I-W Theoretical Studies on Dynamical Foundation of Chemical Reactions and Proteins

Recent experimental developments in single molecule spectroscopy have shed light on the distinct nonergodic features and the heterogeneity of the state space and non-Markovian process of biomolecules. This project focuses on the dynamical foundation of chemical reactions, *i.e.*, why and how do the reacting systems climb through the saddle? and on the developments of new time series analyses to extract the dynamical information regarding the underlying state space structure from single molecule time series.

I-W-1 Phase Space Reaction Network on Multibasin Energy Landscapes

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Recent theoretical developments[1–4] in chemical reactions have greatly improved our understanding of the definability of the no-return dividing hypersurface and the reaction path along which all reacting species follow. By using the HCN/CNH isomerization reaction as an illustrative vehicle of chemical reactions on multibasin energy landscapes, we give explicit visualizations of molecular motions associated with straight-through reaction tube in the phase space inside which all reactive trajectories pass from one basin to another, with eliminating recrossing trajectories in the configuration space. This visualization provides us with a chemical intuition of how chemical species "walk along" the reaction rate slope in the multi-dimensional phase space compared with the intrinsic reaction path in the configuration space. The distinct nonergodic features in the two different HCN and CNH wells can be easily demonstrated by a section of Poincaré surface of section in those potential minima, which predicts *a priori* the pattern of trajectories residing in the potential well. We elucidate the global phase space structure which gives rise to non-Markovian dynamics or dynamical correlation of sequential multi-basin chemical reactions. The controllability of the product state in chemical reactions is also presented in terms of the phase space structure.

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I-W-2 A Construction of Multidimensional Free Energy Landscape from an Ensemble of Single Molecule Time Series

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Recent experimental developments in single molecule spectroscopy hold great promise to shed light on the complexity of dynamics of biomolecules. However, without any knowledge about the potential energy function and the number of energy basins with the metric relation among them, what can we learn from an observed single molecule scalar time series about the multivariate free energy landscape or, in general, state space structure buried in the observations?

Using local ergodicity ansatz as a 0^{th} order description, we developed a new empirical self-consistent scheme to elucidate the local ergodic state distribution function from an ensemble of short single molecule time series and construct an effective multidimensional free energy landscape where local ergodic states are located with preserving the "metric" relationship among them as possible in the projected space. We also proposed the transition sequence analysis to elucidate the degree of memory along each transition sequence path.

I-W-3 A New Technique to Differentiate the Origin of Observed non-Brownian Dynamics in the Principal Component Space

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The dimensional reduction is crucial to focus on some important degrees of freedom in manybody protein dynamics. The principal component (PC) analysis is one of the most widely used methods and the projection of protein dynamics on the PC space have often shown large deviations from a simple normal Brownian picture, for example, in Crambin in crystal,[1)] Cytochrome *c* in water,[2)] Plastocyanin in water.[3)] However, it was derived analytically[4)] that multidimensional normal Brownian motion can also exhibit the regular behavior on the PC space deviated from normal Brownian motion. What can we learn from the projection of complex protein dynamics onto the PC space?

We developed a new diagnostic technique to differentiate the origin of the observed regular behavior in order to extract essential (rather than artifact) informa-

tion inherent to the dynamics of the protein by using finite size Liapunov exponent concept[5),6)] and the PC eigenvalue spectrum.[7)]

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I-W-4 Polypeptide in Water on the Lagrange Picture in Fluid Dynamics

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The (overdamped) Langevin formulation has been one of the most utilized methods in describing complex dynamics of biomolecules in solution. This is based on an implicit assumption of the existence of separable time scales between the global dynamics of biomolecules and those of the surrounding solvents. However, recently, it was revealed for human Lysozyme in solution[1),2)] that the rotational diffusion of *local dipole field*, which is defined as a short time ensemble average of the dipole moment vectors of many individual water molecules at a solvent site through which they pass or visit, has dynamical memory up to 70 times longer than the rotational relaxation of the individual water molecules in the vicinity of human Lysozyme. This indicates that the time separability required for validating the Langevin formulation does not necessarily hold and water molecules may not necessarily retard the protein motions as "friction." We examined a dynamic inseparability of helix-coil transition of polyalanine and the surrounding water rearrangement by investigating the correlation between individual site dipole vector field and turn moiety dynamics of polyalanine. We found that, at the turn formation, the site-dipole field dynamics and turn formation is correlated more significant than those before and after the formation, that is consistent with the computational mechanics analysis for Leu-Enkephalin in solution.[3)]

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