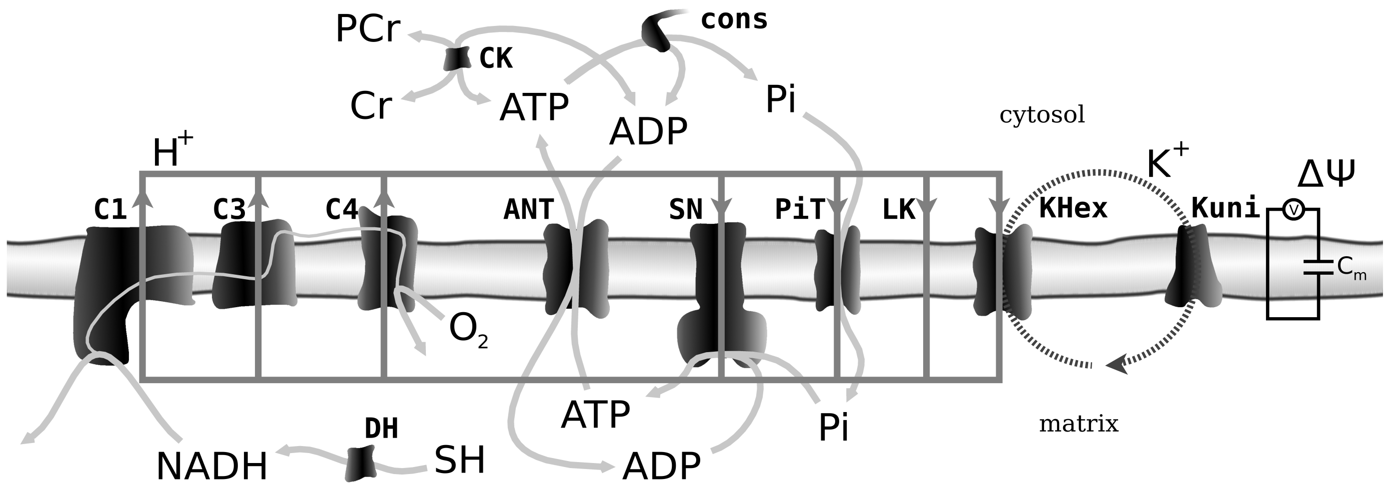

In calculations all concentrations are expressed in μM, all rates in $\mu M \cdot min^{-1}$ and electrostatic and redox potentials in mV

I. INDEPENDENT MODEL VARIABLES

a) protons concentration in matrix	$[H^+]_i$
b) protons concentration in cytosol	$[H^+]_e$
c) potassium concentration in matrix	$[K^+]_i$
d) potassium concentration in cytosol	$[K^+]_e$
e) phosphate concentration in matrix	$[Pi]_i$
f) phosphate concentration in cytosol	$[Pi]_e$
g) ADP concentration in cytosol	$[ADP]_e$
h) ATP concentration in matrix	$[ATP]_i$
i) ATP concentration in cytosol	$[ATP]_e$
j) creatine phosphate concentration	$[PCr]$
k) oxygen concentration	$[O_2]$
l) NAD^+ concentration	$[NAD_r]$
m) ubiquinol concentration	$[UQ_r]$
n) reduced cytochrome c concentration	$[cytc_r]$
o) transmembrane potential	$\Delta\Psi$

II. MODEL CONSTANTS

a)	total adenine nucleotides concentration in matrix	$[AXP]_i$	16.26 mM
b)	total adenine nucleotides concentration in cytosol	$[AXP]_e$	6.7 mM
c)	creatine pool size	$[Cr_t]$	25 mM
d)	total nicotinamide dinucleotide concentration	$[NAD_t]$	2.79 mM
e)	total ubiquinone/ubiquinol concentration	$[UQ_t]$	1.35 mM
f)	total cytochrome c concentration	$[cytc_t]$	0.27 mM
g)	total cytochrome a concentration	$[cyta_t]$	0.135 mM
h)	matrix magnesium concentration	$[Mg^{2+}]_i$	0.38 mM
i)	cytosol magnesium concentration	$[Mg^{2+}]_e$	4 mM
j)	phosphate dissociation constant	pK_{Pi}	6.8
k)	ADP magnesium binding constant in matrix	$k_{d,ADP,i}$	282 μM^{-1}
l)	ADP magnesium binding constant in cytosol	$k_{d,ADP,e}$	347 μM^{-1}
m)	ATP magnesium binding constant in matrix	$k_{d,ATP,i}$	17 μM^{-1}
n)	ATP magnesium binding constant in cytosol	$k_{d,ATP,e}$	24 μM^{-1}
o)	NAD standard redox potential	$Em_{NAD,0}$	-320 mV
p)	UQ standard redox potential	$Em_{UQ,0}$	40 mV
q)	cytochrome c standard redox potential	$Em_{cytc,0}$	250 mV
r)	cytochrome a standard redox potential	$Em_{cyta,0}$	540 mV
s)	ATP synthase proton stoichiometry	n_A	2.5
t)	cell to mitochondrial volume ratio	R_{cm}	4.35
u)	NAD buffering capacity coefficient	$buff_{NAD}$	5
v)	inner membrane electrical capacitance	C_m	1 $\mu M \cdot mV^{-1}$

