Theoretical Studies on Condensed Phase Dynamics

Department of Theoretical and Computational Molecular Science
Division of Computational Molecular Science

SAITO, Shinji	Professor
KIM, Kang	Assistant Professor
HIGASHI, Masahiro	IMS Fellow
KOBAYASHI, Chigusa	Post-Doctoral Fellow
YAGASAKI, Takuma	Post-Doctoral Fellow
SUMIKAMA, Takashi	Post-Doctoral Fellow
IMOTO, Sho	Graduate Student*
UENO, Harumi	Secretary

Liquids and biological systems show complicated dynamics because of their structural flexibility and dynamical hierarchy. Understanding these complicated dynamics is indispensable to elucidate chemical reactions and relaxation in solutions and functions of proteins. We have been investigating complex dynamics in supercooled liquids[1–3] and chemical reactions in biological systems using molecular dynamics simulation and electronic structure calculation. In addition, we have been analyzing liquid dynamics by using multi-dimensional spectroscopy.[4,5]

1. Multiple Time Scales Hidden in Heterogeneous Dynamics of Glass-Forming Liquids[1]

A multi-time probing of density fluctuations is introduced to investigate hidden time scales of heterogeneous dynamics in glass-forming liquids. Molecular-dynamics simulations for simple glass-forming liquids are performed and a three-time correlation function is numerically calculated for general time intervals. It is demonstrated that the three-time correlation function is sensitive to the heterogeneous dynamics and that it reveals couplings of correlated motions over a wide range of time scales. Furthermore, the time scale of the heterogeneous dynamics τ_{hetero} is determined by the change in the second time interval in the three-time correlation function. The present results show that the time scale of the heterogeneous dynamics τ_{hetero} becomes larger than the α-relaxation time at low temperatures and large wavelengths. We also find a dynamical scaling relation between the time scale τ_{hetero} and the length scale ξ of dynamical heterogeneity as $\tau_{\mathrm{hetero}} \sim \xi^z$ with $z = 3$.

2. Slow Dynamics in Random Media: Crossover from Glass to Localization Transition[2]

We study slow dynamics of particles moving in a matrix of immobile obstacles using molecular dynamics simulation. The glass transition point decreases drastically as the obstacle density increases. At higher obstacle densities, dynamics of mobile particles changes qualitatively from glass-like to a Lorentz-gas-like relaxation. This crossover is studied by the density correlation functions, non-ergodic parameters, mean square displacement, and nonlinear dynamic susceptibility. Our finding is qualitatively consistent with results of recent numerical and theoretical studies on various spatially heterogeneous systems. Furthermore, we show that slow dynamics is surprisingly rich and sensitive to the obstacle configurations. Especially, reentrant transition is observed for a particular configuration, though its origin is not directly linked to the similar prediction based on the mode-coupling theory.

3. Conformational Changes and Fluctuations of Molecular Switch Ras

Ras superfamily works as a molecular switch for cell growth. Ras is cycled between two states of guanine nucleotide, the GTP- and GDP-bound states, by hydrolysis. Ras binds to effectors for regulation of cell proliferation in the GTP-bound state, whereas it is inactivated in the GDP-bound state. X-ray crystallography studies revealed conformational changes of two regions, *i.e.* switch I and switch II, around a nucleotide binding site in these two states. We analyze the conformational changes and fluctuations between these states by carrying out molecular dynamics (MD) simulation. We find that the change in the coordinations of Thr35-Mg^{2+} and Gly60-γ-phosphate due to the hydrolysis of GTP induces the changes in the conformations of sidechains as well as the backbone in the GTP- and GDP-bound states. We perform the principle coordinate analysis of the structural change between these states and indeed find the important structural change arising from the switch regions.

