

*Invited Presentation***BIOMEDICAL ENGINEERING SEMINAR**

11:00 a.m.-12:00 noon, Friday, June 12, 2009
Mann Hall, Medical Sciences Building

Title: The Electromechanics of Cells and Patches

**Presenter: Frederick Sachs, Ph.D.
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Abstract: We discovered mechanosensitive ion channels in skeletal muscle some twenty years ago. Thus began a diverse collection of studies on channel biophysics which included studies of patch anatomy, cell mechanics the structure of water¹ and electrophysiology² using methods ranging from patch clamp³ to light⁴ and high voltage electron microscopy⁵, AFM¹, fluorescence⁶, natural products chemistry⁷.

The “mechanical membrane” is not a bilayer but a rather undefined object. The structure of a patch is even visible in the light microscope. When a patch is mechanically stressed with pipette pressure, the stresses are distributed among multiple proteins and lipids so that precise control of the stimulus is not possible. All patches are intrinsically stressed by the adhesion energy of the gigaseal and that stress is a significant fraction of the lytic tension of a bilayer. Most channels that have been tested, including all the voltage sensitive channels, are mechanosensitive since they change dimensions between states⁸.

Despite the complexity of the patch, it remains the simplest preparation to study the cell cortex and mechanosensitive channels but it would be useful to have a simpler screening assay. Researchers often apply osmotic pressure as a mechanical stimulus, but rarely found a matching mechanical response. Why? We measured the cell stiffness under hypotonic stress using an AFM and found that cells never became stiffer and often became softer. This makes sense if the osmotic stress is constrained primarily by the cytoskeleton and not the cell membrane. Animal cells appear to behave like sponges, not semipermeable bags - they swell and become soft with the uptake of water. Sponges don't lyse since the mechanical stress in the latticework raises the internal water pressure to match the external free energy. Since crosslinking decreases the osmotic pressure of the component parts, we predict that cells should be able to pump water without moving solutes. Constraining osmotic stress by an external structure or an internal structure is a major feature distinguishing plants from animals¹.

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 3. Suchyna, T. & Sachs, F. Mechanical and electrical properties of membranes from dystrophic and normal mouse muscle. *J.Physiol.(Lond)* **581**, 369-387 (2007).
 4. Sokabe, M. & Sachs, F. The structure and dynamics of patch-clamped membranes: a study by differential interference microscopy. *Journal of Cell Biology* **111**, 599-606 (1990).
 5. Ruknudin, A., Song, M.J. & Sachs, F. The ultrastructure of patch-clamped membranes: a study using high voltage electron microscopy. *Journal of Cell Biology* **112**, 125-134 (1991).
 6. Meng, F., Suchyna, T.M. & Sachs, F. A fluorescence energy transfer-based mechanical stress sensor for specific proteins in situ. *Febs Journal* **275**, 3072-3087 (2008).
 7. Bowman, C., Gottlieb, P.A., Suchyna, T., Murphy, Y.K. & Sachs, F. Mechanosensitive Ion Channels and the Peptide Inhibitor GsMTx4: History, Properties, Mechanisms and Pharmacology. *Toxicol* (2006).
 8. Honore, E., Suchyna, T., Patel, A.A. & Sachs, F. Desensitization of cloned 2P domain K channels. *Proceedings of the National Academy of Sciences* **103**, 6859-6864 (2006).

Host: Gianrico Farrugia, Ph.D.

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