Sets of rate equations and kinetic parameters used for mathematical modelling.

V_{max} values of the glycolytic enzymes and all kinetic parameters for the TPI reaction were determined experimentally. The rate equations and additional kinetic parameters used for computation of the whole glycolytic pathway were taken from the model of Mulquiney and Kuchel [10] for the glycolytic enzymes. Expressions for bisphosphoglycerate mutase (BPGM), bisphosphoglycerate phosphatase (BPGP) and their parameters were based on the results described in reference [9].

v^{HK}	Glucose + ATP = G6P + ADP
v^{GPI}	G6P = F6P
v^{PFK}	F6P + ATP = FBP + ADP
$v^{Aldolase}$	FBP = DHAP + GAP
v^{TPI}	GAP = DHAP
v^{GAPDH}	GAP + NAD + Pi = G1,3DP + NADH + H$^+$
v^{PGK}	G1,3DP + ADP = 3-PG + ATP
v^{PGM}	3-PG = 2-PG
$v^{Enolase}$	2-PG = PEP
v^{PK}	PEP + ADP = Pyruvate + ATP + Pi
v^{LDH}	Pyruvate + NADH = Lactate + NAD
v^{BPGM}	G1,3DP = G2,3DP
v^{BPGM}	G2,3DP = 3-PG + Pi

HK   **EC 2.7.1.1**

$$v^{HK} = \frac{V_{max}^{HK} * (\frac{[Glu\cos e]*[ATP]}{K_M^{HK} * K_{M1}^{HK}} - \frac{[G6P]*[ADP]}{Ke^{HK}})}{1 + \frac{[Glu\cos e]}{K_M^{HK}} + \frac{[ATP]}{K_{M1}^{HK}} + \frac{[G6P]}{K_{M2}^{HK}} + \frac{[ADP]}{K_{M3}^{HK}} + \frac{[Glu\cos e]*[ATP]}{K_M^{HK} * K_{M1}^{HK}} + \frac{[G6P]*[ADP]}{K_{M2}^{HK} * K_{M3}^{HK}}}$$

K_M^{HK}= 50 μM, K_{M1}^{HK}= 1000 μM, K_{M2}^{HK}= 50 μM, K_{M3}^{HK}= 1000 μM, Ke^{HK}= 7.75 * 10^6 μM^2

V_{max}^{HK}= 0.62 U/g Hb for control, V_{max}^{HK}= 1.47 U/g Hb for patient

GPI   **EC 5.3.1.9**

$$v^{GPI} = \frac{V_{max}^{GPI}}{K_M^{GPI}} * \frac{[G6P] - \dfrac{[F6P]}{Ke^{GPI}}}{1 + \dfrac{[G6P]}{K_M^{GPI}} + \dfrac{[F6P]}{K_{M1}^{GPI}}}$$

K_M^{GPI}= 200 µM, K_{M1}^{GPI}= 80 µM, Ke^{GPI}= 0.329

V_{max}^{GPI}= 30 U/g Hb for control, V_{max}^{GPI}= 30 U/g Hb for patient

PFK   **EC 2.7.1.11**

$$v^{PFK} = \frac{V_{max}^{PFK} * \left(\dfrac{[F6P]*[ATP]}{K_M^{PFK} * K_{M1}^{PFK}} - \dfrac{[FBP]*[ADP]}{Ke^{PFK}}\right)}{1 + \dfrac{[F6P]}{K_M^{PFK}} + \dfrac{[ATP]}{K_{M1}^{PFK}} + \dfrac{[FBP]}{K_{M2}^{PFK}} + \dfrac{[ADP]}{K_{M3}^{PFK}} + \dfrac{[F6P]*[ATP]}{K_M^{PFK} * K_{M1}^{PFK}} + \dfrac{[FBP]*[ADP]}{K_{M2}^{PFK} * K_{M3}^{PFK}}} * \frac{1}{1+f}$$

$$f = \frac{(\dfrac{h}{Ka})^n * (1 + \dfrac{[ATP]}{K_{M1}^{PFK}})^4 * (1 + \dfrac{[Mg^{2+}]}{K_{M4}^{PFK}})^4}{(1 + \dfrac{[F6P]}{K_M^{PFK}} + \dfrac{[FBP]}{K_{M2}^{PFK}})^4 * (1 + \dfrac{[P_i]}{K_{M5}^{PFK}})^4}$$

