Theoretical Studies on Reactions, Functions, and Fluctuations in Condensed-Phase Systems

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Our research centers on complex fluctuations in condensed systems, including supercooled liquids and biomolecules. These fluctuations significantly influence various properties, functions, and reactions. By investigating the dynamics and fluctuations in these molecular systems, we aim to uncover the molecular origins of these properties, functions, and reactions.

We have pioneered advanced computational methods for multi-dimensional nonlinear spectroscopy, enabling us to elucidate the molecular basis of ultrafast energy relaxation and the temporal evolution of nonuniform fluctuations in liquid water that conventional linear spectroscopy has not revealed. Additionally, we have delved into the dynamical heterogeneity of supercooled liquids, characterized by slow, inhomogeneous structural changes driven by fluctuations. Using a three-time correlation function, we unveiled the dynamic coupling of structural fluctuations across different time scales in proteins.

Our research has also focused on the anomalous properties of water, establishing a link between these anomalies and previously hidden structural and dynamical characteristics. Recently, we developed a novel analytical method for studying dynamical disorder based on stochastic process theory, elucidating the mechanisms behind slowing structural changes as systems approach the glass transition.

In the realm of biomolecular systems, structural fluctuations and conformational changes are crucial for functional expression. Our studies on enzymatic reactions underscore the importance of specific prepared conformational states that facilitate these reactions. Furthermore, we have probed the molecular origins of dynamic disorder within protein conformational dynamics, revealing the complexity of these processes. Our investigations also extend to the molecular mechanisms underlying efficient excitation energy transfer in photosynthetic systems.

Through these efforts, we are engaged in a broad spectrum of theoretical and computational studies to unravel the dynamical phenomena that govern condensed-phase systems.

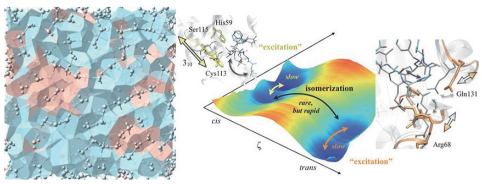

Figure 1. Snapshot of two-state model in supercooled water consisting of high- and low-density liquids (left) and schematic of 2D free energy surface for enzymatic reaction (right).

Selected Publications

- T. Yagasaki and S. Saito, *Annu. Rev. Phys. Chem.* **64**, 55–75 (2013), T. L. C. Jansen, S. Saito, J. Jeon and M. Cho, *J. Chem. Phys. (Perspective)* **150**, 100901 (17 pages) (2019), C. R. Baiz *et al.*, *Chem. Rev.* **120**, 7152–7218 (2020).
- K. Kim and S. Saito, *J. Chem. Phys. (Special Topic on Glass Transition)* **138**, 12A506 (12 pages) (2013).
- S. Saito, B. Bagchi and I. Ohmine, *J. Chem. Phys.* **149**, 124504 (8 pages) (2018), S. Saito and B. Bagchi, *J. Chem. Phys.* **150**, 054502 (14 pages) (2019), S. Saito, *J. Chem. Phys.* **160**, 194506 (13 pages) (2024).
- J. Ono, Y. Matsumura, T. Mori and S. Saito, *J. Phys. Chem. B (Perspective)* **128**, 20–32 (2024).
- S. Saito, M. Higashi and G. R. Fleming, *J. Phys. Chem. B* **123**, 9762–9772 (2019).

1. Flat-Bottom Elastic Network Model for Generating Improved Plausible Reaction Paths[1)]

Rapid generation of a plausible reaction path connecting a given reactant and product in advance is crucial for the efficient computation of precise reaction paths or transition states. We propose a computationally efficient potential energy based on the molecular structure to generate such paths. This potential energy has a flat bottom consisting of structures without atomic collisions while preserving nonreactive chemical bonds, bond angles, and partial planar structures. By combining this potential energy with the direct MaxFlux method, a recently developed reaction-path/transition-state search method, we can find the shortest plausible path passing within the bottom. Numerical results show that this combination yields lower energy paths compared to the paths obtained by the well-known image-dependent pair potential. We also theoretically investigate the differences between these two potential energies. The proposed potential energy and path generation routine are implemented in our Python version of the direct MaxFlux method, available on GitHub.

