Supplementary Table 1. Molecular components of the model

Reaction number	Abbreviation	Protein name/description	SwissProt ID/TrEMBL entry	Compound/EC number	pathway(s)
v1	GK	Glucokinase	P35557	E.C.2.7.1.2	glycolysis
v1	GLC	Glucose		C00267	glycolysis
v1,v2	F6P	Fructose-6-phosphate		C00085	glycolysis
v1,v2,v5,v6,v23,v28, v36,v40	ADP	Adenosine Diphosphate		C00008	glycolysis, TCA cycle
v1,v2,v5,v6,v23,v28, v36,v43	ATP	Adenosine Triphosphate		C00002	glycolysis, TCA cycle
v2	PFK	6-phosphofructokinase	P17858	E.C.2.7.1.11	glycolysis
v2,v3	FBP	Fructose-1,6-bisphosphate		C00354	glycolysis
v3	FBA	fructose-bisphosphate aldolase (B/C/A)	P05062/P09972/P04075	E.C.4.1.2.13	glycolysis
v3,v4	GAP	Glyceraldehyde 3-phosphate		C00118	glycolysis
v4	GAPD	glyceraldehyde 3-phosphate dehydrogenase	P04406	E.C.1.2.1.12	glycolysis
v4,v5	DPG	1,3-bisphospho-D-glycerate		C00236	glycolysis
v4,v7,v9,v12,v14,v18, v24,v31	NAD+	Nicotinamide Adenine Dinucleotides		C00003	glycolysis, TCA cycle.NADH shuttles, respiratory chain, pyruvate cycle
v4,v7,v9,v12,v14,v18, v24,v31	NADH	Nicotinamide Adenine Dinucleotides		C00004	glycolysis, TCA cycle.NADH shuttles, respiratory chain, pyruvate cycle

v5	PGP	bisphosphoglycerate phosphatase (1/2)	P18669/P15259	E.C.5.4.2.1/E.C.5.4.2.4	glycolysis
v5,v6	PEP	Phosphoenol Pyruvate		C00074	glycolysis
v6	PK	Pyruvate kinase	P30613	E.C.2.7.1.40	glycolysis
v6,v7,v8,v9,v20,v36,v44	PYR	Pyruvate		C00022	glycolysis, TCA cycle
v7	LDH	Lactate dehydrogenase	P00338/P07195	E.C.1.1.1.27	glycolysis
v7	LAC	Lactate		C00186	glycolysis
v8	PYC	Pyruvate Carrier	Q4Q5H1		metabolite transport
v9	PDC	Pyruvate Dehydrogenase Complex	P08559/P11177/P29803	E.C.1.2.4.1.	TCA cycle
v9	CO2	Carbon Dioxide		C00011	TCA cycle
v10,v11,v27,v29,v33	Cit	Citrate		C00158	TCA cycle, pyruvate cycle
v10,v15	CoA	Coenzyme A		C00010	TCA cycle
v10,v18,v21,v31,v32,v36	OXA	Oxaloacetate		C000036	TCA cycle,NADH shuttles
v10,v27	CS	Citrate Synthase	O75390	E.C.2.3.3.1/E.C.2.3.3.3	TCA cycle, pyruvate cycle
v10,v27	Acetyl_CoA			C00024	TCA cycle
v11,v12,v29,v41,v42	IsoCit	Isocitrate		C00311	TCA cycle, pyruvate cycle
v11,v29	ACO	Aconitase	Q99798	E.C.4.2.1.3	TCA cycle, pyruvate cycle
v12	IDHa	Isocitrate Dehydrogenase (NAD+) (alpha/beta/gamma)	P50213/O43837/P51553	E.C.1.1.1.41	TCA cycle, pyruvate cycle
v12,v14,v21,v30,v32	OG	Oxoglutarate		C00026	TCA cycle,NADH shuttles

v13	PiC	Phosphate Carrier	Q00325		metabolite transport
v13,v15,v28	Pi	Phosphate		C00009	metabolite transport
v14	OGDC	Oxoglutarate Dehydrogenase Complex	Q02218	E.C.1.2.4.2	TCA cycle
v14,v15	SCoA	Succinyl-CoA		C00091	TCA cycle
v15	SCS	Succinyl-CoA synthetase	P53597/Q96I99	E.C.6.2.1.4	TCA cycle
v15,v16	Suc	Succinate		C00042	TCA cycle
v15,v23	GDP	Guanosine Diphosphate		C00035	TCA cycle
v15,v23	GTP	Guanosine Triphosphate		C00044	TCA cycle
v16	SDH	Succinate Dehydrogenase	P21912/P31040	E.C.1.3.5.1	TCA cycle,respiratory chain
v16,v17	Fum	Fumarate		C00122	TCA cycle,respiratory chain
v16,v24,v25	Q	Ubiquinone		C00399	respiratory chain, NADH shuttles
v16,v24,v25	QH2	Ubiquinol		C00390	respiratory chain, NADH shuttles
v17	FM	Fumarase	P07954	E.C.4.2.1.2	TCA cycle, NADH shuttle
v17,v18,v19,v30,v31, v33v39,v42,v44	Mal	Malate		C00149	TCA cycle, NADH shuttle, pyruvate cycle
v18,v31	MDH	Malate Dehydrogenase(mitochondrion & cytosol)	P40926	E.C.1.1.1.37	TCA cycle, NADH shuttles
v19	DIC	Dicarboxyrate Carrier			metabolite transport

v20	AlaTA	Alanine Transaminase	P24298	E.C.2.6.1.2	NADH shuttle (malate-aspartate shuttle)
v20	Ala	Alanine		C00041	TCA cycle
v20,v21	Glu	Glutamate		C00025	TCA cycle, NADH shuttles
v21,v22	Asp	Aspartate		C00049	TCA cycle
v21,v32	AspTA	Aspartate Transaminase	P00505	E.C.2.6.1.1	NADH shuttle (malate-aspartate shuttle)
v22	AGC	Aspartate/ Glutamate Carrier	Q59GB0		NADH shuttle (malate-aspartate shuttle)
v23	NDK	Nucleoside Diphosphate Kinase	O00746	E.C.2.7.4.6	TCA cycle
v24	Complex-I	NADH :Ubiquinone oxidoreductase		E.C.1.6.5.3	respiratory chain
v25	Complex-III	Ubiquinol: Cytochrome c Oxidoreductase	P08574	E.C.1.10.2.2	respiratory chain
v25,v26	Cyt_c2+	Ferricytochrome c		C00125	respiratory chain
v25,v26	Cyt_c3+	Ferrocytochrome c		C00126	respiratory chain
v26	Complex-IV	Cytochrome c Oxidase	P14854/P00403/P10176 /P20674/P13073/P09669 /P24311/P00395/O14548 /P15954	E.C.1.9.3.1	respiratory chain
v26,v28	H2O	Water		C00001	
v28	Complex-V	ATPase complex		E.C.3.6.1.3/E.C.3.6.1.5	respiratory chain
v30	OGC	Oxoglutarate Carrier	Q02978		NADH shuttle (malate-aspartate shuttle),pyruvate cycle

v33	CIC	Citrate Carrier	P53007		metabolite transport
v34	ETF-QO	ETF:Q oxidoreductase	Q16134	E.C.1.5.5.1	NADH shuttle (glycerophosphate shuttle)
v34,v35	ETFox	Electron Transfer Flavoprotein (oxidised form)			NADH shuttle (glycerophosphate shuttle)
v34,v35	ETFred	Electron Transfer Flavoprotein (reduced form)			NADH shuttle (glycerophosphate shuttle)
v35	GSSGR	Glutathione reductase	P00390	E.C.1.8.1.7	glutathione pathway
v35,v37	FAD			C00016	NADH shuttle (glycerophosphate shuttle)
v35,v37	FADH2			C01352	NADH shuttle (glycerophosphate shuttle)
v36	PC	Pyruvate Carboxylase	P11498	E.C.6.4.1.1	TCA cycle, pyruvate cycle
v37	GUT2P	Glycerol-3-phosphate dehydrogenase (FAD dependent)	P43304	E.C.1.1.99.5	NADH shuttle (glycerophosphate shuttle)
v37,v38	DHAP	Dihydroxyacetone-phosphate		C00111	NADH shuttle (glycerophosphate shuttle)

v37,v38	G3P	Glycerol-3-phosphate		C00093	NADH shuttle (glycerophosphate shuttle)
v38	G3PD	Glycerol-3-phosphate dehydrogenase (NAD+)	P21695	E.C.1.1.1.8	NADH shuttle (glycerophosphate shuttle)
v39,v41,v44	NADP+			C00006	pyruvate cycle
v39,v41,v44	NADPH			C00005	pyruvate cycle
v39,v44	ME	Malate Dehydrogenase (oxaloacetate-decarboxylating)(NADP+)	P48163/Q16798	E. C. 1.1.1.40	pyruvate cycle
v40,v43	AAC	ATP/ADP carrier	P12236		metabolite transport
v41	IDHc	cytosolic Isocitrate Dehydrogenase (NADP+)	P48735/O75874	E.C.1.1.1.42	pyruvate cycle

Supplementary Table 2. Reactions

Glycolysis:

	Reaction	Rate expression	Source
GK (v1)	GLC+ATP → F6P+ADP	$\frac{V_1[ATP][GLC]}{(K_{1GLC}+[GLC])(K_{1ATP}+[ATP])}$	[Nielsen, et al. 1998]
PFK (v2)	F6P+ATP → FBP+ADP	$\frac{V_2[F6P]^2[ATP]}{(K_2(1+k_2(\frac{[ATP]}{[AMP]})^2)+[F6P]^2)(K_{2ATP}+[ATP])}$	[Nielsen, et al. 1998]
FBA (v3)	FBP ↔ 2GAP	$v_{\rightarrow}=k_{3f}[FBP]$ $v_{\leftarrow}=k_{3b}[GAP]^2$	[Nielsen, et al. 1998]
GAPD (v4)	GAP+NAD → DPG+NADH	$\frac{V_4[GAP][NAD]}{(K_{4GAP}+[GAP])(K_{4NAD}+[NAD])}$	[Nielsen, et al. 1998]
V5	DPG+ADP ↔ PEP+ATP	$v_{\rightarrow}=k_{5f}[DPG][ADP]$ $v_{\leftarrow}=k_{5b}[PEP][ATP]$	[Nielsen, et al. 1998]
V6	PEP+ADP → PYR+ATP	$\frac{V_6[PEP][ADP]}{(K_{6PEP}+[PEP])(K_{6ADP}+[ADP])}$	[Nielsen, et al. 1998]
V7	PYR +NADH → LAC +NAD	$\frac{V_7[PYR]}{(K_{7PYR}+[PYR])}$	[Nielsen, et al. 1998]

