A supplementary document of

A general computational model of mitochondrial metabolism in a whole organelle scale

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Contents

1 Abbreviations

1.1 Species and organs

Table 1: Abbreviations for species and organs

Abbreviation	Species, Organ
BH	Bovine Heart
BHM	Bovine Heart Mitochondria
BL	Bovine Liver
BLM	Bovine Liver Mitochondria
CL	Chicken Liver
HLC	Human Liver Cytosol
IMS	Intermembrane Space (Mitochondrial)
MAT	Matrix (Mitochondrial)
PH	Pig Heart
PHM	Pig Heart Mitochondria
PL	Pig Liver
PLM	Pig Liver Mitochondria
RbHM	Rabbit Heart Mitochondria
RB	Rat Brain
RH	Rat Heart
RHM	Rat Heart Mitochondria
RK	Rat Kidney
RLM	Rat Liver Mitochondria

1.2 Metabolites and enzymes: A-G

Table 2: Abbreviations for metabolites

Abbreviation	Substance name	Compound/EC number
AAC	ATP/ADP Carrier	
ACD	Acyl-CoA Dehydrogenase	EC1.3.99.3
Acetoacetyl-CoA		C00332
Acetyl-CoA		C00024
ACO	Aconitase	EC4.2.1.3
ADP	Adenosine Diphosphate	C00008
AGC	Aspartate/Glutamate Carrier	
Ala	Alanine	C00041
AlaTA	Alanine Transaminase	EC2.6.1.2
Asp	Aspartate	C00049
AspTA	Aspartate Transaminase	EC2.6.1.1
ATP	Adenosine Triphosphate	C00002
CAC	Carnitine Carrier	
Car	Carnitine	C00318
CIC	Citrate Carrier	
Cit	Citrate	C00158
CPT-I	Carnitine Palmitoyl Transferase I	EC2.3.1.21
CPT-II	Carnitine Palmitoyl Transferase II	EC2.3.1.21
CoA	Coenzyme A	C00010
Complex-I	NADH Dehydrogenase	EC1.6.5.3
Complex-III	Ubiquinol:Cytochrome c Oxidoreductase	EC1.10.2.2
Complex-IV	Cytochrome c Oxidase	EC1.9.3.1
Complex-V	ATP Synthetase	EC3.6.1.34
CO2	Carbon Dioxide	C00011
CS	Citrate Synthase	EC4.1.3.7
Cyt-c2+	Ferricytochrome c	C00125
Cyt-c3+	Ferrocytochrome c	C00126
DIC	Dicarboxyrate Carrier	
ECH	Enoyl-CoA Hydratase	EC4.2.1.17
ETFox	Electron Transfer Flavoprotein (oxidised form)	
ETFred	Electron Transfer Flavoprotein (reduced form)	
ETF-QO	ETF:Q Oxidoreductase	
FM	Fumarase	EC4.2.1.2
Fum	Fumarate	C00122
GDP	Guanosine Diphosphate	C00035
Glu	Glutamate	C00025
GTP	Guanosine Triphosphate	C00044

1.3 Metabolites and enzymes: H-Z

Table 3: Abbreviations for metabolites (cont'd)

Abbreviation	Substance name	Compound/EC number
HCD	Hydroxyacyl-CoA Dehydrogenase	EC1.1.1.35
H+	Hydrogen ion (proton)	C00080
IDHa	Isocitrate Dehydrogenase (NAD+)	EC1.1.1.41
IDHb	Isocitrate Dehydrogenase (NADP+)	EC1.1.1.42
IsoCit	Isocitrate	C00311
Mal	Malate	C00149
MDH	Malate Dehydrogenase	EC1.1.1.37
NAD+		C00003
NADH		C00004
NADP+		C00006
NADPH		C00005
NDK	Nucleoside Diphosphate Kinase	EC2.7.4.6
OCT	Oxoacyl-CoA Thiolase	EC2.3.1.16
OG	Oxoglutarate	C00026
OGC	Oxoglutarate Carrier	
OGDC	Oxoglutarate Dehydrogenase Complex	EC1.2.4.2 etc.
OXA	Oxaloacetate	C00036
PalCar	Palmitoylcarnitine	C02990
PC	Pyruvate Carboxylase	EC6.4.1.1
PDC	Pyruvate Dehydrogenase Complex	EC1.2.4.1 etc.
Pi	Phosphate	C00009
PiC	Pi Carrier	
Pyr	Pyruvate	C00022
PYC	Pyruvate Carrier	
Q	Ubiquinone	C00399
QH2	Ubiquinol	C00390
SCoA	Succinyl-CoA	C00091
SCS	Succinyl-CoA synthetase	EC6.2.1.4
SDH	Succinate Dehydrogenase	EC1.3.5.1
Suc	Succinate	C00042

1.4 Other metabolites

Table 4: Abbreviations for metabolites (cont'd)

Abbreviation	Substance name	Compound/EC number
10Acyl-CoA	Decanoyl-CoA	C05274
10Enoyl-CoA	trans-Dec-2-enoyl-CoA	C05275
10Hydroxyacyl-CoA	(S)-3-Hydroxydedecanoyl-CoA	C05264
10Oxoacyl-CoA	3-Oxodecanoyl-CoA	C05265
12Acyl-CoA	Lauroyl-CoA	C01832
12Enoyl-CoA	trans-Dodec-2-enoyl-CoA	C03221
12Hydroxyacyl-CoA	(S)-3-Hydroxydodecanoyl-CoA	C05262
12Oxoacyl-CoA	3-Oxododecanoyl-CoA	C05263
14Acyl-CoA	Myristoyl-CoA	C02593
14Enoyl-CoA	trans-Tetradec-2-enoyl-CoA	C05273
14Hydroxyacyl-CoA	(S)-3-Hydroxytetradecanoyl-CoA	C05260
14Oxoacyl-CoA	3-Oxotetradecanoyl-CoA	C05261
16Acyl-CoA	Palmitoyl-CoA	C00154
16Enoyl-CoA	trans-Hexadec-2-enoyl-CoA	C05272
16Hydroxyacyl-CoA	(S)-3-Hydroxyhexadecanoyl-CoA	C05258
16Oxoacyl-CoA	3-Oxohexadecanoyl-CoA	C05259
4Acyl-CoA	Butanoyl-CoA	C00136
4Enoyl-CoA	Crotonyl-CoA	C00877
4Hydroxyacyl-CoA	(S)-3-Hydroxybutanoyl-CoA	C01144
6Acyl-CoA	Hexanoyl-CoA	C05270
6Enoyl-CoA	trans-Hex-2-enoyl-CoA	C05271
6Hydroxyacyl-CoA	(S)-3-Hydroxyhexanoyl-CoA	C05268
6Oxoacyl-CoA	3-Oxohexanoyl-CoA	C05269
8Acyl-CoA	Octanoyl-CoA	C01944
8Enoyl-CoA	trans-Oct-2-enoyl-CoA	C05276
8Hydroxyacyl-CoA	(S)-3-Hydroxyoctanoyl-CoA	C05266
8Oxoacyl-CoA	3-Oxooctaanoyl-CoA	C05267

2 Reactions

2.1 Respiratory chain

Table 5: Reactions in the respiratory chain (where H^+_{MAT} denotes H^+ in the matrix, H^+_{IMS} is H^+ in the intermembrane space)

complex	reaction	reaction mechanism	source
I	$\mathrm{NADH} + \mathrm{Q} + 5\mathrm{H}^+_{MAT}$ $\longleftrightarrow \mathrm{NAD}^+ + \mathrm{QH}_2 + 4\mathrm{H}^+_{IMS}$	Ping-Pong Bi Bi [Fato et al., 1996]	BHM
II(SDH)	$\mathrm{Suc} + \mathrm{Q} \quad \longleftrightarrow \quad \mathrm{Fum} + \mathrm{QH}_2$	Ping-Pong Bi Bi [Grivennikova et al., 1993]	BHM
III	$\mathrm{QH}_2 + 2\mathrm{cyt}\ c^{3+} + 2\mathrm{H}^+_{MAT}$ $\rightarrow \mathrm{Q} + 2\mathrm{cyt}\ c^{2+} + 4\mathrm{H}^+_{IMS}$	See [Kubota et al., 1992]	BHM
IV	$4\mathrm{cyt}\ c^{2+} + \mathrm{O}_2 + 8\mathrm{H}^+_{MAT}$ $\longrightarrow 4\mathrm{cyt}\ c^{3+} + 2\mathrm{H}_2\mathrm{O} + 4\mathrm{H}^+_{IMS}$	Michaelis Uni Uni [Malmström and Andréasson, 1985]	-
V	$\mathrm{ADP} + \mathrm{Pi} + 3\mathrm{H}^+_{IMS}$ $\longleftrightarrow \mathrm{ATP} + \mathrm{H}_2\mathrm{O} + 3\mathrm{H}^+_{MAT}$	See [Kholodenko, 1993]	-

2.2 TCA cycle

Table 6: The enzymes in/around the TCA cycle

enzyme	reaction	reaction mechanism	source
PDC	Pyr + NAD^+ + CoA $\longrightarrow$ Acetyl-CoA + NADH + CO_2	See [Hamada et al., 1975]	PHM
PC	Pyr + ATP + CO_2 $\longleftrightarrow$ OXA + ADP + Pi	See [Barden et al., 1972]	CL
AspTA	Asp + OG $\longleftrightarrow$ OXA + Glu	Ping-Pong Bi Bi [Velick and Vavra, 1962, Henson and Cleland, 1964]	PH
AlaTA	Ala + OG $\longleftrightarrow$ Glu + Pyr	Ping-Pong Bi Bi [De Rosa et al., 1979]	PL
NDK	ATP + GDP $\longleftrightarrow$ ADP + GTP	Ping-Pong Bi Bi [Garces and Cleland, 1969]	yeast
CS	OXA + Acetyl-CoA $\longleftrightarrow$ Cit + CoA	Random Bi Bi [Shepherd and Garland, 1969, Matsuoka and Srere, 1973]	RK, RB
ACO	Cit $\longleftrightarrow$ IsoCit	Uni Uni Reversible [Guarriero-Bobyleva et al., 1978]	RLM
IDHa	IsoCit + NAD^+ $\longrightarrow$ OG + NADH	See [Plaut et al., 1974]	BH
IDHb	IsoCit + $NADP^+$ $\longleftrightarrow$ OG + NADPH	See [Londesborough and Dalziel, 1970]	BHM
OGDC	OG + NAD^+ + CoA $\longrightarrow$ SCoA + NADH + CO_2	See [Hamada et al., 1975]	PHM
SCS	SCoA + GDP + Pi $\longleftrightarrow$ Suc + CoA + GTP	See [Cha and Parks Jr., 1964]	PH
SDH	Suc + Q $\longleftrightarrow$ Fum + QH_2	Ping-Pong Bi Bi [Grivennikova et al., 1993]	BHM
FM	Fum $\longleftrightarrow$ Mal	Uni Uni Reversible	
MDH	Mal + NAD^+ $\longleftrightarrow$ OXA + NADH	Ordered Bi Bi [Crow et al., 1983]	HLC

