Supplementary Documents

An adaptable *in silico* model of the arachidonic acid cascade

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Supplementary Table S1. Description of the event reactions within the model. The table includes the reaction number and reaction scheme of event reactions in the model. Abbreviations: Membrane phospholipid which contain esterified AA (MAA), arachidonic acid (AA), phospholipase A_2 (PLA2), generic pool (Φ**)**, cyclooxygenase 2 (COX-2).

Network Reaction Number	Reaction
1	$\text{MAA} \underset{}{\overset{PLA2}{\rightleftarrows}} \text{AA}$
95	Φ→ AA
112	Φ→ COX-2
113	MAA → AA

Supplementary Table S2. Description of the enzymatic reactions in the model. The table includes the reaction number and reaction scheme for each enzymatic reaction included in the model. All reactions take place in the intracellular compartment. Abbreviations: Arachidonic acid (AA), Prostaglandin H_2 (PGH_2), Cyclooxygenase 2 (COX2), Prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$), Prostaglandin F synthase (PGFS), Thromboxane A_2 (TXA_2), Thromboxane A synthase (TXAS), Prostaglandin I_2 (PGI_2), Prostaglandin I synthase (PGIS), Prostaglandin E_2 (PGE_2), Prostaglandin E synthase (PGES), 5-Hydroperoxy-eicosatetraenoic acid (5-HPETE), 5-Lipoxygeanse (5-LOX), 5-Hydroxy-eicosatetraenoic acid (5-HETE), Phospholipid hydroperoxide glutathione peroxidase (PHGPx), Leukotriene A_4 (LTA_4), Arachidonate 5-lipoxygenase-activating protein (FLAP), 5-Oxo-eicosatetraenoic acid (5-oxo-ETE), 5-Hydroxyeicosanoid dehydrogenase (5-HEDH), Leukotriene A_4 hydrolase (LTA_4H), Leukotriene B_4 (LTB_4), Leukotriene C_4 (LTC_4), Leukotriene C_4 synthase (LTC_4S), 15-Hydroperoxy-eicosatetraenoic acid (15-HPETE), 15-Lipoxygenase (15-LOX), 12-Hydroperoxy-eicosatetraenoic acid (12-HPETE), 12-Lipoxygenase (12-LOX), 15-Hydroxy-eicosatetraenoic acid (15-HETE), Prostaglandin D_2 (PGD_2), Prostaglandin D synthase (PGDS), 15-Keto-prostaglandin E_2 (15-keto-PGE_2), 15-Hydroxyprostaglandin dehydrogenase (15-PGDH), 13,14-Dihydro-15-keto-prostalgandin E_2 (13,14-dihydro-15-keto-PGE_2), Prostaglandin reductase 2 (PTGR2).

Network Reaction Number	**Reaction**
2	$\mathrm{AA} \overset{COX-2}{\rightleftarrows} \mathrm{PGH_2}$
3	$\mathrm{PGH_2} \overset{PGFS}{\rightleftarrows} \mathrm{PGF_{2\alpha}}$
4	$\mathrm{PGH_2} \overset{TXAS}{\rightleftarrows} \mathrm{TXA_2}$

5	$PGIS$ PGH_2 ⇄ PGI_2
10	$PGES$ PGH_2 ⇄ PGE_2
11	$5-LOX$ AA ⇄ 5-HPETE
12	$PHGPx$ 5-HPETE ⇄ 5-HETE
13	$5-LOX/FLAP$ 5-HPETE ⇄ LTA_4
14	$5-HEDH$ 5-HETE ⇄ 5-oxo-ETE
15	LTA_4H LTA_4 ⇄ LTB_4
16	LTC_4S LTA_4 ⇄ LTC_4
17	$15-LOX$ AA ⇄ 15-HPETE
18	$PHGPx$ 15-HPETE ⇄ 15-HETE
19	$12-LOX$ AA ⇄ 12-HPETE
20	$PHGPx$ 12-HPETE ⇄ 12-HETE
21	$PGDS$ PGH_2 ⇄ PGD_2
65	$COX-1$ AA ⇄ PGH_2
66	$15-PGDH$ PGE_2 ⇄ 15-keto-PGE_2

69	$PTGR2$ 15-keto-PGE_2 ⇄ 13,14-dihydro-15-keto-PGE_2

Supplementary Table S3. Description of the non-enzymatic reactions included in the model. The table includes the reaction number and reaction scheme for each non-enzymatic reaction in the model. Reactions 6–9 take place in the intracellular compartment and reactions 96–99 take place within the extracellular compartment. The prefix "ex" refers to the metabolite located in the extracellular compartment. Abbreviations: Thromboxane A_2 (TXA_2), Thromboxane B_2 (TXB_2), Prostaglandin I_2 (PGI_2), 6-Keto-prostaglandin $F_{1\alpha}$ (6-keto-$PGF_{1\alpha}$), Prostaglandin D_2 (PGD_2), Prostaglandin J_2 (PGJ_2), 15-Deoxy-prostalgandin J_2 (15-deoxy-PGJ_2), Extracellular thromboxane A_2 (exTXA_2), Extracellular thromboxane B_2 (exTXB_2), Extracellular prostaglandin I_2 (exPGI_2), Extracellular 6-keto-prostaglandin $F_{1\alpha}$ (ex6-keto-$PGF_{1\alpha}$), Extracellular prostaglandin D_2 (exPGD_2), Extracellular prostaglandin J_2 (exPGJ_2), Extracellular 15-deoxy-prostaglandin J_2 (ex15-deoxy-PGJ_2).

Network Reaction Number	Reaction
6	$TXA_2 \rightleftarrows TXB_2$
7	$PGI_2 \rightleftarrows$ 6-keto-$PGF_{1\alpha}$
8	$PGD_2 \rightleftarrows PGJ_2$
9	$PGJ_2 \rightleftarrows$ 15-deoxy-PGJ_2
96	ex$TXA_2 \rightleftarrows$ exTXB_2
97	ex$PGI_2 \rightleftarrows$ ex6-keto-$PGF_{1\alpha}$
98	ex$PGD_2 \rightleftarrows$ exPGJ_2
99	ex$PGJ_2 \rightleftarrows$ ex15-deoxy-PGJ_2

Supplementary Table S4. Description of the decay reactions in the model. The table includes the reaction number and reaction scheme each decay reaction in the model. Reactions 72–94 take place in the intracellular compartment and reaction 44–71 take place in the extracellular compartment. The prefix "ex" refers to the metabolite being in the extracellular compartment. Abbreviations: Extracellular prostaglandin $F_{2\alpha}$ ($exPGF_{2\alpha}$), Extracellular thromboxane B_2 ($exTXB_2$), Extracellular thromboxane A_2 ($exTXA_2$), Extracellular 6-keto prostaglandin $F_{1\alpha}$ (ex6-keto-$PGF_{1\alpha}$), Extracellular prostaglandin I_2 ($exPGI_2$), Extracellular prostaglandin E_2 ($exPGE_2$), Extracellular 15-deoxy-prostaglandin J_2 (ex15-deoxy-PGJ_2), Extracellular prostaglandin J_2 ($exPGJ_2$), Extracellular prostaglandin D_2 ($exPGD_2$), Extracellular prostaglandin H_2 ($exPGH_2$), Extracellular 5-oxo- eicosatetraenoic acid (ex5-oxo-ETE), Extracellular 5-hydroxy-eicosatetraenoic acid (ex5-HETE), Extracellular leukotriene B_4 ($exLTB_4$), Extracellular leukotriene C_4 ($exLTC_4$), Extracellular leukotriene A_4 ($exLTA_4$), Extracellular 5-hydroperoxy-eicosatetraenoic acid (ex5-HPETE), Extracellular 15-hydroxy-eicosatetraenoic acid (ex15-HETE), Extracellular 15-hydroperoxy-eicosatetraenoic acid (ex15-HPETE), Extracellular 12-hydroxy-eicosatetraenoic acid (ex12-HETE), Extracellular 12-hydroperoxy-eicosatetraenoic acid (ex12-HPETE), Extracellular arachidonic acid (exAA), Extracellular 15-keto-prostaglandin E_2 (ex15-keto-PGE_2), Extracellular 13,14-dihydro-15-keto-prostaglandin E_2 (ex13,14-dihydro-15-keto-PGE_2), Prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$), Thromboxane B_2 (TXB_2), Thromboxane A_2 (TXA_2), 6-Keto-prostaglandin $F_{1\alpha}$ (6-keto-$PGF_{1\alpha}$), Prostaglandin I_2 (PGI_2), Prostaglandin E_2 (PGE_2), 15-Deoxy-prostaglandin J_2 (15-deoxy-PGJ_2), Prostaglandin J_2 (PGJ_2), Prostaglandin D_2 (PGD_2), Prostaglandin H_2 (PGH_2), 5-Oxo-eicosatetraenoic acid (5-oxo-ETE), 5-Hydroxy-eicosatetraenoic acid (5-HETE), Leukotriene B_4 (LTB_4), Leukotriene C_4 (LTC_4), Leukotriene A_4 (LTA_4), 5-hydroperoxy-eicosatetraenoic acid (5-HPETE), 15-Hydroxy-eicosatetraenoic acid (15-HETE), 15-hydroperoxy-eicosatetraenoic acid (15-HPETE), 12-Hydroxy-eicosatetraenoic acid (12-HETE), 12-hydroperoxy-eicosatetraenoic acid (12-HPETE), Arachidonic acid (AA), 13,14-Dihydro-15-keto-prostaglandin E_2 (13,14-dihydro-15-keto-PGE_2), 15-keto-prostaglandin E_2 (15-keto-PGE_2).

Network Reaction Number	Reaction
44	ex$PGF_{2\alpha}$ → Miscellaneous metabolites
45	exTXB_2 → Miscellaneous metabolites
46	exTXA_2 → Miscellaneous metabolites
47	ex6-keto-$PGF_{1\alpha}$ → Miscellaneous metabolites
48	exPGI_2 → Miscellaneous metabolites
49	exPGE_2 → Miscellaneous metabolites
50	ex15-deoxy-PGJ_2 → Miscellaneous metabolites
51	exPGJ_2 → Miscellaneous metabolites
52	exPGD_2 → Miscellaneous metabolites
53	exPGH_2 → Miscellaneous metabolites
54	ex5-oxo-ETE → Miscellaneous metabolites
55	ex5-HETE → Miscellaneous metabolites
56	exLTB_4 → Miscellaneous metabolites
57	exLTC_4 → Miscellaneous metabolites
58	exLTA_4 → Miscellaneous metabolites
59	ex5-HPETE → Miscellaneous metabolites
60	ex15-HETE → Miscellaneous metabolites
61	ex15-HPETE → Miscellaneous metabolites
62	ex12-HETE → Miscellaneous metabolites
63	ex12-HPETE → Miscellaneous metabolites
64	exAA → Miscellaneous metabolites
68	ex15-keto-PGE_2 → Miscellaneous metabolites
71	ex13,14-dihydro-15-keto-PGE_2→ Miscellaneous metabolites
72	$PGF_{2\alpha}$ → Miscellaneous metabolites
73	TXB_2 → Miscellaneous metabolites

74	TXA_2 → Miscellaneous metabolites
75	6-keto-$PGF_{1\alpha}$ → Miscellaneous metabolites
76	PGI_2 → Miscellaneous metabolites
77	PGE_2 → Miscellaneous metabolites
78	15-deoxy-PGJ_2 → Miscellaneous metabolites
79	PGJ_2 → Miscellaneous metabolites
80	PGD_2 → Miscellaneous metabolites
81	PGH_2 → Miscellaneous metabolites
82	5-oxo-ETE → Miscellaneous metabolites
83	5-HETE → Miscellaneous metabolites
84	LTB_4 → Miscellaneous metabolites
85	LTC_4 → Miscellaneous metabolites
86	LTA_4 → Miscellaneous metabolites
87	5-HPETE → Miscellaneous metabolites
88	15-HETE → Miscellaneous metabolites
89	15-HPETE → Miscellaneous metabolites
90	12-HETE → Miscellaneous metabolites
91	12-HPETE → Miscellaneous metabolites
92	AA → Miscellaneous metabolites
93	13,14-dihydro-15-keto-PGE_2 → Miscellaneous metabolites
94	15-keto-PGE_2 → Miscellaneous metabolites

Supplementary Table S5. Description of the transporter reactions in the model. The table includes the reaction number for each transporter mediated reactions in the model. Reactions 22–42, 67 and 70 are mediated by the ABC transporter, and reactions 101–11 are mediated by the PGT transporter. The prefix "ex" refers to the metabolite being in the extracellular compartment. Abbreviations: ATP-binding cassette transporters (ABC), Prostaglandin transporter (PGT), Prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$), Extracellular prostaglandin $F_{2\alpha}$ ($exPGF_{2\alpha}$), Thromboxane B_2 (TXB_2), Extracellular thromboxane B_2 ($exTXB_2$), 6-Keto-prostaglandin $F_{1\alpha}$ (6-keto-$PGF_{1\alpha}$), Extracellular 6-keto prostaglandin $F_{1\alpha}$ (ex6-keto-$PGF_{1\alpha}$), Prostaglandin E_2 (PGE_2), Extracellular prostaglandin E_2 ($exPGE_2$), 15-Deoxy-prostaglandin J_2 (15-deoxy-PGJ_2), Extracellular 15-deoxy-prostaglandin J_2 (ex15-deoxy-PGJ_2), 5-Oxo-eicosatetraenoic acid (5-oxo-ETE), Extracellular 5-oxo- eicosatetraenoic acid (ex5-oxo-ETE), 15-Hydroxy-eicosatetraenoic acid (15-HETE), Extracellular 15 -hydroxy-eicosatetraenoic acid (ex15-HETE), Leukotriene B_4 (LTB_4), Extracellular leukotriene B_4 ($exLTB_4$), Leukotriene C_4 (LTC_4), Extracellular leukotriene C_4 ($exLTC_4$), 12-Hydroxy-eicosatetraenoic acid (12-HETE), Extracellular 12-hydroxy-eicosatetraenoic acid (ex12-HETE), Thromboxane A_2 (TXA_2), Extracellular thromboxane A_2 ($exTXA_2$), Prostaglandin I_2 (PGI_2), Extracellular prostaglandin I_2 ($exPGI_2$), Prostaglandin H_2 (PGH_2), Extracellular prostaglandin H_2 ($exPGH_2$), Prostaglandin D_2 (PGD_2), Extracellular prostaglandin D_2 ($exPGD_2$), Prostaglandin J_2 (PGJ_2), Extracellular prostaglandin J_2 ($exPGJ_2$), 12-hydroperoxy-eicosatetraenoic acid (12-HPETE), Extracellular 12-hydroperoxy-eicosatetraenoic acid (ex12-HPETE), 15-hydroperoxy-eicosatetraenoic acid (15-HPETE), Extracellular 15-hydroperoxy-eicosatetraenoic acid (ex15-HPETE), 5-hydroperoxy-eicosatetraenoic acid (5-HPETE), Extracellular 5-hydroperoxy-eicosatetraenoic acid (ex5-HPETE), 5-Hydroxy-eicosatetraenoic acid (5-HETE), Extracellular 5-hydroxy-eicosatetraenoic acid (ex5-HETE), Leukotriene A_4 (LTA_4), Extracellular leukotriene A_4 ($exLTA_4$), Arachidonic acid (AA), Extracellular arachidonic acid (exAA), 15-keto-prostaglandin E_2 (15-keto-PGE_2), Extracellular 15-keto-prostaglandin E_2 (ex15-keto-PGE_2), 13,14-Dihydro-15-keto-prostaglandin E_2 (13,14-dihydro-15-keto-PGE_2), Extracellular 13,14-dihydro-15-keto-prostaglandin E_2 (ex13,14-dihydro-15-keto-PGE_2).

Network Reaction Number	Reaction
22	$PGF_{2\alpha} \overset{ABC}{\rightleftarrows} exPGF_{2\alpha}$
23	$TXB_2 \overset{ABC}{\rightleftarrows} exTXB_2$
24	$6\text{-keto-}PGF_{1\alpha} \overset{ABC}{\rightleftarrows} ex6\text{-keto-}PGF_{1\alpha}$
25	$PGE_2 \overset{ABC}{\rightleftarrows} exPGE_2$
26	$15\text{-deoxy-}PGJ_2 \overset{ABC}{\rightleftarrows} ex15\text{-deoxy-}PGJ_2$
27	$5\text{-oxo-ETE} \overset{ABC}{\rightleftarrows} ex5\text{-oxo-ETE}$
28	$15\text{-HETE} \overset{ABC}{\rightleftarrows} ex15\text{-HETE}$
29	$LTB_4 \overset{ABC}{\rightleftarrows} exLTB_4$
30	$LTC_4 \overset{ABC}{\rightleftarrows} exLTC_4$
31	$12\text{-HETE} \overset{ABC}{\rightleftarrows} ex12\text{-HETE}$
32	$TXA_2 \overset{ABC}{\rightleftarrows} exTXA_2$

33	$\overset{ABC}{PGI_2 \rightleftarrows exPGI_2}$
34	$\overset{ABC}{PGH_2 \rightleftarrows exPGH_2}$
35	$\overset{ABC}{PGD_2 \rightleftarrows exPGD_2}$
36	$\overset{ABC}{PGJ_2 \rightleftarrows exPGJ_2}$
37	$\overset{ABC}{\text{12-HPETE} \rightleftarrows \text{ex12-HPETE}}$
38	$\overset{ABC}{\text{15-HPETE} \rightleftarrows \text{ex15-HPETE}}$
39	$\overset{ABC}{\text{5-HPETE} \rightleftarrows \text{ex5-HPETE}}$
40	$\overset{ABC}{\text{5-HETE} \rightleftarrows \text{ex5-HETE}}$
41	$\overset{ABC}{LTA_4 \rightleftarrows exLTA_4}$
42	$\overset{ABC}{AA \rightleftarrows exAA}$
67	$\overset{ABC}{\text{15-keto-PGE}_2 \rightleftarrows \text{ex15-keto-PGE}_2}$
70	$\overset{ABC}{\text{13,14-dihydro-15-keto-PGE}_2 \rightleftarrows \text{ex13,14-dihydro-15-keto-PGE}_2}$
101	$\overset{PGT}{PGF_{2\alpha} \rightleftarrows exPGF_{2\alpha}}$
102	$\overset{PGT}{PGE_2 \rightleftarrows exPGE_2}$
103	$\overset{PGT}{PGI_2 \rightleftarrows exPGI_2}$

104	$PGD_2 \overset{PGT}{\rightleftarrows} exPGD_2$
105	$PGJ_2 \overset{PGT}{\rightleftarrows} exPGJ_2$
106	$TXB_2 \overset{PGT}{\rightleftarrows} exTXB_2$
107	$13,14\text{-dihydro-15-keto-}PGE_2 \overset{PGT}{\rightleftarrows} ex13,14\text{-dihydro-15-keto-}PGE_2$
108	$15\text{-keto-}PGE_2 \overset{PGT}{\rightleftarrows} ex15\text{-keto-}PGE_2$
109	$6\text{-keto-}PGF_{1\alpha} \overset{PGT}{\rightleftarrows} ex6\text{-keto-}PGF_{1\alpha}$
110	$TXA_2 \overset{PGT}{\rightleftarrows} exTXA_2$
111	$15\text{-deoxy-}PGJ_2 \overset{PGT}{\rightleftarrows} ex15\text{-deoxy-}PGJ_2$

Supplementary Table S6. Equations used to calculate enzyme kinetic parameters in the AA cascade *in silico* model. Where K_{eq} is the equilibrium constant, ΔG is the change in Gibbs Free Energy, R is the gas constant, T is the temperature of the reaction (Kelvin), K_{Decay} is the decay constant, [E] is the enzyme concentration, K_f forward reaction rate constant for non-enzymatic reactions, A is the pre-exponential constant of the Arrhenius equation, and E_a is the activation energy.

S.6.1. Calculations

S.Eq.6.1.1. $$K_{eq} = e^{-\Delta G/RT}$$

S.Eq.6.1.2. $$K_{Decay} = \frac{Ln(2)}{\text{Half-life } (min)}$$

S.Eq.6.1.3. $$[E](mM) = \frac{[E](ppm) \times Average\ number\ of\ proteins\ in\ a\ human\ cell\ (10000)}{Avagradro's\ Number\ (6.023 \times 10^{23}) \times Cell\ volume\ (3 \times 10^{-12} L)} \times 1000$$

S.Eq.6.1.4. $$K_f = Ae^{\frac{-Ea}{RT}}$$

S.6.2. Protein concentration conversion

S.Eq.6.2.1.1 $$Protein\ (mol) = \frac{abundance(ppm) \times \Sigma\ proteins\ in\ a\ cell\ (10^6)}{Na\ (mol)}$$

S.Eq.6.2.2. $$Protein\ (mM) = \frac{\text{Protein (mol)}}{volume\ of\ a\ cell\ (L)}$$

Supplementary Document S7. Enzymatic Reaction Structure and Parameterisation.

Documentation of parameter values obtained for all enzymatic reactions in the model (Reactions 2–5, 10–21, 65–66, 69; Supplementary Table S2) from the literature and associated uncertainty for the eicosanoid network model. Parameterisation was performed using the method of Tsigkinopoulou *et al.,* (2018). The table includes information regarding each reaction and its respective parameters are documented. This includes information such as the reaction rate law and the literature values that were used to define parameters, including experimental conditions, total weights and literature references from which the data were obtained. In this model some parameters are referred as "Dependent parameters", meaning that the log-normal distribution for that parameter was calculated using multivariate distributions (discussed in **Section 2.6.2**). As a result, no confidence interval factor or literature values were cited for the Dependent parameters.

Contents

S.7.1 Reaction 2: AA ⇌ PGH2

The inducible isoform of COX, COX-2, catalyses the two-step reaction of cycloooxygenation and oxygenation, followed by a hydroperoxide reduction. This isoform is transiently induced in response to inflammatory stimuli, hormones and growth factors (Coffey et al., 1997; DeWitt and Meade, 1993; Fang et al., 2013; Herschman, 1994; Kargman et al., 1995; Kujubu et al., 1993; Lee et al., 1992; Ristimaki et al., 1994). This is a two-step reaction of cycloooxygenation and oxygenation, followed by a hydroperoxide reduction. The cyclooxygenase reaction occurs in the hydrophobic channel within the core of the protein and generates PGG_2. The subsequent peroxidase reaction produces PGH_2 and occurs at the heme-containing active site near the protein surface. The two step reaction results in the insertion of molecular oxygen across the C-9 and C-11 double bonds.

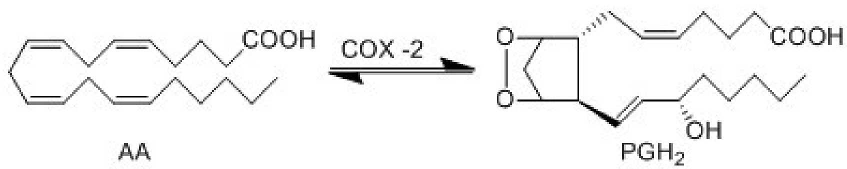


Figure SF.7.1. The cycloooxygenation and oxygenation reaction, followed by a hydroperoxide reduction of arachidonic acid (AA) into prostaglandin H_2 (PGH_2) by cyclooxygenase 2 (COX-2) (Reaction 2).

SEq.7.1. Reaction rate law for Reaction 2.

$$v_2 = \frac{k_{cat} \cdot [COX-2]\left([AA] - {[PGH_2]}/{K_{eq}}\right)}{K_{m_s}\left(1 + \frac{[PGH_2]}{K_{m_p}}\right) + [AA]}$$

S.7.1.1. Reaction parameters

S.7.1.1.1. Parameter: COX-2 K_{ms}

Parameter values for the K_{ms} of Reaction 2 were obtained from the literature and summarised in Table ST.7.1.1.1.1. The log-normal distribution properties for the K_{ms} of Reaction 2 are shown in Table ST.7.1.1.1.2 and plotted in Figure SF.7.1.1.1.1.

Table ST.7.1.1.1.1. Literature information used to design the COX-2 K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
2.10×10^{-3}	4.00×10^{-4}	Human	Baculovirus	Wild Type Cycloxygenase-2	7.2	30		128	0	(Bambai et al., 2004)
2.10×10^{-3}	4.00×10^{-4}	Human	E. coli	Wild Type Cycloxygenase-2	8.5	30		64	0	(Rogge et al., 2004)
5.14×10^{-3}	2.90×10^{-4}	Mouse	Baculovirus	COX-2	8	37	1–200 µM of substrate	128	0	(Vecchio et al., 2010)
1.62×10^{-2}	2.20×10^{-3}	Human	Embryonic kidney cells	COX-2	Not specified	Not specified		128	0	(Kim et al., 2005)

Table ST.7.1.1.1.2. The log-normal distribution properties of the COX-2 K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Confidence Interval	Location parameter (µ)	Scale parameter (σ)
4.90×10^{-3}	5.70	-4.72	7.77×10^{-1}

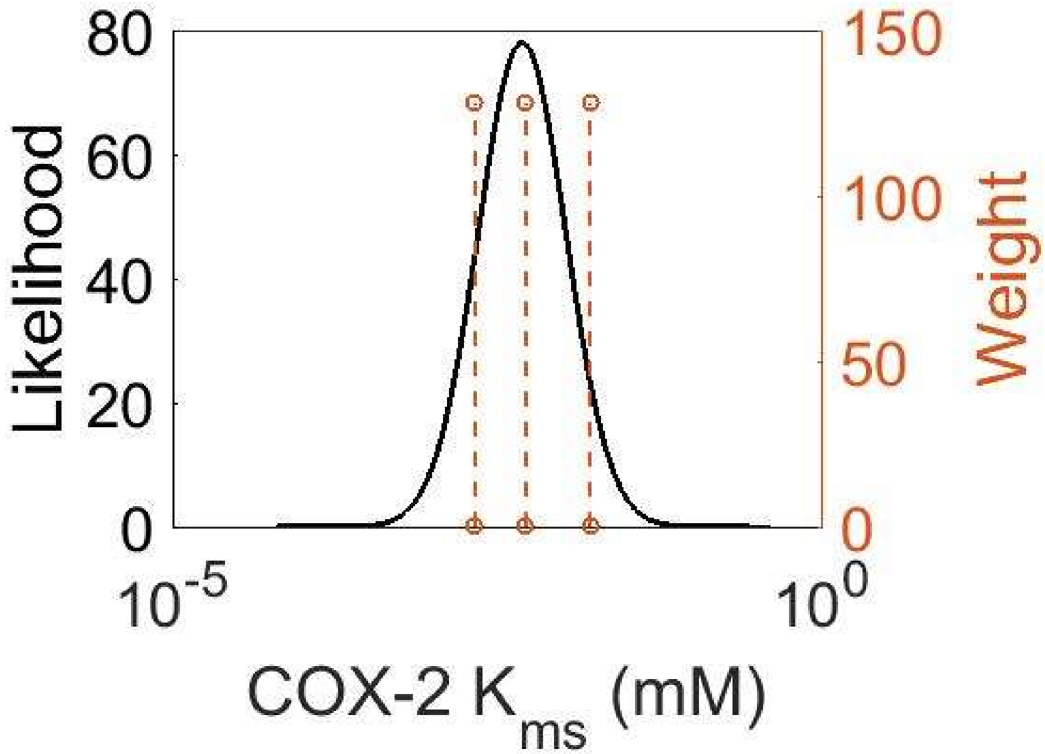


Figure SF.7.1.1.1.1. The estimated probability distribution for COX-2 K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.1.1.2. Parameter: COX-2 K_{mp} (Dependent parameter)

The log-normal distribution for the parameter for the K_{mp} of Reaction 2 was calculated using multivariate distributions. The log-normal distribution properties for the K_{mp} of Reaction 2 are shown in Table ST.7.1.1.2.1 and plotted in Figure SF.7.1.1.2.1.

Table ST.7.1.1.2.1. The log-normal distribution properties of the COX-2 K_{mp} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Location parameter (μ)	Scale parameter (σ)
4.70 $\times10^{-3}$	-4.75	7.87 $\times10^{-1}$

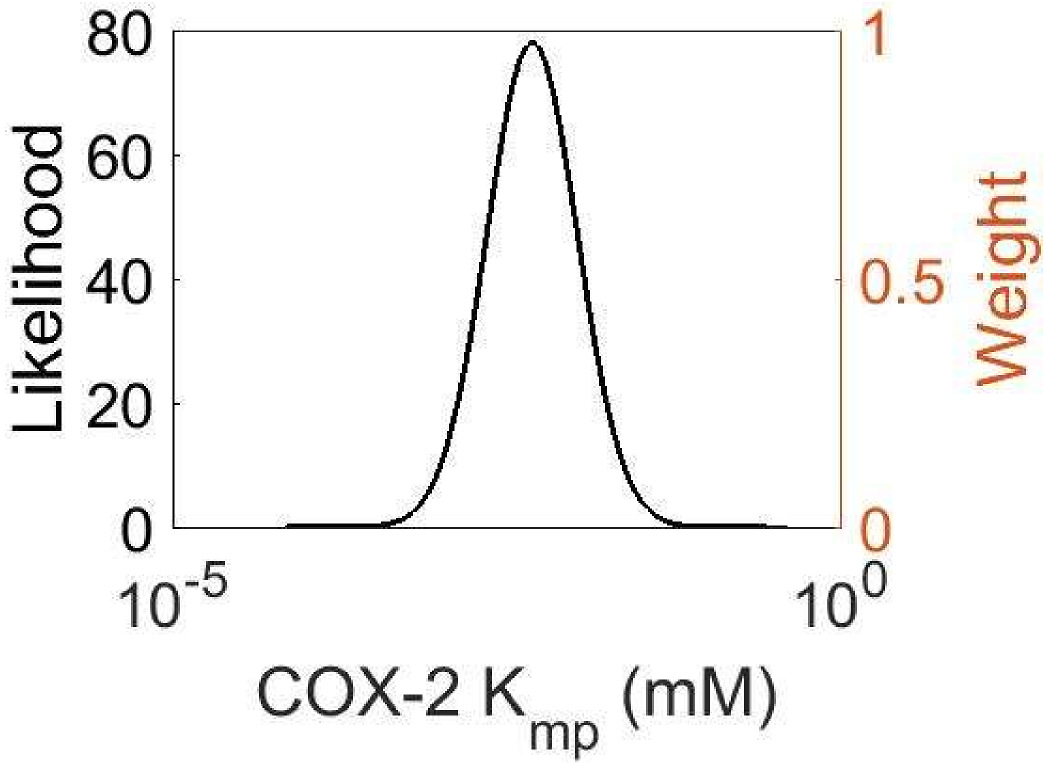


Figure SF.7.1.1.2.1. The estimated probability distribution for COX-2 K_{mp}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.1.1.3. Parameter: COX-2 k_{cat}

Parameter values for the k_{cat} of Reaction 2 were obtained from the literature and summarised in Table ST.7.1.1.3.1. The log-normal distribution properties for the k_{cat} of Reaction 2 are shown in Table ST.7.1.1.3.2 and plotted in Figure SF.7.1.1.3.1.

Table ST.7.1.1.3.1. Literature information used to design the COX-2 k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.62×10^{3}	2.40×10^{1}	Mouse	Baculovirus	COX-2	8	37	1–200 µM of substrate	128	0	(Vecchio et al., 2010)

Table ST.7.1.1.3.2. The log-normal distribution properties of the COX-2 k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (µ)	Scale parameter (σ)
1.62×10^{3}	1.01	7.39	1.48×10^{-2}

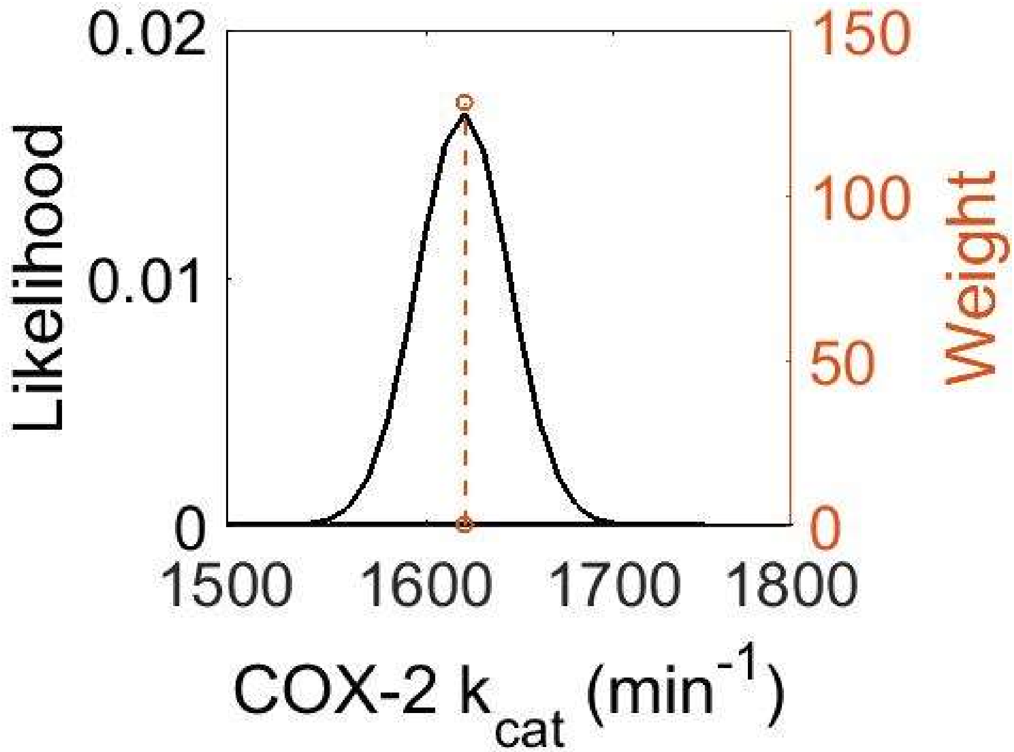


Figure SF.7.1.1.3.1. The estimated probability distribution for COX-2 k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.1.1.4. Parameter: COX-2 K_{eq}

Parameter values for the K_{eq} of Reaction 2 were obtained from the literature and summarised in Table ST.7.1.1.4.1. The log-normal distribution properties for the K_{eq} of Reaction 2 are shown in Table ST.7.1.1.4.2 and plotted in Figure SF.7.1.1.4.1.

Table ST.7.1.1.4.1. Literature information used to design the COX-2 K_{eq} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

ΔG (kcal/mol)	K_{eq}	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
-3.90×10^{1}	4.18×10^{28}	Human	Unknown	COX-2	7	Unknown		64	0	(Caspi et al., 2018)

Table ST.7.1.1.4.2. The log-normal distribution properties of the COX-2 K_{eq} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
4.18×10^{28}	1.00×10^{1}	6.67×10^{1}	8.90×10^{-1}

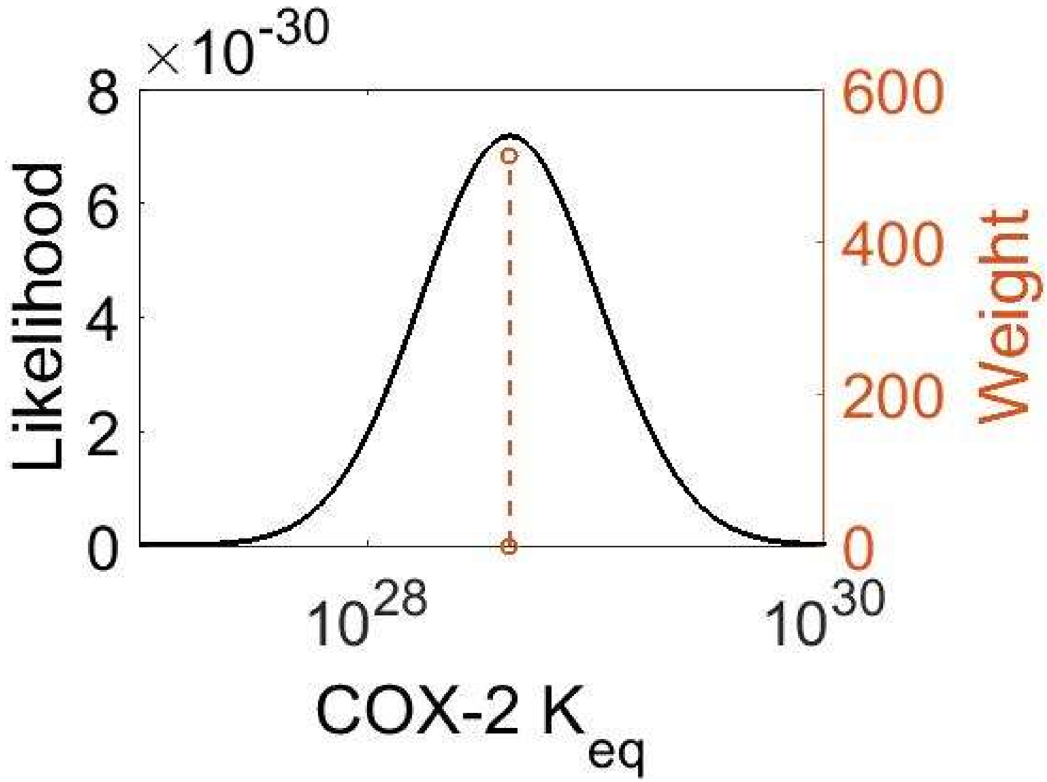


Figure SF.7.1.1.4.1. The estimated probability distribution for COX-2 K_{eq}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.1.1.5. Parameter: COX-2 concentration

Parameter values for the COX-2 concentration of Reaction 2 were obtained from the literature and summarised in Table ST.7.1.1.5.1. The abundance of COX-2 (ppm) was converted to COX-2 (mM) using **Equation S.7.2.** As a result, the concentration of COX-2 in unstimulated tissue was estimated as 2.27 x10^{-5} mM. The upregulation of COX-2 in HaCaT keratinocytes was estimated using western blotting in (Kiezel-Tsugunova, 2017), Figure SF.7.1.1.5.1. shows an example. Using this information, *in silico* experiments which included an upregulation of COX-2, included the concentration of COX-2 reaching 100 times higher concentration than the estimated unstimulated concentration. Therefore, the COX-2 induction event includes the concentration of COX-2 eventually reaching a concentration of 2.27 x10^{-3} mM after 6h post irradiation.

Table ST.7.1.1.5.1. Literature information used to determine the concentration of COX-2 in a selection of human tissues. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
4.11	NaN	Human	Stomach	COX-2	7.5	37		**1024**	0	(Wilhelm et al., 2014)

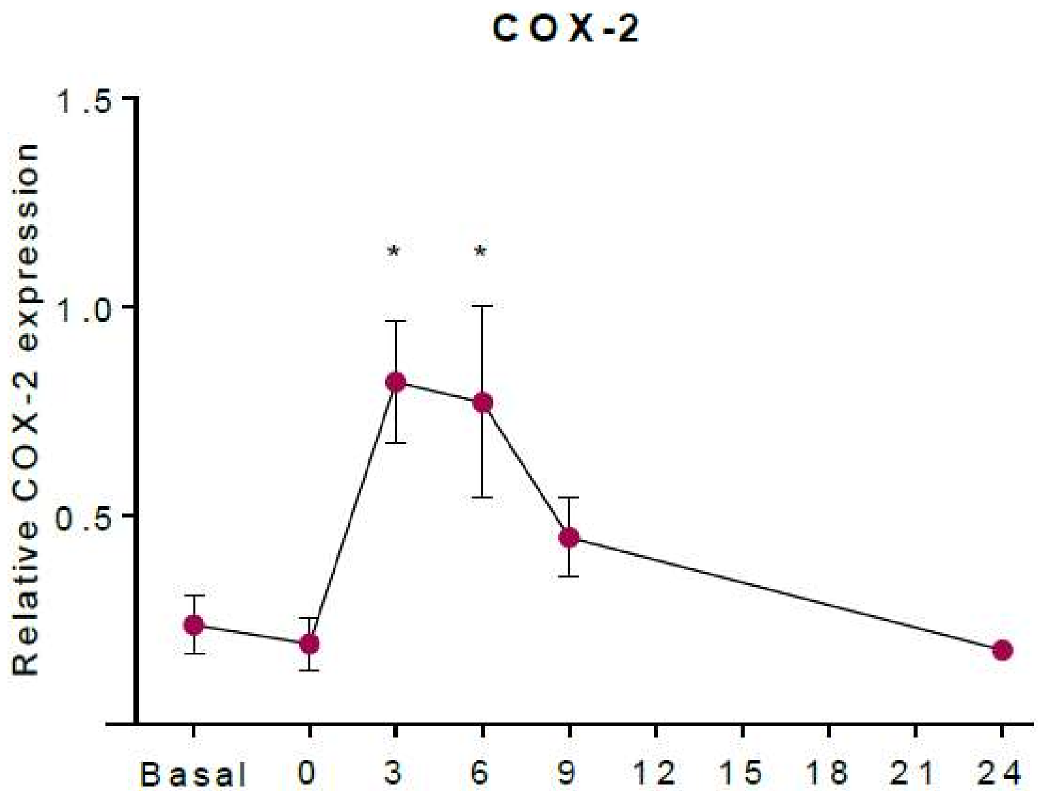


Figure SF.7.1.1.5.1. The relative expression of COX-2 protein in HaCaT keratinocytes (Kiezel-Tsugunova, 2017).

S.7.2 Reaction 3: $PGH_2 \rightleftharpoons PGF_{2\alpha}$

The isomerisation of PGH_2 to $PGF_{2\alpha}$ is performed by prostaglandin F synthase (PGFS). This reaction results in the formation of two hydroxyl groups at C9 and C11 of PGH_2.

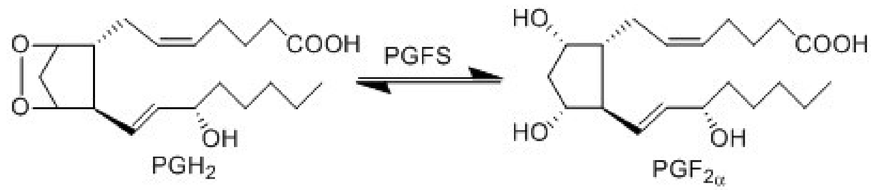


Figure SF.7.2. Isomerisation of prostaglandin H_2 (PGH) into prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) by prostaglandin F synthase (PGFS) (Reaction 3).

SEq.7.2. Reaction rate law for Reaction 3.

$$\boldsymbol{v_3} = \frac{k_{cat}\cdot[PGFS]\left([PGH_2]-{[PGF_{2\alpha}]}/{K_{eq}}\right)}{K_{m_s}\left(1+\frac{[PGF_{2\alpha}]}{K_{m_p}}\right)+[PGH_2]}$$

S.7.2.1. Reaction parameters

S.7.2.1.1. Parameter: PGFS K_{ms}

Parameter values for the K_{ms} of Reaction 3 were obtained from the literature and summarised in Table ST.7.2.1.1.1. The log-normal distribution properties for the K_{ms} of Reaction 3 are shown in Table ST.7.2.1.1.2 and plotted in Figure SF.7.2.1.1.1.

Table ST.7.2.1.1.1. Literature information used to design the PGFS K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.80 $\times10^{-2}$		Human	E. coli	PGFS	7	37	Placental Aldose Reductase (AKR1B1)	512	0	(Kabututu et al., 2009)
1.90 $\times10^{-3}$	1.50 $\times10^{-3}$	Human	E. coli	PGFS	7	37	Lung PGF2a Synthase (AKR1C3)	512	0	(Kabututu et al., 2009)

Table ST.7.2.1.1.2. The log-normal distribution properties of the PGFS K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.33 $\times10^{-2}$	3.81	-3.45	9.33 $\times10^{-1}$

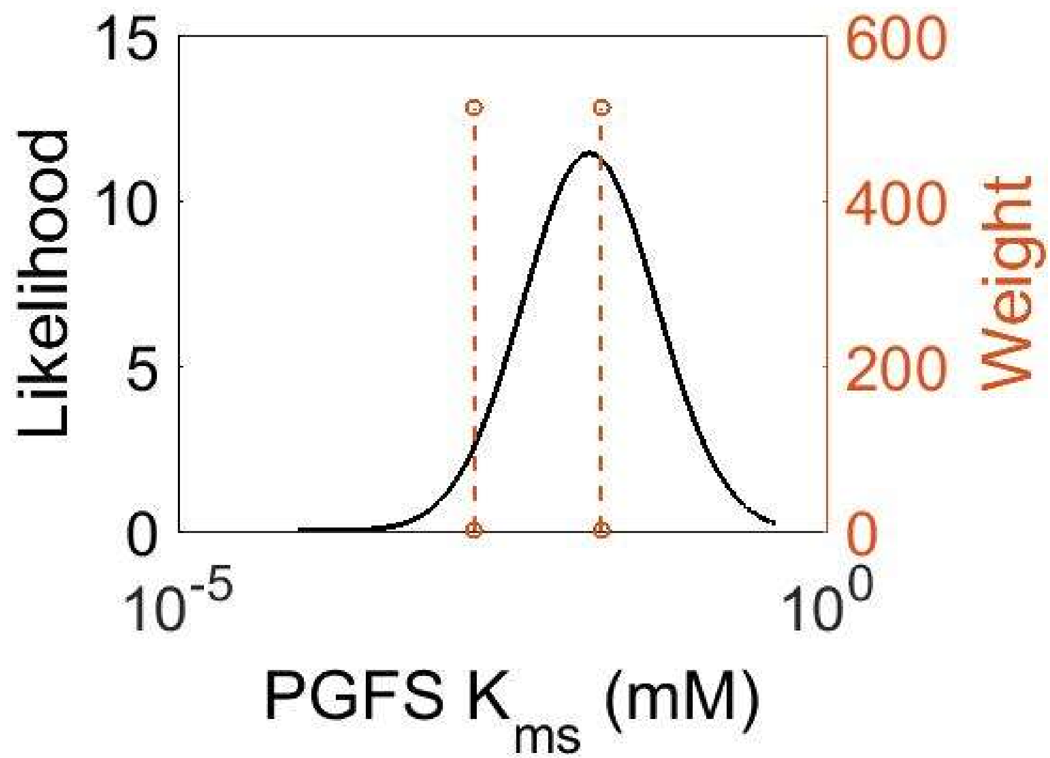


Figure SF.7.2.1.1.1. The estimated probability distribution for PGFS K_{ms}, plotted on a log-scale. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line.

S.7.2.1.2. Parameter: PGFS K_{mp} (Dependent parameter)

The log-normal distribution for the parameter for the K_{mp} of Reaction 3 was calculated using multivariate distributions. The log-normal distribution properties for the K_{mp} of Reaction 3 are shown in Table ST.7.2.1.2.1 and plotted in Figure SF.7.2.1.2.1.

Table ST.7.2.1.2.1. The log-normal distribution properties of the PGFS-2 K_{mp} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Location parameter (μ)	Scale parameter (σ)
1.46 $x10^{-2}$	-2.86	1.17

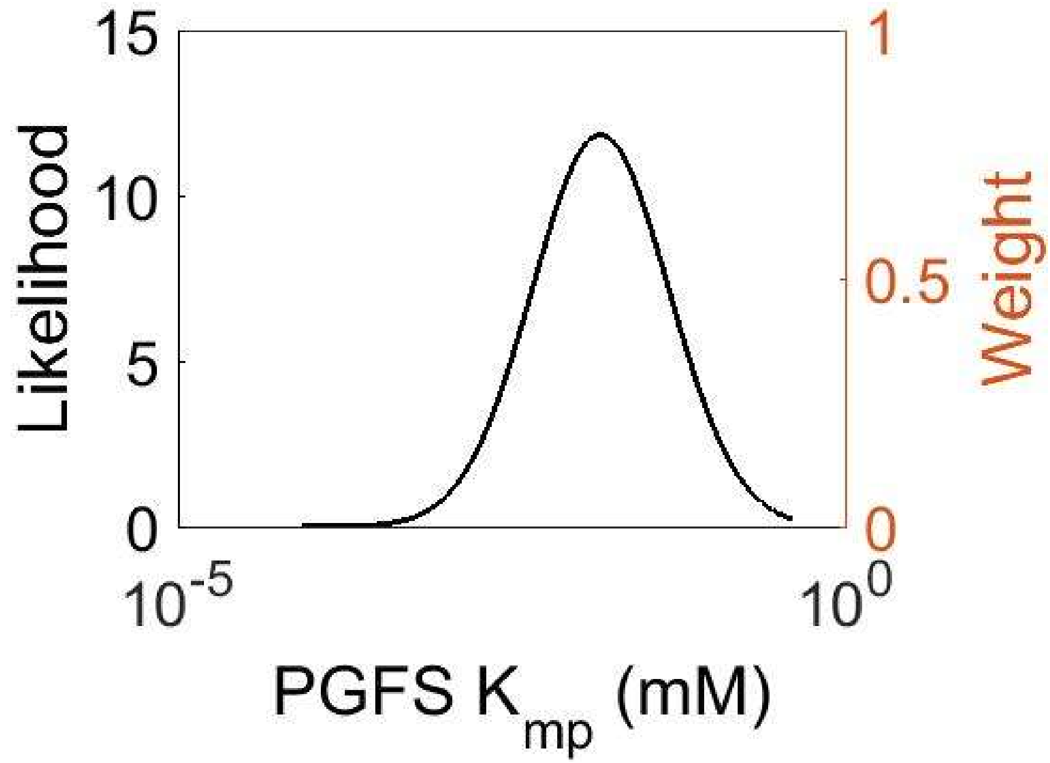


Figure SF.7.2.1.2.1. The estimated probability distribution for PGFS K_{mp}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.2.1.3. Parameter: PGFS k_{cat}

Parameter values for the k_{cat} of Reaction 3 were obtained from the literature and summarised in Table ST.7.2.1.3.1. The log-normal distribution properties for the k_{cat} of Reaction 3 are shown in Table ST.7.2.1.3.2 and plotted in Figure SF.7.2.1.3.1.

Table ST.7.2.1.3.1. Literature information used to design the PGFS k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.49×10^{1}	NaN	Mouse/Swine	E. coli	Prostamide/PGF Synthase	7	37		128	0	(Moriuchi et al., 2008)

Table ST.7.2.1.3.2. The log-normal distribution properties of the PGFS k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.48×10^{1}	1.10	2.71	9.49×10^{-2}

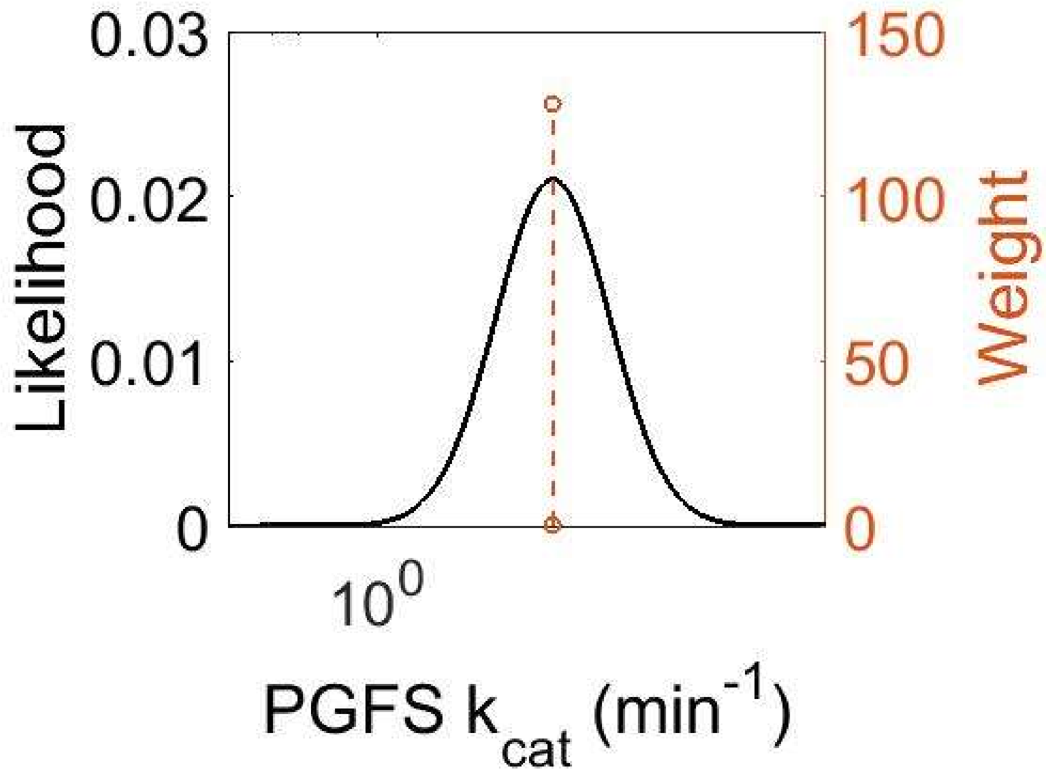


Figure SF.7.2.1.3.1. The estimated probability distribution for PGFS k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.2.1.4. Parameter: PGFS K_{eq}

Parameter values for the K_{eq} of Reaction 3 were obtained from the literature and summarised in Table ST.7.2.1.4.1. The log-normal distribution properties for the K_{eq} of Reaction 3 are shown in Table ST.7.2.1.4.2 and plotted in Figure SF.7.2.1.4.1.

Table ST.7.2.1.4.1. Literature information used to design the PGFS K_{eq} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

ΔG (kcal/mol)	K_{eq}	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
-6.64	7.46 x10^{4}	Human	Unknown	PGFS	7	Unknown		64	0	(Caspi et al., 2018)

Table ST.7.2.1.4.2. The log-normal distribution properties of the PGFS K_{eq} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
7.46 x10^{4}	1.00 x10^{1}	1.20 x10^{1}	8.90 x10^{-1}

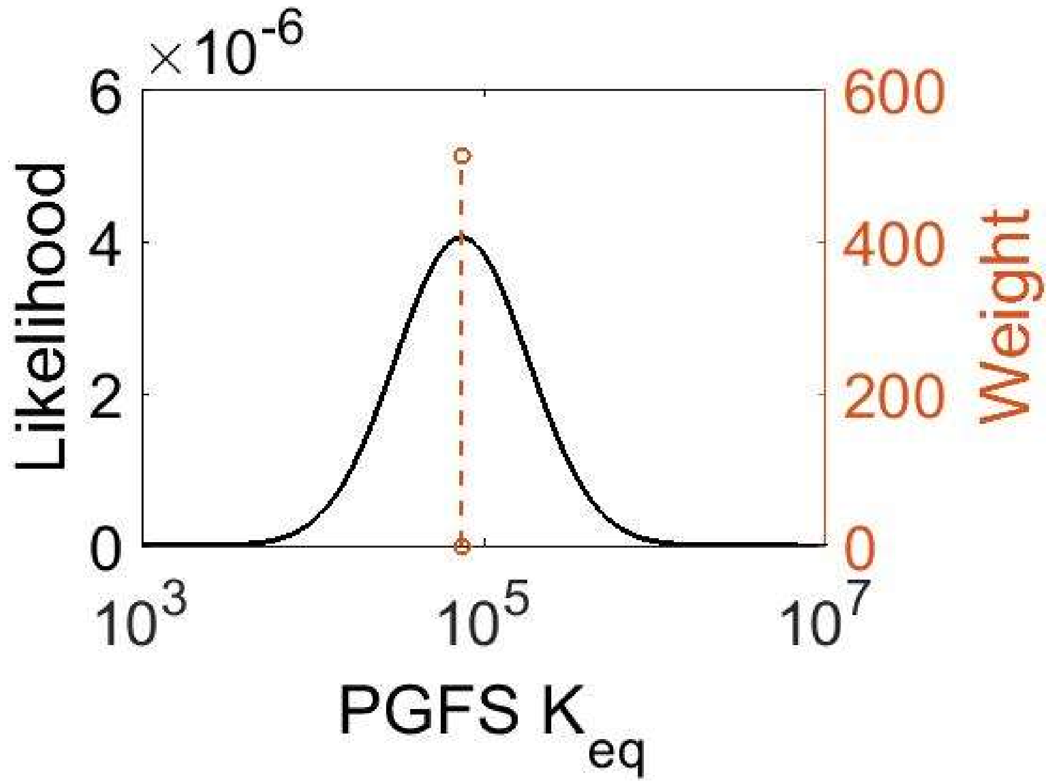


Figure SF.7.2.1.4.1. The estimated probability distribution for PGFS K_{eq}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.2.1.5. Parameter: PGFS concentration

Parameter values for the PGFS concentration of Reaction 3 were obtained from the literature and summarised in Table ST.7.2.1.5.1. The log-normal distribution properties for the PGFS concentration of Reaction 3 are shown in Table ST.7.2.1.5.2 and plotted in Figure SF.7.2.1.5.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.7.2.1.5.1. Literature information used to design the PGFS concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.99 x10^{1}	NaN	Human	Lung	PGFS	7.5	37		**1024**	0	(Wilhelm et al., 2014)
4.03 x10^{1}	NaN	Human	Oesophagus	PGFS	7.5	37		**1024**	0	(Wilhelm et al., 2014)
1.05 x10^{2}	NaN	Human	Platelet	PGFS	7.5	37		**1024**	0	(Kim et al., 2014)
1.10 x10^{2}	NaN	Human	Oral cavity	PGFS	7.5	37		**1024**	0	(Wilhelm et al., 2014)

Table ST.7.2.1.5.2. The log-normal distribution properties of the PGFS concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
6.41 x10^{1}	3.55 x10^{-4}	2.05	4.53	6.06 x10^{-1}

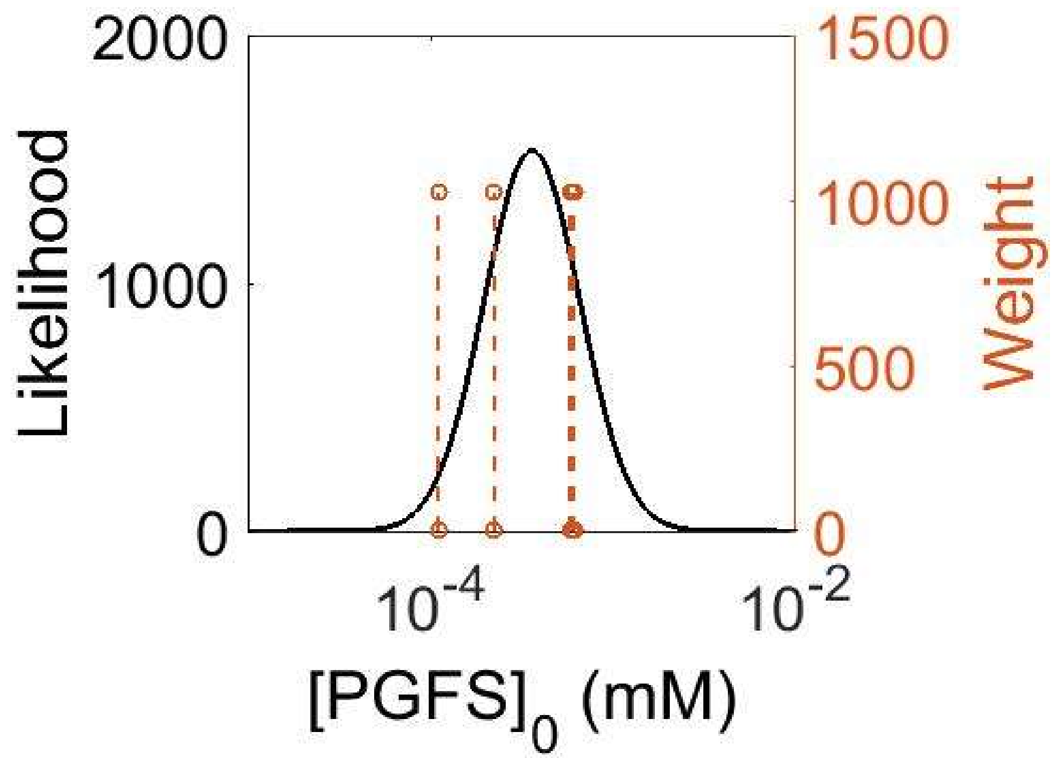


Figure SF.7.2.1.5.1. The estimated probability distribution for the PGFS concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.3 Reaction 4: $PGH_2 \rightleftharpoons TXA_2$

The isomerisation of PGH_2 to TXA_2 is performed by TXAS. This reaction includes the rearrangement of the peroxide functional group by the protein's heme group, whereby one oxygen is incorporated into the cyclopentane ring between C11 and C12 to form an oxane ring, whilst the other forms an epoxide group across the oxane ring between C9 and C11.

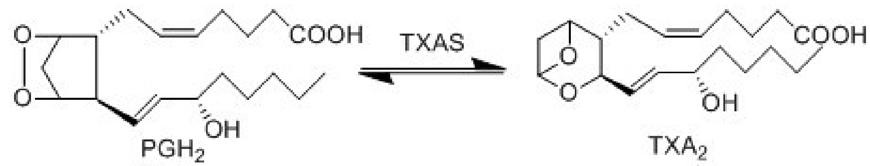


Figure SF.7.3. Isomerisation of prostaglandin H_2 (PGH_2) into thromboxane A_2 (TXA_2) by thromboxane A synthase (TXAS) (Reaction 4).

SEq.7.3. Reaction rate law for Reaction 4.

$$\boldsymbol{v_4} = \frac{\boldsymbol{K_{cat}} \cdot [\boldsymbol{TXAS}] \left([\boldsymbol{PGH_2}] - {[\boldsymbol{TXA_2}]}/{\boldsymbol{K_{eq}}} \right)}{\boldsymbol{K_{m_s}} \left(\mathbf{1} + \frac{[\boldsymbol{TXA_2}]}{\boldsymbol{K_{m_p}}} \right) + [\boldsymbol{PGH_2}]}$$

S.7.3.1. Reaction parameters

S.7.3.1.1. Parameter: TXAS K_{ms}

Parameter values for the K_{ms} of Reaction 4 were obtained from the literature and summarised in Table ST.7.3.1.1.1. The log-normal distribution properties for the K_{ms} of Reaction 4 are shown in Table ST.7.3.1.1.2 and plotted in Figure SF.7.3.1.1.1.

Table ST.7.3.1.1.1. Literature information used to design the TXAS K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
4.00×10^{-3}	NaN	Human	Platelet Free Human Monocyte	TXAS	7.4	37		2048	0	(Orlandi et al., 1994)
1.00×10^{-2}	NaN	Human	Microsome	TXAS	7.4	Unknown		512	0	(Nusing et al., 1990)
2.20×10^{-2}	NaN	Human	Platelet	TXAS	7.4	37		2048	0	(Hecker and Ullrich, 1989)

Table ST.7.3.1.1.2. The log-normal distribution properties of the TXAS K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
9.96×10^{-3}	2.25	-3.9721	0.78374

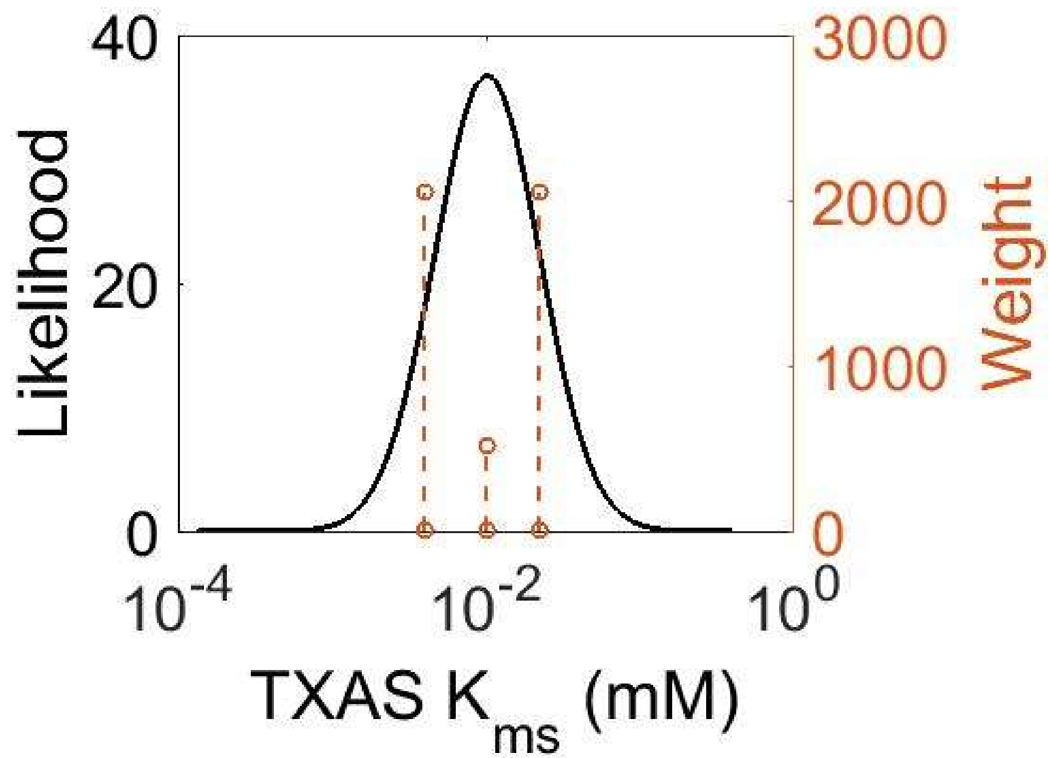


Figure SF.7.3.1.1.1. The estimated probability distribution for TXAS K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.3.1.2. Parameter: TXAS K_{mp} (Dependent Parameter)

The log-normal distribution for the parameter for the K_{mp} of Reaction 4 was calculated using multivariate distributions. The log-normal distribution properties for the K_{mp} of Reaction 4 are shown in Table ST.7.3.1.2.1 and plotted in Figure SF.7.3.1.2.1.

Table ST.7.3.1.2.1. The log-normal distribution properties of the TXAS K_{mp} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Location parameter (μ)	Scale parameter (σ)
1.03 $x10^{-2}$	-3.942048511	0.797944323

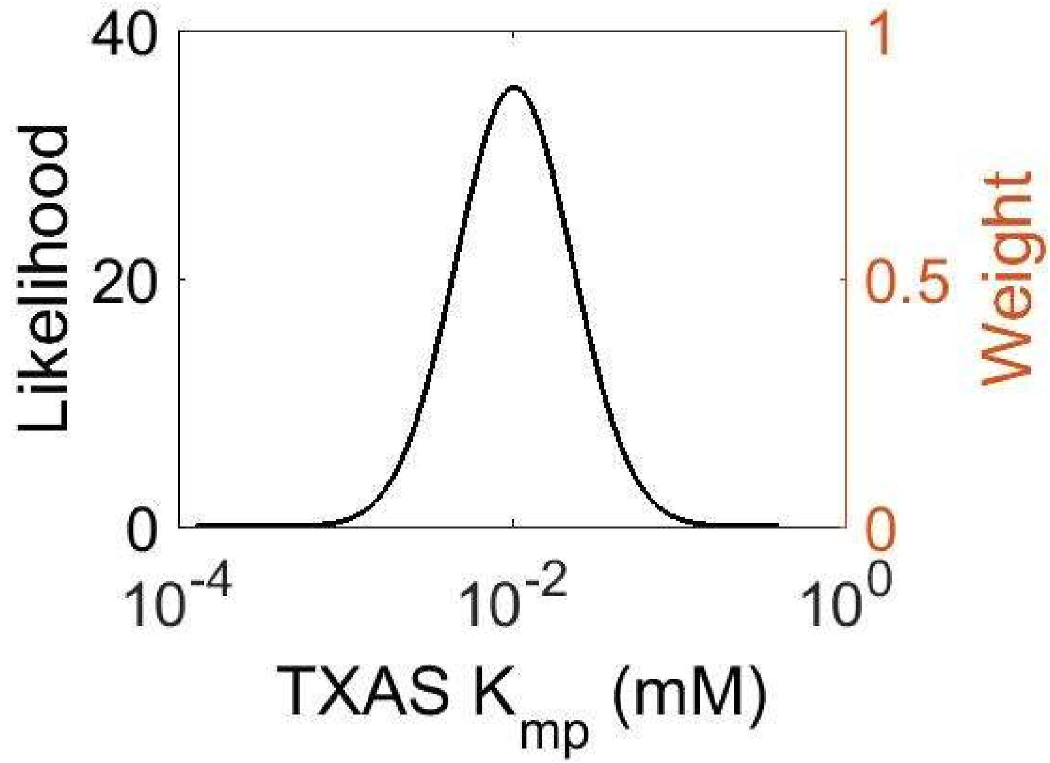


Figure SF.7.3.1.2.1. The estimated probability distribution for TXAS K_{mp}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.3.1.3. Parameter: TXAS k_{cat}

Parameter values for the k_{cat} of Reaction 4 were obtained from the literature and summarised in Table ST.7.3.1.3.1. The log-normal distribution properties for the k_{cat} of Reaction 4 are shown in Table ST.7.3.1.3.2 and plotted in Figure SF.7.3.1.3.1.

Table ST.7.3.1.3.1. Literature information used to design the TXAS k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min-1)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.63 x10^3	NaN	Human	Platelet microsomes	TXAS	7.4	37		2048	0	(Haurand and Ullrich, 1985)
2.69 x10^3	NaN	Human	Platelet	TXAS	7.4	30		512	0	(Hecker et al., 1987)

Table ST.7.3.1.3.2. The log-normal distribution properties of the TXAS k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.67 x10^3	1.25	7.467597712	0.216816683

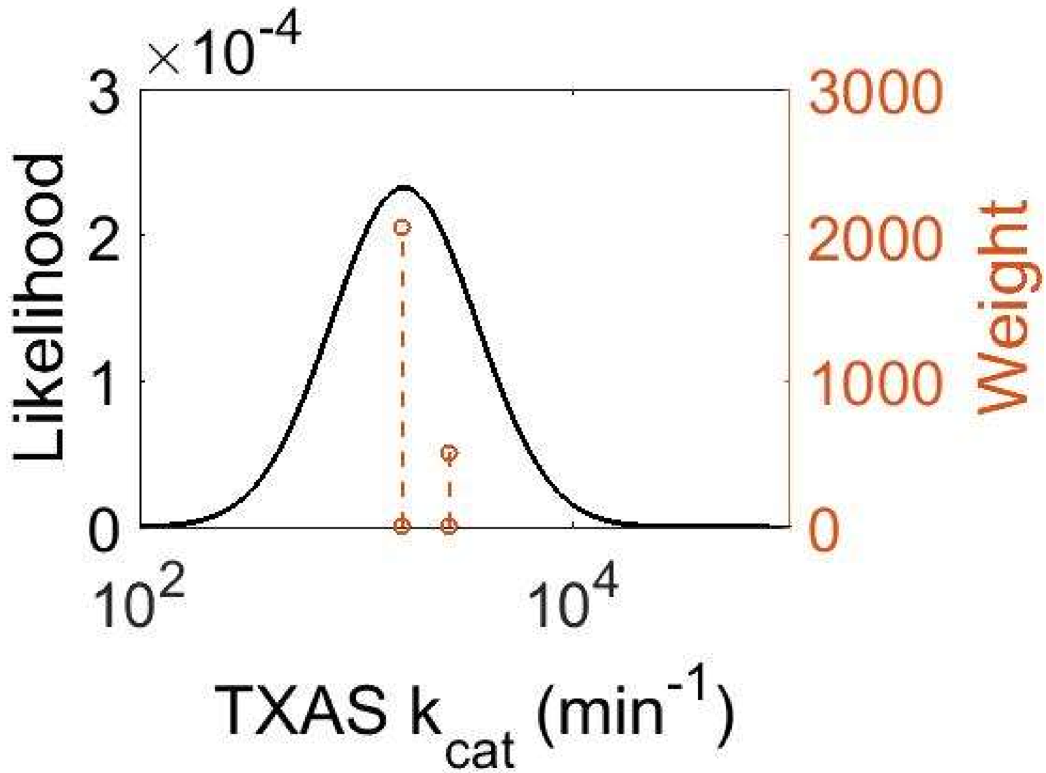


Figure SF.7.3.1.3.1. The estimated probability distribution for TXAS k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.3.1.4. Parameter: TXAS K_{eq}

Parameter values for the K_{eq} of Reaction 4 were obtained from the literature and summarised in Table ST.7.3.1.4.1. The log-normal distribution properties for the K_{eq} of Reaction 4 are shown in Table ST.7.3.1.4.2 and plotted in Figure SF.7.3.1.4.1.

Table ST.7.3.1.4.1. Literature information used to design the TXAS K_{eq} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

ΔG (kcal/mol)	Keq	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
4.00 x10^{-2}	9.35 x10^{-1}	Human	Unknown	PGIS	7	Unknown	The Gibbs free value for TXAS is 41.08 kcal/mol. This value was much higher than other reactions of similar activity, therefore the value for PGIS was used.	64	0	(Caspi et al., 2018)

Table ST.7.3.1.4.2. The log-normal distribution properties of the TXAS K_{eq} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
9.35×10^{-1}	1.00×10^{1}	7.30×10^{-1}	8.90×10^{-1}

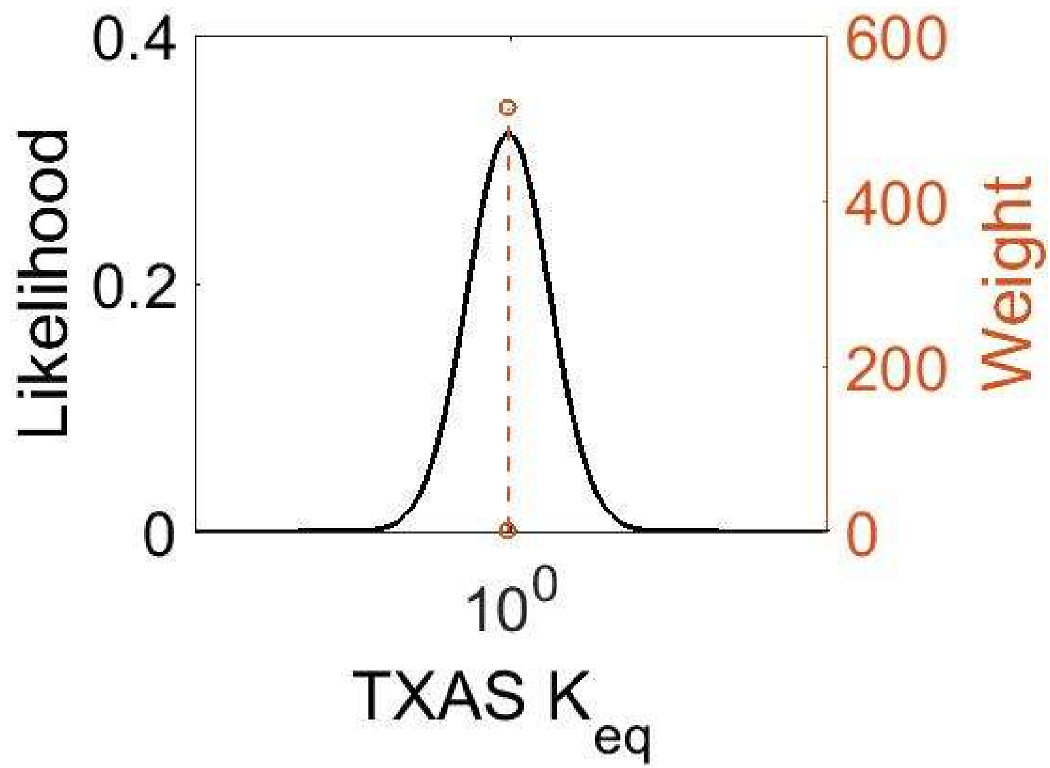


Figure SF.7.3.1.4.1. The estimated probability distribution for TXAS K_{eq}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.3.1.5. Parameter: TXAS concentration

Parameter values for the TXAS concentration of Reaction 4 were obtained from the literature and summarised in Table ST.7.3.1.5.1. The log-normal distribution properties for the TXAS concentration of Reaction 4 are shown in Table ST.7.3.1.5.2 and plotted in Figure SF.7.3.1.5.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

ST.7.3.1.5.1. Literature information used to design the TXAS concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
4.58	NaN	Human	Urinary bladder	TXAS	7.5	37		**1024**	0	(Kim et al., 2014)
5.62 x10^{1}	NaN	Human	Lung	TXAS	7.5	37		**1024**	0	(Kim et al., 2005)
1.01 x10^{2}	NaN	Human	Oral cavity	TXAS	7.5	37		**1024**	0	(Wilhelm et al., 2014)
9.49 x10^{2}	NaN	Human	Platelet	TXAS	7.5	37		**1024**	0	(Kim et al., 2014)

Table ST.7.3.1.5.2. The log-normal distribution properties of the TXAS concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
7.50 x10^{1}	4.15 x10^{-4}	6.69	5.66	1.16

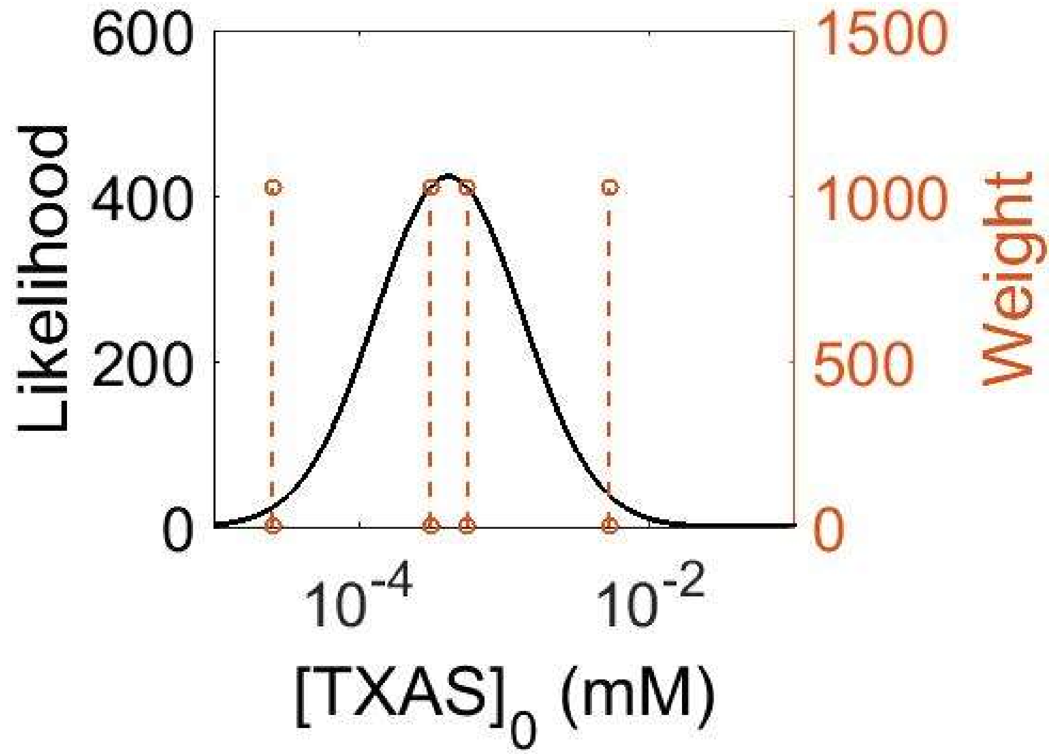


Figure SF.7.3.1.5.1. The estimated probability distribution for the TXAS concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.4 Reaction 5: $PGH_2 \rightleftharpoons PGI_2$

PGH_2 is metabolised into the prostacyclin, PGI_2, by prostaglandin I synthase (PGIS). This protein is a member of the CYP P450 family, but unlike most CYP P450 enzymes it does not oxidise PGH_2. PGI_2 is generated by the rearrangement of the peroxide functional group, whereby a hydroxyl group is formed at C11, and a new epoxide ring is formed between C9 and C6.

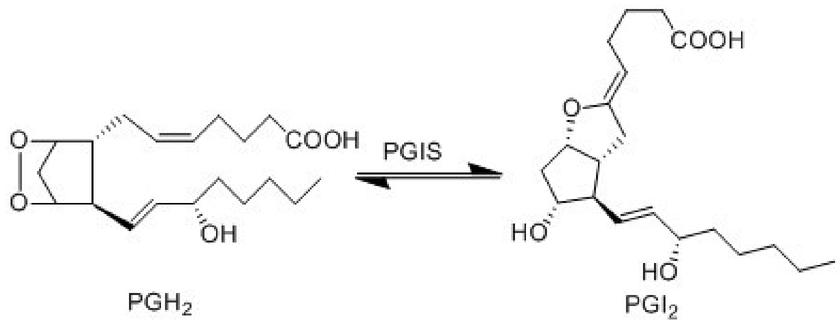


Figure SF.7.4. The metabolism of prostaglandin H_2 (PGH_2) into prostaglandin I_2 (PGI_2) by prostaglandin I synthase (PGIS) (Reaction 5).

SEq.7.4. Reaction rate law for Reaction 5.

$$v_5 = \frac{K_{cat} \cdot [PGIS]\left([PGH_2] - {[PGI_2]}/{K_{eq}}\right)}{K_{m_s}\left(1 + \frac{[PGI_2]}{K_{m_p}}\right) + [PGH_2]}$$

S.7.4.1. Reaction parameters

S.7.4.1.1. Parameter: PGIS K_{ms}

Parameter values for the K_{ms} of Reaction 5 were obtained from the literature and summarised in Table ST.7.4.1.1.1. The log-normal distribution properties for the K_{ms} of Reaction 5 are shown in Table ST.7.4.1.1.2 and plotted in Figure SF.7.4.1.1.1.

Table ST.7.4.1.1.1. Literature information used to design the PGIS K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
9.00 x10^{-3}	5.00 x10^{-3}	Bovine	Bovine Endothelial and Aorta Cells	PGIS	7.4	24		192	0	(Hara et al., 1994)
1.33 x10^{-2}	1.40 x10^{-3}	Human	Bovine Endothelial and Aorta Cells	PGIS	7.4	23		256	0	(Yeh et al., 2005)

Table ST.7.4.1.1.2. The log-normal distribution properties of the PGIS K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.24 x10^{-2}	2.46	-4.22	4.20 x10^{-1}

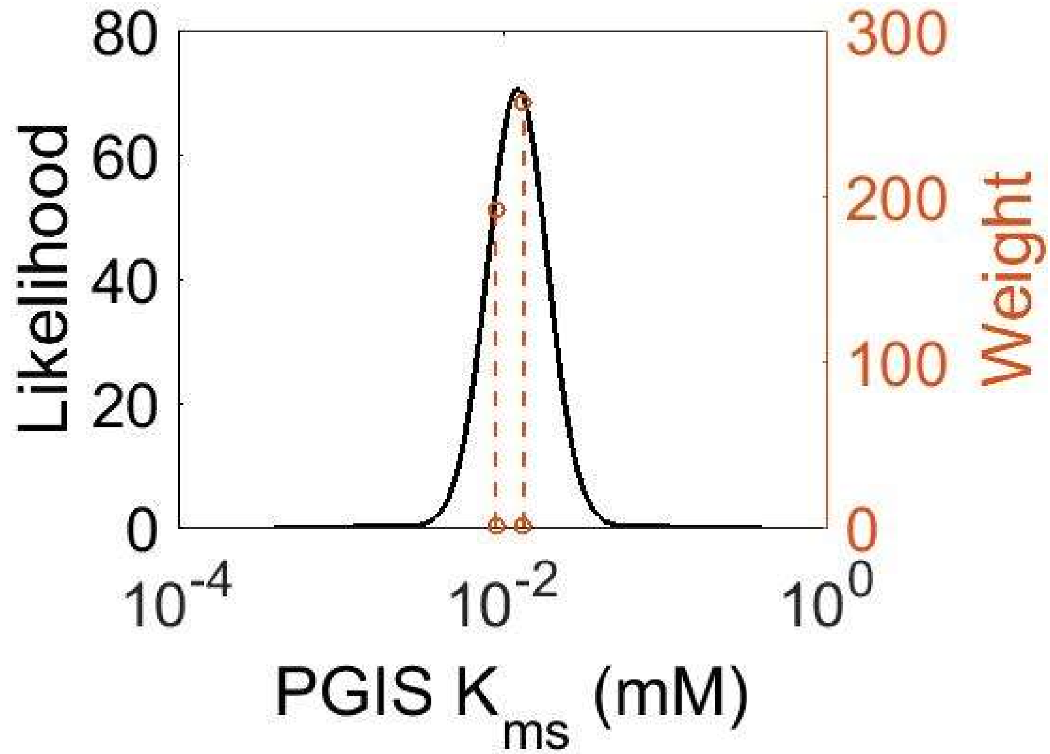


Figure SF.7.4.1.1.1. The estimated probability distribution for PGIS K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.4.1.2. Parameter: PGIS K_{mp} (Dependent parameter)

The log-normal distribution for the parameter for the K_{mp} of Reaction 5 was calculated using multivariate distributions. The log-normal distribution properties for the K_{mp} of Reaction 5 are shown in Table ST.7.4.1.2.1 and plotted in Figure SF.7.4.1.2.1.

Table ST.7.4.1.2.1. The log-normal distribution properties of the PGIS K_{mp} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Location parameter (μ)	Scale parameter (σ)
1.29×10^{-2}	-4.182022605	0.414183521

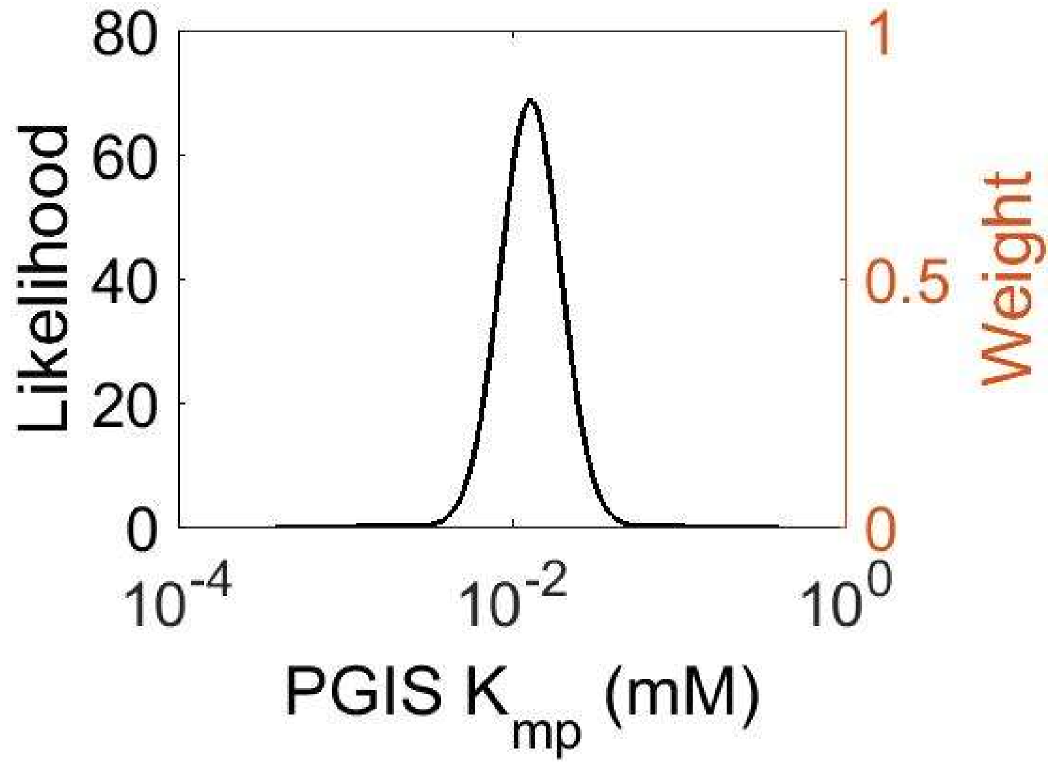


Table SF.7.4.1.2.1. The estimated probability distribution for PGIS K_{mp}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.4.1.3. Parameter: PGIS k_{cat}

Parameter values for the k_{cat} of Reaction 5 were obtained from the literature and summarised in Table ST.7.4.1.3.1. The log-normal distribution properties for the k_{cat} of Reaction 5 are shown in Table ST.7.4.1.3.2 and plotted in Figure SF.7.4.1.3.1.

Table ST.7.4.1.3.1. Literature information used to design the PGIS k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min-1)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.47 x10^2	4.50 x10^1	Bovine	E. coli	PGIS	7.4	24		192	0	(Hara et al., 1994)

Table ST.7.4.1.3.2. The log-normal distribution properties of the PGIS k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.41 x10^2	1.35	5.028213628	0.287348692

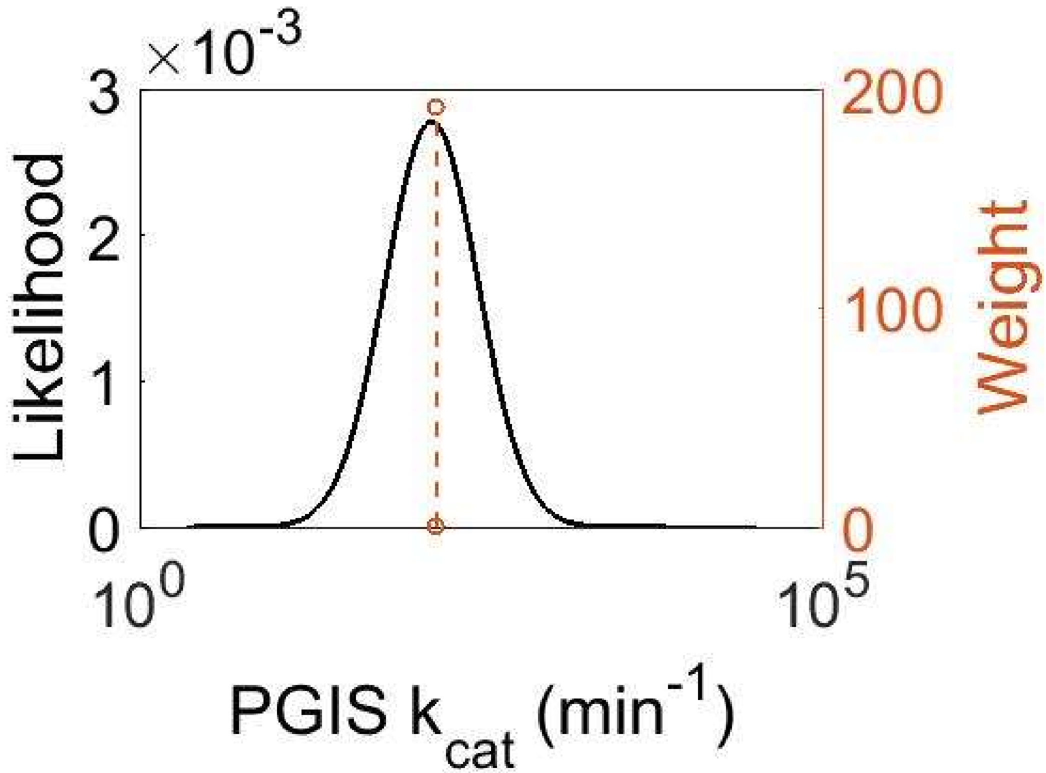


Figure SF.7.4.1.3.1. The estimated probability distribution for PGIS k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.4.1.4. Parameter: PGIS K_{eq}

Parameter values for the K_{eq} of Reaction 5 were obtained from the literature and summarised in Table ST.7.4.1.4.1. The log-normal distribution properties for the K_{eq} of Reaction 5 are shown in Table ST.7.4.1.4.2 and plotted in Figure SF.7.4.1.4.1.

Table ST.7.4.1.4.1. Literature information used to design the PGIS K_{eq} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

ΔG (kcal/mol)	Keq	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
4.00 x10^{-2}	9.35 x10^{-1}	Human	Unknown	PGIS	7	Unknown		64	0	(Caspi et al., 2018)

Table ST.7.4.1.4.2. The log-normal distribution properties of the PGIS K_{eq} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
9.35 x10^{-1}	1.00 x10^{1}	7.30 x10^{-1}	8.90 x10^{-1}

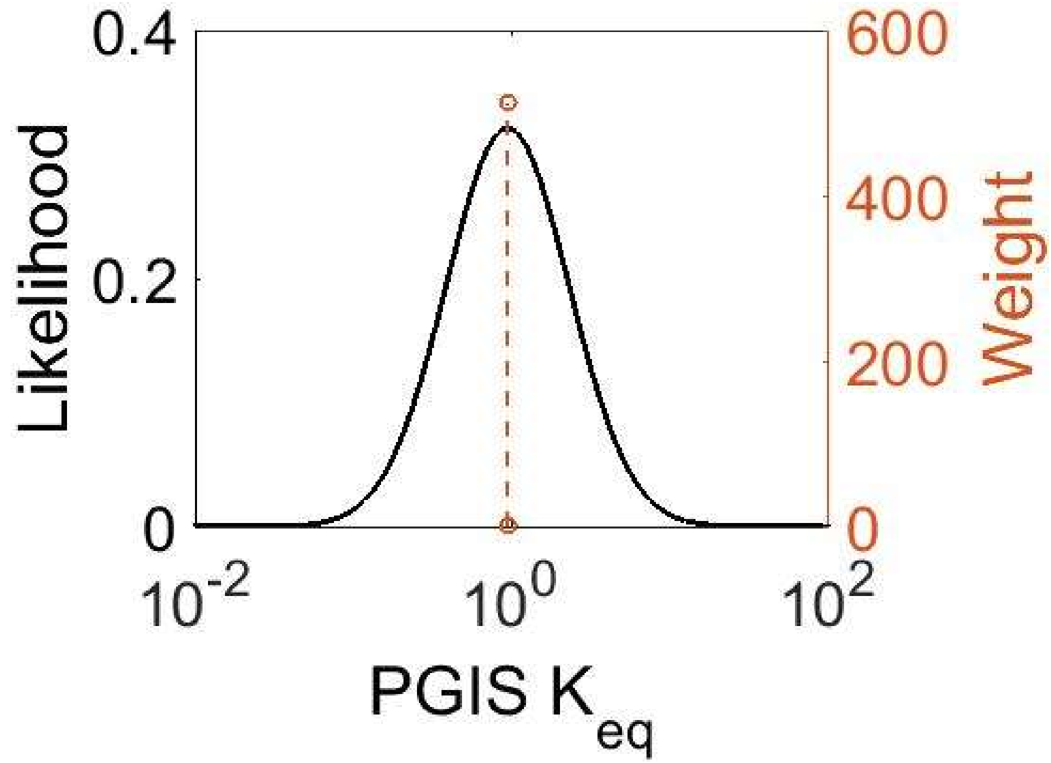


Figure SF.7.4.1.4.1. The estimated probability distribution for PGIS K_{eq}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.4.1.5. Parameter: PGIS concentration

Parameter values for the PGIS concentration of Reaction 5 were obtained from the literature and summarised in Table ST.7.4.1.5.1. The log-normal distribution properties for the PGIS concentration of Reaction 5 are shown in Table ST.7.4.1.5.2 and plotted in Figure SF.7.4.1.5.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.7.4.1.5.1. Literature information used to design the PGIS concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
9.93	NaN	Human	Oral cavity	PGIS	7.5	37		**1024**	0	(Wilhelm et al., 2014)
6.01×10^{1}	NaN	Human	Oesophagus	PGIS	7.5	37		**1024**	0	(Kim et al., 2014)
2.06×10^{2}	NaN	Human	Lung	PGIS	7.5	37		**1024**	0	(Kim et al., 2014)
4.12×10^{2}	NaN	Human	Urinary bladder	PGIS	7.5	37		**1024**	0	(Kim et al., 2014)

Table ST.7.4.1.5.2. The log-normal distribution properties of the PGIS concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.13×10^{2}	6.25×10^{-4}	4.13	5.67	9.68×10^{-1}

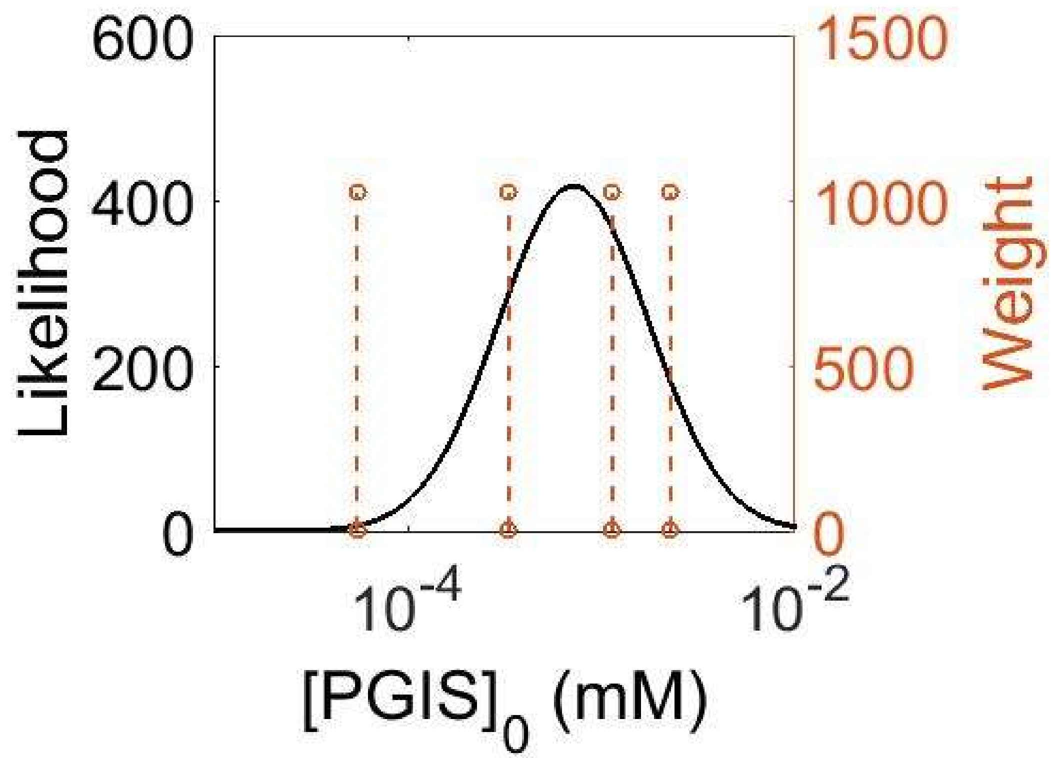


Figure SF.7.4.1.5.1. The estimated probability distribution for the PGIS concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.5 Reaction 10: $PGH_2 \rightleftharpoons PGE_2$

PGE_2 is produced by the isomerisation of the PGH_2 peroxide, into a ketone at C9 and an alcohol at C11 by PGES, yielding PGE_2.

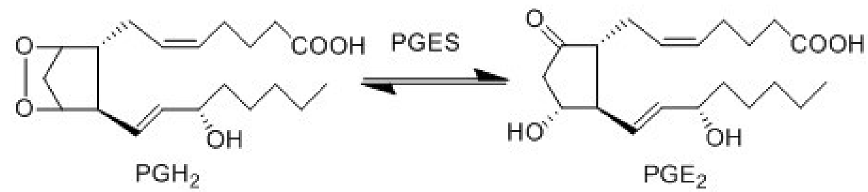


Figure SF.7.5. The metabolism of prostaglandin H_2 (PGH_2) into prostaglandin E_2 (PGE_2) by prostaglandin E synthase (PGES) (Reaction 10).

SEq.7.5. Reaction rate law for Reaction 10.

Eq.S.7.1 $$\boldsymbol{v_{10}} = \frac{K_{cat} \cdot [PGES]\left([PGH_2] - {[PGE_2]}/{K_{eq}}\right)}{K_{m_s}\left(1 + \frac{[PGE_2]}{K_{m_p}}\right) + [PGH_2]}$$

S.7.5.1. Reaction parameters

S.7.5.1.1. Parameter: PGES K_{ms}

Parameter values for the K_{ms} of Reaction 10 were obtained from the literature and summarised in Table ST.7.5.1.1.1. The log-normal distribution properties for the K_{ms} of Reaction 10 are shown in Table ST.7.5.1.1.2 and plotted in Figure SF.7.5.1.1.1.

Table ST.7.5.1.1.1. Literature information used to design the PGES K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.49 $\times10^{-2}$	NaN	Human	E. coli.	PGES (cPGES)	Unknown	Unknown		64	0	(Kobayashi et al., 2004)
6.66 $\times10^{-2}$	NaN	Human	E. coli.	PGES (cPGES)	Unknown	Unknown		64	0	(Kobayashi et al., 2004)
1.60 $\times10^{-1}$	4.00 $\times10^{-3}$	Human	E. coli.	PGES (mPGES-1)	8	37		512	0	(Pettersson et al., 2005)
2.15 $\times10^{-1}$	NaN	Human	E. coli.	PGES (mPGES-1)	7.2	37		1024	0	(Hamza et al., 2010)

Table ST.7.5.1.1.2. The log-normal distribution properties of the PGES K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.97 $\times10^{-1}$	1.73	-1.39	4.91 $\times10^{-1}$

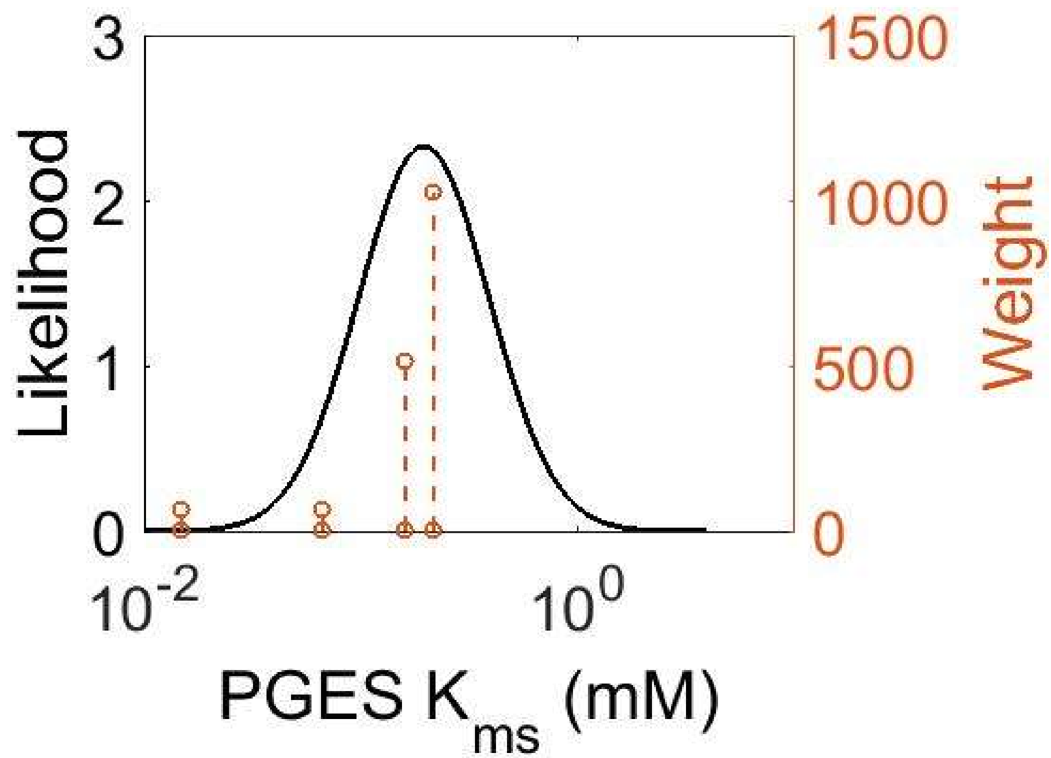


Table SF.7.5.1.1.1. The estimated probability distribution for PGES K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.5.1.2. Parameter: PGES K_{mp} (Dependent Parameter)

The log-normal distribution for the parameter for the K_{mp} of Reaction 10 was calculated using multivariate distributions. The log-normal distribution properties for the K_{mp} of Reaction 10 are shown in Table ST.7.5.1.2.1 and plotted in Figure SF.7.5.1.2.1.

Table ST.7.5.1.2.1. The log-normal distribution properties of the PGES K_{mp} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Location parameter (μ)	Scale parameter (σ)
1.93×10^{-1}	-1.15	7.02×10^{-1}

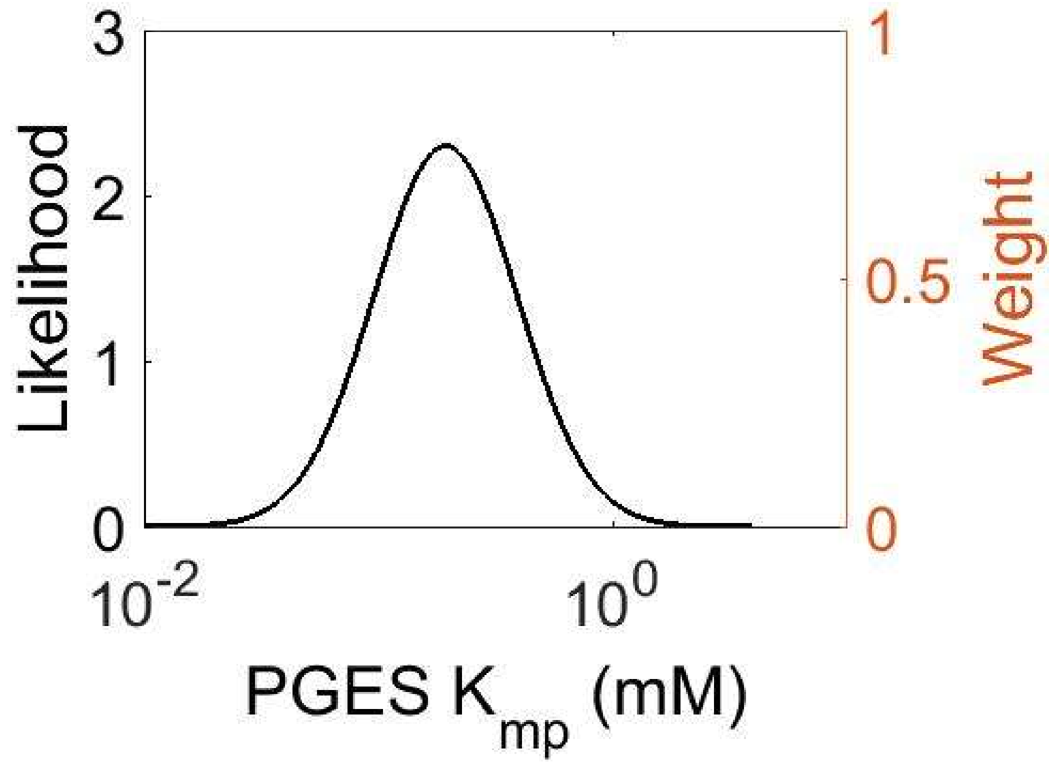


Figure SF.7.5.1.2.1. The estimated probability distribution for PGES K_{mp}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.5.1.3. Parameter: PGES k_{cat}

Parameter values for the k_{cat} of Reaction 10 were obtained from the literature and summarised in Table ST.7.5.1.3.1. The log-normal distribution properties for the k_{cat} of Reaction 10 are shown in Table ST.7.5.1.3.2 and plotted in Figure SF.7.5.1.3.1.

Table ST.7.5.1.3.1. Literature information used to design the PGES k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
3.00 x10^3	3.60 x10^2	Human	E. coli.	PGES (mPGES-1)	7.5	37		1024	0	(Pettersson et al., 2005)

Table ST.7.5.1.3.2. The log-normal distribution properties of the PGES k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
2.98 x10^3	1.13	8.01	1.19 x10^{-1}

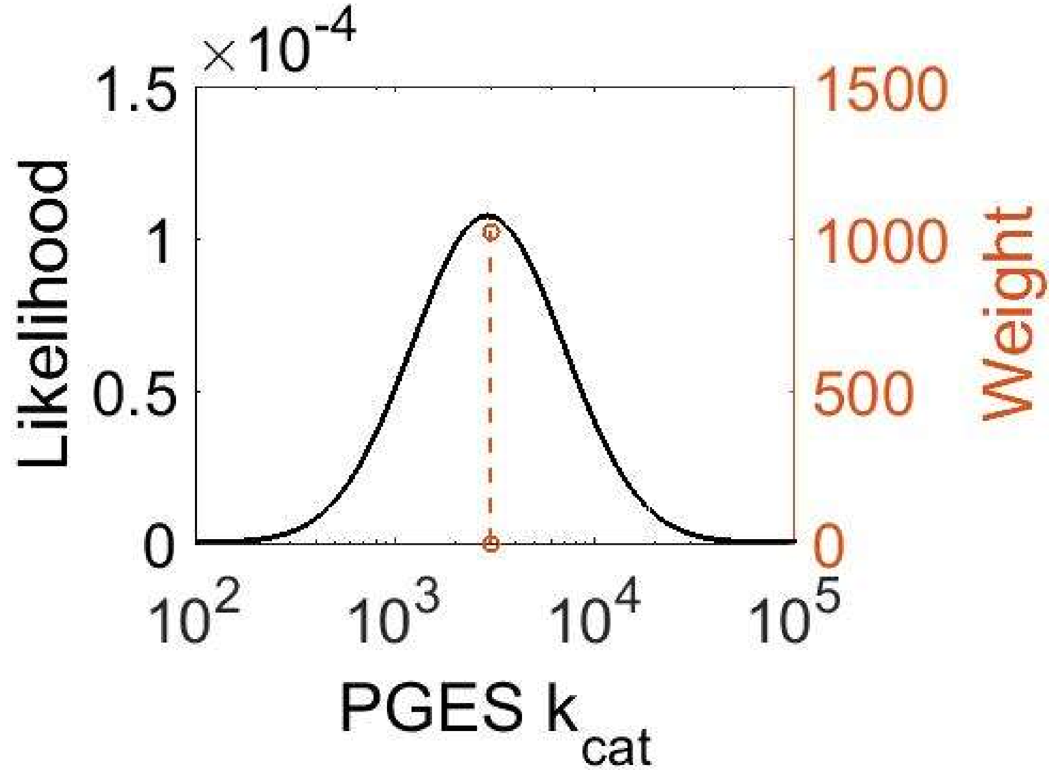


Figure SF.7.5.1.3.1. The estimated probability distribution for PGES k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.5.1.4. Parameter: PGES K_{eq}

Parameter values for the K_{eq} of Reaction 10 were obtained from the literature and summarised in Table ST.7.5.1.4.1. The log-normal distribution properties for the K_{eq} of Reaction 10 are shown in Table ST.7.5.1.4.2 and plotted in Figure SF.7.5.1.4.1.

Table ST.7.5.1.4.1. Literature information used to design the PGES K_{eq} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

ΔG (kcal/mol)	K_{eq}	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
-6.64	7.46 x10^{4}	Human	Unknown	PGES	7	Unknown		64	0	(Caspi et al., 2018)

Table ST.7.5.1.4.2. The log-normal distribution properties of the PGES K_{eq} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
7.46 x10^{4}	1.00 x10^{1}	1.20 x10^{1}	8.90 x10^{-1}

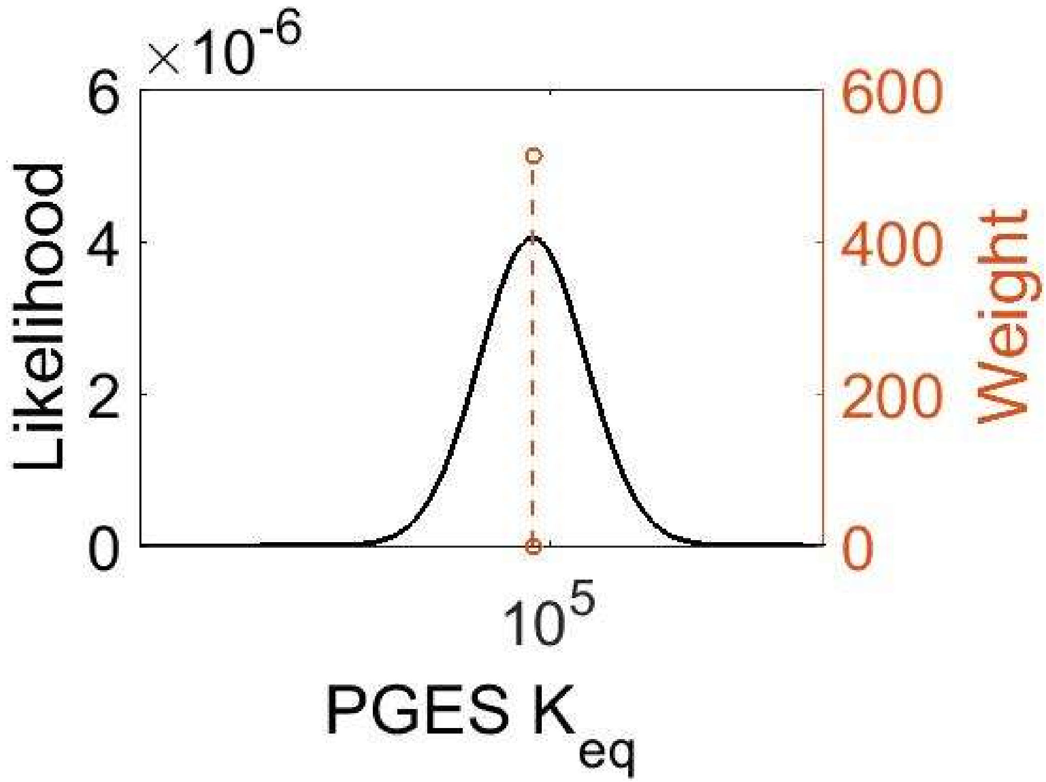


Figure SF.7.5.1.4.1. The estimated probability distribution for PGES K_{eq}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.5.1.5. Parameter: PGES concentration

Parameter values for the PGES concentration of Reaction 10 were obtained from the literature and summarised in Table ST.7.5.1.5.1. The log-normal distribution properties for the PGES concentration of Reaction 10 are shown in Table ST.7.5.1.5.2 and plotted in Figure SF.7.5.1.5.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.7.5.1.5.1. Literature information used to design the PGES K_{eq} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.16 x10^{1}	NaN	Human	Colon	PGES	7.5	37		**1024**	0	(Kim et al., 2014)
2.81 x10^{1}	NaN	Human	Lung	PGES	7.5	37		**1024**	0	(Kim et al., 2014)
7.53 x10^{1}	NaN	Human	Urinary bladder	PGES	7.5	37		**1024**	0	(Kim et al., 2014)
2.08 x10^{2}	NaN	Human	Stomach	PGES	7.5	37		**1024**	0	(Wilhelm et al., 2014)
2.20 x10^{2}	NaN	Human	Placenta	PGES	7.5	37		**1024**	0	(Wilhelm et al., 2014)

Table ST.7.5.1.5.2 The log-normal distribution properties of the PGES concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
7.49 x10^{1}	4.15 x10^{-4}	3.15	5.03	8.44 x10^{-1}

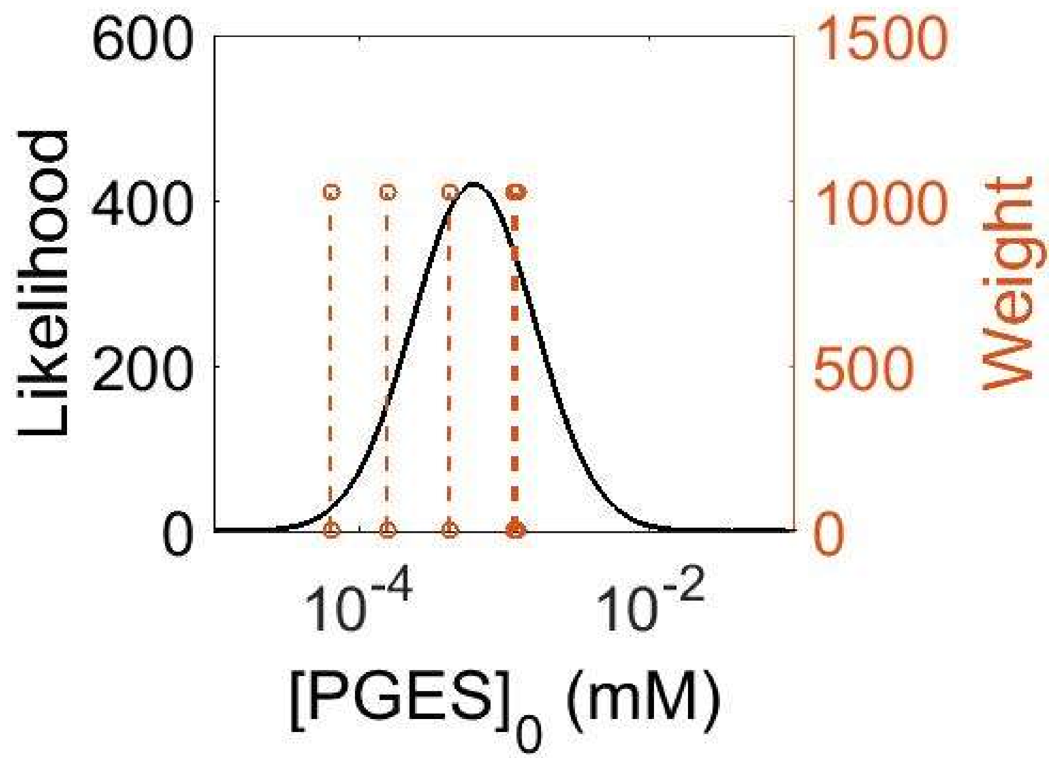


Figure SF.7.5.1.5.1. The estimated probability distribution for the PGES concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.6 Reaction 11: AA ⇌ 5-HPETE

The gene ALOX5 encodes the protein 5-LOX, which is responsible for the generation of 5-HPETE from AA. The formation of the hydroperoxy fatty acids (HPETE) begins with the abstraction of a hydrogen radical at the allylic position between two double bonds. The structure undergoes a rearrangement reaction which results in the formation of a conjugated diene system. The insertion of molecular oxygen and a hydrogen leads to the formation of the final structure, a hydroperoxy fatty acid.

Figure SF.7.6. The metabolism of arachidonic acid (AA) into 5-hydroperoxyeicosatetraenoic acid (5-HPETE) by 5-lipoxygenase (5-LOX) (Reaction 11).

SEq.7.6. Reaction rate law for Reaction 11.

$$\boldsymbol{v_{11}} = \frac{K_{cat}\cdot[5-LOX]\left([AA]-{[5-HPETE]}/{K_{eq}}\right)}{K_{m_s}\left(1+\frac{[5-HPETE]}{K_{m_p}}\right)+[AA]}$$

S.7.6.1. Reaction parameters

S.7.6.1.1. Parameter: 5-LOX K_{ms}

Parameter values for the K_{ms} of Reaction 11 were obtained from the literature and summarised in Table ST.7.6.1.1.1. The log-normal distribution properties for the K_{ms} of Reaction 11 are shown in Table ST.7.6.1.1.2 and plotted in Figure SF.7.6.1.1.1.

Table ST.7.6.1.1.1. Literature information used to design the 5-LOX K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
5.10 x10^{-3}	NaN	Human	Baculovirus	5-LOX	5.6	37		256	0	(Shirumalla et al., 2006)
1.20 x10^{-2}	NaN	Human	Polymorphonuclear Leukocytes	5-LOX	7.5	22		512	0	(Soberman, 1988)
6.31 x10^{-2}	NaN	Human	Polymorphonuclear Leukocytes	5-LOX	7.5	22		512	0	(Soberman et al., 1985)

Table ST.7.6.1.1.2. The log-normal distribution properties of the 5-LOX K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.27 x10^{-2}	2.74	-3.76	7.73 x10^{-1}

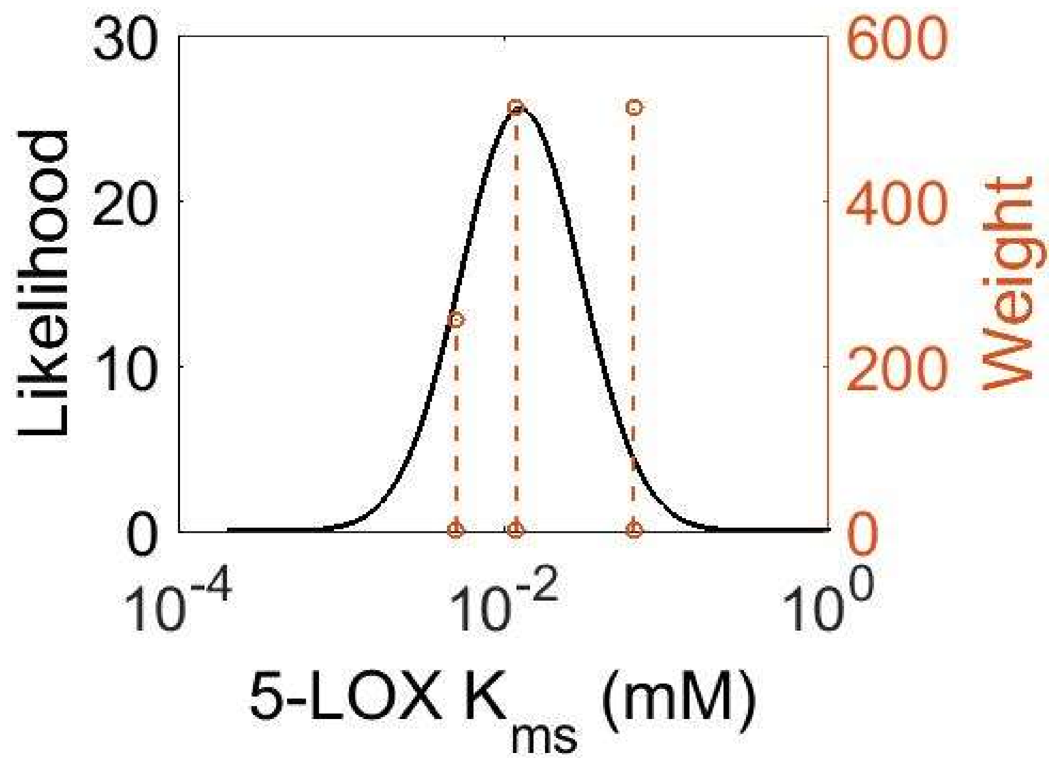


Figure SF.7.6.1.1.1. The estimated probability distribution for 5-LOX K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.6.1.2. Parameter: 5-LOX K_{mp} (Dependent parameter)

The log-normal distribution for the parameter for the K_{mp} of Reaction 11 was calculated using multivariate distributions. The log-normal distribution properties for the K_{mp} of Reaction 11 are shown in Table ST.7.6.1.2.1 and plotted in Figure SF.7.6.1.2.1.

Table ST.7.6.1.2.1. The log-normal distribution properties of the 5-LOX K_{mp} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Location parameter (μ)	Scale parameter (σ)
1.25×10^{-2}	-3.63	8.68×10^{-1}

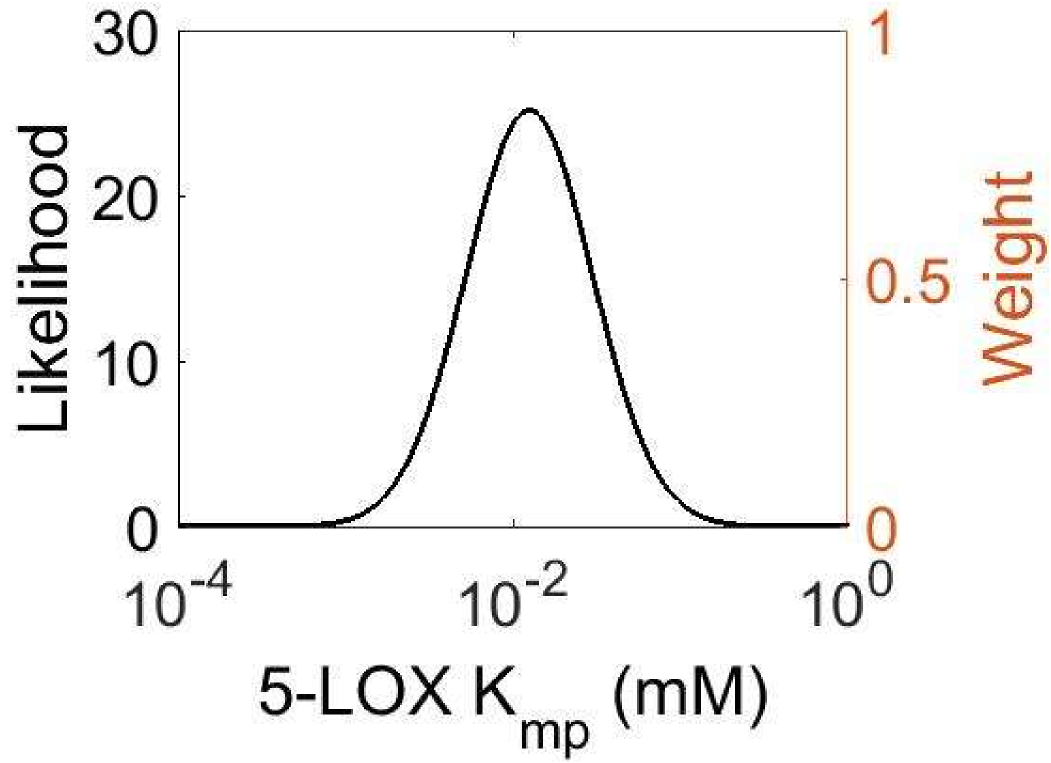


Figure SF.7.6.1.2.1. The estimated probability distribution for 5-LOX K_{mp}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.6.1.3. Parameter: 5-LOX k_{cat}

Parameter values for the k_{cat} of Reaction 11 were obtained from the literature and summarised in Table ST.7.6.1.3.1. The log-normal distribution properties for the k_{cat} of Reaction 11 are shown in Table ST.7.6.1.3.2 and plotted in Figure SF.7.6.1.3.1.

Table ST.7.6.1.3.1. Literature information used to design the 5-LOX k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.50×10^{3}	7.50×10^{1}	Potato	Potato	5-LOX	5.5	23		16	0	(Mulliez et al., 1987)

Table ST.7.6.1.3.2. The log-normal distribution properties of the 5-LOX k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.50×10^{3}	1.05	7.31	4.99×10^{-2}

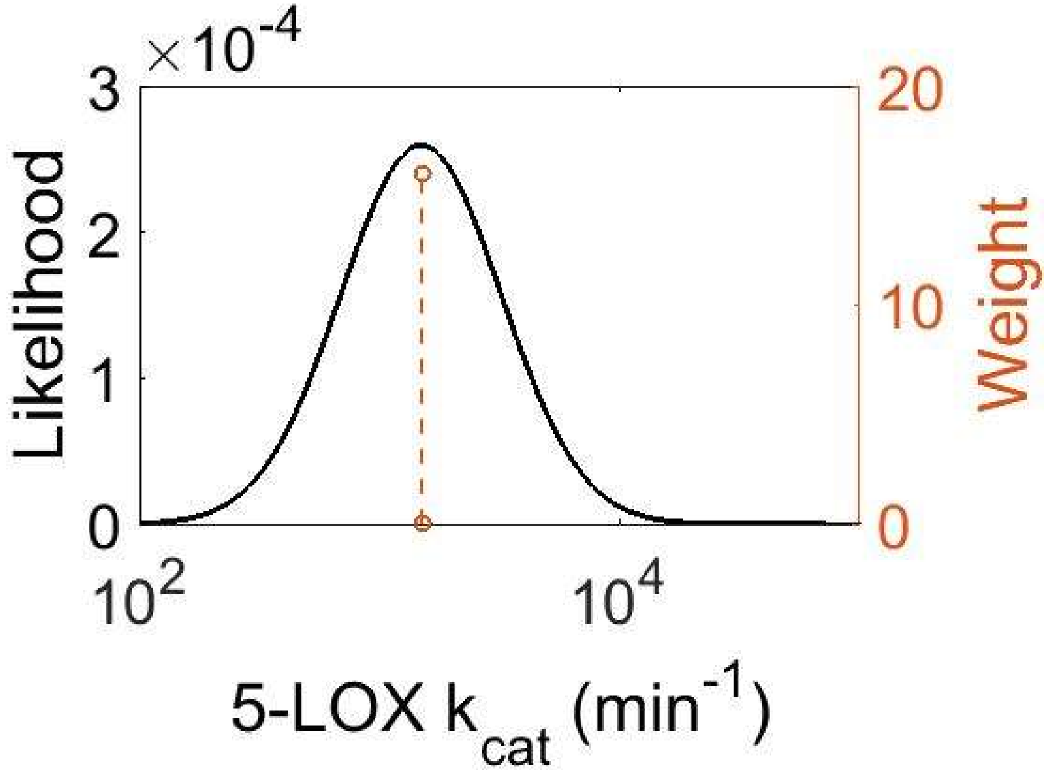


Figure SF.7.6.1.3.1. The estimated probability distribution for 5-LOX k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.6.1.4. Parameter: 5-LOX K_{eq}

Parameter values for the K_{eq} of Reaction 11 were obtained from the literature and summarised in Table ST.7.6.1.4.1. The log-normal distribution properties for the K_{eq} of Reaction 11 are shown in Table ST.7.6.1.4.2 and plotted in Figure SF.7.6.1.4.1.

Table ST.7.6.1.4.1. Literature information used to design the 5-LOX K_{eq} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

ΔG (kcal/mol)	K_{eq}	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
-7.00 x10^{1}	2.27 x10^{51}	Human	Unknown	5-LOX	7	Unknown		64	0	(Caspi et al., 2018)

Table ST.7.6.1.4.2. The log-normal distribution properties of the 5-LOX K_{eq} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
2.27 x10^{51}	1.00 x10^{1}	1.19 x10^{2}	8.90 x10^{-1}

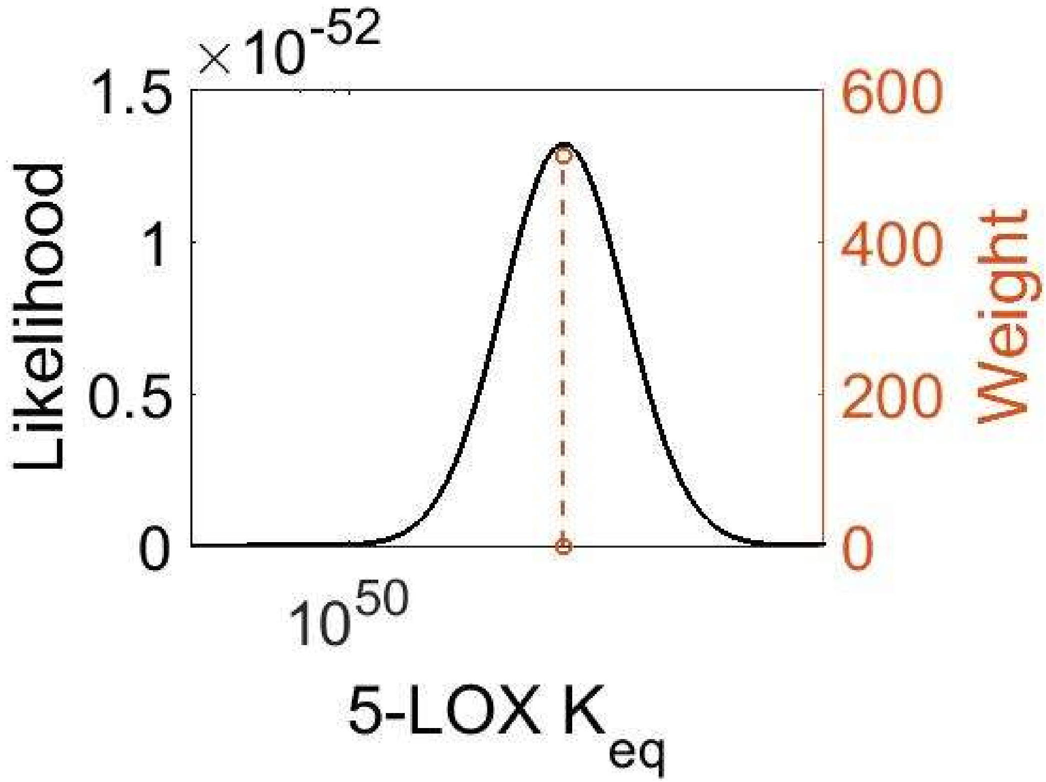


Figure SF.7.6.1.4.1. The estimated probability distribution for 5-LOX K_{eq}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.6.1.5. Parameter: 5-LOX concentration

Parameter values for the 5-LOX concentration of Reaction 11 were obtained from the literature and summarised in Table ST.7.6.1.5.1. The log-normal distribution properties for the 5-LOX concentration of Reaction 11 are shown in Table ST.7.6.1.5.2 and plotted in Figure SF.7.6.1.5.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.7.6.1.5.1. Literature information used to design the 5-LOX concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
3.19×10^{1}	NaN	Human	Oral cavity	5-LOX	7.5	37		**1024**	0	(Wilhelm et al., 2014)
4.98×10^{1}	NaN	Human	Oesophagus	5-LOX	7.5	37		**1024**	0	(Wilhelm et al., 2014)
9.73×10^{1}	NaN	Human	Lung	5-LOX	7.5	37		**1024**	0	(Kim et al., 2014)

Table ST.7.6.1.5.2. The log-normal distribution properties of the 5-LOX concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
4.96×10^{1}	2.74×10^{-4}	1.60	4.09	4.28×10^{-1}

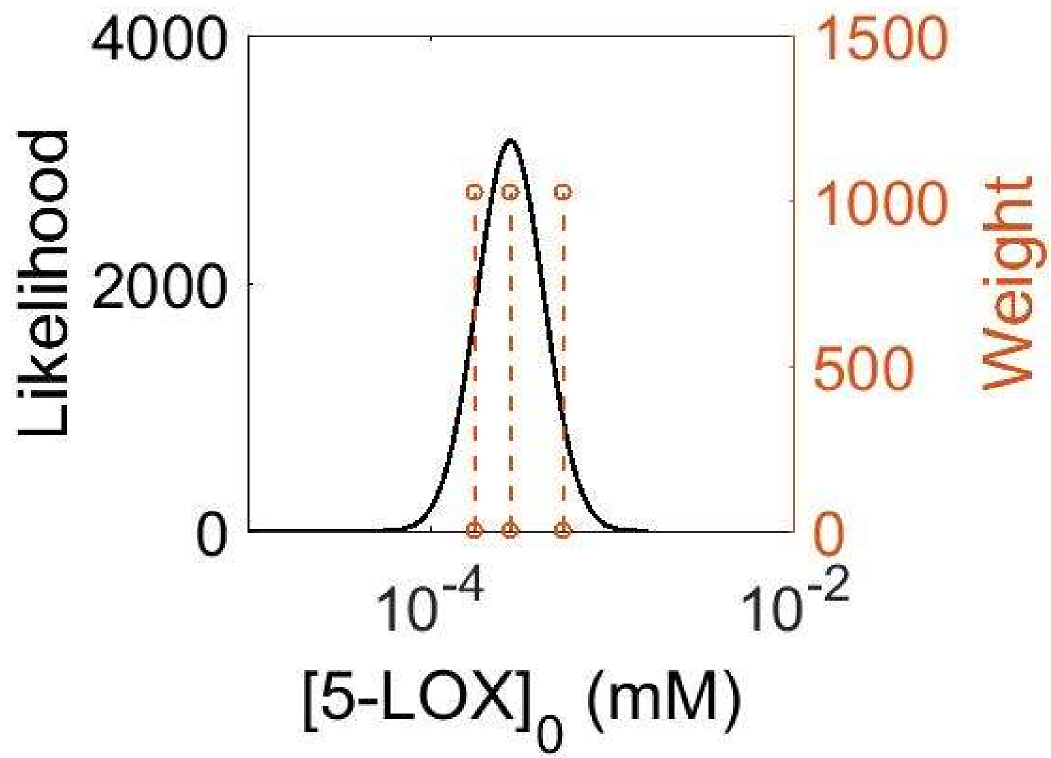


Figure SF.7.6.1.5.1. The estimated probability distribution for the 5-LOX concentration The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.7 Reaction 12: 5-HPETE ⇌ 5-HETE

Upon being generated, 5-HPETE is reduced by an oxidoreductase enzyme, phospholipid hydroperoxide glutathione peroxidase (PHGPx), to form 5-HETE.

Figure SF.7.7. The metabolism of 5-hydroperoxyeicosatetraenoic acid (5-HPETE) into 5-hydroxyeicosatetraenoic acid (5-HETE) by phospholipid hydroperoxide glutathione peroxidase (PHGPx) (Reaction 12).

SEq.7.7. Reaction rate law for Reaction 12.

$$\boldsymbol{v_{12}} = \frac{\boldsymbol{K_{cat}} \cdot [\boldsymbol{PHGPx}]\left([\mathbf{5}-\boldsymbol{HPETE}\mathbf{5}]-{[\mathbf{5}-\boldsymbol{HETE}]}/{\boldsymbol{K_{eq}}}\right)}{\boldsymbol{K_{m_s}}\left(\mathbf{1}+\frac{[\mathbf{5}-\boldsymbol{HETE}]}{\boldsymbol{K_{m_p}}}\right)+[\mathbf{5}-\boldsymbol{HPETE}]}$$

S.7.7.1. Reaction parameters

S.7.7.1.1. Parameter: PHGPx K_{ms}

Parameter values for the K_{ms} of Reaction 12 were obtained from the literature and summarised in Table ST.7.7.1.1.1. The log-normal distribution properties for the K_{ms} of Reaction 12 are shown in Table ST.7.7.1.1.2 and plotted in Figure SF.7.7.1.1.1.

Table ST.7.7.1.1.1. Literature information used to design the PHGPx K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
4.00×10^{-3}	NaN	Rat	Liver	PHGPx	7.4	37		768	0	(Hiratsuka et al., 1997)
3.00×10^{-1}	NaN	Human	Bio imprinted Enzyme	PHGPx	7	37		512	0	(Liu et al., 2008)
1.11×10^{1}	2.90×10^{-1}	Human	E. coli.	PHGPx	7	37		1024	0	(Zheng et al., 2008)

Table ST.7.7.1.1.2. The log-normal distribution properties of the PHGPx K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
3.19×10^{-1}	1.02×10^{3}	2.54	1.92

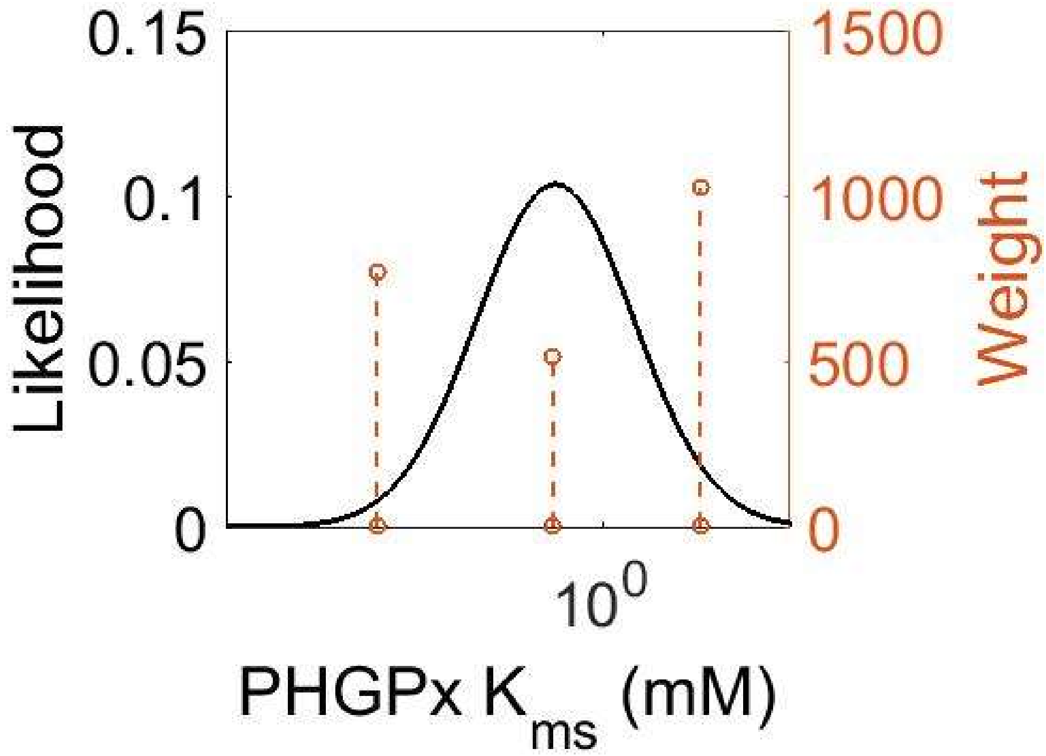


Figure SF.7.7.1.1.1. The estimated probability distribution for PHGPx K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.7.1.2. Parameter: PHGPx K_{mp} (Dependent parameter)

The log-normal distribution for the parameter for the K_{mp} of Reaction 12 was calculated using multivariate distributions. The log-normal distribution properties for the K_{mp} of Reaction 12 are shown in Table ST.7.7.1.2.1 and plotted in Figure SF.7.7.1.2.1.

Table ST.7.7.1.2.1. The log-normal distribution properties of the PHGPx K_{mp} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Location parameter (μ)	Scale parameter (σ)
3.15 x10^{-1}	2.53	1.92

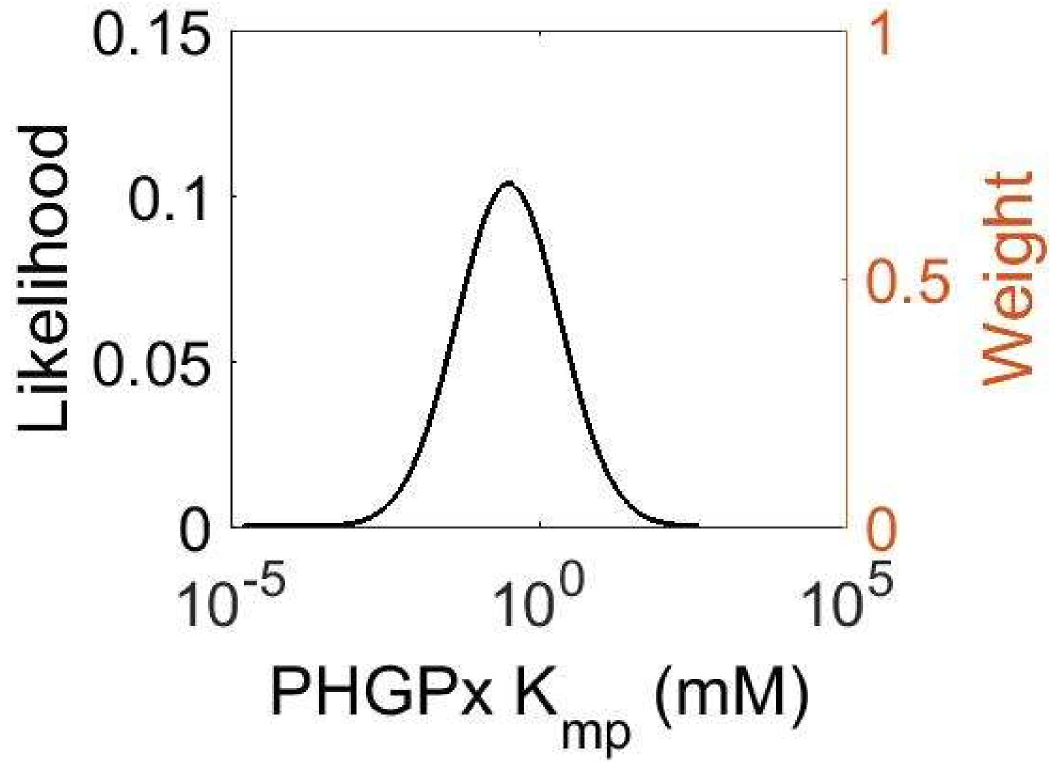


Figure SF.7.7.1.2.1. The estimated probability distribution for PHGPx K_{mp}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.7.1.3. Parameter: PHGPx k_{cat}

Parameter values for the k_{cat} of Reaction 12 were obtained from the literature and summarised in Table ST.7.7.1.3.1. The log-normal distribution properties for the k_{cat} of Reaction 12 are shown in Table ST.7.7.1.3.2 and plotted in Figure SF.7.7.1.3.1.

Table ST.7.7.1.3.1. Literature information used to design the PHGPx k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.17×10^3	5.00×10^1	Human	Bio imprinted Enzyme	PHGPx	7	37		512	0	(Liu et al., 2008)
2.45×10^4	1.50×10^2	Human	E. coli.	PHGPx	7	37		1024	0	(Zheng et al., 2008)

Table ST.7.7.1.3.2. The log-normal distribution properties of the PHGPx k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
2.44×10^4	4.20	1.11×10^1	9.75×10^{-1}

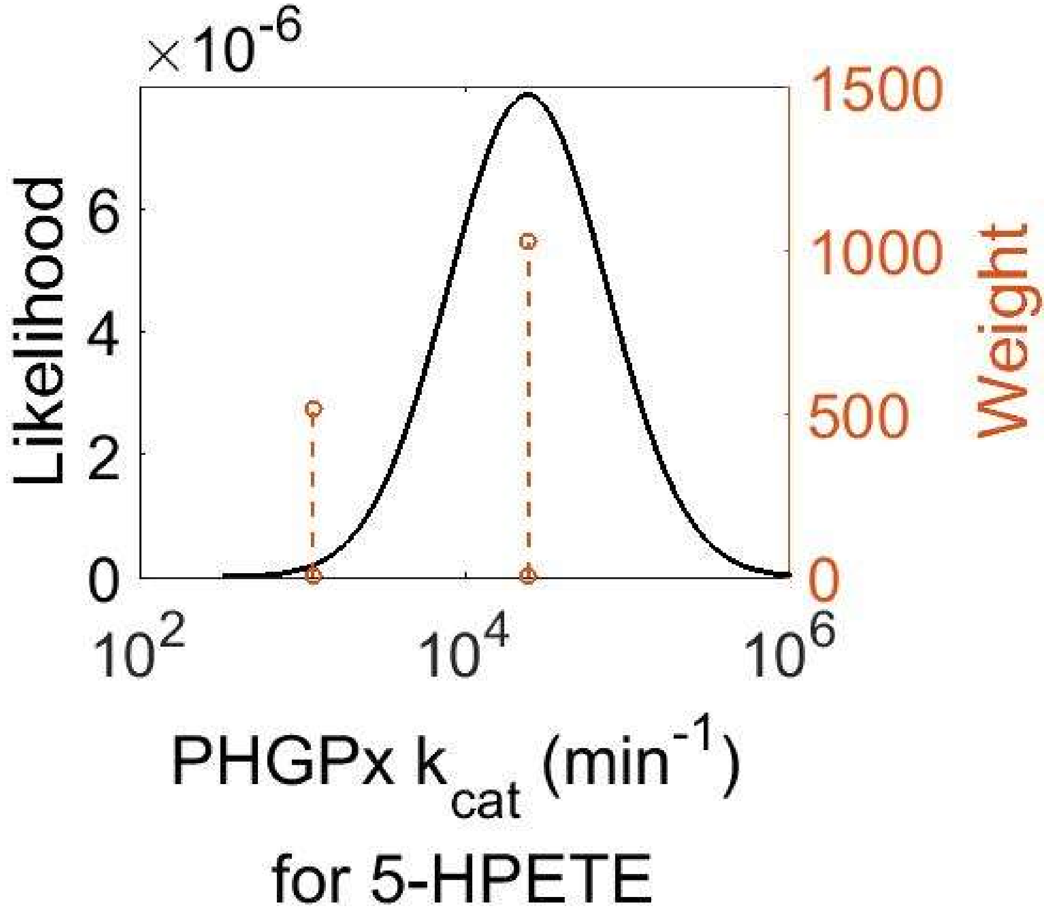


Figure SF.7.7.1.3.1. The estimated probability distribution for PHGPx k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.7.1.4. Parameter: PHGPx K_{eq}

Parameter values for the K_{eq} of Reaction 12 were obtained from the literature and summarised in Table ST.7.7.1.4.1. The log-normal distribution properties for the K_{eq} of Reaction 12 are shown in Table ST.7.7.1.4.2 and plotted in Figure SF.7.7.1.4.1.

