**Model constants**

|  |  |  |  |
| --- | --- | --- | --- |
| **Units** | **Value** | **Description** | **Symbol** |
| **General model constants** | | | |
| C/m | 96847 | Faraday's constant | F |
| mJ/(M·K˚) | 8314 | Gas constant | R |
| K° | 308 | Temperature | T |
| pF | 0.05 | Cell capacitance | Cm |
| mM | 0.000071 | Intracellular Ca2+ | [Ca2+]i |
| mM | 2.5 | Extracellular Ca2+ | [Ca2+]o |
| mM | 8.4 | Intracellular Na+ | [Na+]i |
| mM | 140 | Extracellular Na+ | [Na+]o |
| mM | 140 | Intracellular K+ | [K+]i |
| mM | 5 | Extracellular K+ | [K+]c |
| nL | 0.0126 | Cytoplasmic volume | Vi |
| nL | 0.005884 | Ca2+ intracellular volume | VCa |
| nL | 0.0025 | Cell volume | Vc |
| nL | 0.0003969 | SR uptake compartment volume | Vup |
| nL | 0.000044 | SR release compartment volume | Vrel |
| pA | -15000 | Stimulus current | Is |
| **Current constants** | | | |
| nS | 3.5 | Maximal conductance for fast delayed rectifying K+ channels | gK,r |
| nS | 2.5 | Maximal conductance for slow delayed rectifying K+ channels | gK,s |
| nS | 3.5 | Maximal conductance for inward rectifying K+ channels | gK1 |
| [] | 0.59 | Equilibrium binding constant for K+ dependence of the IK1 channels | km,K1 |
| nS | 50.02 | Maximal conductance for transient outward K+ channels | gK,to |
| nS | 2.4 | Maximal conductance for sustained outward K+ channels | gsus |
| [pA] | 64.41 | Maximal current of the Na-K pumps | INaK,max |
| [] | 1 | Equilibrium binding constant of K to the pump | km,k |
| [] | 11 | Equilibrium binding constant of Na to the pump | km,Na |
| [] | 0.45 | Position of Eyring rate theory energy barrier controlling voltage dependence of NCX | γNaCa |
| [] | 0.0003 | Denominator constant for INaCa | dNaCa |
| nS | 0.0014 | Maximal conductance for Na+ channels | gNa |
| pA | 9.509 | Maximal current of the membranal Ca2+ pumps | ICaP,max |
| mV | 50 | Reversal potential of L-type Ca2+ channels | ECa,L |
| nS | 4 | Maximal conductance of L-type Ca2+ channels | gCa,L |
| mV | 38 | Reversal potential of T-type Ca2+ channels | ECa,T |
| nS | 6 | Maximal conductance of T-type Ca2+ channels | gCa,T |
| nS | 0.03 | Leakage conductance for Na | gNa,b |
| nS | 0.03 | Leakage conductance for Ca | gCa,b |
| pA | 2800 | Maximal Ca2+ uptake current by the SR | Iup,max |
| [] | 0.0003 | Equilibrium binding Ca2+ concentration on the cytosol side | Kcy,Ca |
| [] | 0.5 | Equilibrium binding Ca2+ concentration on uptake compartment of the SR side | Ksr,Ca |
| [] | 0.4 | Translocation constant | Kxcs |
| pA/mM | 200000 | Rate constant for Ca2+ release | αrel |
| 1/s | 0.815 | Rate constant for recovery of the Ca2+-dependent-Ca2+ release channels from inactivated state | krecov |
| mM | 0.0003 | Equilibrium binding constant of SR Ca2+ release gate for [Ca2+]in | KM,rel |
| **Force generation constants** | | | |
| µm | 0.8 | A constant coefﬁcient that describes the effect of the actin- and myosin-ﬁlament lengths on the single overlap length. Actin- and myosin-ﬁlament lengths on the single overlap length | SL0 |
| 1/mm2 | 2\*1013 | The SAN cross-section area | NC |
| 1/mM | 350 | The cross-bridge independent coefﬁcient of calcium  afﬁnity. | Fk0 |
| 1/mM | 3000 | The cooperativity coefﬁcient. Describes the dependence of calcium afﬁnity on the number of strong cross-bridges | Fk1 |
|  | 3.5 | Hill coefficient | FN |
| 1/mm3 | 2.5\*109 | Half-maximal cross-bridge Ca2+ affinity | Fk,0.5 |
| 1/mM/ms | 60 | The rate constant of calcium binding to troponin low-afﬁnity sites. | Fkl |
| 1/ms | 0.04 | The cross-bridge turnover rate from the weak to the strong conformation. | Ff |
| 1/ms | 0.03 | The cross-bridge weakening rate at isometric regime | Fg0 |
