Additional tables

Additional Table S1 Elasticities. 0.00 means -0.005 < 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	$K_m^{UDP\text{-}Glc}$	0,85	0,44	1,12	0,35
	$K_0^{UDP\text{-}Glc}$	0,76	0,15	1,03	0,12

	K_a^{Glc6P}	0,49	0,13	0,75	0,11
	$K_b^{UDP\text{-}Glc}$	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
	$k_m^{CO_{2mito}}$	-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 µmol/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]
Vmm	-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

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

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

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

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

Transfer function of external hormones to phosphorylation state

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

Stoichiometric matrix

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

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

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

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

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

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

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

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

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

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

$$\frac{d}{dt}Glc6P = v_{GK} + v_{G6PT_{ER}} - v_{GPI} + v_{G1PI}$$

$$\frac{d}{dt}Glc6P_{ER} = -v_{G6P_{ER}} - v_{Glc6PT_{ER}}$$

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Reaction kinetics

ALD (Aldolase)

$Fru16P_2 \leftrightarrow GAP + DHAP$

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

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

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

$k_{m}^{Fru16P_2} = 0.004$ mM [38]

k_{m}^{GAP} =0.48 mM [39]

$K_{m}^{DHAP} = 0.38$ mM [39]

EN (Enolase)

$2PG \leftrightarrow PEP$

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

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

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

$k_{m}^{2PG} = 0.14\ mM$ [41]

$k_{m}^{PEP} = 0.31\ mM$ [41]

FBP1 (Fructose-1,6-bisphosphatase)

$Fru16P_2 \rightarrow Fru6P + P$

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

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

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

$k_{m^{native}}^{Fru16P_2} = 0.0029$mM [42]

$k_{i}^{Fru26P_2} = 0.00113$ mM [42]

$n = 1.26$ [42]

n_{AMP} = 2.43 [42]

K_{i}^{AMP} = 0.023 mM [42]

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

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

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

$n = 1.26$ [42]

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

$n_{AMP} = 2.43$ [42]

GAPDH (Glyceraldehyde 3-phosphate dehydrogenase)

$$GAP + P + NAD^+ \leftrightarrow 13P2G + NADH + H^+$$

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

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

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

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

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

$k_m^P = 3.8$ mM [45]

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

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

GK (Glucokinase)

$$Glc + ATP \rightarrow Glc6P + ADP$$

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

$$V_{max}^{GK} = V_0^{GK} \cdot \frac{(Glc)^{n2}}{(Glc)^{n2} + (k_a^{Glc})^{n2}} \cdot \left(1 - f \cdot \frac{Fru6P}{Fru6P + k_i^{Fru6P}}\right)$$

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

$n = 1.5$ [46]

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

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

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

$f = 0.75$ [48]

$n2 = 3.7$ [49]

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

GlcT$_{ER}$ (Glucose transport to ER)

$Glc_{ER} \leftrightarrow Glc$

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

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

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

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

GLUT2 (Glucose transporter 2)

$Glc_{ext} \leftrightarrow Glc$

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

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

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

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

GP (Glycogen phosphorylase) [53, 54]

$$Glyc + P \leftrightarrow Glc1P$$

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

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

$$store = 300 \; mM$$

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

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

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

$K_{a_{native}}^{AMP} = 0.36$ 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]

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

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

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

G6P$_{ER}$ (Glucose-6-phosphate phosphatase in the ER) [56, 57]

$Glc6P_{ER} \rightarrow Glc_{ER} + P$

$$v_{G6P\,ER} = V_{max}^{G6P_{ER}} \cdot \frac{Glc6P_{ER}}{Glc6P_{ER} + k_m^{Glc6P_{ER}}}$$

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

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

GPI (Glucose-6-phosphate isomerase)

$Glc6P \leftrightarrow Fru6P$

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

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

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

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

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

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

$Glc1P \leftrightarrow Glc6P$

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

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

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

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

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

G6PT$_{ER}$ (Glucose-6-phosphate transport to ER)

$Glc6P_{ER} \leftrightarrow Glc6P$

$$v_{G6PT_{ER}} = V_{max}^{G6PT_{ER}} \cdot \frac{(Glc6P - Glc6P_{ER})}{1 + \frac{Glc6P}{k_m^{Glc6P}} + \frac{Glc6P_{ER}}{k_m^{Glc6P_{ER}}}}$$

$V_{max}^{G6PT_{ER}} = 1.94 \cdot 10^{10}\ h^{-1}$

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

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

GS (Glycogen synthase)