K_M^{PFK}= 100 µM, K_{M1}^{PFK}= 100 µM, K_{M2}^{PFK}= 600 µM, K_{M3}^{PFK}= 600 µM,

K_{M4}^{PFK}= 4 mM,

K_{M5}^{PFK}= 30 mM, Ke^{PFK}= 1.44 * 10^7 µM², h = [H⁺], pKa = 7.05, n =5

V_{max}^{PFK}= 17.3 U/g Hb for control, V_{max}^{PFK}= 34.3 U/g Hb for patient

Aldolase   **EC 4.1.2.13**

$$v^{ALD} = \frac{V_{max}^{ALD} * \left(\dfrac{[FBP]}{K_M^{ALD}} - \dfrac{[DHAP]*[GAP]}{Ke^{ALD}}\right)}{1 + \dfrac{[FBP]}{K_M^{ALD}} + \dfrac{[DHAP]}{K_{M1}^{ALD}} + \dfrac{(K_{M3}^{ALD}*[GAP]) + ([DHAP]*[GAP])}{K_{M1}^{ALD} * K_{M2}^{ALD}} + \dfrac{K_{M3}^{ALD}*[FBP]*[GAP]}{K_{M1}^{ALD} * K_{M2}^{ALD} * K_{M4}^{ALD}}}$$

K_M^{ALD}= 8 µM, K_{M1}^{ALD}= 10 µM, K_{M2}^{ALD}= 40 µM, K_{M3}^{ALD}= 40 µM,

K_{M4}^{ALD}= 15 µM, Ke^{ALD}= 140 µM²,

V_{max}^{ALD}= 4.6 U/g Hb for control, V_{max}^{ALD}= 6.7 U/g Hb for patient

TPI EC 5.3.1.1

$$v^{TPI} = \frac{V_{max}^{TPI}}{K_M^{TPI}} * \frac{[GAP] - \dfrac{[DHAP]}{Ke^{TPI}}}{1 + \dfrac{[GAP]}{K_M^{TPI}} + \dfrac{[DHAP]}{K_{M1}^{TPI}}}$$

K_M^{TPI}= 650 µM, K_{M1}^{TPI}= 1300 µM, Ke^{TPI}= 9, V_{max}^{TPI}= 1750 U/g Hb for control,

V_{max}^{TPI}= 36.5 U/g Hb for patient

GAPDH EC 1.2.1.12

$$v^{GAPDH} = \frac{V_{max}^{GAPDH} * \left(\dfrac{[GAP]*[NAD]*[P_i]}{K_M^{GAPDH} * K_{M1}^{GAPDH} * K_{M2}^{GAPDH}} - \dfrac{[G1,3DP]*[NADH]*[H^+]}{K_e^{GAPDH} * K_{M3}^{GAPDH} * K_{M4}^{GAPDH}} \right)}{\left(\dfrac{[GAP]}{K_{M2}^{GAPDH}} + \dfrac{[G1,3DP]}{K_{M3}^{GAPDH}} + \dfrac{[GAP]*[P_i]}{K_{M1}^{GAPDH} * K_{M2}^{GAPDH}} \right)\left(1 + \dfrac{[GAP]}{K_{M5}^{GAPDH}}\right) + w1 + w2 + w3 + w4}$$

$$w1 = \frac{K_{M6}^{GAPDH} *[NADH]*[H^+]}{K_{M3}^{GAPDH} * K_{M4}^{GAPDH}} + \frac{K_{M7}^{GAPDH} *[NAD]*[P_i]}{K_M^{GAPDH} * K_{M1}^{GAPDH} * K_{M2}^{GAPDH}} + \frac{[NAD]*[GAP]}{K_{M8}^{GAPDH} * K_{M2}^{GAPDH}}$$