2.3 Fatty acid β oxidation

Table 7: The enzymes in the fatty acid β oxidation

enzyme	reaction	reaction mechanism	source
ACD	Acyl-CoA + ETF_{ox} $\longleftrightarrow$ Enoyl-CoA + ETF_{red}	Ordered Bi Bi [McKean et al., 1979]	PLM
ECH	Enoyl-CoA + H_2O $\longleftrightarrow$ 3-hydroxyacyl-CoA	Uni Uni Reversible [Yang and Schulz, 1987]	BL
HCD	3-hydroxyacyl-CoA + NAD^+ $\longrightarrow$ 3-oxoacyl-CoA + NADH	Michaelis Uni Uni [Yang and Schulz, 1987]	PH
OCT	3-oxoacyl-CoA + CoA $\longleftrightarrow$ Acyl-CoA + Acetyl-CoA	Ping-Pong Bi Bi [Miyazawa et al., 1981]	RLM
ETF-QO	ETF_{red} + Q $\longleftrightarrow$ ETF_{ox} + QH_2	Ping-Pong Bi Bi [Beckmann and Frerman, 1985]	PLM
CPT I	16Acyl-CoA + Car $\longleftrightarrow$ CoA + PalCar	Rapid Equilibrium Random Bi Bi [Ramsay et al., 1987]	BLM
CPT II	CoA + PalCar $\longleftrightarrow$ 16Acyl-CoA + Car	Ordered Bi Bi [Mann et al., 1995]	RLM
CAC	$PalCar_{IMS}$ + Car_{MAT} $\leftrightarrow$ $PalCar_{MAT}$ + Car_{IMS}	Ping-Pong Bi Bi [Indiveri et al., 1994]	RLM

2.4 Metabolite transporting system

Table 8: Metabolite carriers on the inner membrane

enzyme	reaction	reaction mechanism	source
AAC	$\mathrm{ATP}_{MAT} \longrightarrow \mathrm{ATP}_{IMS}$ $\mathrm{ADP}_{MAT} \longleftarrow \mathrm{ADP}_{IMS}$	See [Krämer and Klingenberg, 1982]	RHM
PiC	$\mathrm{Pi}_{IMS} + \mathrm{H}^{+}_{IMS}$ $\longleftrightarrow \mathrm{Pi}_{MAT} + \mathrm{H}^{+}_{MAT}$	Rapid Equilibrium Random Bi Bi [Stappen and Krämer, 1994]	RHM
PYC	$\mathrm{Pyr}_{IMS} + \mathrm{H}^{+}_{MAT}$ $\longleftrightarrow \mathrm{Pyr}_{MAT} + \mathrm{H}^{+}_{IMS}$	Rapid Equilibrium Random Bi Bi ("Sequential Mechanism" [Nalecz, 1994])	RLM
OGC	$\mathrm{OG}_{IMS} + \mathrm{Mal}_{MAT}$ $\longleftrightarrow \mathrm{OG}_{MAT} + \mathrm{Mal}_{IMS}$	Rapid Equilibrium Random Bi Bi [Indiveri et al., 1991a]	BHM
DIC	$\mathrm{Mal}_{IMS} + \mathrm{Pi}_{MAT}$ $\longleftrightarrow \mathrm{Mal}_{MAT} + \mathrm{Pi}_{IMS}$	Rapid Equilibrium Random Bi Bi [Indiveri et al., 1993]	RLM
CIC	$\mathrm{Cit}_{IMS} + \mathrm{Mal}_{MAT}$ $\longleftrightarrow \mathrm{Cit}_{MAT} + \mathrm{Mal}_{IMS}$	Rapid Equilibrium Random Bi Bi [Bisaccia et al., 1993]	RLM
AGC	$\mathrm{Asp}_{IMS} + \mathrm{Glu}_{MAT}$ $\longleftrightarrow \mathrm{Asp}_{MAT} + \mathrm{Glu}_{IMS}$	Rapid Equilibrium Random Bi Bi [Sluse et al., 1991]	RHM
CAC	$\mathrm{PalCar}_{IMS} + \mathrm{Car}_{MAT}$ $\leftrightarrow \mathrm{PalCar}_{MAT} + \mathrm{Car}_{IMS}$	Ping-Pong Bi Bi [Indiveri et al., 1994]	RLM

3 Parameter classification

We classified all the kinetic parameters into four classes to distinguish their background as follows. This classification rule was applied for annotating the parameters shown in 4.1 ∼ 4.33.

Table 9: The four classes for annotating the kinetic parameters

Class	Definition	Example
class 0	Found in the literature	$K_{mA} = 2.3\mathrm{E} - 3(\mathrm{M})$, $K_{mB} = 2.3 \pm 0.2\mathrm{E} - 3(\mathrm{M})$
class 1	Estimated around the values in the literature	$K_m = 2.3\mathrm{E} - 3(\mathrm{M})$ $\longrightarrow K_m = 2.6\mathrm{E} - 3(\mathrm{M})$
class 2	Estimated around the values of analogous metabolites	$K_m\mathrm{ATP} = 2.3\mathrm{E} - 3(\mathrm{M})$ $\longrightarrow 0 \leq K_m\mathrm{GTP} \leq 3\mathrm{E} - 3(\mathrm{M})$
class 3	Estimated arbitrarily	$? \leq k \leq ?$ $\longrightarrow k = 1.2\mathrm{E} + 9\ \mathrm{sec}^{-1}$

4 Kinetic parameters

4.1 AAC

Table 10: Kinetic parameters and their sources(AAC)

Parameter		class	notice
kf0	0.9	class 0	velocity model, at mp = 0, kf0 = kr0
kr0	0.9	class 0	velocity model, at mp = 0
normalize	2.21	class 0	normalizing factor of kf0, kr0
Kd1	5.9E-4	class 3	Kd1 → Kd, velocity model, Kd1 = Kd2
Kd2	5.9E-4	class 3	Kd2 → Kd′ Kd accepts no effects from membrane potential
Cf	3.30	class 0	kf0 × exp(Cf × ΔΨ) = kf(ΔΨ)
Cr	-3.34	class 0	kr0 × exp(Cr × ΔΨ) = kr(ΔΨ)
T	310.0	-	absolute temperature

kinetic mechanism	see [Krämer and Klingenberg, 1982]
rate equation	See 7.1
source for parameter estimation	[Krämer and Klingenberg, 1982] Figure 2(B) $V^D_{\rightarrow}(\Delta\Psi = 0, 180\text{mV})$

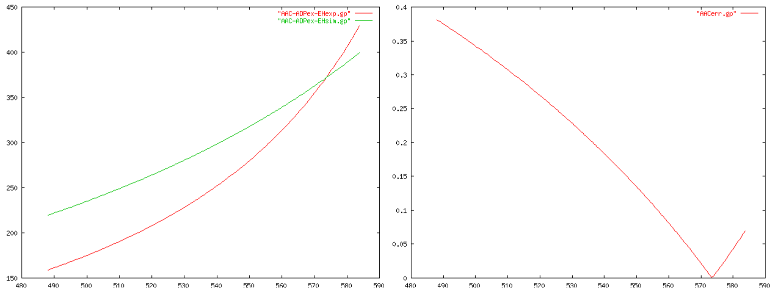

Figure 1: Comparison between experimental data and computed ones from estimated parameters(AAC)

left: Comparison between experimental data and computed ones
abscissa = reaction rate (sec^{-1})
ordinate = substrate concentration (M)
right: Percent error between experimental data and computed ones
abscissa = substrate concentration (M)
ordinate = percent error

4.2 ACD

Table 11: Kinetic parameters and their sources(ACD)

Parameter		class	notice
KmS1	39E-6	class 0	[McKean et al., 1979, Table 1]
KmS2	0.12E-6	class 0	
KmP1	1.08E-6	class 2	
KmP2	2.42E-5	class 2	
KiS1	76E-6	class 0	
KiS2	0.24E-6	class 0	
KiP1	7.53E-5	class 2	
KiP2	1.19E-5	class 2	
Keq	8.99	class 3	
KcF	2.18	class 0	
KcR	0.30	class 2	
kinetic mechanism			Ordered Bi Bi [McKean et al., 1979]
rate equation			See 7.9
source for parameter estimation			[McKean et al., 1979]

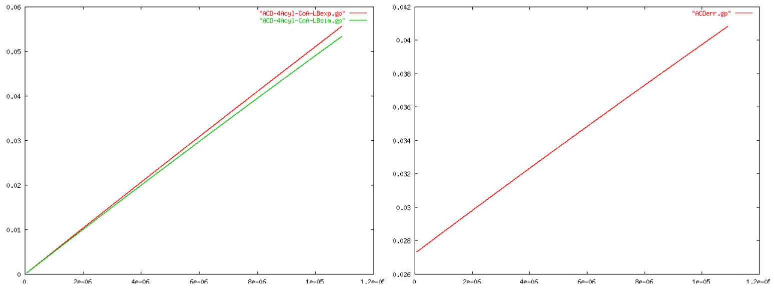

Figure 2: Comparison between experimental data and Computed data from estimated parameters(ACD)

left: Comparison between experimental data and computed ones
abscissa = reaction rate (sec^{-1})
ordinate = substrate concentration (M)
right: Percent error between experimental data and computed ones
abscissa = substrate concentration (M)
ordinate = percent error

4.3 ACO

Table 12: Kinetic parameters and their sources(ACO)

Parameter		class	notice
Ks	0.50E-3	class 0	
Kp	0.11E-3	class 0	
KcF	20.47	class 0	calculated from the graph
KcR	31.44	class 0	calculated from the graph
kinetic mechanism			Uni Uni Reversible [Guarriero-Bobyleva et al., 1978]
rate equation			See 7.14

4.4 AGC

Table 13: Kinetic parameters and their sources(AGC)

Parameter		class	notice
KiS1	80E-6	class 0	[Dierks and Krämer, 1988]
KiS2	3.2E-3	class 0	[Dierks and Krämer, 1988]
KiP1	180E-6	class 0	[Dierks and Krämer, 1988]
KiP2	2.8E-3	class 0	[Dierks and Krämer, 1988]
KcF	10.0	class 3	
KcR	10.0	class 3	
alpha	1.0	class 0	
beta	1.0	class 0	
gamma	1.0	class 0	
delta	1.0	class 0	
kinetic mechanism			Rapid Equilibrium Random Bi Bi [Sluse et al., 1991]
rate equation			See 7.12
source for parameter estimation			-

4.5 AlaTA

Table 14: Kinetic parameters and their sources(AlaTA)