III.DEPENDENT MODEL VARIABLES

a) monovalent phosphate ion concentration in matrix $$[Pi]_{i,j}=\frac{[Pi]_i}{1+10^{(pH_i-pK_{Pi})}}$$

b) monovalent phosphate ion concentration in cytosol $$[Pi]_{e,j}=\frac{[Pi]_e}{1+10^{(pH_e-pK_{Pi})}}$$

c) AMP concentration in cytosol $$[AMP]_e=[AXP]_e-([ATP]_e+[ADP]_e)$$

d) ADP concentration in matrix $$[ADP]_i=[AXP]_i-[ATP]_i$$

e) free ADP in matrix $$[ADP]_{i,f}=\frac{[ADP]_i}{1+\frac{[Mg^{2+}]_i}{k_{d,ADP,i}}}$$

f) magnesium bound ADP in matrix $$[ADP]_{i,m}=[ADP]_i-[ADP]_{i,f}$$

g) free ADP in cytosol $$[ADP]_{e,f}=\frac{[ADP]_e}{1+\frac{[Mg^{2+}]_e}{k_{d,ADP,e}}}$$

h) magnesium bound ADP in cytosol $$[ADP]_{e,m}=[ADP]_e-[ADP]_{e,f}$$

i) free ATP in matrix $$[ATP]_{i,f}=\frac{[ATP]_i}{1+\frac{[Mg^{2+}]_i}{k_{d,ATP,i}}}$$

j) magnesium bound ATP in matrix $$[ATP]_{i,m}=[ATP]_i-[ATP]_{i,f}$$

k) free ATP in cytosol $$[ATP]_{e,f}=\frac{[ATP]_e}{1+\frac{[Mg^{2+}]_e}{k_{d,ATP,e}}}$$

l) magnesium bound ATP in cytosol $$[ATP]_{e,m}=[ATP]_e-[ATP]_{e,f}$$

m) creatine concentration $$[Cr]=[Cr_t]-[PCr]$$

n) NAD redox potential $$Em_{NAD}=Em_{NAD,0}+\frac{1}{2}\cdot\frac{R\cdot T}{F}\cdot\ln\left(\frac{[NAD_o]}{[NAD_r]}\right)$$

o) NADH concentration $$[NAD_o]=[NAD_t]-[NAD_r]$$

p) ubiquinone redox potential $$Em_{UQ}=Em_{UQ,0}+\frac{1}{2}\cdot\frac{R\cdot T}{F}\cdot\ln\left(\frac{[UQ_o]}{[UQ_r]}\right)$$

q) ubiquinone concentration $$[UQ_o]=[UQ_t]-[UQ_r]$$

r) cytochrome c redox potential $$Em_{cytc}=Em_{cytc,0}+\frac{R\cdot T}{F}\cdot\ln\left(\frac{[cytc_o]}{[cytc_r]}\right)$$

s) oxidized cytochrome c concentration $$[cytc_o]=[cytc_t]-[cytc_r]$$

III.DEPENDENT MODEL VARIABLES

t) cytochrome a redox potential $Em_{cyta}=Em_{cytc}+\Delta p-\Delta\Psi$

u) reduced cytochrome a concentration $$[cyta_r]=\frac{[cyta_t]}{1+e^{\frac{F}{R\cdot T}\cdot(Em_{cyta}-Em_{cyta,0})}}$$

v) oxidized cytochrome a concentration $[cyta_o]=[cyta_t]-[cyta_r]$

w) H^+ buffering capacity coefficient for matrix $$buff_{H_i^+}=0.022\cdot\left(\frac{\left(10^{-pH_i}-10^{-pH_i-0.001}\right)}{0.001}\right)^{-1}$$

x) H^+ buffering capacity coefficient for cytosol $$buff_{H_e^+}=0.025\cdot\left(\frac{\left(10^{-pH_e}-10^{-pH_e-0.001}\right)}{0.001}\right)^{-1}$$

