upf. Universitat Pompeu Fabra Barcelona

Master in Bioinformatics for Health Sciences

Master project 2021-2022

Personal Information

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Project

Structural bioinformatics

Project Title:

Computational elucidation of large-scale activation dynamics in a multi domain protein

Keywords:

Multi-domain, state transition, metadynamics, conformational transition, gelsolin, amyloidosis, calcium.

Summary:

Gelsolin (GSN) is the prototype of a family of Ca2+ dependent proteins that regulate actin oligomerization state through their severing, capping and nucleating activities. Due to this polyvalent function and modular construction, gelsolin-like proteins are involved in several physiological processes. However, an exhaustive model of its physiologic mechanism of action is not yet available due to the highly dynamic structures of both gelsolin and actin. This project aims to develop a robust model of GSN activation by combining experimental and computational approaches. We will use extensive ("big data") molecular dynamics simulations with state-of-the art methodologies to elucidate the rare events and pathways underlying state transitions that are both physiologically relevant for the maintenance of the cell cytoskeleton, as well as in the pathology of diseases such as AGel amyloidosis. The work is essentially computational. The student will work with the direction of Dr. T. Giorgino [www.giorginolab.it] of the Institute of Biophysics of the Italian National Research Council. The work is part of an active scientific line conducted with the close collaboration of experimentalists (SAXS, crystallography, mutagenesis, stability assays). Due to the coronavirus situation, remote collaboration will be strongly preferred.

References:

- Giorgino T, Mattioni D, Hassan A, Milani M, Mastrangelo E, Barbiroli A, et al. Nanobody interaction unveils structure, dynamics and proteotoxicity of the Finnish-type amyloidogenic gelsolin variant. Biochimica et Biophysica Acta (BBA) - Molecular Basis of Disease. 2019 Mar 1;1865(3):648–60. - Chumnarnsilpa S, Robinson RC, Grimes JM, Leyrat C. Calcium-controlled conformational choreography in the N-terminal half of adseverin. Nat Commun. 2015 Nov;6(1):8254. - Nag S, Larsson M, Robinson RC, Burtnick LD. Gelsolin: The tail of a molecular gymnast. Cytoskeleton. 2013;70(7):360–84.

Expected skills::

The project is computationally oriented. Familiarity with Unix and interest in molecular simulations are essential. A degree of scientific independence is a plus.

Possibility of funding::

No

Possible continuity with PhD: :

To be discussed