

INTERNSHIP PROPOSAL

Institute and Group: Institut de Biologie Structurale, Groupe Microscopie Electronique et Méthodes (MEM)

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Research project title: Using atomic force microscopy topography to reconstruct large biological complexes.

5 Keywords to describe the project: Atomic force microscopy; structure reconstruction; image processing; simulation; modelling

**Description of the project (aims, experimental techniques, recommended background):
10 to 15 lines:**

As of today, more than 100,000 structures of biological macromolecules have been determined by x-ray diffraction. The majority of them are small to medium size globular proteins. There is a lack of representation of membrane proteins as well as large complexes. Currently, there is a huge effort coming from the recently revolutionized electron microscopy in which high-resolution structures of large complexes are determined.

The aim of the project is to pursue the development of methods that enable the laboratory to reconstruct large protein complexes using high-resolution topographic surfaces from atomic force microscopy. Our hypothesis is that it is possible to build large structures using their individual components with the aid of topographical surfaces obtained with AFM. The reconstruction protocol is based on a six-dimensional docking of individual components. The core of the project is the testing of different scoring methods from docking orientations. The candidate will work in a Linux-based computer environment and should be familiar with basic knowledge in structural biology. The candidate will be trained on our high-resolution atomic force microscope.

Justification that the internship's subject fits with the general theme of GRAL (3 lines):

This project aims at using novel structural information obtained by atomic force microscopy which is an additional technique toward integrating knowledge on the structure and dynamics of proteins and their function. Therefore, it expands the goal of the GRAL Labex.

Relevant publications of the team (3 max):



Grenoble Alliance for Integrated
Structural & Cell Biology

Chaves RC, Dahmane S, Odorico M, Nicolaes GAF and Pellequer J-L (2014) Factor Va alternative conformation reconstruction using Atomic Force Microscopy. *Thromb. Haemost.* **112**: 1167-1173.

Chaves RC and Pellequer JL (2013) DockAFM: benchmarking protein structures by docking under AFM topographs. *Bioinformatics* **29**: 3230-3231.

Trinh M-H, Odorico M, Pique ME, Teulon J-M, Roberts VA, Ten Eyck LF, Getzoff ED, Parot P, Chen S-wW and Pellequer J-L (2012) Computational reconstruction of multidomain proteins using atomic force microscopy data. *Structure* **20**: 113-120.