

Additional tables**Additional Table S1 Elasticities.** 0.00 means $-0.005 < \text{value} < 0.005$.

Enzyme	Parameter	Fasted state		Fed state	
		4 mM glucose	10 mM glucose	4 mM glucose	10 mM glucose
FBP1	$k_i^{Fru26P_2}$	0,18	1,23	0,68	1,26
	K_i^{AMP}	2,20	2,47	2,24	2,49
	$k_m^{Fru16P_2}$	-0,69	-0,74	-0,59	-0,88
FBP2	k_i^{Fru6P}	0,77	0,82	0,80	0,84
	$k_m^{Fru26P_2}$	-0,64	-0,22	-0,27	-0,14
GlcT	k_m^{Glc}	0,14	0,26	0,15	0,27
	$k_m^{Glc_{ext}}$	0,19	0,25	0,17	0,22
GK	k_a^{Glc}	-3,26	-2,91	-3,19	-3,31
	f	-2,10	-1,77	-2,30	-1,87
	k_i^{Fru6P}	0,20	0,26	0,15	0,25
	k_m^{ATP}	-0,14	-0,14	-0,14	-0,14
	K_m^{Glc}	-1,01	-0,69	-1,03	-0,80
GP	K_a^{AMP}	0,09	0,15	0,07	0,19
	k_m^{Glyc}	-0,88	-1,30	-0,67	-1,60
	k_m^P	-0,69	-0,88	-0,52	-1,08
	K_m^{Glc1P}	0,00	0,00	0,00	0,00
	$K_{a_{Glc1P}}^{AMP}$	0,00	0,00	0,00	0,00
G6P _{ER}	$k_m^{G6P_{ER}}$	-0,94	-0,92	-0,93	-0,91
GS	$K_m^{UDP-Glc}$	0,85	0,44	1,12	0,35
	$K_0^{UDP-Glc}$	0,76	0,15	1,03	0,12

	K_a^{Glc6P}	0,49	0,13	0,75	0,11
	$K_b^{UDP-Glc}$	0,09	0,30	0,09	0,24
PC	$k_m^{ATP_{mito}}$	-0,01	-0,01	-0,01	-0,01
	$k_m^{Pyr_{mito}}$	-0,70	-0,58	-0,68	-0,48
	$k_m^{CO_2_{mito}}$	-0,45	-0,45	-0,46	-0,45
PEPCK	k_m^{OA}	0,26	0,37	0,38	0,58
	k_m^{GTP}	0,43	0,51	0,54	0,65
	k_m^{PEP}	0,04	0,04	0,04	0,01
	k_m^{GDP}	-0,08	-0,06	0,02	0,00
	$k_m^{CO_2}$	-0,05	-0,04	0,04	0,00
PFK1	K_m^{ATP}	-0,05	-0,01	-0,04	0,00
	$K_m^{ATP} : K_a^{Fru26P_2}$	0,00	-0,01	-0,01	0,00
	K_i^{ATP}	4,37	3,96	4,29	3,97
	$K_i^{ATP} : f_{Fru26P_2}$	0,02	1,03	0,09	1,52
	$K_i^{ATP} : K_a^{Fru26P_2}$	-0,02	-0,97	-0,08	-1,39
	k_m^{Fru6P}	-2,30	-1,47	-2,19	-1,41
	$k_m^{Fru6P} : k_i^{ATP}$	2,17	1,25	2,04	1,21
	$k_m^{Fru6P} : k_i^{Cit}$	0,46	0,27	0,43	0,26
	$k_m^{Fru6P} : f_{AMP}$	3,33	1,87	3,10	1,81
	$k_m^{Fru6P} : K_a^{AMP}$	-1,52	-0,95	-1,44	-0,92
	$k_m^{Fru6P} : f_P$	9,84	4,97	9,15	4,85
	$k_m^{Fru6P} : K_a^P$	-0,87	-0,53	-0,82	-0,51
	$k_m^{Fru6P} : f_{Fru26P_2}$	0,09	6,41	0,52	10,09
	$k_m^{Fru6P} : K_a^{Fru26P_2}$	-0,09	-0,92	-0,46	-0,68
	$n^{Fru6P} : k_i^{ATP}$	0,02	0,01	0,01	0,00

	$n^{Fru6P}:f_{Cit}$	-0,68	-0,27	-0,52	-0,21
	$n^{Fru6P}:K_i^{Cit}$	0,01	0,00	0,01	0,00
	$n^{Fru6P}:f_{AMP}$	3,95	1,43	2,95	1,11
	$n^{Fru6P}:K_a^{AMP}$	-1,56	-0,63	-1,20	-0,49
	$n^{Fru6P}:f_P$	3,22	1,18	2,41	0,91
	$n^{Fru6P}:K_a^P$	0,00	0,00	0,00	0,00
	$n^{Fru6P}:f_{Fru26P_2}$	0,00	1,80	0,34	1,39
	$n^{Fru6P}:K_a^{Fru26P_2}$	0,00	0,00	-1,03	0,00
PFK2	k_m^{Fru6P}	-0,97	-0,43	-0,60	-0,42
	k_m^{ATP}	-0,13	-0,07	-0,13	-0,07
	n_0	-0,17	-0,16	-0,20	-0,09
	k_i^{PEP}	0,14	0,13	0,16	0,07
PK	k_m^{PEP}	-0,21	-0,21	-0,21	-0,23
	k_i^{ATP}	0,00	0,00	0,00	0,00
	$k_a^{Fru16P_2}$	-0,09	-0,08	-0,12	-0,03
	k_m^{ADP}	-0,33	-0,33	-0,33	-0,33

Additional Table S2 Fixed metabolite concentrations. Concentrations given in $\mu\text{mol/g}$ wet weight were converted to mM

by deviding with the factor 0.46 and corrected for the liver density of 1.067 g/ml [35].

Metabolite	Value	Reference
ADP	0.5 mM	[1]
ADP _{mito}	7.5 mM	[1, 2]
AMP	0.16 mM	[3, 4]
ATP	3.25 mM	[1]
ATP _{mito}	17.5 mM	[1, 2]

CO ₂	5 mM	[5]
GDP + GTP	0.8 mM	[6, 7]
GDP _{mito} + GTP _{mito}	0.8 mM	[1, 2, 8]
NAD	1.13 mM	[9, 10]
NAD/NADH	1130	[11, 12]
NAD _{mito}	0.046 mM	[13]
NAD _{mito} /NADH _{mito}	11.5	[11, 12, 14]
P	5 mM	[3]
P _{mito}	8 mM	[15, 16]
PP	0.008 mM	[17]
UDP + UDP-Glc + UTP	1.2 mM	[3, 6, 7, 18, 19]
V _{mm}	-155 mV	[20]

Additional Table S3 Data for the GHT functions – insulin (Figure 18A).

