

“Fenton reaction” module

Table S1. Model parameter values for reactions in the Module “Fenton reaction”

Reaction	Value	Ref
$\text{Fe}^{2+} + \text{H}_2\text{O}_2 \rightarrow \text{Fe}^{3+} + \cdot\text{OH} + \text{OH}^-$	$5.7 * 10^2 \text{ M}^{-1}\text{s}^{-1}$	[1]
$\text{Fe}^{3+} + \cdot\text{O}_2^- \rightarrow \text{Fe}^{2+} + \text{O}_2$	$3.1 * 10^5 \text{ M}^{-1}\text{s}^{-1}$	[1]
$\text{Fe}^{2+} + \text{H}_2\text{O}_2 \rightarrow \text{Fe}^{3+} + \text{OH}^- + \cdot\text{OH}$		

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“Iron Metabolism” module

Table S2. Model parameter values for reactions in the Module “Iron Metabolism”

Compartment/Reaction	Value	Ref
Extracellular space		
$\text{Fe}^{3+} -\text{Ceruloplasmin} \rightarrow \text{Fe}^{2+}$	Rate of oxidation of the Cu^{1+} to Cu^{2+} in ceruloplasmin by O_2 $\mu\text{M}^{-1} \text{ min}^{-1} 5.93\text{E}+0$ Rate coefficient of oxidation of Fe^{2+} to Fe^{3+} by ceruloplasmin $\mu\text{M}^{-1} \text{ min}^{-1} 8.99\text{E}+1$ (1.5 s)	[1]
$\text{Fe}^{3+} + \text{Transferrin} \rightarrow \text{Transferrin_Fe}$	$K_{\text{C-domain}} = 4,7 \times 10^{20} \text{ M}^{-1}$ and $K_{\text{N-domain}} = 2,4 \times 10^{19} \text{ M}^{-1}$ for C-domain and N-domain respectively $K_d = 10^{-23} \text{ M}$	[2,3,4,14]
Cell Membrane		
$\text{Transferrin_1} + \text{Transferrin_Receptor} \rightarrow \text{TF_TFR1}$	Rate constant Association rate of HT and R proteins $1.7 \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$	[5,12]
$\text{TF_TFR1} \rightarrow \text{Fe}^{3+}_1 + \text{TF_TFR1_1}$	Rate coefficient of dissociation of (Fe^{3+}) Tf from complex with TfR $\mu\text{M} 3.38\text{E}-2$ $1.125 \times 10^{-3} \text{ s}^{-1}$	[6, 16]
$\text{TF_TFR1_1} \rightarrow \text{Transferrin_Receptor} + \text{Transferrin}$	$K_d = 5 \times 10^{-9} \text{ M}$ Ph 7.4 K562 cells	[4]
$\text{Ferroportin_Fe}^{3+} \rightarrow \text{Fe}^{3+} + \text{Ferroportin}$	K_m of $1.9 \pm 0.26 \mu\text{M}$ and V_{max} of $0.13 \pm 0.09 \text{ min}^{-1} 4.3 \times 10^{-2} \text{ s}^{-1}$	[13, 16]
$\text{Fe}^{2+} -\text{ZIP8/14} \rightarrow \text{Fe}^{2+}$	$V_{maxFe} = 1,0 \pm 0,1 \text{ pmol/min}$, $KdCa = 0,39 \pm 0,12 \text{ mM}$ $0,00000000015 \text{ mM/s}$	[7,15]
Cell		
$\text{Fe} + \text{Ferritin} \rightarrow \text{Ferritin_Fe}$	$K_{d1} = 0.2$; $K_{d2} = 5.3$	[8]
Cell (Lysosome)		
$\text{Fe}^{3+} -\text{STEAP3/4} \rightarrow \text{Fe}^{2+}$	$V_{max} = 3.0$ (0.05 s); $K_m = 5.0$	[9]
$\text{Fe}^{2+} -\text{DMT1} \rightarrow \text{Fe}^{2+}$	$V_{max} = 2.2193$ (0,0369883 s); $K_m = 1.22$	[10,16]
$\text{Fe}^{2+} -\text{ZIP8/14} \rightarrow \text{Fe}^{2+}$	$V_{maxFe} = 1,0 \pm 0,1 \text{ pmol/min}$, $KdCa = 0,39 \pm 0,12 \text{ mM}$ $0,00000000015 \text{ mM/s}$	[7,15]
Cell (Mitochondrion)		
$\text{Fe}^{2+} -\text{MCU} \rightarrow \text{Fe}^{2+}$	Dissociation constant for Ca^{2+} translocation by the MCU $6 \mu\text{M}$	[11]

	Dissociation constant for MCU activation by Ca ²⁺ 0.38 μM Rate constant of the MCU 0.0006 μM.s ⁻¹	
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“Lipid Synthesis” module

Table S3. Model parameter values for reactions in the Module “Lipid Synthesis”

Reaction	Value	Ref
CoA + PUFAs (Cat.ACRL4) → CoA-PUFAs	Km = 6.7 Vmax = 3444	[1,3]
CoA-PUFAs + LysoPE (Cat.LPCAT3) → PE-PUFAs	Km = 71.56 Vmax = 6,247	[2,3]

