

Table S1, adjustable model parameters,

Parameter name	Description	Value original model	Value optimized model (Figure 1A)	Parameter range sampled in MC simulations (Figure 1B)	Unit
R	Dehydrogenase parameter	4.559	7.61	0.4559 – 9.118	unitless
$k_{Pi,1}$	Dehydrogenase parameter	0.1553	0.317	0.01553 – 0.3106	mM
$k_{Pi,2}$	Dehydrogenase parameter	0.8222	3.70	0.08222 – 1.6444	mM
X_{DH}	Dehydrogenase activity	0.16	0.735	0.016 – 0.32	$\text{mol s}^{-1} \text{M}^{-1} (\text{L mito})^{-1}$
X_{CI}	Complex I activity	4405	14057	440.5 – 8810	$\text{mol s}^{-1} \text{M}^{-2} (\text{L mito})^{-1}$
X_{C3}	Complex III activity	4.887	4.10	0.4887 – 9.774	$\text{mol s}^{-1} \text{M}^{-3/2} (\text{L mito})^{-1}$
$k_{Pi,3}$	Complex III parameter	0.3601	0.560	0.03601 – 0.7202	mM
$k_{Pi,4}$	Complex III parameter	5.651	0.334	0.5651 – 11.302	mM
X_{C4}	Complex IV activity	6.766×10^{-5}	10.6×10^{-5}	$6.766 \times 10^{-6} - 1.3532 \times 10^{-4}$	$\text{mol s}^{-1} \text{M}^{-1} (\text{L mito})^{-1}$
k_{O2}	Complex IV parameter	0.12	0.11	0.012 – 0.24	mM
X_{FI}	F_0F_1 -ATPase activity	1000.0	699.8	100 – 2000	$\text{mol s}^{-1} \text{M}^{-1} (\text{L mito})^{-1}$
X_{ANT}	ANT activity	0.041	0.112	0.0041 – 0.082	$\text{mol s}^{-1} (\text{L mito})^{-1}$
$K_{m,ADP}$	Michaelis constant ANT	3.5×10^{-3}	13.0×10^{-3}	$3.5 \times 10^{-4} - 7.0 \times 10^{-3}$	mM
k_{PiHt}	H^+/Pi^- cotransporter parameter	0.2542	0.270	0.02542 – 0.5084	mM
X_{PiHt}	H^+/Pi^- cotransporter activity	3.850×10^{-5}	18.9×10^{-5}	$3.850 \times 10^{-6} - 7.7 \times 10^{-5}$	$\text{mol s}^{-1} \text{M}^{-1} (\text{L mito})^{-1}$
X_{KH}	K^+/H^+ antiporter activity	5.651×10^7	11.9×10^7	$5.651 \times 10^6 - 1.1302 \times 10^8$	$\text{mol s}^{-1} \text{M}^{-2} (\text{L mito})^{-1}$

P_{pi}	Mitochondrial membrane permeability to inorganic phosphate	327	796.5	32.7 – 654	$\mu\text{m s}^{-1}$
P_A	Mitochondrial outer membrane permeability to nucleotides	85.0	117.2	8.5 – 170	$\mu\text{m s}^{-1}$
C_{tot}	total cytochrom C concentration	2.7	3.97	0.27 – 5.4	$\text{mmol (L IM water)}^{-1}$
Q_{tot}	total ubiquinol concentration - Q+QH2	1.35	1.26	0.135 – 2.7	$\text{mmol (L matrix water)}^{-1}$
NAD_{tot}	total matrix NAD(H) concentration - NAD+NADH	2.97	2.59	0.297 – 5.94	$\text{mmol (L matrix water)}^{-1}$
X_{buff}	matrix buffering coefficient	100	118.64	10 – 200	M^{-1}
K_{DT}	Mg-ATP binding constant	24×10^{-6}	231.9×10^{-6}	$2.4 \times 10^{-6} - 48 \times 10^{-6}$	M
K_{DD}	Mg-ADP binding constant	347×10^{-6}	309.1×10^{-6}	$34.7 \times 10^{-6} - 694 \times 10^{-6}$	M
gamma	mito membrane area per cell volume	5.99	15.1	0.599 – 11.98	μm^{-1}
θ	ANT parameter	1	0.960	0 – 1	unitless
Total matrix ADP+ATP	Total matrix ADP+ATP	10	8.66	0.1 – 2	$\text{mmol (L matrix water)}^{-1}$
