**TABLE S1. Parameters used in complex I model**

|  |  |  |  |
| --- | --- | --- | --- |
| Parameter | Description | Value | Reference |
| ρC1 | concentration of complex I | 8.8490mM | fit using data from (22) |
| ΔΨB | phase boundary potential | 50mV | (4) |
| a12\* |  | 6.3396·1011 mM-2s-1 | fit using data from (22) |
| a21 |  | 5 s-1 | (4) |
| a56 |  | 100 s-1 | (4) |
| a65\* |  | 2.5119·1013 mM-2s-1 | fit using data from (22) |
| a61\* |  | 107 s-1 | fit using data from (22) |
| a16\* |  | 130 s-1 | (4) |
| a23\* |  | 3.8867·103 mM-1/2s-1 | fit using data from (22) |
| a32 |  | 9.1295·106 s-1 | fit using data from (22) |
| a34 |  | 639.1364 s-1 | fit using data from (22) |
| a43\* |  | 3.2882 mM-1/2s-1 | fit using data from (22) |
| a47\* |  | 1.5962·107 mM-1s-1 | fit using data from (22) |
| a74 |  | 65.2227 s-1 | fit using data from (22) |
| a75 |  | 2.4615·104 s-1 | fit using data from (22) |
| a57\* |  | 1.1667·103 mM-1/2s-1 | fit using data from (22) |
| EFMN | Midpoint potential of flavin mononucleotide | -0.375mV | (24) |
| EO2.- | Midpoint potential of superoxide | -0.15mV | (25) |
| a42\* |  | 6.0318 mM-1s-1 | fit using data from (22) |

**TABLE S2. Parameters used in the complexes II and III models**

|  |  |  |  |
| --- | --- | --- | --- |
| Parameter | Description | Value | Reference |
| Vsucc | Maximum velocity of SDH | 250 mM/min | fit using data from (26) |
| Km\_succ | Michaelis constant for SDH | 0.6 | (25) |
| k03 | Reverse rate constant for reaction 3 | 9.9998·104 | fit using data from (26) |
| Keq3 | Equilibrium constant for reaction 3 | 0.6877 | (25) |
| k04 | Reverse rate constant for reaction 3 | 3.6402·103 | fit using data from (26) |
| Keq4\_bHox | Equilibrium constant for reaction 4  (bH oxidized) | 129.9853 | fit using data from (26) |
| Keq4\_bHred | Equilibrium constant for reaction 4  (bH reduced) | 13.7484 | fit using data from (26) |
| δ1 | Fraction of ΔΨ at energy barrier peak for reaction 4 | 0.5 | (25) |
| α | Fraction of ΔΨ affecting Qp.- to bL e- transfer | 0.2497 | Derived from β value, assuming membrane symmetry |
| kd | Rate of diffusion across the membrane for Q and QH2 | 1.32·106 /min | (25) |
| k06 | Reverse rate constant for reaction 6 | 10,000 | fit using data from (26) |
| Keq6 | Equilibrium constant for reaction 6 | 9.4546 | fit using data from (26) |
| δ2 | Fraction of ΔΨ at energy barrier peak for reaction 6 | 0.5 | (25) |
| β | Fraction of ΔΨ affecting bL to bH e- transfer | 0.5006 | fit using data from (26) |
| k07\_bLox | Reverse rate constant for reaction 7  (bL oxidized) | 800 | fit using data from (26) |
| Keq7\_bLox | Equilibrium constant for reaction 7  (bL oxidized) | 3.0748 | (25) |
| k07\_bLred | Reverse rate constant for reaction 7  (bL reduced) | 100 | fit using data from (26) |
| Keq7\_bLred | Equilibrium constant for reaction 7  (bL reduced) | 29.0714 | Adjusted from (25) by for anticooperativity as given in (26) |
| δ3 | Fraction of ΔΨ at energy barrier peak for reaction 7 | 0.5 | (25) |
| γ | Fraction of ΔΨ affecting bH to Qn e- transfer | 0.2497 | Derived from β value,  assuming membrane symmetry |
| k08\_bLox | Reverse rate constant for reaction 8  (bL oxidized) | 5000 | fit using data from (26) |
| Keq8\_bLox | Equilibrium constant for reaction 8  (bL oxidized) | 129.9853 | (26) |
| k08\_bLred | Reverse rate constant for reaction 8  (bL oxidized) | 500 | fit using data from (26) |
| Keq8\_bLred | Equilibrium constant for reaction 8  (bL reduced) | 9.4546 | (26) |
| k09 | Reverse rate constant for reaction 9 | 4.9949·104 | fit using data from (26) |
| Keq9 | Equilibrium constant for reaction 9 | 0.2697 | (25) |
| k010 | Reverse rate constant for reaction 10 | 50 | fit using data from (26) |
| Keq10 | Equilibrium constant for reaction 10 | 1.4541 | (26) |

|  |  |  |  |
| --- | --- | --- | --- |
| k33 |  | 148,148 | (29) |
| Keq33 | Equilibrium constant for reaction 33 | 2.1145 | (26) |
| C3tot | Total complex III protein | 0.325mM | (29) |