Parameter		class	notice
KmS1	2E-3	class 0	
KmS2	0.4E-3	class 0	
KmP1	32E-3	class 0	
KmP2	0.4E-3	class 0	
KiS1	8.7E-3	class 2	KiP2
KiP2	12E-3	class 0	
Keq	0.69	class 2	0.16, AspTA
KcF	337	class 0	at MW = 78000, activity = 210 micromol/min/mg
KcR	0.15	class 3	
kinetic mechanism			Ping-Pong Bi Bi [De Rosa et al., 1979]
rate equation			See 7.11
source for parameter estimation			[De Rosa et al., 1979], Figure 3 with 5mM glutamate

4.6 AspTA

Table 15: Kinetic parameters and their sources(AspTA)

Parameter		class	notice
KmS1	0.9E-3	class 0	[Velick and Vavra, 1962, Table II]
KmS2	0.1E-3	class 0	[Velick and Vavra, 1962, Table II]
KmP1	0.04E-3	class 0	[Velick and Vavra, 1962, Table II]
KmP2	4E-3	class 0	[Velick and Vavra, 1962, Table II]
KiS1	2E-3	class 0	[Velick and Vavra, 1962, Table VII]
KiP2	8.3E-3	class 0	[Velick and Vavra, 1962, Table VII]
Keq	6.2	class 0	
KcF	300	class 0	
KcR	1000	class 0	from k4 and k10
kinetic mechanism			Ping-Pong Bi Bi [Velick and Vavra, 1962]
rate equation			See 7.11

4.7 CAC

Table 16: Kinetic parameters and their sources(CAC)

Parameter		class	notice
KmS1	0.6E-3	class 0	[Indiveri et al., 1994]
KmS2	9.4E-3	class 0	[Indiveri et al., 1994]
KmP1	43.4E-6	class 1	11.6E-6, the value of Car/Car reaction
KmP2	0.4E-3	class 1	1.2E-3, the value of Car/Car reaction
KiS1	8.7E-6	class 1	5.1E-6 [Indiveri et al., 1991b]
KiP2	250E-6	class 1	510E-6 [Indiveri et al., 1991b]
Keq	243.3	class 3	
KcF	1.22	class 2	
KcR	1.08	class 1	0.92, [Indiveri et al., 1991b]
kinetic mechanism			Ping-Pong Bi Bi [Indiveri et al., 1994]
rate equation			See 7.11
source for parameter estimation			[Indiveri et al., 1991b] Figure 4 with 13mM acetylcarnitine

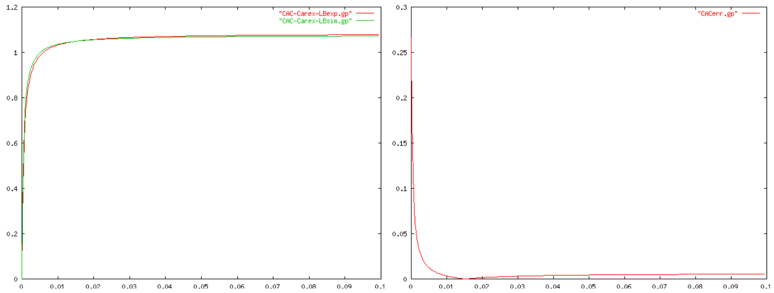

Figure 3: Comparison between experimental data and Computed data from estimated parameters(CAC)

left: Comparison between experimental data and computed ones
abscissa = reaction rate (sec^{-1})
ordinate = substrate concentration (M)
right: Percent error between experimental data and computed ones
abscissa = substrate concentration (M)
ordinate = percent error

4.8 CIC

Table 17: Kinetic parameters and their sources(CIC)

Parameter		class	notice
KiS1	1.3E-4	class 2	11.2 mmol/min/g prot. × 30kDa 2.1, [Bisaccia et al., 1993, Table II]
KiS2	4.4E-4	class 2	
KiP1	3.3E-4	class 0	
KiP2	4.18E-5	class 0	
KcF	5.6	class 0	
KcR	3.5	class 1	
alpha	1.0	class 0	
beta	1.0	class 0	
gamma	1.0	class 0	
delta	1.0	class 0	
kinetic mechanism			Rapid Equilibrium Random Bi Bi [Bisaccia et al., 1993]
rate equation			See 7.12
source for parameter estimation			Figure 1(A) with 0.05mM citrate, (C) with 0.05mM malate [Bisaccia et al., 1993]

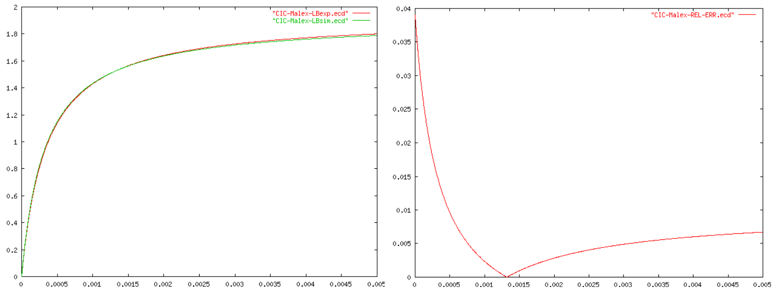

Figure 4: Comparison between experimental data and Computed data from estimated parameters(CIC)

left: Comparison between experimental data and computed ones
abscissa = reaction rate (sec^{-1})
ordinate = substrate concentration (M)
right: Percent error between experimental data and computed ones
abscissa = substrate concentration (M)
ordinate = percent error

4.9 Complex I

Table 18: Kinetic parameters and their sources(Complex I)

Parameter		class	notice
KmS1	9.2E-6	class 0	KiS1 = 1 / k_{min}
KmS2	2.6E-4	class 0	
KmP1	9.9E-6	class 2	
KmP2	5.9E-5	class 2	
KiS1	2.1E-8	class 0	
KiP2	9.8E-8	class 2	
Keq	407.9	class 3	
KcF	498	class 0	
KcR	229	class 2	
kinetic mechanism			Ping-Pong Bi Bi [Fato et al., 1996]
rate equation			See 7.11
source for parameter estimation			[Fato et al., 1996] Figure 1(C) with 2.4 μM reduced CoQ_2

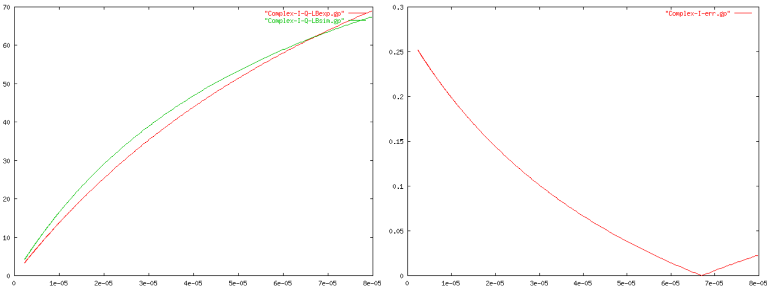

Figure 5: Comparison between experimental data and Computed data from estimated parameters(Complex I)

left: Comparison between experimental data and computed ones
abscissa = reaction rate (sec^{-1})
ordinate = substrate concentration (M)
right: Percent error between experimental data and computed ones
abscissa = substrate concentration (M)
ordinate = percent error

4.10 Complex III

Table 19: Kinetic parameters and their sources(Complex III)

Parameter		class	notice
KmA	2.8E-5	class 0	$K_5 \times$ KcF
KmB	3.0E-6	class 0	$K_6 \times$ KcF
Kb1	5.4E-6	class 2	k_5/k_4 $K_3 = K_4 \times$ Kb1
Kb2	5.7E-6	class 2	k_{10}/k_9, $K_1 = K_2 \times$ Kb2
Kq1	2.8E-6	class 2	k_7/k_6, $K_4 =$ Kq1$/k_8$
Kq2	1.9E-6	class 2	k_{12}/k_{11}, $K_2 = K_5 \times$ Kq2
k8	622.1	class 2	
KcF	426.8	class 0	1 / K_7
kinetic mechanism			[Kubota et al., 1992, Scheme 3]
rate equation			See 7.3
source for parameter estimation			[Kubota et al., 1992] Figure 6 with 15 μM Q_2H_2

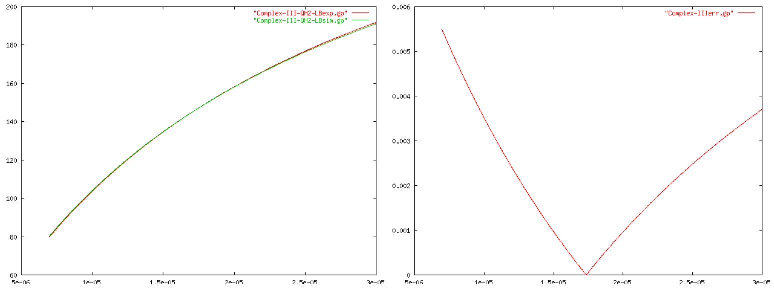

Figure 6: Comparison between experimental data and Computed data from estimated parameters(Complex III)

left: Comparison between experimental data and computed ones
abscissa = reaction rate ($\sec^{-1}$)
ordinate = substrate concentration (M)
right: Percent error between experimental data and computed ones
abscissa = substrate concentration (M)
ordinate = percent error

4.11 Complex IV

Table 20: Kinetic parameters and their sources(Complex IV)

Parameter		class	notice
Ks	110E-6	class 0	Value at pH = 7
KcF	93.5	class 0	Value at pH = 7, $\frac{d[cyt2+]}{dt} \times \frac{1}{4}$
kinetic mechanism			Michaelis Uni Uni [Malmström and Andréasson, 1985]
rate equation			See 7.7

4.12 Complex V

Table 21: Kinetic parameters and their sources(Complex V)

Parameter		class	notice
Kd	2.67E-7	class 3	
Kp	9.02E-5	class 3	
Kt	4.33E-5	class 3	
KcF	14.5	class 0	2340nmol/min/mg × 371kDa
Khx	1.3E-4	class 3	
Khy	1.6E-4	class 3	
klt_f	1.35E+8	class 3	
klt_r	0.00018	class 3	
ax	0.1	class 3	
ay	0.6	class 3	
beta	0.3	class 3	
T	310	-	
kinetic mechanism			see [Kholodenko, 1993]
rate equation			See 7.4
source for parameter estimation			[Matsuno-Yagi and Hatefi, 1985] Figure 2 with NADH respiration

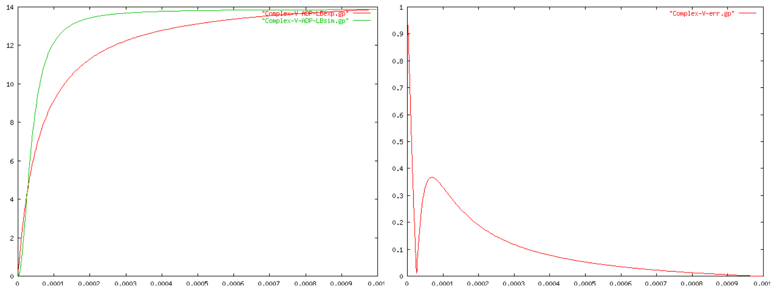

Figure 7: Comparison between experimental data and computed data from estimated parameters(Complex V)

left: Comparison between experimental data and computed ones
abscissa = reaction rate (sec^{-1})
ordinate = substrate concentration (M)
right: Percent error between experimental data and computed ones
abscissa = substrate concentration (M)
ordinate = percent error