	Reaction	Rate expression	Source
PYC (v8)	$PYR_{IMS}+H_{MAT}$ ↔ $PYR_{MAT}+H_{IMS}$	$\frac{V[E][PYR]}{(K+[PYR])}$	[Halestrap, 1975]
PDC (v9)	Pyr+NAD++CoA → Acetyl-CoA +NADH+CO2	$\frac{K_{cf}[E][Pyc][CoA][NAD^+]}{denom}$ $denom=K_{mC}[Pyc][CoA]+K_{mB}[Pyc][NAD^+]+K_{mA}[CoA][NAD^+]+[Pyc][CoA][NAD^+]+\frac{K_{mA}K_{mP}K_{ib}K_{ic}[Acetyl-CoA][NADH]}{K_{mR}K_{ip}K_{iq}}$ $+\frac{K_{mC}[Pyc][CoA][NADH]}{K_{ir}}+\frac{K_{mB}[Pyc][NAD^+][Acetyl-CoA]}{K_{iq}}+\frac{K_{mA}K_{mP}K_{ib}K_{ic}[Pyc][Acetyl-CoA][NADH]}{K_{mR}K_{ip}K_{ia}K_{iq}}$	[Yugi & Tomita, 2004] [Hamada et al., 1975]

CS (v10& v27)	OXA+Acetyl-CoA ↔ Cit+CoA	$\frac{V[Acetyl-CoA][OXA]}{[Acetyl-CoA][OXA]+K_a[OXA]+K_b[Acetyl-CoA]+K_{ia}K_b}$	[Matsuoka & Srere, 1973]
ACO (v11 & v29)	Cit ↔ IsoCit	$\frac{[E](K_{cf}K_p[Cit]-K_{cr}K_s[IsoCit])}{K_s[IsoCit]+K_p[Cit]+K_sK_p}$	[Yugi & Tomita, 2004] [Guarriero-bobyleva et al., 1978]
IDHa (v12)	IsoCit+NAD+ → OG+NADH	$\frac{K_{cf}[E]([IsoCit]^2+b[ADP][IsoCit])}{[IsoCit]^2+c[IsoCit]+d[ADP]+e[ADP][IsoCit]+f}$	[Yugi & Tomita, 2004] [Plaut et al., 1974]
PiC (v13)	$Pi_{IMS}+H^+_{IMS}$ ↔ $Pi_{MAT}+H^+_{MAT}$	$\frac{\frac{[Pi_{IMS}][H_{MAT}]}{\alpha K_{1Pi}K_{1H}}k^f_{cat}[PiC]-\frac{[Pi_{MAT}][H_{IMS}]}{\beta K_{2Pi}K_{2H}}k^r_{cat}[PiC]}{1+\frac{[Pi_{IMS}]}{K_{1Pi}}+\frac{[H_{MAT}]}{K_{1H}}+\frac{[Pi_{MAT}]}{K_{2Pi}}+\frac{[H_{IMS}]}{K_{2H}}+\frac{[Pi_{IMS}][H_{MAT}]}{\alpha K_{1Pi}K_{1H}}+\frac{[Pi_{MAT}][H_{IMS}]}{\beta K_{2Pi}K_{2H}}+\frac{[H_{MAT}][Pi_{MAT}]}{\gamma K_{1H}K_{2Pi}}+\frac{[[Pi_{IMS}][H_{IMS}]}{\delta K_{1Pi}K_{2H}}}$	[Yugi & Tomita, 2004] [Stappen & Kramer, 1994]
OGDC (v14)	OG+NAD^++CoA → SCoA+ NADH+CO_2	$\frac{K_{cf}[E][OG][CoA][NAD^+]}{denom}$ $denom=K_{mC}[OG][CoA]+K_{mB}[OG][NAD^+]+K_{mA}[CoA][NAD^+]+[OG][CoA][NAD^+]+\frac{K_{mA}K_{mP}K_{ib}K_{ic}[SCoA][NADH]}{K_{mR}K_{ip}K_{iq}}$ $+\frac{K_{mC}[OG][CoA][NADH]}{K_{ir}}+\frac{K_{mB}[OG][NAD^+][SCoA]}{K_{iq}}+\frac{K_{mA}K_{mP}K_{ib}K_{ic}[OG][SCoA][NADH]}{K_{mR}K_{ip}K_{ia}K_{iq}}$	[Yugi & Tomita, 2004] [Hamada et al., 1975]
SCS (v15)	SCoA+GDP+Pi ↔ Suc+CoA+GTP	$\frac{([GDP][SCoA][Pi]-\frac{[Suc][GTP][CoA]}{K_{eq}})\{K_{c1}[E]+K_{c2}[E](\frac{K_{mC}[Suc]}{K_{mC2}K_{ip}}+\frac{[Pi]}{K_{mC2}})\}}{denom}$	[Yugi & Tomita, 2004] [Cha & Parks Jr., 1964]

		$$denom = K_{ia}K_{mB}[pi] + K_{mB}[GDP][Pi] + K_{mA}[SCoA][Pi] + K_{mC}[GDP][SCoA] + [GDP][SCoA][Pi] + \frac{[GDP][SCoA][Pi]^2}{K_{mC2}}$$ $$+ \frac{K_{ia}K_{mB}K_{mC}[Suc]}{K_{ip}} + \frac{K_{ia}K_{mB}K_{mC}[Suc][GTP]}{K_{ip}K_{iq}} + \frac{K_{ia}K_{mB}K_{mC}[Suc][CoA]}{K_{ip}K_{ir}} + \frac{K_{ia}K_{mB}K_{ic}[GTP][CoA]}{K_{mQ}K_{ir}}$$ $$+ \frac{K_{ia}K_{mB}K_{mC}[Suc][GTP][CoA]}{K_{ip}K_{mQ}K_{ir}} + \frac{K_{ia}K_{mB}K_{mC}[Suc]^2[GTP][CoA]}{K_{ip}K_{mP2}K_{mQ}K_{ir}} + \frac{K_{ia}K_{mB}[Pi][GTP]}{K_{iq}} + \frac{K_{ia}K_{mB}[Pi][CoA]}{K_{ir}}$$ $$+ \frac{K_{ia}K_{mB}[Pi][GTP][CoA]}{K_{mQ}K_{ir}} + \frac{K_{ia}K_{mB}[Pi][Suc][GTP][CoA]}{K_{mP2}K_{mQ}K_{ir}} + \frac{K_{mB}K_{mC}[GDP][Suc]}{K_{ip}} + \frac{K_{mA}K_{mC}[SCoA][Suc]}{K_{ip}}$$ $$+ \frac{K_{mC}[GDP][SCoA][Suc]}{K_{ip}} + \frac{K_{mC}[GDP][SCoA][Pi][Suc]}{K_{mC2}K_{ip}} + \frac{K_{mA}[SCoA][Pi][GTP]}{K_{iq}} + \frac{K_{mB}[GDP][Pi][CoA]}{K_{ir}}$$ $$+ \frac{K_{mA}K_{mC}[SCoA][Suc][GTP]}{K_{ip}K_{iq}} + \frac{K_{mB}K_{mC}[GDP][Suc][CoA]}{K_{ip}K_{ir}}$$	
SDH (v16)	Suc+Q ↔ Fum+QH_2	$$\frac{K_{cf}K_{cr}[E]([Suc][Q] - \frac{[Fum][QH_2]}{K_{eq}})}{denom}$$ $$denom = K_{cr}K_{mS2}[Suc] + K_{cr}K_{mS1}[Q] + \frac{K_{cf}K_{mP2}[Fum]}{K_{eq}} + \frac{K_{cf}K_{mP1}[QH_2]}{K_{eq}} + K_{cr}[Suc][Q] + \frac{K_{cf}K_{mP2}[Suc][Fum]}{K_{eq}K_{iS1}} + \frac{K_{cf}[Fum][QH_2]}{K_{eq}}$$ $$+ \frac{K_{cr}K_{mS1}[Q][QH_2]}{K_{iP2}}$$	[Yugi & Tomita, 2004] [Grivennikova et al., 1993]
FM (v17)	Fum ↔ Mal	$$\frac{[E](K_{cf}K_p[Fum] - K_{cr}K_s[Mal])}{K_s[Mal] + K_p[Fum] + K_sK_p}$$	[Yugi & Tomita, 2004]
MDH (v18 & v31)	Mal+NAD^+ ↔ OXA+NADH	$$\frac{[E](\frac{K_{cf}[Mal][NAD^+]}{K_{iS1}K_{mS2}} - \frac{K_{cr}[OXA][NADH]}{K_{mP1}K_{iP2}})}{denom}$$ $$denom = 1 + \frac{[Mal]}{K_{iS1}} + \frac{K_{mS1}[NAD^+]}{K_{iS1}K_{mS2}} + \frac{K_{mP2}[OXA]}{K_{mP1}K_{iP2}} + \frac{[NADH]}{K_{iP2}} + \frac{[Mal][NAD^+]}{K_{iS1}K_{mS2}} + \frac{K_{mP2}[Mal][OXA]}{K_{iS1}K_{mP1}K_{iP2}} + \frac{K_{mS1}[NAD^+][NADH]}{K_{iS1}K_{mS2}K_{iP2}}$$ $$+ \frac{[OXA][NADH]}{K_{mP1}K_{iP2}} + \frac{[Mal][NAD^+][OXA]}{K_{iS1}K_{mS2}K_{iP1}} + \frac{[NAD^+][OXA][NADH]}{K_{iS2}K_{mP1}K_{iP2}}$$	[Yugi & Tomita, 2004] [Crow et al., 1983]