Glc [mM]	Insulin [pM]	Reference
5.92	490.2	[21]
6.36	524.6	
6.37	656.2	
6.46	627.2	
6.48	489.1	
6.66	627.2	
6.77	592.8	
6.80	619.5	
6.80	613.7	
6.88	541.5	

6.91	481.8
6.91	388.7
7.01	560.9
7.02	415.8
7.34	652.5
7.34	432.7
7.41	592.8
7.41	751.8
7.42	634.5
7.42	913.0
7.44	634.2
7.44	564.6
7.52	605.2
7.62	817.7
7.97	766.1
8.16	722.5
9.13	1337.9
9.47	818.8
10.01	835.7
10.19	1384.1
14.67	1433.2
18.33	1170.5
20.47	1180.0
24.09	1440.2
25.45	1538.0

25.79	1748.3	
5.20	607.7	[22]
5.60	448.6	
5.90	448.6	
5.90	448.6	
5.90	448.6	
5.90	448.6	
5.90	390.7	
6.20	549.8	
6.20	405.1	
6.60	752.4	
7.60	1056.3	
7.70	1215.4	
7.70	1099.7	
8.70	1114.1	
9.40	1461.4	
9.80	1504.8	
12.60	1823.2	
15.70	1967.8	
3.86	30.2	[23]
3.96	61.8	
3.96	59.3	
3.98	47.0	
4.04	50.3	
4.18	30.2	

4.36	84.0
4.55	57.9
4.63	121.1
5.05	113.2
5.18	155.7
5.49	113.2
5.77	168.1
5.77	200.2
5.79	197.7
5.83	242.2
5.92	151.0
6.01	197.7
6.05	207.6
6.20	205.1
6.22	185.4
6.32	171.1
6.46	168.6
6.63	244.1
6.71	198.8
6.73	181.2
6.75	151.0
6.79	158.5

Additional Table S4 Data for the GHT functions – glucagon (Figure 18B).

Glc [mM]	Glucagon [pM]	Reference
6.17	30.18	[24]
6.19	30.18	
6.28	30.65	
6.45	33.79	
6.60	43.54	
6.62	34.73	
6.65	44.17	
6.73	46.52	
6.92	27.50	
7.28	35.68	
5.31	56.41	[25]
5.93	32.32	
6.00	28.30	
6.35	29.37	
8.18	31.25	
8.70	26.70	
1.69	368.32	[26]
7.68	9.78	
1.93	210.74	[27]
2.22	324.83	
7.78	36.73	
7.78	40.01	

1.30	254.93	[28]
1.30	268.79	
2.24	199.49	
5.08	136.62	
5.97	188.60	
6.05	163.36	
6.27	185.63	

Additional Table S5 Data for the phosphorylation states of enzymes as function of glucagon concentrations (Figure 19A).

Enzyme	Glucagon [pM]	Relative activity	Reference
FBP2	1.00E-03	1.00	[29]
	1.00E+01	1.00	
	5.00E+01	0.83	
	1.00E+02	0.56	
	5.00E+02	0.33	
	1.00E+03	0.00	
	1.00E+05	0.00	
	2.00E-03	1.00	[30]
	2.00E+01	0.24	
	2.00E+02	0.00	
	2.00E+03	0.00	
PFK2	1.00E-03	1.00	[29]
	1.00E+01	1.00	
	5.00E+01	0.86	
	1.00E+02	0.52	

	5.00E+02	0.29	
	1.00E+03	0.10	
	1.00E+05	0.00	
PK	1.00E-03	1.00	[29]
	1.00E+01	1.00	
	5.00E+01	1.00	
	1.00E+02	0.30	
	5.00E+02	0.09	
	1.00E+03	0.00	
	1.00E+05	0.00	
	1.00E-02	1.00	[31]
	1.00E+02	0.69	
	3.00E+02	0.23	
	1.00E+03	0.00	
	3.00E+03	0.00	
	1.00E+04	0.00	
	1.00E+01	1.00	[32]
	2.20E+01	1.00	
	4.50E+01	0.54	
	1.00E+02	0.15	
	2.20E+02	0.08	
	4.50E+02	0.03	
	1.00E+03	0.00	
	1.00E-03	1.00	[33]
	1.00E+02	0.84	

	5.00E+02	0.39	
	1.00E+03	0.23	
	5.00E+03	0.00	
	1.00E+04	0.02	
	2.00E-03	1.00	[30]
	2.00E+01	1.00	
	2.00E+02	0.38	
	2.00E+03	0.00	

Additional Table S6 Data for the phosphorylation states of enzymes as function of insulin concentrations (Figure 19B).

Enzyme	Insulin[pM]	rel. Activity	Reference
GP	1.00E+00	0.00	[34]
	1.00E+02	0.15	
	5.00E+02	0.29	
	1.00E+03	0.33	
	1.00E+04	0.42	
	1.00E+05	1.00	
	1.00E-03	0.00	[35]
	1.00E+01	0.14/0.27	
	1.00E+02	0.36/0.64	
	1.00E+03	0.68/0.82	
	1.00E+04	0.77/0.91	
	1.00E+05	1.00	
GS	1.00E+01	0.00	[34]
	1.00E+02	0.03	

	5.00E+02	0.11	
	1.00E+03	0.16	
	1.00E+04	0.45	
	1.00E+05	1.00	
	1.00E-03	0.18	[36]
	1.00E+00	0.00	
	1.00E+01	0.12	
	1.00E+02	0.06	
	5.00E+02	0.35	
	1.00E+03	0.65	
	5.00E+03	1.00	
	1.00E+04	1.00	

Signaling transfer functions

Hormone dependency on glucose

$$Ins = 1.55 \text{ nM} * \frac{(Glc_{ext})^{5.7}}{(Glc_{ext})^{5.7} + (7.7 \text{ mM})^{5.7}}$$

$$Glucagon = 0.253 \text{ nM} * \left(1 - \frac{(Glc_{ext})^{5.65}}{(Glc_{ext})^{5.65} + (4.7 \text{ mM})^{5.65}}\right) + 0.02 \text{ nM}$$

$$Ins_{diab} = 0.155 \text{ nM} * \frac{(Glc_{ext})^{5.7}}{(Glc_{ext})^{5.7} + (7.7 \text{ mM})^{5.7}}$$

$$Glucagon_{diab} = 0.506 \text{ nM} * \left(1 - \frac{(Glc_{ext})^{5.65}}{(Glc_{ext})^{5.65} + (4.7 \text{ mM})^{5.65}}\right) + 0.04 \text{ nM}$$

Transfer function of external hormones to phosphorylation state

$$\gamma = \frac{1}{2} * \left(1 - \frac{Ins^{1.75}}{Ins^{1.75} + (0.70 \text{ nM})^{1.75}} + \frac{Glucagon^{3.6}}{Glucagon^{3.6} + (0.08 \text{ nM})^{3.6}}\right)$$

