

# SCIENCE AT THE EDGE

2017 SEMINAR SERIES

Quantitative Biology Graduate Program | Gene Expression in Development and Disease

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### “Proton Pumping and Electron Tunneling to Power the Cell”

A transmembrane proton gradient is established in cells by proton pumping through membrane embedded proteins from the N-side of the membrane, with fewer protons, to the more positive P-side. The energy to build the gradient comes from sunlight in photosynthesis or from energy liberated by redox chemistry such as in the reduction of oxygen in cytochrome c oxidase. The proton gradient fuels the transfer of ions and substrates across the membrane needed for cell signaling and metabolism and the production of ATP, the universal energy currency for biochemical reactions. To pump protons the protein must change the proton affinity of specific groups that serve as intermediate proton donors and acceptors. A hydrogen bond pathway connects proton donors and acceptors. The accessibility of proton transfer pathways to the N- and P-sides of the membrane must also change during the reaction cycle to ensure that the proton transfers do not dissipate the proton gradient. The gates that change the conductivity of proton transfer have been difficult to identify as they must be transient and may occur anywhere along the proton transfer pathways. MCCE (Multiconformation Continuum Electrostatics) has been used to access the proton affinity of key groups through the reaction cycle in cytochrome c oxidase and bacteriorhodopsin. Local structures in proteins that help groups gain and lose protons will be described.

#### REFERENCES

- Molecular mechanisms for generating transmembrane proton gradients. (2013) MR Gunner, Muhamed Amin, Xuyu Zhu, Jianxun Lu. *Biochim Biophys Acta* 827:892-913. doi: 10.1016/j.bbabi.2013.03.001
- Characterizing the proton loading site in cytochrome c oxidase. (2014) Lu, J, Gunner, MR. *Proc. Natl. Acad. Sci. USA* 111(34):12414-9. doi: 10.1073/pnas.1407187111.
- Halorhodopsin pumps Cl<sup>-</sup> and bacteriorhodopsin pumps protons by a common mechanism that uses conserved electrostatic interactions. Song Y, Gunner MR. *Proc Natl Acad Sci U S A*. 2014; DOI: 10.1073/pnas.1411191111.
- The design features cells use to build their transmembrane proton gradient. Gunner, M.R. and Koder, R. (2016) *Physical Biology*. *Phys Biol*. 2017 Feb 7;14(1):013001

**FRIDAY, MARCH 17, 2017**  
**11:30 AM, ROOM 1400 BPS**

*Refreshments at 11:15*