**Computational modelling of protein dynamics in heart and muscle disease**

The research activity of the group is focused on the computational modelling of structural and dynamical properties of proteins involved in heart and skeletal muscle contraction using Molecular Dynamics simulations.

At the molecular level, muscle contraction arises from the complex motions of proteins that compose the sarcomere, the basic repeating unit of muscle cells. The normal functioning of muscles relies on the correct regulation and coordination of these motions, so that amino acid mutations affecting single proteins can damage the whole sarcomeric machinery. Indeed, a large number of mutations in sarcomeric proteins have been linked to inherited cardiac and skeletal muscle diseases.
The identification of new therapies for myopathies and cardiomyopathies relies on a deep understanding of these mechanisms at the atomistic level. In particular, knowledge of the fundamental interactions that determine the protein motions can guide the design of drugs that can target sarcomeric proteins. Using a combination of state-of-the-art modelling techniques, the student will investigate how myopathy-related mutations affect the motion and stability of key muscle proteins and how small molecules can be designed to restore their normal function.

**Techniques and Training:** the student will be trained in a wide range of computational techniques for the study of biomolecules and for in silico drug design, including basic and advanced Molecular Dynamics simulation techniques, Homology Modelling of protein structures, Molecular Docking, Virtual Screening and Structural Bioinformatics tools. Moreover, the student will gain experience in Unix-based operating systems and in scripting and programming languages for biomolecular analyses. The training will also include the development of skills essential for career progression, including management of research projects, presentation and writing skills.

**References:**

* Fornili A, Hashem S, Davies WG (2020). Heart Failure Drug Modifies the Intrinsic Dynamics of the Pre-Power Stroke State of Cardiac Myosin. Journal of Chemical Information and Modeling. 10.1021/acs.jcim.0c00953.
* Tiberti M, Lechner BD, Fornili A (2019). Binding Pockets in Proteins Induced by Mechanical Stress . Journal of Chemical Theory and Computation. 10.1021/acs.jctc.8b00755.
* Hashem S, Tiberti M, Fornili A (2017). Allosteric modulation of cardiac myosin dynamics by omecamtiv mecarbil . PLOS Computational Biology. 10.1371/journal.pcbi.1005826.

**Requirements:** BSc in Chemistry/Pharmaceutical Chemistry/Biochemistry