Stoichiometric matrix

$$\frac{d}{dt}DHAP = v_{ALD} - v_{TPI}$$

$$\frac{d}{dt}Fru16P_2 = v_{PFK1} - v_{FBP1} - v_{ALD}$$

$$\frac{d}{dt}Fru26P_2 = v_{PFK2} - v_{FBP2}$$

$$\frac{d}{dt}Fru6P = v_{GPI} - v_{PFK1} - v_{PFK2} + v_{FBP1} + v_{FBP2}$$

$$\frac{d}{dt}GAP = v_{ALD} + v_{TPI} - v_{GAPDH}$$

$$\frac{d}{dt}GDP = -v_{NDK^{GTP}} + v_{PEPCK}$$

$$\frac{d}{dt}GDP_{mito} = -v_{NDK^{GTP}_{mito}} + v_{PEPCK_{mito}}$$

$$\frac{d}{dt}Glc = v_{GLUT2} - v_{GK} + v_{GlcTER}$$

$$\frac{d}{dt}Glc_{ER} = v_{G6P_{ER}} - v_{GlcTER}$$

$$\frac{d}{dt}Glc1P = v_{GP} - v_{G1PI} - v_{UGT}$$

$$\frac{d}{dt}Glc6P = v_{GK} + v_{G6P_{TER}} - v_{GPI} + v_{G1PI}$$

$$\frac{d}{dt}Glc6P_{ER} = -v_{G6P_{ER}} - v_{Glc6P_{TER}}$$

$$\frac{d}{dt}Glyc = v_{GS} - v_{GP}$$

$$\frac{d}{dt}GTP = v_{NDK^{GTP}} - v_{PEPCK}$$

$$\frac{d}{dt}GTP_{mito} = v_{NDK^{GTP}_{mito}} - v_{PEPCK_{mito}}$$

$$\frac{d}{dt}Lac = v_{LacT} + v_{LDH}$$

$$\frac{d}{dt}Mal = v_{MalT} - v_{MDH} + v_{PyrMalT}$$

$$\frac{d}{dt}Mal_{mito} = -v_{MalT} - v_{MDH_{mito}} - v_{PyrMalT}$$

$$\frac{d}{dt}OA = v_{MDH} - v_{PEPCK}$$

$$\frac{d}{dt}OA_{mito} = v_{PC} - v_{PEPCK_{mito}} + v_{MDH_{mito}}$$

$$\frac{d}{dt}PEP = v_{EN} - v_{PK} + v_{PEPCK} - v_{PEPT}$$

$$\frac{d}{dt}PEP_{mito} = v_{PEPCK_{mito}} + v_{PEPT}$$

$$\frac{d}{dt}13P2G = v_{GAPDH} - v_{PGK}$$

$$\frac{d}{dt}2PG = v_{PGM} - v_{EN}$$

$$\frac{d}{dt}3PG = v_{PGK} - v_{PGM}$$

$$\frac{d}{dt}Pyr = v_{PK} - v_{LDH} - v_{PyrT} - v_{PyrMalT}$$

$$\frac{d}{dt}Pyr_{mito} = v_{PyrT} - v_{PC} + v_{PyrMalT}$$

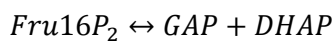
$$\frac{d}{dt}UDP = -v_{NDK^{UTP}} + v_{GS}$$

$$\frac{d}{dt}UDP-Glc = v_{UGT} - v_{GS}$$

$$\frac{d}{dt}UTP = v_{NDK^{UTP}} - v_{UGT}$$

Reaction kinetics

ALD (Aldolase)



$$v_{ALD} = v_{max}^{ALD} \cdot \frac{Fru16P_2 - GAP \cdot DHAP / k_{eq}^{ALD}}{\left(1 + \frac{Fru16P_2}{k_m^{Fru16P_2}}\right) + \left(1 + \frac{GAP}{k_m^{GAP}}\right) \left(1 + \frac{DHAP}{k_m^{DHAP}}\right) - 1}$$

$$v_{max}^{ALD} = 7.78 \cdot 10^8 \text{ h}^{-1}$$

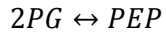
$$k_{eq}^{ALD} = 0.099 \text{ mM [37]}$$

$$k_m^{Fru16P_2} = 0.004 \text{ mM [38]}$$

$$k_m^{GAP} = 0.48 \text{ mM [39]}$$

$$K_m^{DHAP} = 0.38 \text{ mM [39]}$$

EN (Enolase)



$$v_{EN} = v_{max}^{EN} \cdot \frac{2PG - PEP/k_{eq}^{EN}}{1 + \frac{2PG}{k_m^{2PG}} + \frac{PEP}{k_m^{PEP}}}$$

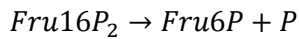
$$v_{max}^{EN} = 1.94 \cdot 10^{10} h^{-1}$$

$$k_{eq}^{EN} = 1.7 [40]$$

$$k_m^{2PG} = 0.14 \text{ mM [41]}$$

$$k_m^{PEP} = 0.31 \text{ mM [41]}$$

FBP1 (Fructose-1,6-bisphosphatase)



$$v_{FBP1} = V_{max}^{FBP1} \cdot \left((1 - \gamma^{FBP1}) \cdot v_{FBP1}^{native} + \gamma^{FBP1} \cdot v_{FBP1}^{phospho} \right)$$

$$V_{max}^{FBP1} = 2.92 \cdot 10^4 \text{ mM} \cdot h^{-1}$$

$$v_{FBP1}^{native} = \frac{Fru16P_2}{Fru16P_2 + k_m^{Fru16P_2}} / \left(1 + \frac{Fru26P_2^n}{(k_i^{Fru26P_2})^n} \right) / \left(1 + \left(\frac{AMP}{K_i^{AMP}} \right)^{n_{AMP}} \right)$$

$$k_m^{Fru16P_2} = 0.0029 \text{ mM [42]}$$

$$k_i^{Fru26P_2} = 0.00113 \text{ mM [42]}$$

$$n = 1.26 [42]$$

$$n_{AMP} = 2.43 [42]$$

$$K_i^{AMP} = 0.023 \text{ mM [42]}$$

$$v_{FBP1}^{phospho} = \frac{Fru16P_2}{Fru16P_2 + k_{m^{phospho}}^{Fru16P_2}} / \left(1 + \frac{Fru26P_2^n}{(k_i^{Fru26P_2})^n} \right) / \left(1 + \left(\frac{AMP}{K_i^{AMP}} \right)^{n_{AMP}} \right)$$

$$k_{m^{phospho}}^{Fru16P_2} = 0.0019 \text{ mM [42]}$$

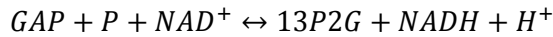
$$k_i^{Fru26P_2} = 0.00113 \text{ mM [42]}$$

$$n = 1.26 \text{ [42]}$$

$$K_i^{AMP} = 0.023 \text{ mM [42]}$$

$$n_{AMP} = 2.43 \text{ [42]}$$

GAPDH (Glyceraldehyde 3-phosphate dehydrogenase)



$$v_{GAPDH} = v_{max}^{GAPDH} * \frac{NAD^+ \cdot GAP \cdot P - 13P2G \cdot NADH / k_{eq}^{GAPDH}}{\left(1 + \frac{NAD^+}{k_m^{NAD^+}} \right) \cdot \left(1 + \frac{GAP}{k_m^{GAP}} \right) \cdot \left(1 + \frac{P}{k_m^P} \right) + \left(1 + \frac{NADH}{k_m^{NADH}} \right) \cdot \left(1 + \frac{13P2G}{k_m^{13P2G}} \right) - 1}$$

$$v_{max}^{GAPDH} = 2.92 \cdot 10^8 h^{-1} \cdot mM^{-2}$$

$$k_{eq}^{GAPDH} = 10^{-4} mM^{-1} \text{ [43]}$$

$$k_m^{NAD^+} = 0.010 \text{ mM [44]}$$

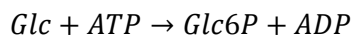
$$k_m^{GAP} = 0.035 \text{ mM [44]}$$

$$k_m^P = 3.8 \text{ mM [45]}$$

$$k_m^{NADH} = 0.006 \text{ mM [45]}$$

$$k_m^{13P2G} = 0.01 \text{ mM [44]}$$

GK (Glucokinase)



$$v_{GK} = V_{max}^{GK} \cdot \frac{ATP}{ATP + k_m^{ATP}} \cdot \frac{(Glc)^n}{(Glc)^n + (k_m^{Glc})^n}$$

$$V_{max}^{GK} = V_0^{GK} \cdot \frac{(Glc)^{n_2}}{(Glc)^{n_2} + (k_a^{Glc})^{n_2}} \cdot \left(1 - f \cdot \frac{Fru6P}{Fru6P + k_i^{Fru6P}} \right)$$

$$V_0^{GK} = 1.05 \cdot 10^4 \text{ mM h}^{-1}$$

$$n = 1.5 [46]$$

$$K_m^{Glc} = 9 \text{ mM} [46]$$

$$k_m^{ATP} = 0.55 \text{ mM} [47]$$

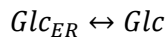
$$k_i^{Fru6P} = 0.005 \text{ mM} [48]$$

$$f = 0.75 [48]$$

$$n_2 = 3.7 [49]$$

$$k_a^{Glc} = 15.9 \text{ mM} [49]$$

GlcT_{ER} (Glucose transport to ER)



