Driveshaft torque for ATP synthase

Congratulations to everybody who had a stab at this calculation. Here is my analysis of the problem, which might well contain errors. I would be delighted to hear from any students (or staff) who think they have a better answer. A bottle of wine is on offer for the first person to find a mistake.

1) This enzyme consists of two reversible molecular motors coupled "back to back" through a rotating driveshaft, analogous to a motor - generator set. When the chemical reactions are close to equilibrium, you should get approximately the same answers starting from either the F1 or the F0 end of the complete assembly.

2) Under near-equilibrium conditions, the driveshaft torque depends on the free energy for ATP hydrolysis in the mitochondrial matrix compartment, multiplied by the number of ATP molecules synthesised by the F1 head group per driveshaft revolution.

3) Alternatively, the torque depends on the proton motive force, multiplied by the number of protons translocated by the F0 base piece per driveshaft revolution. [This should give the same answer as (2) above.]

Assume that ΔG for ATP hydrolysis in the matrix space the is 75% of the cytoplasmic value (because of the extra energy supplied from the proton motive force to the adenine nucleotide and phosphate translocators) then:

matrix $\Delta G = 37.5$ kJ/mole of ATP

After dividing by Avogadro's number [6.022×10^{23}] this is equivalent to 6×10^{-20} Joules per individual ATP (in the matrix space). Three ATP are synthesised per driveshaft revolution.

chemical work done per enzyme, per driveshaft revolution = 1.8×10^{-19} J

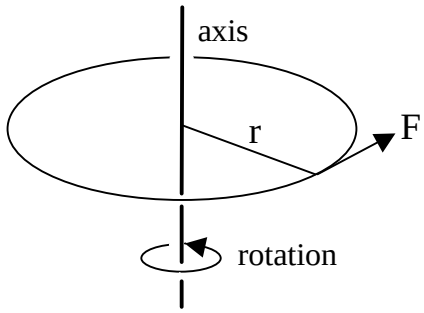
physical work done per enzyme, per driveshaft revolution = $2\pi \times$ torque

$\therefore$ torque $= 1.8 \times 10^{-19} / 2\pi$ Nm

$= 28.6$ pN.nm

[units are picoNewton nanometres]

Torque is a measure of the turning force about some axis of rotation.



Imagine a force of F Newtons acting tangentially at a radius of r metres

Torque T = r.F Newton metres [Nm]

Exactly the same torque would result from a
force of 2 F Newtons at radius 0.5 r
or 0.5 F Newtons at radius 2 r

Work done per revolution = force x distance

Work done per revolution = 2π r F = 2π T
(independent of where the force acts)

4) I would hypothesise that this torque approaches the ultimate torsional strength of the two α helices that make up the driveshaft, and that evolutionary selection pressures have driven this design about as far as it can be pushed.

5) The driveshaft angular velocity depends on the turnover number for a single F1 active site, divided by the number of ATP molecules synthesised per revolution.

6) Alternatively, the angular velocity depends on the turnover number for the F0 proton channels, divided by the number of protons translocated per revolution. [This should give the same answer as (5) above.]

7) I am astonished by the agreement between my own calculation of the angular driveshaft velocity in cardiac muscle and the published values for the bacterial enzyme. I have yet to find a mistake, but perhaps some of you can help me? My calculations go as follows:

A rat heart (1g wet weight) perfused with blood-free salt solution (gassed with 95% oxygen) extracts about 75% of the available oxygen from the perfusion medium. At the maximum possible left ventricular pressures the coronary flow with low viscosity inorganic media approaches 35 ml/min. The oxygen consumption is about 25 μmol/min/heart.

The wet weight / dry weight ratio for heart muscle is about 4:1, so the oxygen consumption is 100 μmol/min/g dry weight. If the P:O ratio is 2.5, or 5 ATP per oxygen molecule, then the ATP turnover is 500 μmol/min/g dry weight.

Mitochondria make up 30% of the cardiac muscle, and the F1/F0 ATP synthase is about 10% of the mitochondrial protein. So there are 30mg ATP synthase per gram dry weight. The molecular weight for the enzyme is about 500,000 and there are 3 active centres per F1 head group.

active centre concentration = $3 \times 0.03 / 500{,}000 = 1.8 \times 10^{-7}$ moles / g dry weight

turnover number per active site = $5 \times 10^{-4} / 1.8 \times 10^{-7} = 2.8 \times 10^{3}$ per minute

The drive shaft revolves once for each active site turnover. [It is important not to allow twice for the three active centres in this calculation.]

So the drive shafts are spinning at 2,800 rpm in working heart muscle at 37ºC.

[This is 47 revolutions per second, or about 3 times faster than the value estimated by Noji et al (1997) Nature **386,** 299 - 302 for their chemically modified bacterial enzyme at 25ºC. The 12ºC difference in temperature would normally produce a two to three fold increase in rate. These workers estimated a maximum torque of 45 pN nm for the F1 head groups turning fluorescent actin filaments. (Beware of the misprint < pN nm^{-1} > in the summary, although the units in the main part are correct.) They noted that all their motors quickly failed under load, suggesting that their torque limit had been reached. Not bad performance for a 5 nm diameter motor. Not bad arithmetical agreement either!]

8) If there is "slippage" (rotation unlinked to chemistry) then the results depend on which part is slipping, and which end is supplying the power. In general, the fluxes and angular velocity will be increased on the upstream side of the "slip".

9) When the enzyme is operating under non-equilibrium conditions, at very high fluxes, there might be additional frictional losses, generally leading to lower torques than the power consumption would imply.

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