DIC (v19)	$Mal_{IMS} + Pi_{MAT} \leftrightarrow Mal_{MAT} + Pi_{IMS}$	$\frac{\frac{[Mal_{IMS}][Pi_{MAT}]}{\alpha K_{1Mal} K_{1Pi}} k_{cat}^{f}[DIC] - \frac{[Mal_{MAT}][Pi_{IMS}]}{\beta K_{2Mal} K_{2Pi}} k_{cat}^{r}[DIC]}{1 + \frac{[Mal_{IMS}]}{K_{1Mal}} + \frac{[Pi_{MAT}]}{K_{1Pi}} + \frac{[Mal_{MAT}]}{K_{2Mal}} + \frac{[Pi_{IMS}]}{K_{2Pi}} + \frac{[Mal_{IMS}][Pi_{MAT}]}{\alpha K_{1Mal} K_{1Pi}} + \frac{[Mal_{MAT}][Pi_{IMS}]}{\beta K_{2Mal} K_{2Pi}} + \frac{[Pi_{MAT}][Mal_{MAT}]}{\gamma K_{1Pi} K_{2Mal}} + \frac{[[Mal_{IMS}][Pi_{IMS}]}{\delta K_{1Mal} K_{2Pi}}}$	[Yugi & Tomita, 2004] [Indiveri et al., 1993]
AlaTA (v20)	Ala+OG ↔ Glu+Pyr	$\frac{K_{cf} K_{cr}[E]([Ala][OG] - \frac{[Glu][Pyr]}{K_{eq}})}{denom}$ $denom = K_{cr} K_{mS2}[Ala] + K_{cr} K_{mS1}[OG] + \frac{K_{cf} K_{mP2}[Glu]}{K_{eq}} + \frac{K_{cf} K_{mP1}[Pyr]}{K_{eq}} + K_{cr}[Ala][OG] + \frac{K_{cf} K_{mP2}[Ala][Glu]}{K_{eq} K_{iS1}} + \frac{K_{cf}[Glu][Pyr]}{K_{eq}} + \frac{K_{cr} K_{mS1}[OG][Pyr]}{K_{iP2}}$	[Yugi & Tomita, 2004] [De Rosa et al., 1979]
AspTA (v21 & v32)	Asp+OG ↔ OXA+Glu	$\frac{K_{cf} K_{cr}[E]([Asp][OG] - \frac{[OXA][Glu]}{K_{eq}})}{denom}$ $denom = K_{cr} K_{mS2}[Asp] + K_{cr} K_{mS1}[OG] + \frac{K_{cf} K_{mP2}[OXA]}{K_{eq}} + \frac{K_{cf} K_{mP1}[Glu]}{K_{eq}} + K_{cr}[Asp][OG] + \frac{K_{cf} K_{mP2}[Asp][OXA]}{K_{eq} K_{iS1}} + \frac{K_{cf}[OXA][Glu]}{K_{eq}} + \frac{K_{cr} K_{mS1}[OG][Glu]}{K_{iP2}}$	[Yugi & Tomita, 2004] [Velick & Vavra, 1962] [Henson & Cleland, 1964]
AGC (v22)	$Asp_{IMS} + Glu_{MAT} \leftrightarrow Asp_{MAT} + Glu_{IMS}$	$\frac{\frac{[Asp_{IMS}][Glu_{MAT}]}{\alpha K_{1Asp} K_{1Glu}} k_{cat}^{f}[AGC] - \frac{[Asp_{MAT}][Glu_{IMS}]}{\beta K_{2Asp} K_{2Glu}} k_{cat}^{r}[AGC]}{1 + \frac{[Asp_{IMS}]}{K_{1Asp}} + \frac{[Glu_{MAT}]}{K_{1Glu}} + \frac{[Asp_{MAT}]}{K_{2Asp}} + \frac{[Glu_{IMS}]}{K_{2Glu}} + \frac{[Asp_{IMS}][Glu_{MAT}]}{\alpha K_{1Asp} K_{1Glu}} + \frac{[Asp_{MAT}][Glu_{IMS}]}{\beta K_{2Asp} K_{2Glu}} + \frac{[Glu_{MAT}][Asp_{MAT}]}{\gamma K_{1Glu} K_{2Asp}} + \frac{[[Asp_{IMS}][Glu_{IMS}]}{\delta K_{1Asp} K_{2Glu}}}$	[Yugi & Tomita, 2004] [Sluse et al., 1991]
NDK (v23)	ATP + GDP ↔ ADP + GTP	$\frac{K_{cf} K_{cr}[E]([ATP][GDP] - \frac{[ADP][GTP]}{K_{eq}})}{denom}$ $denom = K_{cr} K_{mS2}[ATP] + K_{cr} K_{mS1}[GDP] + \frac{K_{cf} K_{mP2}[ADP]}{K_{eq}} + \frac{K_{cf} K_{mP1}[GTP]}{K_{eq}} + K_{cr}[ATP][GDP] + \frac{K_{cf} K_{mP2}[ATP][ADP]}{K_{eq} K_{iS1}} + \frac{K_{cf}[ADP][GTP]}{K_{eq}} + \frac{K_{cr} K_{mS1}[GDP][GTP]}{K_{iP2}}$	[Yugi & Tomita, 2004] [Garces & Cleland, 1969]
I (v24)	$NADH+Q+5H^{+}_{MAT} \leftrightarrow NAD^{+}+QH_2 + 4H^{+}_{IMS}$	$\frac{K_{cf} K_{cr}[E]([NADH][Q] - \frac{[NAD^{+}][QH_2]}{K_{eq}})}{denom}$	[Yugi & Tomita, 2004] [Fato et al., 1996]

		$denom = K_{cr}K_{mS2}[NADH] + K_{cr}K_{mS1}[Q] + \frac{K_{cf}K_{mP2}[NAD^+]}{K_{eq}} + \frac{K_{cf}K_{mP1}[QH_2]}{K_{eq}} + K_{cr}[NADH][Q] + \frac{K_{cf}K_{mP2}[NADH][NAD^+]}{K_{eq}K_{iS1}}$ $+ \frac{K_{cf}[NAD^+][QH_2]}{K_{eq}} + \frac{K_{cr}K_{mS1}[Q][QH_2]}{K_{iP2}}$	
III (v25)	QH_2+2cyt c^{3+}+ $2H^+_{MAT} \leftrightarrow$ Q + 2cyt c^{2+} +$4H^+_{IMS}$	$\frac{K_{cf}[E][QH_2][cyt\,c^{3+}]}{[Q](K_{mA}K_{q2}K_{b2} + K_{mA}K_{q2}[cyt\,c^{3+}] + \frac{K_{cf}}{k_8}K_{q1}[QH_2]K_{b1} + \frac{K_{cf}}{k_8}K_{q1}[QH_2][cyt\,c^{3+}]) + K_{mA}[cyt\,c^{3+}] + K_{mB}[QH_2] + [QH_2][cyt\,c^{3+}]}$	[Yugi & Tomita, 2004] [Kubota et al., 1992]
IV (v26)	4cyt c^{2+}+O_2+ $8H^+_{MAT} \leftrightarrow$ 4cyt c^{3+} +$2H_2O$+$4H^+_{IMS}$	$\frac{K_{cf}[E][cyt\,c^{2+}]}{K_s + [cyt\,c^{2+}]}$	[Yugi & Tomita, 2004] [Malmstrom & Andreasson, 1985]
V (v28)	ADP+Pi+$3H^+_{IMS} \leftrightarrow$ ATP+H_2O+$3H^+_{MAT}$	$\frac{K_{cf}[E]\{\frac{[ADP][Pi]}{K_dK_p}klt_f(\frac{H_{IMS}}{H_{MAT}})^{-3(\beta-ax)}(\frac{[H^+_{IMS}]}{K_{hx}(\frac{H_{IMS}}{H_{MAT}})^{ax}})^3 - \frac{[ATP]}{K_t}klt_r(\frac{H_{IMS}}{H_{MAT}})^{3(1-\beta-ay)}(\frac{[H^+_{MAT}]}{K_{hy}(\frac{H_{IMS}}{H_{MAT}})^{-ay}})^3\}}{(1+\frac{[H^+_{IMS}]}{K_{hx}(\frac{H_{IMS}}{H_{MAT}})^{ax}} + \frac{[H^+_{MAT}]}{K_{hy}(\frac{H_{IMS}}{H_{MAT}})^{-ay}})^3(3+\frac{[ADP][Pi]}{K_dK_p} + \frac{[ATP]}{K_t})}$	[Yugi & Tomita, 2004] [Kholodenko, 1993]
OGC (v30)	OG_{IMS} + Mal_{MAT} $\leftrightarrow$ OG_{MAT} + Mal_{IMS}	$\frac{\frac{[OG_{IMS}][Mal_{MAT}]}{\alpha K_{1OG}K_{1Mal}}k^f_{cat}[OGC] - \frac{[OG_{MAT}][Mal_{IMS}]}{\beta K_{2OG}K_{2Mal}}k^r_{cat}[OGC]}{1+\frac{[OG_{IMS}]}{K_{1OG}} + \frac{[Mal_{MAT}]}{K_{1Mal}} + \frac{[OG_{MAT}]}{K_{2OG}} + \frac{[Mal_{IMS}]}{K_{2Mal}} + \frac{[OG_{IMS}][Mal_{MAT}]}{\alpha K_{1OG}K_{1Mal}} + \frac{[OG_{MAT}][Mal_{IMS}]}{\beta K_{2OG}K_{2Mal}} + \frac{[Mal_{MAT}][OG_{MAT}]}{\gamma K_{1Mal}K_{2OG}} + \frac{[[OG_{IMS}][Mal_{IMS}]}{\delta K_{1OG}K_{2Mal}}}$	[Yugi & Tomita, 2004] [Indiveri et al., 1991]
CIC (v33 & v42)	Cit_{IMS} + Mal_{MAT} $\leftrightarrow$ Cit_{MAT} + Mal_{IMS} $IsoCit_{IMS}$ + Mal_{MAT} $\leftrightarrow$ $IsoCit_{MAT}$ + Mal_{IMS}	$\frac{\frac{[Cit_{IMS}][Mal_{MAT}]}{\alpha K_{1Cit}K_{1Mal}}k^f_{cat}[CIC] - \frac{[Cit_{MAT}][Mal_{IMS}]}{\beta K_{2Cit}K_{2Mal}}k^r_{cat}[CIC]}{1+\frac{[Cit_{IMS}]}{K_{1Cit}} + \frac{[Mal_{MAT}]}{K_{1Mal}} + \frac{[Cit_{MAT}]}{K_{2Cit}} + \frac{[Mal_{IMS}]}{K_{2Mal}} + \frac{[Cit_{IMS}][Mal_{MAT}]}{\alpha K_{1Cit}K_{1Mal}} + \frac{[Cit_{MAT}][Mal_{IMS}]}{\beta K_{2Cit}K_{2Mal}} + \frac{[Mal_{MAT}][Cit_{MAT}]}{\gamma K_{1Mal}K_{2Cit}} + \frac{[[Cit_{IMS}][Mal_{IMS}]}{\delta K_{1Cit}K_{2Mal}}}$	[Yugi & Tomita, 2004] [Bisaccia et al., 1993]
ETF-QO (v34)	ETFred +Q $\leftrightarrow$ ETFox + QH2	$\frac{K_{cf}K_{cr}[E]([ETF_{red}][Q] - \frac{[ETF_{ox}][QH_2]}{K_{eq}})}{denom}$ $denom = K_{cr}K_{mS2}[ETF_{red}] + K_{cr}K_{mS1}[Q] + \frac{K_{cf}K_{mP2}[ETF_{ox}]}{K_{eq}} + \frac{K_{cf}K_{mP1}[QH_2]}{K_{eq}} + K_{cr}[ETF_{red}][Q] + \frac{K_{cf}K_{mP2}[ETF_{red}][ETF_{ox}]}{K_{eq}K_{iS1}}$ $+ \frac{K_{cf}[ETF_{ox}][QH_2]}{K_{eq}} + \frac{K_{cr}K_{mS1}[Q][QH_2]}{K_{iP2}}$	[Yugi & Tomita, 2004] [Beckmann and Frerman, 1985]

