ENS – IISER Network / BIOSANTEXC Project

Internship Proposal Form
France to India

(Discipline/Field name)

Single Molecule Biophysics

Internship title: Deciphering the aging of mechanoresponsive proteins under repetitive exposure to mechanical tension

Keywords related with the subject (minimum 3): Gating-springs, Mechanoresponsive proteins, Magnetic Tweezers

Name of the IISER: Indian Institute of Science, Education and Research Mohali

Name of the laboratory(ies): Single Molecule Mechanobiology

Name of the internship supervisor(s): Dr. Sabyasachi Rakshit

Email(s): srakshit@iisermohali.ac.in

Prerequisites for the internship: Basic understanding of molecular biology, statistics, and comfortable working with high-precision Instruments.

Requested level: Masters / Graduates

Foreseen internship dates: April 2025- September 2025

Internship type (refer to page 1):
☑ 3–6-month internship ☐ Research stays ☐ 6+6 months internship

For 3 to 6 months internships, please indicate the desired duration: 6 months

For 6+6 months internships, please also fill in:

- **Name of the internship co-supervisor:**
- **Name of the co-supervisor's laboratory/entity:**
- **Email of the co-supervisor:**

Internship proposal (description and expected training outcomes / half page min, 1 page max):

Objective:

1. Measure the elasticity of tip-link proteins using magnetic tweezers.
2. Understand how tip-link stiffness changes under repetitive (oscillatory) forces, similar to sound waves.

Hypothesis: Sound travels through air as vibrations, which create an oscillating force that is sensed by the ear for converting mechanical signals into electrical signals (mechano-electro-transduction). Unlike common experiments that use steady or gradually increasing force, we believe that under real-life oscillating forces, tip-link proteins will show different stiffness depending on the frequency and duration of the signal. When exposed to natural sound with changing intensity and frequency, the tip-link may adapt its elasticity and demonstrate a flexible mechano-response.

Background: Tip-link proteins act like springs that transmit mechanical signals to ion channels, allowing us to hear. Even though tip-links receive strong external forces, only a specific amount is passed on to the ion channels. Our recent studies, using steady force, show that tip-links not only transmit signals but also manage excessive force to protect the ear. However, while these studies reveal how tip-links protect ion channels, they don't mimic the repetitive nature of sound waves. How tip-links behave under continuous vibrations, and how their elasticity changes with these forces, has yet to be explored.

Current Gaps: Most studies so far have used steady or linearly changing forces, which don't represent the complex and non-linear nature of real-world mechanical inputs, such as sound waves. Natural mechanical signals vary in both strength and frequency. To understand how our hearing works from a single-molecule perspective, experiments should better simulate these natural, changing conditions.

Approach: We plan to use experiments that apply a consistent oscillating force, which more closely resembles how natural sound waves work. By varying the frequency and strength of the force, we can gain a better understanding of how tip-link proteins adapt during the process of hearing.

Expected Project Outcomes: Studying how oscillating forces affect hearing at the molecular level is a largely unexplored field. Our goal is to examine how tip-links dynamically adjust and adapt when exposed to different sound frequencies. This research could provide insights into issues like age-related hearing loss and shed light on the fundamental process of hearing mechanotransduction.

Expected training outcomes:

The research trainee will be exposed to the following systems and protocols and acquire hands-on experience-

1. Basic protein biology and molecular biology, Surface Preparation techniques for Single-molecule studies
2. Performing experiments using our laboratory-built Magnetic tweezers, custom-built AFM, and learn MATLAB programming for automated data analysis and presentation.

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