Table ST.7.7.1.4.1. Literature information used to design the PHGPx K_{eq} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

ΔG (kcal/mol)	K_{eq}	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
-2.69 x10^{1}	5.90 x10^{19}	Human	Unknown	PHGPx	7	Unknown		64	0	(Caspi et al., 2018)

Table ST.7.7.1.4.2. The log-normal distribution properties of the PHGPx K_{eq} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
5.90 x10^{19}	1.00 x10^{1}	4.63 x101	8.90 x10^{-1}

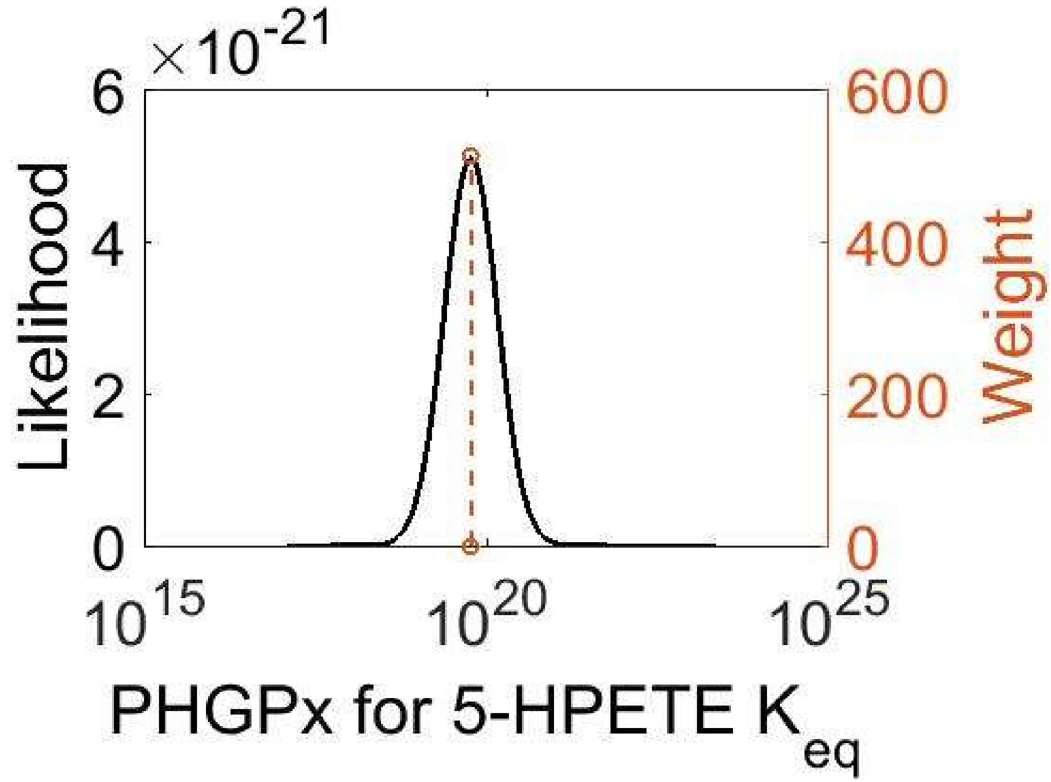


Figure SF.7.7.1.4.1. The estimated probability distribution for PHGPx K_{eq}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.7.1.5. Parameter: PHGPx concentration

Parameter values for the PHGPx concentration of Reaction 12 were obtained from the literature and summarised in Table ST.7.7.1.5.1. The log-normal distribution properties for the PHGPx concentration of Reaction 12 are shown in Table ST.7.7.1.5.2 and plotted in Figure SF.7.7.1.5.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.7.7.1.5.1. Literature information used to design the PHGPx concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
2.04 x10^{2}	NaN	Human	Gut	PHGPx	7.5	37		**1024**	0	(Kim et al., 2014)
2.82 x10^{2}	NaN	Human	Oesophagus	PHGPx	7.5	37		**1024**	0	(Wilhelm et al., 2014)
3.07 x10^{2}	NaN	Human	Lung	PHGPx	7.5	37		**1024**	0	(Wilhelm et al., 2014)
4.59 x10^{2}	NaN	Human	Skin	PHGPx	7.5	37		**2048**	0	(Wilhelm et al., 2014)

Table ST.7.7.1.5.2. The log-normal distribution properties of the PHGPx concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
3.14 x10^{2}	1.74x10^{-3}	1.38	5.85	3.09 x10^{-1}

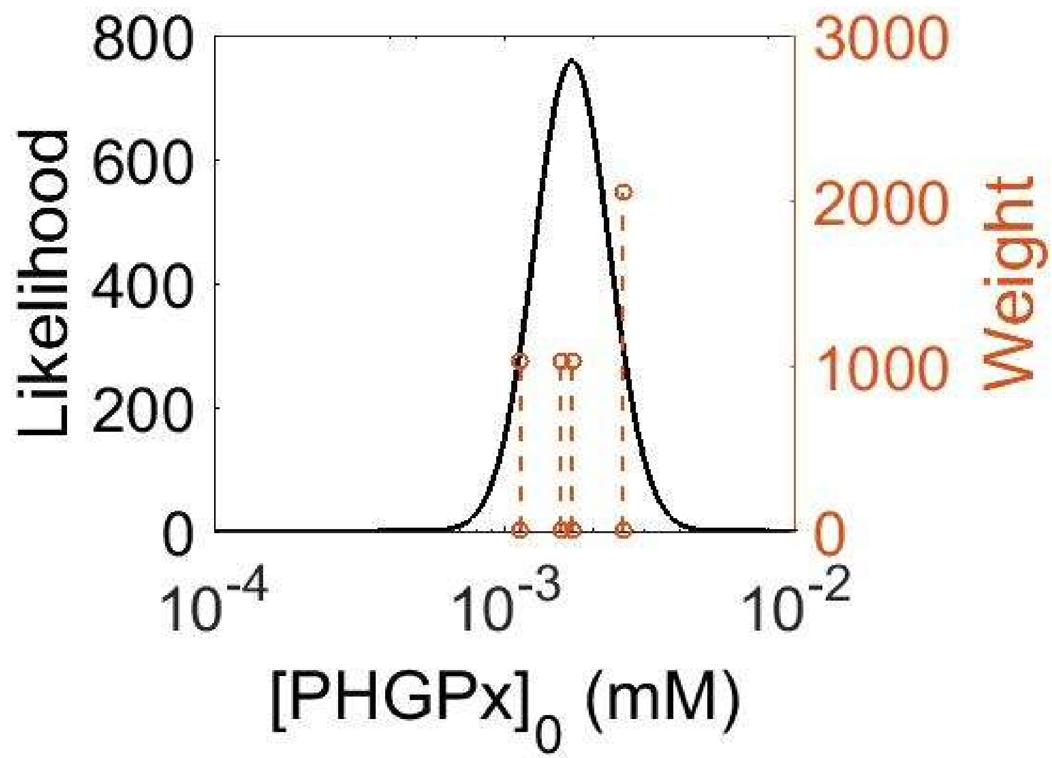


Figure SF.7.7.1.5.1. The estimated probability distribution for the PHGPx concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.8 Reaction 13: 5-HPETE ⇌ LTA_4

5-HPETE is further metabolised by 5-LOX. This dehydration reaction converts the peroxide functional group of 5(S)-HPETE to an epoxide functional group, generating LTA_4 (Shimizu et al., 1984). 5-LOX performs this reaction by abstracting the pro-R hydrogen at C10 and rearranging the structure so that the radical relocates to C6. The double bonds within the structure then rearrange to form a conjugated triene system and an epoxide. This reaction is promoted when 5-LOX colocalises with 5-lipoxygenase-activating protein (FLAP) on the nuclear membrane or the ER (Abramovitz et al., 1993; Brock et al., 1994).

Figure SF.7.8. The metabolism of 5-hydroperoxyeicosatetraenoic acid (5-HPETE) into leukotriene A_4 (LTA_4) by 5-lipoxygenase/5-lipoxygenase-activating protein (5-LOX/FLAP) (Reaction 13).

SEq.7.8. Reaction rate law for Reaction 13.

$$v_{13} = \frac{K_{cat} \cdot [5-LOX]\left([5-HPETE] - {[LTA_4]}/{K_{eq}}\right)}{K_{m_s}\left(1+\frac{[LTA_4]}{K_{m_p}}\right)+[5-HPETE]}$$

S.7.8.1. Reaction parameters

S.7.8.1.1. Parameter: 5-LOX/FLAP K_{ms}

Parameter values for the K_{ms} of Reaction 13 were obtained from the literature and summarised in Table ST.7.8.1.1.1. The log-normal distribution properties for the K_{ms} of Reaction 13 are shown in Table ST.7.8.1.1.2 and plotted in Figure SF.7.8.1.1.1.

Table ST.7.8.1.1.1. Literature information used to design the 5-LOX/FLAP K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
5.10 $x10^{-3}$	NaN	Human	Baculovirus	5-LOX	5.6	37		256	0	(Shirumalla et al., 2006)
1.20 $x10^{-2}$	NaN	Human	Polymorphonuclear Leukocytes	5-LOX	7.5	22		512	0	(Soberman, 1988)
6.31 $x10^{-2}$	NaN	Human	Polymorphonuclear Leukocytes	5-LOX	7.5	22		512	0	(Soberman et al., 1985)

Table ST.7.8.1.1.2. The log-normal distribution properties of the 5-LOX/FLAP K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.28 $x10^{-2}$	8.70	-3.64	8.50 $x10^{-1}$

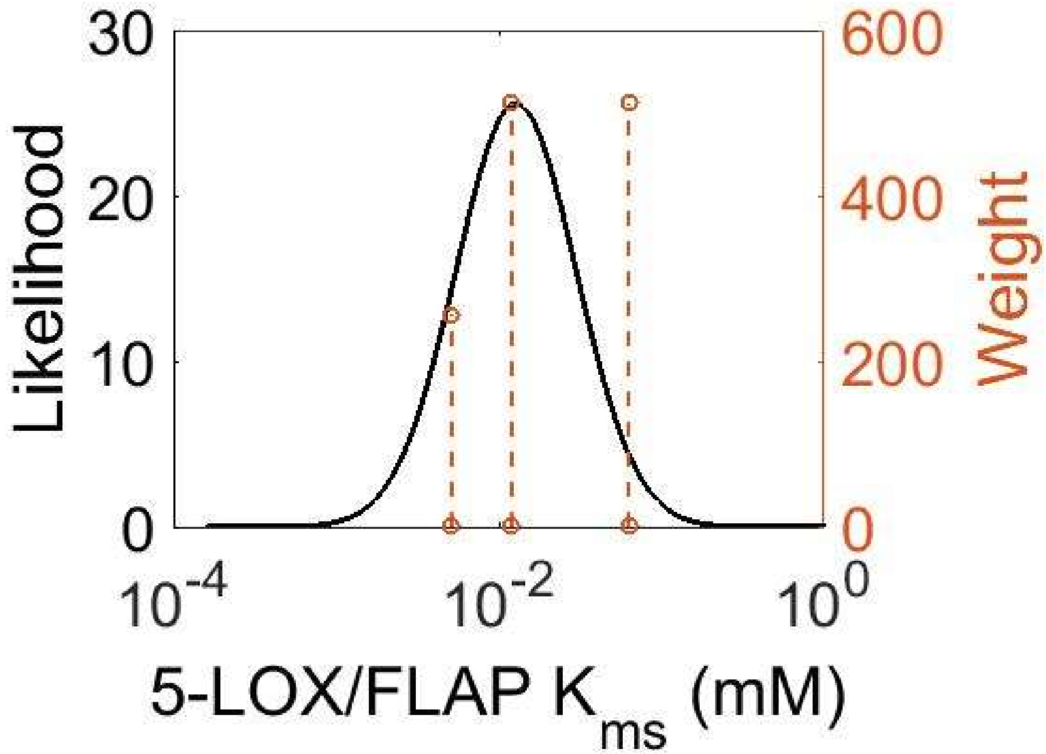


Figure SF.7.8.1.1.1. The estimated probability distribution for 5-LOX/FLAP K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.8.1.2. Parameter: 5-LOX/FLAP K_{mp} (Dependent parameter)

The log-normal distribution for the parameter for the K_{mp} of Reaction 13 was calculated using multivariate distributions. The log-normal distribution properties for the K_{mp} of Reaction 13 are shown in Table ST.7.8.1.2.1 and plotted in Figure SF.7.8.1.2.1.

Table ST.7.8.1.2.1. The log-normal distribution properties of the 5-LOX/FLAP K_{mp} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	**Location parameter (μ)**	**Scale parameter (σ)**
1.30×10^{-2}	-3.65	8.31×10^{-1}

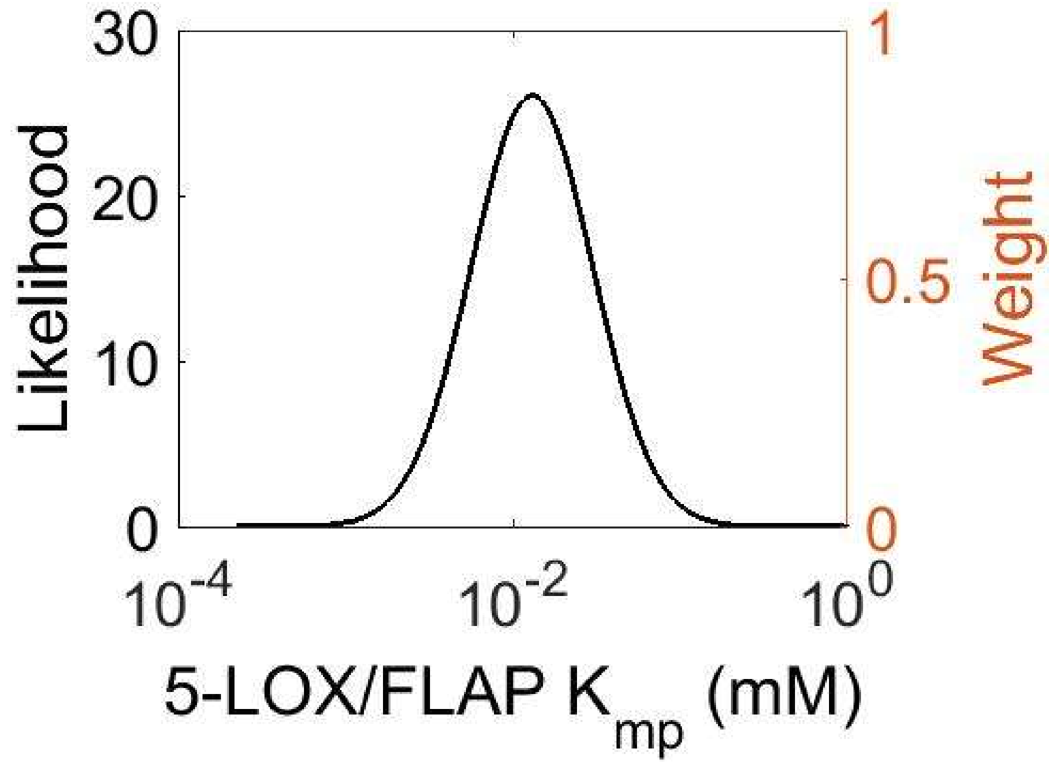


Figure SF.7.8.1.2.1. The estimated probability distribution for 5-LOX/FLAP K_{mp}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.8.1.3. Parameter: 5-LOX/FLAP k_{cat}

Parameter values for the k_{cat} of Reaction 13 were obtained from the literature and summarised in Table ST.7.8.1.3.1. The log-normal distribution properties for the k_{cat} of Reaction 13 are shown in Table ST.7.8.1.3.2 and plotted in Figure SF.7.8.1.3.1.

Table ST.7.8.1.3.1. Literature information used to design the 5-LOX/FLAP k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.50 x10^3	7.50 x10^1	Potato	Potato	5-LOX	5.5	23		16	0	(Mulliez et al., 1987)

Table ST.7.8.1.3.2. The log-normal distribution properties of the 5-LOX/FLAP k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.49 x10^3	6.66	7.90	7.69 x10^{-1}

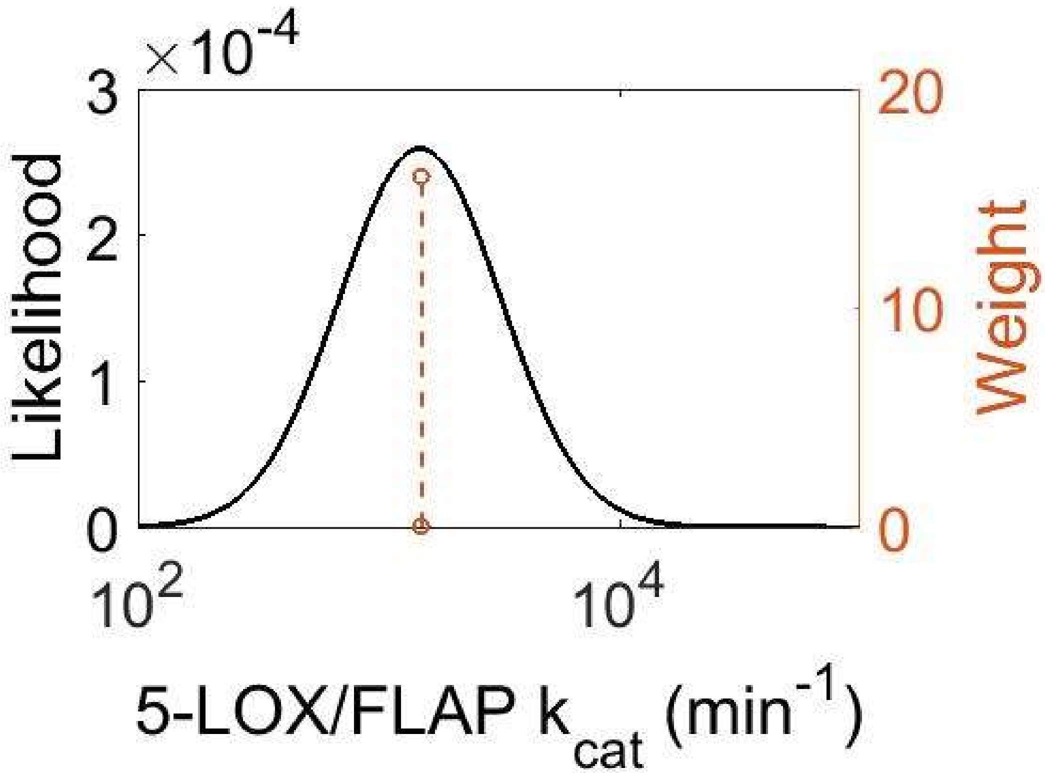


Figure SF.7.8.1.3.1. The estimated probability distribution for 5-LOX/FLAP k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.8.1.4. Parameter: 5-LOX/FLAP K_{eq}

Parameter values for the K_{eq} of Reaction 13 were obtained from the literature and summarised in Table ST.7.8.1.4.1. The log-normal distribution properties for the K_{eq} of Reaction 13 are shown in Table ST.7.8.1.4.2 and plotted in Figure SF.7.8.1.4.1.

Table ST.7.8.1.4.1. Literature information used to design the 5-LOX/FLAP K_{eq} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

ΔG (kcal/mol)	K_{eq}	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
-8.60×10^{1}	1.31×10^{63}	Human	Unknown	5-LOX/FLAP	7	Unknown		64	0	(Caspi et al., 2018)

Table ST.7.8.1.4.2. The log-normal distribution properties of the 5-LOX/FLAP K_{eq} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.31×10^{63}	1.00×10^{1}	1.46×10^{2}	8.90×10^{-1}

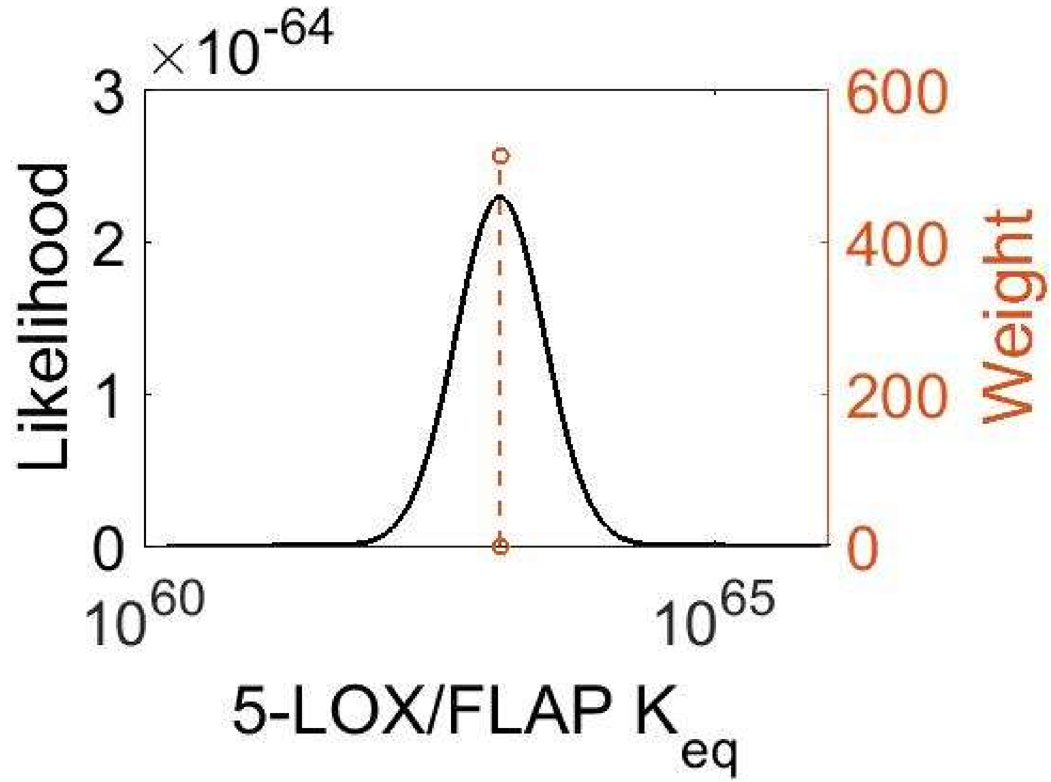


Figure SF.7.8.1.4.1. The estimated probability distribution for 5-LOX/FLAP K_{eq}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.8.1.5. Parameter: 5-LOX/FLAP concentration

Parameter values for the 5-LOX/FLAP concentration of Reaction 13 were obtained from the literature and summarised in Table ST.7.8.1.5.1. The log-normal distribution properties for the 5-LOX/FLAP concentration of Reaction 13 are shown in Table ST.7.8.1.5.2 and plotted in Figure SF.7.8.1.5.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.7.8.1.5.1. Literature information used to design the 5-LOX/FLAP concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
3.19×10^{1}	NaN	Human	Oral cavity	5-LOX	7.5	37		**1024**	0	(Wilhelm et al., 2014)
4.98×10^{1}	NaN	Human	Oesophagus	5-LOX	7.5	37		**1024**	0	(Wilhelm et al., 2014)
9.73×10^{1}	NaN	Human	Lung	5-LOX	7.5	37		**1024**	0	(Kim et al., 2014)

Table ST.7.8.1.5.2. The log-normal distribution properties of the 5-LOX/FLAP concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
4.96×10^{1}	2.74×10^{-4}	1.60	4.09	4.28×10^{-1}

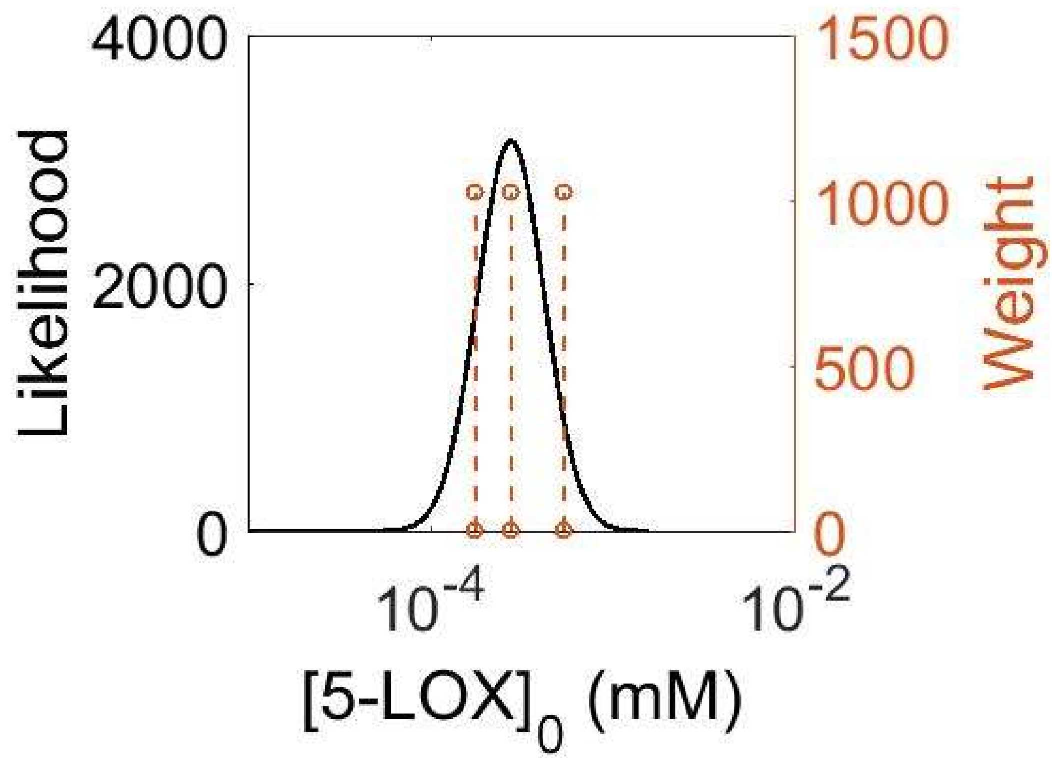
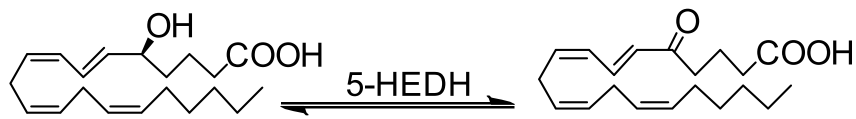


Figure SF.7.8.1.5.1. The estimated probability distribution for the 5-LOX concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.9 Reaction 14: 5-HETE ⇌ 5-oxo-ETE

5-HETE is then oxidised by 5-hydroxyeicosanoid dehydrogenase (5-HEDH) to 5-oxo-ETE (Powell et al., 1992). This reaction is selective for 5(S)-HETE and the cofactor is $NADP^+$ (Powell et al., 1992). 5-HEDH is a microsomal enzyme which catalyses the conversion of the C5 alcohol to a ketone by transferring the hydrogen cation to $NADP^+$ via a ping-pong mechanism (K.-R. Erlemann et al., 2007; Powell et al., 1992).



5-HETE 5-oxo-ETE

Figure SF.7.9. The metabolism of 5-hydroxyeicosatetraenoic acid (5-HETE) into 5-oxo-eicosatetraenoic acid (5-oxo-ETE) by 5-hydroxyeicosanoid dehydrogenase (5-HEDH) (Reaction 14).

SEq.7.9. Reaction rate law for Reaction 14.

$$\boldsymbol{v_{14}} = \frac{K_{cat} \cdot [5-HEDH]\left([5-HETE] - {[5-oxo-ETE]}/{K_{eq}}\right)}{K_{m_s}\left(1 + \frac{[5-oxo-ETE]}{K_{m_p}}\right) + [5-HETE]}$$

S.7.9.1. Reaction parameters

S.7.9.1.1. Parameter: 5-HEDH K_{ms}

Parameter values for the K_{ms} of Reaction 14 were obtained from the literature and summarised in Table ST.7.9.1.1.1. The log-normal distribution properties for the K_{ms} of Reaction 14 are shown in Table ST.7.9.1.1.2 and plotted in Figure SF.7.9.1.1.1.

Table ST.7.9.1.1.1. Literature information used to design the 5-HEDH K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
6.00 $x10^{-4}$		Human	Unknown	5-HEDH	Unknown	Unknown		64		(Steinhilber, 2016)
6.70 $x10^{-4}$		Human	Cell line	5-HEDH	7.4	37		2048		(K. R. Erlemann et al., 2007)
5.16 $x10^{-4}$	1.90 $x10^{-4}$	Human	Cell line	5-HEDH	7.4	37		2048		(Patel P., 2009)

Table ST.7.9.1.1.2. The log-normal distribution properties of the 5-HEDH K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
6.34 $x10^{-4}$	1.63 $x10^{1}$	-6.31	1.03

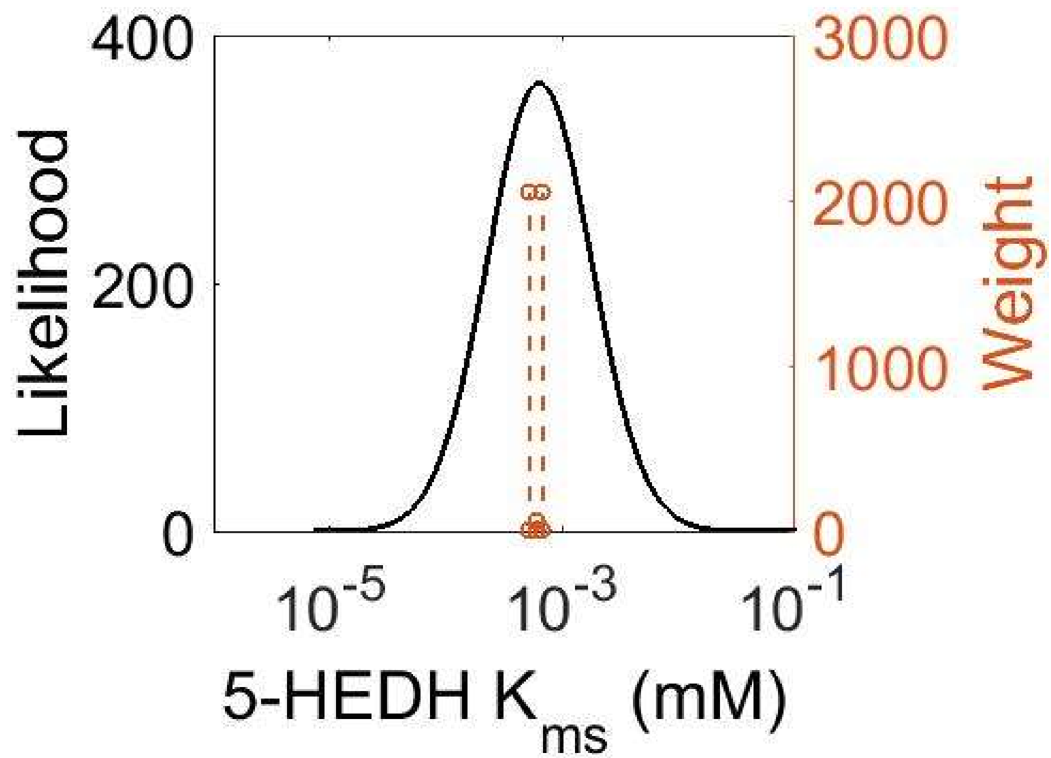


Figure SF.7.9.1.1.1. The estimated probability distribution for 5-HEDH K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.9.1.2. Parameter: 5-HEDH K_{mp} (Dependent parameter)

The log-normal distribution for the parameter for the K_{mp} of Reaction 14 was calculated using multivariate distributions. The log-normal distribution properties for the K_{mp} of Reaction 14 are shown in Table ST.7.9.1.2.1 and plotted in Figure SF.7.9.1.2.1.

Table ST.7.9.1.2.1. The log-normal distribution properties of the 5-HEDH K_{mp} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	**Location parameter (μ)**	**Scale parameter (σ)**
1.14×10^{4}	1.09×10^{1}	1.25

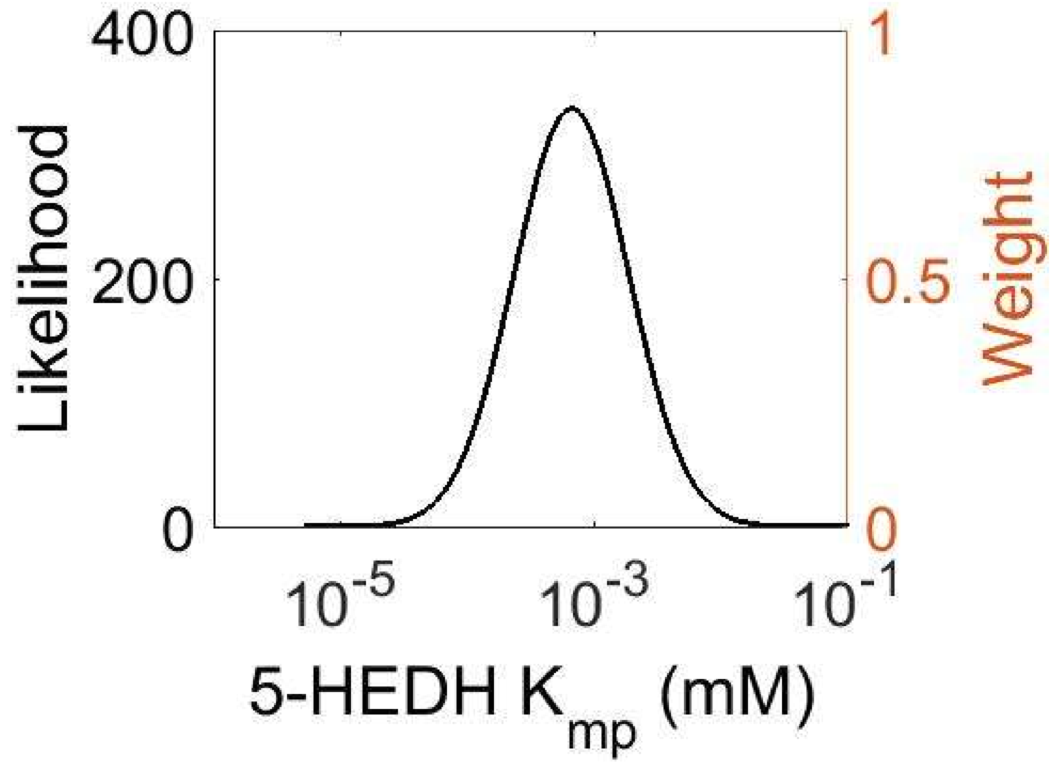


Figure SF.7.9.1.2.1. The estimated probability distribution for 5-HEDH K_{mp}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.9.1.3. Parameter: 5-HEDH k_{cat}

Parameter values for the k_{cat} of Reaction 14 were obtained from the literature and summarised in Table ST.7.9.1.3.1. The log-normal distribution properties for the k_{cat} of Reaction 14 are shown in Table ST.7.9.1.3.2 and plotted in Figure SF.7.9.1.3.1.

Table ST.7.9.1.3.1. Literature information used to design the 5-HEDH k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.16×10^4	8.40×10^2	Yokenella	E. coli.	5-HEDH	6.5	65		128		(Wei, 2012)

Table ST.7.9.1.3.2. The log-normal distribution properties of the 5-HEDH k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.15×10^4	4.02×10^1	1.09×10^1	1.25

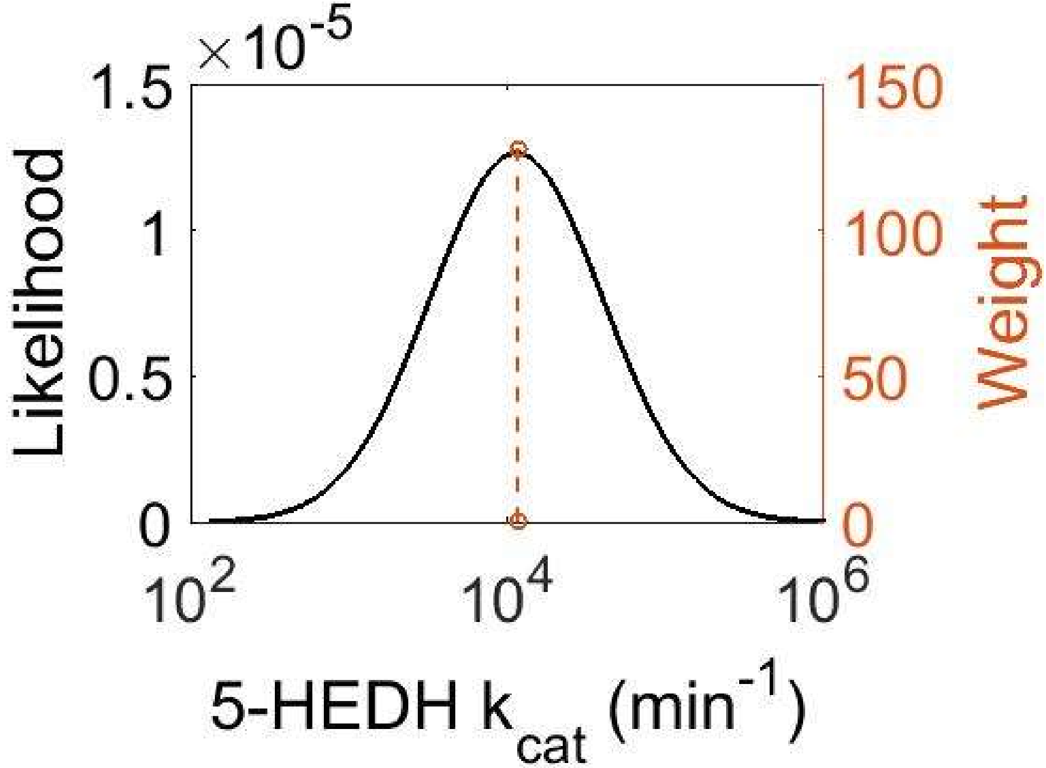


Figure SF.7.9.1.3.1. The estimated probability distribution for 5-HEDH k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.9.1.4. Parameter: 5-HEDH K_{eq}

Parameter values for the K_{eq} of Reaction 14 were obtained from the literature and summarised in Table ST.7.9.1.4.1. The log-normal distribution properties for the K_{eq} of Reaction 14 are shown in Table ST.7.9.1.4.2 and plotted in Figure SF.7.9.1.4.1.

Table ST.7.9.1.4.1. Literature information used to design the 5-HEDH K_{eq} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

ΔG (kcal/mol)	K_{eq}	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.29	1.12 x10^{-1}	Human	Unknown	5-HEDH	7	Unknown		64	0	(Caspi et al., 2018)

Table ST.7.9.1.4.2. The log-normal distribution properties of the 5-HEDH K_{eq} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.12 x10^{-1}	1.00 x10^{1}	-1.39	8.91 x10^{-1}

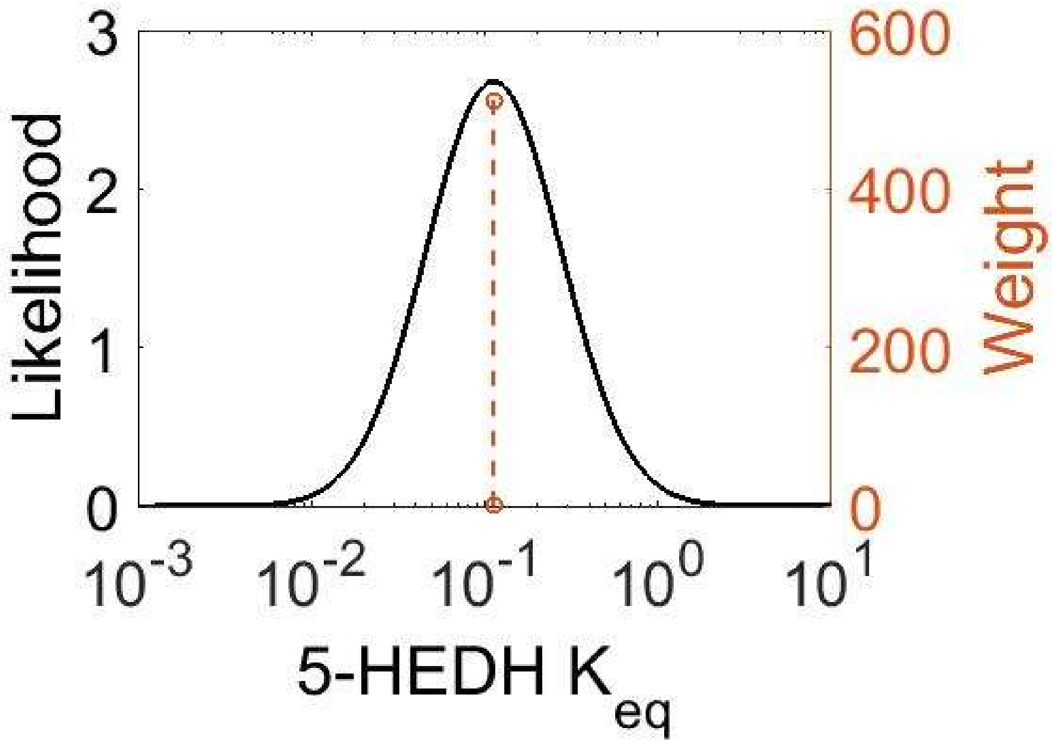


Figure SF.7.9.1.4.1. The estimated probability distribution for 5-HEDH K_{eq}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.9.1.5. Parameter: 5-HEDH concentration

Parameter values for the 5-HEDH concentration of Reaction 14 were obtained from the literature and summarised in Table ST.7.9.1.5.1. The log-normal distribution properties for the 5-HEDH concentration of Reaction 14 are shown in Table ST.7.9.1.5.2 and plotted in Figure SF.7.9.1.5.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.7.9.1.5.1. Literature information used to design the 5-HEDH concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
4.90 $x10^2$		Human	Skin	5-HEDH	7.5	37		**2048**		(Wilhelm et al., 2014)
6.25 $x10^2$		Human	Oral cavity	5-HEDH	7.5	37		1024		(Wilhelm et al., 2014)
7.28 $x10^2$		Human	Oesophagus	5-HEDH	7.5	37		1024		(Kim et al., 2014)
1.15 $x10^1$		Human	Skin	5-HEDH	7.5	37		**2048**		(Kim et al., 2014)

Table ST.7.9.1.5.2. The log-normal distribution properties of the 5-HEDH concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
4.88 $x10^2$	2.70 $x10^{-3}$	6.37	7.49	1.14

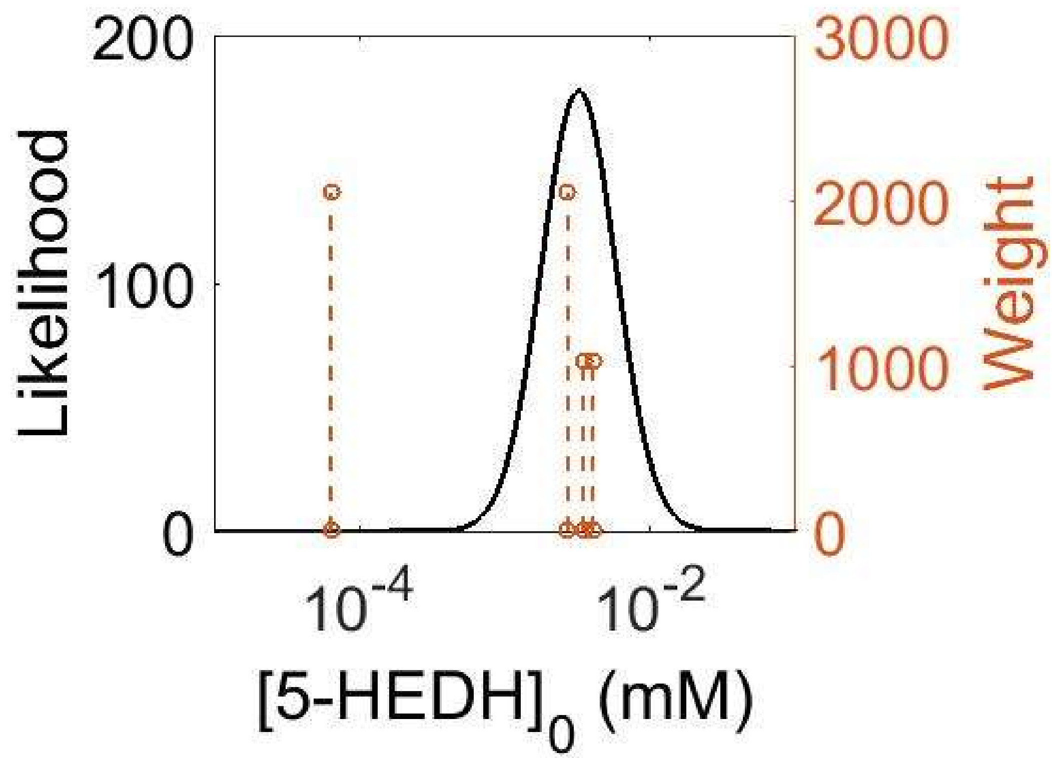


Figure SF.7.9.1.5.1. The estimated probability distribution for the 5-HEDH concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.10 Reaction 15: $LTA_4 \rightleftharpoons LTB_4$

LTA_4 is subsequently enzymatically hydrolysed to LTB_4 by LTA_4 hydrolase (LTA_4H). This reaction is stereospecific (Haeggstrom et al., 2007) and relies on the Zn^{2+} at the active site of LTA_4H. . The enzyme performs this reaction by opening the epoxide and creating a carbocation intermediate. The charge of the carbocation delocalises over the triene system and is subsequently subject to nucleophilic attack by water at C12, resulting in the stereospecific addition of a hydroxyl group and the generation of LTB_4.

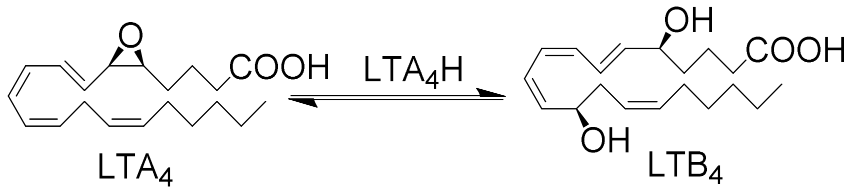


Figure SF.7.10. The metabolism of leukotriene A_4 (LTA_4) into leukotriene B_4 (LTB_4) by LTA_4 hydrolase (LTA_4H) (Reaction 15).

SEq.7.10. Reaction rate law for Reaction 15.

$$\boldsymbol{v_{15}} = \frac{K_{cat} \cdot [LTA_4H]\left([LTA_4] - {[LTB_4]}/{K_{eq}}\right)}{K_{m_s}\left(1 + \frac{[LTB_4]}{K_{mp}}\right) + [LTA_4]}$$

S.7.10.1. Reaction parameters

S.7.10.1.1. Parameter: LTA_4H K_{ms}

Parameter values for the K_{ms} of Reaction 15 were obtained from the literature and summarised in Table ST.7.10.1.1.1. The log-normal distribution properties for the K_{ms} of Reaction 15 are shown in Table ST.7.10.1.1.2 and plotted in Figure SF.7.10.1.1.1.

Table ST.7.10.1.1.1. Literature information used to design the LTA_4H K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
2.30×10^{-3}	NaN	Human	Leukocytes	LTA_4H	8	37		1024	0	(Radmark et al., 1984)
2.70×10^{-3}	NaN	Frog	Oocytes	LTA_4H	8	20		16	0	(Stromberg-Kull and Haeggstrom, 1998)
5.80×10^{-3}	NaN	Human	E. coli.	LTA_4H	8	20		128	0	(Mueller et al., 1996)
2.20×10^{-2}	NaN	Human	Leukocytes	LTA_4H	8	2		256	0	(Radmark et al., 1984)

Table ST.7.10.1.1.2. The log-normal distribution properties of the LTA_4H K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
2.40 x10^{-3}	5.77	-5.51	7.20 x10^{-1}

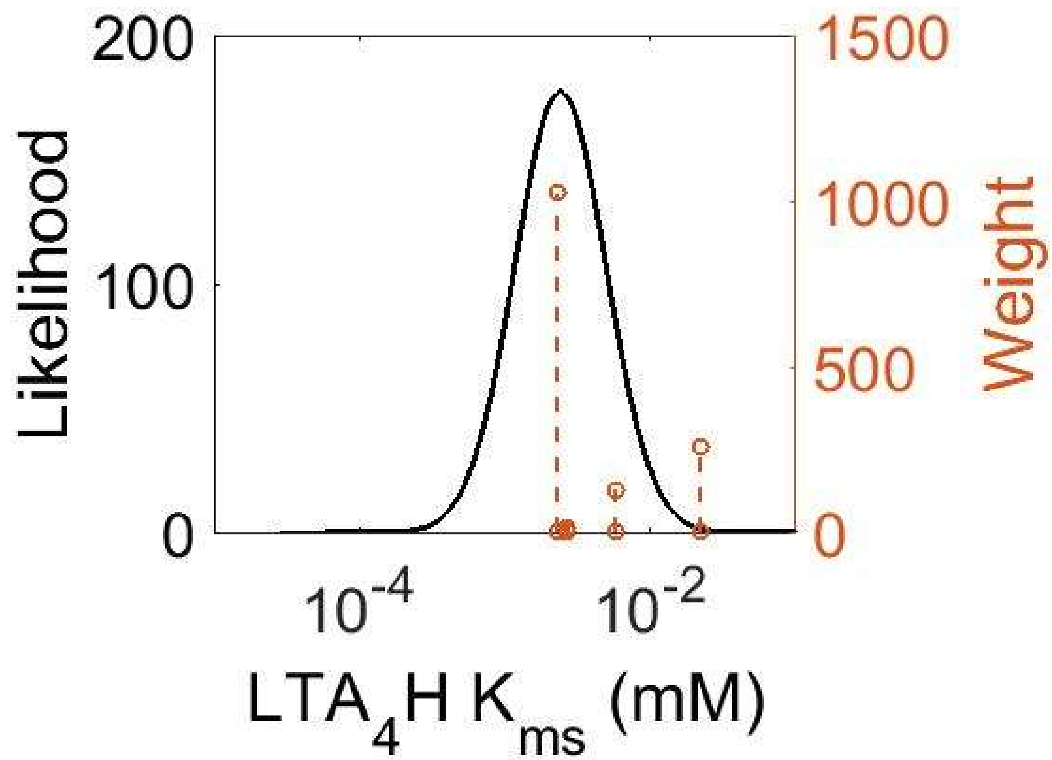


Figure SF.7.10.1.1.1. The estimated probability distribution for LTA_4H K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.10.1.2. Parameter: LTA_4H K_{mp} (Dependent parameters)

The log-normal distribution for the parameter for the K_{mp} of Reaction 15 was calculated using multivariate distributions. The log-normal distribution properties for the K_{mp} of Reaction 15 are shown in Table ST.7.10.1.2.1 and plotted in Figure SF.7.10.1.2.1.

Table ST.7.10.1.2.1. The log-normal distribution properties of the LTA_4H K_{mp} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Location parameter (μ)	Scale parameter (σ)
2.40 $x10^{-3}$	-5.51	7.17 $x10^{-1}$

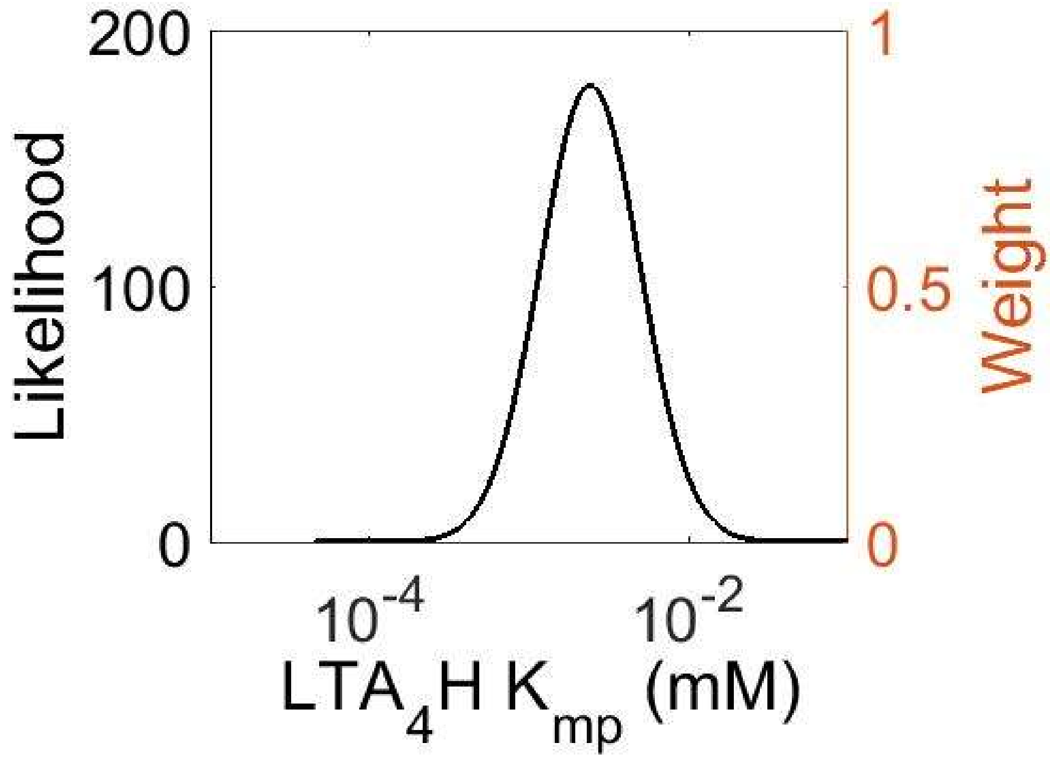


Figure SF.7.10.1.2.1. The estimated probability distribution for LTA_4H K_{mp}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.10.1.3. Parameter: LTA_4H k_{cat}

Parameter values for the k_{cat} of Reaction 15 were obtained from the literature and summarised in Table ST.7.10.1.3.1. The log-normal distribution properties for the k_{cat} of Reaction 15 are shown in Table ST.7.10.1.3.2 and plotted in Figure SF.7.10.1.3.1.

Table ST.7.10.1.3.1. Literature information used to design the LTA_4H k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.26×10^1	NaN	Human	E. coli.	LTA4H	7.4	37		1024	0	(Rudberg et al., 2002)
2.82×10^1	NaN	Human	E. coli.	LTA4H	7.4	37		1024	0	(Rudberg et al., 2002)
5.10×10^1	NaN	Human	E. coli.	LTA4H	8	20		128	0	(Mueller et al., 1996)
9.00×10^1	NaN	Frog	Oocytes	LTA4H	8	20		16	0	(Stromberg-Kull and Haeggstrom, 1998)
1.25×10^2	NaN	Human	Leukocytes	LTA4H	8	37		1024	0	(Radmark et al., 1984)

Table ST.7.10.1.3.2. The log-normal distribution properties of the LTA_4H k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
2.85×10^{1}	6.56	3.94	7.60×10^{-1}

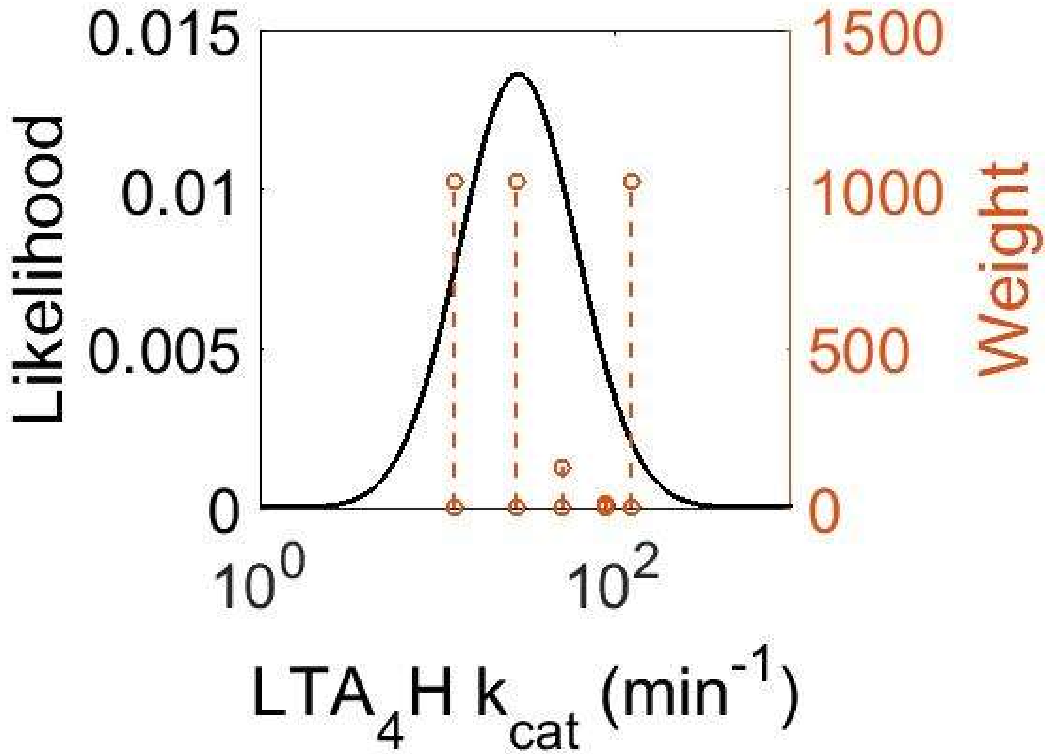


Figure SF.7.10.1.3.1. The estimated probability distribution for LTA_4H k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.10.1.4. Parameter: LTA_4H K_{eq}

Parameter values for the K_{eq} of Reaction 15 were obtained from the literature and summarised in Table ST.7.10.1.4.1. The log-normal distribution properties for the K_{eq} of Reaction 15 are shown in Table ST.7.10.1.4.2 and plotted in Figure SF.7.10.1.4.1.

Table ST.7.10.1.4.1. Literature information used to design the LTA_4H K_{eq} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

ΔG (kcal/mol)	K_{eq}	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
-3.63	4.64 x10^{2}	Human	Unknown	LTA4H	7	Unknown		64	0	(Caspi et al., 2018)

Table ST.7.10.1.4.2. The log-normal distribution properties of the LTA_4H K_{eq} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
4.64 x10^{2}	1.00 x10^{1}	6.93	8.90 x10^{-1}

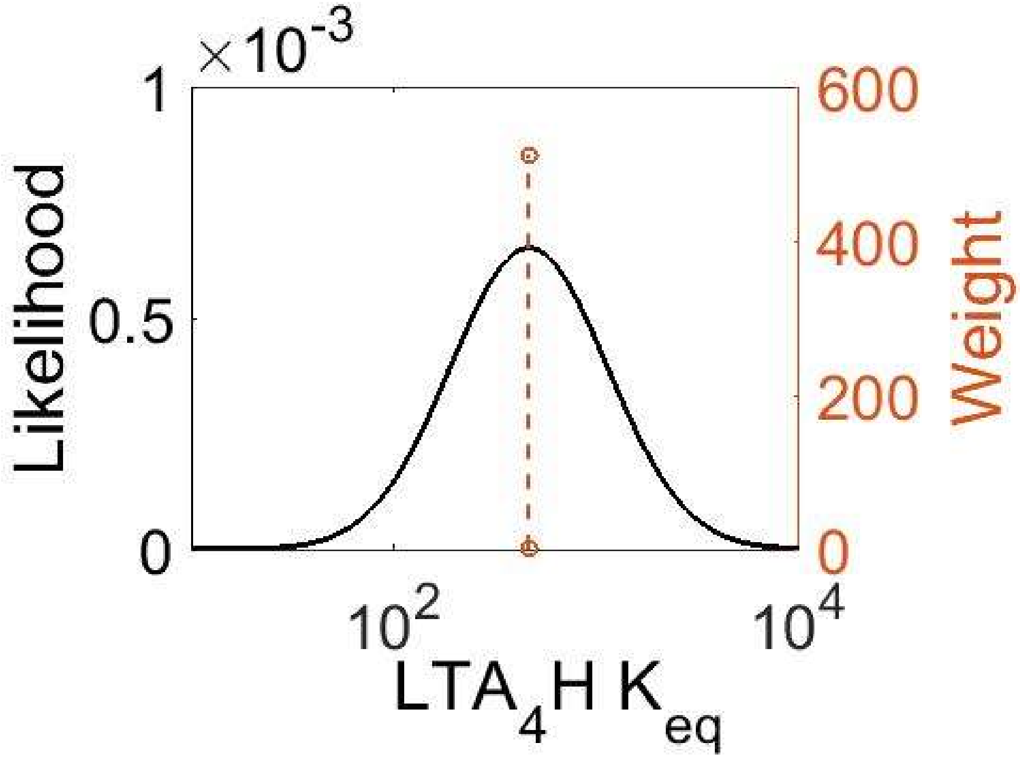


Figure SF.7.10.1.4.1. The estimated probability distribution for LTA_4H K_{eq}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.10.1.5. Parameter: LTA_4H concentration

Parameter values for the LTA_4H concentration of Reaction 15 were obtained from the literature and summarised in Table ST.7.10.1.5.1. The log-normal distribution properties for the LTA_4H concentration of Reaction 15 are shown in Table ST.7.10.1.5.2 and plotted in Figure SF.7.10.1.5.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.7.10.1.5.1. Literature information used to design the LTA_4H concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
4.10×10^{2}	NaN	Human	Oral cavity	LTA4H	7.5	37		**1024**	0	(Wilhelm et al., 2014)
4.89×10^{2}	NaN	Human	Skin	LTA4H	7.5	37		**2048**	0	(Wilhelm et al., 2014)
7.14×10^{2}	NaN	Human	Lung	LTA4H	7.5	37		**1024**	0	(Kim et al., 2014)

Table ST.7.10.1.5.2. The log-normal distribution properties of the LTA_4H concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
4.88×10^{2}	2.70×10^{-3}	1.25	6.24	2.19×10^{-1}

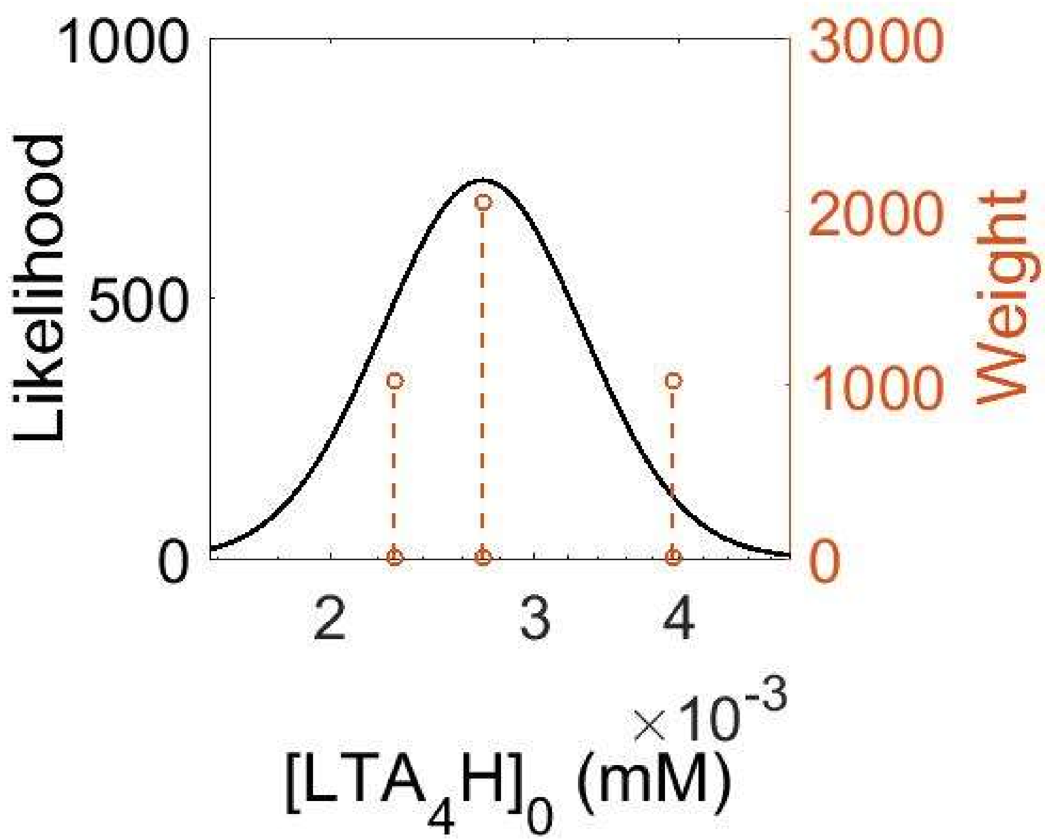


Figure SF.7.10.1.5.1. The estimated probability distribution for the LTA_4H concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.11 Reaction 16: $LTA_4 \rightleftharpoons LTC_4$

LTA_4 can be metabolised by leukotriene C_4 synthase (LTC_4S), into LTC_4. This reaction involves the conjugation of the LTA_4 epoxide and glutathione.

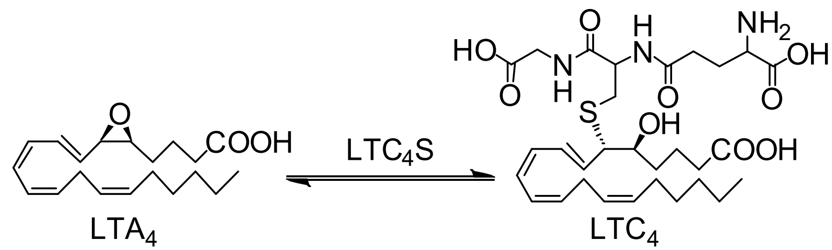


Figure SF.7.11. The metabolism of leukotriene A_4 (LTA_4) into leukotriene C_4 (LTC_4) by leukotriene C_4 synthase (LTC_4S) (Reaction 16).

SEq.7.11. Reaction rate law for Reaction 16.

$$\boldsymbol{v_{16}} = \frac{K_{cat}\cdot[LTC_4S]\left([LTA_4]-{[LTC_4]}/{K_{eq}}\right)}{K_{m_s}\left(1+\frac{[LTC_4]}{K_{m_p}}\right)+[LTA_4]}$$

S.7.11.1. Reaction parameters

S.7.11.1.1. Parameter: LTC_4S K_{ms}

Parameter values for the K_{ms} of Reaction 16 were obtained from the literature and summarised in Table ST.7.11.1.1.1. The log-normal distribution properties for the K_{ms} of Reaction 16 are shown in Table ST.7.11.1.1.2 and plotted in Figure SF.7.11.1.1.1.

Table ST.7.11.1.1.1. Literature information used to design the LTC_4S K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
3.00×10^{-1}	6.00×10^{-2}	Human	E. coli.	hLTC4S	7.8	20		256	0	(Rinaldo-Matthis et al., 2010)
3.00×10^{-2}	1.00×10^{-2}	Human	E. coli.	LTC4S	7.8	37		1024	0	(Niegowski et al., 2013)

Table ST.7.11.1.1.2. The log-normal distribution properties of the LTC_4S K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
3.15×10^{-2}	7.18	-2.83	7.90×10^{-1}

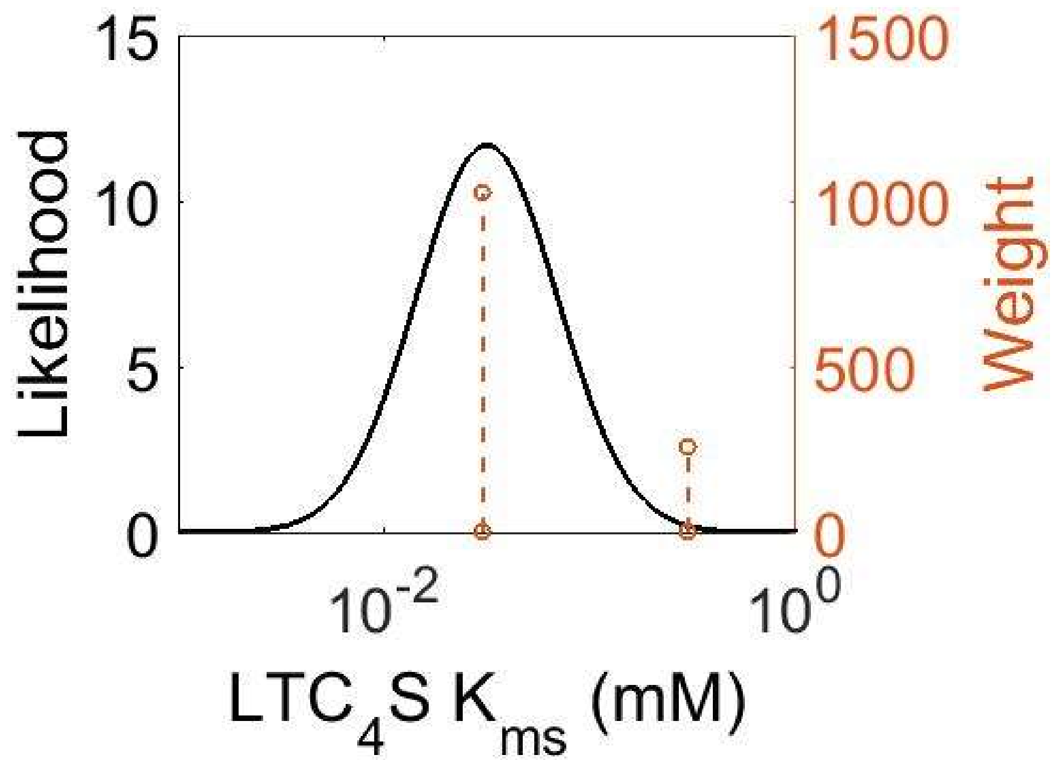


Figure SF.7.11.1.1.1. The estimated probability distribution for the LTC_4S K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.11.1.2. Parameter: LTC_4S K_{mp} (Dependent parameter)

The log-normal distribution for the parameter for the K_{mp} of Reaction 16 was calculated using multivariate distributions. The log-normal distribution properties for the K_{mp} of Reaction 16 are shown in Table ST.7.11.1.2.1 and plotted in Figure SF.7.11.1.2.1.

Table ST.7.11.1.2.1. The log-normal distribution properties of the LTC_4S K_{mp} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	**Location parameter (μ)**	**Scale parameter (σ)**
3.18×10^{-2}	-2.82	7.92×10^{-1}

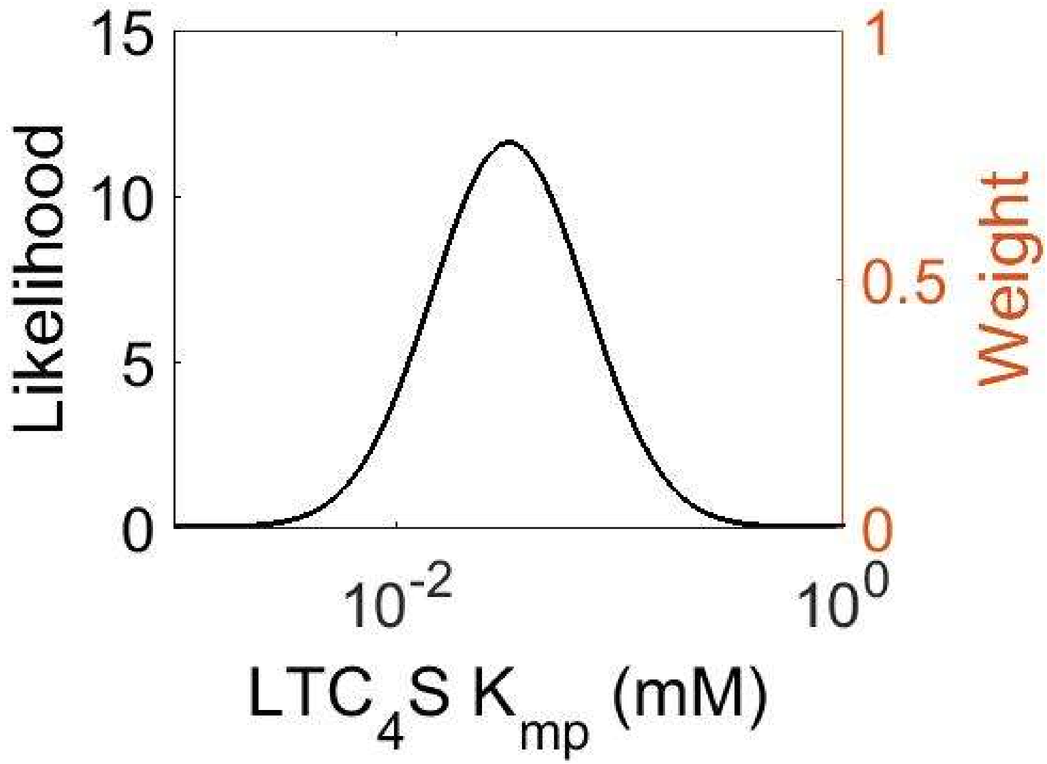


Figure SF.7.11.1.2.1. The estimated probability distribution for the LTC_4S K_{mp}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.11.1.3. Parameter: LTC_4S k_{cat}

Parameter values for the k_{cat} of Reaction 16 were obtained from the literature and summarised in Table ST.7.11.1.3.1. The log-normal distribution properties for the k_{cat} of Reaction 16 are shown in Table ST.7.11.1.3.2 and plotted in Figure SF.7.11.1.3.1.

Table ST.7.11.1.3.1. Literature information used to design the LTC_4S k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
7.02×10^{2}	NaN	Human	E. coli.	hLTC4S	7.8	20		256	0	(Rinaldo-Matthis et al., 2010)
1.56×10^{3}	2.40×10^{2}	Human	E. coli.	LTC4S	7.8	37		1024	0	(Niegowski et al., 2013)

Table ST.7.11.1.3.2. The log-normal distribution properties of the LTC_4S k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.47×10^{3}	1.42	7.40	3.29×10^{-1}

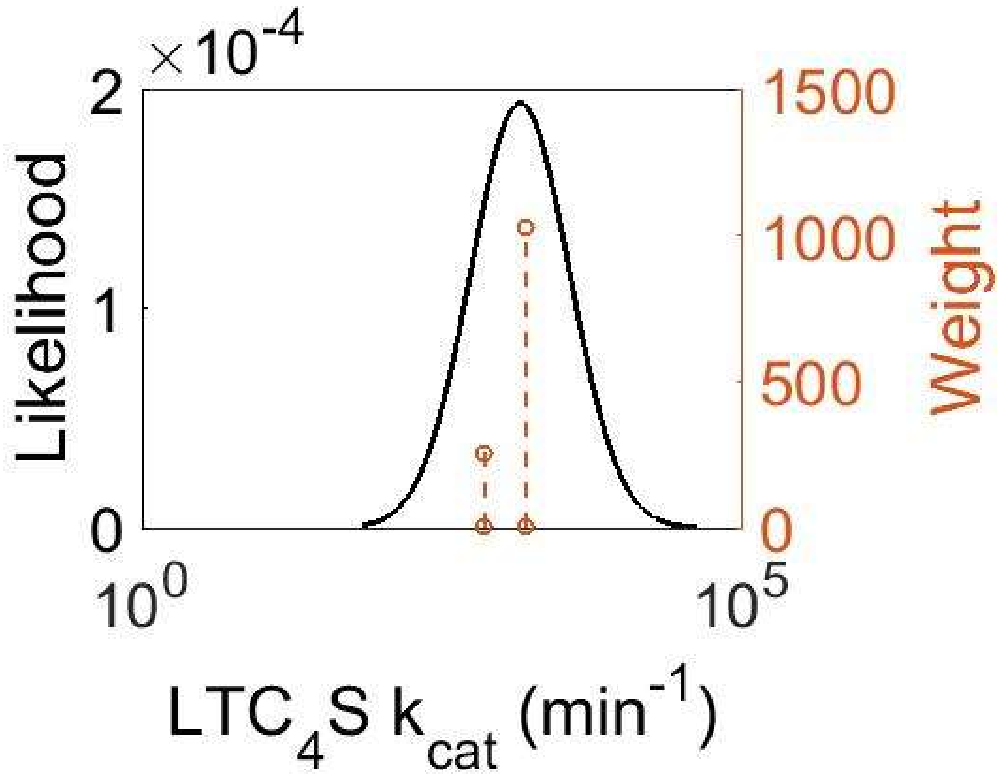


Figure SF.7.11.1.3.1. The estimated probability distribution for the LTC_4S k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.11.1.4. Parameter: LTC4S K_{eq}

Parameter values for the K_{eq} of Reaction 16 were obtained from the literature and summarised in Table ST.7.11.1.4.1. The log-normal distribution properties for the K_{eq} of Reaction 16 are shown in Table ST.7.11.1.4.2 and plotted in Figure SF.7.11.1.4.1.

Table ST.7.11.1.4.1. Literature information used to design the LTC4S K_{eq} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

ΔG (kcal/mol)	K_{eq}	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
9.93	5.13 x10^{-8}	Human	Unknown	LTC4S	7	Unknown		64	0	(Caspi et al., 2018)

Table ST.7.11.1.4.2. The log-normal distribution properties of the LTC4S K_{eq} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
5.13 x10^{-8}	1.00 x10^{1}	-1.60 x10^{1}	8.90 x10^{-1}

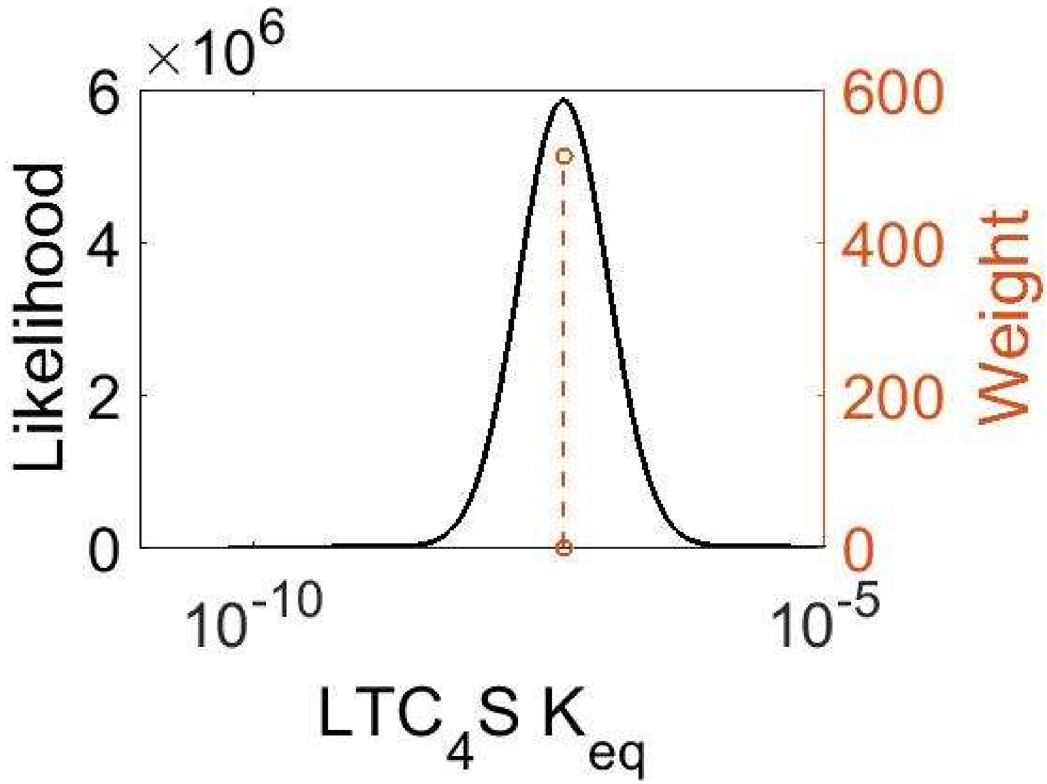


Figure SF.7.11.1.4.1. The estimated probability distribution for the LTC_4S K_{eq}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.11.1.5. Parameter: LTC_4S concentration

Parameter values for the LTC_4S concentration of Reaction 16 were obtained from the literature and summarised in Table ST.7.11.1.5.1. The log-normal distribution properties for the LTC_4S concentration of Reaction 16 are shown in Table ST.7.11.1.5.2 and plotted in Figure SF.7.11.1.5.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.7.11.1.5.1. Literature information used to design the LTC_4S concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.39×10^{1}	NaN	Human	Adrenal gland	LTC4S	7.5	37		**1024**	0	(Kim et al., 2014)
2.68×10^{1}	NaN	Human	Lung	LTC4S	7.5	37		**1024**	0	(Kim et al., 2014)
3.30×10^{1}	NaN	Human	Oesophagus	LTC4S	7.5	37		**2048**	0	(Kim et al., 2014)

Table ST.7.11.1.5.2. The log-normal distribution properties of the LTC_4S concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
2.90×10^{1}	1.60×10^{-4}	1.44	3.49	3.46×10^{-1}

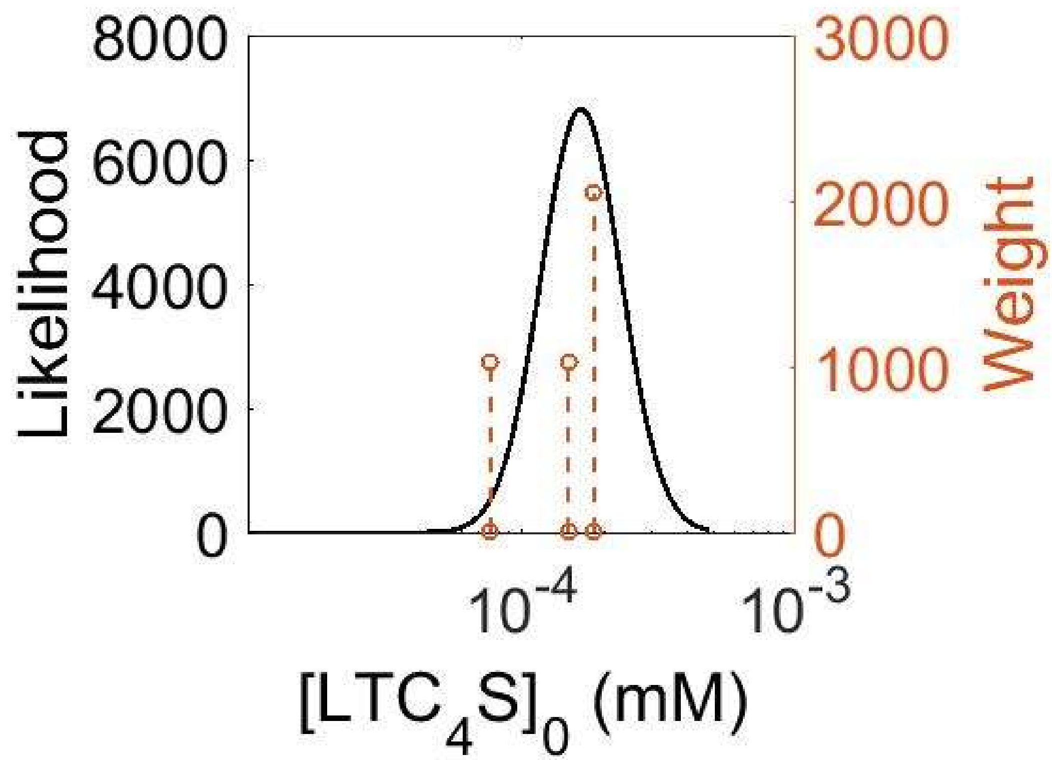


Figure SF.7.11.1.5.1. The estimated probability distribution for the LTC_4S concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.12 Reaction 17: AA ⇌ 15-HPETE

The gene ALOX15B encodes the formation of 15-LOX-2, which converts AA exclusively into 15(S)-HPETE. Whereas the gene ALOX15 encodes the 15-LOX-1 protein, which converts AA into both 12(S)-HPETE and 15(S)-HPETE in a ratio of 1 to 16 (Bryant, Bailey et al. 1982). The formation of the hydroperoxy fatty acids (HPETE) begins with the abstraction of a hydrogen radical at the allylic position between two double bonds. The structure undergoes a rearrangement reaction which results in the formation of a conjugated diene system. The insertion of molecular oxygen and a hydrogen leads to the formation of the final structure, a hydroperoxy fatty acid.

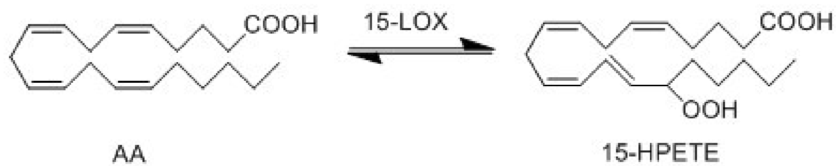


Figure SF.7.17. The metabolism of arachidonic acid (AA) into 15-hydroperoxyeicosatetraenoic acid (15-HPETE) by 15-lipoxygenase (15-LOX) (Reaction 17).

S.7.12.1. **Reaction rate law for Reaction 17.**

$$\boldsymbol{v_{17}} = \frac{K_{cat} \cdot [15-LOX] \left([AA] - {[15-HPETE]}/{K_{eq}} \right)}{K_{m_S}\left(1 + \frac{[15-HPETE]}{K_{m_P}}\right) + [AA]}$$

S.7.12.2. Reaction parameters

S.7.12.2.1. Parameter: 15-LOX K_{ms}

Parameter values for the K_{ms} of Reaction 17 were obtained from the literature and summarised in Table ST.7.12.1.1.1. The log-normal distribution properties for the K_{ms} of Reaction 17 are shown in Table ST.7.12.1.1.2 and plotted in Figure SF.7.12.1.1.1.

Table ST.7.12.1.1.1. Literature information used to design the 15-LOX K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.17×10^{-2}	9.00×10^{-4}	Human	Baculovirus	15-LOX	6.8	37		512	0	(Sloane et al., 1995)
3.70×10^{-3}	3.00×10^{-4}	Human	Epithelium	15-LOX	7.5	25		512	0	(C. Jacquot et al., 2008)
5.00×10^{-3}	NaN	Human	Reticulocyte	15-LOX	7.5	Unknown		512	0	(Cyril Jacquot et al., 2008)
1.06×10^{-2}	NaN	Human	Keratinocyte	15-LOX	6.7	37		2048	0	(Burrall et al., 1988)

Table ST.7.12.1.1.2. The log-normal distribution properties of the 15-LOX K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.02×10^{-2}	2.40	-4.42	4.10×10^{-1}

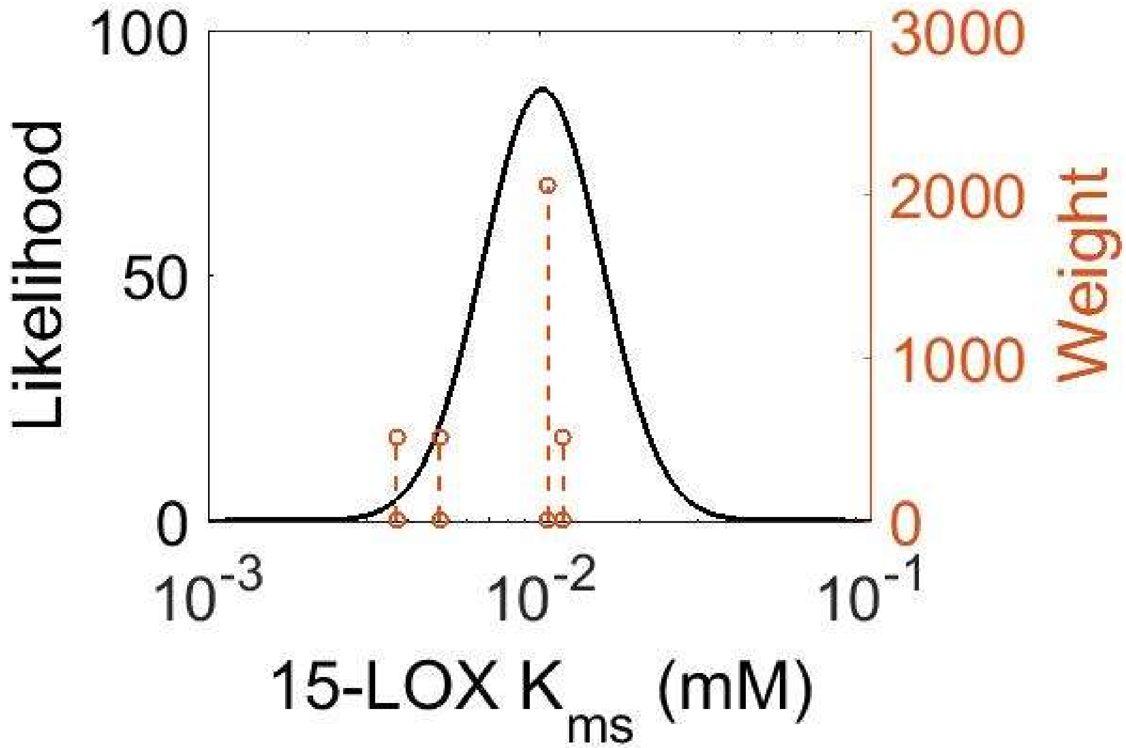


Figure SF.7.12.1.1.1. The estimated probability distribution for the 15-LOX K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.12.2.2. Parameter: 15-LOX K_{mp} (Dependent parameters)

The log-normal distribution for the parameter for the K_{mp} of Reaction 17 was calculated using multivariate distributions. The log-normal distribution properties for the K_{mp} of Reaction 17 are shown in Table ST.7.12.1.2.1 and plotted in Figure SF.7.12.1.2.1.

Table ST.7.12.1.2.1. The log-normal distribution properties of the 15-LOX K_{mp} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Location parameter (μ)	Scale parameter (σ)
1.02×10^{-2}	-4.42	4.11×10^{-1}

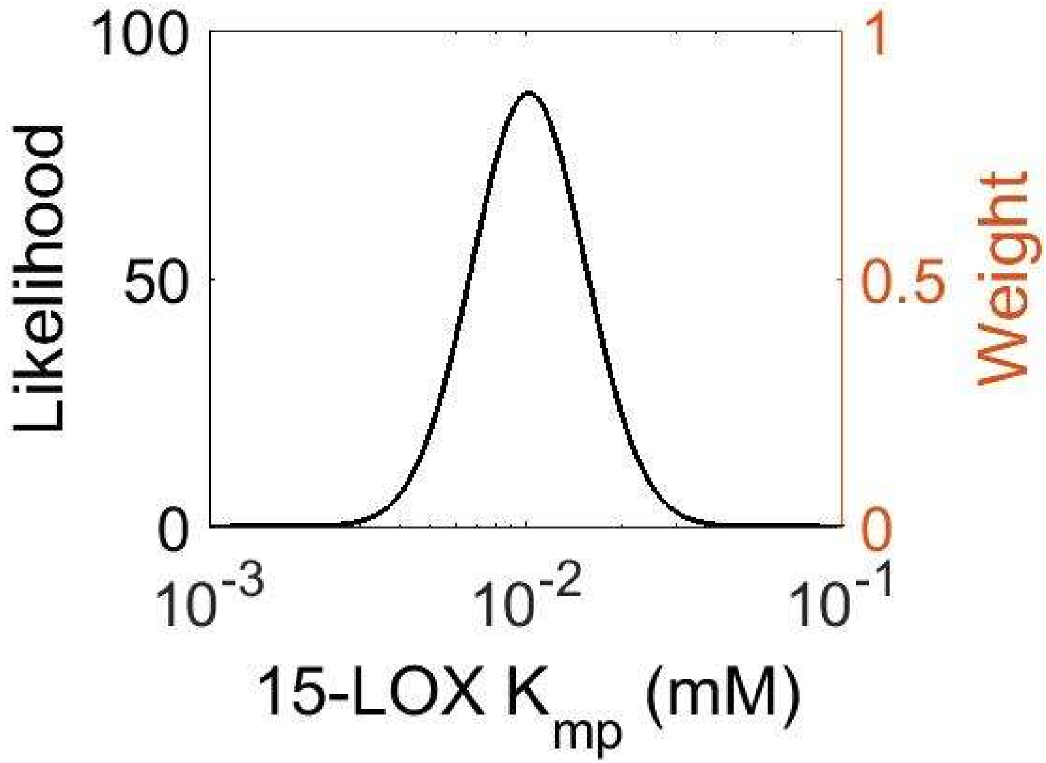


Figure SF.7.12.1.2.1. The estimated probability distribution for the 15-LOX K_{mp}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.12.2.3. Parameter: 15-LOX k_{cat}

Parameter values for the k_{cat} of Reaction 17 were obtained from the literature and summarised in Table ST.7.12.1.3.1. The log-normal distribution properties for the k_{cat} of Reaction 17 are shown in Table ST.7.12.1.3.2 and plotted in Figure SF.7.12.1.3.1.

Table ST.7.12.1.3.1. Literature information used to design the 15-LOX k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
3.42×10^{1}	6.00×10^{-1}	Human	Epithelial	15-LOX-2	7.5	15		512	0	(A. T. Wecksler et al., 2009)
3.72×10^{1}	1.80	Human	Epithelial	15-LOX-2	7	22		512	0	(A. T. Wecksler et al., 2009)
4.44×10^{1}	2.40	Human	Epithelial	15-LOX-2	8	22		256	0	(A. T. Wecksler et al., 2009)
4.50×10^{1}	1.20	Human	Epithelial	15-LOX-2	7.5	22		512	0	(A. T. Wecksler et al., 2009)
4.50×10^{1}	1.20	Human	Epithelial	15-LOX-2	7.5	22		512	0	(A. T. Wecksler et al., 2009)
6.24×10^{1}	4.20	Human	Epithelial	15-LOX-2	7.5	30		512	0	(A. T. Wecksler et al., 2009)
8.28×10^{1}	4.80	Human	Epithelial	15-LOX-2	7.5	37		2048	0	(A. T. Wecksler et al., 2009)

5.96 x10^{2}	1.68 x10^{1}	Human	Epithelial	15-LOX	7.5	25		512	0	(C. Jacquot et al., 2008)

Table ST.7.12.1.3.2. The log-normal distribution properties of the 15-LOX k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
6.51 x10^{1}	4.62	4.60	6.50 x10^{-1}

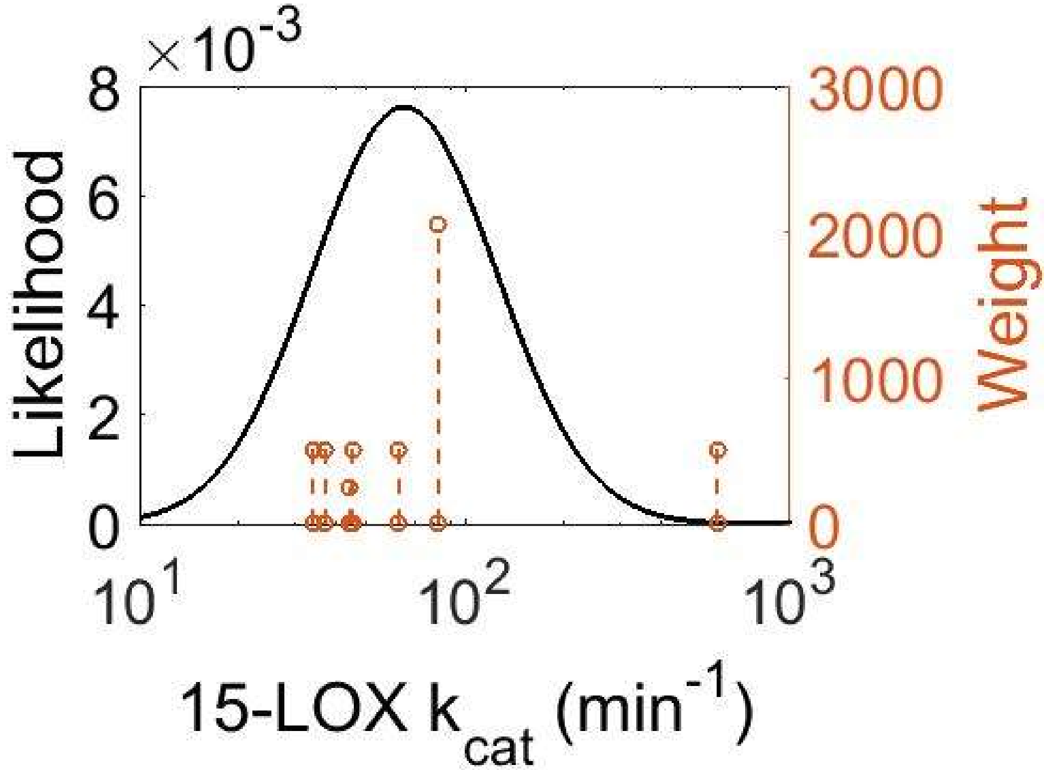


Figure SF.7.12.1.3.1. The estimated probability distribution for the 15-LOX k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.12.2.4. Parameter: 15-LOX K_{eq}

Parameter values for the K_{eq} of Reaction 17 were obtained from the literature and summarised in Table ST.7.12.1.4.1. The log-normal distribution properties for the K_{eq} of Reaction 17 are shown in Table ST.7.12.1.4.2 and plotted in Figure SF.7.12.1.4.1.

Table ST.7.12.1.4.1. Literature information used to design the 15-LOX K_{eq} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

ΔG (kcal/mol)	K_{eq}	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
-7.00 x10^{1}	2.27 x10^{51}	Human	Unknown	5-LOX	7	Unknown		64	0	(Caspi et al., 2018)

Table ST.7.12.1.4.2. The log-normal distribution properties of the 15-LOX K_{eq} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode	Confidence Interval	Location parameter (µ)	Scale parameter (σ)
2.27 x10^{51}	1.00 x10^{1}	1.19 x10^{2}	8.90 x10^{-1}

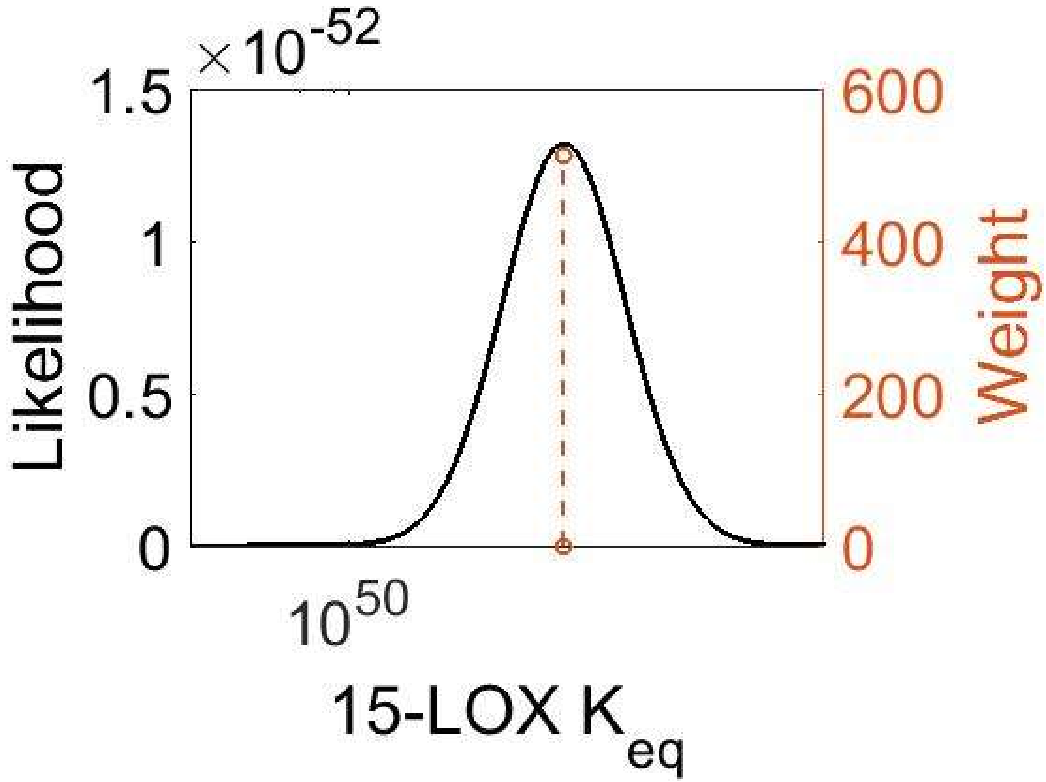


Figure SF.7.12.1.4.1. The estimated probability distribution for the 15-LOX K_{eq}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.12.2.5. Parameter: 15-LOX concentration

Parameter values for the 15-LOX concentration of Reaction 17 were obtained from the literature and summarised in Table ST.7.12.1.5.1. The log-normal distribution properties for the 15-LOX concentration of Reaction 17 are shown in Table ST.7.12.1.5.2 and plotted in Figure SF.7.12.1.5.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.7.12.1.5.1. Literature information used to design the 15-LOX concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.40	NaN	Human	Gut	15-LOX	7.5	37		**1024**	0	(Kim et al., 2014)
4.09	NaN	Human	Lung	15-LOX	7.5	37		**1024**	0	(Kim et al., 2014)
3.74×10^{1}	NaN	Human	Spleen	15-LOX	7.5	37		**1024**	0	(Wilhelm et al., 2014)

Table ST.7.12.1.5.2. The log-normal distribution properties of the 15-LOX concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
4.07	2.25E-05	7.23	7.12×10^{-1}	1.19

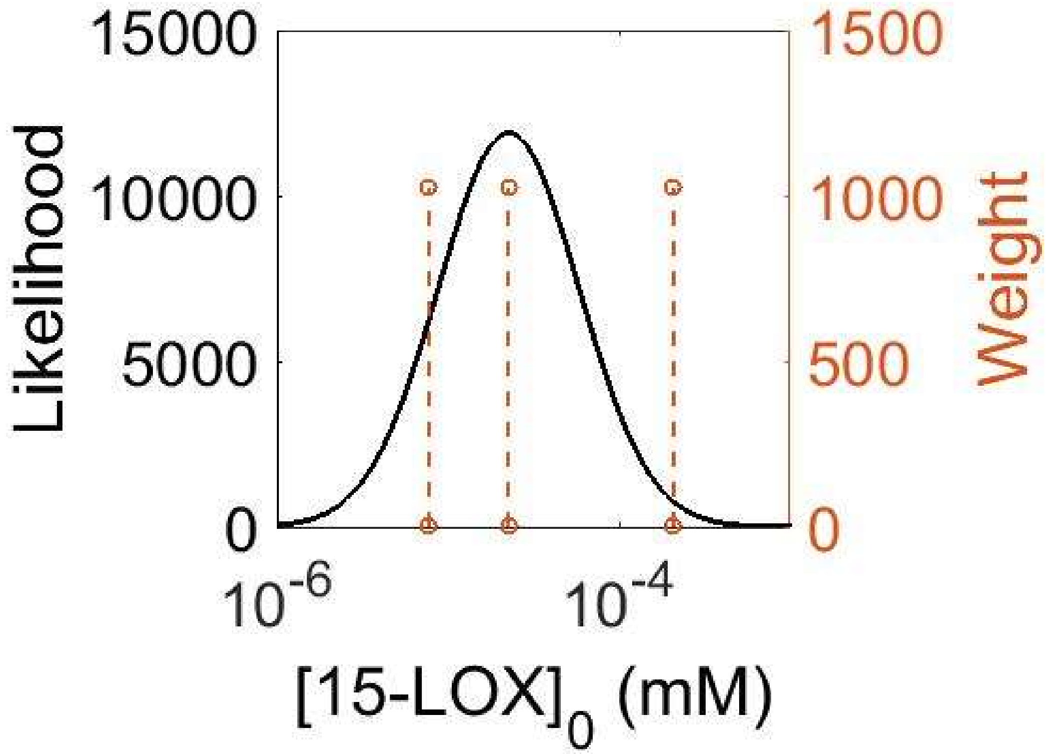


Figure SF.7.12.1.5.1. The estimated probability distribution for the 15-LOX concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.13 Reaction 18: 15-HPETE ⇌ 15-HETE

15-HPETE is reduced by an oxidoreductase enzyme (PHGPx) to form 15-HETE.

15-HPETE 15-HETE

Figure SF.7.13. The metabolism of 15-hydroperoxyeicosatetraenoic acid (15-HPETE) into 15-hydroxyeicosatetraenoic acid (15-HETE) by hydroperoxide glutathione peroxidase (PHGPx) (Reaction 18).

SEq.7.13. Reaction rate law for Reaction 18.

$$\boldsymbol{v_{18}} = \frac{K_{cat}\cdot[PHGPx]\left([15-HPETE]-{[15-HETE]}/{K_{eq}}\right)}{K_{m_s}\left(1+\frac{[15-HETE]}{K_{m_p}}\right)+[15-HPETE]}$$

S.7.13.1. Reaction parameters

S.7.13.1.1. Parameter: PHGPx K_{ms}

Parameter values for the K_{ms} of Reaction 18 were obtained from the literature and summarised in Table ST.7.13.1.1.1. The log-normal distribution properties for the K_{ms} of Reaction 18 are shown in Table ST.7.13.1.1.2 and plotted in Figure SF.7.13.1.1.1.

Table ST.7.13.1.1.1. Literature information used to design the PHGPx K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
4.00 x10^{-3}	NaN	Rat	Liver	PHGPx	7.4	37		768	0	(Hiratsuka et al., 1997)
3.00 x10^{-1}	NaN	Human	Bio imprinted Enzyme	PHGPx	7	37		512	0	(Liu et al., 2008)
1.11 x10^{1}	2.90 x10^{-1}	Human	E. coli.	PHGPx	7	37		1024	0	(Zheng et al., 2008)

Table ST.7.13.1.1.2. The log-normal distribution properties of the PHGPx K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
3.19 x10^{-1}	1.02 x10^{3}	2.54	1.92

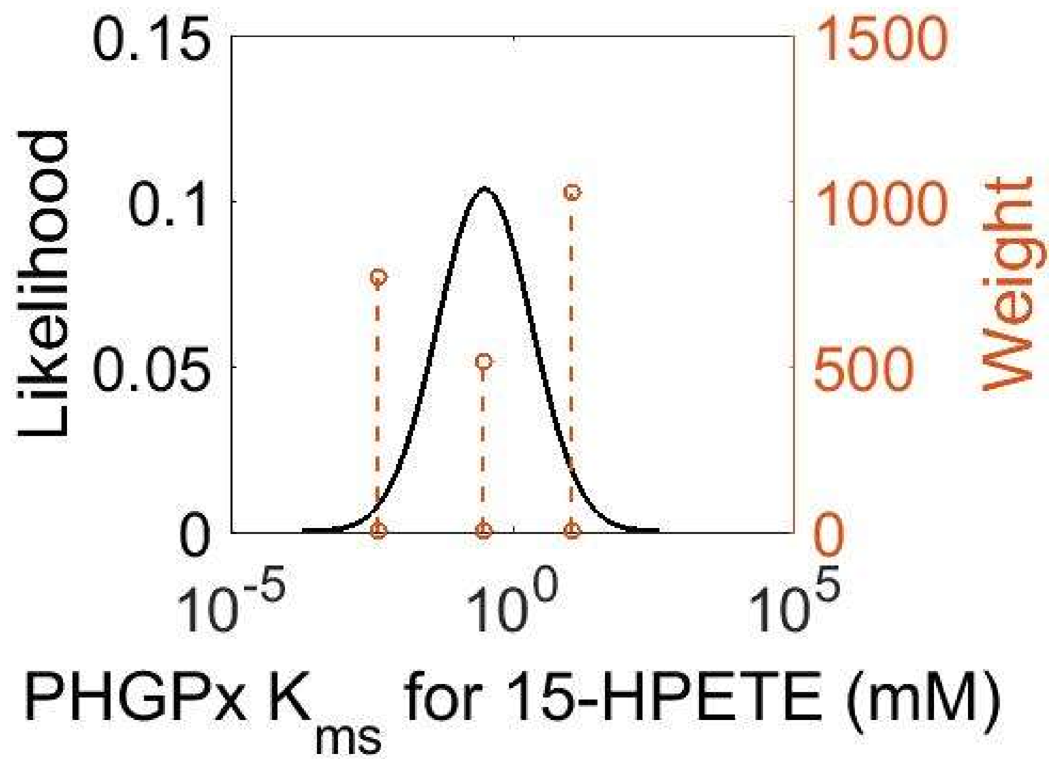


Figure SF.7.13.1.1.1. The estimated probability distribution for the PHGPx K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.13.1.2. Parameter: PHGPx K_{mp} (Dependent parameter)

The log-normal distribution for the parameter for the K_{mp} of Reaction 18 was calculated using multivariate distributions. The log-normal distribution properties for the K_{mp} of Reaction 18 are shown in Table ST.7.13.1.2.1 and plotted in Figure SF.7.13.1.2.1.

Table ST.7.13.1.2.1. The log-normal distribution properties of the PHGPx K_{mp} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Location parameter (μ)	Scale parameter (σ)
3.15×10^{-1}	2.53	1.92

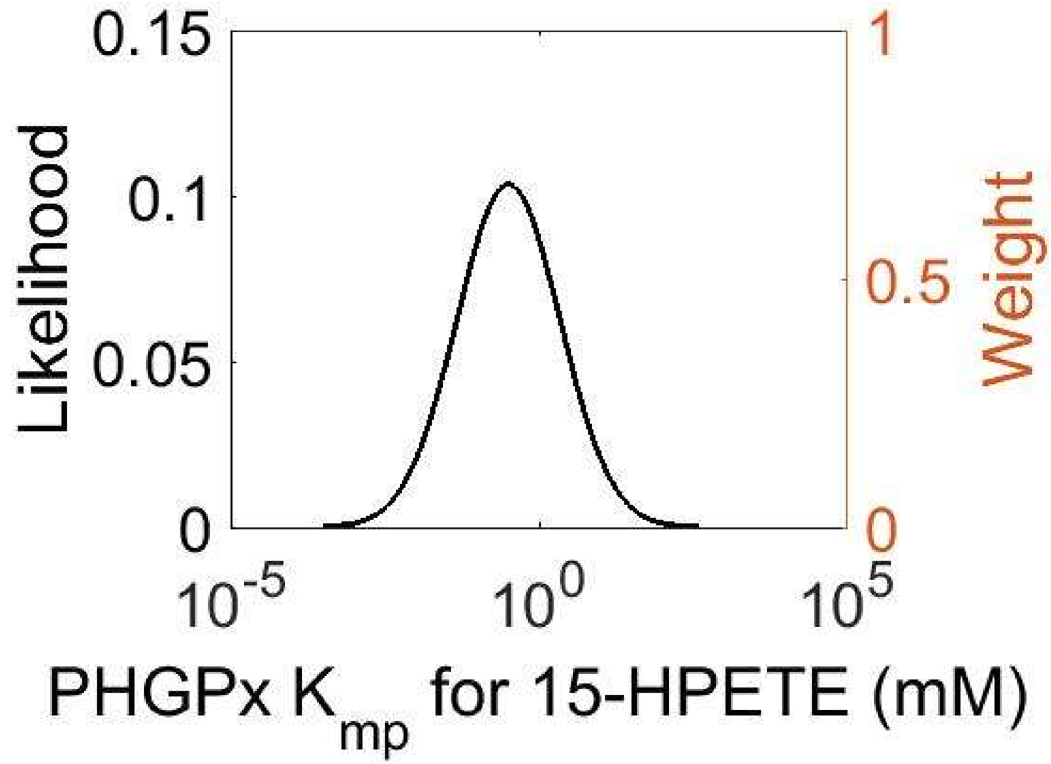


Figure SF.7.13.1.2.1. The estimated probability distribution for the PHGPx K_{mp}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.13.1.3. Parameter: PHGPx k_{cat}

Parameter values for the k_{cat} of Reaction 18 were obtained from the literature and summarised in Table ST.7.13.1.3.1. The log-normal distribution properties for the k_{cat} of Reaction 18 are shown in Table ST.7.13.1.3.2 and plotted in Figure SF.7.13.1.3.1.

Table ST.7.13.1.3.1. Literature information used to design the PHGPx k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.17 x10^3	5.00 x10^1	Human	Bio imprinted Enzyme	PHGPx	7	37		512	0	(Liu et al., 2008)
2.45 x10^4	1.50 x10^2	Human	E. coli.	PHGPx	7	37		1024	0	(Zheng et al., 2008)

Table ST.7.13.1.3.2. The log-normal distribution properties of the PHGPx k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
2.44 x10^4	4.20	1.11 x10^1	9.75 x10^{-1}

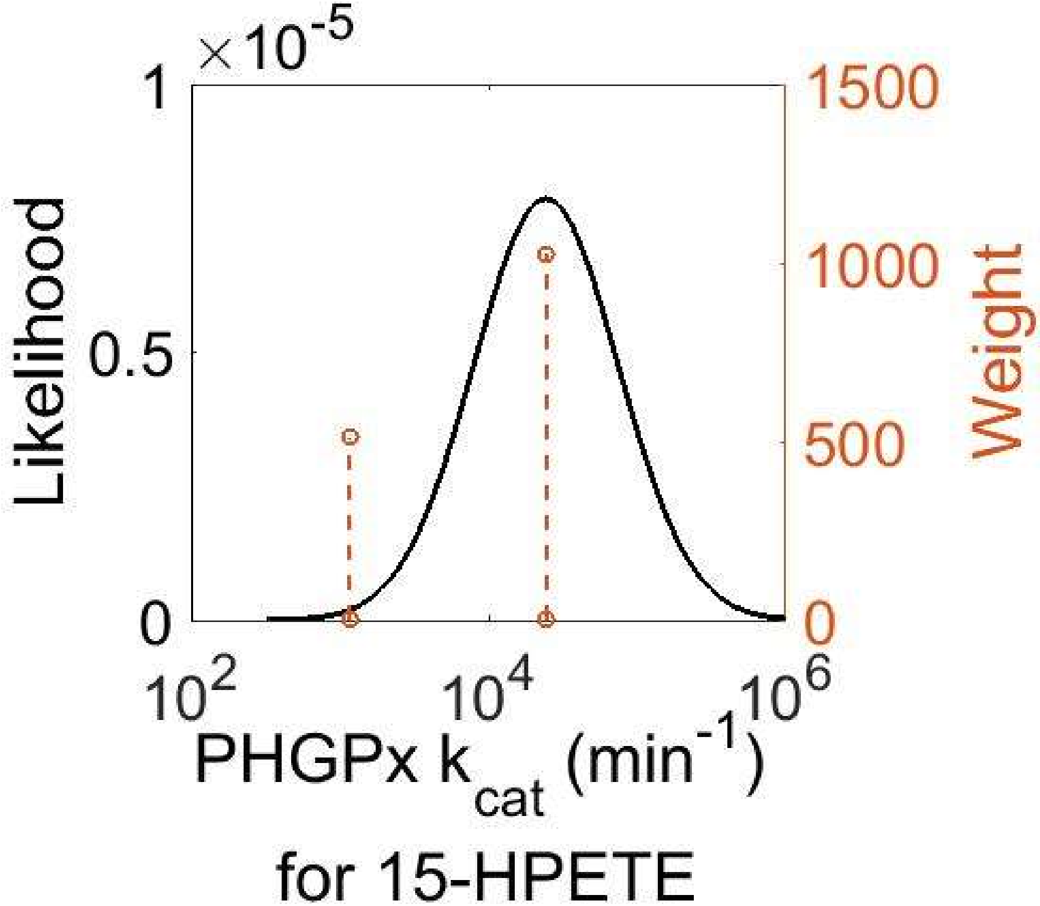


Figure SF.7.13.1.3.1. The estimated probability distribution for the PHGPx k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.13.1.4. Parameter: PHGPx K_{eq}

Parameter values for the K_{eq} of Reaction 18 were obtained from the literature and summarised in Table ST.7.13.1.4.1. The log-normal distribution properties for the K_{eq} of Reaction 18 are shown in Table ST.7.13.1.4.2 and plotted in Figure SF.7.13.1.4.1.

Table ST.7.13.1.4.1. Literature information used to design the PHGPx K_{eq} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

ΔG (kcal/mol)	K_{eq}	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
-2.69 x10^{1}	5.90 x10^{19}	Human	Unknown	PHGPx	7	Unknown		64	0	(Caspi et al., 2018)

Table ST.7.13.1.4.2. The log-normal distribution properties of the PHGPx K_{eq} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
5.90 x10^{19}	1.00 x10^{1}	4.63 x10^{1}	8.90 x10^{-1}

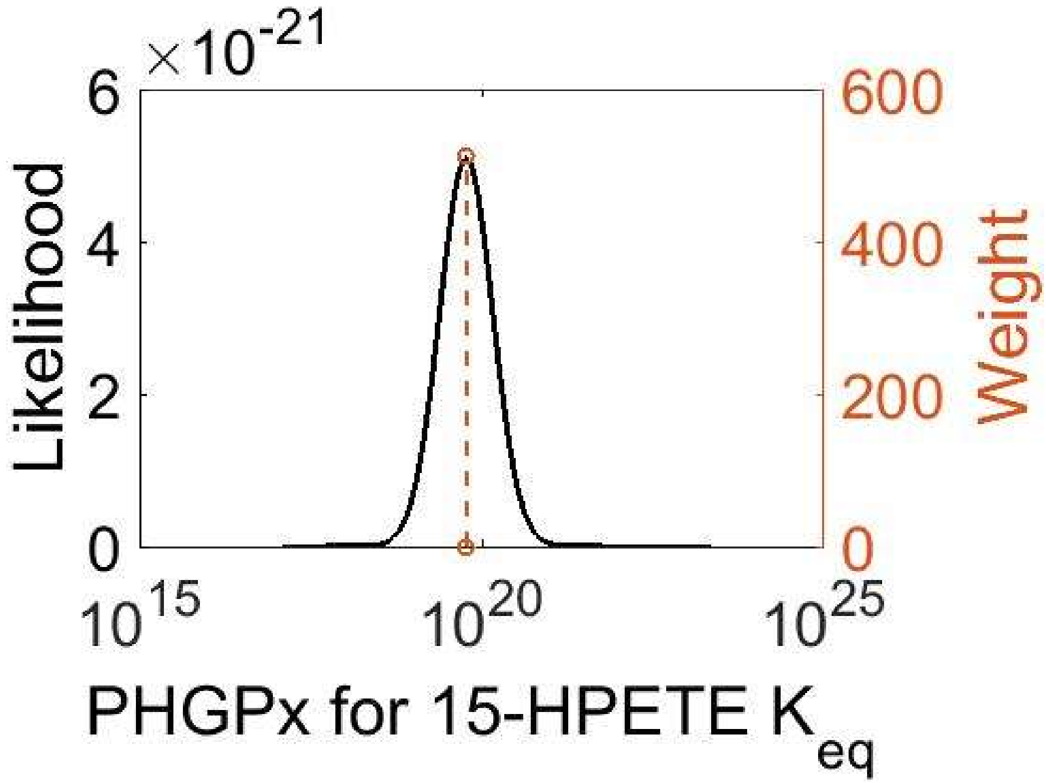


Figure SF.7.13.1.4.1. The estimated probability distribution for the PHGPx K_{eq}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.13.1.5. Parameter: PHGPx concentration

Parameter values for the PHGPx concentration of Reaction 18 were obtained from the literature and summarised in Table ST.7.13.1.5.1. The log-normal distribution properties for the PHGPx concentration of Reaction 18 are shown in Table ST.7.13.1.5.2 and plotted in Figure SF.7.13.1.5.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.7.13.1.5.1. Literature information used to design the PHGPx concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
2.04 x10^{2}	NaN	Human	Gut	PHGPx	7.5	37		**1024**	0	(Kim et al., 2014)
2.82 x10^{2}	NaN	Human	Oesophagus	PHGPx	7.5	37		**1024**	0	(Wilhelm et al., 2014)
3.07 x10^{2}	NaN	Human	Lung	PHGPx	7.5	37		**1024**	0	(Wilhelm et al., 2014)
4.59 x10^{2}	NaN	Human	Skin	PHGPx	7.5	37		**2048**	0	(Wilhelm et al., 2014)

Table ST.7.13.1.5.2. The log-normal distribution properties of the PHGPx concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
3.14 x10^{2}	1.74 x10^{-3}	1.38	5.85	3.09 x10^{-1}

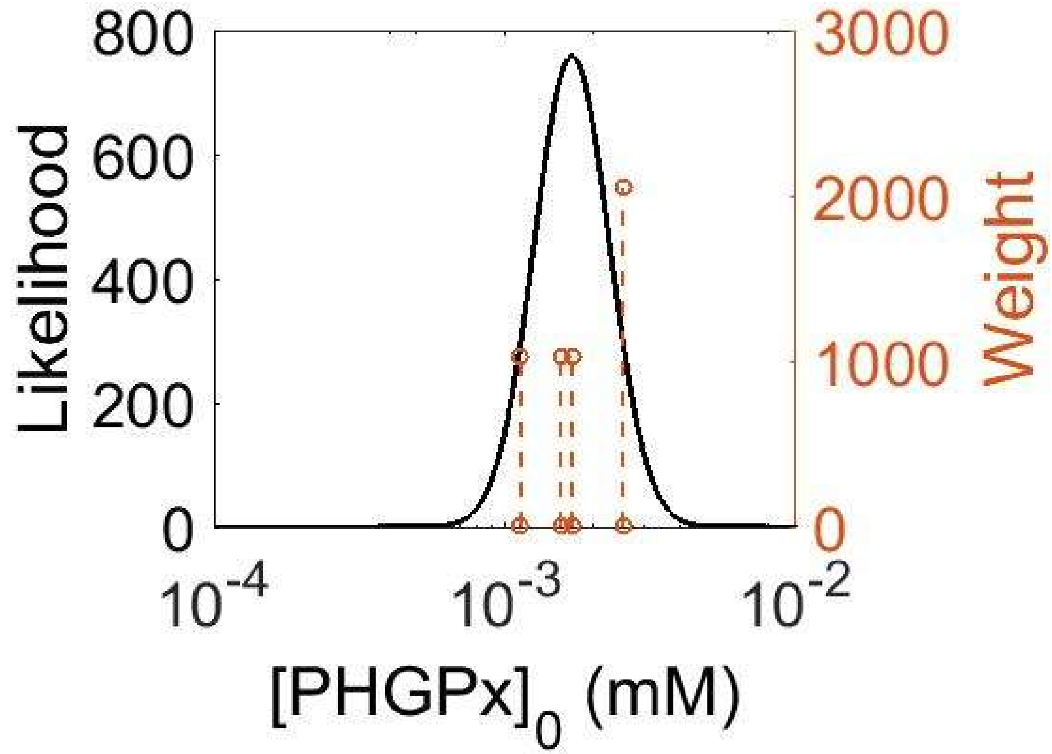


Figure SF.7.13.1.5.1. The estimated probability distribution for the PHGPx concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.14 Reaction 19: AA ⇌ 12-HPETE

The gene ALOX12 encodes 12-LOX, which converts AA into the S enantiomer of 12-HPETE, 12(S)-HPETE (Izumi et al., 1990). The genes ALOX12B and ALOXE3 encode the proteins 12R-LOX and eLOX3 respectively, these proteins are responsible for the generation of the R enantiomer of 12-HPETE, 12(R)-HPETE (Schwartzman et al., 1987). Interestingly, ALOX15 which encodes the 15-LOX-1 protein, is capable of producing both 12(S)-HPETE and 15(S)-HPETE in a ratio of 1 to 16 (Bryant et al., 1982). The formation of the hydroperoxy fatty acids (HPETE) begins with the abstraction of a hydrogen radical at the allylic position between two double bonds. The structure undergoes a rearrangement reaction which results in the formation of a conjugated diene system. The insertion of molecular oxygen and a hydrogen leads to the formation of the final structure, a hydroperoxy fatty acid.

Figure SF.7.14. The metabolism of arachidonic acid (AA) into 12-hydroperoxyeicosatetraenoic acid (12-HPETE) by 12-lipoxygenase (12-LOX) (Reaction 19).

SEq.7.14. Reaction rate law for Reaction 19.

$$v_{19} = \frac{K_{cat}\cdot[12\text{-}LOX]\left([AA]-{[12\text{-}HPETE]}/{K_{eq}}\right)}{K_{m_s}\left(1+\frac{[12\text{-}HPETE]}{K_{m_p}}\right)+[AA]}$$

S.7.14.1. Reaction parameters

S.7.14.1.1. Parameter: 12-LOX K_{ms}

Parameter values for the K_{ms} of Reaction 18 were obtained from the literature and summarised in Table ST.7.14.1.1.1. The log-normal distribution properties for the K_{ms} of Reaction 18 are shown in Table ST.7.14.1.1.2 and plotted in Figure SF.7.14.1.1.1.

Table ST.7.14.1.1.1. Literature information used to design the 12-LOX K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
7.20 x10^{-3}	NaN	Human	Platelet	12-LOX	7.4	37		2048	0	(Lagarde et al., 1984)
7.90 x10^{-3}	8.00 x10^{-4}	Human	Platelet	12-LOX	7.4	37		2048	0	(Romano et al., 1993)
1.00 x10^{-2}	NaN	Human	Baculovirus	12-LOX	8	37		256	0	(Chen et al., 1993)
8.00 x10^{-2}	NaN	Human	Platelet	12-LOX	7.4	24		512	0	(Hada et al., 1991)

Table ST.7.14.1.1.2. The log-normal distribution properties of the 12-LOX K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Confidence Interval	Location parameter (σ)	Scale parameter (σ)
7.60 x10^{-3}	4.34	-4.48	6.30 x10^{-1}

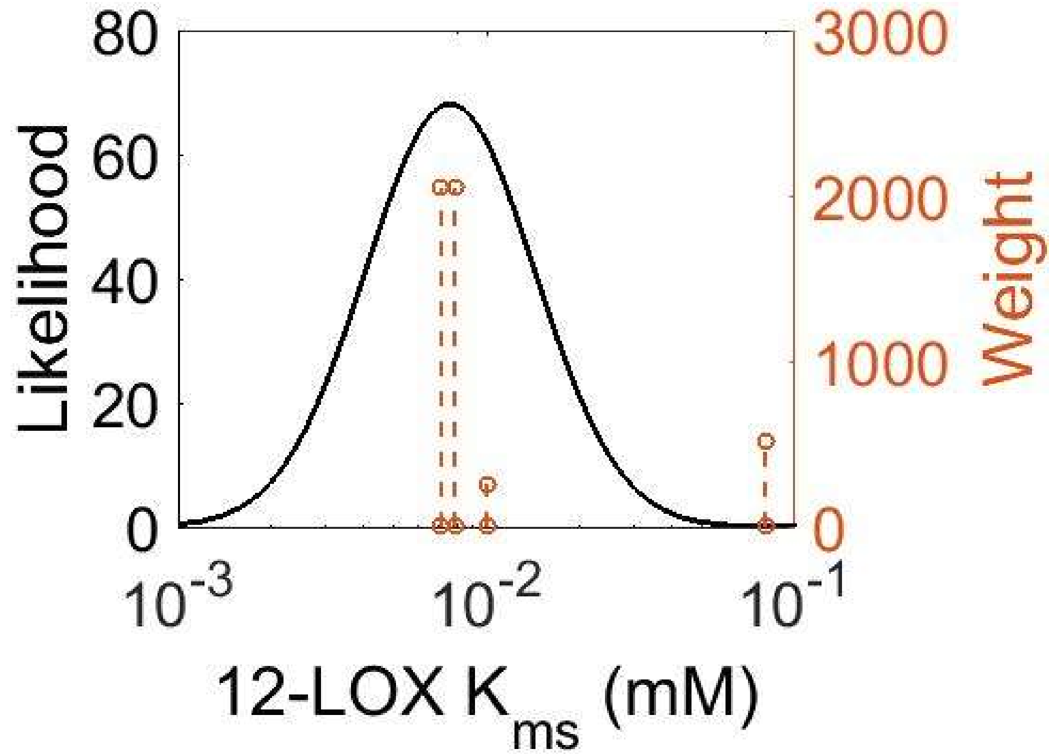


Figure SF.7.14.1.1.1. The estimated probability distribution for the 12-LOX K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.14.1.2. Parameter: 12-LOX K_{mp} (Dependent parameter)

he log-normal distribution for the parameter for the K_{mp} of Reaction 18 was calculated using multivariate distributions. The log-normal distribution properties for the K_{mp} of Reaction 18 are shown in Table ST.7.14.1.2.1 and plotted in Figure SF.7.14.1.2.1.

Table ST.7.14.1.2.1. The log-normal distribution properties of the 12-LOX K_{mp} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Location parameter (μ)	Scale parameter (σ)
7.30 $\times 10^{-3}$	-4.52	6.28 $\times 10^{-1}$

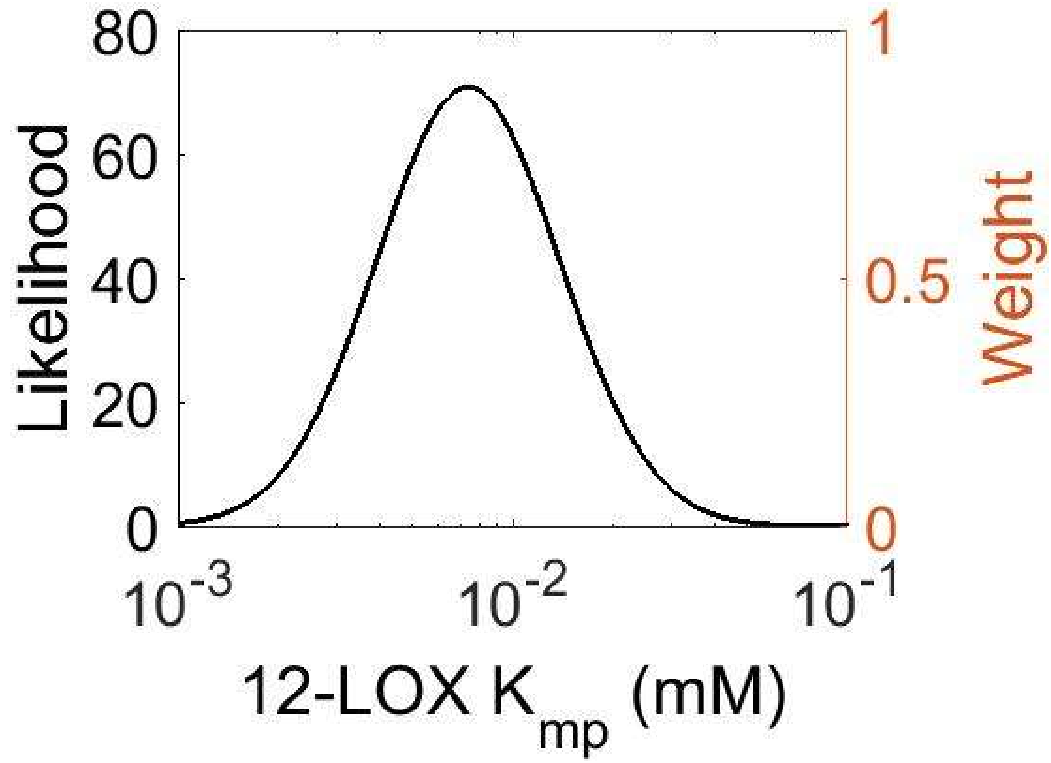


Figure SF.7.14.1.2.1. The estimated probability distribution for the 12-LOX K_{mp}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.14.1.3. Parameter: 12-LOX k_{cat}

Parameter values for the k_{cat} of Reaction 18 were obtained from the literature and summarised in Table ST.7.14.1.3.1. The log-normal distribution properties for the k_{cat} of Reaction 18 are shown in Table ST.7.14.1.3.2 and plotted in Figure SF.7.14.1.3.1.

Table ST.7.14.1.3.1. Literature information used to design the 12-LOX k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
5.04 $x10^2$	NaN	Boar	E. coli.	12-LOX	7.4	37		1024	0	(Richards and Marnett, 1997)
3.36 $x10^2$	1.20 $x10^1$	Human	Reticulocyte	12-LOX	7.5	25		256	0	(Aaron T. Wecksler et al., 2009)

Table ST.7.14.1.3.2. The log-normal distribution properties of the 12-LOX k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
4.87 $x10^2$	1.20	6.22	1.80 $x10^{-1}$

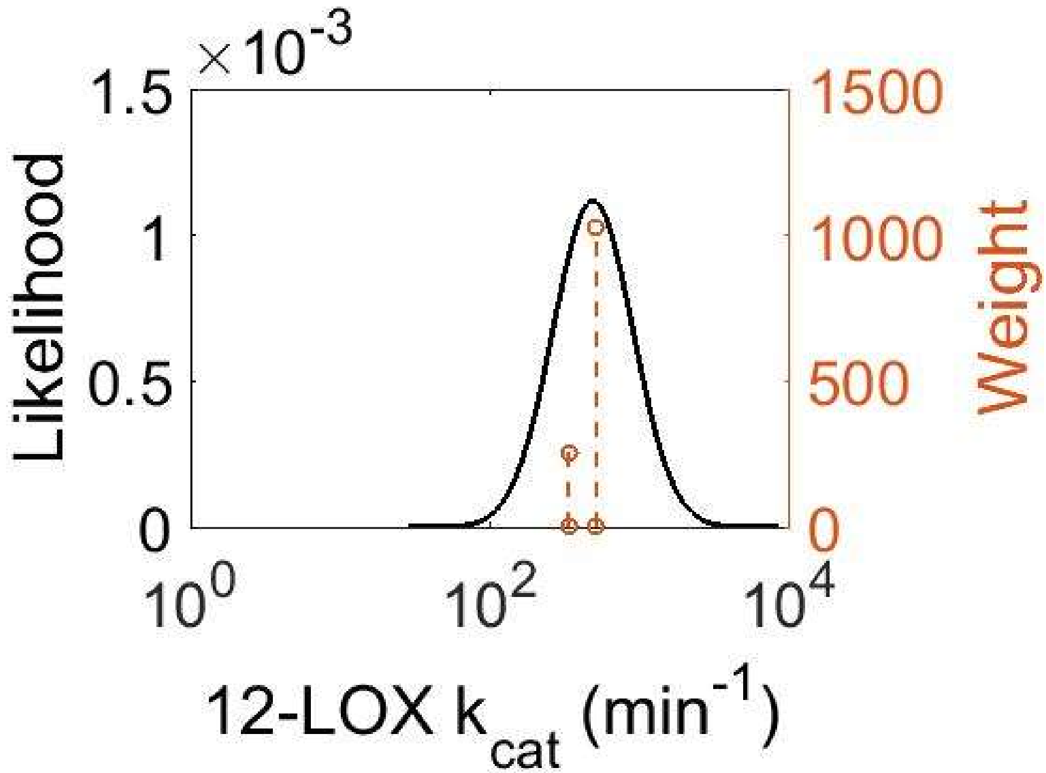


Figure SF.7.14.1.3.1. The estimated probability distribution for the 12-LOX k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.14.1.4. Parameter: 12-LOX K_{eq}

Parameter values for the K_{eq} of Reaction 18 were obtained from the literature and summarised in Table ST.7.14.1.4.1. The log-normal distribution properties for the K_{eq} of Reaction 18 are shown in Table ST.7.14.1.4.2 and plotted in Figure SF.7.14.1.4.1.

Table ST.7.14.1.4.1. Literature information used to design the 12-LOX K_{eq} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

ΔG (kcal/mol)	K_{eq}	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
-7.00×10^{1}	2.27×10^{51}	Human	Unknown	5-LOX	7	Unknown		64	0	(Caspi et al., 2018)

Table ST.7.14.1.4.2. The log-normal distribution properties of the 12-LOX K_{eq} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
2.27×10^{51}	1.00×10^{1}	1.19×10^{2}	8.90×10^{-1}

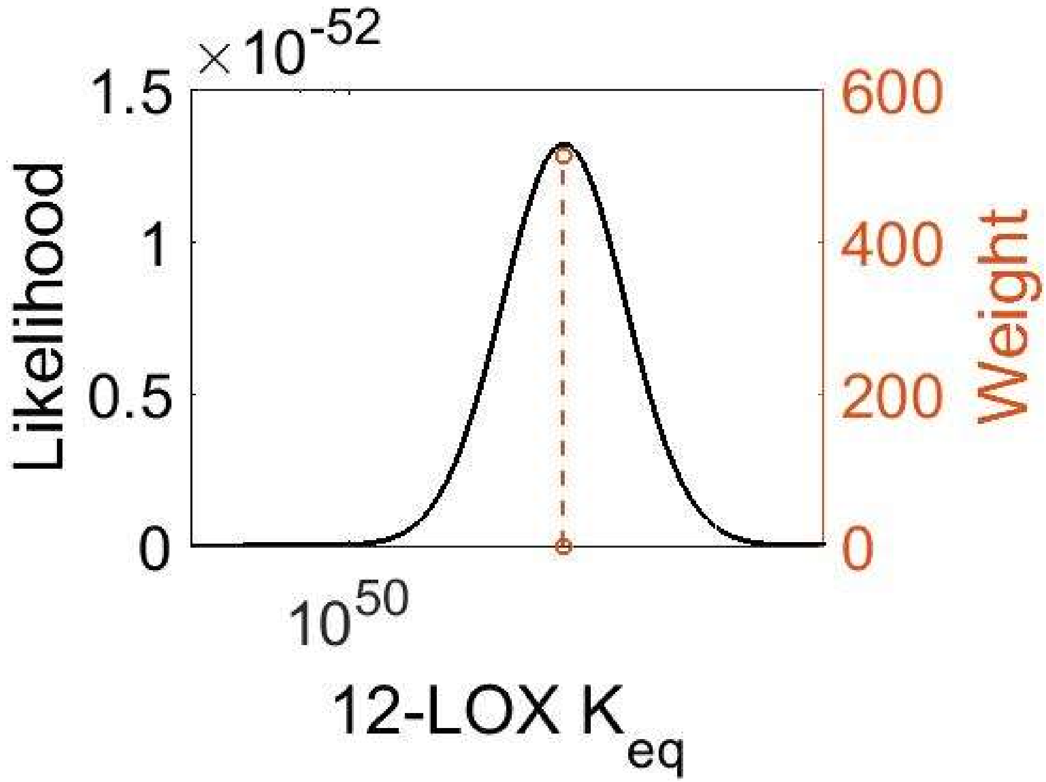


Figure SF.7.14.1.4.1. The estimated probability distribution for the 12-LOX K_{eq}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.14.1.5. Parameter: 12-LOX concentration

Parameter values for the 12-LOX concentration of Reaction 18 were obtained from the literature and summarised in Table ST.7.14.1.5.1. The log-normal distribution properties for the 12-LOX concentration of Reaction 18 are shown in Table ST.7.14.1.5.2 and plotted in Figure SF.7.14.1.5.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.7.14.1.5.1. Literature information used to design the 12-LOX concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.10 $\times 10^{-1}$	NaN	Human	Pancreas	12-LOX	7.5	37		**1024**	0	(Kim et al., 2014)
2.80 $\times 10^{-1}$	NaN	Human	Gut	12-LOX	7.5	37		**1024**	0	(Kim et al., 2014)
1.60	NaN	Human	Liver	12-LOX	7.5	37		**1024**	0	(Kim et al., 2014)
1.98 $\times 10^{1}$	NaN	Human	Spleen	12-LOX	7.5	37		**1024**	0	(Wilhelm et al., 2014)

Table ST.7.14.1.5.2. The log-normal distribution properties of the 12-LOX concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
4.98 $\times 10^{-1}$	2.76 $\times 10^{-6}$	7.23	7.12 $\times 10^{-1}$	1.19

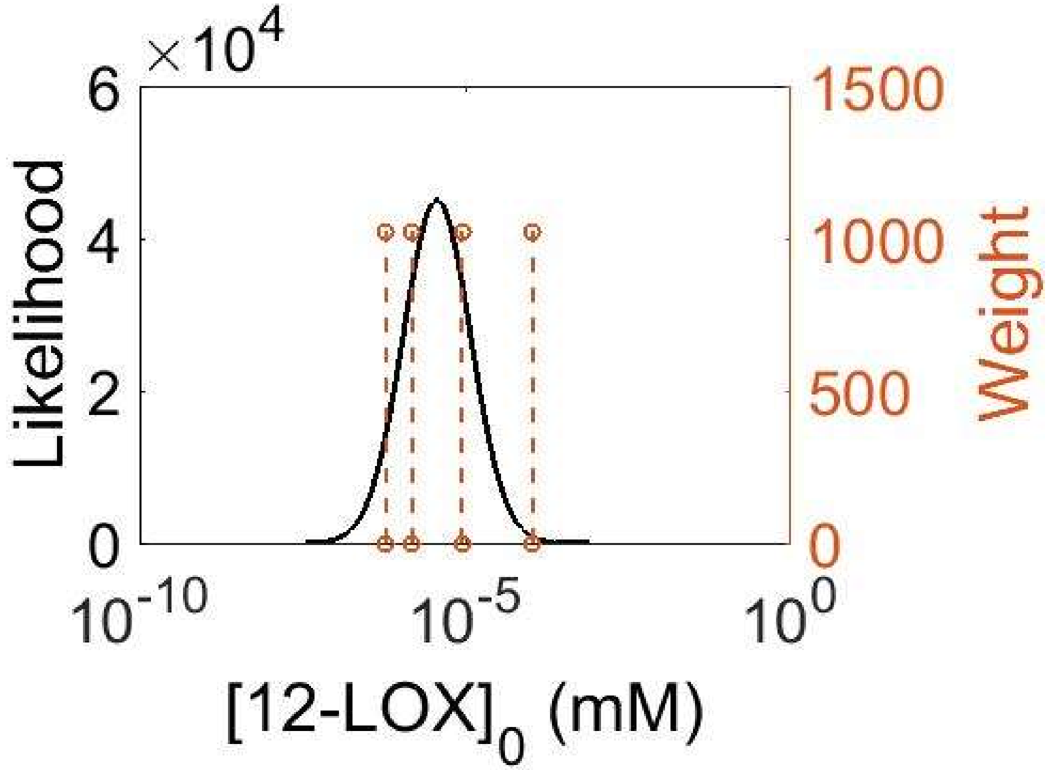


Figure SF.7.14.1.5.1. The estimated probability distribution for the 12-LOX concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.15 Reaction 20: 12-HPETE ⇌ 12-HETE

Both enantiomers of 12-HPETE can be reduced by an oxidoreductase enzyme (PHGPx), to form 12(R)-HETE and 12(S)-HETE.

Figure SF.7.15. The metabolism of 12-hydroperoxyeicosatetraenoic acid (12-HPETE) to 12-hydroxyeicosatetraenoic acid (12-HETE) by phospholipid hydroperoxide glutathione peroxidase (PHGPx) (Reaction 20).

SEq.7.15. Reaction rate law for Reaction 20.

$$\boldsymbol{v_{20}} = \frac{K_{cat} \cdot [PHGPx]\left([12-HPETE] - {[12-HETE]}/{K_{eq}}\right)}{K_{m_s}\left(1 + \frac{[12-HPETE]}{K_{m_p}}\right) + [12-HETE]}$$

S.7.15.1. Reaction parameters

S.7.15.1.1. Parameter: PHGPx K_{ms}

Parameter values for the K_{ms} of Reaction 20 were obtained from the literature and summarised in Table ST.7.15.1.1.1. The log-normal distribution properties for the K_{ms} of Reaction 20 are shown in Table ST.7.15.1.1.2 and plotted in Figure SF.7.15.1.1.1.

Table ST.7.15.1.1.1. Literature information used to design the PHGPx K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
4.00×10^{-3}	NaN	Rat	Liver	PHGPx	7.4	37		768	0	(Hiratsuka et al., 1997)
3.00×10^{-1}	NaN	Human	Bio imprinted Enzyme	PHGPx	7	37		512	0	(Liu et al., 2008)
1.11×10^{1}	2.90×10^{-1}	Human	E. coli.	PHGPx	7	37		1024	0	(Zheng et al., 2008)

Table ST.7.15.1.1.2. The log-normal distribution properties of the PHGPx K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
3.19×10^{-1}	1.02×10^{3}	2.54	1.92

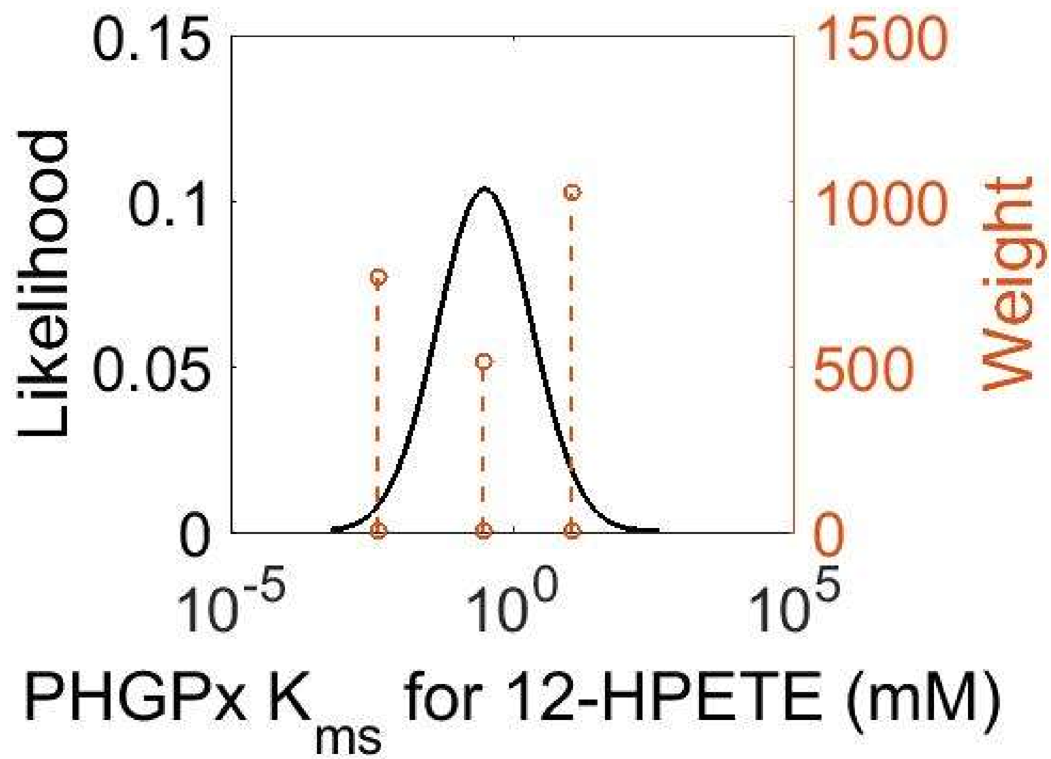


Figure SF.7.15.1.1.1. The estimated probability distribution for the PHGPx K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.15.1.2. Parameter: PHGPx K_{mp} (Dependent parameter)

The log-normal distribution for the parameter for the K_{mp} of Reaction 20 was calculated using multivariate distributions. The log-normal distribution properties for the K_{mp} of Reaction 20 are shown in Table ST.7.15.1.2.1 and plotted in Figure SF.7.15.1.2.1.