V35	FAD + ETF_{red} ↔ FADH2 +ETF_{ox}	$$\frac{[E]\left(\frac{K_{cf}[FAD][ETF_{red}]}{K_{iS1}K_{mS2}} - \frac{K_{cr}[FADH2][ETF_{ox}]}{K_{mP1}K_{iP2}}\right)}{denom}$$ $$denom = 1 + \frac{[FAD]}{K_{iS1}} + \frac{K_{mS1}[ETF_{red}]}{K_{iS1}K_{mS2}} + \frac{K_{mP2}[FADH2]}{K_{mP1}K_{iP2}} + \frac{[ETF_{ox}]}{K_{iP2}} + \frac{[FAD][ETF_{red}]}{K_{iS1}K_{mS2}} + \frac{K_{mP2}[FAD][FADH2]}{K_{iS1}K_{mP1}K_{iP2}}$$ $$+ \frac{K_{mS1}[ETF_{red}][ETF_{ox}]}{K_{iS1}K_{mS2}K_{iP2}} + \frac{[FADH2][ETF_{ox}]}{K_{mP1}K_{iP2}} + \frac{[FAD][ETF_{red}][FADH2]}{K_{iS1}K_{mS2}K_{iP1}} + \frac{[ETF_{red}][FADH2][ETF_{ox}]}{K_{iS2}K_{mP1}K_{iP2}}$$	[Yugi & Tomita, 2004] [McKean et al., 1979]
PC (v36)	Pyr+ATP+CO2 ↔ OXA+ADP+Pi	$$\frac{K_{cf}K_{cr}[PC]([ATP][CO_2][Pyr] - \frac{[Pi][ADP][OXA]}{K_{eq}}}{denom}$$ $$denom = (K_{ia}K_{mB}K_{cr}[Pyr] + K_{mC}K_{cr}[ATP][CO_2] + K_{mA}K_{cr}[CO_2][Pyr] + K_{mB}K_{cr}[ATP][Pyr] + K_{cr}[ATP][CO_2][Pyr]$$ $$+ \frac{K_{ip}K_{mQ}K_{cf}[OXA]}{K_{eq}} + \frac{K_{mQ}K_{cf}[Pi][OXA]}{K_{eq}} + \frac{K_{mP}K_{cf}[ADP][OXA]}{K_{eq}} + \frac{K_{mR}K_{cf}[Pi][ADP]}{K_{eq}} + \frac{K_{cf}[Pi][ADP][OXA]}{K_{eq}}$$ $$+ \frac{K_{ia}K_{mB}K_{cr}[Pyr][Pi]}{K_{ip}} + \frac{K_{ia}K_{mB}K_{cr}[Pyc][ADP]}{K_{ip}} + \frac{K_{iq}K_{mP}K_{cf}[CO_2][OXA]}{K_{ib}K_{eq}} + \frac{K_{iq}K_{mP}K_{cf}[ATP][OXA]}{K_{ia}K_{eq}}$$ $$+ \frac{K_{ia}K_{cr}[ATP][CO_2][OXA]}{K_{ir}} + \frac{K_{mR}K_{cf}[Pyr][Pi][ADP]}{K_{ic}K_{eq}} + \frac{K_{mA}K_{cr}[CO_2][Pyr][ADP]}{K_{iq}} + \frac{K_{mA}K_{cr}[CO_2][Pyr][Pi]}{K_{ip}}$$ $$+ \frac{K_{mP}K_{cf}[CO_2][ADP][OXA]}{K_{ib}K_{eq}} + \frac{K_{mQ}K_{cf}[CO_2][Pi][OXA]}{K_{ib}K_{eq}}$$	[Yugi & Tomita, 2004] [Barden et al., 1972]
v37 & v38	G3P + FAD ↔ DHAP + FADH2 NADH +DHAP ↔ NAD + G3P	$$\frac{V[E][G3P]}{K + [G3P]}$$	[Påhlman et al., 2002]
ME (v39 & v44)	Mal +NADP ↔ PYR +NADPH	$$\frac{K_{cat}[E][Mal][NADP]}{(K_{Mal} + [Mal])(K_{NADP} + [NADP]}$$	[Swierczynski, 1980]

AAC (v40 & v43)	$ATP_{MAT} \rightarrow ATP_{IMS}$ $ADP_{MAT} \leftarrow ADP_{IMS}$	$$v_{\rightarrow} = \frac{\frac{k_{f0}(\frac{H_{IMS}}{H_{MAT}})^{(\frac{RT}{F})C_f} normalize[AAC][ATP_{IMS}]}{1+\frac{k_{f0}(\frac{H_{IMS}}{H_{MAT}})^{(\frac{RT}{F})C_f} normalize}{k_{r0}(\frac{H_{IMS}}{H_{MAT}})^{(\frac{RT}{F})C_{rf}} normalize}(1+\frac{Kd_2}{[ATP_{MAT}]})}}{\frac{Kd_1}{1+\frac{k_{f0}(\frac{H_{IMS}}{H_{MAT}})^{(\frac{RT}{F})C_f} normalize}{k_{r0}(\frac{H_{IMS}}{H_{MAT}})^{(\frac{RT}{F})C_{rf}} normalize}(1+\frac{Kd_2}{[ATP_{MAT}]})}+[ATP_{IMS}]}$$ $$v_{\leftarrow} = \frac{\frac{k_{f0}(\frac{H_{IMS}}{H_{MAT}})^{(\frac{RT}{F})C_f} normalize[AAC][ADP_{IMS}]}{1+\frac{k_{f0}(\frac{H_{IMS}}{H_{MAT}})^{(\frac{RT}{F})C_f} normalize}{k_{r0}(\frac{H_{IMS}}{H_{MAT}})^{(\frac{RT}{F})C_{rf}} normalize}(1+\frac{Kd_2}{[ADP_{MAT}]})}}{\frac{Kd_1}{1+\frac{k_{f0}(\frac{H_{IMS}}{H_{MAT}})^{(\frac{RT}{F})C_f} normalize}{k_{r0}(\frac{H_{IMS}}{H_{MAT}})^{(\frac{RT}{F})C_{rf}} normalize}(1+\frac{Kd_2}{[ADP_{MAT}]})}+[ADP_{IMS}]}$$	[Yugi & Tomita, 2004] [Kramer & Klingenberg, 1982]
IDHc (v41)	IsoCit+NADP+ ↔ OG+NADPH	$$\frac{[E][NADP][IsoCit]}{\phi_0[NADP][IsoCit]+\phi_1[IsoCit]+\phi_2[NADP]+\phi_{12}} - \frac{[E][NADPH][OG][CO_2]}{denom}$$ $$denom = \phi_0^{'}[NADPH][OG][CO_2]+\phi_1^{'}[OG][CO_2]+\phi_2^{'}[NADPH][CO_2]+\phi_3^{'}[NADPH][OG]+\phi_{12}^{'}[CO_2]+\phi_{13}^{'}[OG]$$ $$+\phi_{23}^{'}[NADPH]+\phi_{123}^{'}$$	[Yugi & Tomita, 2004] [Londesborough & Dalziel, 1970]

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Supplementary Table 3. Kinetic Parameters