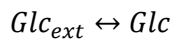
$$v_{GlcT_{ER}} = V_{max}^{GlcT_{ER}} \cdot \frac{(Glc - Glc_{ER})}{1 + \frac{Glc}{k_m^{Glc}} + \frac{Glc_{ER}}{k_m^{Glc_{ER}}}}$$

$$V_{max}^{Glc_{ER}} = 1.94 \cdot 10^{10} \text{ h}^{-1}$$

$$k_m^{Glc_{ER}} = 1.37 \text{ mM} [50, 51]$$

$$k_m^{Glc} = 1.22 \text{ mM} [50, 51]$$

GLUT2 (Glucose transporter 2)



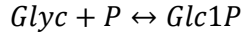
$$v_{GLUT2} = V_{max}^{GLUT2} \cdot \frac{Glc_{ext} - Glc}{1 + \frac{Glc_{ext}}{k_m^{Glc_{ext}}} + \frac{Glc}{k_m^{Glc}}}$$

$$k_m^{Glc} = 17.3 \text{ mM} [52]$$

$$k_m^{Glc_{ext}} = 17.3 \text{ mM} [52]$$

$$V_{max}^{GLUT2} = 9.09 \cdot 10^1 \text{ h}^{-1}$$

GP (Glycogen phosphorylase) [53, 54]



$$v_{GP} = V_{max}^{GP} \cdot \left((1 - \gamma^{GP}) \cdot v_{GP}^{native} + \gamma^{GP} \cdot v_{GP}^{phospho} \right)$$

$$V_{max}^{GP} = 1.29 \cdot 10^2 \cdot \left(\frac{Glyc}{store} \right) mM \cdot h^{-1}$$

$$store = 300 mM$$

$$v_{GP}^{native} = V_{max_{native}}^{GP} \cdot \frac{Glyc \cdot P - Glc1P / k_{eq}^{GP}}{\left(1 + \frac{Glyc}{k_{m_{native}}^{Glyc}} \right) \cdot \left(1 + \frac{P}{k_{m_{native}}^P} \right) + \left(1 + \frac{Glc1P}{k_{m_{native}}^{Glc1P}} \right) - 1}$$

$$V_{max_{native}}^{GP} = V_{0_{native}} \cdot \left(\frac{AMP}{AMP + K_{a_{native}}^{AMP}} \right)$$

$$V_{0_{native}} = \frac{1}{k_{m_{native}}^{Glyc} \cdot k_{m_{native}}^P}$$

$$K_{a_{native}}^{AMP} = 0.36 mM [53]$$

$$k_{eq}^{GP} = 0.21 (mM)^{-1} [55]$$

$$k_{m_{native}}^{Glyc} = 2.5 mM [54]$$

$$k_{m_{native}}^P = 500 mM [54]$$

$$K_{m_{native}}^{Glc1P} = K_0^{Glc1P} \cdot \left(1 - \frac{AMP}{AMP + K_{a_{Glc1P}}^{AMP}} \right)$$

$$K_0^{Glc1P} = 250 mM [54]$$

$$K_{a_{Glc1P}}^{AMP} = 0.5 mM [54]$$

$$v_{GP}^{phospho} = V_{max_{phospho}}^{GP} \cdot \frac{Glyc \cdot P - Glc1P / k_{eq}^{GP}}{\left(1 + \frac{Glyc}{k_{m_{phospho}}^{Glyc}} \right) \cdot \left(1 + \frac{P}{k_{m_{phospho}}^P} \right) + \left(1 + \frac{Glc1P}{k_{m_{phospho}}^{Glc1P}} \right) - 1}$$

$$V_{max_{phospho}}^{GP} = V_{0_{phospho}} \cdot \left(\frac{AMP}{AMP + K_{a_{phospho}}^{AMP}} \right)$$

$$V_{0_{phospho}} = \frac{1}{k_{m_{phospho}}^{Glyc} \cdot k_{m_{phospho}}^P}$$

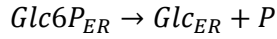
$$K_{a_{phospho}}^{AMP} = 0.017 mM [53]$$

$$k_{m_{phospho}}^{Glyc} = 1.8 \text{ mM} [54]$$

$$k_{m_{phospho}}^P = 2.1 \text{ mM} [54]$$

$$k_{m_{phospho}}^{Glc1P} = 0.7 \text{ mM} [54]$$

G6P_{ER} (Glucose-6-phosphate phosphatase in the ER) [56, 57]



$$v_{G6P_{ER}} = V_{max}^{G6P_{ER}} \cdot \frac{Glc6P_{ER}}{Glc6P_{ER} + k_m^{Glc6P_{ER}}}$$

$$k_m^{Glc6P_{ER}} = 1.84 \text{ mM} [56]$$

$$V_{max}^{G6P_{ER}} = 4.57 \cdot 10^2 \text{ mM} \cdot h^{-1}$$

GPI (Glucose-6-phosphate isomerase)



$$v_{GPI} = V_{max}^{GPI} \cdot \frac{Glc6P - Fru6P/k_{eq}^{GPI}}{1 + \frac{Glc6P}{k_m^{Glc6P}} + \frac{Fru6P}{k_m^{Fru6P}}}$$

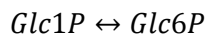
$$V_{max}^{GPI} = 1.07 \cdot 10^9 h^{-1}$$

$$k_{eq}^{GPI} = 0.3 [58]$$

$$k_m^{Glc6P} = 0.055 \text{ mM} [59]$$

$$K_m^{Fru6P_{cyt}} = 0.12 \text{ mM} [59]$$

G1PI (Glucose-1-phosphate isomerase) [60]



$$v_{G1PI} = v_{max}^{G1PI} \cdot \frac{Glc1P - Glc6P/k_{eq}^{G1PI}}{1 + \frac{Glc1P}{k_m^{Glc1P}} + \frac{Glc6P}{k_m^{Glc6P}}}$$

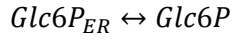
$$v_{max}^{G1PI} = 7.78 \cdot 10^7 h^{-1}$$

$$k_{eq}^{G1PI} = 16.2 [61]$$

$$k_m^{Glc1P} = 0.045 \text{ mM [60]}$$

$$k_m^{Glc6P} = 0.67 \text{ mM [60]}$$

G6P_{ER} (Glucose-6-phosphate transport to ER)



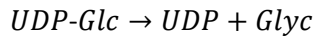
$$v_{G6P_{ER}} = V_{max}^{G6P_{ER}} \cdot \frac{(Glc6P - Glc6P_{ER})}{1 + \frac{Glc6P}{k_m^{Glc6P}} + \frac{Glc6P_{ER}}{k_m^{Glc6P_{ER}}}}$$

$$V_{max}^{G6P_{ER}} = 1.94 \cdot 10^{10} \text{ h}^{-1}$$

$$k_m^{Glc6P_{ER}} = 1.12 \text{ mM [50]}$$

$$k_m^{Glc6P} = 1.12 \text{ mM [50]}$$

GS (Glycogen synthase)



$$v_{GS} = V_{max}^{GS} \cdot \left((1 - \gamma^{GS}) \cdot v_{GS}^{native} + \gamma^{GS} \cdot v_{GS}^{phospho} \right)$$

$$V_{max}^{GS} = 1.16 \cdot 10^2 \frac{(store - glyc)}{(store - glyc) + 0.1 \cdot store} \text{ mM} \cdot \text{h}^{-1}$$

