Structure and Dynamics of Biomolecular Systems by Combining Enhanced Sampling Molecular Simulations and Experimental Data

Biomolecular systems are typically described by an ensemble of thermodynamic states that interconvert between them at characteristic timescales. Atomistic molecular simulations can assist in determining structural ensembles, yet their accuracy depends on the quality of the forcefield and of the sampling. In this talk I will address the ergodicity problem by evoking VIE-TPS [1], a newly developed coordinate-free enhanced sampling method, able to simultaneously estimate free energy surfaces and interconversion rates between stable states. The forcefield problem will be addressed by Metainference [2], a Bayesian inference method that can optimally combine prior information of the system such as the forcefield with experimental data to provide refined thermodynamic ensembles, with specific focus on Cryo-EM data and the amyloidogenic protein tau. Finally, despite its utter significance, no method so far has been able to correct prior atomistic ensembles in a reweighting fashion, given experimental rate data constraints. By combining the Maximum Caliber principle and VIE-TPS, we develop a new approach able to obtain posterior free energy and committor surfaces that comply with experimental rate constants [3].

1. ZF Brotzakis, P. Bolhuis. JCP 151 (17) ,174111 (2019)

2. M. Bonomi , C. Camilloni ,A. Cavalli, M. Vendruscolo: Sci Adv, 2 (2018)

3. ZFBrotzakis, P. Bolhuis in Prep.