Table ST.7.15.1.2.1. The log-normal distribution properties of the PHGPx K_{mp} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Location parameter (μ)	Scale parameter (σ)
3.15×10^{-1}	2.53	1.92

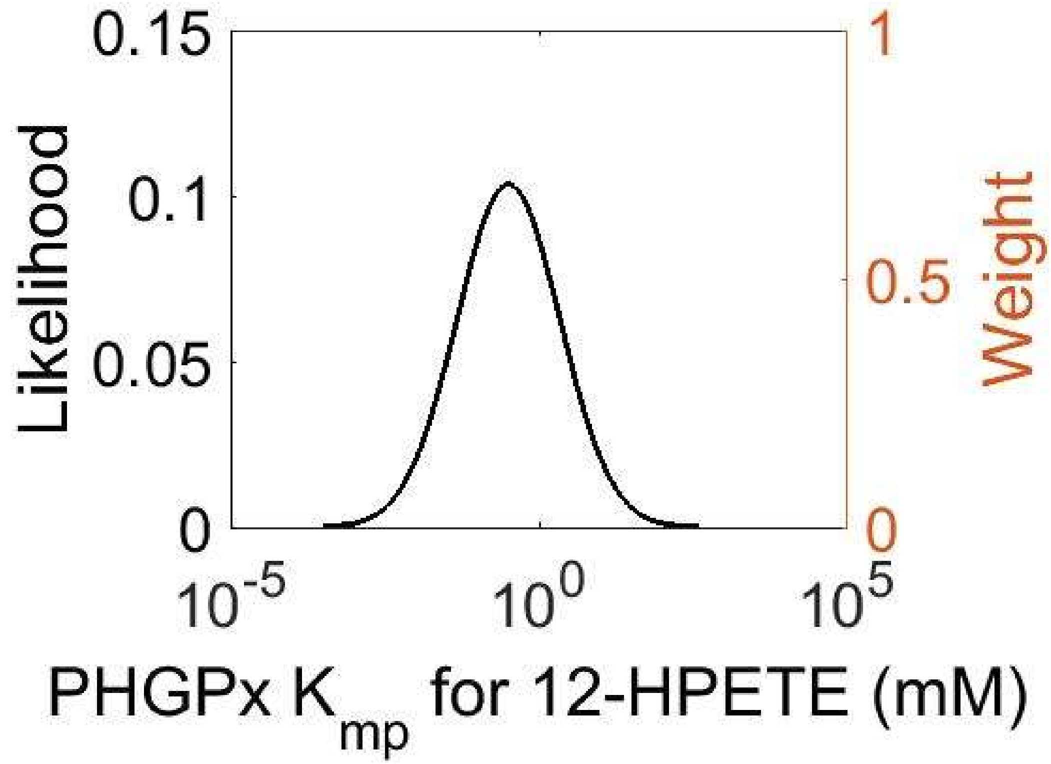


Figure SF.7.15.1.2.1. The estimated probability distribution for the PHGPx K_{mp}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.15.1.3. Parameter: PHGPx k_{cat}

Parameter values for the k_{cat} of Reaction 20 were obtained from the literature and summarised in Table ST.7.15.1.3.1. The log-normal distribution properties for the k_{cat} of Reaction 20 are shown in Table ST.7.15.1.3.2 and plotted in Figure SF.7.15.1.3.1.

Table ST.7.15.1.3.1. Literature information used to design the PHGPx k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.17×10^3	5.00×10^1	Human	Bio imprinted Enzyme	PHGPx	7	37		512	0	(Liu et al., 2008)
2.45×10^4	1.50×10^2	Human	E. coli.	PHGPx	7	37		1024	0	(Zheng et al., 2008)

Table ST.7.15.1.3.2. The log-normal distribution properties of the PHGPx k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
2.44×10^4	4.20	1.11×10^1	9.75×10^{-1}

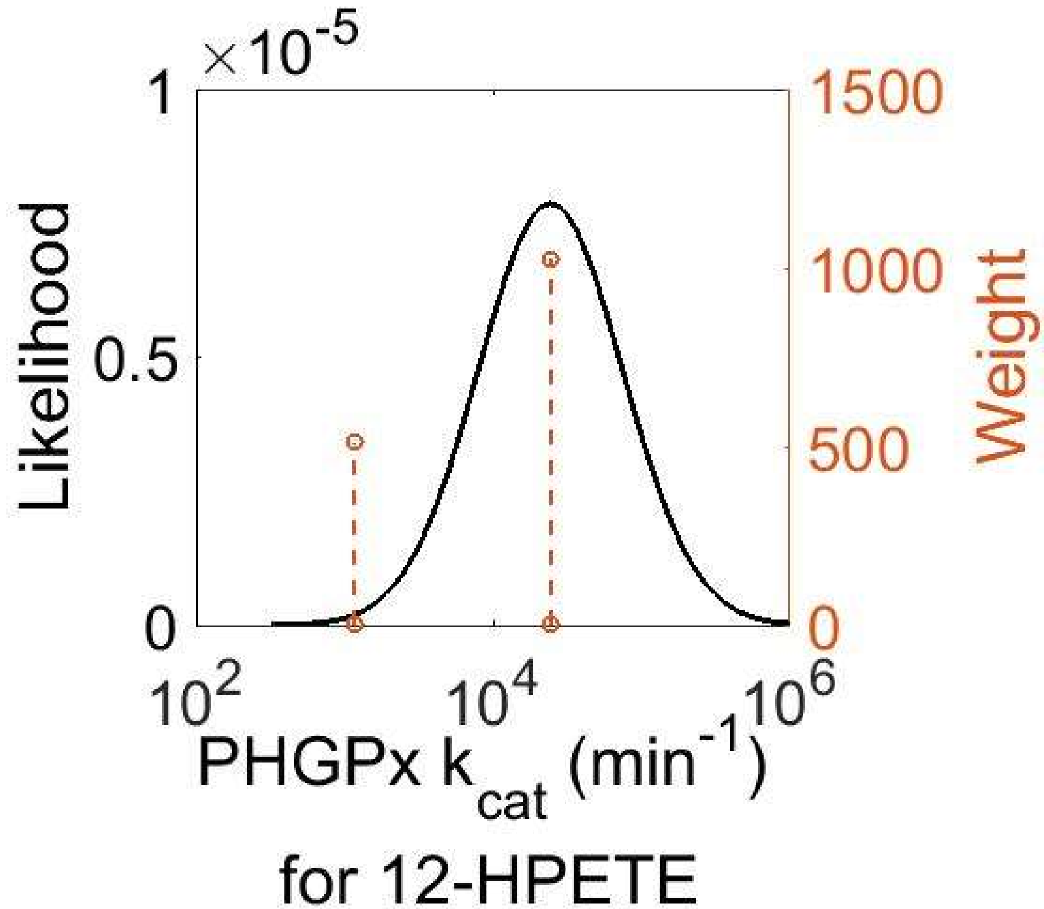


Figure SF.7.15.1.3.1. The estimated probability distribution for the PHGPx k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.15.1.4. Parameter: PHGPx K_{eq}

Parameter values for the K_{eq} of Reaction 20 were obtained from the literature and summarised in Table ST.7.15.1.4.1. The log-normal distribution properties for the K_{eq} of Reaction 20 are shown in Table ST.7.15.1.4.2 and plotted in Figure SF.7.15.1.4.1.

Table ST.7.15.1.4.1. Literature information used to design the PHGPx K_{eq} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

ΔG (kcal/mol)	K_{eq}	Experimental details						Weight	Type of error	Reference
		Species	**Expression Vector**	**Enzyme**	**pH**	**Temperature (°C)**	**Other**			
-2.69×10^{1}	5.90×10^{19}	Human	Unknown	PHGPx	7	Unknown		64	0	(Caspi et al., 2018)

Table ST.7.15.1.4.2. The log-normal distribution properties of the PHGPx K_{eq} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
5.90×10^{19}	1.00×10^{1}	4.63×10^{1}	8.90×10^{-1}

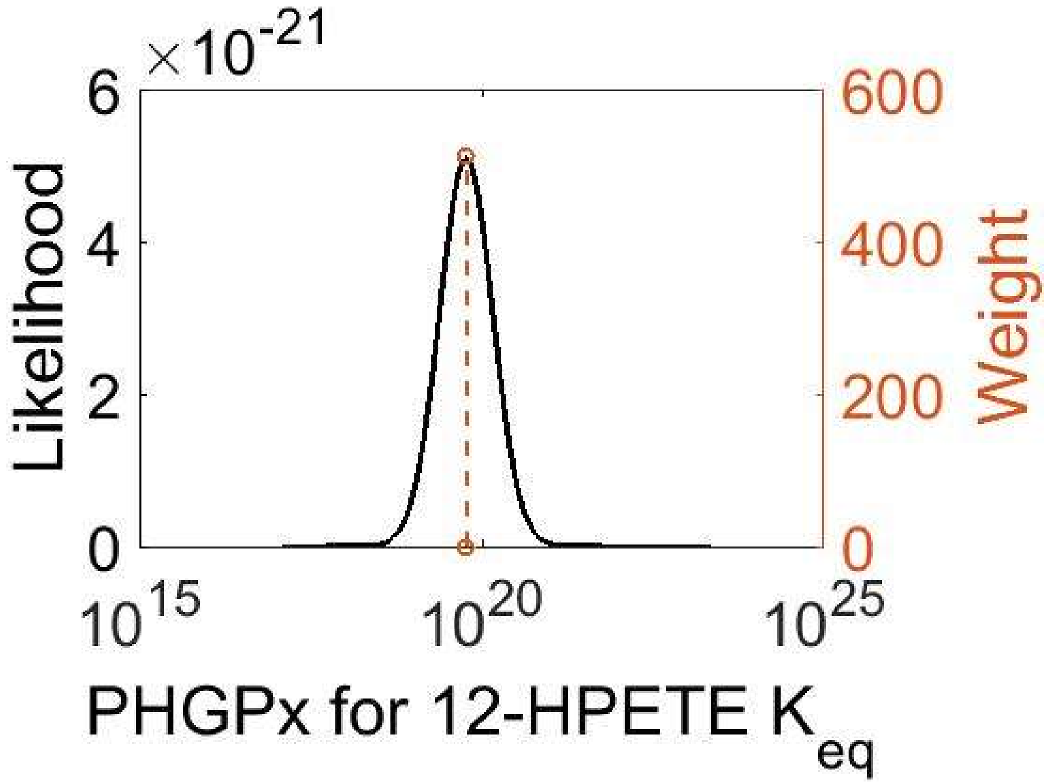


Figure SF.7.15.1.4.1. The estimated probability distribution for the PHGPx K_{eq}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.15.1.5. Parameter: PHGPx concentration

Parameter values for the PHGPx concentration of Reaction 20 were obtained from the literature and summarised in Table ST.7.15.1.5.1. The log-normal distribution properties for the PHGPx concentration of Reaction 20 are shown in Table ST.7.15.1.5.2 and plotted in Figure SF.7.15.1.5.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.7.15.1.5.1. Literature information used to design the PHGPx concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
2.04×10^{2}	NaN	Human	Gut	PHGPx	7.5	37		**1024**	0	(Kim et al., 2014)
2.82×10^{2}	NaN	Human	Oesophagus	PHGPx	7.5	37		**1024**	0	(Wilhelm et al., 2014)
3.07×10^{2}	NaN	Human	Lung	PHGPx	7.5	37		**1024**	0	(Wilhelm et al., 2014)
4.59×10^{2}	NaN	Human	Skin	PHGPx	7.5	37		**2048**	0	(Wilhelm et al., 2014)

Table ST.7.15.1.5.2. The log-normal distribution properties of the PHGPx concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
3.14×10^{2}	1.74×10^{-3}	1.38	5.85	3.09×10^{-1}

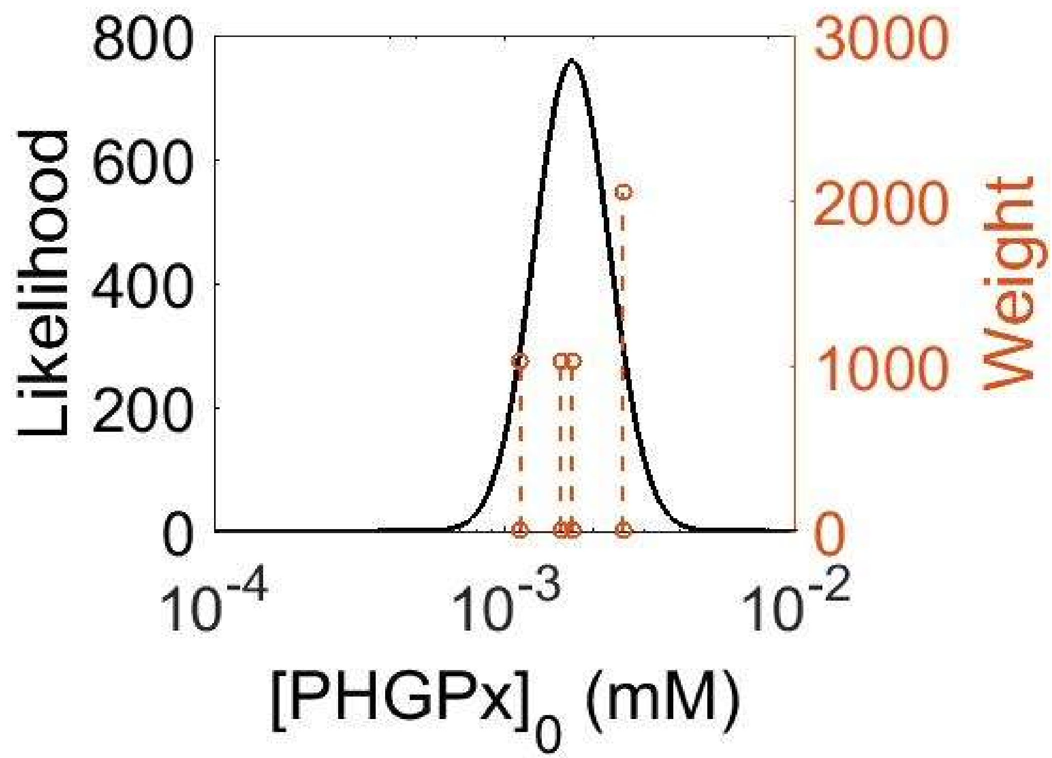


Figure SF.7.15.1.5.1. The estimated probability distribution for the PHGPx concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.16 Reaction 21: $PGH_2 \rightleftharpoons PGD_2$

The isomerisation of PGH_2 to PGD_2 is performed by prostaglandin D synthase (PGDS), to yield a hydroxyl group at C9 and a ketone group at C11.

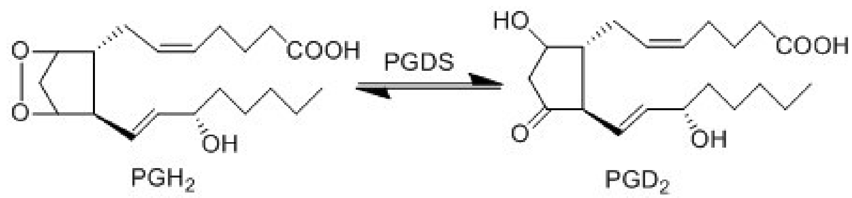


Figure SF.7.16. The metabolism of prostaglandin H_2 (PGH_2) into prostaglandin D_2 (PGD_2) by prostaglandin D synthase (PGDS) (Reaction 21).

SEq.7.16. Reaction rate law for Reaction 21.

$$\boldsymbol{v_{21}} = \frac{k_{cat} \cdot [PGDS] \left([PGH_2] - {[PGD_2]}/{K_{eq}} \right)}{K_{m_s} \left(1 + \frac{[PGD_2]}{K_{m_p}} \right) + [PGH_2]}$$

S.7.16.1. Reaction parameters

S.7.16.1.1. Parameter: PGDS K_{ms}

Parameter values for the K_{ms} of Reaction 21 were obtained from the literature and summarised in Table ST.7.16.1.1.1. The log-normal distribution properties for the K_{ms} of Reaction 21 are shown in Table ST.7.16.1.1.2 and plotted in Figure SF.7.16.1.1.1.

Table ST.7.16.1.1.1. Literature information used to design the PGDS K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
4.00×10^{-3}	NaN	Human	Cerebrospinal Fluid	PGDS	10	Unknown		256	0	(Watanabe et al., 1994)
1.38×10^{-2}	NaN	Human	Human cell	PGDS	8	25		512	0	(Zhou et al., 2010)
5.00×10^{-1}	NaN	Human	E. coli.	PGDS	6.5	Unknown		128	0	(Pinzar et al., 2000)
1.40×10^{-2}	NaN	Rat	Cerebrospinal Fluid	PGDS	7	25		256	0	(Urade et al., 1985)

Table ST.7.16.1.1.2. The log-normal distribution properties of the PGDS K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.35×10^{-2}	3.78	-3.44	9.29×10^{-1}

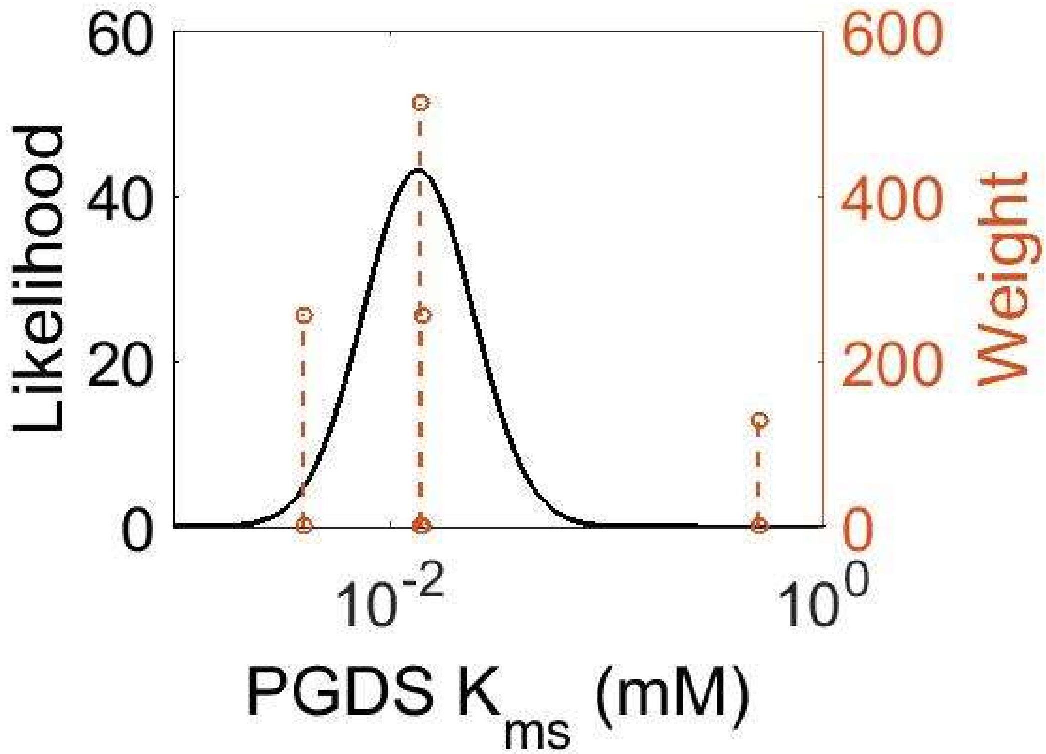


Figure SF.7.16.1.1.1. The estimated probability distribution for the PGDS K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.16.1.2. Parameter: PGDS K_{mp} (Dependent parameter)

The log-normal distribution for the parameter for the K_{mp} of Reaction 21 was calculated using multivariate distributions. The log-normal distribution properties for the K_{mp} of Reaction 21 are shown in Table ST.7.16.1.2.1 and plotted in Figure SF.7.16.1.2.1.

Table ST.7.16.1.2.1. The log-normal distribution properties of the PGDS K_{mp} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Location parameter (μ)	Scale parameter (σ)
1.30 $x10^{-2}$	-4.02	5.69 $x10^{-1}$

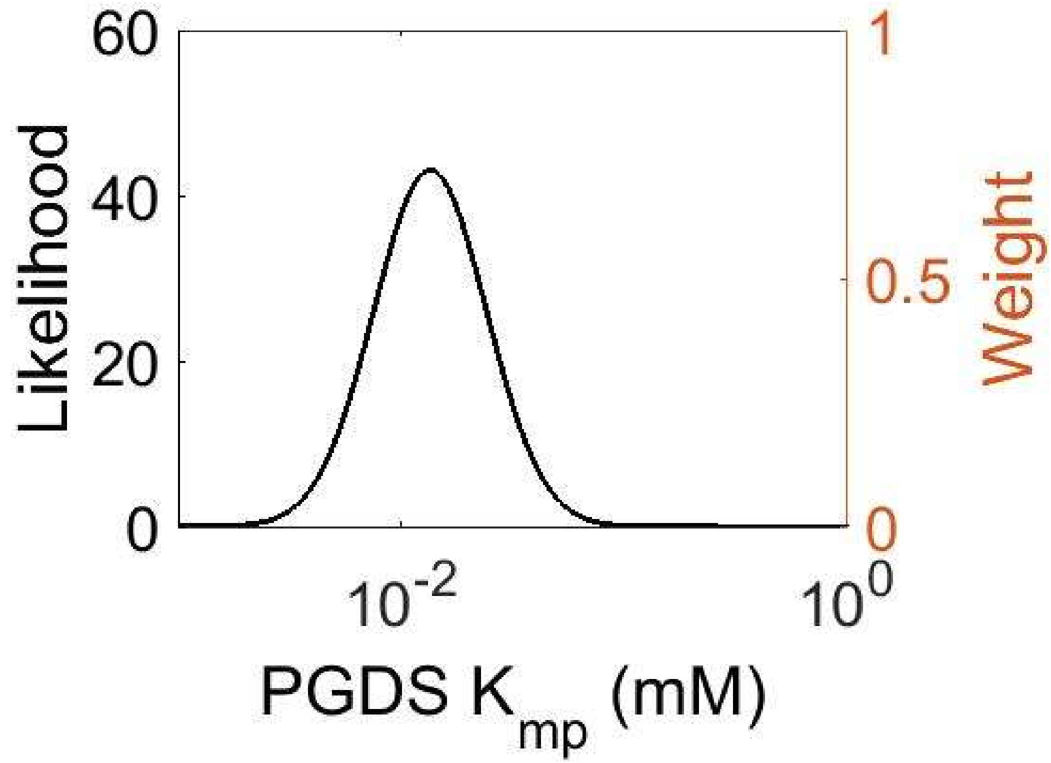


Figure SF.7.16.1.2.1. The estimated probability distribution for the PGDS K_{mp}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.16.1.3. Parameter: PGDS k_{cat}

Parameter values for the k_{cat} of Reaction 21 were obtained from the literature and summarised in Table ST.7.16.1.3.1. The log-normal distribution properties for the k_{cat} of Reaction 21 are shown in Table ST.7.16.1.3.2 and plotted in Figure SF.7.16.1.3.1.

Table ST.7.16.1.3.1. Literature information used to design the PGDS k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.58 x10^2	NaN	Human	Human cell	PGDS	8	25		256	0	(Zhou et al., 2010)
1.30 x10^3		Human	E. coli.	PGDS	6.5	Unknown		128		(Pinzar et al., 2000)

Table ST.7.16.1.3.2. The log-normal distribution properties of the PGDS k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.58 x10^2	1.50	5.10	2.00 x10^{-1}

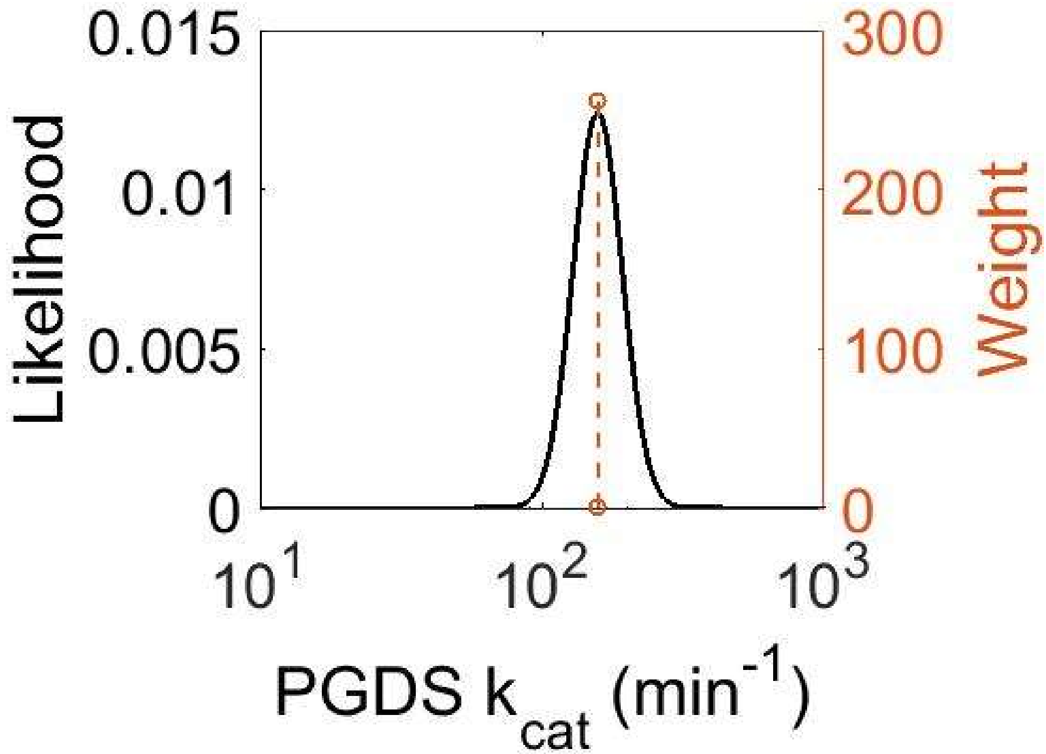


Figure SF.7.16.1.3.1. The estimated probability distribution for the PGDS k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.16.1.4. Parameter: PGDS K_{eq}

Parameter values for the K_{eq} of Reaction 21 were obtained from the literature and summarised in Table ST.7.16.1.4.1. The log-normal distribution properties for the K_{eq} of Reaction 21 are shown in Table ST.7.16.1.4.2 and plotted in Figure SF.7.16.1.4.1.

Table ST.7.16.1.4.1. Literature information used to design the PGDS K_{eq} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

ΔG (kcal/mol)	K_{eq}	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
-6.64	7.46 x10^{4}	Human	Unknown	PGDS	7	Unknown		64	0	(Caspi et al., 2018)

Table ST.7.16.1.4.2. The log-normal distribution properties of the PGDS K_{eq} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
7.46 x10^{4}	1.00 x10^{1}	1.20 x10^{1}	8.90 x10^{-1}

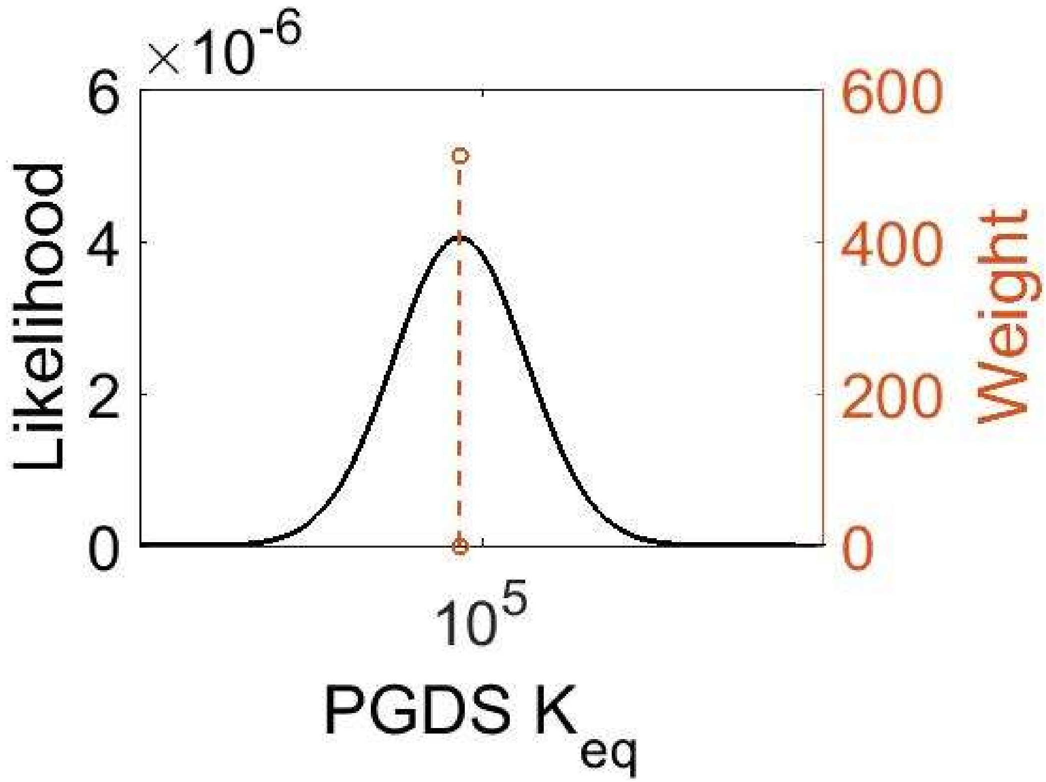


Figure SF.7.16.1.4.1. The estimated probability distribution for the PGDS K_{eq}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.16.1.5. Parameter: PGDS concentration

Parameter values for the PGDS concentration of Reaction 21 were obtained from the literature and summarised in Table ST.7.16.1.5.1. The log-normal distribution properties for the PGDS concentration of Reaction 21 are shown in Table ST.7.16.1.5.2 and plotted in Figure SF.7.16.1.5.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.7.16.1.5.1. Literature information used to design the PGDS concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
4.45 x10^{1}	NaN	Human	Skin	PGDS	7.5	37		**2048**	0	(Wilhelm et al., 2014)
6.79 x10^{1}	NaN	Human	Oesophagus	PGDS	7.5	37		**1024**	0	(Kim et al., 2014)
1.01 x10^{2}	NaN	Human	Oral cavity	PGDS	7.5	37		**1024**	0	(Wilhelm et al., 2014)
1.56 x10^{2}	NaN	Human	Pancreas	PGDS	7.5	37		**1024**	0	(Kim et al., 2014)

Table ST.7.16.1.5.2. The log-normal distribution properties of the PGDS concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
6.76 x10^{1}	3.74 x10^{-4}	1.64	4.41	4.49 x10^{-1}

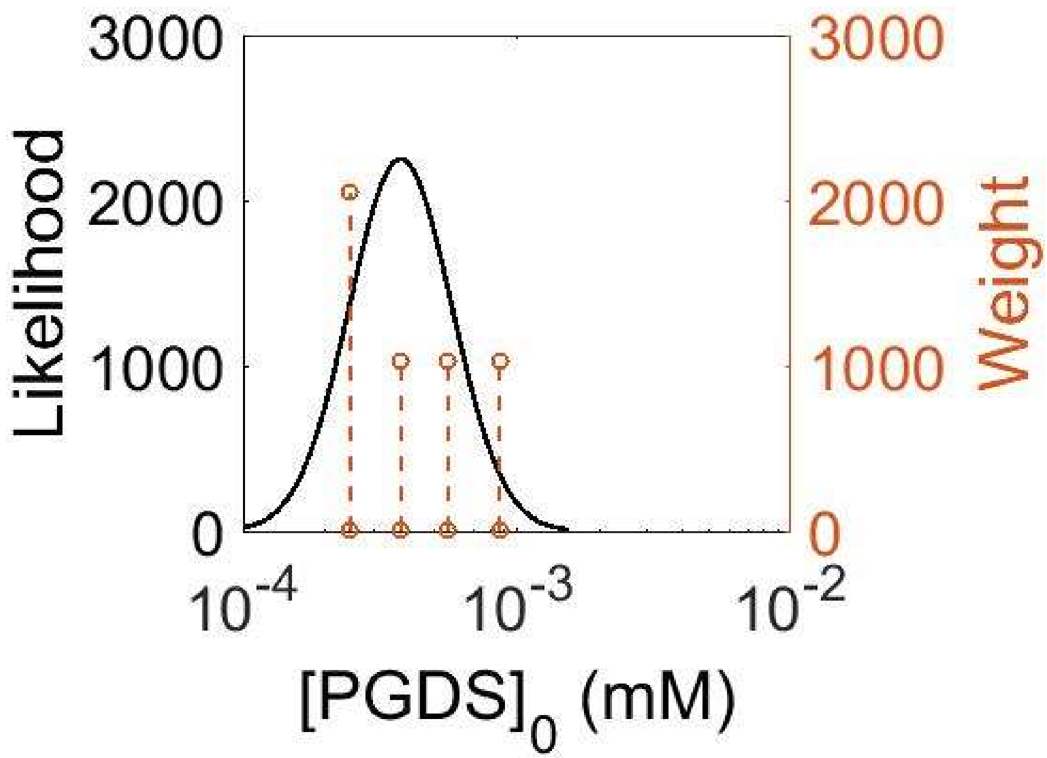


Figure SF.7.16.1.5.1. The estimated probability distribution for the PGDS concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.17 Reaction 65: AA = PGH_2

COX-1, the constitutively expressed isoform of COX, mediates the production of PGH2 from AA. This is a two-step reaction of cyclooxygenation and oxygenation, followed by a hydroperoxide reduction. The cyclooxygenase reaction occurs in the hydrophobic channel within the core of the protein and generates PGG_2. The subsequent peroxidase reaction produces PGH_2 and occurs at the heme-containing active site near the protein surface. The two step reaction results in the insertion of molecular oxygen across the C-9 and C-11 double bonds.

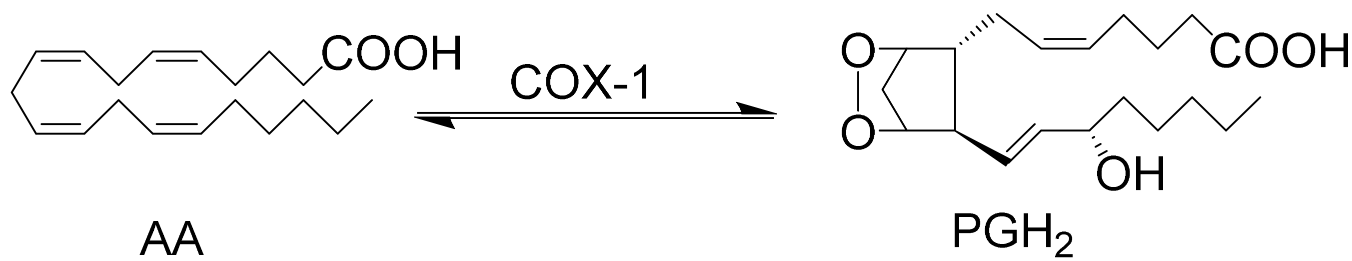


Figure SF.7.17. The cyclooxygenation and oxygenation reaction, followed by a hydroperoxide reduction of arachidonic acid (AA) into prostaglandin H_2 (PGH_2) by cyclooxygenase 1 (COX-1) (Reaction 65).

SEq.7.17. Reaction rate law for Reaction 65.

$$v_{65} = \frac{K_{cat} \cdot [COX-1]\left([AA] - {[PGH_2]}/{K_{eq}}\right)}{K_{m_S}\left(1 + \frac{[PGH_2]}{K_{m_P}}\right) + [AA]}$$

S.7.17.1. Reaction parameters

S.7.17.1.1. Parameter: COX-1 K_{ms}

Parameter values for the K_{ms} of Reaction 65 were obtained from the literature and summarised in Table ST.7.17.1.1.1. The log-normal distribution properties for the K_{ms} of Reaction 65 are shown in Table ST.7.17.1.1.2 and plotted in Figure SF.7.17.1.1.1.

Table ST.7.17.1.1.1. Literature information used to design the COX-1 K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
8.80 $\times 10^{-3}$	2.20 $\times 10^{-3}$	Human	Human cell	COX-1	7.6	37		2048	0	(Noreen et al., 1998)
1.90 $\times 10^{-3}$	2.00 $\times 10^{-4}$	Ram	Ram cell	COX-1	8	30		192	0	(Mukherjee et al., 2007)

Table ST.7.17.1.1.2. The log-normal distribution properties of the COX-1 K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
8.30 $\times 10^{-3}$	1.62	-4.60	4.41 $\times 10^{-1}$

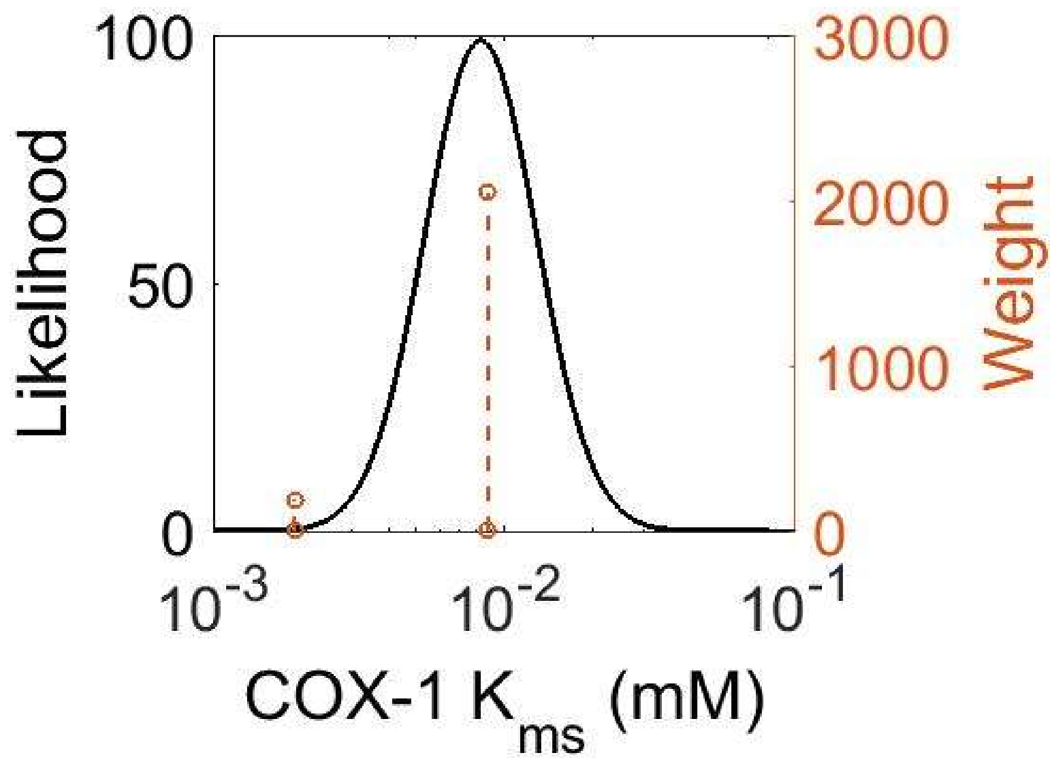


Figure SF.7.17.1.1.1. The estimated probability distribution for COX-1 K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.17.1.2. Parameter: COX-1 K_{mp}

The log-normal distribution for the parameter for the K_{mp} of Reaction 65 was calculated using multivariate distributions. The log-normal distribution properties for the K_{mp} of Reaction 65 are shown in Table ST.7.17.1.2.1 and plotted in Figure SF.7.17.1.2.1.

Table ST.7.17.1.2.1. The log-normal distribution properties of the COX-1 K_{mp} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Location parameter (μ)	Scale parameter (σ)
8.20×10^{-3}	-4.60	4.49×10^{-1}

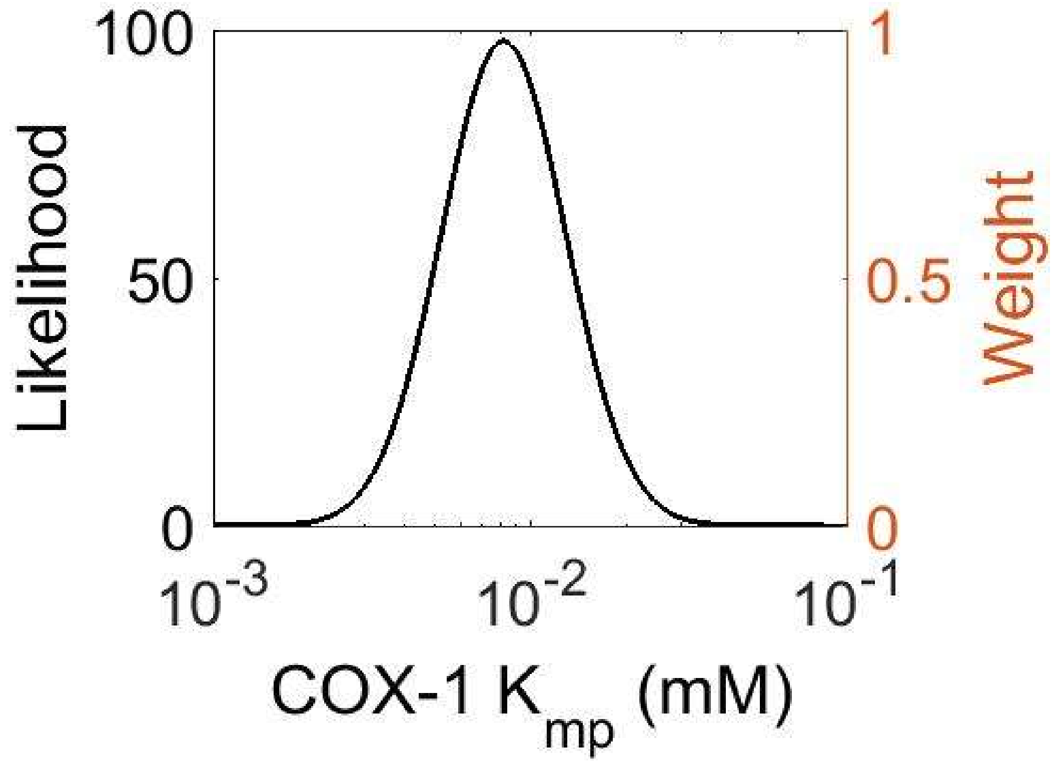


Figure SF.7.17.1.2.1. The estimated probability distribution for COX-1 K_{mp}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.17.1.3. Parameter: COX-1 k_{cat}

Parameter values for the k_{cat} of Reaction 65 were obtained from the literature and summarised in Table ST.7.17.1.3.1. The log-normal distribution properties for the k_{cat} of Reaction 65 are shown in Table ST.7.17.1.3.2 and plotted in Figure SF.7.17.1.3.1.

Table ST.7.17.1.3.1. Literature information used to design the COX-1 k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
8.82×10^{3}	3.60×10^{2}	Ram	Ram cell	COX-1	8	30		192	0	(Mukherjee et al., 2007)

Table ST.7.17.1.3.2. The log-normal distribution properties of the COX-1 K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
8.81×10^{3}	1.04	9.09	4.08×10^{-2}

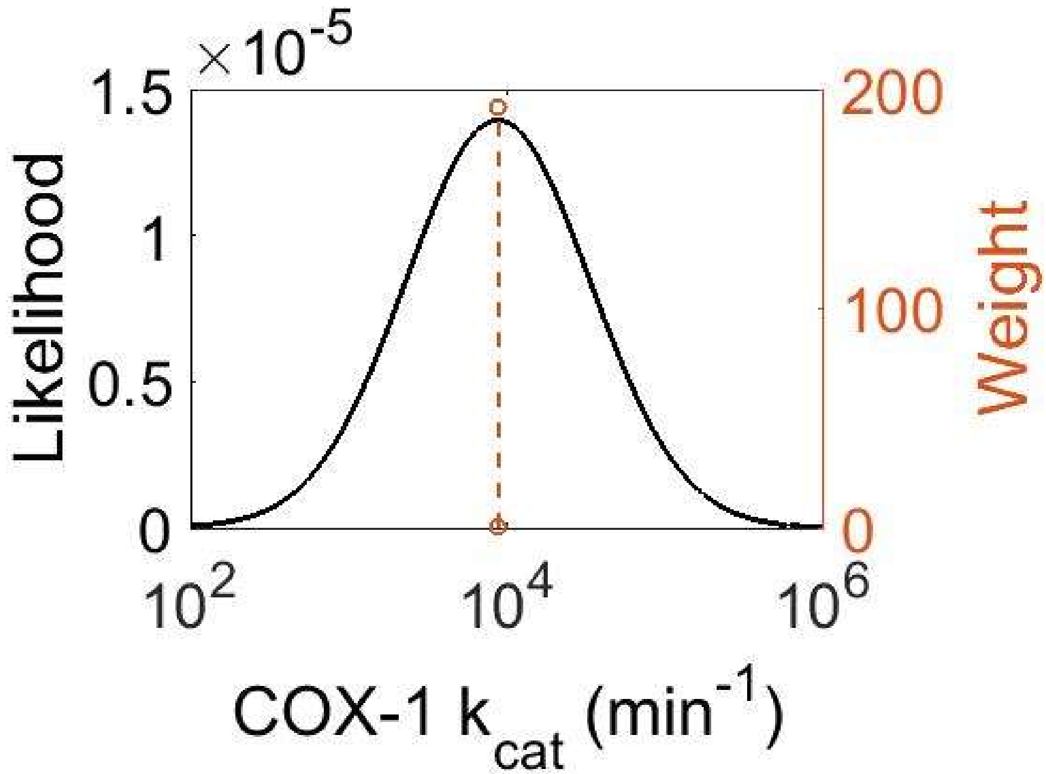


Figure SF.7.17.1.3.1. The estimated probability distribution for COX-1 k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.17.1.4. Parameter: COX-1 Keq

Parameter values for the K_{eq} of Reaction 65 were obtained from the literature and summarised in Table ST.7.17.1.4.1. The log-normal distribution properties for the K_{eq} of Reaction 65 are shown in Table ST.7.17.1.4.2 and plotted in Figure SF.7.17.1.4.1.

Table ST.7.17.1.4.1. Literature information used to design the COX-1 K_{eq} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

ΔG (kcal/mol)	K_{eq}	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
-3.90 x10^{1}	4.18 x10^{28}	Human	Unknown	COX-1	7	Unknown		64	0	(Caspi et al., 2018)

Table ST.7.17.1.4.2. The log-normal distribution properties of the COX-1 K_{eq} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
4.18 x10^{28}	1.00 x10^{1}	6.67 x10^{1}	8.90 x10^{-1}

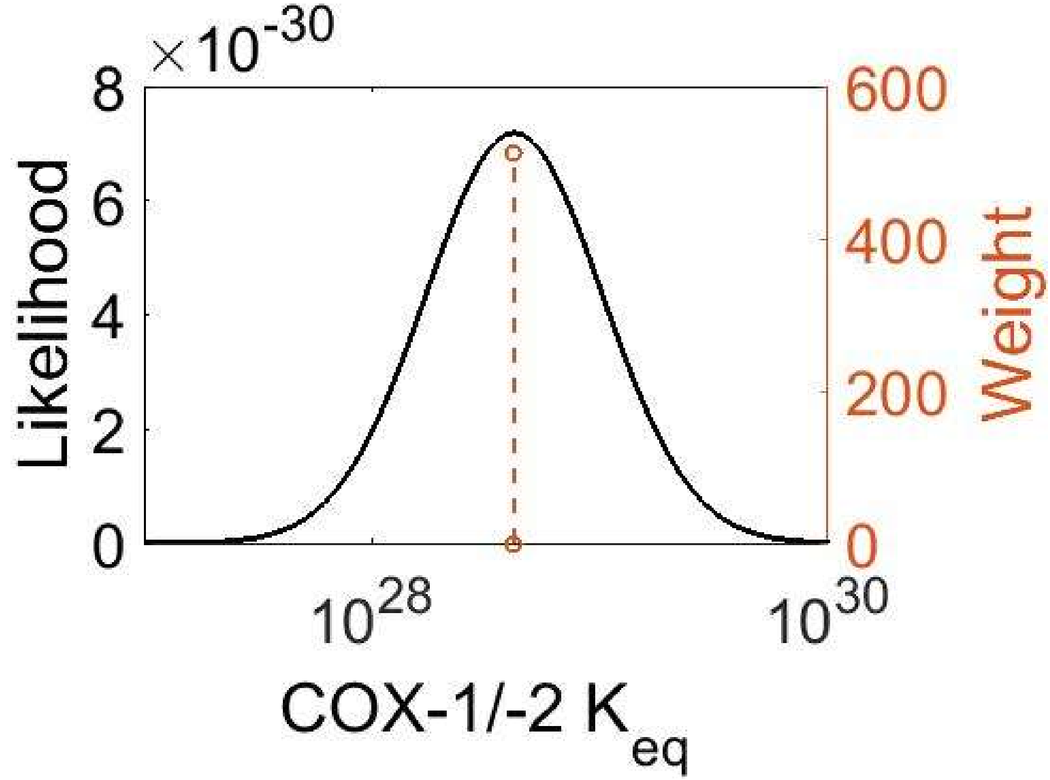


Figure SF.7.17.1.4.1. The estimated probability distribution for COX-1 K_{eq}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.17.1.5. Parameter: COX-1 concentration

Parameter values for the COX-1 concentration of Reaction 65 were obtained from the literature and summarised in Table ST.7.17.1.5.1. The log-normal distribution properties for the COX-1 concentration of Reaction 65 are shown in Table ST.7.17.1.5.2 and plotted in Figure SF.7.17.1.5.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.7.17.1.5.1. Literature information used to design the COX-1 concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.91×10^{1}	NaN	Human	Lung	COX-1	7.5	37		**1024**	0	(Kim et al., 2014)
7.08×10^{1}	NaN	Human	Oral cavity	COX-1	7.5	37		**1024**	0	(Wilhelm et al., 2014)
1.30×10^{2}	NaN	Human	Oesophagus	COX-1	7.5	37		**1024**	0	(Wilhelm et al., 2014)
2.08×10^{2}	NaN	Human	Stomach	COX-1	7.5	37		**1024**	0	(Wilhelm et al., 2014)
8.49×10^{2}	NaN	Human	Platelet	COX-1	7.5	37		**1024**	0	(Kim et al., 2014)

Table ST.7.17.1.5.2. The log-normal distribution properties of the COX-1 concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.29×10^{2}	7.14×10^{-4}	3.49	5.66	8.94×10^{-1}

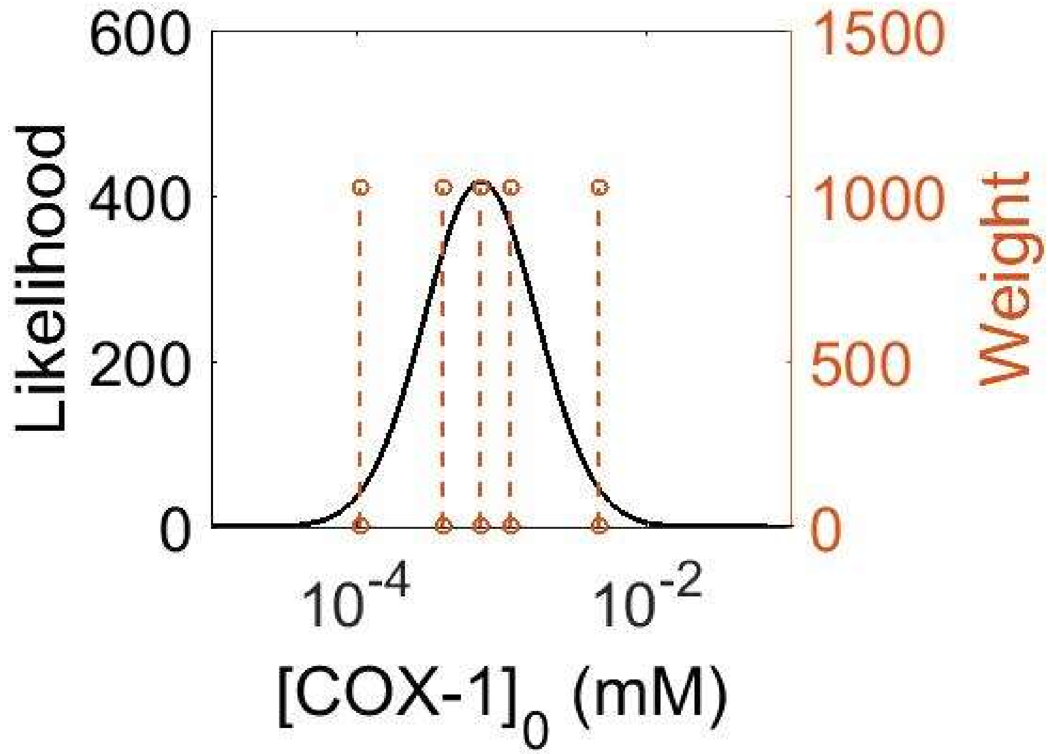


Figure SF.7.17.1.5.1. The estimated probability distribution for the COX-1 concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.18 Reaction 66: $PGE_2 \rightleftharpoons$ 15-keto-PGE_2

PGE_2 is metabolised by 15-prostoglandin dehydrogenase (15-PGDH), via the oxidation of the 15(S)-hydroxyl group of PGE_2 into a ketone (Anggard and Samuelsson, 1965). The product of this reaction, 15-keto-PGE_2, has less biological activity than PGE_2 therefore is of therapeutic interest (Lim et al., 2010; Myung et al., 2006).

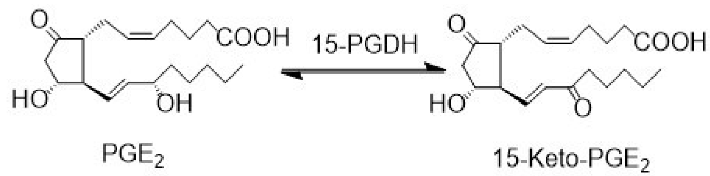


Figure SF.7.18. The oxidation reaction of prostaglandin E_2 (PGE_2) into 15-keto-prostaglandin E_2 (15-keto-PGE_2), by 15-prostoglandin dehydrogenase (15-PGDH) (Reaction 66).

SEq.7.18. Reaction rate law for Reaction 66.

$$v_{66} = \frac{K_{cat} \cdot [15-PGDH]\left([PGE_2] - {[15-\text{keto}-\text{PGE}_2]}/{K_{eq}}\right)}{K_{m_s}\left(1 + \frac{[15-\text{keto}-\text{PGE}_2]}{K_{m_p}}\right) + [PGE_2]}$$

S.7.18.1. Reaction parameters

S.7.18.1.1. Parameter: 15-PGDH K_{ms}

Parameter values for the K_{ms} of Reaction 66 were obtained from the literature and summarised in Table ST.7.18.1.1.1. The log-normal distribution properties for the K_{ms} of Reaction 66 are shown in Table ST.7.18.1.1.2 and plotted in Figure SF.7.18.1.1.1.

Table ST.7.18.1.1.1. Literature information used to design the 15-PGDH K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
8.00 x10^{-3}		Rat	Skin	15-PGDH	7	37		1024		(Fincham and Camp, 1983)
7.50 x10^{-3}		Rat	Skin	15-PGDH	7	37		1024		(Fincham and Camp, 1983)
2.40 x10^{-2}		Rat	Skin	15-PGDH	7	37		1024		(Fincham and Camp, 1983)
2.30 x10^{-2}		Rat	Skin	15-PGDH	7	37		1024		(Fincham and Camp, 1983)
3.90 x10^{-3}		Human	E. coli.	15-PGDH	7	37		1024		(Zhou et al., 2001)
9.90 x10^{-3}		Rat	E. coli.	15-PGDH	7	37		512		(Zhou et al., 2001)
5.50 x10^{-3}	6.00 x10^{-4}	Human	E. coli.	15-PGDH	7	37		1024		(Niesen et al., 2010)

Table ST.7.18.1.1.2. The log-normal distribution properties of the 15-PGDH K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
7.64 $x10^{-3}$	5.05	-4.41	6.80 $x10^{-1}$

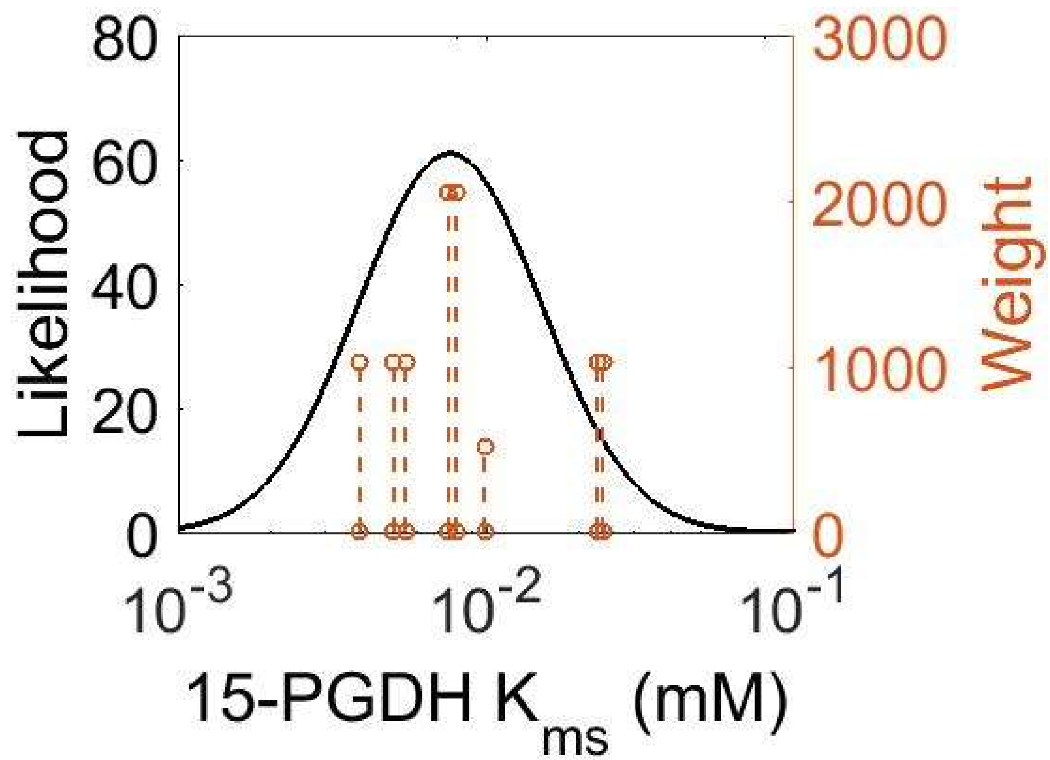


Figure SF.7.18.1.1.1. The estimated probability distribution for 15-PGDH K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.18.1.2. Parameter: 15-PGDH K_{mp} (Dependent parameter)

The log-normal distribution for the parameter for the K_{mp} of Reaction 66 was calculated using multivariate distributions. The log-normal distribution properties for the K_{mp} of Reaction 66 are shown in Table ST.7.18.1.2.1 and plotted in Figure SF.7.18.1.2.1.

Table ST.7.18.1.2.1. The log-normal distribution properties of the 15-PGDH K_{mp} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Location parameter (μ)	Scale parameter (σ)
7.70 x10^{-3}	-4.41	6.72 x10^{-1}

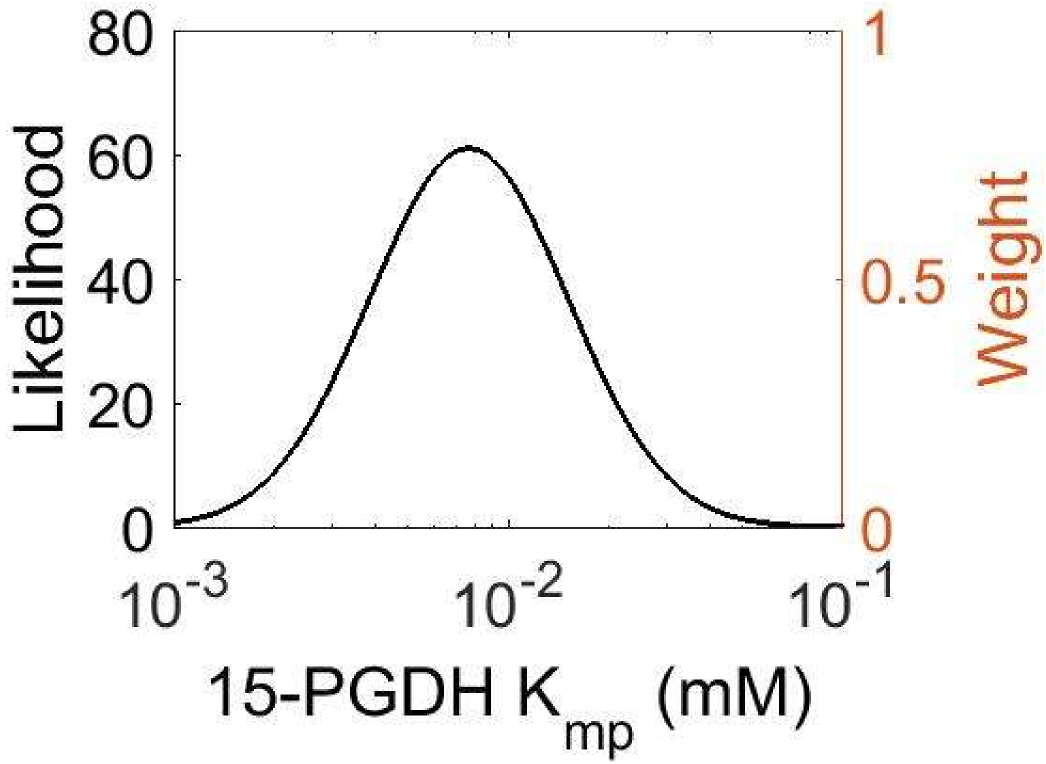


Figure SF.7.18.1.2.1. The estimated probability distribution for 15-PGDH K_{mp}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.18.1.3. Parameter: 15-PGDH kcat

Parameter values for the k_{cat} of Reaction 66 were obtained from the literature and summarised in Table ST.7.18.1.3.1. The log-normal distribution properties for the k_{cat} of Reaction 66 are shown in Table ST.7.18.1.3.2 and plotted in Figure SF.7.18.1.3.1.

Table ST.7.18.1.3.1. Literature information used to design the 15-PGDH k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
8.16 x10^{2}	1.80 x10^{1}	Human	E. coli.	15-PGDH	8	25		128	0	(Niesen et al., 2010)
3.66 x10^{2}	1.20 x10^{1}	Human	E. coli.	15-PGDH	8	25		128		(Niesen et al., 2010)
8.46 x10^{2}	1.20 x10^{1}	Human	E. coli.	15-PGDH	8	25		128		(Niesen et al., 2010)

Table ST.7.18.1.3.2. The log-normal distribution properties of the 15-PGDH k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
8.12 x10^{2}	5.38	7.19	7.01 x10^{-1}

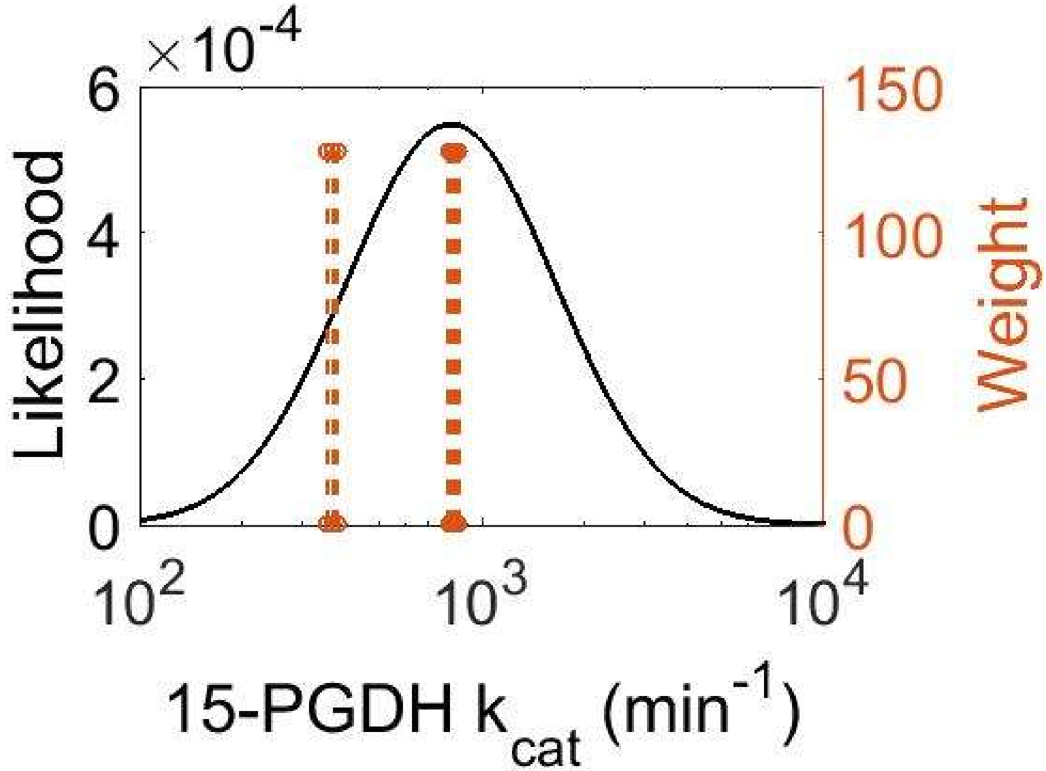


Figure SF.7.18.1.3.1. The estimated probability distribution for 15-PGDH k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.18.1.4. Parameter: 15-PGDH K_{eq}

Parameter values for the K_{eq} of Reaction 66 were obtained from the literature and summarised in Table ST.7.18.1.4.1. The log-normal distribution properties for the K_{eq} of Reaction 66 are shown in Table ST.7.18.1.4.2 and plotted in Figure SF.7.18.1.4.1.

Table ST.7.18.1.4.1. Literature information used to design the 15-PGDH K_{eq} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

ΔG (kcal/mol)	K_{eq}	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
-4.68×10^{-1}	2.21	Human	Unknown	15-PGDH	7	Unknown		64	0	(Caspi et al., 2018)

Table ST.7.18.1.4.2. The log-normal distribution properties of the 15-PGDH K_{eq} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
2.21	1.00×10^{1}	1.58	8.91×10^{-1}

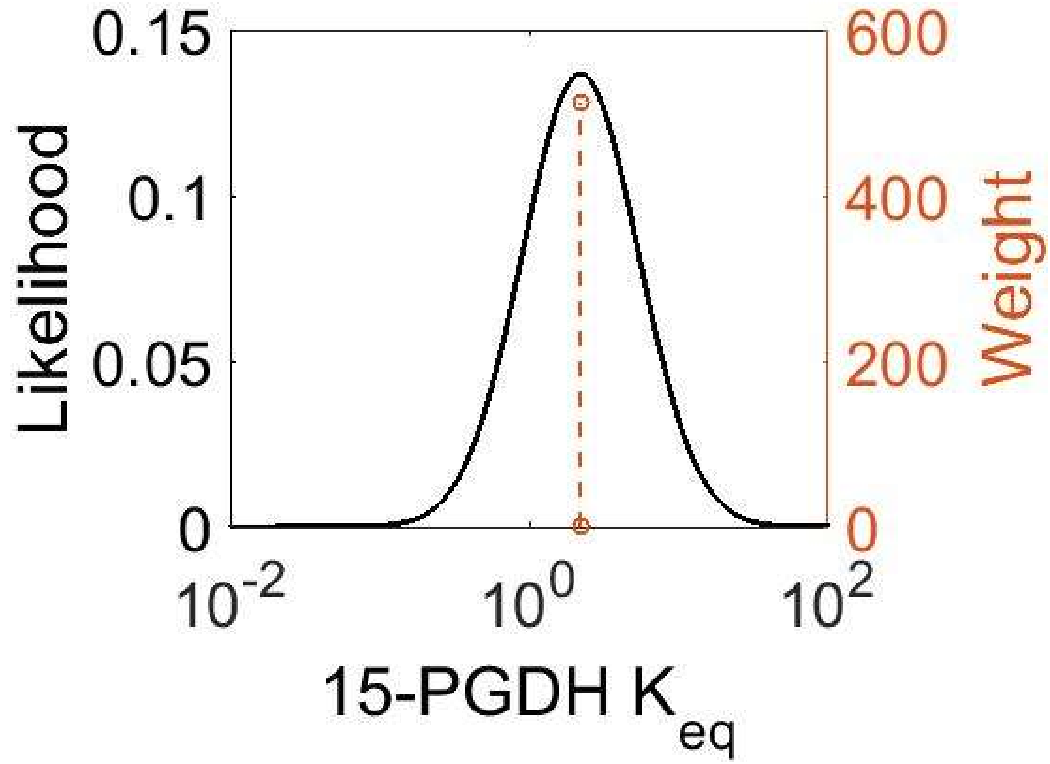


Figure SF.7.18.1.4.1. The estimated probability distribution for 15-PGDH K_{eq}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.18.1.5. Parameter: 15-PGDH concentration

Parameter values for the 15-PGDH concentration of Reaction 66 were obtained from the literature and summarised in Table ST.7.18.1.5.1. The log-normal distribution properties for the 15-PGDH concentration of Reaction 66 are shown in Table ST.7.18.1.5.2 and plotted in Figure SF.7.18.1.5.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.7.18.1.5.1. Literature information used to design the 15-PGDH concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
7.68	NaN	Human	Skin	15-PGDH	7.5	37		**2048**	0	(Kim et al., 2014)
1.12 x10^{1}	NaN	Human	Oesophagus	15-PGDH	7.5	37		**1024**	0	(Kim et al., 2014)
2.21 x10^{1}	NaN	Human	Heart	15-PGDH	7.5	37		**1024**	0	(Kim et al., 2014)
6.98 x10^{1}	NaN	Human	Oesophagus	15-PGDH	7.5	37		**1024**	0	(Wilhelm et al., 2014)

Table ST.7.18.1.5.2. The log-normal distribution properties of the 15-PGDH concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.12 x10^{1}	6.20 x10^{-5}	2.32	2.87	6.80 x10^{-1}

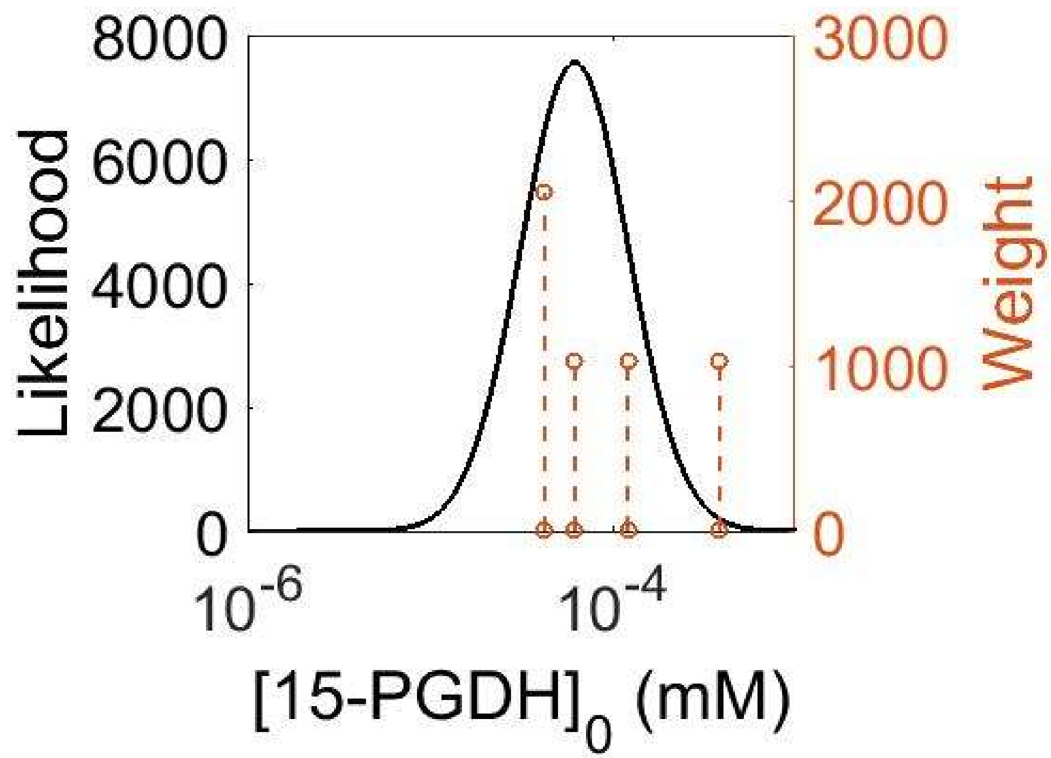


Figure SF.7.18.1.5.1. The estimated probability distribution for the 15-PGDH concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.19 Reaction 69: 15-keto-PGE$_2$ ⇌ 13,14-dihydro-15-keto-PGE$_2$

15-keto-PGE$_2$ is a substrate for prostaglandin reductase 2 (PTGR-2), which catalyses the formation of 13,14-dihydro-15-keto-PGE$_2$. In this reaction, the conjugated α, β-unsaturated double bond between C13 and C14 is reduced.

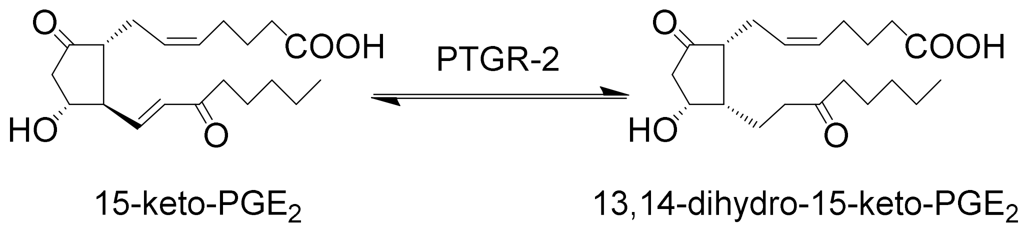


Figure SF.7.19. The reduction of 15-keto-prostaglandin E$_2$ (15-keto-PGE$_2$) to 13,14-dihydro-15-keto-prostaglandin E$_2$ (13,14-dihydro-15-keto-PGE$_2$), by prostaglandin reductase 2 (PTGR-2) (Reaction 69).

SEq.7.19. Reaction rate law for Reaction 69.

$$\boldsymbol{v_{69}} = \frac{K_{cat}\cdot[\mathrm{PTGR2}]\left([\mathrm{15-keto-PGE_2}] - {[\mathrm{13{,}14-dihydro-15-keto-PGE_2}]}/{K_{eq}}\right)}{K_{m_s}\left(1+\frac{[\mathrm{13{,}14-dihydro-15-keto-PGE_2}]}{K_{m_p}}\right)+[\mathrm{15-keto-PGE_2}]}$$

S.7.19.1. Reaction parameters

S.7.19.1.1. Parameter: PTGR-2 K_{ms}

Parameter values for the K_{ms} of Reaction 69 were obtained from the literature and summarised in Table ST.7.19.1.1.1. The log-normal distribution properties for the K_{ms} of Reaction 69 are shown in Table ST.7.19.1.1.2 and plotted in Figure SF.7.19.1.1.1.

Table ST.7.19.1.1.1. Literature information used to design the PTGR-2 K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.12 $\times10^{-2}$	1.40 $\times10^{-4}$	Human	E Coli	PTGR2	7	37		**512**		(Wu et al., 2008)
1.59 $\times10^{-2}$	1.71 $\times10^{-3}$	Human	E Coli	PTGR2	7	37		**512**		(Wu et al., 2008)

Table ST.7.19.1.1.2. The log-normal distribution properties of the PTGR-2 K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.20 $\times10^{-2}$	4.92	-3.97	6.71 $\times10^{-1}$

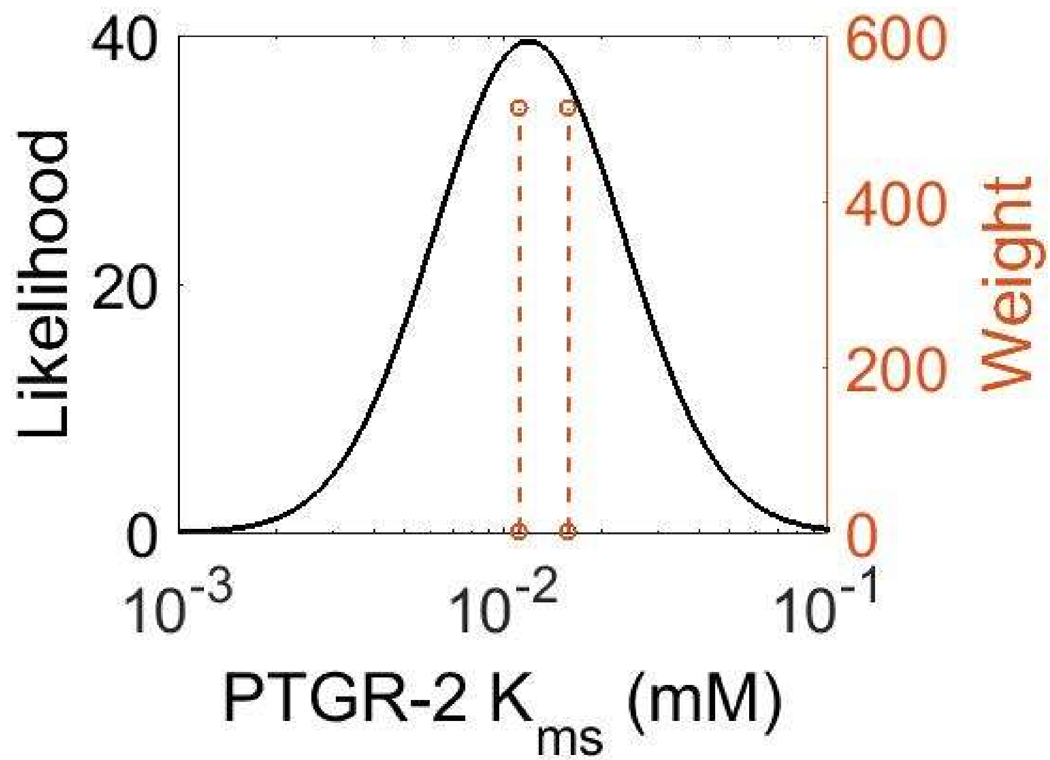


Figure SF.7.19.1.1.1. The estimated probability distribution for PTGR-2 K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.19.1.2. Parameter: PTGR-2 K_{mp}

The log-normal distribution for the parameter for the K_{mp} of Reaction 69 was calculated using multivariate distributions. The log-normal distribution properties for the K_{mp} of Reaction 69 are shown in Table ST.7.19.1.2.1 and plotted in Figure SF.7.19.1.2.1.

Table ST.7.19.1.2.1. The log-normal distribution properties of the PTGR-2 K_{mp} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Location parameter (μ)	Scale parameter (σ)
1.19 x10^{-2}	-3.97	6.81 x10^{-1}

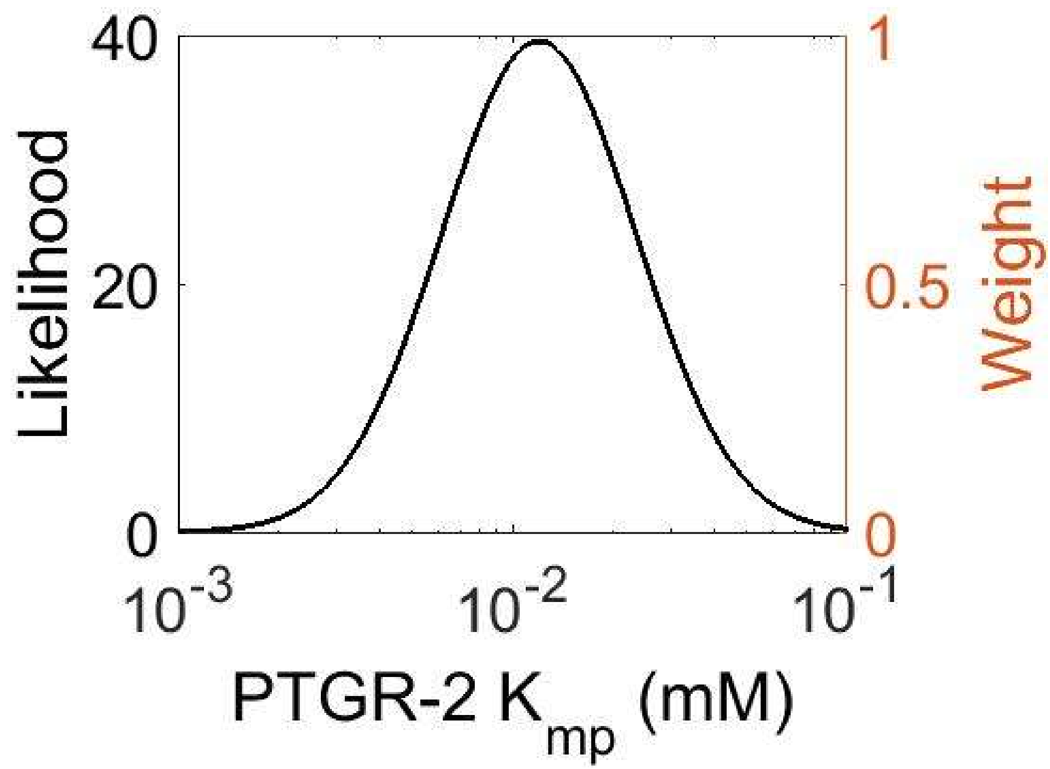


Figure SF.7.19.1.2.1. The estimated probability distribution for PTGR-2 K_{mp}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.19.1.3. Parameter: PTGR-2 k_{cat}

Parameter values for the k_{cat} of Reaction 69 were obtained from the literature and summarised in Table ST.7.19.1.3.1. The log-normal distribution properties for the k_{cat} of Reaction 69 are shown in Table ST.7.19.1.3.2 and plotted in Figure SF.7.19.1.3.1.

Table ST.7.19.1.3.1. Literature information used to design the PTGR-2 k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.14 x10^{1}	9.00 x10^{-1}	Mouse	Mouse cell	13,14-dehydro-15-oxoprostaglandin 13-reductase	7.4	37		384		(Wu et al., 2008)

Table ST.7.19.1.3.2. The log-normal distribution properties of the PTGR-2 k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.14 x10^{1}	9.86	3.22	8.87 x10^{-1}

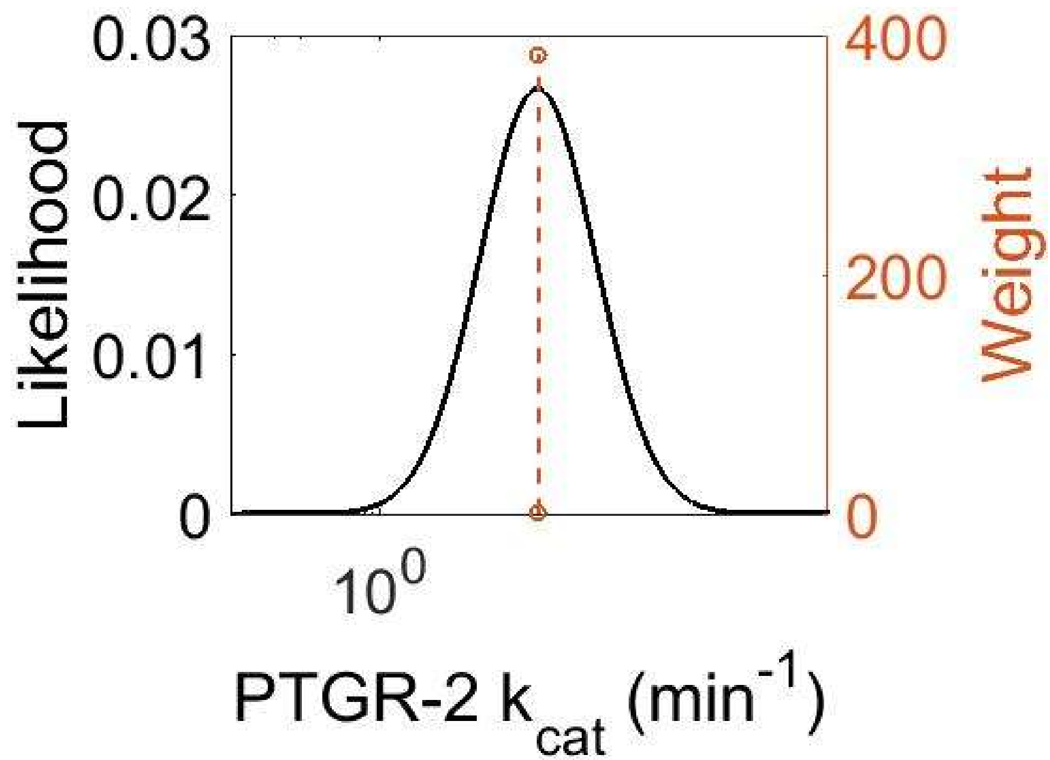


Figure SF.7.19.1.3.1. The estimated probability distribution for PTGR-2 k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.19.1.4. Parameter: PTGR-2 K_{eq}

Parameter values for the K_{eq} of Reaction 69 were obtained from the literature and summarised in Table ST.7.19.1.4.1. The log-normal distribution properties for the K_{eq} of Reaction 69 are shown in Table ST.7.19.1.4.2 and plotted in Figure SF.7.19.1.4.1.

Table ST.7.19.1.4.1. Literature information used to design the PTGR-2 K_{eq} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

ΔG (kcal/mol)	K_{eq}	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
3.60	2.28 x10^{-3}	Human	Unknown	15-PGDH	7	Unknown		64	0	(Caspi et al., 2018)

Table ST.7.19.1.4.2. The log-normal distribution properties of the PTGR-2 K_{eq} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
2.28 x10^{-3}	1.00 x10^{1}	-5.29	8.91 x10^{-1}

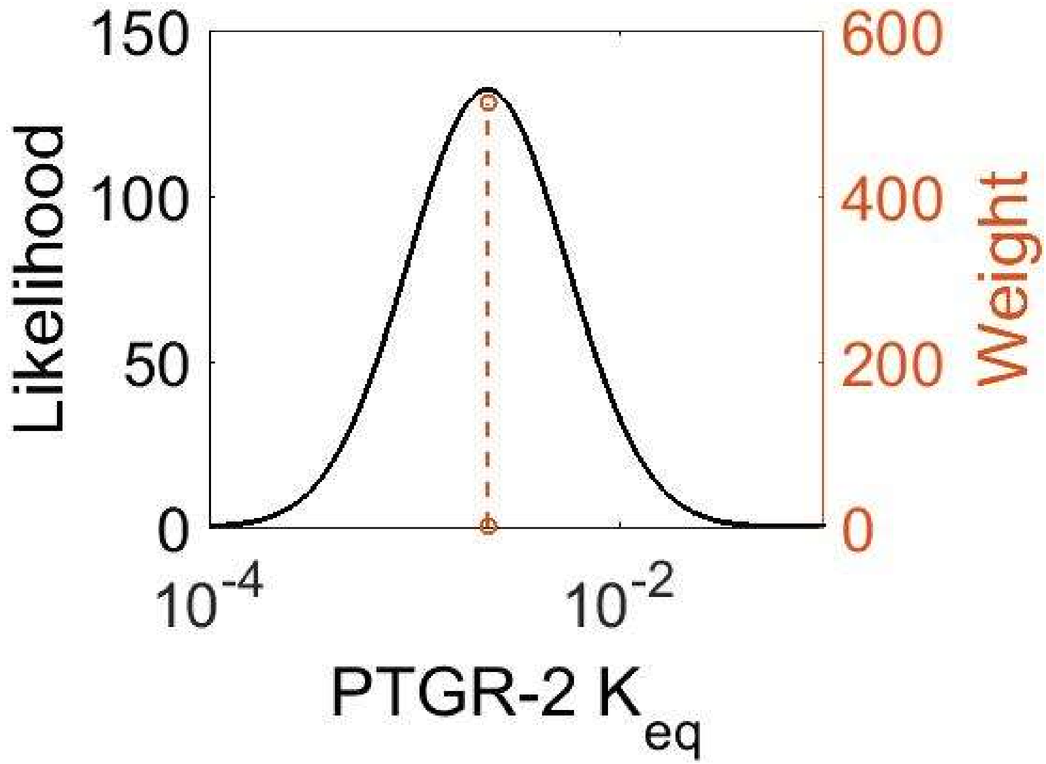


Figure SF.7.19.1.4.1. The estimated probability distribution for PTGR-2 K_{eq}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.7.19.1.5. Parameter: PTGR-2 concentration

Parameter values for the PTGR-2 concentration of Reaction 69 were obtained from the literature and summarised in Table ST.7.19.1.5.1. The log-normal distribution properties for the PTGR-2 concentration of Reaction 69 are shown in Table ST.7.19.1.5.2 and plotted in Figure SF.7.19.1.5.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.7.19.1.5.1. Literature information used to design the PTGR-2 concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.62×10^{2}		Human	Skin	PTGR2	7.5	37		2048		(Wilhelm et al., 2014)
8.09×10^{1}		Human	Skin	PTGR2	7.5	37		2048		(Wilhelm et al., 2014)
7.41×10^{1}		Human	Oral cavity	PTGR2	7.5	37		1024		(Wilhelm et al., 2014)

Table ST.7.19.1.5.2. The log-normal distribution properties of the PTGR-2 concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
8.65×10^{1}	4.79×10^{-4}	1.45	4.58	3.47×10^{-1}

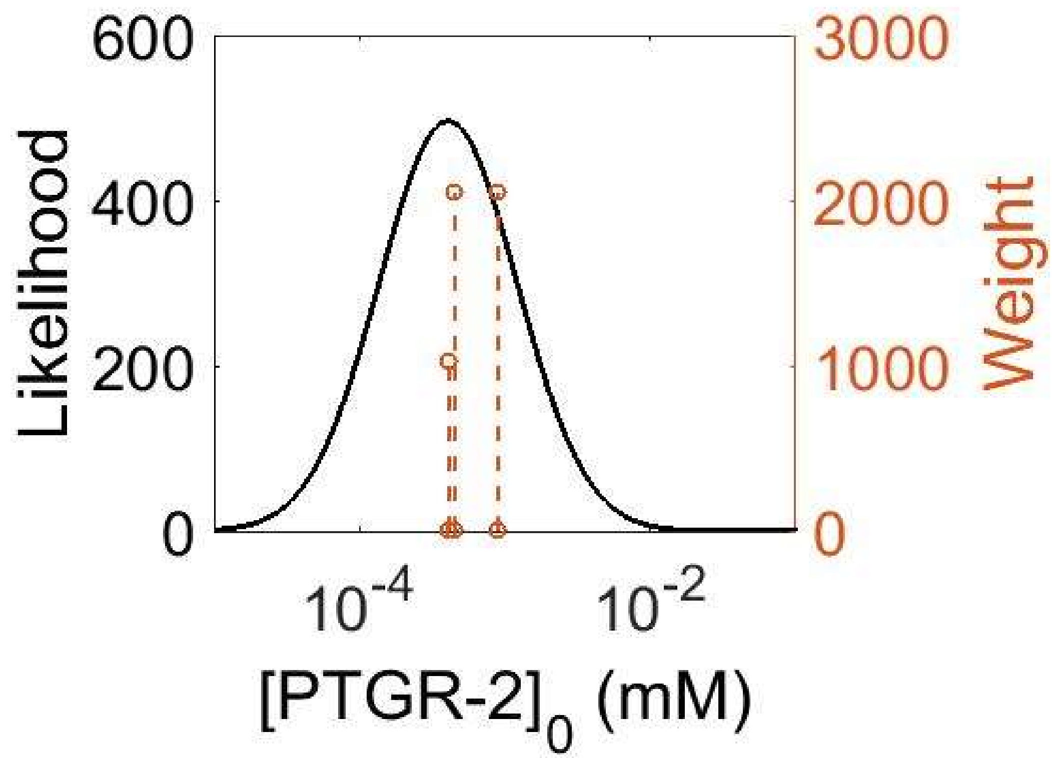


Figure SF.7.19.1.5.1. The estimated probability distribution for the PTGR-2 concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

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Supplementary Document S8. Non-enzymatic Reaction Structure and Parameterisation.

Documentation of parameter values obtained for all non-enzymatic reactions in the model (Reactions 6–9, 96–99; Supplementary Table S3) from the literature and associated uncertainty for the eicosanoid network model. Parameterisation was performed using the method of Tsigkinopoulou *et al.,* (2018). The table includes information regarding each reaction and its respective parameters are documented. This includes information such as the reaction rate law and the literature values that were used to define parameters, including experimental conditions, total weights and literature references from which the data were obtained. In this model some parameters are referred as "Dependent parameters", meaning that the log-normal distribution for that parameter was calculated using multivariate distributions (discussed in **Section 2.6.2**). As a result, no confidence interval factor or literature values were cited for the Dependent parameters.

Contents

S.8.1 Reaction 6: $TXA_2 \rightleftharpoons TXB_2$

Upon generating the unstable metabolite TXA_2, it is rapidly hydrolysed into TXB_2 via a non-enzymatic reaction. This inactive metabolite is produced by the incorporation of two hydrogens and one oxygen at C9 and C11, resulting in the opening of the trimethylene oxide ring, and the generation of two hydroxyl groups on the tetrahydropyran ring.

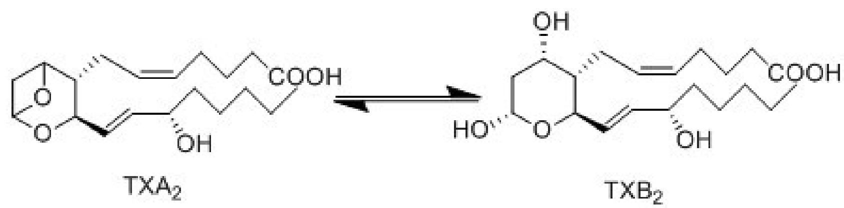

Figure SF.8.11. The non-enzymatic hydrolysis reaction of thromboxane A_2 (TXA_2) into thromboxane B_2 (TXB_2) (Reaction 6).

Equation SEq.8.2. Reaction rate law for Reaction 6.

$$v_6 = K_f[TXA_2] - K_r[TXB_2]$$

S.8.1.1. Reaction 6 parameters

S.8.1.1.1. Parameter: K_f

Parameter values for the K_f of Reaction 6 were obtained from the literature and summarised in Table ST.8.1.1.1.1. The log-normal distribution properties for the K_f of Reaction 6 are shown in Table ST.8.1.1.1.2 and plotted in Figure SF.8.1.1.1.1.

Table ST.8.1.1.1.1. Literature information used to design the Reaction 6 K_f parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (M^{-1} s^{-1})	Error (M^{-1} s^{-1})	Experimental details				Weight	Type of error	Reference
		Substrate type	Functional group	Temperature (°C)	Other			
3.70 x10^3	1.00 x10^2	Different cycle	Epoxide	25		**32**		(Ross et al., 1982)
8.70 x10^3		Different cycle	Epoxide	25		**32**		(Ross et al., 1982)
1.10 x10^4	1.00 x10^3	6 ring cycle	Epoxide	25		**48**		(Ross et al., 1982)
2.40 x10^4		6 ring cycle	Epoxide	25		**48**		(Ross et al., 1982)
3.70 x10^3	1.00 x10^2	Different cycle	Epoxide	25		**32**		(Ross et al., 1982)
3.60	2.00 x10^{-1}	Different cycle	Epoxide	25		**32**		(Ross et al., 1982)
1.70	1.00 x10^{-1}	Different cycle	Epoxide	25		**32**		(Ross et al., 1982)

2.67 x10^{1}	9.00 x10^{-1}	Different cycle	Epoxide	25		**32**		(Ross et al., 1982)
3.50 x10^{1}		Different cycle	Epoxide	25		**32**		(Ross et al., 1982)

Table ST.8.1.1.1.2. The log-normal distribution properties of the Reaction 6 K_f distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (M^{-1} s^{-1})	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
3.70 x10^{3}	3.44 x10^{1}	1.10 x10^{1}	1.66

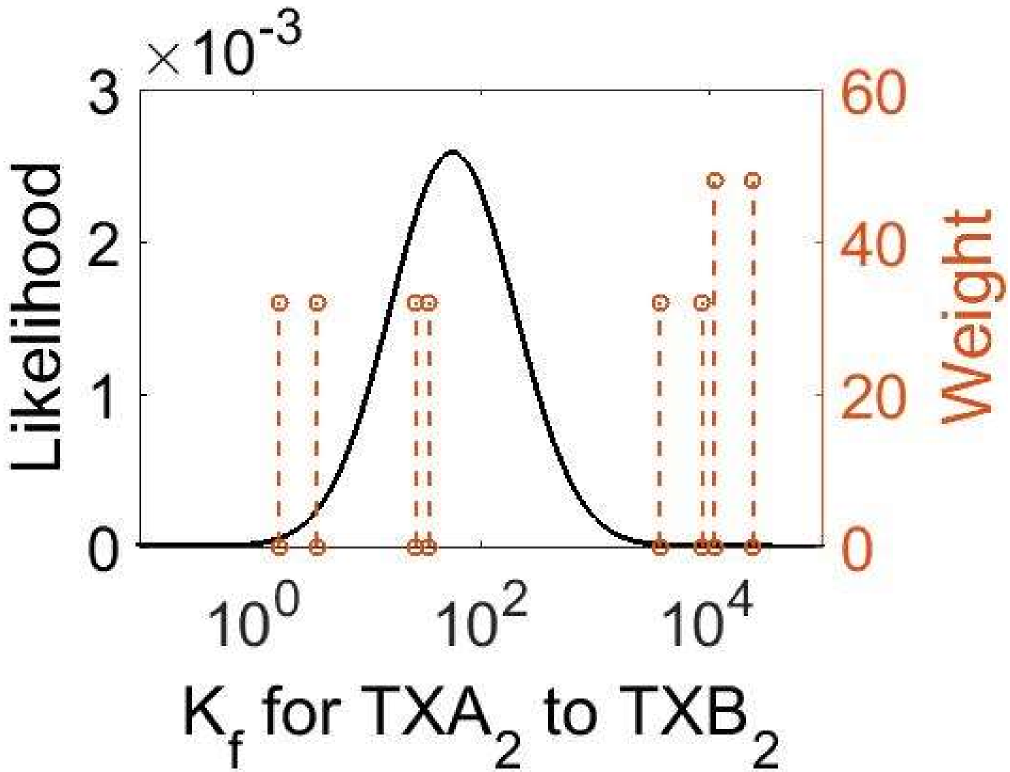

Figure SF.8.1.1.1.1. The estimated probability distribution for the Reaction 6 K_f. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.8.1.1.2. Parameter: K_D

Parameter values for the K_D of Reaction 6 were obtained from the literature and summarised in Table ST.8.1.1.2.1. The log-normal distribution properties for the K_D of Reaction 6 are shown in Table ST.8.1.1.2.2 and plotted in Figure SF.8.1.1.2.1.

Table ST.8.1.1.2.1. Literature information used to design the Reaction 6 K_D parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (M^{-1} min^{-1})	**Error (M^{-1} min^{-1})**	**Experimental details**				**Weight**	**Type of error**	**Reference**
		Species	**Substrate type**	**Temperature (°C)**	**Other**			
0.000038	NaN	Mosquito	Carbocyclic TXA2	35		**24**		(Alvarenga et al., 2010)
0.00000023	NaN	Rabbit	TXA2 antagonist	35		**36**		(Nakahata et al., 1992)
1500	500	N/A	Hydroxysulfamic acid	25		**16**		(D. LITTLEJOHN, 1988)
1.75×10^{-12}	NaN	N/A	H2O2			**16**		(D. LITTLEJOHN, 1988)
5.90×10^{-8}	NaN	N/A	Oxaplatin			**16**		(Jerremalm et al., 2003)

Table ST.8.1.1.2.2. The log-normal distribution properties of the Reaction 6 K_D distribution. These values were calculated using the functions described in Section 2.6.2.

Mode **(M^{-1} min^{-1})**	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
2.35 $x10^{-7}$	1.76 $x10^{4}$	-6.86	2.90

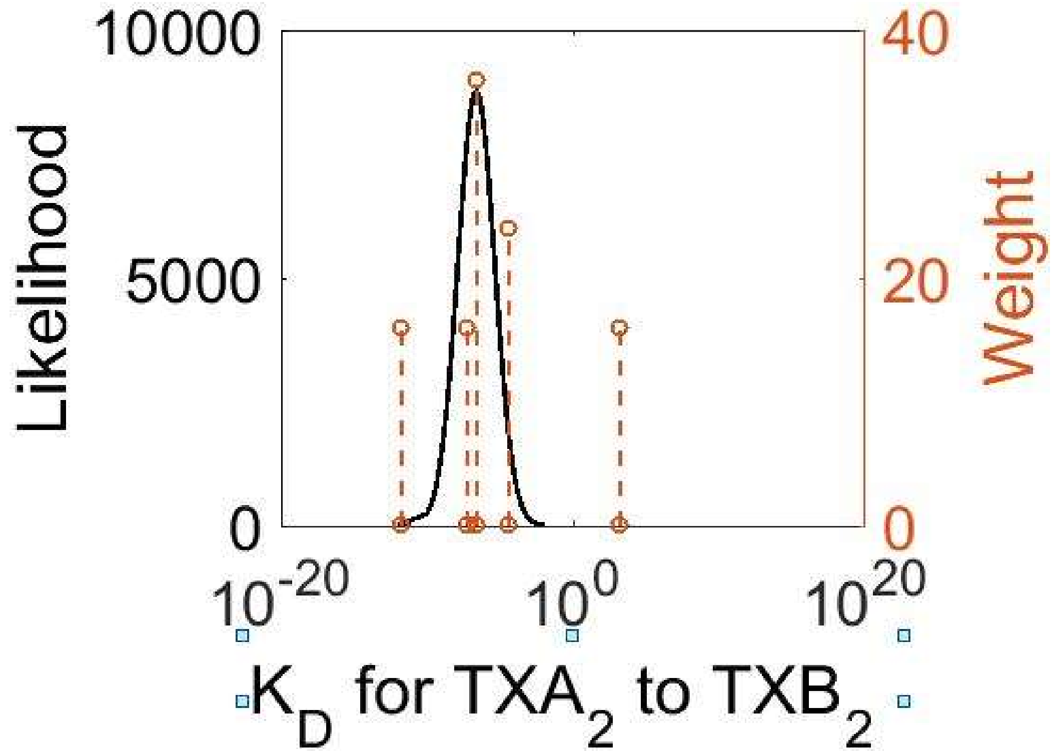

Figure SF.8.1.1.2.1. The estimated probability distribution for the Reaction 6 K_D. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.8.1.1.3. Parameter: K_r (Dependent parameter)

The log-normal distribution for the parameter for the K_r of Reaction 6 was calculated using multivariate distributions. The log-normal distribution properties for the K_r of Reaction 6 are shown in Table ST.8.1.1.3.1 and plotted in Figure SF.8.1.1.3.1.

Table ST.8.1.1.3.1. The log-normal distribution properties of the Reaction 6 K_r distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (M^{-1} min^{-1})	**Location parameter (μ)**	**Scale parameter (σ)**
5.28 $x10^1$	5.63	1.29

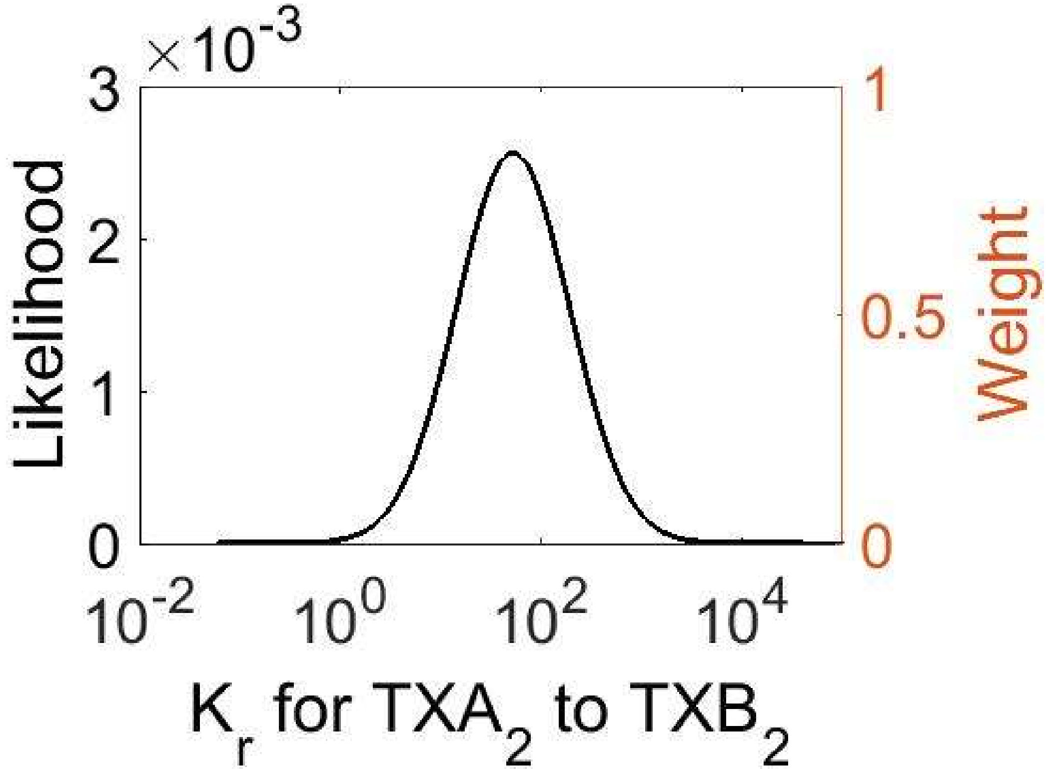

Figure SF.8.1.1.3.1. The estimated probability distribution Reaction 6 K_r. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.8.2. Reaction 7: $PGI_2 \rightleftharpoons$ 6-keto-$PGF_{1\alpha}$

Due to ring strain, PGI_2 is rapidly hydrolysed to 6-keto-$PGF_{1\alpha}$. This is a non-enzymatic reaction and results in the formation of a hydroxyl group at C9 and a ketone at C6, by incorporating two hydrogens and one oxygen.

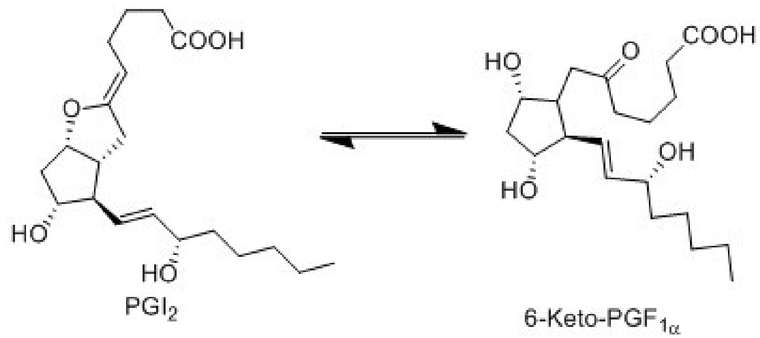

Figure SF.8.2. The non-enzymatic transformation of prostaglandin I_2 (PGI_2) into 6-keto-prostaglandin $F_{1\alpha}$ (6-keto-$PGF_{1\alpha}$) (Reaction 7).

Equation Seq.8.2. Reaction rate law for Reaction 7.

$$\boldsymbol{\nu_7 = K_f[PGI_2] - K_r[6 - keto - PGF_{1\alpha}]}$$

S.8.2.1. Reaction parameters

S.8.2.1.1. Parameter: K_f

Parameter values for the K_f of Reaction 7 were obtained from the literature and summarised in Table ST.8.2.1.1.1. The log-normal distribution properties for the K_f of Reaction 7 are shown in Table ST.8.2.1.1.2 and plotted in Figure SF.8.2.1.1.1.

Table ST.8.2.1.1.1. Literature information used to design the Reaction 7 K_f parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (M^{-1} s^{-1})	Error (M^{-1} s^{-1})	Experimental details				Weight	Type of error	Reference
		Substrate type	Functional group	Temperature (°C)	Other			
3.70 x10^3	1.00 x10^2	Different cycle	Epoxide	25		**32**		(Ross et al., 1982)
8.70 x10^3		Different cycle	Epoxide	25		**32**		(Ross et al., 1982)
1.10 x10^4	1.00 x10^3	6 ring cycle	Epoxide	25		**48**		(Ross et al., 1982)
2.40 x10^4		6 ring cycle	Epoxide	25		**48**		(Ross et al., 1982)
3.70 x10^3	1.00 x10^2	Different cycle	Epoxide	25		**32**		(Ross et al., 1982)
3.60	2.00 x10^{-1}	Different cycle	Epoxide	25		**32**		(Ross et al., 1982)

1.70	1.00 x10^{-1}	Different cycle	Epoxide	25		**32**		(Ross et al., 1982)
2.67 x10^{1}	9.00 x10^{-1}	Different cycle	Epoxide	25		**32**		(Ross et al., 1982)
3.50 x10^{1}		Different cycle	Epoxide	25		**32**		(Ross et al., 1982)

Table ST.8.2.1.1.2. The log-normal distribution properties of the Reaction 7 K_f distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (M^{-1} s^{-1})	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
3.70 x10^{3}	3.44 x10^{1}	1.10 x10^{1}	1.66

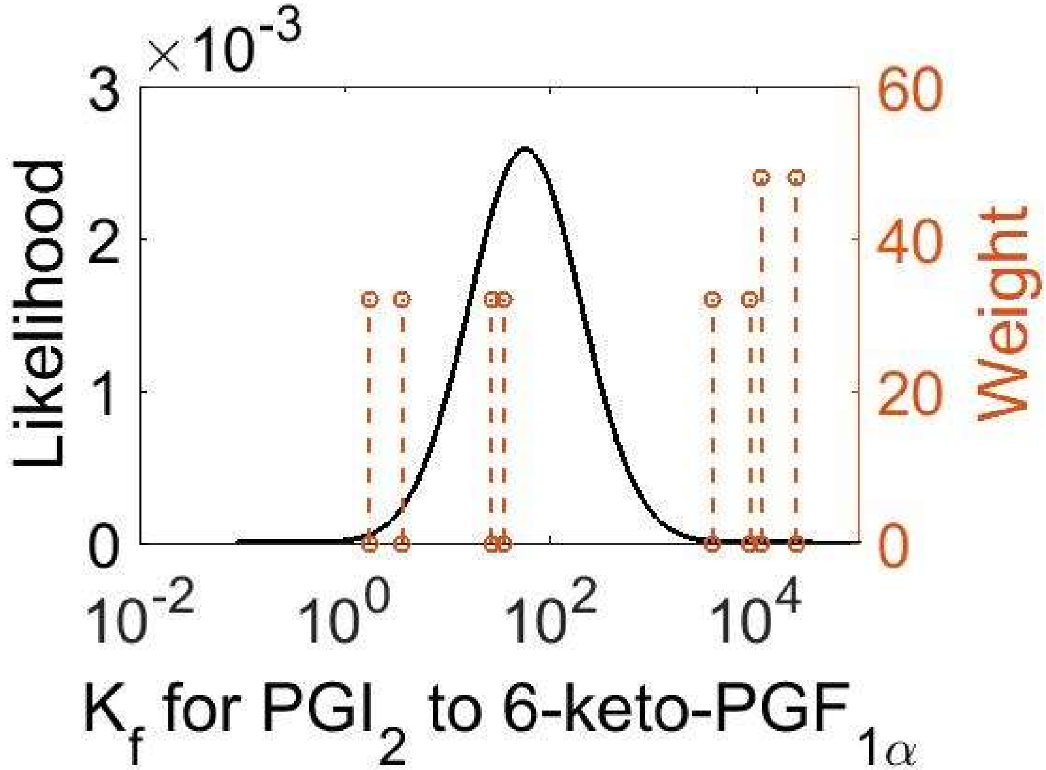

Figure SF.8.2.1.1.1. The estimated probability distribution for the Reaction 7 K_f. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.8.2.1.2. Parameter: K_D

Parameter values for the K_D of Reaction 7 were obtained from the literature and summarised in Table ST.8.2.1.2.1. The log-normal distribution properties for the K_D of Reaction 7 are shown in Table ST.8.2.1.2.2 and plotted in Figure SF.8.2.1.2.1.

Table ST.8.2.1.2.1. Literature information used to design the Reaction 7 K_D parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (M^{-1} min^{-1})	**Error (M^{-1} min^{-1})**	**Experimental details**				**Weight**	**Type of error**	**Reference**
		Species	**Substrate type**	**Temperature (°C)**	**Other**			
0.000038	NaN	Mosquito	Carbocyclic TXA2	35		**24**		(Alvarenga et al., 2010)
0.00000023	NaN	Rabbit	TXA2 antagonist	35		**36**		(Nakahata et al., 1992)
1500	500	N/A	Hydroxysulfamic acid	25		**16**		(D. LITTLEJOHN, 1988)
1.75×10^{-12}	NaN	N/A	H2O2			**16**		(D. LITTLEJOHN, 1988)
5.90×10^{-8}	NaN	N/A	Oxaplatin			**16**		(Jerremalm et al., 2003)

Table ST.8.2.1.2.2. The log-normal distribution properties of the Reaction 7 K_D distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (M^{-1} min^{-1})	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
2.35 $x10^{-7}$	1.76 $x10^{4}$	-6.86	2.90

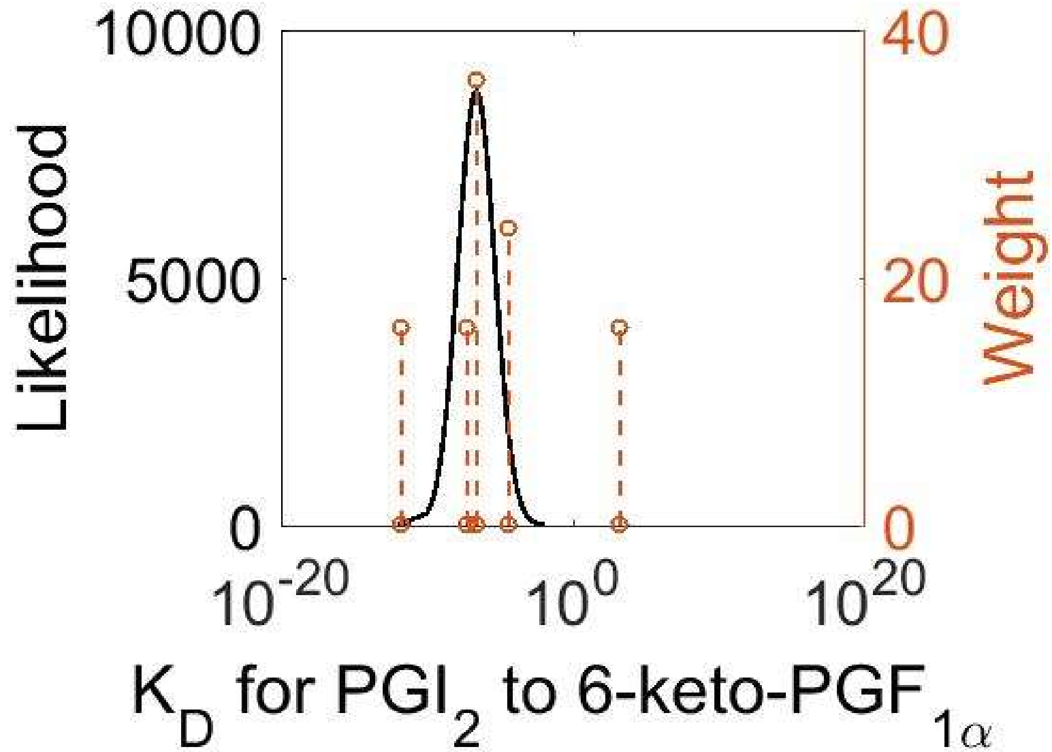

Figure SF.8.2.1.2.1. The estimated probability distribution for Reaction 7 K_D. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.8.2.1.3. Parameter: K_r (Dependent parameter)

The log-normal distribution for the parameter for the K_r of Reaction 7 was calculated using multivariate distributions. The log-normal distribution properties for the K_r of Reaction 7 are shown in Table ST.8.2.1.3.1 and plotted in Figure SF.8.2.1.3.1.

Table ST.8.2.1.3.1. The log-normal distribution properties of the Reaction 7 K_r distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (M^{-1} min^{-1})	**Location parameter (μ)**	**Scale parameter (σ)**
5.81 $x10^1$	5.60	1.24

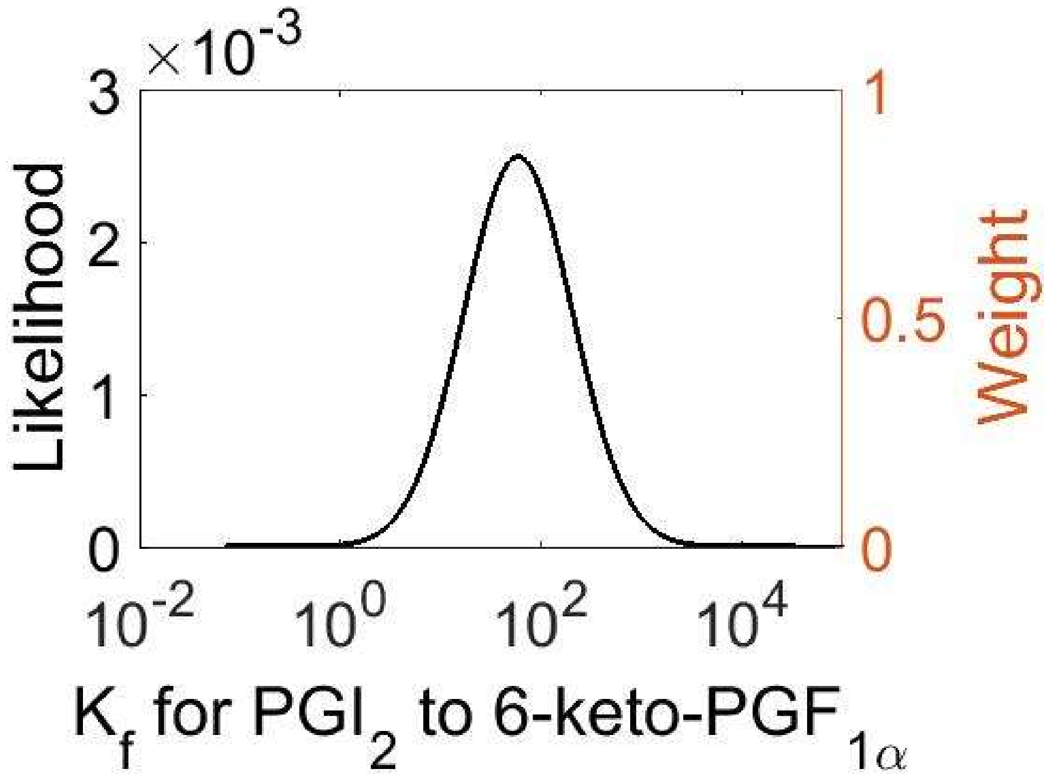

Figure SF.8.2.1.3.1. The estimated probability distribution for Reaction 7 K_f. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.8.3. Reaction 8: $PGD_2 \rightleftharpoons PGJ_2$

PGD_2 is subsequently converted to PGJ_2 via a non-enzymatic reaction (Fitzpatrick and Wynalda, 1983). This dehydration reaction includes the removal of two hydrogens and one oxygen molecule, and occurs across the C9 hydroxyl and the C10 carbon axis, to form a double bond between C9 and 10.

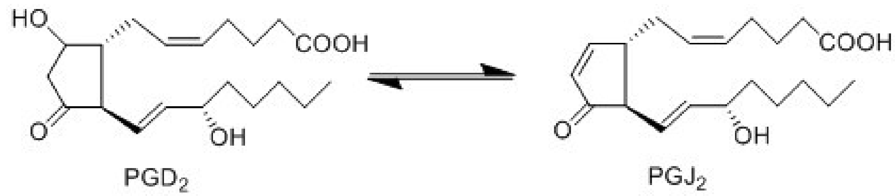

Figure SF.8.2. The non-enzymatic transformation of prostaglandin D_2 (PGD_2) into prostaglandin J_2 (PGJ_2) (Reaction 8).

SEq.8.3. Reaction rate law for Reaction 8.

$$\boldsymbol{v_8 = K_f[PGD_2] - K_r[PGJ_2]}$$

S.8.3.1. Reaction parameters

S.8.3.1.1. Parameter: K_f

Parameter values for the K_f of Reaction 8 were obtained from the literature and summarised in Table ST.8.3.1.1.1. The log-normal distribution properties for the K_f of Reaction 8 are shown in Table ST.8.3.1.1.2 and plotted in Figure SF.8.3.1.1.1.

Table ST.8.3.1.1.1. Literature information used to design the Reaction 8 K_f parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (M^{-1} min^{-1})	Error (M^{-1} min^{-1})	Experimental details				Weight	Type of error	Reference
		Substrate type	Functional group	Temperature (°C)	Other			
3.30 x10^{6}		Different	Carboxylic acid	25		32		(B. H. GIBBONS, 1963)
4.50		Different		20		32		(Tur'yan, 1998)
4.20 x10^{-1}		Different		20		32		(Ranney and Ziemann, 2016)

Table ST.8.3.1.1.2. The log-normal distribution properties of the Reaction 8 k_f distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (M^{-1} min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
4.48	1.09×10^3	7.34	2.42

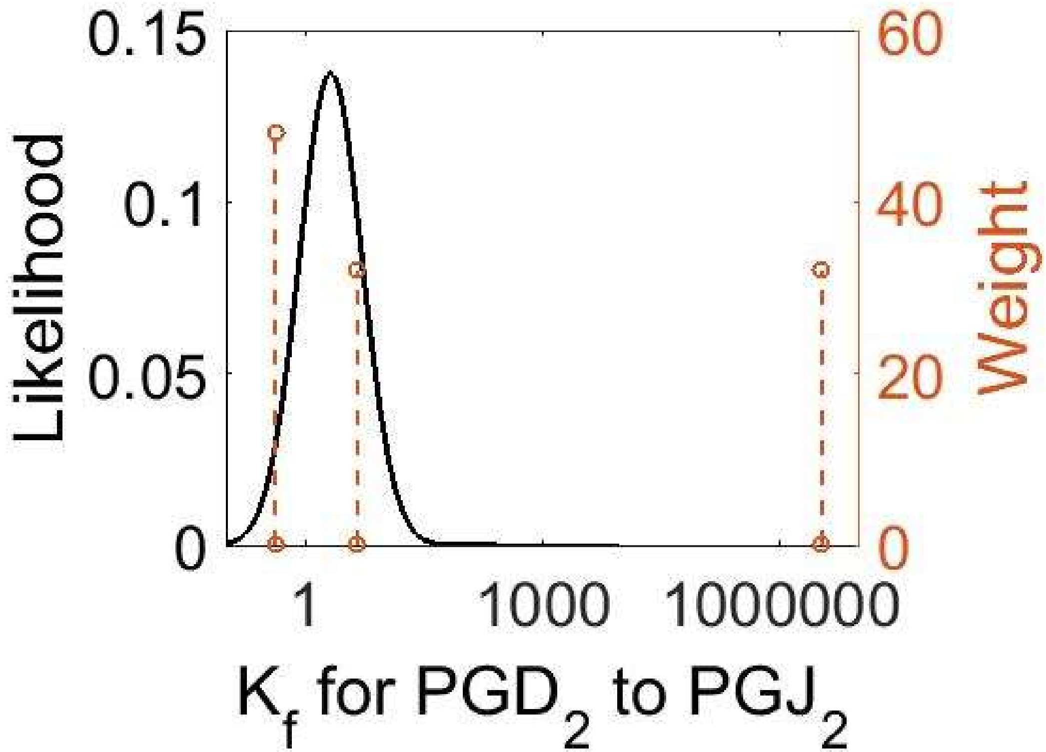

Figure SF.8.3.1.1.1. The estimated probability distribution for the Reaction 8 K_f. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.8.3.1.2. Parameter: K_D

Parameter values for the K_D of Reaction 8 were obtained from the literature and summarised in Table ST.8.3.1.2.1. The log-normal distribution properties for the K_D of Reaction 8 are shown in Table ST.8.3.1.2.2 and plotted in Figure SF.8.3.1.2.1.

Table ST.8.3.1.2.1. Literature information used to design the Reaction 8 K_D parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (M^{-1} min^{-1})	**Error (M^{-1} min^{-1})**	**Experimental details**				**Weight**	**Type of error**	**Reference**
		Substrate	**Functional group**	**Temperature (°C)**	**Other**			
8.00 x10^{-4}	NaN	OH radicals	tetrahydrofuran	Unknown		**8**		(Ranney and Ziemann, 2016)
4.00 x10^{-4}	NaN	H2CO3	carbonate			**8**		(Buytendyk et al., 1927)
4.40 x10^{-4}	NaN	H2CO3	carbonate			**8**		(Thiel and Strohecker, 1914)

Table ST.8.3.1.2.2. The log-normal distribution properties of the Reaction 8 K_D distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (M^{-1} min^{-1})	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
4.49×10^{-4}	1.38	-7.61	3.07×10^{-1}

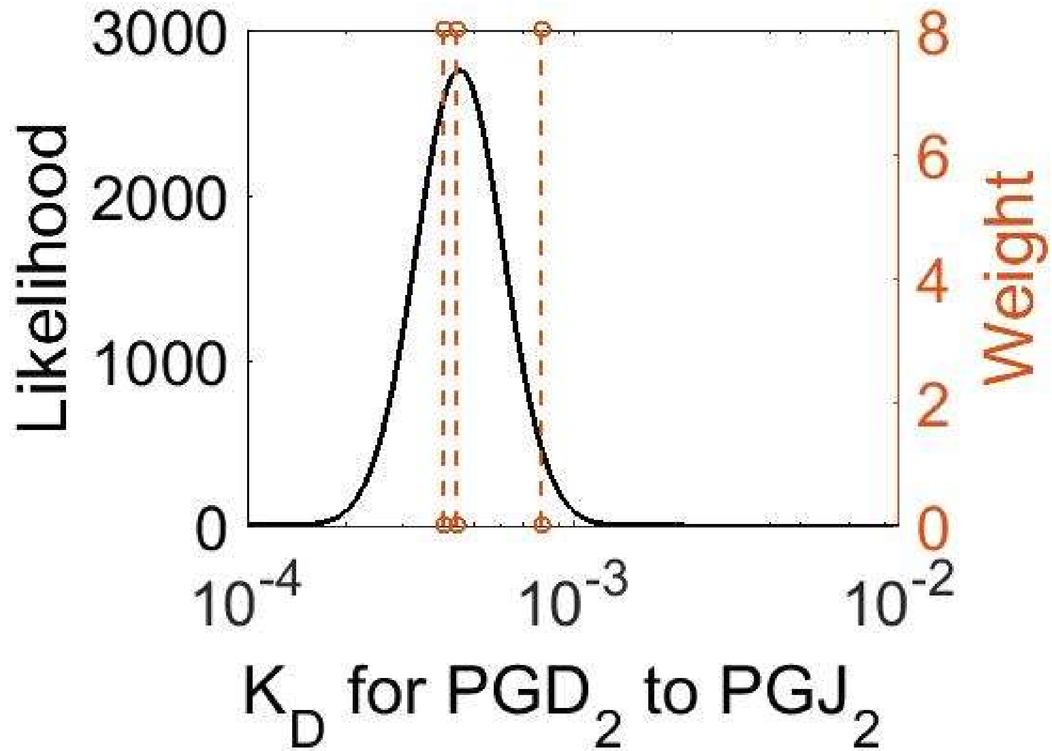

Figure SF.8.3.1.2.1. The estimated probability distribution for the Reaction 8 K_D. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.8.3.1.3. Parameter: K_r (Dependent parameter)

The log-normal distribution for the parameter for the K_r of Reaction 8 was calculated using multivariate distributions. The log-normal distribution properties for the K_r of Reaction 6 are shown in Table ST.8.3.1.3.1 and plotted in Figure SF.8.3.1.3.1.

Table ST.8.3.1.3.1. The log-normal distribution properties of the Reaction 8 K_r distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (M^{-1} min^{-1})	**Location parameter (μ)**	**Scale parameter (σ)**
9.25 x10^{-4}	-6.07	9.57 x10^{-1}

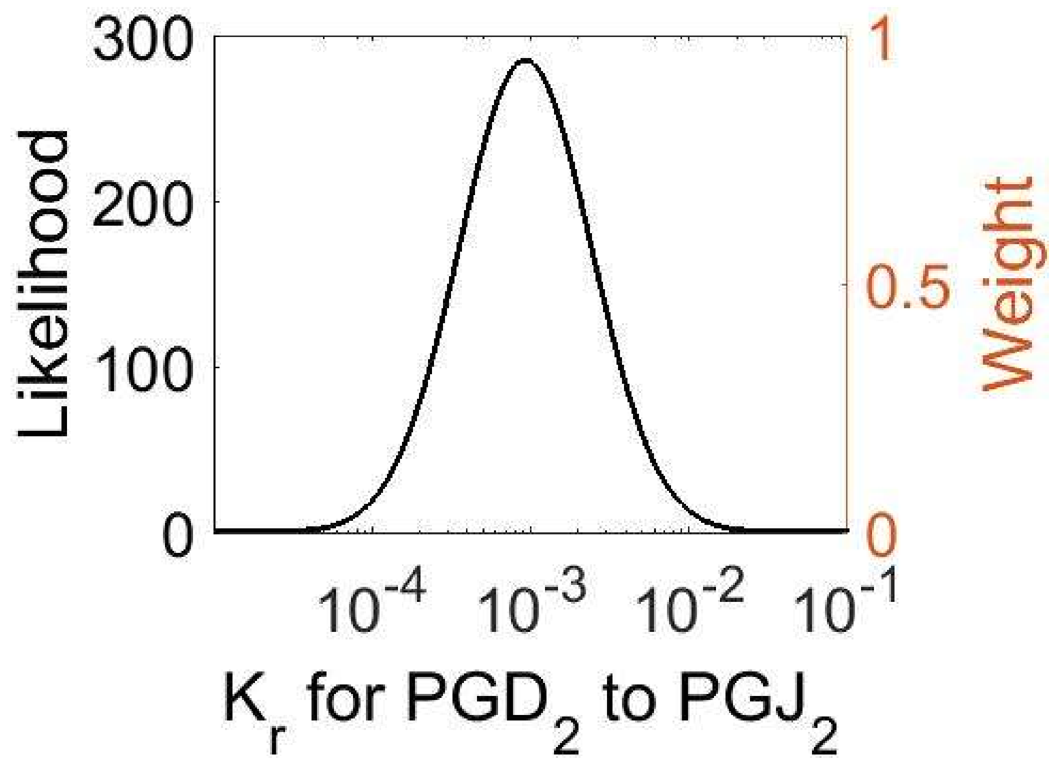

Figure SF.8.3.1.3.1. The estimated probability distribution for Reaction 8 K_r. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.8.4. Reaction 9: $PGJ_2 \rightleftharpoons$ 15-deoxy-PGJ_2

PGJ_2 is subject to a non-enzymatic dehydration reaction to yield 15-deoxy-PGJ_2. This dehydration reaction includes the removal of two hydrogens and one oxygen molecule, and occurs across the C15 hydroxyl and the C14 carbon axis, to form a double bond between C15 and 14.

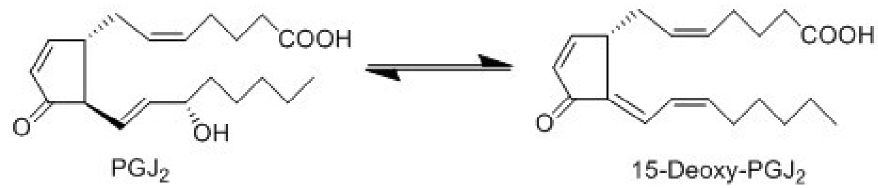

Figure SF.8.4. The non-enzymatic transformation of prostaglandin J_2 (PGJ_2) into 15-deoxy-prostaglandin J_2 (15-deoxy-PGJ_2) (Reaction 9).

Equation SEq.8.4. Reaction rate law for Reaction 9.

$$\boldsymbol{v_9 = K_f[PGJ_2] - K_r[15 - deoxy - PGJ_2]}$$

S.8.4.1. Reaction parameters

S.8.4.1.1. Parameter: K_f

Parameter values for the K_f of Reaction 9 were obtained from the literature and summarised in Table ST.8.4.1.1.1. The log-normal distribution properties for the K_f of Reaction 9 are shown in Table ST.8.4.1.1.2 and plotted in Figure SF.8.4.1.1.1.

Table ST.8.4.1.1.1. Literature information used to design the Reaction 9 K_f parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (M^{-1} min^{-1})	Error (M^{-1} min^{-1})	Experimental details				Weight	Type of error	Reference
		Substrate type	Functional group	Temperature (°C)	Other			
3.30 x10^6		Different	Carboxylic acid	25		32		(B. H. GIBBONS, 1963)
4.50		Different		20		32		(Tur'yan, 1998)
4.20 x10^{-1}		Different		20		32		(Ranney and Ziemann, 2016)

Table ST.8.4.1.1.2. The log-normal distribution properties of the Reaction 9 k_f distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (M^{-1} min^{-1})	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
4.48	1.09 x10^3	7.34	2.42

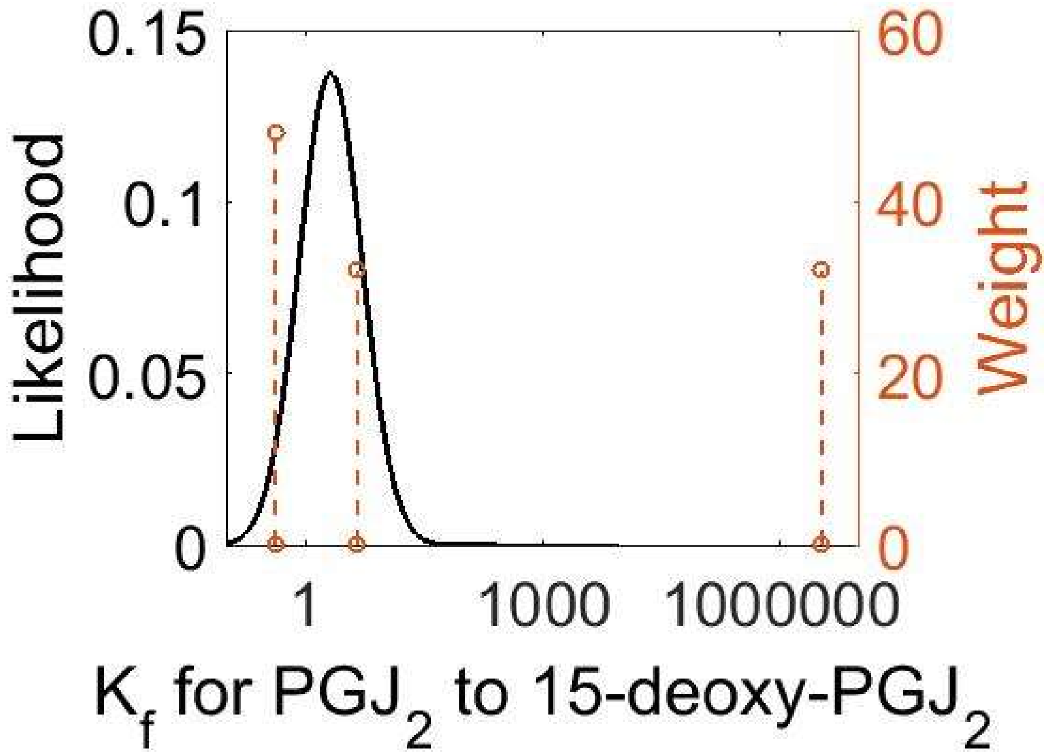

Figure SF.8.4.1.1.1. The estimated probability distribution for Reaction 9 K_f. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.8.4.1.2 Parameter: K_D

Parameter values for the K_D of Reaction 9 were obtained from the literature and summarised in Table ST.8.4.1.2.1. The log-normal distribution properties for the K_D of Reaction 9 are shown in Table ST.8.4.1.2.2 and plotted in Figure SF.8.2.1.2.1.

Table ST.8.4.1.2.1. Literature information used to design the Reaction 9 K_D parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (M^{-1} min^{-1})	**Error (M^{-1} min^{-1})**	**Experimental details**				**Weight**	**Type of error**	**Reference**
		Substrate	**Functional group**	**Temperature (°C)**	**Other**			
8.00 x10^{-4}	NaN	OH radicals	tetrahydrofuran	Unknown		**8**		(Ranney and Ziemann, 2016)
4.00 x10^{-4}	NaN	H2CO3	carbonate			**8**		(Buytendyk et al., 1927)
4.40 x10^{-4}	NaN	H2CO3	carbonate			**8**		(Thiel and Strohecker, 1914)

Table ST.8.4.1.2.2. The log-normal distribution properties of the Reaction 9 K_D distribution. These values were calculated using the functions described in Section 2.6.2.

Mode **(M^{-1} min^{-1})**	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
4.49 $x10^{-4}$	1.38	-7.61	$3.07x10^{-1}$

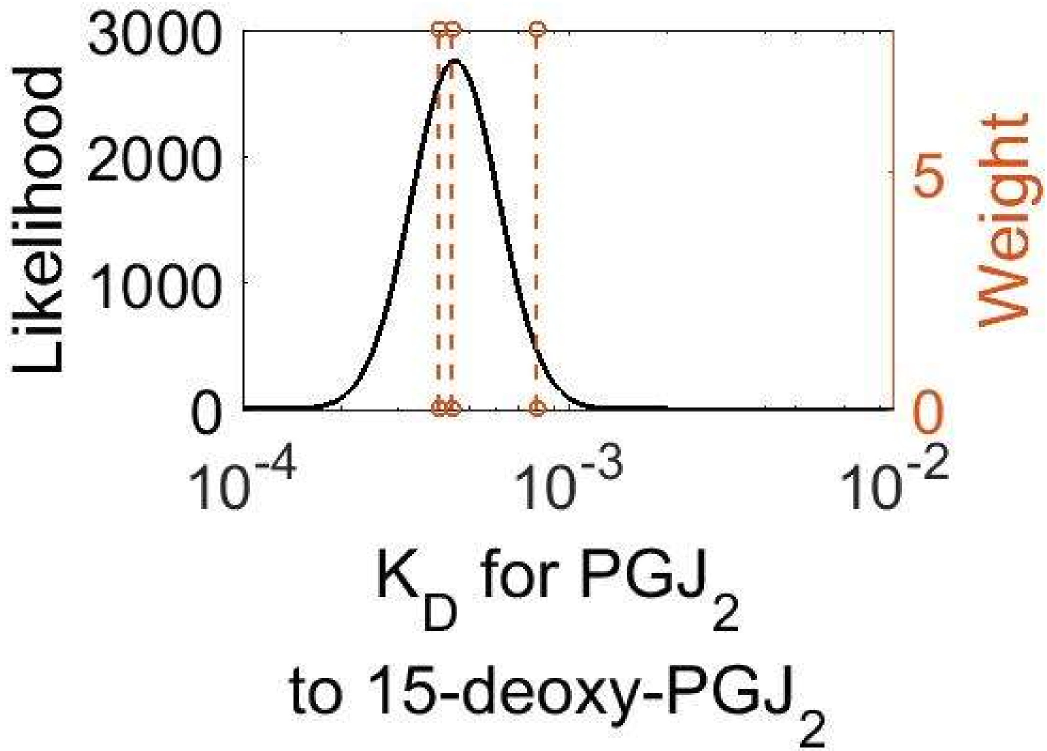

Figure SF.8.2.1.2.1. The estimated probability distribution for the Reaction 9 K_D. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.8.4.1.3. Parameter: K_r (Dependent parameter)

The log-normal distribution for the parameter for the K_r of Reaction 9 was calculated using multivariate distributions. The log-normal distribution properties for the K_r of Reaction 9 are shown in Table ST.8.4.1.3.1 and plotted in Figure SF.8.4.1.3.1.

Table ST.8.4.1.3.1. The log-normal distribution properties of the Reaction 9 k_r distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (M^{-1} min^{-1})	**Location parameter (μ)**	**Scale parameter (σ)**
9.63 $x10^{-4}$	-6.02	9.62 $x10^{-1}$

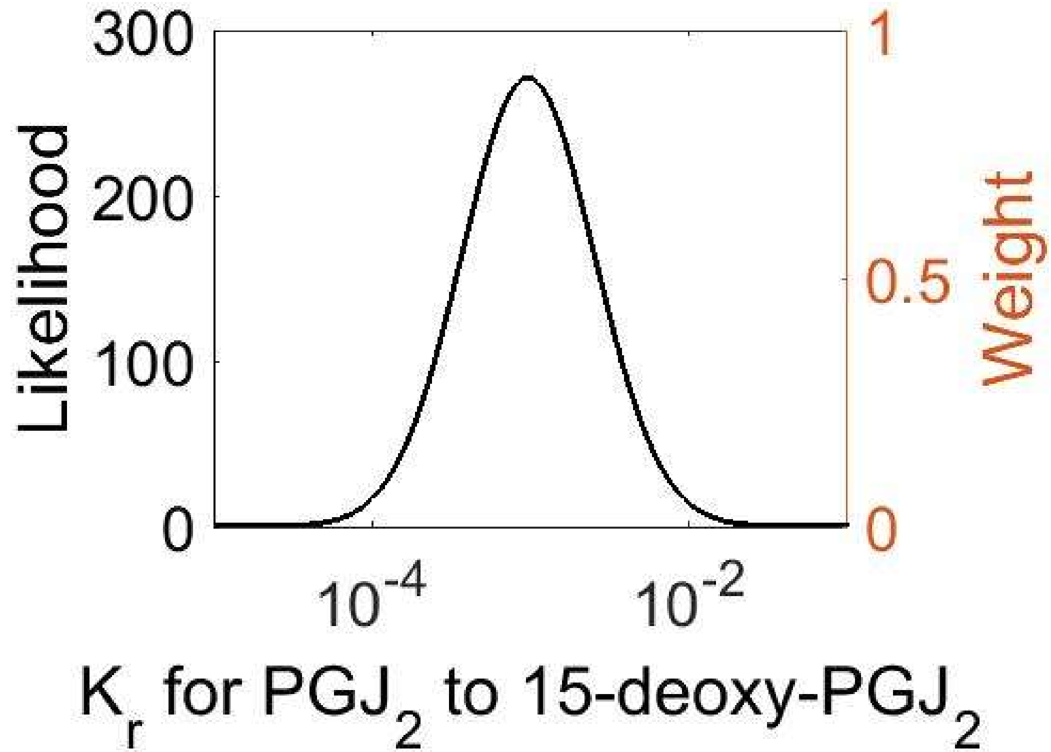

Figure SF.8.4.1.3.1. The estimated probability distribution for Reaction 9 K_r. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.8.5. Reaction 96: $exTXA_2 \rightleftharpoons exTXB_2$

TXA_2 is rapidly hydrolysed into TXB_2 via a non-enzymatic reaction. This inactive metabolite is produced by the incorporation of two hydrogens and one oxygen at C9 and C11, resulting in the opening of the trimethylene oxide ring, and the generation of two hydroxyl groups on the tetrahydropyran ring.

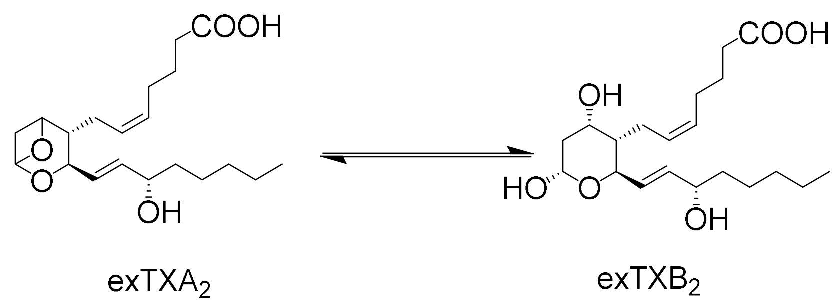

Figure SF.8.5. The non-enzymatic hydrolysis reaction of thromboxane A_2 (TXA_2) into thromboxane B_2 (TXB_2) in the extracellular compartment (Reaction 96).

SEq.8.5. Reaction rate law for Reaction 96.

$$\boldsymbol{v_{96} = K_f[exTXA_2] - K_r[exTXB_2]}$$

S.8.5.1. Reaction parameters

S.8.5.1.1. Parameter: K_f

Parameter values for the K_f of Reaction 96 were obtained from the literature and summarised in Table ST.8.5.1.1.1. The log-normal distribution properties for the K_f of Reaction 96 are shown in Table ST.8.5.1.1.2 and plotted in Figure SF.8.5.1.1.1.