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“Lipid peroxidation” module

Table S4. Model parameter values for reactions in the Module “Lipid peroxidation”

Reaction	Value	Ref
HO* + PE-PUFAs → PE-PUFAs*	100,000,000,000.0000000	[1]
PE-PUFAs + PE-PUFAs-O* → PE-PUFAs* + PE-PUFAs-OH	12,600,000.0000000	[1]
PE-PUFAs* → PE-PUFAs-OO*	1,000,000,000.0000000	[2]
PE-PUFAs-OOH + Fe ²⁺ → Fe ³⁺ + O-PE-PUFAs-OO*	3,500,000.0000000	[3]
PE-PUFAs (Cat.LOXs) → PE-PUFAs-OOH	0.0600000	[4]
O-PE-PUFAs-OO* + PE-PUFAs → PE-PUFAs* + O-PE-PUFAs-OOH	70.0000000	[2]

PE-PUFAs-OO* + PE-PUFAs → PE-PUFAs* + PE-PUFAs-OOH	70.0000000	[2]
PE-PUFAs-OOH + Fe2+ → PE-PUFAs-O* + Fe3+	320.0000000	[5]
2PE-PUFAs-OO* → PE-PUFAs-OH	100,000.0000000	[2]

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“Pentose phosphate pathway” module

Table S5. Model parameter values for reactions in the Module “Pentose phosphate pathway”

Reaction	Value	Ref
6-phosphogluconate dehydrogenase (GND1, GND2) NADP ⁺ + 6-Phosphogluconate (Cat. PGD) → NADPH + Rebulose-5-phosphate	Kcat 28.0 s ⁻¹ Kp6g 0.062 mM Knadp 0.094 mM Kru5p 0.1 mM Knadph 0.055 mM	[1]
Glucose-6-phosphate dehydrogenase (ZWF1) Glucose-6-phosphate (Cat. G6PD) → NADPH + NADP ⁺ + 6-Phosphogluconate	Kcat 189 s ⁻¹ Kg6p 0.042 mM Knadp 0.045 mM Kg6l 0.1 mM Knadph 0.017 mM	[1]

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“Antioxidant system” module

Table S6. Model parameter values for reactions in the Module “Antioxidant system”

Reaction	Value	Ref
GSH + PE-PUFAs-O-OH (Cat.GPx4) → GSSH + PE-PUFAs-OH	21 000 000,0000000	[1]
GSSH + NADPH (Cat.GR) → GSH + NADP+	0,0000500	[2]
GSH + PE-PUFAs-O* (Cat.GPx4) → PE-PUFAs-O-OH + GSSH	21 000 000,0000000	[1]
GSH + H2O2 (Cat.GPx4) → GSSH + H2O	180 000 000,0000000	[4]
GSH + O* (Cat.GPx4) → GSSH + O2	150 000,0000000	[5]
O-PE-PUFAs-OO* + aT-OH → O-PE-PUFAs-OOH + aT-O*	1 850 000,0000000	[6]
aT-O* (Cat.Ascorbate) → aT-OH	200 000,0000000	[7]

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“GSH Synthesis” module

Table S7. Model parameter values for reactions in the Module “GSH Synthesis module”

Reaction	Value	Ref
Cysteinylglycine (Cat. Peptidase) → Cycteine + Glycine	(Mn ²⁺) K _m = 0.4 mM, K _{cat} = 86.5 s ⁻¹ ; (Zn ²⁺) K _m = 0.8 mM, K _{cat} = 76.9 s ⁻¹	[4]
Cyctine + GSH + AA (Cat.GGT) → Cysteinylglycine + γ-glu-AA	V _{max} = 1200 min (20 s) γ-Glutamyl (K _m = 1.4 mM) Glycylglycine (K _m = 10 mM)	[1,2]
Glutamate + AA (Cat.GCL) → γ-glu-AA	K _{cat} = 6.1 min ⁻¹ (0.1 s); K _m = 9.1 mM	[6]
5-oxoproline → Glutamate	K _m = 51 mM; V _{max} = 167 mM/h (0.046 s)	[5]
γ-glu-AA (Cat.GGCT) → 5-oxoproline	K _m = 3.13 mM; V _{max} = 980 mmol/(h*mg) (0.272 s)	[3]
Cysteine + Glutamate -GSH, GCL→ GGC	0.1016 s	[7]
GGC + Glycine -GSS → GSH	V _{max} = 7.91 s	[8]
Cystine -TXNRD1→ Cysteine	K _m = 0.8, k _{cat} = 1.8 min ⁻¹ (0.03 s)	[9,10]
GSH → GSH	V(cytosole-blood) = 1152 h (0.32 s), V(blood-outside) = 9 h (0.00247 s)	[11]
Cystine + Glutamate -System_Xc-→ Cystine + Glutamate	K _i for glutamate inhibition of cystine uptake = 150 mM K _i for cystine inhibition of glutamate uptake = 33 mM K _m glutamate = 78 mM K _m cystine = 45 mM	[12,14]
Glycine → Glycine	V _{max} = 47 h (0.01305 s), K _m = 67	[13]
Cysteine → Cysteine	V _{max} = 92 h (0.0255 s), K _m = 27	[13]

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