v1-3	$V_1 = 0.50mM/s$; $K_{1GLC} = 0.1mM$; $K_{1ATP} = 0.063mM$
v2-4	$V_2 = 1.5mM/s$; $K_2 = 0.0016mM^2$; $k_2 = 0.017$; $K_{2ATP} = 0.01mM$
v3-2	$k_{3f} = 1/s$; $k_{3b} = 50mM/s$
v4-3	$V_4 = 20mM/s$; $K_{4GAP} = 1mM$; $K_{4NAD} = 1mM$
v5-2	$k_{5f} = 1mM/s$; $k_{5b} = 0.5mM/s$
v6-3	$V_6 = 10mM/s$; $K_{6PEP} = 0.2mM$; $K_{6ADP} = 0.3mM$
v7-2	$V_7 = 2.0mM/s$; $K_{7PYR} = 0.3mM$
PYC (v8-10)	$\alpha = 1.0$; $\beta = 1.0$; $\gamma = 1.0$; $\delta = 1.0$; $K_{1PYR} = 6.1e-4$; $K_{1H} = 5.9e-4$; $K_{2PYR} = 4.1e-4$; $K_{2H} = 2.6e-4$; $k_{cat}^f = 0.84$; $k_{cat}^r = 0.78$
PDC (v9-12)	$K_{cf} = 856$; $K_{mA} = 25e-6$; $K_{mB} = 13e-6$; $K_{mC} = 50e-6$; $K_{mP} = 5.9e-7$; $K_{mR} = 6.9e-7$; $K_{ia} = 5.5e-4$; $K_{ib} = 3.0e-4$; $K_{ic} = 1.8e-4$; $K_{ip} = 6.0e-5$; $K_{iq} = 35e-6$; $K_{ir} = 36e-6$
CS (v10-16)	$k1 = 6.8e10$; $k\_1 = 8.1e8$; $k2 = 3.0e10$; $k\_2 = 7.2e8$; $k3 = 6.2e10$; $k\_3 = 5.1e8$; $k4 = 1.2e10$; $k\_4 = 4.0e8$; $k5 = 1.4e9$; $k\_5 = 2.4e8$; $k6 = 4.1e10$; $k\_6 = 1.1e8$; $k7 = 5e10$; $k\_7 = 9.8e8$; $k8 = 5.3e10$; $k\_8 = 7.7e8$
ACO (v11-4)	$K_{cf} = 20.47$; $K_{cr} = 31.44$; $K_s = 0.50e-3$; $K_p = 0.11e-3$
IDHa (v12-6)	$K_{cf} = 105$; $b = 29.6$; $c = 0.00023$; $d = 7.8e-05$; $e = 0.00064$; $f = 0.00036$
PiC (v13-10)	$\alpha = 1.0$; $\beta = 1.0$; $\gamma = 1.0$; $\delta = 1.0$; $K_{1Pi} = 0.87$; $K_{1H} = 1.86e-8$; $K_{2Pi} = 32.84e-9$; $K_{2H} = 11.12e-3$; $k_{cat}^f = 37.9$; $k_{cat}^r = 37.0$
OGDC (v14-12)	$K_{cf} = 177$; $K_{mA} = 0.22e-3$; $K_{mB} = 0.025e-3$; $K_{mC} = 0.05e-3$; $K_{mP} = 3e-4$; $K_{mR} = 6e-4$; $K_{ia} = 7.2e-4$; $K_{ib} = 7.4e-4$; $K_{ic} = 1e-4$; $K_{ip} = 1.1e-6$; $K_{iq} = 81e-6$; $K_{ir} = 25e-6$
SCS (v15-16)	$K_{eq} = 8.375$; $K_{mA} = 5e-6$; $K_{mB} = 3.5e-5$; $K_{mC} = 4.5e-4$; $K_{mP} = 6e-4$; $K_{mQ} = 7.5e-6$; $K_{mC2} = 4.5e-4$; $K_{mP2} = 6e-4$; $K_{ia} = 4e-4$; $K_{ib} = 2e-5$; $K_{ic} = 3e-5$; $K_{ip} = 7e-2$; $K_{iq} = 5e-6$; $K_{ir} = 6.7e-6$; $K_{c1} = 100$; $K_{c2} = 100$
SDH (vv16-9)	$K_{cf} = 69.3$; $K_{cr} = 1.73$; $K_{eq} = 0.037$; $K_{mS1} = 30e-6$; $K_{mS2} = 69e-6$; $K_{mP1} = 0.3e-6$; $K_{mP2} = 1.5e-6$; $K_{iS1} = 4.1e-6$; $K_{iP2} = 5.6e-6$
FM (v17-4)	$K_{cf} = 800$; $K_{cr} = 900$; $K_s = 0.50e-5$; $K_p = 2.5e-5$
MDH (v18&v32-10)	$K_{cf} = 0.390$; $K_{cr} = 0.040$; $K_{mS1} = 72e-6$; $K_{mS2} = 110e-6$; $K_{mP1} = 1600e-6$; $K_{mP2} = 170e-6$; $K_{iS1} = 11e-6$; $K_{iS2} = 100e-6$; $K_{iP1} = 7100e-6$; $K_{iP2} = 1900e-6$
DIC (v19-10)	$\alpha = 1.0$; $\beta = 1.0$; $\gamma = 1.0$; $\delta = 1.0$; $K_{1Mal} = 0.20e-3$; $K_{1Pi} = 0.72e-3$; $K_{2Mal} = 90.e-4$; $K_{2Pi} = 7.6e-4$; $k_{cat}^f = 2.7$; $k_{cat}^r = 4.1$
AlaTA (v20-9)	$K_{cf} = 337$; $K_{cr} = 0.15$; $K_{eq} = 0.69$; $K_{mS1} = 2e-3$; $K_{mS2} = 0.4e-3$; $K_{mP1} = 32e-3$; $K_{mP2} = 0.4e-3$; $K_{iS1} = 8.7e-3$; $K_{iP2} = 12e-3$
AspTA (v21-9)	$K_{cf} = 300$; $K_{cr} = 1000$; $K_{eq} = 6.2$; $K_{mS1} = 0.9e-3$; $K_{mS2} = 0.1e-3$; $K_{mP1} = 0.04e-3$; $K_{mP2} = 4e-3$; $K_{iS1} = 2e-3$; $K_{iP2} = 8.3e-3$

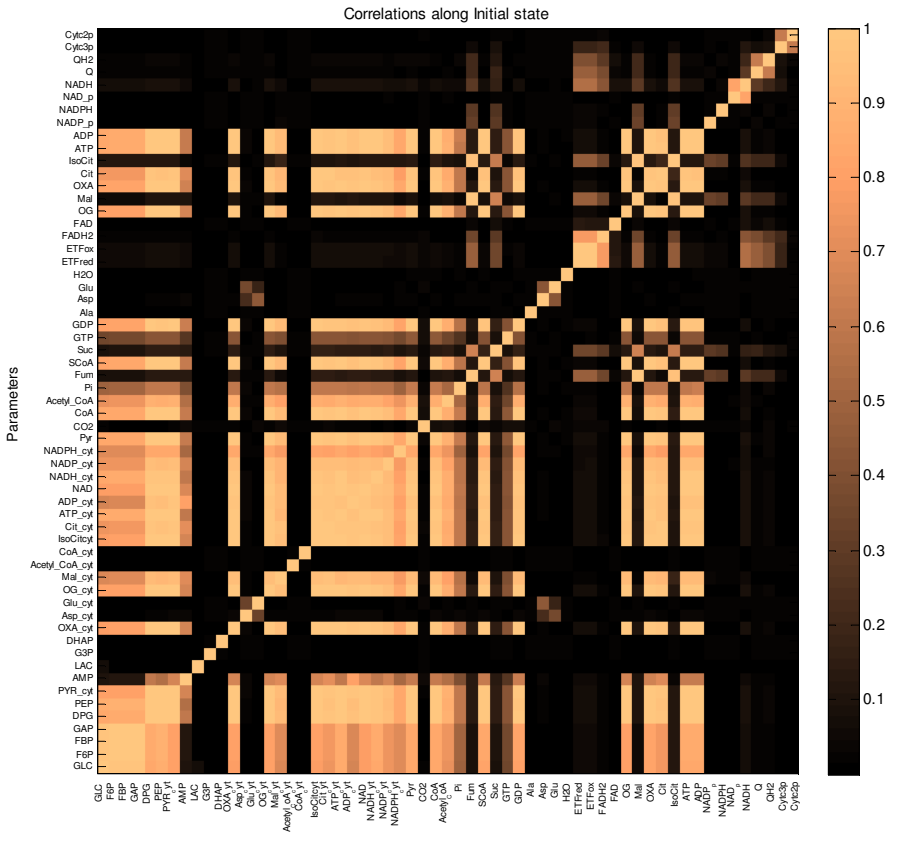
AGC (v22-10)	$\alpha = 1.0$; $\beta = 1.0$; $\gamma = 1.0$; $\delta = 1.0$; $K_{1Asp} = 80e-6$; $K_{1Glu} = 3.2e-3$; $K_{2Asp} = 180e-6$; $K_{2Glu} = 2.8e-3$; $k_{cat}^{f} = 10.0$; $k_{cat}^{r} = 10.0$
NDK (v23-9)	$K_{mS1} = 0.31e-3M$; $K_{mS2} = 0.043e-3M$; $K_{mP1} = 0.050e-3M$; $K_{mP2} = 0.25e-3M$; $K_{iS1} = 0.21e-3M$; $K_{iP2} = 0.35e-3M$; $K_{eq} = 1.28$; $K_{cf} = 6883$; $K_{cr} = 5950$
I (v24-9)	$K_{cf} = 498$; $K_{cr} = 229$; $K_{eq} = 407.9$; $K_{mS1} = 9.2e-6$; $K_{mS2} = 2.6e-4$; $K_{mP1} = 9.9e-6$; $K_{mP2} = 5.9e-5$; $K_{iS1} = 2.1e-8$; $K_{iP2} = 9.8e-8$
III (v25-8)	$K_{cf} = 426.8$; $K_{mA} = 2.8e-5$; $K_{mB} = 3.0e-6$; $K_{b1} = 5.4e-6$; $K_{b2} = 5.7e-6$; $K_{q1} = 2.8e-6$; $K_{q2} = 1.9e-6$; $k_8 = 622.1$
IV (v26-2)	$K_{cf} = 93.5$; $K_s = 110e-6$
V (v28-12)	$K_{cf} = 14.5$; $K_d = 2.67e-7$; $K_p = 9.02e-5$; $K_t = 4.33e-5$; $K_{hx} = 1.3e-4$; $K_{hy} = 1.6e-4$; $klt_f = 1.35e+8$; $klt_r = 0.00018$; $ax = 0.1$; $ay = 0.6$; $\beta = 0.3$; $T = 310$
OGC (v30-10)	$K_{iS1} = 0.3e-3M$; $K_{iS2} = 0.7e-3M$; $K_{iP1} = 1.4e-3M$; $K_{iP2} = 0.17e-3M$; $K_{cf} = 3.675$; $K_{cr} = 4.83$; $\alpha = 1.0$; $\beta = 1.0$; $\gamma = 1.0$; $\delta = 1.0$
CIC (v33- 10)	$K_{iS1} = 0.13e-3M$; $K_{iS2} = 0.44e-3M$; $K_{iP1} = 0.33e-3M$; $K_{iP2} = 4.18e-5M$; $K_{cf} = 5.6$; $K_{cr} = 3.5$; $\alpha = 1.0$; $\beta = 1.0$; $\gamma = 1.0$; $\delta = 1.0$
ETF-QO (v34-9)	$K_{mS1} = 0.31e-6M$; $K_{mS2} = 0.39e-6M$; $K_{mP1} = 0.32e-6M$; $K_{mP2} = 4.2e-9M$; $K_{iS1} = 0.31e-6M$; $K_{iP2} = 0.3e-6M$; $K_{eq} = 0.66$; $K_{cf} = 78$; $K_{cr} = 101$
V35 (11)	$K_{mS1} = 39e-6M$; $K_{mS2} = 0.12e-6M$; $K_{mP1} = 1.08e-6M$; $K_{mP2} = 2.42e-5M$; $K_{iS1} = 76e-6M$; $K_{iS2} = 0.24e-6M$; $K_{iP1} = 7.53e-5M$; $K_{iP2} = 1.19e-5M$; $K_{eq} = 8.99$; $K_{cf} = 2.18$; $K_{cr} = 0.30$
PC (v36-15)	$K_{cf} = 200$; $K_{cr} = 20$; $K_{eq} = 9.0$; $K_{ia} = 0.15e-3$; $K_{ib} = 1.6e-3$; $K_{ic} = 0.13e-3$; $K_{ip} = 7.9e-3$; $K_{iq} = 0.19e-3$; $K_{ir} = 0.24e-3$; $K_{mA} = 0.11e-3$; $K_{mB} = 1.63e-3$; $K_{mC} = 0.37e-3$; $K_{mP} = 16e-3$; $K_{mQ} = 0.24e-3$; $K_{mR} = 0.051e-3$
V37 (2)	$V = 0.0399e-6M/s$; $K = 34.0e-6M$
ME (v39- 3)	$K_{cat} = 0.333$; $K_{Mal} = 0.125e-3$; $K_{NADP} = 11e-3$
AAC→ (v40-10)	$k_{f0} = 1.0$; $k_{r0} = 1.0$; $normalize = 2.21$; $Kd_1 = 5.9e-4$; $Kd_2 = 5.9e-4$; $C_f = 10.2$; $C_r = -10.2$; $T = 310$; $R = 8.3145$; $F = 96485$
IDHc (v41-12)	$\phi_0 = 5.1e-2$; $\phi_1 = 9.5e-8$; $\phi_2 = 0.96e-6$; $\phi_{12} = 9e-8$; $\phi_0' = 6.6e-2$; $\phi_1' = 0.37e-6$; $\phi_2' = 29e-6$; $\phi_3' = 2.5e-4$; $\phi_{12}' = 6e-12$; $\phi_{13}' = 1.3e-10$; $\phi_{23}' = 9.4e-8$; $\phi_{123}' = 4.6e-14$
AAC← (v43-10)	$k_{f0} = 0.9$; $k_{r0} = 0.9$; $normalize = 2.21$; $Kd_1 = 5.9e-4$; $Kd_2 = 5.9e-4$; $C_f = 3.3$; $C_r = -3.34$; $T = 310$; $R = 8.3145$; $F = 96485$

