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Energy Equivalence of Information in the Mitochondrion and the Thermodynamic Efficiency of ATP Synthase

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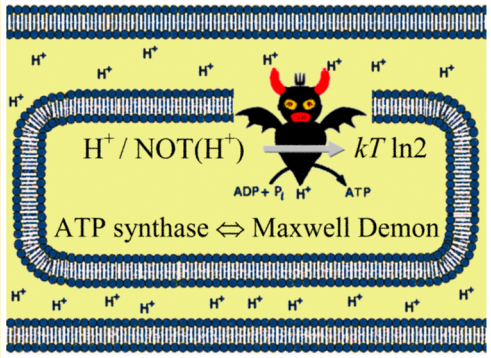
ABSTRACT: Half a century ago, Johnson and Knudsen resolved the puzzle of the apparent low efficiency of the kidney (~0.5%) compared to most other bodily organs (~40%) by taking into account the entropic cost of ion sorting, the principal function of this organ. Similarly, it is shown that the efficiency of energy transduction of the chemiosmotic proton-motive force by ATP synthase is closer to 90% instead of the oft-quoted textbook value of only 60% when information theoretic considerations are applied to the mitochondrion. This high efficiency is consistent with the mechanical energy transduction of ATP synthase known to be close to the 100% thermodynamic limit. It would have been wasteful for evolution to maximize the mechanical energy transduction to 100% while wasting 40% of the chemiosmotic free energy in the conversion of the proton-motive force into mechanical work before being captured as chemical energy in adenosine 5′-triphosphate.



The efficiency of mitochondrial energy transduction is of prime interest given its role as the main energy source of eukaryotic cells. Metabolic energy obtained from the oxidation of nutrients and harnessed in the form of nucleoside 5′-triphosphate such as adenosine 5′-triprosphate (ATP) is converted by the cell to mechanical, biosynthetic, electrical, and osmotic work, in addition to useful and wasteful thermal energy. As suggested in the past by Johnson and Knudsen,[1−3] it is argued that information theoretic work equivalent of acts of sorting (gathering information) constitutes an additional channel that must be taken into account in estimations of energy utilization efficiency of a cell organelle, cell, organ, or organism. These considerations bring the efficiency of the mitochondrion to nearly 85−90% in its role as an energy transduction device, as opposed to the oft-encountered textbook estimates of ~60%.[4] It appears, hence, that evolution has fine-tuned the working of the mitochondrion close to maximal efficiency.

The kidney had long been thought to be an exceptionally thermodynamically inefficient organ where the ratio of power output (osmotic work) to power input (ATP) is on the order of ~1%,[5] an order of magnitude lower than those of other organs. This low thermodynamic efficiency has been shown to be only apparent and due to missing the energetic cost of the sorting of ions performed by the kidney. Johnson and Knudsen, in a remarkable but largely forgotten *Nature* article[1] (cited only ~15 times), resolved the paradox and brought the kidney's efficiency into alignment with those of most other organs in the body (~30−40%). These authors argue that whenever an organ performs a regulatory function such as sorting ions or molecules following a molecular recognition event this organ can be considered as a physical realization of Maxwell's demon.[6,7] In such situations, the energy cost associated with gathering information (i.e., associated with negentropy)[8] must be taken into account.[1−3]

Because the entropy associated with the reduction of uncertainty by half, that is in acquiring 1 bit of information, is $S = -k_B \ln 2$, the minimal energy associated with this reduction of uncertainty is equal to $k_B T \ln 2$.[8] A common feature of the work of the kidney (an entire organ) and the work of mitochondrial F_oF_1 ATP synthase (a component of a cell organelle) is the role of the organ and enzyme as information-gathering devices (realizations of Maxwell's demon). The pioneering work of Johnson and Knudsen on the efficiency of the kidney is adapted in this work to the coupling of ATP synthesis with re-entry of protons into the mitochondrion matrix through F_oF_1 ATP synthase according to Mitchell's chemiosmotic theory.[9−11]

RESULTS

Proton Recognition by ATP Synthase as an Information-Gathering Event and Its Thermodynamic Consequences. According to the now well-established chemiosmotic theory,[9−11] the transfer of electrons across the electron transport chain within the inner mitochondrial membrane is coupled with the pumping of protons from the mitochondrial matrix to the intermembrane space creating chemical and

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electric charge gradients. The subsequent F_oF_1 ATP synthase-dependent phosporylation of ADP to ATP is driven by the "proton-motive force" (PMF) resulting from the pumping of a proton in the intermembrane space. The ΔG associated with the proton gradient can be used to synthesize ATP as discussed herein.