IV.EXTRAMITOCHONDRIAL PROCESSES

a) ATP consumption $$v_{cons}=\frac{k_{cons}}{1+\frac{Km_{cons,ATP}}{[ATP]_e}}$$

$k_{cons}=13937\ \mu M\cdot min^{-1}$

$Km_{cons,ATP}=150\ \mu M$

b) creatine kinase $v_{CK}=k_{CK,f}\cdot[ADP]_e\cdot[PCr]-k_{CK,b}\cdot[ATP]_e\cdot[Cr]$

$k_{CK,f}=6.60560\ \mu M^{-1}\cdot min^{-1}$

$k_{CK,f}=0.0030025441\ \mu M^{-1}\cdot min^{-1}$

c) adenylate kinase $v_{AK}=k_{AK,f}\cdot[ADP]_{e,f}\cdot[ADP]_{e,m}-k_{AK,b}\cdot[ATP]_{e,m}\cdot[AMP]_e$

$k_{AK,f}=2956.98\ \mu M^{-1}\cdot min^{-1}$

$k_{AK,b}=78.0208\ \mu M^{-1}\cdot min^{-1}$

d) glycolysis $v_{glyc}=0.2\cdot v_{DH}$

e) proton efflux $v_{EFF}=k_{EFF}\cdot(7.0-pH_e)$

$k_{EFF}=10000\ \mu M\cdot min^{-1}\cdot pH\ unit^{-1}$

V.INTRAMITOCHONDRIAL PROCESSES

a) substrate dehydrogenation $$v_{DH}=k_{DH}\cdot\frac{1}{1+\frac{Km_{DH,NAD}}{\left(\frac{[NAD_o]}{[NAD_r]}\right)^{pD_{DH}}}}$$

$k_{DH}=96293\ \mu M\cdot min^{-1}$

$Km_{DH,NAD}=100$

$pD_{DH}=0.8$

VI.INNER MITOCHONDRIAL MEMBRANE PROCESSES

a) complex I

$$v_{C1}=k_{C1}\cdot\Delta G_{C1}$$
$$k_{C1}=819.61\ \mu M\cdot min^{-1}\cdot mV^{-1}$$
$$\Delta G_{C1}=Em_{UQ}-Em_{NAD}-2\cdot\Delta p$$

b) complex III

$$v_{C3}=k_{C3}\cdot\Delta G_{C3}$$
$$k_{C3}=467.9\ \mu M\cdot min^{-1}\cdot mV^{-1}$$
$$\Delta G_{C3}=Em_{cytc}-Em_{UQ}-2\cdot\Delta p+\Delta\Psi$$

c) complex IV

$$v_{C4}=k_{C4}\cdot[cytc_r]\cdot[cyta_r]\cdot\frac{1}{1+\frac{Km_{C4,O_2}}{[O_2]}}$$
$$k_{C4}=24.696\ \mu M^{-1}\cdot min^{-1}$$
$$Km_{C4,O_2}=150\ \mu M$$

d) proton leak

$$v_{LK}=k_{LK,1}\cdot\left(e^{k_{LK,2}\cdot\Delta p}-1\right)$$
$$k_{LK,1}=8.5758\ \mu M\cdot min^{-1}$$
$$k_{LK,2}=0.038\ mV^{-1}$$

e) ATP synthase

$$v_{SN}=k_{SN}\cdot\frac{\gamma_{SN}-1}{\gamma_{SN}+1}$$
$$k_{SN}=117706\ \mu M\cdot min^{-1}$$
$$\ln(\gamma_{SN})=n_A\cdot\frac{F\cdot\Delta p}{R\cdot T}-\left(\frac{\Delta G_{SN,0}}{R\cdot T}+\ln\left(\frac{[ATP]_i\cdot 10^6\mu M}{[ADP]_i\cdot[Pi]_i}\right)\right)$$
$$\Delta G_{SN,0}=31.9\ kJ\cdot mol^{-1}$$