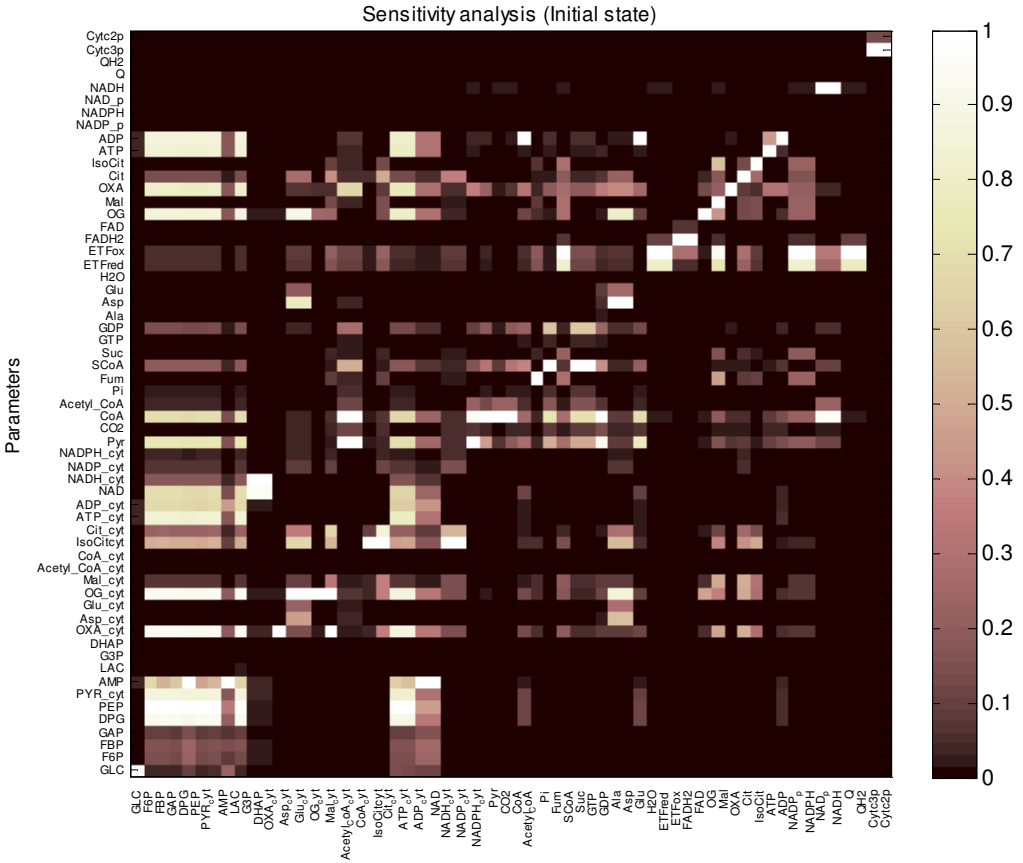
Table 4. Initialisation conditions

$[ATP\_cyt]_0 = 4.49064 mM/l$; $[ADP\_cyt]_0 = 0.108367 mM/l$; $[NADH\_cyt]_0 = 0.616118 mM/l$; $[NAD^+]_0 = 3.62057 mM/l$;
$[GLC]_0 = 0.0112817 mM/l$; $[F6P]_0 = 0.65939 mM/l$; $[FBP]_0 = 0.00770135 mM/l$; $[GAP]_0 = 0.00190919 mM/l$;
$[DPG]_0 = 0.299109 mM/l$; $[PEP]_0 = 0.0021125 mM/l$; $[PYR\_cyt]_0 = 0.00422702 mM/l$; $[AMP]_0 = 0.00261149 mM/l$;
$[Pyr]_0 = 0.1025 mM/l$; $[H_{MAT}]_0 = 1.0e-5 mM/l$; $[ATP_{MAT}]_0 = 4.5 mM/l$; $[ADP_{MAT}]_0 = 0.45 mM/l$; $[GTP]_0 = 4.5 mM/l$;
$[GDP]_0 = 0.45 mM/l$; $[CO_2]_0 = 1.63 mM/l$; $[Pi]_0 = 4.0 mM/l$; $[OXA]_0 = 4.0e-3 mM/l$; $[CoA]_0 = 0.272 mM/l$; $[NAD^+]_0 = 0.17 mM/l$;
$[NADH]_0 = 0.072 mM/l$; $[Acetyl\_CoA]_0 = 0.03 mM/l$; $[Cit]_0 = 0.42 mM/l$; $[IsoCit]_0 = 0.42 mM/l$; $[OG]_0 = 0.021 mM/l$;
$[NADP^+]_0 = 0.17 mM/l$; $[NADPH]_0 = 0.072 mM/l$; $[Asp]_0 = 1.14 mM/l$; $[Glu]_0 = 3.03 mM/l$; $[Ala]_0 = 3.44 mM/l$;
$[SCoA]_0 = 0.2941 mM/l$; $[Suc]_0 = 2.95 mM/l$; $[Fum]_0 = 0.065 mM/l$; $[Mal]_0 = 0.5 mM/l$; $[PC]_0 = 3.8617e-4 mM/l$;
$[PDC]_0 = 3.8617e-4 mM/l$; $[CS]_0 = 3.8617e-4 mM/l$; $[AspTA]_0 = 3.8617e-4 mM/l$; $[FM]_0 = 3.8617e-4 mM/l$;
$[SCS]_0 = 3.8617e-4 mM/l$; $[OGDC]_0 = 3.8617e-4 mM/l$; $[MDH]_0 = 3.8617e-4 mM/l$; $[AlaTA]_0 = 3.8617e-4 mM/l$;
$[ACO]_0 = 3.8617e-4 mM/l$; $[IDHa]_0 = 3.8617e-4 mM/l$; $[IDHb]_0 = 3.8617e-4 mM/l$; $[Pyr_{IMS}]_0 = 0.1025 mM/l$;
$[H_{IMS}]_0 = 0.001 mM/l$; $[Q]_0 = 0.26 mM/l$; $[QH_2]_0 = 0.028 mM/l$; $[Cyt\,c^{3+}]_0 = 0.003 mM/l$; $[Cyt\,c^{2+}]_0 = 0.11 mM/l$;
$[PYC_{IM}]_0 = 0.33211 mM/l$; $[SDH_{IM}]_0 = 0.33211 mM/l$; $[Complex\_I_{IM}]_0 = 0.33211 mM/l$; $[Complex\_III_{IM}]_0 = 0.99632 mM/l$;
$[Complex\_IV_{IM}]_0 = 2.3248 mM/l$; $[Complex\_V_{IM}]_0 = 0.2989 mM/l$