Equilibrium constants were adjusted to 37°C

**TABLE S3. Parameters used in complex IV model**

|  |  |  |  |
| --- | --- | --- | --- |
| Parameter | Description | Value | Reference |
| cyt ctot | Total cytochrome c | 0.325mM | (29) |
| C4tot | Total complex IV protein | 0.325mM | (29) |
| k34 |  | 1.7667·1028 | Adjusted from (29) to fit (26) |
| k-34 |  | 1.7402 | Adjusted from (29) to fit (26) |
| k35 |  | 45,000 | (30) |
| k36 |  | 2.8955·1025 | Adjusted from (29) to fit (26) |
| k-36 |  | 2.8955·1010 | Adjusted from (29) to fit (26) |
| k37 |  | 1.7542·1012 | Adjusted from (29) to fit (26) |
| k-37 |  | 1.7542·104 | Adjusted from (29) to fit (26) |
| δ5 |  | 0.5 | (29) |
| O2 | Matrix oxygen concentration | 6·10-3mM | (29) |
| O2.- | Matrix superoxide concentration | 0.1·10-3mM | (29) |

**TABLE S4. Parameters for ATP generation and proton leak systems**

|  |  |  |  |
| --- | --- | --- | --- |
| Parameter | Description | Value | Reference |
| Cmito | Mitochondrial membrane capacitance | 1.812·10-3mM/mV | (1) |
| KATPase\_app | Apparent equilibrium constant for ATPase | 4.1175· 106 |  |
| Pi | total concentration of inorganic phosphate | 8.6512mM |  |
| HADP | concentration of proton-bound ATP | 0.0026mM |  |
| ρF1 | concentration of ATPase | 5mM |  |
| pa |  | 9.936·10-4 min-1 | (4) |
| pb |  | 2.0238·10-5 min-1 | (4) |
| p1 |  | 1.346·10-4 | (4) |
| p2 |  | 7.739·10-7 | (4) |
| p3 |  | 6.65·10-15 | (4) |

**TABLE S5. Simulation parameters for Figs. 2A-C**

|  |  |
| --- | --- |
| Parameter | Value |
| pHp | 7.0 |
| pHn | 7.3 |
| ΔΨ | clamped to values ranging from 70 to 200mV |
| NADH | 1mM |
| NAD+ | 9mM |
| SDH activity | 60% |
| gh | 0.12mM/min/mV |
| ATP | 0.01mM |
| ADP | 0.0110mM |

NADH:NAD ratio comes from most reduced estimate by Mintz and Robin (31) for alveolar

macrophages to compare to Kim et al. (26) RAW macrophages. SDH activity was increased to fit the Q/QH2 redox data in accordance with the observation from a previously published mitochondria model (13) that SDH activity is increased as NADH becomes oxidized.

**TABLE S16. Parameters for scavenging model**

|  |  |  |
| --- | --- | --- |
| Parameter | Description | Value |
| ETGPX | concentration of GPx | 0.0034mM |
| Φ1 | GPx activity constant | 1.1337·10-7/min |
| Φ2 | GPx activity constant | 2.5·10-5/min |
| ETGR | concentration of GR | 5·10-3mM |
| kGR | rate constant of GR | 1500/min |
| KMGSSG | KM of GR for oxidized GSH | 0.12mM |
| KMNADPH | KM of GR for NADPH | 0.015mM |
| Gtot | total glutathione pool | 3mM |
| ETPRX | concentration of Prx | 1mM |
| ΦP1 | Prx activity constant | 6.3833·10-6/min |
| ΦP2 | Prx activity constant | 3.0833·10-7/min |
| KMTrx(SS) | KM of TrxR for Trx(SS) | 0.006 |
| KM T-NADPH | KM of TrxR for NADPH | 0.012 |
| kTrxR | rate constant of TrxR | 1.32·103/min |
| ETTrxR | concentration of TrxR | 0.01 |
| kTxPx | rate constant of Prx | 1.5·105/min |
| Trxtot | total thioredoxin pool | 0.025 |
| Prxtot | total peroxiredoxin pool | 0.15 |
| k1 | rate constant of H2O2 transport from mitochondria | 0.002 |

**TABLE S17. Initial conditions**

|  |  |
| --- | --- |
| **State variable** | **Value** |
| Qn | 1.2518 mM |
| Q.- | 0.5578 mM |
| (QH2)n | 0.4199 mM |
| (QH2)p | 0.4197 mM |
| Q.- | 0.0988 mM |
| Qp | 1.2520 mM |
| b1 | 0.0618 mM |
| b2 | 0.1500 mM |
| b3 | 0.0954 mM |
| b4 | 0.0179 mM |
| FeSox | 0.0900 mM |
| FeSred | 0.2350 mM |
| cyt c1ox | 0.2266 mM |
| cyt cox | 0.1785 mM |
| cyt c1red | 0.0984 mM |
| cyt cred | 0.1465 mM |
| ΔΨ (only relevant if unclamped) | 180mV |
| H2O2 (only with scavenging model) | 0 mM |
| GSH (only with scavenging model) | 2.8 mM |
| Trx(SH)2 (only with scavenging model) | 0.002 mM |
| Prx(SH)2 (only with scavenging model) | 0.0281 mM |