$$store = 300 \text{ mM (average hepatocyte)}$$

$$v_{GS}^{native} = \frac{UDP-Glc}{UDP-Glc + K_{m-native}^{UDP-Glc}}$$

$$K_{m-native}^{UDP-Glc} = K_{0-native}^{UDP-Glc} \cdot \left(1 - \frac{Glc6P}{Glc6P + K_{a-native}^{Glc6P}} \right) + K_{b-native}^{UDP-Glc}$$

$$K_{0-native}^{UDP-Glc} = 1.4 \text{ mM [62]}$$

$$K_{a-native}^{Glc6P} = 0.007 \text{ mM [62]}$$

$$K_{b-native}^{UDP-Glc} = 0.2 \text{ mM [62]}$$

$$v_{GS}^{phospho} = \frac{UDP-Glc}{UDP-Glc + K_{m-phospho}^{UDP-Glc}}$$

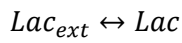
$$k_{m_{phospho}}^{UDP-Glc} = K_{0_{phospho}}^{UDP-Glc} \cdot \left(1 - \frac{Glc6P}{Glc6P + K_{a_{phospho}}^{Glc6P}} \right) + K_{b_{phospho}}^{UDP-Glc}$$

$$K_{0_{phospho}}^{UDP-Glc} = 32 \text{ mM [62]}$$

$$K_{a_{phospho}}^{Glc6P} = 0.09 \text{ mM [62]}$$

$$K_{b_{phospho}}^{UDP-Glc} = 0.3 \text{ mM [62]}$$

LacT (Lactate transporter)



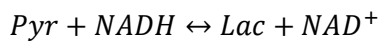
$$v_{LacT} = v_{max}^{LacT} \cdot \frac{Lac_{ext} - Lac}{1 + \frac{Lac}{k_m^{Lac}} + \frac{Lac_{ext}}{k_m^{Lac_{ext}}}}$$

$$v_{max}^{LacT} = 5.83 \cdot 10^2 \text{ h}^{-1}$$

$$k_m^{Lac} = 2.42 \text{ mM [63]}$$

$$k_m^{Lac_{ext}} = 2.42 \text{ mM [63]}$$

LDH (Lactate dehydrogenase) [64, 65]



$$v_{LDH} = v_{max}^{LDH} \cdot \frac{Pyr \cdot NADH - Lac \cdot NAD^+ / k_{eq}^{LDH}}{\left(1 + \frac{NADH}{k_m^{NADH}} \right) \cdot \left(1 + \frac{Pyr}{k_m^{Pyr}} \right) + \left(1 + \frac{Lac}{k_m^{Lac}} \right) \cdot \left(1 + \frac{NAD^+}{k_m^{NAD^+}} \right) - 1}$$

$$v_{max}^{LDH} = 1.56 \cdot 10^{11} \text{ h}^{-1} \cdot \text{mM}^{-1}$$

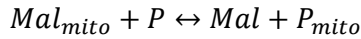
$$k_{eq}^{LDH} = 9000 \text{ [66]}$$

$$k_m^{NADH} = 0.015 \text{ mM [65]}$$

$$k_m^{Pyr} = 0.15 \text{ mM [65]}$$

$$k_m^{Lac} = 36 \text{ mM [64]}$$

$$k_m^{NAD^+} = 0.11 \text{ mM [65]}$$

MalT (Malate transporter)

$$v_{MalT} = v_{max}^{MalT} \cdot \left(\frac{Mal_{mito} \cdot P - Mal \cdot P_{mito}}{\left(1 + \frac{Mal_{mito}}{K_m^{Mal_{mito}}}\right) \cdot \left(1 + \frac{P}{K_m^P}\right) + \left(1 + \frac{Mal}{K_m^{Mal}}\right) \cdot \left(1 + \frac{P_{mito}}{K_m^{P_{mito}}}\right) - 1} \right)$$

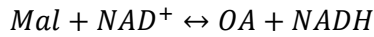
$$v_{max}^{MalT} = 1.94 \cdot 10^3 h^{-1} \cdot mM^{-1}$$

$$k_m^P = 1.41 \text{ mM [67]}$$

$$k_m^{Mal_{mito}} = 0.49 \text{ mM [67]}$$

$$k_m^{P_{mito}} = 1.41 \text{ mM [67]}$$

$$k_m^{Mal} = 0.49 \text{ mM [67]}$$

MDH (Malate dehydrogenase)

$$v_{MDH} = v_{max}^{MDH} \cdot \frac{Mal \cdot NAD^+ - OA \cdot NADH / k_{eq}^{MDH}}{\left(1 + \frac{Mal}{k_m^{Mal}}\right) \cdot \left(1 + \frac{NAD^+}{k_m^{NAD^+}}\right) + \left(1 + \frac{OA}{k_m^{OA}}\right) \cdot \left(1 + \frac{NADH}{k_m^{NADH}}\right) - 1}$$

$$v_{max}^{MDH} = 1.94 \cdot 10^9 h^{-1} \cdot mM^{-1}$$

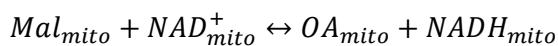
$$k_{eq}^{MDH} = 3 \cdot 10^{-5} \text{ [68]}$$

$$k_m^{Mal} = 1.1 \text{ mM [69]}$$

$$k_m^{NAD^+} = 0.114 \text{ mM [69]}$$

$$k_m^{OA} = 0.088 \text{ mM [69]}$$

$$k_m^{NADH} = 0.026 \text{ mM [69]}$$

MDH_{mito} (Mitochondrial malate dehydrogenase)

$$v_{MDH_{mito}} = V_{max}^{MDH_{mito}}$$

$$\cdot \left(\frac{Mal_{mito} \cdot NAD_{mito}^+ - 1/K_{eq}^{MDH_{mito}} \cdot OA_{mito} \cdot NADH_{mito}}{\left(1 + \frac{Mal_{mito}}{K_m^{Mal_{mito}}}\right) \cdot \left(1 + \frac{NAD_{mito}}{K_m^{NAD_{mito}}}\right) + \left(1 + \frac{OA_{mito}}{K_m^{OA_{mito}}}\right) \cdot \left(1 + \frac{NADH_{mito}}{K_m^{NADH_{mito}}}\right) - 1} \right)$$

$$V_{max}^{MDH_{mito}} = 6.80 \cdot 10^{11} h^{-1} \cdot mM^{-1}$$

$$K_{eq}^{MDH_{mito}} = 3.1 \cdot 10^{-5} \text{ (pH 7.5) [68]}$$

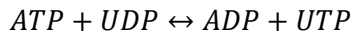
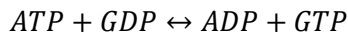
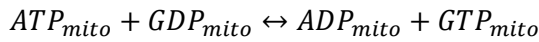
$$K_m^{Mal_{mito}} = 0.33 \text{ mM [70]}$$

$$K_m^{NAD_{mito}} = 0.06 \text{ mM [71]}$$

$$K_m^{OA_{mito}} = 0.017 \text{ mM [71]}$$

$$K_m^{NADH_{mito}} = 0.044 \text{ mM [71]}$$

NDK^{GTP}, NDK^{UTP}, NDK^{GTP}_{mito} (Cytosolic and mitochondrial nucleoside-diphosphate kinases)



$$v_{NDK^{GTP}} = v_{max}^{NDK^{GTP}} \cdot \frac{ATP \cdot GDP - ADP \cdot GTP / k_{eq}^{NDK}}{\left(1 + \frac{ATP}{k_m^{ATP}}\right) \left(1 + \frac{GDP}{k_m^{GDP}}\right) + \left(1 + \frac{ADP}{k_m^{ADP}}\right) \left(1 + \frac{GTP}{k_m^{GTP}}\right) - 1}$$