4.13 CPT I

Table 22: Kinetic parameters and their sources(CPT I)

Parameter		class	notice
KiS1	182E-6	class 0	[Ramsay et al., 1987]
KiS2	0.82E-6	class 0	
KiP1	6.7E-6	class 0	
KiP2	21E-6	class 0	
KcF	61.4	class 0	
KcR	32.8	class 0	
alpha	1.0	class 0	
beta	1.0	class 0	
gamma	1.0	class 0	
delta	1.0	class 0	
kinetic mechanism			Rapid Equilibrium Random Bi Bi
			[Ramsay et al., 1987]
rate equation			See 7.12

4.14 CPT II

Table 23: Kinetic parameters and their sources(CPT II)

Parameter		class	notice
KmS1	6.3E-4	class 2	
KmS2	3.3E-4	class 2	
KmP1	950E-6	class 0	
KmP2	34E-6	class 0	
KiS1	2.4E-4	class 2	
KiS2	2.7E-4	class 2	
KiP1	41E-6	class 0	
KiP2	7E-6	class 0	
Keq	23540	class 3	
KcF	8.0	class 2	
KcR	2.4	class 0	1.8 Unit/mg × 80kDa
			[Mann et al., 1995, Woeltje et al., 1987]
kinetic mechanism			Ordered Bi Bi
			[Mann et al., 1995]
rate equation			See 7.9
source for parameter estimation			[Mann et al., 1995]
			Figure 1 with 0μM SDZ

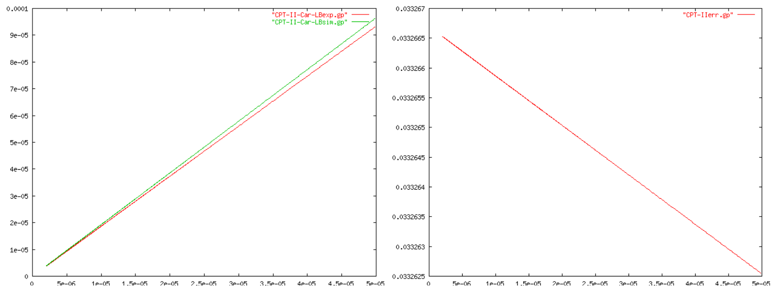

Figure 8: Comparison between experimental data and Computed data from estimated parameters(CPT II)

left: Comparison between experimental data and computed ones
abscissa = reaction rate (sec^{-1})
ordinate = substrate concentration (M)
right: Percent error between experimental data and computed ones
abscissa = substrate concentration (M)
ordinate = percent error

4.15 CS

Table 24: Kinetic parameters and their sources(CS)

Parameter	class	notice
k1 6.8E10	class 3	
k_1 8.1E8	class 3	
k2 3.0E10	class 3	
k_2 7.2E8	class 3	
k3 6.2E10	class 3	
k_3 5.1E8	class 3	
k4 1.2E10	class 3	
k_4 4.0E8	class 3	
k5 1.4E9	class 3	
k_5 2.4E8	class 3	
k6 4.1E10	class 3	
k_6 1.1E8	class 3	
k7 5E10	class 3	
k_7 9.8E8	class 3	
k8 5.3E10	class 3	
k_8 7.7E8	class 3	
kinetic mechanism		Random Bi Bi, [Shepherd and Garland, 1969], [Matsuoka and Srere, 1973], [Mukherjee and Srere, 1976]
source for parameter estimation		[Matsuoka and Srere, 1973]

4.16 DIC

Table 25: Kinetic parameters and their sources(DIC)

Parameter		class	notice
KiS1	0.20E-3	class 0	[Indiveri et al., 1993, Fig. 5]
KiS2	0.72E-3	class 0	[Indiveri et al., 1993, Fig. 5]
KiP1	9.0E-4	class 2	
KiP2	7.6E-4	class 2	
KcF	2.7	class 0	6.7E-6 mol/min/mg × 28kDa
KcR	4.1	class 1	
alpha	1.0	class 0	
beta	1.0	class 0	
gamma	1.0	class 0	
delta	1.0	class 0	

kinetic mechanism	Rapid Equilibrium Random Bi Bi [Indiveri et al., 1993]
rate equation	See 7.12
source for parameter estimation	Figure 5(A) with 0.05mM phosphate, (C) with 0.10mM malate [Indiveri et al., 1993]

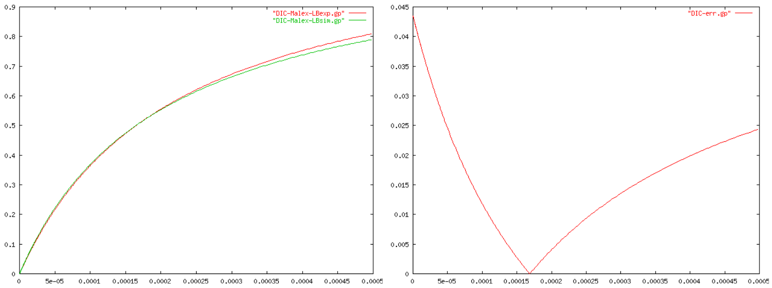

Figure 9: Comparison between experimental data and Computed data from estimated parameters(DIC)

left: Comparison between experimental data and computed ones
abscissa = reaction rate (sec^{-1})
ordinate = substrate concentration (M)
right: Percent error between experimental data and computed ones
abscissa = substrate concentration (M)
ordinate = percent error

4.17 ECH

Table 26: Kinetic parameters and their sources(ECH)

Parameter		class	notice
Ks	16.9E-6	class 0	
Kp	12.1E-6	class 0	
KcF	8.9166667	class 0	
KcR	2154.1667	class 0	

kinetic mechanism	Uni Uni Reversible [Yang and Schulz, 1987]
rate equation	See 7.14

4.18 ETF-QO

Table 27: Kinetic parameters and their sources(ETF-QO)

Parameter		class	notice
KmS1	0.31E-6	class 0	
KmS2	0.39E-6	class 2	
KmP1	0.32E-6	class 0	
KmP2	4.2E-9	class 2	
KiS1	0.31E-6	class 0	
KiP2	0.3E-6	class 2	
Keq	0.66	class 0	
KcF	78	class 0	
KcR	101	class 2	
kinetic mechanism			Ping-Pong Bi Bi, [Beckmann and Frerman, 1985]
rate equation			See 7.11
source for parameter estimation			Figure 4 with 1.5μM ETF hydroquinone [Beckmann and Frerman, 1985]

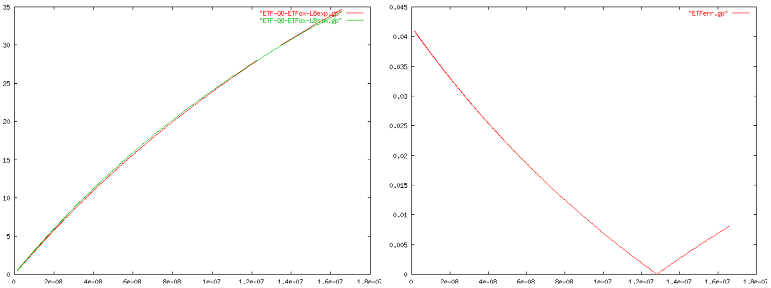

Figure 10: Comparison between experimental data and Computed data from estimated parameters(ETF:QO)

left: Comparison between experimental data and computed ones
abscissa = reaction rate ($\sec^{-1}$)
ordinate = substrate concentration (M)
right: Percent error between experimental data and computed ones
abscissa = substrate concentration (M)
ordinate = percent error

4.19 FM

Table 28: Kinetic parameters and their sources(FM)

Parameter		class	notice
Ks	0.5E-5	class 0	[Boyer, 1970, Vol. V, chap. 19, Table V]
Kp	2.5E-5	class 0	
KcF	800	class 0	
KcR	900	class 0	
kinetic mechanism			Uni Uni Reversible
rate equation			See 7.14

4.20 HCD

Table 29: Kinetic parameters and their sources(HCD)

Parameter	class	notice
Ks 1.5E-6	class 0	
KcF 41.483333	class 0	
kinetic mechanism		Michaelis Uni Uni [Yang and Schulz, 1987]
rate equation		See 7.7

4.21 IDHa

Table 30: Kinetic parameters and their sources(IDHa)

Parameter	class	notice
KcF 105	class 0	28 U/mg × 224000 Da [Plaut et al., 1974, Ehrlich et al., 1981]
b 29.6	class 3	
c 0.00023	class 3	
d 7.8e-05	class 3	
e 0.00064	class 3	
f 0.00036	class 3	
kinetic mechanism		[Plaut et al., 1974]
rate equation		See 7.5
source for parameter estimation		Figure 4 with 1.0mM ADP, [Plaut et al., 1974]

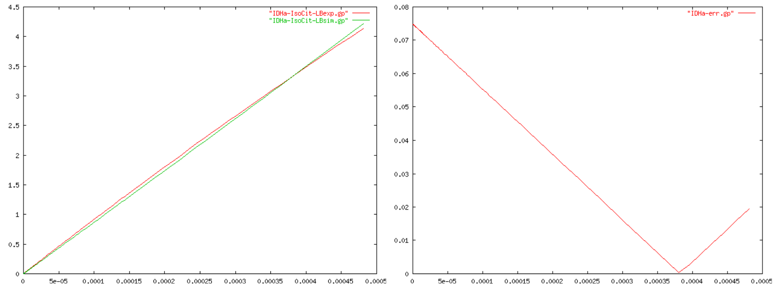

Figure 11: Comparison between experimental data and Computed data from estimated parameters(IDHa)

left: Comparison between experimental data and computed ones
abscissa = reaction rate (sec^{-1})
ordinate = substrate concentration (M)
right: Percent error between experimental data and computed ones
abscissa = substrate concentration (M)
ordinate = percent error

4.22 IDHb

Table 31: Kinetic parameters and their sources(IDHb)

Parameter		class	notice
phi0	5.1E-2	class 0	[Londesborough and Dalziel, 1970, Table 1]
phi1	9.5E-8	class 0	
phi2	0.96E-6	class 0	
phi12	9E-8	class 0	
phir0	6.6E-2	class 0	
phir1	0.37E-6	class 0	
phir2	29E-6	class 0	
phir3	2.5E-4	class 0	
phir12	6E-12	class 0	
phir13	1.3E-10	class 0	
phir23	9.4E-8	class 0	
phir123	4.6E-14	class 0	
kinetic mechanism			See [Londesborough and Dalziel, 1970]
rate equation			See 7.6