| 1/m | 4.4\*106 | The mechanical-feedback coefﬁcient. Describes the dependence of the XB weakening rate on the shortening velocity | Fg1 |
| mN | 2\*10-9 | The unitary force per cross-bridge at isometric regime | FXB |
| **Energy and oxygen consumption** | | | |
| mM | 0.02533 | Maximal ATP consumption by the sarcomeres | ATPmax |
| mM | 2.6 | ATP concentration in the cytoplasm | CATPi |
| 1/min | 0.016 | Non- Ca2+ AC activity | KACI |
| 1/min | 0.0735 | Non-Ca2+ AC activation | KAC |
| ms-1 | 0.5421 | Ca2+ dissociation constant for calmodulin | kbCM |
| mM | 0.000178 | Maximal Ca2+ AC activation | KCa |
| mM -1· ms-1 | 227.7 | Ca2+ association constant for calmodulin | kfCM |
| mM | 0.000024 | Half-maximal Ca2+ AC activation | KACCa |
| [] | 0.03 | Constant representing the dependence of force generation on the energy state of the cell | kXBATP |
| [] | 0.26 | Constant representing the dependence of force generation on the energy state of the cell | kXBADP |
| **Mitochondrial Ca2+ handling parameters** | | | |
| mM/ms | 0.0275 | Maximal uniporter Ca2+ transport | Vunimax |
| mV | 91 | Offset membrane potential | 0Ψ |
| mM | 3.8·10-4 | Activation constant | Kact |
| mM | 0.019 | Kd for translocated Ca2+ | Ktrans |
| [] | 110 | Keq for conformational transitions in uniporter | L |
| [] | 2.8 | Uniporter activation cooperativity | na |
| mM/ms | 10-4 | Vmax of Na/Ca antiporter | VNaCa max |
| [] | 0.5 | ΔΨm dependence of Na/Ca antiporter | b |
| mM | 9.4 | Antiporter Na+ constant | KNa |
| mM | 3.75·10-4 | Antiporter Ca2+ constant | KCa |
| [] | 3 | Na/Ca antiporter cooperativity | n |
| [] | 3·10-4 | Fraction of free mitochondrial Ca2+ | Δ |
| **Oxidative phosphorylation parameters** | | | |
| 1/ms | 6.394·10-13 | Sum of products of rate constants | ra |
| 1/ms | 1.76·10-16 | Sum of products of rate constants | rb |
| 1/ms | 2.656·10-22 | Sum of products of rate constants | rc1 |
| 1/ms | 8.632·10-30 | Sum of products of rate constants | rc2 |
| [] | 2.077·10-18 | Sum of products of rate constants | r1 |
| [] | 1.728·10-9 | Sum of products of rate constants | r2 |
| [] | 1.059·10-26 | Sum of products of rate constants | r3 |
| mM | 3·10-3 | Electron carriers concentration (respiratory complexes I-III-IV) | ρres |
| [] | 1.35·1018 | Equilibrium constant of respiration | Kres |
| mM | 3.75·10-3 | Electron carriers concentration (respiratory complexes II-III-IV) | ρresF |
| mV | 50 | Phase boundary potential | ΨB |
| [] | 0.85 | Voltage correction factor | G |
| [] | 5.765·1013 | Equilibrium constant of FADH2 oxidation | KresF |
| mM | 1.24 | FADH2 concentration (reduced) | FADH2 |
| mM | 0.02 | FADH concentration (oxidized) | FADH |
| 1/ms | 1.656·10-8 | Sum of products of rate constants | pa |
| 1/ms | 3.337·10-10 | Sum of products of rate constants | pb |
| 1/ms | 9.651·10-17 | Sum of products of rate constants | pc1 |
| 1/ms | 7.739·10-17 | Sum of products of rate constants | pc2 |
| [] | 1.346·10-8 | Sum of products of rate constants | p1 |
| [] | 7.739·10-7 | Sum of products of rate constants | p2 |
| [] | 3.65·10-15 | Sum of products of rate constants | p3 |
| mM | 1.5 | F1-F0 ATPase concentration | ρF1 |
| [] | 1.71·106 | ATP hydrolysis equilibrium constant | KF1 |
| mM | 2 | Inorganic phosphate concnetration | Pi |
| mM | 1.5 | Total sum of mitochondrial adenine nucleotides | CA |
| mM/ms | 0.025 | ANT maximal rate | VANT,max |
| [] | 0.5 | Fraction of ΔΨm | hANT |
| mM/(ms·mV) | 10-8 | Inner membrane ionic conductance | gH |
| [] | -0.6 | pH gradients across the inner membrane | pHΔ |
| mM | 10 | Total sum of mitochondrial pyridine nucleotides | CPN |
| mM/mV | 1.812·10-3 | Inner membrane capacitance | Cmito |
| mM | 25 | Total concentration of creatine metabolites | Cc |
| **Tricarboxylic acid cycle parameters** | | | |
