



RESEARCH ACTIVITIES

Theoretical and Computational Molecular Science

It is our goal to develop new theoretical and computational methods based on quantum mechanics and statistical mechanics to predict and understand the structures, chemical reactions, and functions of molecules in gas and condensed phases including nano- and bio-systems.

Theoretical Studies of Heterogeneous Dynamics and Protein Functions

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Keywords Spatiotemporal Heterogeneous Dynamics, Functions, Liquids

Nonlinear intermolecular interactions cause complicated motions in condensed phases, *e.g.* liquids and biological systems. These motions are spatially and temporally heterogeneous with a wide range of time and spatial scales and yield both static and dynamic properties of the systems. The spatiotemporal non-uniform motions known as dynamic heterogeneity are considered to be a clue to understand supercooled liquids and glass transition. Furthermore, heterogeneous reaction rates have been found in biological systems. Therefore, understanding of spatiotemporal heterogeneous dynamics is essential to the elucidation of the structure, thermodynamics, dynamics, and functions of the condensed phase systems.

We have investigated inter- and intra-molecular dynamics of water by using third-order nonlinear spectroscopy which can provide the detailed dynamics that are not available from conventional IR spectroscopy. We have examined the detailed fluctuations in water by calculating two-dimensional IR spectra of water. We have revealed the molecular mechanism of ultrafast energy relaxation, which is one of dynamical features of water, *i.e.* the fast energy relaxation is caused by the nonlinear strong coupling between the libration motion and other intra- and inter-molecular vibrational motions.

We have also investigated the dynamics of supercooled liquids. We quantified the lifetime of dynamic heterogeneity by introducing the three-time correlation function of density fluctuation, which is sensitive to the time evolution of dy-

namic heterogeneity. Our systematic analysis for various systems shows that the lifetime of dynamic heterogeneity is intimately related to configurational entropy and thus the temperature dependence of lifetime of dynamic heterogeneity is more sensitive to the fragility than that of α -relaxation time determined by one-time correlation function. In addition to the analysis of dynamic heterogeneity with multi-time correlation function, we have revealed the molecular origin of anomalous temperature dependence of isobaric specific heat of water by examining the spatiotemporal fluctuations in terms of complex specific heat.

We currently investigate how chemical reactions proceed in biological systems, *e.g.* clock protein KaiC, under complex conformational fluctuations. We also examine heterogeneous conformational dynamics of proteins by exploiting the ideas of multi-dimensional spectroscopy and glassy dynamics.

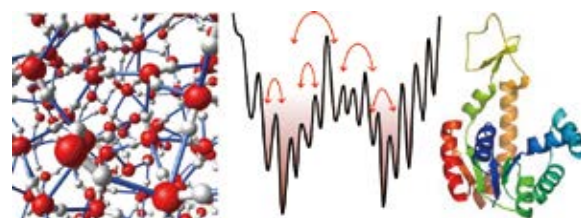


Figure 1. Schematic figure of rugged energy landscape (center) in supercooled water (left) and adenylate kinase (right).

Selected Publications

- T. Yagasaki and S. Saito, *Acc. Chem. Res.* **42**, 1250–1258 (2009), *Annu. Rev. Phys. Chem.* **64**, 55–75 (2013).
- S. Imoto, S. Xantheas and S. Saito, *J. Phys. Chem. B* **119**, 11068–11078 (2015).
- K. Kim and S. Saito, *J. Chem. Phys. (Special Topic on Glass Transition)* **138**, 12A506 (12 pages) (2013).
- S. Saito, I. Ohmine and B. Bagchi, *J. Chem. Phys.* **138**, 094503 (7 pages) (2013).
- J. Ono, S. Takada and S. Saito, *J. Chem. Phys. (Special Topic on Multidimensional Spectroscopy)* **142**, 212404 (13 pages) (2015).

1. Quantitative Evaluation of Site Energies and Their Pigment Fluctuations in the Fenna-Matthews-Olson Complex with an Efficient Method for Generating Potential Energy Surfaces¹⁾

We develop an efficient method to generate an accurate semi-global potential energy surface of a molecule in condensed phases with low computational cost. We apply the method to the analysis of the site energies and their fluctuations of bacteriochlorophyll (BChl) a pigments in the Fenna-Matthews-Olson (FMO) complex using the density functional properly describing the ground and excited states of BChl a in solution in our previous work (*J. Phys. Chem. B* **118**, 10906–10918 (2014)). The errors of the potential energies calculated from the present and QM/MM methods are small: ~1 kcal/mol for both the ground and excited states. The calculated site energies are in good agreement with the experimentally fitted results. The calculated spectral density also agrees with the experimentally available data. The spectral densities of BChl 2 and BChl 5 are much larger than those of the other five sites. The present method is expected to reveal the efficient excitation energy transfer in light-harvesting antennas.