4.23 MDH

Table 32: Kinetic parameters and their sources(MDH)

Parameter		class	notice
KmS1	72E-6	class 0	
KmS2	110E-6	class 0	
KmP1	1600E-6	class 0	
KmP2	170E-6	class 0	
KiS1	11E-6	class 0	
KiS2	100E-6	class 0	
KiP1	7100E-6	class 0	
KiP2	1900E-6	class 0	
KcF	0.390	class 0	specific activity = 0.33 U/mg, MW = 72000 [Crow et al., 1983, Table I]
KcR	0.040	class 0	$\frac{V_f}{V_r} = 9.8$ [Crow et al., 1983, Table III]
kinetic mechanism			Ordered Bi Bi [Crow et al., 1983]
rate equation			See 7.2

4.24 NDK

Table 33: Kinetic parameters and their sources(NDK)

Parameter		class	notice
KmS1	0.31E-3	class 0	[Garces and Cleland, 1969]
KmS2	0.043E-3	class 0	[Garces and Cleland, 1969],UDP
KmP1	0.050E-3	class 0	[Garces and Cleland, 1969]
KmP2	0.25E-3	class 0	[Garces and Cleland, 1969],UTP
KiS1	0.21E-3	class 2	[Garces and Cleland, 1969]
KiP2	0.35E-3	class 2	[Garces and Cleland, 1969],UTP
Keq	1.28	class 0	[Garces and Cleland, 1969]
KcF	6883	class 0	MW = 70000 Da [Colomb et al., 1969]
KcR	5950	class 0	MW = 70000 Da [Colomb et al., 1969]

kinetic mechanism	Ping-Pong Bi Bi [Garces and Cleland, 1969, Colomb et al., 1969]
rate equation	See 7.11
source for parameter estimation	[Colomb et al., 1969, Figure 4 with 0.18mM ATP]

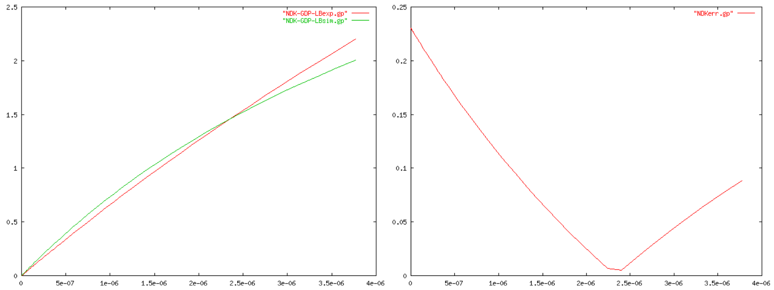

Figure 12: Comparison between experimental data and Computed data from estimated parameters(NDK)

left: Comparison between experimental data and computed ones
abscissa = reaction rate (sec^{-1})
ordinate = substrate concentration (M)
right: Percent error between experimental data and computed ones
abscissa = substrate concentration (M)
ordinate = percent error

4.25 OCT

Table 33: Kinetic parameters and their sources(OCT)

Parameter		class	notice
KmS1	1.1E-6	class 0	OCTa
	1.1E-6	class 0	OCTb, value for 16Oxoacyl-CoA
	1.3E-6	class 0	OCTc
	2.1E-6	class 0	OCTd
	3.2E-6	class 0	OCTe
	6.7E-6	class 0	OCTf
	12.4E-6	class 0	OCTg
KmS2	28.6E-6	class 0	
	28.6E-6	class 0	OCTb, value for 16Oxoacyl-CoA
	38.4E-6	class 0	OCTc
	35.7E-6	class 0	OCTd
	35.5E-6	class 0	OCTe
	18.9E-6	class 0	OCTf
	2.2E-6	class 0	OCTg
KmP1	7.2E-5	class 2	
KmP2	8.7E-5	class 2	
KiS1	1.1E-5	class 2	
KiP2	8.7E-5	class 2	
Keq	160.98	class 3	
KcF	137.86	class 0	$V_{max} \times$ 178000Da
	137.86	class 0	OCTb, value for 16Oxoacyl-CoA
	253.52	class 0	OCTc
	272.94	class 0	OCTd
	277.38	class 0	OCTe
	264.07	class 0	OCTf
	80.244	class 0	OCTg
KcR	87.253	class 2	
	87.253	class 2	OCTb, value for 16Oxoacyl-CoA
	160.46	class 2	OCTc
	172.75	class 2	OCTd
	175.56	class 2	OCTe
	167.13	class 2	OCTf
	51.615	class 2	OCTg

kinetic mechanism	Ping-Pong Bi Bi, [Miyazawa et al., 1981]
rate equation	See 7.11
source for parameter estimation	Figure 5(B) with 200μM Acetyl-CoA, [Miyazawa et al., 1981]

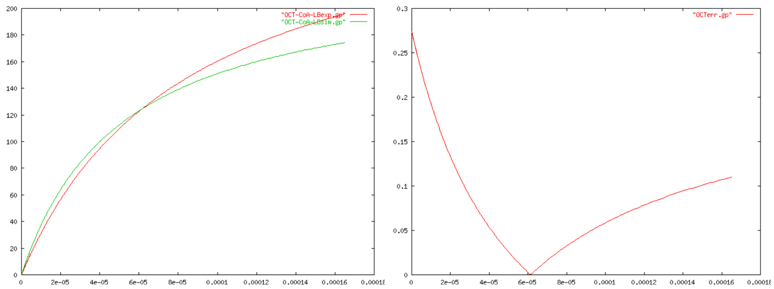

Figure 13: Comparison between experimental data and Computed data from estimated parameters(OCT)

left: Comparison between experimental data and computed ones
abscissa = reaction rate (sec^{-1})
ordinate = substrate concentration (M)
right: Percent error between experimental data and computed ones
abscissa = substrate concentration (M)
ordinate = percent error

4.26 OGC

Table 34: Kinetic parameters and their sources(OGC)

Parameter		class	notice
KiS1	0.3E-3	class 0	
KiS2	0.7E-3	class 2	
KiP1	1.4E-3	class 0	
KiP2	0.17E-3	class 2	
KcF	3.675	class 0	
KcR	4.83	class 0	
alpha	1.0	class 0	
beta	1.0	class 0	
gamma	1.0	class 0	
delta	1.0	class 0	
kinetic mechanism			Rapid Equilibrium Random Bi Bi, [Indiveri et al., 1991a]
rate equation			See 7.12
source for parameter estimation			Figure 2 with 20mM malate, [Indiveri et al., 1991a]

4.27 OGDC

Table 35: Kinetic parameters and their sources(OGDC)

Parameter		class	notice
KmA	0.22E-3	class 0	Pig Heart [Hamada et al., 1975]
KmB	0.025E-3	class 0	Pig Heart [Hamada et al., 1975]
KmC	0.050E-3	class 0	Pig Heart [Hamada et al., 1975]
KmP	3E-4	class 2	
KmR	6E-4	class 2	
Kia	7.2E-4	class 2	0.75E-3, Dictyostelium, [Heckert et al., 1989]
Kib	7.4E-4	class 2	
Kic	1E-4	class 2	
Kip	1.1E-6	class 2	
Kiq	81E-6	class 0	Human Heart [Kiselevsky et al., 1990]
Kir	25E-6	class 0	Human Heart [Kiselevsky et al., 1990]
KcF	177	class 2	estimated, 270 at MW = 2700000Da

kinetic mechanism	Multisite Ping-Pong [Cleland, 1973, Hamada et al., 1975]
rate equation	See 7.8
source for parameter estimation	Figure 1(A) with 0.010mM CoA, (B) with 0.20mM NAD, (C) with 0.10mM oxoglutarate [Hamada et al., 1975]

4.28 PC

Table 36: Kinetic parameters and their sources(PC)

Parameter		class	notice
KmA	0.11E-3	class 0	ATP, Table III, inhibitor=MgADP
KmB	1.63E-3	class 0	HCO_3^-, Table III, inhibitor=OXA
KmC	0.37E-3	class 0	Pyr, Table III, inhibitor=OXA
KmP	16E-3	class 0	Pi, Table III, inhibitor=MgATP
KmQ	0.24E-3	class 0	ADP, Table III, inhibitor=MgATP
KmR	0.051E-3	class 0	OXA, Table III, inhibitor=Pyr
Keq	9.0	class 0	
Kia	0.15E-3	class 0	ATP, Table I
Kib	1.6E-3	class 0	HCO_3^-, Table I
Kic	0.13E-3	class 0	Pyr, Table III, vs. OXA
Kip	7.9E-3	class 0	Pi, Table I
Kiq	0.19E-3	class 0	ADP, Table I
Kir	0.24E-3	class 0	OXA, Table III, vs. Pyr
KcF	200	class 0	specific activity = 20, MW=600000
KcR	20	class 0	$\frac{V_1}{V_2} = 10$

kinetic mechanism	[Barden et al., 1972]
rate equation	See 7.10

4.29 PDC

Table 37: Kinetic parameters and their sources(PDC)

Parameter		class	notice
KmA	25E-6	class 0	[Kiselevsky et al., 1990]
KmB	13E-6	class 0	[Kiselevsky et al., 1990]
KmC	50E-6	class 0	[Kiselevsky et al., 1990]
KmP	5.9E-7	class 2	
KmR	6.9E-7	class 2	
Kia	5.5E-4	class 2	Dictyostelium, [Heckert et al., 1989]
Kib	3.0E-4	class 2	
Kic	1.8E-4	class 2	
Kip	6.0E-5	class 2	
Kiq	35E-6	class 0	Human Heart [Kiselevsky et al., 1990]
Kir	36E-6	class 0	Human Heart [Kiselevsky et al., 1990]
KcF	856	class 1	specific activity = 4.8 U/mg protein [Kiselevsky et al., 1990]

kinetic mechanism	Multisite Ping-Pong, [Cleland, 1973, Hamada et al., 1975]
rate equation	See 7.8
source for parameter estimation	Figure 2(A) with 0.015mM CoA, (B) with 0.050mM NAD, (C) with 0.050mM pyruvate [Hamada et al., 1975]

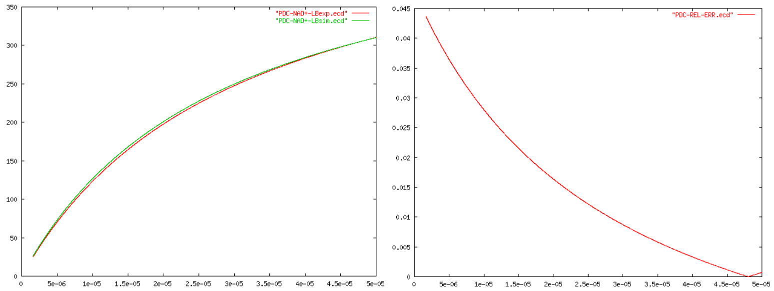

Figure 14: Comparison between experimental data and Computed data from estimated parameters(PDC)

left: Comparison between experimental data and computed ones
abscissa = reaction rate ($\sec^{-1}$)
ordinate = substrate concentration (M)
right: Percent error between experimental data and computed ones
abscissa = substrate concentration (M)
ordinate = percent error