2. Development of Molecular Dynamics Parameters and Theoretical Analysis of Excitonic and Optical Properties in the Light-Harvesting Complex II[2)]

The light-harvesting complex II (LHCII) in green plants exhibits highly efficient excitation energy transfer (EET). A comprehensive understanding of the EET mechanism in LHCII requires quantum chemical, molecular dynamics (MD), and statistical mechanics calculations that can adequately describe pigment molecules in heterogeneous environments. Herein, we develop MD simulation parameters that accurately reproduce the quantum mechanical/molecular mechanical energies of both the ground and excited states of all chlorophyll (Chl) molecules in membrane embedded LHCII. The present simulations reveal that Chl *a* molecules reside in more inhomogeneous environments than Chl *b* molecules. We also find a narrow gap between the exciton energy levels of Chl *a* and Chl *b*. In addition, we investigate the nature of the exciton states of Chl molecules, such as delocalization, and analyze the optical spectra of LHCII, which align with experimental results. Thus, the MD simulation parameters developed in this study successfully reproduce the excitonic and optical properties of the Chl molecules in LHCII, validating their effectiveness.

3. Fast Diffusion of Water along Carbon Nanotube near the Wall[3)]

The diffusion of water in carbon nanotubes (CNTs) is debated, particularly whether it is faster near the CNT wall or at the center and how the temperature influences this effect. Using molecular dynamics (MD) simulations, we study radially resolved water diffusion in CNT(26,26) (3.57 nm diameter) over a wide temperature range. Diffusion along the CNT axis is significantly enhanced compared to that of bulk water, with the effect intensifying at lower temperatures. Supercooling further amplifies this enhancement following near-Arrhenius behavior. Confinement has a smaller impact on the rotational dynamics. By resolving water motion into radial layers, we find that both translational and rotational dynamics are higher near the CNT wall due to weakened hydrogen bonding. The presence of dangling O−H bonds reduces friction at the CNT−water interface. Revisiting an NMR study, we suggest that the high-intensity peak corresponds to central layers, aligning with our MD results and refining our insights into confined water dynamics.

4. Correlated Flat-Bottom Elastic Network Model for Improved Bond Rearrangement in Reaction Paths[4)]

This study introduces correlated flat-bottom elastic network model (CFB-ENM), an extension of our recently developed flat-bottom elastic network model (FB-ENM) for generating plausible reaction paths, *i.e.*, collision-free paths preserving nonreactive parts. While FB-ENM improved upon the widely used image-dependent pair potential (IDPP) by addressing unintended structural distortion and bond breaking, it still struggled with regulating the timing of series of bond breaking and formation. CFB-ENM overcomes this limitation by incorporating structure-based correlation terms. These terms impose constraints on pairs of atom pairs, ensuring immediate formation of new bonds after breaking of existing bonds. Using the direct MaxFlux method, we generated paths for 121 reactions involving main group elements and 35 reactions involving transition metals. We found that CFB-ENM significantly improves reaction paths compared to FB-ENM. CFB-ENM paths exhibited lower maximum DFT energies along the paths in most reactions, with nearly half showing significant energy reductions of several tens of kcal/mol. In the few cases where CFB-ENM yielded higher energy paths, most increases were below 10 kcal/mol. We also confirmed that CFB-ENM reduces computational costs in subsequent precise reaction path or transition state searches compared to FB-ENM. An implementation of CFB-ENM based on the Atomic Simulation Environment is available on GitHub for use in computational chemistry research.

References

1) S.-i. Koda and S. Saito, *J. Chem. Theory Comput.* **20**, 7176–7187 (2024).
2) Z. Zhu, M. Higashi and S. Saito, *J. Chem. Theory Comput.* **21**, 413–427 (2025).
3) G. R. Kahn, S. Saito and S. Daschakraborty, *J. Phys. Chem. B* **129**, 6561–6573 (2025).
4) S.-i. Koda and S. Saito, *J. Chem. Theory Comput.* **21**, 3513–3522 (2025).