Concise complete kinetic description of the dynamic model of oxidative phosphorylation in intact skeletal muscle. Subscripts: e, external (cytosolic); i, internal (mitochondrial); t, total; f, free; m, magnesium complex; j, monovalent.

KINETIC EQUATIONS

(All reaction rates are expressed in μM min^{-1}).

Substrate dehydrogenation:

$$v_{DH} = k_{DH} \frac{1}{\left(1 + \frac{K_{mN}}{NAD^{+}/NADH}\right)^{p_D}}$$

k_{DH}= 28074 μM min^{-1}, K_{mN}=100, p_D=0.8

Complex I:

$$v_{C1} = k_{C1} \cdot \Delta G_{C1}$$

k_{C1}= 238.95 μM mV^{-1} min^{-1}

Complex III:

$$v_{C3} = k_{C3} \cdot \Delta G_{C3}$$

k_{C3}= 136.41 μM mV^{-1} min^{-1}

Complex IV:

$$v_{C4} = k_{C4} \cdot a^{2+} \cdot c^{2+} \frac{1}{1 + \frac{K_{mO}}{O_2}}$$

k_{C4}= 3.600 μM^{-1} min^{-1}, K_{mO}=120 μM (apparent K_{mO}=0.8 μM)

ATP synthase:

$$v_{SN} = k_{SN} \frac{\gamma - 1}{\gamma + 1}$$

k_{SN}= 34316 μM min^{-1}, $\gamma = 10^{\Delta G_{SN}/Z}$

ATP/ADP carrier:

$$v_{EX} = k_{EX} \cdot \left(\frac{ADP_{fe}}{ADP_{fe} + ATP_{fe} \cdot 10^{-\Psi_e/Z}} - \frac{ADP_{fi}}{ADP_{fi} + ATP_{fi} \cdot 10^{-\Psi_i/Z}} \right) \cdot \left(\frac{1}{1 + K_{mADP} / ADP_{fe}} \right)$$

k_{EX}= 54572 μM min^{-1}, K_{mADP}=3.5 μM

Phosphate carrier:

$$v_{PI} = k_{PI} \cdot \left(Pi_{je} \cdot H_e - Pi_{ji} \cdot H_i \right)$$

k_{PI}= 69.421 μM^{-1} min^{-1}

ATP usage:

$$v_{UT} = k_{UT} \frac{1}{1 + \frac{K_{mA}}{ATP_{te}}}$$

k_{UT}= 686.50 μM min^{-1} (resting state), K_{mA}=150 μM

Proton leak:

$$v_{LK} = k_{LK1} \cdot \left(e^{k_{LK2} \cdot \Delta p} - 1 \right)$$

k_{LK1}= 2.500 μM min^{-1}, k_{LK2}=0.038 mV^{-1}

Adenylate kinase:

$$v_{AK} = k_{fAK} \cdot ADP_{fe} \cdot ADP_{me} - k_{bAK} \cdot ATP_{me} \cdot AMP_e$$

k_{fAK}= 862.10 μM^{-1} min^{-1}, k_{bAK}= 22.747 μM^{-1} min^{-1}

Creatine kinase:

$$v_{CK} = k_{fCK} \cdot ADP_{te} \cdot PCr \cdot H_e^+ - k_{bCK} \cdot ATP_{te} \cdot Cr$$

k_{fCK} = 1.9258 μM^{-2} min^{-1}, k_{bCK} = 0.00087538 μM^{-1} min^{-1}

Proton efflux:

$$v_{EFF} = k_{EFF} \cdot (pH_0 - pH_e)$$

k_{EFF} = 10000 μM min^{-1}, pH_0 = 7.0

SET OF DIFFERENTIAL EQUATIONS

$$\dot{NADH} = (v_{DH} - v_{C1}) \cdot R_{cm} / B_N$$

$$\dot{UQH}_2 = (v_{C1} - v_{C3}) \cdot R_{cm}$$

$$\dot{c}^{2+} = (v_{C3} - 2 \cdot v_{C4}) \cdot 2 \cdot R_{cm}$$

$\dot{O}_2 = 0$ (constant saturated oxygen concentration = 240 μM) or $\dot{O}_2 = -v_{C4}$