4.30 PiC

Table 38: Kinetic parameters and their sources(PiC)

Parameter		class	notice
KiS1	0.87	class 2	
KiS2	1.86E-8	class 2	
KiP1	32.84E-9	class 0	Fig. 4, [Stappen and Krämer, 1994]
KiP2	11.12E-3	class 0	Fig. 4, [Stappen and Krämer, 1994]
KcF	37.9	class 0	Fig. 4, [Stappen and Krämer, 1994], 34kDa
KcR	37.0	class 0	Fig. 4, [Stappen and Krämer, 1994], 34kDa
alpha	1.0	class 0	
beta	1.0	class 0	
gamma	1.0	class 0	
delta	1.0	class 0	
kinetic mechanism			Rapid Equilibrium Random Bi Bi, [Stappen and Krämer, 1994]
rate equation			See 7.12
source for parameter estimation			Figure 4(A) with pH5.85, (B) with 4mM phosphate]stappen94

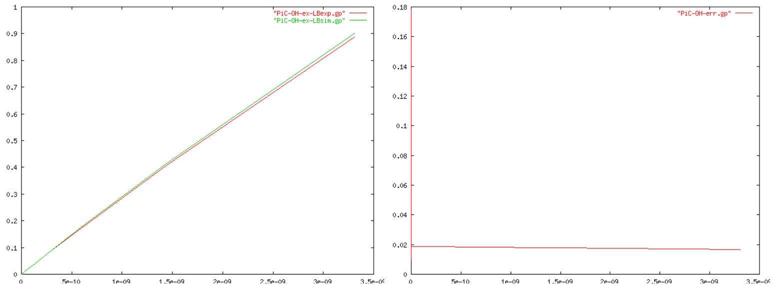

Figure 15: Comparison between experimental data and Computed data from estimated parameters(PiC)

left: Comparison between experimental data and computed ones
abscissa = reaction rate (sec^{-1})
ordinate = substrate concentration (M)
right: Percent error between experimental data and computed ones
abscissa = substrate concentration (M)
ordinate = percent error

4.31 PYC

Table 39: Kinetic parameters and their sources(PYC)

Parameter		class	notice
KiS1	6.1E-4	class 2	
KiS2	5.9E-4	class 2	
KiP1	2.6E-4	class 2	
KiP2	4.1E-4	class 2	
KcF	0.84	class 1	0.67 [Capuano et al., 1990]
KcR	0.78	class 1	0.61 [Capuano et al., 1990]
alpha	1.0	class 0	
beta	1.0	class 0	
gamma	1.0	class 0	
delta	1.0	class 0	
kinetic mechanism			Rapid Equilibrium Random Bi Bi, (sequential) [Nalecz, 1994]
rate equation			See 7.12
source for parameter estimation			[Capuano et al., 1990, Figure 3]

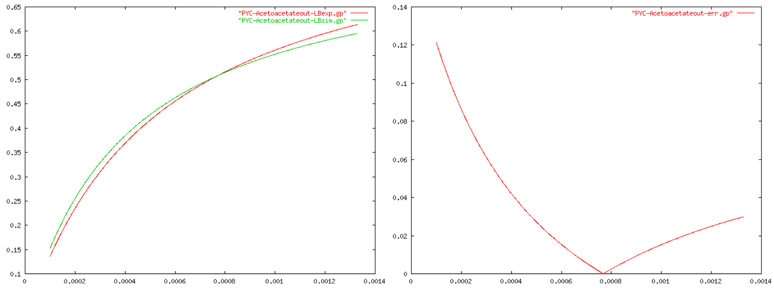

Figure 16: Comparison between experimental data and Computed data from estimated parameters(PYC)

left: Comparison between experimental data and computed ones
abscissa = reaction rate (sec^{-1})
ordinate = substrate concentration (M)

right: Percent error between experimental data and computed ones
abscissa = substrate concentration (M)
ordinate = percent error

4.32 SCS

Table 40: Kinetic parameters and their sources(SCS)

Parameter		class	notice
KmA	5E-6	class 0	GDP (2 - 8E-6)
KmB	3.5E-5	class 0	Succinyl-CoA (1 - 6E-5)
KmC	4.5E-4	class 0	Pi (2 - 7E-4)
KmP	6E-4	class 0	Succinate (4 - 8E-4)
KmQ	7.5E-6	class 0	GTP (5 - 10E-6)
KmC2	4.5E-4	class 0	Pi (2 - 7E-4)
KmP2	6E-4	class 0	Succinate (4 - 8E-4)
Keq	8.375	class 0	From Haldane relationships
Kia	4E-4	class 0	GDP (Table II)
Kib	2E-5	class 0	Succinyl-CoA, (vs. CoA, Fig. 7)
Kic	3E-5	class 0	Pi (Table II)
Kip	7E-2	class 0	Succinate (Table II)
Kiq	5E-6	class 0	GTP (Table II)
Kir	6.7E-6	class 0	CoA, from a Haldane relationship, Kq * Kir = Kiq * Kr where Kr (CoA) = 10E-6 M
Kc1	100	class 0	kcat = Kc2 = 25 to 287.5 (20 to 230 U/mg * 75000 Dalton)
Kc2	100	class 3	guess, V1 / V2 = 0.20, V2' / V1' = 30
kinetic mechanism			See [Cha and Parks Jr., 1964]
rate equation			See 7.13

4.33 SDH

Table 41: Kinetic parameters and their sources(SDH)

Parameter		class	notice
KmS1	30E-6	class 0	30-130E-6
KmS2	69E-6	class 0	
KmP1	0.3E-6	class 0	
KmP2	1.5E-6	class 0	
KiS1	4.1E-6	class 2	Ki for carboxin = 3.0E-6 M
KiP2	5.6E-6	class 2	Ki for carboxin = 3.0E-6 M
Keq	0.037	class 0	from Haldane
KcF	69.3	class 0	MW = 104000 Da
KcR	1.73	class 0	MW = 104000 Da
kinetic mechanism			Ping-Pong Bi Bi [Grivennikova et al., 1993]
rate equation			See 7.11
source for parameter estimation			[Grivennikova et al., 1993, Figure 2(B)]

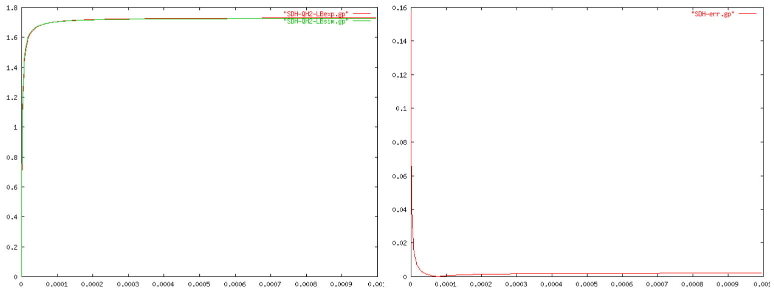

Figure 17: Comparison between experimental data and Computed data from estimated parameters(SDH)
left: Comparison between experimental data and computed ones
abscissa = reaction rate (sec^{-1})
ordinate = substrate concentration (M)
right: Percent error between experimental data and computed ones
abscissa = substrate concentration (M)
ordinate = percent error

5 Initial condition

5.1 The respiratory chain

Table 42: Initial condition of enzymes (respiratory chain)

name	localization	number of molecules
Complex-I	MT-IM	1000
Complex-III	MT-IM	3000
Complex-IV	MT-IM	7000
Complex-V	MT-IM	900

Table 43: Initial condition of metabolites (respiratory chain)

name	localization	concentration
Q	MT-IMS	0.26E-3 M
QH2	MT-IMS	0.028E-3 M
Cyt-c3+	MT-IMS	3E-6 M
Cyt-c2+	MT-IMS	0.11E-3 M
H+	MT-IMS	1E-6 M (fix)
H+	MATRIX	1E-8 M (fix)

5.2 The TCA cycle

Table 44: Initial condition of enzymes (TCA cycle)

name	localization	number of molecules
CS	MATRIX	100
ACO	MATRIX	100
IDHa	MATRIX	100
IDHb	MATRIX	100
OGDC	MATRIX	100
SCS	MATRIX	100
SDH	MT-IM	100
FM	MATRIX	100
MDH	MATRIX	100
AlaTA	MATRIX	100
AspTA	MATRIX	100
NDK	MATRIX	100
PDC	MATRIX	100
PC	MATRIX	100

Table 45: Initial condition of metabolites (TCA cycle)

name	localization	concentration
Cit	MT-IMS	0.42E-3 M (fix)
Cit	MATRIX	0.42E-3 M
IsoCit	MATRIX	0.42E-3 M
OG	MT-IMS	0.021E-3 M (fix)
OG	MATRIX	0.021E-3 M
SCoA	MATRIX	76168
Suc	MATRIX	2.95E-3 M
Fum	MATRIX	0.065E-3 M
Mal	MT-IMS	0.50E-3 M (fix)
Mal	MATRIX	0.50E-3 M
OXA	MATRIX	0.004E-3 M
Asp	MATRIX	1.14E-3 M
Asp	MT-IMS	1.14E-3 M (fix)
Glu	MATRIX	3.03E-3 M
Glu	MT-IMS	3.03E-3 M (fix)
Ala	MATRIX	3.44E-3 M
Pyr	MT-IMS	0.1025E-3 M (fix)
Pyr	MATRIX	0.1025E-3 M (fix)
CoA	MT-IMS	700 (fix)
CoA	MATRIX	70435
Acetyl-CoA	MATRIX	0.03E-3 M
NADH	MATRIX	0.072E-3 M
NAD+	MATRIX	0.170E-3 M
NADPH	MATRIX	0.072E-3 M
NADP+	MATRIX	0.170E-3 M
CO2	MATRIX	1.63E-3 M

Table 46: Initial condition of metabolites

name	localization	concentration
ATP	MT-IMS	4.5E-3 M (fix)
ATP	MATRIX	4.5E-3 M
ADP	MT-IMS	0.45E-3 M (fix)
ADP	MATRIX	0.45E-3 M (fix)
GTP	MATRIX	4.5E-3 M
GDP	MATRIX	0.45E-3 M
Pi	MT-IMS	4E-3 M (fix)
Pi	MATRIX	4E-3 M

5.3 Fatty acid β oxidation

Table 47: Initial condition of enzymes (fatty acid β oxidation)

name	localization	number of molecules
CPT-I	MT-OM	100
CAC	MT-IM	100
ACD	MT-IM	100
ECH	MT-IM	100
HCD	MT-IM	100
OCT	MT-IM	100
ETF-QO	MT-IM	100