f) adenine nucleotides antiport

$$v_{ANT}=\quad k_{ANT}\cdot\frac{1}{1+\frac{Km_{ANT,ADP}}{[ADP]_{e,f}}}\cdot$$
$$\cdot\left(\frac{[ADP]_{e,f}}{[ADP]_{e,f}+[ATP]_{e,f}\cdot e^{-\frac{F}{R\cdot T}\cdot(1-f_{ANT})\cdot\Delta\Psi}}-\frac{[ADP]_{i,f}}{[ADP]_{i,f}+[ATP]_{i,f}\cdot e^{-\frac{F}{R\cdot T}\cdot f_{ANT}\cdot\Delta\Psi}}\right)$$
$$k_{ANT}=187185\ \mu M\cdot min^{-1}$$
$$Km_{ANT,ADP}=3.5\ \mu M$$
$$f_{ANT}=0.65$$

g) phosphate translocator

$$v_{PiT}=k_{PiT}\cdot\left([Pi]_{e,j}\cdot[H^+]_e-[Pi]_{i,j}\cdot[H^+]_i\right)$$
$$k_{PiT}=238.1\ \mu M^{-1}\cdot min^{-1}$$

h) potassium uniport

$$v_{Kuni}=k_{Kuni}\cdot\left([K^+]_e\cdot e^{\frac{F}{R\cdot T}\cdot\frac{-\Delta\Psi}{2}}-[K^+]_i\cdot e^{\frac{F}{R\cdot T}\cdot\frac{\Delta\Psi}{2}}\right)$$
$$k_{Kuni}=0.00001\ min^{-1}$$

i) H^+/K^+ exchanger

$$v_{KHex}=k_{KHex}\cdot\left([K^+]_i\cdot[H^+]_e-[K^+]_e\cdot[H^+]_i\right)$$
$$k_{KHex}=0.003452\ \mu M^{-1}\cdot min^{-1}$$

VII.DIFFERENTIAL EQUATIONS

a) protons concentration in matrix
$$[\dot{H^+}]_i = \begin{pmatrix} -4\cdot v_{C1} - 2\cdot v_{C3} - 4\cdot v_{C4} + \\ + n_A\cdot v_{SN} + v_{PiT} + v_{LK} + v_{KHex} \end{pmatrix} \cdot R_{cm} \cdot buff_{H_i^+}^{-1}$$

b) protons concentration in cytosol
$$[\dot{H^+}]_e = \begin{pmatrix} 4\cdot v_{C1} + 4\cdot v_{C3} + 2\cdot v_{C4} + \\ - n_A\cdot v_{SN} - v_{PiT} - v_{LK} - v_{KHex} - v_{EFF} \end{pmatrix} \cdot buff_{H_e^+}^{-1}$$

c) potassium concentration in matrix
$$[\dot{K^+}]_i = (v_{Kuni} - v_{KHex})\cdot R_{cm}$$

d) potassium concentration in cytosol
$$[\dot{K^+}]_e = 0$$

e) phosphate concentration in matrix
$$[\dot{Pi}]_i = (v_{PiT} - v_{SN})\cdot R_{cm}$$

f) phosphate concentration in cytosol
$$[\dot{Pi}]_e = v_{cons} - v_{PiT} - v_{glyc}$$

g) ADP concentration in cytosol
$$[\dot{ADP}]_e = v_{cons} - v_{ANT} - 2\cdot v_{AK} - v_{CK} - v_{glyc}$$

h) ATP concentration in matrix
$$[\dot{ATP}]_i = (v_{SN} - v_{ANT})\cdot R_{cm}$$

i) ATP concentration in cytosol
$$[\dot{ATP}]_e = v_{ANT} - v_{cons} + v_{AK} + v_{CK} + v_{glyc}$$

j) creatine phosphate concentration
$$[\dot{PCr}] = -v_{CK}$$

k) oxygen concentration
$$[\dot{O_2}] = 0$$

l) NAD^+ concentration
$$[\dot{NAD_r}] = (v_{DH} - v_{C1})\cdot R_{cm}\cdot buff_{NAD}^{-1}$$

m) ubiquinol concentration
$$[\dot{UQ_r}] = (v_{C1} - v_{C3})\cdot R_{cm}$$

n) reduced cytochrome c concentration
$$[\dot{cytc_r}] = (v_{C3} - v_{C4})\cdot R_{cm}$$

o) transmembrane potential
$$\Delta\dot{\Psi} = \begin{pmatrix} -4\cdot v_{C1} - 2\cdot v_{C3} - 4\cdot v_{C4} + \\ + n_A\cdot v_{SN} + v_{ANT} + v_{LK} + v_{Kuni} \end{pmatrix} \cdot R_{cm}\cdot C_m^{-1}$$