

IC-3i International PhD Program
PhD thesis project
2017 Call for application



**Size Control of the Hair-Cell Bundle
for Frequency-Selective Auditory Detection**

General information

Call	2017
Reference	2016-06-MARTIN
Keyword(s)	hair cell, mechanosensitivity, hearing, actin, biophysics

Director(s) and team

Thesis director(s)	Pascal Martin. Codirector: Christine Petit (Institut Pasteur)
Research team	Active Mechano-Sensitivity by Hair Cells in the Inner Ear
Research department	UMR 168 - Physical Chemistry

Description of the PhD thesis project

Auditory processing of complex sounds like speech or music relies on acute frequency discrimination over a broad range of sound frequencies. To cope with this requirement, the cochlea of the inner ear is endowed with specialized mechanosensory “hair cells” that are each tuned to detect a particular frequency of sound-evoked vibration. Tuning results in part from the mechanical properties of the hair bundle, the mechanosensory antenna of the hair cell. Morphological gradients within the cochlea suggest that the hair bundle operates as a (living) tuning fork for which size helps select the preferred frequency of vibration. Despite its critical importance for hearing, the mechanism that specifies the morphology of the hair bundle in relation to the characteristic frequency of the corresponding hair cell is largely unknown.

To clarify this major question of auditory physiology, the PhD candidate will study the role played by mechanical tension in proteinaceous links that interconnect the “hairs” (stereocilia) of the hair bundle. The work will benefit from an ongoing collaboration between our group at the Curie Institute, which brings the biophysical tools to experimentally probe and theoretically describe the effect of mechanical force on the hair bundle, and the group led by Prof Christine Petit (Institut Pasteur), which brings genetically modified mice that present defects in the morphology of the hair bundle as well as a biochemical know-how to identify, visualize and interfere with molecular constituents of this organelle.

Defects in the morphology of the hair-cell bundle result in severe hearing deficits. By better understanding how this morphology is tuned according to the bundle’s function as a frequency-selective mechanosensor, as well as by finding the physical origin of its deterioration in deaf animals, we hope to lay the groundwork for some future therapeutic approaches of deafness of genetic or environmental origin.

International, interdisciplinary & intersectoral aspects of the project

The project involves international collaborations with a Korean group (Prof Jinwoo Cheon, Yonsei University) for the development of magnetic nanoparticles to apply forces to the hair bundle and with Oticon Medical, an industrial partner located in Denmark that develops hearing aids and cochlear implants. The work will be co-supervised by Dr Pascal Martin, a biophysicist (leader of the project), and Prof Christine petit, a biologist (partner), who bring the interdisciplinary expertise between physics and biology that will be necessary for the success of the project.

Recent publications

1. Bormuth V, Barral J, Joanny JF, Jülicher F, **Martin P**.
Transduction channels'gating can control friction on vibrating hair-cell bundles in the ear.
Proc Natl Acad Sci U S A. 2014 May 20;111(20):7185-90. doi: 10.1073/pnas.1402556111.
2. Barral J, **Martin P**.
Phantom tones and suppressive masking by active nonlinear oscillation of the hair-cell bundle.
Proc Natl Acad Sci U S A. 2012 May 22;109(21):E1344-51. doi: 10.1073/pnas.1202426109.
3. Barral J, Dierkes K, Lindner B, Jülicher F, **Martin P**.
Coupling a sensory hair-cell bundle to cyber clones enhances nonlinear amplification.
Proc Natl Acad Sci U S A. 2010 May 4;107(18):8079-84. doi: 10.1073/pnas.0913657107.
4. Hudspeth AJ, Jülicher F, **Martin P**.
A critique of the critical cochlea: Hopf, a bifurcation, is better than none.
J Neurophysiol. 2010 Sep;104(3):1219-29. doi: 10.1152/jn.00437.2010.
5. Tinevez J-Y, Jülicher F, **Martin P**.
Unifying the various incarnations of active hair-bundle motility by the vertebrate hair cell.
Biophys J. 2007 Dec 1;93(11):4053-67.

Expected profile of the candidate

Applicants should have a strong desire to work at the interface between physics and biology on living cells, and should show solid capacity for independent, quantitative and creative thinking. Background in biophysics is strongly recommended. Background in cell mechanics, the cytoskeleton, sensory systems, or mechanobiology is a plus but not compulsory. The project highly relies on microscopy and micromanipulation of cells, for which the applicant should have either experience or a strong motivation to learn.