Table ST.8.5.1.1.1. Literature information used to design the Reaction 96 K_f parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (M^{-1} s^{-1})	**Error (M^{-1} s^{-1})**	**Experimental details**				**Weight**	**Type of error**	**Reference**
		Substrate type	**Functional group**	**Temperature (°C)**	**Other**			
3.70 x10^3	1.00 x10^2	Different cycle	Epoxide	25		**32**		(Ross et al., 1982)
8.70 x10^3		Different cycle	Epoxide	25		**32**		(Ross et al., 1982)
1.10 x10^4	1.00 x10^3	6 ring cycle	Epoxide	25		**48**		(Ross et al., 1982)
2.40 x10^4		6 ring cycle	Epoxide	25		**48**		(Ross et al., 1982)
3.70 x10^3	1.00 x10^2	Different cycle	Epoxide	25		**32**		(Ross et al., 1982)
3.60	2.00 x10^{-1}	Different cycle	Epoxide	25		**32**		(Ross et al., 1982)

1.70	1.00 x10^{-1}	Different cycle	Epoxide	25		**32**		(Ross et al., 1982)
2.67 x10^{1}	9.00 x10^{-1}	Different cycle	Epoxide	25		**32**		(Ross et al., 1982)
3.50 x10^{1}		Different cycle	Epoxide	25		**32**		(Ross et al., 1982)

Table ST.8.5.1.1.2. The log-normal distribution properties of the Reaction 96 K_f distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (M^{-1} s^{-1})	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
3.70 x10^{3}	3.44 x10^{1}	1.10 x10^{1}	1.66

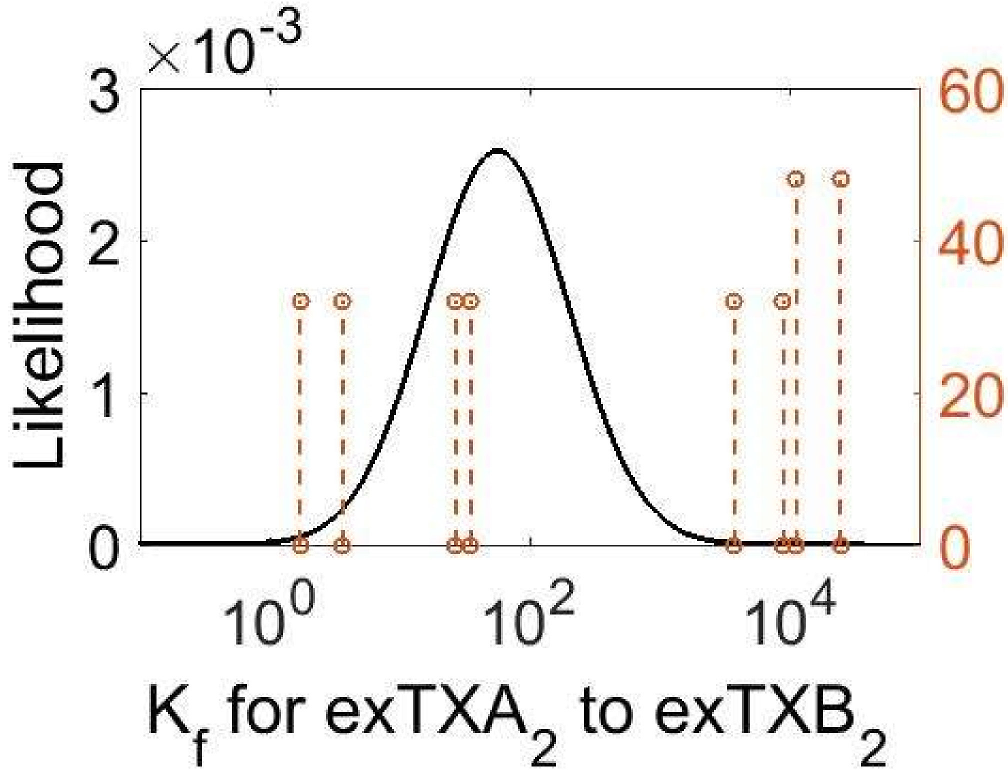

Figure SF.8.5.1.1.1. The estimated probability distribution for the Reaction 96 K_f. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.8.5.1.2. Parameter: K_D

Parameter values for the K_D of Reaction 96 were obtained from the literature and summarised in Table ST.8.5.1.2.1. The log-normal distribution properties for the K_D of Reaction 96 are shown in Table ST.8.5.1.2.2 and plotted in Figure SF.8.5.1.2.1.

Table ST.8.5.1.2.1. Literature information used to design the Reaction 96 K_D parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (M^{-1} min^{-1})	**Error (M^{-1} min^{-1})**	**Experimental details**				**Weight**	**Type of error**	**Reference**
		Species	**Substrate type**	**Temperature (°C)**	**Other**			
0.000038	NaN	Mosquito	Carbocyclic TXA_2	35		**24**		(Alvarenga et al., 2010)
0.00000023	NaN	Rabbit	TXA_2 antagonist	35		**36**		(Nakahata et al., 1992)
1500	500	N/A	Hydroxysulfamic acid	25		**16**		(D. LITTLEJOHN, 1988)
1.75 $\times 10^{-12}$	NaN	N/A	H2O2			**16**		(D. LITTLEJOHN, 1988)
5.90 $\times 10^{-8}$	NaN	N/A	Oxaplatin			**16**		(Jerremalm et al., 2003)

Table ST.8.5.1.2.2. The log-normal distribution properties of the Reaction 96 K_D distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (M^{-1} min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
2.35 $x10^{-7}$	1.76 $x10^{4}$	-6.86	2.90

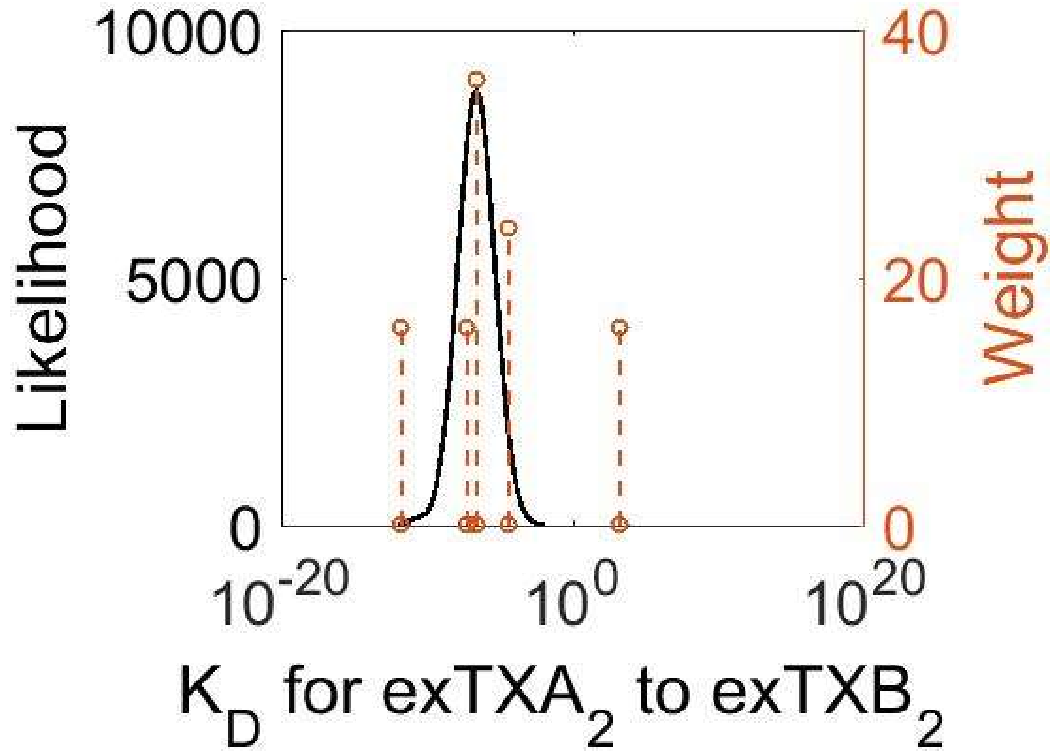

Figure SF.8.5.1.2.1. The estimated probability distribution for the Reaction 96 K_D. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.8.5.1.3. Parameter: K_r (Dependent parameter)
The log-normal distribution for the parameter for the K_r of Reaction 96 was calculated using multivariate distributions. The log-normal distribution properties for the K_r of Reaction 96 are shown in Table ST.8.5.1.3.1 and plotted in Figure SF.8.5.1.3.1.

Table ST.8.5.1.3.1. The log-normal distribution properties of the Reaction 96 K_r distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (M^{-1} min^{-1})	Location parameter (μ)	Scale parameter (σ)
5.28×10^{1}	5.63	1.29

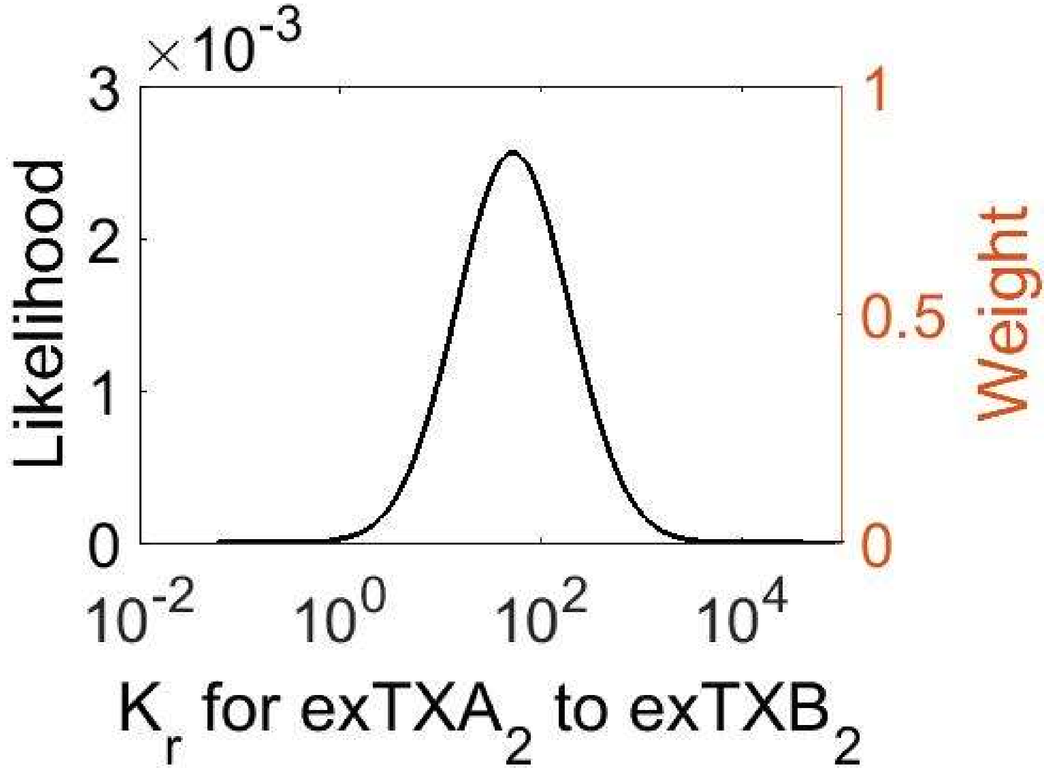

Figure SF.8.5.1.3.1. The estimated probability distribution for the Reaction 96 K_r. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.8.6. Reaction 97: $exPGI_2 \rightleftharpoons ex6\text{-}keto\text{-}PGF_{1\alpha}$

Due to ring strain, PGI_2 is rapidly hydrolysed to 6-keto-$PGF_{1\alpha}$. This is a non-enzymatic reaction and results in the formation of a hydroxyl group at C9 and a ketone at C6, by incorporating two hydrogens and one oxygen.

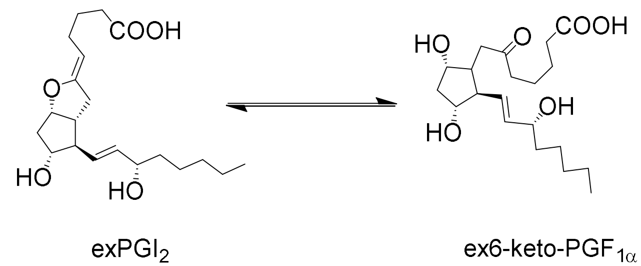

Figure SF.8.6. The non-enzymatic hydrolysis of prostaglandin I_2 (PGI_2) into 6-keto-prostaglandin $F_{1\alpha}$ (6-keto-$PGF_{1\alpha}$) in the extracellular compartment (Reaction 97).

SEq.8.6. Reaction rate law for Reaction 97.

$$\boldsymbol{v_{97} = K_f[exPGI_2] - K_r[ex6 - keto - PGF_{1\alpha}]}$$

S.8.6.1. Reaction parameters

S.8.6.1.1. Parameter: K_f

Parameter values for the K_f of Reaction 97 were obtained from the literature and summarised in Table ST.8.6.1.1.1. The log-normal distribution properties for the K_f of Reaction 97 are shown in Table ST.8.6.1.1.2 and plotted in Figure SF.8.6.1.1.1.

Table ST.8.6.1.1.1. Literature information used to design the Reaction 97 K_f parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (M^{-1} s^{-1})	Error (M^{-1} s^{-1})	Experimental details				Weight	Type of error	Reference
		Substrate type	Functional group	Temperature (°C)	Other			
3.70 $x10^3$	1.00 $x10^2$	Different cycle	Epoxide	25		**32**		(Ross et al., 1982)
8.70 $x10^3$		Different cycle	Epoxide	25		**32**		(Ross et al., 1982)
1.10 $x10^4$	1.00 $x10^3$	6 ring cycle	Epoxide	25		**48**		(Ross et al., 1982)
2.40 $x10^4$		6 ring cycle	Epoxide	25		**48**		(Ross et al., 1982)
3.70 $x10^3$	1.00 $x10^2$	Different cycle	Epoxide	25		**32**		(Ross et al., 1982)
3.60	2.00 $x10^{-1}$	Different cycle	Epoxide	25		**32**		(Ross et al., 1982)

1.70	1.00 x10^{-1}	Different cycle	Epoxide	25		**32**		(Ross et al., 1982)
2.67 x10^{1}	9.00 x10^{-1}	Different cycle	Epoxide	25		**32**		(Ross et al., 1982)
3.50 x10^{1}		Different cycle	Epoxide	25		**32**		(Ross et al., 1982)

Table ST.8.6.1.1.2. The log-normal distribution properties of the Reaction 97 K_f distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (M^{-1} s^{-1})	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
3.70 x10^{3}	3.44 x10^{1}	1.10 x10^{1}	1.66

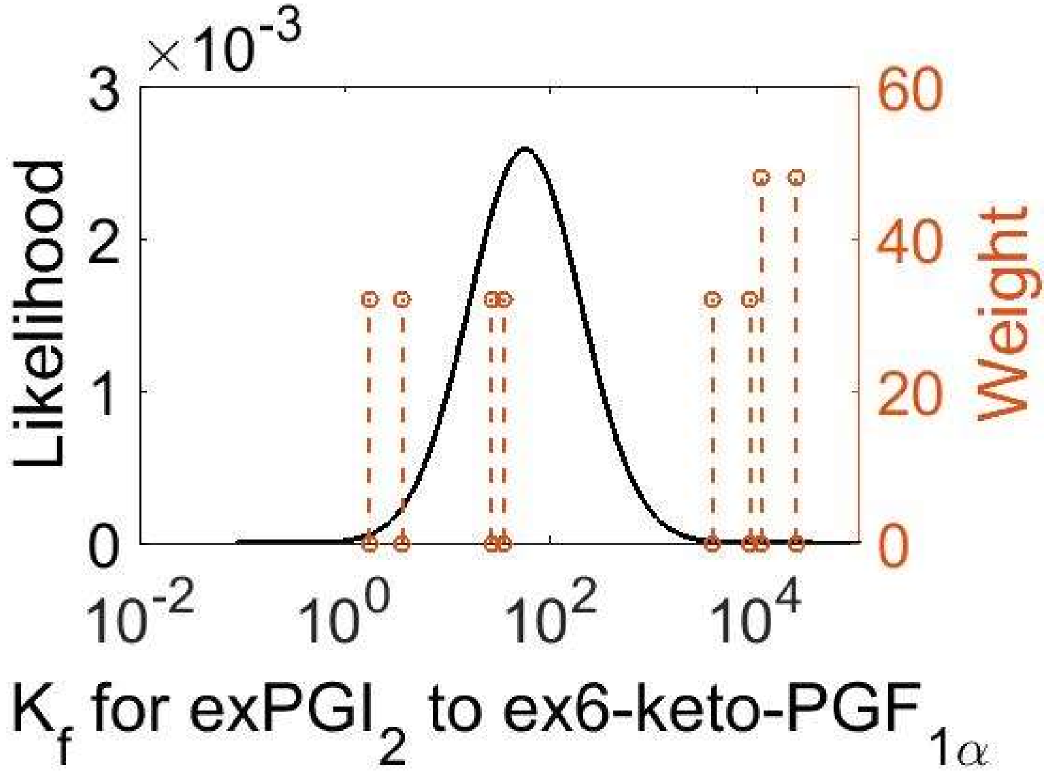

Figure SF.8.6.1.1.1. The estimated probability distribution for the Reaction 97 K_f. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.8.6.1.2. Parameter: K_D

Parameter values for the K_D of Reaction 97 were obtained from the literature and summarised in Table ST.8.6.1.2.1. The log-normal distribution properties for the K_D of Reaction 97 are shown in Table ST.8.6.1.2.2 and plotted in Figure SF.8.6.1.2.1.

Table ST.8.6.1.2.1. Literature information used to design the Reaction 97 K_D parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (M^{-1} min^{-1})	**Error (M^{-1} min^{-1})**	**Experimental details**				**Weight**	**Type of error**	**Reference**
		Species	**Substrate type**	**Temperature (°C)**	**Other**			
0.000038	NaN	Mosquito	Carbocyclic TXA2	35		**24**		(Alvarenga et al., 2010)
0.00000023	NaN	Rabbit	TXA2 antagonist	35		**36**		(Nakahata et al., 1992)
1500	500	N/A	Hydroxysulfamic acid	25		**16**		(D. LITTLEJOHN, 1988)
1.75 $x10^{-12}$	NaN	N/A	H2O2			**16**		(D. LITTLEJOHN, 1988)
5.90 $x10^{-8}$	NaN	N/A	Oxaplatin			**16**		(Jerremalm et al., 2003)

Table ST.8.6.1.2.2. The log-normal distribution properties of the Reaction 97 K_D distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (M^{-1} min^{-1})	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
2.35×10^{-7}	1.76×10^{4}	-6.86	2.90

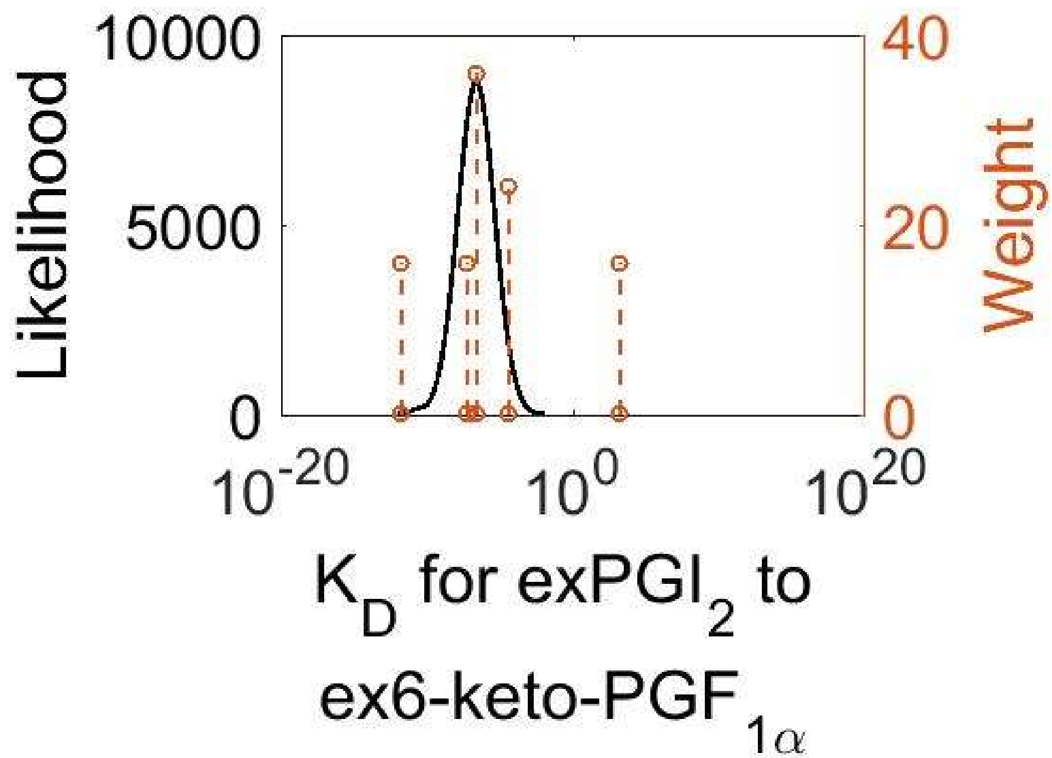

Figure SF.8.6.1.2.1. The estimated probability distribution for the Reaction 97 K_D. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.8.6.1.3. Parameter: K_r (Dependent parameter)
The log-normal distribution for the parameter for the K_r of Reaction 97 was calculated using multivariate distributions. The log-normal distribution properties for the K_r of Reaction 97 are shown in Table ST.8.6.1.3.1 and plotted in Figure SF.8.6.1.3.1.

Table ST.8.6.1.3.1. The log-normal distribution properties of the Reaction 97 K_r distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (M^{-1} min^{-1})	Location parameter (μ)	Scale parameter (σ)
5.81 $x10^1$	5.60	1.24

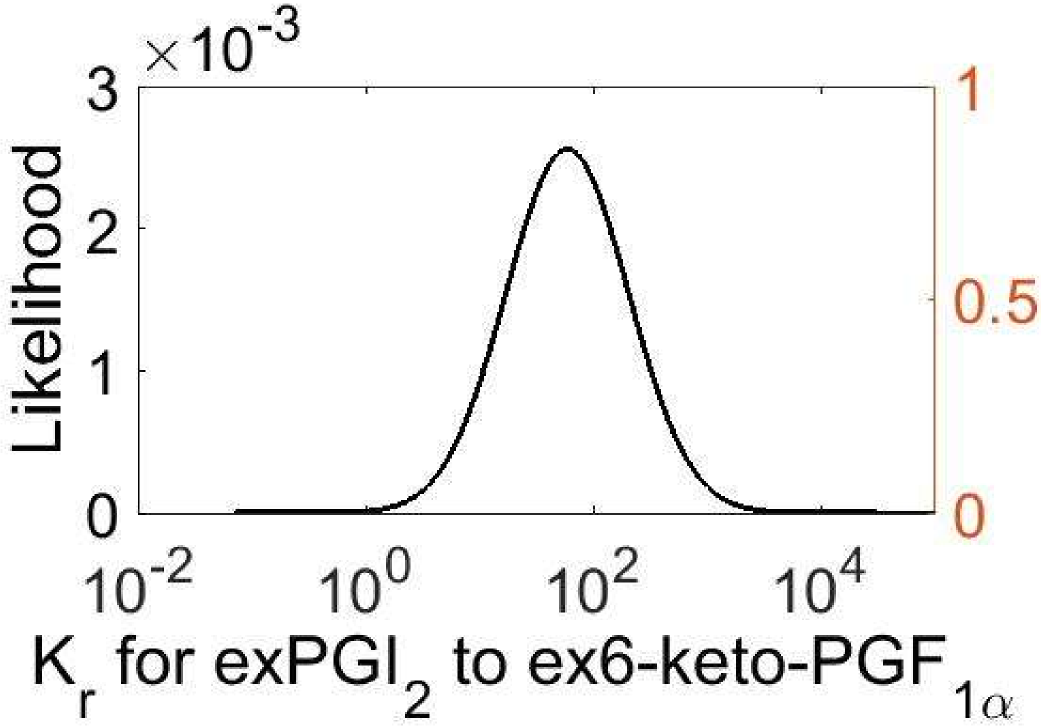

Figure SF.8.6.1.3.1. The estimated probability distribution for the Reaction 97 K_r. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.8.7. Reaction 98: $exPGD_2 \rightleftharpoons exPGJ_2$

PGD_2 is subsequently converted to PGJ_2 via a non-enzymatic reaction (Fitzpatrick and Wynalda, 1983). This dehydration reaction includes the removal of two hydrogens and one oxygen molecule, and occurs across the C9 hydroxyl and the C10 carbon axis, to form a double bond between C9 and 10.

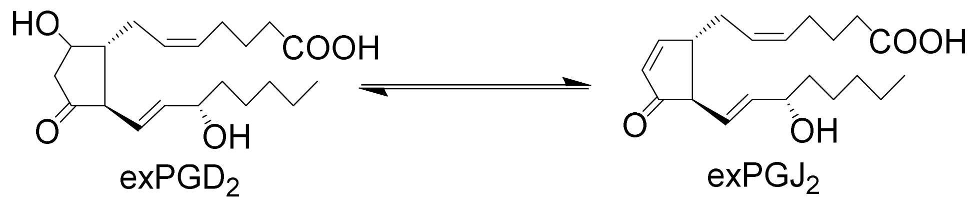

Figure SF.8.7. The non-enzymatic dehydration of prostaglandin D_2 (PGD_2) into prostaglandin J_2 (PGJ_2) in the extracellular compartment (Reaction 98).

SEq.8.7. Reaction rate law for Reaction 98.

$$\boldsymbol{v_{98} = K_f[exPGD_2] - K_r[exPGJ_2]}$$

S.8.7.1. Reaction parameters

S.8.7.1.1. Parameter: K_f

Parameter values for the K_f of Reaction 98 were obtained from the literature and summarised in Table ST.8.7.1.1.1. The log-normal distribution properties for the K_f of Reaction 98 are shown in Table ST.8.7.1.1.2 and plotted in Figure SF.8.7.1.1.1.

Table ST.8.7.1.1.1. Literature information used to design the Reaction 98 K_f parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (M^{-1} min^{-1})	Error (M^{-1} min^{-1})	Experimental details				Weight	Type of error	Reference
		Substrate type	Functional group	Temperature (°C)	Other			
3.30 x10^{6}		Different	Carboxylic acid	25		32		(B. H. GIBBONS, 1963)
4.50		Different		20		32		(Tur'yan, 1998)
4.20 x10^{-1}		Different		20		32		(Ranney and Ziemann, 2016)

Table ST.8.7.1.1.2. The log-normal distribution properties of the Reaction 98 K_f distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (M^{-1} min^{-1})	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
4.48	1.09 x10^3	7.34	2.42

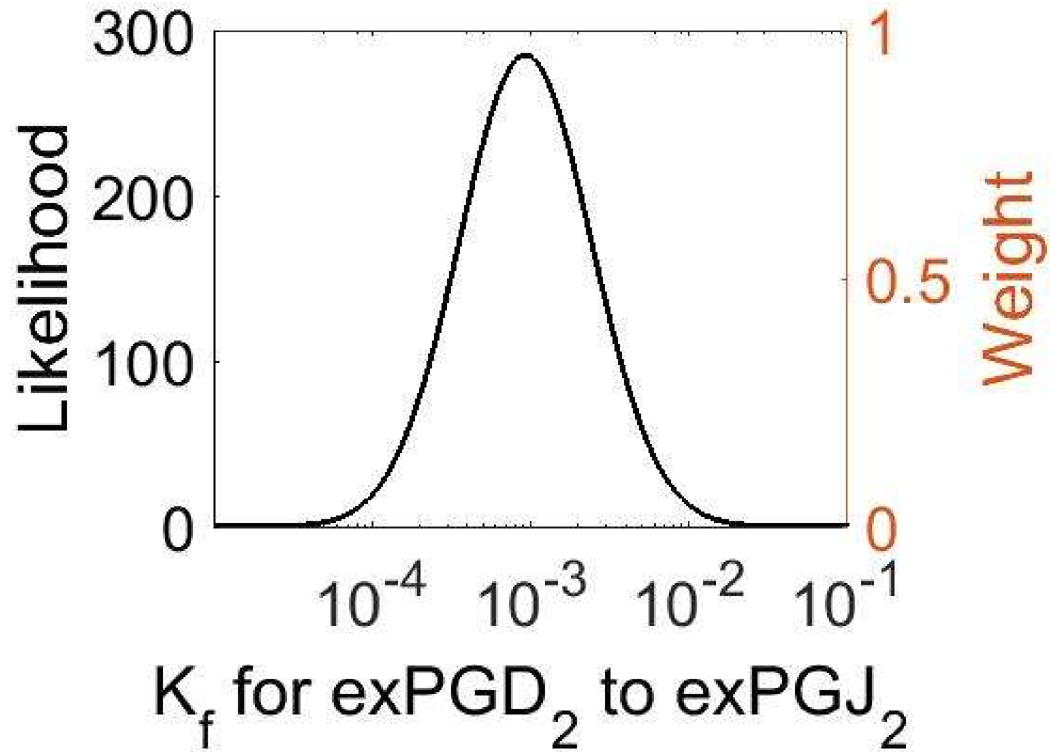

Figure SF.8.7.1.1.1. The estimated probability distribution for the Reaction 98 K_f. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.8.7.1.2. Parameter: K_D

Parameter values for the K_D of Reaction 98 were obtained from the literature and summarised in Table ST.8.7.1.2.1. The log-normal distribution properties for the K_D of Reaction 98 are shown in Table ST.8.7.1.2.2 and plotted in Figure SF.8.7.1.2.1.

Table ST.8.7.1.2.1. Literature information used to design the Reaction 98 K_D parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (M^{-1} min^{-1})	**Error (M^{-1} min^{-1})**	**Experimental details**				**Weight**	**Type of error**	**Reference**
		Substrate	**Functional group**	**Temperature (°C)**	**Other**			
8.00×10^{-4}	NaN	OH radicals	tetrahydrofuran	Unknown		**8**		(Ranney and Ziemann, 2016)
4.00×10^{-4}	NaN	H2CO3	carbonate			**8**		(Buytendyk et al., 1927)
4.40×10^{-4}	NaN	H2CO3	carbonate			**8**		(Thiel and Strohecker, 1914)

Table ST.8.7.1.2.2 The log-normal distribution properties of the Reaction 98 K_D distribution. These values were calculated using the functions described in Section 2.6.2.

Mode **(M^{-1} min^{-1})**	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
4.49 $x10^{-4}$	1.38	-7.61	3.07 $x10^{-1}$

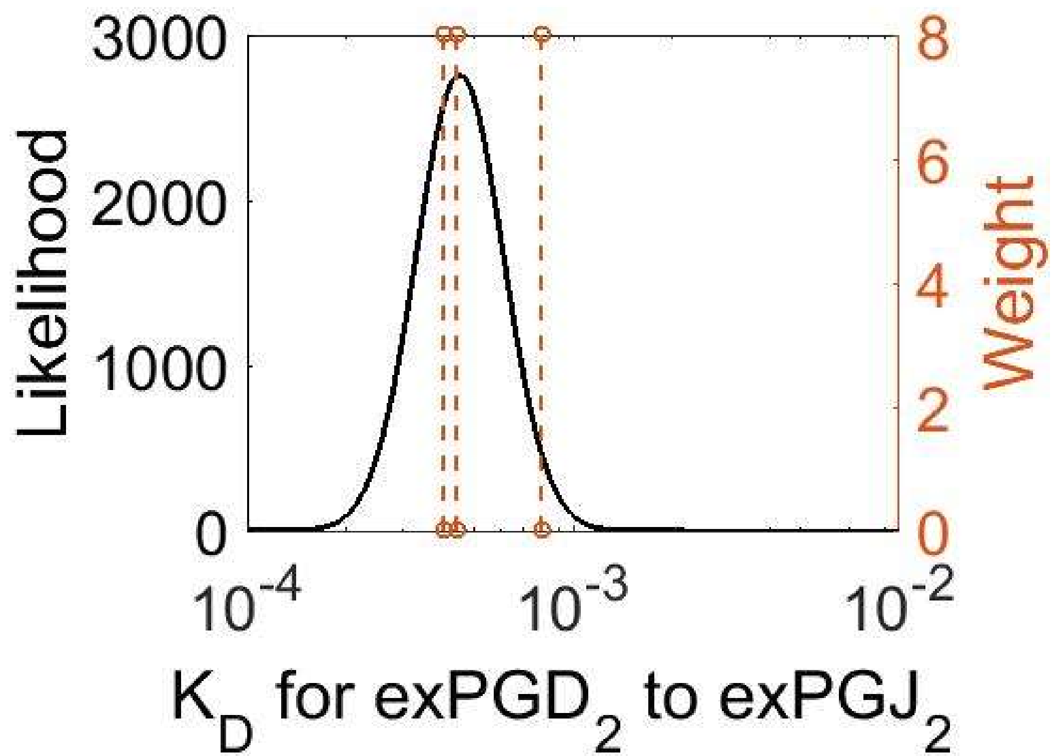

Figure SF.8.7.1.2.1. The estimated probability distribution for the Reaction 98 K_D. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.8.7.1.3. Parameter: K_r (Dependent parameter)

The log-normal distribution for the parameter for the K_r of Reaction 98 was calculated using multivariate distributions. The log-normal distribution properties for the K_r of Reaction 98 are shown in Table ST.8.7.1.3.1 and plotted in Figure SF.8.7.1.3.1.

Table ST.8.7.1.3.1. The log-normal distribution properties of the Reaction 98 K_r distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (M^{-1} min^{-1})	**Location parameter (μ)**	**Scale parameter (σ)**
9.25 $x10^{-4}$	-6.07	$9.57x10^{-1}$

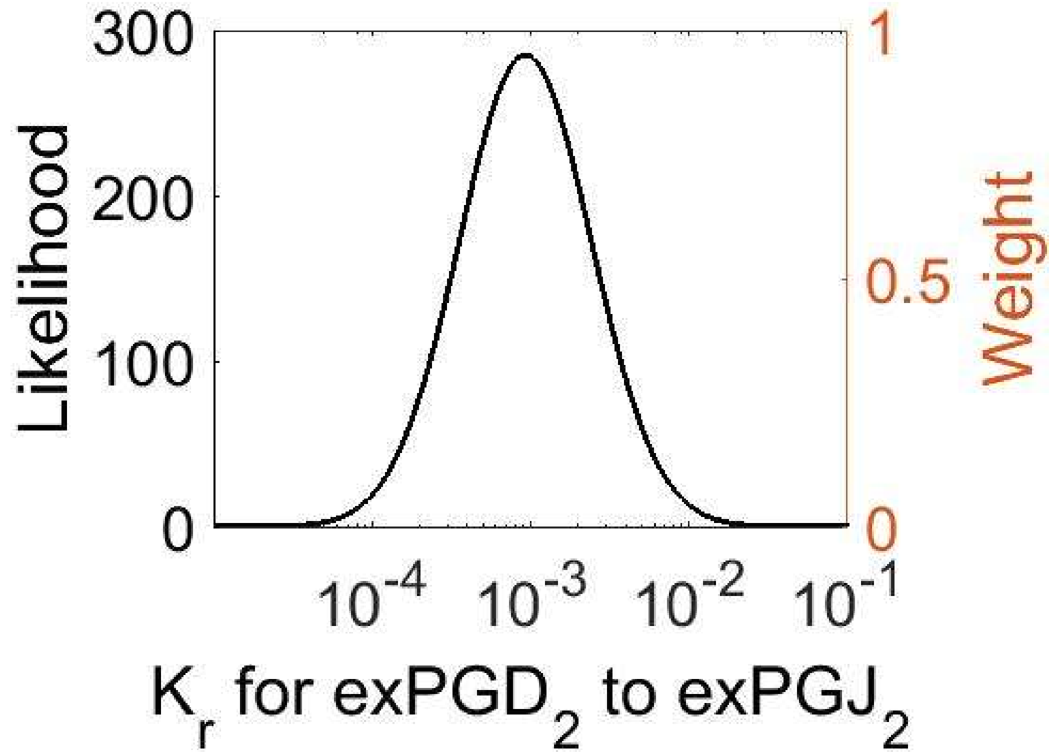

Figure SF.8.7.1.3.1. The estimated probability distribution for the Reaction 98 K_r. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.8.8. Reaction 99: exPGJ$_2$ ⇌ ex15-deoxy-PGJ$_2$

PGJ$_2$ is subject to a non-enzymatic dehydration reaction to yield 15-deoxy-PGJ$_2$. This dehydration reaction includes the removal of two hydrogens and one oxygen molecule, and occurs across the C15 hydroxyl and the C14 carbon axis, to form a double bond between C15 and 14.

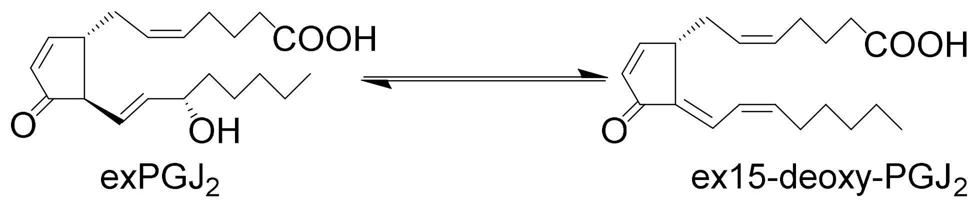

Figure SF.8.8. The non-enzymatic dehydration of prostaglandin J$_2$ (PGJ$_2$) into 15-deoxy-PGJ$_2$ (15-deoxy-PGJ$_2$) in the extracellular compartment (Reaction 99).

SEq.8.8. Reaction rate law for Reaction 99.

$$\boldsymbol{v_{99} = K_f[exPGJ_2] - K_r[ex15 - deoxy - PGJ_2]}$$

S.8.8.1. Reaction parameters

S.8.8.1.1. Parameter: K_f

Parameter values for the K_f of Reaction 99 were obtained from the literature and summarised in Table ST.8.8.1.1.1. The log-normal distribution properties for the K_f of Reaction 99 are shown in Table ST.8.8.1.1.2 and plotted in Figure SF.8.8.1.1.1.

Table ST.8.8.1.1.1. Literature information used to design the Reaction 99 K_f parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (M^{-1} min^{-1})	Error (M^{-1} min^{-1})	Experimental details				Weight	Type of error	Reference
		Substrate type	Functional group	Temperature (°C)	Other			
3.30 x10^{6}		Different	Carboxylic acid	25		32		(B. H. GIBBONS, 1963)
4.50		Different		20		32		(Tur'yan, 1998)
4.20 x10^{-1}		Different		20		32		(Ranney and Ziemann, 2016)

Table ST.8.8.1.1.2. The log-normal distribution properties of the Reaction 99 K_f distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (M^{-1} min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
4.48	1.09 $x10^3$	7.34	2.42

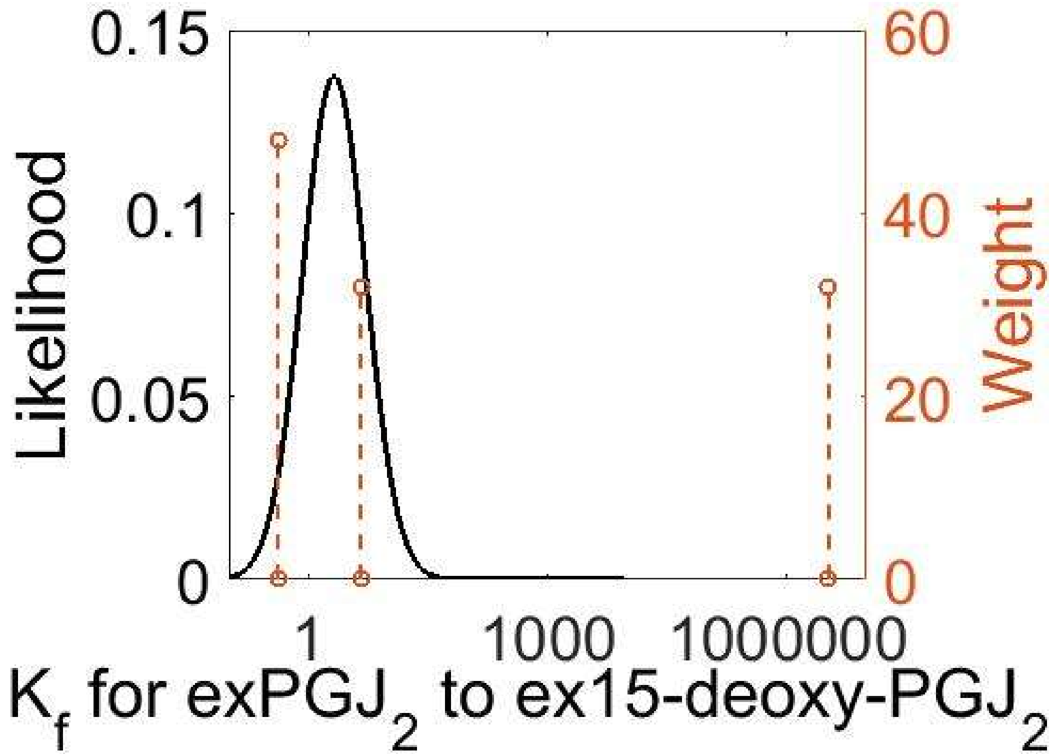

Figure SF.8.8.1.1.1. The estimated probability distribution for the Reaction 99 K_f. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.8.8.1.2. Parameter: K_D

Parameter values for the K_D of Reaction 99 were obtained from the literature and summarised in Table ST.8.8.1.2.1. The log-normal distribution properties for the K_D of Reaction 99 are shown in Table ST.8.8.1.2.2 and plotted in Figure SF.8.8.1.2.1.

Table ST.8.8.1.2.1. Literature information used to design the Reaction 99 K_D parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (M^{-1} min^{-1})	Error (M^{-1} min^{-1})	Experimental details				Weight	Type of error	Reference
		Substrate	**Functional group**	**Temperature (°C)**	**Other**			
8.00 x10^{-4}	NaN	OH radicals	tetrahydrofuran	Unknown		**8**		(Ranney and Ziemann, 2016)
4.00 x10^{-4}	NaN	H2CO3	carbonate			**8**		(Buytendyk et al., 1927)
4.40 x10^{-4}	NaN	H2CO3	carbonate			**8**		(Thiel and Strohecker, 1914)

Table ST.8.8.1.2.2. The log-normal distribution properties of the Reaction 99 K_D distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (M^{-1} min^{-1})	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
4.49×10^{-4}	1.38	-7.61	3.07×10^{-1}

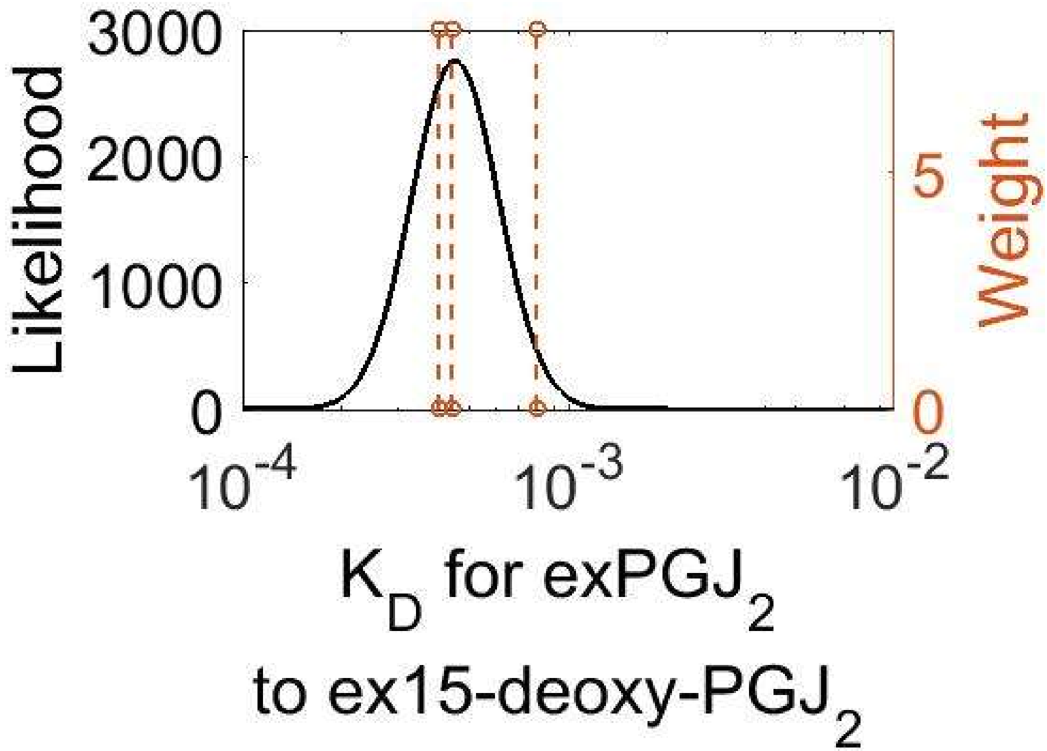

Figure SF.8.8.1.2.1. The estimated probability distribution for the Reaction 99 K_D. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.8.8.1.3. Parameter: K_r (Dependent parameter)

The log-normal distribution for the parameter for the K_r of Reaction 99 was calculated using multivariate distributions. The log-normal distribution properties for the K_r of Reaction 99 are shown in Table ST.8.8.1.3.1 and plotted in Figure SF.8.8.1.3.1.

Table ST.8.8.1.3.1. The log-normal distribution properties of the Reaction 99 K_r distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (M^{-1} min^{-1})	Location parameter (μ)	Scale parameter (σ)
9.63 $x10^{-4}$	-6.02	9.62 $x10^{-1}$

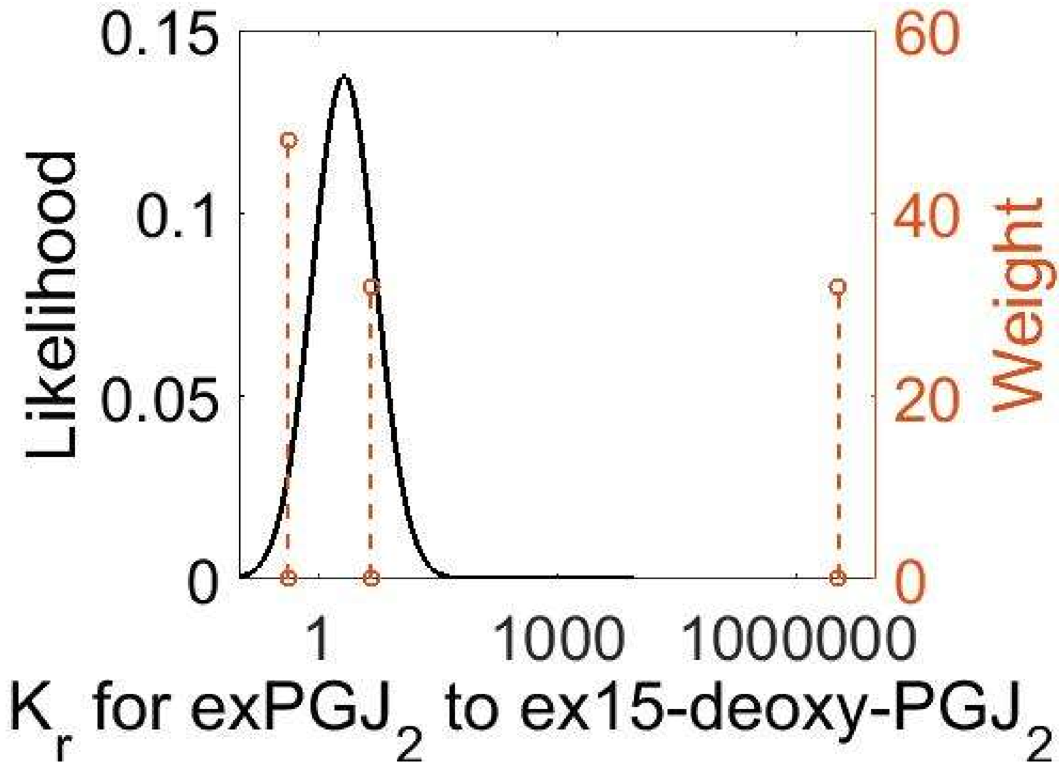

Figure SF.8.8.1.3.1. The estimated probability distribution for the Reaction 99 K_r. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

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Tur'yan, Y. I. (1998). 'Kinetics and equilibrium of the dehydration-hydration and recombination-dissociation reactions of glyoxylic acid investigated by electrochemical methods' *Croat Chem Acta*, 71 (1), pp. 727-743.

Supplementary Document S9. Decay Reaction Structure and Parameterisation.

Documentation of parameter values obtained for all decay reactions in the model (Reactions 44–64, 68, 71–94; Supplementary Table S4) from the literature and associated uncertainty for the eicosanoid network model. Parameterisation was performed using the method of Tsigkinopoulou *et al.,* (2018). The table includes information regarding each reaction and its respective parameters are documented. This includes information such as the reaction rate law and the literature values that were used to define parameters, including experimental conditions, total weights and literature references from which the data were obtained. In this model some parameters are referred as "Dependent parameters", meaning that the log-normal distribution for that parameter was calculated using multivariate distributions (discussed in **Section 2.6.2**). As a result, no confidence interval factor or literature values were cited for the Dependent parameters.

Contents

S.9.1 Reaction 44: $exPGF_{2\alpha} \rightarrow \phi$

The decay of $PGF_{2\alpha}$ in the extracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

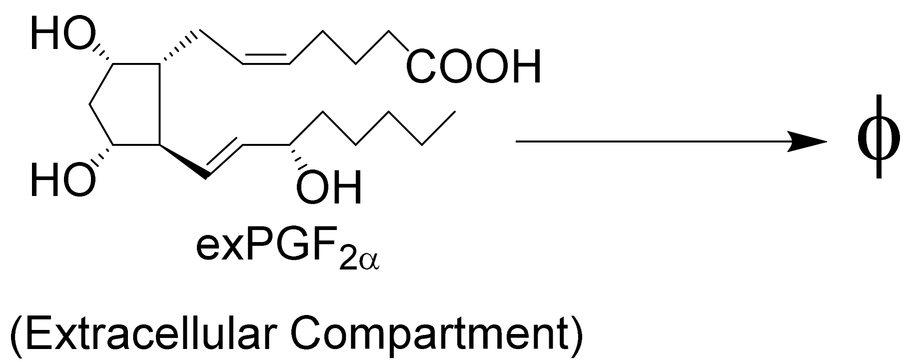

Figure SF.9.1. The decay of prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) in the extracellular compartment (Reaction 44).

SEq. 9.1. Reaction rate law for Reaction 44.

$$\boldsymbol{v_{44} = K[exPGF_{2\alpha}]}$$

S.9.1.1. Reaction parameters

S.9.1.1.1. Parameter: K

Parameter values for the K of Reaction 44 were obtained from the literature and summarised in Table ST.9.1.1.1.1. The log-normal distribution properties for the K of Reaction 44 are shown in Table ST.9.1.1.1.2 and plotted in Figure SF.9.1.1.1.1.

Table ST.9.1.1.1.1. Literature information used to design the exPGF$_{2\alpha}$ decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	Reference
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other		
900	492	0.001	0.001	In vivo	PGF2a	Human	Decidual stromal cells and macrophages	Unknown	Unknown		8	(Ishihara et al., 1991)

Table ST.9.1.1.1.2. The log-normal distribution properties of the exPGF$_{2\alpha}$ decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
7.07 x10^{-4}	2.30	-6.80	6.7610^{-1}

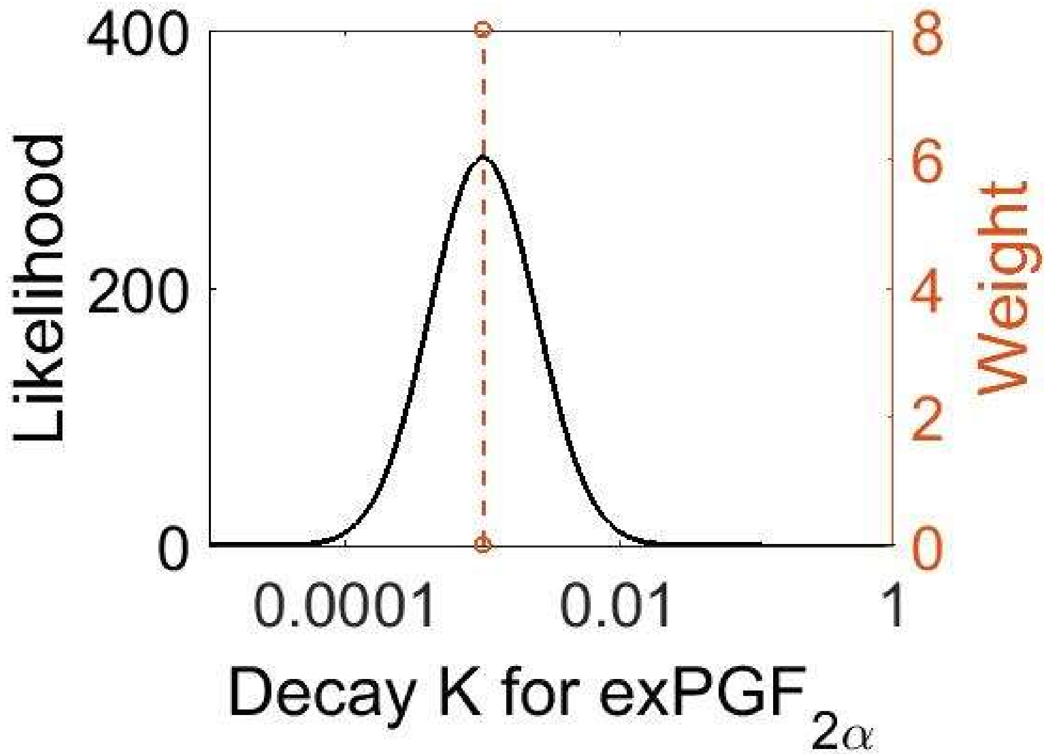

Figure SF.9.1.1.1.1. The estimated probability distribution for $exPGF_{2\alpha}$ decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.9.2. Reaction 45: $exTXB_2 \rightarrow \phi$

The decay of TXB_2 in the extracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

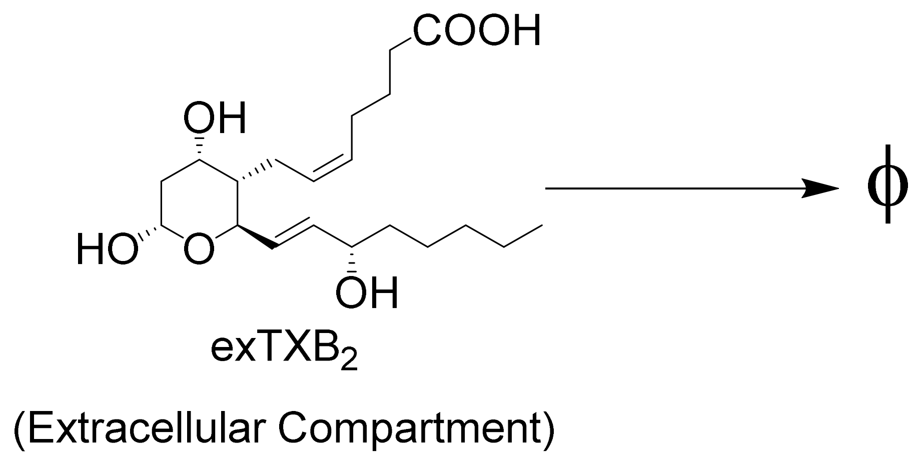

Figure SF.9.2. The decay of thromboxane B_2 (TXB_2) in the extracellular compartment (Reaction 45).

SEq.9.2. Reaction rate law for Reaction 45.

$$\boldsymbol{v_{45} = K[exTXB_2]}$$

S.9.2.1. Reaction parameters

S.9.2.1.1. Parameter: K

Parameter values for the K of Reaction 45 were obtained from the literature and summarised in Table ST.9.2.1.1.1. The log-normal distribution properties for the K of Reaction 45 are shown in Table ST.9.2.1.1.2 and plotted in Figure SF.9.2.1.1.1.

Table ST.9.2.1.1.1. Literature information used to design the exTXB$_2$ decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	Reference
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other		
20		0.035		Unknown, assume in vitro	TXB2	Unknown	Unknown	Unknown	Unknown	Textbook with no reference	8	(Wild, 2005)

Table ST.9.2.1.1.2. The log-normal distribution properties of the exTXB$_2$ decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
3.48 x10^{-2}	1.10	-3.35	9.4910^{-2}

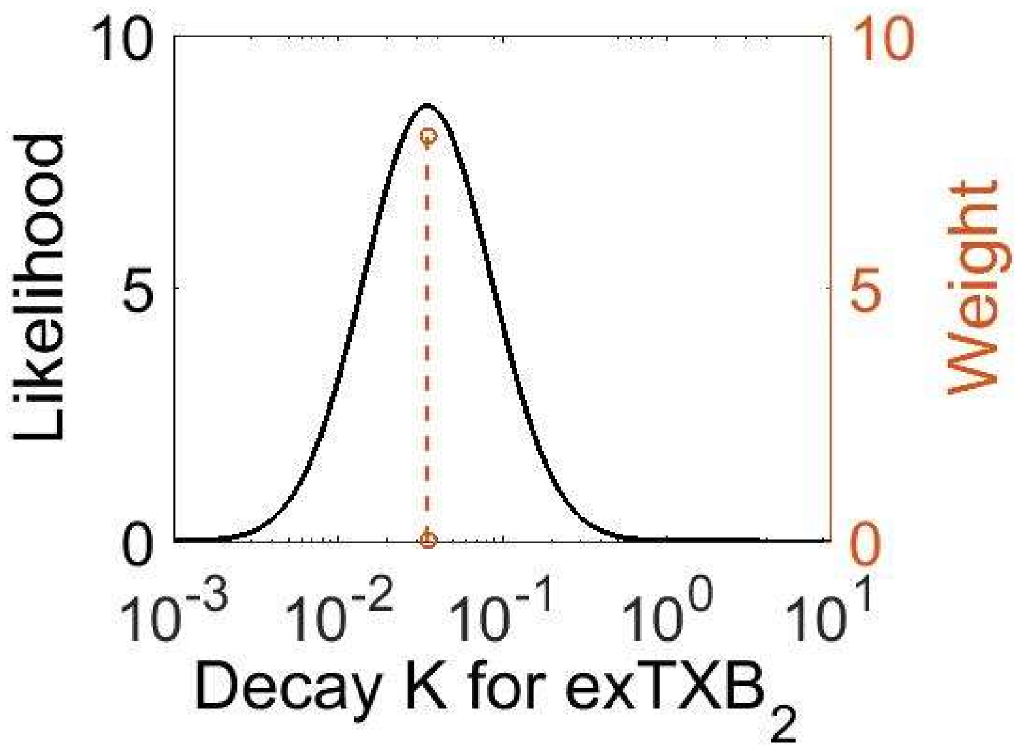

Figure SF.9.2.1.1.1. The estimated probability distribution for $exTXB_2$ decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.9.3. Reaction 46: $exTXA_2 \rightarrow \phi$

The decay of TXA_2 in the extracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

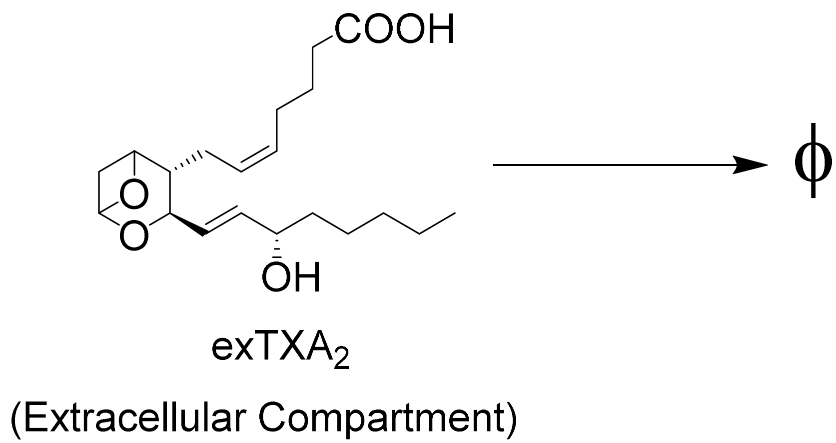

Figure SF.9.3. The decay of thromboxane A_2 (TXA_2) in the extracellular compartment (Reaction 46).

SEq.9.3. Reaction rate law for Reaction 46.

$$\boldsymbol{v_{46} = K[ex\mathbf{TXA_2}]}$$

S.9.3.1. Reaction parameters

S.9.3.1.1. Parameter: K

Parameter values for the K of Reaction 46 were obtained from the literature and summarised in Table ST.9.3.1.1.1. The log-normal distribution properties for the K of Reaction 46 are shown in Table ST.9.3.1.1.2 and plotted in Figure SF.9.3.1.1.1.

Table ST.9.3.1.1.1. Literature information used to design the $exTXA_2$ decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	Reference
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other		
0.333		2.079		Unknown, assume in vitro	TXA2	Unknown	Unknown	Unknown	Unknown	Textbook with no reference	8	(Wild, 2005)

Table ST.9.3.1.1.2 The log-normal distribution properties of the $exTXA_2$ decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
2.07	1.10	7.37×10^{-1}	9.4910^{-2}

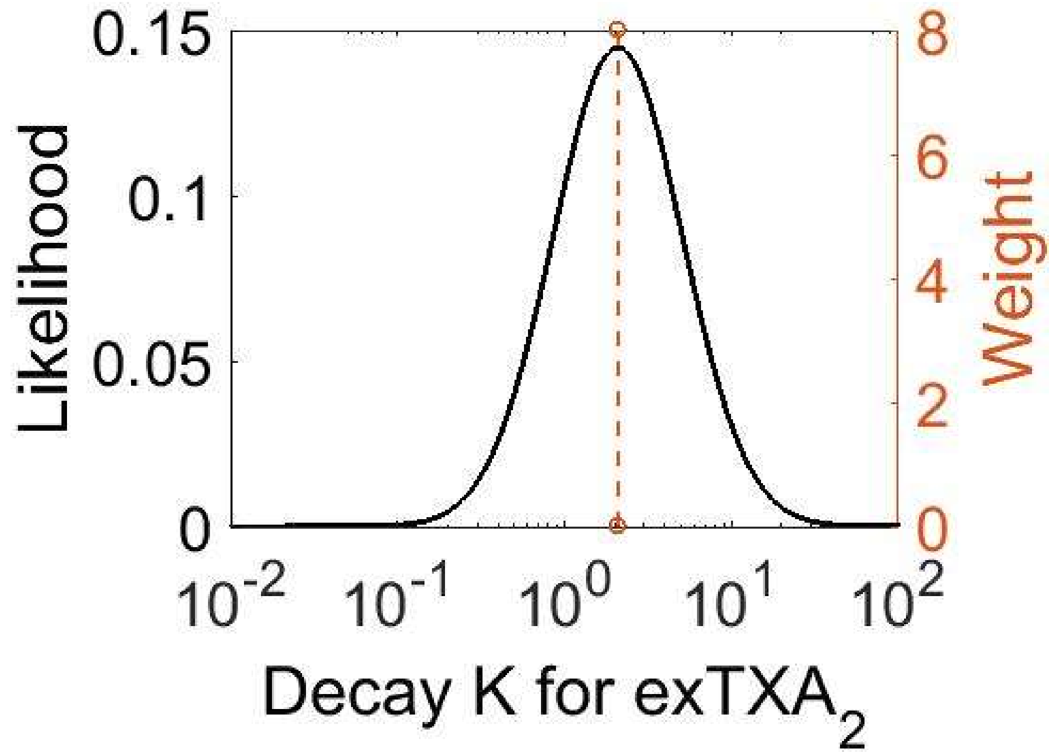

Figure SF.9.3.1.1.1. The estimated probability distribution for $exTXA_2$ decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.9.4. Reaction 47: ex6-keto-PGF$_{1\alpha}$ →ϕ

The decay of 6-keto-PGF$_{1\alpha}$ in the extracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

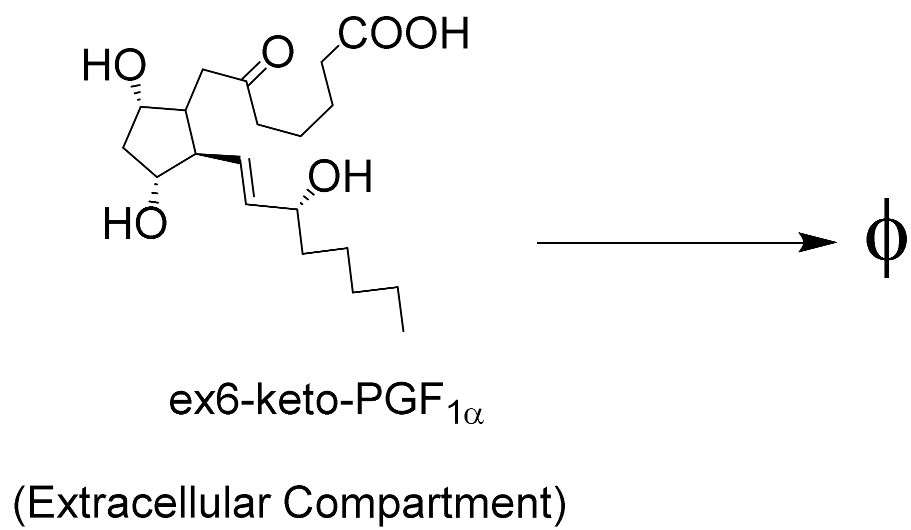

Figure SF.9.4. The decay of 6-keto-prostaglandin F$_{1\alpha}$ (6-keto-PGF$_{1\alpha}$) in the extracellular compartment (Reaction 47).

SEq.9.4. Reaction rate law for Reaction 47.

$$\boldsymbol{v_{47} = K[ex6 - keto - \mathrm{PGF}_{1\alpha}]}$$

S.9.4.1. Reaction parameters

S.9.4.1.1. Parameter: K

Parameter values for the K of Reaction 47 were obtained from the literature and summarised in Table ST.9.4.1.1.1. The log-normal distribution properties for the K of Reaction 47 are shown in Table ST.9.4.1.1.2 and plotted in Figure SF.9.4.1.1.1.

Table ST.9.4.1.1.1. Literature information used to design the ex6-keto-$PGF_{1\alpha}$ decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	Reference
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other		
30		0.023104906		In vivo	6-KETO-PGF1A	Human	Plasma	Unknown	Unknown		8	(Ylikorkala and Viinikka, 1981)

Table ST.9.4.1.1.2. The log-normal distribution properties of the ex6-keto-$PGF_{1\alpha}$ decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
2.30 $x10^{-2}$	1.10	-3.76	9.49 $x10^{-2}$

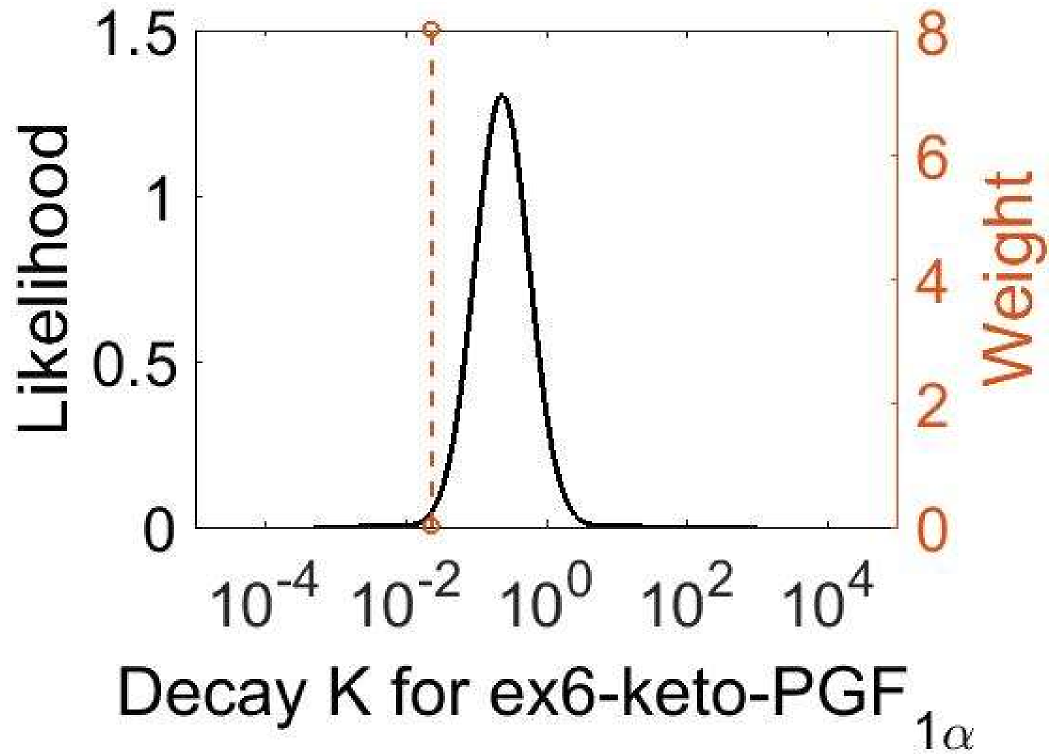

Figure SF.9.4.1.1.1. The estimated probability distribution for ex6-keto-$PGF_{1\alpha}$ decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.9.5. Reaction 48: exPGI$_2$ →ϕ

The decay of PGI$_2$ in the extracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

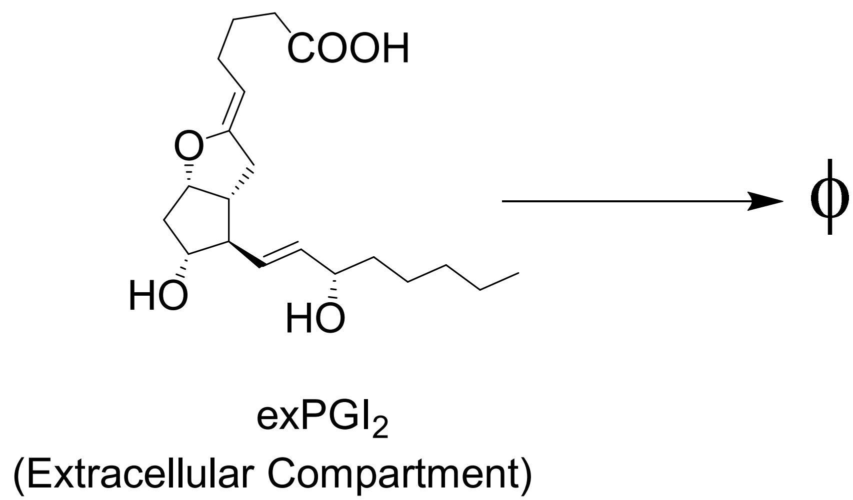

Figure SF.9.5. The decay of prostaglandin I$_2$ (PGI$_2$) in the extracellular compartment (Reaction 48).

SEq.9.5. Reaction rate law for Reaction 48.

$$\boldsymbol{v_{48} = K[exPGI_2]}$$

S.9.5.1. Reaction parameters

S.9.5.1.1. Parameter: K

Parameter values for the K of Reaction 48 were obtained from the literature and summarised in Table ST.9.5.1.1.1. The log-normal distribution properties for the K of Reaction 48 are shown in Table ST.9.5.1.1.2 and plotted in Figure SF.9.5.1.1.1.

Table ST.9.5.1.1.1. Literature information used to design the exPGI$_2$ decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	Reference
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other		
3		0.231		Unknown	PGI2	Unknown	Unknown	Unknown	Unknown	Textbook with no reference	8	(Cawello et al., 1994)

Table ST.9.5.1.1.2. The log-normal distribution properties of the exPGI$_2$ decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
2.30×10^{-1}	1.10	-1.46	9.4910^{-2}

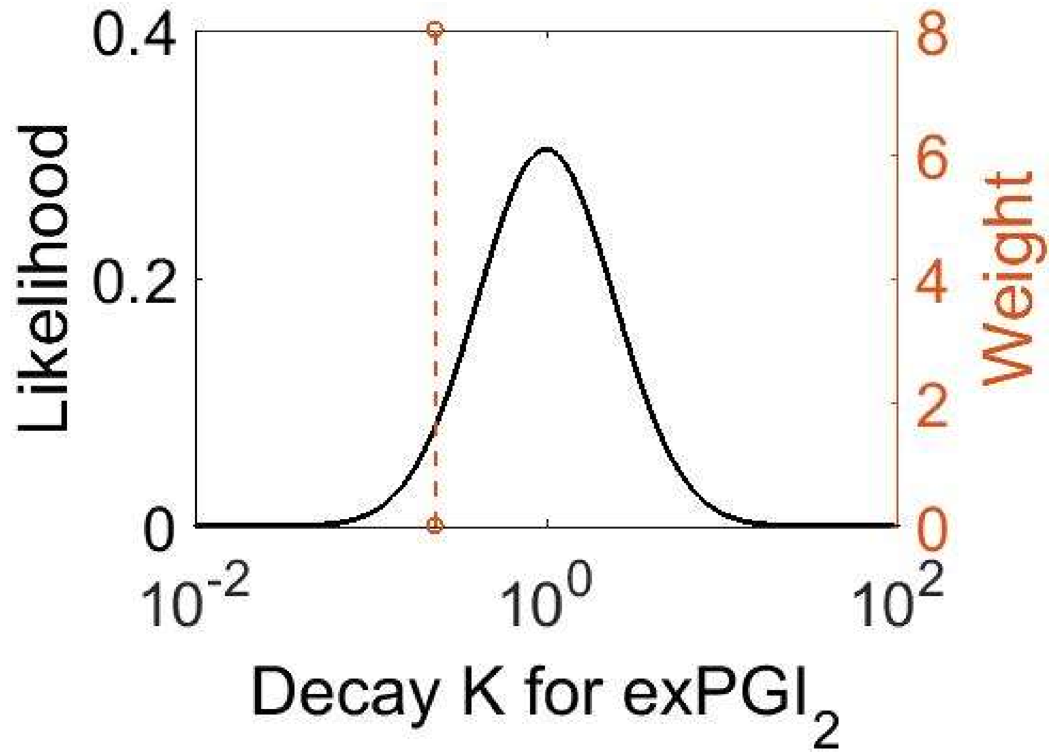

Figure SF.9.5.1.1.1. The estimated probability distribution for $exPGI_2$ decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.9.6. Reaction 49: $exPGE_2 \rightarrow \phi$

The decay of PGE_2 in the extracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

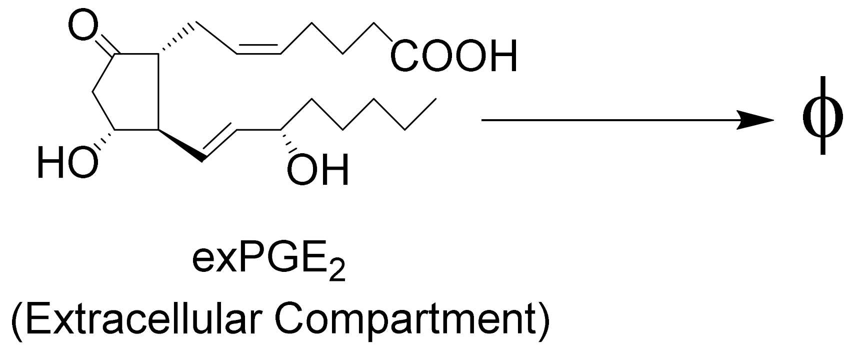

Figure SF.9.6. The decay of prostaglandin E_2 (PGE_2) in the extracellular compartment (Reaction 49).

SEq.9.6. Reaction rate law for Reaction 49.

$$\boldsymbol{v_{49} = K[exPGE_2]}$$

S.9.6.1. Reaction parameters

S.9.6.1.1. Parameter: K

Parameter values for the K of Reaction 49 were obtained from the literature and summarised in Table ST.9.6.1.1.1. The log-normal distribution properties for the K of Reaction 49 are shown in Table ST.9.6.1.1.2 and plotted in Figure SF.9.6.1.1.1.

Table ST.9.6.1.1.1. Literature information used to design the exPGE$_2$ decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	Reference
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other		
528	204	0.001	0.003	In vivo	PGE2	Human	Decidual stromal cells and macrophages	Unknown	Unknown		8	(Ishihara et al., 1991)

Table ST.9.6.1.1.2. The log-normal distribution properties of the exPGE$_2$ decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
3.16×10^{-4}	4.56	-7.04	1.01

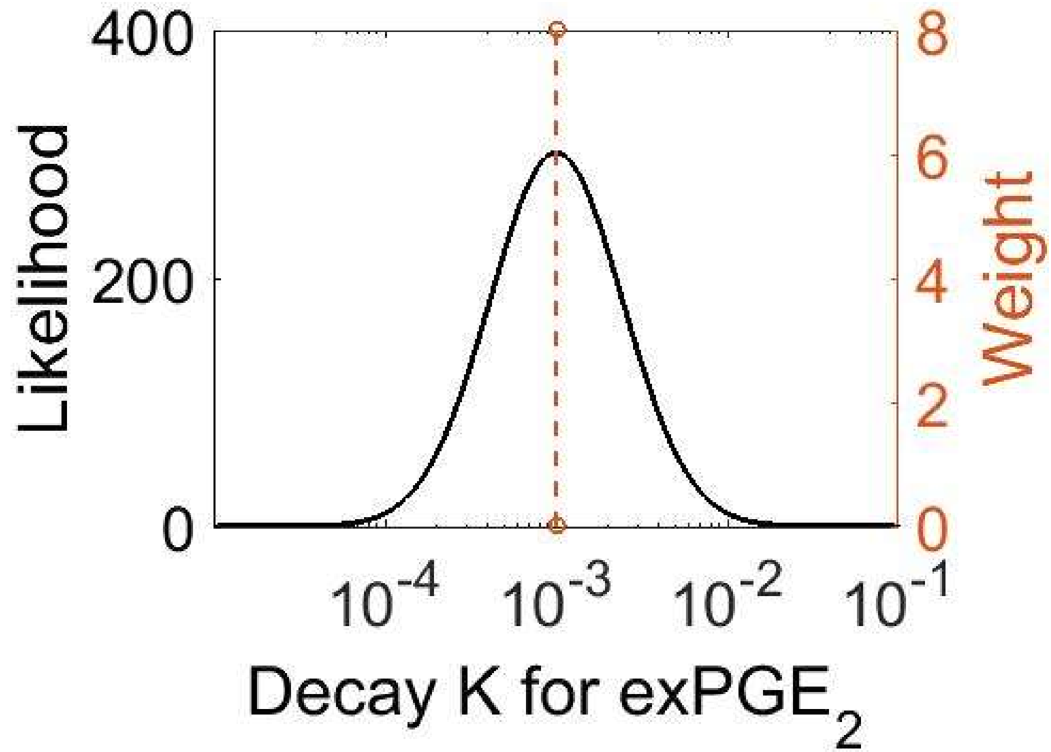

Figure SF.9.6.1.1.1. The estimated probability distribution for $exPGE_2$ decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.9.7. Reaction 50: ex15-deoxy-PGJ_2 →ϕ

The decay of 15-deoxy-PGJ_2 in the extracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

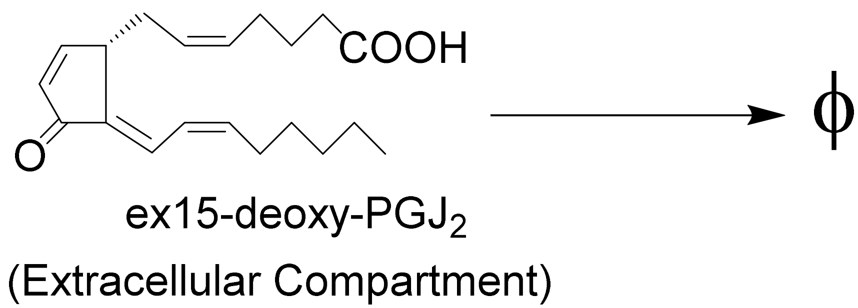

Figure SF.9.7 The decay of 15-deoxy-prostaglandin J_2 (15-deoxy-PGJ_2) in the extracellular compartment (Reaction 50).

SEq.9.7. Reaction rate law for Reaction 50.

$$\boldsymbol{v_{50} = K[ex15 - \mathrm{deoxy} - \mathrm{PGJ_2}]}$$

S.9.7.1. Reaction parameters

S.9.7.1.1. Parameter: K

Parameter values for the K of Reaction 50 were obtained from the literature and summarised in Table ST.9.7.1.1.1. The log-normal distribution properties for the K of Reaction 50 are shown in Table ST.9.7.1.1.2 and plotted in Figure SF.9.7.1.1.1.

Table ST.9.7.1.1.1. Literature information used to design the ex15-deoxy-PGJ_2 decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	Reference
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other		
720		0.001		In vivo	15-Deoxy-PGJ2	Human	Albumin	7.4	37		8	(Fitzpatrick and Wynalda, 1983)

Table ST.9.7.1.1.2. The log-normal distribution properties of the ex15-deoxy-PGJ_2 decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
9.95 $x10^{-4}$	1.10	-6.90	9.4910^{-2}

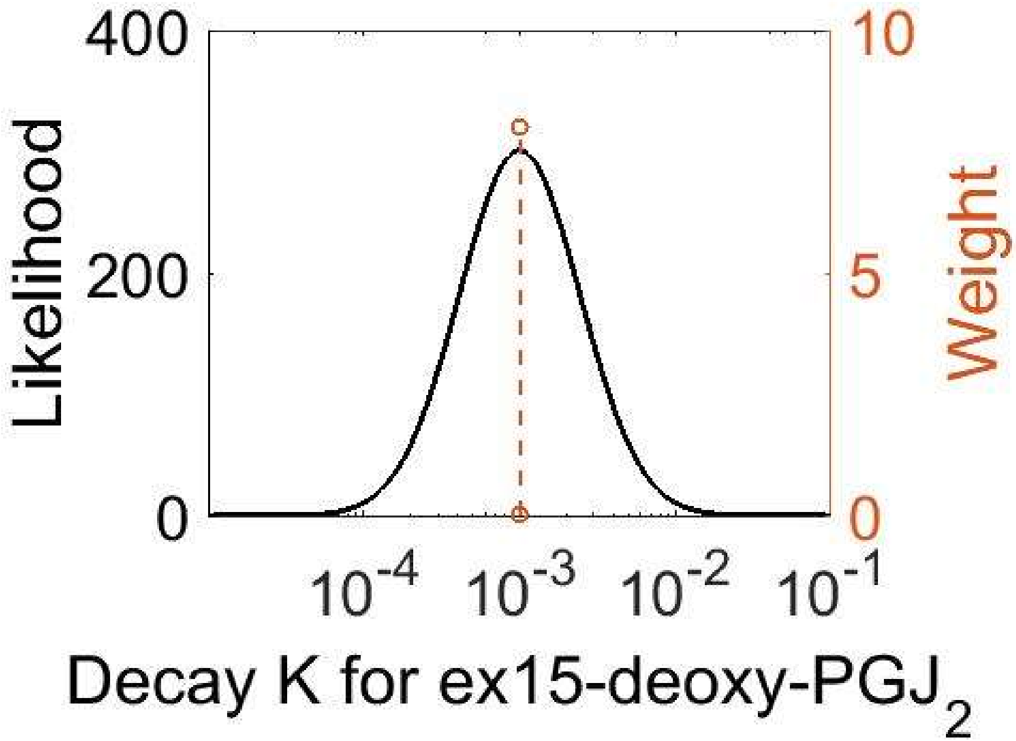

Figure SF.9.7.1.1.1. The estimated probability distribution for ex15-deoxy-PGJ$_2$ decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.9.8. Reaction 51: exPGJ$_2$ →ϕ

The decay of PGJ$_2$ in the extracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

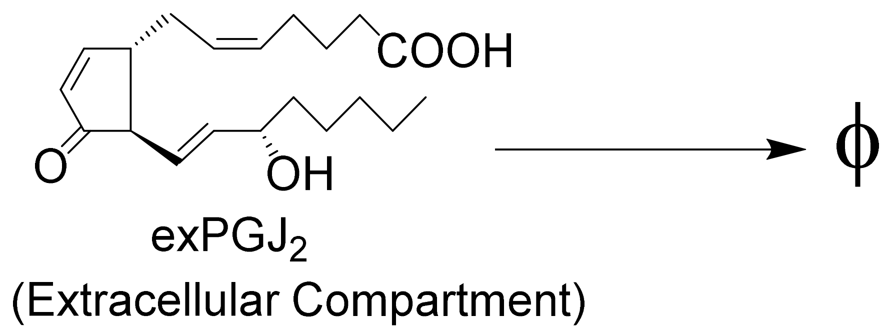

Figure SF.9.8. The decay of prostaglandin J$_2$ (PGJ$_2$) in the extracellular compartment (Reaction 51).

SEq.9.8. Reaction rate law for Reaction 51.

$$\boldsymbol{v_{51} = K[ex\mathrm{PGJ}_2\,]}$$

S.9.8.1. Reaction parameters

S.9.8.1.1. Parameter: K

Parameter values for the K of Reaction 51 were obtained from the literature and summarised in Table ST.9.8.1.1.1. The log-normal distribution properties for the K of Reaction 51 are shown in Table ST.9.8.1.1.2 and plotted in Figure SF.9.8.1.1.1.

Table ST.9.8.1.1.1. Literature information used to design the $exPGJ_2$ decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	Reference
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other		
720		0.001		In vivo	**15-Deoxy-PGJ2**	Human	Albumin	7.4	37		8	(Fitzpatrick and Wynalda, 1983)

Table ST.9.8.1.1.2. The log-normal distribution properties of the $exPGJ_2$ decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
9.95×10^{-4}	1.10	-6.90	9.4910^{-2}

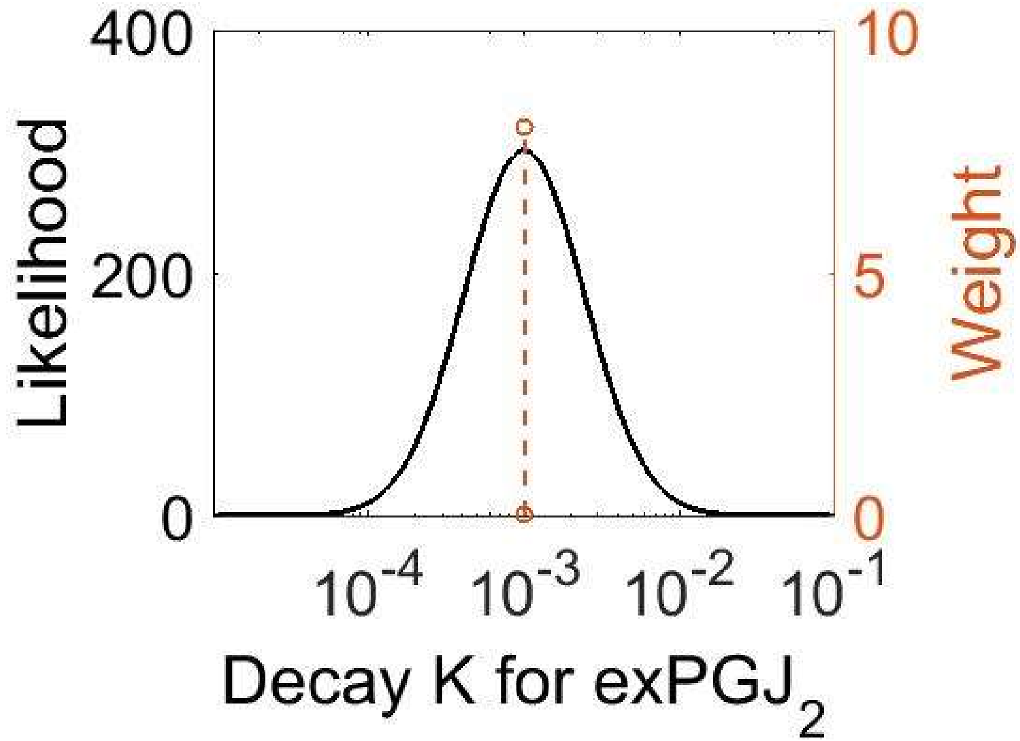

Figure SF.9.8.1.1.1. The estimated probability distribution for $exPGJ_2$ decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.9.9. Reaction 52: $exPGD_2 \rightarrow \phi$

The decay of PGD_2 in the extracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

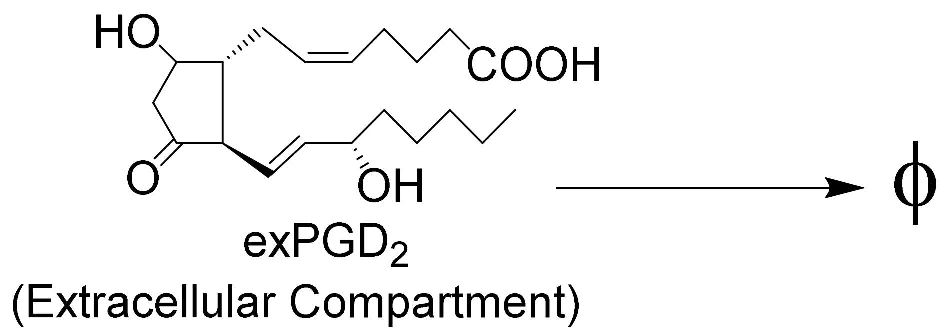

Figure SF.9.9. The decay of prostaglandin D_2 (PGD_2) in the extracellular compartment (Reaction 52).

SEq.9.9. Reaction rate law for Reaction 52.

$$\boldsymbol{v_{52} = K[exPGD_2]}$$

S.9.9.1. Reaction parameters

S.9.9.1.1. Parameter: K

Parameter values for the K of Reaction 52 were obtained from the literature and summarised in Table ST.9.9.1.1.1. The log-normal distribution properties for the K of Reaction 52 are shown in Table ST.9.9.1.1.2 and plotted in Figure SF.9.9.1.1.1.

Table ST.9.9.1.1.1. Literature information used to design the exPGD$_2$ decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	Reference
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other		
30		0.023		In vivo	PGD2	Human	Plasma	7	37		8	(Schuligoi et al., 2007)
1.5		0.462		In vivo	PGD2	Human	Brain	7.4	Unknown		8	(Suzuki et al., 1986)

Table ST.9.9.1.1.2. The log-normal distribution properties of the exPGD$_2$ decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
2.30 x10^{-2}	1.10	-3.76	9.4910^{-2}

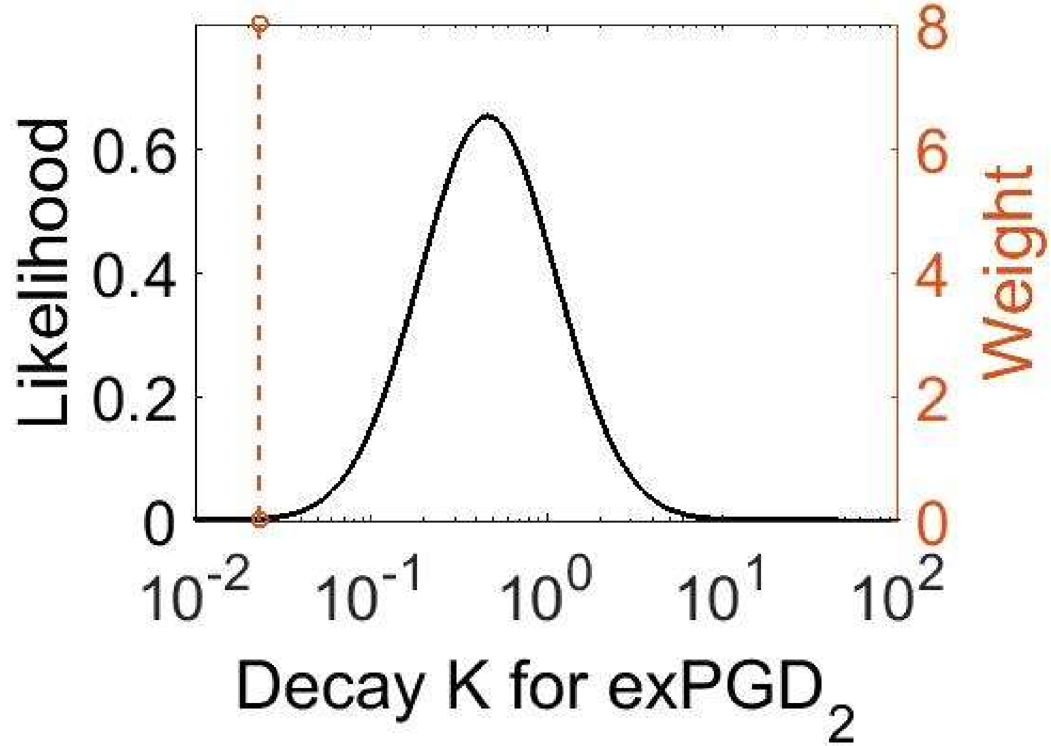

Figure SF.9.9.1.1.1. The estimated probability distribution for $exPGD_2$ decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.9.10. Reaction 53: $exPGH_2 \rightarrow \phi$

The decay of PGH_2 in the extracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

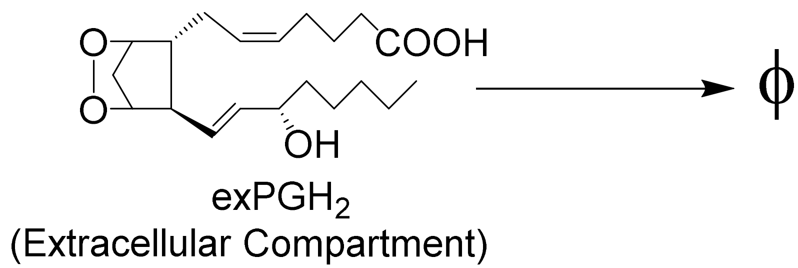

Figure SF.9.10. The decay of prostaglandin H_2 (PGH_2) in the extracellular compartment (Reaction 53).

SEq.9.10. Reaction rate law for Reaction 53.

$$\boldsymbol{v_{53} = K[exPGH_2]}$$

S.9.10.1. Reaction parameters

S.9.10.1.1. Parameter: K

Parameter values for the K of Reaction 53 were obtained from the literature and summarised in Table ST.9.10.1.1.1. The log-normal distribution properties for the K of Reaction 53 are shown in Table ST.9.10.1.1.2 and plotted in Figure SF.9.10.1.1.1.

Table ST.9.10.1.1.1. Literature information used to design the exPGH$_2$ decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	References
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other		
5		0.139		In vivo	PGH2	Unknown	Unknown	Unknown	Unknown	Textbook with no reference	8	(Sciences, 2019)

Table ST.9.10.1.1.2. The log-normal distribution properties of the exPGH$_2$ decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.38 x10^{-1}	1.10	-1.97	9.49 x10^{-2}

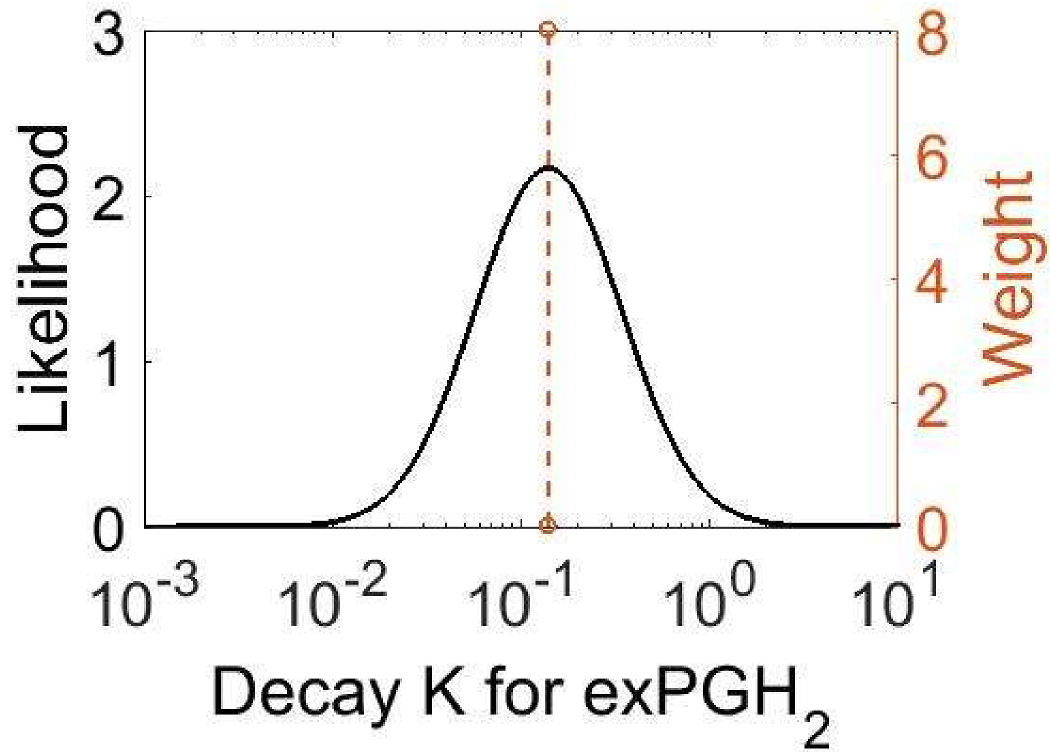

Figure SF.9.10.1.1.1. The estimated probability distribution for $exPGH_2$ decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.9.11. Reaction 54: ex5-oxo-ETE →ϕ

The decay of 5-oxo-ETE in the extracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

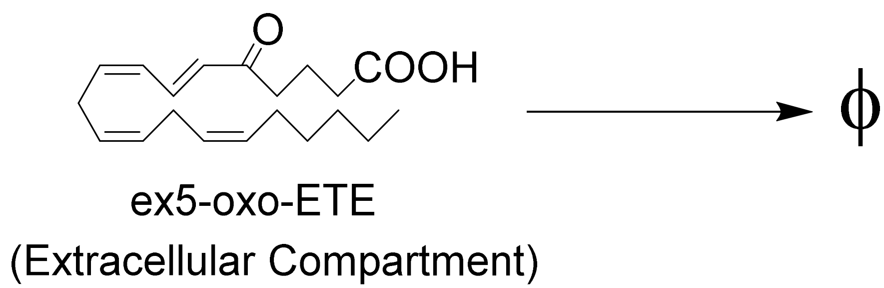

Figure SF.9.11. The decay of 5-oxo-eicosatetraenoic acid (5-oxo-ETE) in the extracellular compartment (Reaction 54).

SEq.9.11. Reaction rate law for Reaction 54.

$$\boldsymbol{v_{54}} = \boldsymbol{K}[\boldsymbol{ex}\mathbf{5} - \mathbf{oxo} - \mathbf{ETE}]$$

S.9.11.1. Reaction parameters

S.9.11.1. Parameter: K

Parameter values for the K of Reaction 54 were obtained from the literature and summarised in Table ST.9.11.1.1.1. The log-normal distribution properties for the K of Reaction 54 are shown in Table ST.9.11.1.1.2 and plotted in Figure SF.9.11.1.1.1.

Table ST.9.11.1.1.1. Literature information used to design the ex5-oxo-ETE decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	References
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other		
11		0.064		In vivo	**15-OXO-ETE**	Human	R15L Cells	Unknown	37		8	(Wei et al., 2009)

Table ST.9.11.1.1.2. The log-normal distribution properties of the ex5-oxo-ETE decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
6.37 x10^{-2}	1.10	-2.74	9.49$10^{-2}$

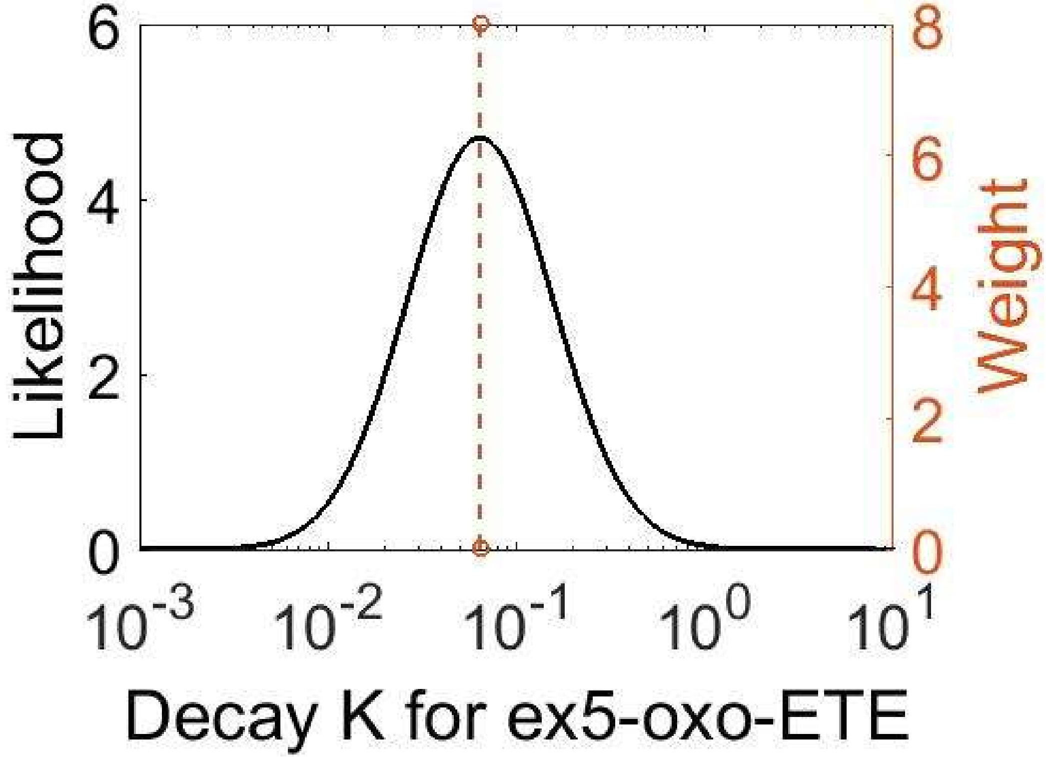

Figure SF.9.11.1.1.1. The estimated probability distribution for ex5-oxo-ETE decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.9.12. Reaction 55: ex5-HETE →ϕ

The decay of 5-HETE in the extracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

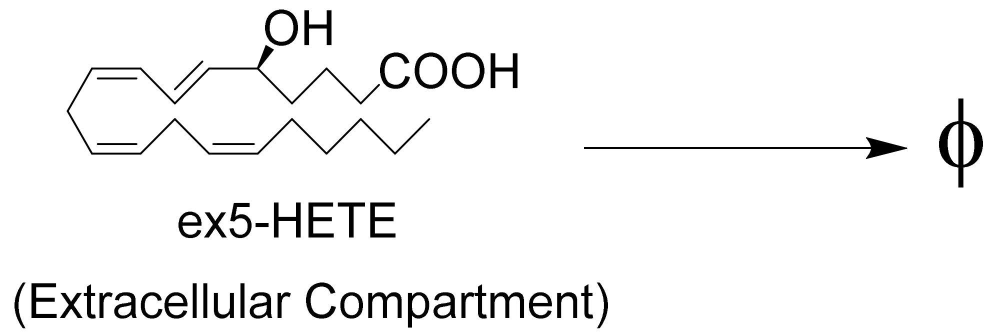

Figure SF.9.12. The decay of 5-hydroxyeicosatetraenoic acid (5-HETE) in the extracellular compartment (Reaction 55).

SEq.9.12. Reaction rate law for Reaction 55.

$$\boldsymbol{v_{55} = K[ex5 - \mathbf{HETE}]}$$

S.9.11.1. Reaction parameters

S.9.11.1.1. Parameter: K

Parameter values for the K of Reaction 55 were obtained from the literature and summarised in Table ST.9.11.1.1.1. The log-normal distribution properties for the K of Reaction 55 are shown in Table ST.9.11.1.1.2 and plotted in Figure SF.9.11.1.1.1.

Table ST.9.11.1.1.1. Literature information used to design the ex5-HETE decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	References
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other		
21		0.033		In vivo	**15-HETE**	Human	R15L Cells	Unknown	37		8	(Wei et al., 2009)

Table ST.9.11.1.1.2. The log-normal distribution properties of the ex5-HETE decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
3.30 $x10^{-2}$	1.10	-3.40	9.4910^{-2}

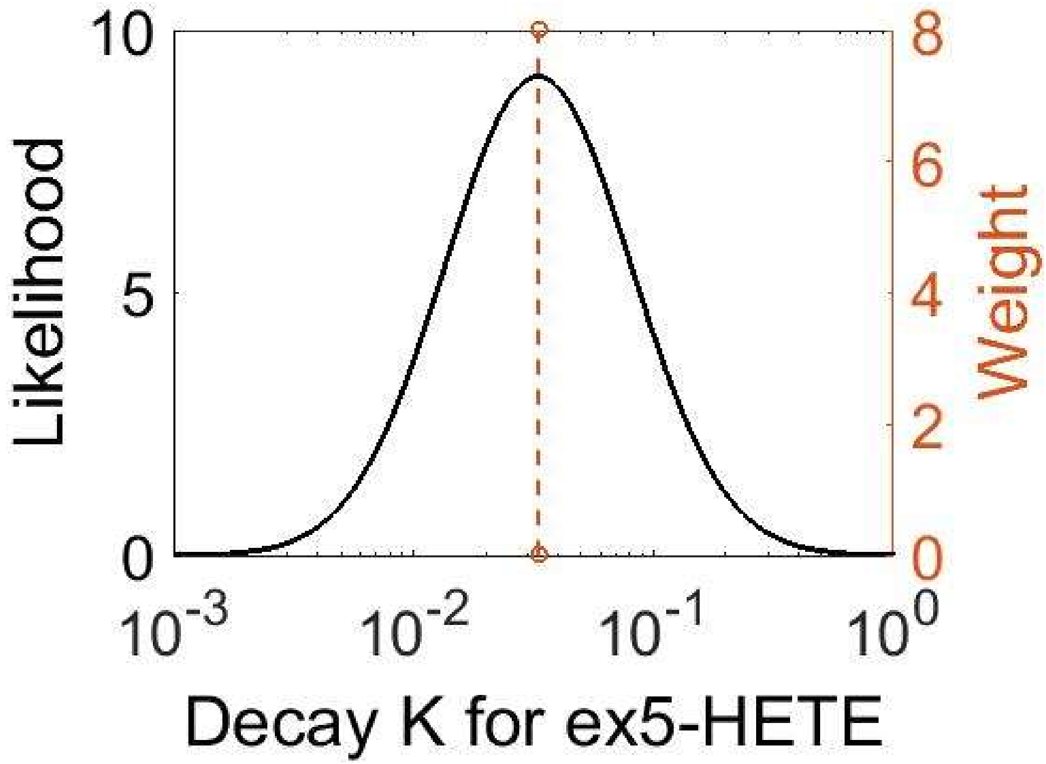

Figure SF.9.11.1.1.1. The estimated probability distribution for ex5-HETE decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.9.12. Reaction 56: $exLTB_4 \rightarrow \phi$

The decay of LTB_4 in the extracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

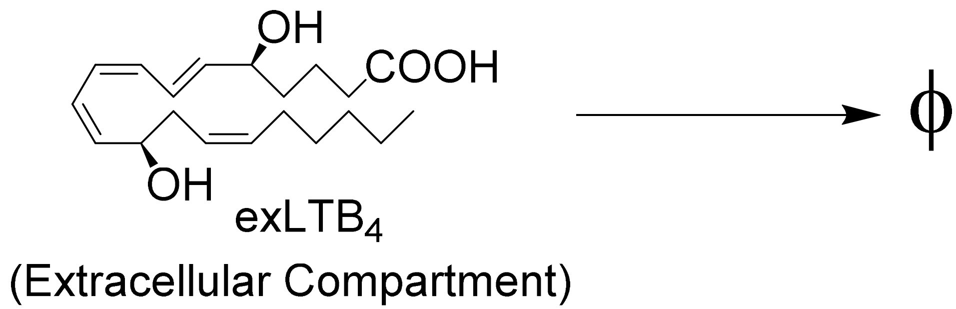

Figure SF.9.12. The decay of leukotriene B_4 (LTB_4) in the extracellular compartment (Reaction 56).

SEq.9.12. Reaction rate law for Reaction 56.

$$\boldsymbol{v_{56} = K[exLTB_4]}$$

S.9.12.1. Reaction parameters

S.9.12.1.1. Parameter: K

Parameter values for the K of Reaction 56 were obtained from the literature and summarised in Table ST.9.12.1.1.1. The log-normal distribution properties for the K of Reaction 56 are shown in Table ST.9.12.1.1.2 and plotted in Figure SF.9.12.1.1.1.

Table ST.9.12.1.1.1. Literature information used to design the exLTB$_4$ decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	References
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other		
0.47		1.475		In vivo	LTB4	Rabbit	Plasma	7.4	Unknown		8	(Marleau et al., 1994)

Table ST.9.12.1.1.2. The log-normal distribution properties of the exLTB$_4$ decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.47	1.10	3.93 x10^{-1}	9.4910^{-2}

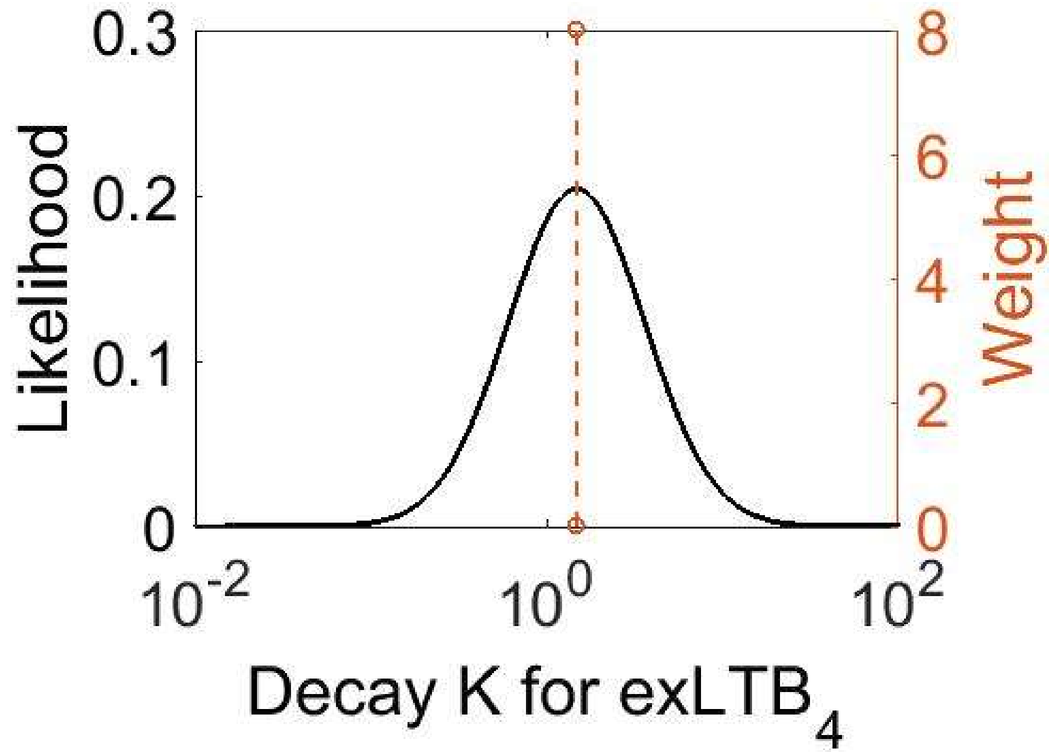

Figure SF.9.12.1.1.1. The estimated probability distribution for exLTB$_4$ decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.9.13. Reaction 57: $exLTC_4 \rightarrow \phi$

The decay of LTC_4 in the extracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

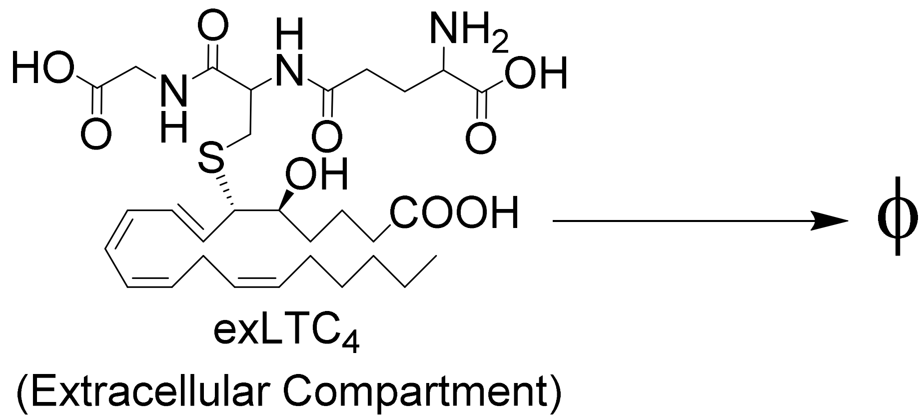

Figure SF.9.13. The decay of leukotriene C_4 (LTC_4) in the extracellular compartment (Reaction 57).

SEq.9.13. Reaction rate law for Reaction 57.

$$\boldsymbol{v_{57} = K[exLTC_4\,]}$$

S.9.13.1. Reaction parameters

S.9.13.1.1. Parameter: K

Parameter values for the K of Reaction 57 were obtained from the literature and summarised in Table ST.9.13.1.1.1. The log-normal distribution properties for the K of Reaction 57 are shown in Table ST.9.13.1.1.2 and plotted in Figure SF.9.13.1.1.1.

Table ST.9.13.1.1.1. Literature information used to design the exLTC$_4$ decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	References
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other		
0.47		1.475		In vivo	**LTB4**	Rabbit	Plasma	7.4	Unknown		8	(Marleau et al., 1994)

Table ST.9.13.1.1.2. The log-normal distribution properties of the exLTC$_4$ decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.47	1.10	3.93×10^{-1}	9.4910^{-2}

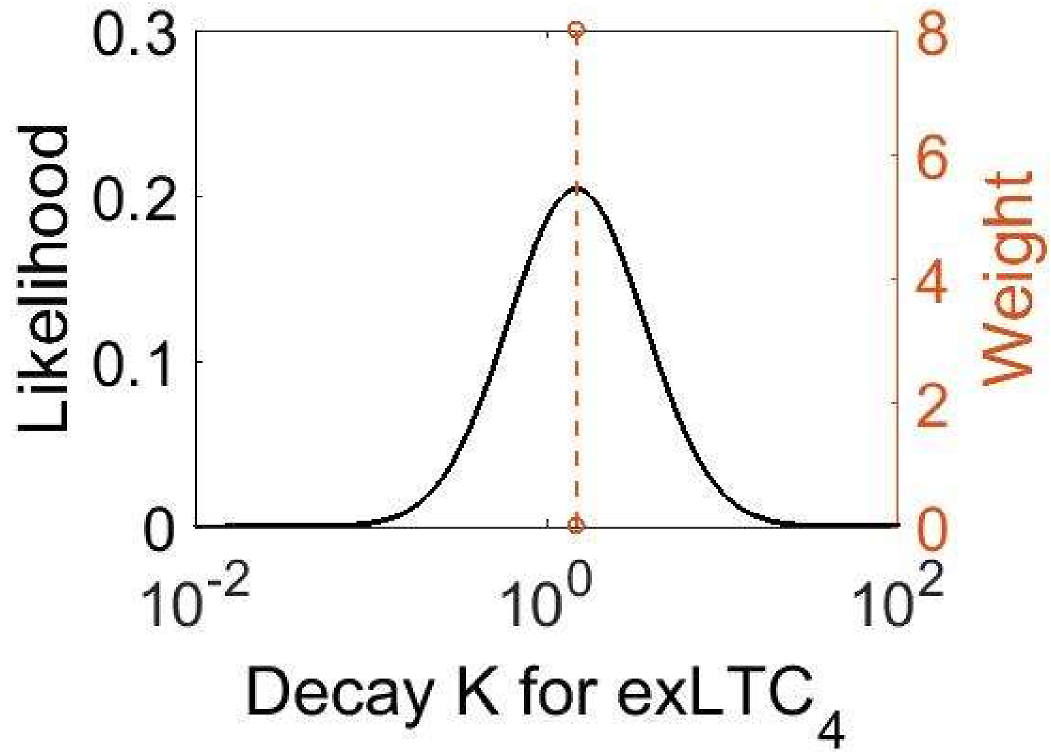

Figure SF.9.13.1.1.1. The estimated probability distribution for $exLTC_4$ decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.9.14. Reaction 58: exLTA$_4$ →ϕ

The decay of LTA$_4$ in the extracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

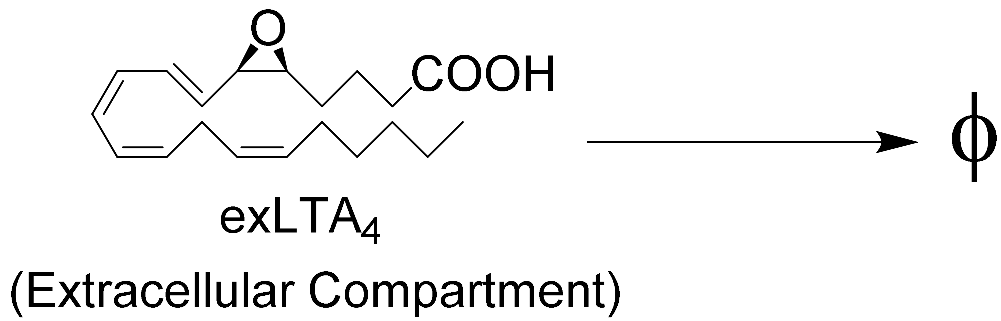

Figure SF.9.14. The decay of leukotriene A$_4$ (LTA$_4$) in the extracellular compartment (Reaction 58).

SEq.9.14. Reaction rate law for Reaction 58.

$$\boldsymbol{v_{58} = K[ex\mathbf{LTA_4}]}$$

S.9.14.1. Reaction parameters

S.9.14.1.1. Parameter: K

Parameter values for the K of Reaction 58 were obtained from the literature and summarised in Table ST.9.14.1.1.1. The log-normal distribution properties for the K of Reaction 58 are shown in Table ST.9.14.1.1.2 and plotted in Figure SF.9.14.1.1.1.

Table ST.9.14.1.1.1. Literature information used to design the $exLTA_4$ decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	References
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other		
0.05		13.863		In vivo	LTA4	Unknown	Unknown	7	37		8	(Dickinson Zimmer et al., 2004)

Table ST.9.14.1.1.2. The log-normal distribution properties of the $exLTA_4$ decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.38×10^{1}	1.10	2.63	9.4910^{-2}

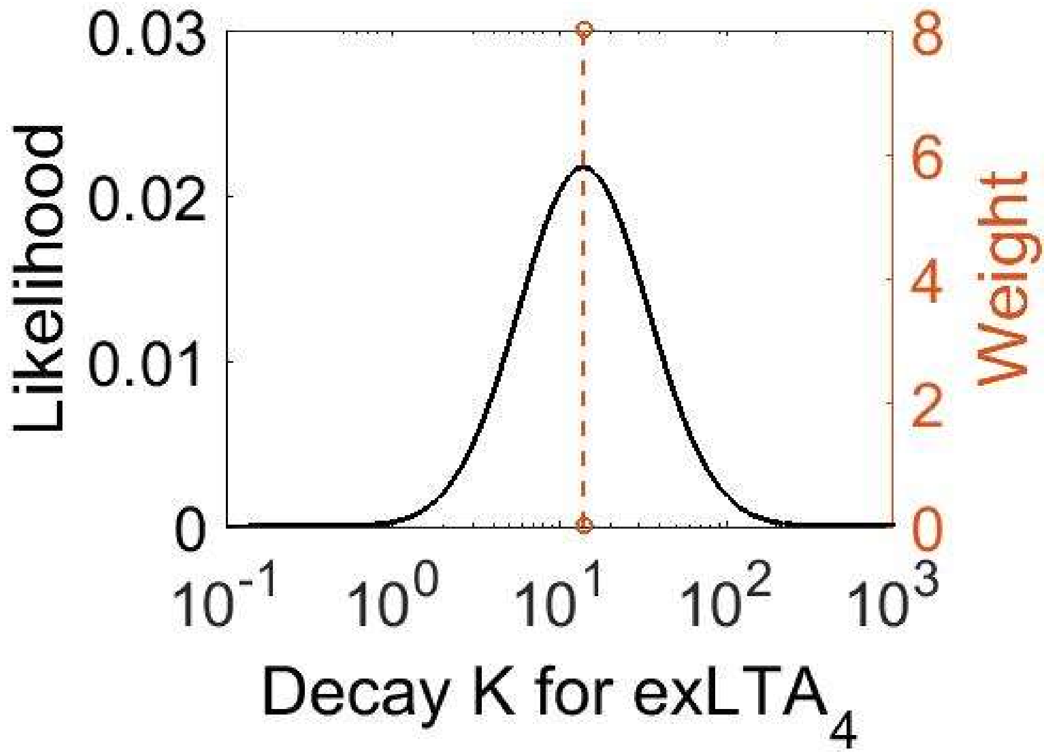

Figure SF.9.14.1.1.1. The estimated probability distribution for $exLTA_4$ decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.9.15. Reaction 59: ex5-HPETE →ϕ

The decay of 5-HPETE in the extracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

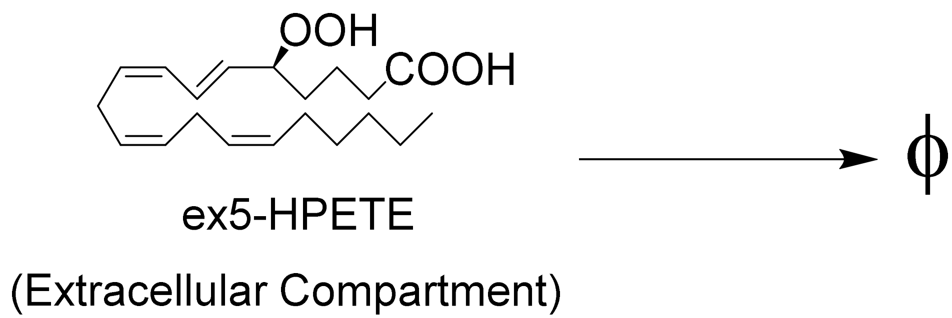

Figure SF.9.15. The decay of 5-hydroperoxyeicosatetraenoic acid (5-HPETE) in the extracellular compartment (Reaction 59).

SEq.9.15. Reaction rate law for Reaction 59.

$$\boldsymbol{v_{59} = K[ex5 - \mathbf{HPETE}\,]}$$

S.9.15.1. Reaction parameters

S.9.15.1.1. Parameter: K

Parameter values for the K of Reaction 59 were obtained from the literature and summarised in Table ST.9.15.1.1.1. The log-normal distribution properties for the K of Reaction 59 are shown in Table ST.9.15.1.1.2 and plotted in Figure SF.9.15.1.1.1.

Table ST.9.15.1.1.1. Literature information used to design the ex5-HPETE decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	References
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other		
0.5		1.386		In vivo	**12-HPETE**	Unknown	Unknown	Unknown	Unknown		8	(Maclouf et al., 1982)

Table ST.9.15.1.1.2. The log-normal distribution properties of the ex5-HPETE decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.38	1.10	3.31×10^{-1}	9.4910^{-2}

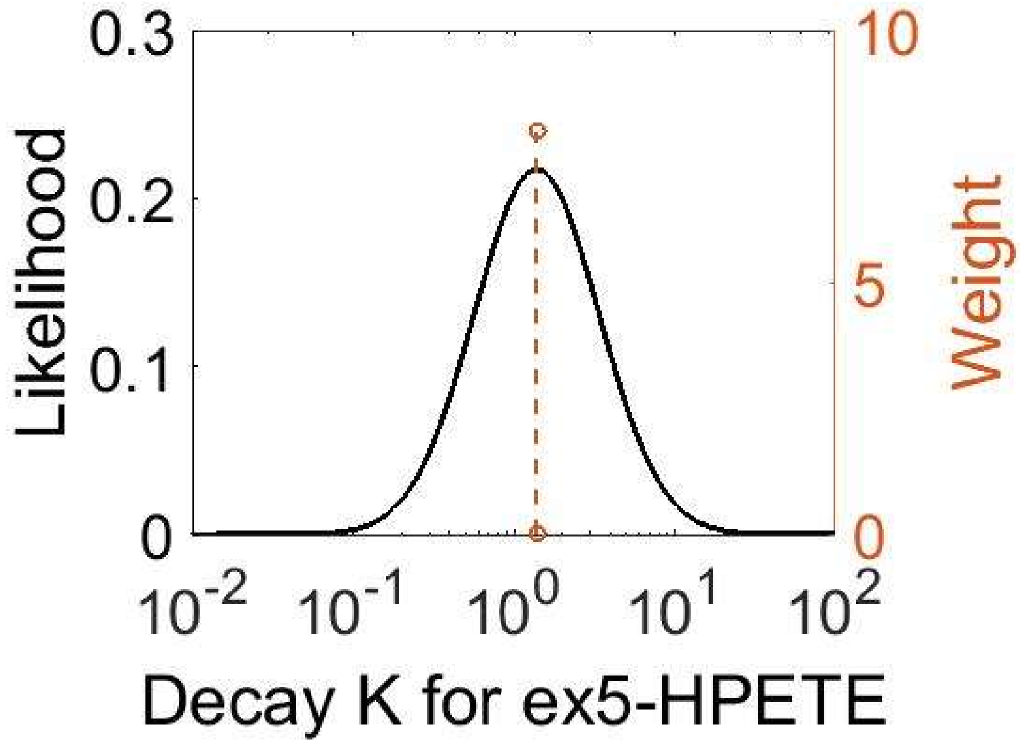

Figure SF.9.15.1.1.1. The estimated probability distribution for ex5-HPETE decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.9.16. Reaction 60: ex15-HETE→ϕ

The decay of 15-HETE in the extracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

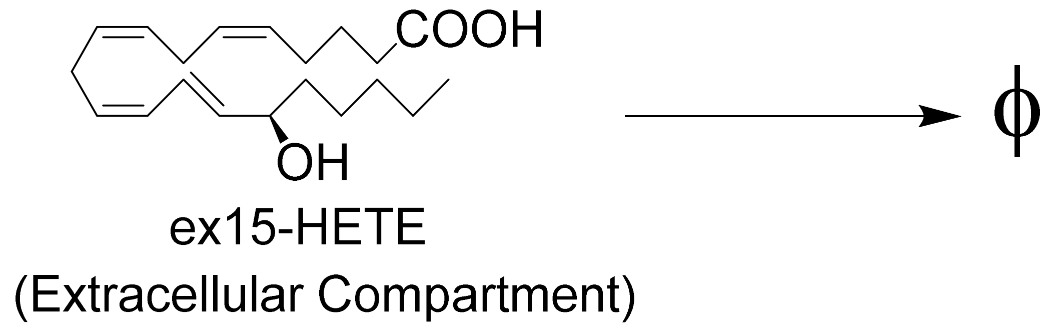

Figure SF.9.16. The decay of 15-hydroxyeicosatetraeonic acid (15-HETE) in the extracellular compartment (Reaction 60).

SEq.9.16. Reaction rate law for Reaction 60.

$$\boldsymbol{v_{60} = K[ex15 - \mathbf{HETE}\,]}$$

S.9.16.1. Reaction parameters

S.9.16.1.1. Parameter: K

Parameter values for the K of Reaction 60 were obtained from the literature and summarised in Table ST.9.16.1.1.1. The log-normal distribution properties for the K of Reaction 60 are shown in Table ST.9.16.1.1.2 and plotted in Figure SF.9.16.1.1.1.

Table ST.9.16.1.1.1. Literature information used to design the ex15-HETE decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	References
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other		
21		0.033		In vivo	15-HETE	Human	R15L Cells	Unknown	37		8	(Wei et al., 2009)

Table ST.9.16.1.1.2. The log-normal distribution properties of the ex15-HETE decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
3.30×10^{-2}	1.10	-3.40	9.4910^{-2}

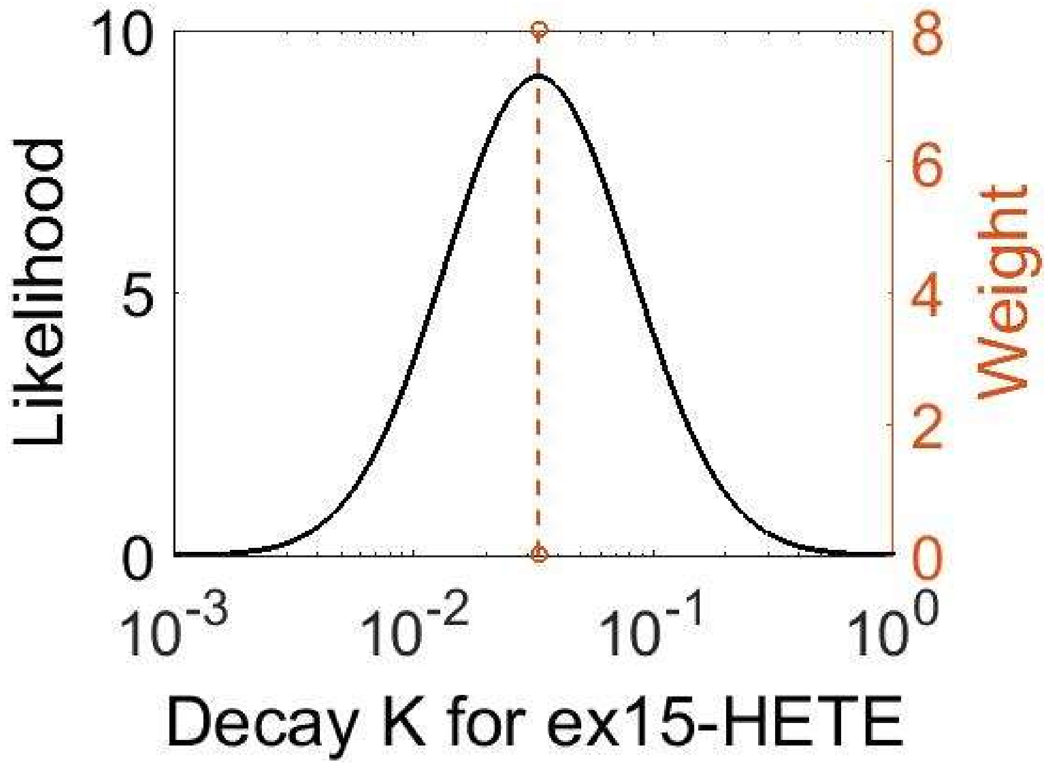

Figure SF.9.16.1.1.1. The estimated probability distribution for ex15-HETE decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.9.17. Reaction 61: ex15-HPETE→ϕ

The decay of 15-HPETE in the extracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

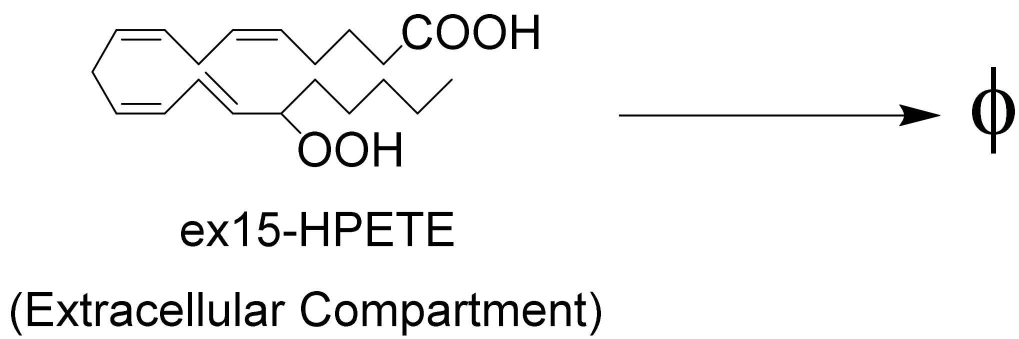

Figure SF.9.17. The decay of 15-hydroperoxyeicosatetraenoic acid (15-HPETE) in the extracellular compartment (Reaction 61).

SEq.9.17. Reaction rate law for Reaction 61.

$$\boldsymbol{v_{61}} = \boldsymbol{K}[\boldsymbol{ex15} - \mathbf{HPETE}]$$

S.9.17.1. Reaction parameters

S.9.17.1.1. Parameter: K

Parameter values for the K of Reaction 61 were obtained from the literature and summarised in Table ST.9.17.1.1.1. The log-normal distribution properties for the K of Reaction 61 are shown in Table ST.9.17.1.1.2 and plotted in Figure SF.9.17.1.1.1.

Table ST.9.17.1.1.1. Literature information used to design the ex15-HPETE decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	References
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other		
0.5		1.386		In vivo	**12-HPETE**	Unknown	Unknown	Unknown	Unknown		8	(Maclouf et al., 1982)

Table ST.9.17.1.1.2. The log-normal distribution properties of the ex15-HPETE decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.38	1.10	3.31×10^{-1}	9.4910^{-2}

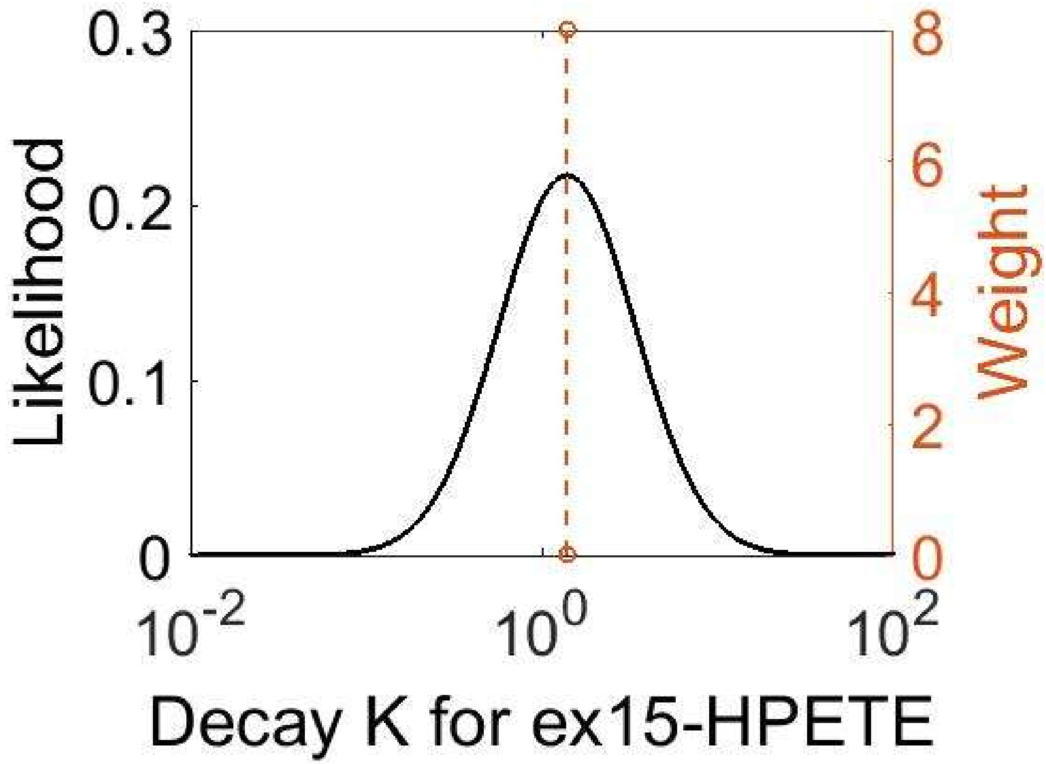

Figure SF.9.17.1.1.1. The estimated probability distribution for ex15-HPETE decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale**.**

S.9.18. Reaction 62: ex12-HETE →ϕ

The decay of 12-HETE in the extracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

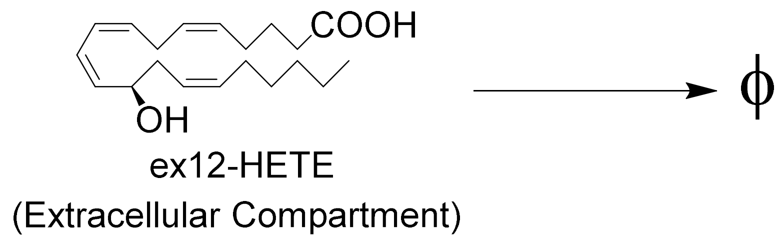

Figure SF.9.18. The decay of 12-hydroxyeicosatetraenoic acid (12-HETE) in the extracellular compartment (Reaction 62).

SEq.9.18. Reaction rate law for Reaction 62.

$$\boldsymbol{v_{62} = K[ex12 - \mathrm{HETE}]}$$

S.9.18.1. Reaction parameters

S.9.18.1.1. Parameter: K

Parameter values for the K of Reaction 62 were obtained from the literature and summarised in Table ST.9.18.1.1.1. The log-normal distribution properties for the K of Reaction 62 are shown in Table ST.9.18.1.1.2 and plotted in Figure SF.9.18.1.1.1.

Table ST.9.18.1.1.1. Literature information used to design the ex12-HETE decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	References
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other		
180		0.004		In vivo	12-HETE	Rabbit	Platelets	Unknown	37		8	(Dadaian et al., 1998)

Table ST.9.18.1.1.2. The log-normal distribution properties of the ex12-HETE decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
3.83 $x10^{-3}$	1.10	-5.56	9.4910^{-2}

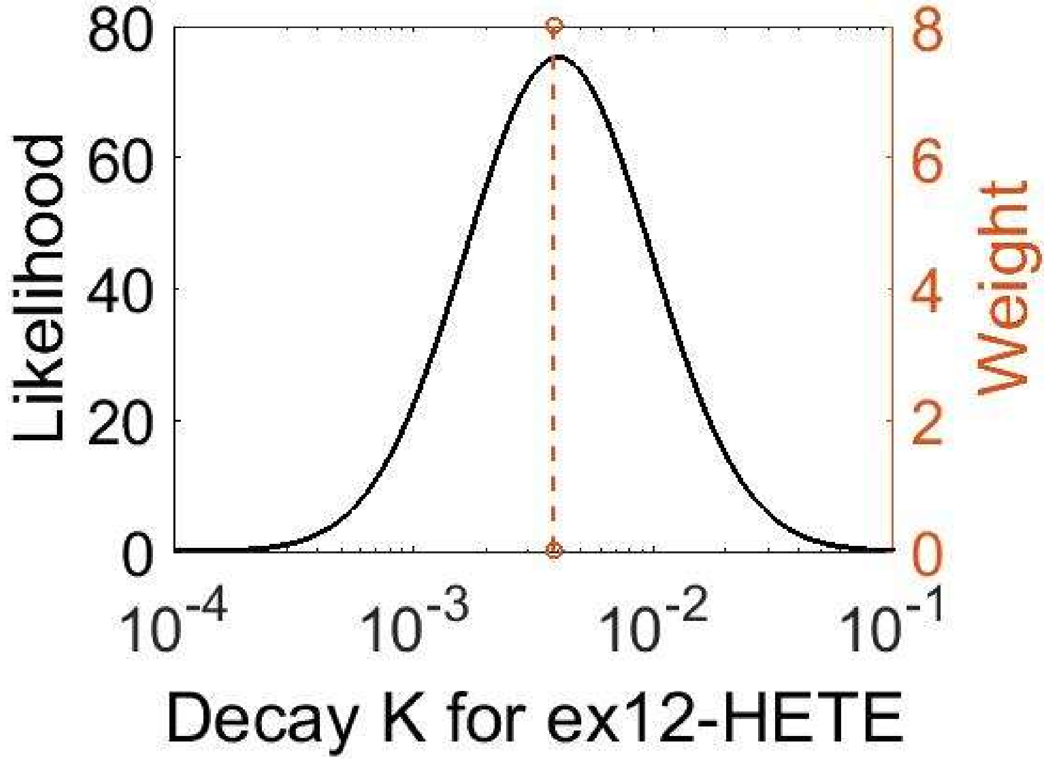

Figure SF.9.18.1.1.1. The estimated probability distribution for ex12-HETE decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-**scale.**

S.9.19. Reaction 63: ex12-HPETE→ϕ

The decay of 12-HPETE in the extracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

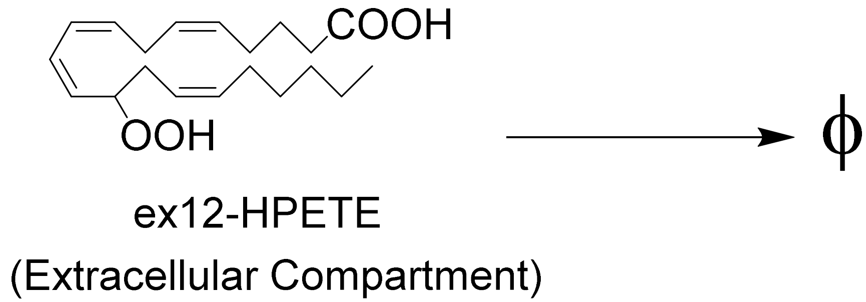

Figure SF.9.19. The decay of 12-hydroperoxyeicosatetraenoic acid (12-HPETE) in the extracellular compartment (Reaction 63).

SEq.9.19. Reaction rate law for Reaction 63.

$$\boldsymbol{v_{63}} = \boldsymbol{K}[\boldsymbol{ex12} - \mathbf{HPETE}]$$

S.9.19.1. Reaction parameters

S.9.19.1.1. Parameter: K

Parameter values for the K of Reaction 63 were obtained from the literature and summarised in Table ST.9.19.1.1.1. The log-normal distribution properties for the K of Reaction 63 are shown in Table ST.9.19.1.1.2 and plotted in Figure SF.9.19.1.1.1.

Table ST.9.19.1.1.1. Literature information used to design the ex12-HPETE decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	References
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other		
0.5		1.386		Unknown	12-HPETE	Unknown	Unknown	Unknown	Unknown	Textbook with no reference	8	(Maclouf et al., 1982)

Table ST.9.19.1.1.2. The log-normal distribution properties of the ex12-HPETE decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.85×10^{-1}	7.46	-2.52×10^{-1}	1.20

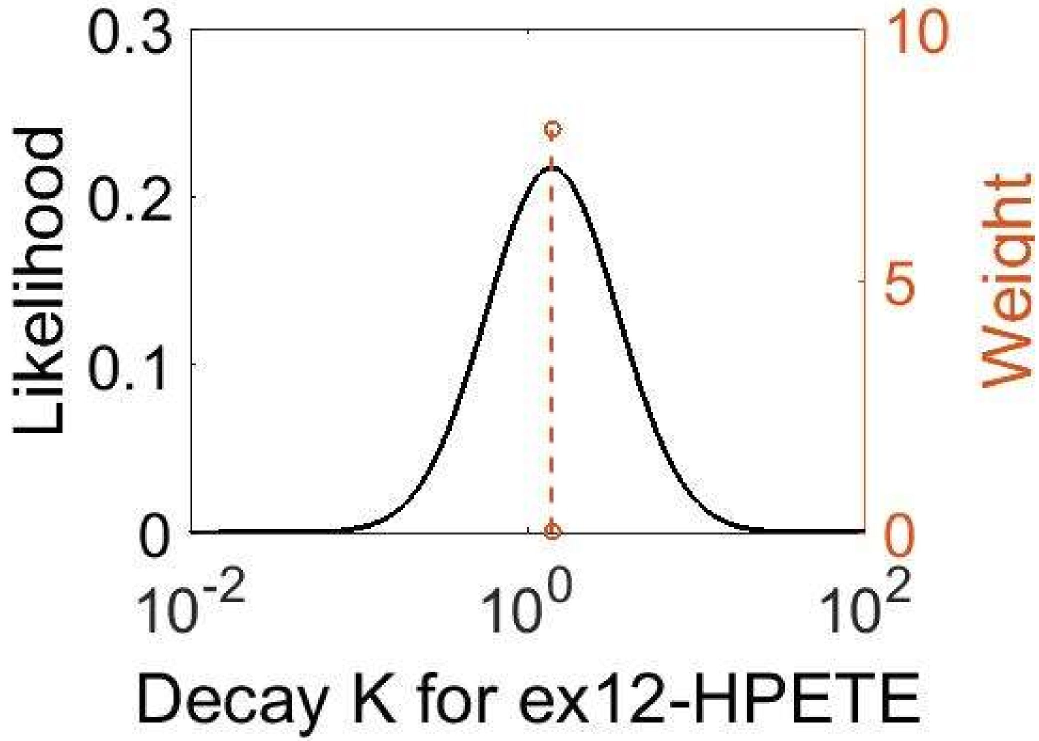

Figure SF.9.19.1.1.1. The estimated probability distribution for ex12-HPETE decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.9.20. Reaction 64: exAA →ϕ

The decay of AA in the extracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

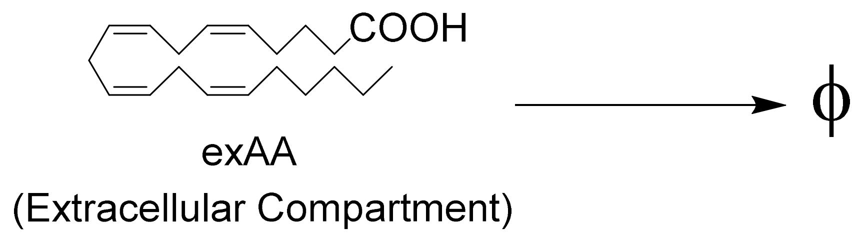

Figure SF.9.20. The decay of arachidonic acid (AA) in the extracellular compartment (Reaction 64).

SEq.9.20. Reaction rate law for Reaction 64.

$$\boldsymbol{v_{64} = K[exAA]}$$

S.9.20.1. Reaction parameters

S.9.20.1. Parameter: K

Parameter values for the K of Reaction 64 were obtained from the literature and summarised in Table ST.9.20.1.1.1. The log-normal distribution properties for the K of Reaction 64 are shown in Table ST.9.20.1.1.2 and plotted in Figure SF.9.20.1.1.1.