$$v_{NDK^{UTP}} = v_{max}^{NDK^{UTP}} \cdot \frac{ATP \cdot UDP - ADP \cdot UTP / k_{eq}^{NDK}}{\left(1 + \frac{ATP}{k_m^{ATP}}\right) \left(1 + \frac{UDP}{k_m^{UDP}}\right) + \left(1 + \frac{ADP}{k_m^{ADP}}\right) \left(1 + \frac{UTP}{k_m^{UTP}}\right) - 1}$$

$$v_{NDK^{GTP}_{mito}} = v_{max}^{Ndk^{GTP}_{mito}} \cdot \frac{ATP_{mito} \cdot GDP_{mito} - ADP_{mito} \cdot GTP_{mito} / k_{eq}^{NDK}}{\left(1 + \frac{ATP_{mito}}{k_m^{ATP_{mito}}}\right) \left(1 + \frac{GDP_{mito}}{k_m^{GDP_{mito}}}\right) + \left(1 + \frac{ADP_{mito}}{k_m^{ADP_{mito}}}\right) \left(1 + \frac{GTP_{mito}}{k_m^{GTP_{mito}}}\right) - 1}$$

$$v_{max}^{NDK^{GTP}} = 1.94 \cdot 10^{11} h^{-1} \cdot mM^{-1}$$

$$v_{max}^{NDK^{UTP}} = 1.94 \cdot 10^7 h^{-1} \cdot mM^{-1}$$

$$v_{max}^{NDK^{GTP}_{mito}} = 1.94 \cdot 10^7 h^{-1} \cdot mM^{-1}$$

$$k_{eq}^{NDK} = 1 [72]$$

$$k_m^{ATP} = 1.33 \text{ mM} [73]$$

$$k_m^{GDP} = 3.1 \cdot 10^{-2} \text{ mM} [73]$$

$$k_m^{ADP} = 4.2 \cdot 10^{-2} \text{ mM} [73]$$

$$k_m^{GTP} = 0.15 \text{ mM} [74]$$

$$K_m^{ATP_{mito}} = 1.66 \text{ mM} [73]$$

$$K_m^{GDP_{mito}} = 0.036 \text{ mM} [73]$$

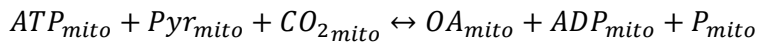
$$K_m^{ADP_{mito}} = 0.073 \text{ mM} [73]$$

$$K_m^{GTP_{mito}} = 0.15 \text{ mM} [74]$$

$$k_m^{UTP} = 16 \text{ mM} [74]$$

$$k_m^{UDP} = 0.19 \text{ mM} [73]$$

PC (Pyruvate carboxylase) [75, 76]



$$v_{PC} = v_{max}^{PC} \cdot \frac{ATP_{mito} \cdot Pyr_{mito} \cdot CO_{2mito} - OA_{mito} \cdot ADP_{mito} \cdot P_{mito} / k_{eq}^{PC}}{(ATP_{mito} + k_m^{ATP_{mito}}) \cdot (Pyr_{mito} + k_m^{Pyr_{mito}}) \cdot (CO_{2mito} + k_m^{CO_{2mito}})}$$

$$v_{max}^{PC} = 3.59 \cdot 10^3 \text{ mM} \cdot h^{-1}$$

$$k_m^{ATP_{mito}} = 0.14 \text{ mM} [75]$$

$$k_m^{Pyr_{mito}} = 0.33 \text{ mM} [75]$$

$$k_m^{CO_{2mito}} = 4.2 \text{ mM} [75]$$

$$k_{eq}^{PC} = 6.55 [76]$$

PEPCK (Phosphoenolpyruvate carboxykinase)



$$v_{PEPCK} = v_{max}^{PEPCK} \cdot \frac{OA \cdot GTP - PEP \cdot GDP \cdot CO_2 / k_{eq}^{PEPCK}}{\left(1 + \frac{OA}{k_m^{OA}}\right) \cdot \left(1 + \frac{GTP}{k_m^{GTP}}\right) + \left(1 + \frac{PEP}{k_m^{PEP}}\right) \cdot \left(1 + \frac{GDP}{k_m^{GDP}}\right) \cdot \left(1 + \frac{CO_2}{k_m^{CO_2}}\right) - 1}$$

$$v_{max}^{PEPCK} = 5.11 \cdot 10^5 h^{-1} \cdot mM^{-1}$$

$$k_{eq}^{PEPCK} = 110 \text{ mM} [77]$$

$$k_m^{OA} = 0.024 \text{ mM} [78]$$

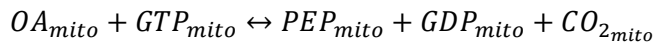
$$k_m^{GTP} = 0.021 \text{ mM} [79]$$

$$k_m^{PEP} = 0.4 \text{ mM} [80]$$

$$k_m^{GDP} = 0.02 \text{ mM} [81]$$

$$k_m^{CO_2} = 1.194 \text{ mM} [82]$$

PEPCK_{mito} (Mitochondrial phosphoenolpyruvate carboxykinase)



$$v_{PEPCK_{mito}}$$

$$= v_{max}^{PEPCK_{mito}}$$

$$\cdot \frac{OA_{mito} \cdot GTP_{mito} - PEP_{mito} \cdot GDP_{mito} \cdot CO_{2mito} / k_{eq}^{PEPCK_{mito}}}{\left(1 + \frac{OA_{mito}}{k_m^{OA_{mito}}}\right) \cdot \left(1 + \frac{GTP_{mito}}{k_m^{GTP_{mito}}}\right) + \left(1 + \frac{PEP_{mito}}{k_m^{PEP_{mito}}}\right) \cdot \left(1 + \frac{GDP_{mito}}{k_m^{GDP_{mito}}}\right) \cdot \left(1 + \frac{CO_{2mito}}{k_m^{CO_{2mito}}}\right) - 1}$$

$$v_{max}^{PEPCK_{mito}} = 1.0 \cdot 10^6 h^{-1} \cdot mM^{-1}$$

$$k_{eq}^{PEPCK_{mito}} = 160 \text{ mM} [77]$$

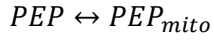
$$k_m^{OA_{mito}} = 0.0085 \text{ mM} [83]$$

$$k_m^{GTP_{mito}} = 0.022 \text{ mM} [81]$$

$$k_m^{PEP_{mito}} = 0.4 \text{ mM} [80]$$

$$k_m^{GDP_{mito}} = 0.02 \text{ mM} [81]$$

$$k_m^{CO_{2mito}} = 1.06 \text{ mM} [84]$$

PEPT (Phosphoenolpyruvate transporter)

