Mathsys project: Modelling actin curling and contraction under protein interaction
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Background: Actin is an essential structural protein in animal, plant and bacterial cells and fulfils a multitude of roles from shaping cells to gene regulation. This versality is due to the ability of actin to polymerize into filaments of several micrometers in length and its interaction with other proteins that can modulate the actin filament dynamics, alter its mechanical properties or link actin to other cellular structures. In particular, two phenomena have attracted the interest of experimental and theoretical physicists and mathematicians: interactions of actin filaments with i) molecular motors giving rise to active gels and ii) actin filament interactions with lipid membranes, which give rise to excitable systems. In recent studies, Köster identified a protein (called Rng2) that, when placed in a lipid membrane, can bend actin filaments into tight curls (1-4 um diameter), Figure 1. Addition of motors increases the curling and can even lead to actin ring contraction. The molecular mechanisms behind this phenomenon are not yet understood. This project aims to yield a better understanding of the physical and molecular mechanisms by modeling these processes.

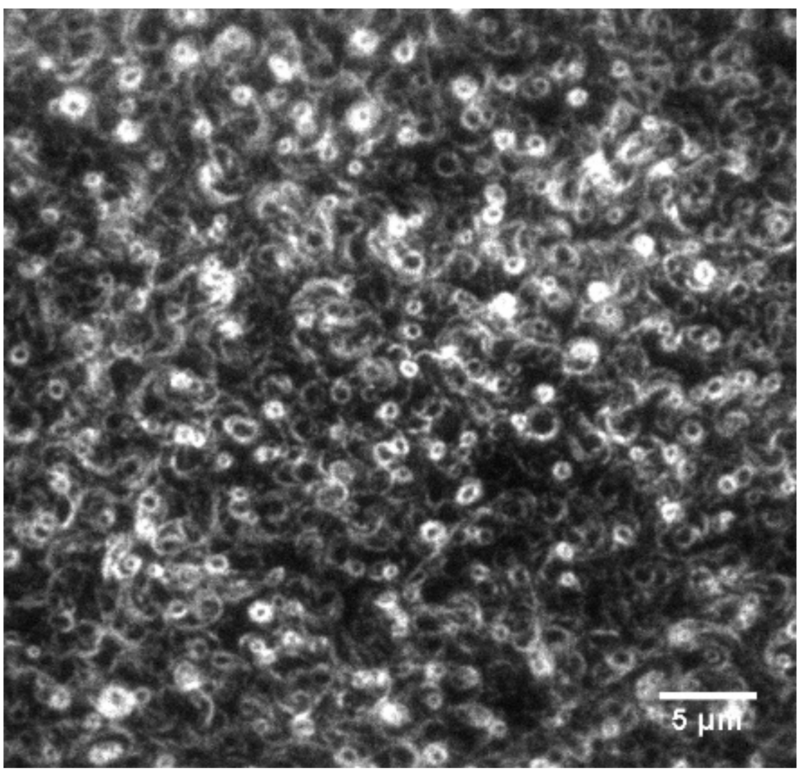

Fig. 1. Image of fluorescently labelled actin filaments binding to a Rng2[1-189] decorated lipid membrane.

The project: This is a computational project, using MatLab, C++ or python. You will build two types of models, firstly a bead-spring model of the actin filament - actin is in fact a spiral, Figure 2, and an elastic ribbon continuum model [1,2] to capture the filament twist. The latter may allow analytical treatment. The Rng2 protein has 2 actin binding sites, so upon binding it could either change the filament twist, resulting in curvature when attached to a surface, or bring two of the actin monomers within the filament closer together, i.e. create curvature. You will test these two hypotheses with your models to examine if they can recreate the data and a number of key observations. Motors can also be modeled; these crosslink the actin filaments.

Desirable skills. A keen interest in using modeling and computation to address biological problems. Experience with Monte carlo methods will be useful. An understanding of mechanics and geometry (for parametrisation of curves in 3D) will also be useful.

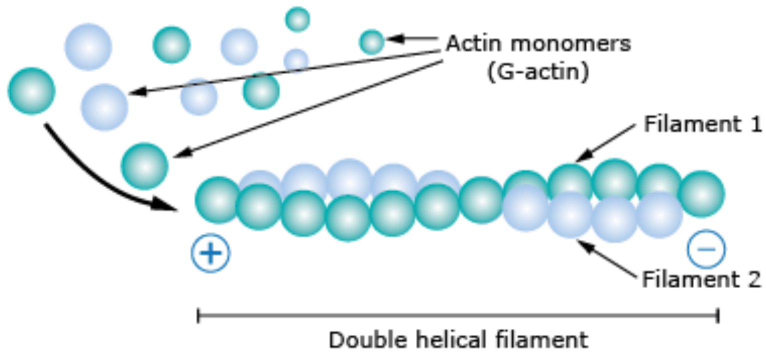

Figure 2. Actin filament showing helix structure.

Possibilities of a PhD.

There are a number of potential options for making this into a PhD. For instance:

i) Actin-protein dynamics. There is tremendous interest in protein interactions with actin. Another well studied system is cofilin, that cuts actin, but can generate complex dynamics in association with capping proteins [3]. This PhD would examine protein-actin interactions and its impact on mechanics and dynamics. A suitable external would be contacted in CNRS, Paris, France.

ii) Generalisation to DNA origami, examining DNA filament shapes and interaction with motors. Creating DNA with specific mechanical properties may also be possible leading to predictive modeling and testing against new experimental data. A suitable external would be contacted in Fraunhofer Institute in Leipzig, Germany.

Other possibilities include modeling the actin cortex and the actomyosin ring (yeast cell division).

References.

[1] Roadmap to the Morphological Instabilities of a Stretched Twisted Ribbon. Julien Chopin, Vincent Démery, Benny Davidovitch. 2015. *J. Elasticity* 119;137-89.

[2] Buckling of Naturally Curved Elastic Strips: The Ribbon Model Makes a Difference. Audoly B., Seffen K.A. (2016). In: Fosdick R., Fried E. (eds) *The Mechanics of Ribbons and Möbius Bands.* Springer, Dordrecht.

[3] ADF/Cofilin Accelerates Actin Dynamics by Severing Filaments and Promoting Their Depolymerization at Both Ends. Hugo Wioland, Berengere Guichard, Yosuke Senju, Sarah Myram, Pekka Lappalainen, Antoine Jégou, Guillaume Romet-Lemonne. *Curr Biol*. 2017; 27, 1956-67.