

Department of Chemistry

Departmental Seminar Series

You are cordially invited to a lecture presented by



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Date: Tuesday, 13 December 2022
Time: 11:30
Venue: The Orbital (Room 3-1 Chemistry Building)

ATP Synthase Beyond Catalysis:

Novel biological functions of ATP synthase have been recently proposed. This enzyme is now believed to interfere with the *energetics of the reaction itself* and *not only the rate of the reaction*. This unusual role is due to the enzyme's electrostatic potential. Five accurate crystallographic structures of ATP synthase are used to compare their electrostatic potentials (ESP) and fields by solving the Poisson-Boltzmann's equation in an environment simulating the mitochondrion. The ESP is found to be of the order of magnitude of the chemiosmotic potential difference itself (*ca.* 0.2 volt) and, hence, cannot be ignored. It is suggested, therefore, that a new term, previously overlooked, must be added in the textbook ΔG expression of chemiosmotic theory which is revised to read:

$$\Delta G = \Delta G_{\text{chem.}} + \Delta G_{\text{elec.}} + \underbrace{+\Delta G_{\text{ATPase}}}_{\text{NEW TERM}}$$
$$= 2.3nRT\Delta\text{pH} + n\mathcal{F}Z\Delta\psi + \underbrace{+n\mathcal{F}Z\Delta\psi_{\text{ATPase}}}_{\text{NEW TERM}}$$

In summary, one can assign three different roles to ATP synthase:

- (1) Its known putative role, and that is the catalysis (lowering the ΔG^\ddagger) of the reaction:
 $\text{ADP} + \text{P}_i \rightleftharpoons \text{ATP} + \text{H}_2\text{O}.$
- (2) A *novel role*, which is, altering the ΔG of the reaction of translocation of protons from the inter-membrane gap to the mitochondrial matrix.
- (3) Another *novel role*, and that it to create a potential barrier regulating the rate of proton translocation itself. Said differently, due to the enzyme's very structure, ATP synthase functions over and above its role as an enzyme as a biological catalyst. How

this term has been overlooked will be discussed in the context of a larger research programme.

Time permitting, a proposed reconciliation of a million-fold disagreement between theory and experiment regarding the temperature of the mitochondrion where ATP synthase operates will be touched upon.

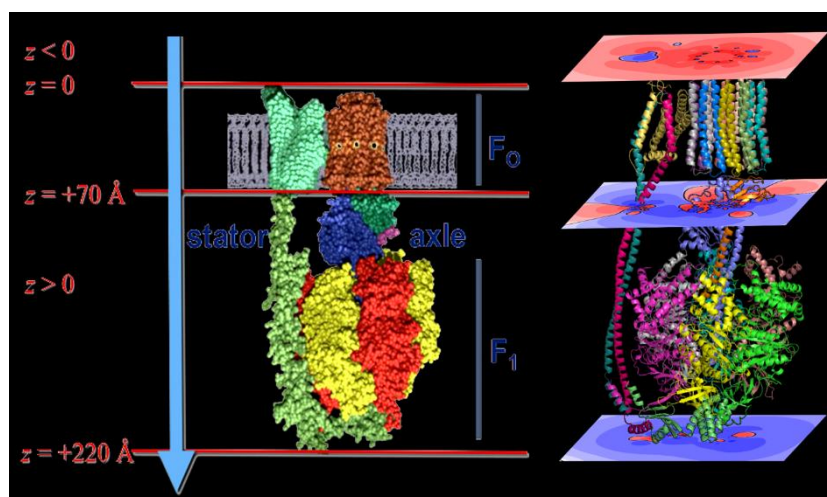


Fig. 1 A representation of ATP synthase, with its F_0 subunit spanning the inner mitochondrial membrane, along with the calculated electrostatic potential of the protein at 3 key planes perpendicular to the long molecular axis (z -axis, shown to the left (in Å)). At its point of entry (around $z = 0$ Å), the proton “sees” a positive (red) potential and when it exits ($z \approx 70$ Å) it encounters a negative potential (blue), with a potential difference of the order of a 0.1 volt.

REFERENCES:

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3. Fahimi, P.; Matta, C. F. “The hot mitochondrion paradox: Reconciling theory and experiment”, *Trends Chem.* **4**, 96-110, 2022.
4. Nasr, M. A.; Dovbeshko, G. I.; Bearne, S. L.; El-Badri, N.; Matta, C. F. “Heat shock proteins and their putative roles in the hot mitochondrion”, *BioEssays* **41**, Article 1900055, 2019.
5. Matta, C. F., Massa, L. “Notes on the energy equivalence of information”, *J. Phys. Chem. A* **121**, 9131-9135, 2017.

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