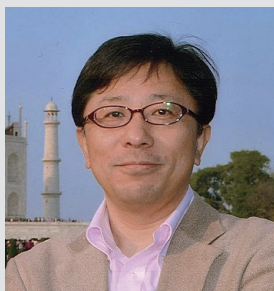


# Theoretical Studies of Reactions, Functions, and Fluctuations in Many-Body Molecular Systems

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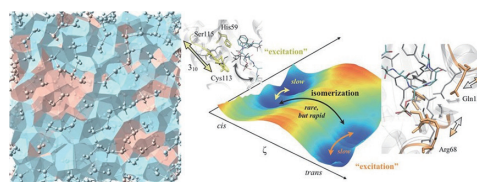
Many-body molecular systems, such as (supercooled) liquids and biomolecules, exhibit complex fluctuations. Furthermore, in these systems, various physical properties and biological functions are created and chemical reactions proceed under the fluctuations. We aim to elucidate the properties, functions, and reactions by investigating fluctuations and dynamics of the many-body molecular systems.

We have investigated fluctuations and dynamics of liquids by developing computational method for multi-dimensional nonlinear spectroscopy that can reveal detailed dynamical information not available from conventional linear spectroscopy. Consequently, we revealed the molecular origins of the ultrafast energy relaxation and time evolution of inhomogeneous fluctuations in liquid water. In supercooled liquids, rare and non-uniform structural changes, called dynamic heterogeneity, are induced by fluctuations. We elucidated the relationship between the lifetime of the dynamic heterogeneity and the fragility using the three-time correlation function of density fluctuations.

We study the molecular origin of anomalous properties of liquid water. We revealed that the anomalies of liquid water are related to the structural and dynamical instabilities hidden in the experimentally inaccessible region and the physical reason of the low glass transition of liquid water. Now we

investigate how rare but persistent structural relaxations proceed at low temperatures towards the glass transition temperature.

Complex conformational fluctuations and changes are also found in biomolecular systems. In addition, the conformational dynamics are considered to be essential for biological functions. We examine the relationship between fluctuation and biomolecular function found in the robust circadian rhythm of the clock protein KaiC and the efficient excitation energy transfer in photosynthetic systems. We investigate dynamic effects of enzymatic reactions, and find the importance of prearranged states for the rare but persistent enzymatic reactions. Furthermore, we examine dynamic disorder in conformational changes of proteins at the molecular level.



**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

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## 1. Molecular Mechanism of Acceleration and Retardation of Collective Orientation Relaxation of Water Molecules in Aqueous Solutions<sup>1)</sup>

The collective orientation relaxation (COR) of water molecules in aqueous solutions is faster or slower with an increase in the concentration of the solutions than that in pure water; for example, acceleration (deceleration) of the COR is observed in a solution of sodium chloride (tetramethyl ammonium chloride) with increasing concentration. However, the molecular mechanism of the solution and concentration dependence of the relaxation time of the COR has not yet been clarified. We theoretically investigate the concentration dependence of the COR of water molecules in solutions of tetramethylammonium chloride (TMACl), guanidinium chloride (GdmCl), and sodium chloride (NaCl). Based on the Mori–Zwanzig equation, we identify two opposing factors that determine the COR of water molecules in any aqueous solution: The correlation of dipole moments and the single-molecule orientation relaxation. We reveal the molecular mechanism of the concentration dependence of the relaxation time of the COR in the TMACl, GdmCl, and NaCl solutions in terms of these two factors.

## 2. Effects of Interfaces on Structure and Dynamics of Water Droplets on a Graphene Surface: A Molecular Dynamics Study<sup>2)</sup>

The structure and dynamics of water droplets on a bilayer graphene surface are investigated using molecular dynamics simulations. The effects of solid/water and air/water interfaces on the local structure of water droplets are analyzed in terms of the hydrogen bond distribution and tetrahedral order parameter. It is found that the local structure in the core region of a water droplet is similar to that in liquid water. On the other hand, the local structure of water molecules at the solid/water and air/water interfaces, referred to as the interface and surface regions, respectively, consists mainly of three-coordinated molecules that are greatly distorted from a tetrahedral structure. This study reveals that the dynamics in different regions of the water droplets affects the intermolecular vibrational density of states: It is found that in the surface and interface regions, the intensity of vibrational density of states at  $\sim 50\text{ cm}^{-1}$  is enhanced, whereas those at  $\sim 200$  and  $\sim 500\text{ cm}^{-1}$  are weakened and redshifted. These changes are attributed to the increase in the number of molecules having fewer hydrogen bonds in the interface and surface regions. Both single-molecule and collective orientation relaxations are also examined. Single-molecule orientation relaxation is found to be marginally slower than that in liquid water. On the other hand, the collective orientation relaxation of water droplets is found to be significantly faster than that of liquid water because of the destructive correlation of dipole moments in the

droplets. The negative correlation between distinct dipole moments also yields a blue-shifted libration peak in the absorption spectrum. It is also found that the water–graphene interaction affects the structure and dynamics of the water droplets, such as the local water structure, collective orientation relaxation, and the correlation between dipole moments. This study reveals that the water/solid and water/air interfaces strongly affect the structure and intermolecular dynamics of water droplets and suggests that the intermolecular dynamics, such as energy relaxation dynamics, in other systems with interfaces are different from those in liquid water.

## 3. Microscopic Insights into Dynamic Disorder in the Isomerization Dynamics of the Protein BPTI<sup>3)</sup>

Understanding the dynamic disorder behind a process, *i.e.*, the dynamic effect of fluctuations that occur on a timescale slower or comparable with the timescale of the process, is essential for elucidating the dynamics and kinetics of complicated molecular processes in biomolecules and liquids. Despite numerous theoretical studies of single-molecule kinetics, our microscopic understanding of dynamic disorder remains limited. In the present study, we investigate the microscopic aspects of dynamic disorder in the isomerization dynamics of the Cys14–Cys38 disulfide bond in the protein bovine pancreatic trypsin inhibitor, which has been observed by nuclear magnetic resonance. We use a theoretical model with a stochastic transition rate coefficient, which is calculated from the 1-ms-long time molecular dynamics trajectory obtained by Shaw *et al.* [*Science* **330**, 341–346 (2010)]. The isomerization dynamics are expressed by the transitions between coarse-grained states consisting of internal states, *i.e.*, conformational sub-states. In this description, the rate for the transition from the coarse-grained states is stochastically modulated due to fluctuations between internal states. We examine the survival probability for the conformational transitions from a coarse-grained state using a theoretical model, which is a good approximation to the directly calculated survival probability. The dynamic disorder changes from a slow modulation limit to a fast modulation limit depending on the aspects of the coarse-grained states. Our analysis of the rate modulations behind the survival probability, in relation to the fluctuations between internal states, reveals the microscopic origin of dynamic disorder.

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