Table ST.9.20.1.1.1. Literature information used to design the exAA decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	References
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other		
240		0.003		In vivo	AA	Human	Platelets	Unknown	37		8	(Vinge, 1985)

Table ST.9.20.1.1.2. The log-normal distribution properties of the exAA decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
2.88×10^{-3}	1.10	-5.84	9.4910^{-2}

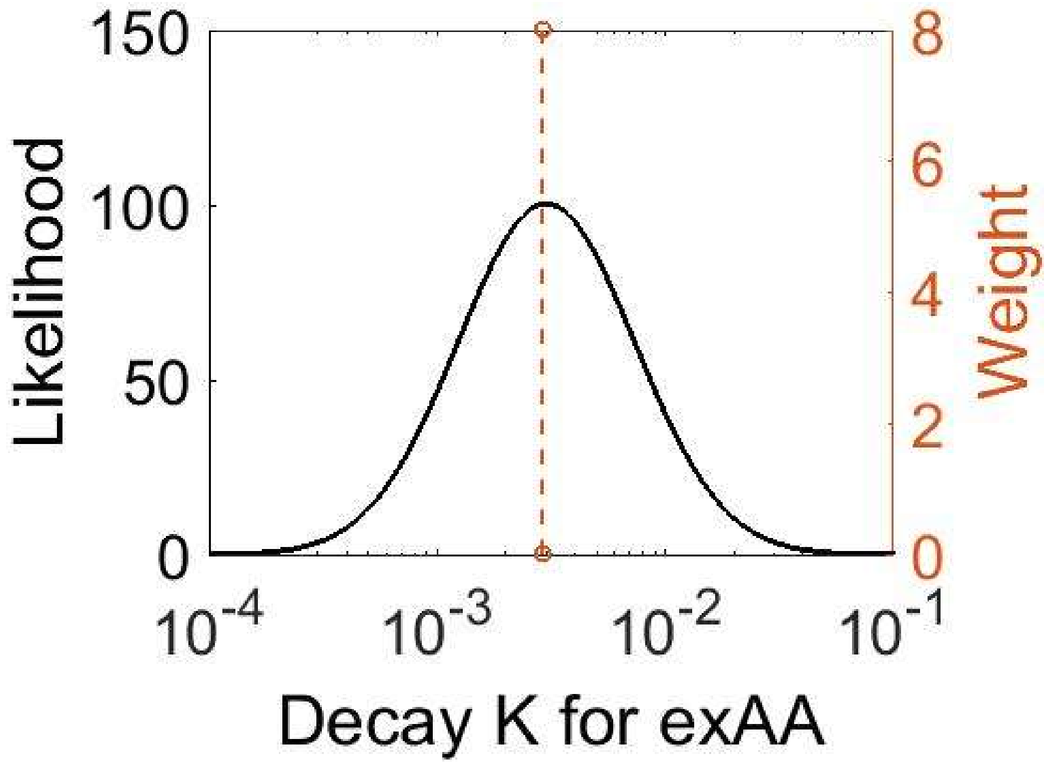

Figure SF.9.20.1.1.1. The estimated probability distribution for exAA decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.9.21. Reaction 68: ex15-keto-PGE$_2$ →ϕ

The decay of 15-keto-PGE$_2$ in the extracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

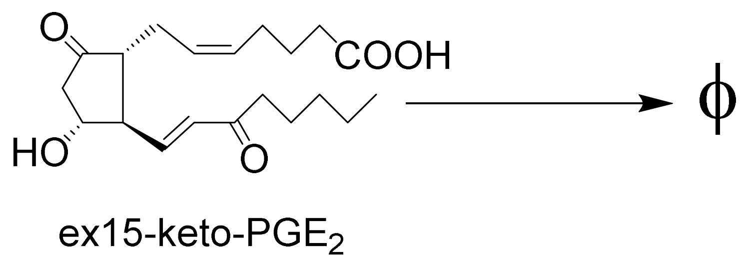

Figure SF.9.21. The decay of 15-keto-prostaglandin E$_2$ (15-keto-PGE$_2$) in the extracellular compartment (Reaction 68).

S.7.1.1. Reaction rate law for Reaction 68.

$$\boldsymbol{v_{68} = K[\mathbf{ex15-keto-PGE_2}]}$$

S.9.21.1. Reaction parameters

S.9.21.1.1. Parameter: K

Parameter values for the K of Reaction 68 were obtained from the literature and summarised in Table ST.9.21.1.1.1. The log-normal distribution properties for the K of Reaction 68 are shown in Table ST.9.21.1.1.2 and plotted in Figure SF.9.21.1.1.1.

Table ST.9.21.1.1.1. Literature information used to design the ex15-keto-PGE_2 decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	Type of error	Reference
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other			
9.9		0.07		In vivo	**13,14-Dihydro-15-Keto-PGE2**	Unknown	Unknown	Unknown	Unknown		8		(Bothwell et al., 1982)

Table ST.9.21.1.1.2. The log-normal distribution properties of the ex15-keto-PGE_2 decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
6.97 $x10^{-3}$	1.10	-4.96	9.49 $x10^{-2}$

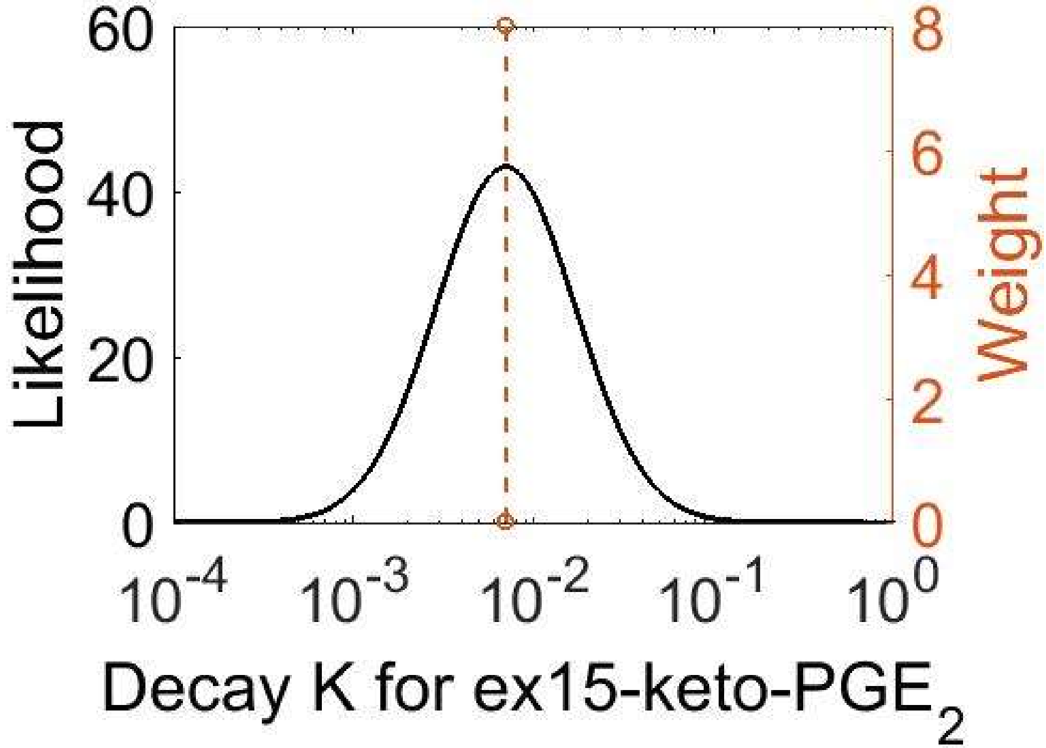

Figure SF.9.21.1.1.1. The estimated probability distribution for the ex15-keto-PGE$_2$ decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale**.**

S.9.22. Reaction 71: ex13,14-dihydro-15-keto-PGE$_2$ →ϕ

The decay of 13,14-dihydro-15-keto-PGE$_2$ in the extracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

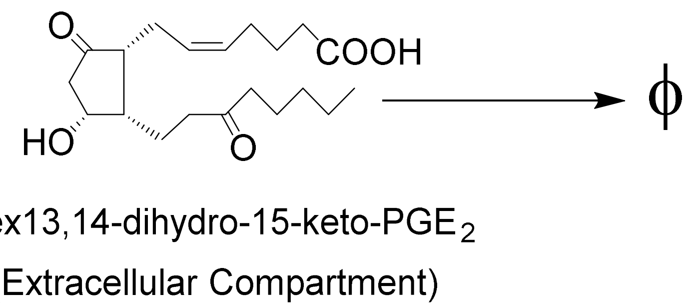

Figure SF.9.22. The decay of 13,14-dihydro-15-keto-prostaglandin E$_2$ (13,14-dihydro-15-keto-PGE$_2$) in the extracellular compartment (Reaction 71).

SEq.9.22. Reaction rate law for Reaction 71.

$$\boldsymbol{v_{64}} = \boldsymbol{K}[\mathbf{ex13,14-dihydro-15-keto-PGE_2}]$$

S.9.22.1. Reaction parameters

S.9.22.1.1. Parameter: K

Parameter values for the K of Reaction 71 were obtained from the literature and summarised in Table ST.9.22.1.1.1. The log-normal distribution properties for the K of Reaction 71 are shown in Table ST.9.22.1.1.2 and plotted in Figure SF.9.22.1.1.1.

Table ST.9.22.1.1.1. Literature information used to design the ex13,14-dihydro-15-keto-PGE$_2$ parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	Type of error	Reference
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other			
9.9		0.07		In vivo	**13,14-Dihydro-15-Keto-PGE2**	Unknown	Unknown	Unknown	Unknown		8		(Bothwell et al., 1982)

Table ST.9.22.1.1.2. The log-normal distribution properties of the 13,14-dihydro-15-keto-PGE$_2$ decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
6.97 x10^{-3}	1.10	-4.96	9.4910^{-2}

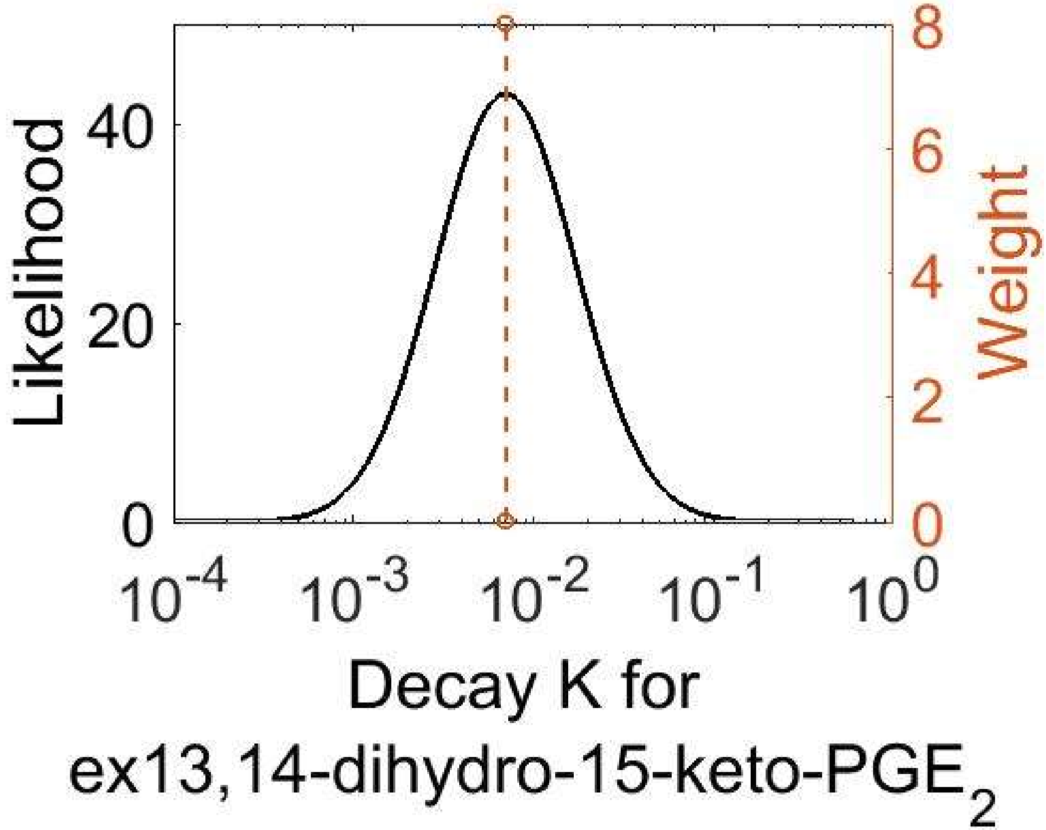

Figure SF.9.22.1.1.1. The estimated probability distribution for the ex13,14-dihydro-15-keto-PGE$_2$ decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.9.23. Reaction 72: AA →ϕ

The decay of AA in the intracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

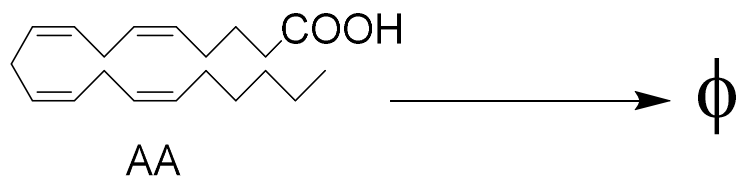

Figure SF.9.23. The decay of arachidonic acid (AA) in the intracellular compartment (Reaction 72).

SEq.9.23. Reaction rate law for Reaction 72.

$$\boldsymbol{v_{72} = K[\mathrm{AA}]}$$

S.9.23.1. Reaction parameters

S.9.23.1.1. Parameter: K

Parameter values for the K of Reaction 72 were obtained from the literature and summarised in Table ST.9.23.1.1.1. The log-normal distribution properties for the K of Reaction 72 are shown in Table ST.9.23.1.1.2 and plotted in Figure SF.9.23.1.1.1.

Table ST.9.23.1.1.1. Literature information used to design the AA decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	Type of error	Reference
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other			
240		0.003		In vivo	AA	Human	Platelets	Unknown	37		8		(Vinge, 1985)

Table ST.9.23.1.1.2. The log-normal distribution properties of the AA decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
2.88×10^{-3}	1.10	-5.84	9.49×10^{-2}

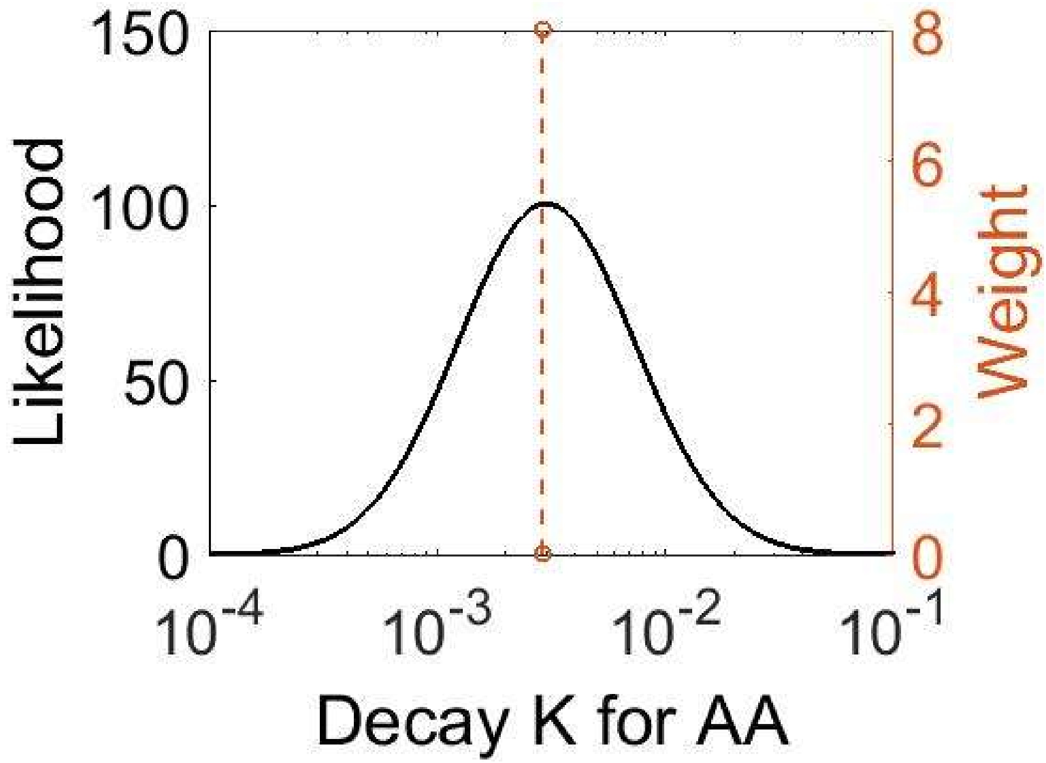

Figure SF.9.23.1.1.1. The estimated probability distribution for the AA decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.9.24. Reaction 73: $PGH_2 \rightarrow \phi$

The decay of PGH_2 in the intracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

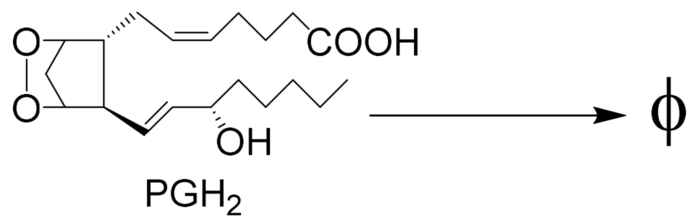

Figure SF.9.24. The decay of prostaglandin H_2 (PGH_2) in the intracellular compartment (Reaction 73).

SEq.9.24. Reaction rate law for Reaction 73.

$$\boldsymbol{v_{73} = K[\mathbf{PGH_2}]}$$

S.9.24.1. Reaction parameters

S.9.24.1.1. Parameter: K

Parameter values for the K of Reaction 73 were obtained from the literature and summarised in Table ST.9.24.1.1.1. The log-normal distribution properties for the K of Reaction 73 are shown in Table ST.9.24.1.1.2 and plotted in Figure SF.9.24.1.1.1.

Table ST.9.24.1.1.1. Literature information used to design the PGH_2 decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	Type of error	Reference
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other			
5		0.139		In vivo	PGH2	Unknown	Unknown	Unknown	Unknown	Textbook with no reference	8		(Sciences, 2019)

Table ST.9.24.1.1.2. The log-normal distribution properties of the PGH_2 decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.38×10^{-1}	1.10	-1.97	9.49×10^{-2}

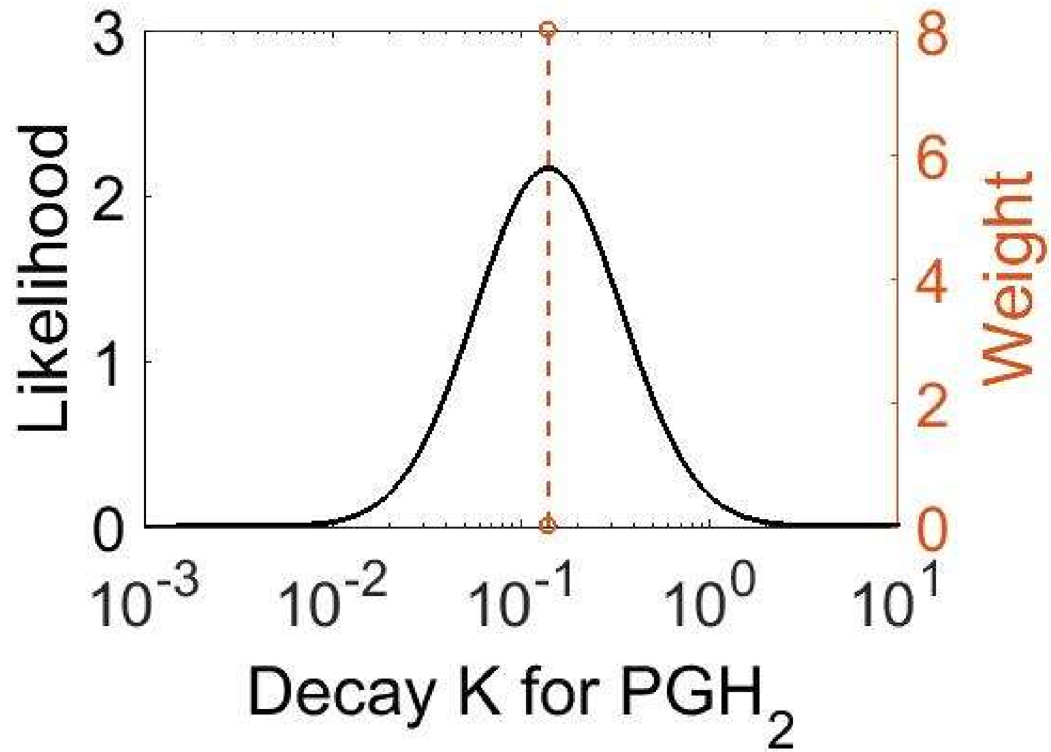

Figure SF.9.24.1.1.1. The estimated probability distribution for PGH_2 decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.9.25. Reaction 74: $PGF_{2\alpha}$→ϕ

The decay of $PGF_{2\alpha}$ in the intracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

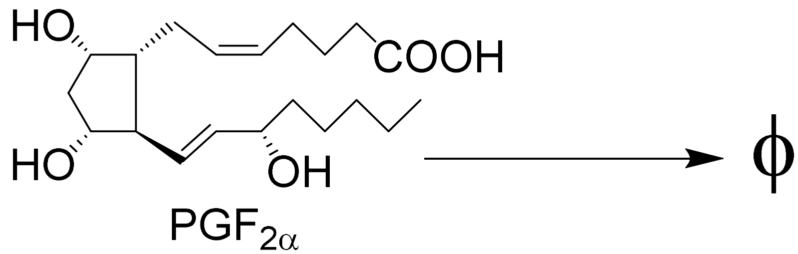

Figure S.9.25. The decay of prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) in the intracellular compartment (Reaction 74).

SEq.9.25. Reaction rate law for Reaction 74.

$$\boldsymbol{v_{74} = K[\mathbf{PGF_{2\alpha}}]}$$

S.9.25.1. Reaction parameters

S.9.25.1.1. Parameter: K

Parameter values for the K of Reaction 74 were obtained from the literature and summarised in Table ST.9.25.1.1.1. The log-normal distribution properties for the K of Reaction 74 are shown in Table ST.9.25.1.1.2 and plotted in Figure SF.9.25.1.1.1.

Table ST.9.25.1.1.1. Literature information used to design the $PGF_{2\alpha}$ decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	Type of error	Reference
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other			
900	492	0.001	0.001	In vivo	PGF2a	Human	Decidual stromal cells and macrophages	Unknown	Unknown		8		(Ishihara et al., 1991)

Table ST.9.25.1.1.2. The log-normal distribution properties of the PGH_2 decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
7.07×10^{-4}	2.30	-6.80	6.7610^{-1}

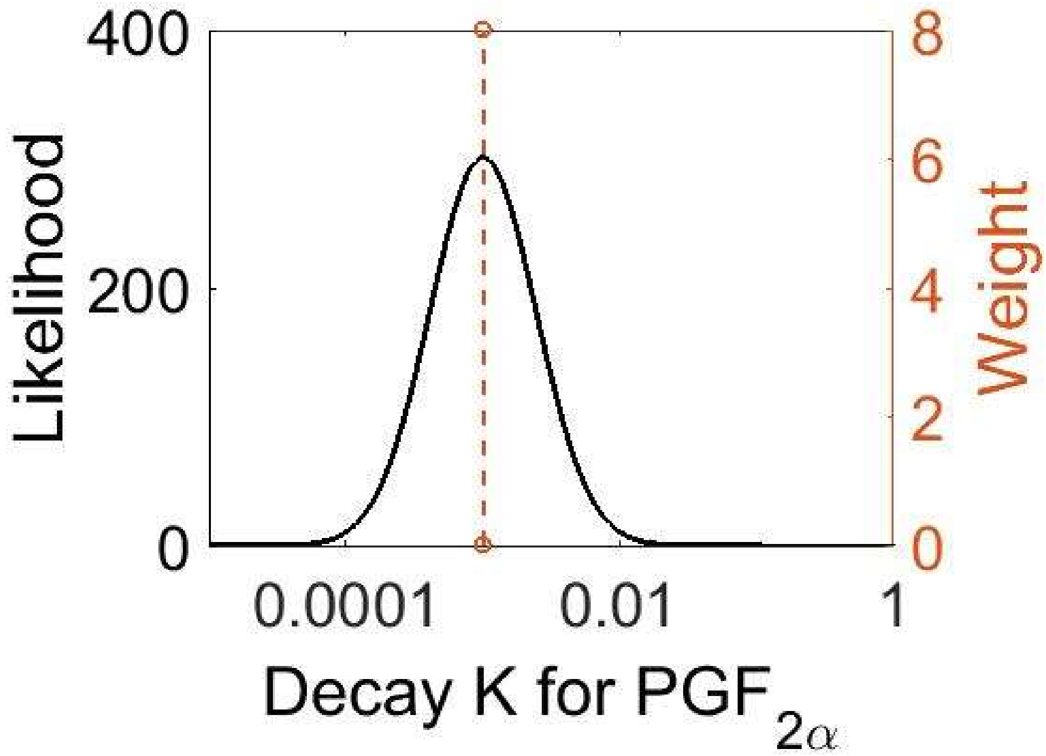

Figure SF.9.25.1.1.1. The estimated probability distribution for $PGF_{2\alpha}$ decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.9.26. Reaction 75: $TXA_2 \rightarrow \phi$

The decay of TXA_2 in the intracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

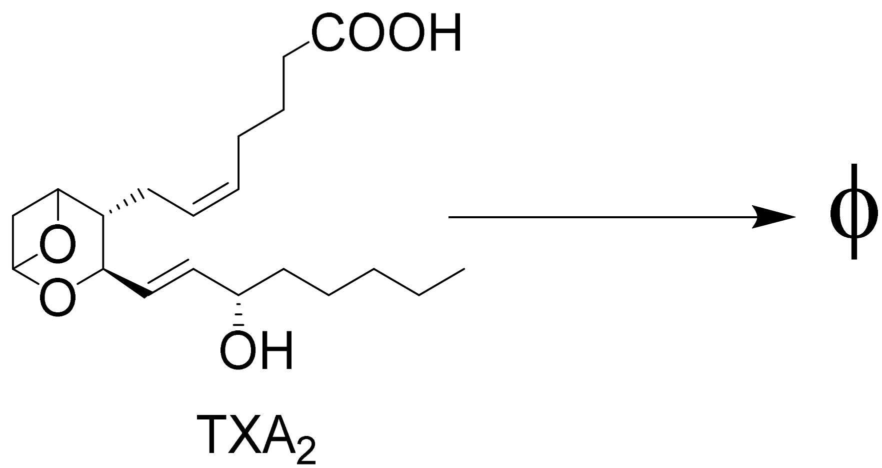

Figure SF.9.26. The decay of thromboxane A_2 (TXA_2) in the intracellular compartment (Reaction 75).

SEq.9.26. Reaction rate law for Reaction 75.

$$\boldsymbol{v_{75} = K[\mathrm{TXA_2}]}$$

S.9.26.1. Reaction parameters

S.9.26.1.1. Parameter: K

Parameter values for the K of Reaction 75 were obtained from the literature and summarised in Table ST.9.26.1.1.1. The log-normal distribution properties for the K of Reaction 75 are shown in Table ST.9.26.1.1.2 and plotted in Figure SF.9.26.1.1.1.

Table ST.9.26.1.1.1. Literature information used to design the TXA_2 decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	Type of error	Reference
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other			
0.333		2.079		Unknown, assume in vitro	TXA2	Unknown	Unknown	Unknown	Unknown	Textbook with no reference	8		(Wild, 2005)

Table ST.9.26.1.1.2. The log-normal distribution properties of the TXA_2 decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
2.07	1.10	7.37×10^{-1}	9.49×10^{-2}

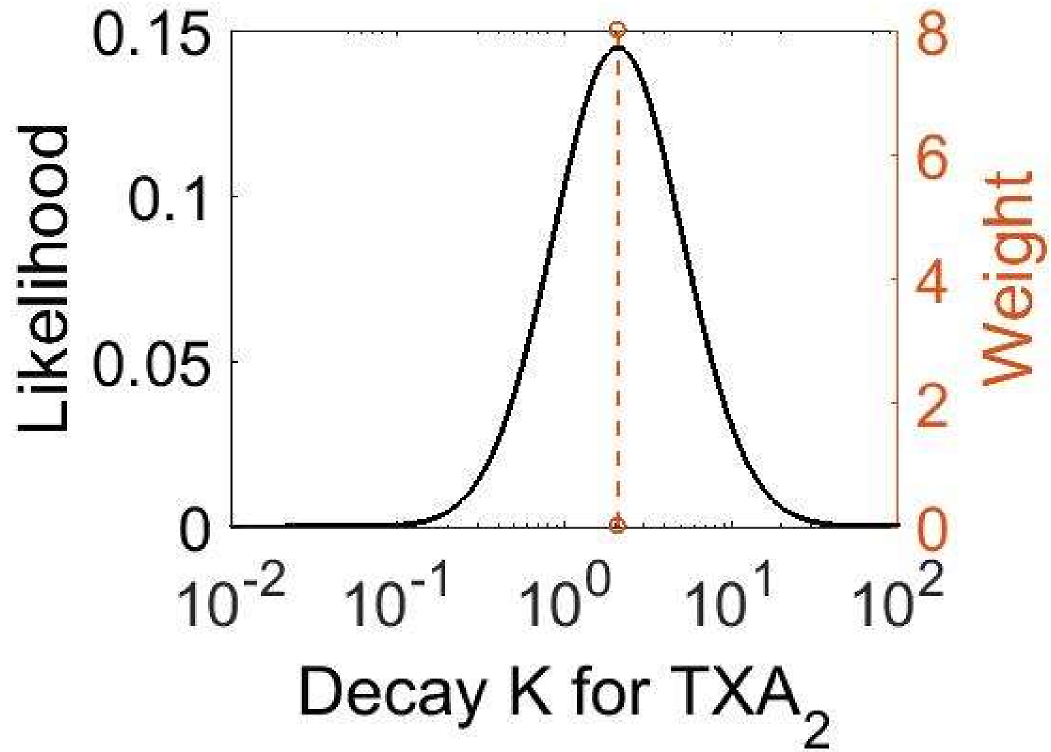

Figure SF.9.26.1.1.1. The estimated probability distribution for the TXA_2 decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.9.27. Reaction 76: $PGE_2 \rightarrow \phi$

The decay of PGE_2 in the intracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

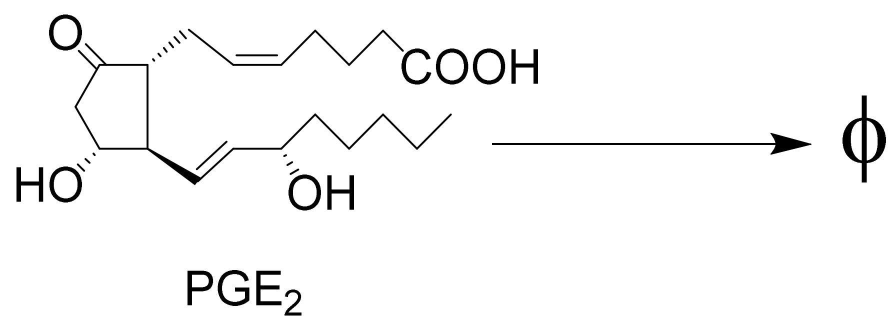

Figure SF.9.27. The decay of prostaglandin E_2 (PGE_2) in the intracellular compartment (Reaction 76).

SEq.9.27. Reaction rate law for Reaction 76.

$$\boldsymbol{v_{76} = K[\mathbf{PGE_2}]}$$

S.9.27.1. Reaction parameters

S.9.27.1.1 Parameter: K

Parameter values for the K of Reaction 76 were obtained from the literature and summarised in Table ST.9.27.1.1.1. The log-normal distribution properties for the K of Reaction 76 are shown in Table ST.9.27.1.1.2 and plotted in Figure SF.9.27.1.1.1.

Table ST.9.27.1.1.1. Literature information used to design the PGE_2 decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	Type of error	Reference
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other			
528	204	0.001	0.003	In vivo	PGE2	Human	Decidual stromal cells and macrophages	Unknown	Unknown		8		(Ishihara et al., 1991)

Table ST.9.27.1.1.2. The log-normal distribution properties of the PGE_2 decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
3.16 x10^{-4}	4.56	-7.04	1.01

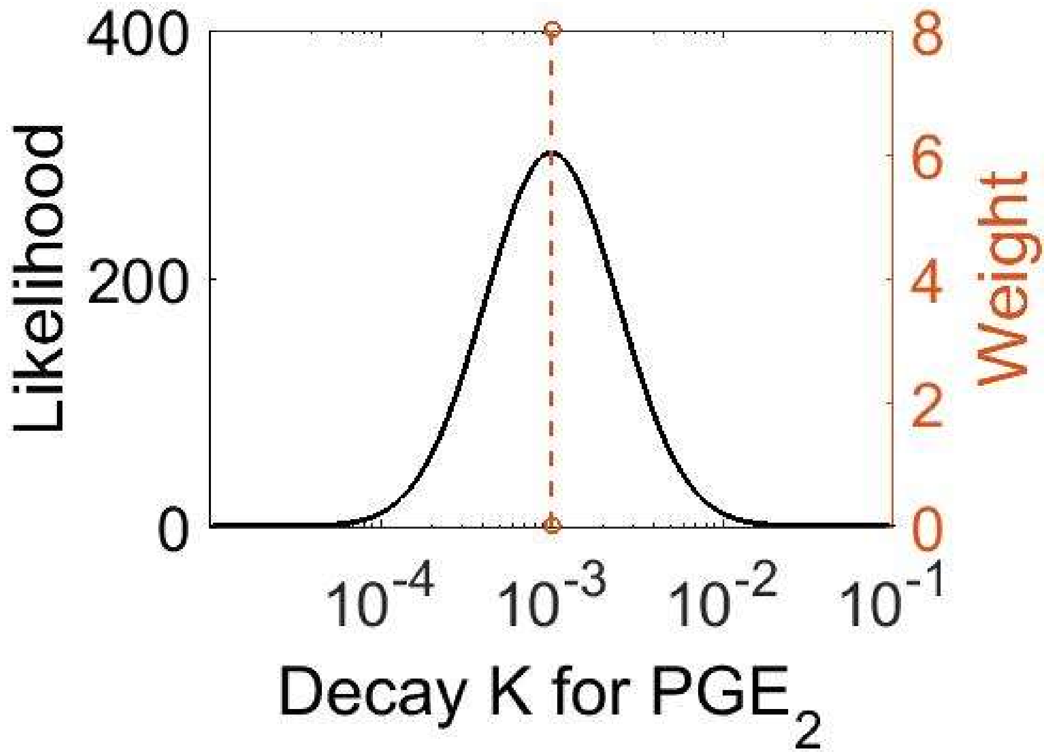

Figure SF.9.27.1.1.1. The estimated probability distribution for the PGE_2 decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.9.28. Reaction 77: $PGI_2 \rightarrow \phi$

The decay of PGI_2 in the intracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

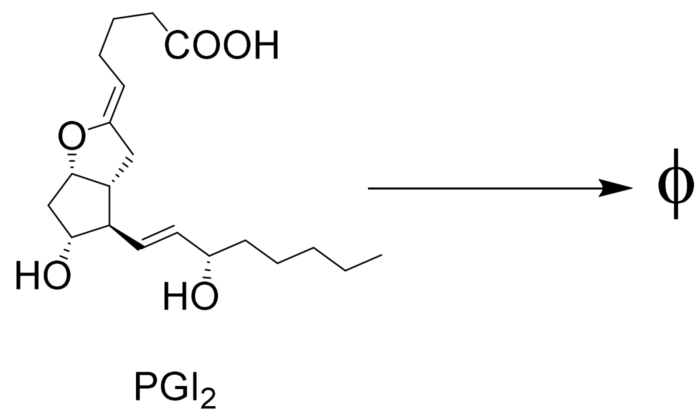

Figure SF.9.28. The decay of prostaglandin I_2 (PGI_2) in the intracellular compartment (Reaction 77).

SEq.9.28. Reaction rate law for Reaction 77.

$$\boldsymbol{v_{77} = K[\mathrm{PGI_2}]}$$

S.9.28.1. Reaction parameters

S.9.28.1.1. Parameter: K

Parameter values for the K of Reaction 77 were obtained from the literature and summarised in Table ST.9.28.1.1.1. The log-normal distribution properties for the K of Reaction 77 are shown in Table ST.9.28.1.1.2 and plotted in Figure SF.9.28.1.1.1.

Table ST.9.28.1.1.1. Literature information used to design the PGI_2 decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	Type of error	Reference
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other			
3		0.231		Unknown	PGI2	Unknown	Unknown	Unknown	Unknown	Textbook with no reference	8		(Cawello et al., 1994)

Table ST.9.28.1.1.2. The log-normal distribution properties of the PGI_2 decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
2.30×10^{-1}	1.10	-1.46	9.49×10^{-2}

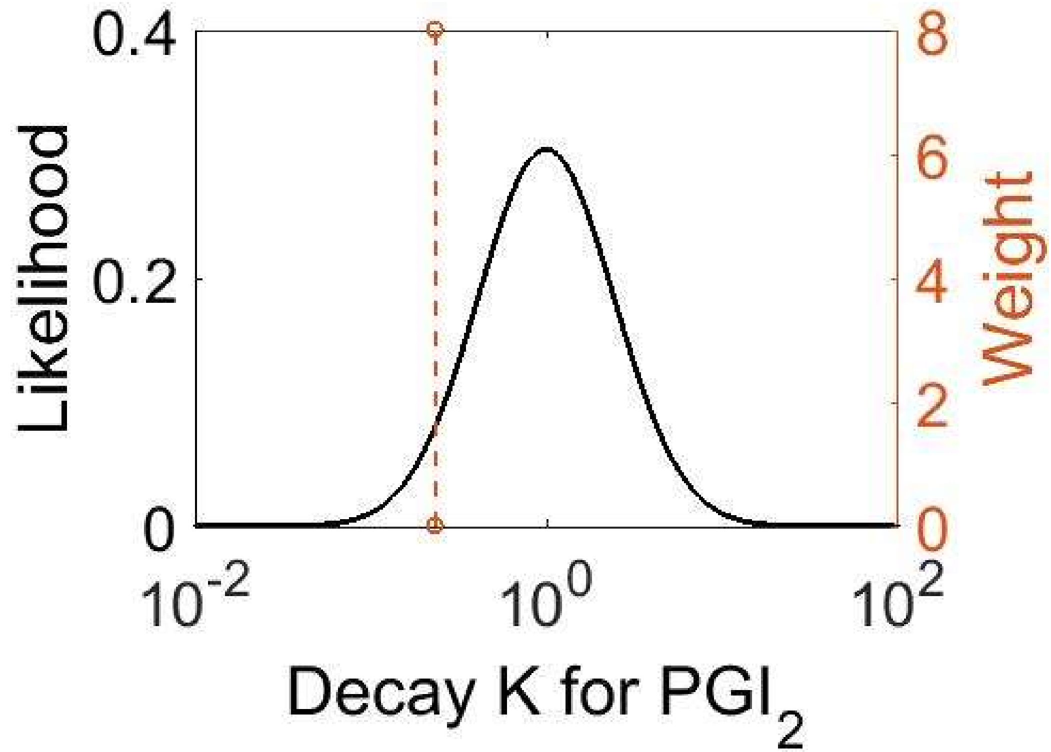

Figure SF.9.28.1.1.1. The estimated probability distribution for the PGI_2 decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.9.29. Reaction 78: $PGD_2 \rightarrow \phi$

The decay of PGD_2 in the intracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

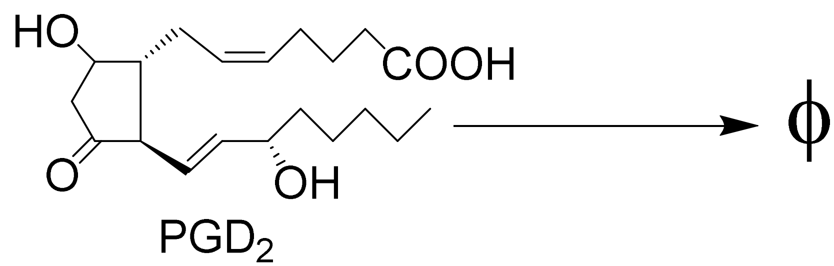

Figure SF.9.29. The decay of prostaglandin D_2 (PGD_2) in the intracellular compartment (Reaction 78).

SEq.9.29. Reaction rate law for Reaction 78.

$$\boldsymbol{v_{78} = K[PGD_2]}$$

S.9.29.1. Reaction parameters

S.9.29.1.1. Parameter: K
Parameter values for the K of Reaction 78 were obtained from the literature and summarised in Table ST.9.29.1.1.1. The log-normal distribution properties for the K of Reaction 78 are shown in Table ST.9.29.1.1.2 and plotted in Figure SF.9.29.1.1.1.

Table ST.9.29.1.1.1. Literature information used to design the PGD_2 decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	Type of error	Reference
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other			
30		0.023		In vivo	PGD2	Human	Plasma	7	37		8		(Schuligoi et al., 2007)
1.5		0.462		In vivo	PGD2	Human	Brain	7.4	Unknown		8		(Suzuki et al., 1986)

Table ST.9.29.1.1.2. The log-normal distribution properties of the PGD_2 decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
2.30 x10^{-2}	1.10	-3.76	9.49 x10^{-2}

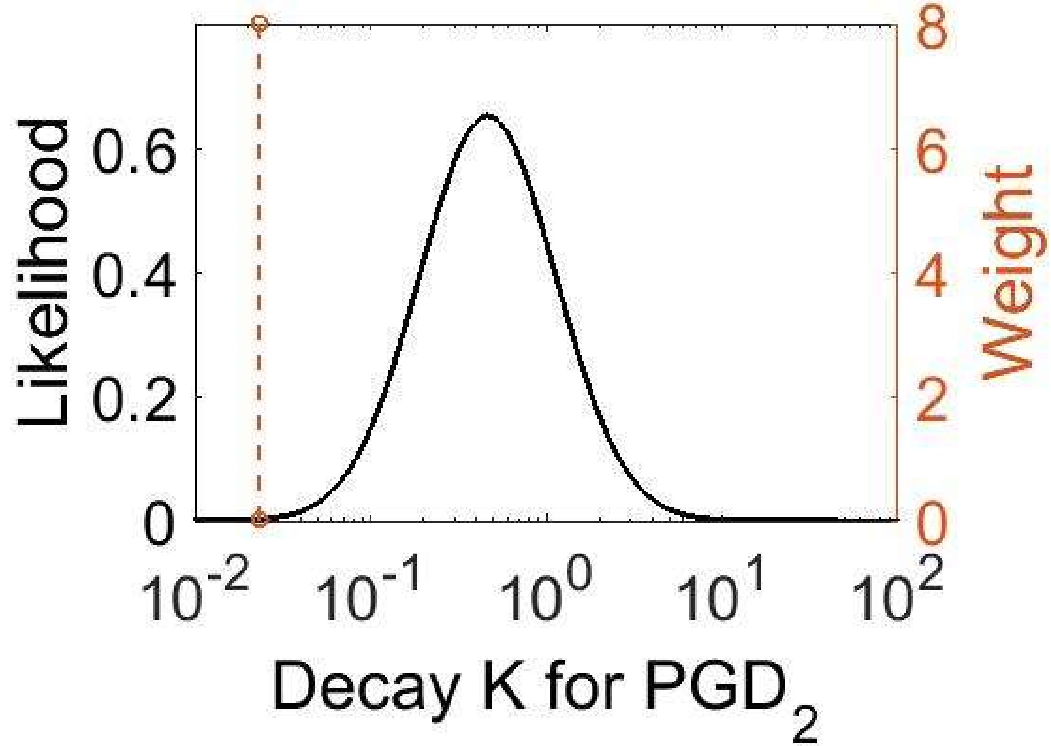

Figure SF.9.29.1.1.1. The estimated probability distribution for the PGD_2 decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.9.30. Reaction 79: 15-keto-PGE_2 →ϕ

The decay of 15-keto-PGE_2 in the intracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

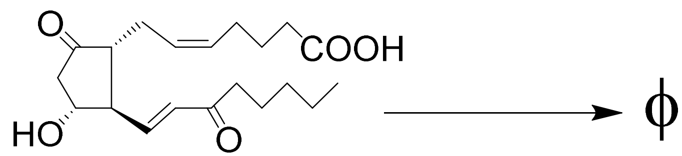

Figure SF.9.30. The decay of 15-keto-prostaglandin E_2 (15-keto-PGE_2) in the intracellular compartment (Reaction 79).

SEq.9.30. Reaction rate law for Reaction 79.

$$\boldsymbol{v_{79} = K[15 - \mathrm{keto} - \mathrm{PGE_2}]}$$

S.9.30.1. Reaction parameters

S.9.30.1.1. Parameter: K

Parameter values for the K of Reaction 79 were obtained from the literature and summarised in Table ST.9.30.1.1.1. The log-normal distribution properties for the K of Reaction 79 are shown in Table ST.9.30.1.1.2 and plotted in Figure SF.9.30.1.1.1.

Table ST.9.30.1.1.1. Literature information used to design the 15-keto-PGE$_2$ decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	Type of error	Reference
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other			
99		0.007		In vivo	**13,14-Dihydro-15-Keto-PGE2**	Unknown	Unknown	Unknown	Unknown		8		(Bothwell et al., 1982)

Table ST.9.30.1.1.2 The log-normal distribution properties of the 15-keto-PGE$_2$ decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
6.97 x10^{-3}	1.10	-4.96	9.49 x10^{-2}

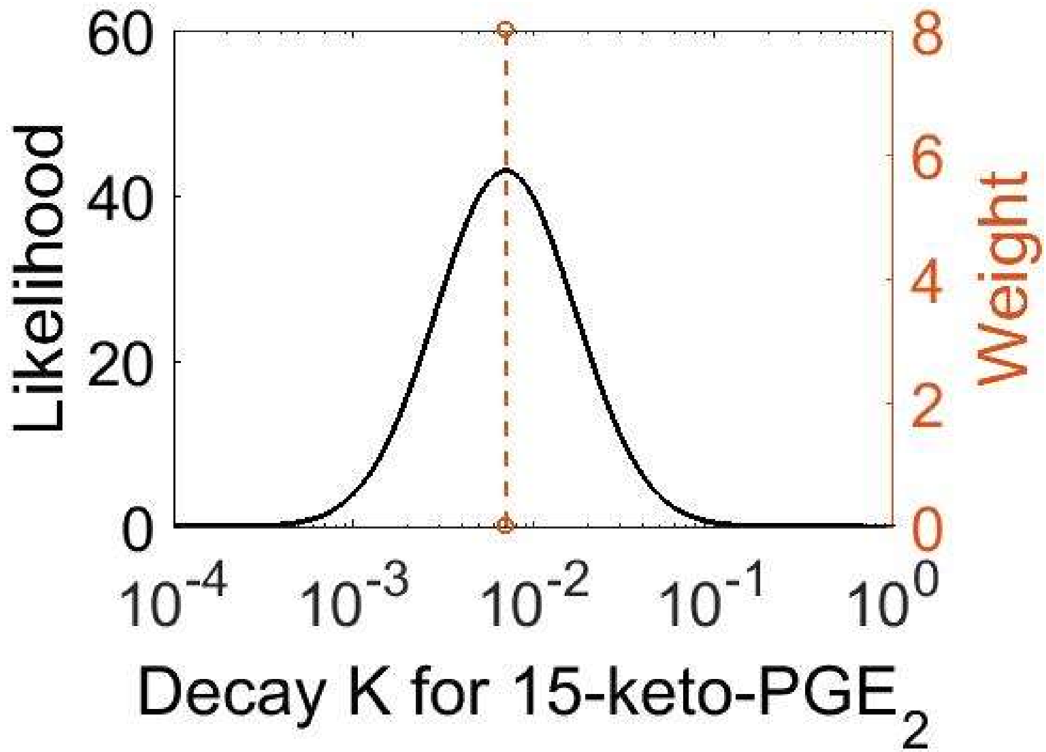

Figure SF.9.30.1.1.1. The estimated probability distribution for the 15-keto-PGE_2 decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.9.31. Reaction 80: 13,14-dihydro-15-keto-PGE_2 →ϕ

The decay of 13,14-dihydro-15-keto-PGE_2 in the intracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

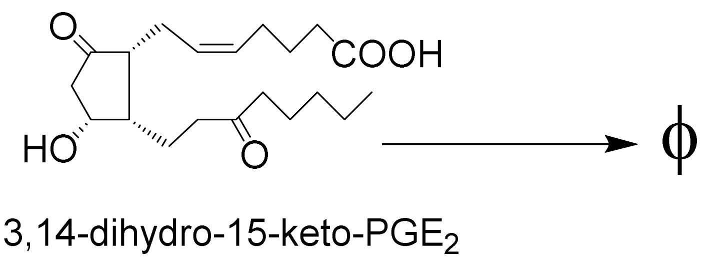

Figure SF.9.31. The decay of 13,14-dihydro-15-keto-prostaglandin E_2 (13,14-dihydro-15-keto-PGE_2) in the intracellular compartment (Reaction 80).

SEq.9.31. Reaction rate law for Reaction 80.

$$\boldsymbol{v_{80} = K[13,14 - \mathbf{dihydro} - 15 - \mathbf{keto} - \mathbf{PGE_2}\,]}$$

S.9.31.1. Reaction parameters

S.9.31.1.1. Parameter: K

Parameter values for the K of Reaction 80 were obtained from the literature and summarised in Table ST.9.31.1.1.1. The log-normal distribution properties for the K of Reaction 80 are shown in Table ST.9.31.1.1.2 and plotted in Figure SF.9.31.1.1.1.

Table ST.9.31.1.1.1. Literature information used to design the 13,14-dihydro-15-keto-PGE_2 decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	Type of error	Reference
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other			
99		0.007		In vivo	13,14-Dihydro-15-Keto-PGE2	Unknown	Unknown	Unknown	Unknown		8		(Bothwell et al., 1982)

Table ST.9.31.1.1.2. The log-normal distribution properties of the 15-keto-PGE_2 decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
6.97×10^{-3}	1.10	-4.96	9.49×10^{-2}

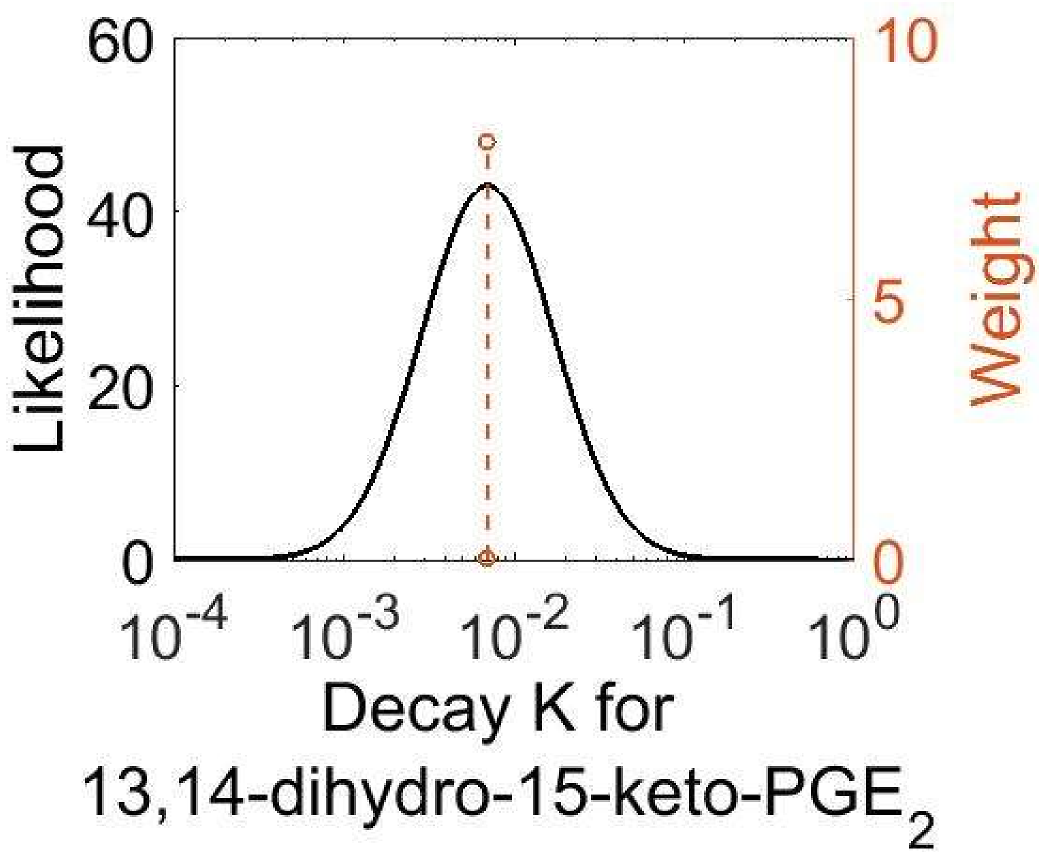

Figure SF.9.31.1.1.1. The estimated probability distribution for the 13,14-dihydro-15-keto-PGE$_2$ decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.9.32. Reaction 81: $TXB_2 \rightarrow \phi$

The decay of TXB_2 in the intracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

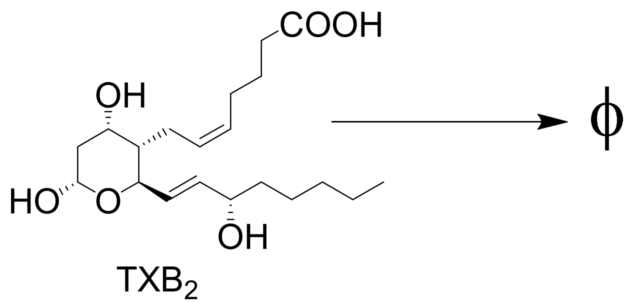

Figure SF.9.32. The decay of thromboxane B_2 (TXB_2) in the intracellular compartment (Reaction 81).

SEq.9.32. Reaction rate law for Reaction 81.

$$\boldsymbol{v_{81} = K[\mathrm{TXB_2}]}$$

S.9.32.1. Reaction parameters

S.9.32.1.1. Parameter: K

Parameter values for the K of Reaction 81 were obtained from the literature and summarised in Table ST.9.32.1.1.1. The log-normal distribution properties for the K of Reaction 81 are shown in Table ST.9.32.1.1.2 and plotted in Figure SF.9.32.1.1.1.

Table ST.9.32.1.1.1. Literature information used to design the TXB_2 decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	Type of error	Reference
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other			
20		0.035		Unknown, assume in vitro	TXB2	Unknown	Unknown	Unknown	Unknown	Textbook with no reference	8		(Wild, 2005)

Table ST.9.32.1.1.2. The log-normal distribution properties of the TXB_2 decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
3.48×10^{-2}	1.10	-3.35	9.49×10^{-2}

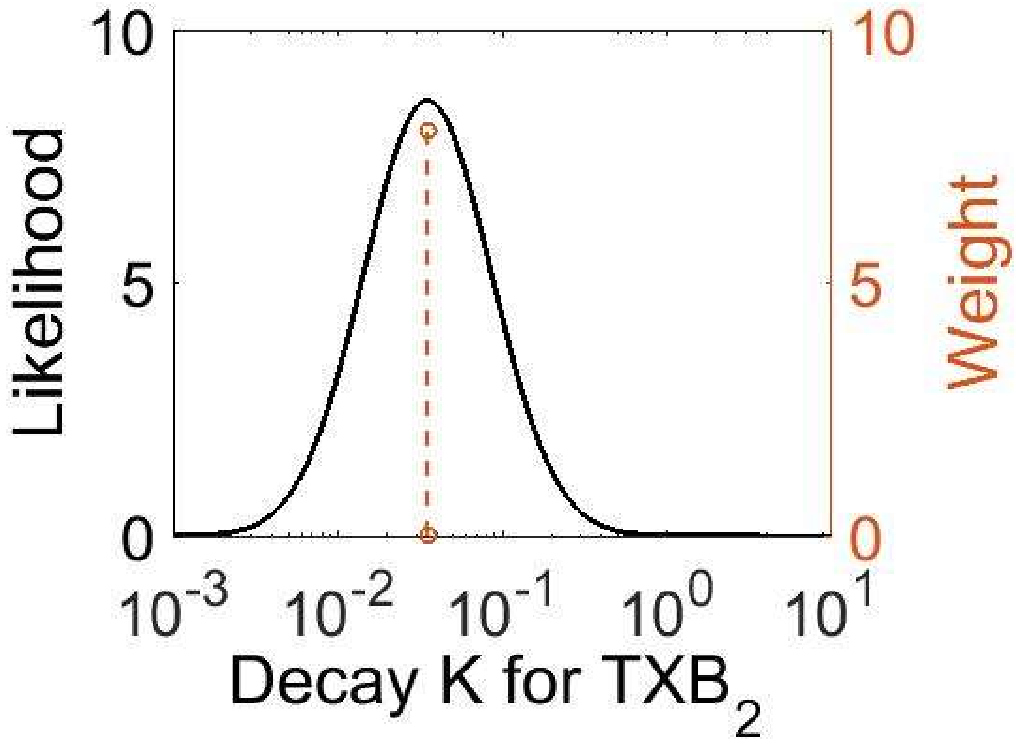

Figure SF.9.32.1.1.1. The estimated probability distribution for the TXB_2 decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale**.**

S.9.33. Reaction 82: 6-keto-PGF$_{1\alpha}$→ϕ
The decay of 6-keto-PGF$_{1\alpha}$ in the intracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

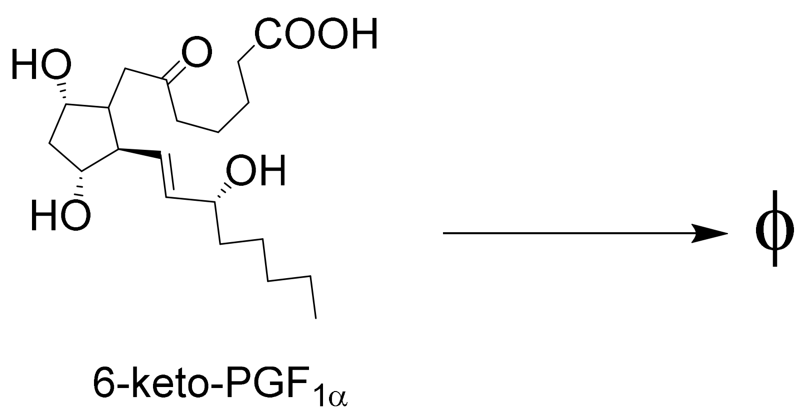

Figure SF.9.33. The decay of 6-keto-prostaglandin F$_{1\alpha}$ (6-keto-PGF$_{1\alpha}$) in the intracellular compartment (Reaction 82).

SEq.9.33. Reaction rate law for Reaction 82.

$$\boldsymbol{v_{82}} = \boldsymbol{K}[\mathbf{6 - keto - PGF_{1\alpha}}]$$

S.9.33.1. Reaction parameters

S.9.33.1.1. Parameter: K

Parameter values for the K of Reaction 82 were obtained from the literature and summarised in Table ST.9.33.1.1.1. The log-normal distribution properties for the K of Reaction 82 are shown in Table ST.9.33.1.1.2 and plotted in Figure SF.9.33.1.1.1.

Table ST.9.33.1.1.1. Literature information used to design the 6-keto-PGF$_{1\alpha}$ decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	Type of error	Reference
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other			
30		0.023104906		In vivo	6-KETO-PGF1A	Human	Plasma	Unknown	Unknown		8		(Ylikorkala and Viinikka, 1981)

Table ST.9.33.1.1.2. The log-normal distribution properties of the 6-keto-PGF$_{1\alpha}$ decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
2.30 x10^{-2}	1.10	-3.76	9.4910^{-2}

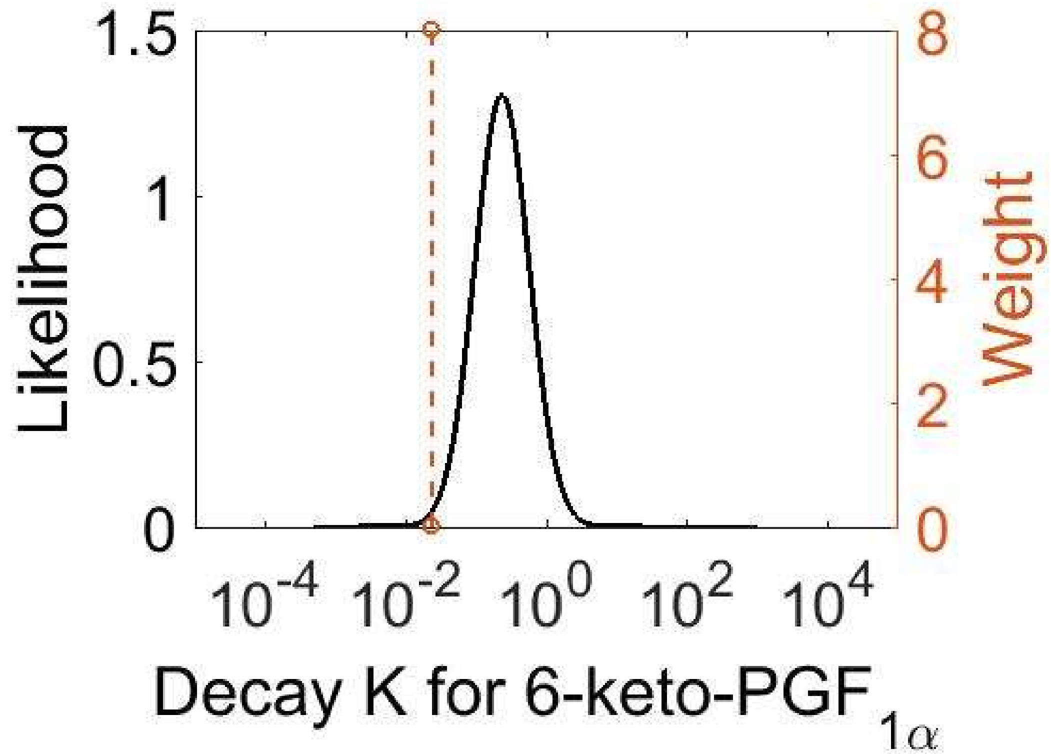

Figure SF.9.33.1.1.1. The estimated probability distribution for the 6-keto-$PGF_{1\alpha}$ decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.9.34. Reaction 83: $PGJ_2 \rightarrow \phi$

The decay of PGJ_2 in the intracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

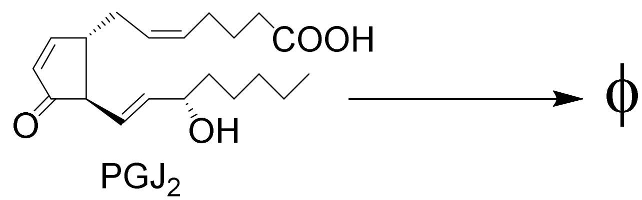

Figure S.9.34. The decay of prostaglandin J_2 (PGJ_2) in the intracellular compartment (Reaction 83).

SEq.9.34. Reaction rate law for Reaction 83.

$$\boldsymbol{v}_{83} = \boldsymbol{K}[\mathbf{PGJ_2}]$$

S.9.34.1. Reaction parameters

S.9.34.1.1. Parameter: K

Parameter values for the K of Reaction 83 were obtained from the literature and summarised in Table ST.9.34.1.1.1. The log-normal distribution properties for the K of Reaction 83 are shown in Table ST.9.34.1.1.2 and plotted in Figure SF.9.34.1.1.1.

Table ST.9.34.1.1.1. Literature information used to design the PGJ_2 decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	Type of error	Reference
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other			
720		0.001		In vivo	15-Deoxy-PGJ2	Human	Albumin	7.4	37		8		(Fitzpatrick and Wynalda, 1983)

Table ST.9.34.1.1.2. The log-normal distribution properties of the PGJ_2 decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
9.95×10^{-4}	1.10	-6.90	9.4910^{-2}

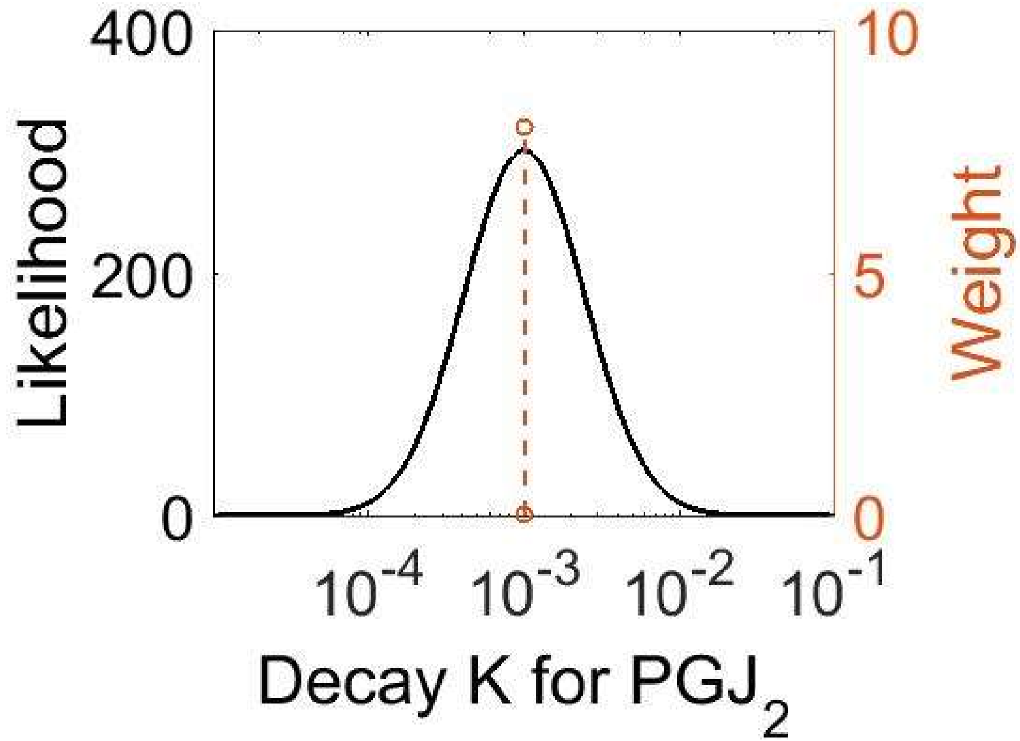

Figure SF.9.34.1.1.1. The estimated probability distribution for the PGJ_2 decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.9.35. Reaction 84: 15-deoxy-PGJ$_2$ →ϕ

The decay of 15-deoxy-PGJ$_2$ in the intracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

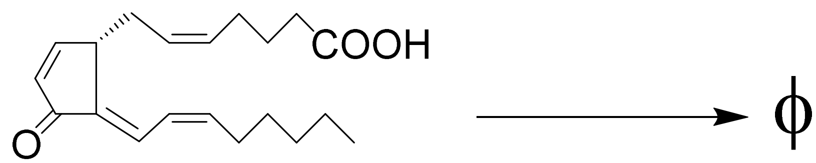

Figure SF.9.35. The decay of 15-deoxy-prostaglandin J$_2$ (15-deoxy-PGJ$_2$) in the intracellular compartment (Reaction 84).

SEq.9.35. Reaction rate law for Reaction 84.

$$\boldsymbol{v_{84}} = \boldsymbol{K}[\mathbf{15-deoxy-PGJ_2}]$$

S.9.35.1. Reaction parameters

S.9.35.1.1 Parameter: K

Parameter values for the K of Reaction 84 were obtained from the literature and summarised in Table ST.9.35.1.1.1. The log-normal distribution properties for the K of Reaction 84 are shown in Table ST.9.35.1.1.2 and plotted in Figure SF.9.35.1.1.1.

Table ST.9.35.1.1.1. Literature information used to design the 15-deoxy-PGJ_2 decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	Type of error	Reference
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other			
720		0.001		In vivo	15-Deoxy-PGJ_2	Human	Albumin	7.4	37		8		(Fitzpatrick and Wynalda, 1983)

Table ST.9.35.1.1.2 The log-normal distribution properties of the 15-deoxy-PGJ_2 decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
9.95 $x10^{-4}$	1.10	-6.90	9.4910^{-2}

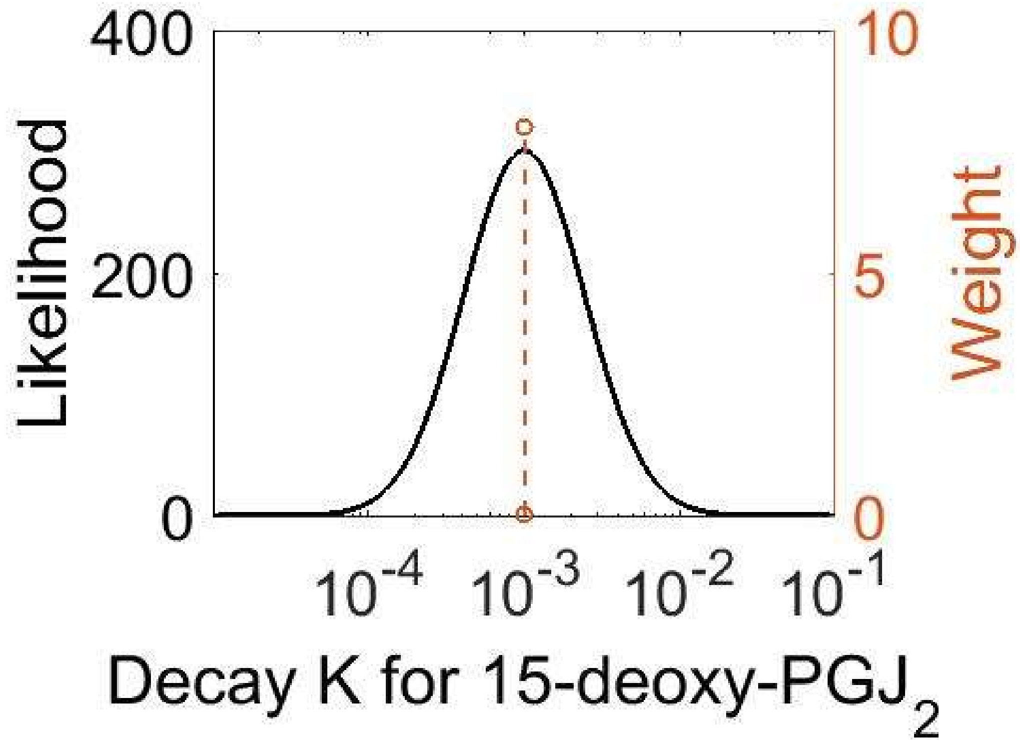

Figure SF.9.35.1.1.1. The estimated probability distribution for the 15-deoxy-PGJ_2 decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.9.36. Reaction 85: 15-HPETE →ϕ

The decay of 15-HPETE in the intracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

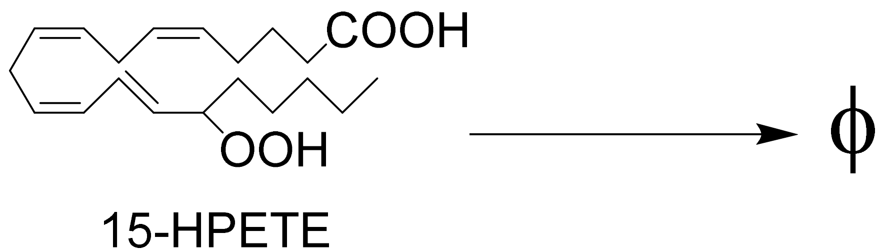

Figure SF.9.36. The decay of 15-hydroperoxyeicosatetraenoic acid (15-HPETE) in the intracellular compartment (Reaction 85).

SEq.9.36. Reaction rate law for Reaction 85.

$$\boldsymbol{v_{85} = K[15 - \mathbf{HPETE}\,]}$$

S.9.36.1. Reaction parameters

S.9.36.1.1. Parameter: K

Parameter values for the K of Reaction 85 were obtained from the literature and summarised in Table ST.9.36.1.1.1. The log-normal distribution properties for the K of Reaction 85 are shown in Table ST.9.36.1.1.2 and plotted in Figure SF.9.36.1.1.1.

Table ST.9.36.1.1.1. Literature information used to design the 15-HPETE decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	Type of error	Reference
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other			
0.5		1.386		In vivo	12-HPETE	Unknown	Unknown	Unknown	Unknown		8		(Maclouf et al., 1982)

Table ST.9.36.1.1.2. The log-normal distribution properties of the 15-HPETE decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.38	1.10	3.31×10^{-1}	9.4910^{-2}

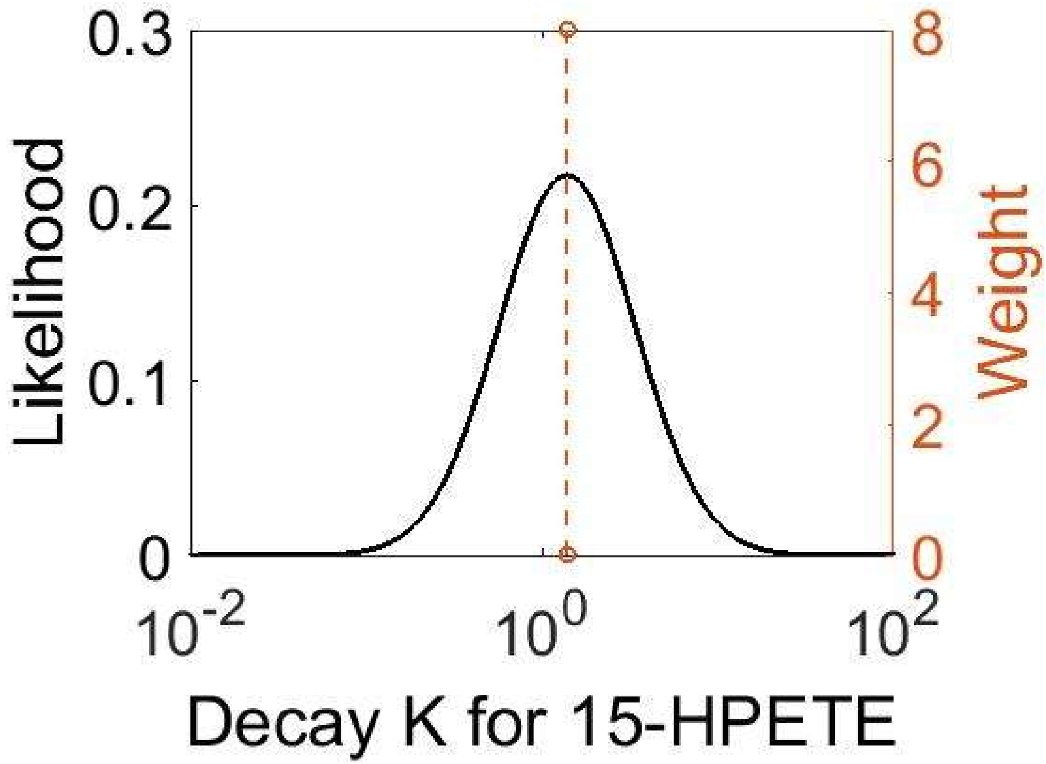

Figure SF.9.36.1.1.1. The estimated probability distribution for the 15-HPETE decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.9.37. Reaction 86: 12-HPETE →ϕ
The decay of 12-HPETE in the intracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

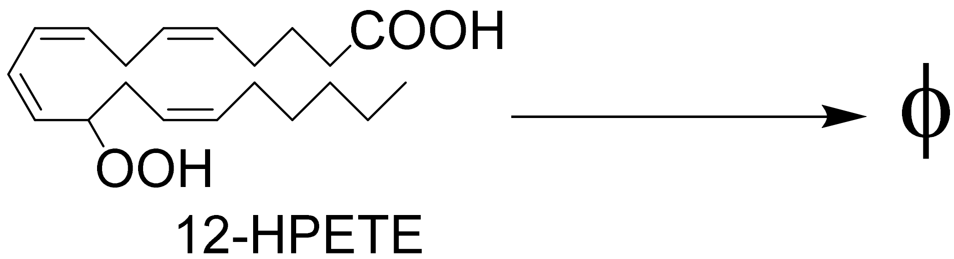

Figure SF.9.37. The decay of 12-hydroperoxyeicosatetraenoic acid (12-HPETE) in the intracellular compartment (Reaction 86).

SEq.9.37. Reaction rate law for Reaction 86.
$$\boldsymbol{v_{86} = K[12 - \mathrm{HPETE}]}$$

S.9.37.1. Reaction parameters

S.9.37.1.1. Parameter: K

Parameter values for the K of Reaction 86 were obtained from the literature and summarised in Table ST.9.37.1.1.1. The log-normal distribution properties for the K of Reaction 86 are shown in Table ST.9.37.1.1.2 and plotted in Figure SF.9.37.1.1.1.

Table ST.9.37.1.1.1. Literature information used to design the 12-HPETE decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	Type of error	Reference
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other			
0.5		1.386		Unknown	12-HPETE	Unknown	Unknown	Unknown	Unknown	Textbook with no reference	8		(Maclouf et al., 1982)

Table ST.9.37.1.1.2. The log-normal distribution properties of the 12-HPETE decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.85×10^{-1}	7.46	-2.52×10^{-1}	1.20

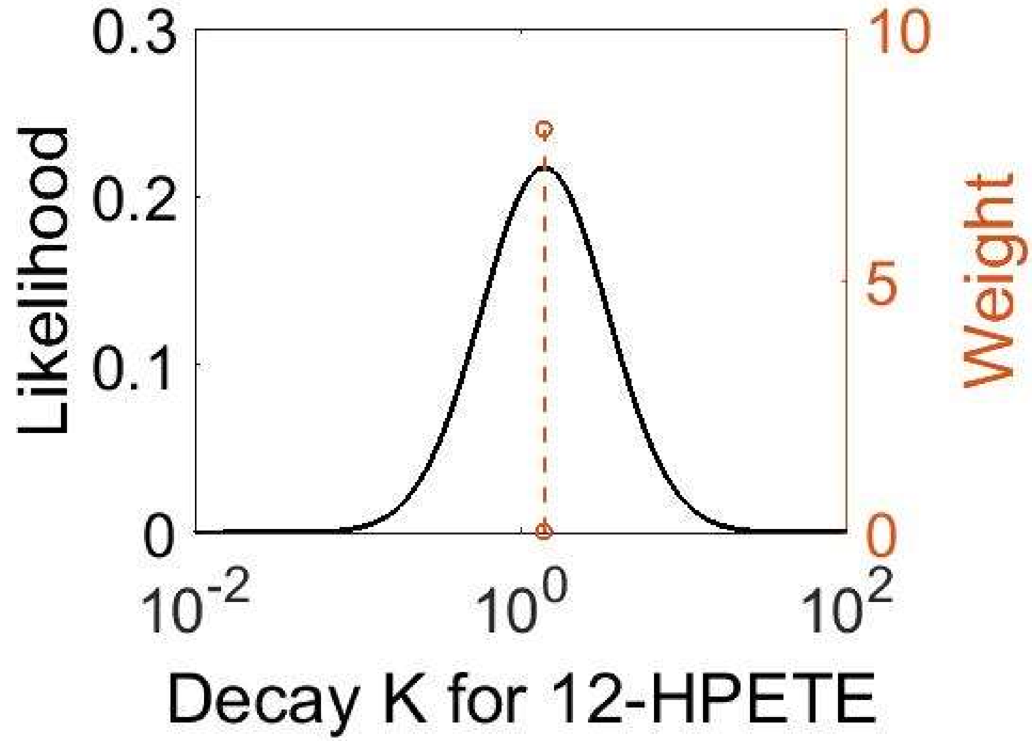

Figure SF.9.37.1.1.1. The estimated probability distribution for the 12-HPETE decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.9.38. Reaction 87: 5-HPETE →ϕ

The decay of 5-HPETE in the intracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

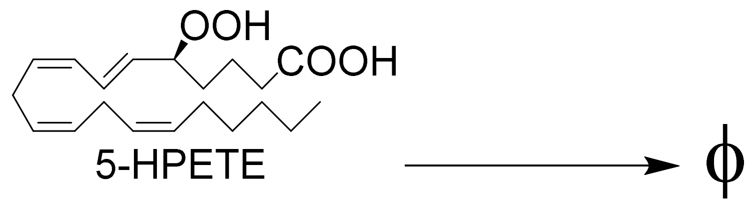

Figure SF.9.38. The decay of 5-hydroperoxyeicosatetraenoic acid (5-HPETE) in the intracellular compartment (Reaction 87).

SEq.9.38. Reaction rate law for Reaction 87.

$$\boldsymbol{v_{87} = K[5 - \mathbf{HPETE}]}$$

S.9.38.1. Reaction parameters

S.9.38.1.1. Parameter: K

Parameter values for the K of Reaction 87 were obtained from the literature and summarised in Table ST.9.38.1.1.1. The log-normal distribution properties for the K of Reaction 87 are shown in Table ST.9.38.1.1.2 and plotted in Figure SF.9.38.1.1.1.

Table ST.9.38.1.1.1. Literature information used to design the 5-HPETE decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	Type of error	Reference
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other			
0.5		1.386		In vivo	12-HPETE	Unknown	Unknown	Unknown	Unknown		8		(Maclouf et al., 1982)

Table ST.9.38.1.1.2. The log-normal distribution properties of the 5-HPETE decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.38	1.10	3.31×10^{-1}	9.4910^{-2}

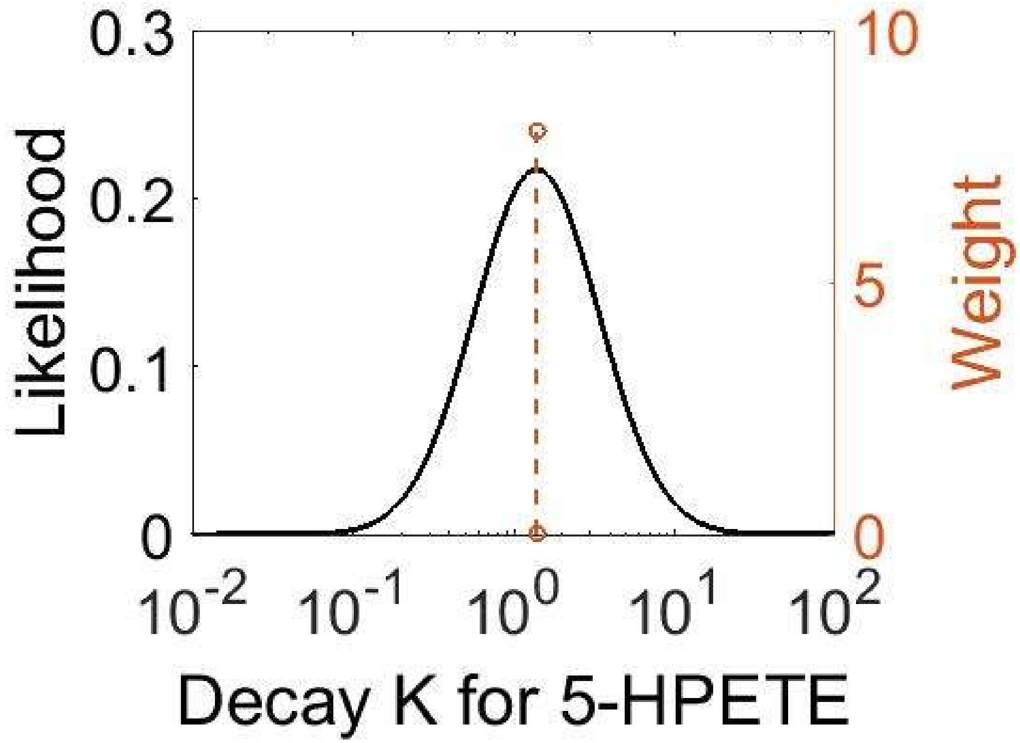

Figure SF.9.38.1.1.1. The estimated probability distribution for the 5-HPETE decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.9.39. Reaction 88: 15-HETE →ϕ

The decay of 15-HETE in the intracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

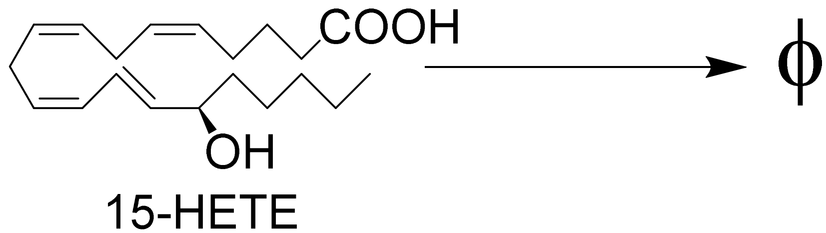

Figure SF.9.39. The decay of 15-hydroxyeicosatetraenoic acid (15-HETE) in the intracellular compartment (Reaction 88).

SEq.9.39. Reaction rate law for Reaction 88.

$$\boldsymbol{v_{88} = K[15 - \mathrm{HETE}]}$$

S.9.39.1. Reaction parameters

S.9.39.1.1. Parameter: K

Parameter values for the K of Reaction 88 were obtained from the literature and summarised in Table ST.9.39.1.1.1. The log-normal distribution properties for the K of Reaction 88 are shown in Table ST.9.39.1.1.2 and plotted in Figure SF.9.39.1.1.1.

Table ST.9.39.1.1.1. Literature information used to design the 15-HETE decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	Type of error	Reference
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other			
21		0.033		In vivo	15-HETE	Human	R15L Cells	Unknown	37		8		(Wei et al., 2009)

Table ST.9.39.1.1.2. The log-normal distribution properties of the 15-HETE decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
3.30 x10^{-2}	1.10	-3.40	9.49$10^{-2}$

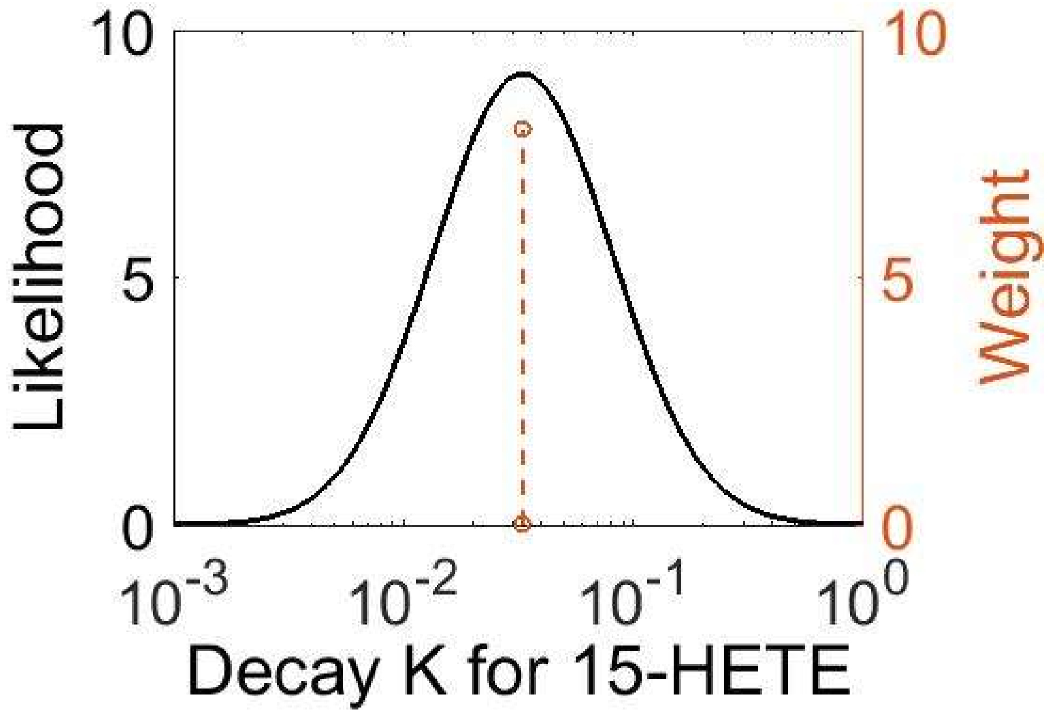

Figure SF.9.39.1.1.1. The estimated probability distribution for the 15-HETE decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.9.40. Reaction 89: 12-HETE →ϕ

The decay of 12-HETE in the intracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

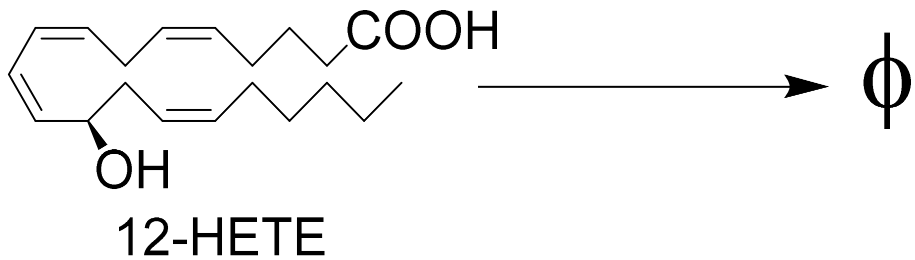

Figure SF.9.40. The decay of 12-hydroxyeicosatetraenoic acid (12-HETE) in the intracellular compartment (Reaction 89).

SEq.9.40. Reaction rate law for Reaction 89.

$$\boldsymbol{v_{89} = K[12 - \mathrm{HETE}]}$$

S.9.40.1. Reaction parameters

S.9.40.1.1. Parameter: K

Parameter values for the K of Reaction 89 were obtained from the literature and summarised in Table ST.9.40.1.1.1. The log-normal distribution properties for the K of Reaction 89 are shown in Table ST.9.40.1.1.2 and plotted in Figure SF.9.40.1.1.1.

Table ST.9.40.1.1.1. Literature information used to design the 12-HETE decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	Type of error	Reference
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other			
180		0.004		In vivo	12-HETE	Rabbit	Platelets	Unknown	37		8		(Dadaian et al., 1998)

Table ST.9.40.1.1.2. The log-normal distribution properties of the 12-HETE decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
3.83×10^{-3}	1.10	-5.56	9.49×10^{-2}

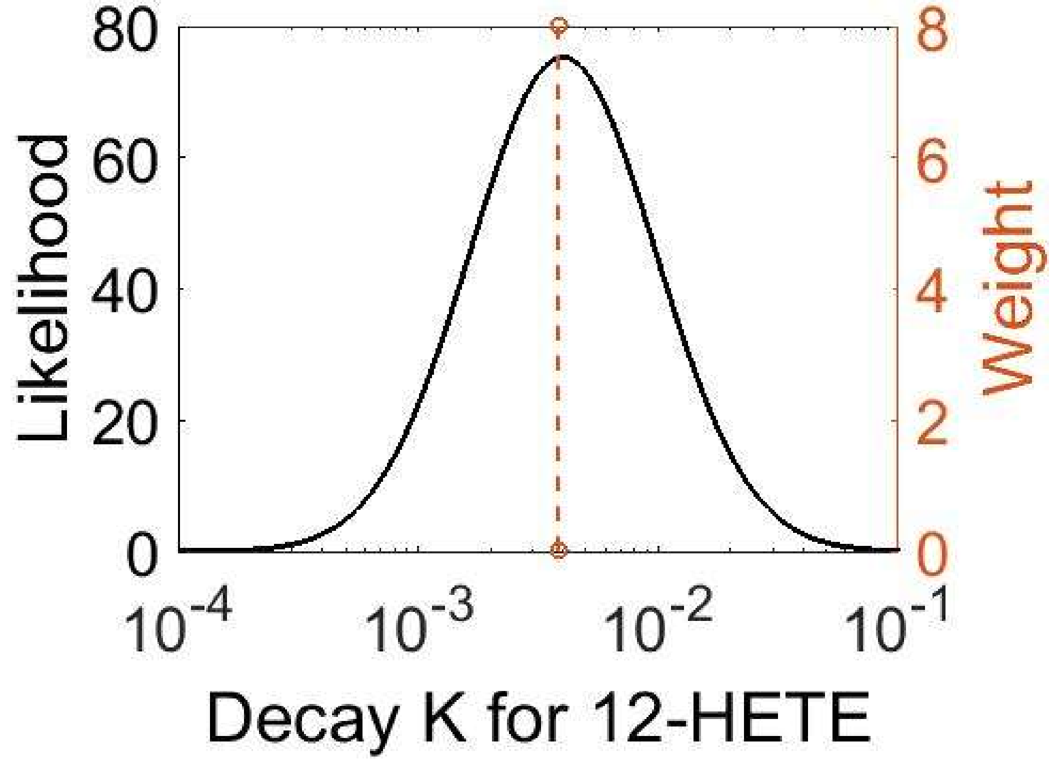

Figure SF.9.40.1.1.1. The estimated probability distribution for the 12-HETE decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.9.41. Reaction 90: 5-HETE→ϕ

The decay of 5-HETE in the intracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

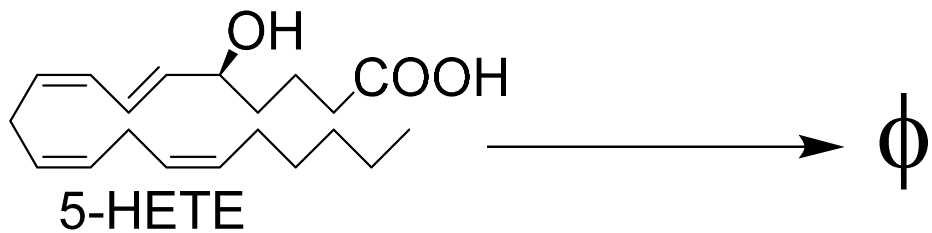

Figure SF.9.41. The decay of 5-hydroxyeicosatetraenoic acid (5-HETE) in the intracellular compartment (Reaction 90).

SEq.9.41. Reaction rate law for Reaction 90.

$$\boldsymbol{v_{90} = K[5 - \mathrm{HETE}]}$$

S.9.41.1. Reaction parameters

S.9.41.1.1. Parameter: K

Parameter values for the K of Reaction 90 were obtained from the literature and summarised in Table ST.9.41.1.1.1. The log-normal distribution properties for the K of Reaction 90 are shown in Table ST.9.41.1.1.2 and plotted in Figure SF.9.41.1.1.1.

Table ST.9.41.1.1.1. Literature information used to design the 5-HETE decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	Type of error	Reference
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other			
21		0.033		In vivo	15-HETE	Human	R15L Cells	Unknown	37		8		(Wei et al., 2009)

Table ST.9.41.1.1.2. The log-normal distribution properties of the 5-HETE decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
3.30×10^{-2}	1.10	-3.40	9.4910^{-2}

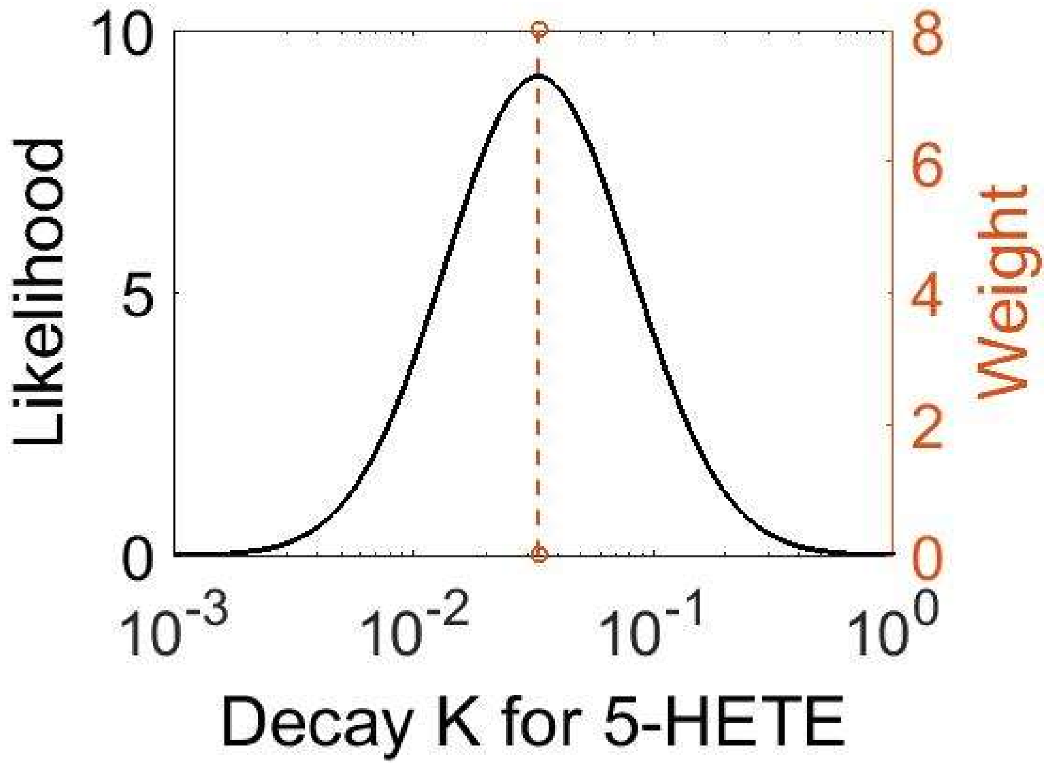

Figure SF.9.41.1.1.1. The estimated probability distribution for the 5-HETE decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.9.42. Reaction 91: 5-oxo-ETE→ϕ

The decay of 5-oxo-ETE in the intracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

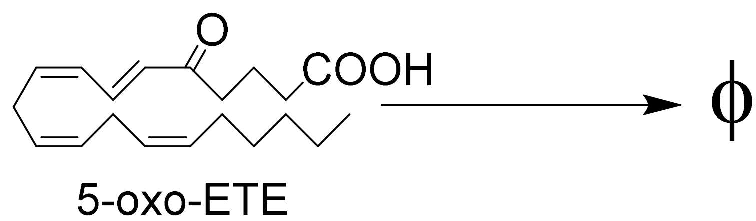

Figure SF.9.42. The decay of 5-oxo-eicosatetraenoic acid (5-oxo-ETE) in the intracellular compartment (Reaction 91).

SEq.9.42. Reaction rate law for Reaction 91.

$$\boldsymbol{v_{91} = K[5 - \mathrm{oxo} - \mathrm{ETE}]}$$

S.9.42.1. Reaction parameters

S.9.42.1.1. Parameter: K

Parameter values for the K of Reaction 91 were obtained from the literature and summarised in Table ST.9.42.1.1.1. The log-normal distribution properties for the K of Reaction 91 are shown in Table ST.9.42.1.1.2 and plotted in Figure SF.9.42.1.1.1.

Table ST.9.42.1.1.1. Literature information used to design the 5-oxo-ETE decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	Type of error	Reference
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other			
11		0.064		In vivo	15-OXO-ETE	Human	R15L Cells	Unknown	37		8		(Wei et al., 2009)

Table ST.9.42.1.1.2. The log-normal distribution properties of the 5-oxo-ETE decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
6.37×10^{-2}	1.10	-2.74	9.4910^{-2}

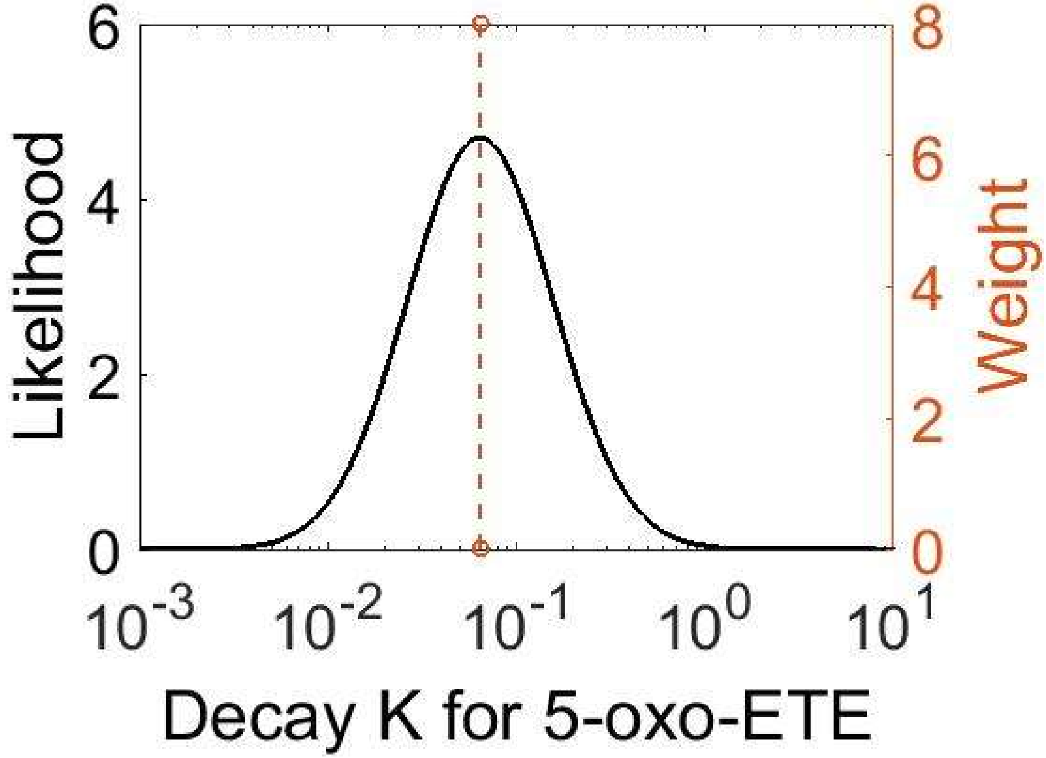

Figure SF.9.42.1.1.1. The estimated probability distribution for the 5-oxo-ETE decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.9.43. Reaction 92: $LTA_4 \rightarrow \phi$

The decay of LTA_4 in the intracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

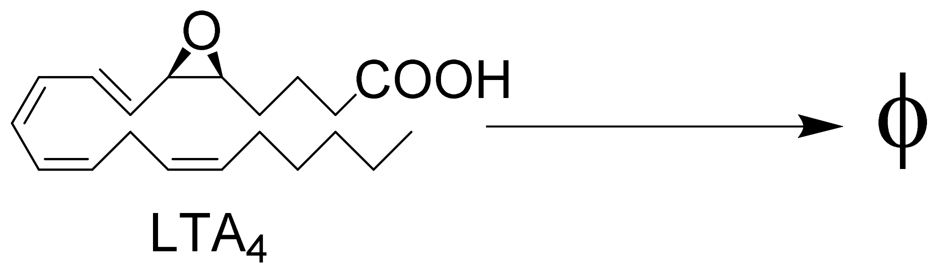

Figure SF.9.43. The decay of leukotriene A_4 (LTA_4) in the intracellular compartment (Reaction 92).

SEq.9.43. Reaction rate law for Reaction 92.

$$\boldsymbol{\nu_{92} = K[\mathrm{LTA_4}]}$$

S.9.43.1. Reaction parameters

S.9.43.1.1. Parameter: K

Parameter values for the K of Reaction 92 were obtained from the literature and summarised in Table ST.9.43.1.1.1. The log-normal distribution properties for the K of Reaction 92 are shown in Table ST.9.43.1.1.2 and plotted in Figure SF.9.43.1.1.1.

Table ST.9.43.1.1.1. Literature information used to design the LTA_4 decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	Type of error	Reference
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other			
0.05		13.863		In vivo	LTA_4	Unknown	Unknown	7	37		8		(Dickinson Zimmer et al., 2004)

Table ST.9.43.1.1.2. The log-normal distribution properties of the LTA_4 decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.38×10^{1}	1.10	2.63	9.4910^{-2}

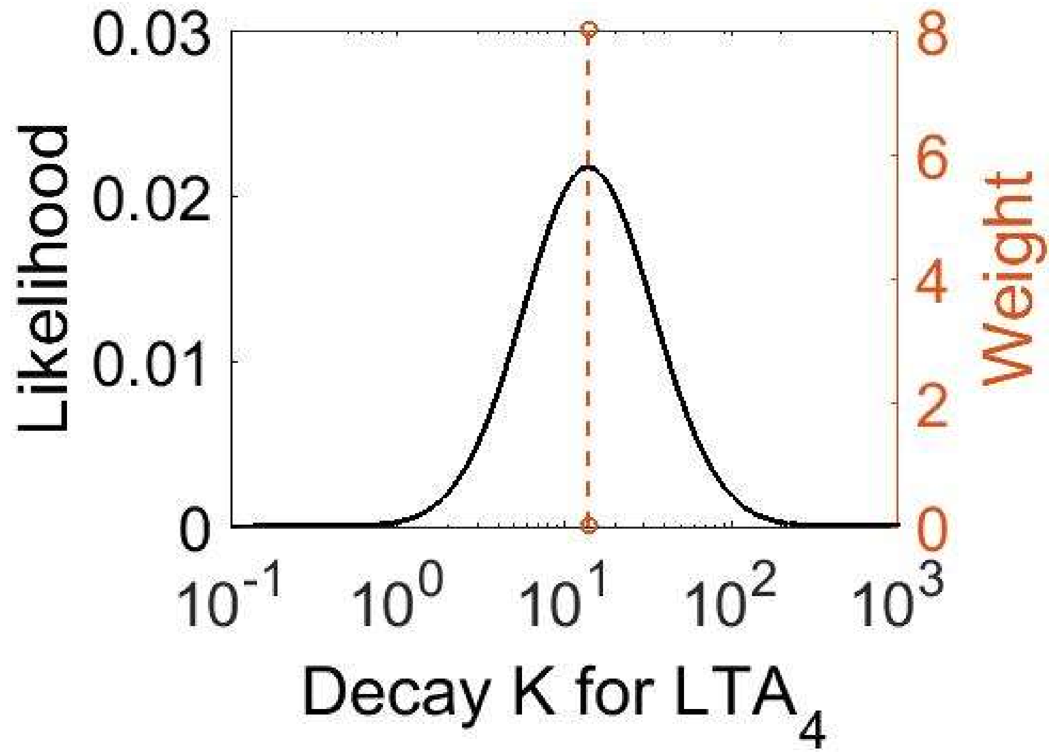

Figure SF.9.43.1.1.1. The estimated probability distribution for the LTA_4 decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.9.44. Reaction 93: $LTB_4 \rightarrow \phi$

The decay of LTB_4 in the intracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

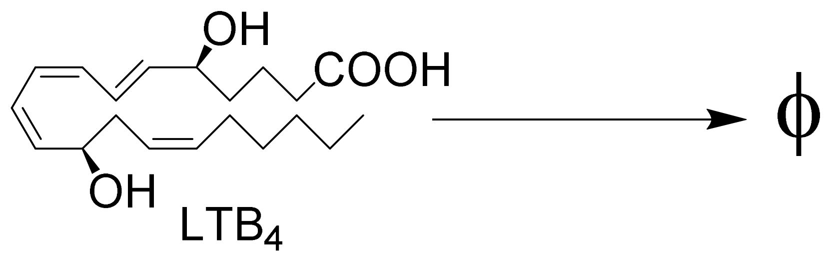

Figure SF.9.44. The decay of leukotriene B_4 (LTB_4) in the intracellular compartment (Reaction 93).

SEq.9.44. Reaction rate law for Reaction 93.

$$\boldsymbol{v_{93} = K[\mathrm{LTB_4}]}$$

S.9.44.1. Reaction parameters

S.9.44.1.1. Parameter: K

Parameter values for the K of Reaction 93 were obtained from the literature and summarised in Table ST.9.44.1.1.1. The log-normal distribution properties for the K of Reaction 93 are shown in Table ST.9.44.1.1.2 and plotted in Figure SF.9.44.1.1.1.

Table ST.9.44.1.1.1. Literature information used to design the LTB_4 decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	Type of error	Reference
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other			
0.47		1.475		In vivo	LTB_4	Rabbit	Plasma	7.4	Unknown		8		(Marleau et al., 1994)

Table ST.9.44.1.1.2. The log-normal distribution properties of the LTB_4 decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.47	1.10	3.93×10^{-1}	9.4910^{-2}

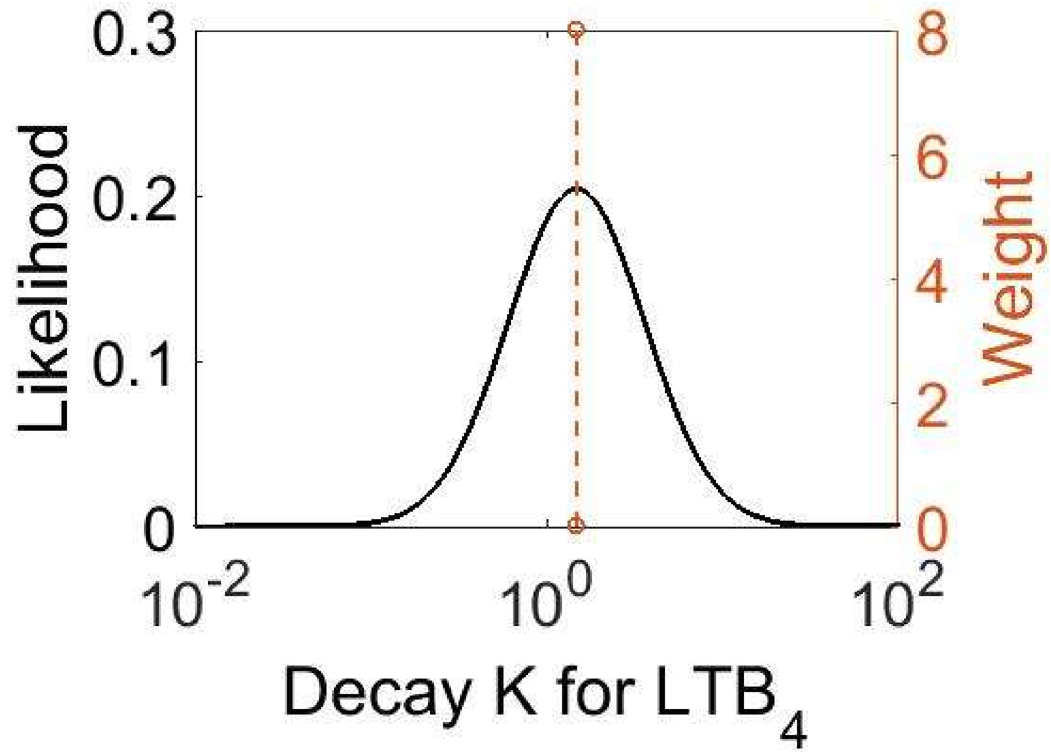

Figure SF.9.44.1.1.1. The estimated probability distribution for the LTB_4 decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale**.**

S.9.45. Reaction 94: $LTC_4 \rightarrow \phi$

The decay of LTC_4 in the intracellular compartment into metabolites outside of the scope of this model. An example of metabolites outside of the scope of this model includes metabolites which have been removed from the extracellular compartment into the systemic circulation or are degraded into metabolites not of interest to this model, the term decay reaction refers to the decrease in metabolite concentration by this collection of unspecified processes.

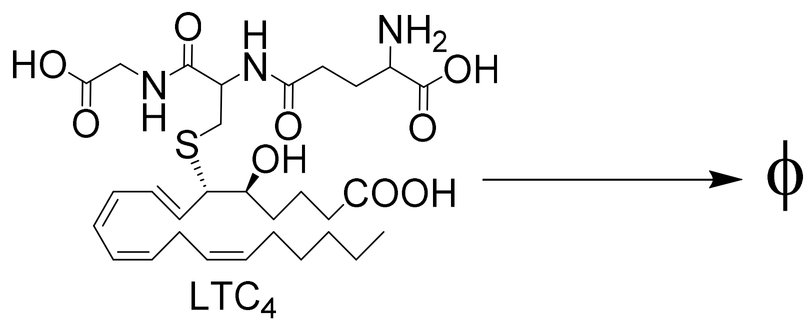

Figure S.9.45 The decay of leukotriene C_4 (LTC_4) in the intracellular compartment (Reaction 94).

SEq.9.45. Reaction rate law for Reaction 94.

$$\boldsymbol{v_{94} = K[LTC_4]}$$

S.9.45.1. Reaction parameters

S.9.45.1.1. Parameter: K

Parameter values for the K of Reaction 94 were obtained from the literature and summarised in Table ST.9.45.1.1.1. The log-normal distribution properties for the K of Reaction 94 are shown in Table ST.9.45.1.1.2 and plotted in Figure SF.9.45.1.1.1.

Table ST.9.45.1.1.1. Literature information used to design the LTC_4 decay constant parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Half Life (min)	Error (min)	Rate constant (min^{-1})	Error (min^{-1})	Experimental details							Weight	Type of error	Reference
				Experiment type	Substrate	Species	Expression Vector	pH	Temperature (°C)	Other			
0.47		1.475		In vivo	LTB_4	Rabbit	Plasma	7.4	Unknown		8		(Marleau et al., 1994)

Table ST.9.45.1.1.2. The log-normal distribution properties of the LTC_4 decay constant distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.47	1.10	3.93×10^{-1}	9.49×10^{-2}

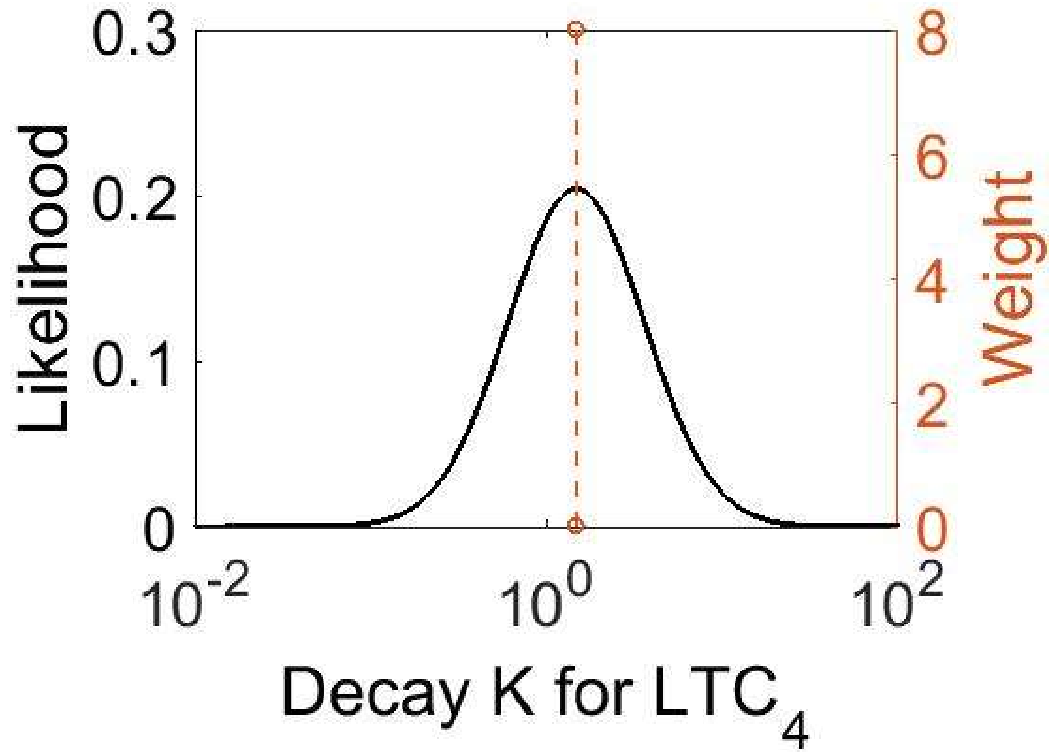

Figure SF.9.45.1.1.1. The estimated probability distribution for the LTC_4 decay constant. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

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Supplementary Document S10. Transporter-mediated Reaction Structure and Parameterisation.

Documentation of parameter values obtained for all transporter-mediated reactions in the model (Reactions 22–42, 67, 70, 101–111; Supplementary Table S5) from the literature and associated uncertainty for the eicosanoid network model. Parameterisation was performed using the method of Tsigkinopoulou *et al.,* (2018). The table includes information regarding each reaction and its respective parameters are documented. This includes information such as the reaction rate law and the literature values that were used to define parameters, including experimental conditions, total weights and literature references from which the data were obtained. In this model some parameters are referred as "Dependent parameters", meaning that the log-normal distribution for that parameter was calculated using multivariate distributions (discussed in **Section 2.6.2**). As a result, no confidence interval factor or literature values were cited for the Dependent parameters.

Contents

S.10.1. Reaction 22: $PGF_{2\alpha} \rightleftharpoons exPGF_{2\alpha}$

$PGF_{2\alpha}$ is relocated from the intracellular compartment to the extracellular compartment via the ATP-binding cassette (ABC) transporter.

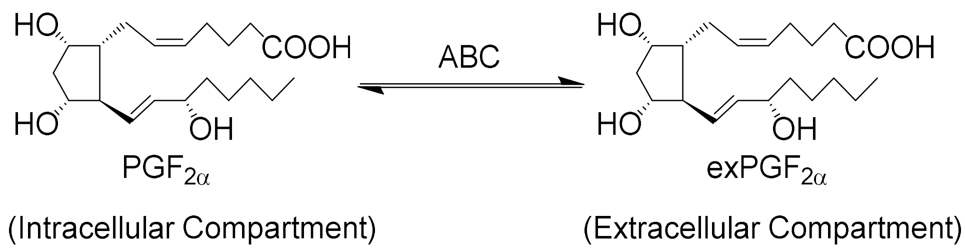


Figure SF.10.1. The transport of prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) from the intracellular compartment to the extracellular compartment by ATP Binding Cassette protein (ABC) (Reaction 22).

SEq.10.1. Reaction rate law for Reaction 22.

$$\boldsymbol{v_{22}} = [\boldsymbol{ABC}] \cdot \boldsymbol{k_{cat}} \cdot \frac{\mathbf{PGF_{2\alpha}}/K_m \cdot \left(1 - \frac{\mathbf{exPGF_{2\alpha}}}{\mathbf{PGF2\alpha} \cdot e^{-0.5 \cdot \left(G + R \cdot T \cdot \ln\left(\frac{ATP}{ADP}\right)\right)/R \cdot T}}\right)}{1 + \frac{\mathbf{PGF2\alpha}}{K_m} + \frac{\mathbf{exPGF2\alpha}}{K_m} + \mathbf{ABC\_CI}}$$

S.10.1.1. Reaction parameters

S.10.1.1.1. Parameter: ABC k_{cat}

Parameter values for the ABC k_{cat} of Reaction 22 were obtained from the literature and summarised in Table ST.10.1.1.1.1. The log-normal distribution properties for the ABC k_{cat} of Reaction 22 are shown in Table ST.10.1.1.1.2 and plotted in Figure SF.10.1.1.1.1.

Table ST.10.1.1.1.1. Literature information used to design the ABC k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
3.50	NaN	Bacteria	E. coli.	Glucose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Waygood and Steeves, 1980)
3.30×10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
8.30×10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
3.28	NaN	Yeast	Saccharomyces cerevisiae	HXT7 transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Ye et al., 2001)
1.13×10^{1}		Primate	Baculovirus	MRP2	7	37		512		(Yasunaga et al., 2008)

Table ST.10.1.1.1.2 The log-normal distribution properties of the ABC k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
1.13×10^{1}	1.00×10^{1}	3.22	8.91×10^{-1}

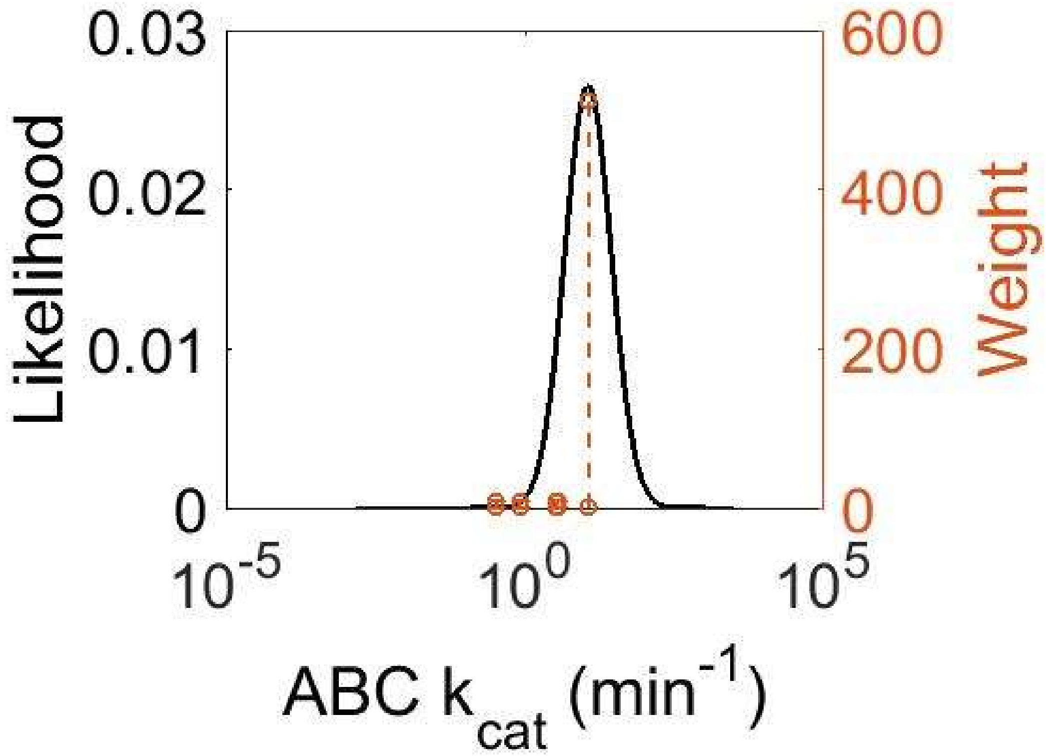


Figure SF.10.1.1.1.1. The estimated probability distribution for ABC k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.1.1.2. Parameter: ABC K_{ms}

Parameter values for the ABC K_{ms} of Reaction 22 were obtained from the literature and summarised in Table ST.10.1.1.2.1. The log-normal distribution properties for the ABC K_{ms} of Reaction 22 are shown in Table ST.10.1.1.2.2 and plotted in Figure SF.10.1.1.2.1.

Table ST.10.1.1.2.1. Literature information used to design the ABC K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.09×10^{-2}	4.10×10^{-3}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
3.66×10^{-5}	3.80×10^{-6}	Unknown	H69AR plasma membrane	MRP1	7.4	37		**128**	0	(Mao et al., 2000)
5.30×10^{-3}	2.60×10^{-3}	Human	HEK293 cells	MRP3	7.4	37		**128**	0	(Zeng et al., 2000)
1.95×10^{-1}	6.12×10^{-2}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
1.10×10^{-1}	3.91×10^{-2}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
2.07×10^{-2}	NaN	Human	HepG2 hepatoma	ABCB1	7.4	37		**2048**	0	(Fong et al., 2007)

Table ST.10.1.1.2.2 The log-normal distribution properties of the ABC K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
2.10 $\times 10^{-2}$	2.37 $\times 10^{1}$	-2.60	1.12

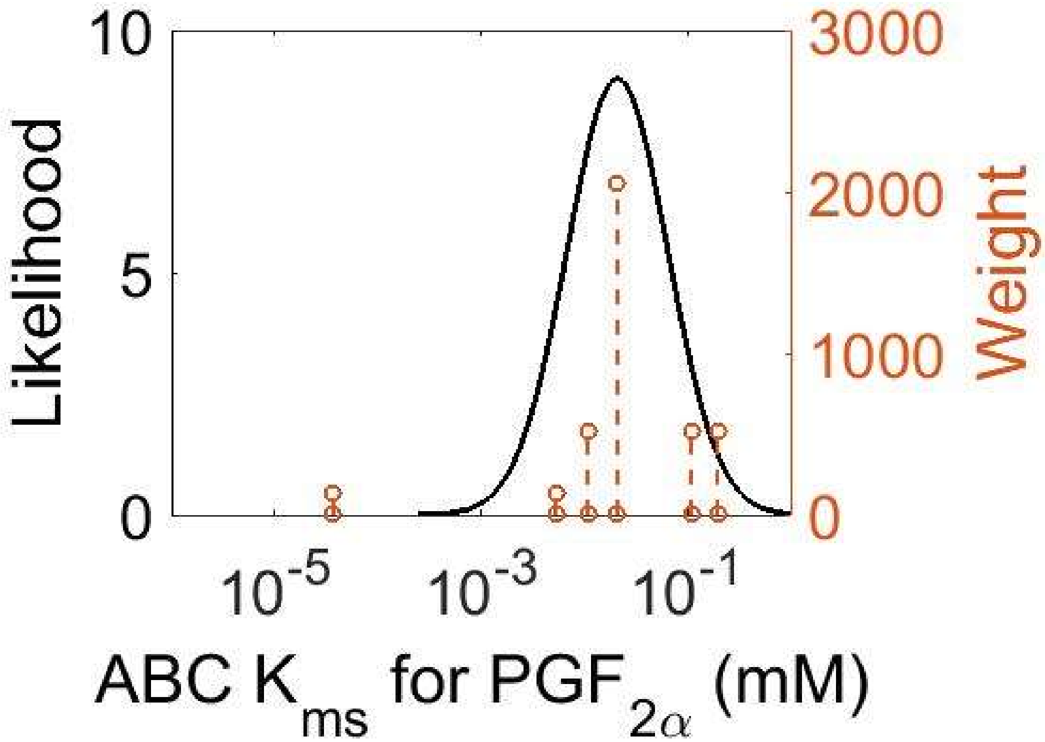


Figure SF.10.1.1.2.1. The estimated probability distribution for ABC K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.1.1.3. Parameter: ABC concentration

Parameter values for the ABC concentration of Reaction 22 were obtained from the literature and summarised in Table ST.10.1.1.3.1. The log-normal distribution properties for the ABC concentration of Reaction 22 are shown in Table ST.10.1.1.3.2 and plotted in Figure SF.10.1.1.3.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.10.1.1.3.1. Literature information used to design the ABC concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
5.15	NaN	Human	Stomach	ABC	7.5	37		2048	0	(Wilhelm et al., 2014)
5.94	NaN	Human	Lung	ABC	7.5	37		2048	0	(Kim et al., 2014)
2.66	NaN	Human	Gut	ABC	7.5	37		2048	0	(Kim et al., 2014)

Table ST.10.1.1.3.2. The log-normal distribution properties of the ABC concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
5.06	2.80×10^{-5}	1.44	1.74	3.42×10^{-1}

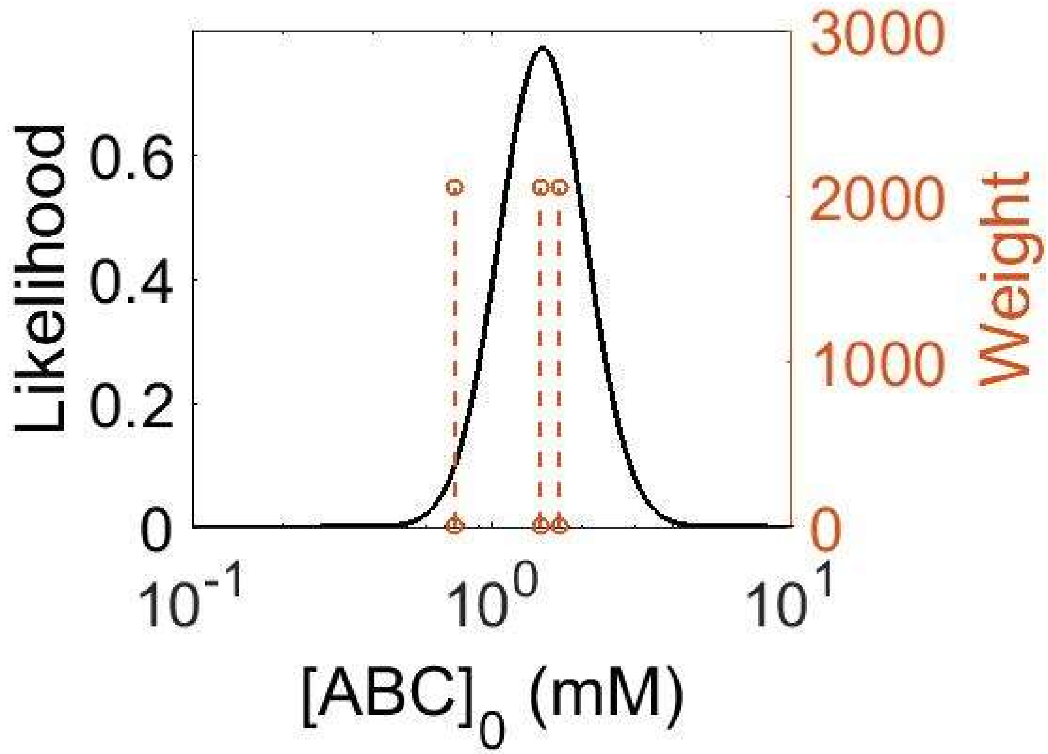


Figure SF.10.1.1.3.1. The estimated probability distribution for the ABC concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.2. Reaction 23: $TXB_2 \rightleftharpoons exTXB_2$

TXB_2 is relocated from the intracellular compartment to the extracellular compartment via the ATP-binding cassette (ABC) transporter.

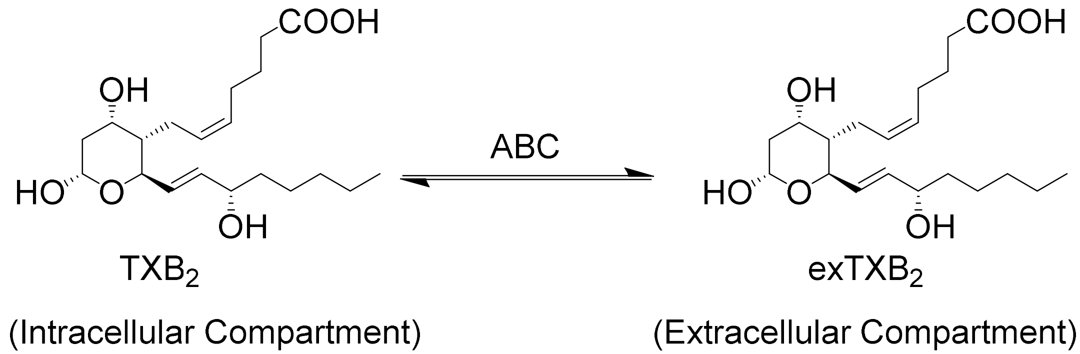


Figure SF.10.2. The transport of thromboxane (TXB_2) from the intracellular compartment to the extracellular compartment by ATP Binding Cassette protein (ABC) (Reaction 23).

SEq.10.2. Reaction rate law for Reaction 23.

$$\boldsymbol{v_{23}} = [\boldsymbol{ABC}] \cdot \boldsymbol{k_{cat}} \cdot \frac{\mathbf{TXB_2}/\boldsymbol{K_m} \cdot \left(1 - \dfrac{\mathbf{exTXB_2}}{\mathbf{TXB2} \cdot \boldsymbol{e}^{-0.5 \cdot \left(G + R \cdot T \cdot \ln\left(\frac{ATP}{ADP}\right)\right)/_{R \cdot T}}}\right)}{1 + \dfrac{\mathbf{TXB_2}}{\boldsymbol{K_m}} + \dfrac{\mathbf{exTXB_2}}{\boldsymbol{K_m}} + \mathbf{ABC\_CI}}$$

S.10.2.1. Reaction parameters

S.10.2.1.1. Parameter: ABC k_{cat}

Parameter values for the ABC k_{cat} of Reaction 23 were obtained from the literature and summarised in Table ST.10.2.1.1.1. The log-normal distribution properties for the ABC k_{cat} of Reaction 23 are shown in Table ST.10.2.1.1.2 and plotted in Figure SF.10.2.1.1.1.

Table ST.10.2.1.1.1. Literature information used to design the ABC k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
3.50	NaN	Bacteria	E. coli.	Glucose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Waygood and Steeves, 1980)
3.30 x10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
8.30 x10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
3.28	NaN	Yeast	Saccharomyces cerevisiae	HXT7 transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Ye et al., 2001)
1.13 x10^{1}		Primate	Baculovirus	MRP2	7	37		512		(Yasunaga et al., 2008)

Table ST.10.2.1.1.2. The log-normal distribution properties of the ABC k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.13 x10^{1}	1.00 x10^{1}	3.22	8.91$10^{-1}$

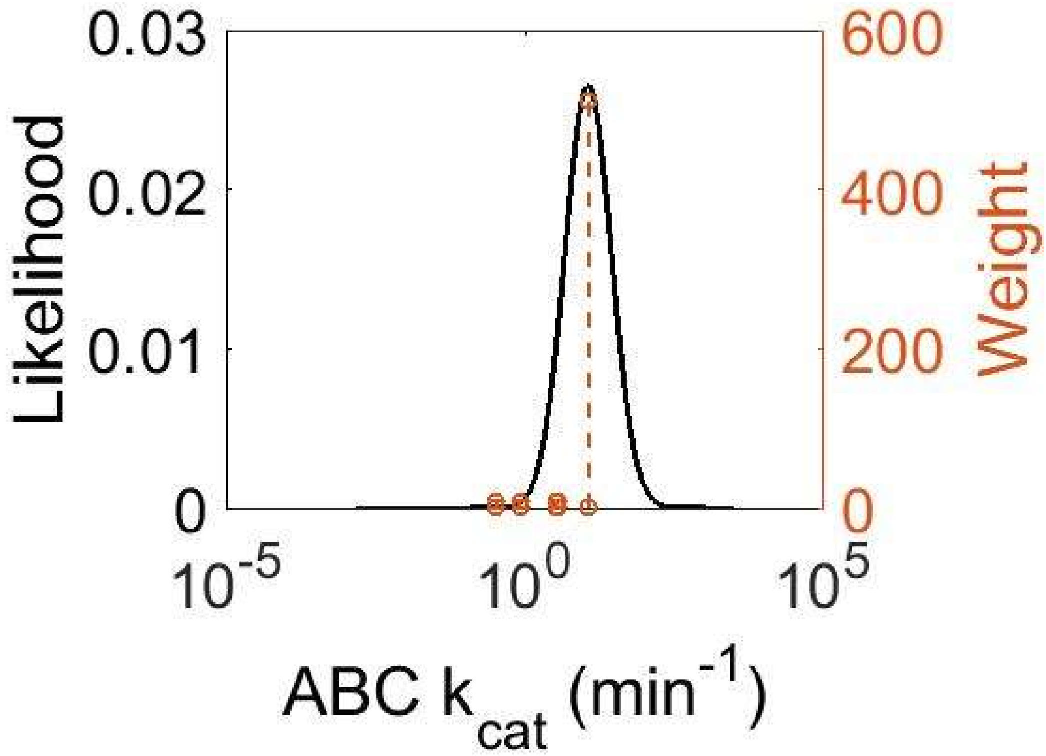


Figure SF.10.2.1.1.1. The estimated probability distribution for ABC k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.2.1.2. Parameter: ABC K_{ms}

Parameter values for the ABC K_{ms} of Reaction 23 were obtained from the literature and summarised in Table ST.10.2.1.2.1. The log-normal distribution properties for the ABC K_{ms} of Reaction 23 are shown in Table ST.10.2.1.2.2 and plotted in Figure SF.10.2.1.2.1.

Table ST.10.2.1.2.1. Literature information used to design the ABC K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.09 x10^{-2}	4.10 x10^{-3}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
3.66 x10^{-5}	3.80 x10^{-6}	Unknown	H69AR plasma membrane	MRP1	7.4	37		**128**	0	(Mao et al., 2000)
5.30 x10^{-3}	2.60 x10^{-3}	Human	HEK293 cells	MRP3	7.4	37		**128**	0	(Zeng et al., 2000)
1.95 x10^{-1}	6.12 x10^{-2}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
1.10 x10^{-1}	3.91 x10^{-2}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
2.07 x10^{-2}	NaN	Human	HepG2 hepatoma	ABCB1	7.4	37		**2048**	0	(Fong et al., 2007)

Table ST.10.2.1.2.2. The log-normal distribution properties of the ABC K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
2.10 $x10^{-2}$	2.37 $x10^{1}$	-2.60	1.12

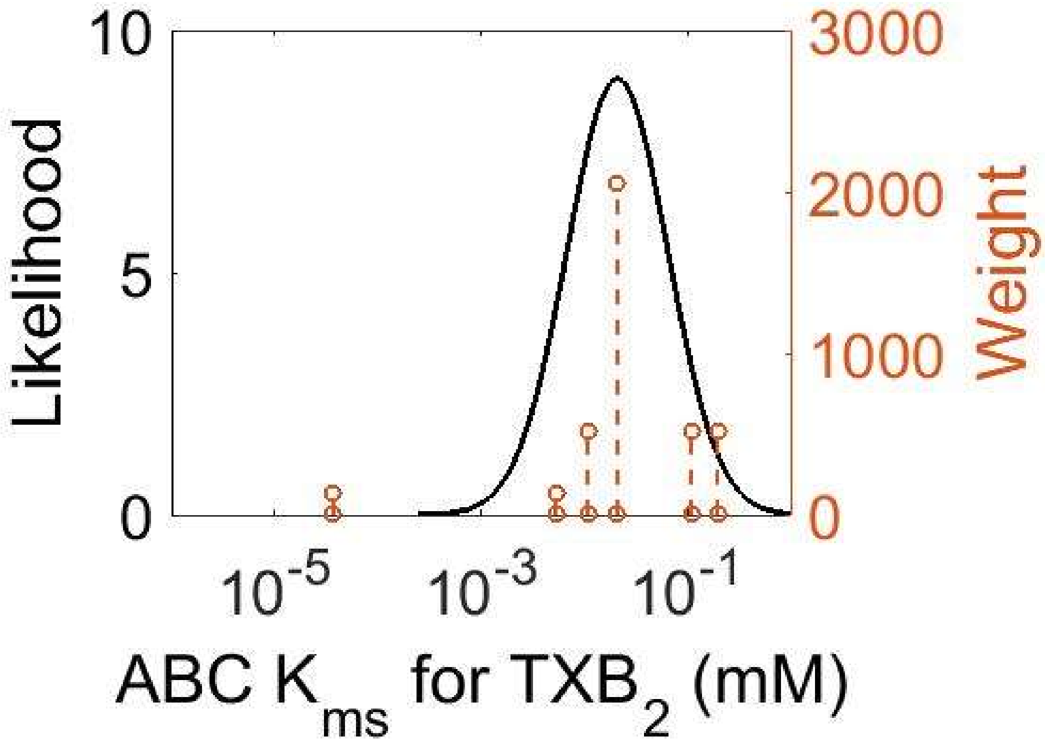


Figure SF.10.2.1.2.1. The estimated probability distribution for ABC K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S10.2.1.3. Parameter: ABC concentration

Parameter values for the ABC concentration of Reaction 23 were obtained from the literature and summarised in Table ST.10.2.1.3.1. The log-normal distribution properties for the ABC concentration of Reaction 23 are shown in Table ST.10.2.1.3.2 and plotted in Figure SF.10.2.1.3.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.10.2.1.3.1. Literature information used to design the ABC concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
5.15	NaN	Human	Stomach	ABC	7.5	37		2048	0	(Wilhelm et al., 2014)
5.94	NaN	Human	Lung	ABC	7.5	37		2048	0	(Kim et al., 2014)
2.66	NaN	Human	Gut	ABC	7.5	37		2048	0	(Kim et al., 2014)

Table ST.10.2.1.3.2. The log-normal distribution properties of the ABC concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
5.06	2.80×10^{-5}	1.44	1.74	3.4210^{-1}

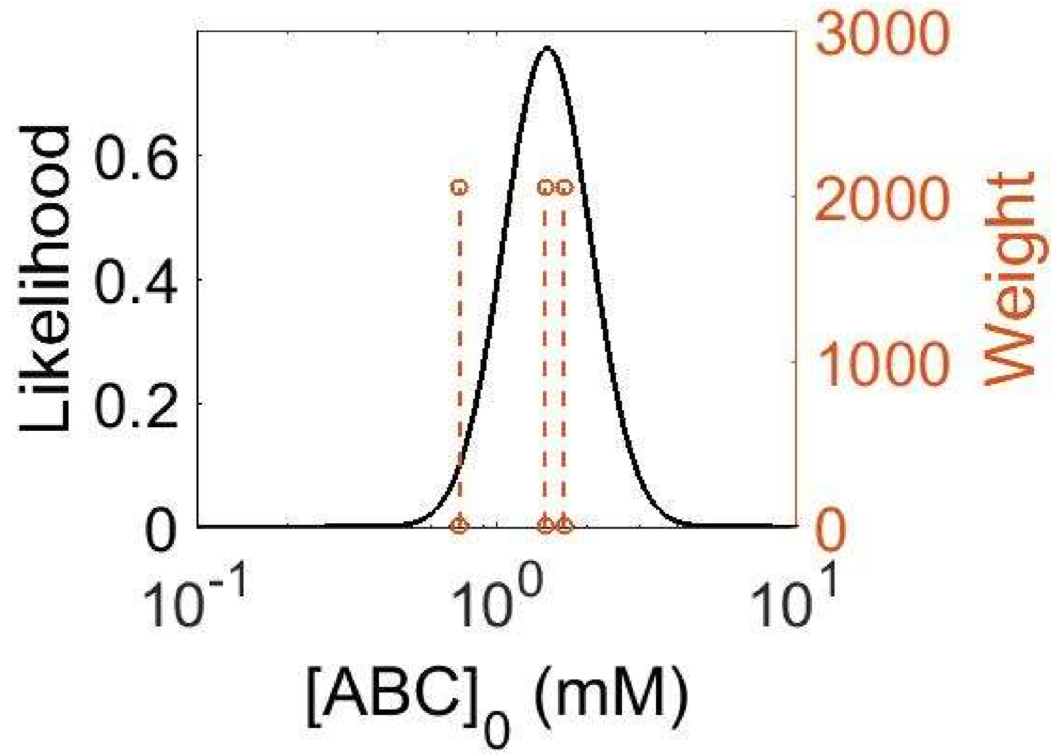
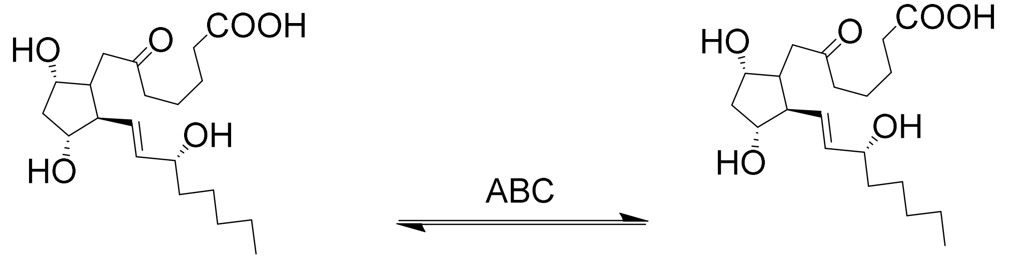


Figure SF.10.2.1.3.1. The estimated probability distribution for the ABC concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.3. Reaction 24: 6-keto-PGF$_{1\alpha}$ ⇌ ex6-keto-PGF$_{1\alpha}$

6-keto-PGF$_{1\alpha}$ is relocated from the intracellular compartment to the extracellular compartment via the ATP-binding cassette (ABC) transporter.



6-keto-PGF$_{1\alpha}$ (Intracellular Compartment)

ex6-keto-PGF$_{1\alpha}$ (Extracellular Compartment)

Figure SF.10.3. The transport of 6-keto-prostaglandin F$_{1\alpha}$ (6-keto-PGF$_{1\alpha}$) from the intracellular compartment to the extracellular compartment by ATP Binding Cassette protein (ABC) (Reaction 24).

SEq.10.3. Reaction rate law for Reaction 24.

$$\boldsymbol{v_{24}} = [\boldsymbol{ABC}] \cdot \boldsymbol{k_{cat}} \cdot \frac{{}^{6-\text{keto}-\text{PGF}_{1\alpha}}/_{K_m} \cdot \left(1 - \frac{\text{ex6}-\text{keto}-\text{PGF}_{1\alpha}}{6-\text{keto}-\text{PGF1}\alpha \cdot e^{-0.5 \cdot \left(G + R \cdot T \cdot \ln\left(\frac{ATP}{ADP}\right)\right) / R \cdot T}}\right)}{1 + \frac{6-\text{keto}-\text{PGF}_{1\alpha}}{K_m} + \frac{\text{ex6}-\text{keto}-\text{PGF}_{1\alpha}}{K_m} + \text{ABC\_CI}}$$

S.10.3.1. Reaction parameters

S.10.3.1.1. Parameter: ABC k_{cat}

Parameter values for the ABC k_{cat} of Reaction 24 were obtained from the literature and summarised in Table ST.10.3.1.1.1. The log-normal distribution properties for the ABC k_{cat} of Reaction 24 are shown in Table ST.10.3.1.1.2 and plotted in Figure SF.10.3.1.1.1.

Table ST.10.3.1.1.1. Literature information used to design the ABC k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	**Error (min^{-1})**	**Experimental details**						**Weight**	**Type of error**	**Reference**
		Species	**Expression Vector**	**Enzyme**	**pH**	**Temperature (°C)**	**Other**			
3.50	NaN	Bacteria	E. coli.	Glucose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Waygood and Steeves, 1980)
3.30×10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
8.30×10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
3.28	NaN	Yeast	Saccharomyces cerevisiae	HXT7 transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Ye et al., 2001)
1.13×10^{1}		Primate	Baculovirus	MRP2	7	37		512		(Yasunaga et al., 2008)

Table ST.10.3.1.1.2. The log-normal distribution properties of the ABC k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
1.13 $x10^{1}$	1.00 x101	3.22	8.9110^{-1}

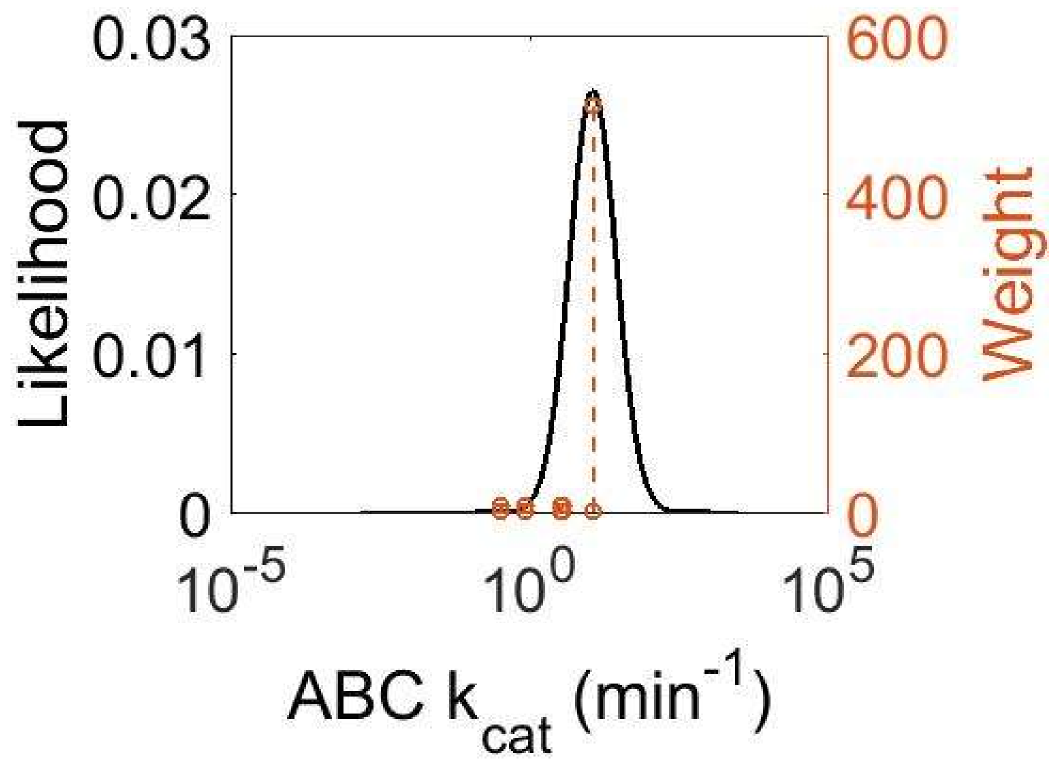


Figure SF.10.3.1.1.1. The estimated probability distribution for ABC k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.3.1.2. Parameter: ABC K_{ms}

Parameter values for the ABC K_{ms} of Reaction 24 were obtained from the literature and summarised in Table ST.10.3.1.2.1. The log-normal distribution properties for the ABC K_{ms} of Reaction 24 are shown in Table ST.10.3.1.2.2 and plotted in Figure SF.10.3.1.2.1.