Table 48: Initial condition of metabolites (fatty acid β oxidation 1)

name	localization	concentration
Car	MT-IMS	0.2E-3 M (fix)
Car	MATRIX	0.95E-3 M
PalCar	MT-IMS	0.6E-3 M (fix)
PalCar	MATRIX	0.012E-3 M
16Acyl-CoA	MT-IMS	0.039E-3 M (fix)
ETFred	MATRIX	0.31E-6 M
ETFox	MATRIX	0.32E-6 M

Table 49: Initial condition of metabolites (fatty acid β oxidation 2)

name	localization	concentration
16Acyl-CoA	MATRIX	0.039E-3 M
16Enoyl-CoA	MATRIX	0.017E-3 M
16Hydroxyacyl-CoA	MATRIX	0.012E-3 M
16Oxoacyl-CoA	MATRIX	0.0011E-3 M
14Acyl-CoA	MATRIX	0.039E-3 M
14Enoyl-CoA	MATRIX	0.017E-3 M
14Hydroxyacyl-CoA	MATRIX	0.012E-3 M
14Oxoacyl-CoA	MATRIX	0.0011E-3 M
12Acyl-CoA	MATRIX	0.087E-3 M
12Enoyl-CoA	MATRIX	0.017E-3 M
12Hydroxyacyl-CoA	MATRIX	0.012E-3 M
12Oxoacyl-CoA	MATRIX	0.0013E-3 M
10Acyl-CoA	MATRIX	0.087E-3 M
10Enoyl-CoA	MATRIX	0.017E-3 M
10Hydroxyacyl-CoA	MATRIX	0.012E-3 M
10Oxoacyl-CoA	MATRIX	0.0021E-3 M
8Acyl-CoA	MATRIX	0.087E-3 M
8Enoyl-CoA	MATRIX	0.017E-3 M
8Hydroxyacyl-CoA	MATRIX	0.012E-3 M
8Oxoacyl-CoA	MATRIX	0.0032E-3 M
6Acyl-CoA	MATRIX	0.087E-3 M
6Enoyl-CoA	MATRIX	0.017E-3 M
6Hydroxyacyl-CoA	MATRIX	0.012E-3 M
6Oxoacyl-CoA	MATRIX	0.0067E-3 M
4Acyl-CoA	MATRIX	0.087E-3 M
4Enoyl-CoA	MATRIX	0.017E-3 M
4Hydroxyacyl-CoA	MATRIX	0.012E-3 M
Acetoacetyl-CoA	MATRIX	0.0124E-3 M

5.4 The inner-membrane transport

Table 50: Initial condition of enzymes (inner-membrane transport)

name	localization	number of molecules
AAC	MT-IM	1000
AGC	MT-IM	1000
PiC	MT-IM	1000
PYC	MT-IM	1000
OGC	MT-IM	1000
DIC	MT-IM	1000
CIC	MT-IM	1000

6 Steady-state condition

This metabolic model reached in a steady-state around t=93000sec with the initial condition. Number of molecules at the steady-state are shown below. Obtaining a steady-state, this system clears requirements for Metabolic Control Analysis[Fell, 1992].

6.1 The respiratory chain

Table 51: Steady-state concentration of metabolites (respiratory chain)

name	localization	number of molecules
Q	MT-IMS	77547
QH2	MT-IMS	500
Cyt-c3+	MT-IMS	29624
Cyt-c2+	MT-IMS	999
H+	MT-IMS	3
H+	MATRIX	3

Table 52: Steady-state concentration of metabolites

name	localization	number of molecules
ATP	MT-IMS	13550(fix)
ATP	MATRIX	180
ADP	MT-IMS	1355(fix)
ADP	MATRIX	121948(fix)
GTP	MATRIX	2579
GDP	MATRIX	1338852
Pi	MT-IMS	12044(fix)
Pi	MATRIX	2507395

6.2 The TCA cycle and the inner-membrane transport

Table 53: Steady-state concentration of metabolites (TCA cycle)

name	localization	number of molecules
Cit	MT-IMS	1265 (fix)
Cit	MATRIX	583455
IsoCit	MATRIX	74758
OG	MT-IMS	63 (fix)
OG	MATRIX	424
SCoA	MATRIX	32
Suc	MATRIX	1133
Fum	MATRIX	231567
Mal	MT-IMS	1506 (fix)
Mal	MATRIX	1028383
OXA	MATRIX	302
Asp	MATRIX	244090
Asp	MT-IMS	3433 (fix)
Glu	MATRIX	801482
Glu	MT-IMS	9124 (fix)
Ala	MATRIX	1016709
Pyr	MT-IMS	27777 (fix)
Pyr	MATRIX	309(fix)
CoA	MT-IMS	700 (fix)
CoA	MATRIX	286
Acetyl-CoA	MATRIX	104498
NADH	MATRIX	3672
NAD+	MATRIX	61909
NADPH	MATRIX	7508
NADP+	MATRIX	58073
CO2	MATRIX	42631671

6.3 Fatty acid β oxidation

Table 54: Steady-state concentration of metabolites (fatty acid β oxidation 1)

name	localization	number of molecules
Car	MT-IMS	602 (fix)
Car	MATRIX	47418
PalCar	MT-IMS	1807 (fix)
PalCar	MATRIX	213280
16Acyl-CoA	MT-IMS	117 (fix)
ETFred	MATRIX	89
ETFox	MATRIX	82

Table 55: Steady-state concentration of metabolites (fatty acid β oxidation 2)

name	localization	number of molecules
16Acyl-CoA	MATRIX	331
16Enoyl-CoA	MATRIX	698
16Hydroxyacyl-CoA	MATRIX	3
16Oxoacyl-CoA	MATRIX	769
14Acyl-CoA	MATRIX	331
14Enoyl-CoA	MATRIX	699
14Hydroxyacyl-CoA	MATRIX	3
14Oxoacyl-CoA	MATRIX	771
12Acyl-CoA	MATRIX	330
12Enoyl-CoA	MATRIX	700
12Hydroxyacyl-CoA	MATRIX	2
12Oxoacyl-CoA	MATRIX	763
10Acyl-CoA	MATRIX	331
10Enoyl-CoA	MATRIX	700
10Hydroxyacyl-CoA	MATRIX	2
10Oxoacyl-CoA	MATRIX	762
8Acyl-CoA	MATRIX	332
8Enoyl-CoA	MATRIX	701
8Hydroxyacyl-CoA	MATRIX	2
8Oxoacyl-CoA	MATRIX	763
6Acyl-CoA	MATRIX	332
6Enoyl-CoA	MATRIX	701
6Hydroxyacyl-CoA	MATRIX	3
6Oxoacyl-CoA	MATRIX	764
4Acyl-CoA	MATRIX	331
4Enoyl-CoA	MATRIX	702
4Hydroxyacyl-CoA	MATRIX	2
Acetoacetyl-CoA	MATRIX	239686

7 Rate equations

7.1 AAC

$$v = \frac{\frac{k^D_{\rightarrow}(\Delta\psi)[E_{total}][ADP_{out}]}{1+\frac{k^D_{\rightarrow}(\Delta\psi)}{k^D_{\leftarrow}(\Delta\psi)}\left(1+\frac{K^{D'}}{[ADP_{in}]}\right)}}{\frac{K^{D'}}{1+\frac{k^D_{\rightarrow}(\Delta\psi)}{k^D_{\leftarrow}(\Delta\psi)}\left(1+\frac{K^{D'}}{[ADP_{in}]}\right)}+[ADP_{out}]}$$

$$k^D_{\rightarrow}(\Delta\psi) = k^D_{0\rightarrow}e^{\phi C_f}\cdot \text{normalize}$$

$$k^D_{\leftarrow}(\Delta\psi) = k^D_{0\leftarrow}e^{\phi C_r}\cdot \text{normalize}$$

$$\phi = \frac{RT}{F}ln\frac{[H_{IMS}]}{[H_{MAT}]}$$

7.2 CB Ordered Bi Bi

$$v = \frac{\left(\frac{KcF[S1][S2]}{K_{iS1}K_{mS2}} - \frac{KcR[P1][P2]}{K_{mP1}K_{iP2}}\right)[E]}{\text{denom}}$$

$$\begin{aligned}\text{denom} &= 1+\frac{[S1]}{K_{iS1}}+\frac{K_{mS1}[S2]}{K_{iS1}K_{mS2}}+\frac{K_{mP2}[P1]}{K_{mP1}K_{iP2}}+\frac{[P2]}{K_{iP2}}+\frac{[S1][S2]}{K_{iS1}K_{mS2}}\\ &+ \frac{K_{mP2}[S1][P1]}{K_{iS1}K_{mP1}K_{iP2}}+\frac{K_{mS1}[S2][P2]}{K_{iS1}K_{mS2}K_{iP2}}+\frac{[P1][P2]}{K_{mP1}K_{iP2}}+\frac{[S1][S2][P1]}{K_{iS1}K_{mS2}K_{iP1}}+\frac{[S2][P1][P2]}{K_{iS2}K_{mP1}K_{iP2}}\end{aligned}$$

7.3 Complex III

$$\begin{aligned} v &= \tfrac{K_{cF}[E_t][A][B]}{\text{denom}} \\ \text{denom} &= \left(K_{mA}K_{q2}K_{b2} + K_{mA}K_{q2}[B] + \tfrac{K_{cF}}{k_8}K_{q1}[A]K_{b1} + \tfrac{K_{cF}}{k_8}K_{q1}[A][B]\right)[Q] \\ &+ K_{mA}[B] + K_{mB}[A] + [A][B] \end{aligned}$$

7.4 Complex V

$$v = \frac{KcF[E]\left\{\frac{[ADP][Pi]}{K_dK_p}klt_f e^{-3(\beta-a_x)\phi}\left(\frac{[H^+_{IMS}]}{Khxe^{ax\phi}}\right)^3 - \frac{[ATP]}{K_t}K_{eq}klt_r e^{3(1-\beta-a_y)\phi}\left(\frac{[H^+_{MAT}]}{Khye^{-ay\phi}}\right)^3\right\}}{\left(1+\frac{[H^+_{IMS}]}{Khxe^{ax\phi}}+\frac{[H^+_{MAT}]}{Khye^{-ay\phi}}\right)^3\left(3+\frac{[ADP][Pi]}{K_dK_p}+\frac{[ATP]}{K_t}\right)}$$

where $\phi = ln\frac{[H_{IMS}]}{[H_{MAT}]}$

7.5 IDHa

$$v = \frac{k_{cat}[E]([IsoCit]^2 + b[ADP][IsoCit])}{[IsoCit]^2 + c[IsoCit] + d[ADP] + e[ADP][IsoCit] + f}$$

7.6 IDHb

$$\begin{aligned} v &= \frac{[E][NADP][IsoCit]}{\text{denom1}} - \frac{[E][NADPH][OG][CO_2]}{\text{denom2}} \\ \text{denom1} &= \phi_0[NADP][IsoCit] + \phi_1[IsoCit] + \phi_2[NADP] + \phi_{12} \\ \text{denom2} &= \phi'_0[NADPH][OG][CO_2] + \phi'_1[OG][CO_2] + \phi'_2[NADPH][CO_2] + \phi'_3[NADPH][OG] \\ &+ \phi'_{12}[CO_2] + \phi'_{13}[OG] + \phi'_{23}[NADPH] + \phi'_{123} \end{aligned}$$

