

**Master 2 internship project
Year 2022-2023**

Laboratory/Institute: MEM/IBS

Team: AFM

Director: W. Weissenhorn

Head of the team: J.L. Pellequer

Name and status of the scientist in charge of the project: JL Pellequer HDR: yes no

Address: 71 avenue des Martyrs

Phone: 045742 87 56

e-mail: jean-luc.pellequer@ibs.fr

Program of the Master's degree in Biology:

- Microbiology, Infectious Diseases and Immunology Structural Biology of Pathogens
 Physiology, Epigenetics, Differentiation, Cancer Neurosciences and Neurobiology

Title of the project: Atomic force microscopy topography and reconstruction of large biological complexes

Objectives (up to 3 lines):

Screening computational models of full-length coagulation factors to test their topographical agreement with experimental data obtained from atomic force microscopy. Application performed on coagulation factors VIII and XIII.

Abstract (up to 10 lines):

With the recent revolution of Artificial Intelligence protein structure prediction (alpha-fold), there is not much doubt that very soon most of individual protein chains will have a D structure available. However, it is not yet the case for dimers, tetramers and oligomers of proteins. In case, we rely on integrative structural biology approaches that combine multiple technique toward a synergetic goal of determining the 3D structures of large protein assemblies. We participate in this effort by applying topographical information obtained from atomic force microscopy. We developed a computer pipeline that aims at building/selecting large protein assemblies. The internship will consist of applying this pipeline of two large multimeric assemblies: coagulation factors VIII and XIII. These two critical coagulation factors act at different levels in the coagulation cascade but their global and intact structure remains unknown. The candidate will pursue the refinement of the pipeline by defining a novel scoring energy function to select best assemblies.

Methods (up to 3 lines):

Application of the AFM-Assembly pipeline that runs on Linux workstations. Definition of appropriate computational parameters. Set-up automated run and analyze computational results with homemade programs or scripts. Important implication in data management plans.

Up to 3 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* 9: 765.

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.

Requested domains of expertise (up to 5 keywords):

Structural biology, bioinformatics, Linux.