Table ST.10.3.1.2.1. Literature information used to design the ABC K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	**Expression Vector**	**Enzyme**	**pH**	**Temperature (°C)**	**Other**			
1.09×10^{-2}	4.10×10^{-3}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
3.66×10^{-5}	3.80×10^{-6}	Unknown	H69AR plasma membrane	MRP1	7.4	37		**128**	0	(Mao et al., 2000)
5.30×10^{-3}	2.60×10^{-3}	Human	HEK293 cells	MRP3	7.4	37		**128**	0	(Zeng et al., 2000)
1.95×10^{-1}	6.12×10^{-2}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
1.10×10^{-1}	3.91×10^{-2}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
2.07×10^{-2}	NaN	Human	HepG2 hepatoma	ABCB1	7.4	37		**2048**	0	(Fong et al., 2007)

Table ST.10.3.1.2.2. The log-normal distribution properties of the ABC K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
2.10×10^{-2}	2.37×10^{1}	-2.60	1.12

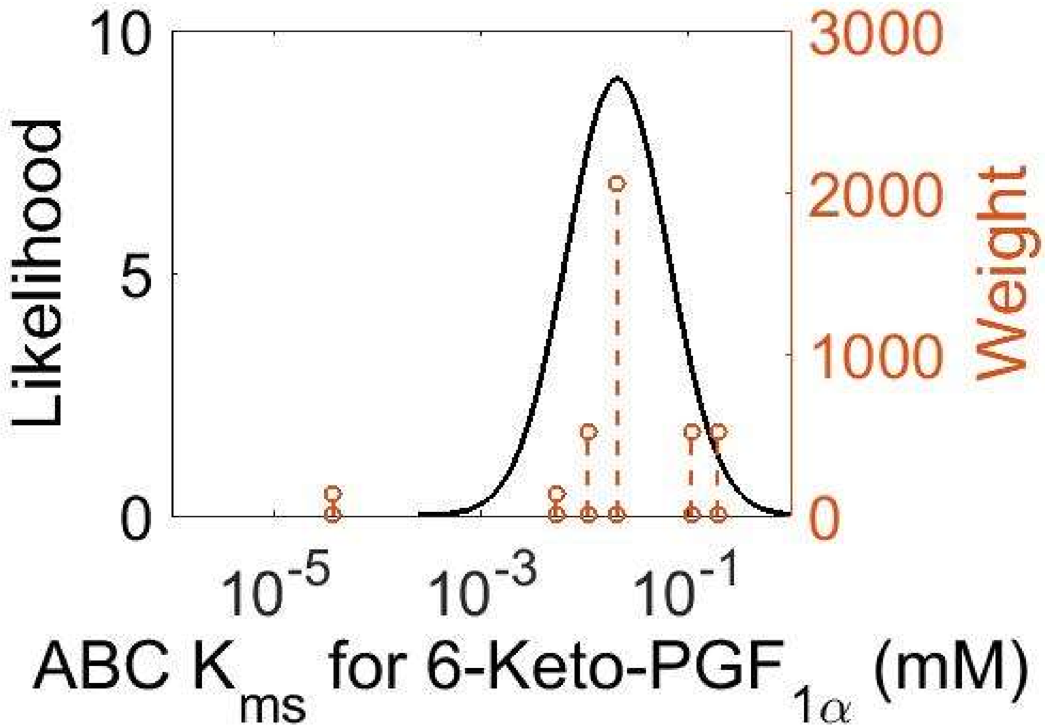


Figure SF.10.3.1.2.1. The estimated probability distribution for ABC K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.3.1.3. Parameter: ABC concentration

Parameter values for the ABC concentration of Reaction 24 were obtained from the literature and summarised in Table ST.10.3.1.3.1. The log-normal distribution properties for the ABC concentration of Reaction 24 are shown in Table ST.10.3.1.3.2 and plotted in Figure SF.10.3.1.3.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.10.3.1.3.1. Literature information used to design the ABC concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
5.15	NaN	Human	Stomach	ABC	7.5	37		2048	0	(Wilhelm et al., 2014)
5.94	NaN	Human	Lung	ABC	7.5	37		2048	0	(Kim et al., 2014)
2.66	NaN	Human	Gut	ABC	7.5	37		2048	0	(Kim et al., 2014)

Table ST.10.3.1.3.2. The log-normal distribution properties of the ABC concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
5.06	2.80×10^{-5}	1.44	1.74	3.4210^{-1}

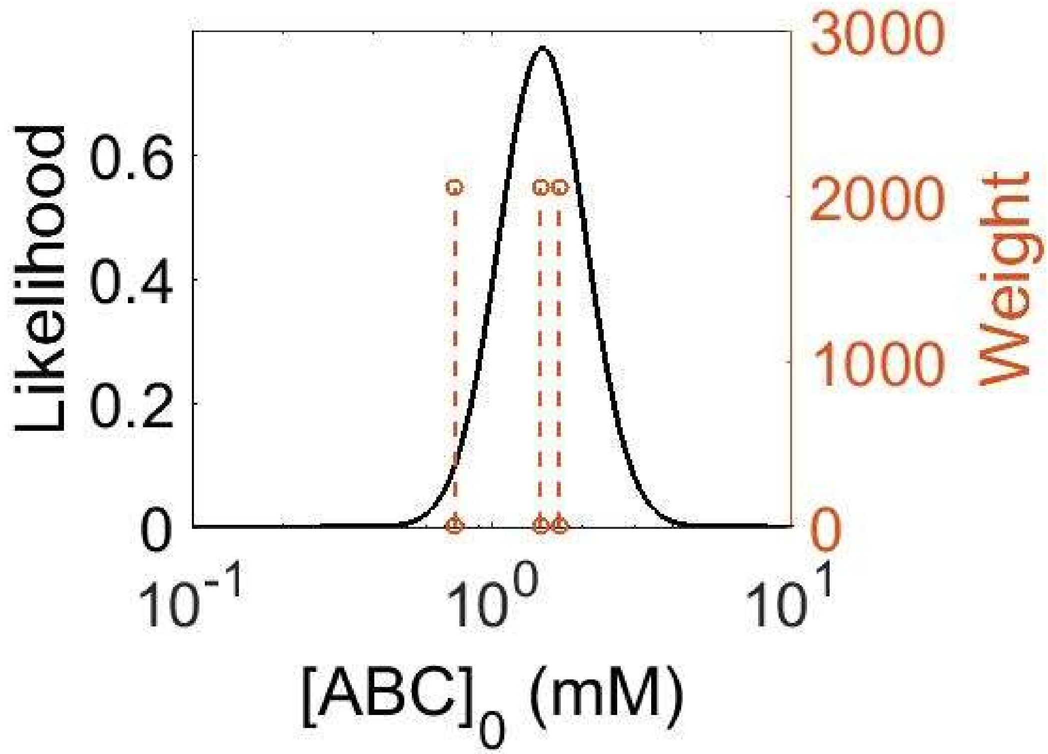


Figure SF.10.3.1.3.1. The estimated probability distribution for the ABC concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.4. Reaction 25: $PGE_2 \rightleftharpoons exPGE_2$

PGE_2 is relocated from the intracellular compartment to the extracellular compartment via the ATP-binding cassette (ABC) transporter.

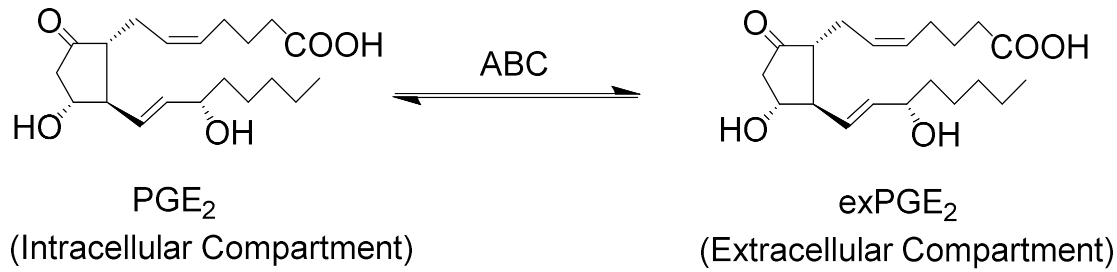


Figure SF.10.4. The transport of prostaglandin E_2 (PGE_2) from the intracellular compartment to the extracellular compartment by ATP Binding Cassette protein (ABC) (Reaction 25).

SEq.10.4. Reaction rate law for Reaction 25.

$$v_{25} = [ABC] \cdot k_{cat} \cdot \frac{\mathrm{PGE_2}/K_m \cdot \left(1 - \frac{\mathrm{exPGE_2}}{\mathrm{PGE2} \cdot e^{-0.5 \cdot \left(G + R \cdot T \cdot \ln\left(\frac{ATP}{ADP}\right)\right)/R \cdot T}}\right)}{1 + \frac{\mathrm{PGE_2}}{K_m} + \frac{\mathrm{exPGE_2}}{K_m} + \mathrm{ABC\_CI}}$$

S.10.4.1. Reaction parameters

S.10.4.1.1. Parameter: ABC k_{cat}

Parameter values for the ABC k_{cat} of Reaction 25 were obtained from the literature and summarised in Table ST.10.4.1.1.1. The log-normal distribution properties for the ABC k_{cat} of Reaction 25 are shown in Table ST.10.4.1.1.2 and plotted in Figure SF.10.4.1.1.1.

Table ST.10.4.1.1.1. Literature information used to design the ABC k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative**.**

Value (min^{-1})	**Error (min^{-1})**	**Experimental details**						**Weight**	**Type of error**	**Reference**
		Species	**Expression Vector**	**Enzyme**	**pH**	**Temperature (°C)**	**Other**			
3.50	NaN	Bacteria	E. coli.	Glucose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Waygood and Steeves, 1980)
3.30×10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
8.30×10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
3.28	NaN	Yeast	Saccharomyces cerevisiae	HXT7 transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Ye et al., 2001)
1.13×10^{1}		Primate	Baculovirus	MRP2	7	37		512		(Yasunaga et al., 2008)

Table ST.10.4.1.1.2. The log-normal distribution properties of the ABC k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
1.13 $x10^{1}$	1.00 $x10^{1}$	3.22	8.9110^{-1}

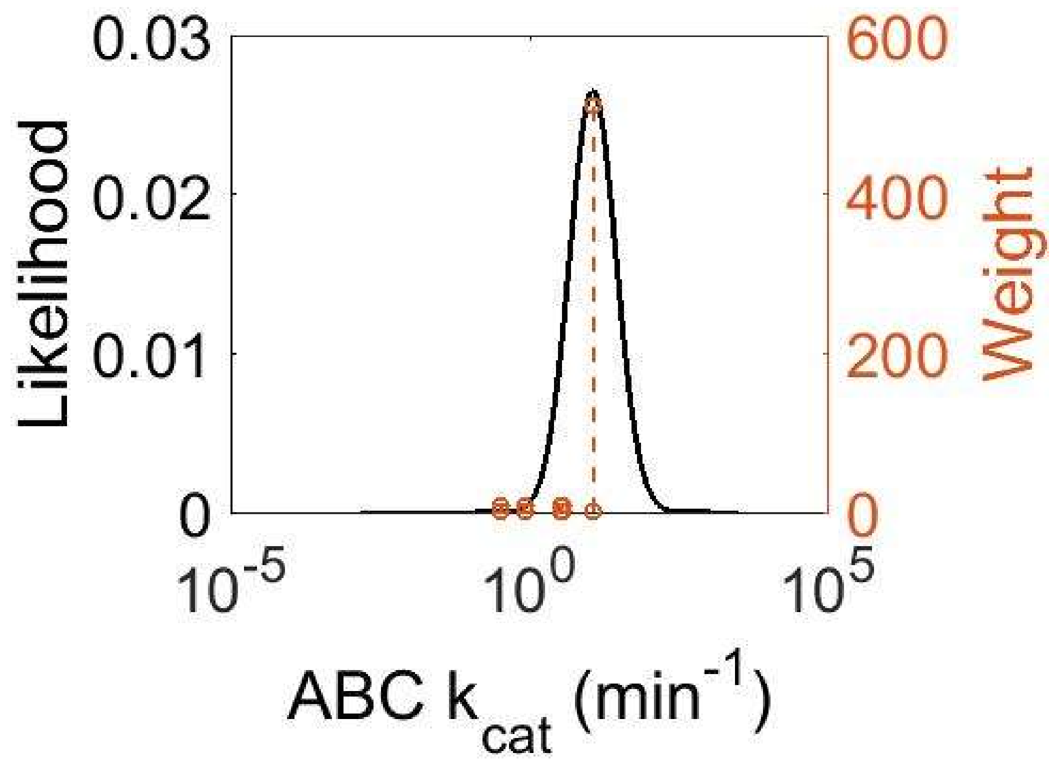


Figure SF.10.4.1.1.1. The estimated probability distribution for ABC k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.4.1.2. Parameter: ABC K_{ms}

Parameter values for the ABC K_{ms} of Reaction 25 were obtained from the literature and summarised in Table ST.10.4.1.2.1. The log-normal distribution properties for the ABC K_{ms} of Reaction 25 are shown in Table ST.10.4.1.2.2 and plotted in Figure SF.10.4.1.2.1.

Table ST.10.4.1.2.1. Literature information used to design the ABC K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.09×10^{-2}	4.10×10^{-3}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
3.66×10^{-5}	3.80×10^{-6}	Unknown	H69AR plasma membrane	MRP1	7.4	37		**128**	0	(Mao et al., 2000)
5.30×10^{-3}	2.60×10^{-3}	Human	HEK293 cells	MRP3	7.4	37		**128**	0	(Zeng et al., 2000)
1.95×10^{-1}	6.12×10^{-2}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
1.10×10^{-1}	3.91×10^{-2}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
2.07×10^{-2}	NaN	Human	HepG2 hepatoma	ABCB1	7.4	37		**2048**	0	(Fong et al., 2007)

Table ST.10.4.1.2.2. The log-normal distribution properties of the ABC K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
2.10×10^{-2}	2.37×10^{1}	-2.60	1.12

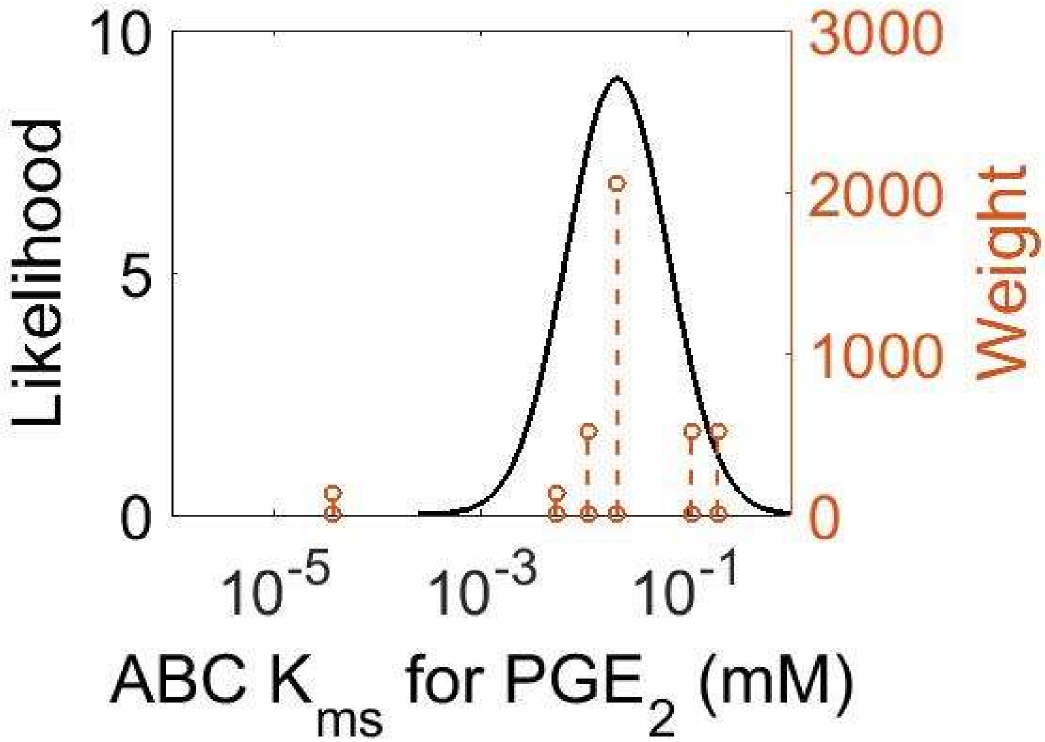


Figure SF.10.4.1.2.1. The estimated probability distribution for ABC K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.4.1.3. Parameter: ABC concentration

Parameter values for the ABC concentration of Reaction 25 were obtained from the literature and summarised in Table ST.10.4.1.3.1. The log-normal distribution properties for the ABC concentration of Reaction 25 are shown in Table ST.10.4.1.3.2 and plotted in Figure SF.10.4.1.3.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.10.4.1.3.1. Literature information used to design the ABC concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
5.15	NaN	Human	Stomach	ABC	7.5	37		2048	0	(Wilhelm et al., 2014)
5.94	NaN	Human	Lung	ABC	7.5	37		2048	0	(Kim et al., 2014)
2.66	NaN	Human	Gut	ABC	7.5	37		2048	0	(Kim et al., 2014)

Table ST.10.4.1.3.2. The log-normal distribution properties of the ABC concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
5.06	2.80×10^{-5}	1.44	1.74	3.42×10^{-1}

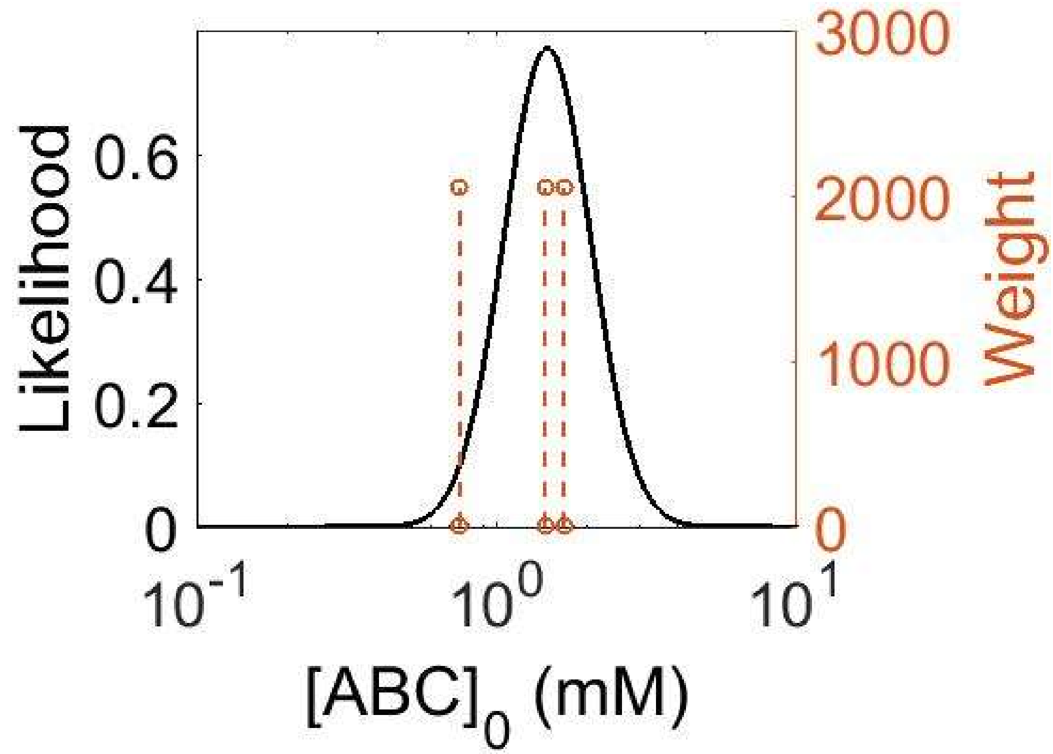


Figure SF.10.4.1.3.1. The estimated probability distribution for the ABC concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.5. Reaction 26: 15-deoxy-PGJ$_2$ ⇌ ex15-deoxy-PGJ$_2$

15-deoxy-PGJ$_2$ is relocated from the intracellular compartment to the extracellular compartment via the ATP-binding cassette (ABC) transporter.

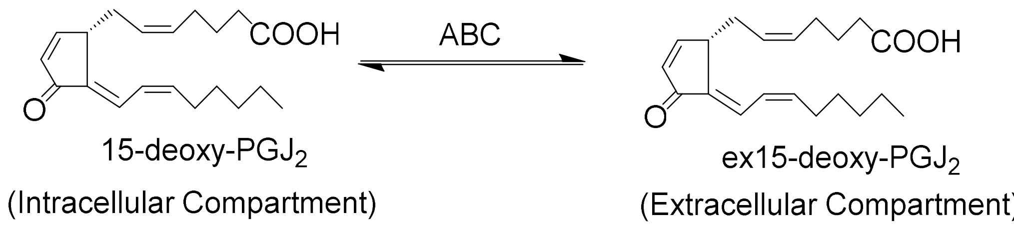


Figure SF.10.5. The transport of 15-deoxy-prostaglandin J$_2$ (15-deoxy-PGJ$_2$) from the intracellular compartment to the extracellular compartment by ATP Binding Cassette protein (ABC) (Reaction 26).

SEq.10.5. Reaction rate law for Reaction 26.

$$\boldsymbol{v_{26} = [ABC] \cdot k_{cat} \cdot \frac{15-deoxy-PGJ_2 / K_m \cdot \left(1 - \frac{ex15-deoxy-PGJ_2}{15-deoxy-PGJ_2 \cdot e^{-0.5 \cdot \left(G + R \cdot T \cdot \ln\left(\frac{ATP}{ADP}\right)\right) / R \cdot T}}\right)}{1 + \frac{15-deoxy-PGJ_2}{K_m} + \frac{ex15-deoxy-PGJ_2}{K_m} + ABC\_CI}}$$

S.10.5.1. Reaction parameters

S.10.5.1.1. Parameter: ABC k_{cat}

Parameter values for the ABC k_{cat} of Reaction 26 were obtained from the literature and summarised in Table ST.10.5.1.1.1. The log-normal distribution properties for the ABC k_{cat} of Reaction 26 are shown in Table ST.10.5.1.1.2 and plotted in Figure SF.10.5.1.1.1.

Table ST.10.5.1.1.1. Literature information used to design the ABC k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	**Error (min^{-1})**	**Experimental details**						**Weight**	**Type of error**	**Reference**
		Species	**Expression Vector**	**Enzyme**	**pH**	**Temperature (°C)**	**Other**			
3.50	NaN	Bacteria	E. coli.	Glucose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Waygood and Steeves, 1980)
3.30×10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
8.30×10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
3.28	NaN	Yeast	Saccharomyces cerevisiae	HXT7 transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Ye et al., 2001)
1.13×10^{1}		Primate	Baculovirus	MRP2	7	37		512		(Yasunaga et al., 2008)

Table ST.10.5.1.1.2. The log-normal distribution properties of the ABC k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
1.13 $x10^{1}$	1.00 $x10^{1}$	3.22	8.9110^{-1}

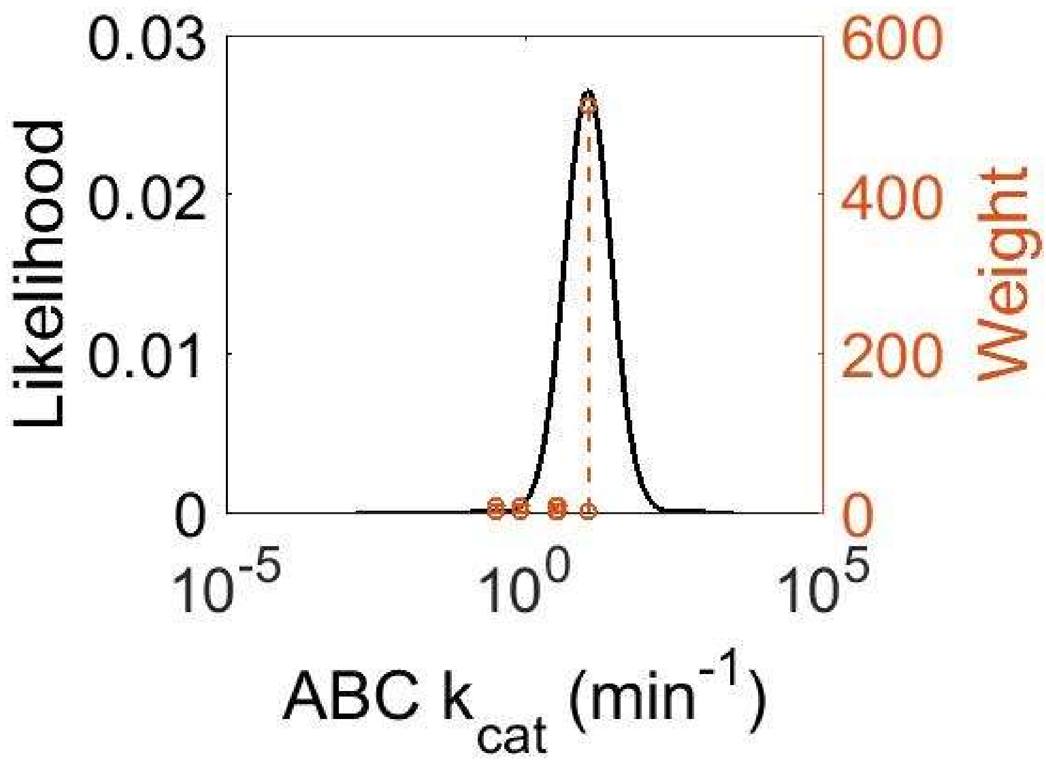


Figure SF.10.5.1.1.1. The estimated probability distribution for ABC k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.5.1.2. Parameter: ABC K_{ms}

Parameter values for the ABC K_{ms} of Reaction 26 were obtained from the literature and summarised in Table ST.10.5.1.2.1. The log-normal distribution properties for the ABC K_{ms} of Reaction 26 are shown in Table ST.10.5.1.2.2 and plotted in Figure SF.10.5.1.2.1.

Table ST.10.5.1.2.1. Literature information used to design the ABC K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.09×10^{-2}	4.10×10^{-3}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
3.66×10^{-5}	3.80×10^{-6}	Unknown	H69AR plasma membrane	MRP1	7.4	37		**128**	0	(Mao et al., 2000)
5.30×10^{-3}	2.60×10^{-3}	Human	HEK293 cells	MRP3	7.4	37		**128**	0	(Zeng et al., 2000)
1.95×10^{-1}	6.12×10^{-2}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
1.10×10^{-1}	3.91×10^{-2}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
2.07×10^{-2}	NaN	Human	HepG2 hepatoma	ABCB1	7.4	37		**2048**	0	(Fong et al., 2007)

Table ST.10.5.1.2.2. The log-normal distribution properties of the ABC K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
2.10×10^{-2}	2.37×10^{1}	-2.60	1.12

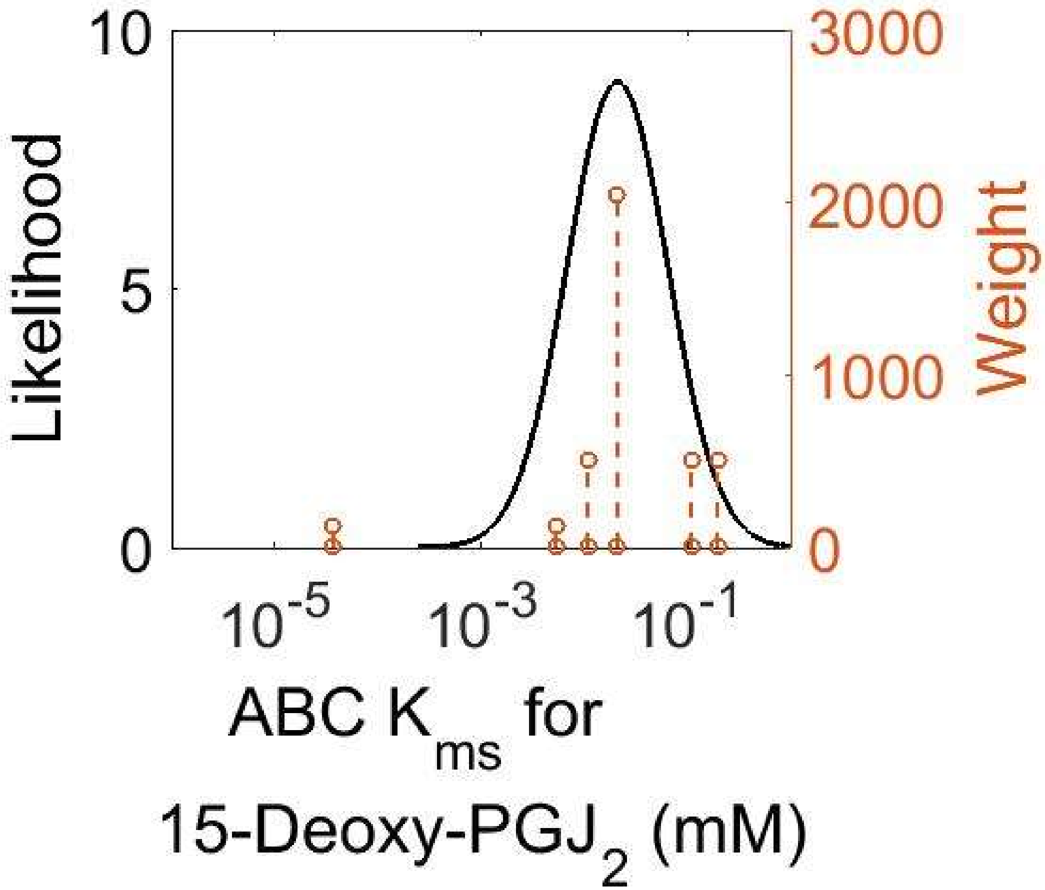


Figure SF.10.5.1.2.1. The estimated probability distribution for ABC K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.5.1.3. Parameter: ABC concentration

Parameter values for the ABC concentration of Reaction 26 were obtained from the literature and summarised in Table ST.10.5.1.3.1. The log-normal distribution properties for the ABC concentration of Reaction 26 are shown in Table ST.10.5.1.3.2 and plotted in Figure SF.10.5.1.3.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.10.5.1.3.1. Literature information used to design the ABC concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
5.15	NaN	Human	Stomach	ABC	7.5	37		2048	0	(Wilhelm et al., 2014)
5.94	NaN	Human	Lung	ABC	7.5	37		2048	0	(Kim et al., 2014)
2.66	NaN	Human	Gut	ABC	7.5	37		2048	0	(Kim et al., 2014)

Table ST.10.5.1.3.2. The log-normal distribution properties of the ABC concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
5.06	2.80×10^{-5}	1.44	1.74	3.42×10^{-1}

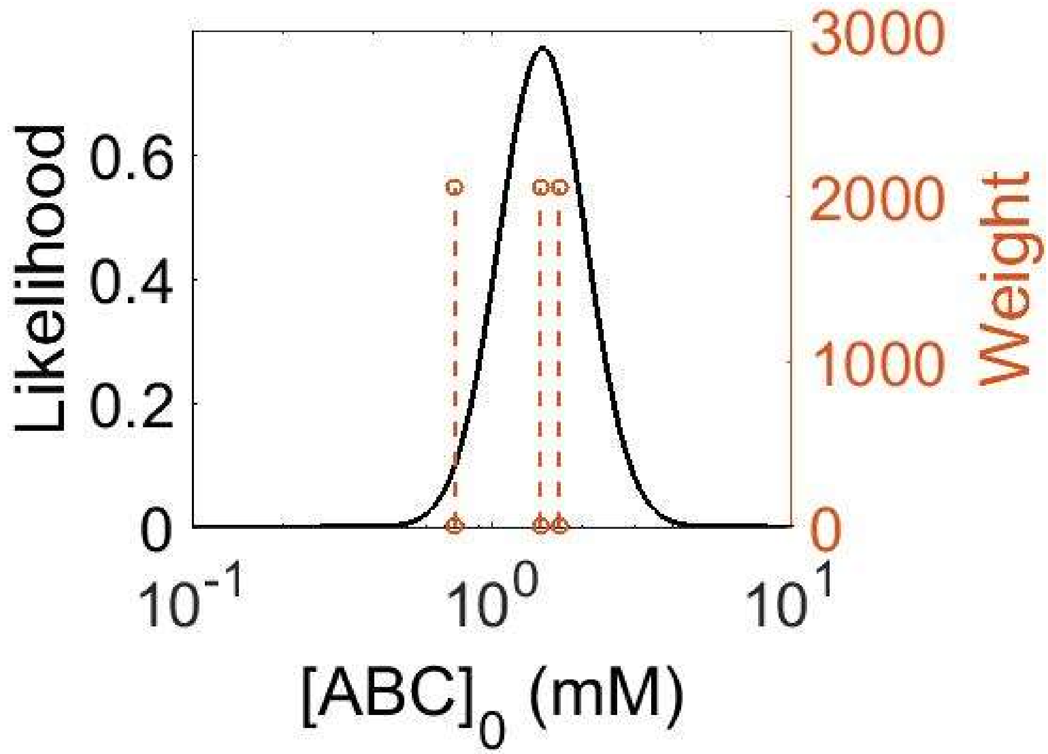
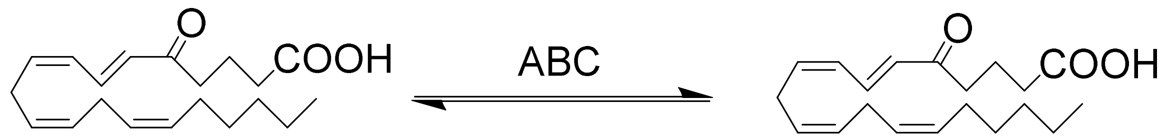


Figure SF.10.5.1.3.1. The estimated probability distribution for the ABC concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.6. Reaction 27: 5-oxo-ETE ⇌ ex5-oxo-ETE

5-oxo-ETE is relocated from the intracellular compartment to the extracellular compartment via the ATP-binding cassette (ABC) transporter.



5-oxo-ETE (Intracellular Compartment)

ex5-oxo-ETE (Extracellular Compartment)

Figure SF.10.6. The transport of 5-oxo-eicosatetraenoic acid (5-oxo-ETE) from the intracellular compartment to the extracellular compartment by ATP Binding Cassette protein (ABC) (Reaction 27).

SEq.10.6. Reaction rate law for Reaction 27.

$$v_{27} = [ABC] \cdot k_{cat} \cdot \frac{{}^{\text{5-oxo-ETE}}/_{K_m} \cdot \left(1 - \frac{\text{ex5-oxo-ETE}}{\text{5-oxo-ETE} \cdot e^{-0.5 \cdot \left(G + R \cdot T \cdot \ln\left(\frac{ATP}{ADP}\right)\right)/_{R \cdot T}}}\right)}{1 + \frac{\text{5-oxo-ETE}}{K_m} + \frac{\text{ex5-oxo-ETE}}{K_m} + \text{ABC\_CI}}$$

S.10.6.1. Reaction parameters

S.10.6.1.1. Parameter: ABC k_{cat}

Parameter values for the ABC k_{cat} of Reaction 27 were obtained from the literature and summarised in Table ST.10.6.1.1.1. The log-normal distribution properties for the ABC k_{cat} of Reaction 27 are shown in Table ST.10.6.1.1.2 and plotted in Figure SF.10.6.1.1.1.

Table ST.10.6.1.1.1. Literature information used to design the ABC k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	**Expression Vector**	**Enzyme**	**pH**	**Temperature (°C)**	**Other**			
3.50	NaN	Bacteria	E. coli.	Glucose transporter	Unknown	Unknown	Bionumbers calculation	8	0	(Waygood and Steeves, 1980)
3.30 x10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	8	0	(Naftalin et al., 2007)
8.30 x10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	8	0	(Naftalin et al., 2007)
3.28	NaN	Yeast	Saccharomyces cerevisiae	HXT7 transporter	Unknown	Unknown	Bionumbers calculation	8	0	(Ye et al., 2001)
1.13 x10^{1}		Primate	Baculovirus	MRP2	7	37		512		(Yasunaga et al., 2008)

Table ST.10.6.1.1.2. The log-normal distribution properties of the ABC k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
1.13 $x10^{1}$	1.00 $x10^{1}$	3.22	8.9110^{-1}

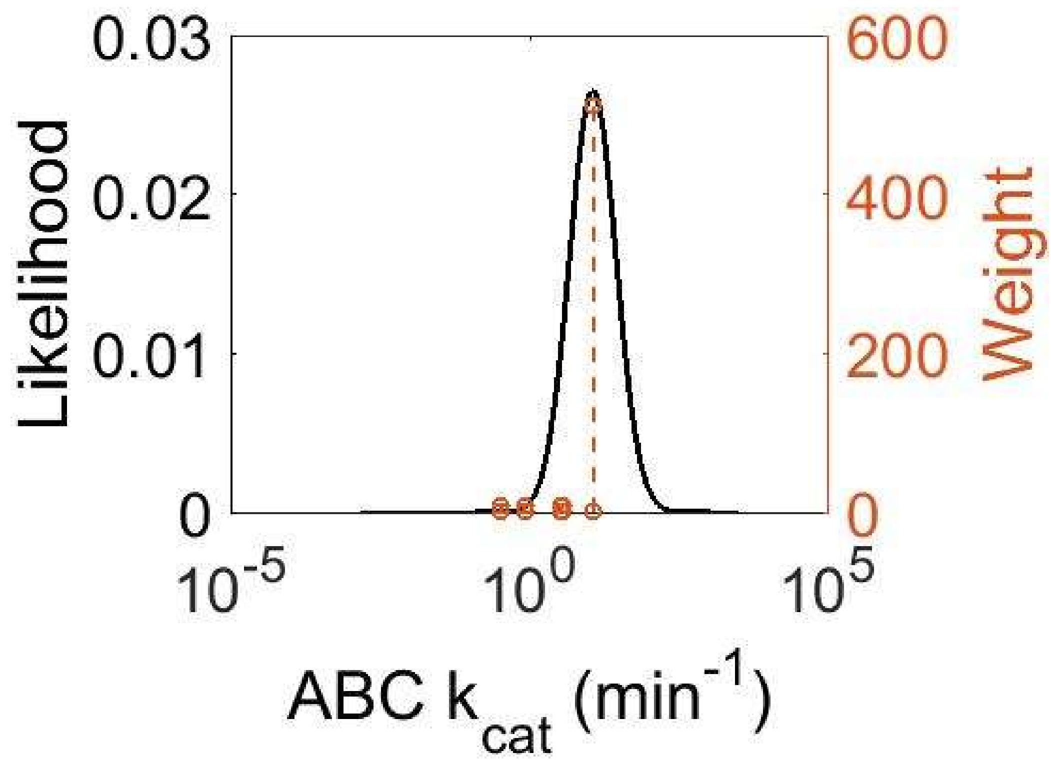


Figure SF.10.6.1.1.1. The estimated probability distribution for ABC k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.6.1.2. Parameter: ABC K_{ms}

Parameter values for the ABC K_{ms} of Reaction 27 were obtained from the literature and summarised in Table ST.10.6.1.2.1. The log-normal distribution properties for the ABC K_{ms} of Reaction 27 are shown in Table ST.10.6.1.2.2 and plotted in Figure SF.10.6.1.2.1.

Table ST.10.6.1.2.1. Literature information used to design the ABC K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.09×10^{-2}	4.10×10^{-3}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
3.66×10^{-5}	3.80×10^{-6}	Unknown	H69AR plasma membrane	MRP1	7.4	37		**128**	0	(Mao et al., 2000)
5.30×10^{-3}	2.60×10^{-3}	Human	HEK293 cells	MRP3	7.4	37		**128**	0	(Zeng et al., 2000)
1.95×10^{-1}	6.12×10^{-2}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
1.10×10^{-1}	3.91×10^{-2}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
2.07×10^{-2}	NaN	Human	HepG2 hepatoma	ABCB1	7.4	37		**2048**	0	(Fong et al., 2007)

Table ST.10.6.1.2.2. The log-normal distribution properties of the ABC K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
2.10×10^{-2}	2.37×10^{1}	-2.60	1.12

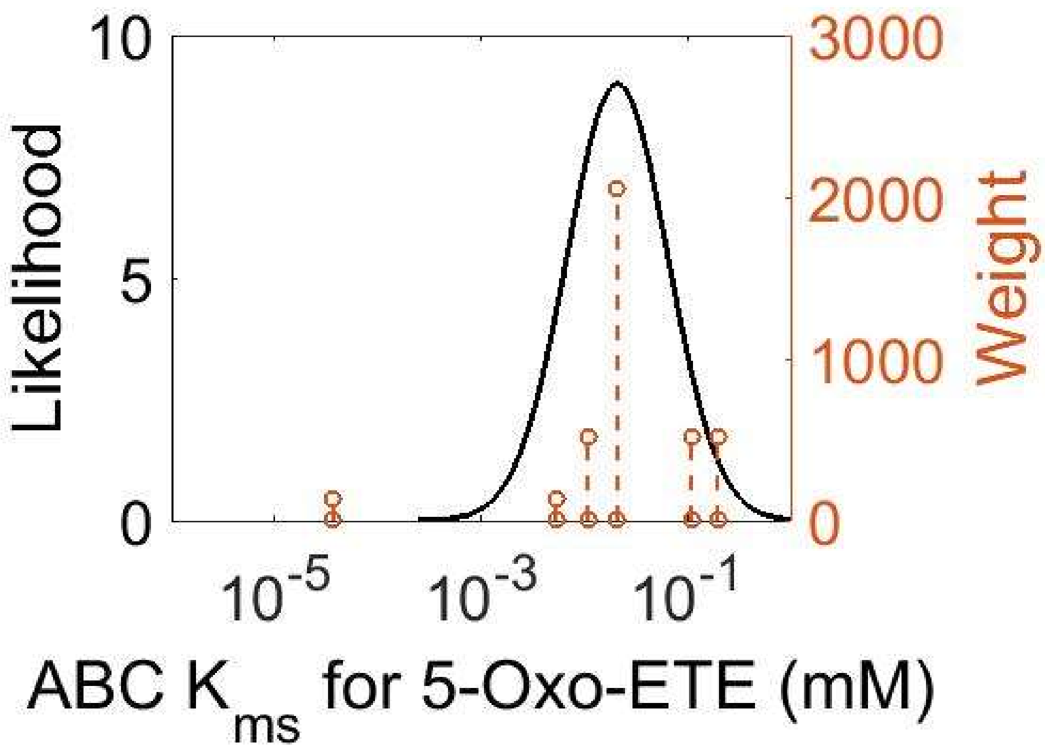


Figure SF.10.6.1.2.1. The estimated probability distribution for ABC K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.6.1.3. Parameter: ABC concentration

Parameter values for the ABC concentration of Reaction 27 were obtained from the literature and summarised in Table ST.10.6.1.3.1. The log-normal distribution properties for the ABC concentration of Reaction 27 are shown in Table ST.10.6.1.3.2 and plotted in Figure SF.10.6.1.3.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.10.6.1.3.1. Literature information used to design the ABC concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
5.15	NaN	Human	Stomach	ABC	7.5	37		2048	0	(Wilhelm et al., 2014)
5.94	NaN	Human	Lung	ABC	7.5	37		2048	0	(Kim et al., 2014)
2.66	NaN	Human	Gut	ABC	7.5	37		2048	0	(Kim et al., 2014)

Table ST.10.6.1.3.2. The log-normal distribution properties of the ABC concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
5.06	2.80×10^{-5}	1.44	1.74	3.42×10^{-1}

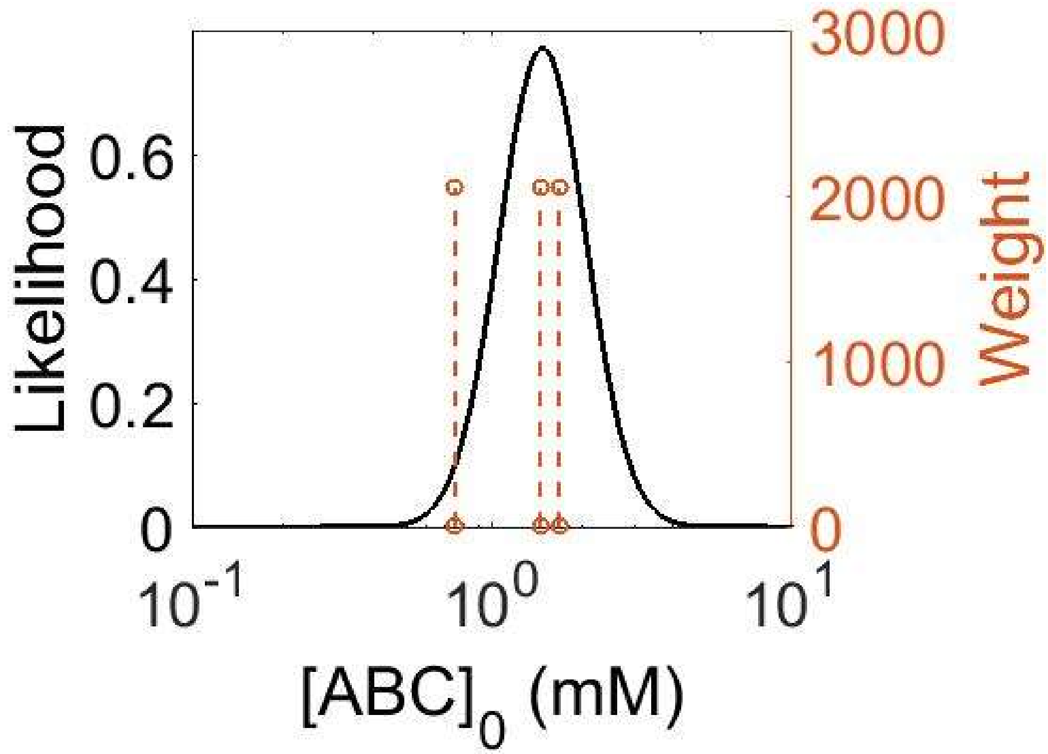


Figure SF.10.6.1.3.1. The estimated probability distribution for the ABC concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.7. Reaction 28: 15-HETE⇌ ex15-HETE

15-HETE is relocated from the intracellular compartment to the extracellular compartment via the ATP-binding cassette (ABC) transporter.

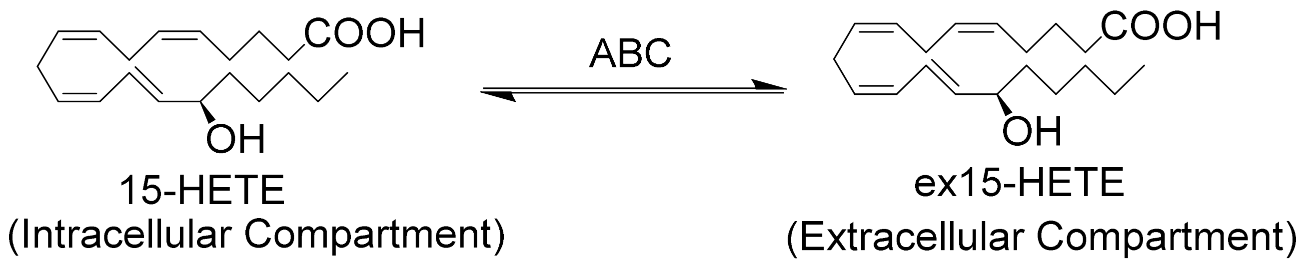


Figure SF.10.7. The transport of 15-hydroxyeicosatetraenoic acid (15-HETE) from the intracellular compartment to the extracellular compartment by ATP Binding Cassette protein (ABC) (Reaction 28).

SEq.10.7. Reaction rate law for Reaction 28.

$$\boldsymbol{v_{28}} = [\boldsymbol{ABC}] \cdot \boldsymbol{k_{cat}} \cdot \frac{\mathbf{15-HETE}/\boldsymbol{K_m} \cdot \left(\mathbf{1} - \frac{\mathbf{ex15-HETE}}{\mathbf{15-HETE} \cdot \boldsymbol{e}^{-0.5\cdot\left(G+R\cdot T\cdot \ln\left(\frac{ATP}{ADP}\right)\right)/_{R\cdot T}}}\right)}{\mathbf{1} + \frac{\mathbf{15-HETE}}{\boldsymbol{K_m}} + \frac{\mathbf{ex15-HETE}}{\boldsymbol{K_m}} + \mathbf{ABC\_CI}}$$

S.10.7.1. Reaction parameters

S.10.7.1.1. Parameter: ABC k_{cat}

Parameter values for the ABC k_{cat} of Reaction 28 were obtained from the literature and summarised in Table ST.10.7.1.1.1. The log-normal distribution properties for the ABC k_{cat} of Reaction 28 are shown in Table ST.10.7.1.1.2 and plotted in Figure SF.10.7.1.1.1.

Table ST.10.7.1.1.1. Literature information used to design the ABC k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
3.50	NaN	Bacteria	E. coli.	Glucose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Waygood and Steeves, 1980)
3.30 $x10^{-1}$	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
8.30 $x10^{-1}$	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
3.28	NaN	Yeast	Saccharomyces cerevisiae	HXT7 transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Ye et al., 2001)
1.13 $x10^{1}$		Primate	Baculovirus	MRP2	7	37		512		(Yasunaga et al., 2008)

Table ST.10.7.1.1.2. The log-normal distribution properties of the ABC k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
1.13 $x10^{1}$	1.00 $x10^{1}$	3.22	8.9110^{-1}

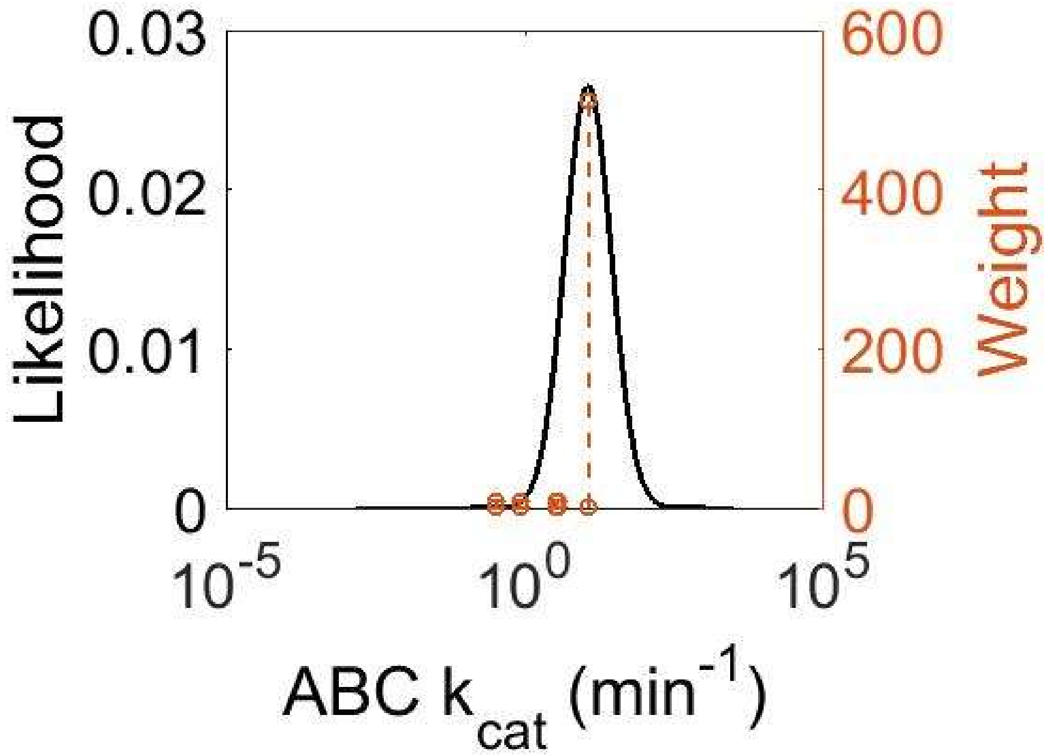


Figure SF.10.7.1.1.1. The estimated probability distribution for ABC k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.7.1.2. Parameter: ABC K_{ms}

Parameter values for the ABC K_{ms} of Reaction 28 were obtained from the literature and summarised in Table ST.10.7.1.2.1. The log-normal distribution properties for the ABC K_{ms} of Reaction 28 are shown in Table ST.10.7.1.2.2 and plotted in Figure SF.10.7.1.2.1.

Table ST.10.7.1.2.1. Literature information used to design the ABC K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.09×10^{-2}	4.10×10^{-3}	Human	Primate	MRP2	7	37		512	0	(Yasunaga et al., 2008)
3.66×10^{-5}	3.80×10^{-6}	Unknown	H69AR plasma membrane	MRP1	7.4	37		128	0	(Mao et al., 2000)
5.30×10^{-3}	2.60×10^{-3}	Human	HEK293 cells	MRP3	7.4	37		128	0	(Zeng et al., 2000)
1.95×10^{-1}	6.12×10^{-2}	Human	Primate	MRP2	7	37		512	0	(Yasunaga et al., 2008)
1.10×10^{-1}	3.91×10^{-2}	Human	Primate	MRP2	7	37		512	0	(Yasunaga et al., 2008)
2.07×10^{-2}	NaN	Human	HepG2 hepatoma	ABCB1	7.4	37		2048	0	(Fong et al., 2007)

Table ST.10.7.1.2.2. The log-normal distribution properties of the ABC K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
2.10 $x10^{-2}$	2.37 $x10^{1}$	-2.60	1.12

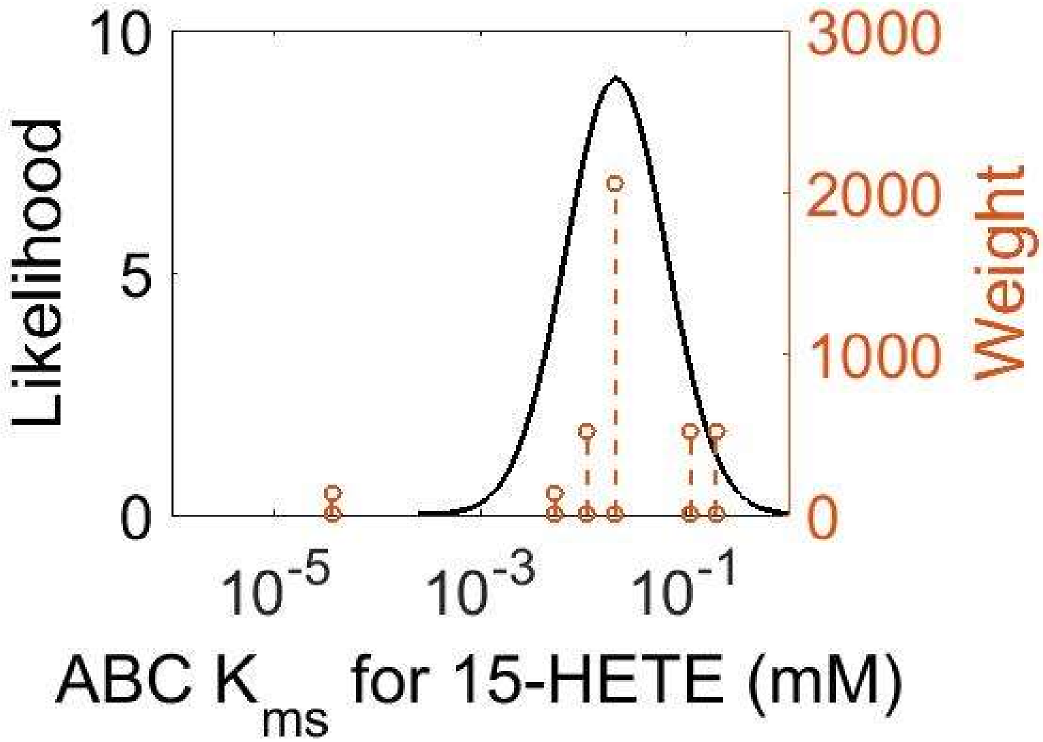


Figure SF.10.7.1.2.1. The estimated probability distribution for ABC K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.7.1.3. Parameter: ABC concentration

Parameter values for the ABC concentration of Reaction 28 were obtained from the literature and summarised in Table ST.10.7.1.3.1. The log-normal distribution properties for the ABC concentration of Reaction 28 are shown in Table ST.10.7.1.3.2 and plotted in Figure SF.10.7.1.3.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.10.7.1.3.1. Literature information used to design the ABC concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
5.15	NaN	Human	Stomach	ABC	7.5	37		2048	0	(Wilhelm et al., 2014)
5.94	NaN	Human	Lung	ABC	7.5	37		2048	0	(Kim et al., 2014)
2.66	NaN	Human	Gut	ABC	7.5	37		2048	0	(Kim et al., 2014)

Table ST.10.7.1.3.2. The log-normal distribution properties of the ABC concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
5.06	2.80×10^{-5}	1.44	1.74	3.42×10^{-1}

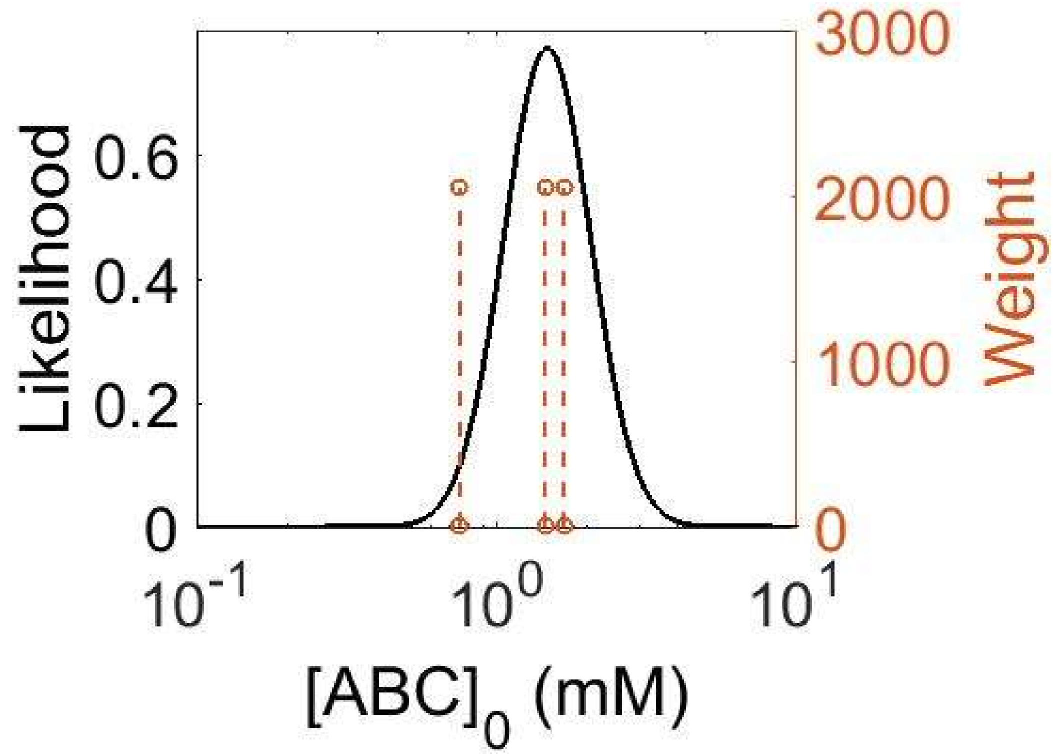


Figure SF.10.7.1.3.1. The estimated probability distribution for the ABC concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.8. Reaction 29: $LTB_4 \rightleftharpoons exLTB_4$

LTB_4 is relocated from the intracellular compartment to the extracellular compartment via the ATP-binding cassette (ABC) transporter.

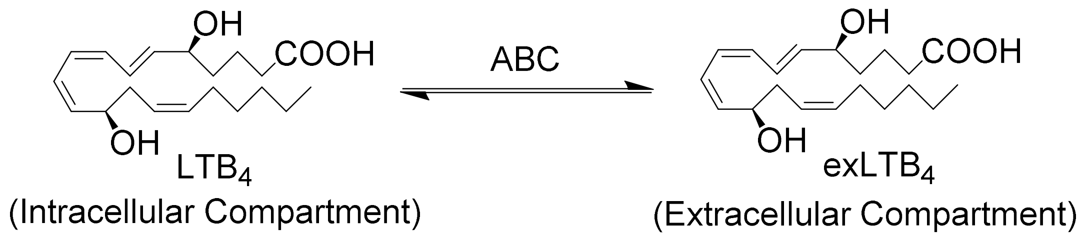


Figure SF.10.8. The transport of leukotriene B_4 (LTB_4) from the intracellular compartment to the extracellular compartment by ATP Binding Cassette protein (ABC) (Reaction 29).

SEq.10.8. Reaction rate law for Reaction 29.

$$v_{29} = [ABC] \cdot k_{cat} \cdot \frac{\mathrm{LTB_4}/K_m \cdot \left(1 - \frac{\mathrm{exLTB_4}}{\mathrm{LTB_4} \cdot e^{-0.5 \cdot \left(G + R \cdot T \cdot \ln\left(\frac{ATP}{ADP}\right)\right)/R \cdot T}}\right)}{1 + \frac{\mathrm{LTB_4}}{K_m} + \frac{\mathrm{exLTB_4}}{K_m} + \mathrm{ABC\_CI}}$$

S.10.8.1. Reaction parameters

S.10.8.1.1. Parameter: ABC k_{cat}

Parameter values for the ABC k_{cat} of Reaction 29 were obtained from the literature and summarised in Table ST.10.8.1.1.1. The log-normal distribution properties for the ABC k_{cat} of Reaction 29 are shown in Table ST.10.8.1.1.2 and plotted in Figure SF.10.8.1.1.1.

Table ST.10.8.1.1.1. Literature information used to design the ABC k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
3.50	NaN	Bacteria	E. coli.	Glucose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Waygood and Steeves, 1980)
3.30 x10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
8.30 x10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
3.28	NaN	Yeast	Saccharomyces cerevisiae	HXT7 transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Ye et al., 2001)
1.13 x10^{1}		Primate	Baculovirus	MRP2	7	37		512		(Yasunaga et al., 2008)

Table ST.10.8.1.1.2. The log-normal distribution properties of the ABC k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.13 $x10^{1}$	1.00 $x10^{1}$	3.22	8.91 $x10^{-1}$

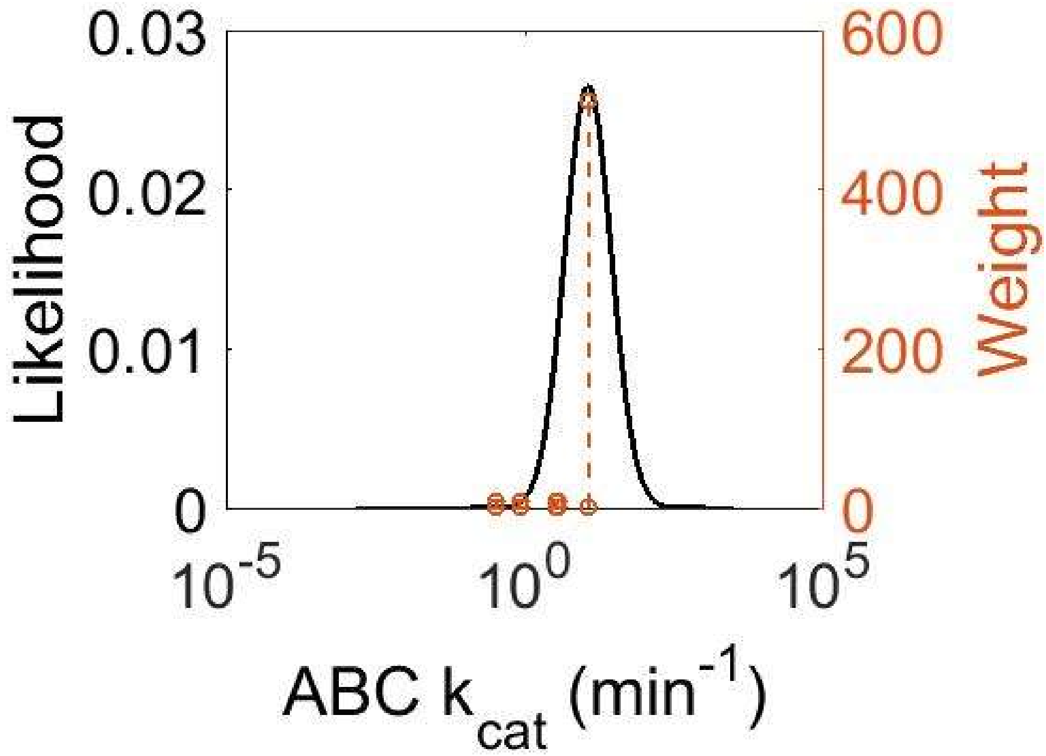


Figure SF.10.8.1.1.1. The estimated probability distribution for ABC k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.8.1.2. Parameter: ABC K_{ms}

Parameter values for the ABC K_{ms} of Reaction 29 were obtained from the literature and summarised in Table ST.10.8.1.2.1. The log-normal distribution properties for the ABC K_{ms} of Reaction 29 are shown in Table ST.10.8.1.2.2 and plotted in Figure SF.10.8.1.2.1.

Table ST.10.8.1.2.1. Literature information used to design the ABC K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.09×10^{-2}	4.10×10^{-3}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
3.66×10^{-5}	3.80×10^{-6}	Unknown	H69AR plasma membrane	MRP1	7.4	37		**128**	0	(Mao et al., 2000)
5.30×10^{-3}	2.60×10^{-3}	Human	HEK293 cells	MRP3	7.4	37		**128**	0	(Zeng et al., 2000)
1.95×10^{-1}	6.12×10^{-2}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
1.10×10^{-1}	3.91×10^{-2}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
2.07×10^{-2}	NaN	Human	HepG2 hepatoma	ABCB1	7.4	37		**2048**	0	(Fong et al., 2007)

Table ST.10.8.1.2.2. The log-normal distribution properties of the ABC K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
2.10×10^{-2}	2.37×10^{1}	-2.60	1.12

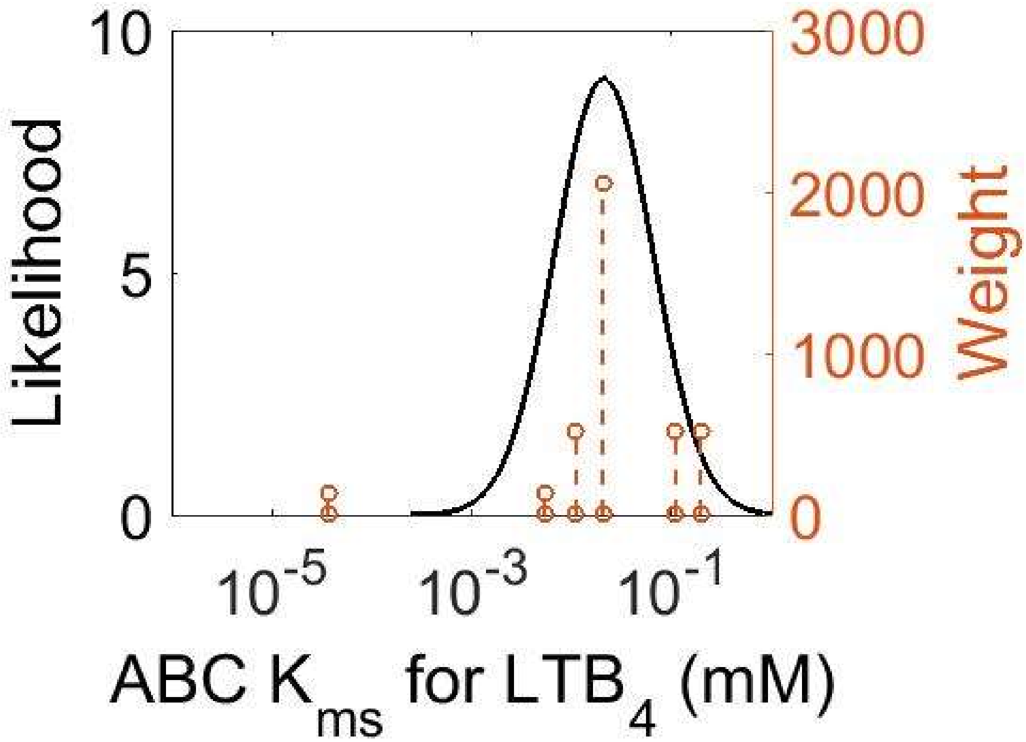


Figure SF.10.8.1.2.1. The estimated probability distribution for ABC K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.8.1.3. Parameter: ABC concentration

Parameter values for the ABC concentration of Reaction 29 were obtained from the literature and summarised in Table ST.10.8.1.3.1. The log-normal distribution properties for the ABC concentration of Reaction 29 are shown in Table ST.10.8.1.3.2 and plotted in Figure SF.10.8.1.3.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.10.8.1.3.1. Literature information used to design the ABC concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
5.15	NaN	Human	Stomach	ABC	7.5	37		2048	0	(Wilhelm et al., 2014)
5.94	NaN	Human	Lung	ABC	7.5	37		2048	0	(Kim et al., 2014)
2.66	NaN	Human	Gut	ABC	7.5	37		2048	0	(Kim et al., 2014)

Table ST.10.8.1.3.2. The log-normal distribution properties of the ABC concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
5.06	2.80×10^{-5}	1.44	1.74	3.4210-1

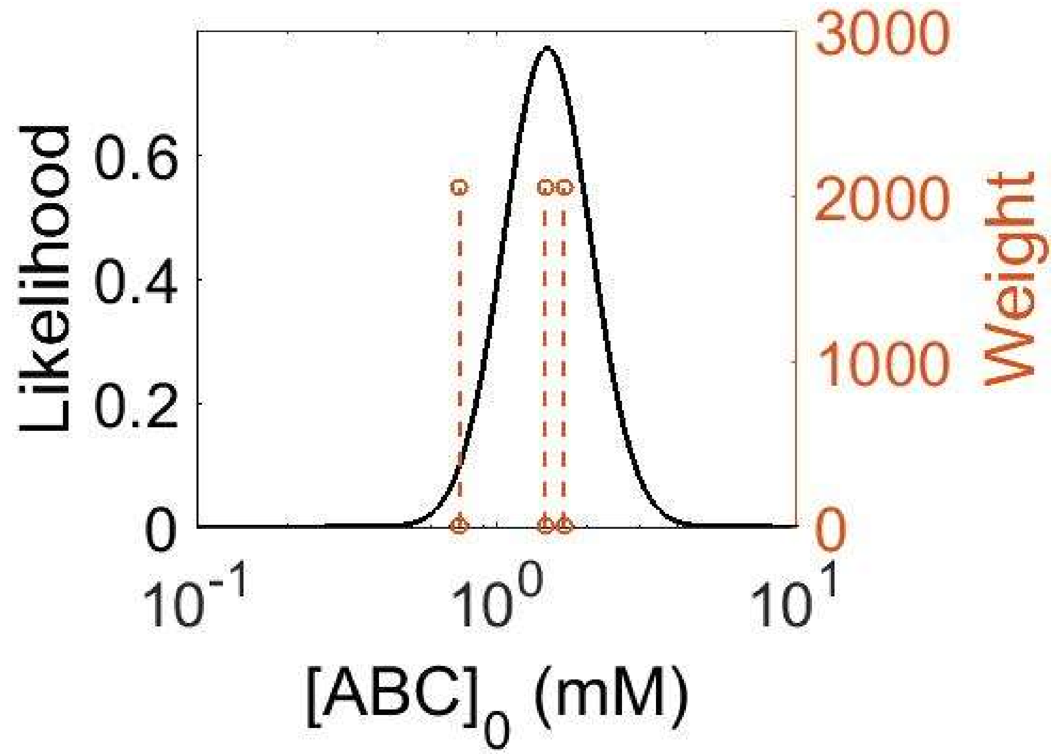


Figure SF.10.8.1.3.1. The estimated probability distribution for the ABC concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.9. Reaction 30: $LTC_4 \rightleftharpoons exLTC_4$

LTC_4 is relocated from the intracellular compartment to the extracellular compartment via the ATP-binding cassette (ABC) transporter.

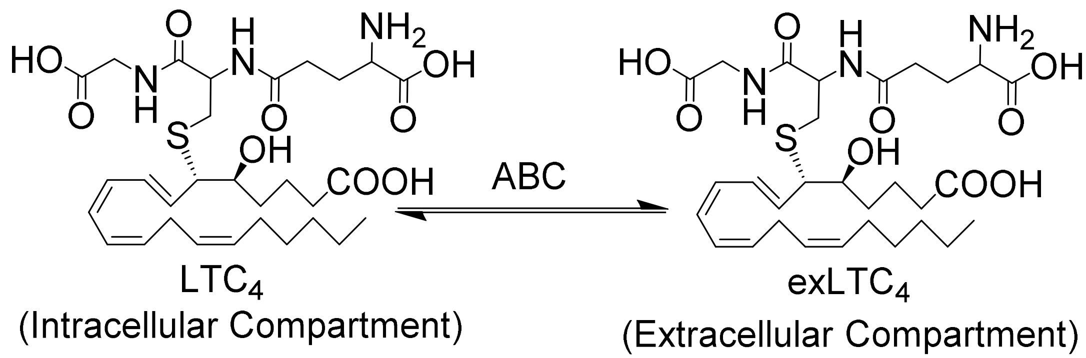


Figure SF.10.9. The transport of leukotriene C_4 (LTC_4) from the intracellular compartment to the extracellular compartment by ATP Binding Cassette protein (ABC) (Reaction 30).

SEq.10.9. Reaction rate law Reaction 30.

$$\boldsymbol{v_{30}} = [\boldsymbol{ABC}] \cdot \boldsymbol{k_{cat}} \cdot \frac{{}^{\mathbf{LTC_4}}/_{\boldsymbol{K_m}} \cdot \left(\mathbf{1} - \frac{\mathbf{exLTC_4}}{\mathbf{LTC_4} \cdot \boldsymbol{e}^{-0.5 \cdot \left(\boldsymbol{G} + \boldsymbol{R} \cdot \boldsymbol{T} \cdot \ln\left(\frac{\boldsymbol{ATP}}{\boldsymbol{ADP}} \right) \right) / \boldsymbol{R \cdot T}}} \right)}{\mathbf{1} + \frac{\mathbf{LTC_4}}{\boldsymbol{K_m}} + \frac{\mathbf{exLTC_4}}{\boldsymbol{K_m}} + \mathbf{ABC\_CI}}$$

S.10.9.1. Reaction parameters

S.10.9.1.1. Parameter: ABC k_{cat}

Parameter values for the ABC k_{cat} of Reaction 30 were obtained from the literature and summarised in Table ST.10.9.1.1.1. The log-normal distribution properties for the ABC k_{cat} of Reaction 30 are shown in Table ST.10.9.1.1.2 and plotted in Figure SF.10.9.1.1.1.

Table ST.10.9.1.1.1. Literature information used to design the ABC k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min-1)	Error (min-1)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
3.50	NaN	Bacteria	E. coli.	Glucose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Waygood and Steeves, 1980)
3.30 x10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
8.30 x10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
3.28	NaN	Yeast	Saccharomyces cerevisiae	HXT7 transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Ye et al., 2001)
1.13 x10^{1}		Primate	Baculovirus	MRP2	7	37		512		(Yasunaga et al., 2008)

Table ST.10.9.1.1.2. The log-normal distribution properties of the ABC k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.13 x10^{1}	1.00 x10^{1}	3.22	8.91$10^{-1}$

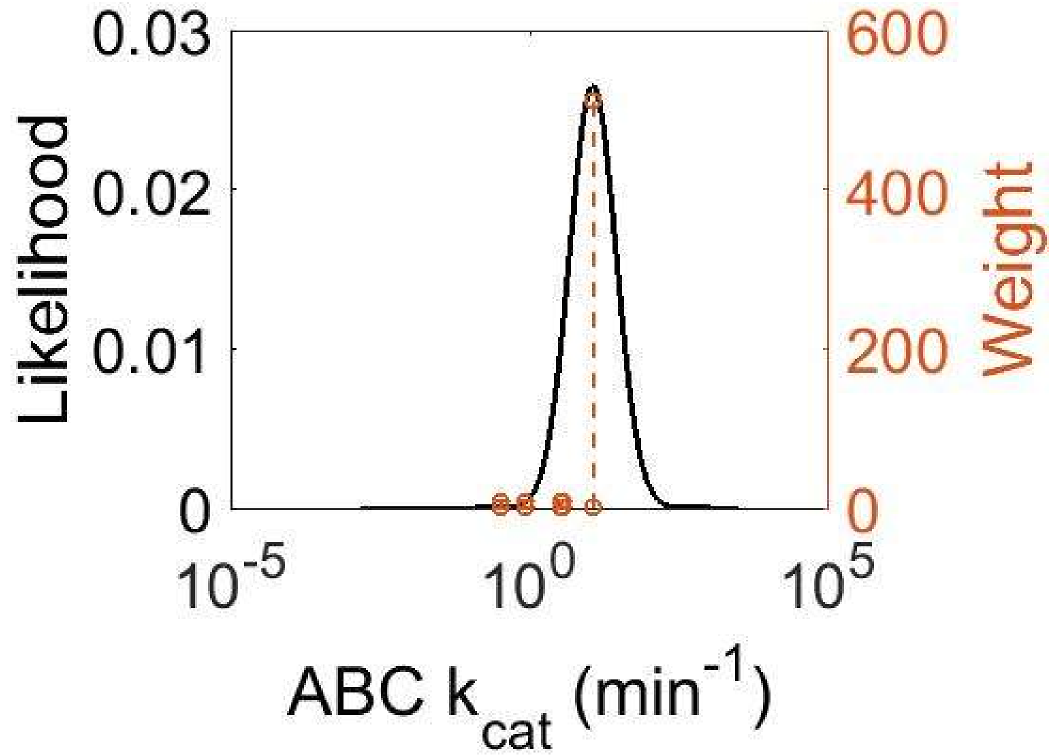


Figure SF.10.9.1.1.1. The estimated probability distribution for ABC k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.9.1.2. Parameter: ABC K_{ms}

Parameter values for the ABC K_{ms} of Reaction 30 were obtained from the literature and summarised in Table ST.10.9.1.2.1. The log-normal distribution properties for the ABC K_{ms} of Reaction 30 are shown in Table ST.10.9.1.2.2 and plotted in Figure SF.10.9.1.2.1.

Table ST.10.9.1.2.1. Literature information used to design the ABC K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.09×10^{-2}	4.10×10^{-3}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
3.66×10^{-5}	3.80×10^{-6}	Unknown	H69AR plasma membrane	MRP1	7.4	37		**128**	0	(Mao et al., 2000)
5.30×10^{-3}	2.60×10^{-3}	Human	HEK293 cells	MRP3	7.4	37		**128**	0	(Zeng et al., 2000)
1.95×10^{-1}	6.12×10^{-2}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
1.10×10^{-1}	3.91×10^{-2}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
2.07×10^{-2}	NaN	Human	HepG2 hepatoma	ABCB1	7.4	37		**2048**	0	(Fong et al., 2007)

Table ST.10.9.1.2.2. The log-normal distribution properties of the ABC K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
2.10×10^{-2}	2.37×10^{1}	-2.60	1.12

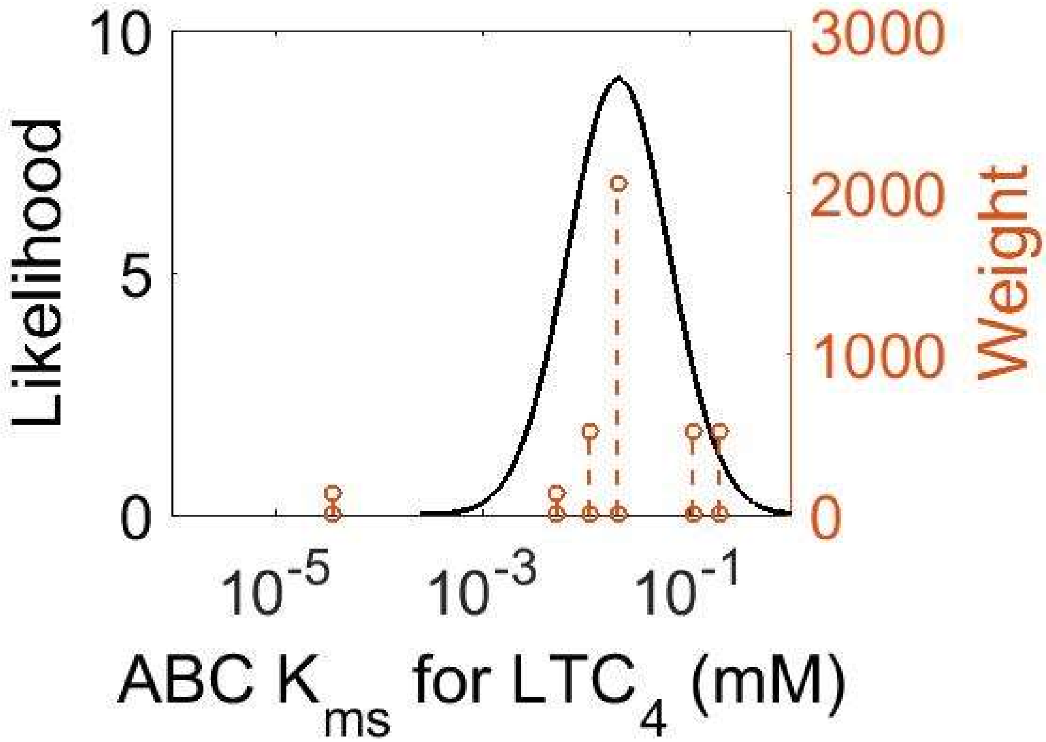


Figure SF.10.9.1.2.1. The estimated probability distribution for ABC K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.9.1.3. Parameter: ABC concentration

Parameter values for the ABC concentration of Reaction 30 were obtained from the literature and summarised in Table ST.10.9.1.3.1. The log-normal distribution properties for the ABC concentration of Reaction 30 are shown in Table ST.10.9.1.3.2 and plotted in Figure SF.10.9.1.3.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.10.9.1.3.1. Literature information used to design the ABC concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
5.15	NaN	Human	Stomach	ABC	7.5	37		2048	0	(Wilhelm et al., 2014)
5.94	NaN	Human	Lung	ABC	7.5	37		2048	0	(Kim et al., 2014)
2.66	NaN	Human	Gut	ABC	7.5	37		2048	0	(Kim et al., 2014)

Table ST.10.9.1.3.2. The log-normal distribution properties of the ABC concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
5.06	2.80×10^{-5}	1.44	1.74	3.4210^{-1}

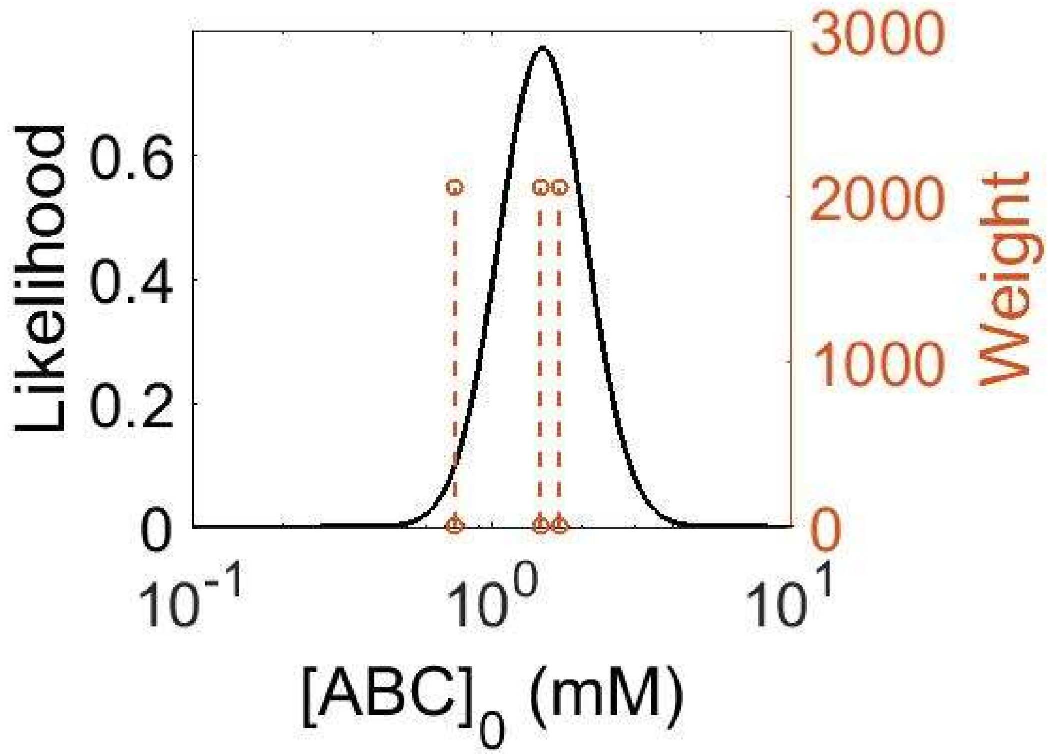


Figure SF.10.9.1.3.1. The estimated probability distribution for the ABC concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.10. Reaction 31: 12-HETE ⇌ ex12-HETE

12-HETE is relocated from the intracellular compartment to the extracellular compartment via the ATP-binding cassette (ABC) transporter.

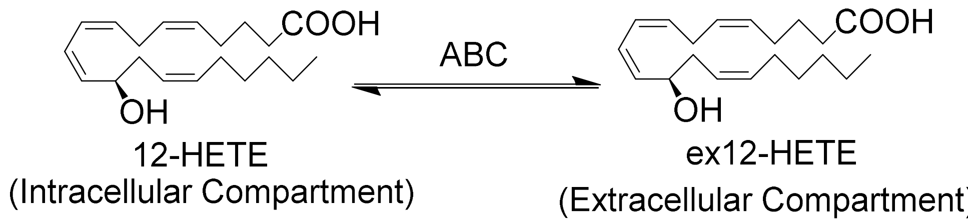


Figure SF.10.10. The transport of 12-hydroxyeicosatetraenoic acid (12-HETE) from the intracellular compartment to the extracellular compartment by ATP Binding Cassette protein (ABC) (Reaction 31).

SEq.10.10. Reaction rate law for Reaction 31.

$$\boldsymbol{v_{31}} = [\boldsymbol{ABC}] \cdot \boldsymbol{k_{cat}} \cdot \frac{\mathbf{12-HETE}/\boldsymbol{K_m} \cdot \left(\mathbf{1} - \dfrac{\mathbf{ex12-HETE}}{\mathbf{12-HETE} \cdot \boldsymbol{e}^{-0.5\cdot\left(\boldsymbol{G}+\boldsymbol{R}\cdot\boldsymbol{T}\cdot\ln\left(\frac{\boldsymbol{ATP}}{\boldsymbol{ADP}}\right)\right)/\boldsymbol{R}\cdot\boldsymbol{T}}}\right)}{\mathbf{1} + \dfrac{\mathbf{12-HETE}}{\boldsymbol{K_m}} + \dfrac{\mathbf{ex12-HETE}}{\boldsymbol{K_m}} + \mathbf{ABC\_CI}}$$

S.10.10.1. Reaction parameters

S.10.10.1.1. Parameter: ABC k_{cat}

Parameter values for the ABC k_{cat} of Reaction 31 were obtained from the literature and summarised in Table ST.10.10.1.1.1. The log-normal distribution properties for the ABC k_{cat} of Reaction 31 are shown in Table ST.10.10.1.1.2 and plotted in Figure SF.10.10.1.1.1.

Table ST.10.10.1.1.1. Literature information used to design the ABC k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	**Error (min^{-1})**	**Experimental details**						**Weight**	**Type of error**	**Reference**
		Species	**Expression Vector**	**Enzyme**	**pH**	**Temperature (°C)**	**Other**			
3.50	NaN	Bacteria	E. coli.	Glucose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Waygood and Steeves, 1980)
3.30×10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
8.30×10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
3.28	NaN	Yeast	Saccharomyces cerevisiae	HXT7 transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Ye et al., 2001)
1.13×10^{1}		Primate	Baculovirus	MRP2	7	37		512		(Yasunaga et al., 2008)

Table ST.10.10.1.1.2. The log-normal distribution properties of the ABC k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.13 $x10^{1}$	1.00 $x10^{1}$	3.22	8.9110^{-1}

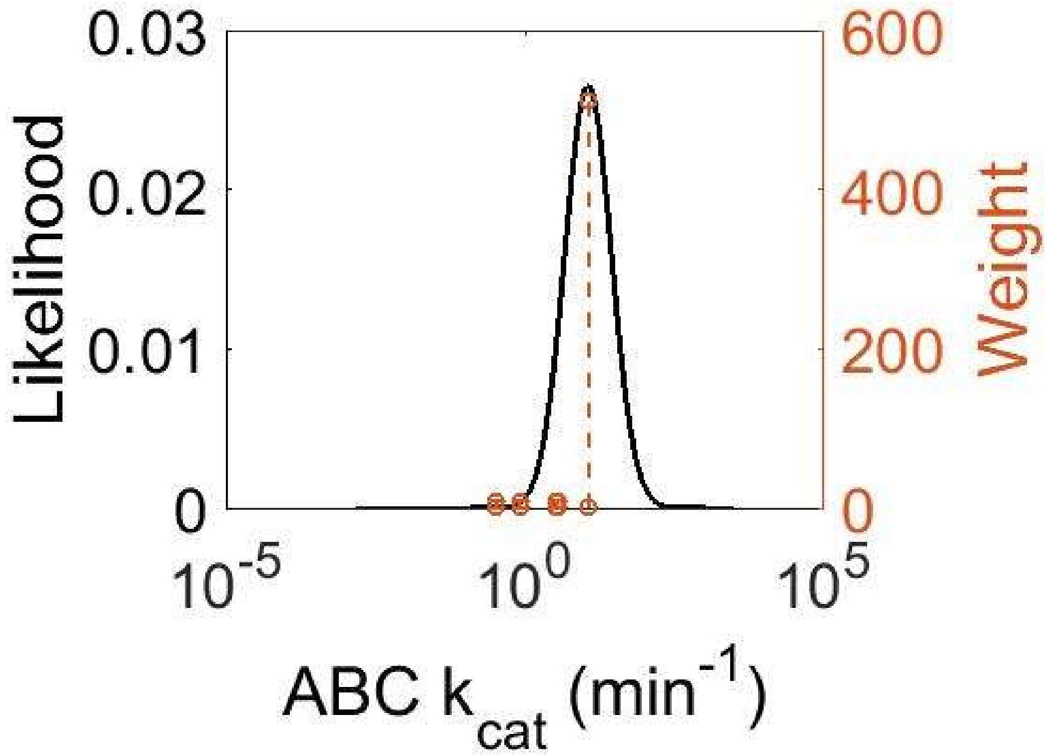


Figure SF.10.10.1.1.1. The estimated probability distribution for ABC k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.10.1.2. Parameter: ABC K_{ms}

Parameter values for the ABC K_{ms} of Reaction 31 were obtained from the literature and summarised in Table ST.10.10.1.2.1. The log-normal distribution properties for the ABC K_{ms} of Reaction 31 are shown in Table ST.10.10.1.2.2 and plotted in Figure SF.10.10.1.2.1.

Table ST.10.10.1.2.1. Literature information used to design the ABC K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.09×10^{-2}	4.10×10^{-3}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
3.66×10^{-5}	3.80×10^{-6}	Unknown	H69AR plasma membrane	MRP1	7.4	37		**128**	0	(Mao et al., 2000)
5.30×10^{-3}	2.60×10^{-3}	Human	HEK293 cells	MRP3	7.4	37		**128**	0	(Zeng et al., 2000)
1.95×10^{-1}	6.12×10^{-2}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
1.10×10^{-1}	3.91×10^{-2}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
2.07×10^{-2}	NaN	Human	HepG2 hepatoma	ABCB1	7.4	37		**2048**	0	(Fong et al., 2007)

Table ST.10.10.1.2.2. The log-normal distribution properties of the ABC K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
2.10×10^{-2}	2.37×10^{1}	-2.60	1.12

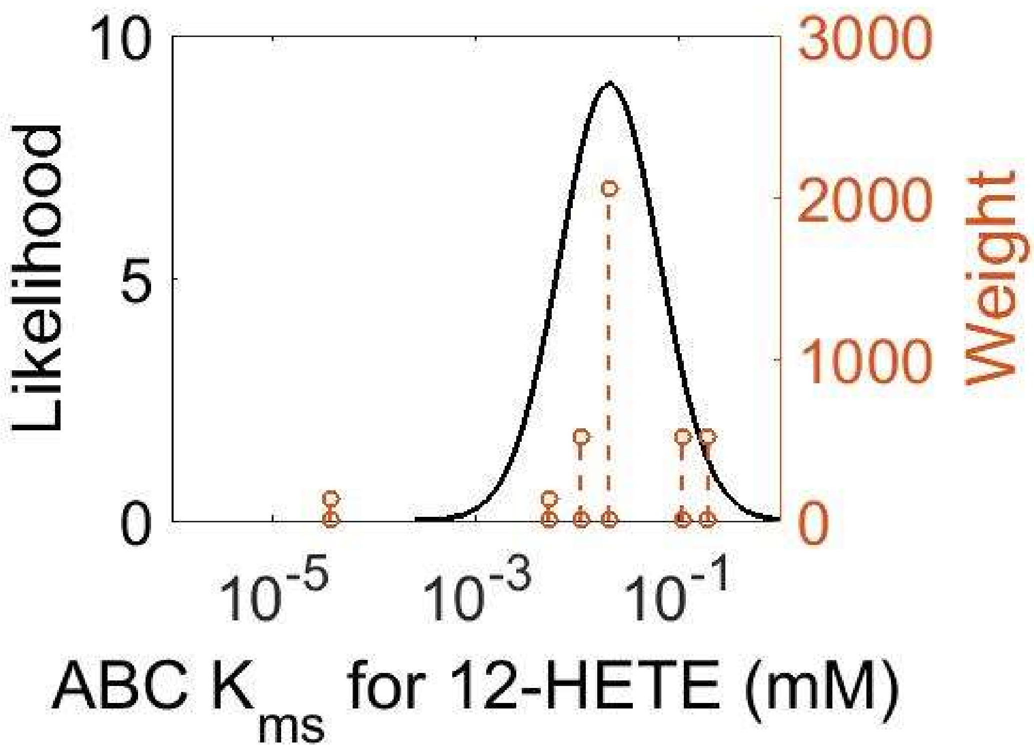


Figure SF.10.10.1.2.1. The estimated probability distribution for ABC K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.10.1.3. Parameter: ABC concentration

Parameter values for the ABC concentration of Reaction 31 were obtained from the literature and summarised in Table ST.10.10.1.3.1. The log-normal distribution properties for the ABC concentration of Reaction 31 are shown in Table ST.10.10.1.3.2 and plotted in Figure SF.10.10.1.3.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.10.10.1.3.1. Literature information used to design the ABC concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
5.15	NaN	Human	Stomach	ABC	7.5	37		2048	0	(Wilhelm et al., 2014)
5.94	NaN	Human	Lung	ABC	7.5	37		2048	0	(Kim et al., 2014)
2.66	NaN	Human	Gut	ABC	7.5	37		2048	0	(Kim et al., 2014)

Table ST.10.10.1.3.2. The log-normal distribution properties of the ABC concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
5.06	2.80×10^{-5}	1.44	1.74	3.4210^{-1}

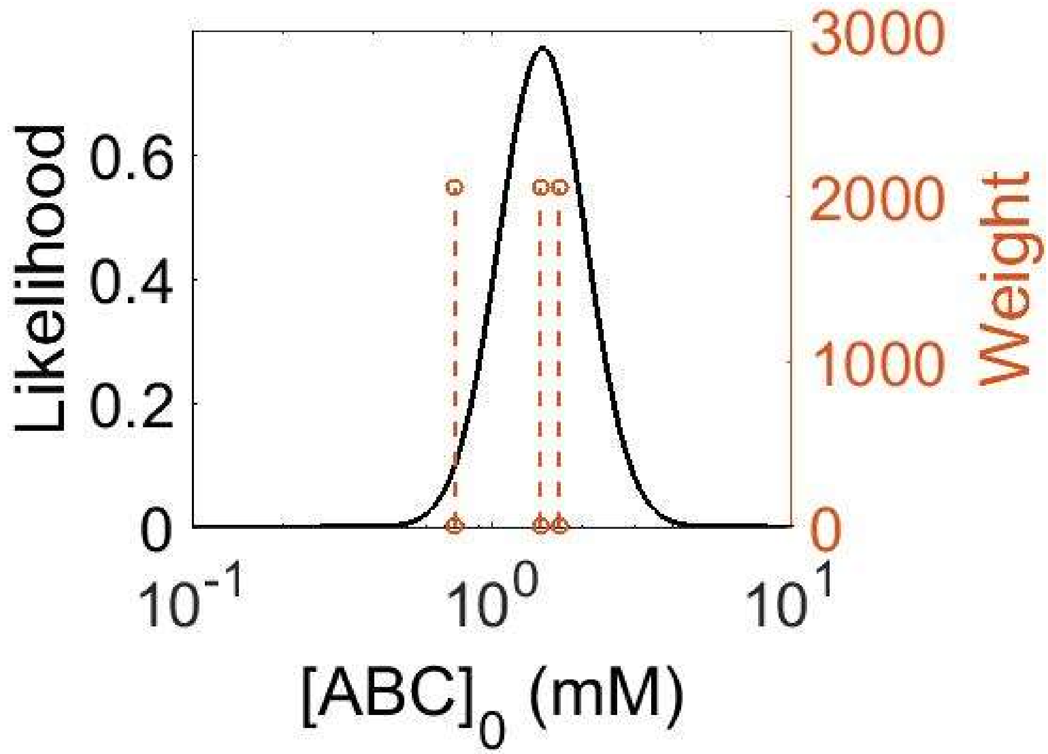


Figure SF.10.10.1.3.1. The estimated probability distribution for the ABC concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.11. Reaction 32: $TXA_2 \rightleftharpoons exTXA_2$

TXA_2 is relocated from the intracellular compartment to the extracellular compartment via the ATP-binding cassette (ABC) transporter.

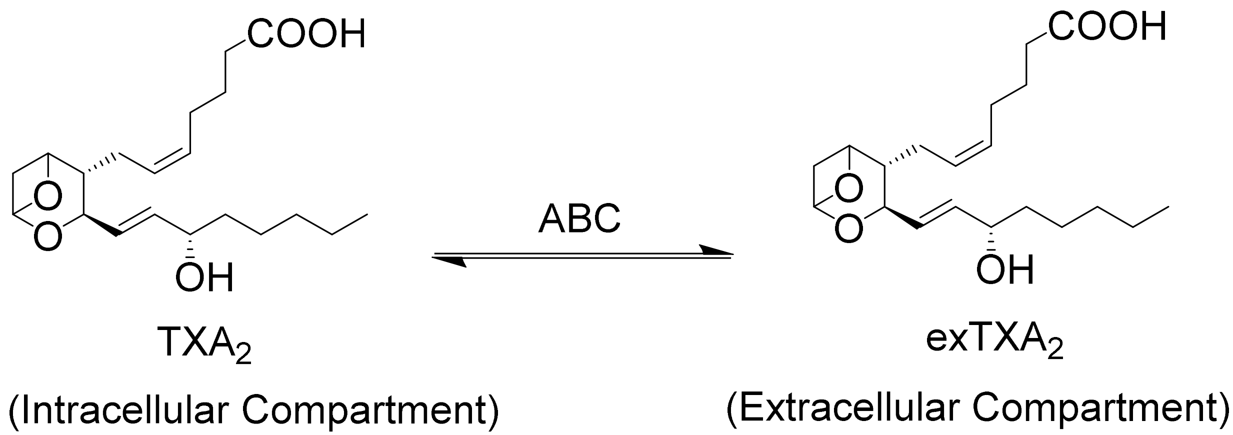


Figure SF.10.11. The transport of thromboxane A_2 (TXA_2) from the intracellular compartment to the extracellular compartment by ATP Binding Cassette protein (ABC) (Reaction 32).

SEq.10.11. Reaction rate law for Reaction 32.

$$\boldsymbol{v_{32}} = [\boldsymbol{ABC}] \cdot \boldsymbol{k_{cat}} \cdot \frac{\mathbf{TXA_2}/\boldsymbol{K_m} \cdot \left(1 - \dfrac{\mathbf{exTXA_2}}{\mathbf{TXA_2} \cdot e^{-0.5 \cdot \left(G + R \cdot T \cdot \ln\left(\frac{ATP}{ADP}\right)\right)/R \cdot T}}\right)}{1 + \dfrac{\mathbf{TXA_2}}{\boldsymbol{K_m}} + \dfrac{\mathbf{exTXA_2}}{\boldsymbol{K_m}} + \mathbf{ABC\_CI}}$$

S.10.11.1. Reaction parameters

S.10.11.1.1 Parameter: ABC k_{cat}

Parameter values for the ABC k_{cat} of Reaction 32 were obtained from the literature and summarised in Table ST.10.11.1.1.1. The log-normal distribution properties for the ABC k_{cat} of Reaction 32 are shown in Table ST.10.11.1.1.2 and plotted in Figure SF.10.11.1.1.1.

Table ST.10.11.1.1.1. Literature information used to design the ABC k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
3.50	NaN	Bacteria	E. coli.	Glucose transporter	Unknown	Unknown	Bionumbers calculation	8	0	(Waygood and Steeves, 1980)
3.30 $x10^{-1}$	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	8	0	(Naftalin et al., 2007)
8.30 $x10^{-1}$	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	8	0	(Naftalin et al., 2007)
3.28	NaN	Yeast	Saccharomyces cerevisiae	HXT7 transporter	Unknown	Unknown	Bionumbers calculation	8	0	(Ye et al., 2001)
1.13 $x10^{1}$		Primate	Baculovirus	MRP2	7	37		512		(Yasunaga et al., 2008)

Table ST.10.11.1.1.2. The log-normal distribution properties of the ABC k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
1.13 $x10^{1}$	1.00 $x10^{1}$	3.22	8.9110^{-1}

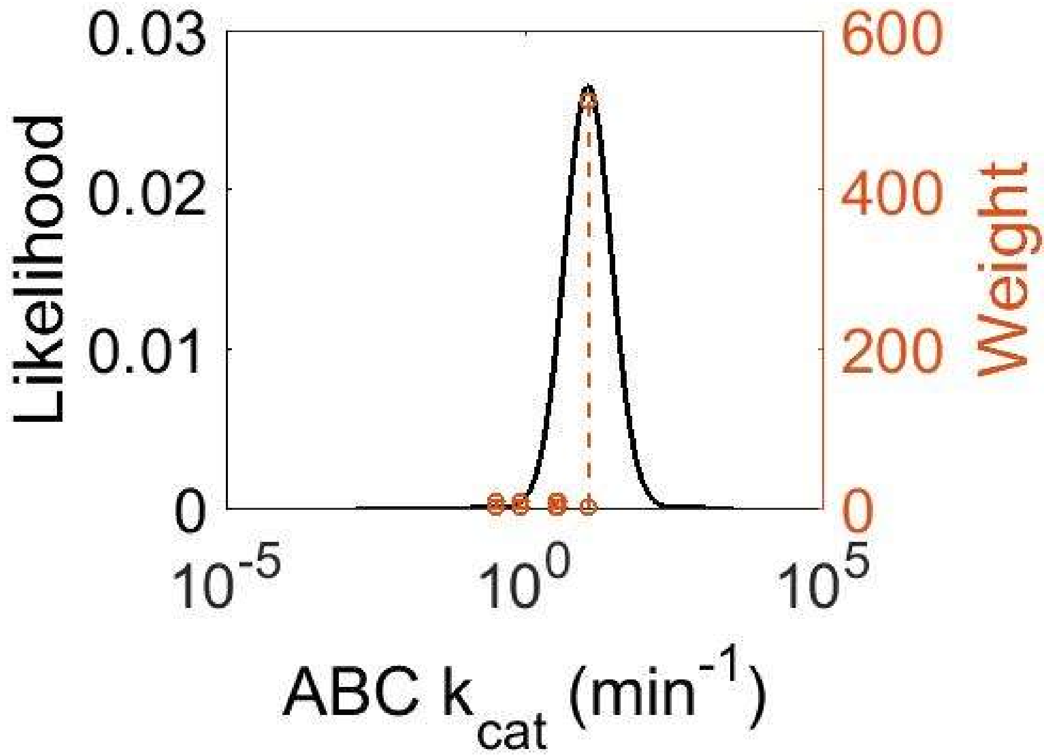


Figure SF.10.11.1.1.1. The estimated probability distribution for ABC k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.11.1.2. Parameter: ABC K_{ms}

Parameter values for the ABC K_{ms} of Reaction 32 were obtained from the literature and summarised in Table ST.10.11.1.2.1. The log-normal distribution properties for the ABC K_{ms} of Reaction 32 are shown in Table ST.10.11.1.2.2 and plotted in Figure SF.10.11.1.2.1.

Table ST.10.11.1.2.1. Literature information used to design the ABC K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.09×10^{-2}	4.10×10^{-3}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
3.66×10^{-5}	3.80×10^{-6}	Unknown	H69AR plasma membrane	MRP1	7.4	37		**128**	0	(Mao et al., 2000)
5.30×10^{-3}	2.60×10^{-3}	Human	HEK293 cells	MRP3	7.4	37		**128**	0	(Zeng et al., 2000)
1.95×10^{-1}	6.12×10^{-2}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
1.10×10^{-1}	3.91×10^{-2}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
2.07×10^{-2}	NaN	Human	HepG2 hepatoma	ABCB1	7.4	37		**2048**	0	(Fong et al., 2007)

Table ST.10.11.1.2.2. The log-normal distribution properties of the ABC K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
2.10×10^{-2}	2.37×10^{1}	-2.60	1.12

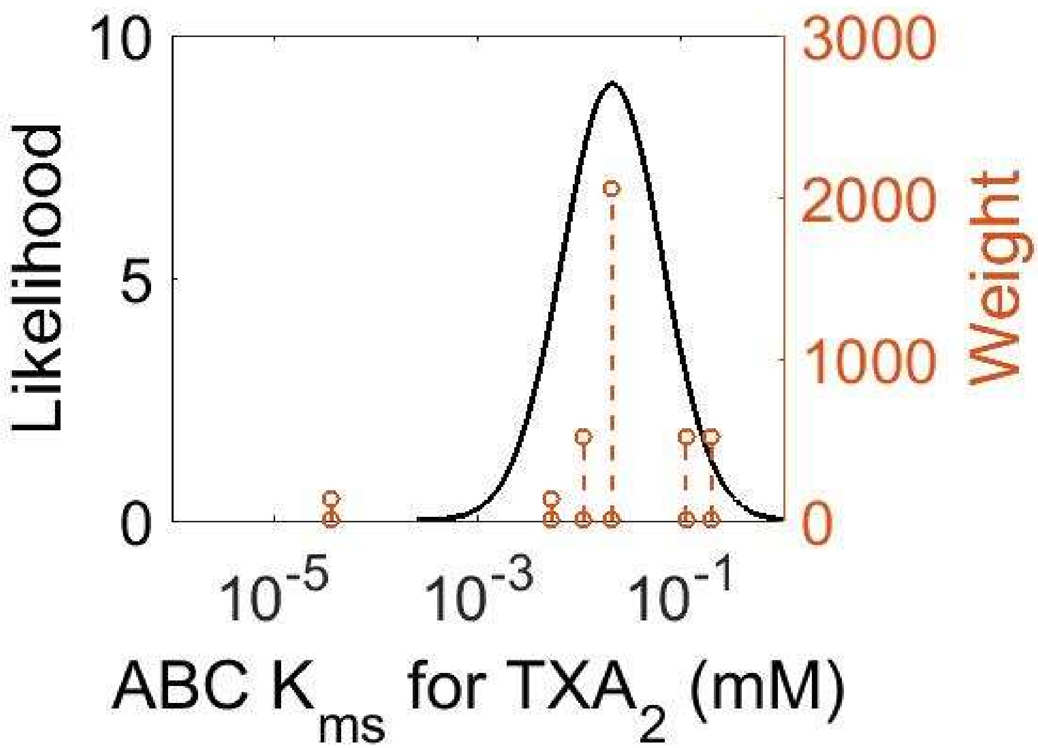


Figure SF.10.11.1.2.1. The estimated probability distribution for ABC K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.11.1.3. Parameter: ABC concentration

Parameter values for the ABC concentration of Reaction 32 were obtained from the literature and summarised in Table ST.10.11.1.3.1. The log-normal distribution properties for the ABC concentration of Reaction 32 are shown in Table ST.10.11.1.3.2 and plotted in Figure SF.10.11.1.3.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.10.11.1.3.1. Literature information used to design the ABC concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
5.15	NaN	Human	Stomach	ABC	7.5	37		2048	0	(Wilhelm et al., 2014)
5.94	NaN	Human	Lung	ABC	7.5	37		2048	0	(Kim et al., 2014)
2.66	NaN	Human	Gut	ABC	7.5	37		2048	0	(Kim et al., 2014)

Table ST.10.11.1.3.2. The log-normal distribution properties of the ABC concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
5.06	2.80×10^{-5}	1.44	1.74	3.42×10^{-1}

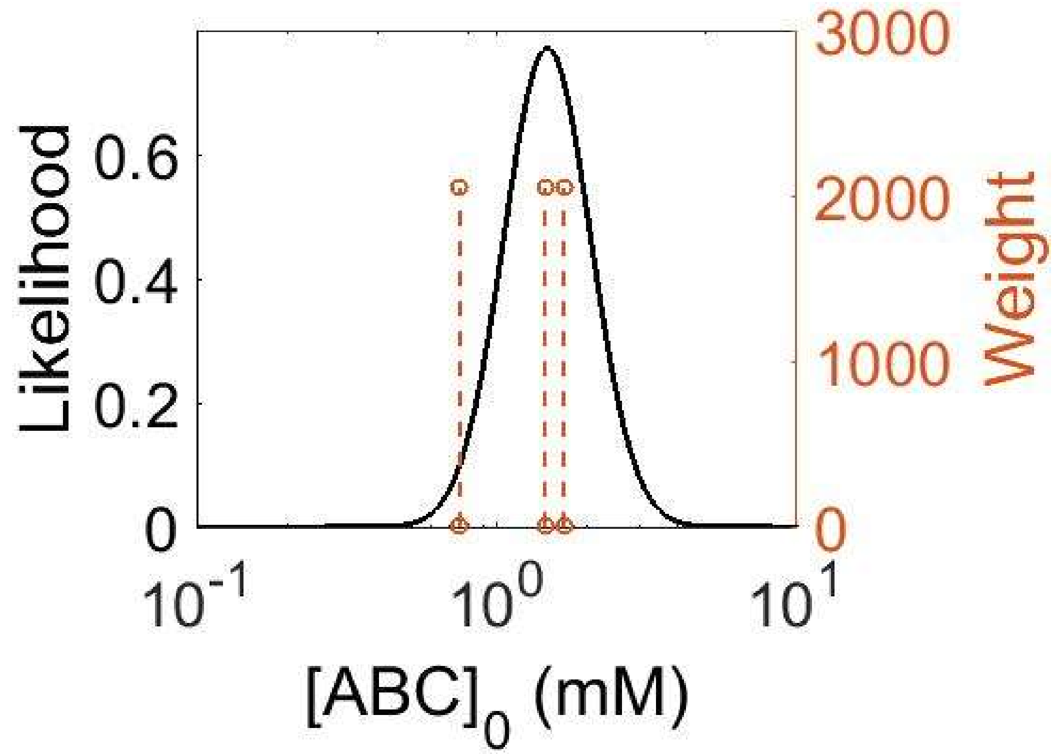


Figure SF.10.11.1.3.1. The estimated probability distribution for the ABC concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.12. Reaction 33: $PGI_2 \rightleftharpoons exPGI_2$

PGI_2 is relocated from the intracellular compartment to the extracellular compartment via the ATP-binding cassette (ABC) transporter.

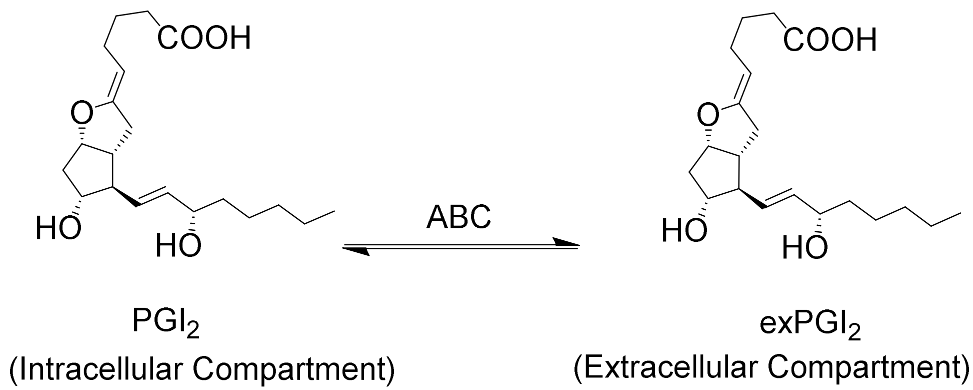


Figure SF.10.12. The transport of prostaglandin I_2 (PGI_2) from the intracellular compartment to the extracellular compartment by ATP Binding Cassette protein (ABC) (Reaction 33).

SEq.10.12. Reaction rate law for Reaction 33.

$$v_{33} = [ABC] \cdot k_{cat} \cdot \frac{\mathrm{PGI_2}/K_m \cdot \left(1 - \frac{\mathrm{exPGI_2}}{\mathrm{PGI_2} \cdot e^{-0.5 \cdot \left(G + R \cdot T \cdot \ln\left(\frac{ATP}{ADP}\right)\right)/R \cdot T}}\right)}{1 + \frac{\mathrm{PGI_2}}{K_m} + \frac{\mathrm{exPGI_2}}{K_m} + \mathrm{ABC\_CI}}$$

S.10.12.1. Reaction parameters

S.10.12.1.1. Parameter: ABC k_{cat}

Parameter values for the ABC k_{cat} of Reaction 33 were obtained from the literature and summarised in Table ST.10.12.1.1.1. The log-normal distribution properties for the ABC k_{cat} of Reaction 33 are shown in Table ST.10.12.1.1.2 and plotted in Figure SF.10.12.1.1.1.

Table ST.10.12.1.1.1. Literature information used to design the ABC k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
3.50	NaN	Bacteria	E. coli.	Glucose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Waygood and Steeves, 1980)
3.30 x10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
8.30 x10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
3.28	NaN	Yeast	Saccharomyces cerevisiae	HXT7 transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Ye et al., 2001)
1.13 x10^{1}		Primate	Baculovirus	MRP2	7	37		512		(Yasunaga et al., 2008)

Table ST.10.12.1.1.2. The log-normal distribution properties of the ABC k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.13 x10^{1}	1.00 x10^{1}	3.22	8.91$10^{-1}$

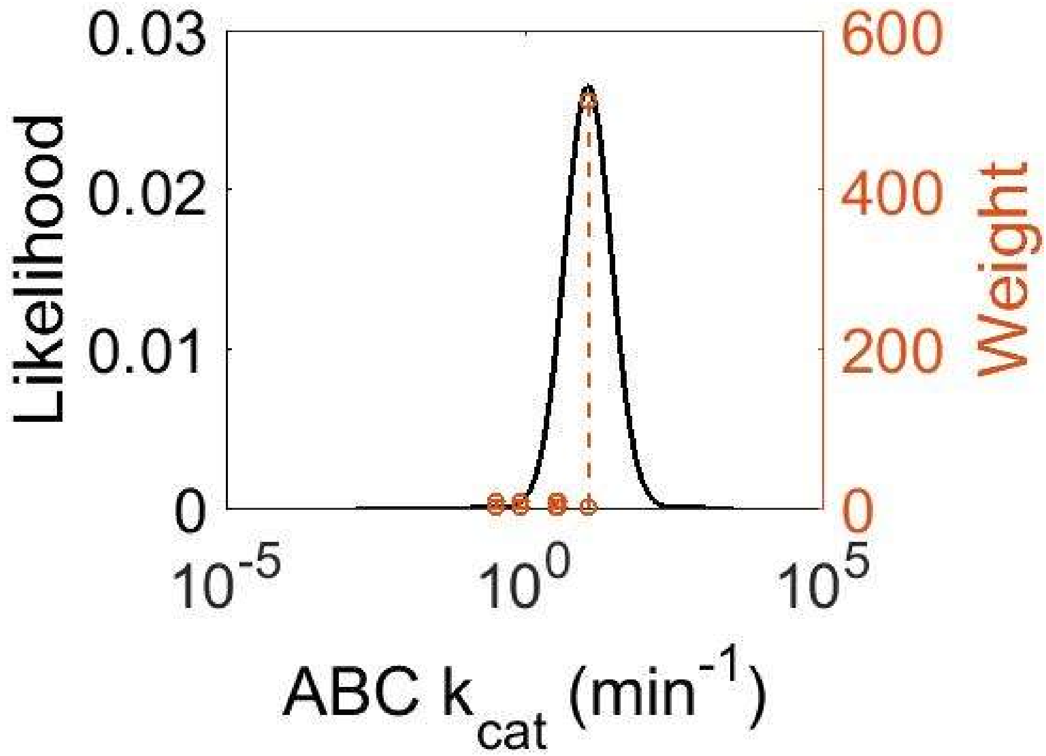


Figure SF.10.12.1.1.1. The estimated probability distribution for ABC k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.12.1.2. Parameter: ABC K_{ms}

Parameter values for the ABC K_{ms} of Reaction 33 were obtained from the literature and summarised in Table ST.10.12.1.2.1. The log-normal distribution properties for the ABC K_{ms} of Reaction 33 are shown in Table ST.10.12.1.2.2 and plotted in Figure SF.10.12.1.2.1.

Table ST.10.12.1.2.1. Literature information used to design the ABC K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.09×10^{-2}	4.10×10^{-3}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
3.66×10^{-5}	3.80×10^{-6}	Unknown	H69AR plasma membrane	MRP1	7.4	37		**128**	0	(Mao et al., 2000)
5.30×10^{-3}	2.60×10^{-3}	Human	HEK293 cells	MRP3	7.4	37		**128**	0	(Zeng et al., 2000)
1.95×10^{-1}	6.12×10^{-2}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
1.10×10^{-1}	3.91×10^{-2}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
2.07×10^{-2}	NaN	Human	HepG2 hepatoma	ABCB1	7.4	37		**2048**	0	(Fong et al., 2007)

Table ST.10.12.1.2.2. The log-normal distribution properties of the ABC K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
2.10×10^{-2}	2.37×10^{1}	-2.60	1.12

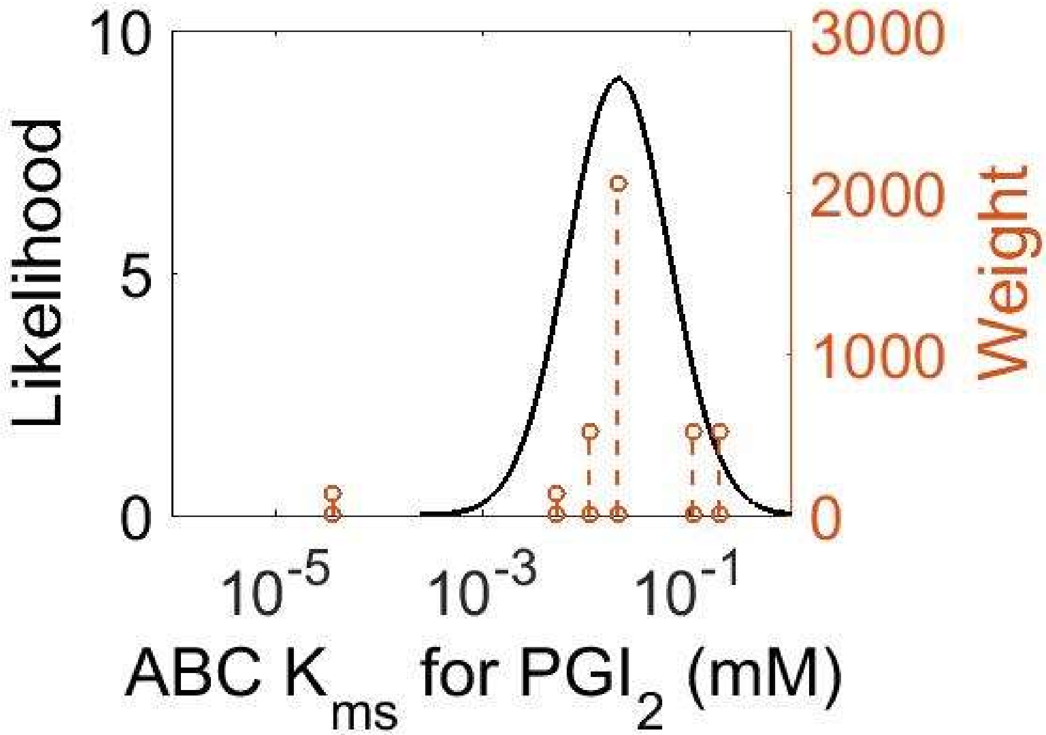


Figure SF.10.12.1.2.1. The estimated probability distribution for ABC K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.12.1.3. Parameter: ABC concentration

Parameter values for the ABC concentration of Reaction 33 were obtained from the literature and summarised in Table ST.10.12.1.3.1. The log-normal distribution properties for the ABC concentration of Reaction 33 are shown in Table ST.10.12.1.3.2 and plotted in Figure SF.10.12.1.3.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.10.12.1.3.1. Literature information used to design the ABC concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
5.15	NaN	Human	Stomach	ABC	7.5	37		2048	0	(Wilhelm et al., 2014)
5.94	NaN	Human	Lung	ABC	7.5	37		2048	0	(Kim et al., 2014)
2.66	NaN	Human	Gut	ABC	7.5	37		2048	0	(Kim et al., 2014)

Table ST.10.12.1.3.2. The log-normal distribution properties of the ABC concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
5.06	1.44	1.74	3.42×10^{-1}

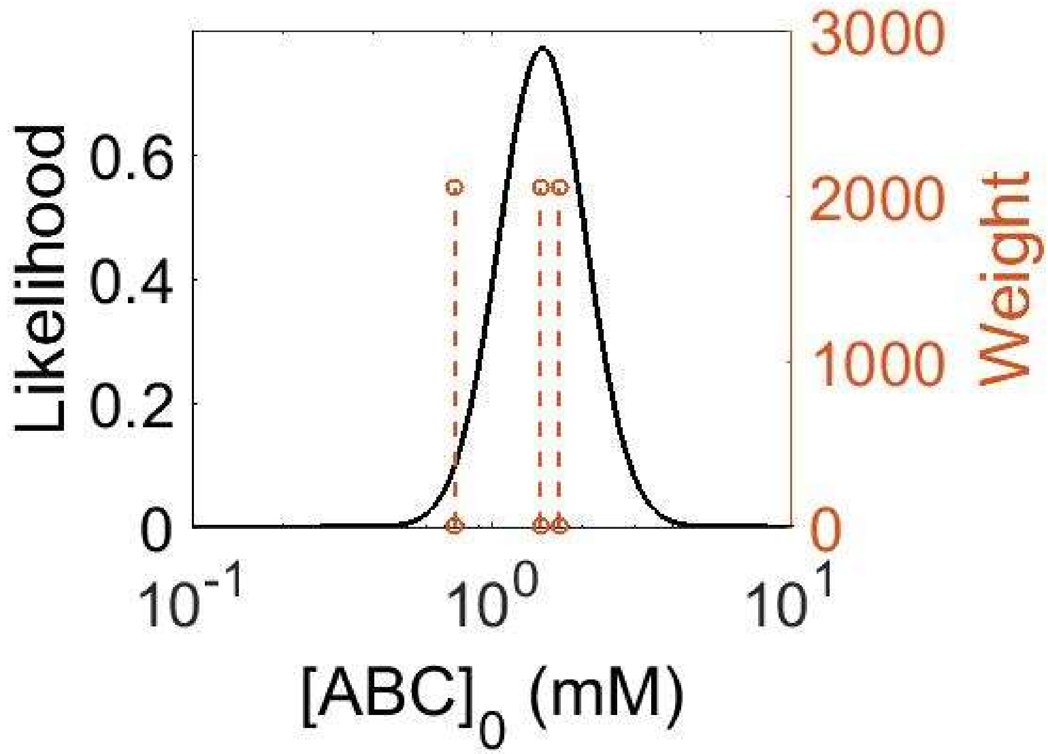


Figure SF.10.12.1.3.1. The estimated probability distribution for the ABC concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.13. Reaction 34: $PGH_2 \rightleftharpoons exPGH_2$

PGH_2 is relocated from the intracellular compartment to the extracellular compartment via the ATP-binding cassette (ABC) transporter.

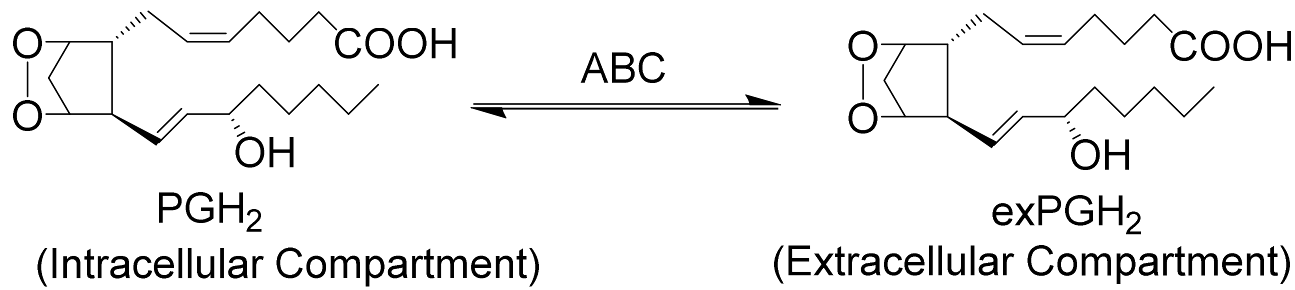


Figure SF.10.13. The transport of prostaglandin H_2 (PGH_2) from the intracellular compartment to the extracellular compartment by ATP Binding Cassette protein (ABC) (Reaction 34).

SEq.10.13. Reaction rate law for Reaction 34.

$$v_{34} = [ABC] \cdot k_{cat} \cdot \frac{\mathbf{PGH_2}/K_m \cdot \left(1 - \frac{\mathbf{exPGH_2}}{\mathbf{PGH_2} \cdot e^{-0.5 \cdot \left(G + R \cdot T \cdot \ln\left(\frac{ATP}{ADP}\right)\right)/_{R \cdot T}}}\right)}{1 + \frac{\mathbf{PGH_2}}{K_m} + \frac{\mathbf{exPGH_2}}{K_m} + \mathbf{ABC\_CI}}$$

S.7.1.1. Reaction parameters

Parameter: ABC k_{cat}

Parameter values for the ABC k_{cat} of Reaction 34 were obtained from the literature and summarised in Table ST.10.13.1.1.1. The log-normal distribution properties for the ABC k_{cat} of Reaction 34 are shown in Table ST.10.13.1.1.2 and plotted in Figure SF.10.13.1.1.1.

Table ST.10.13.1.1.1. Literature information used to design the ABC k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
3.50	NaN	Bacteria	E. coli.	Glucose transporter	Unknown	Unknown	Bionumbers calculation	8	0	(Waygood and Steeves, 1980)
3.30×10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	8	0	(Naftalin et al., 2007)
8.30×10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	8	0	(Naftalin et al., 2007)
3.28	NaN	Yeast	Saccharomyces cerevisiae	HXT7 transporter	Unknown	Unknown	Bionumbers calculation	8	0	(Ye et al., 2001)
1.13×10^{1}		Primate	Baculovirus	MRP2	7	37		512		(Yasunaga et al., 2008)

Table ST.10.13.1.1.2. The log-normal distribution properties of the ABC k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.13 $x10^{1}$	1.00 $x10^{1}$	3.22	8.91 $x10^{-1}$

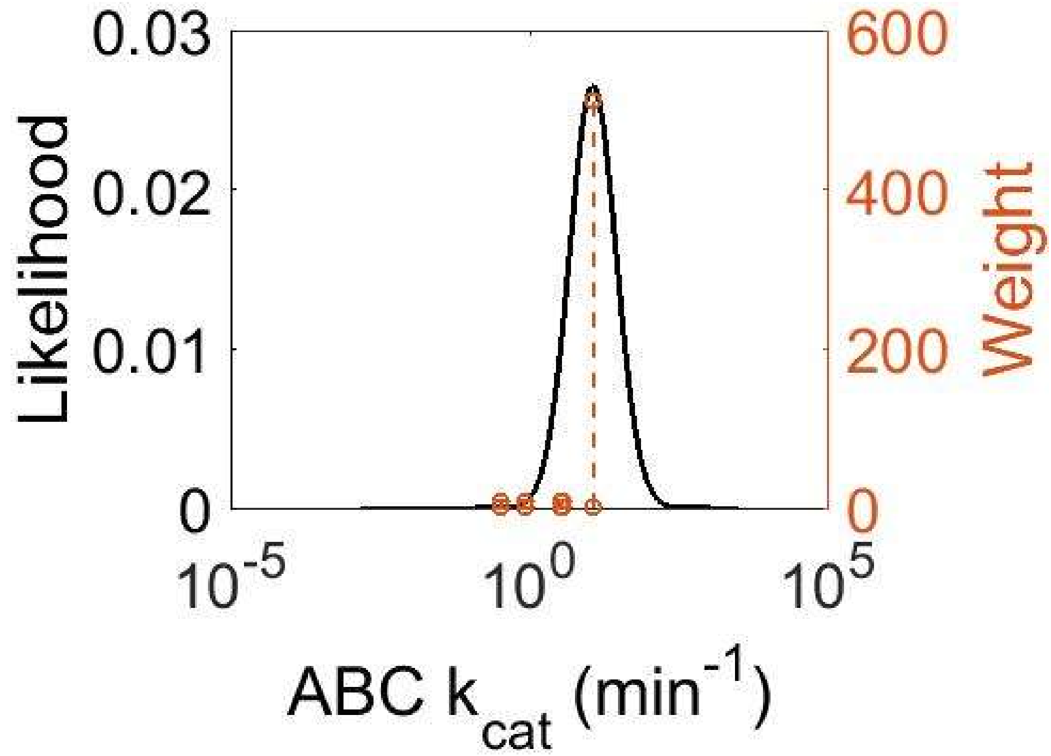


Figure SF.10.13.1.1.1. The estimated probability distribution for ABC k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.13.1.2. Parameter: ABC K_{ms}

In this model numerous simplifications have been made and as a result, intermediate metabolites, such as PGH_2, occur in higher concentrations than are found in reality. To prevent a large percentage of PGH_2 being exported before it is metabolised, the K_{ms} of the ABC transporter has been increased (mode= 25 mM, CIF=10, μ = 4.01, σ = 0.89) (Table ST.10.13.1.2.1.). This is plotted in Figure SF.10.13.1.2.1.

Table ST.10.13.1.2.1. The log-normal distribution properties of the ABC K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
25	10	4.01	8.9010^{-1}

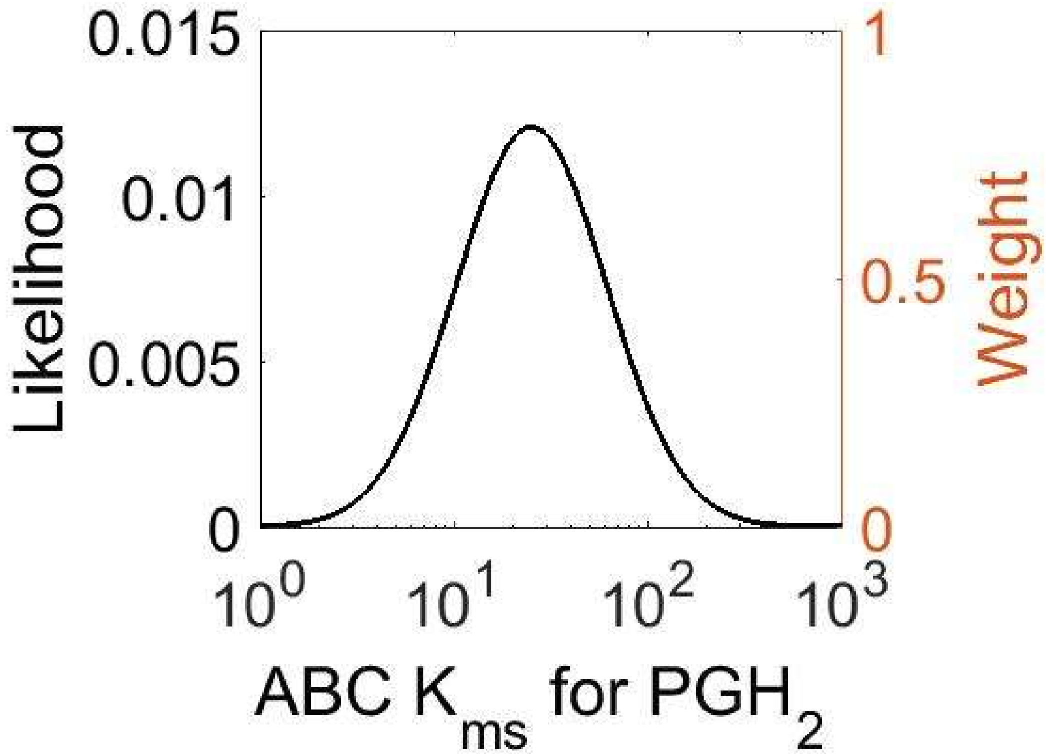


Figure SF.10.13.1.2.1. The estimated probability distribution for ABC K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.13.1.3. Parameter: ABC concentration

Parameter values for the ABC concentration of Reaction 34 were obtained from the literature and summarised in Table ST.10.13.1.3.1. The log-normal distribution properties for the ABC concentration of Reaction 34 are shown in Table ST.10.13.1.3.2 and plotted in Figure SF.10.13.1.3.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.10.13.1.3.1. Literature information used to design the ABC concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
5.15	NaN	Human	Stomach	ABC	7.5	37		2048	0	(Wilhelm et al., 2014)
5.94	NaN	Human	Lung	ABC	7.5	37		2048	0	(Kim et al., 2014)
2.66	NaN	Human	Gut	ABC	7.5	37		2048	0	(Kim et al., 2014)

Table ST.10.13.1.3.2. The log-normal distribution properties of the ABC concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
5.06	2.80×10^{-5}	1.44	1.74	3.4210^{-1}

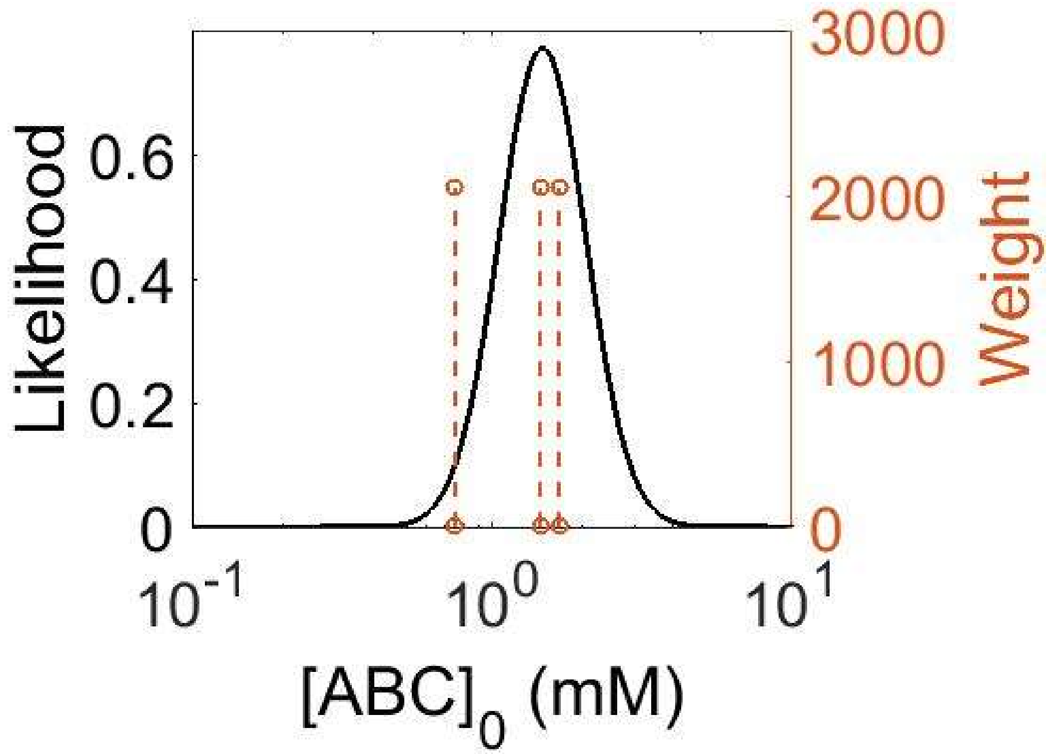
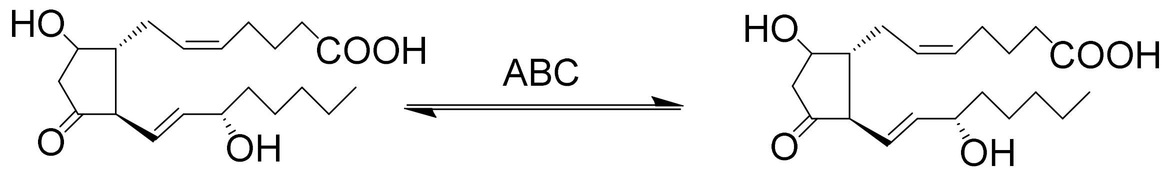


Figure SF.10.13.1.3.1. The estimated probability distribution for the ABC concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.14. Reaction 35: $PGD_2 \rightleftharpoons exPGD_2$

PGD_2 is relocated from the intracellular compartment to the extracellular compartment via the ATP-binding cassette (ABC) transporter.



PGD_2 (Intracellular Compartment) | $exPGD_2$ (Extracellular Compartment)

Figure SF.10.14. The transport of prostaglandin D_2 (PGD_2) from the intracellular compartment to the extracellular compartment by ATP Binding Cassette protein (ABC) (Reaction 35).

SEq.10.14. Reaction rate law for Reaction 35.

$$\boldsymbol{v_{35}} = [\boldsymbol{ABC}] \cdot \boldsymbol{k_{cat}} \cdot \frac{\mathbf{PGD_2}/K_m \cdot \left(1 - \frac{\mathbf{exPGD_2}}{\mathbf{PGD_2} \cdot e^{-0.5 \cdot \left(G + R \cdot T \cdot \ln\left(\frac{ATP}{ADP}\right)\right)/_{R \cdot T}}}\right)}{1 + \frac{\mathbf{PGD_2}}{K_m} + \frac{\mathbf{exPGD_2}}{K_m} + \mathbf{ABC\_CI}}$$

S.10.14.1. Reaction parameters

S.10.14.1.1. Parameter: ABC k_{cat}

Parameter values for the ABC k_{cat} of Reaction 35 were obtained from the literature and summarised in Table ST.10.14.1.1.1. The log-normal distribution properties for the ABC k_{cat} of Reaction 35 are shown in Table ST.10.14.1.1.2 and plotted in Figure SF.10.14.1.1.1.

Table ST.10.14.1.1.1. Literature information used to design the ABC k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
3.50	NaN	Bacteria	E. coli.	Glucose transporter	Unknown	Unknown	Bionumbers calculation	8	0	(Waygood and Steeves, 1980)
3.30×10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	8	0	(Naftalin et al., 2007)
8.30×10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	8	0	(Naftalin et al., 2007)
3.28	NaN	Yeast	Saccharomyces cerevisiae	HXT7 transporter	Unknown	Unknown	Bionumbers calculation	8	0	(Ye et al., 2001)
1.13×10^{1}		Primate	Baculovirus	MRP2	7	37		512		(Yasunaga et al., 2008)

Table ST.10.14.1.1.2. The log-normal distribution properties of the ABC k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.13 $x10^{1}$	1.00 $x10^{1}$	3.22	8.9110^{-1}

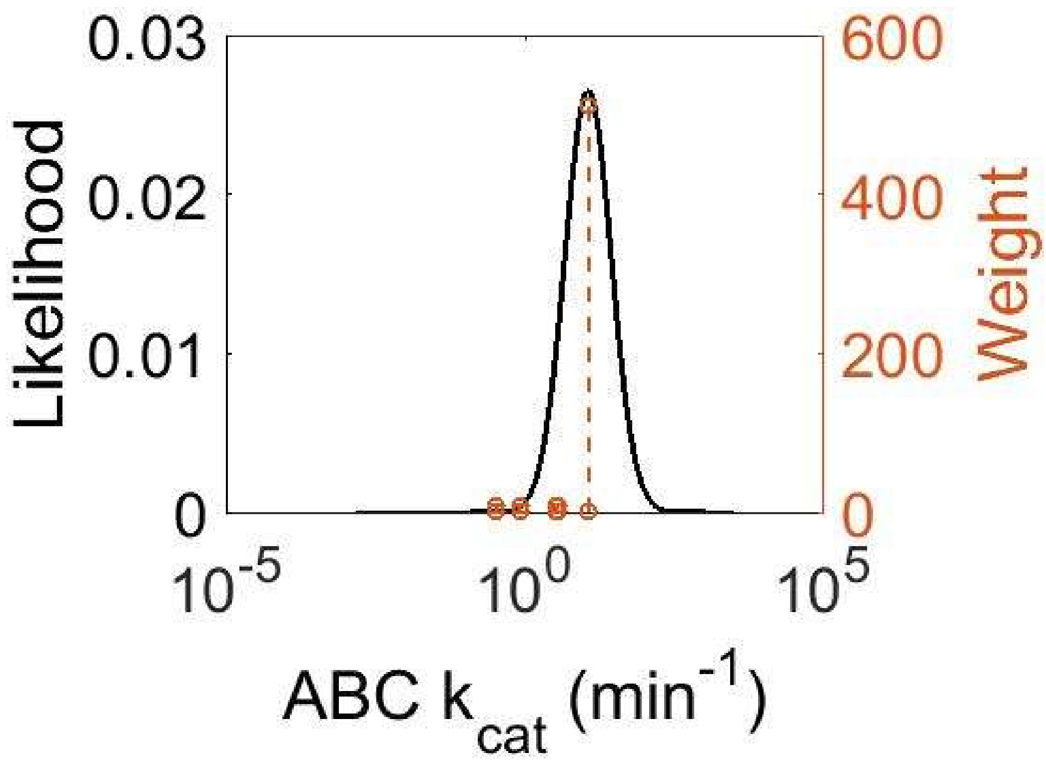


Figure SF.10.14.1.1.1. The estimated probability distribution for ABC k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.14.1.2. Parameter: ABC K_{ms}

Parameter values for the ABC K_{ms} of Reaction 35 were obtained from the literature and summarised in Table ST.10.14.1.2.1. The log-normal distribution properties for the ABC K_{ms} of Reaction 35 are shown in Table ST.10.14.1.2.2 and plotted in Figure SF.10.14.1.2.1.