| mM | 1 | Acetyl CoA concentration | CAcCoA |
| 1/ms | 0.05 | Catalytic constant of CS | kcatCS |
| mM | 0.4 | CS concentration | ET CS |
| mM | 1.26·10-2 | AcCoA Michaelis constant | KMAcCoA |
| mM | 6.4·10-4 | OAA Michaelis constant | KMOAA |
| mM | 1 | Sum of TCA cycle intermediates' concentration | CKint |
| 1/ms | 1.25·10-2 | ACO forward rate constant | kfACO |
| [] | 2.22 | ACO equilibrium constant | KEACO |
| mM | 0.62 | ADP activation constant | Ka ADP |
| mM | 0.0005 | Ca2+ activation constant | Ka Ca |
| mM | 0.19 | NADH inhibition constant | Ki,NADH |
| 1/ms | 0.03 | IDH rate constant | kIDH cat |
| mM | 0.109 | IDH concentration | ET IDH |
| mM | 2.5·10-5 | Matrix proton concentration | [H+] |
| mM | 8.1·10-5 | Ionization constant of IDH | kh,1 |
| mM | 5.98·10-5 | Ionization constant of IDH | kh,2 |
| mM | 1.52 | Isocitrate Michaelis constant | KM ISOC |
| [] | 2 | Isocitrate cooperativity | Ni |
| mM | 0.923 | NAD+ Michaelis constant | KM NAD |
| mM | 0.0308 | Mg2+ Activation constant | KD Mg2+ |
| mM | 1.27·10-3 | Ca2+ Activation constant | KD Ca2+ |
| mM | 0.5 | KGDH concentration | ET KGDH |
| 1/ms | 0.05 | KGDH rate constant | kcat KGDH |
| mM | 1.94 | αKG Michaelis constant | KM αKG |
| mM | 38.7 | NAD Michaelis constant | KM NAD |
| [] | 1.2 | Hill coefficient of KGDH for αKG | nαKG |
| mM | 0.4 | Mg2+ mitochondrial concentration | Mg2+ |
| 1/(mM·ms) | 5·10-4 | SL forward rate constant | kfSL |
| [] | 3.115 | SL reaction equilibrium constant | KESL |
| mM | 0.02 | Coenzyme A concentration | [CoA] |
| 1/ms | 3·10-3 | SDH rate constant | kcat SDH |
| mM | 0.5 | SDH enzyme concentration | ET SDH |
| mM | 0.03 | Succinate Michaelis constant | KMSuc |
| mM | 1.3 | Fumarate inhibition constant | KiFUM |
| mM | 0.15 | Oxaloacetate inhibition constant | Ki,sdhOAA |
| 1/ms | 3.32·10-3 | FH forward rate constant | kf FH |
| [] | 1 | FH equilibrium constant | KEFH |
| mM | 1.13·10-5 | MDH ionization constant | kh1 |
| mM | 26.7 | MDH ionization constant | kh2 |
| mM | 6.68·10-9 | MDH ionization constant | kh3 |
| mM | 5.62·10-6 | MDH ionization constant | kh4 |
| [] | 3.99·10-2 | pH-independent term in the pH activation factor of MDH | koffset |
| 1/ms | 0.111 | MDH rate constant | kcat MDH |
| mM | 0.154 | Total MDH enzyme concentration | ET MDH |
| mM | 1.493 | Malate Michaelis constant | KMMAL |
| mM | 3.1·10-3 | Oxaloacetate inhibition constant | KiOAA |
| mM | 0.2244 | NAD+ Michaelis constant | KMNAD |
| mM | 10 | Glutamate concentration | [GLU] |
| 1/ms | 6.44·10-4 | AAT forward rate constant | kf AAT |
| [] | 6.6 | AAT equilibrium constant | KE AAT |
| 1/ms | 1.5·10-6 | Aspartate consumption rate constant | kASP |
| **Cytoplasmic Energy Handling Parameters** | | | |
| mM | 25 | Total concentration of creatine metabolites (both compartment) | CT |
| 1/ms | 1.4·10-4 | Cytoplasmic CK forward rate constant | kCK cyto |
| 1/ms | 1.33·10-6 | Mitochondrial CK forward rate constant | kCK mito |
| 1/ms | 2·10-3 | CrP transfer rate constant | ktr Cr |
| [] | 0.0095 | CK equilibrium constant | KEQ |
| mM/ms | 10-5 | Constitutive cytosolic ATP consumption rate | VATPase cyto |
| **Mitochondrial Ca2+ Parameters** | | | |
| 1/ms | 2.159 | Uniporter Ca2+ permeability | PCa |
| [] | 2 | Ca2+ valence | ZCa |
| [] | 0.2 | Mitochondrial Ca2+ activity coefficient | mα |
| [] | 0.341 | Extramitochondrial Ca2+ activity coefficient | αe |
| mM/ms | 1.863·10-2 | Na/Ca exchanger maximal velocity | VNC |
| mM | 5 | Extramitochondrial Na+ concentration | [Na] e |
| mM | 3.96 | Mitochondrial Na+ concentration | [Na]m |
| [] | 0.1 | Ca2+ fraction that binds to Ca2+ buffers in the mitochondria | βCa |
| mM | 1.27·10-3 | KGDHC Ca2+ binding constant | KDCa |
| mM | 0.15 | KGDHC Mg2+ binding constant | KDMg |