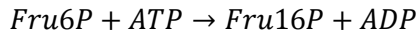
$$v_{PEPT} = v_{max}^{PEPT} \cdot \frac{PEP_{mito} - PEP/k_{eq}^{PEPT}}{1 + \frac{PEP}{k_m^{PEPT}} + \frac{PEP_{mito}}{k_m^{PEPT_{mito}}}}$$

$$v_{max}^{PEPT} = 1.94 \cdot 10^5 \text{ h}^{-1}$$

$$k_{eq}^{PEPT} = \exp\left(-\frac{Vmm \cdot F}{R \cdot T}\right)$$

$$k_m^{PEPT} = 0.1 \text{ mM} [85]$$

$$k_m^{PEPT_{mito}} = 0.1 \text{ mM} [85]$$

PFK1 (Phosphofructokinase 1)

$$v_{PFK1} = v_{max}^{PFK1} \cdot \frac{ATP}{ATP + K_m^{ATP}} \cdot \left(1 - \frac{ATP^{n_i}}{ATP^{n_i} + (K_i^{ATP})^{n_i}}\right) \cdot \frac{(Fru6P)^{n_{Fru6P}}}{(Fru6P)^{n_{Fru6P}} + (k_m^{Fru6P})^{n_{Fru6P}}}$$

$$v_{max}^{PFK1} = 7.68 \cdot 10^4 \text{ mM} \cdot \text{h}^{-1}$$

$$K_m^{ATP} = K_0^{ATP} \cdot \left(1 - \frac{Fru26P_2}{Fru26P_2 + K_a^{Fru26P_2}}\right)$$

$$K_0^{ATP} = 0.2 \text{ mM} [86, 87]$$

$$K_a^{Fru26P_2} = 0.0027 \text{ mM} [86, 87]$$

$$K_i^{ATP} = K_{i0}^{ATP} \cdot \left(1 + f_{Fru26P_2} \frac{Fru26P_2}{Fru26P_2 + K_{a2}^{Fru26P_2}}\right)$$

$$K_{i0}^{ATP} = 0.7 \text{ mM} [86, 87]$$

$$f_{Fru26P_2} = 9 [86, 87]$$

$$K_{a2}^{Fru26P_2} = 0.54 \text{ mM} [86, 87]$$

$$n_i = 4 [86, 87]$$

$$k_m^{Fru6P} = K_0^{Fru6P} \cdot \left(1 + \frac{ATP}{k_i^{ATP}}\right) \cdot \left(1 + \frac{Cit}{k_i^{Cit}}\right) \cdot \left(1 - f_{AMP} \frac{AMP^{n_{AMP}}}{AMP^{n_{AMP}} + (K_a^{AMP})^{n_{AMP}}}\right) \\ \cdot \left(1 - f_P \frac{P}{P + K_a^P}\right) \cdot \left(1 - f_{Fru26P_2} \frac{Fru26P_2^{n_{Fru26P_2}}}{Fru26P_2^{n_{Fru26P_2}} + (K_a^{Fru26P_2})^{n_{Fru26P_2}}}\right)$$

$$K_0^{Fru6P} = 1.14 \text{ mM [88]}$$

$$k_i^{ATP} = 0.6 \text{ mM [88]}$$

$$k_i^{Cit} = 3.27 \text{ mM [88]}$$

$$f_{AMP} = 0.77 \text{ [88]}$$

$$K_a^{AMP} = 0.1 \text{ mM [88]}$$

$$n_{AMP} = 1.84 \text{ [88]}$$

$$f_P = 0.85 \text{ [88]}$$

$$K_a^P = 0.69 \text{ mM [88]}$$

$$f_{Fru26P_2} = 0.92 \text{ [86]}$$

$$K_a^{Fru26P_2} = 0.0045 \text{ mM [86]}$$

$$n_{Fru26P_2} = 1.2 \text{ [86]}$$

$$n^{Fru6P} = \left(n_0 + \frac{ATP^{n_{ATP}}}{ATP^{n_{ATP}} + (K_i^{ATP})^{n_{ATP}}}\right) \cdot \left(1 - f_{AMP} \frac{AMP^{n_{AMP}}}{AMP^{n_{AMP}} + (K_a^{AMP})^{n_{AMP}}}\right) \\ \cdot \left(1 + f_{Cit} \frac{Cit^{n_{Cit}}}{Cit^{n_{Cit}} + (K_i^{Cit})^{n_{Cit}}}\right) \cdot \left(1 - f_P \frac{P^{n_P}}{P^{n_P} + (K_a^P)^{n_P}}\right) \cdot \\ \cdot \left(1 - f_{Fru26P_2} \frac{Fru26P_2^{n_{Fru26P_2}}}{Fru26P_2^{n_{Fru26P_2}} + (K_a^{Fru26P_2})^{n_{Fru26P_2}}}\right)$$

$$n_0 = 3.67 \text{ [88]}$$

$$K_i^{ATP} = 0.13 \text{ mM [88]}$$

$$n_{ATP} = 1.59 \text{ [88]}$$

$$f_{AMP} = 0.4 \text{ [88]}$$

$$K_a^{AMP} = 0.086 \text{ mM [88]}$$

$$n_{AMP} = 2.22 \text{ [88]}$$

$$f_{Cit} = 0.1 \text{ [88]}$$

$$K_i^{Cit} = 0.18 \text{ mM [88]}$$

$$n_{Cit} = 4 \text{ [88]}$$

$$f_P = 0.28 \text{ [88]}$$

$$K_a^P = 0.53 \text{ mM [88]}$$

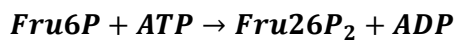
$$n_P = 4 \text{ [88]}$$

$$f_{Fru26P_2} = 0.37 \text{ [86]}$$

$$K_a^{Fru26P_2} = 0.0021 \text{ mM [86]}$$

$$n^{Fru26P_2} = 4 \text{ [86]}$$

PFK2/FBP2 (Phosphofructokinase 2/Fructose-2,6-bisphosphatase)



$$v_{PFK2} = (1 - \gamma^{PFK2}) \cdot v_{PFK2}^{native} + \gamma^{PFK2} \cdot v_{PFK2}^{phospho}$$

$$v_{PFK2}^{native} = V_{max}^{PFK2} \frac{Fru6P^n}{Fru6P^n + (k_m^{Fru6P})^n} \cdot \frac{ATP}{ATP + k_m^{ATP}} \cdot \left(1 - n_0 \cdot \frac{PEP}{PEP + k_i^{PEP}}\right)$$

$$V_{max}^{PFK2} = 1.51 \cdot 10^2 \text{ mM} \cdot \text{h}^{-1}$$

$$k_m^{Fru6P} = 0.015 \text{ mM [89]}$$

$$n = 1.3 \text{ [89]}$$

$$k_m^{ATP} = 0.25 \text{ mM [89]}$$

$$k_i^{PEP} = 0.25 \text{ mM [90]}$$

$$n_0 = 0.85 \text{ [90]}$$

$$v_{PFK2}^{phospho} = V_{max}^{PFK2} \frac{Fru6P^n}{Fru6P^n + k_m^{Fru6P}^n} \cdot \frac{ATP}{ATP + k_m^{ATP}} \cdot \left(1 - n_0 \cdot \frac{PEP}{PEP + k_i^{PEP}}\right)$$

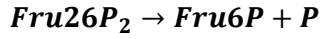
$$k_m^{Fru6P}^{phospho} = 0.05 \text{ mM [89]}$$

$$n = 2 \text{ [89]}$$

$$k_m^{ATP} = 0.5 \text{ mM} [89]$$

$$k_i^{PEP} = 0.25 \text{ mM} [90]$$

$$n_0 = 0.85 [90]$$



$$v_{FBP2} = V_{max}^{FBP2} * \left((1 - \gamma^{FBP2}) \cdot v_{FBP2}^{native} + \gamma^{FBP2} \cdot v_{FBP2}^{phospho} \right)$$

$$V_{max}^{FBP2} = 5.49 \cdot 10^2 \text{ mM} \cdot \text{h}^{-1}$$

$$v_{FBP2}^{native} = \frac{\text{Fru26P}_2}{\text{Fru26P}_2 + k_m^{Fru26P2}} / \left(1 + \frac{\text{Fru6P}}{k_i^{Fru6P}} \right)$$

$$k_m^{Fru26P2} = 0.01 \text{ mM} [91]$$

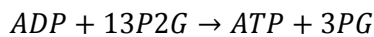
$$k_i^{Fru6P} = 0.0035 \text{ mM} [89]$$

$$v_{FBP2}^{phospho} = \frac{\text{Fru26P}_2}{\text{Fru26P}_2 + k_m^{Fru26P2}} / \left(1 + \frac{\text{Fru6P}}{k_i^{Fru6P}} \right)$$