$UDP\text{-}Glc \rightarrow UDP + Glyc$

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

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

$store = \ 300\ mM\ (average\ hepatocyte)$

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

$$K_{m_{native}}^{UDP\text{-}Glc} = K_{0_{native}}^{UDP\text{-}Glc} \cdot \left(1 - \frac{Glc6P}{Glc6P + K_{a_{native}}^{Glc6p}}\right) + K_{b_{native}}^{UDP\text{-}Glc}$$

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

$K_{a_{native}}^{Glc6P} = 0.007$ mM [62]

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

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

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

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

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

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

LacT (Lactate transporter)

$Lac_{ext} \leftrightarrow Lac$

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

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

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

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

LDH (Lactate dehydrogenase) [64, 65]

$Pyr + NADH \leftrightarrow Lac + NAD^+$

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

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

k_{eq}^{LDH} = 9000 [66]

k_m^{NADH} = 0.015 mM [65]

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

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

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

MalT (Malate transporter)

$$Mal_{mito} + P \leftrightarrow Mal + P_{mito}$$

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

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

k_m^P = 1.41 mM [67]

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

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

k_m^{Mal} = 0.49 mM [67]

MDH (Malate dehydrogenase)

$$Mal + NAD^+ \leftrightarrow OA + NADH$$

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

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

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

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

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

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

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

MDH$_{mito}$ (Mitochondrial malate dehydrogenase)

$$Mal_{mito} + NAD_{mito}^+ \leftrightarrow OA_{mito} + NADH_{mito}$$

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

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

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

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

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

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

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

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

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

$ATP_{mito} + GDP_{mito} \leftrightarrow ADP_{mito} + GTP_{mito}$

$ATP + GDP \leftrightarrow ADP + GTP$

$ATP + UDP \leftrightarrow ADP + UTP$

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

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

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

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

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

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

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

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

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

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

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

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

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

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

$K_m^{GTP\_mito}$ = 0.15 mM [74]

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

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

PC (Pyruvate carboxylase) [75, 76]

$ATP_{mito} + Pyr_{mito} + CO_{2_{mito}} \leftrightarrow OA_{mito} + ADP_{mito} + P_{mito}$

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

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

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

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

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

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

PEPCK (Phosphoenolpyruvate carboxykinase)

$OA + GTP \leftrightarrow PEP + GDP + CO_2$

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

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

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

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

k_m^{GTP} =0.021 mM [79]

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

k_m^{GDP} = 0.02 mM [81]

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

PEPCK$_{mito}$ (Mitochondrial phosphoenolpyruvate carboxykinase)

$OA_{mito} + GTP_{mito} \leftrightarrow PEP_{mito} + GDP_{mito} + CO_{2_{mito}}$

$$v_{PEPCK_{mito}} = v_{max}^{PEPCK_{mito}} \cdot \frac{OA_{mito} \cdot GTP_{mito} - PEP_{mito} \cdot GDP_{mito} \cdot CO_{2_{mito}}/k_{eq}^{PEPCK_{mito}}}{\left(1+\frac{OA_{mito}}{k_{m^{mito}}^{OA}}\right)\cdot\left(1+\frac{GTP_{mito}}{k_{m^{mito}}^{GTP}}\right)+\left(1+\frac{PEP_{mito}}{k_m^{PEP_{mito}}}\right)\cdot\left(1+\frac{GDP_{mito}}{k_m^{GDP_{mito}}}\right)\cdot\left(1+\frac{CO_{2_{mito}}}{k_m^{CO_{2_{mito}}}}\right)-1}$$

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

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

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

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

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

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

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

PEPT (Phosphoenolpyruvate transporter)

$PEP \leftrightarrow PEP_{mito}$

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

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

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

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

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

PFK1 (Phosphofructokinase 1)

$Fru6P + ATP \rightarrow Fru16P + ADP$

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

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

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

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

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

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

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

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

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

$n_i = 4$ [86, 87]

$$k_m^{Fru6P} = K_0^{Fru6p} \cdot \left(1 + \frac{ATP}{k_i^{ATP}}\right) \cdot \left(1 + \frac{Cit}{k_i^{Cit}}\right) \cdot \left(1 - f_{AMP} \frac{AMP^{n_{AMP}}}{AMP^{n_{AMP}} + (K_a^{AMP})^{n_{AMP}}}\right)$$

$$\cdot \left(1 - f_P \frac{P}{P + K_a^P}\right) \cdot \left(1 - f_{Fru26P_2} \frac{Fru26P_2^{n_{Fru26P_2}}}{Fru26P_2^{n_{Fru26P_2}} + \left(K_a^{Fru26P_2}\right)^{n_{Fru26P_2}}}\right)$$

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

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

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

$f_{AMP} = 0.77$ [88]

