INTERNSHIP PROPOSAL

Laboratory name: Physics of Cells and Cancer
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Thesis possibility after internship: YES **Funding:** PENDING

TITLE: Electrical control of hair-cell mechanosensitivity.

SUMMARY: Sounds are detected in the inner ear by mechano-sensory "hair cells" which convert vibrations of their hair bundles into electrical signals (Fig. 1). Mechano-electrical transduction happens from the direct mechanical activation of ion channels by force, which is transmitted by so-called tip links. The mechanical correlates of channel gating—the gating force and the gating swing—are fundamental determinants of hair-cell mechanosensitivity but are poorly understood. We have recently shown that varying the electrical potential across the sensory hair-cell epithelium modulates the gating force, by up to ±100%, and discovered an unexpected transition between two functional states at a threshold value of the transepithelial potential: a state of low gating force ('OFF STATE'), for which mechanosensitivity is low and the hair bundle quiescent, and a state of large gating force ('ON STATE'), for which mechanosensitivity is high and the hair bundle oscillates spontaneously. The aim of the traineeship will be to study this transition and modulate its properties by external biochemical perturbations. Our observations are strongly suggestive of a first-order phase transition, which is thought to occur through a collective rearrangement of the transduction-channel protein complex (at least 10 proteins). Its demonstration would constitute a change of paradigm from a protein-centric view of mechanosensitivity (one protein, one function), for collective effects are largely ignored in the field. Experiments will combine force application on single hair bundles (range: 1-100 pN), application of transepithelial potentials (range: ±100 mV), and biochemical perturbations. This project involves a collaboration with Tony Ricci (Stanford University) and could be followed up by a thesis.

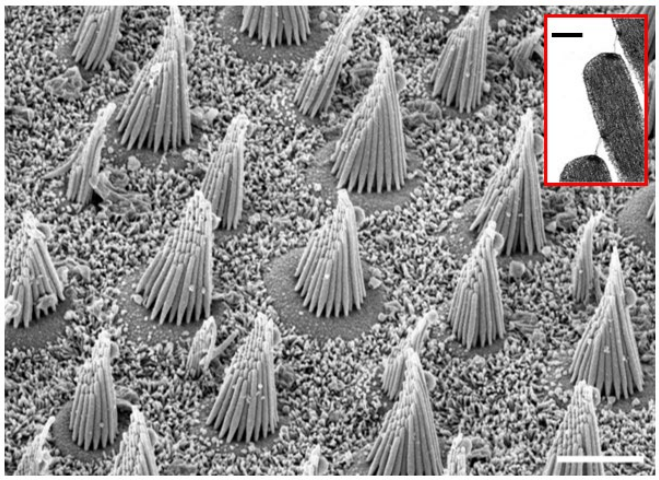

Figure 1: Electron micrograph of hair bundles protruding from the apical surface of the sensory epithelium in a frog's ear; the inset shows the "tip links". Scale bars: 5 µm (bottom), 200 nm (inset).

Keywords: bioelectricity, cell mechanics, hearing, ion channels, mechanosensitivity, oscillations, phase transitions.

References:

Joliot A, Stickel L, Martin P (2024) Electrical control of the transduction channels' gating force in sensory hair cells. BioRxiv. DOI: 10.1101/2024.12.13.628311.

Hudspeth AJ, Martin P (2024) The Critical Thing about the Ear's Sensory Hair Cells. J Neurosci 44:e1583242024.

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