**Table S7:** List of parameters for the computational mitochondrial model (equations 2 – 20 in the Methods)

|  |  |  |  |
| --- | --- | --- | --- |
| **Parameter** | **Description** | **Value (Unit)** | **References** |
| cmito | Mitochondrial inner membrane divided by Faraday constant | 1.8 (µM.mV -1) | 1 |
| fm | Fraction of free over buffer-bound [Ca2+] in mitochondria | 0.00025 | This work |
| L | Allosteric equilibrium constant for uniporter conformations | 50 | 2 |
| αc | Cytosolic ADP and ATP buffering coefficient | 0.111 | 3 |
| αm | Mitochondrial ADP and ATP buffering coefficient | 0.139 | 3 |
| vAGC | Maximum rate constant of NADH production via malate-aspartate shuttle | 25 (µMs-1) | 4 |
| vMCU | Maximum rate constant of the MCU | 0.00001 (µMs-1) | 4 |
| vNCX | Maximum rate constant of the NCX | 0.00035 (µMs-1) | 4 |
| vF1F0 | Maximum rate constant of the F1F0 ATPase | Varies (µMs-1) | This work |
| vANT | Maximum rate constant of the Adenine Nucleotide Translocator | 5000 (µMs-1) | 1,5 |
| vp | Maximum rate constant of the SERCA pumps | 120 (µMs-1) | 6 |
|  | Total concentration of cytosolic adenine nucleotides | 4000 (µM) | This work |
|  | Total concentration of mitochondrial adenine nucleotides | 15000 (µM) | 1 |
|  | Total concentration of mitochondrial pyridine nucleotides | 250 (µM) | 4 |
| K1 | Dissociation constant for [Ca2+] translocation by MCU | 6 (µM) | 4 |
| K2 | Dissociation constant for MCU activation by [Ca2+] | 0.38 (µM) | 2 |
| Kp | Dissociation constant of [Ca2+] from SERCA | 0.35 (µM) | 6 |
| Kh | Michaelis-Menten constant for ATP hydrolysis | 1000 (µM) | 4 |
| kAGC | Dissociation constant of [Ca2+] from AGC | 0.14 (µM) | 7 |
| ke | Dissociation constant of ATP from SERCA pumps | 0.05 (µM) | 4,8 |
| ko | Rate constant of NADH oxidation by ETC | Varies (µMs-1) | This work |
| kGLY | Velocity of glycolysis (empirical) | Varies (µMs-1) | This work |
| kHYD | Maximum rate of ATP hydrolysis | 100 (µMs-1) | 4 |
| kx | Maximum rate constant of bidirectional [Ca2+] leak from mitochondria | 0.008 (s-1) | 4 |
| b1 | Scaling factor between NADH consumption and change in membrane voltage | Varies | This work |
| b2 | Scaling factor between ATP production by ATPase and change in membrane voltage | 3.43 | 1 |
| δ | Ratio between mitochondrial volume to cytosolic volume | 0.0733 | 1 |
| p1 | Voltage dependence coefficient of MCU activity | 0.1 (mV -1) | 4 |
| p2 | Voltage dependence coefficient of NCX activity | 0.016 (mV-1) | 4 |
| p3 | Voltage dependence coefficient of [Ca2+] leak | 0.05 (mV-1) | 4 |
| p4 | Voltage dependence coefficient of AGC activity | 0.01 (mV-1) | 4 |
| F | Faraday’s constant | 96480 (Cmol-1) |  |
| T | Temperature | 310.16 (K) |  |
| R | Ideal gas constant | 8315 (mJ.mol-1 K-1) |  |
| q1 | Michaelis-Menten-like constant for NAD+ consumption by the TCA cycle | 1 (µM) | 1 |
| q2 | Half-maximal activating of the TCA cycle by mitochondrial [Ca2+] | 0.1 (µM) | 4 |
|  | Half-maximal activating for indirect inhibition of the AGC by cytosolic [Ca2+] | 0.1 (µM) | 4 |
| q3 | Michaelis-Menten constant for NADH consumption by the ETC | 100 (µM) | 1 |
| q4 | Voltage dependence coefficient 1 of ETC activity | 177 (mV) | 1 |
| q5 | Voltage dependence coefficient 2 of ETC activity | 5 (mV) | 1 |
| q6 | Inhibition constant of ATPase activity by ATP | 10000 (µM) | 1 |
| q7 | Voltage dependence coefficient of ATPase activity | 190 (mV) | 1 |
| q8 | Voltage dependence coefficient of ATPase activity | 8.5 (mV) | 1 |
| q9 | Voltage dependence of the proton leak | 2 (µMs-1mV-1) | 1 |
| q10 | Rate constant of voltage-independent proton leak | -30 (µMs-1) | 1 |

**References**

1 Bertram, R., Pedersen, M. G., Luciani, D. S. & Sherman, A. A simplified model for mitochondrial ATP production. *Journal of theoretical biology* **243**, 575-586 (2006).

2 Magnus, G. & Keizer, J. Model of beta-cell mitochondrial calcium handling and electrical activity. I. Cytoplasmic variables. *Am J Physiol* **274**, C1158-1173 (1998). https://doi.org/10.1152/ajpcell.1998.274.4.C1158

3 Fall, C. & Keizer, J. Mitochondrial Modulation of Intracellular Ca2+Signaling. *Journal of theoretical biology* **210**, 151-165 (2001). https://doi.org/10.1006/jtbi.2000.2292

4 Wacquier, B., Combettes, L., Van Nhieu, G. T. & Dupont, G. Interplay Between Intracellular Ca(2+) Oscillations and Ca(2+)-stimulated Mitochondrial Metabolism. *Sci Rep* **6**, 19316 (2016). https://doi.org/10.1038/srep19316

5 Cortassa, S., Aon, M. A., Marbán, E., Winslow, R. L. & O’Rourke, B. An integrated model of cardiac mitochondrial energy metabolism and calcium dynamics. *Biophysical journal* **84**, 2734-2755 (2003).

6 Tran Van Nhieu, G. *et al.* Actin-based confinement of calcium responses during Shigella invasion. *Nature Communications* **4**, 1567 (2013). https://doi.org/10.1038/ncomms2561

7 Contreras, L. *et al.* Ca2+ Activation Kinetics of the Two Aspartate-Glutamate Mitochondrial Carriers, Aralar and Citrin: ROLE IN THE HEART MALATE-ASPARTATE NADH SHUTTLE\*. *Journal of Biological Chemistry* **282**, 7098-7106 (2007). https://doi.org/https://doi.org/10.1074/jbc.M610491200

8 Lytton, J., Westlin, M., Burk, S. E., Shull, G. E. & MacLennan, D. H. Functional comparisons between isoforms of the sarcoplasmic or endoplasmic reticulum family of calcium pumps. *Journal of Biological Chemistry* **267**, 14483-14489 (1992). https://doi.org/https://doi.org/10.1016/S0021-9258(19)49738-X