7.7 Michaelis Uni Uni

$$v = \frac{K_{cF}[E][S]}{K_s + [S]}$$

7.8 Multisite Ping-Pong

$$\begin{aligned} v &= \frac{k_{cat}[E_{total}][A][B][C]}{\text{denom}} \\ \text{denom} &= K_{mC}[A][B] + K_{mB}[A][C] + K_{mA}[B][C] + [A][B][C] \\ &+ \frac{K_{mA}K_{mP}K_{ib}K_{ic}[Q][R]}{K_{mR}K_{ip}K_{iq}} + \frac{K_{mC}[A][B][R]}{K_{ir}} + \frac{K_{mB}[A][C][Q]}{K_{iq}} + \frac{K_{mA}K_{mP}K_{ib}K_{ic}[A][Q][R]}{K_{mR}K_{ip}K_{ia}K_{iq}} \end{aligned}$$

7.9 Ordered Bi Bi

$$\begin{array}{ccccccccc} & S_1 & & S_2 & & P_1 & & P_2 & \\ & \downarrow & & \downarrow & & \uparrow & & \uparrow & \\ \hline \text{E} & & ES_1 & & (ES_1S_2 \rightleftharpoons EP_1P_2) & & EP_2 & & \text{E} \end{array}$$

$$\begin{aligned} v &= \frac{K_{cF}K_{cR}[E]([S1][S2] - \frac{[P1][P2]}{K_{eq}})}{\text{denom}} \\ \text{denom} &= K_{cR}K_{iS1}K_{mS2} + K_{cR}K_{mS2}[S1] + K_{cR}K_{mS1}[S2] + \frac{K_{cF}K_{mP2}[P1]}{K_{eq}} + \frac{K_{cF}K_{mP1}[P2]}{K_{eq}} \\ &+ K_{cR}[S1][S2] + \frac{K_{cF}K_{mP2}[S1][P1]}{K_{eq}K_{iS_1}} + \frac{K_{cF}[P1][P2]}{K_{eq}} + \frac{K_{cR}K_{mS1}[S2][P2]}{K_{iq}} + \frac{K_{cR}[S1][S2][P1]}{K_{iP1}} \\ &+ \frac{K_{cF}[S2][P1][P2]}{K_{iS2}K_{eq}} \end{aligned}$$

7.10 PC

$$\begin{aligned} v &= \frac{V_1V_2[A][B][C] - \frac{V_1V_2[P][Q][R]}{K_{eq}}}{\text{denom}} \\ \text{denom} &= K_{ia}K_{mB}V_2[C] + K_{mC}V_2[A][B] + K_{mA}V_2[B][C] + K_{mB}V_2[B][C] + K_{mB}V_2[A][C] + V_2[A][B][C] \\ &+ \frac{K_{ip}K_{mQ}V_1[R]}{K_{eq}} + \frac{K_{mQ}V_1[P][R]}{K_{eq}} + \frac{K_{mP}V_1[Q][R]}{K_{eq}} + \frac{K_{mR}V_1[P][Q]}{K_{eq}} + \frac{V_1[P][Q][R]}{K_{eq}} \\ &+ \frac{K_{ia}K_{mB}V_2[C][P]}{K_{ip}} + \frac{K_{ia}K_{mB}V_2[C][Q]}{K_{ip}} + \frac{K_{iq}K_{mP}V_1[B][R]}{K_{ib}K_{eq}} + \frac{K_{iq}K_{mP}V_1[A][R]}{K_{ia}K_{eq}} \\ &+ \frac{K_{ia}V_2[A][B][R]}{K_{ir}} + \frac{K_{mR}V_1[C][P][Q]}{K_{ic}K_{eq}} + \frac{K_{mA}V_2[B][C][Q]}{K_{iq}} + \frac{K_{mA}V_2[B][C][P]}{K_{ip}} \\ &+ \frac{K_{mP}V_1[B][Q][R]}{K_{ib}K_{eq}} + \frac{K_{mQ}V_1[B][P][R]}{K_{ib}K_{eq}} \end{aligned}$$

7.11 Ping-Pong Bi Bi

$$\begin{array}{ccccccccc} & S_1 & & P_1 & & S_2 & & P_2 & \\ & \downarrow & & \uparrow & & \downarrow & & \uparrow & \\ \hline \text{E} & & (ES_1 \rightleftharpoons FP_1) & & F & & (FS_2 \rightleftharpoons EP_2) & & \text{E} \end{array}$$

$$\begin{aligned} v &= \frac{K_{cF}K_{cR}[E]([S1][S2] - \frac{[P1][P2]}{K_{eq}})}{\text{denom}} \\ \text{denom} &= K_{cR}K_{mS2}[S1] + K_{cR}K_{mS1}[S2] + \frac{K_{cF}K_{mP2}[P1]}{K_{eq}} + \frac{K_{cF}K_{mP1}[P2]}{K_{eq}} + K_{cR}[S1][S2] \\ &+ \frac{K_{cF}K_{mP2}[S1][P1]}{K_{eq}K_{iS1}} + \frac{K_{cF}[P1][P2]}{K_{eq}} + \frac{K_{cR}K_{mS1}[S2][P2]}{K_{iq}} \end{aligned}$$

7.12 Rapid Equilibrium Random Bi Bi

$$v = \frac{\frac{[A][B]}{\alpha K_{iA}K_{iB}} k_{cat}^{f}[E]_{total} - \frac{[P][Q]}{\beta K_{iP}K_{iQ}} k_{cat}^{r}[E]_{total}}{1 + \frac{[A]}{K_{iA}} + \frac{[B]}{K_{iB}} + \frac{[P]}{K_{iP}} + \frac{[Q]}{K_{iQ}} + \frac{[A][B]}{\alpha K_{iA}K_{iB}} + \frac{[P][Q]}{\beta K_{iP}K_{iQ}} + \frac{[B][Q]}{\gamma K_{iB}K_{iQ}} + \frac{[A][P]}{\delta K_{iA}K_{iP}}}$$

7.13 SCS

$$\begin{aligned}
v &= \frac{\left([A][B][C] - \frac{[P][Q][R]}{K_{eq}}\right)\left\{V_1 + V_2\left(\frac{K_{mC}[P]}{K_{mC2}K_{ip}} + \frac{[C]}{K_{mC2}}\right)\right\}}{\text{denom}} \\
\text{denom} &= K_{ia}K_{mB}[C] + K_{mB}[A][C] + K_{mA}[B][C] + K_{mC}[A][B] + [A][B][C] \\
&+ \frac{[A][B][C]^2}{K_{mC2}} + \frac{K_{ia}K_{mB}K_{mC}[P]}{K_{ip}} + \frac{K_{ia}K_{mB}K_{mC}[P][Q]}{K_{ip}K_{iq}} + \frac{K_{ia}K_{mB}K_{mC}[P][R]}{K_{ip}K_{ir}} \\
&+ \frac{K_{ia}K_{mB}K_{ic}[Q][R]}{K_{mQ}K_{ir}} + \frac{K_{ia}K_{mB}K_{mC}[P][Q][R]}{K_{ip}K_{mQ}K_{ir}} + \frac{K_{ia}K_{mB}K_{mC}[P]^2[Q][R]}{K_{ip}K_{mP2}K_{mQ}K_{ir}} \\
&+ \frac{K_{ia}K_{mB}[C][Q]}{K_{iq}} + \frac{K_{ia}K_{mB}[C][R]}{K_{ir}} + \frac{K_{ia}K_{mB}[C][Q][R]}{K_{mQ}K_{ir}} + \frac{K_{ia}K_{mB}[C][P][Q][R]}{K_{mP2}K_{mQ}K_{ir}} \\
&+ \frac{K_{mB}K_{mC}[A][P]}{K_{ip}} + \frac{K_{mA}K_{mC}[B][P]}{K_{ip}} + \frac{K_{mC}[A][B][P]}{K_{ip}} + \frac{K_{mC}[A][B][C][P]}{K_{mC2}K_{ip}} \\
&+ \frac{K_{mA}[B][C][Q]}{K_{iq}} + \frac{K_{mB}[A][C][R]}{K_{ir}} + \frac{K_{mA}K_{mC}[B][P][Q]}{K_{ip}K_{iq}} + \frac{K_{mB}K_{mC}[A][P][R]}{K_{ip}K_{ir}}
\end{aligned}$$

7.14 Uni Uni Reversible

$$v = \frac{(K_{cF}K_p[S] - K_{cR}K_s[P])[E]}{K_s[P] + K_p[S] + KsKp}$$

8 MeSH term and literature search

The mitochondrial model was built through comprehensive literature search. Here we show the tendency of MeSH terms embedded in the articles that were crucial for determination of the rate equations.

Table 56: The MeSH term tendency of the articles on the reaction mechanism of each enzyme

Literature	Kinetics	Models	Mathematics	enzyme name	substrate name
[Barden et al., 1972]	+	+, Chemical	+	-	+
[Beckmann and Frerman, 1985]	+	-	-	+	-
[Crow et al., 1983]	+	-	+	+	+
[Davisson and Schulz, 1985]	+	+, Biological	-	+	+
[De Rosa et al., 1979]	-	-	-	+	-
[Dierks and Krämer, 1988]	+	-	-	+	-
[Fato et al., 1996]	+	-	-	+	+
[Grivennikova et al., 1993]	-	-	-	+	-
[Guarriero-Bobyleva et al., 1978]	+	-	-	+	+
[Hamada et al., 1975]	+	-	-	+	+
[Indiveri et al., 1991b]	+	-	-	+	+
[Indiveri et al., 1991a]	+	-	-	+	+
[Indiveri et al., 1994]	+	-	-	+	+
[Kholodenko, 1993]	+	+	-	+	+
[Krämer and Klingenberg, 1982]	+	-	-	+	+
[Kubota et al., 1992]	+	-	-	+	+
[Malmström and Andréasson, 1985]	+	-	-	+	+
[Mann et al., 1995]	+	-	-	+	+
[Matsuoka and Srere, 1973]	+	-	+	+	+
[McKean et al., 1979]	+	-	-	-	+
[Miyazawa et al., 1981]	+	-	-	+	-
[Mukherjee and Srere, 1976]	-	-	-	-	+
[Plaut et al., 1974]	+	+, Chemical	+	+	+
[Ramsay et al., 1987]	+	-	-	+	+
[Sluse et al., 1991]	+	-	-	+	+
[Stappen and Krämer, 1994]	+	-	-	+	-
[Yang and Schulz, 1987]	+	+, Theoretical	+	+	+
Frequency	24/27	5/27	5/27	24/27	21/27

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