The Energy of Life: Linking Biophysical approaches to real world applications.

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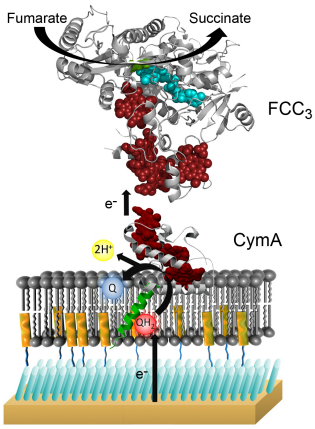
Membrane-bound enzymes utilizing proton/electron transfer play a central role in the respiration of all life on earth. Enzymes called quinone oxidoreductases catalyse the two-electron, two-proton conversion of lipophilic quinol to quinone, driving the generation of transmembrane proton (ΔpH) and electrical gradients (ΔΨ). These gradients are then used to power an enzyme called the ATP synthase, the key enzyme in producing chemical cellular energy (ATP) and effectively a proton 'sink'. Despite the importance of these enzymes, little is known about quinone-quinol interconversions in the membrane environment, and even less is know about the transfer of protons between oxidoreductases and the ATP synthase.

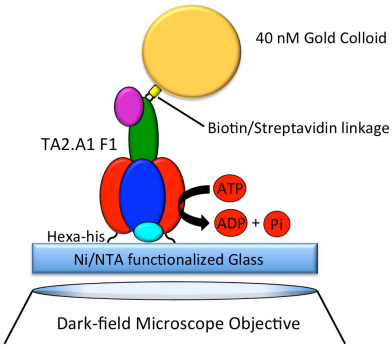
Presented here are biomimetic lipid bilayer systems to examine proton and electron movement using both enzymes and native lipid environments. Also presented are two example biological systems in which single-molecule mechanics and proton movements have been examined.



In the first example I demonstrate electron transfer through a nano-architecture using the fumarate reductase system of the model organism for metal reduction *Shewanella oneidensis* MR-1. This system involves two proteins, CymA, a monotopic membrane tetraheme *c*-type cytochrome belonging to the NapC/NirT family and the physiological binding partner, fumarate-reducing flavocytochrome *c* (Fcc_3).

In the second example I describe a novel method to monitor single molecule resolution of the proton pumping activity of the quinol heme-copper oxidase, cytochrome bo_3 reconstituted in liposomes. Using surface tethered liposomes and coupling electrochemistry with fluorescent microscopy allowed us to *in situ* activate and simultaneously monitor cytochrome oxidase proton pumping activity in liposomes.

In the third example I examine the rotary dynamics of $TA2F_1$, a thermoalkaliphilic ATP synthase from *Caldalkalibacillus thermarum* TA2.A1, with two robust forms of single-molecule analysis, a magnetic bead or a gold nanoparticle. Torque measurements revealed not only the highest torque (52pN) observed for an F_1 molecule using fluctuation theorem, but also a novel mechanistic profile. The mechanism of LDAO activation and implications of a high torque in terms of extreme environment adaptation are presented.



Lastly I present the future directions and applications of such approaches for an array of different fields, from bioelectricity and bioremediation to nanomotors – with particular focus on the study of pathogen respiratory chains and their adaptation to environment.