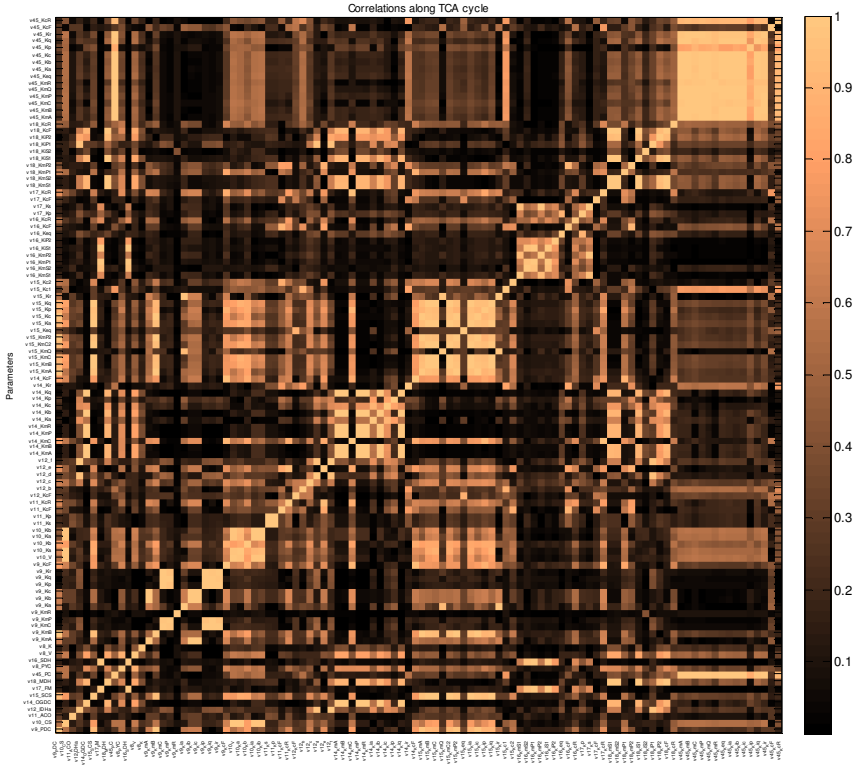
Core model of GSIS

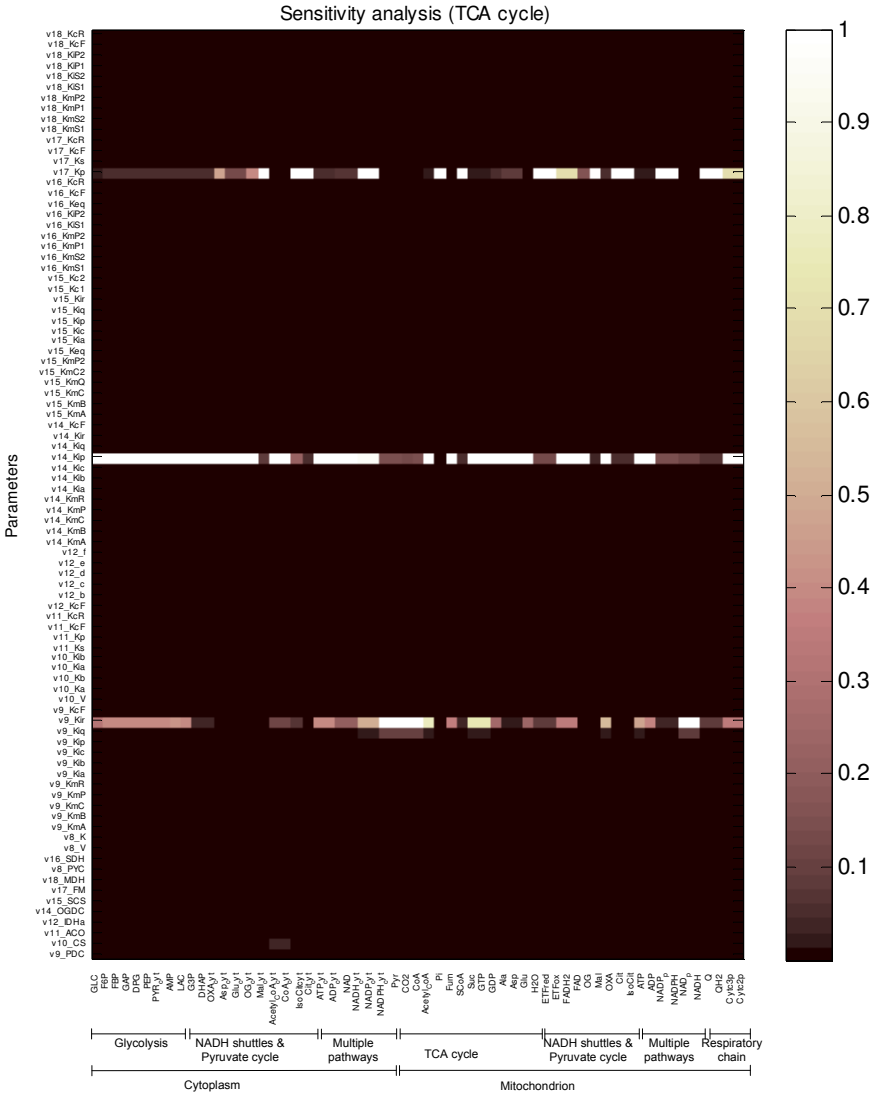
1) The sensitivity and correlation analysis for initial state



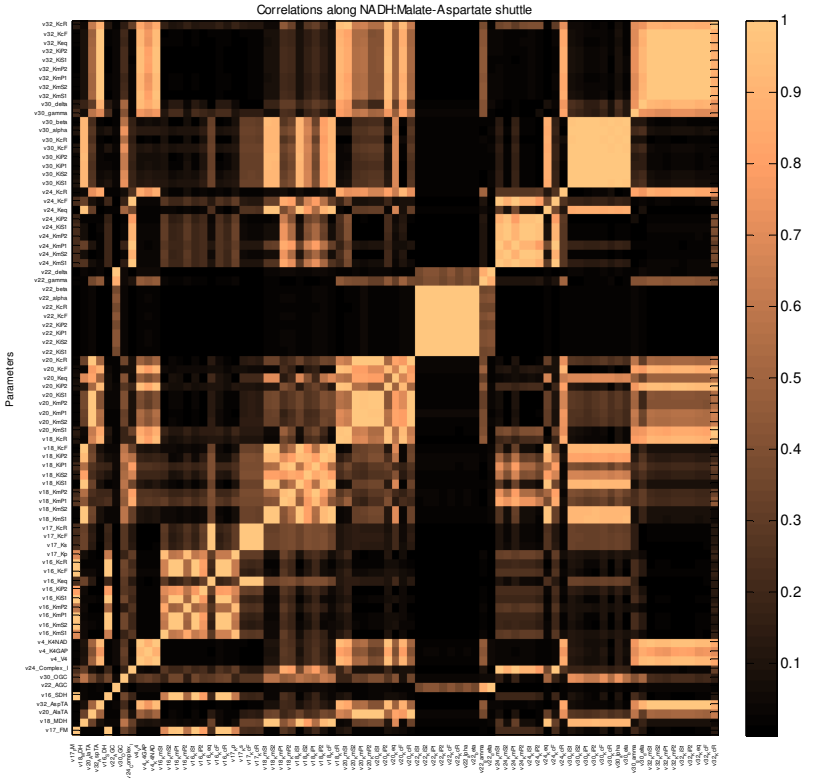


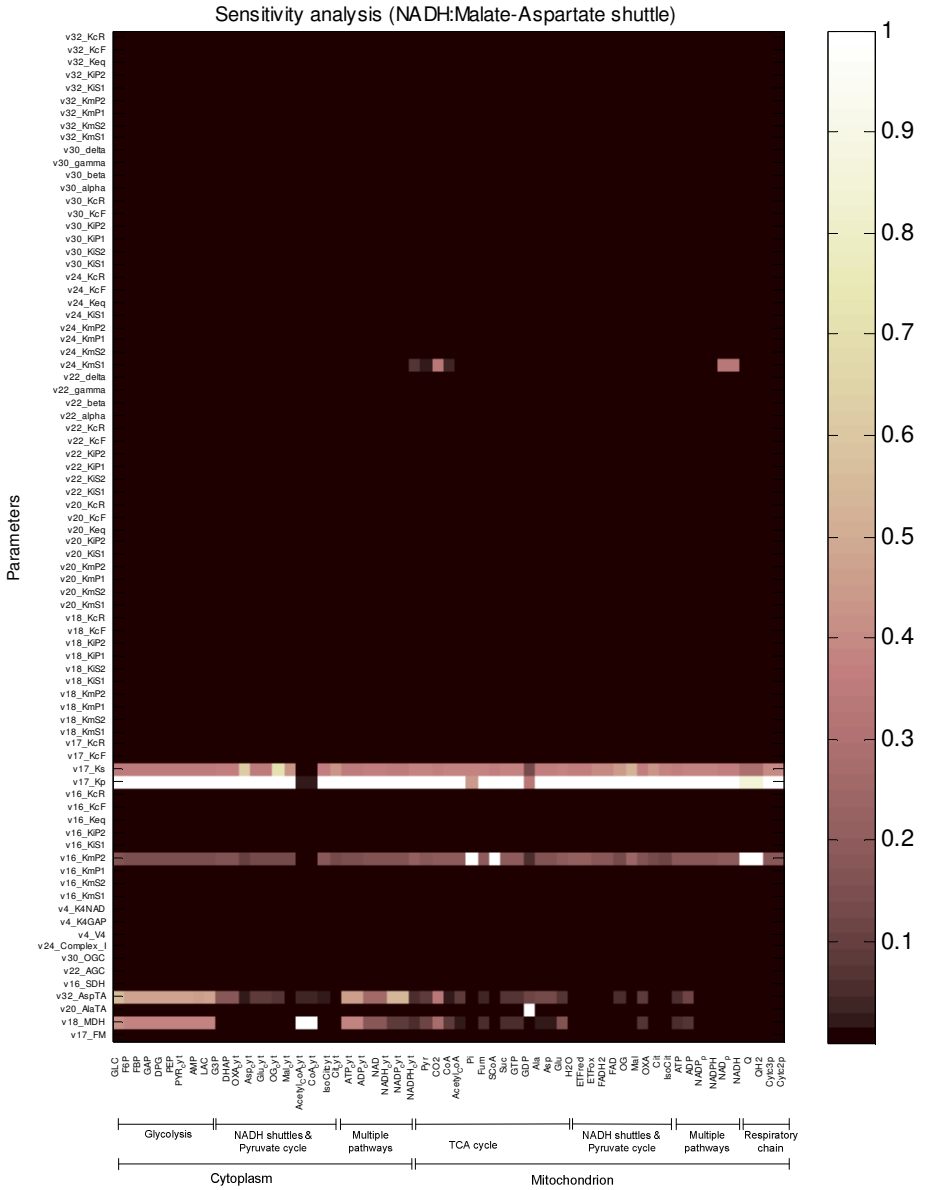
2) The sensitivity and correlation analysis for parameters along TCA cycle