$$\dot{H}_i^+ = -(2 \cdot (2 + 2 \cdot u) \cdot v_{C4} + (4 - 2 \cdot u) \cdot v_{C3} + 4 \cdot v_{C1} - n_A \cdot v_{SN} - u \cdot v_{EX} - (1 - u) \cdot v_{PI} - v_{LK}) \cdot R_{cm} / r_{buffi}$$

$$\dot{ATP}_{ti} = (v_{SN} - v_{EX}) \cdot R_{cm}$$

$$\dot{Pi}_{ti} = (v_{PI} - v_{SN}) \cdot R_{cm}$$

$$\dot{ATP}_{te} = v_{EX} - v_{UT} + v_{AK} + v_{CK}$$

$$\dot{ADP}_{te} = v_{UT} - v_{EX} - 2 \cdot v_{AK} - v_{CK}$$

$$\dot{Pi}_{te} = v_{UT} - v_{PI}$$

$$\dot{PCr} = -v_{CK}$$

$$\dot{H}_e^+ = \begin{pmatrix} 2 \cdot (2 + 2 \cdot u) \cdot v_{C4} + (4 - 2 \cdot u) \cdot v_{C3} + 4 \cdot v_{C1} - n_A \cdot v_{SN} - u \cdot v_{EX} - (1 - u) \cdot v_{PI} - v_{LK} - \\ s \cdot v_{CK} - v_{EFF} \end{pmatrix} / r_{buffe}$$

$s = 0.63-(pH_e-6.0)*0.43$ (proton stoichiometry for creatine kinase Lohman reaction)

$R_{cm} = 15$ (cell volume/mitochondria volume ratio)

$B_N = 5$ (buffering capacity coefficient for NAD)

CALCULATIONS

$c^{3+} = c_t - c^{2+}$

$c_t = 270\ \mu M$ (= $c^{2+} + c^{3+}$, total concentration of cytochrome c)

$UQ = U_t - UQH_2$

$U_t = 1350\ \mu M$ (= $UQH_2 + UQ$, total concentration of ubiquinone)

$NAD^+ = N_t - NADH$

$N_t = 2970\ \mu M$ (= $NADH + NAD^+$, total concentration of NAD)

$AMP_e = A_{eSUM} - ATP_{te} - ADP_{te}$

$A_{eSUM} = 6700.2\ \mu M$ (= $ATP_{te} + ADP_{te} + AMP_e$, total external adenine nucleotide concentration)

$ADP_{ti} = A_{iSUM} - ATP_{ti}$

$A_{iSUM} = 16260\ \mu M$ (= $ATP_{ti} + ADP_{ti}$, total internal adenine nucleotide concentration)

$Cr = C_{SUM} - PCr$

$C_{SUM} = 35000\ \mu M$ (= $Cr + PCr$, total creatine concentration)

$P_{SUM} = 55659\ \mu M$ (= $PCr+3ATP_{te}+2ADP_{te}+AMP_e+Pi_{te}+(3ATP_{ti}+2ADP_{ti}+Pi_{ti})/R_{cm}$, total phosphate pool)

$Mg_{fe} = 4000\ \mu M$ (free external magnesium concentration)

$ATP_{fe} = ATP_{te}/(1+Mg_{fe}/k_{DTe})$

$k_{DTe} = 24\ \mu M$ (magnesium dissociation constant for external ATP)

$ATP_{me} = ATP_{te} - ATP_{fe}$

$ADP_{fe} = ADP_{te}/(1+Mg_{fe}/k_{DDe})$

$k_{DDe} = 347\ \mu M$ (magnesium dissociation constant for external ADP)

$ADP_{me} = ADP_{te} - ADP_{fe}$

$Mg_{fi} = 380\ \mu M$ (free internal magnesium concentration)

$ATP_{fi} = ATP_{ti}/(1+Mg_{fi}/k_{DTi})$

$k_{DTi} = 17\ \mu M$ (magnesium dissociation constant for internal ATP)

