Proposed TFM (Trabajo Final de Master) in Biophysics, year 2020-2021

Dynamical couplings between functional sites of protein complexes with the torsional network model (TNM)

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Protein dynamics in the native state plays a key role for biological function, in particular ligand binding, allosteric regulation and catalysis. Normal mode approximation of structure-based models, termed Elastic network model (ENM), constitutes a physically based approach for computing analytical aspects of protein dynamics in the native state under the hypothesis that the experimentally known native structures is at the minimum of the native free energy basin and that native interactions are not frustrated, i.e. they can all be fulfilled perfectly and simultaneously. This approach provides useful information on protein flexibility and conformational changes. Our laboratory developed an ENM based on torsional degrees of freedom of proteins (TNM) that has several advantages: reduced number of degrees of freedom and faster computations, conservation of the covalent structure and (approximately) of the secondary structure and, most important, better agreement between normal modes and experimental conformational changes.
Through this model, we computed the dynamical couplings between functional sites of proteins, which help characterizing the allosteric communication within protein structure (Alfayate et al., Predicted dynamical couplings of protein residues characterize catalysis, transport and allostery. Bioinformatics 2019 35:4971-4978), and we applied this method to the transport reaction of pentameric ion channels (Hu, Howard, Bastolla, Lindahl, Delarue. Structural basis for allosteric transitions of a multidomain pentameric ligand-gated ion channel. Proc Natl Acad Sci USA 2020 117:13437-13446).

As ion channels, many enzymes form homo-oligomeric complexes in which protein chains with identical sequence are structurally related through conformational changes. The proposed work is aimed at systematically characterize these conformational changes and relate them with the corresponding dynamical couplings, in order to gain some insight on the structural basis of allosteric communication in proteins.

The study will use the computational infrastructure of the Centro de Biologia Molecular Severo Ochoa (CBMSO) in the UAM campus but, due to the Covid-19 pandemics, most of the work will take place online.