The complete oxidation of a glucose molecule results in the formation of approximately 32−34 molecules of ATP produced from ADP and P_i depending on whether glycerol phosphate or malate aspartate, respectively, is the shuttle.[4] The efficiency of the electron transport chain and oxidative phosphorylation is calculated as the percent ratio of the total Gibbs energy of formation of these 32−34 ATP molecules to the theoretical ΔG released from the oxidation of 1 mol of glucose ($C_6H_{12}O_6 + 6O_6 \rightarrow 6CO_2 + 6H_2O$) under a given set of thermodynamic conditions (usually standard or cellular). Under cellular conditions, the Gibbs energy of hydrolysis of ATP is approximately −50 kJ mol^{-1}.[4,12] The formation of 32−34 ATP molecules, then, captures 1600−1700 kJ mol^{-1} of the total energy released from the combustion of 1 mol of glucose, which is estimated to release 2937 kJ mol^{-1}, yielding an estimated efficiency of ∼55−58%.[4]

Of the 32−34 ATPs, 28−30, respectively, are formed in the mitochondrion by oxidative phosphorylation, while two of the remaining ATP molecules are produced in the cytoplasm during glycolysis and the other two are produced from the Krebs cycle. The lower limit of this range, 32, will be taken because other texts have suggested as few as ∼30 ATPs per glucose molecule as a realistic yield.[13] The formation of one ATP molecule is believed to require that three protons be channeled through F_oF_1 ATP synthase from the intermembrane space to the mitochondrial matrix. This step requires the enzyme to recognize the approaching ions as "proton" or "non-proton", a step that necessitates a signal-to-noise ratio of at least 4 (for 98% recognition fidelity).[8]

The thermal noise at body temperature can be taken as RT, the quadruple of which yields a minimal discernible signal of 10.3 kJ mol^{-1} for every recognition of a proton. The energy cost of recognition per ATP molecule is then triple this figure (∼30.9 kJ mol^{-1}). Now, four ATP molecules are formed in glycolysis without the necessity of a proton recognition step. Thus, only 28 ATP molecules occur concomitant with proton recognition costing $\Delta G_{inform.} \approx 866.1$ kJ mol^{-1}. The free energy captured in the pyrophosphate bonds of all 32 ATP molecules formed (4 + 28) $\Delta G_{ATP} \approx 1600$ kJ mol^{-1}. We then write $\Delta G = \Delta G_{ATP} + \Delta G_{inform.} = 1600$ kJ mol^{-1} + 866 kJ mol^{-1} = 2466 kJ mol^{-1}. Taking useful work to be the sum of ΔG_{ATP} (∼55%) and $\Delta G_{inform.}$ (∼30%) yields an efficiency of (2466/2937) × 100 ≈ 84%. This efficiency is the lower limit for ATP synthase, and hence, ∼90% is not an unreasonable figure given its consistency with the near 100% efficiency of the rotation of the "rotor" of this molecular machine.[14]

DISCUSSION AND CLOSING REMARKS

F_oF_1 ATPase/synthase is reversible depending on the energy status of the cell. When the cell has a low energy status, it catalyzes the formation of ATP from ADP and P_i (ATP synthase) but it can also work in the reverse direction of creating a proton gradient by actively pumping protons against the concentration gradient at the expense of ATP hydrolysis (ATPase). In this paper, we calculate this enzyme's efficiency when it works in the ATPase mode. In this case, it acts as a Maxwell's demon because it decreases the entropy of the inter-membrane compartment (excluding the demon). Then, as noted first by Szilard,[15] the entropy of the demon must increase during the process as a consequence of the information gathering events.

The efficiency of the F_oF_1 ATP synthase transforming mechanical rotation energy to chemical energy has been shown to be very high,[14] but this work is the first to show that so too is the efficiency of the mitochondrial conversion of the chemiosmotic gradient into ATP. That is to say, the process beginning with glycolysis and ending with the creation of ATP occurs with an efficiency approaching the theoretical limit. It appears that transforming the proton gradient into chemical energy is more efficient than previously believed.

What we have described here in relation to the mitochondrion is expected to have wider implications because ATP synthase plays a role similar to that discussed here in bacterial membranes and in chloroplasts. Information theoretic considerations are relevant to any and all processes involving selection such as the selection of K^+ and Na^+ by specific membrane-bound gate proteins necessary for nerve pulse generation, membrane transporters, etc. The Gibbs free energy of a proton gradient can be used to drive active transport and to power flagellar rotation and can be converted to electron potential or heat (see Figure 18.44 of ref 13). Textbooks should perhaps consider revising the figure often quoted for the efficiency of the energy transduction in the mitochondrion from around 60% to around 90%. This efficiency accounts for the sorting of protons which is tantamount to information gathering work akin to the operation of Maxwell's demon.

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Notes

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