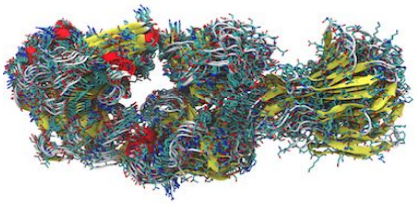

IV ASBioSim – Advanced School on Biomolecular Simulation: Protein Engineering with Rosetta, from fundamental principles to tutorials
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DYNAMICS AND STRUCTURE REFINEMENT OF A TWO-DOMAIN PROTEIN USING SAXS

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Abstract:
Small-angle scattering (SAS) of X-rays (SAXS) has proven to be a powerful tool to study structure and dynamics of multi-domain proteins and protein complexes aided by complimentary techniques to increment the resolution information. SAXS allows the determination of the overall shape and shape changes of biological macromolecules in solution, as well as the investigation of macromolecules stability over time, and the degree of monodispersity. In recent years considerable effort has been devoted to explore the synergy between SAS and other biophysical strategies in order to better characterize multi-domain proteins and protein complexes. The overall possibilities of the application of SAXS and its use as a tool for the characterization of structure and dynamics of a two-domain protein, CBD12, will be presented. The *Drosophila* Na^+/Ca^{2+} exchanger (CALX) is a membrane protein that catalyzes the exchange of Na^+ and Ca^{2+} across the lipid bilayer. Regulation of the CALX transport function requires the binding of Ca^{2+} to a sensor domain, CBD12, located a large intracellular loop of the exchanger. CBD12 consists of two domains, CBD1 and CBD2, connected by a short linker. The literature indicates that Ca^{2+}-binding to CBD1 modulates the dynamics between CBD1 and CBD2, which is a key to understand the mechanism behind the exchanger regulation. We will present SAXS experiments carried out in the presence of different calcium concentrations that made possible the observation of changes in protein flexibility in solution, as well as *ab initio* simulations of CBD12 in the unbound and Ca^{2+}-bound states with available computational tools.