

GRAL MSc RESEARCH SCHOLARSHIP 2020-2021  
RESEARCH INTERNSHIP PROPOSAL

**Institute / Group**

IRIG / IBS - EBEV

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**Research Project Title**

Using atomic force microscopy topography to reconstruct large biological complexes

**Description of the project**

As of today, more than 150,000 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, but a gap persists for individual structures around 100 kDa.

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.

**Keywords**

Atomic force microscopy, structure reconstruction, image processing, simulation, modelling

**Relevant publications of the team**

Singh S, Nazabal A, Kanniyappan S, Pellequer J-L, Wolberg AS, Imhof D, Oldenburg J and Biswas A (2019) The plasma Factor XIII heterotetrameric complex structure: unexpected unequal pairing within a symmetric complex. *Biomolecules*.

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.

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.

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