

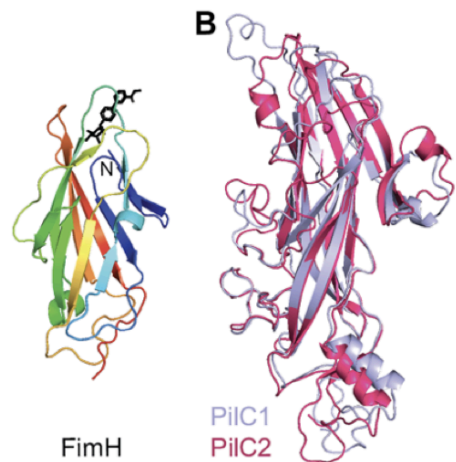
Thesis Project 2024-2025

Rigidity sensing through pilC/pilY1

The role of mechanical cues in controlling biological fate is being appreciated each day a little more. While mechanosensing has been mostly studied in eukaryotic cells, there is growing evidence that organisms as simple as bacteria also display a "sense of touch".

Type 4 pili (T4P), which are ubiquitous filamentous nano-machines in prokaryotes, have been postulated to play a role in mechanosensing in bacteria, in addition to an amazingly wide range of functions (motility, cell adhesion, DNA uptake *etc.*). The molecular mechanisms at play in **T4P-mediated mechanosensing** are still to be elucidated, which is the goal of this project.

In particular the key role of the protein **pilC/pilY1** located at the tip of the pili of many different bacterial species has recently emerged. This protein is modular, presenting two domains with separate functions. With a consortium of collaborators from Marseille and Necker hospital, we have identified mutants in pilC/pilY1 that affect either the biogenesis, dynamics or adherence of pili in multiple species. Focusing first on the human pathogen *Neisseria meningitidis*, we will use different biophysical characterizations of the force exerted by the pili and its adherence to different substrates to dissect the mechanisms behind mechanotransduction. In particular, the candidate will learn to make **microfabricated substrates**, use **flow-chambers**, and **perform image analysis from live imaging**. In case of a pursuit for a PhD thesis, **optical and magnetic tweezers** will also be used to fully characterize biophysically the different mutants. With this knowledge, we hope to be able to establish a precise molecular motor of the involvement of the protein pilC/pilY1 in pili-mediated mechanotransduction. Given the abundance of bacterial species carrying this protein in their genome that will give us means to control many aspects of bacterial life mediated by this appendage, from adhesion, colonization to DNA uptake and potentially antibiotic resistance. We are looking for a **motivated PhD candidate**, with either a **physics or biology background**, to join this project. **Please reply by July 11th.**



Nicolas Biais, Professor of Cellular Biomechanics, Laboratoire Jean Perrin,
Nicolas@mechano-micro-biology.org or Nicolas.Biais@sorbonne-universite.fr