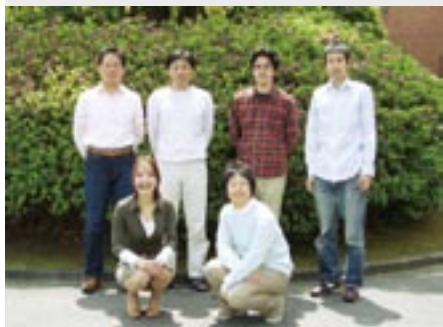


Theoretical Studies on Condensed Phase Dynamics

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Liquids and biological systems show complicated dynamics because of their structural flexibility and dynamical hierarchy. Understanding these complicated dynamics is indispensable to elucidate the chemical reactions in solutions and the functions of proteins. We have been investigating liquid dynamics and chemical reactions in biological systems using molecular dynamics and electronic structure calculations. In addition, we have been analyzing complicated dynamics in terms of multi-dimensional spectroscopy.

1. Glass Transition in Porous Media: Test of Mode-Coupling Theory via Molecular Dynamics Simulation

When a liquid is supercooled below its freezing temperature, it becomes a metastable supercooled state. When the temperature is lowered further and crystallization could be avoided, the supercooled liquid undergoes the glass transition. In the glass transition region a drastic slowing-down occurs in dynamical properties, *e.g.* structural relaxation time, diffusion constant, and viscosity, whereas the static structure is almost the same as that of normal liquids.

The dynamics of glass forming liquids under confinement has attracted attention for its unusual thermodynamic properties; the glass transition temperature in a spatially confined system, *i.e.* a thin film or a porous media, is different from that in the bulk. A theoretical study for glass forming liquids confined in disordered immobile particles has been recently reported. In the study, the liquid-glass transition points for various densities of fluid and immobile particles were determined by using the mode-coupling theory (MCT).

We carried out molecular dynamics simulations of sphere supercooled liquids in order to examine the above theoretical predictions, because the MCT is considered to be violated in the limit of low density for fluid particles. We confirmed that the structural relaxation becomes slow with the

increase in immobile particles. It is also found that the relaxation profile of the intermediate scattering function changes from the type B to the type A with the decrease in the density of fluid particles. In the type B, dynamics for high density of fluid particles, the well-known two-step relaxation is found and gradually stretched with increasing density of immobile particles. On the other hand, in the type A, dynamics for low density of fluid particles, the dynamics is significantly different from that of the type B, where the single-step relaxation decay with the long time tail has been observed. This long time tail is thought to be due to the diffusion localization, *i.e.* the fluid particles are trapped by the immobile obstacle particles for a long time. Moreover, we revealed that the system shows a reentry in the limit of low density for fluid particles at a certain high density for immobile particles as the prediction of the theoretical study. In the reentrant phenomenon, some delocalization is expected to occur due to fluid-fluid collisions. We are now examining this scenario and investigating the physical mechanism of the reentrant phenomenon using simulations.

2. Conformational Changes Associated with GTP Hydrolysis in Ras

Ras superfamily is a well-known signal transduction protein. Ras is activated by binding of GTP and binds to some effectors for regulation of cell proliferation, whereas it is inactivated by the hydrolysis of Ras-bound GTP. The hydrolysis rate is accelerated by five orders of magnitude by binding of GTPase-activating protein, GAP. Therefore, it is essential to investigate the binding effect of GAP on Ras for understanding the reaction.

We analyze the hydrolysis by dividing into the following four states; (i) active (reactant), (ii) GAP-bound, (iii) intermediate of hydrolysis, and (iv) inactive (product) states. We performed molecular dynamics (MD) calculation for the four states and analyzed the conformational changes and fluctuation.

tuations of Ras and GAP in these states. We also carried out QM/MM calculation to examine the details of structures.

In the step from the active to GAP-bound state, salt bridges between acidic residues in Ras and basic residues in GAP are formed. These bonds between Ras and GAP change the HB network structure around the active site and the structures in the switches I and II. In addition, the exchange of a water molecule near GTP is significantly suppressed by the binding of GAP to RAS. The present result implies that the bound water molecule near GTP makes the hydrolysis reaction facile.

GTP is converted to GDP and Pi by the hydrolysis. With MD and QM/MM methods we successfully constructed a stable intermediate state which was found in a recent experimental study. We found that the HB network structure around the active site and the conformation between Ras and GAP in the intermediate state are almost the same as those in the GAP-bound state. We clarified that the invasion of water required for the release of Pi and GAP does not take place in this state. We are also investigating how Pi and GAP are released from Ras in the last step.