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

$n_{AMP} = 1.84$ [88]

$f_P = 0.85$ [88]

$K_a^P = 0.69$ mM [88]

$f_{Fru26P_2} = 0.92$ [86]

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

$n_{Fru26P_2} = 1.2$ [86]

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

$$\cdot \left(1 + f_{Cit} \frac{Cit^{n_{Cit}}}{Cit^{n_{Cit}} + \left(K_i^{Cit}\right)^{n_{Cit}}}\right) \cdot \left(1 - f_P \frac{P^{n_P}}{P^{n_P} + (K_a^P)^{n_P}}\right) \cdot$$

$$\cdot \left(1 - f_{Fru26P_2} \frac{Fru26P_2{}^{n_{Fru26bp}}}{Fru26P_2^{n_{Fru26P_2}} + \left(K_a^{Fru26P_2}\right)^{n_{Fru26P_2}}}\right)$$

$n_0 = 3.67$ [88]

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

$n_{ATP} = 1.59$ [88]

$f_{AMP} = 0.4$ [88]

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

$n_{AMP} = 2.22$ [88]

$f_{Cit} = 0.1$ [88]

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

$n_{Cit} = 4$ [88]

$f_P = 0.28$ [88]

$K_a^P = 0.53$ mM [88]

$n_P = 4$ [88]

$f_{Fru26P_2} = 0.37$ [86]

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

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

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

$\boldsymbol{Fru6P + ATP \rightarrow Fru26P_2 + ADP}$

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

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

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

$k_{m^{native}}^{Fru6P} = 0.015$ mM [89]

$n = 1.3$ [89]

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

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

$n_0 = 0.85$ [90]

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

$k_{m^{phospho}}^{Fru6P} = 0.05$ mM [89]

$n = 2$ [89]

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

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

$n_0 = 0.85$ [90]

$\boldsymbol{Fru26P_2 \rightarrow Fru6P + P}$

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

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

$$v_{FBP2}^{native} = \frac{Fru26P_2}{Fru26P_2 + k_{m^{native}}^{Fru26P_2}} / \left(1 + \frac{Fru6P}{k_{i_{native}}^{Fru6P}}\right)$$

$k_{m^{native}}^{Fru26P_2} = 0.01\ mM$ [91]

$k_{i_{native}}^{Fru6P} = 0.0035$ mM [89]

$$v_{FBP2}^{phospho} = \frac{Fru26P_2}{Fru26P_2 + k_{m^{phospho}}^{Fru26P_2}} / \left(1 + \frac{Fru6P}{k_{i_{phospho}}^{Fru6P}}\right)$$

$k_{m^{phospho}}^{Fru26P_2} = 0.0005$ mM [89]

$k_{i_{phospho}}^{Fru6P} = 0.01\ mM$ [89]

PGK (Phosphoglycerate kinase)

$ADP + 13P2G \rightarrow ATP + 3PG$

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

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

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

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

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

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

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

PGM (Phosphoglycerate mutase)

$3PG \leftrightarrow 2PG$

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

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

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

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

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

PK (Pyruvate kinase)

$PEP + ADP \leftrightarrow Pyr + ATP$

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

$$v_{PK}^{native} = \frac{PEP}{PEP + k_{m^{native}}^{PEP} \cdot \left(1 + \frac{ATP}{k_{i^{native}}^{ATP}}\right) \cdot \left(1 - \frac{Fru16P_2}{Fru16P_2 + k_{a^{native}}^{Fru16P_2}}\right)} \cdot \frac{ADP}{ADP + k_m^{ADP}}$$

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

$k_{m^{native}}^{PEP}$ =0.13 mM [97]

$k_{i^{native}}^{ATP}$ =1 mM [97]

$k_{a^{native}}^{Fru16P_2}$ =0.0078 mM [98]

k_m^{ADP} = 0.25 mM [99]

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

$k_{m^{phospho}}^{PEP}$ = 5.8 mM [97]

$n = 2.9$ [97]

$k_{a_{phospho}}^{Fru16P_2} = 0.0095$ mM [98]

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

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

PyrMalT (Pyruvate/malate antiporter)

$Mal_{mito} + Pyr \leftrightarrow Mal + Pyr_{mito}$

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

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

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

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

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

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

PyrT (Pyruvate transporter)

$Pyr \leftrightarrow Pyr_{mito}$

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

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

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

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

TPI (Triosephosphate isomerase)

$DHAP \leftrightarrow GAP$

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

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

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

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

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

UGT (Uridine diphospho-glucuronosyltransferase)

$UTP + Glc1P \leftrightarrow UDP\text{-}Glc + PP$

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

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

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

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

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

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

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

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