Table ST.10.14.1.2.1. Literature information used to design the ABC K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.09×10^{-2}	4.10×10^{-3}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
3.66×10^{-5}	3.80×10^{-6}	Unknown	H69AR plasma membrane	MRP1	7.4	37		**128**	0	(Mao et al., 2000)
5.30×10^{-3}	2.60×10^{-3}	Human	HEK293 cells	MRP3	7.4	37		**128**	0	(Zeng et al., 2000)
1.95×10^{-1}	6.12×10^{-2}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
1.10×10^{-1}	3.91×10^{-2}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
2.07×10^{-2}	NaN	Human	HepG2 hepatoma	ABCB1	7.4	37		**2048**	0	(Fong et al., 2007)

Table ST.10.14.1.2.2. The log-normal distribution properties of the ABC K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
2.10×10^{-2}	2.37×10^{1}	-2.60	1.12

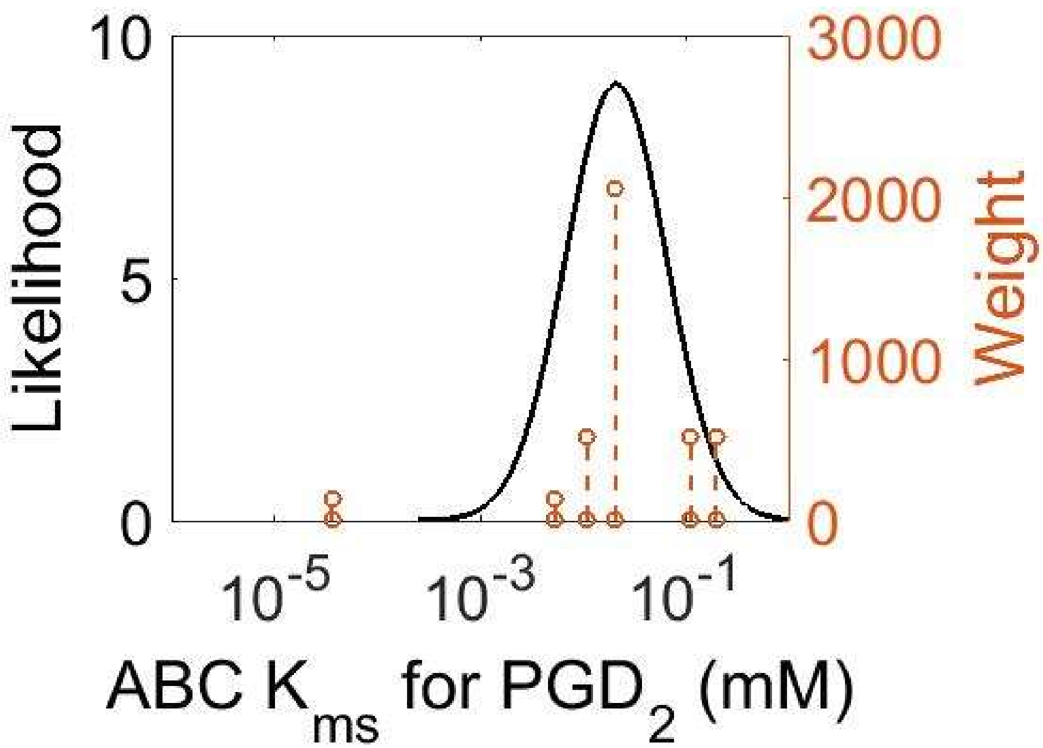


Figure SF.10.14.1.2.1. The estimated probability distribution for ABC K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.14.1.3. Parameter: ABC concentration

Parameter values for the ABC concentration of Reaction 35 were obtained from the literature and summarised in Table ST.10.14.1.3.1. The log-normal distribution properties for the ABC concentration of Reaction 35 are shown in Table ST.10.14.1.3.2 and plotted in Figure SF.10.14.1.3.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.10.14.1.3.1. Literature information used to design the ABC concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
5.15	NaN	Human	Stomach	ABC	7.5	37		2048	0	(Wilhelm et al., 2014)
5.94	NaN	Human	Lung	ABC	7.5	37		2048	0	(Kim et al., 2014)
2.66	NaN	Human	Gut	ABC	7.5	37		2048	0	(Kim et al., 2014)

Table ST.10.14.1.3.2. The log-normal distribution properties of the ABC concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
5.06	2.80×10^{-5}	1.44	1.74	3.42×10^{-1}

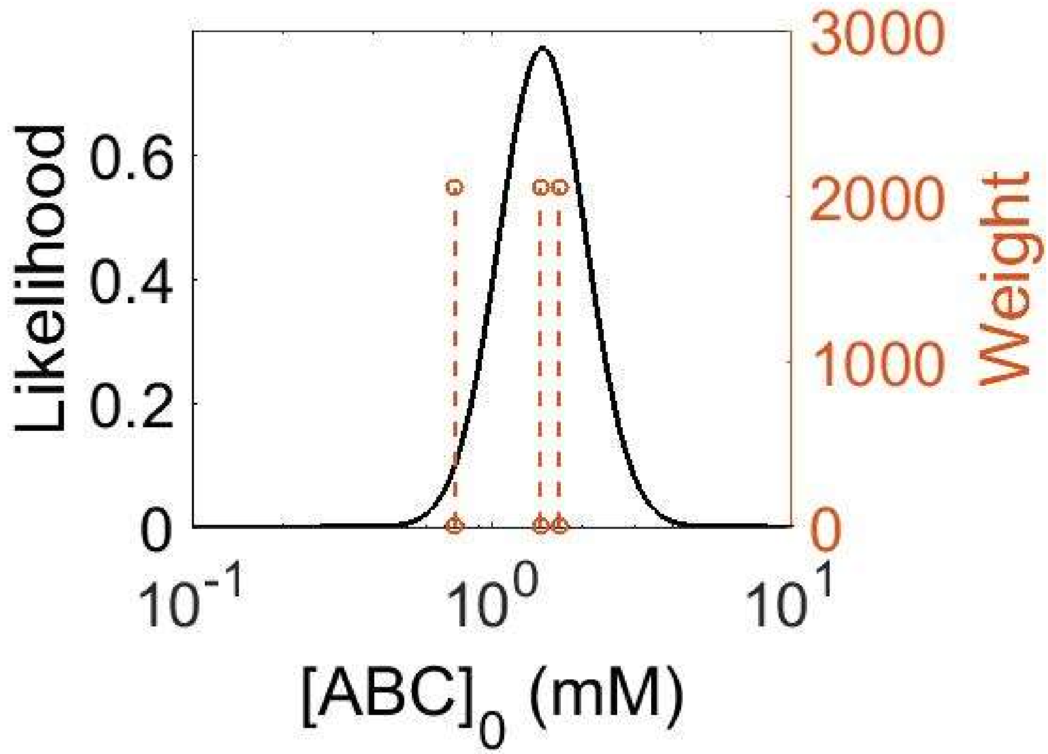


Figure SF.10.14.1.3.1. The estimated probability distribution for the ABC concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.15. Reaction 36: $PGJ_2 \rightleftharpoons exPGJ_2$

PGJ_2 is relocated from the intracellular compartment to the extracellular compartment via the ATP-binding cassette (ABC) transporter.

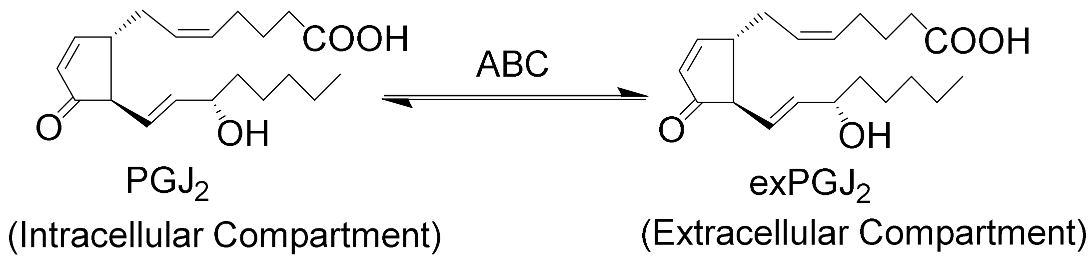


Figure SF.10.15. The transport of prostaglandin J_2 (PGJ_2) from the intracellular compartment to the extracellular compartment by ATP Binding Cassette protein (ABC) (Reaction 36).

SEq.10.15. Reaction rate law for Reaction 36.

$$\boldsymbol{v_{36}} = [\boldsymbol{ABC}] \cdot \boldsymbol{k_{cat}} \cdot \frac{\mathbf{PGJ_2} / K_m \cdot \left(1 - \frac{\mathbf{exPGJ_2}}{\mathbf{PGJ_2} \cdot e^{-0.5 \cdot \left(G + R \cdot T \cdot \ln\left(\frac{ATP}{ADP}\right)\right) / R \cdot T}}\right)}{1 + \frac{\mathbf{PGJ_2}}{K_m} + \frac{\mathbf{exPGJ_2}}{K_m} + \mathbf{ABC\_CI}}$$

S.10.15.1 Reaction parameters

S.10.15.1.1 Parameter: ABC k_{cat}

Parameter values for the ABC k_{cat} of Reaction 36 were obtained from the literature and summarised in Table ST.10.15.1.1.1. The log-normal distribution properties for the ABC k_{cat} of Reaction 36 are shown in Table ST.10.15.1.1.2 and plotted in Figure SF.10.15.1.1.1.

Table ST.10.15.1.1.1. Literature information used to design the ABC k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
3.50	NaN	Bacteria	E. coli.	Glucose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Waygood and Steeves, 1980)
3.30×10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
8.30×10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
3.28	NaN	Yeast	Saccharomyces cerevisiae	HXT7 transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Ye et al., 2001)
1.13×10^{1}		Primate	Baculovirus	MRP2	7	37		512		(Yasunaga et al., 2008)

Table ST.10.15.1.1.2. The log-normal distribution properties of the ABC k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
1.13×10^{1}	1.00×10^{1}	3.22	8.91×10^{-1}

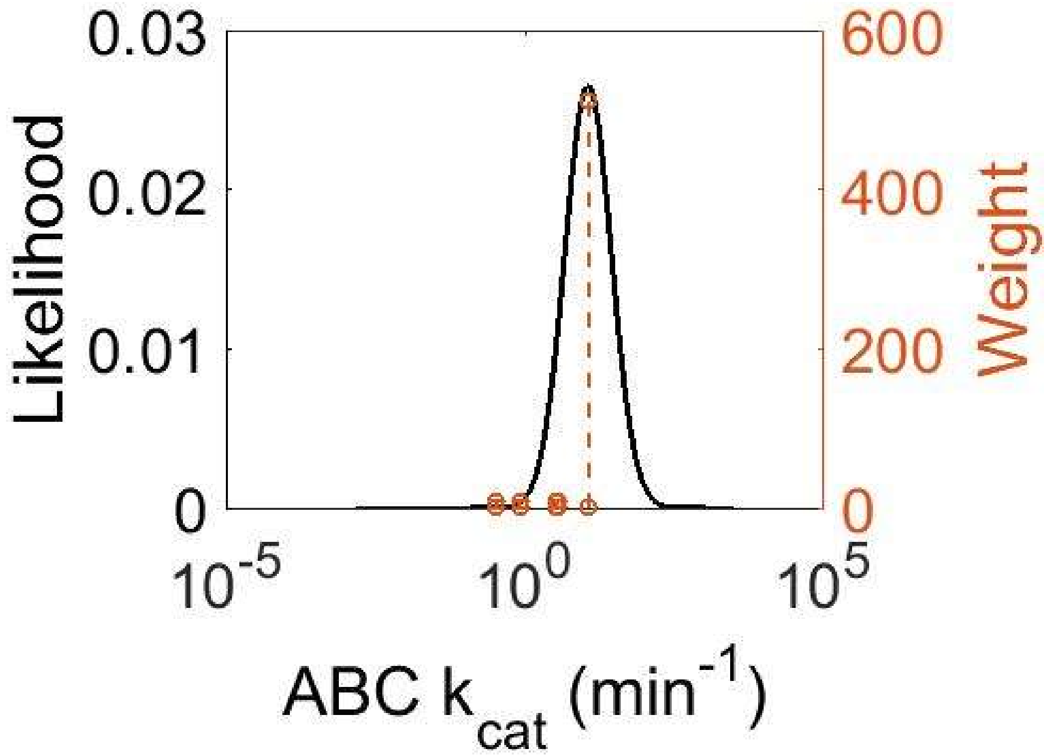


Figure SF.10.15.1.1.1. The estimated probability distribution for ABC k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.15.1.2. Parameter: ABC K_{ms}

Parameter values for the ABC K_{ms} of Reaction 36 were obtained from the literature and summarised in Table ST.10.15.1.2.1. The log-normal distribution properties for the ABC K_{ms} of Reaction 36 are shown in Table ST.10.15.1.2.2 and plotted in Figure SF.10.15.1.2.1.

Table ST.10.15.1.2.1. Literature information used to design the ABC K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.09×10^{-2}	4.10×10^{-3}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
3.66×10^{-5}	3.80×10^{-6}	Unknown	H69AR plasma membrane	MRP1	7.4	37		**128**	0	(Mao et al., 2000)
5.30×10^{-3}	2.60×10^{-3}	Human	HEK293 cells	MRP3	7.4	37		**128**	0	(Zeng et al., 2000)
1.95×10^{-1}	6.12×10^{-2}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
1.10×10^{-1}	3.91×10^{-2}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
2.07×10^{-2}	NaN	Human	HepG2 hepatoma	ABCB1	7.4	37		**2048**	0	(Fong et al., 2007)

Table ST.10.15.1.2.2. The log-normal distribution properties of the ABC K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
2.10 $x10^{-2}$	2.37 $x10^{1}$	-2.60	1.12

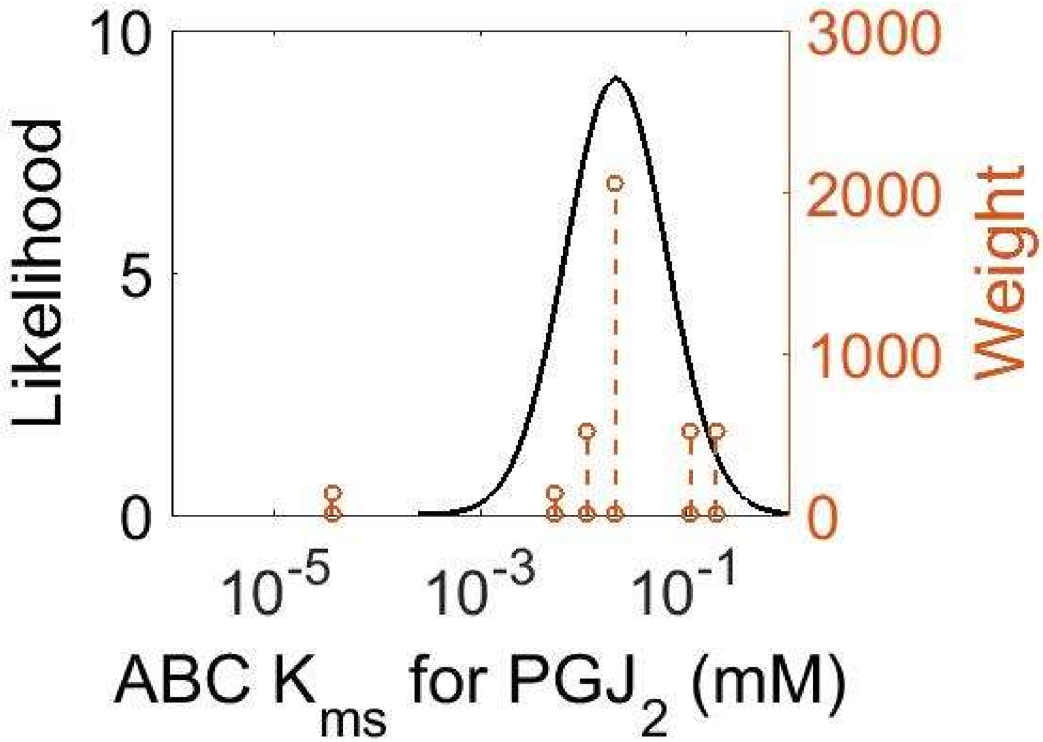


Figure SF.10.15.1.2.1. The estimated probability distribution for ABC K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.15.1.3. Parameter: ABC concentration

Parameter values for the ABC concentration of Reaction 36 were obtained from the literature and summarised in Table ST.10.15.1.3.1. The log-normal distribution properties for the ABC concentration of Reaction 36 are shown in Table ST.10.15.1.3.2 and plotted in Figure SF.10.15.1.3.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.10.15.1.3.1. Literature information used to design the ABC concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
5.15	NaN	Human	Stomach	ABC	7.5	37		2048	0	(Wilhelm et al., 2014)
5.94	NaN	Human	Lung	ABC	7.5	37		2048	0	(Kim et al., 2014)
2.66	NaN	Human	Gut	ABC	7.5	37		2048	0	(Kim et al., 2014)

Table ST.10.15.1.3.2. The log-normal distribution properties of the ABC concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
5.06	2.80×10^{-5}	1.44	1.74	3.42×10^{-1}

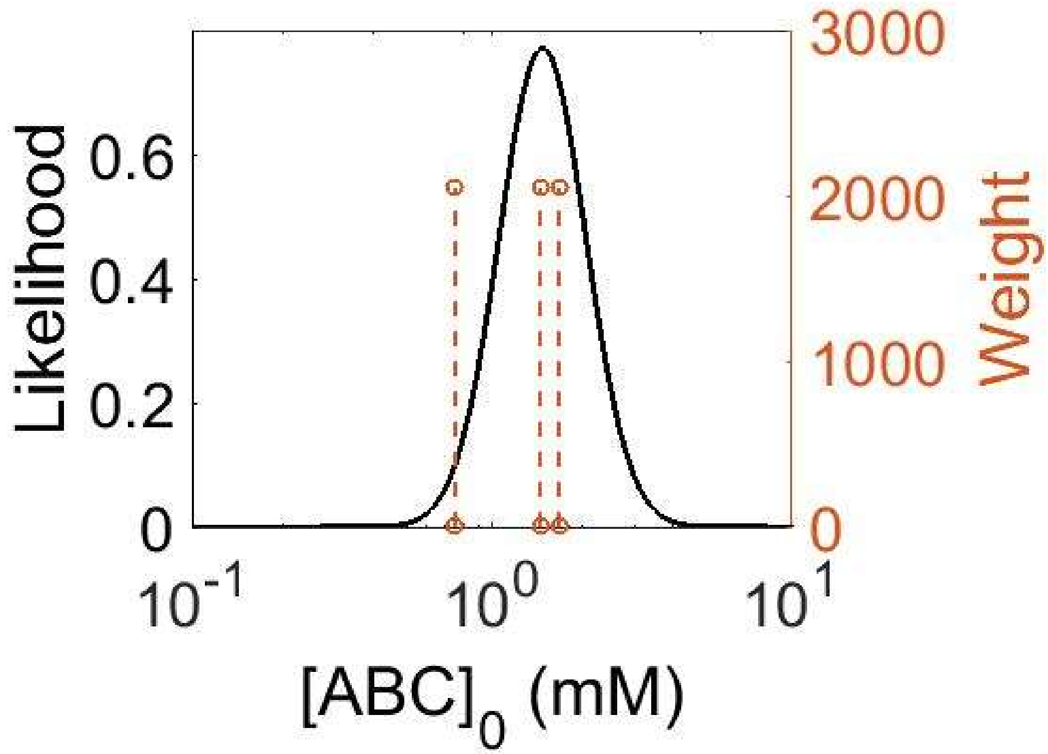
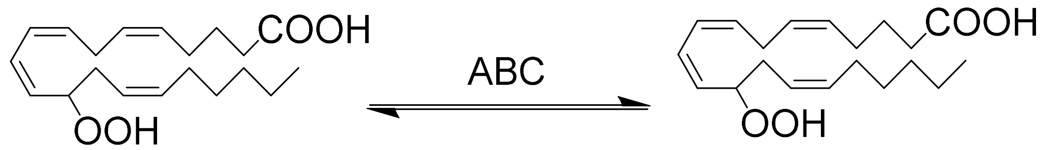


Figure SF.10.15.1.3.1. The estimated probability distribution for the ABC concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.16. Reaction 37: 12-HPETE ⇌ ex12-HPETE
12-HPETE is relocated from the intracellular compartment to the extracellular compartment via the ATP-binding cassette (ABC) transporter.



12-HPETE
(Intracellular Compartment)

ex12-HPETE
(Extracellular Compartment)

Figure SF.10.16. The transport of 12-hydroperoxyeicosatetraenoic acid (12-HPETE) from the intracellular compartment to the extracellular compartment by ATP Binding Cassette protein (ABC) (Reaction 37).

SEq.10.16. Reaction rate law for Reaction 37.

$$v_{37} = [ABC] \cdot k_{cat} \cdot \frac{\mathrm{12{-}HPETE}/K_m \cdot \left(1 - \frac{\mathrm{ex12{-}HPETE}}{\mathrm{12{-}HPETE} \cdot e^{-0.5 \cdot \left(G + R \cdot T \cdot \ln\left(\frac{ATP}{ADP}\right)\right)/R \cdot T}}\right)}{1 + \frac{\mathrm{12{-}HPETE}}{K_m} + \frac{\mathrm{ex12{-}HPETE}}{K_m} + \mathrm{ABC\_CI}}$$

S.10.16.1. Reaction parameters

S.10.16.1.1. Parameter: ABC k_{cat}

Parameter values for the ABC k_{cat} of Reaction 37 were obtained from the literature and summarised in Table ST.10.16.1.1.1. The log-normal distribution properties for the ABC k_{cat} of Reaction 37 are shown in Table ST.10.16.1.1.2 and plotted in Figure SF.10.16.1.1.1.

Table ST.10.16.1.1.1. Literature information used to design the ABC k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	**Expression Vector**	**Enzyme**	**pH**	**Temperature (°C)**	**Other**			
3.50	NaN	Bacteria	E. coli.	Glucose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Waygood and Steeves, 1980)
3.30×10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
8.30×10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
3.28	NaN	Yeast	Saccharomyces cerevisiae	HXT7 transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Ye et al., 2001)
1.13×10^{1}		Primate	Baculovirus	MRP2	7	37		512		(Yasunaga et al., 2008)

Table ST.10.16.1.1.2. The log-normal distribution properties of the ABC k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.13×10^{1}	1.00×10^{1}	3.22	8.91×10^{-1}

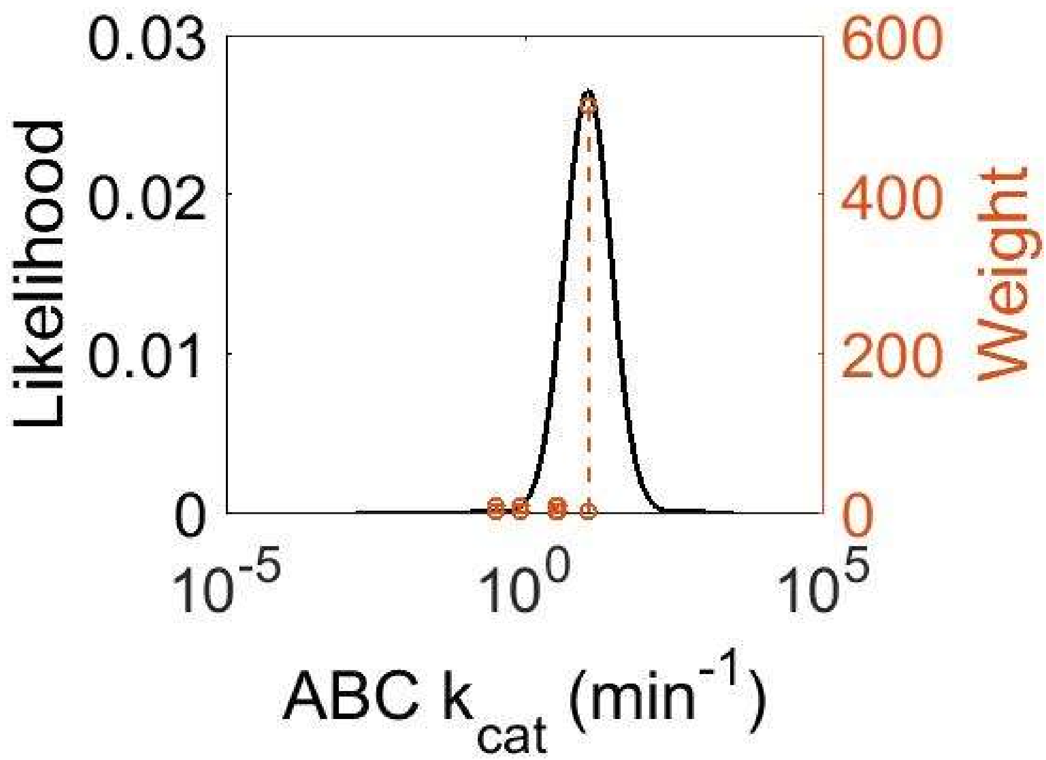


Figure SF.10.16.1.1.1. The estimated probability distribution for ABC k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.16.1.2. Parameter: ABC K_{ms}

Parameter values for the ABC K_{ms} of Reaction 37 were obtained from the literature and summarised in Table ST.10.16.1.2.1. The log-normal distribution properties for the ABC K_{ms} of Reaction 37 are shown in Table ST.10.16.1.2.2 and plotted in Figure SF.10.16.1.2.1.

Table ST.10.16.1.2.1. Literature information used to design the ABC K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.09×10^{-2}	4.10×10^{-3}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
3.66×10^{-5}	3.80×10^{-6}	Unknown	H69AR plasma membrane	MRP1	7.4	37		**128**	0	(Mao et al., 2000)
5.30×10^{-3}	2.60×10^{-3}	Human	HEK293 cells	MRP3	7.4	37		**128**	0	(Zeng et al., 2000)
1.95×10^{-1}	6.12×10^{-2}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
1.10×10^{-1}	3.91×10^{-2}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
2.07×10^{-2}	NaN	Human	HepG2 hepatoma	ABCB1	7.4	37		**2048**	0	(Fong et al., 2007)

Table ST.10.16.1.2.2. The log-normal distribution properties of the ABC K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
2.10×10^{-2}	2.37×10^{1}	-2.60	1.12

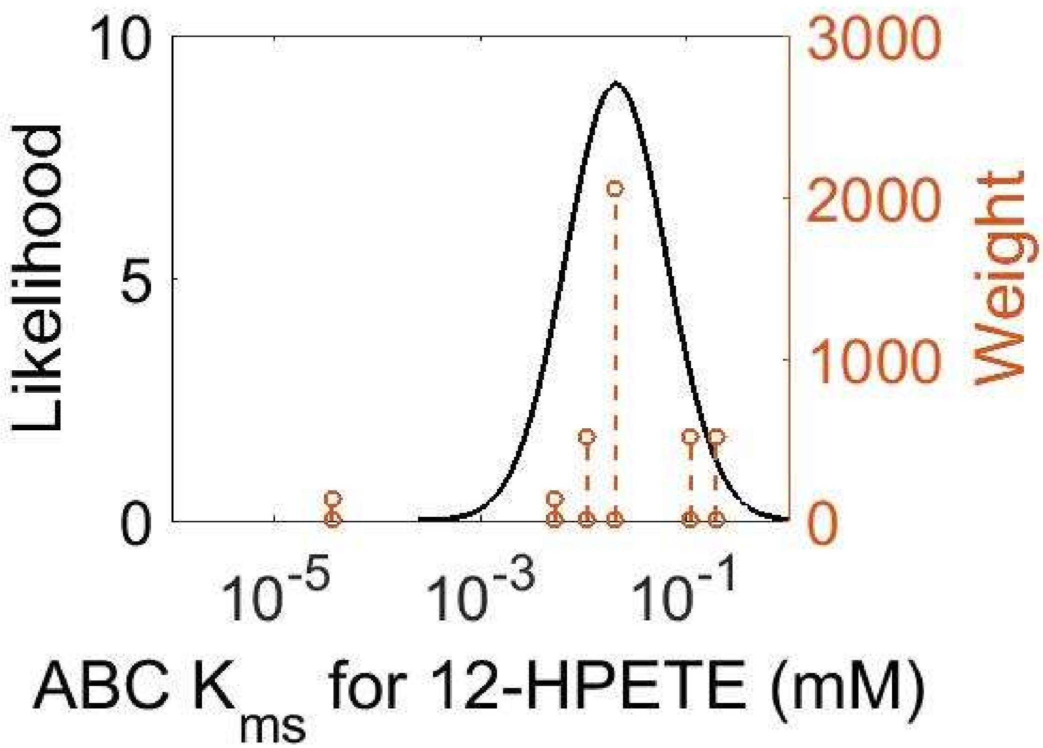


Figure SF.10.16.1.2.1. The estimated probability distribution for ABC K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.16.1.3. Parameter: ABC concentration

Parameter values for the ABC concentration of Reaction 37 were obtained from the literature and summarised in Table ST.10.16.1.3.1. The log-normal distribution properties for the ABC concentration of Reaction 37 are shown in Table ST.10.16.1.3.2 and plotted in Figure SF.10.16.1.3.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.10.16.1.3.1. Literature information used to design the ABC concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
5.15	NaN	Human	Stomach	ABC	7.5	37		2048	0	(Wilhelm et al., 2014)
5.94	NaN	Human	Lung	ABC	7.5	37		2048	0	(Kim et al., 2014)
2.66	NaN	Human	Gut	ABC	7.5	37		2048	0	(Kim et al., 2014)

Table ST.10.16.1.3.2. The log-normal distribution properties of the ABC concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
5.06	2.80×10^{-5}	1.44	1.74	3.42×10^{-1}

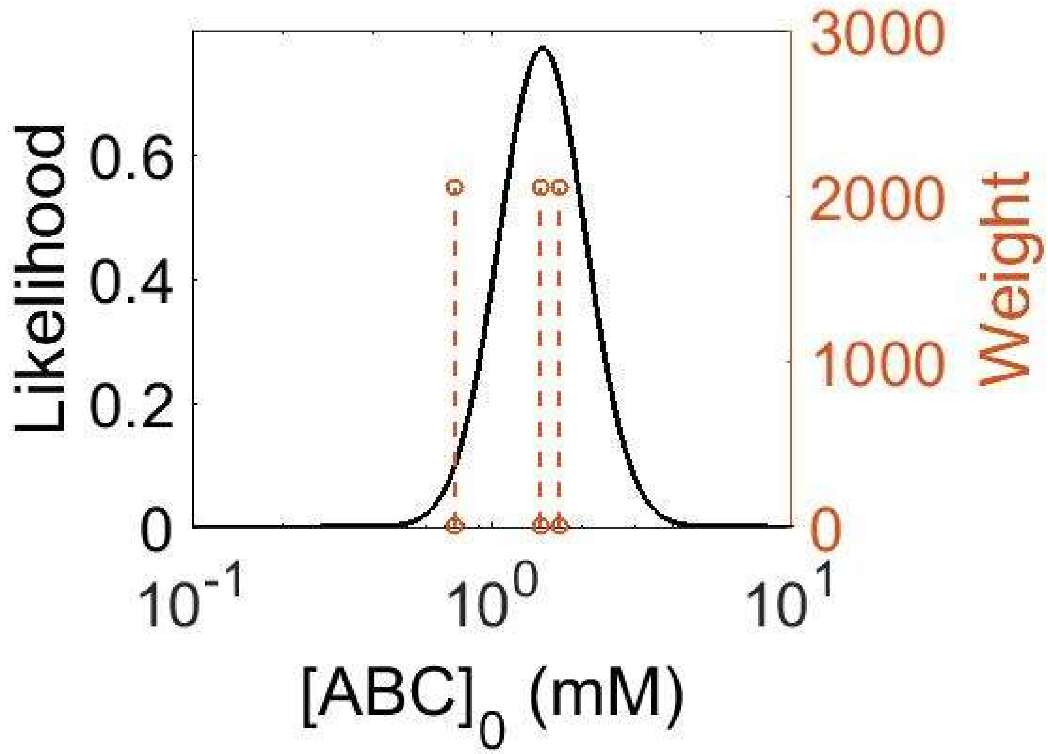


Figure SF.10.16.1.3.1. The estimated probability distribution for the ABC concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.17. Reaction 38: 15-HPETE ⇌ ex15-HPETE
15-HPETE is relocated from the intracellular compartment to the extracellular compartment via the ATP-binding cassette (ABC) transporter.

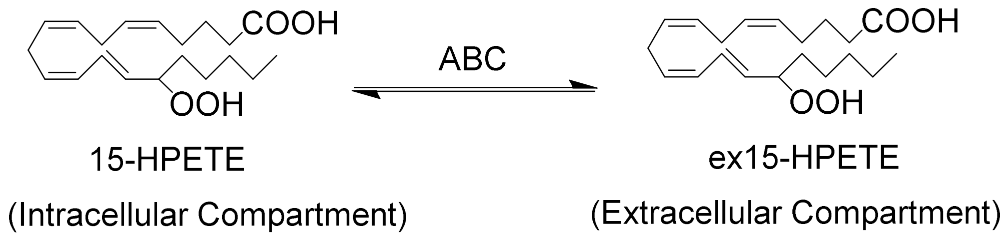


Figure SF.10.17. The transport of 15-hydroperoxyeicosatetraenoic acid (15-HPETE) from the intracellular compartment to the extracellular compartment by ATP Binding Cassette protein (ABC) (Reaction 38).

SEq.10.17. Reaction rate law for Reaction 38.

$$v_{38} = [ABC] \cdot k_{cat} \cdot \frac{\text{15-HPETE}/K_m \cdot \left(1 - \frac{\text{ex15-HPETE}}{\text{15-HPETE} \cdot e^{-0.5 \cdot \left(G + R \cdot T \cdot \ln\left(\frac{ATP}{ADP}\right)\right) / R \cdot T}}\right)}{1 + \frac{\text{15-HPETE}}{K_m} + \frac{\text{ex15-HPETE}}{K_m} + \text{ABC\_CI}}$$

S.10.17.1 Reaction parameters

S.10.17.1.1. Parameter: ABC k_{cat}

Parameter values for the ABC k_{cat} of Reaction 38 were obtained from the literature and summarised in Table ST.10.17.1.1.1. The log-normal distribution properties for the ABC k_{cat} of Reaction 38 are shown in Table ST.10.17.1.1.2 and plotted in Figure SF.10.17.1.1.1.

Table ST.10.17.1.1.1. Literature information used to design the ABC k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
3.50	NaN	Bacteria	E. coli.	Glucose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Waygood and Steeves, 1980)
3.30×10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
8.30×10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
3.28	NaN	Yeast	Saccharomyces cerevisiae	HXT7 transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Ye et al., 2001)
1.13×10^{1}		Primate	Baculovirus	MRP2	7	37		512		(Yasunaga et al., 2008)

Table ST.10.17.1.1.2. The log-normal distribution properties of the ABC k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.13 $x10^{1}$	1.00 $x10^{1}$	3.22	8.91 $x10^{-1}$

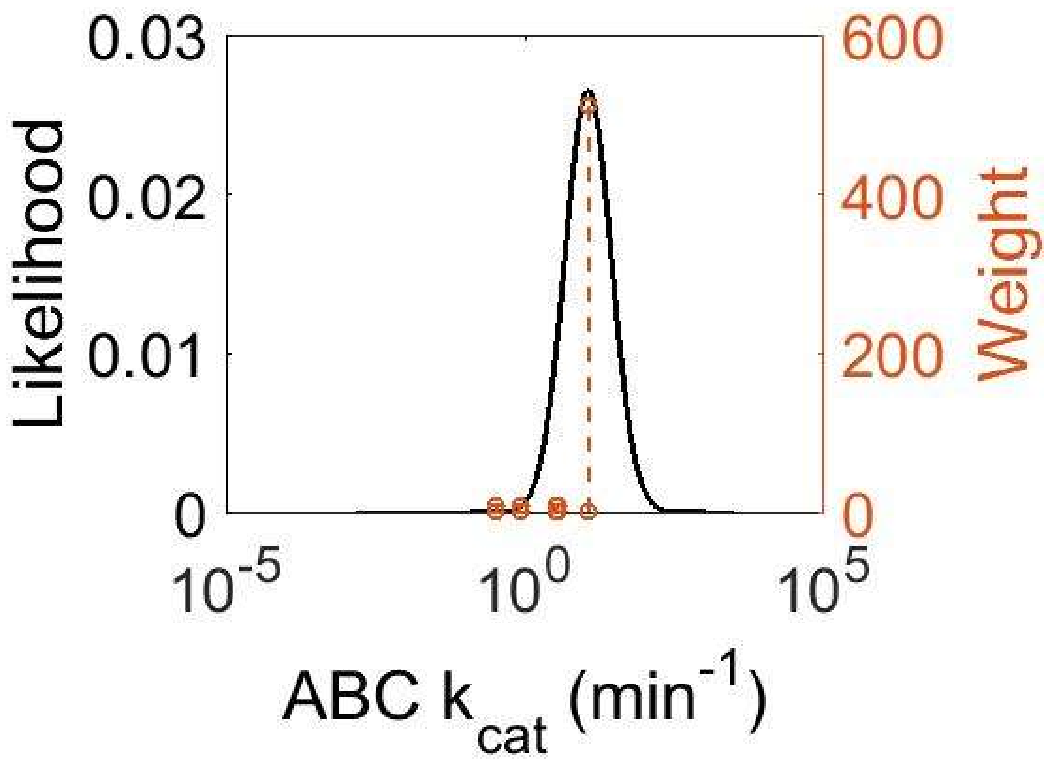


Figure SF.10.17.1.1.1. The estimated probability distribution for ABC k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.17.1.2. Parameter: ABC K_{ms}

Parameter values for the ABC K_{ms} of Reaction 38 were obtained from the literature and summarised in Table ST.10.17.1.2.1. The log-normal distribution properties for the ABC K_{ms} of Reaction 38 are shown in Table ST.10.17.1.2.2 and plotted in Figure SF.10.17.1.2.1.

Table ST.10.17.1.2.1. Literature information used to design the ABC K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.09×10^{-2}	4.10×10^{-3}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
3.66×10^{-5}	3.80×10^{-6}	Unknown	H69AR plasma membrane	MRP1	7.4	37		**128**	0	(Mao et al., 2000)
5.30×10^{-3}	2.60×10^{-3}	Human	HEK293 cells	MRP3	7.4	37		**128**	0	(Zeng et al., 2000)
1.95×10^{-1}	6.12×10^{-2}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
1.10×10^{-1}	3.91×10^{-2}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
2.07×10^{-2}	NaN	Human	HepG2 hepatoma	ABCB1	7.4	37		**2048**	0	(Fong et al., 2007)

Table ST.10.17.1.2.2. The log-normal distribution properties of the ABC K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
2.10×10^{-2}	2.37×10^{1}	-2.60	1.12

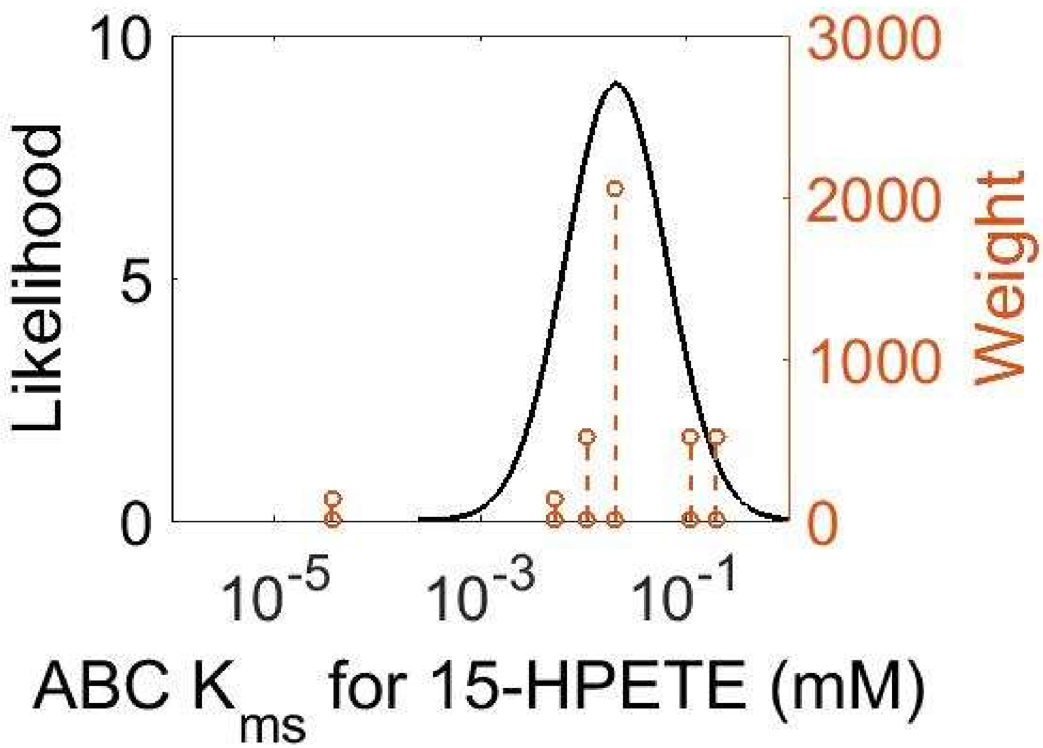


Figure SF.10.17.1.2.1. The estimated probability distribution for ABC K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.17.1.3. Parameter: ABC concentration

Parameter values for the ABC concentration of Reaction 38 were obtained from the literature and summarised in Table ST.10.17.1.3.1. The log-normal distribution properties for the ABC concentration of Reaction 38 are shown in Table ST.10.17.1.3.2 and plotted in Figure SF.10.17.1.3.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.10.17.1.3.1. Literature information used to design the ABC concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
5.15	NaN	Human	Stomach	ABC	7.5	37		2048	0	(Wilhelm et al., 2014)
5.94	NaN	Human	Lung	ABC	7.5	37		2048	0	(Kim et al., 2014)
2.66	NaN	Human	Gut	ABC	7.5	37		2048	0	(Kim et al., 2014)

Table ST.10.17.1.3.2. The log-normal distribution properties of the ABC concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
5.06	2.80×10^{-5}	1.44	1.74	3.42×10^{-1}

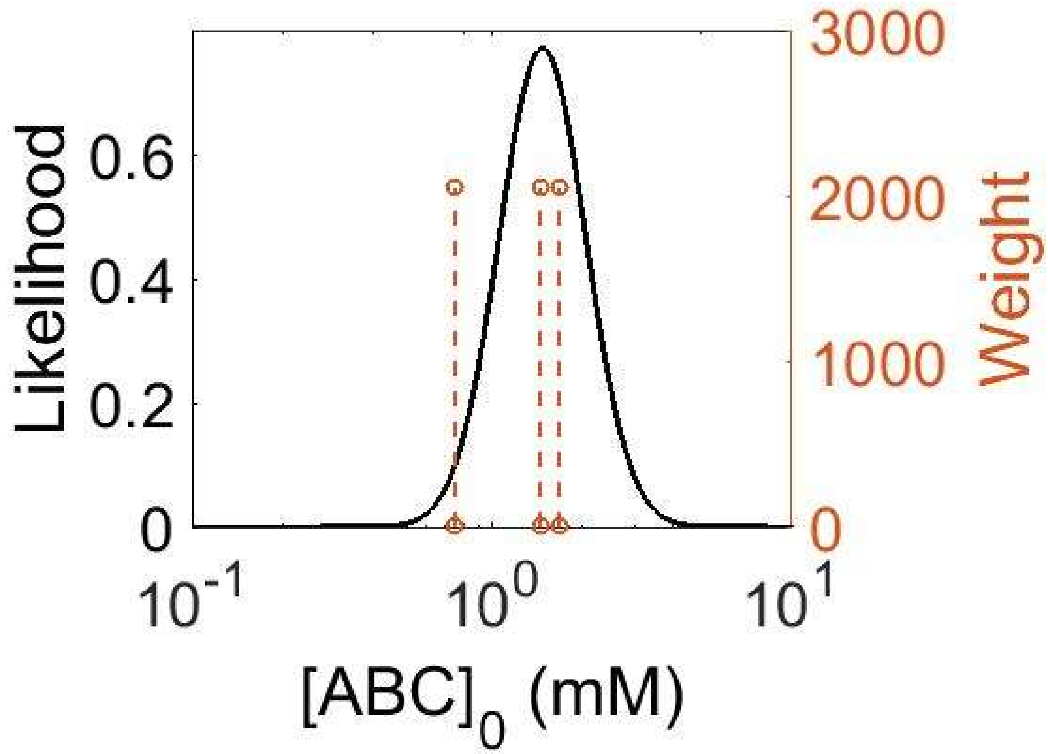


Figure SF.10.17.1.3.1. The estimated probability distribution for the ABC concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.18. Reaction 39: 5-HPETE ⇌ ex5-HPETE

5-HPETE is relocated from the intracellular compartment to the extracellular compartment via the ATP-binding cassette (ABC) transporter.

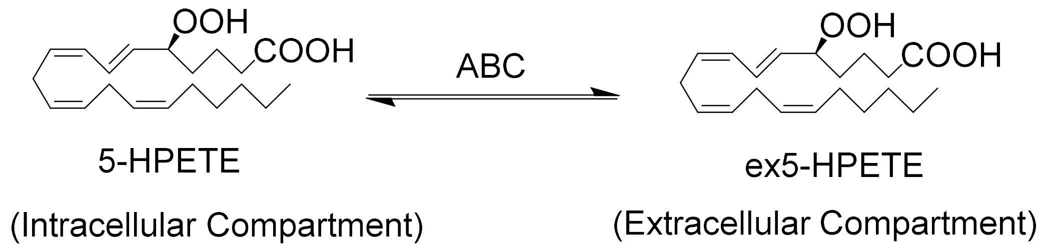


Figure SF.10.18. The transport of 5-hydroperoxyeicosatetraenoic acid (5-HPETE) from the intracellular compartment to the extracellular compartment by ATP Binding Cassette protein (ABC) (Reaction 39).

SEq.10.18. Reaction rate law for Reaction 39.

$$\boldsymbol{v_{39}} = [\boldsymbol{ABC}] \cdot \boldsymbol{k_{cat}} \cdot \frac{\mathbf{5{-}HPETE}/\boldsymbol{K_m} \cdot \left(\mathbf{1} - \frac{\mathbf{ex5{-}HPETE}}{\mathbf{5{-}HPETE} \cdot \boldsymbol{e}^{-0.5\cdot\left(\boldsymbol{G}+\boldsymbol{R}\cdot\boldsymbol{T}\cdot\ln\left(\frac{\boldsymbol{ATP}}{\boldsymbol{ADP}}\right)\right)/\boldsymbol{R}\cdot\boldsymbol{T}}}\right)}{\mathbf{1} + \frac{\mathbf{5{-}HPETE}}{\boldsymbol{K_m}} + \frac{\mathbf{ex5{-}HPETE}}{\boldsymbol{K_m}} + \mathbf{ABC\_CI}}$$

S.10.18.1. Reaction parameters

S.10.18.1.1. Parameter: ABC k_{cat}

Parameter values for the ABC k_{cat} of Reaction 39 were obtained from the literature and summarised in Table ST.10.18.1.1.1. The log-normal distribution properties for the ABC k_{cat} of Reaction 39 are shown in Table ST.10.18.1.1.2 and plotted in Figure SF.10.18.1.1.1.

Table ST.10.18.1.1.1. Literature information used to design the ABC k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
3.50	NaN	Bacteria	E. coli.	Glucose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Waygood and Steeves, 1980)
3.30 $x10^{-1}$	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
8.30 $x10^{-1}$	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
3.28	NaN	Yeast	Saccharomyces cerevisiae	HXT7 transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Ye et al., 2001)
1.13 $x10^{1}$		Primate	Baculovirus	MRP2	7	37		512		(Yasunaga et al., 2008)

Table ST.10.18.1.1.2. The log-normal distribution properties of the ABC k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
1.13 $x10^{1}$	1.00 $x10^{1}$	3.22	8.91 $x10^{-1}$

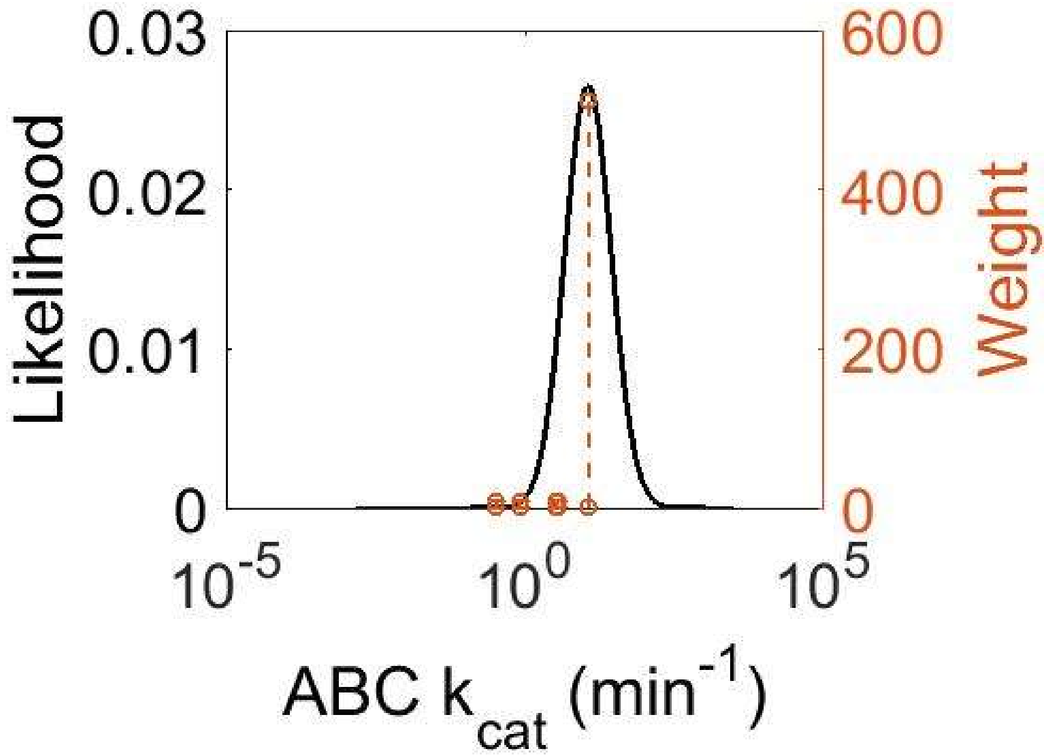


Figure SF.10.18.1.1.1. The estimated probability distribution for ABC k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.18.1.2. Parameter: ABC K_{ms}

Parameter values for the ABC K_{ms} of Reaction 39 were obtained from the literature and summarised in Table ST.10.18.1.2.1. The log-normal distribution properties for the ABC K_{ms} of Reaction 39 are shown in Table ST.10.18.1.2.2 and plotted in Figure SF.10.18.1.2.1.

Table ST.10.18.1.2.1. Literature information used to design the ABC K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.09 x10^{-2}	4.10 x10^{-3}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
3.66 x10^{-5}	3.80 x10^{-6}	Unknown	H69AR plasma membrane	MRP1	7.4	37		**128**	0	(Mao et al., 2000)
5.30 x10^{-3}	2.60 x10^{-3}	Human	HEK293 cells	MRP3	7.4	37		**128**	0	(Zeng et al., 2000)
1.95 x10^{-1}	6.12 x10^{-2}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
1.10 x10^{-1}	3.91 x10^{-2}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
2.07 x10^{-2}	NaN	Human	HepG2 hepatoma	ABCB1	7.4	37		**2048**	0	(Fong et al., 2007)

Table ST.10.18.1.2.2. The log-normal distribution properties of the ABC K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
2.10×10^{-2}	2.37×10^{1}	-2.60	1.12

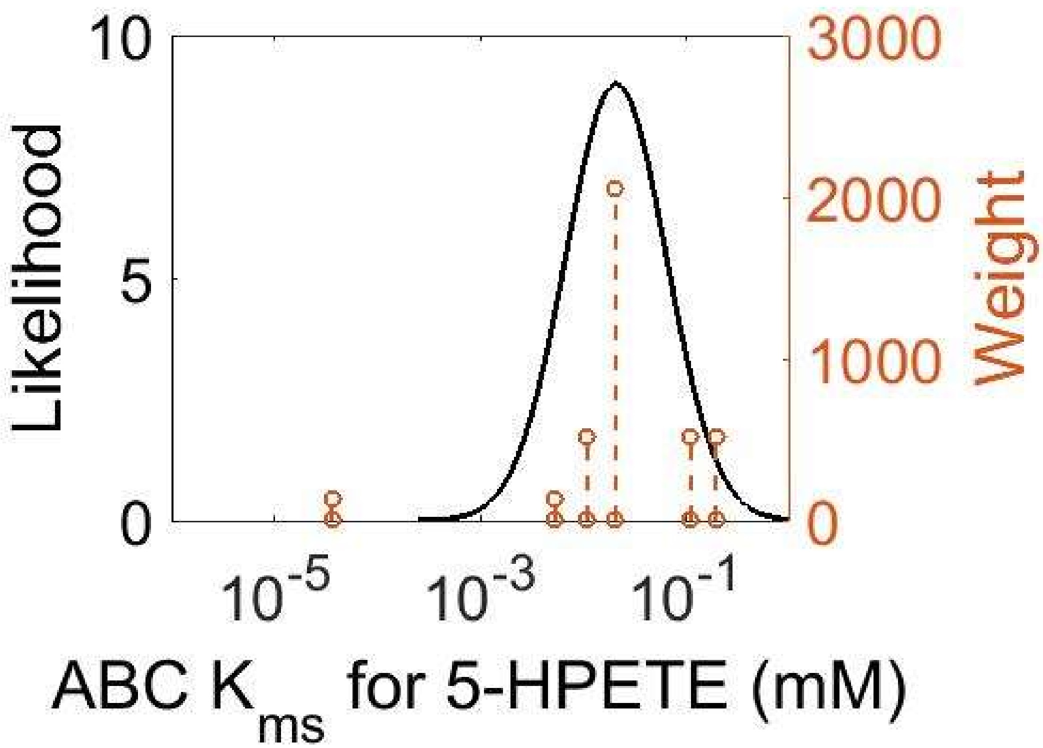


Figure SF.10.18.1.2.1. The estimated probability distribution for ABC K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.18.1.3. Parameter: ABC concentration

Parameter values for the ABC concentration of Reaction 39 were obtained from the literature and summarised in Table ST.10.18.1.3.1. The log-normal distribution properties for the ABC concentration of Reaction 39 are shown in Table ST.10.18.1.3.2 and plotted in Figure SF.10.18.1.3.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.10.18.1.3.1. Literature information used to design the ABC concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
5.15	NaN	Human	Stomach	ABC	7.5	37		2048	0	(Wilhelm et al., 2014)
5.94	NaN	Human	Lung	ABC	7.5	37		2048	0	(Kim et al., 2014)
2.66	NaN	Human	Gut	ABC	7.5	37		2048	0	(Kim et al., 2014)

Table ST.10.18.1.3.2. The log-normal distribution properties of the ABC concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
5.06	2.80×10^{-5}	1.44	1.74	3.42×10^{-1}

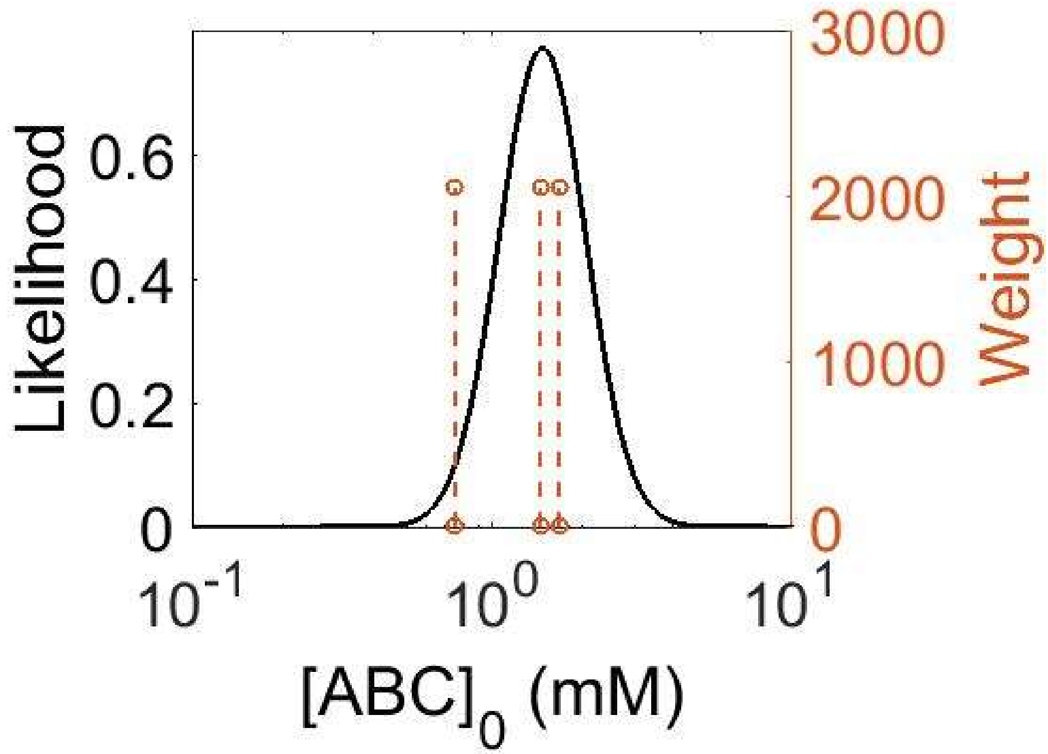


Figure SF.10.18.1.3.1. The estimated probability distribution for the ABC concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.19. Reaction 40: 5-HETE ⇌ ex5-HETE
5-HETE is relocated from the intracellular compartment to the extracellular compartment via the ATP-binding cassette (ABC) transporter.

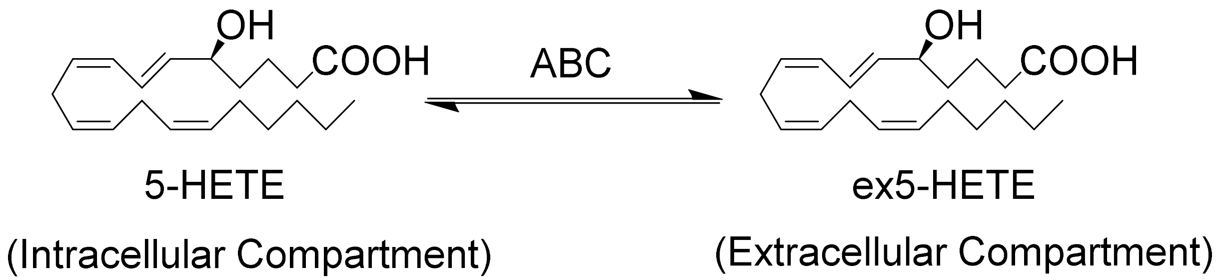


Figure SF.10.19. The transport of 5-hydroxyeicosatetraenoic acid (5-HETE) from the intracellular compartment to the extracellular compartment by ATP Binding Cassette protein (ABC) (Reaction 40).

SEq.10.19. Reaction rate law for Reaction 40.

$$\boldsymbol{v_{40}} = [\boldsymbol{ABC}] \cdot \boldsymbol{k_{cat}} \cdot \frac{\mathbf{5{-}HETE}/K_m \cdot \left(1 - \frac{\mathbf{ex5{-}HETE}}{\mathbf{5{-}HETE} \cdot e^{-0.5\cdot\left(G + R\cdot T\cdot \ln\left(\frac{ATP}{ADP}\right)\right)/R\cdot T}}\right)}{1 + \frac{\mathbf{5{-}HETE}}{K_m} + \frac{\mathbf{ex5{-}HETE}}{K_m} + \mathbf{ABC\_CI}}$$

S.10.19.1. Reaction parameters

S.10.19.1.1. Parameter: ABC k_{cat}

Parameter values for the ABC k_{cat} of Reaction 40 were obtained from the literature and summarised in Table ST.10.19.1.1.1. The log-normal distribution properties for the ABC k_{cat} of Reaction 40 are shown in Table ST.10.19.1.1.2 and plotted in Figure SF.10.19.1.1.1.

Table ST.10.19.1.1.1. Literature information used to design the ABC k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
3.50	NaN	Bacteria	E. coli.	Glucose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Waygood and Steeves, 1980)
3.30×10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
8.30×10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
3.28	NaN	Yeast	Saccharomyces cerevisiae	HXT7 transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Ye et al., 2001)
1.13×10^{1}		Primate	Baculovirus	MRP2	7	37		512		(Yasunaga et al., 2008)

Table ST.10.19.1.1.2. The log-normal distribution properties of the ABC k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.13 $x10^{1}$	1.00 $x10^{1}$	3.22	8.9110^{-1}

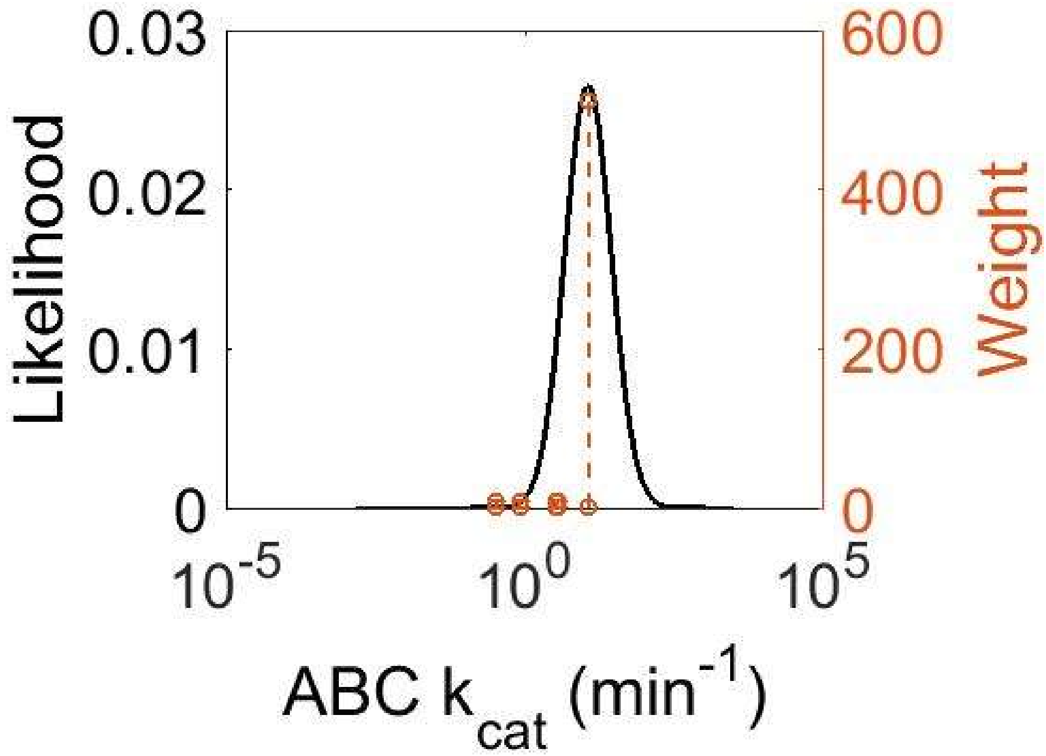


Figure SF.10.19.1.1.1. The estimated probability distribution for ABC k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.19.1.2. Parameter: ABC K_{ms}

Parameter values for the ABC K_{ms} of Reaction 40 were obtained from the literature and summarised in Table ST.10.19.1.2.1. The log-normal distribution properties for the ABC K_{ms} of Reaction 40 are shown in Table ST.10.19.1.2.2 and plotted in Figure SF.10.19.1.2.1.

Table ST.10.19.1.2.1. Literature information used to design the ABC K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.09×10^{-2}	4.10×10^{-3}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
3.66×10^{-5}	3.80×10^{-6}	Unknown	H69AR plasma membrane	MRP1	7.4	37		**128**	0	(Mao et al., 2000)
5.30×10^{-3}	2.60×10^{-3}	Human	HEK293 cells	MRP3	7.4	37		**128**	0	(Zeng et al., 2000)
1.95×10^{-1}	6.12×10^{-2}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
1.10×10^{-1}	3.91×10^{-2}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
2.07×10^{-2}	NaN	Human	HepG2 hepatoma	ABCB1	7.4	37		**2048**	0	(Fong et al., 2007)

Table ST.10.19.1.2.2. The log-normal distribution properties of the ABC K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
2.10×10^{-2}	2.37×10^{1}	-2.60	1.12

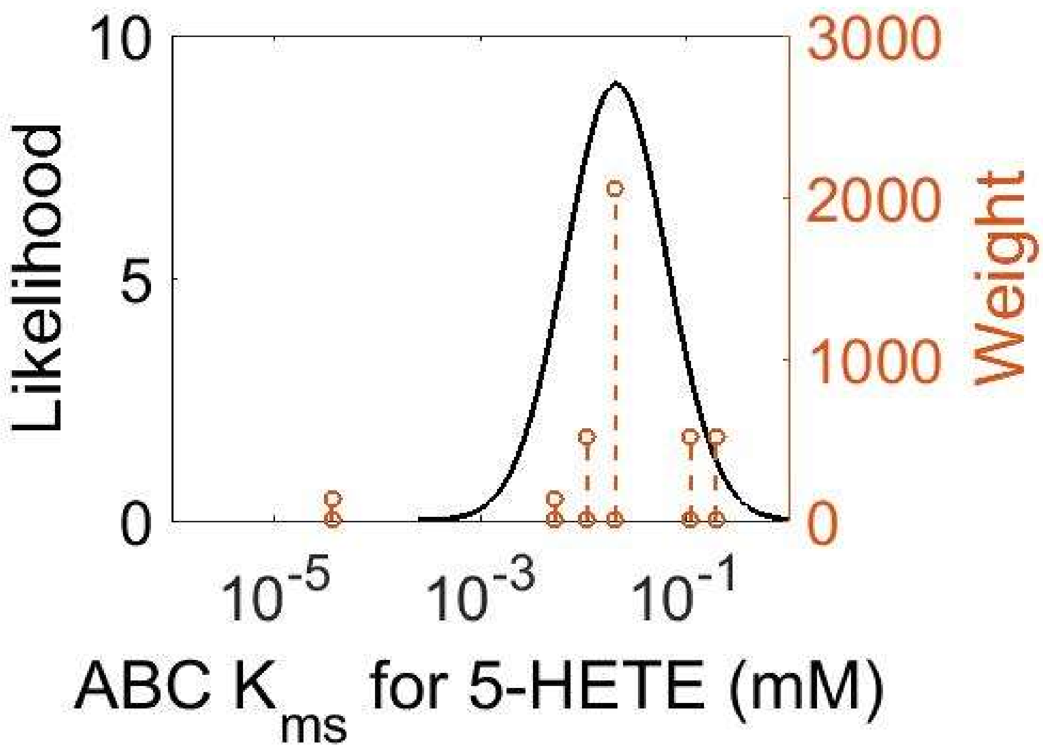


Figure SF.10.19.1.2.1. The estimated probability distribution for ABC K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.19.1.3. Parameter: ABC concentration

Parameter values for the ABC concentration of Reaction 40 were obtained from the literature and summarised in Table ST.10.19.1.3.1. The log-normal distribution properties for the ABC concentration of Reaction 40 are shown in Table ST.10.19.1.3.2 and plotted in Figure SF.10.19.1.3.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.10.19.1.3.1. Literature information used to design the ABC concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
5.15	NaN	Human	Stomach	ABC	7.5	37		2048	0	(Wilhelm et al., 2014)
5.94	NaN	Human	Lung	ABC	7.5	37		2048	0	(Kim et al., 2014)
2.66	NaN	Human	Gut	ABC	7.5	37		2048	0	(Kim et al., 2014)

Table ST.10.19.1.3.2. The log-normal distribution properties of the ABC concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
5.06	2.80×10^{-5}	1.44	1.74	3.4210^{-1}

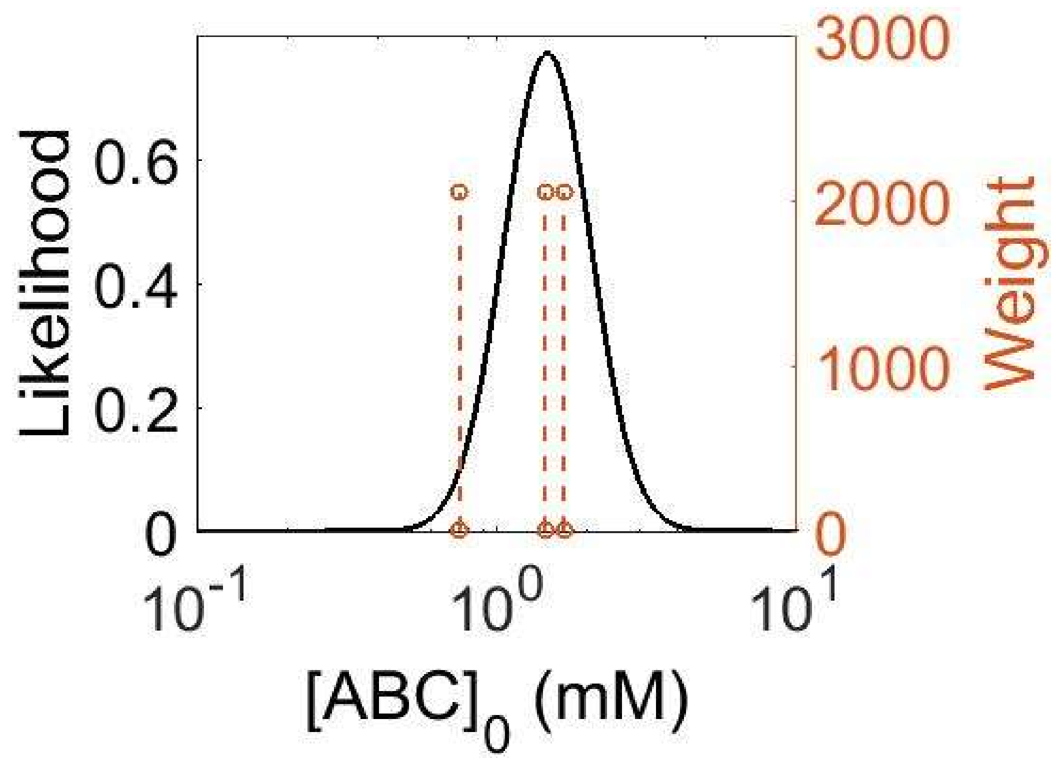


Figure SF.10.19.1.3.1. The estimated probability distribution for the ABC concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.20. Reaction 41: $LTA_4 \rightleftharpoons exLTA_4$

LTA_4 is relocated from the intracellular compartment to the extracellular compartment via the ATP-binding cassette (ABC) transporter.

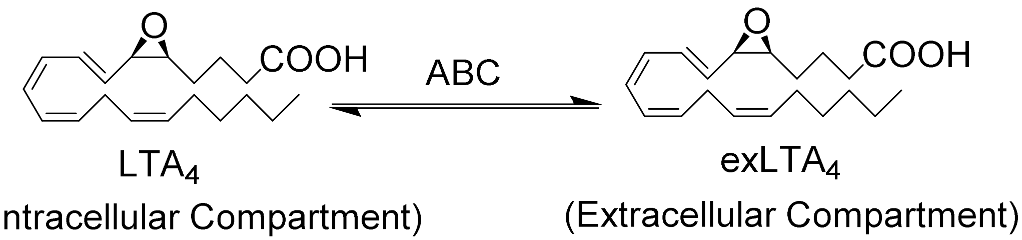


Figure SF.10.20. The transport of leukotriene A_4 (LTA_4) from the intracellular compartment to the extracellular compartment by ATP Binding Cassette protein (ABC) (Reaction 41).

SEq.10.20. Reaction rate law for Reaction 41.

$$\boldsymbol{v_{41}} = [\boldsymbol{ABC}] \cdot \boldsymbol{k_{cat}} \cdot \frac{\mathbf{LTA_4}/K_m \cdot \left(1 - \frac{\mathbf{exLTA_4}}{\mathbf{LTA_4} \cdot e^{-0.5 \cdot \left(G + R \cdot T \cdot \ln\left(\frac{ATP}{ADP}\right)\right)/R \cdot T}}\right)}{1 + \frac{\mathbf{LTA_4}}{K_m} + \frac{\mathbf{exLTA_4}}{K_m} + \mathbf{ABC\_CI}}$$

S.10.20.1. Reaction parameters

S.10.20.1.1. Parameter: ABC k_{cat}

Parameter values for the ABC k_{cat} of Reaction 41 were obtained from the literature and summarised in Table ST.10.20.1.1.1. The log-normal distribution properties for the ABC k_{cat} of Reaction 41 are shown in Table ST.10.20.1.1.2 and plotted in Figure SF.10.20.1.1.1.

Table ST.10.20.1.1.1. Literature information used to design the ABC k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
3.50	NaN	Bacteria	E. coli.	Glucose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Waygood and Steeves, 1980)
3.30×10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
8.30×10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
3.28	NaN	Yeast	Saccharomyces cerevisiae	HXT7 transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Ye et al., 2001)
1.13×10^{1}		Primate	Baculovirus	MRP2	7	37		512		(Yasunaga et al., 2008)

Table ST.10.20.1.1.2. The log-normal distribution properties of the ABC k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
1.13×10^{1}	1.00×10^{1}	3.22	8.91×10^{-1}

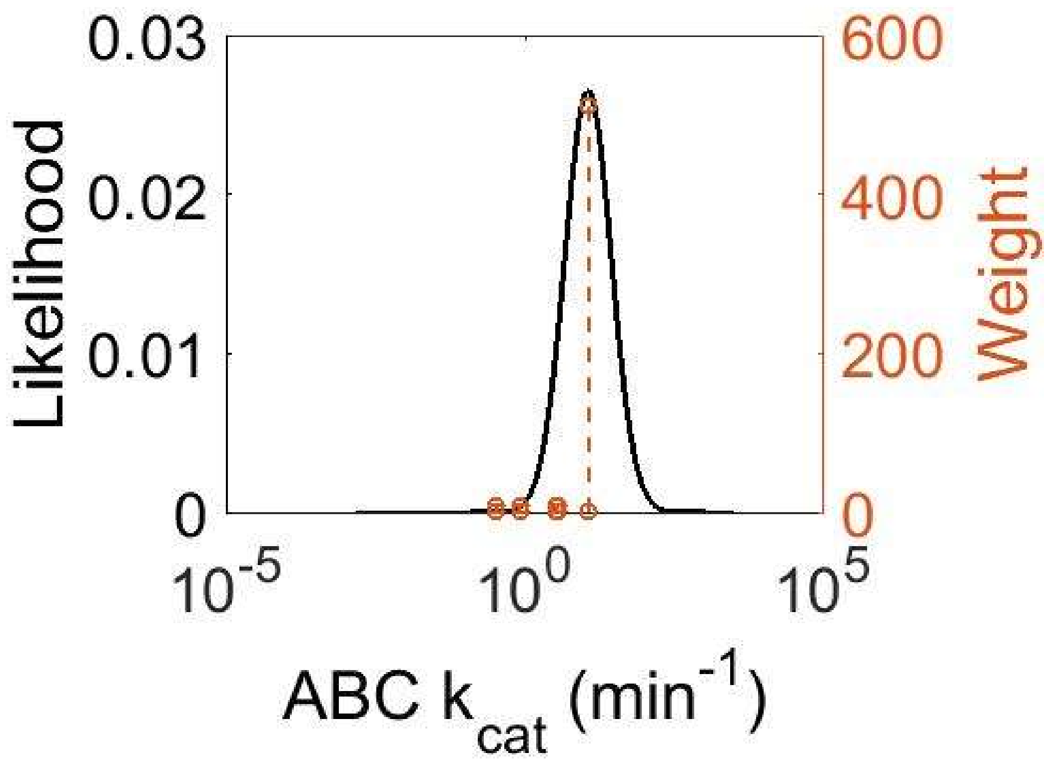


Figure SF.10.20.1.1.1. The estimated probability distribution for ABC k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.20.1.2. Parameter: ABC K_{ms}

Parameter values for the ABC K_{ms} of Reaction 41 were obtained from the literature and summarised in Table ST.10.20.1.2.1. The log-normal distribution properties for the ABC K_{ms} of Reaction 41 are shown in Table ST.10.20.1.2.2 and plotted in Figure SF.10.20.1.2.1.

Table ST.10.20.1.2.1. Literature information used to design the ABC K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.09×10^{-2}	4.10×10^{-3}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
3.66×10^{-5}	3.80×10^{-6}	Unknown	H69AR plasma membrane	MRP1	7.4	37		**128**	0	(Mao et al., 2000)
5.30×10^{-3}	2.60×10^{-3}	Human	HEK293 cells	MRP3	7.4	37		**128**	0	(Zeng et al., 2000)
1.95×10^{-1}	6.12×10^{-2}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
1.10×10^{-1}	3.91×10^{-2}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
2.07×10^{-2}	NaN	Human	HepG2 hepatoma	ABCB1	7.4	37		**2048**	0	(Fong et al., 2007)

Table ST.10.20.1.2.2. The log-normal distribution properties of the ABC K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
2.10 $x10^{-2}$	2.37 $x10^{1}$	-2.60	1.12

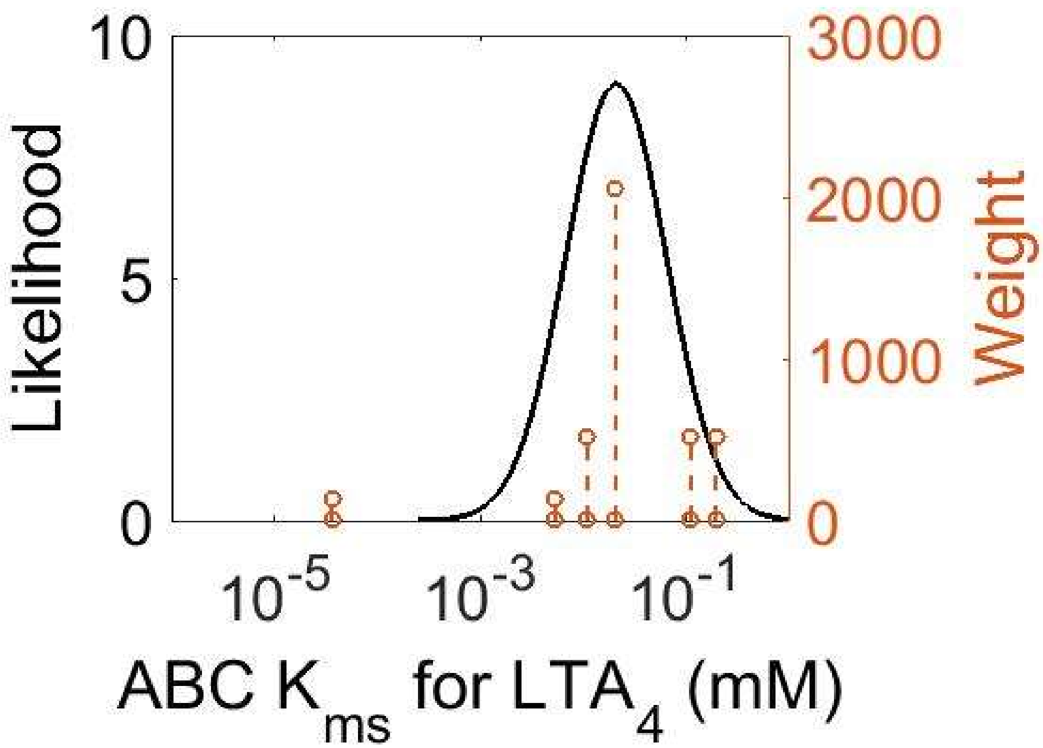


Figure SF.10.20.1.2.1. The estimated probability distribution for ABC K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.20.1.3. Parameter: ABC concentration

Parameter values for the ABC concentration of Reaction 41 were obtained from the literature and summarised in Table ST.10.20.1.3.1. The log-normal distribution properties for the ABC concentration of Reaction 41 are shown in Table ST.10.20.1.3.2 and plotted in Figure SF.10.20.1.3.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.10.20.1.3.1. Literature information used to design the ABC concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
5.15	NaN	Human	Stomach	ABC	7.5	37		2048	0	(Wilhelm et al., 2014)
5.94	NaN	Human	Lung	ABC	7.5	37		2048	0	(Kim et al., 2014)
2.66	NaN	Human	Gut	ABC	7.5	37		2048	0	(Kim et al., 2014)

Table ST.10.20.1.3.2. The log-normal distribution properties of the ABC concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
5.06	2.80×10^{-5}	1.44	1.74	3.42 x10-1

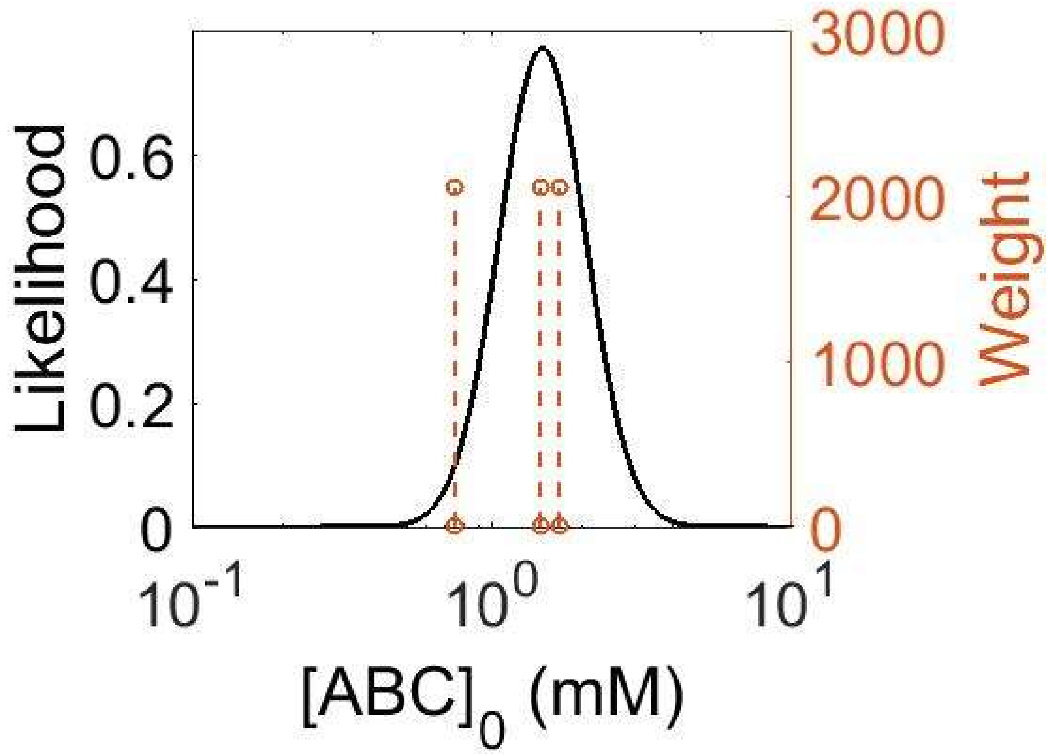


Figure SF.10.20.1.3.1. The estimated probability distribution for the ABC concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.21. Reaction 42: AA ⇌ exAA

AA is relocated from the intracellular compartment to the extracellular compartment via the ATP-binding cassette (ABC) transporter.

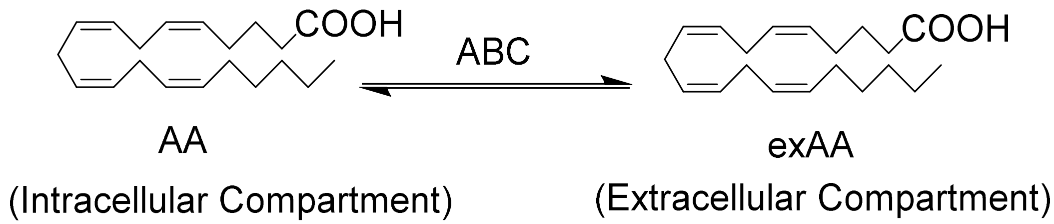


Figure SF.10.21. The transport of arachidonic acid (AA) from the intracellular compartment to the extracellular compartment by ATP Binding Cassette protein (ABC) (Reaction 42).

SEq.10.21. Reaction rate law for Reaction 42.

$$\boldsymbol{v_{42}} = [\boldsymbol{ABC}] \cdot \boldsymbol{k_{cat}} \cdot \frac{\mathbf{AA}/K_m \cdot \left(1 - \dfrac{\mathbf{exAA}}{\mathbf{AA} \cdot e^{-0.5 \cdot \left(G + R \cdot T \cdot \ln\left(\frac{ATP}{ADP}\right)\right)/R \cdot T}}\right)}{1 + \frac{\mathbf{AA}}{K_m} + \frac{\mathbf{exAA}}{K_m} + \mathbf{ABC\_CI}}$$

S.10.21.1. Reaction parameters

S.10.21.1.1. Parameter: ABC k_{cat}

Parameter values for the ABC k_{cat} of Reaction 42 were obtained from the literature and summarised in Table ST.10.21.1.1.1. The log-normal distribution properties for the ABC k_{cat} of Reaction 42 are shown in Table ST.10.21.1.1.2 and plotted in Figure SF.10.21.1.1.1.

Table ST.10.21.1.1.1. Literature information used to design the ABC k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
3.50	NaN	Bacteria	E. coli.	Glucose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Waygood and Steeves, 1980)
3.30×10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
8.30×10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
3.28	NaN	Yeast	Saccharomyces cerevisiae	HXT7 transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Ye et al., 2001)
1.13×10^{1}		Primate	Baculovirus	MRP2	7	37		512		(Yasunaga et al., 2008)

Table ST.10.21.1.1.2. The log-normal distribution properties of the ABC k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.13 $x10^{1}$	1.00 $x10^{1}$	3.22	8.9110^{-1}

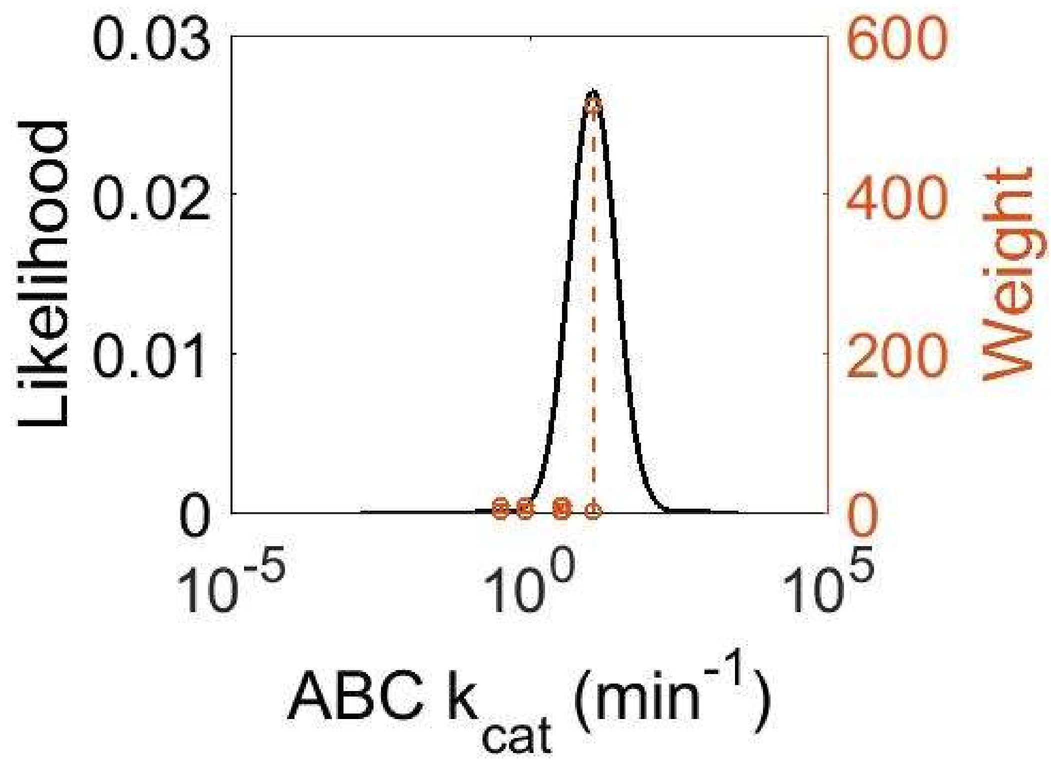


Figure SF.10.21.1.1.1. The estimated probability distribution for ABC k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.21.1.2. Parameter: ABC K_{ms}

In this model numerous simplifications have been made and as a result, metabolites, such as AA, occur in higher concentrations than are found in reality. To prevent a large percentage of AA being exported before it is metabolised, the K_{ms} of the ABC transporter has been increased (mode= 25 mM, CIF=10, μ = 4.01, σ = 0.89) (Table ST.10.21.1.2.1.). This is plotted in Figure SF.10.21.1.2.1.

Table ST.10.21.1.2.1. The log-normal distribution properties of the ABC K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
25	10	4.01	0.89

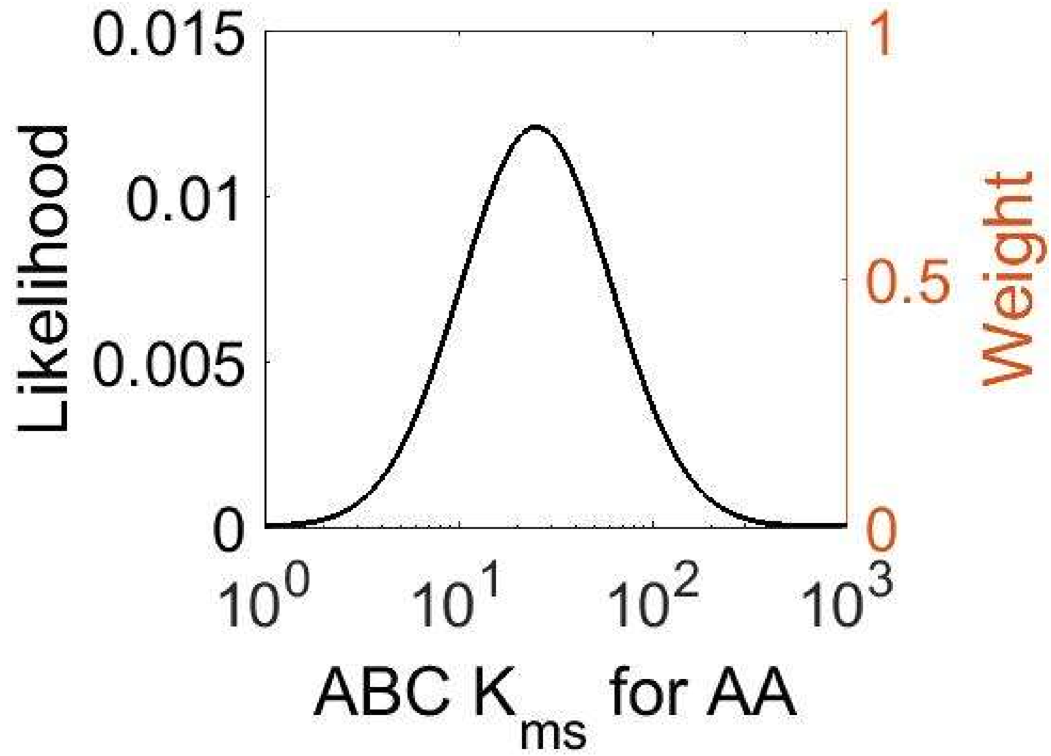


Figure SF.10.21.1.2.1. The estimated probability distribution for ABC K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.21.1.3. Parameter: ABC concentration

Parameter values for the ABC concentration of Reaction 42 were obtained from the literature and summarised in Table ST.10.21.1.3.1. The log-normal distribution properties for the ABC concentration of Reaction 42 are shown in Table ST.10.21.1.3.2 and plotted in Figure SF.10.21.1.3.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.10.21.1.3.1. Literature information used to design the ABC concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
5.15	NaN	Human	Stomach	ABC	7.5	37		2048	0	(Wilhelm et al., 2014)
5.94	NaN	Human	Lung	ABC	7.5	37		2048	0	(Kim et al., 2014)
2.66	NaN	Human	Gut	ABC	7.5	37		2048	0	(Kim et al., 2014)

Table ST.10.21.1.3.2. The log-normal distribution properties of the ABC concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
5.06	2.80×10^{-5}	1.44	1.74	3.42×10^{-1}

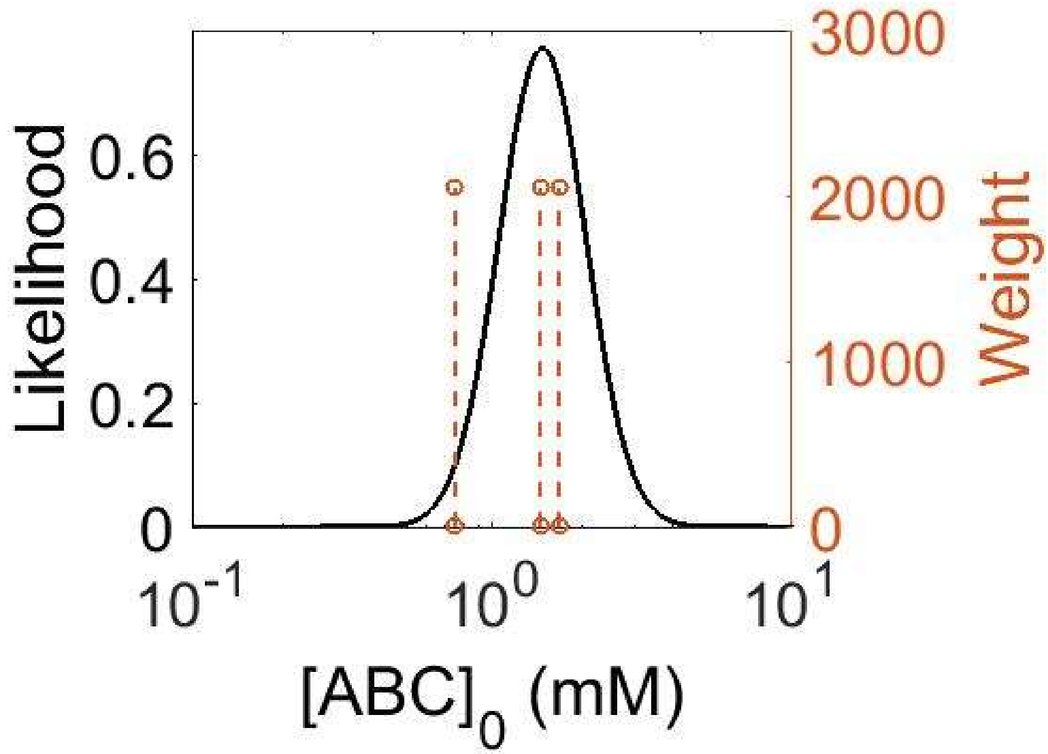
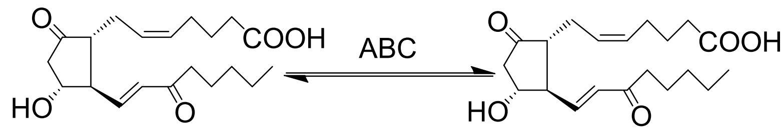


Figure SF.10.21.1.3.1. The estimated probability distribution for the ABC concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.22. Reaction 67: 15-keto-PGE$_2$ ⇌ ex15-keto-PGE$_2$

15-keto-PGE$_2$ is relocated from the intracellular compartment to the extracellular compartment via the ATP-binding cassette (ABC) transporter.



15-keto-PGE$_2$
(Intracellular Compartment)

ex15-keto-PGE$_2$
(Extracellular Compartment)

Figure SF.10.22. The transport of 15-keto-prostaglandin E$_2$ (15-keto-PGE$_2$) from the intracellular compartment to the extracellular compartment by ATP Binding Cassette protein (ABC) (Reaction 67).

SEq.10.22. Reaction rate law for Reaction 67.

$$\boldsymbol{v_{67}} = [\boldsymbol{ABC}] \cdot \boldsymbol{k_{cat}} \cdot \frac{\text{15-keto-PGE}_2/K_m \cdot \left(1 - \frac{\text{ex15-keto-PGE}_2}{\text{15-keto-PGE}_2 \cdot e^{-0.5 \cdot \left(G + R \cdot T \cdot \ln\left(\frac{ATP}{ADP}\right)\right)/R \cdot T}}\right)}{1 + \frac{\text{15-keto-PGE}_2}{K_m} + \frac{ex\text{15-keto-PGE}_2}{K_m} + ABC\_CI}$$

S.10.22.1. Reaction parameters

S.10.22.1.1. Parameter: ABC k_{cat}

Parameter values for the ABC k_{cat} of Reaction 67 were obtained from the literature and summarised in Table ST.10.22.1.1.1. The log-normal distribution properties for the ABC k_{cat} of Reaction 67 are shown in Table ST.10.22.1.1.2 and plotted in Figure SF.10.22.1.1.1.

Table ST.10.22.1.1.1. Literature information used to design the ABC k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
3.50	NaN	Bacteria	E. coli.	Glucose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Waygood and Steeves, 1980)
3.30×10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
8.30×10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
3.28	NaN	Yeast	Saccharomyces cerevisiae	HXT7 transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Ye et al., 2001)
1.13×10^{1}		Primate	Baculovirus	MRP2	7	37		512		(Yasunaga et al., 2008)

Table ST.10.22.1.1.2. The log-normal distribution properties of the ABC k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
1.14×10^{1}	9.86	3.22	8.87×10^{-1}

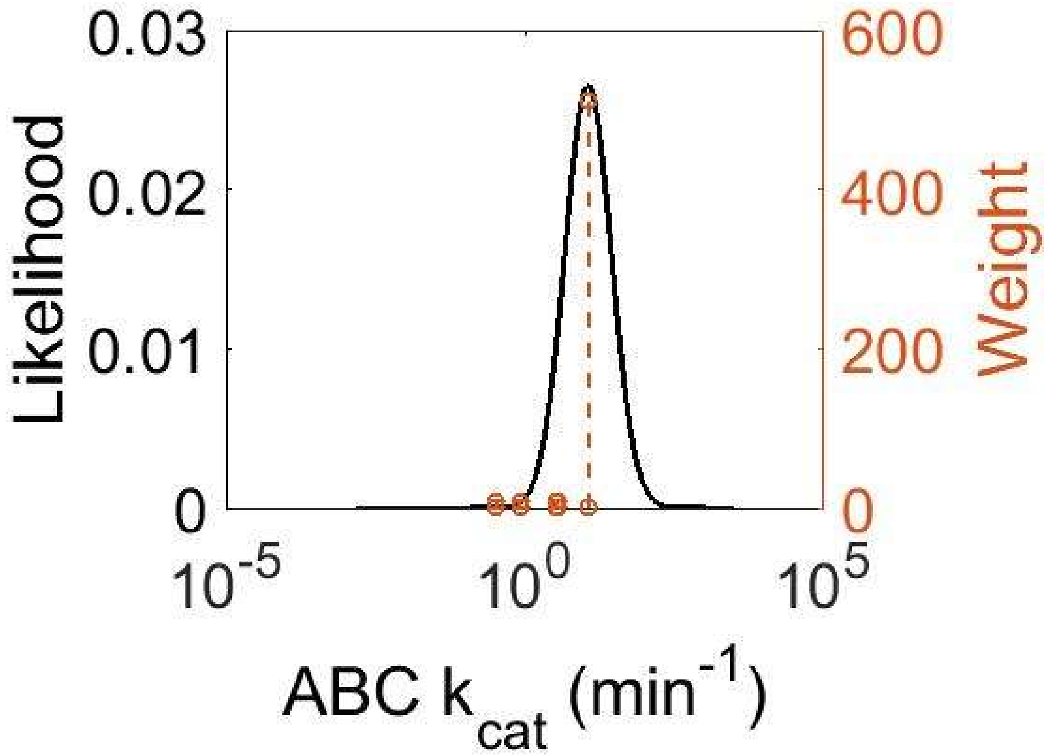


Figure SF.10.22.1.1.1. The estimated probability distribution for ABC k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.22.1.2. Parameter: ABC K_{ms}

Parameter values for the ABC K_{ms} of Reaction 67 were obtained from the literature and summarised in Table ST.10.22.1.2.1. The log-normal distribution properties for the ABC K_{ms} of Reaction 67 are shown in Table ST.10.22.1.2.2 and plotted in Figure SF.10.22.1.2.1.

Table ST.10.22.1.2.1. Literature information used to design the ABC K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.09×10^{-2}	4.10×10^{-3}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
3.66×10^{-5}	3.80×10^{-6}	Unknown	H69AR plasma membrane	MRP1	7.4	37		**128**	0	(Mao et al., 2000)
5.30×10^{-3}	2.60×10^{-3}	Human	HEK293 cells	MRP3	7.4	37		**128**	0	(Zeng et al., 2000)
1.95×10^{-1}	6.12×10^{-2}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
1.10×10^{-1}	3.91×10^{-2}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
2.07×10^{-2}	NaN	Human	HepG2 hepatoma	ABCB1	7.4	37		**2048**	0	(Fong et al., 2007)

Table ST.10.22.1.2.2. The log-normal distribution properties of the ABC K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
1.20 $x10^{-2}$	4.92	-3.97	8.7110^{-1}

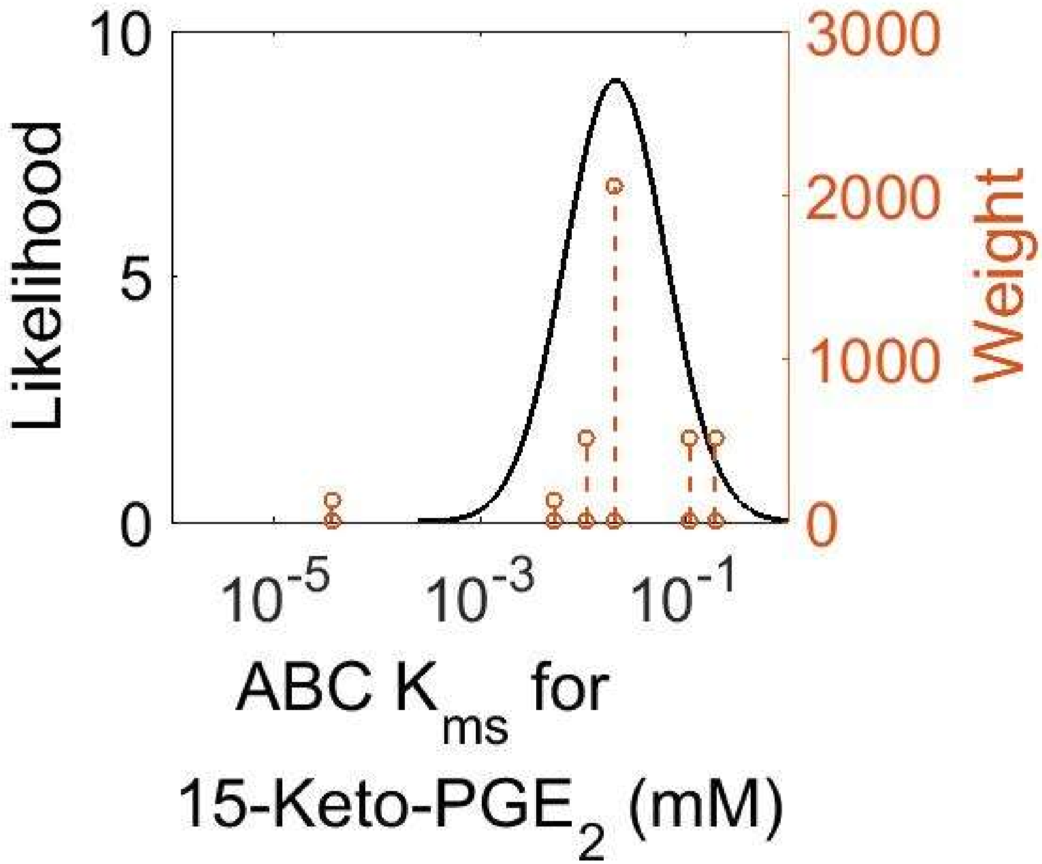


Figure SF.10.22.1.2.1. The estimated probability distribution for ABC K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.22.1.3. Parameter: ABC concentration

Parameter values for the ABC concentration of Reaction 67 were obtained from the literature and summarised in Table ST.10.22.1.3.1. The log-normal distribution properties for the ABC concentration of Reaction 67 are shown in Table ST.10.22.1.3.2 and plotted in Figure SF.10.22.1.3.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.10.22.1.3.1. Literature information used to design the ABC concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
5.15	NaN	Human	Stomach	ABC	7.5	37		2048	0	(Wilhelm et al., 2014)
5.94	NaN	Human	Lung	ABC	7.5	37		2048	0	(Kim et al., 2014)
2.66	NaN	Human	Gut	ABC	7.5	37		2048	0	(Kim et al., 2014)

Table ST.10.22.1.3.2. The log-normal distribution properties of the ABC concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
5.06	2.80×10^{-5}	1.44	1.74	3.42×10^{-1}

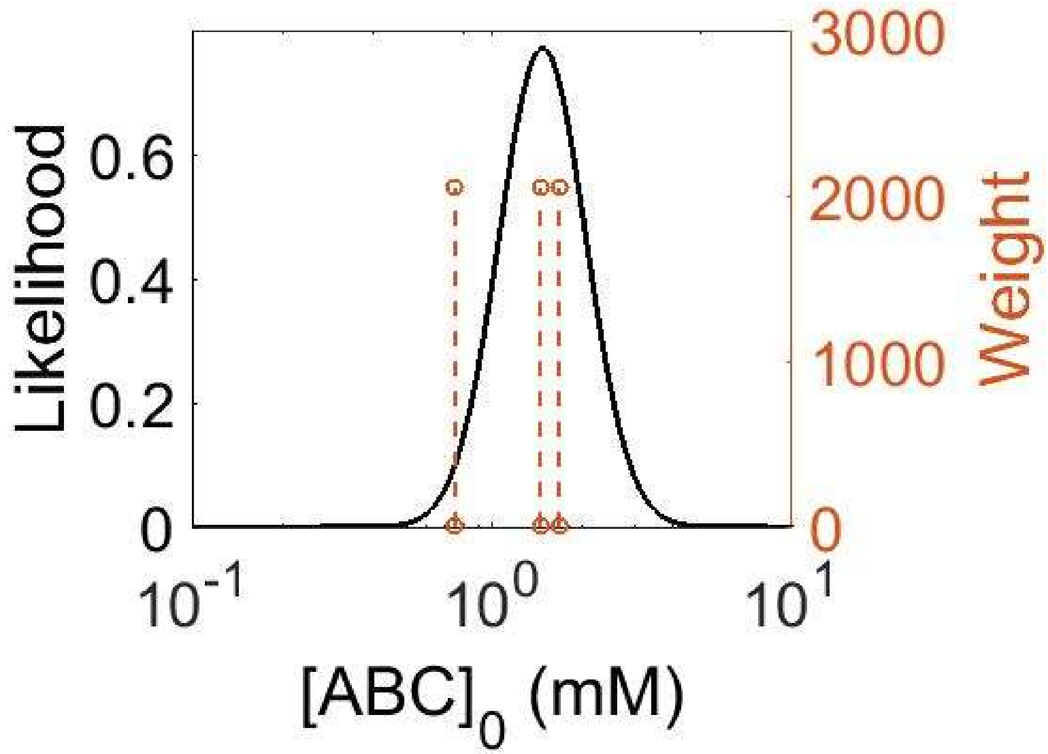


Figure SF.10.22.1.3.1. The estimated probability distribution for the ABC concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.23. Reaction 70: 13,14-dihydro-15-keto-PGE$_2$ ⇌ ex13,14-dihydro-15-keto-PGE$_2$

13,14-dihydro-15-keto-PGE$_2$ is relocated from the intracellular compartment to the extracellular compartment via the ATP-binding cassette (ABC) transporter.

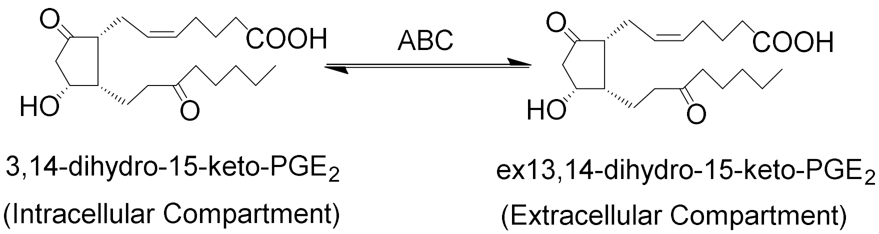


Figure SF.10.23. The transport of 13,14-dihydro-15-keto-prostaglandin E$_2$ (13,14-dihydro-15-keto-PGE$_2$) from the intracellular compartment to the extracellular compartment by ATP Binding Cassette protein (ABC) (Reaction 70).

SEq.10.23. Reaction rate law for Reaction 70.

$$v_{70} = [ABC] \cdot k_{cat} \cdot \frac{13,14-\text{dihydro}-15-\text{keto}-\text{PGE}_2 / K_m \cdot \left(1 - \frac{ex13,14-\text{dihydro}-15-\text{keto}-\text{PGE}_2}{13,14-\text{dihydro}-15-\text{keto}-\text{PGE}_2 \cdot e^{-0.5\cdot\left(G+R\cdot T\cdot \ln\left(\frac{ATP}{ADP}\right)\right)/R\cdot T}}\right)}{1 + \frac{13,14-\text{dihydro}-15-\text{keto}-\text{PGE}_2}{K_m} + \frac{ex13,14-\text{dihydro}-15-\text{keto}-\text{PGE}_2}{K_m} + ABC\_CI}$$

S.10.23.1. Reaction parameters

S.10.23.1.1. Parameter: ABC k_{cat}

Parameter values for the ABC k_{cat} of Reaction 70 were obtained from the literature and summarised in Table ST.10.23.1.1.1. The log-normal distribution properties for the ABC k_{cat} of Reaction 70 are shown in Table ST.10.23.1.1.2 and plotted in Figure SF.10.23.1.1.1.

Table ST.10.23.1.1.1. Literature information used to design the ABC k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
3.50	NaN	Bacteria	E. coli.	Glucose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Waygood and Steeves, 1980)
3.30×10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
8.30×10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
3.28	NaN	Yeast	Saccharomyces cerevisiae	HXT7 transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Ye et al., 2001)
1.13×10^{1}		Primate	Baculovirus	MRP2	7	37		512		(Yasunaga et al., 2008)

Table ST.10.23.1.1.2. The log-normal distribution properties of the ABC k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
1.13×10^{1}	1.00×10^{1}	3.22	8.91×10^{-1}

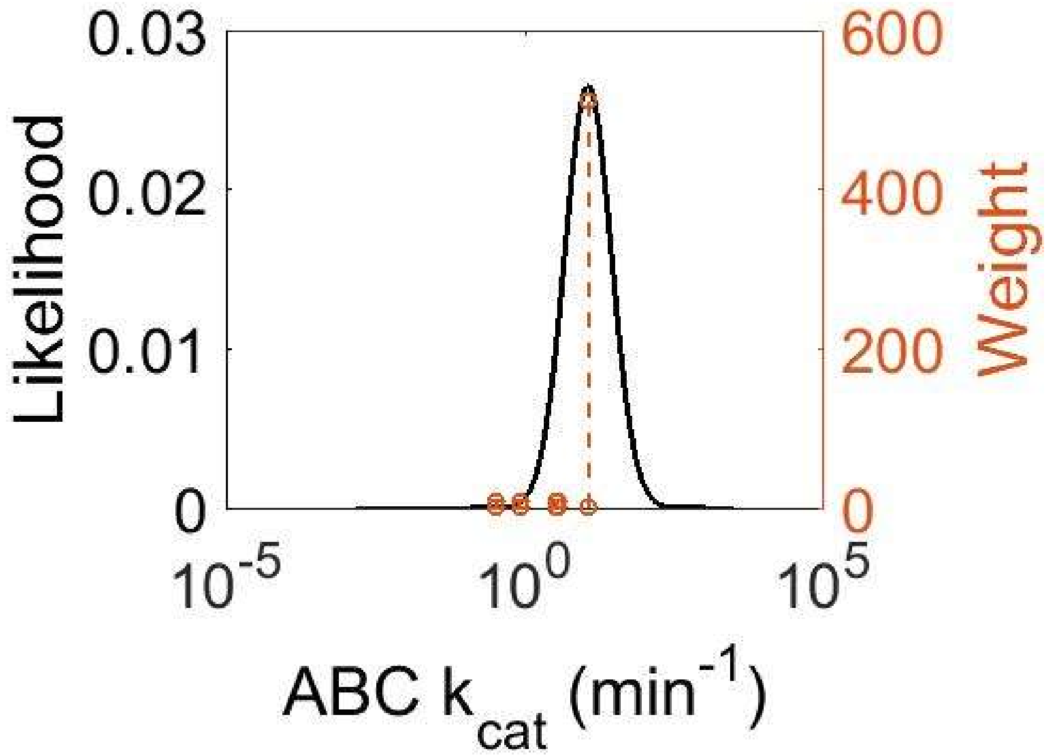


Figure SF.10.23.1.1.1. The estimated probability distribution for ABC k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.23.1.2. Parameter: ABC K_{ms}

Parameter values for the ABC K_{ms} of Reaction 70 were obtained from the literature and summarised in Table ST.10.23.1.2.1. The log-normal distribution properties for the ABC K_{ms} of Reaction 70 are shown in Table ST.10.23.1.2.2 and plotted in Figure SF.10.23.1.2.1.

Table ST.10.23.1.2.1. Literature information used to design the ABC K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
1.09×10^{-2}	4.10×10^{-3}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
3.66×10^{-5}	3.80×10^{-6}	Unknown	H69AR plasma membrane	MRP1	7.4	37		**128**	0	(Mao et al., 2000)
5.30×10^{-3}	2.60×10^{-3}	Human	HEK293 cells	MRP3	7.4	37		**128**	0	(Zeng et al., 2000)
1.95×10^{-1}	6.12×10^{-2}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
1.10×10^{-1}	3.91×10^{-2}	Human	Primate	MRP2	7	37		**512**	0	(Yasunaga et al., 2008)
2.07×10^{-2}	NaN	Human	HepG2 hepatoma	ABCB1	7.4	37		**2048**	0	(Fong et al., 2007)

Table ST.10.23.1.2.2. The log-normal distribution properties of the ABC K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
2.10×10^{-2}	2.37×10^{1}	-2.60	1.12

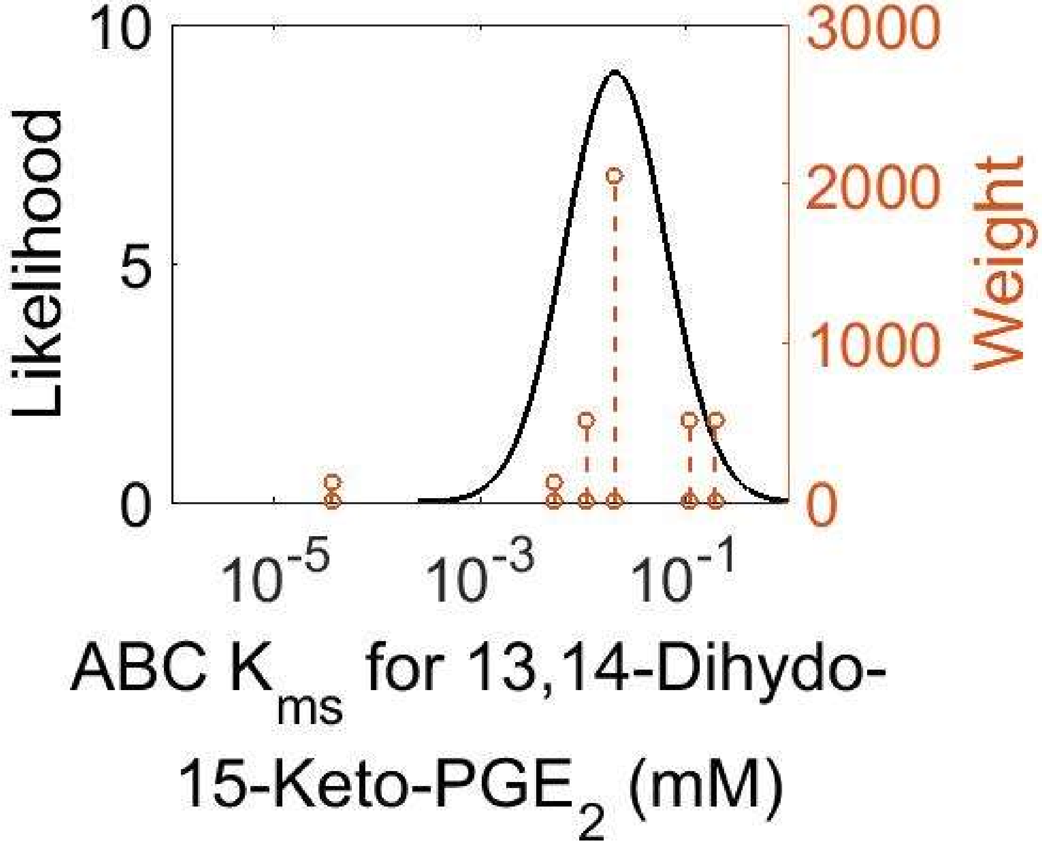


Figure SF.10.23.1.2.1. The estimated probability distribution for ABC K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.23.1.3. Parameter: ABC concentration

Parameter values for the ABC concentration of Reaction 70 were obtained from the literature and summarised in Table ST.10.23.1.3.1. The log-normal distribution properties for the ABC concentration of Reaction 70 are shown in Table ST.10.23.1.3.2 and plotted in Figure SF.10.23.1.3.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.10.23.1.3.1. Literature information used to design the ABC concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
5.15	NaN	Human	Stomach	ABC	7.5	37		2048	0	(Wilhelm et al., 2014)
5.94	NaN	Human	Lung	ABC	7.5	37		2048	0	(Kim et al., 2014)
2.66	NaN	Human	Gut	ABC	7.5	37		2048	0	(Kim et al., 2014)

Table ST.10.23.1.3.2. The log-normal distribution properties of the ABC concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
5.06	2.80×10^{-5}	1.44	1.74	3.42×10^{-1}

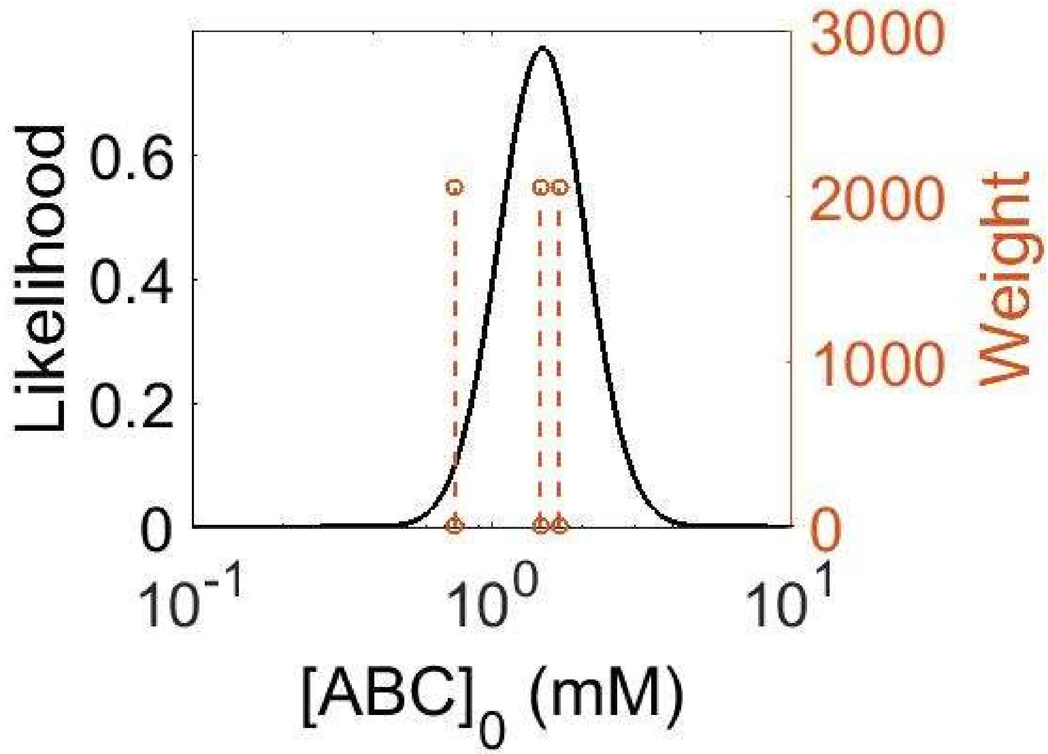


Figure SF.10.23.1.3.1. The estimated probability distribution for the ABC concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.24. Reaction 101: $PGF_{2\alpha} \rightleftharpoons exPGF_{2\alpha}$ (PGT)

$PGF_{2\alpha}$ is relocated from the intracellular compartment to the extracellular compartment via the prostaglandin (PGT) transporter.

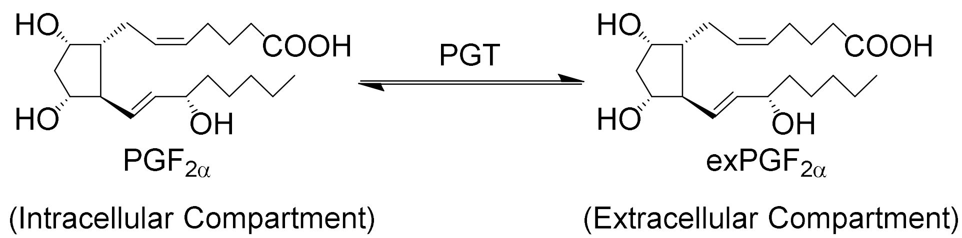


Figure SF.10.24. The transport of prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) from the intracellular compartment to the extracellular compartment by prostaglandin (PGT) transporter (Reaction 101).

SEq.10.24. Reaction rate law for Reaction 101.

$$\boldsymbol{v_{101}} = [\boldsymbol{PGT}] \cdot \boldsymbol{k_{cat}} \cdot \frac{{PGF_{2\alpha}}/{K_m} \cdot \left(1 - \frac{exPGF_{2\alpha}}{PGF_{2\alpha} \cdot e^{-0.5 \cdot \left(G + R \cdot T \cdot \ln\left(\frac{ATP}{ADP}\right)\right)/R \cdot T}}\right)}{1 + \frac{PGF_{2\alpha}}{K_m} + \frac{exPGF_{2\alpha}}{K_m} + \mathrm{PGT\_CI}}$$

S.10.24.1. Reaction parameters

S.10.24.1.1. Parameter: PGT k_{cat}

Parameter values for the PGT k_{cat} of Reaction 101 were obtained from the literature and summarised in Table ST.10.24.1.1.1. The log-normal distribution properties for the PGT k_{cat} of Reaction 101 are shown in Table ST.10.24.1.1.2 and plotted in Figure SF.10.24.1.1.1.

Table ST.10.24.1.1.1. Literature information used to design the PGT k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
3.50	NaN	Bacteria	E. coli.	Glucose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Waygood and Steeves, 1980)
3.30 x10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
8.30 x10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
3.28	NaN	Yeast	Saccharomyces cerevisiae	HXT7 transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Ye et al., 2001)

Table ST.10.24.1.1.2. The log-normal distribution properties of the PGT k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.33	7.30	9.20 $x10^{-1}$	8.0 $x10^{-1}$

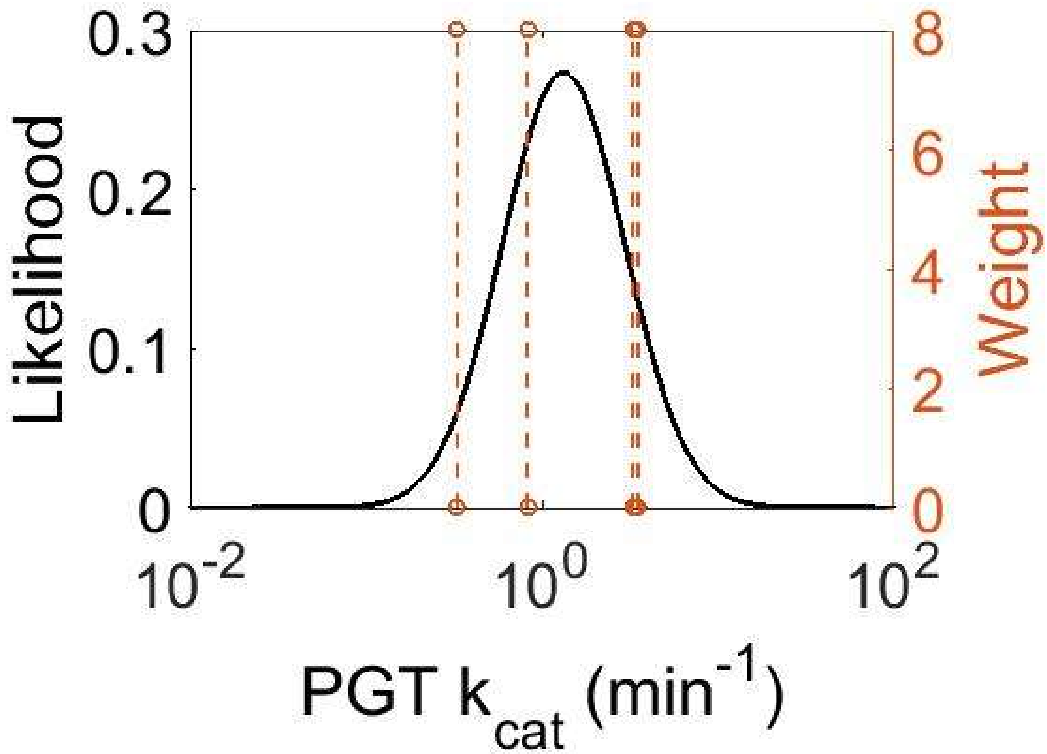


Figure SF.10.24.1.1.1. The estimated probability distribution for the PGT k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.24.1.2. Parameter: PGT K_{ms}

Parameter values for the PGT K_{ms} of Reaction 101 were obtained from the literature and summarised in Table ST.10.24.1.2.1. The log-normal distribution properties for the PGT K_{ms} of Reaction 101 are shown in Table ST.10.24.1.2.2 and plotted in Figure SF.10.24.1.2.1.

Table ST.10.24.1.2.1. Literature information used to design the PGT K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details							Weight	Type of error	Reference
		Substrate	Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
3.31×10^{-5}	1.31×10^{-4}		Human	Eye	PGT	7.5	37		512	0	(Gose et al., 2016)
3.76×10^{-4}	3.40×10^{-5}		Human	Embryonic kidney cells (HEK293)	PGT	Unknown	37		192	0	(Chi and Schuster, 2010)
5.40×10^{-3}	NaN		Human	Embryonic kidney cells (HEK293)	PGT	Unknown	37		2048	0	(Kraft et al., 2010)
7.20×10^{-3}	5.95×10^{-4}		Canine	Madin-Darby Canine Kidney Epithelial Cells (MDCK) cells	PGT	Unknown	Unknown		512	0	(Gose et al., 2016)

9.40 x10^{-5}	NaN	PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Kanai et al., 1995)
4.23 x10^{-4}	NaN	TXB2	Human	HeLa cells	PGT	7	27		**1024**	0	(Kanai et al., 1995)
7.57 x10^{-3}	NaN	6-keto-PGF1a	Human	HeLa cells	PGT	7	27		**1024**	0	(Kanai et al., 1995)
4.87 x10^{-5}	NaN	PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Itoh et al., 1996)
5.02 x10^{-5}	NaN	PGF2a	Human	HeLa cells	PGT	7	27		**1024**	0	(Itoh et al., 1996
5.00 x10^{-3}	NaN	15-keto-PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Itoh et al., 1996
5.00 x10^{-3}	NaN	13,14-dihydro-15-keto-PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Itoh et al., 1996
3.82 x10^{-5}	NaN	PGH2	Human	HeLa cells	PGT	7	27		**2048**	0	(Itoh et al., 1996

Table ST.10.24.1.2.2. The log-normal distribution properties of the PGT K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
1.10 x10^{-3}	9.42 x10^{1}	-4.67	1.45

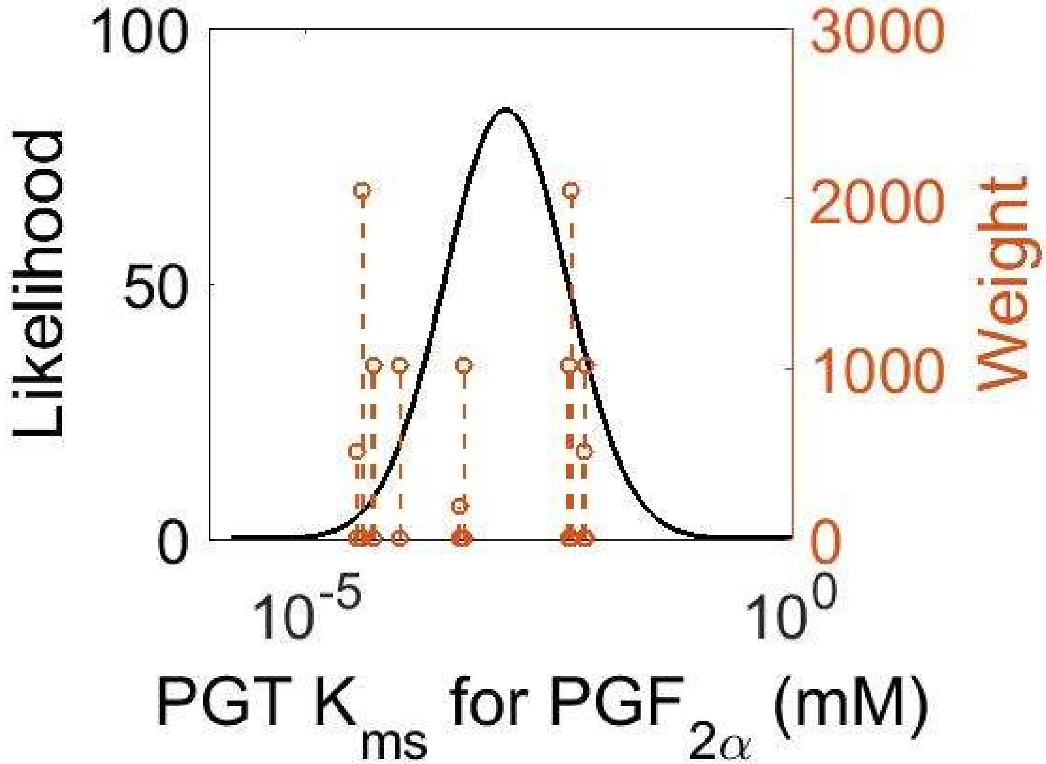


Figure SF.10.24.1.2.1. The estimated probability distribution for the PGT K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.24.1.3. Parameter: PGT concentration

Parameter values for the PGT concentration of Reaction 101 were obtained from the literature and summarised in Table ST.10.24.1.3.1. The log-normal distribution properties for the PGT concentration of Reaction 101 are shown in Table ST.10.24.1.3.2 and plotted in Figure SF.10.24.1.3.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.10.24.1.3.1. Literature information used to design the PGT concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
2.82	NaN	Human	Gut	PGT	7.5	37		2048	0	(Kim et al., 2014)
1.74 x10^{1}	NaN	Human	Oesophagus	PGT	7.5	37		2048	0	(Wilhelm et al., 2014)
1.25 x10^{2}	NaN	Human	Lung	PGT	7.5	37		2048	0	(Kim et al., 2014)

Table ST.10.24.1.3.2. The log-normal distribution properties of the PGT concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.73 x10^{1}	9.57 x10^{-5}	4.72	3.90	1.02

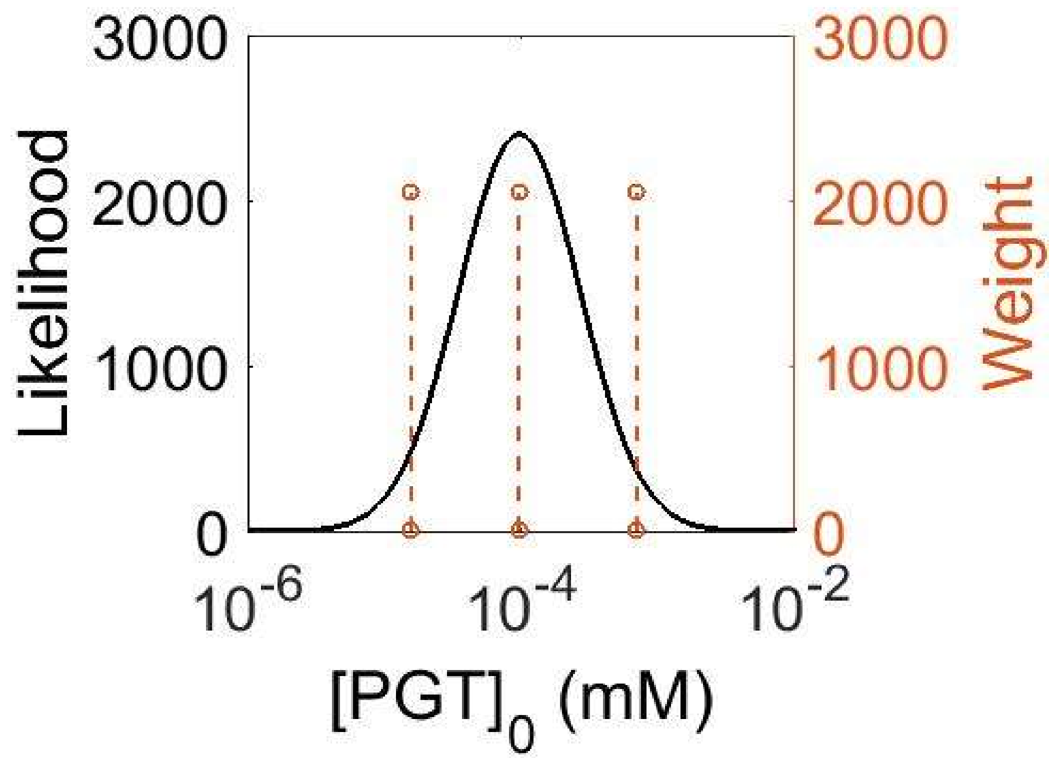


Figure SF.10.24.1.3.1. The estimated probability distribution for the PGT concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.25. Reaction 102: $PGE_2 \rightleftharpoons exPGE_2$ (PGT)

PGH_2 is relocated from the intracellular compartment to the extracellular compartment via the prostaglandin (PGT) transporter.

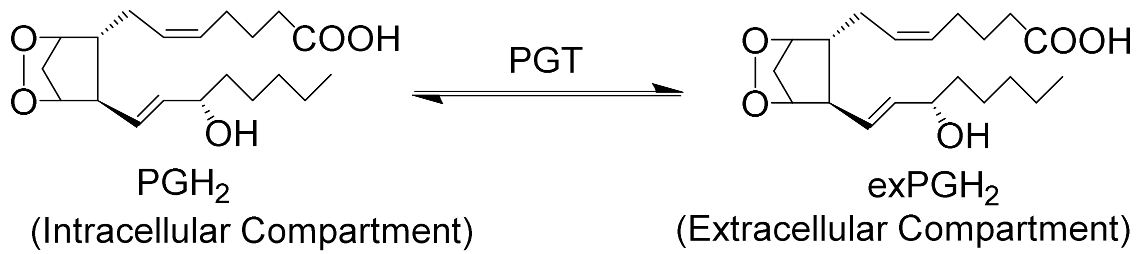


Figure SF.10.25. The transport of prostaglandin H_2 (PGH_2) from the intracellular compartment to the extracellular compartment by prostaglandin (PGT) transporter (Reaction 102).

SEq.10.25. Reaction rate law for Reaction 102.

$$\boldsymbol{v_{102}} = [\boldsymbol{PGT}] \cdot \boldsymbol{k_{cat}} \cdot \frac{\mathbf{PGE_2}/K_m \cdot \left(1 - \dfrac{ex\mathbf{PGE_2}}{\mathbf{PGE_2} \cdot e^{-0.5 \cdot \left(G + R \cdot T \cdot \ln\left(\frac{ATP}{ADP}\right)\right)/R \cdot T}}\right)}{1 + \dfrac{\mathbf{PGE_2}}{K_m} + \dfrac{ex\mathbf{PGE_2}}{K_m} + \mathbf{PGT\_CI}}$$

S.10.25.1. Reaction parameters

S.10.25.1.1. Parameter: PGT k_{cat}

Parameter values for the PGT k_{cat} of Reaction 102 were obtained from the literature and summarised in Table ST.10.25.1.1.1. The log-normal distribution properties for the PGT k_{cat} of Reaction 102 are shown in Table ST.10.25.1.1.2 and plotted in Figure SF.10.25.1.1.1.

Table ST.10.25.1.1.1. Literature information used to design the PGT k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
3.50	NaN	Bacteria	E. coli.	Glucose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Waygood and Steeves, 1980)
3.30 $x10^{-1}$	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
8.30 $x10^{-1}$	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
3.28	NaN	Yeast	Saccharomyces cerevisiae	HXT7 transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Ye et al., 2001)

Table ST.10.25.1.1.2. The log-normal distribution properties of the PGT k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
1.33	7.30	9.20×10^{-1}	$8.0\ 10^{-1}$

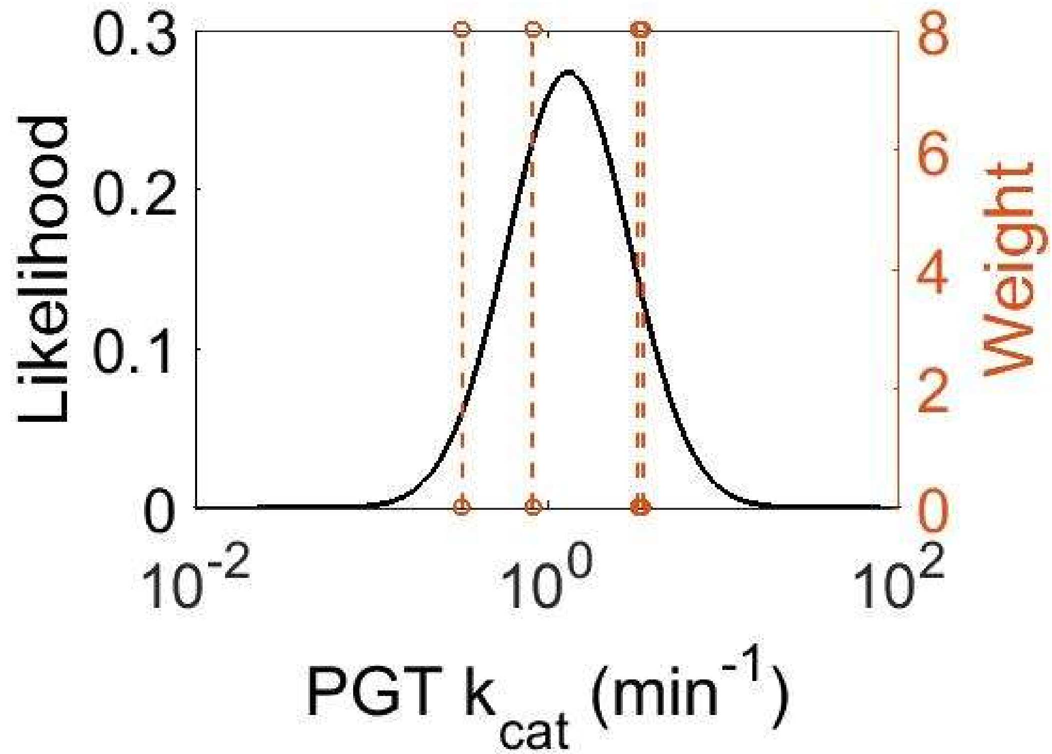


Figure SF.10.25.1.1.1. The estimated probability distribution for the PGT k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.25.1.2. Parameter: PGT K_{ms}

Parameter values for the PGT K_{ms} of Reaction 102 were obtained from the literature and summarised in Table ST.10.25.1.2.1. The log-normal distribution properties for the PGT K_{ms} of Reaction 102 are shown in Table ST.10.25.1.2.2 and plotted in Figure SF.10.25.1.2.1.

Table ST.10.25.1.2.1. Literature information used to design the PGT K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details							Weight	Type of error	Reference
		Substrate	Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
3.31×10^{-5}	1.31×10^{-4}		Human	Eye	PGT	7.5	37		512	0	(Waygood and Steeves, 1980)
3.76×10^{-4}	3.40×10^{-5}		Human	Embryonic kidney cells (HEK293)	PGT	Unknown	37		192	0	(Naftalin et al., 2007)
5.40×10^{-3}	NaN		Human	Embryonic kidney cells (HEK293)	PGT	Unknown	37		2048	0	(Naftalin et al., 2007)
7.20×10^{-3}	5.95×10^{-4}		Canine	Madin-Darby Canine Kidney Epithelial Cells (MDCK) cells	PGT	Unknown	Unknown		512	0	(Ye et al., 2001)

9.40 x10^{-5}	NaN	PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Waygood and Steeves, 1980)
4.23 x10^{-4}	NaN	TXB2	Human	HeLa cells	PGT	7	27		**1024**	0	(Naftalin et al., 2007)
7.57 x10^{-3}	NaN	6-keto-PGF1a	Human	HeLa cells	PGT	7	27		**1024**	0	(Naftalin et al., 2007)
4.87 x10^{-5}	NaN	PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Ye et al., 2001)
5.02 x10^{-5}	NaN	PGF2a	Human	HeLa cells	PGT	7	27		**1024**	0	(Waygood and Steeves, 1980)
5.00 x10^{-3}	NaN	15-K-PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Naftalin et al., 2007)
5.00 x10^{-3}	NaN	DH-15-K-PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Naftalin et al., 2007)
3.82 x10^{-5}	NaN	PGH2	Human	HeLa cells	PGT	7	27		**2048**	0	(Ye et al., 2001)

Table ST.10.25.1.2.2. The log-normal distribution properties of the PGT K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
1.10 x10^{-3}	9.42 x10^{1}	-4.67	1.45

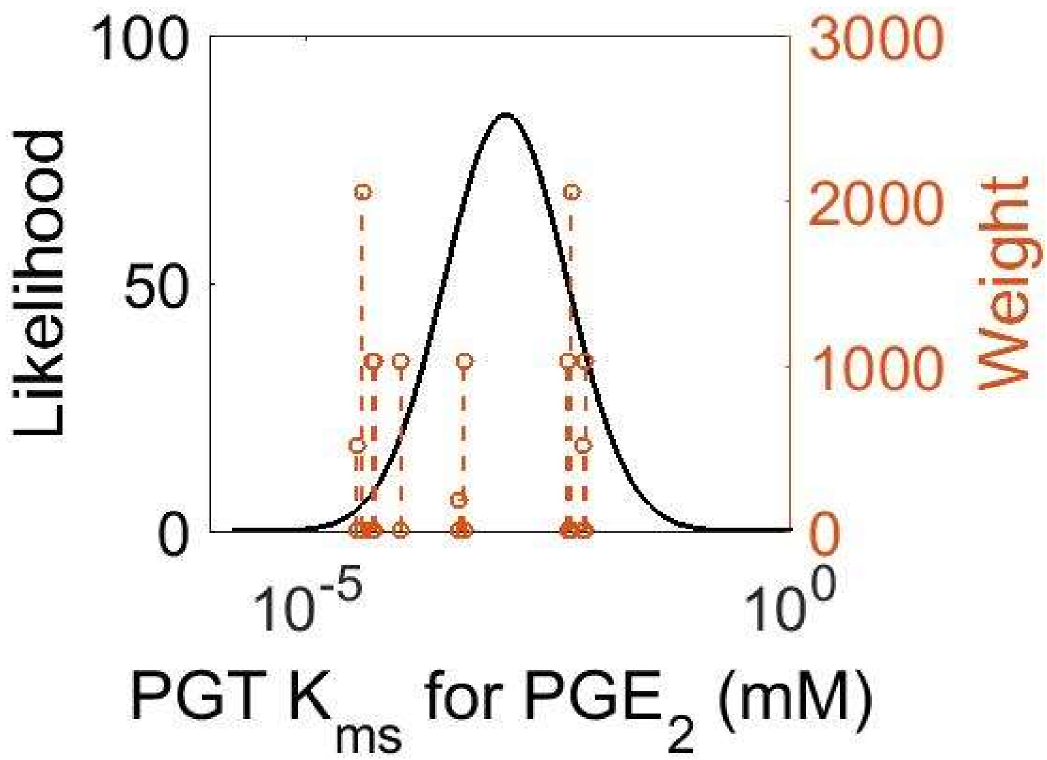


Figure SF.10.25.1.2.1. The estimated probability distribution for the PGT K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.25.1.3. Parameter: PGT concentration

Parameter values for the PGT concentration of Reaction 102 were obtained from the literature and summarised in Table ST.10.25.1.3.1. The log-normal distribution properties for the PGT concentration of Reaction 102 are shown in Table ST.10.25.1.3.2 and plotted in Figure SF.10.25.1.3.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.10.25.1.3.1. Literature information used to design the PGT concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
2.82	NaN	Human	Gut	PGT	7.5	37		2048	0	(Kim et al., 2014)
1.74×10^{1}	NaN	Human	Oesophagus	PGT	7.5	37		2048	0	(Wilhelm et al., 2014)
1.25×10^{2}	NaN	Human	Lung	PGT	7.5	37		2048	0	(Kim et al., 2014)

Table ST.10.25.1.3.2. The log-normal distribution properties of the PGT concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.73×10^{1}	9.57×10^{-5}	4.72	3.90	1.02

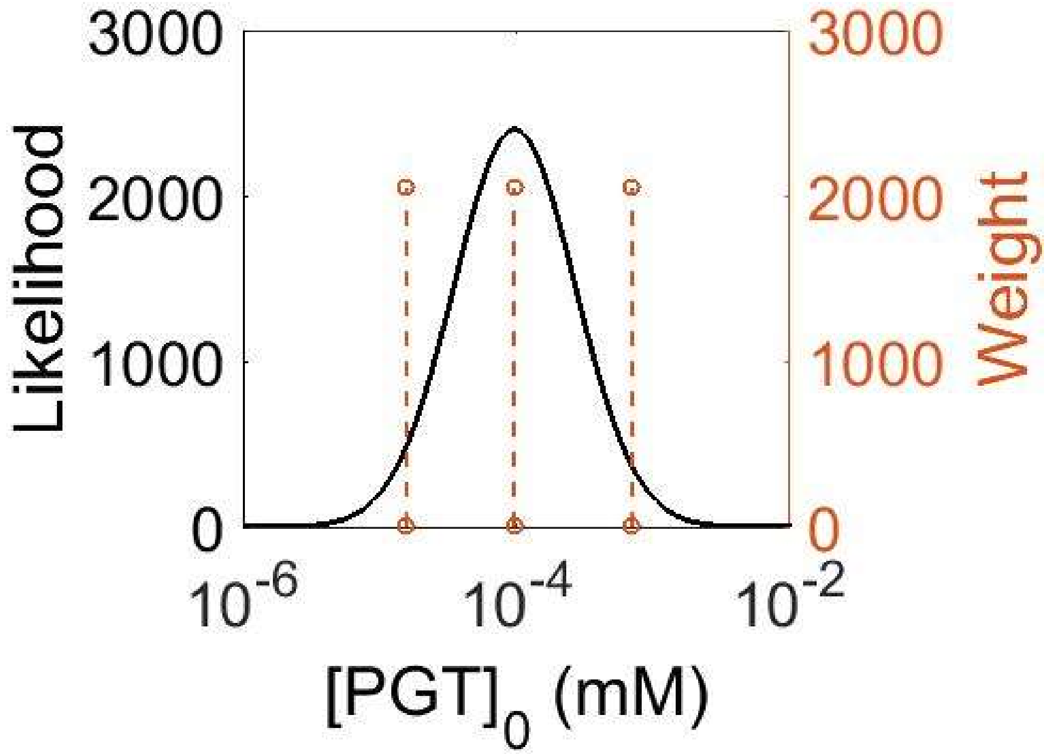
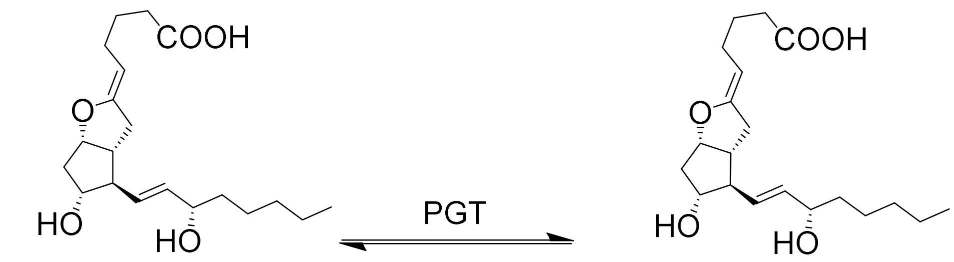


Figure SF.10.25.1.3.1. The estimated probability distribution for the PGT concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.26. Reaction 103: $PGI_2 \rightleftharpoons exPGI_2$ (PGT)

PGI_2 is relocated from the intracellular compartment to the extracellular compartment via the prostaglandin (PGT) transporter.



