Universitat Pompeu Fabra Barcelona | Master in Bioinformatics for Health Sciences

Master project 2020-2021

Personal Information

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Project

Structural bioinformatics

Project Title:

Integrative Structural biology of exocytosis

Keywords:

Integrative Modeling Platform, Python, Integrative structural biology, Exocytosis

Summary:

This project aims to push the limits of integrative structural biology to resolve fundamental problems in cell biology. The student is expected to develop computational tools that strengthen a multidisciplinary team of bioinformaticians, physicists and experimentalists and that provide us with unique capabilities to resolve molecular structures. The biological question that we would like to address is exocytosis, a cellular process responsible to deliver biomolecules to the plasma membrane and extracellular space that is conserved in all eukaryotic cells. Exocytosis controls the growth of cell surface and it is directly coupled with the cell cycle and viability. However, the mechanism that regulates exocytosis is a central question in cell biology that could not be answered yet. Decades of research and the latest developments in gene editing, molecular biology and cryoEM have provided fundamental insight about exocytosis, but failed to resolve the molecular details that control this essential process. The complexity of the protein machinery involved and fast cycles of assembly-activity-disassembly have prevented full understanding of exocytosis. Recently, we developed a new method of fluorescent microscopy capable of resolving 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). However, high-resolution structures and conformational dynamics necessary to understand the mechanism of exocytosis remain elusive. We offer a position for a Master student to push further integrative structural biology and that, together with our collaborators (D. Davos, CABD, Sevilla; J. Ries, EMBL, Heidelberg), works to develop the computational tools that can overcome current technical limitations. The student will use Python and the Integrative Modeling Platform (IMP, developed in A. Sali's lab at UCSF) to integrate in vitro and in cellulo datasets (i.e. live-cell imaging, cryo-EM, homology modeling, super resolution microscopy…) and to reconstruct the high-resolution structure of the supra-assembly that controls exocytosis. The student will team-up with a PhD student from our lab to explore new strategies involving Monte Carlo sampling methods and coarse-grained modeling among others. Overall, he/she is expected to contribute to a larger project aiming to resolve the mechanism of exocytosis.

References:

Picco, A., Irastorza-Azcarate, I., Specht, T., B.ke, 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. Knowledge on structural modeling or molecular dynamics will be a plus.

Possibility of funding::

Yes

Possible continuity with PhD: :

To be discussed

Comments:

High motivation for learning, team work and pushing the project forward is a must.