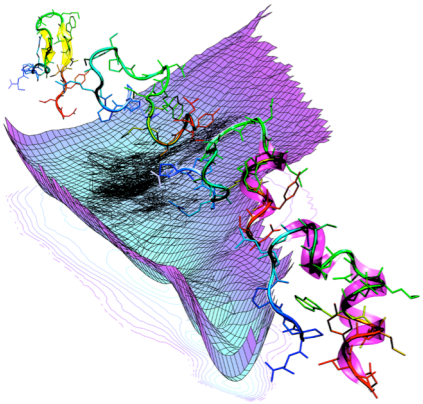
SUMMER INTERNSHIPS 2017

TITLE: Temperature dependent friction in proteins

DESCRIPTION (Objectives, tasks, materials, equipment…):

Protein folding is the process by which protein polypeptide chains are able to acquire their three dimensional (native) structures. Protein folding is essential to living organisms, as proteins usually require a well-defined structure to undertake their biological functions.

The folding reaction usually occurs in solution and is subject to the frictional forces of the solvent against the protein. However, for over 20 years a different source of friction has been invoked, due to interactions of the protein with itself (hence the term "internal friction"). In the last years we have proposed an explanation for the molecular mechanisms of internal friction. In this project we will focus in the temperature dependence of internal friction, which has been resolved experimentally for fast folding proteins, but remains unexplained.



Cartoon representation of the Trp cage mini protein as it traverses the folding energy landscape from a misfolded state (yellow) to its native form (magenta). This barrier crossing process is subject to solvent friction but also to "internal" friction.

In this project we will use computational tools to tackle this problem. We will run atomistic molecular dynamics simulations of model systems (short alanine-based peptides) and analyze simulations of full proteins. From the model systems we expect to recover fundamental aspects of the temperature dependence of internal friction, as we have seen before at a single temperature. Then we will aim for establishing connections between the physics of the simple system and the macroscopic observations of the full proteins.

The work in this project will be fully computational, although the candidate will be trained to think with reference to experimental results. During the internship, the candidate will be equipped with a skillset that is currently in high demand both in academia and in industry, including some basic knowledge of UNIX systems, programming in the Python scripting language, computing in parallel architectures, and using analytics methods akin to those used in Big Data industries. Additionally, the simulation techniques that will be used are essential in drug discovery, making it an excellent skill for those considering a career in Pharma. No prior knowledge of computer programming is required.

References:

- Ken A. Dill and Justin L. MacCallum, The Protein-Folding Problem, 50 Years On, *Science* 338 (2012), doi: 10.1126/science.1219021
- Stephen J. Hagen, Solvent Viscosity and Friction in Protein Folding Dynamics, *Curr. Protein Pept. Sci*. 11 (2010), doi: 10.2174/138920310791330596
- David De Sancho, Anshul Sirur and Robert B. Best, Molecular origins of internal friction effects on protein-folding rates, *Nat. Commun.* 4307 (2014), doi:10.1038/ncomms5307

SUPERVISOR: Dr. David De Sancho

SHORT DESCRIPTION OF THE GROUP: The Nanobiomechanics group is focused on atomic-force microscopy to study the mechanical features of proteins. The group is led by Dr. Perez-Jimenez and uses advanced molecular-biology techniques and cutting-edge force spectrometers to investigate the role of mechanical forces in biology.

More info: http://www.nanogune.eu/nanobiomechanics

TIMETABLE: to be determined

COMMENTS: Internship duration from 1.5 to 2 months (to be discussed).
Applicants should send an email to jm.pitarke@nanogune.eu including their academic record.
More info: http://www.nanogune.eu/summer-internship
Deadline for applications: 5 February 2017

SUITABLE FOR: chemists, biochemists, and physicists with an interest in biology