$$k_m^{Fru26P2} = 0.0005 \text{ mM} [89]$$

$$k_i^{Fru6P} = 0.01 \text{ mM} [89]$$

PGK (Phosphoglycerate kinase)



$$v_{PGK} = v_{max}^{PGK} * \frac{\text{ADP} \cdot 13\text{P2G} - \text{ATP} \cdot 3\text{PG} / k_{eq}^{PGK}}{\left(1 + \frac{\text{ADP}}{k_m^{ADP}} \right) \cdot \left(1 + \frac{13\text{P2G}}{k_m^{13\text{P2G}}} \right) + \left(1 + \frac{\text{ATP}}{k_m^{ATP}} \right) \cdot \left(1 + \frac{3\text{PG}}{k_m^{3\text{PG}}} \right) - 1}$$

$$v_{max}^{PGK} = 1.94 \cdot 10^{10} \text{ h}^{-1} \cdot \text{mM}^{-1}$$

$$k_{eq}^{PGK} = 1830 [92]$$

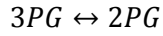
$$k_m^{ADP} = 0.35 \text{ mM} [93]$$

$$k_m^{13\text{P2G}} = 0.0022 \text{ mM} [93]$$

$$k_m^{ATP} = 0.24 \text{ mM} [94]$$

$$k_m^{3PG} = 1.65 \text{ mM [94]}$$

PGM (Phosphoglycerate mutase)



$$v_{PGM} = v_{max}^{PGM} \cdot \frac{3PG - 2PG/k_{eq}^{PGM}}{1 + \frac{3PG}{k_m^{3PG}} + \frac{2PG}{K_m^{2PG}}}$$

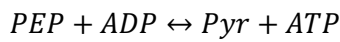
$$v_{max}^{PGM} = 1.94 \cdot 10^{10} \text{ h}^{-1}$$

$$k_{eq}^{PGM} = 0.096 \text{ [95]}$$

$$k_m^{3PG} = 0.52 \text{ mM [96]}$$

$$K_m^{2PG} = 0.24 \text{ mM [96]}$$

PK (Pyruvate kinase)



$$v_{PK} = v_{max}^{PK} \cdot \left((1 - \gamma^{PK}) \cdot v_{PK}^{native} + \gamma^{PK} \cdot v_{PK}^{phospho} \right)$$

$$v_{PK}^{native} = \frac{PEP}{PEP + k_m^{PEP} \cdot \left(1 + \frac{ATP}{k_i^{ATP}} \right) \cdot \left(1 - \frac{Fru16P_2}{Fru16P_2 + k_a^{Fru16P_2}} \right)} \cdot \frac{ADP}{ADP + k_m^{ADP}}$$

$$v_{max}^{PK} = 1.28 \cdot 10^4 \text{ mM} \cdot \text{h}^{-1}$$

$$k_m^{PEP} = 0.13 \text{ mM [97]}$$

$$k_i^{ATP} = 1 \text{ mM [97]}$$

$$k_a^{Fru16P_2} = 0.0078 \text{ mM [98]}$$

$$k_m^{ADP} = 0.25 \text{ mM [99]}$$

$$v_{PK}^{phospho} = \frac{PEP^n}{PEP^n + \left(k_m^{PEP} \cdot \left(1 + \frac{ATP}{k_i^{ATP}} \right) \cdot \left(1 - \frac{Fru16P_2}{Fru16P_2 + k_a^{Fru16P_2}} \right) \right)^n} \cdot \frac{ADP}{ADP + k_m^{ADP}}$$

$$k_m^{PEP} = 5.8 \text{ mM [97]}$$

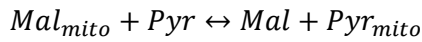
$$n = 2.9 \text{ [97]}$$

$$k_{a^{phospho}}^{Fru16P_2} = 0.0095 \text{ mM [98]}$$

$$k_{i^{phospho}}^{ATP} = 0.32 \text{ mM [32]}$$

$$k_m^{ADP} = 0.33 \text{ mM [99]}$$

PyrMalT (Pyruvate/malate antiporter)



$$v_{PyrMalT} = v_{max}^{PyrMalT} \cdot \left(\frac{Mal_{mito} \cdot Pyr - Mal \cdot Pyr_{mito}}{\left(1 + \frac{Mal_{mito}}{K_m^{Mal_{mito}}}\right) \cdot \left(1 + \frac{Pyr}{K_m^{Pyr}}\right) + \left(1 + \frac{Mal}{K_m^{Mal}}\right) \cdot \left(1 + \frac{Pyr_{mito}}{K_m^{Pyr_{mito}}}\right) - 1} \right)$$

$$v_{max}^{PyrMalT} = 1.94 \cdot 10^4 \text{ h}^{-1} \cdot \text{mM}^{-1}$$

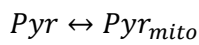
$$k_m^{Pyr} = 0.84 \text{ mM [100]}$$

$$k_m^{Mal} = 0.7 \text{ mM [85]}$$

$$k_m^{Pyr_{mito}} = 0.84 \text{ mM [100]}$$

$$k_m^{Mal_{mito}} = 0.7 \text{ mM [85]}$$

PyrT (Pyruvate transporter)



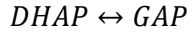
$$v_{PyrT} = v_{max}^{PyrT} \cdot \frac{Pyr \cdot H^+ - Pyr_{mito} \cdot H_{mito}^+}{1 + \frac{Pyr}{k_m^{Pyr}} + \frac{Pyr_{mito}}{k_m^{Pyr_{mito}}}}$$

$$v_{max}^{PyrT} = 1.94 \cdot 10^8 \text{ h}^{-1} \cdot \text{mM}^{-1}$$

$$k_m^{Pyr} = 0.15 \text{ mM [101]}$$

$$k_m^{Pyr_{mito}} = 0.15 \text{ mM [101]}$$

TPI (Triosephosphate isomerase)



$$v_{TPI} = v_{max}^{TPI} \cdot \frac{DHAP - GAP/k_{eq}^{TPI}}{1 + \frac{DHAP}{k_m^{DHAP}} + \frac{GAP}{k_m^{GAP}}}$$

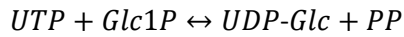
$$v_{max}^{TPI} = 1.94 \cdot 10^8 \text{ h}^{-1}$$

$$k_{eq}^{TPI} = 0.04545 [37]$$

$$k_m^{DHAP} = 0.59 \text{ mM} [102]$$

$$k_m^{GAP} = 0.415 \text{ mM} [102]$$

UGT (Uridine diphospho-glucuronosyltransferase)



$$v_{UGT} = v_{max}^{UGT} \cdot \frac{UTP * Glc1P - UDP-Glc * PP/k_{eq}^{UGT}}{\left(1 + \frac{UTP}{k_m^{UTP}}\right) \left(1 + \frac{Glc1P}{k_m^{Glc1P}}\right) + \left(1 + \frac{UDP-Glc}{k_m^{UDP-Glc}}\right) \left(1 + \frac{PP}{k_m^{PP}}\right) - 1}$$

$$v_{max}^{UGT} = 7.78 \cdot 10^9 \text{ h}^{-1} \cdot \text{mM}^{-1}$$

$$k_{eq}^{UGT} = 0.3122 [103]$$

$$k_m^{UTP} = 0.2 \text{ mM} [103]$$

$$k_m^{Glc1P} = 0.055 \text{ mM} [103]$$

$$k_m^{UDP-Glc} = 0.06 \text{ mM} [103]$$

$$k_m^{PP} = 0.084 \text{ mM} [103]$$

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