

Master project 2021-2022

Personal Information

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Project

Structural bioinformatics

Project Title:

Integrative approaches to resolve protein structures in vivo

Keywords:

Integrative structural biology, Python, ImageJ, Pymol, CryoEM

Summary:

The mechanisms regulating biological processes are central questions in biomedicine. However, these mechanisms rely on protein structures and conformational dynamics that are often unknown. The complexity of the protein machinery involved, and fast cycles of assembly-activity-disassembly have prevented full understanding of the molecular basis that control human biology. For instance, in our group, we investigate the mechanism that drives exocytosis, a process that is essential in neurobiology and cell growth and whose mechanism of action is a long standing question in the field. We have developed a new method of fluorescent microscopy capable to resolve the 3D architecture of protein assemblies directly in living cells. Using this approach and computational integration of structural data we reconstructed de novo the exocytic machinery at the nanometre scale (Picco et al 2017 Cell). Our unpublished data indicates that the exocytic machinery organizes in transient higher-order structures with dimensions similar to the Nuclear Pore Complex, but with a highly dynamic behavior that prevents its purification and reconstitution in vitro. For these reasons, high-resolution structures and conformational dynamics necessary to understand the mechanism of exocytosis remain elusive. We offer a position for a Master student to continue the work published in Cell (Picco et al 2017 Cell). The student will use IMP (Integrative Modelling Platform, developed in A. Sali's lab), Python and image analysis to integrate in vitro and in cellulo datasets (i.e. live-cell imaging, cryo-EM, homology modelling, super resolution microscopy...) and to reconstruct the high-resolution structure of the supra-assembly that controls exocytosis. The project will be done in collaboration with the groups of Daniel Castaño (Biozentrum, Basel, Switzerland) and Alex de Marco (Monash University, Melbourne, Australia). The student is expected to contribute, together with experimentalists, in a larger project aiming to resolve the mechanism of exocytosis.

References:

Picco, A., Irastorza-Azcarate, I., Specht, T., Böke, D., Pazos, I., Rivier-Cordey, A-S., Devos, D.P., Kaksonen, M., Gallego, O., (2017) "The in vivo architecture of the exocyst provides structural basis for exocytosis." Cell 168, 400-412.e18.

Expected skills::

Expertise with Python is required.

Possibility of funding::

Yes

Possible continuity with PhD: :

To be discussed