$$w2 =$$
$$\frac{[NAD]*[G1,3DP]}{K_{M3}^{GAPDH} * K_{M8}^{GAPDH}} + \frac{[GAP]*[NAD]*[P_i]}{K_M^{GAPDH} * K_{M1}^{GAPDH} * K_{M2}^{GAPDH}} + \frac{K_{M7}^{GAPDH} *[NAD]*[P_i]*[G1,3DP]}{K_M^{GAPDH} * K_{M2}^{GAPDH} * K_{M1}^{GAPDH} * K_{M9}^{GAPDH}}$$

$$w3 = \frac{[G1,3DP]*[NADH]*[H^+]}{K_{M3}^{GAPDH} * K_{M4}^{GAPDH}} + \frac{[GAP]*[NADH]*[H^+]}{K_{M10}^{GAPDH} * K_{M2}^{GAPDH}} + \frac{K_{M6}^{GAPDH} *[P_i]*[NADH]*[H^+]}{K_{M1}^{GAPDH} * K_{M3}^{GAPDH} * K_{M4}^{GAPDH}}$$

$$w4 = \frac{[GAP]*[P_i]*[NADH]*[H^+]}{K_{M1}^{GAPDH} * K_{M2}^{GAPDH} * K_{M10}^{GAPDH}} + \frac{K_{M6}^{GAPDH} *[G1,3DP]*[P_i]*[NADH]*[H^+]}{K_{M3}^{GAPDH} * K_{M9}^{GAPDH} * K_{M1}^{GAPDH} * K_{M4}^{GAPDH}}$$

K_M^{GAPDH}= 45 µM, K_{M1}^{GAPDH}= 3200 µM, K_{M2}^{GAPDH}= 1.6*10⁻¹⁴ µM, K_{M3}^{GAPDH}= 1.6*10⁻¹⁵ µM,

K_{M4}^{GAPDH}= 21 µM, K_{M5}^{GAPDH}= 31 µM, K_{M6}^{GAPDH}= 0.67 µM, K_{M7}^{GAPDH}= 100 µM, K_{M8}^{GAPDH}= 45 µM,

K_{M9}^{GAPDH}= 1 µM, K_{M10}^{GAPDH}= 64 µM, K_e^{GAPDH}= 1.34,

V_{max}^{GAPDH}= 130 U/g Hb for control, V_{max}^{GAPDH}= 210 U/g Hb for patient

PGK EC 2.7.2.3

$$v^{PGK} = \frac{V_{max}^{\ PGK} * (\frac{[G1,3DP]*[ADP]}{K_M^{\ PGK} * K_{M1}^{\ PGK}} - \frac{[3-PG]*[ATP]}{Ke^{PGK} * K_{M2}^{\ PGK} * K_{M3}^{\ PGK}})}{1 + \frac{[G1,3DP]}{K_{M4}^{\ PGK}} + \frac{[ADP]}{K_M^{\ PGK}} + \frac{[3-PG]}{K_{M5}^{\ PGK}} + \frac{[ATP]}{K_{M2}^{\ PGK}} + \frac{[G1,3DP]*[ADP]}{K_M^{\ PGK} * K_{M1}^{\ PGK}} + \frac{[3-PG]*[ADP]}{K_{M2}^{\ PGK} * K_{M3}^{\ PGK}}}$$

K_M^{PGK}= 80 μM, K_{M1}^{PGK}=2 μM, K_{M2}^{PGK}=200 μM, K_{M3}^{PGK}=1100 μM, K_{M4}^{PGK}= 1600 μM,

K_{M5}^{PGK}=205 μM, Ke^{PGK}= 2.5,

V_{max}^{PGK}= 290 U/g Hb for control, V_{max}^{PGK}= 290 U/g Hb for patient

PGM EC 5.4.2.1

$$v^{PGM} = \frac{V_{max}^{\ PGM}}{K_M^{\ PGM}} * \frac{[3-PG] - \frac{[2-PG]}{Ke^{PGM}}}{1 + \frac{[3-PG]}{K_M^{\ PGM}} + \frac{[2-PG]}{K_{M1}^{\ PGM}}}$$