In addition to the GTP-bound state with the function of the cell growth, another GTP-bound state with different conformation has been observed experimentally. The GTP-bound state with the function is called state 2, while the other state is referred to as state 1. It is known that state 2 is a predominant form of Ras and interacts with effectors. ^{31}P NMR spectroscopy of some mutants shows the absence of the coordination of Thr35-Mg^{2+} in state 1. It is also shown in X-ray structural analysis that the coordination of Gly60-γ-phosphate is lost in the state 1 of another mutant. We investigate the conformational changes and fluctuations in these two kinds of state 1 by using MD simulation. It is found that the breaking of the coordination of Thr35-Mg^{2+} causes the large scale structural change in the switch I region followed by the steric hindrance between Pro34 and γ-phosphate and then the break of hydrogen bond between ribose in GTP and switch I region. We also find that the conformational fluctuation in the switch I region is substantially large in state 1. We show that the global structural changes of loop4 and α2 helix in the switch II region are induced by the loss of the coordination between Gly60 and γ-phosphate. The presence of multiple states with different conformations in the GTP-bound state is consistent with the experimentally observed interconversion between multiple conformations and with the low affinity to effectors.

We also analyze the GAP-GTP-bound state to understand the role of GAP. We find that the binding of GAP significantly suppressed the unnecessary thermal motions of the water molecule which is involved in the hydrolysis of GTP.

In addition to the above analyses based on MD simulation, we are currently analyzing the reaction pathway of hydrolysis of GTP in the GAP-GTP-bound state, by using the so-called QM/MM method.

4. Molecular Dynamics Simulation of Nonlinear Spectroscopies of Intermolecular Motions in Liquid Water[4,5]

Water is the most extensively studied of liquids because of both its ubiquity and its anomalous thermodynamic and dynamic properties. The properties of water are dominated by hydrogen bonds and hydrogen bond network rearrangements. Fundamental information on the dynamics of liquid water has been provided by linear infrared (IR), Raman, and neutron-scattering experiments; molecular dynamics simulations have also provided insights. Recently developed higher-order nonlinear spectroscopies open new windows into the study of the hydrogen bond dynamics of liquid water. For example, the vibrational lifetimes of stretches and a bend, intramolecular features of water dynamics, can be accurately measured and are found to be on the femtosecond time scale at room temperature. Higher-order nonlinear spectroscopy is expressed by a multi-time correlation function, whereas traditional linear spectroscopy is given by a one-time correlation function. Thus, nonlinear spectroscopy yields more detailed information on the dynamics of condensed media than linear spectroscopy. In this Account, we describe the theoretical background and methods for calculating higher-order nonlinear spectroscopy; equilibrium and non-equilibrium molecular dynamics simulations, and a combination of both, are used. We also present the intermolecular dynamics of liquid water revealed by fifth-order two-dimensional (2D) Raman spectroscopy and third order IR spectroscopy. 2D Raman spectroscopy is sensitive to couplings between modes; the calculated 2D Raman signal of liquid water shows large anharmonicity in the translational motion and strong coupling between the translational and librational motions. Third-order IR spectroscopy makes it possible to examine the time-dependent couplings. The 2D IR spectra and three-pulse photon echo peak shift show the fast frequency modulation of the librational motion. A significant effect of the translational motion on the fast frequency modulation of the librational motion is elucidated by introducing the "translation-free" molecular dynamics simulation. The isotropic pump-probe signal and the polarization anisotropy decay show fast transfer of the librational energy to the surrounding water molecules, followed by relaxation to the hot ground state.

Reference

1) K. Kim and S. Saito, *Phys. Rev. E* **79**, 060501(R) (4 pages) (2009).
2) K. Kim, K. Miyazaki and S. Saito, *Europhys. Lett.* **88**, 36002 (5 pages) (2009).
3) A. Furukawa, K. Kim, S. Saito and H. Tanaka, *Phys. Rev. Lett.* **102**, 016001 (4 pages) (2009).
4) T. Yagasaki and S. Saito, *Acc. Chem. Res.* **42**, 1250–1259 (2009).
5) T. Yagasaki, J. Ono and S. Saito, *J Chem. Phys.* **131**, 164511 (11 pages) (2009).

* carrying out graduate research on Cooperative Education Program of IMS with Nagoya University