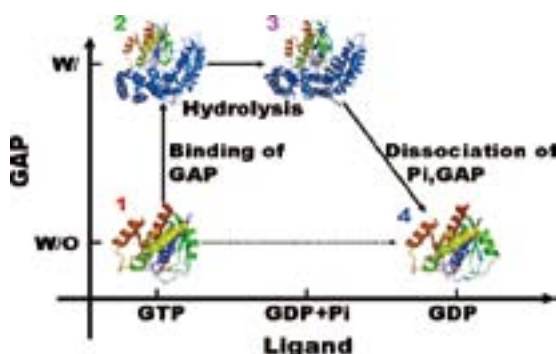


Figure 1. Conformational changes associated with GTP hydrolysis in Ras.

3. Two-Dimensional Infrared Spectroscopy of Intermolecular Modes in Liquid Water

Liquid water is an interesting system with a number of anomalous thermodynamic and dynamic properties. Its complicated dynamics has been analyzed with various kinds of spectroscopies. Great progresses have been achieved in developing multi-dimensional spectroscopies since late 90 s.

We have been investigating intermolecular water dynamics using two-dimensional (2D) infrared (IR) spectroscopy which is a powerful technique to provide detailed information on dynamics. In the 2D IR spectroscopy, the system interacts with electric fields at $t = 0$, t_1 , and $t_1 + T$, and the signal is detected at $t = t_1 + T + t_3$ and thus the response function is expressed in terms of a three-time correlation function. The so-called hybrid method in which equilibrium and non-equilibrium molecular

dynamics simulations are combined is employed in the calculation of 2D IR spectroscopy.

The peak width along the diagonal line in the 2D IR spectroscopy provides a measure of inhomogeneous broadening. The present result shows that the libration motion of water has inhomogeneous contribution. In addition, the present analysis shows that the initial inhomogeneity rapidly decays with ~ 100 fs, by analyzing the waiting time, T , dependence of the diagonal line shape. The loss of initial inhomogeneity slows down about three times, when the intermolecular translation motion which couples with the libration motion is removed. Consequently, we revealed the significant effect of the translation motion on the fast loss of initial inhomogeneity of the libration motion in liquid water.

We can obtain useful information about relaxation dynamics by analyzing off-diagonal peaks of the 2D IR spectroscopy. We found a strong off-diagonal peak located at $(\omega_1, \omega_3) = (\sim 700 \text{ cm}^{-1}, \sim 150 \text{ cm}^{-1})$. The cross peak arises from the coupling between the libration motion during t_1 and the intermolecular translation motion during t_3 . The intensity of the peak decreases for $T < 40$ fs and then it increases for $T > 40$ fs. The increase in the signal intensity can be attributed to the relaxation from the libration motion to intermolecular translation motion during t_2 . The present result shows that the time constant of the relaxation is about 150 fs.

Feynman diagrams for the 2D IR spectroscopy are usually classified into three kinds of Liouville pathways, S_I , S_{II} , and S_{III} : S_I represents rephasing pathways, on the other hand, S_{II} and S_{III} represent non-rephasing ones. We found that the third-order 2D IR response function of water contains several Feynman diagrams which cannot be classified into the above three pathways. The new pathways, S_{IV} , are related to the second overtone of the libration motion due to a three-quantum transition. The existence of the three-quantum transition shows the anharmonic dynamics in the libration motion. It is conceivable that S_{IV} can be observed by the intermolecular 2D IR experiment of water with two colors.

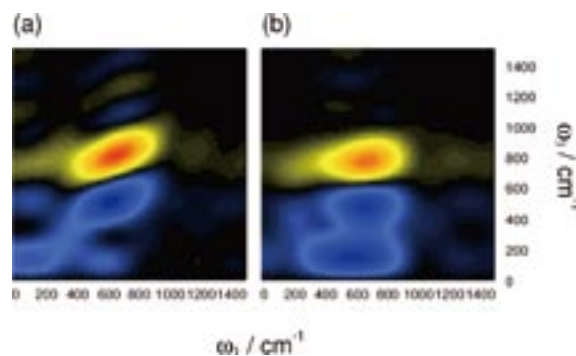


Figure 2. 2D IR spectra of water at (a) $T = 20$ and (b) 200 fs, respectively.