K_M^{PGM}=168 μM, K_{M1}^{PGM}=26 μM, Ke^{PGM}=0.17,

V_{max}^{PGM}= 22 U/g Hb for control, V_{max}^{PGM}= 22 U/g Hb for patient

Enolase EC 4.2.1.11

$$v^{enolase} = \frac{V_{max}^{\ enolase} * (\frac{[2-PG]*[Mg^{2+}]}{K_M^{\ enolase} * K_{M1}^{\ enolase}} - \frac{[PEP]*[Mg^{2+}]}{Ke^{enolase} * K_{M2}^{\ enolase} * K_{M3}^{\ enolase}})}{1 + \frac{[2-PG]}{K_{M4}^{\ enolase}} + \frac{[Mg^{2+}]}{K_M^{\ enolase}} + \frac{[PEP]}{K_{M2}^{\ enolase}} + \frac{[2-PG]*[Mg^{2+}]}{K_M^{\ enolase} * K_{M1}^{\ enolase}} + \frac{[PEP]*[Mg^{2+}]}{K_{M2}^{\ enolase} * K_{M3}^{\ enolase}}}$$

$K_M^{enolase}$=46 μM, $K_{M1}^{enolase}$=140 μM, $K_{M2}^{enolase}$=111 μM, $K_{M3}^{enolase}$=111 μM,

$K_{M4}^{enolase}$= 140 μM, $Ke^{enolase}$=4,

$V_{max}^{enolase}$= 10 U/g Hb for control, $V_{max}^{enolase}$= 10 U/g Hb for patient

PK   **EC 2.7.1.40**

$$v^{PK} = \dfrac{V_{max}^{PK} * \left(\dfrac{[PEP]*[ADP]}{K_M^{PK}*K_{M1}^{PK}} - \dfrac{[Pyr]*[ATP]}{Ke^{PK}*K_{M2}^{PK}*K_{M3}^{PK}}\right)}{1 + \dfrac{[PEP]}{K_M^{PK}} + \dfrac{[ADP]}{K_{M1}^{PK}} + \dfrac{[Pyr]}{K_{M2}^{PK}} + \dfrac{[ATP]}{K_{M3}^{PK}} + \dfrac{[PEP]*[ADP]}{K_M^{PK}*K_{M1}^{PK}} + \dfrac{[Pyr]*[ATP]}{K_{M2}^{PK}*K_{M3}^{PK}}} * \dfrac{1}{1+f^{PK}}$$

$$f^{PK} = \dfrac{\left(\dfrac{h}{Ka}\right)^n * \left(1 + \dfrac{[ATP]}{K_{M4}^{PK}}\right)^4}{\left(1 + \dfrac{[PEP]}{K_{M5}^{PK}} + \dfrac{[Pyr]}{K_{M2}^{PFK}}\right)^4 * \left(1 + \dfrac{[FBP]}{K_{M6}^{PK}}\right)^4}$$

K_M^{PK}= 225 µM, K_{M1}^{PK}= 474 µM, K_{M2}^{PK}= 2000 µM,

K_{M3}^{PK}= 3000 µM, K_{M4}^{PK}=3.4 mM,

K_{M5}^{PK}= 255 µM, K_{M6}^{PK}=5 µM, Ke^{PK}= 425, h = [H⁺], pKa = 6.8, n =1,

V_{max}^{PK}= 14 U/g Hb for control, V_{max}^{PK}= 26 U/g Hb for patient

LDH   **EC 1.1.1.27**

$$v^{LDH} = \dfrac{V_{max}^{LDH} * \left(\dfrac{[NADH]*[Pyr]}{K_M^{LDH}*K_{M1}^{LDH}} - \dfrac{[Lac]*[NAD]}{Ke^{LDH}*K_{M2}^{LDH}*K_{M3}^{LDH}}\right)}{q1 + \dfrac{[NADH]}{K_M^{LDH}} + \dfrac{[NAD]}{K_{M3}^{LDH}} + \dfrac{[NADH]*[Pyr]}{K_M^{LDH}*K_{M1}^{LDH}} + q2 + \dfrac{[Lac]*[NAD]}{K_{M2}^{LDH}*K_{M3}^{LDH}} +}$$