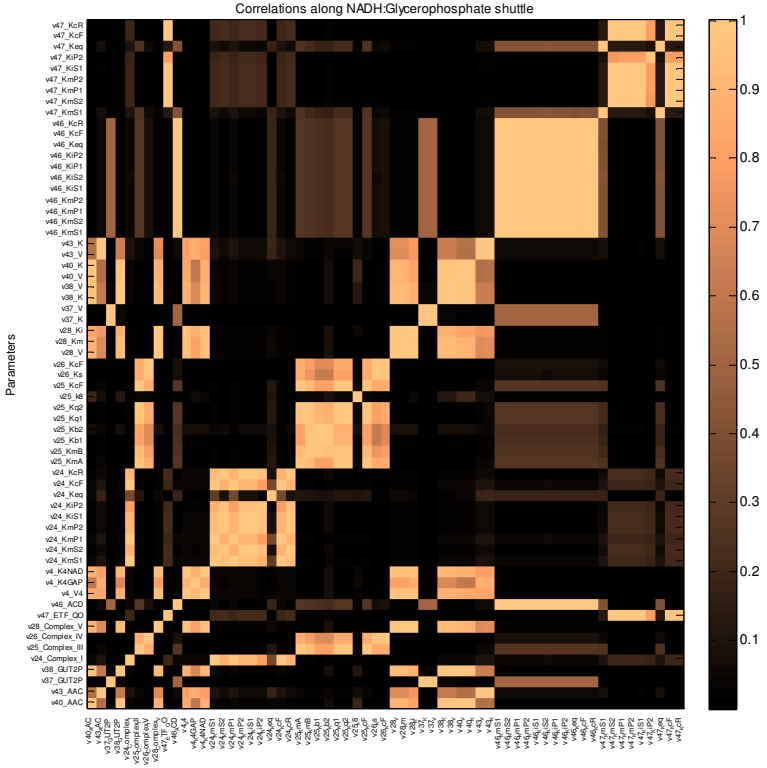


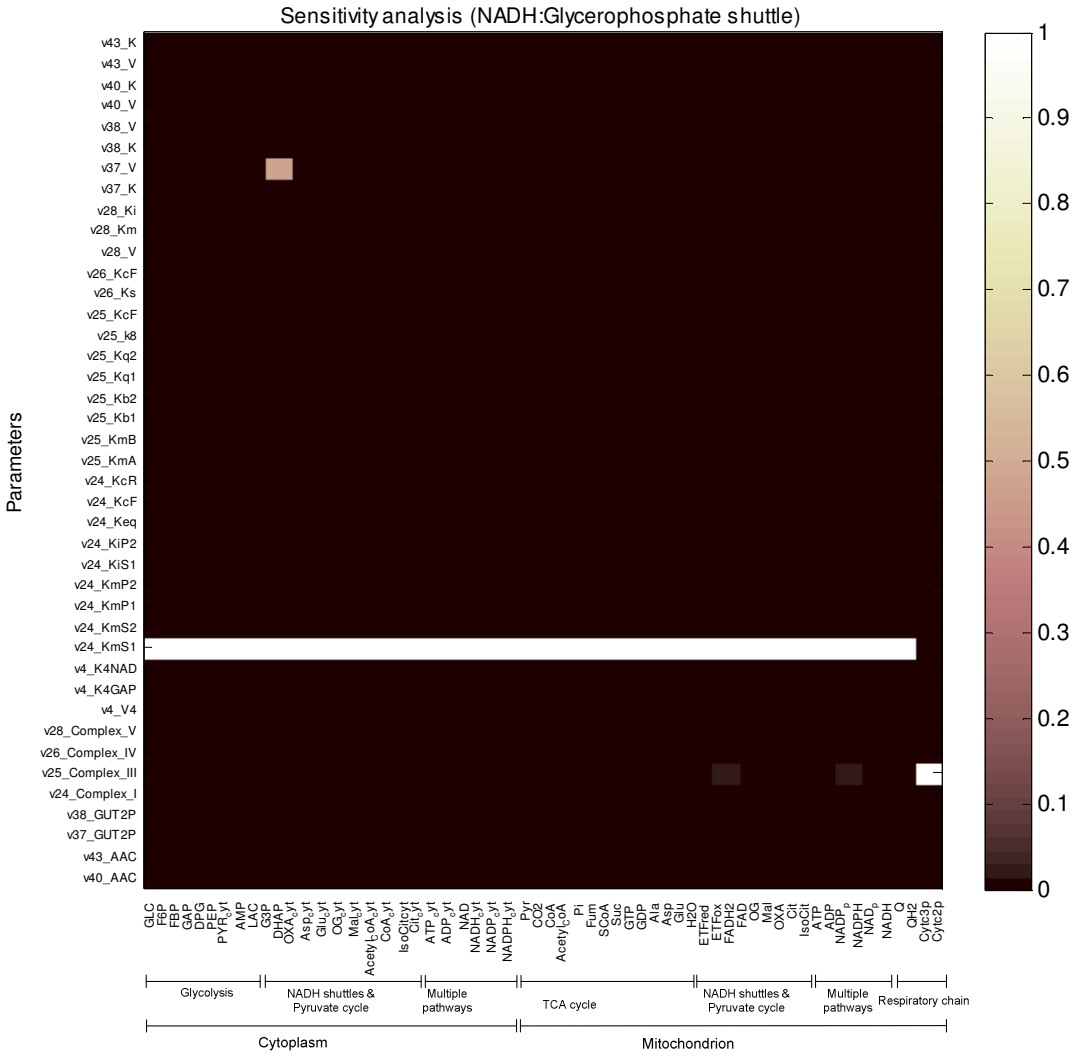
3) The sensitivity and correlation analysis for parameters along NADH: malate-aspartate shuttle



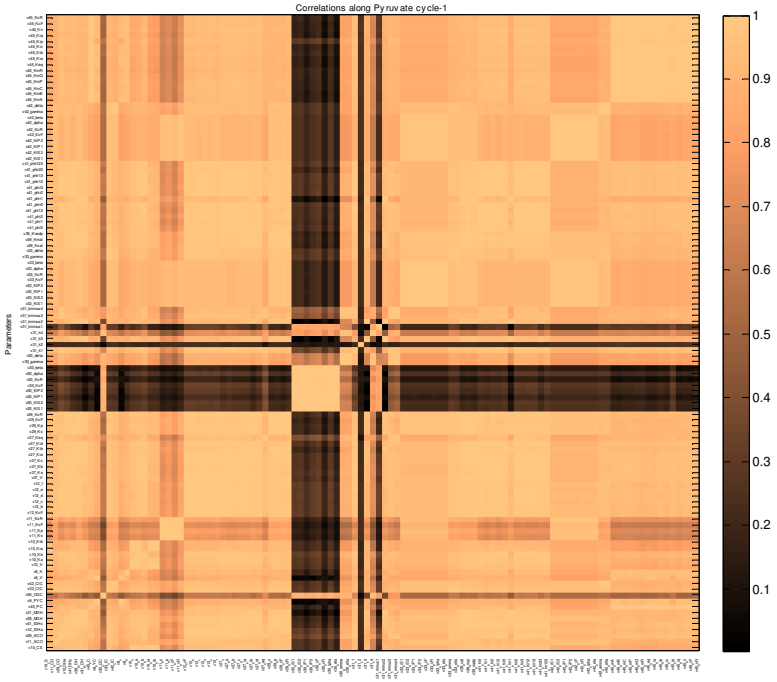


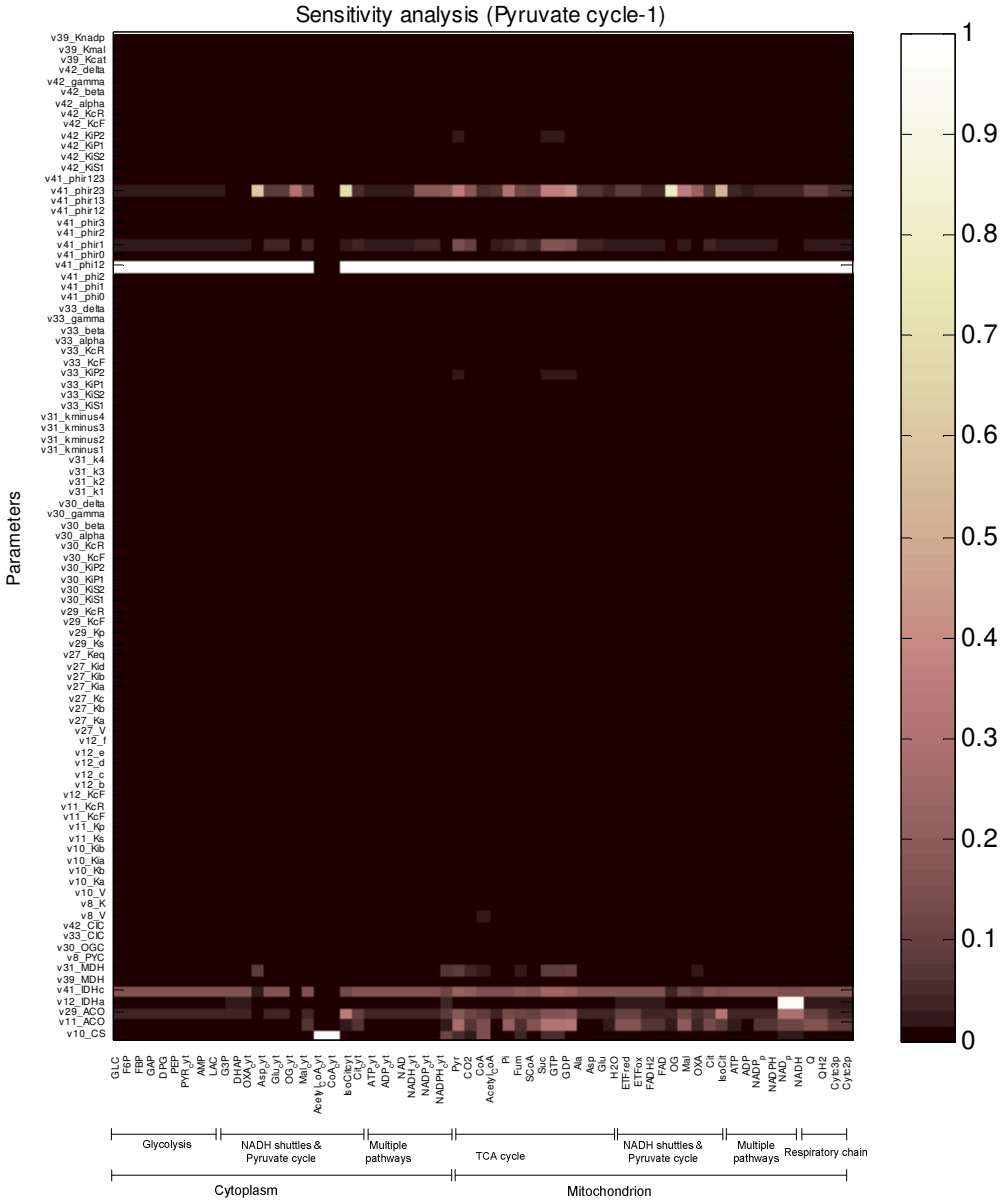
4) The sensitivity and correlation analysis for parameters along NADH: Glycerophosphate shuttle





5) The sensitivity and correlation analysis for parameters along Pyruvate cycle-1





6) The sensitivity and correlation analysis for parameters along Pyruvate cycle-2