Posters

– 11. Computational biophysics –

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Molecular dynamics simulation of engineered β-strand peptide interaction with AqpZ membrane protein

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β-strand peptides can be used to stabilize integral membrane proteins (IMPs); sequestering the hydrophobic surfaces by forming ordered, stabilizing β-barrel-like structures [1]. We are able to design and build hybrid systems crosslinking functionalized β-strand:protein complex to a variety of matrix materials, such as polymers and glass experimentally. The resulted protein-incorporated biomimetic membranes can be used for industrial purposes. Understanding the mechanism underlying b-strand formation and β-strand:protein complexes at the molecular level is essential to control the formation and orientation of the embedded complex in the hybrid device. In this study, AqpZ, the water channel from E. coli, is used as a model protein. We employed a systematic computational approach including molecular dynamics simulations to study the β-strand formation and interaction with the protein, paving the way to rationally design β-strand peptide variants with improved stoichiometric and oriented crosslinking ability on AQP's.

[1] Nat Meth, 2013. 10(8): p. 759-761.

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The order-disorder transition in proteins is a jamming transition

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The order-disorder transitions in grains and glasses, two widely different materials, occurring upon increasing temperature and external load, respectively, have common features. They lead to a universal jamming phase diagram conjecture, but unified theories are lacking, mainly because of the disparate nature of the particle interactions. In my talk I will discuss how the order-disorder transition *in proteins* exhibits signatures common to both glassiness and jamming by using molecular dynamics simulations. Ordered protein regions develop a peak in the interatomic force distributions that is universal with those of jammed matter. Dynamical signatures are found as a dramatic slowdown of stress relaxation upon folding, and a picture of the role of internal interactions emerges. Secondly, in my talk I will also discuss how order parameters (of the type that are typically measured in NMR relaxation) which measure motional disorder at the bond level, are affected by order-disorder transitions and I will link their motional change to a sea-to-lakes transition of the underlying free energy surface. Results have implications for designing stable biopolymers.

(1) P. P. Jose and I. Andricioaei, *Nature Communications* **3**, 1161 (2012)

(2) A.T. Frank, Q. Zhang, H.M. Al-Hashimi, I. Andricioaei, *Biophys. J.* **108**, 2876 (2015)

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Study of a fluid-gel transition process in a lipid bilayer under the influence of an external electric field

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The study of nanoparticles (NPs), their size and their shape has increased importance in many biomedical applications, because of their abilities to pass the phospholipid layer. It is important, hence, to understand how NPs interact with the lipid membrane, and how their surface functionalization drives this interaction. More in details, charged NPS interact with the heads of lipids, perturbing the bilayer, and leading to NP adsorption or bilayer rupture. Wang et al., recently, have experimentally noticed that the adsorption of negatevely charged NP onto the surface of phospholipid layer has restructured the local bilayer phase, promoting a shift from the fluid to the gel one [1]. Through Molecular Dynamics (MD) calculations, we decided to analyze the problem, in order to better focus on the phase shift and on how it occurs under such conditions, by simulating the interaction of the lipid bilayer with an external electric field, amenable to that generated by a negatevely charged NP.

[1] Wang, Bo and Zhang, Liangfang and Bae, Sung Chul and Granick, Steve; *PNAS*, **105**, 18171-18175

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A new protocol to improve the predictive power of molecular docking

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Quantitative understanding of molecular recognition is key for basic research and computer-aided drug design projects. Docking mimics ligand-receptor association *in silico*, providing an atomic-level model structure of their complex. Unfortunately most docking algorithms underestimate receptor flexibility, reducing the rate of success when binding induces large structural changes of partners. Ensemble-docking, where a set of receptor structures (e.g. from MD simulations) is considered, was implemented to overcome this limitation. Clearly, ensemble structures should include conformations prone to host ligands (holo form), which is usually not the case when apo and holo forms are separated by high free energy barriers. To improve generation of holo-like receptor conformations starting only from its apo form, we implemented a computational protocol based on enhanced-sampling MD simulations. We validated our method on proteins whose apo and holo structures were available and previous efforts to generate holo-like structures and native-like docking poses failed. Receptor structures obtained with our method were comparable to those extracted from MD trajectories of the complex. Furthermore, the docking poses generated by using these structures were native-like and top-ranked in score.