Master 2 SBCP

INTERNSHIP PROPOSAL

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Thesis possibility after internship: YES

TITLE: Calcium control of auditory mechanosensitivity by the inner ears' hair cells.

SUMMARY: Sounds are detected in the inner ear's cochlea by active mechano-sensory hair cells (Fig. 1A). Hearing starts with the deflection of the hair bundle, a cohesive tuft of "stereocilia" that works as the hair cell's mechanical antenna (Fig. 1B). Hair-bundle vibrations modulate tension in oblique tip links that pull on mechanosensitive channels at the stereociliary tips (Fig. 1B, inset), producing an electrical signal that is then interpreted by the brain. Reciprocally, channel gating affects tip-link tension and thus produces internal forces on the hair bundle, reducing the bundle's stiffness and increasing its friction (Fig. 1C)(Bormuth et al., 2014). This phenomenon is highly relevant to hearing because hair-bundle mechanics controls mechanosensitivity to sound-evoked forces. Here we propose to study how calcium—whose concentration is tightly controlled in auditory organs--modulates the magnitude of gating forces. To tackle this challenge, the trainee will combine force application on single hair bundles with a recently developed microperfusion system (Fig. 1D) that creates a microcompartment of controlled ionic composition around the hair bundle under study. We will measure force-displacement relations as a function of the calcium concentration in this microcompartment and study the dynamics of mechanical changes upon fast changes of the calcium concentration. The work will be performed in close collaboration with two PhD students in the group.

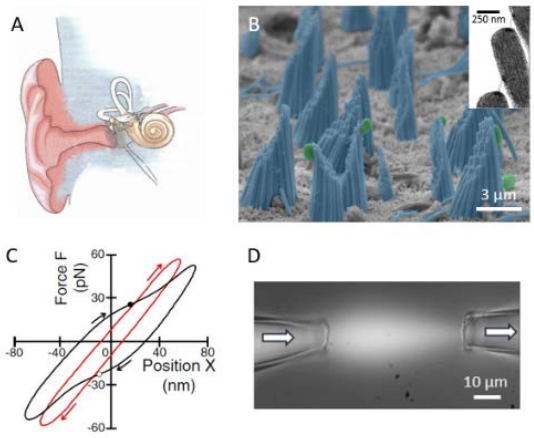

Figure 1: A: schematic of the human inner ear. B: electron micrograph of hair bundles protruding from the apical surface of the sensory epithelium in a frog's ear; the inset shows the "tip links". C: Force-displacement relation of a single hair bundle upon periodic (triangular) stimulation under control conditions (black) and with blocked transduction channels (red), demonstrating the mechanical effects of channel gating. D: microperfusion system to produce a compartment of controlled ionic composition. Confinement between the two micropipette is here demonstrated by using fluorescence microscopy to visualize fluorescein ejected from the left pipette, but absent in the bath..

REFERENCES:

Bormuth V, Barral J, Joanny J-F, Juelicher F, Martin P (2014) Transduction channels' gating can control friction on vibrating hair-cell bundles in the ear. Proc Natl Acad Sci U S A 111:7185–7190.

Tinevez JY, Julicher F, Martin P (2007) Unifying the various incarnations of active hair-bundle motility by the vertebrate hair cell. Biophys J 93:4053–4067.