$ATP_{mi} = ATP_{ti} - ATP_{fi}$

$ADP_{fi} = ADP_{ti}/(1+Mg_{fi}/k_{DDi})$

$k_{DDi} = 282\ \mu M$ (magnesium dissociation constant for internal ADP)

$ADP_{mi} = ADP_{ti} - ADP_{fi}$

$T = 298$

$R = 0.0083\ kJ{*}mol^{-1}{*}K^{-1}$

$F = 0.0965\ kJ{*}mol^{-1}{*}mV^{-1}$

$S = 2.303{*}R{*}T$

$Z = 2.303{*}R{*}T/F$

$u = 0.861$ ($= \Delta\Psi/\Delta p$)

$pH_e = -\log(H_e/1000000)$ (H_e expressed in μM)

$pH_i = -\log(H_i/1000000)$ (H_i expressed in μM)

$\Delta pH = Z\ (pH_i - pH_e)$

$\Delta p = 1/(1-u)\ \Delta pH$

$\Delta\Psi = -\ (\Delta p - \Delta pH)$

$\Psi i = 0.65{*}\Delta\Psi$

$\Psi e = -\ 0.35{*}\Delta\Psi$

$c_{0i} = (10^{-pHi}-10^{-pHi-dpH})/dpH$ ('natural' buffering capacity for H^+ in matrix)

$dpH = 0.001$

$r_{buffi} = c_{buffi}/c_{0i}$ (buffering capacity coefficient for H^+ in matrix)

$c_{buffi} = 0.022\ M\ H^+/pH$ unit (buffering capacity for H^+ in matrix)

$c_{0e} = (10^{-pHe}-10^{-pHe-dpH})/dpH$ ('natural' buffering capacity for H^+ in cytosol)

$dpH = 0.001$

$r_{buffe} = c_{buffe}/c_{0e}$ (buffering capacity coefficient for H^+ in cytosol)

$c_{buffe} = 0.025\ M\ H^+/pH$ unit (buffering capacity for H^+ in cytosol)

$Pi_{je} = Pi_{te}/(1+10^{pHe-pKa})$

$Pi_{ji} = Pi_{ti}/(1+10^{pHi-pKa})$

$pK_a = 6.8$

$\Delta G_{SN} = n_A * \Delta p - \Delta G_P$ (thermodynamic span of ATP synthase)

$\Delta G_P = \Delta G_{P0}/F + Z * \log(1000000 * ATP_{ti}/(ADP_{ti} * Pi_{ti}))$ (concentrations expressed in μM)

$n_A = 2.5$ (phenomenological H^+/ATP stoichiometry of ATP syntahse)

$\Delta G_{P0} = 31.9\ kJ * mol^{-1}$

$E_{mN} = E_{mN0}+Z/2 * \log(NAD^+/NADH)$ (NAD redox potential)

$E_{mN0} = -320\ mV$

$E_{mU} = E_{mU0}+Z/2 * \log(UQ/UQH_2)$ (ubiquinone redox potential)

$E_{mU0} = 85\ mV$

$E_{mc} = E_{mc0}+Z * \log(c^{3+}/c^{2+})$ (cytochrome c redox potential)

$E_{mc0} = 250\ mV$

$E_{ma} = E_{mc}+\Delta p*(2+2u)/2$ (cytochrome a_3 redox potential)

$A_{3/2} = 10^{(Ema-Ema0)/Z}$ (a^{3+}/a^{2+} ratio)

$a^{2+} = a_t/(1+A_{3/2})$ (concentration of reduced cytochrome a_3)

$a^{3+} = a_t - a^{2+}$

$a_t = 135\ \mu M$

$E_{ma0} = 540\ mV$

$\Delta G_{C1} = E_{mU}-E_{mN}-\Delta p*4/2$ (thermodynamic span of complex I)

$\Delta G_{C3} = E_{mc}-E_{mU}-\Delta p*(4-2u)/2$ (thermodynamic span of complex III)