PGI_2
(Intracellular Compartment)

$exPGI_2$
(Extracellular Compartment)

Figure SF.10.26. The transport of prostaglandin I_2 (PGI_2) from the intracellular compartment to the extracellular compartment by prostaglandin (PGT) transporter (Reaction 103).

SEq.10.26. Reaction rate law for Reaction 103.

$$\boldsymbol{v_{103}} = [\boldsymbol{PGT}] \cdot \boldsymbol{k_{cat}} \cdot \frac{\mathrm{PGI_2}/\boldsymbol{K_m} \cdot \left(\mathbf{1} - \frac{\boldsymbol{ex}\mathrm{PGI_2}}{\mathrm{PGI_2} \cdot \boldsymbol{e}^{-0.5 \cdot \left(\boldsymbol{G} + \boldsymbol{R} \cdot \boldsymbol{T} \cdot \ln\left(\frac{\boldsymbol{ATP}}{\boldsymbol{ADP}}\right)\right) / \boldsymbol{R} \cdot \boldsymbol{T}}}\right)}{\mathbf{1} + \frac{\mathrm{PGI_2}}{\boldsymbol{K_m}} + \frac{\boldsymbol{ex}\mathrm{PGI_2}}{\boldsymbol{K_m}} + \mathbf{PGT\_CI}}$$

S.10.26.1. Reaction parameters

S.10.26.1.1. Parameter: PGT k_{cat}

Parameter values for the PGT k_{cat} of Reaction 103 were obtained from the literature and summarised in Table ST.10.26.1.1.1. The log-normal distribution properties for the PGT k_{cat} of Reaction 103 are shown in Table ST.10.26.1.1.2 and plotted in Figure SF.10.26.1.1.1.

Table ST.10.26.1.1.1. Literature information used to design the PGT k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
3.50	NaN	Bacteria	E. coli.	Glucose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Waygood and Steeves, 1980)
3.30 x10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
8.30 x10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
3.28	NaN	Yeast	Saccharomyces cerevisiae	HXT7 transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Ye et al., 2001)

Table ST.10.26.1.1.2. The log-normal distribution properties of the PGT k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
1.33	7.30	9.20×10^{-1}	8.0×10^{-1}

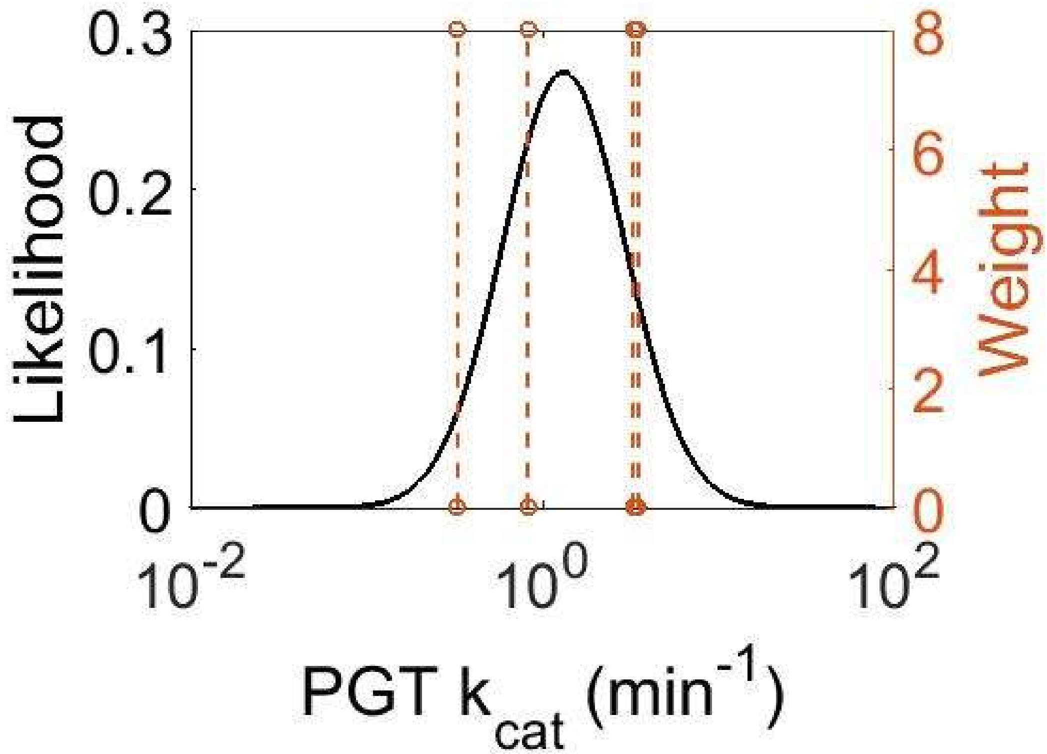


Figure SF.10.26.1.1.1. The estimated probability distribution for the PGT k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.26.1.2. Parameter: PGT K_{ms}

Parameter values for the PGT K_{ms} of Reaction 103 were obtained from the literature and summarised in Table ST.10.26.1.2.1. The log-normal distribution properties for the PGT K_{ms} of Reaction 103 are shown in Table ST.10.26.1.2.2 and plotted in Figure SF.10.26.1.2.1.

Table ST.10.26.1.2.1. Literature information used to design the PGT K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details							Weight	Type of error	Reference
		Substrate	Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
3.31×10^{-5}	1.31×10^{-4}		Human	Eye	PGT	7.5	37		512	0	(Waygood and Steeves, 1980)
3.76×10^{-4}	3.40×10^{-5}		Human	Embryonic kidney cells (HEK293)	PGT	Unknown	37		192	0	(Naftalin et al., 2007)
5.40×10^{-3}	NaN		Human	Embryonic kidney cells (HEK293)	PGT	Unknown	37		2048	0	(Naftalin et al., 2007)
7.20×10^{-3}	5.95×10^{-4}		Canine	Madin-Darby Canine Kidney Epithelial Cells (MDCK) cells	PGT	Unknown	Unknown		512	0	(Ye et al., 2001)

9.40×10^{-5}	NaN	PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Waygood and Steeves, 1980)
4.23×10^{-4}	NaN	TXB2	Human	HeLa cells	PGT	7	27		**1024**	0	(Naftalin et al., 2007)
7.57×10^{-3}	NaN	K6PGF1a	Human	HeLa cells	PGT	7	27		**1024**	0	(Naftalin et al., 2007)
4.87×10^{-5}	NaN	PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Ye et al., 2001)
5.02×10^{-5}	NaN	PGF2a	Human	HeLa cells	PGT	7	27		**1024**	0	(Waygood and Steeves, 1980)
5.00×10^{-3}	NaN	15-K-PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Naftalin et al., 2007)
5.00×10^{-3}	NaN	DH-15-K-PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Naftalin et al., 2007)
3.82×10^{-5}	NaN	PGH2	Human	HeLa cells	PGT	7	27		**2048**	0	(Ye et al., 2001)

Table ST.10.26.1.2.2. The log-normal distribution properties of the PGT K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
1.10×10^{-3}	9.42×10^{1}	-4.67	1.45

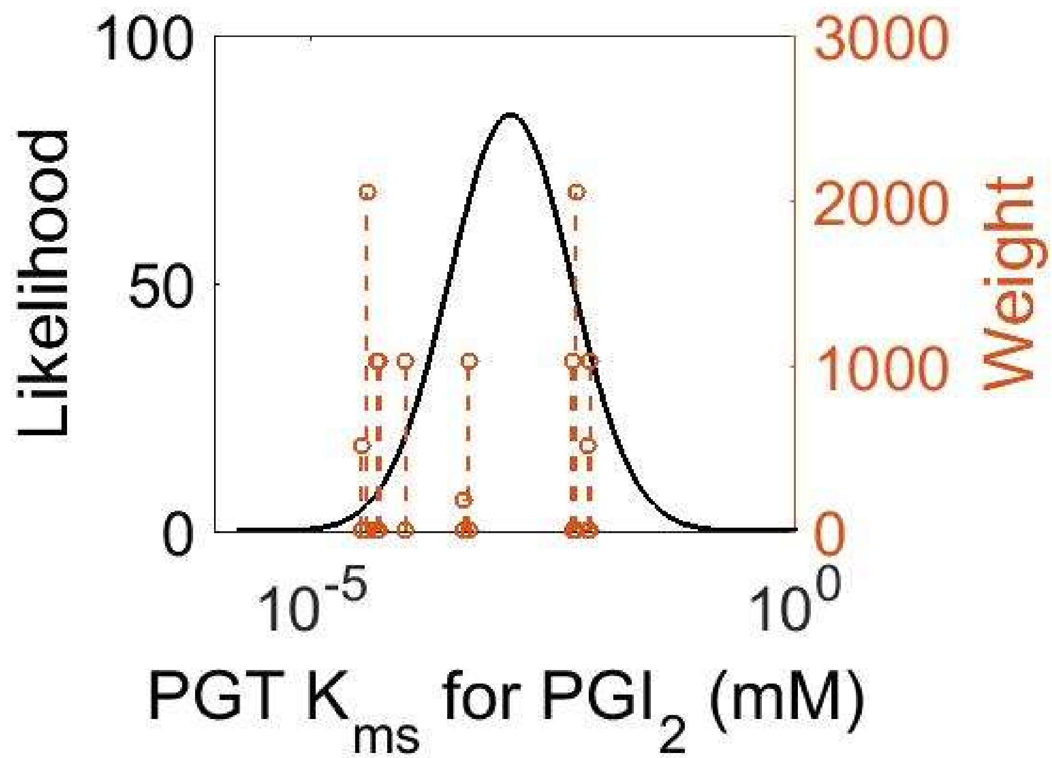


Figure SF.10.26.1.2.1. The estimated probability distribution for the PGT K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.26.1.3. Parameter: PGT concentration

Parameter values for the PGT concentration of Reaction 103 were obtained from the literature and summarised in Table ST.10.26.1.3.1. The log-normal distribution properties for the PGT concentration of Reaction 103 are shown in Table ST.10.26.1.3.2 and plotted in Figure SF.10.26.1.3.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.10.26.1.3.1. Literature information used to design the PGT concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
2.82	NaN	Human	Gut	PGT	7.5	37		2048	0	(Kim et al., 2014)
1.74 $x10^1$	NaN	Human	Oesophagus	PGT	7.5	37		2048	0	(Wilhelm et al., 2014)
1.25 $x10^2$	NaN	Human	Lung	PGT	7.5	37		2048	0	(Kim et al., 2014)

Table ST.10.26.1.3.2 The log-normal distribution properties of the PGT concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.73 $x10^1$	9.57 $x10^{-5}$	4.72	3.90	1.02

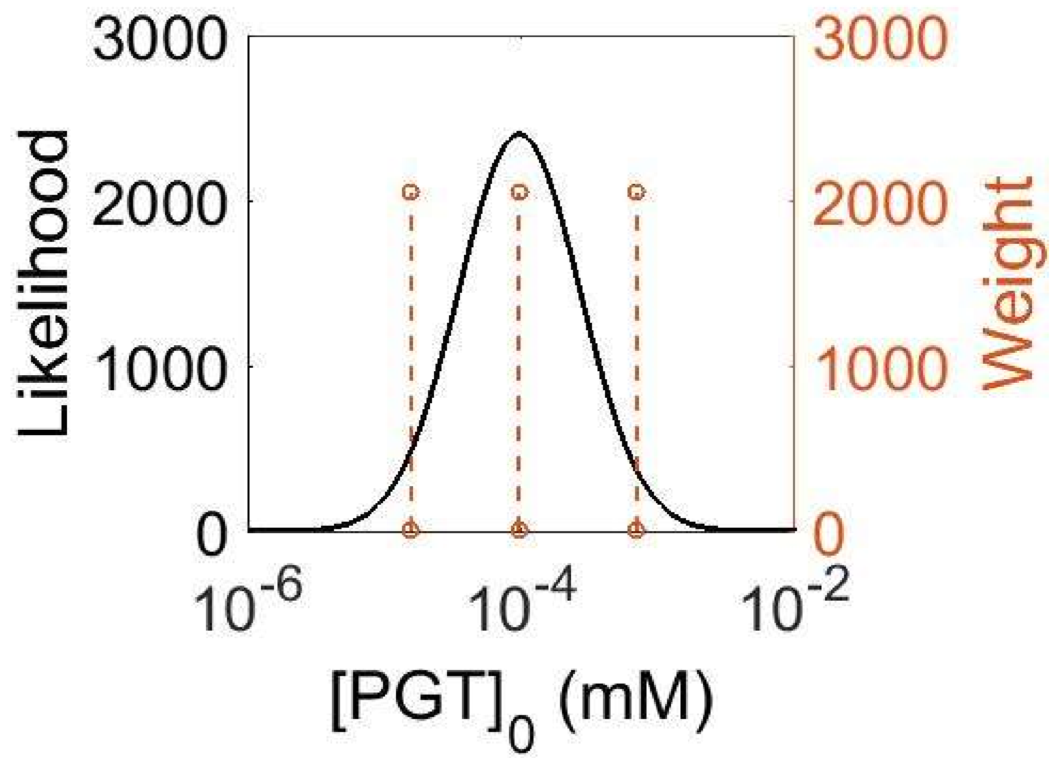


Figure SF.10.26.1.3.1. The estimated probability distribution for the PGT concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.27. Reaction 104: $PGD_2 \rightleftharpoons exPGD_2$ (PGT)

PGD_2 is relocated from the intracellular compartment to the extracellular compartment via the prostaglandin (PGT) transporter.

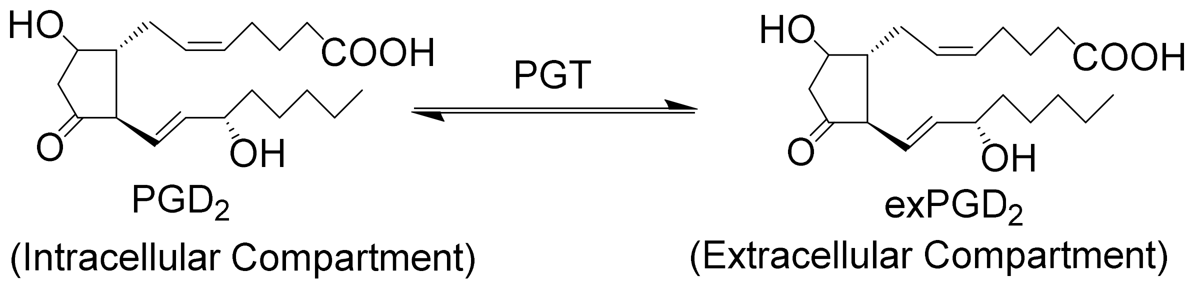


Figure SF.10.27. The transport of prostaglandin D_2 (PGD_2) from the intracellular compartment to the extracellular compartment by prostaglandin (PGT) transporter (Reaction 104).

SEq.10.27. Reaction rate law for Reaction 104.

$$\boldsymbol{v_{104}} = [\boldsymbol{PGT}] \cdot \boldsymbol{k_{cat}} \cdot \frac{\mathbf{PGD_2}/K_m \cdot \left(1 - \frac{ex\mathbf{PGD_2}}{\mathbf{PGD_2} \cdot e^{-0.5 \cdot \left(G + R \cdot T \cdot \ln\left(\frac{ATP}{ADP}\right)\right)/R \cdot T}}\right)}{1 + \frac{\mathbf{PGD_2}}{K_m} + \frac{ex\mathbf{PGD_2}}{K_m} + \mathbf{PGT\_CI}}$$

S.10.27.1. Reaction parameters

S.10.27.1.1. Parameter: PGT k_{cat}

Parameter values for the PGT k_{cat} of Reaction 104 were obtained from the literature and summarised in Table ST.10.27.1.1.1. The log-normal distribution properties for the PGT k_{cat} of Reaction 104 are shown in Table ST.10.27.1.1.2 and plotted in Figure SF.10.27.1.1.1.

Table ST.10.27.1.1.1. Literature information used to design the PGT k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
3.50	NaN	Bacteria	E. coli.	Glucose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Waygood and Steeves, 1980)
3.30×10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
8.30×10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
3.28	NaN	Yeast	Saccharomyces cerevisiae	HXT7 transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Ye et al., 2001)

Table ST.10.27.1.1.2. The log-normal distribution properties of the PGT k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
1.33	7.30	9.20×10^{-1}	8.0×10^{-1}

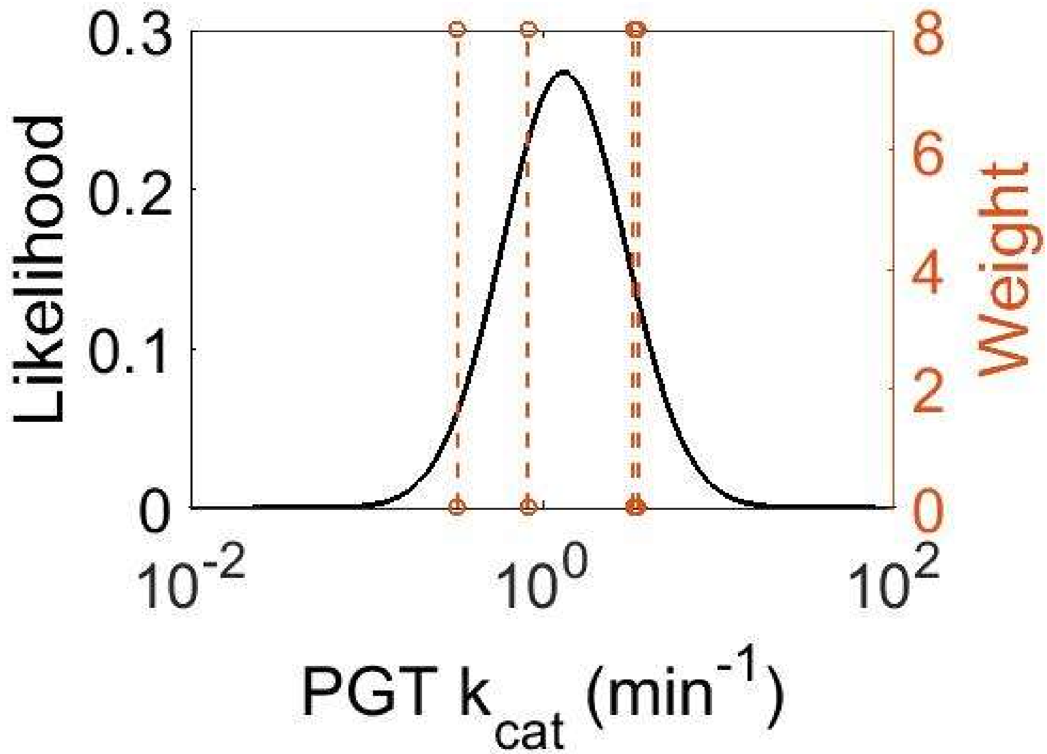


Figure SF.10.27.1.1.1. The estimated probability distribution for the PGT k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.27.1.2. Parameter: PGT K_{ms}

Parameter values for the PGT K_{ms} of Reaction 104 were obtained from the literature and summarised in Table ST.10.27.1.2.1. The log-normal distribution properties for the PGT K_{ms} of Reaction 104 are shown in Table ST.10.27.1.2.2 and plotted in Figure SF.10.27.1.2.1.

Table ST.10.27.1.2.1. Literature information used to design the PGT K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Other	Weight	Type of error	Reference
		Substrate	Species	Expression Vector	Enzyme	pH	Temperature (°C)				
3.31×10^{-5}	1.31×10^{-4}		Human	Eye	PGT	7.5	37		512	0	(Waygood and Steeves, 1980)
3.76×10^{-4}	3.40×10^{-5}		Human	Embryonic kidney cells (HEK293)	PGT	Unknown	37		192	0	(Naftalin et al., 2007)
5.40×10^{-3}	NaN		Human	Embryonic kidney cells (HEK293)	PGT	Unknown	37		2048	0	(Naftalin et al., 2007)
7.20×10^{-3}	5.95×10^{-4}		Canine	Madin-Darby Canine Kidney Epithelial Cells (MDCK) cells	PGT	Unknown	Unknown		512	0	(Ye et al., 2001)

9.40 x10^{-5}	NaN	PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Waygood and Steeves, 1980)
4.23 x10^{-4}	NaN	TXB2	Human	HeLa cells	PGT	7	27		**1024**	0	(Naftalin et al., 2007)
7.57 x10^{-3}	NaN	K6PGF1a	Human	HeLa cells	PGT	7	27		**1024**	0	(Naftalin et al., 2007)
4.87 x10^{-5}	NaN	PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Ye et al., 2001)
5.02 x10^{-5}	NaN	PGF2a	Human	HeLa cells	PGT	7	27		**1024**	0	(Waygood and Steeves, 1980)
5.00 x10^{-3}	NaN	15-K-PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Naftalin et al., 2007)
5.00 x10^{-3}	NaN	DH-15-K-PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Naftalin et al., 2007)
3.82 x10^{-5}	NaN	PGH2	Human	HeLa cells	PGT	7	27		**2048**	0	(Ye et al., 2001)

Table ST.10.27.1.2.2. The log-normal distribution properties of the PGT K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
1.10 x10^{-3}	9.42 x10^{1}	-4.67	1.45

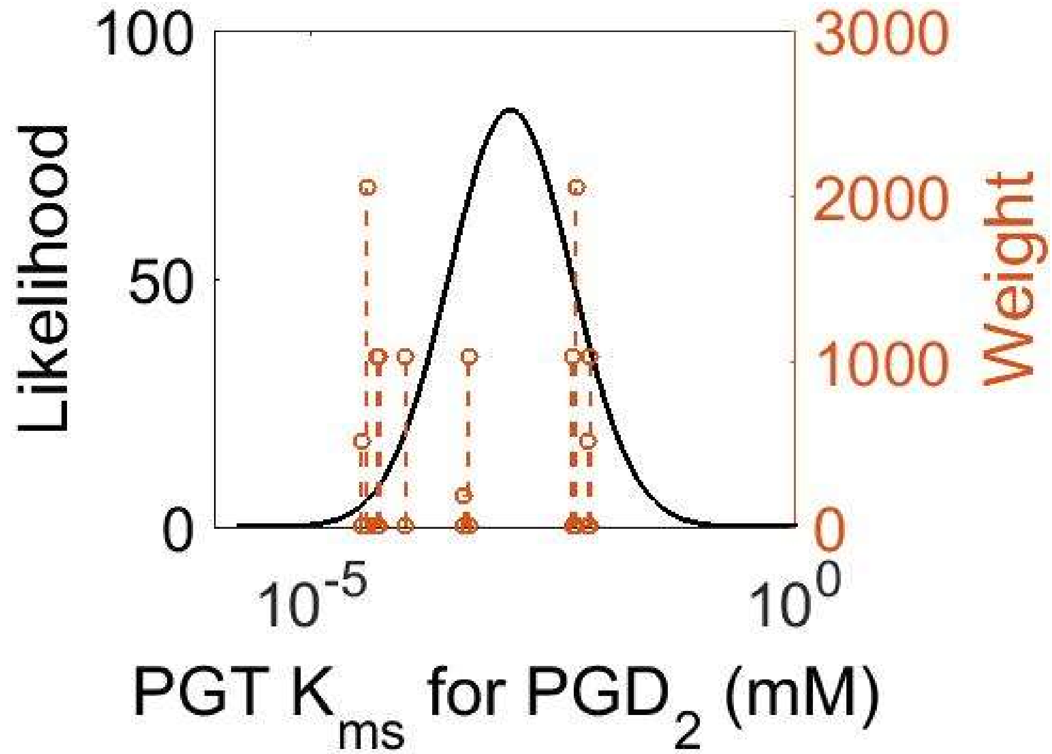


Figure SF.10.27.1.2.1. The estimated probability distribution for the PGT K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.27.1.3. Parameter: PGT concentration

Parameter values for the PGT concentration of Reaction 104 were obtained from the literature and summarised in Table ST.10.27.1.3.1. The log-normal distribution properties for the PGT concentration of Reaction 104 are shown in Table ST.10.27.1.3.2 and plotted in Figure SF.10.27.1.3.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.10.27.1.3.1. Literature information used to design the PGT concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
2.82	NaN	Human	Gut	PGT	7.5	37		2048	0	(Kim et al., 2014)
1.74 x10^{1}	NaN	Human	Oesophagus	PGT	7.5	37		2048	0	(Wilhelm et al., 2014)
1.25 x10^{2}	NaN	Human	Lung	PGT	7.5	37		2048	0	(Kim et al., 2014)

Table ST.10.27.1.3.2. The log-normal distribution properties of the PGT concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.73 x10^{1}	9.57 x10^{-5}	4.72	3.90	1.02

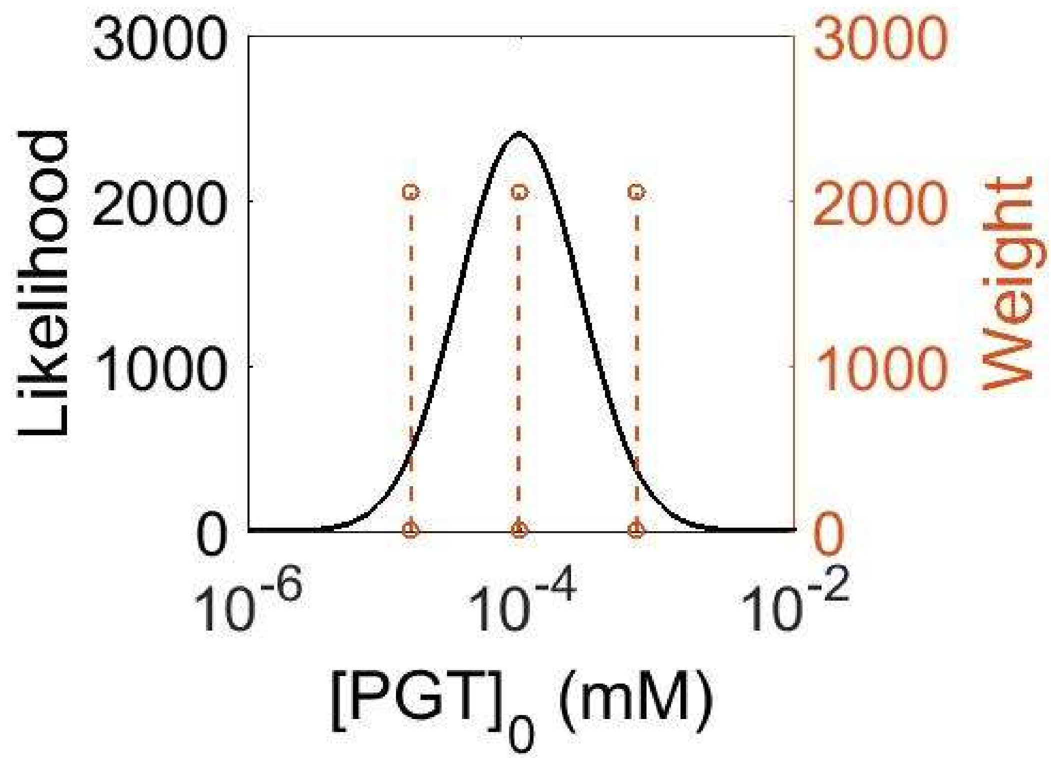


Figure SF.10.27.1.3.1. The estimated probability distribution for the PGT concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.28. Reaction 105: $PGJ_2 \rightleftharpoons exPGJ_2$ (PGT)

PGJ_2 is relocated from the intracellular compartment to the extracellular compartment via the prostaglandin (PGT) transporter.

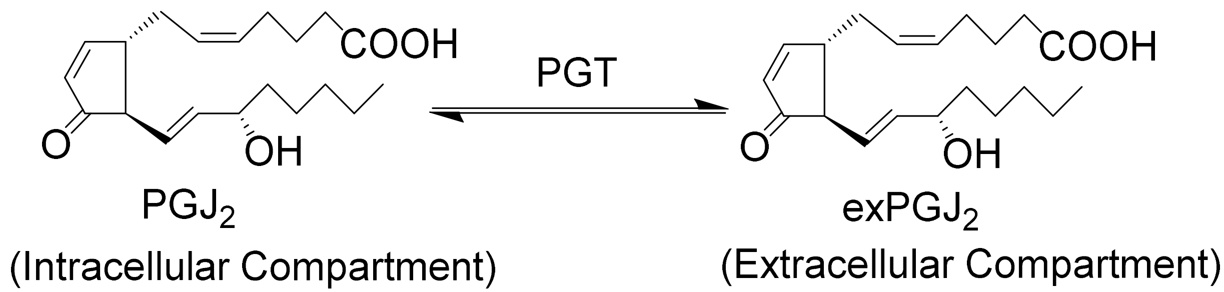


Figure SF.10.28. The transport of prostaglandin J_2 (PGJ_2) from the intracellular compartment to the extracellular compartment by prostaglandin (PGT) transporter (Reaction 105).

SEq.10.28. Reaction rate law for Reaction 105.

$$v_{105} = [PGT] \cdot k_{cat} \cdot \frac{\mathrm{PGJ_2}/K_m \cdot \left(1 - \frac{ex\mathrm{PGJ_2}}{\mathrm{PGJ_2} \cdot e^{-0.5 \cdot \left(G + R \cdot T \cdot \ln\left(\frac{ATP}{ADP}\right)\right)/R \cdot T}}\right)}{1 + \frac{\mathrm{PGJ_2}}{K_m} + \frac{ex\mathrm{PGJ_2}}{K_m} + \mathrm{PGT\_CI}}$$

S.10.28.1 Reaction parameters

S.10.28.1.1. Parameter: PGT k_{cat}

Parameter values for the PGT k_{cat} of Reaction 105 were obtained from the literature and summarised in Table ST.10.28.1.1.1. The log-normal distribution properties for the PGT k_{cat} of Reaction 105 are shown in Table ST.10.28.1.1.2 and plotted in Figure SF.10.28.1.1.1.

Table ST.10.28.1.1.1. Literature information used to design the PGT k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
3.50	NaN	Bacteria	E. coli.	Glucose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Waygood and Steeves, 1980)
3.30 $x10^{-1}$	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
8.30 $x10^{-1}$	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
3.28	NaN	Yeast	Saccharomyces cerevisiae	HXT7 transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Ye et al., 2001)

Table ST.10.28.1.1.2. The log-normal distribution properties of the PGT k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.33	7.30	9.20 x10^{-1}	8.0 10^{-1}

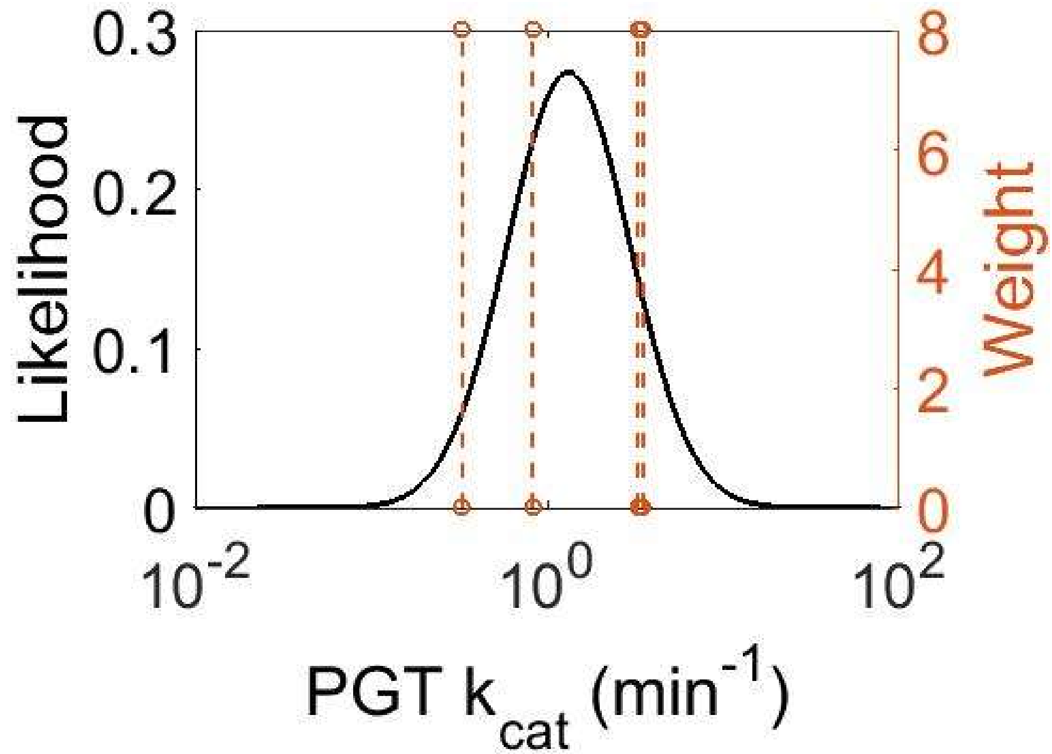


Figure SF.10.28.1.1.1. The estimated probability distribution for the PGT k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.28.1.2. Parameter: PGT K_{ms}

Parameter values for the PGT K_{ms} of Reaction 105 were obtained from the literature and summarised in Table ST.10.28.1.2.1. The log-normal distribution properties for the PGT K_{ms} of Reaction 105 are shown in Table ST.10.28.1.2.2 and plotted in Figure SF.10.28.1.2.1.

Table ST.10.28.1.2.1. Literature information used to design the PGT K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details							Weight	Type of error	Reference
		Substrate	Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
3.31×10^{-5}	1.31×10^{-4}		Human	Eye	PGT	7.5	37		512	0	(Waygood and Steeves, 1980)
3.76×10^{-4}	3.40×10^{-5}		Human	Embryonic kidney cells (HEK293)	PGT	Unknown	37		192	0	(Naftalin et al., 2007)
5.40×10^{-3}	NaN		Human	Embryonic kidney cells (HEK293)	PGT	Unknown	37		2048	0	(Naftalin et al., 2007)
7.20×10^{-3}	5.95×10^{-4}		Canine	Madin-Darby Canine Kidney Epithelial Cells (MDCK) cells	PGT	Unknown	Unknown		512	0	(Ye et al., 2001)

9.40×10^{-5}	NaN	PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Waygood and Steeves, 1980)
4.23×10^{-4}	NaN	TXB2	Human	HeLa cells	PGT	7	27		**1024**	0	(Naftalin et al., 2007)
7.57×10^{-3}	NaN	K6PGF1a	Human	HeLa cells	PGT	7	27		**1024**	0	(Naftalin et al., 2007)
4.87×10^{-5}	NaN	PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Ye et al., 2001)
5.02×10^{-5}	NaN	PGF2a	Human	HeLa cells	PGT	7	27		**1024**	0	(Waygood and Steeves, 1980)
5.00×10^{-3}	NaN	15-K-PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Naftalin et al., 2007)
5.00×10^{-3}	NaN	DH-15-K-PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Naftalin et al., 2007)
3.82×10^{-5}	NaN	PGH2	Human	HeLa cells	PGT	7	27		**2048**	0	(Ye et al., 2001)

Table ST.10.28.1.2.2. The log-normal distribution properties of the PGT K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
1.10×10^{-3}	9.42×10^{1}	-4.67	1.45

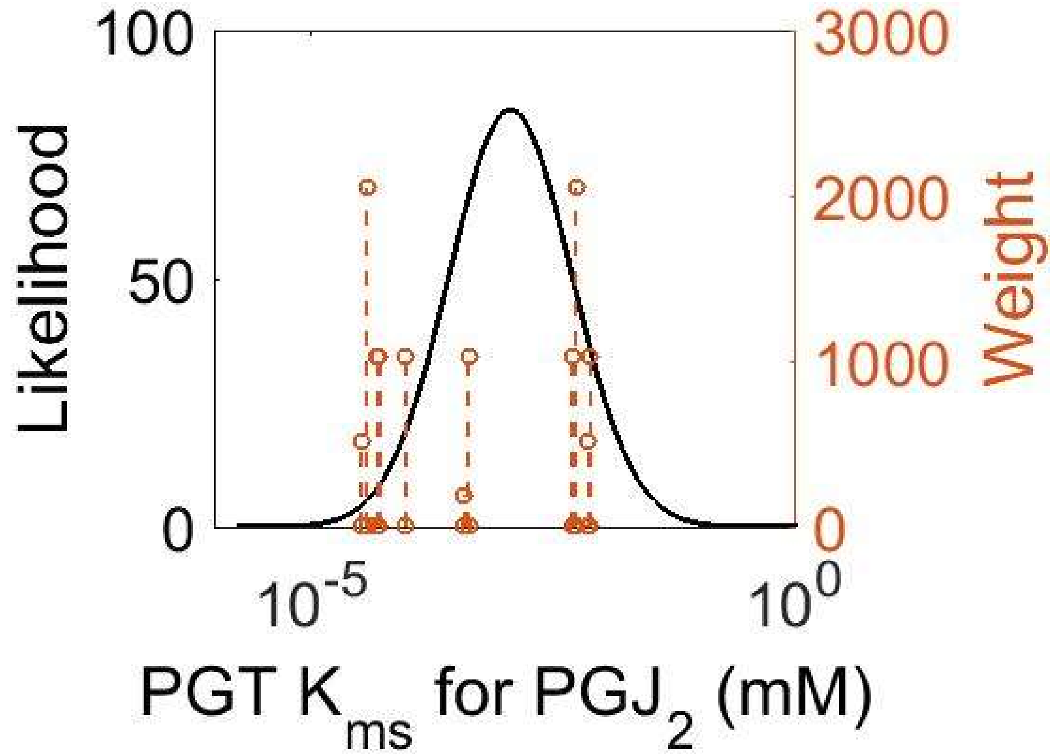


Figure SF.10.28.1.2.1. The estimated probability distribution for the PGT K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.28.1.3. Parameter: PGT concentration

Parameter values for the PGT concentration of Reaction 105 were obtained from the literature and summarised in Table ST.10.28.1.3.1. The log-normal distribution properties for the PGT concentration of Reaction 105 are shown in Table ST.10.28.1.3.2 and plotted in Figure SF.10.28.1.3.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.10.28.1.3.1. Literature information used to design the PGT concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
2.82	NaN	Human	Gut	PGT	7.5	37		2048	0	(Kim et al., 2014)
1.74×10^{1}	NaN	Human	Oesophagus	PGT	7.5	37		2048	0	(Wilhelm et al., 2014)
1.25×10^{2}	NaN	Human	Lung	PGT	7.5	37		2048	0	(Kim et al., 2014)

Table ST.10.28.1.3.2. The log-normal distribution properties of the PGT concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.73×10^{1}	9.57×10^{-5}	4.72	3.90	1.02

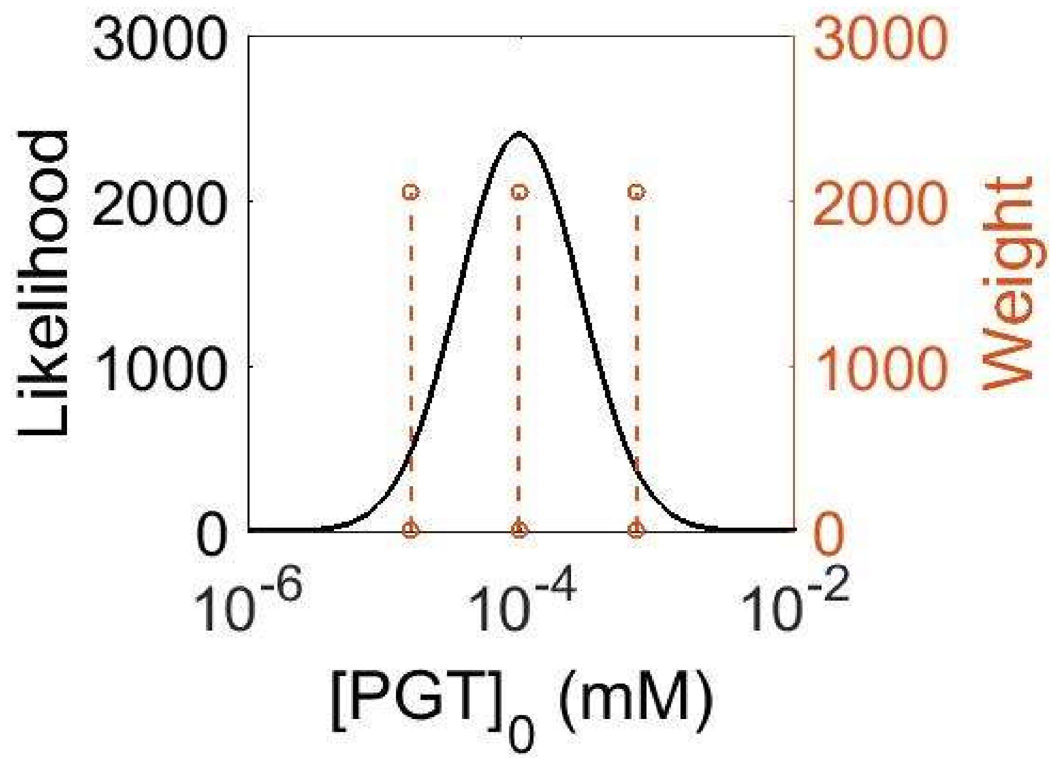
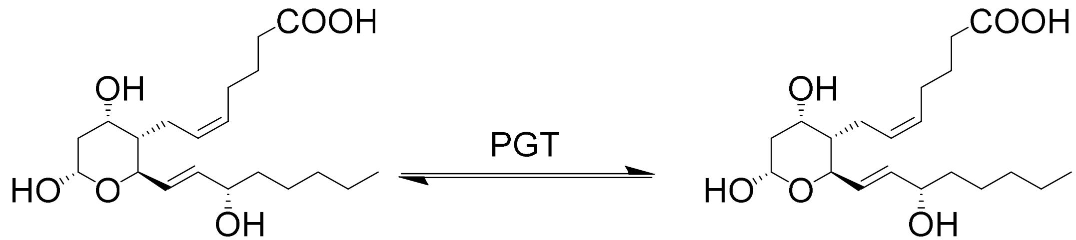


Figure SF.10.28.1.3.1. The estimated probability distribution for the PGT concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.29. Reaction 106: $TXB_2 \rightleftharpoons exTXB_2$ (PGT)

TXB_2 is relocated from the intracellular compartment to the extracellular compartment via the prostaglandin (PGT) transporter.



TXB_2 $\quad$ $exTXB_2$

(Intracellular Compartment) $\quad$ (Extracellular Compartment)

Figure SF.10.29. The transport of thromboxane B_2 (TXB_2) from the intracellular compartment to the extracellular compartment by prostaglandin (PGT) transporter (Reaction 106).

SEq.10.29. Reaction rate law for Reaction 106.

$$\boldsymbol{v_{106}} = [\boldsymbol{PGT}] \cdot \boldsymbol{k_{cat}} \cdot \frac{\mathrm{TXB_2}/K_m \cdot \left(1 - \frac{ex\mathrm{TXB_2}}{\mathrm{TXB_2} \cdot e^{-0.5 \cdot \left(G + R \cdot T \cdot \ln\left(\frac{ATP}{ADP}\right)\right)/R \cdot T}}\right)}{1 + \frac{\mathrm{TXB_2}}{K_m} + \frac{ex\mathrm{TXB_2}}{K_m} + \mathrm{PGT\_CI}}$$

S.10.29.1. Reaction parameters

S.10.29.1.1. Parameter: PGT k_{cat}

Parameter values for the PGT k_{cat} of Reaction 106 were obtained from the literature and summarised in Table ST.10.29.1.1.1. The log-normal distribution properties for the PGT k_{cat} of Reaction 106 are shown in Table ST.10.29.1.1.2 and plotted in Figure SF.10.29.1.1.1.

Table ST.10.29.1.1.1. Literature information used to design the PGT k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
3.50	NaN	Bacteria	E. coli.	Glucose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Waygood and Steeves, 1980)
3.30 x10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
8.30 x10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
3.28	NaN	Yeast	Saccharomyces cerevisiae	HXT7 transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Ye et al., 2001)

Table ST.10.29.1.1.2 The log-normal distribution properties of the PGT k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
1.33	7.30	9.20×10^{-1}	$8.0\ 10^{-1}$

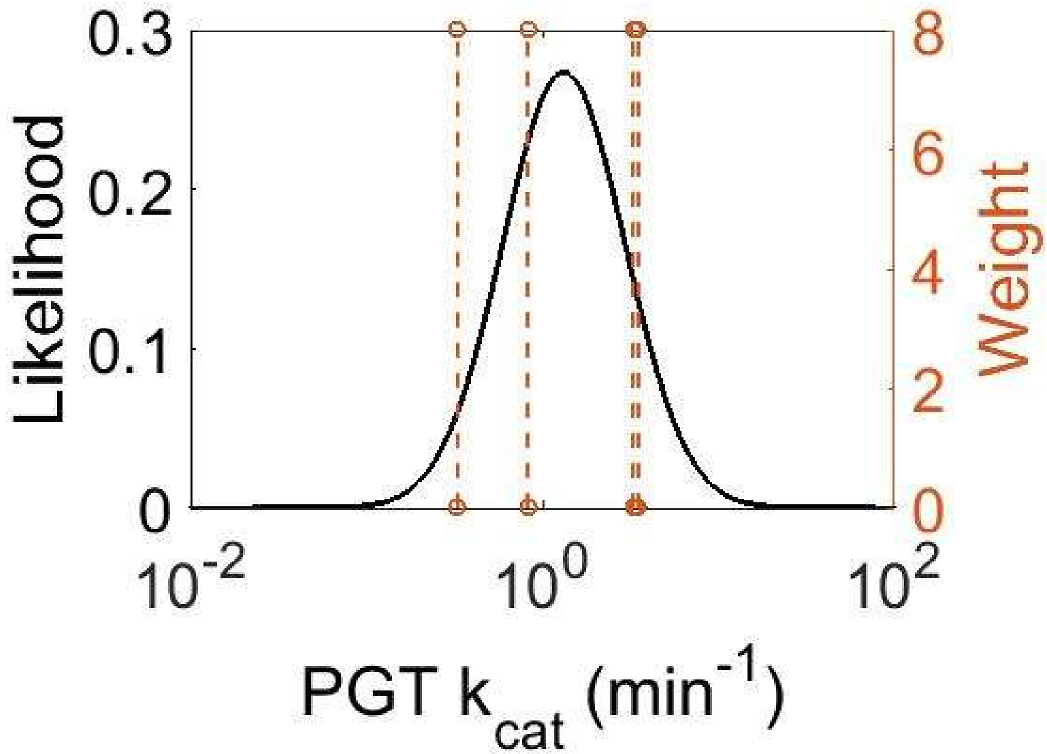


Figure SF.10.29.1.1.1. The estimated probability distribution for the PGT k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.29.1.2. Parameter: PGT K_{ms}

Parameter values for the PGT K_{ms} of Reaction 106 were obtained from the literature and summarised in Table ST.10.29.1.2.1. The log-normal distribution properties for the PGT K_{ms} of Reaction 106 are shown in Table ST.10.29.1.2.2 and plotted in Figure SF.10.29.1.2.1.

Table ST.10.29.1.2.1. Literature information used to design the PGT K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details							Weight	Type of error	Reference
		Substrate	Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
3.31×10^{-5}	1.31×10^{-4}		Human	Eye	PGT	7.5	37		512	0	(Waygood and Steeves, 1980)
3.76×10^{-4}	3.40×10^{-5}		Human	Embryonic kidney cells (HEK293)	PGT	Unknown	37		192	0	(Naftalin et al., 2007)
5.40×10^{-3}	NaN		Human	Embryonic kidney cells (HEK293)	PGT	Unknown	37		2048	0	(Naftalin et al., 2007)
7.20×10^{-3}	5.95×10^{-4}		Canine	Madin-Darby Canine Kidney Epithelial Cells	PGT	Unknown	Unknown		512	0	(Ye et al., 2001)

				(MDCK) cells							
9.40×10^{-5}	NaN	PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Waygood and Steeves, 1980)
4.23×10^{-4}	NaN	TXB2	Human	HeLa cells	PGT	7	27		**1024**	0	(Naftalin et al., 2007)
7.57×10^{-3}	NaN	K6PGF1a	Human	HeLa cells	PGT	7	27		**1024**	0	(Naftalin et al., 2007)
4.87×10^{-5}	NaN	PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Ye et al., 2001)
5.02×10^{-5}	NaN	PGF2a	Human	HeLa cells	PGT	7	27		**1024**	0	(Waygood and Steeves, 1980)
5.00×10^{-3}	NaN	15-K-PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Naftalin et al., 2007)
5.00×10^{-3}	NaN	DH-15-K-PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Naftalin et al., 2007)
3.82×10^{-5}	NaN	PGH2	Human	HeLa cells	PGT	7	27		**2048**	0	(Ye et al., 2001)

Table ST.10.29.1.2.2. The log-normal distribution properties of the PGT K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
1.10×10^{-3}	9.42×10^{1}	-4.67	1.45

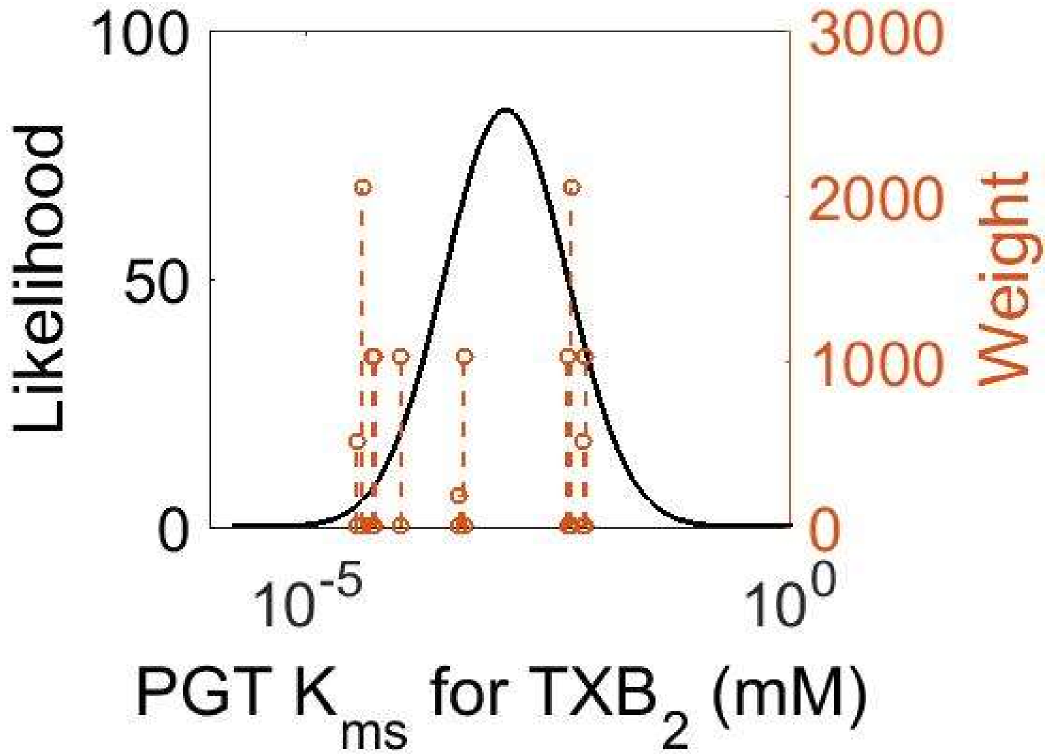


Figure SF.10.29.1.2.1. The estimated probability distribution for the PGT K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.29.1.3. Parameter: PGT concentration

Parameter values for the PGT concentration of Reaction 106 were obtained from the literature and summarised in Table ST.10.29.1.3.1. The log-normal distribution properties for the PGT concentration of Reaction 106 are shown in Table ST.10.29.1.3.2 and plotted in Figure SF.10.29.1.3.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.10.29.1.3.1. Literature information used to design the PGT concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
2.82	NaN	Human	Gut	PGT	7.5	37		2048	0	(Kim et al., 2014)
1.74×10^{1}	NaN	Human	Oesophagus	PGT	7.5	37		2048	0	(Wilhelm et al., 2014)
1.25×10^{2}	NaN	Human	Lung	PGT	7.5	37		2048	0	(Kim et al., 2014)

Table ST.10.29.1.3.2. The log-normal distribution properties of the PGT concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.73×10^{1}	9.57×10^{-5}	4.72	3.90	1.02

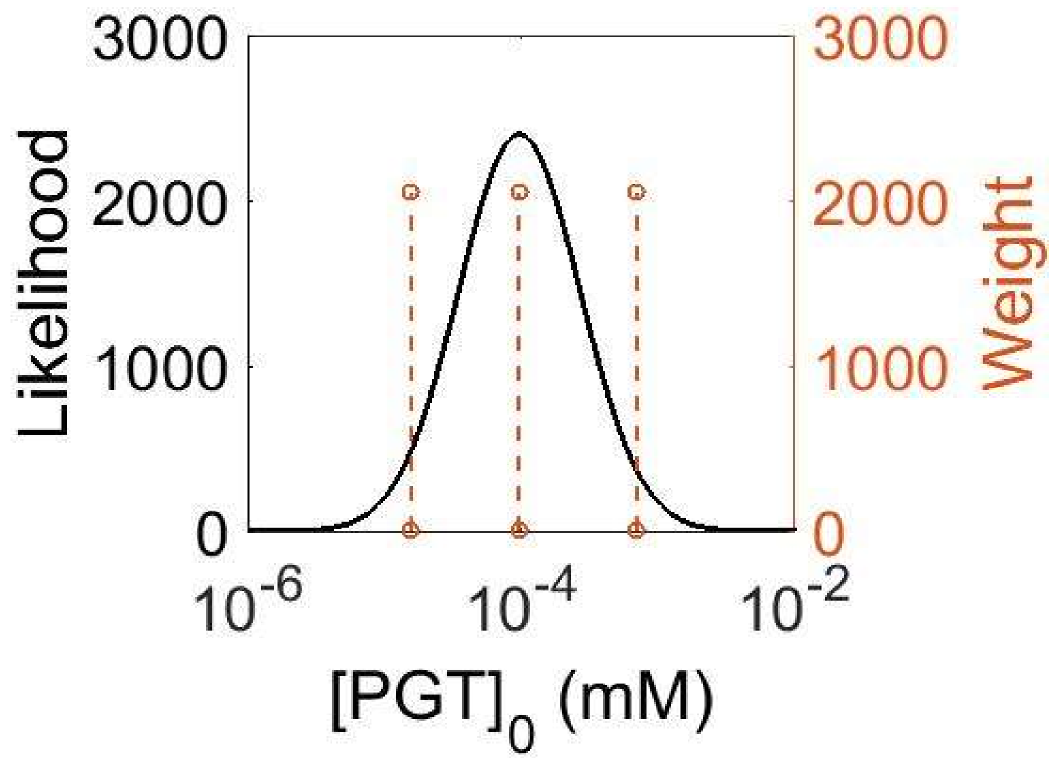


Figure SF.10.29.1.3.1. The estimated probability distribution for the PGT concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.30. Reaction 107: 13,14-dihydro-15-keto-PGE$_2$ ⇌ ex13,14-dihydro-15-keto-PGE$_2$ (PGT)

13,14-dihydro-15-keto-PGE$_2$ is relocated from the intracellular compartment to the extracellular compartment via the prostaglandin (PGT) transporter.

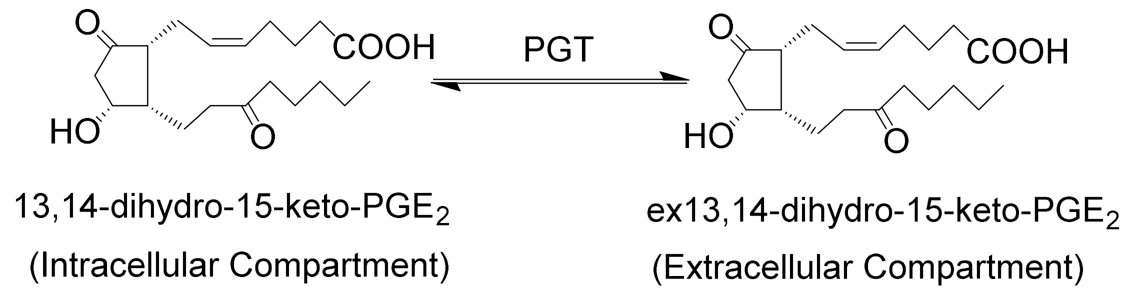


Figure SF.10.30. The transport of 13,14-dihydro-15-keto-prostaglandin E$_2$ (13,14-dihydro-15-keto-PGE$_2$) from the intracellular compartment to the extracellular compartment by prostaglandin (PGT) transporter (Reaction 107).

SEq.10.30. Reaction rate law for Reaction 107.

$$\boldsymbol{v_{107}} = [\boldsymbol{PGT}] \cdot \boldsymbol{k_{cat}} \cdot \frac{\text{13,14}-dihydro-15-keto-\text{PGE}_2 / K_m \cdot \left(1 - \frac{ex\text{13,14}-dihydro-15-keto-\text{PGE}_2}{\text{13,14}-dihydro-15-keto-\text{PGE}_2 \cdot e^{-0.5 \cdot \left(G + R \cdot T \cdot \ln\left(\frac{ATP}{ADP}\right)\right) / R \cdot T}}\right)}{1 + \frac{\text{13,14}-dihydro-15-keto-\text{PGE}_2}{K_m} + \frac{ex\text{13,14}-dihydro-15-keto-\text{PGE}_2}{K_m} + \text{PGT\_CI}}$$

S.10.30.1. Reaction parameters

S.10.30.1.1. Parameter: PGT k_{cat}

Parameter values for the PGT k_{cat} of Reaction 107 were obtained from the literature and summarised in Table ST.10.30.1.1.1. The log-normal distribution properties for the PGT k_{cat} of Reaction 107 are shown in Table ST.10.30.1.1.2 and plotted in Figure SF.10.30.1.1.1.

Table ST.10.30.1.1.1. Literature information used to design the PGT k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
3.50	NaN	Bacteria	E. coli.	Glucose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Waygood and Steeves, 1980)
3.30×10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
8.30×10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
3.28	NaN	Yeast	Saccharomyces cerevisiae	HXT7 transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Ye et al., 2001)

Table ST.10.30.1.1.2. The log-normal distribution properties of the PGT k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
1.33	7.30	9.20×10^{-1}	8.0×10^{-1}

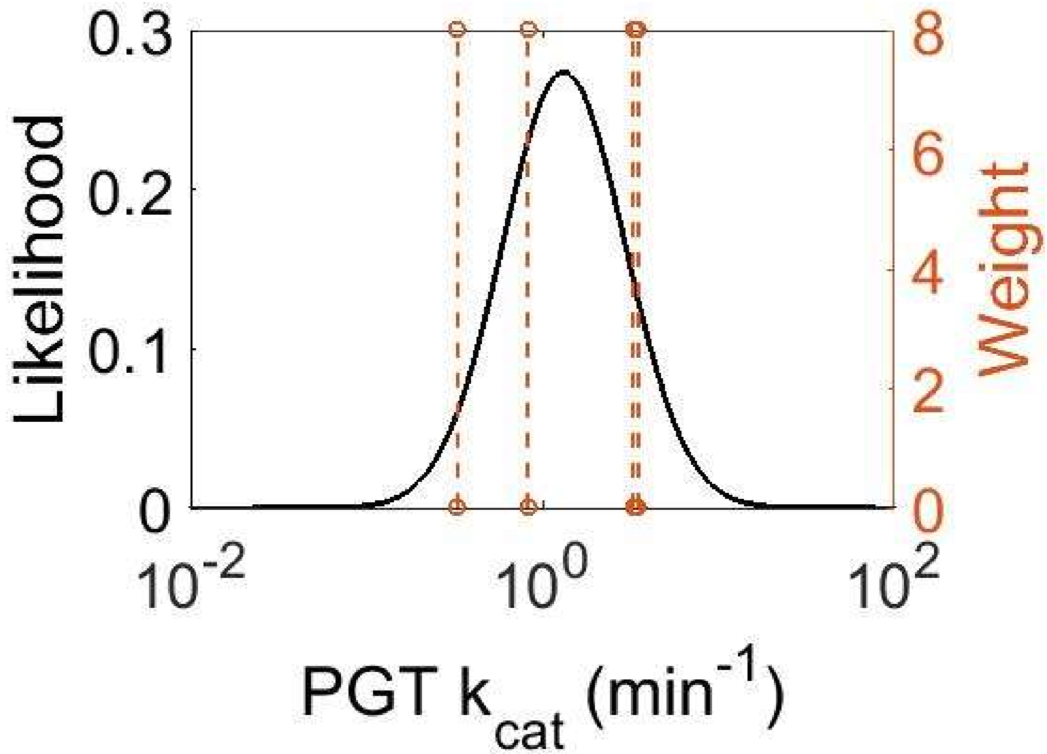


Figure SF.10.30.1.1.1. The estimated probability distribution for the PGT k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.30.1.2. Parameter: PGT K_{ms}

Parameter values for the PGT K_{ms} of Reaction 107 were obtained from the literature and summarised in Table ST.10.30.1.2.1. The log-normal distribution properties for the PGT K_{ms} of Reaction 107 are shown in Table ST.10.30.1.2.2 and plotted in Figure SF.10.30.1.2.1.

Table ST.10.30.1.2.1. Literature information used to design the PGT K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details									
		Substrate	Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other	Weight	Type of error	Reference
3.31×10^{-5}	1.31×10^{-4}		Human	Eye	PGT	7.5	37		512	0	(Waygood and Steeves, 1980)
3.76×10^{-4}	3.40×10^{-5}		Human	Embryonic kidney cells (HEK293)	PGT	Unknown	37		192	0	(Naftalin et al., 2007)
5.40×10^{-3}	NaN		Human	Embryonic kidney cells (HEK293)	PGT	Unknown	37		2048	0	(Naftalin et al., 2007)
7.20×10^{-3}	5.95×10^{-4}		Canine	Madin-Darby Canine Kidney Epithelial Cells	PGT	Unknown	Unknown		512	0	(Ye et al., 2001)

				(MDCK) cells							
9.40 x10^{-5}	NaN	PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Waygood and Steeves, 1980)
4.23 x10^{-4}	NaN	TXB2	Human	HeLa cells	PGT	7	27		**1024**	0	(Naftalin et al., 2007)
7.57 x10^{-3}	NaN	K6PGF1a	Human	HeLa cells	PGT	7	27		**1024**	0	(Naftalin et al., 2007)
4.87 x10^{-5}	NaN	PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Ye et al., 2001)
5.02 x10^{-5}	NaN	PGF2a	Human	HeLa cells	PGT	7	27		**1024**	0	(Waygood and Steeves, 1980)
5.00 x10^{-3}	NaN	15-K-PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Naftalin et al., 2007)
5.00 x10^{-3}	NaN	DH-15-K-PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Naftalin et al., 2007)
3.82 x10^{-5}	NaN	PGH2	Human	HeLa cells	PGT	7	27		**2048**	0	(Ye et al., 2001)

Table ST.10.30.1.2.2. The log-normal distribution properties of the PGT K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
1.10 x10^{-3}	9.42 x10^{1}	-4.67	1.45

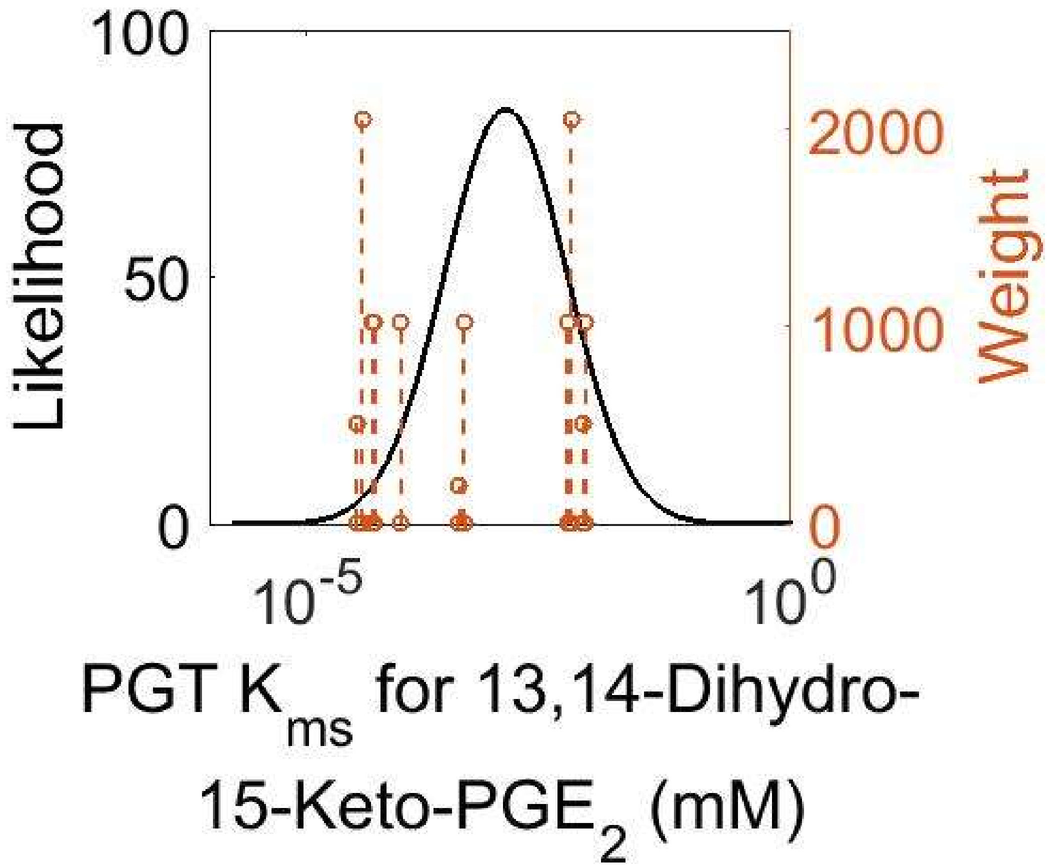


Figure SF.10.30.1.2.1. The estimated probability distribution for the PGT K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.30.1.3. Parameter: PGT concentration

Parameter values for the PGT concentration of Reaction 107 were obtained from the literature and summarised in Table ST.10.30.1.3.1. The log-normal distribution properties for the PGT concentration of Reaction 107 are shown in Table ST.10.30.1.3.2 and plotted in Figure SF.10.30.1.3.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.10.30.1.3.1. Literature information used to design the PGT concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
2.82	NaN	Human	Gut	PGT	7.5	37		2048	0	(Kim et al., 2014)
1.74 $x10^1$	NaN	Human	Oesophagus	PGT	7.5	37		2048	0	(Wilhelm et al., 2014)
1.25 $x10^2$	NaN	Human	Lung	PGT	7.5	37		2048	0	(Kim et al., 2014)

Table ST.10.30.1.3.2. The log-normal distribution properties of the PGT concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.73 $x10^1$	9.57 $x10^{-5}$	4.72	3.90	1.02

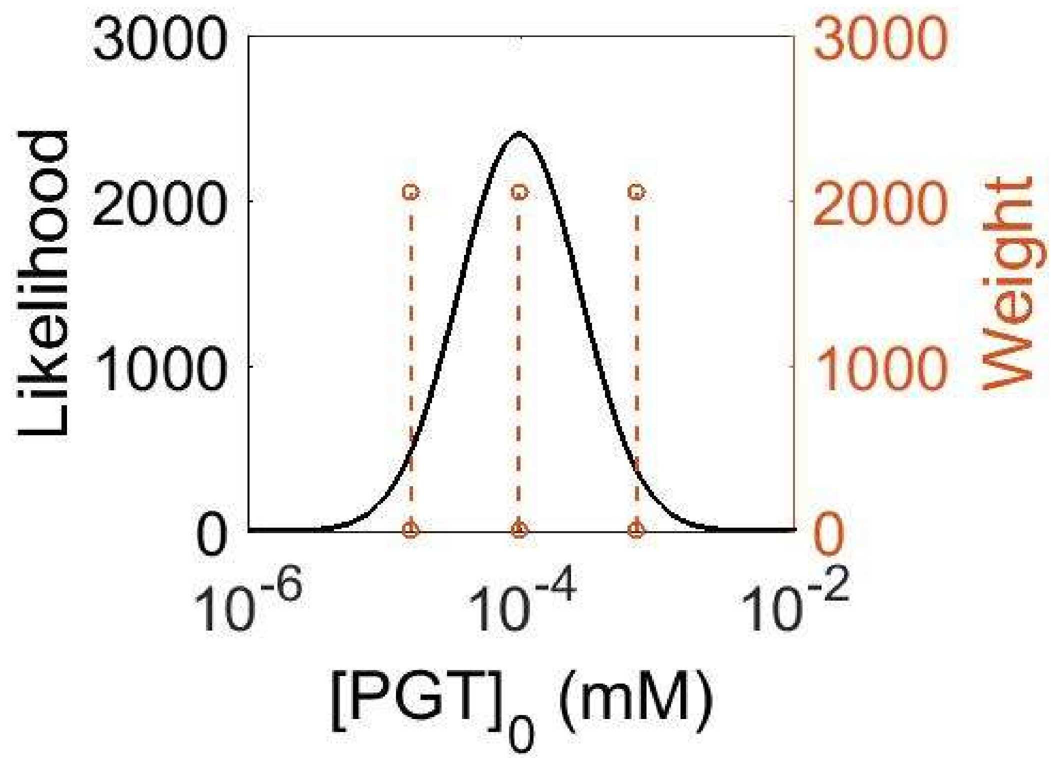


Figure SF.10.30.1.3.1. The estimated probability distribution for the PGT concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.31. Reaction 108: 15-keto-PGE$_2$ ⇌ ex15-keto-PGE$_2$ (PGT)

15-keto-PGE$_2$ is relocated from the intracellular compartment to the extracellular compartment via the prostaglandin (PGT) transporter.

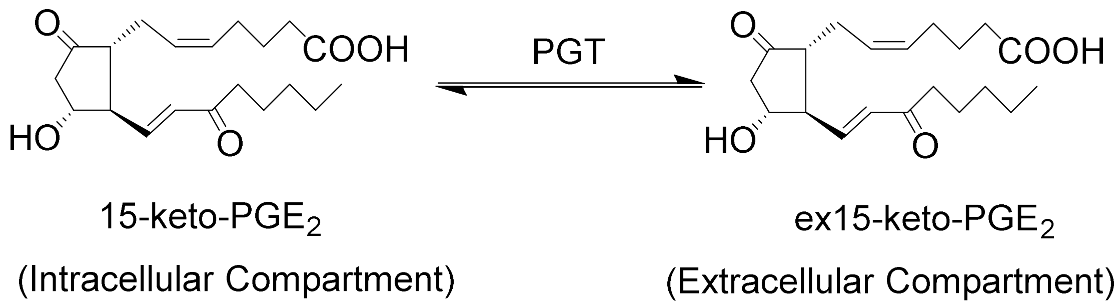


Figure SF.10.31. The transport of 15-keto-prostaglandin E$_2$ (15-keto-PGE$_2$) from the intracellular compartment to the extracellular compartment by prostaglandin (PGT) transporter (Reaction 108).

SEq.10.31. Reaction rate law for Reaction 108.

$$\boldsymbol{v_{108}} = [\boldsymbol{PGT}] \cdot \boldsymbol{k_{cat}} \cdot \frac{\text{15-keto-PGE}_2 / K_m \cdot \left(1 - \frac{\text{ex15-keto-PGE}_2}{\text{15-keto-PGE}_2 \cdot e^{-0.5 \cdot \left(G + R \cdot T \cdot \ln\left(\frac{ATP}{ADP}\right)\right) / R \cdot T}}\right)}{1 + \frac{\text{15-keto-PGE}_2}{K_m} + \frac{\text{ex15-keto-PGE}_2}{K_m} + \text{PGT\_CI}}$$

S.10.31.1. Reaction parameters

S.10.31.1.1. Parameter: PGT k_{cat}

Parameter values for the PGT k_{cat} of Reaction 108 were obtained from the literature and summarised in Table ST.10.31.1.1.1. The log-normal distribution properties for the PGT k_{cat} of Reaction 108 are shown in Table ST.10.31.1.1.2 and plotted in Figure SF.10.31.1.1.1.

Table ST.10.31.1.1.1. Literature information used to design the PGT k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
3.50	NaN	Bacteria	E. coli.	Glucose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Waygood and Steeves, 1980)
3.30 x10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
8.30 x10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
3.28	NaN	Yeast	Saccharomyces cerevisiae	HXT7 transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Ye et al., 2001)

Table ST.10.31.1.1.2. The log-normal distribution properties of the PGT k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
1.33	7.30	9.20×10^{-1}	8.0×10^{-1}

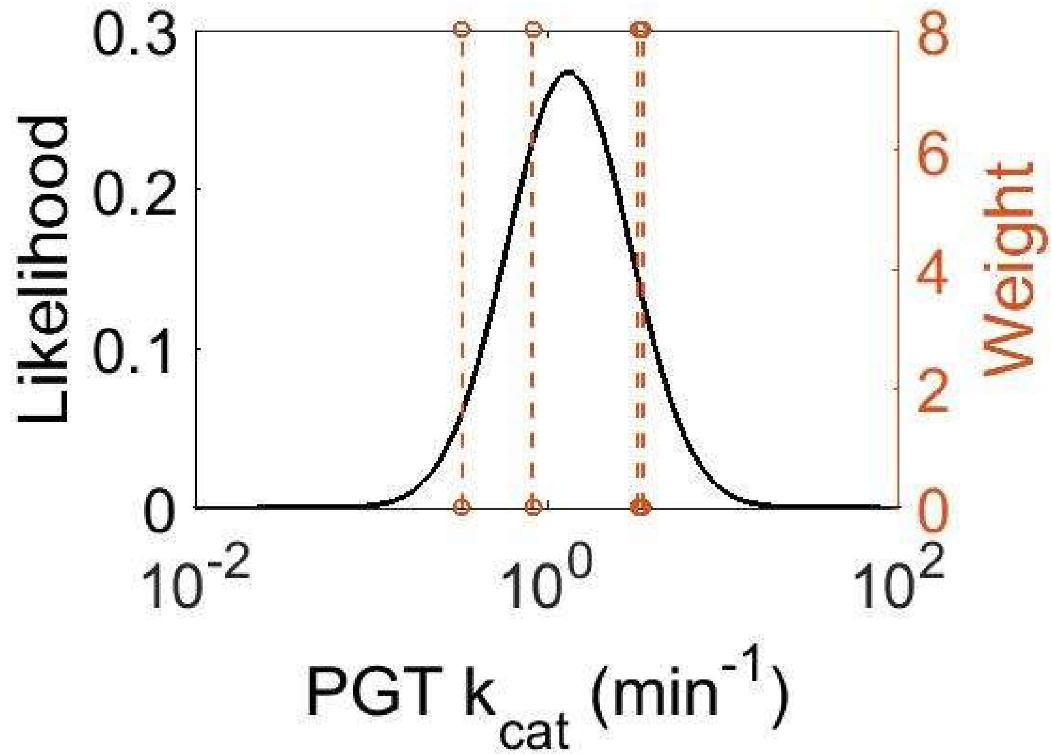


Figure SF.10.31.1.1.1. The estimated probability distribution for the PGT k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.31.1.2. Parameter: PGT K_{ms}

Parameter values for the PGT K_{ms} of Reaction 108 were obtained from the literature and summarised in Table ST.10.31.1.2.1. The log-normal distribution properties for the PGT K_{ms} of Reaction 108 are shown in Table ST.10.31.1.2.2 and plotted in Figure SF.10.31.1.2.1.

Table ST.10.31.1.2.1. Literature information used to design the PGT K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details									
		Substrate	**Species**	**Expression Vector**	**Enzyme**	**pH**	**Temperature (°C)**	**Other**	**Weight**	**Type of error**	**Reference**
3.31×10^{-5}	1.31×10^{-4}		Human	Eye	PGT	7.5	37		512	0	(Waygood and Steeves, 1980)
3.76×10^{-4}	3.40×10^{-5}		Human	Embryonic kidney cells (HEK293)	PGT	Unknown	37		192	0	(Naftalin et al., 2007)
5.40×10^{-3}	NaN		Human	Embryonic kidney cells (HEK293)	PGT	Unknown	37		2048	0	(Naftalin et al., 2007)
7.20×10^{-3}	5.95×10^{-4}		Canine	Madin-Darby Canine Kidney Epithelial Cells	PGT	Unknown	Unknown		512	0	(Ye et al., 2001)

				(MDCK) cells							
9.40 x10^{-5}	NaN	PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Waygood and Steeves, 1980)
4.23 x10^{-4}	NaN	TXB2	Human	HeLa cells	PGT	7	27		**1024**	0	(Naftalin et al., 2007)
7.57 x10^{-3}	NaN	K6PGF1a	Human	HeLa cells	PGT	7	27		**1024**	0	(Naftalin et al., 2007)
4.87 x10^{-5}	NaN	PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Ye et al., 2001)
5.02 x10^{-5}	NaN	PGF2a	Human	HeLa cells	PGT	7	27		**1024**	0	(Waygood and Steeves, 1980)
5.00 x10^{-3}	NaN	15-K-PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Naftalin et al., 2007)
5.00 x10^{-3}	NaN	DH-15-K-PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Naftalin et al., 2007)
3.82 x10^{-5}	NaN	PGH2	Human	HeLa cells	PGT	7	27		**2048**	0	(Ye et al., 2001)

Table ST.10.31.1.2.2. The log-normal distribution properties of the PGT K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.10 x10^{-3}	9.42 x10^{1}	-4.67	1.45

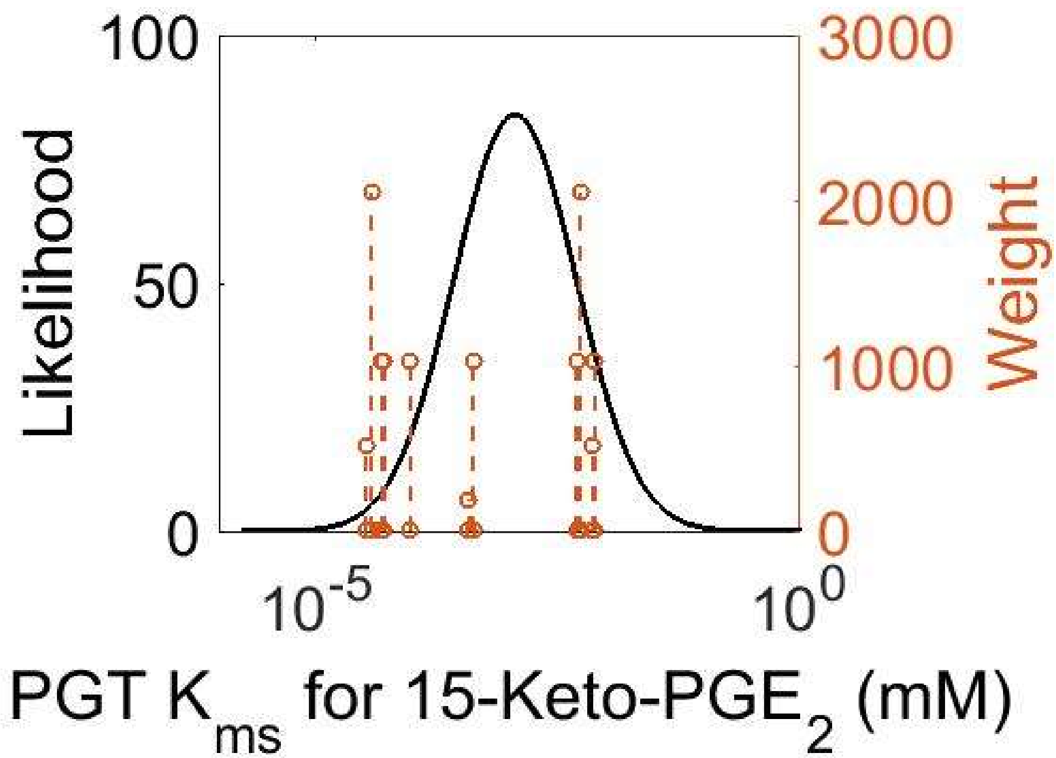


Figure SF.10.31.1.2.1. The estimated probability distribution for the PGT K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.31.1.3. Parameter: PGT concentration

Parameter values for the PGT concentration of Reaction 108 were obtained from the literature and summarised in Table ST.10.31.1.3.1. The log-normal distribution properties for the PGT concentration of Reaction 108 are shown in Table ST.10.31.1.3.2 and plotted in Figure SF.10.31.1.3.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.10.31.1.3.1. Literature information used to design the PGT concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
2.82	NaN	Human	Gut	PGT	7.5	37		2048	0	(Kim et al., 2014)
1.74×10^{1}	NaN	Human	Oesophagus	PGT	7.5	37		2048	0	(Wilhelm et al., 2014)
1.25×10^{2}	NaN	Human	Lung	PGT	7.5	37		2048	0	(Kim et al., 2014)

Table ST.10.31.1.3.2. The log-normal distribution properties of the PGT concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.73×10^{1}	9.57×10^{-5}	4.72	3.90	1.02

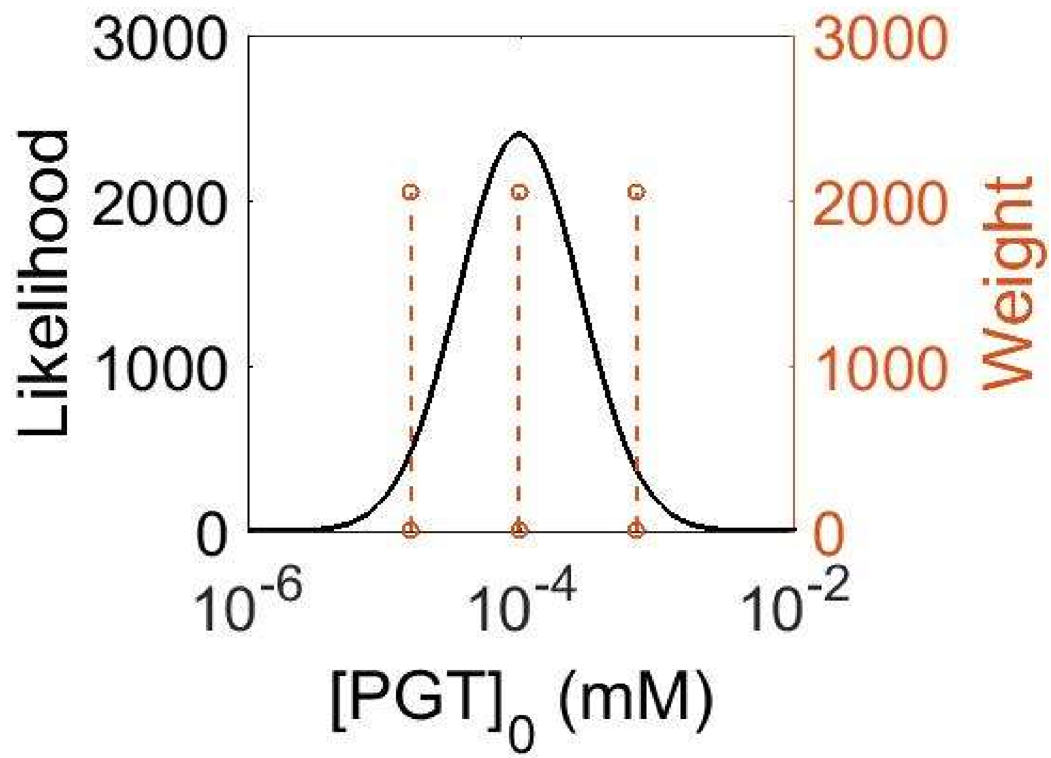


Figure SF.10.31.1.3.1. The estimated probability distribution for the PGT concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.32. Reaction 109: 6-keto-PGF$_{1\alpha}$ ⇌ ex6-keto-PGF$_{1\alpha}$ (PGT)
6-keto-PGF$_{1\alpha}$ is relocated from the intracellular compartment to the extracellular compartment via the prostaglandin (PGT) transporter.

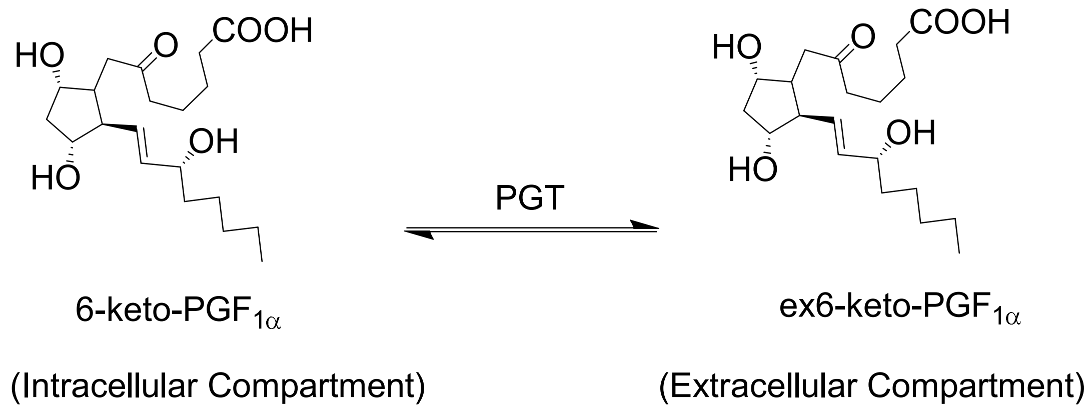


Figure SF.10.32. The transport of 6-keto-prostaglandin F$_{1\alpha}$ (6-keto-PGF$_{1\alpha}$) from the intracellular compartment to the extracellular compartment by prostaglandin (PGT) transporter (Reaction 109).

SEq.10.32. Reaction rate law for Reaction 109.

$$\boldsymbol{v_{109}} = [\boldsymbol{PGT}] \cdot \boldsymbol{k_{cat}} \cdot \frac{\frac{6-\text{keto}-\text{PGF}_{1\alpha}}{K_m} \cdot \left(1 - \frac{\text{ex6}-\text{keto}-\text{PGF}_{1\alpha}}{6-\text{keto}-\text{PGF}_{1\alpha} \cdot e^{-0.5\cdot\left(G+R\cdot T\cdot\ln\left(\frac{ATP}{ADP}\right)\right)/R\cdot T}}\right)}{1+\frac{6-\text{keto}-\text{PGF}_{1\alpha}}{K_m}+\frac{\text{ex6}-\text{keto}-\text{PGF}_{1\alpha}}{K_m}+\text{PGT\_CI}}$$

S.10.32.1. Reaction parameters

S.10.32.1.1. Parameter: PGT k_{cat}

Parameter values for the PGT k_{cat} of Reaction 109 were obtained from the literature and summarised in Table ST.10.32.1.1.1. The log-normal distribution properties for the PGT k_{cat} of Reaction 109 are shown in Table ST.10.32.1.1.2 and plotted in Figure SF.10.32.1.1.1.

Table ST.10.32.1.1.1. Literature information used to design the PGT k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
3.50	NaN	Bacteria	E. coli.	Glucose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Waygood and Steeves, 1980)
3.30×10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
8.30×10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
3.28	NaN	Yeast	Saccharomyces cerevisiae	HXT7 transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Ye et al., 2001)

Table ST.10.32.1.1.2. The log-normal distribution properties of the PGT K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
1.33	7.30	9.20×10^{-1}	8.0×10^{-1}

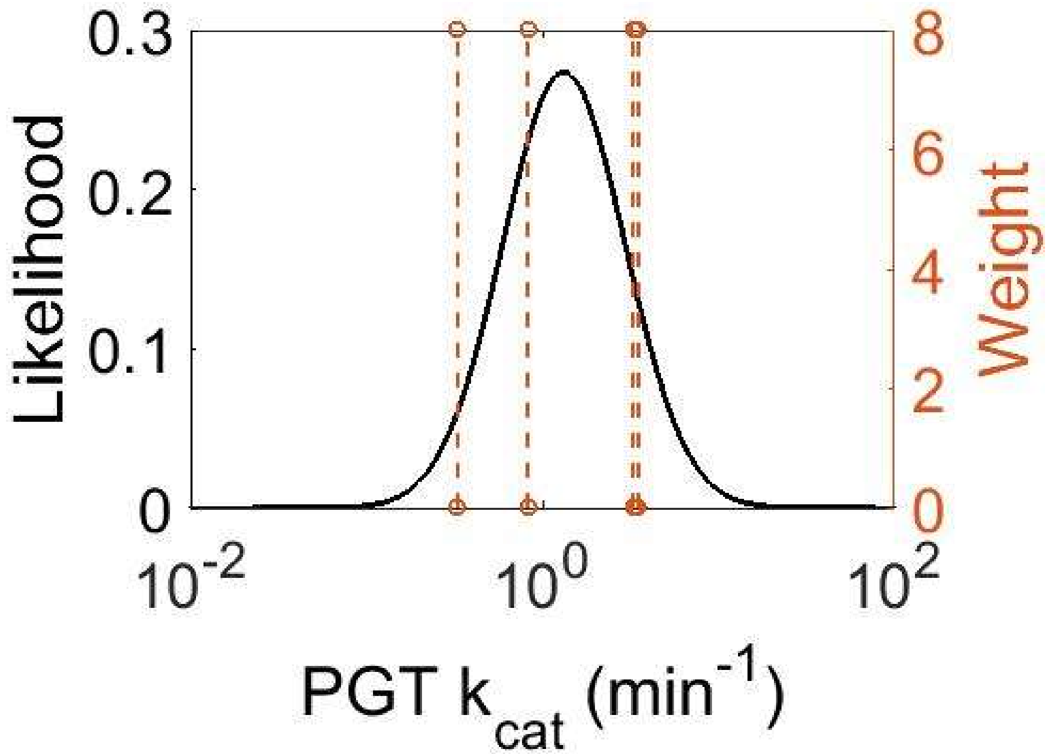


Figure SF.10.32.1.1.1. The estimated probability distribution for the PGT k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.32.1.2. Parameter: PGT K_{ms}

Parameter values for the PGT K_{ms} of Reaction 109 were obtained from the literature and summarised in Table ST.10.32.1.2.1. The log-normal distribution properties for the PGT K_{ms} of Reaction 109 are shown in Table ST.10.32.1.2.2 and plotted in Figure SF.10.32.1.2.1.

Table ST.10.32.1.2.1. Literature information used to design the PGT K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Other	Weight	Type of error	Reference
		Substrate	Species	Expression Vector	Enzyme	pH	Temperature (°C)				
3.31×10^{-5}	1.31×10^{-4}		Human	Eye	PGT	7.5	37		512	0	(Waygood and Steeves, 1980)
3.76×10^{-4}	3.40×10^{-5}		Human	Embryonic kidney cells (HEK293)	PGT	Unknown	37		192	0	(Naftalin et al., 2007)
5.40×10^{-3}	NaN		Human	Embryonic kidney cells (HEK293)	PGT	Unknown	37		2048	0	(Naftalin et al., 2007)
7.20×10^{-3}	5.95×10^{-4}		Canine	Madin-Darby Canine Kidney Epithelial Cells (MDCK) cells	PGT	Unknown	Unknown		512	0	(Ye et al., 2001)

9.40×10^{-5}	NaN	PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Waygood and Steeves, 1980)
4.23×10^{-4}	NaN	TXB2	Human	HeLa cells	PGT	7	27		**1024**	0	(Naftalin et al., 2007)
7.57×10^{-3}	NaN	K6PGF1a	Human	HeLa cells	PGT	7	27		**1024**	0	(Naftalin et al., 2007)
4.87×10^{-5}	NaN	PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Ye et al., 2001)
5.02×10^{-5}	NaN	PGF2a	Human	HeLa cells	PGT	7	27		**1024**	0	(Waygood and Steeves, 1980)
5.00×10^{-3}	NaN	15-K-PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Naftalin et al., 2007)
5.00×10^{-3}	NaN	DH-15-K-PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Naftalin et al., 2007)
3.82×10^{-5}	NaN	PGH2	Human	HeLa cells	PGT	7	27		**2048**	0	(Ye et al., 2001)

Table ST.10.32.1.2.2. The log-normal distribution properties of the PGT K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.10×10^{-3}	9.42×10^{1}	-4.67	1.45

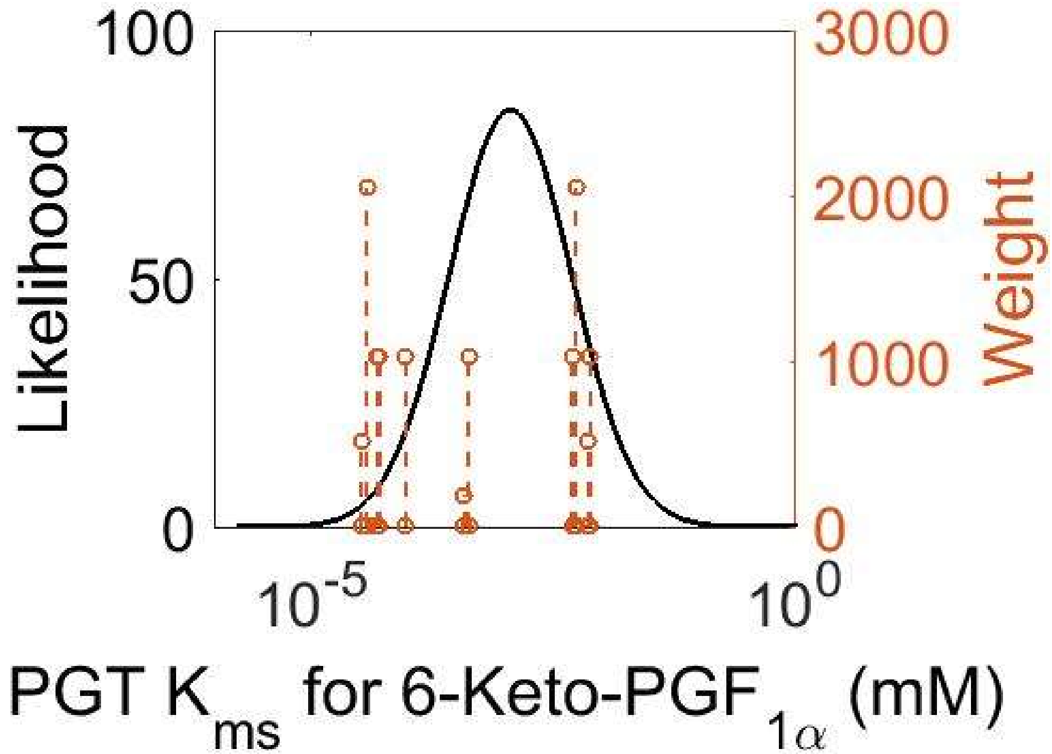


Figure SF.10.32.1.2.1. The estimated probability distribution for the PGT K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.32.1.3. Parameter: PGT concentration

Parameter values for the PGT concentration of Reaction 109 were obtained from the literature and summarised in Table ST.10.32.1.3.1. The log-normal distribution properties for the PGT concentration of Reaction 109 are shown in Table ST.10.32.1.3.2 and plotted in Figure SF.10.32.1.3.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.10.32.1.3.1. Literature information used to design the PGT concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
2.82	NaN	Human	Gut	PGT	7.5	37		2048	0	(Kim et al., 2014)
1.74 $x10^1$	NaN	Human	Oesophagus	PGT	7.5	37		2048	0	(Wilhelm et al., 2014)
1.25 $x10^2$	NaN	Human	Lung	PGT	7.5	37		2048	0	(Kim et al., 2014)

Table ST.10.32.1.3.2. The log-normal distribution properties of the PGT concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.73 $x10^1$	9.57 $x10^{-5}$	4.72	3.90	1.02

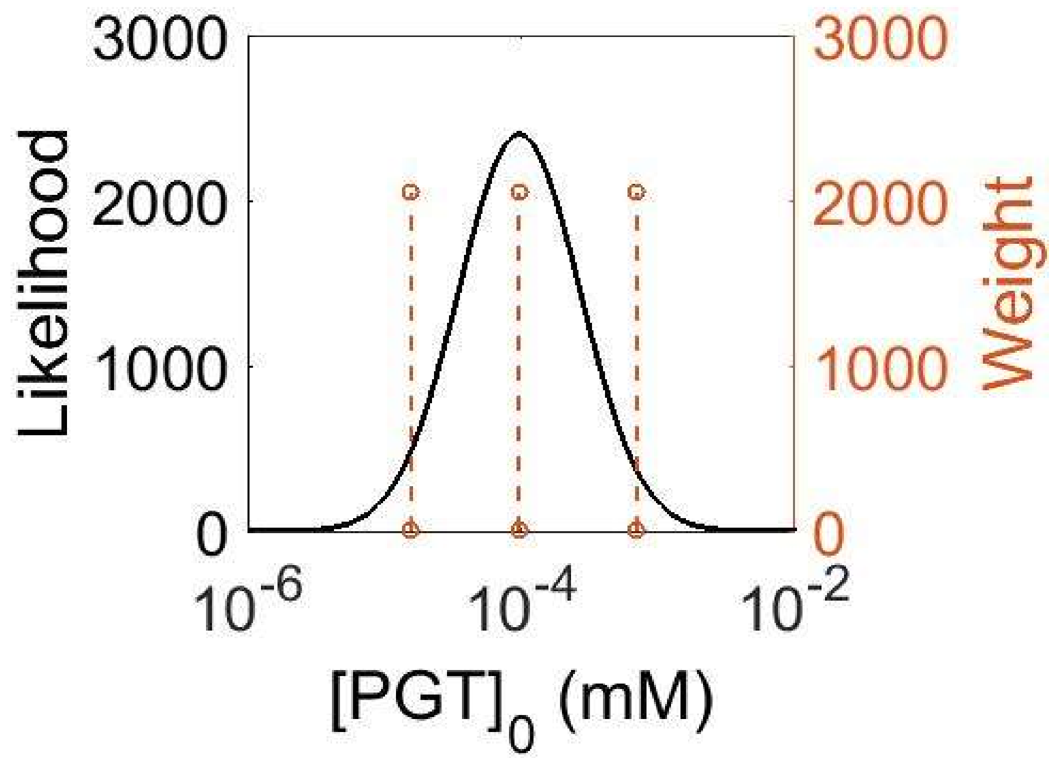


Figure SF.10.32.1.3.1. The estimated probability distribution for the PGT concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.33. Reaction 110: $TXA_2 \rightleftharpoons exTXA_2$ (PGT)
TXA_2 is relocated from the intracellular compartment to the extracellular compartment via the prostaglandin (PGT) transporter.

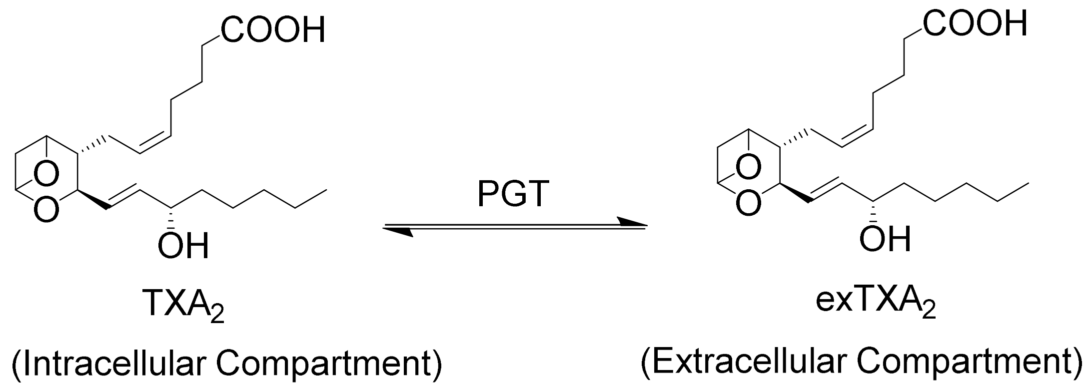


Figure SF.10.33. The transport of thromboxane A_2 (TXA_2) from the intracellular compartment to the extracellular compartment by prostaglandin (PGT) transporter (Reaction 110).

SEq.10.33. Reaction rate law for Reaction 110.

$$\boldsymbol{v_{110}} = [\boldsymbol{PGT}] \cdot \boldsymbol{k_{cat}} \cdot \frac{\mathbf{TXA_2}/K_m \cdot \left(1 - \frac{\mathbf{exTXA_2}}{\mathbf{TXA_2} \cdot e^{-0.5 \cdot \left(G + R \cdot T \cdot \ln\left(\frac{ATP}{ADP}\right)\right)/R \cdot T}}\right)}{1 + \frac{\mathbf{TXA_2}}{K_m} + \frac{\mathbf{exTXA_2}}{K_m} + \mathbf{PGT\_CI}}$$

S.10.33.1. Reaction parameters

S.10.33.1.1. Parameter: PGT k_{cat}

Parameter values for the PGT k_{cat} of Reaction 110 were obtained from the literature and summarised in Table ST.10.33.1.1.1. The log-normal distribution properties for the PGT k_{cat} of Reaction 110 are shown in Table ST.10.33.1.1.2 and plotted in Figure SF.10.33.1.1.1.

Table ST.10.33.1.1.1. Literature information used to design the PGT k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	Error (min^{-1})	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
3.50	NaN	Bacteria	E. coli.	Glucose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Waygood and Steeves, 1980)
3.30 $x10^{-1}$	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
8.30 $x10^{-1}$	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
3.28	NaN	Yeast	Saccharomyces cerevisiae	HXT7 transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Ye et al., 2001)

Table ST.10.33.1.1.2. The log-normal distribution properties of the PGT k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
1.33	7.30	9.20×10^{-1}	$8.0 \ 10^{-1}$

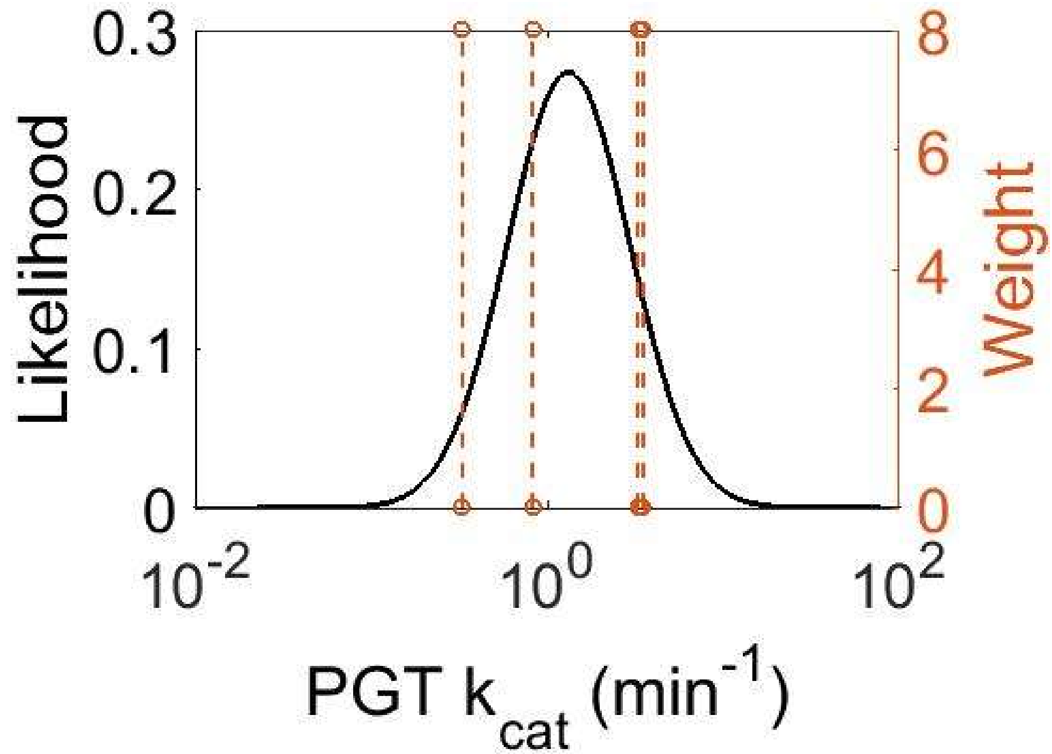


Figure SF.10.33.1.1.1. The estimated probability distribution for the PGT k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.33.1.2. Parameter: PGT K_{ms}

Parameter values for the PGT K_{ms} of Reaction 110 were obtained from the literature and summarised in Table ST.10.33.1.2.1. The log-normal distribution properties for the PGT K_{ms} of Reaction 110 are shown in Table ST.10.33.1.2.2 and plotted in Figure SF.10.33.1.2.1.

Table ST.10.33.1.2.1. Literature information used to design the PGT K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Other	Weight	Type of error	Reference
		Substrate	Species	Expression Vector	Enzyme	pH	Temperature (°C)				
3.31×10^{-5}	1.31×10^{-4}		Human	Eye	PGT	7.5	37		512	0	(Waygood and Steeves, 1980)
3.76×10^{-4}	3.40×10^{-5}		Human	Embryonic kidney cells (HEK293)	PGT	Unknown	37		192	0	(Naftalin et al., 2007)
5.40×10^{-3}	NaN		Human	Embryonic kidney cells (HEK293)	PGT	Unknown	37		2048	0	(Naftalin et al., 2007)
7.20×10^{-3}	5.95×10^{-4}		Canine	Madin-Darby Canine Kidney Epithelial Cells (MDCK) cells	PGT	Unknown	Unknown		512	0	(Ye et al., 2001)

9.40 x10^{-5}	NaN	PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Waygood and Steeves, 1980)
4.23 x10^{-4}	NaN	TXB2	Human	HeLa cells	PGT	7	27		**1024**	0	(Naftalin et al., 2007)
7.57 x10^{-3}	NaN	K6PGF1a	Human	HeLa cells	PGT	7	27		**1024**	0	(Naftalin et al., 2007)
4.87 x10^{-5}	NaN	PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Ye et al., 2001)
5.02 x10^{-5}	NaN	PGF2a	Human	HeLa cells	PGT	7	27		**1024**	0	(Waygood and Steeves, 1980)
5.00 x10^{-3}	NaN	15-K-PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Naftalin et al., 2007)
5.00 x10^{-3}	NaN	DH-15-K-PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Naftalin et al., 2007)
3.82 x10^{-5}	NaN	PGH2	Human	HeLa cells	PGT	7	27		**2048**	0	(Ye et al., 2001)

Table ST.10.33.1.2.2. The log-normal distribution properties of the PGT K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
1.10 x10^{-3}	9.42 x10^{1}	-4.67	1.45

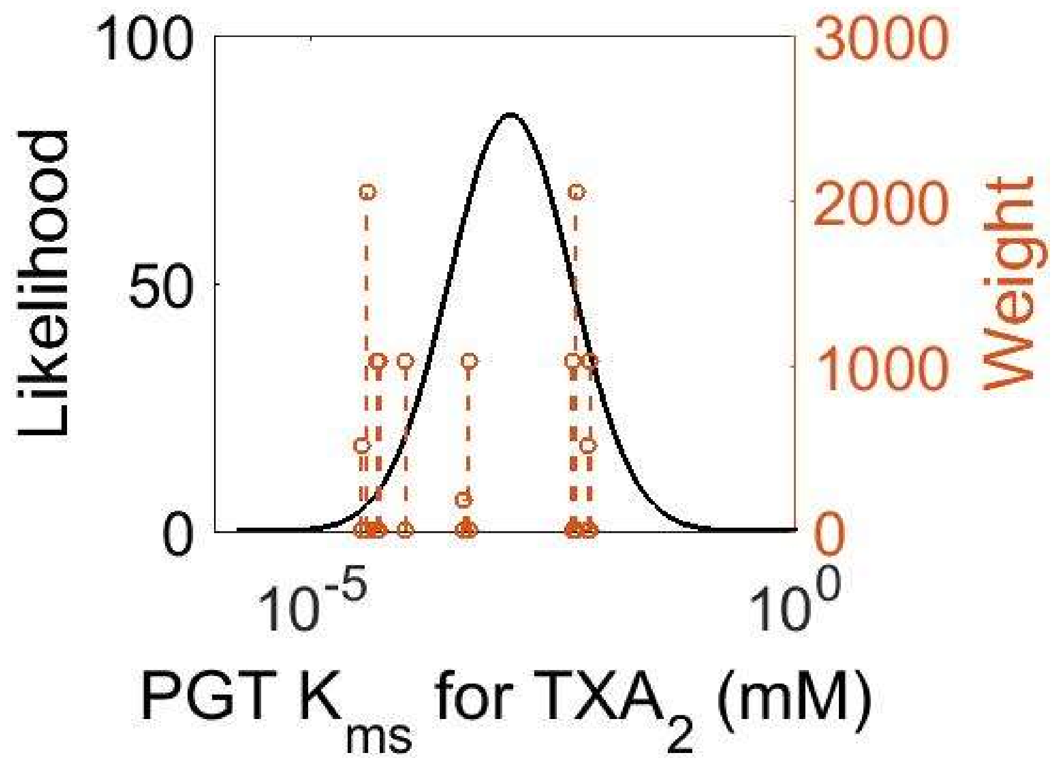


Figure SF.10.33.1.2.1. The estimated probability distribution for the PGT K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.33.1.3. Parameter: PGT concentration

Parameter values for the PGT concentration of Reaction 110 were obtained from the literature and summarised in Table ST.10.33.1.3.1. The log-normal distribution properties for the PGT concentration of Reaction 110 are shown in Table ST.10.33.1.3.2 and plotted in Figure SF.10.33.1.3.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.10.33.1.3.1. Literature information used to design the PGT concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
2.82	NaN	Human	Gut	PGT	7.5	37		2048	0	(Kim et al., 2014)
1.74 x10^{1}	NaN	Human	Oesophagus	PGT	7.5	37		2048	0	(Wilhelm et al., 2014)
1.25 x10^{2}	NaN	Human	Lung	PGT	7.5	37		2048	0	(Kim et al., 2014)

Table ST.10.33.1.3.2. The log-normal distribution properties of the PGT concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.73 x10^{1}	9.57 x10^{-5}	4.72	3.90	1.02

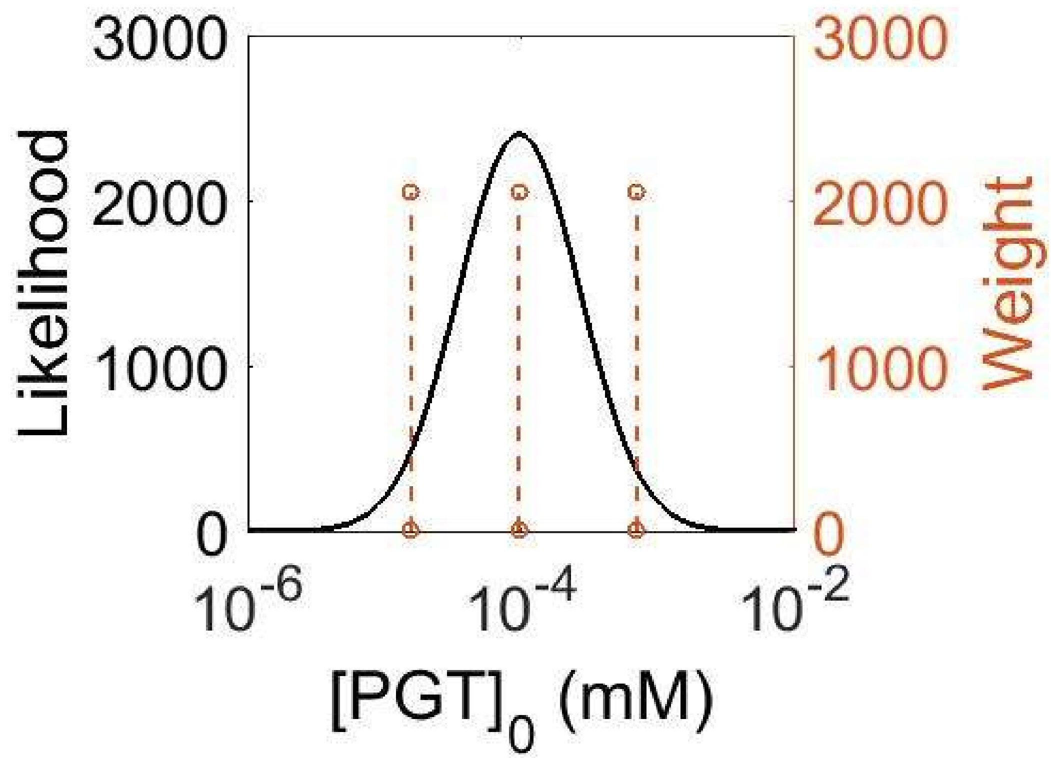


Figure SF.10.33.1.3.1. The estimated probability distribution for the PGT concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.34. Reaction 111: 15-deoxy-PGJ$_2$ ⇌ ex15-deoxy-PGJ$_2$ (PGT)
15-deoxy-PGJ$_2$ is relocated from the intracellular compartment to the extracellular compartment via the prostaglandin (PGT) transporter.

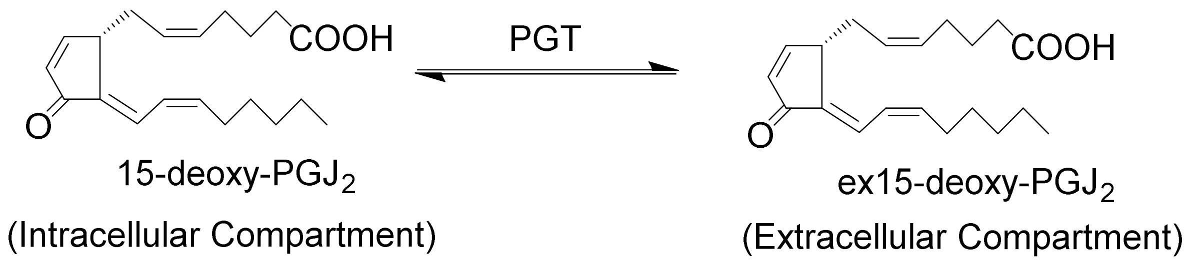


Figure SF.10.34. The transport of 15-deoxy-prostaglandin J$_2$ (15-deoxy-PGJ$_2$) from the intracellular compartment to the extracellular compartment by prostaglandin (PGT) transporter (Reaction 111).

SEq.10.34. Reaction rate law for Reaction 111.

$$\boldsymbol{v_{111}} = [\boldsymbol{PGT}] \cdot \boldsymbol{k_{cat}} \cdot \frac{\mathbf{15{-}deoxy{-}PGJ_2}/K_m \cdot \left(1 - \frac{\mathbf{ex15{-}deoxy{-}PGJ_2}}{\mathbf{15{-}deoxy{-}PGJ_2} \cdot e^{-0.5\cdot\left(G + R\cdot T\cdot \ln\left(\frac{ATP}{ADP}\right)\right)/R\cdot T}}\right)}{1 + \frac{\mathbf{15{-}deoxy{-}PGJ_2}}{K_m} + \frac{\mathbf{ex15{-}deoxy{-}PGJ_2}}{K_m} + \mathbf{PGT\_CI}}$$

S.10.34.1. Reaction parameters

S.10.34.1.1. Parameter: PGT k_{cat}

Parameter values for the PGT k_{cat} of Reaction 111 were obtained from the literature and summarised in Table ST.10.34.1.1.1. The log-normal distribution properties for the PGT k_{cat} of Reaction 111 are shown in Table ST.10.34.1.1.2 and plotted in Figure SF.10.34.1.1.1.

Table ST.10.34.1.1.1. Literature information used to design the PGT k_{cat} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (min^{-1})	**Error (min^{-1})**	**Experimental details**						**Weight**	**Type of error**	**Reference**
		Species	**Expression Vector**	**Enzyme**	**pH**	**Temperature (°C)**	**Other**			
3.50	NaN	Bacteria	E. coli.	Glucose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Waygood and Steeves, 1980)
3.30 x10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
8.30 x10^{-1}	NaN	Bacteria	E. coli.	Lactose transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Naftalin et al., 2007)
3.28	NaN	Yeast	Saccharomyces cerevisiae	HXT7 transporter	Unknown	Unknown	Bionumbers calculation	**8**	0	(Ye et al., 2001)

Table ST.10.34.1.1.2. The log-normal distribution properties of the PGT k_{cat} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (min^{-1})	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
1.33	7.30	9.20×10^{-1}	8.0×10^{-1}

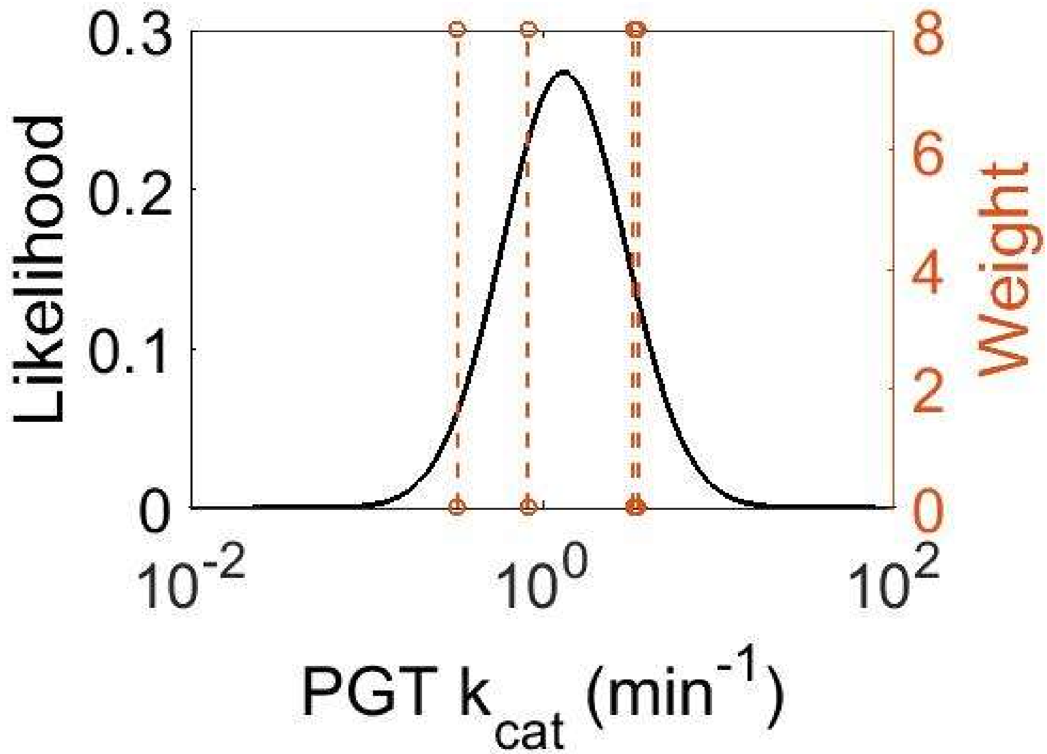


Figure SF.10.34.1.1.1. The estimated probability distribution for the PGT k_{cat}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.34.1.2. Parameter: PGT K_{ms}

Parameter values for the PGT K_{ms} of Reaction 111 were obtained from the literature and summarised in Table ST.10.34.1.2.1. The log-normal distribution properties for the PGT K_{ms} of Reaction 111 are shown in Table ST.10.34.1.2.2 and plotted in Figure SF.10.34.1.2.1.

Table ST.10.34.1.2.1. Literature information used to design the PGT K_{ms} parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (mM)	Error (mM)	Experimental details						Other	Weight	Type of error	Reference
		Substrate	Species	Expression Vector	Enzyme	pH	Temperature (°C)				
3.31×10^{-5}	1.31×10^{-4}		Human	Eye	PGT	7.5	37		512	0	(Waygood and Steeves, 1980)
3.76×10^{-4}	3.40×10^{-5}		Human	Embryonic kidney cells (HEK293)	PGT	Unknown	37		192	0	(Naftalin et al., 2007)
5.40×10^{-3}	NaN		Human	Embryonic kidney cells (HEK293)	PGT	Unknown	37		2048	0	(Naftalin et al., 2007)
7.20×10^{-3}	5.95×10^{-4}		Canine	Madin-Darby Canine Kidney Epithelial Cells (MDCK) cells	PGT	Unknown	Unknown		512	0	(Ye et al., 2001)

9.40×10^{-5}	NaN	PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Waygood and Steeves, 1980)
4.23×10^{-4}	NaN	TXB2	Human	HeLa cells	PGT	7	27		**1024**	0	(Naftalin et al., 2007)
7.57×10^{-3}	NaN	K6PGF1a	Human	HeLa cells	PGT	7	27		**1024**	0	(Naftalin et al., 2007)
4.87×10^{-5}	NaN	PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Ye et al., 2001)
5.02×10^{-5}	NaN	PGF2a	Human	HeLa cells	PGT	7	27		**1024**	0	(Waygood and Steeves, 1980)
5.00×10^{-3}	NaN	15-K-PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Naftalin et al., 2007)
5.00×10^{-3}	NaN	DH-15-K-PGE2	Human	HeLa cells	PGT	7	27		**1024**	0	(Naftalin et al., 2007)
3.82×10^{-5}	NaN	PGH2	Human	HeLa cells	PGT	7	27		**2048**	0	(Ye et al., 2001)

Table ST.10.34.1.2.2. The log-normal distribution properties of the PGT K_{ms} distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (mM)	**Confidence Interval**	**Location parameter (μ)**	**Scale parameter (σ)**
1.10×10^{-3}	9.42×10^{1}	-4.67	1.45

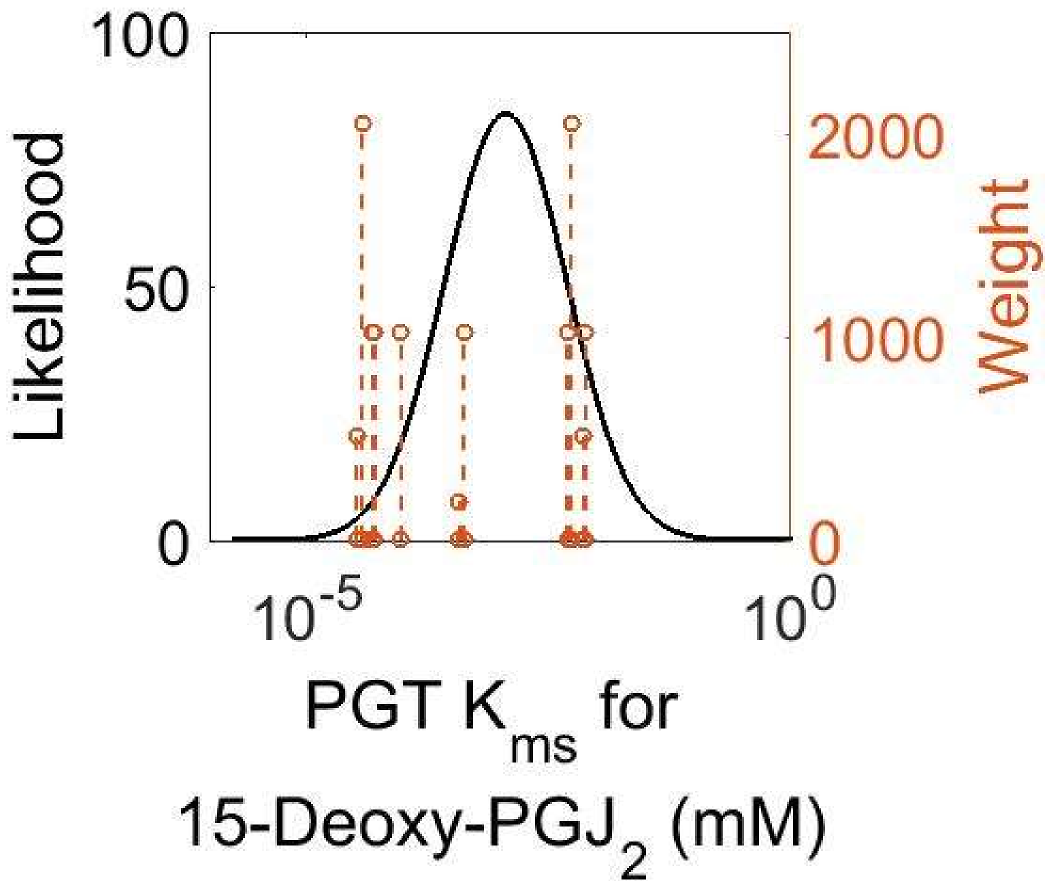


Figure SF.10.34.1.2.1. The estimated probability distribution for the PGT K_{ms}. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

S.10.34.1.3. Parameter: PGT concentration

Parameter values for the PGT concentration of Reaction 111 were obtained from the literature and summarised in Table ST.10.34.1.3.1. The log-normal distribution properties for the PGT concentration of Reaction 111 are shown in Table ST.10.34.1.3.2 and plotted in Figure SF.10.34.1.3.1. To convert the enzyme concentration from ppm to mM, **Equation S.6.2** was used.

Table ST.10.34.1.3.1. Literature information used to design the PGT concentration parameter distribution. Each value was assigned a weight using the protocol described in Section 2.6.2. The type of error was assigned as 0 if it was additive and 1 if it was multiplicative.

Value (ppm)	Error (ppm)	Experimental details						Weight	Type of error	Reference
		Species	Expression Vector	Enzyme	pH	Temperature (°C)	Other			
2.82	NaN	Human	Gut	PGT	7.5	37		2048	0	(Kim et al., 2014)
1.74 $x10^1$	NaN	Human	Oesophagus	PGT	7.5	37		2048	0	(Wilhelm et al., 2014)
1.25 $x10^2$	NaN	Human	Lung	PGT	7.5	37		2048	0	(Kim et al., 2014)

Table SF.10.34.1.3.1. The log-normal distribution properties of the PGT concentration distribution. These values were calculated using the functions described in Section 2.6.2.

Mode (ppm)	Mode (mM)	Confidence Interval	Location parameter (μ)	Scale parameter (σ)
1.73 $x10^1$	9.57 $x10^{-5}$	4.72	3.90	1.02

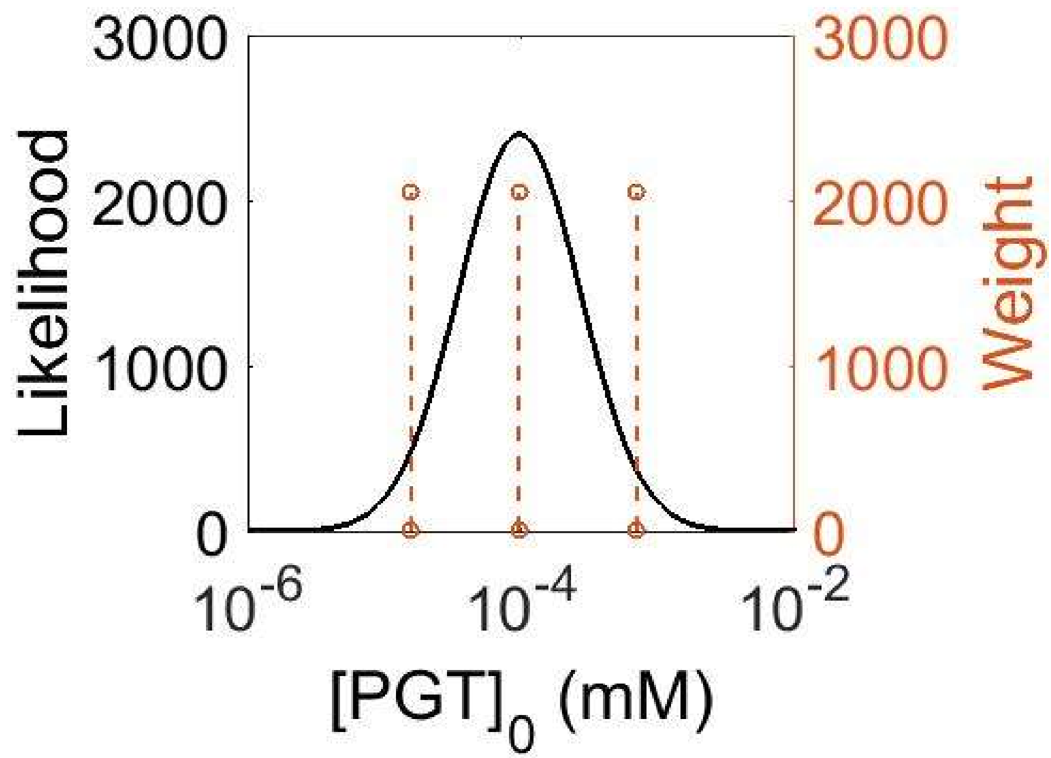


Figure SF.10.34.1.3.1. The estimated probability distribution for the PGT concentration. The value and weight of the literature values used to define the distribution are indicated by an orange dashed line. The x axis is plotted on a log-scale.

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Supplementary Document S11. Initiation Reaction Structure and Parameterisation.

Documentation of parameter values obtained for all transporter-mediated reactions in the model (Reactions 95, 112, 113; Supplementary Table S1) from the literature and associated uncertainty for the eicosanoid network model. Parameterisation was performed using the method of Tsigkinopoulou *et al.,* (2018). The table includes information regarding each reaction and its respective parameters are documented. This includes information such as the reaction rate law and the literature values that were used to define parameters, including experimental conditions, total weights and literature references from which the data were obtained. In this model some parameters are referred as "Dependent parameters", meaning that the log-normal distribution for that parameter was calculated using multivariate distributions (discussed in **Section 2.6.2**). As a result, no confidence interval factor or literature values were cited for the Dependent parameters.

Contents

S.11.1. Reaction 95: ϕ → AA

The liberation of free AA from the phospholipid membrane. As this reaction is performed by a multitude of isoforms of PLA2, all with unique kinetics, this reaction was simplified.

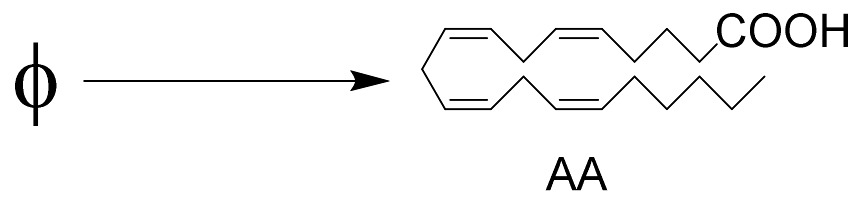

Figure SF.11.1. The release of arachidonic acid into the computational model (Reaction 95).

S.Eq.11.1. Reaction rate law for Reaction 95.

$$\boldsymbol{v_{95}} = \frac{\boldsymbol{c}}{\boldsymbol{AADT}} - \frac{\boldsymbol{c2 \cdot \ln(2) \cdot [AA]}}{\boldsymbol{AAHL}}$$

S.11.1.1. Reaction parameters

Table ST.11.1.1.1. The name, shorthand, initial value, adapted value and justification for each event parameter. These parameters are adapted to represent different model scenarios.

Parameter Name	Parameter Shorthand	Initial Value	Justification
Doubling time of the AA event	AADT	420 min	AA was set to be released for 6h, as this was the length of the inflammatory window in the modelled system. This value was not changed in the modelled scenarios.
Maximum concentration of AA	c	0 mM	The adapted value of this parameter depends on the scenario (Table S13). This value changes 60 min into the simulation for all scenarios.
Decay switch	c2	0	If required the production of AA can decrease over time by amending this value from 0 to 1. This was set to 0 in all scenarios.
Half-life of the AA event	AAHL	420 min	This value was arbitrarily set at 420 min. However, no simulations required AA release to decrease over time.

Table ST.11.1.1.2. Values of the Maximum AA parameter in the eight model scenarios.

	Scenario							
Treatment	**A23187**		**Indomethacin and A23187**		**ATP**		**UVR**	
Cell type	**HaCaT keratinocyte**	**46BR.1N fibroblast**	**HaCaT keratinocyte**	**46BR.1N fibroblast**	**HaCaT keratinocyte**	**46BR.1N fibroblast**	**HaCaT keratinocyte**	**46BR.1N fibroblast**
Σ AA released (pg/million cells)	2.03 $x10^{6}$	5.43 $x10^{5}$	1.64 $x10^{6}$	2.11 $x10^{5}$	8.43 $x10^{5}$	3.29 $x10^{4}$	1.80 $x10^{6}$	4.30 $x10^{5}$
Σ AA released (mM)	5.77 $x10^{-4}$	1.54 $x10^{-4}$	4.65 $x10^{-4}$	6.00 $x10^{-5}$	2.40 $x10^{-4}$	9.36 $x10^{-6}$	5.11 $x10^{-4}$	1.22E $x10^{-4}$

S.11.2. Reaction 112: ϕ → COX-2

The induced expression of COX-2. As this process is as a result of complex transcription and translation processes, this reaction was simplified.

$$\phi \rightarrow \text{COX-2}$$

Figure SF.11.2. The induction of COX-2 in the computational model (Reaction 112).

SEq.11.2. Reaction rate law for Reaction 112.

$$\boldsymbol{v_{112}} = \frac{\boldsymbol{c3}}{\boldsymbol{COX2DT}} - \frac{\boldsymbol{c4} \cdot \ln(2) \cdot [\boldsymbol{COX-2}]}{\boldsymbol{COX2HL}}$$

S.11.2.1. Reaction parameters

S.11.2.1.1. Fixed Parameters

Table ST.11.2.1.1.1. The name, shorthand, initial value, adapted value and justification for the COX-2 event parameter. These parameters are adapted to represent different model scenarios.

Parameter Name	Parameter Shorthand	Initial Value	Justification
Doubling time of the COX-2 event	COX2DT	180 min	This value was upon the unpublished western blot data in (Kiezel-Tsugunova, 2017).
Maximum concentration of COX-2	C3	0 mM	The adapted value of this parameter depends on the scenario (Table S15). This value changes 240 min into the simulation for the UVR scenarios.
Decay switch	C4	0	If required the induced expression of COX-2 can decrease over time by amending this value from 0 to 1. This was set to 0 in all scenarios.
Half-life of the COX-2 event	COX2HL	0 min	This value was arbitrarily set at 0 min. However, no simulations required COX-2 release to decrease over time.

Table ST.11.2.1.1.2. Values of the COX-2 concentration in the eight model scenarios.

	Scenario							
Treatment	**A23187**		**Indomethacin and A23187**		**ATP**		**UVR**	
Cell type	**HaCaT keratinocyte**	**46BR.1N fibroblast**	**HaCaT keratinocyte**	**46BR.1N fibroblast**	**HaCaT keratinocyte**	**46BR.1N fibroblast**	**HaCaT keratinocyte**	**46BR.1N fibroblast**
COX-1 (mM) at 0h	x	x	1.00×10^{-28}	1.00×10^{-28}	x	x	x	x
COX-2 (mM) at 0h	x	x	1.00×10^{-28}	1.00×10^{-28}	x	x	1.00×10^{-28}	1.00×10^{-28}
COX-2 (mM) at 6h	x	x	x	x	x	x	2.27×10^{-2}	2.2710^{-2}

S.11.3. Reaction 113: MAA → AA

In the attempt to improve the AA release mechanism, reaction 113 was added. However, this reaction was not incorporated into all model scenarios as it required further refinement.

$$MAA \rightarrow AA$$

Figure SF.11.2. The alternative release mechanism of arachidonic acid into the computational model (Reaction 113).

SEq.11.3. Reaction rate law for Reaction 113.

$$\boldsymbol{v_{113}} = \boldsymbol{R113K} \times [\boldsymbol{MAA}]$$

Supplementary Table S12. Ordinary differential equations for each metabolite in the model. Where "r" is the reaction number assigned in Supplementary Tables S2-6. Arachidonic acid (AA), Prostaglandin H_2 (PGH_2), Prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$), Thromboxane A_2 (TXA_2), Prostaglandin I_2 (PGI_2), Thromboxane B_2 (TXB_2), 6-Keto-prostaglandin $F_{1\alpha}$ (6-keto-$PGF_{1\alpha}$), Prostaglandin J_2 (PGJ_2), Prostaglandin D_2 (PGD_2), 15-Deoxy-prostaglandin J_2 (15-deoxy-PGJ_2), Prostaglandin E_2 (PGE_2), 5-hydroperoxy-eicosatetraenoic acid (5-HPETE), 5-Hydroxy-eicosatetraenoic acid (5-HETE), Leukotriene A_4 (LTA_4), 5-Oxo-eicosatetraenoic acid (5-oxo-ETE), Leukotriene B_4 (LTB_4), 15-hydroperoxy-eicosatetraenoic acid (15-HPETE), 15-Hydroxy-eicosatetraenoic acid (15-HETE), 12-hydroperoxy-eicosatetraenoic acid (12-HPETE), 12-Hydroxy-eicosatetraenoic acid (12-HETE), Extracellular prostaglandin $F_{2\alpha}$ (ex$PGF_{2\alpha}$), Extracellular thromboxane B_2 (exTXB_2), Extracellular 6-keto prostaglandin $F_{1\alpha}$ (ex6-keto-$PGF_{1\alpha}$), Extracellular prostaglandin E_2 (exPGE_2), Extracellular 15-deoxy-prostaglandin J_2 (ex15-deoxy-PGJ_2), Extracellular 5-oxo- eicosatetraenoic acid (ex5-oxo-ETE), Extracellular 15 -hydroxy-eicosatetraenoic acid (ex15-HETE), Extracellular leukotriene B_4 (exLTB_4), Leukotriene C_4 (LTC_4), Extracellular leukotriene C_4 (exLTC_4), 1 Extracellular 12-hydroxy-eicosatetraenoic acid (ex12-HETE), Extracellular thromboxane A_2 (exTXA_2), Extracellular prostaglandin I_2 (exPGI_2), Extracellular prostaglandin H_2 (exPGH_2), Extracellular prostaglandin D_2 (exPGD_2), Extracellular prostaglandin J_2 (exPGJ_2), Extracellular 12-hydroperoxy-eicosatetraenoic acid (ex12-HPETE), Extracellular 15-hydroperoxy-eicosatetraenoic acid (ex15-HPETE), Extracellular 5-hydroperoxy-eicosatetraenoic acid (ex5-HPETE), Extracellular 5-hydroxy-eicosatetraenoic acid (ex5-HETE), Extracellular leukotriene A_4 (exLTA_4), Extracellular arachidonic acid (exAA), 15-keto-prostaglandin E_2 (15-keto-PGE_2), Extracellular 15-keto-prostaglandin E_2 (ex15-keto-PGE_2), 13,14-Dihydro-15-keto-prostaglandin E_2 (13,14-dihydro-15-keto-PGE_2), Extracellular 13,14-dihydro-15-keto-prostaglandin E_2 (ex13,14-dihydro-15-keto-PGE_2), Cyclooxygenase 2 (COX-2).

Ordinary differential equations
d[AA]/dt=r95+r1-r2-r11-r17-r19-r42-r65-r92-r100+r113
d[PGH_2]/dt=r2+r65-r3-r4-r5-r10-r21-r81-r34
d[$PGF_{2\alpha}$]/dt=r3-r22-r72-r101

d[TXA_2]/dt=r4-r6-r32-r74-r110
d[PGI_2]/dt=r5-r7-r33-r76-r103
d[TXB_2]/dt=r6-r106-r73-r23
d[6-keto-$PGF_{1\alpha}$]/dt=r7-r24-r75-r109
d[PGJ_2]/dt=r8-r9-r36-r79-r105
d[PGD_2]/dt=r21-r8-r35-r80-r104
d[15-deoxy-PGJ_2]/dt=r9-r26-r78-r111
d[PGE_2]/dt=r10-r25-r66-r77-r102
d[5-HPETE]/dt=r11-r12-r13-r39-r87
d[5-HETE]/dt=r12-r14-r40-r83
d[LTA_4]/dt=r13-r15-r16-r41-r86
d[5-oxo-ETE]/dt=r14-r27-r82
d[LTB_4]/dt=r15-r29-r84
d[LTC_4]/dt=r16-r30-r85
d[15-HPETE]/dt=r17-r18-r38-r89
d[15-HETE]/dt=r18-r28-r88
d[12-HPETE]/dt=r19-r20-r37-r91
d[12-HETE]/dt=r20-r31-r90
d[ex$PGF_{2\alpha}$]/dt=r22+r101-r44
d[exTXB_2]/dt=r23+r106-r45+r96
d[ex6-keto-$PGF_{1\alpha}$]/dt=r24+r109-r47+r97
d[exPGE_2]/dt=r25+r102-r49
d[ex15-deoxy-PGJ_2]/dt=r26+r111-r50+r99
d[ex5-oxo-ETE]/dt=r27-r54
d[ex15-HETE]/dt=r28-r60
d[exLTB_4]/dt=r29-r56
d[exLTC_4]/dt=r30-r57
d[ex12-HETE]/dt=r31-r62
d[exTXA_2]/dt=r32+r110-r46-r96
d[exPGI_2]/dt=r33+r103-r48-r97
d[exPGH_2]/dt=-r53
d[exPGD_2]/dt=r35+r104-r52-r98
d[exPGJ_2]/dt=r36+r105-r51+r98-r99
d[ex12-HPETE]/dt=r37-r63
d[ex15-HPETE]/dt=r38-r61
d[ex5-HPETE]/dt=r39-r59
d[ex5-HETE]/dt=r40-r55
d[exLTA_4]/dt=r41-r58
d[exAA]/dt=-r64
d[15-keto-PGE_2]/dt=r66-r67-r69-r94-r108
d[ex15-keto-PGE_2]/dt=r67+r108-r68
d[13,14-dihydro-15-keto-PGE_2]/dt=r69-r70-r93-r107

d[ex13,14-dihydro-15-keto-PGE_2]/dt=r70+r107-r71
d[COX-2]/dt=r112-r2
d[Miscellaneous metabolites]/dt=r44+r45+r46+r47+r48+r49+r50+r51+r52+r53+r54 +r55+r56+r57+r58+r59+r60+r61+r62+r63+r64+r68+r71+r72+r73+r74+r75+r76+r77 +r78+r79+r80+r81+r82+r83+r84+r85+r86+r87+r88+r89+r90+r91+r92

Supplementary Table S13. Parameter changes used to model cell-specific AA release. Depending on the *in silico* experiment, the value of parameters in equation 2 change at set time points in order to recreate experimental observations. The data used for the “maximum 6h concentration of AA” parameter was the approximate difference of AA measured by fatty acid analysis after 6h of stimulation (mean of three independent experiments). Simulated treatments were A23187 (6 h, 5 μM), indomethacin (IND) (1 h, 10 μM) followed by A23187 (6 h, 5 μM), ATP (2 mM), ultraviolet radiation (15 mJ/cm^2). * HaCaT + UVR utilised a minimal initial AA concentration and delayed AA release, so the “*Maximum 6h Concentration of AA*" was set as 1.80×10^{5} pg/10^{6} cells for 0-3 h post-stimulation (10 % of the experimental maximum AA concentration), followed by 1.65×10^{6} pg/10^{6} cells for 3-6 h post-stimulation (90 % of the experimental maximum AA concentration). This represented the delayed AA cascade response to UVR stimulation.

		Parameters					
	***In Silico* Experiment**	“*Maximum 6h Concentration of AA*"			"*Doubling Time of AA*” (h)	“*Decay Switch*”	"*Half Life of AA*” (h)
		Value (pg/10^{6} cells)	Simulation time (h)	Duration (h)			
HaCaT keratinocytes	HaCaT + A23187	2.03×10^{6}	0	6	6	Off	6
	HaCaT + IND + A23187	1.64×10^{6}	0	6	6	Off	6
	HaCaT + ATP	8.43×10^{5}	0	6	6	Off	6
	HaCaT + UVR (*)	1.80×10^{5} 1.65×10^{6}	3	3	3	Off	6
46BR.1N	46BR.1N + A23187	5.43×10^{5}	0	6	6	Off	6
	46BR.1N + IND + A23187	2.11×10^{5}	0	6	6	Off	6
	46BR.1N + ATP	3.29×10^{4}	0	6	6	Off	6

	46BR.1N + UVR	4.30×10^5	0	6	6	Off	6

Supplementary Table S14. Examples of putative patterns of AA release: single release, decaying release, constant release, and delayed release (Figure 7B). The value of parameters in Equation 2 were set to change at set time points in order to recreate the relevant experimental observations.

	Parameters				
Simulation type	$Maximum\ Concentration\ of\ AA$		$Doubling\ Time\ of\ AA$ (min)	$Decay\ Switch$	$Half\ Life\ of\ AA$ (min)
	Time (min)	Duration (min)			
Single release	0	1	1	Off	360
Constant release	0	360	360	Off	360
Decaying release	0	1	1	On	360
Delayed release	180	180	180	Off	360

Supplementary Table S15. Parameter changes used to model the *in silico* COX-2 induction. Parameter changes are described for the "HaCaT + UVR" and "46BR.1N + UVR" *in silico* experiments. The $"Maximum\ 6h\ Concentration\ of\ COX-2"$ increased from its initial value to its final value, starting at the simulation time and occuring across the duration specified. These changes were only made for UVR simulations and represented the delayed AA cascade response to UVR stimulation.

	Parameters						
	$"Maximum\ 6h\ Concentration\ of\ COX-2"$				$"Doubling\ Time\ of\ COX-2"$ (h)	$"Decay\ Switch"$	$"Half\ Life\ of\ COX-2"$ (h)
	Initial Value (mM)	Final Value (mM)	Simulation time (h)	Duration (h)			
HaCaT keratinocyte + UVR	1×10^{-28}	2.27×10^{-2}	0	3	3	Off	1
46BR.1N fibroblast +UVR	1×10^{-28}	2.27×10^{-2}	0	6	6	Off	1

Supplementary Table S16. "Metabolite Ψ" scores used in the cell specific *in silico* experiments for HaCaT keratinocytes and 46BR.1N fibroblasts. The proximity of the predicted and measured concentration of each eicosanoid in each cell type, at four time points (0.5h, 1h, 3h and 6h post stimulation), was used to calculate a quality score. The prediction accuracy was calculated based upon the percentage of model variants with a quality score above -40. In the HaCaT keratinocyte *in vitro* timecourse, prostaglandin E_2 (PGE_2), Prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$), 12-Hydroxy-eicosatetraenoic acid (12-HETE), 15-Hydroxy-eicosatetraenoic acid (15-HETE), 15-Keto-prostaglandin E_2 (15-keto-PGE_2) and 13,14-Dihydro-15-keto-prostaglandin E_2 (13,14-dihydro-15-keto-PGE_2) were all detected so were all included in scoring against *in silico* predictions. In the 46BR.1N fibroblast *in vitro* timecourse, only PGE_2, 12-HETE and 15-HETE were detected so it was only possible to score these species against *in silico* predictions.

	***In Silico* Experiments**							
	HaCaT + A23187	HaCaT + IND + A23187	HaCaT + ATP	HaCaT + UVR	46BR.1N + A23187	46BR.1N + IND + A23187	46BR.1N + ATP	46BR.1N + UVR
PGE_2	91	2	64	0	4	0	7	0
$PGF_{2\alpha}$	84	2	67	77	-	-	-	-
12-HETE	26	26	0	4	61	69	30	22
15-HETE	1	7	1	0	21	25	0	11
15-keto-PGE_2	13	0	0	0	-	-	-	-
13,14-dihydro-15-keto-PGE_2	65	0	68	1	-	-	-	-