Emergence of Converged Reaction Coordinates in Biomolecular Dynamics

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Molecular Dynamics (MD) simulations have been a useful technique in studying protein dynamics and investigating its role in biological function. However, objective identification of reaction coordinates (RCs) to describe the underlying multi-dimensional biomolecular energy landscape has proved to be a formidable challenge. Over the last three decades, dimensionality reduction and/or denoising techniques adopted from multivariate statistics such as principal component analysis (PCA) or time-structured independent component analysis (TICA) and and more recently machine learning approaches employing autoencoders have attempted to address this challenge. A common axiom for the aforementioned approaches is the completeness of the dataset, i.e. global equilibration, which is not practically achievable even for the simplest of biomolecules.

In the previous AWS, I discussed the design of a metric, termed mode evolution metric (MeM), to delineate the changes in reaction coordinates with respect to PCA. In the talk, I will present our hypothesis that the RCs for biomolecular dynamics emerge well before equilibration, and the application of MeM to validate it. I will discuss the basic idea about the generalisation of our metric to other dimensionality reduction and/or denoising methods beyond PCA and its applications to multiple model potential energy surfaces. I will also discuss a framework where we plan to use our metric in order to perform metadynamics and obtain accurate kinetic barriers and thermodynamic free energy differences. Additionally, I will also briefly introduce a software library designed in Python3 and algorithms which can be used to calculate various dynamical properties from a trajectory.