$$q1 = \left(1 + \dfrac{K_{M4}^{LDH}*[Pyr]}{K_M^{LDH}*K_{M1}^{LDH}} + \dfrac{K_{M5}^{LDH}*[Lac]}{K_{M2}^{LDH}*K_{M3}^{LDH}}\right) * \left(1 + \dfrac{[Pyr]}{K_{M6}^{LDH}}\right)$$

$$q2 = \dfrac{[NADH]*[Lac]*K_{M5}^{LDH}}{K_M^{LDH}*K_{M2}^{LDH}*K_{M3}^{LDH}} + \dfrac{[NAD]*[Pyr]*K_{M4}^{LDH}}{K_M^{LDH}*K_{M1}^{LDH}*K_{M3}^{LDH}}$$

$$q3 = \dfrac{[NADH]*[Pyr]*[Lac]}{K_M^{LDH}*K_{M1}^{LDH}*K_{M7}^{LDH}} + \dfrac{[NAD]*[Pyr]*[Lac]}{K_{M8}^{LDH}*K_{M2}^{LDH}*K_{M3}^{LDH}}$$

K_M^{LDH}= 2.45 µM, K_{M1}^{LDH}= 137 µM, K_{M2}^{LDH}= 503 µM, K_{M3}^{LDH}= 1070 µM,

K_{M4}^{LDH}=8.44 µM,

K_{M5}^{LDH}= 107 µM, K_{M6}^{LDH}=101 µM, K_{M7}^{LDH}=7330 µM, K_{M8}^{LDH}=228 µM, Ke^{LDH}= 4,

V_{max}^{LDH}= 185 U/g Hb for control, V_{max}^{LDH}= 185U/g Hb for patient

BPGM   EC 5.4.2.4

$$v^{BPGM} = \frac{V_{\max}^{BPGM}*[G1,3DP]}{K_M^{BPGM} + K_{M1}^{BPGM}*[G1,3DP]+[G2,3DP]}$$

$K_M^{BPGM}= 40\ \mu M$, $K_{M1}^{BPGM}= 0.013$,

$V_{\max}^{BPGM}= 170$ U/g Hb for control, $V_{\max}^{BPGM}= 170$ U/g Hb for patient

BPGP EC 3.1.3.13

$$v^{BPGP} = \frac{V_{\max}^{BPGP}*[G2,3DP]}{K_M^{BPGP}*(1+([2-PG]+[3-PG])/K_{M1}^{BPGP})+[G2,3DP]}$$

$K_M^{BPGP}= 20\ \mu M$, $K_{M1}^{BPGP}= 0.006$,

$V_{\max}^{BPGP}= 0.027$ U/g Hb for control, $V_{\max}^{BPGP}= 0.027$ U/g Hb for patient

$$\frac{d[Glu\cos e]}{dt} = -v^{HK},\ \frac{d[G6P]}{dt} = -v^{GPI}+v^{HK},\ \frac{d[F6P]}{dt} = v^{GPI}-v^{PFK},$$

$$\frac{d[FBP]}{dt} = v^{PFK}-v^{ALD},\ \frac{d[DHAP]}{dt} = v^{ALD}+v^{TPI},$$

$$\frac{d[GAP]}{dt} = v^{ALD}-v^{TPI}-v^{GAPDH},\ \frac{d[G1,3DP]}{dt} = v^{GAPDH}-v^{PGK}-v^{BPGM},$$

$$\frac{d[3-PG]}{dt} = v^{PGK}+v^{BPGP}-v^{PGM},\ \frac{d[2-PG]}{dt} = v^{PGM}-v^{enolase},$$

$$\frac{d[PEP]}{dt} = v^{enolase}-v^{PK},\ \frac{d[NAD]}{dt} = v^{LDH}-v^{GAPDH},\ \frac{d[NADH]}{dt} = v^{GAPDH}-v^{LDH}$$