2. Molecular Mechanism behind the Fast Folding/Unfolding Transitions of Villin Headpiece Subdomain: Hierarchy and Heterogeneity²⁾

Proteins involve motions over a wide range of spatial and temporal scales. While the large conformational changes such as folding and functioning are slow and appear to occur in a highly cooperative manner, how the hierarchical dynamics over different timescales play a role during these slow transitions has been of great interest over the decades. Here we study the folding mechanism of the villin headpiece subdomain (HP35) to understand the molecular mechanism behind this prototypical fast-folding protein. The ~400 μ s molecular dynamics (MD) trajectories obtained by Piana *et al.* [Piana, S. *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **109**, 17845 (2012)] are analyzed in detail. By extracting the slowest mode from the trajectories, which is responsible for the folding/unfolding transitions, and by analyzing the transition events along this mode, we find that the transitions occur in a heterogeneous manner. Detailed analysis of the individual transition events shows that the folding/unfolding transitions occur via two qualitatively different pathways, *i.e.* the unfolding triggered from the C-terminal (α_3 helix) and from the N-terminal (α_1 – α_2 loop). Non-native contacts are also found to contribute in slowing down the transitions. The folding of HP35 thus proceeds in a segmental manner rather than cooperatively at the sub-microsecond timescale. The Lys \rightarrow Nle mutation is found to speed up the transitions by rigidifying the α_3 helix, *i.e.* suppressing one transition pathway. The analysis of the microsecond dynamics in the single-molecule Förster resonance energy transfer efficiency trajectories, which are calcu-

lated from the MD data, reveals that the folding/unfolding transitions in the NleNle mutant can be fitted with a two-state model, whereas those in WT appear to be more complex and involves multiple timescales. This may be due to the similarity in the timescale of the transition events and overall folding/unfolding transitions in WT. The present study demonstrates that a protein as small as HP35 already involves heterogeneous characters during folding/unfolding transitions when the hierarchical dynamics at molecular level is considered, thus heterogeneity can be a general characteristic in protein folding.

3. Multiple Transitions of Water on Its Path to Low Density Amorphous Ice³⁾

Amorphous ice is ubiquitous in the Universe, being a major constituent of meteorites and asteroids. It is mechanically stable at very low temperatures and is different from its crystalline counterpart, ice Ih. However, the mechanism of its formation from low temperature water is still not understood. The amorphous ice, when heated from below, undergoes a glass transition to a highly viscous liquid at 136 K, then crystallizes at 150 K, while liquid water when supercooled below its freezing temperature itself freezes at 227 K. Our difficulty to understand the formation of amorphous ice stems from the inaccessibility of liquid water to experiments between 227 K and 150 K, a temperature range well-known as “no man’s land.” We study the entire process of vitrification of water by extensive molecular dynamics simulations. We find that vitrification of water occurs in three distinct stages, accompanied by two sharp changes in fragility. A large scale density fluctuation between the high density liquid (HDL) and the low density liquid (LDL) that appears near 220 K, profoundly influences the entire transformation process. It undergoes a further dynamical transition at ~195 K where we find the dynamical heterogeneity to decrease sharply, and rather suddenly. This transition occurs by a fragmentation of macroscopic HDL, leading to the formation of a state where small, non-spherical, fast relaxing, high density droplets containing 3- and 5-coordinated defects exist in the slow low density network of 4-coordinated water molecules. The fragmentation scenario explains well the observed density minimum of water at 190 K. We also find that particular 3-coordinated defects with two HB acceptors and one HB donor are involved in structural changes in water. It is found, furthermore, that the presence of LDL predominantly formed by 4-coordinated molecules leads to a significant decrease of the glass transition temperature of water.

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Theory for Optical Response in Nanostructures and Application to Unified Photonic and Electronic Devices

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Keywords Optical Near-Field, Light-Matter Interaction, Nanodevices

Optical response of molecules is undoubtedly essential for understanding their physicochemical properties. In conventional theoretical approaches to optical response of molecules, two conditions are usually assumed:

- (i) A scale of wavelength of incident light is considered to be much longer than molecular size, *i.e.*, dipole approximation. Thus, a target molecule is well approximated by a point dipole and the dipole feels a spatially uniform electromagnetic field.
- (ii) Electric polarization in a molecule induced by incident-light excitation inevitably generates a new electromagnetic field, referred to as an “optical near-field.” However, such a self-consistent light-matter (LM) interaction between electron and electromagnetic field dynamics is ignored.

Recent development of nanofabrication and nano-optical techniques requires a more general optical response theory fully taking account of *nonuniform and self-consistent* LM interactions.

We have developed a generalized theoretical description of full (nonuniform and self-consistent) LM interactions with the aim of understanding the optical near-field excitation dynamics in nanostructures of more than ten-nanometers in size. Electron dynamics in nanostructures interacting with an electromagnetic field is described by the time-dependent

Kohn-Sham (TDKS) equation, whereas electromagnetic field dynamics is represented by the microscopic Maxwell’s equations. The nonuniform LM interaction is taken into account in the vector potential and the self-consistent LM interaction is described by solving the electron and electromagnetic field coupled equations self-consistently. The coupled equations are solved numerically by using our developed computational program (GCEED: *Grid-based Coupled Electron and Electromagnetic field Dynamics*). Our computational approach is based on a finite-difference method in real-time and real-space. Since the approach employs very simple algorithms, it is highly suitable for massively parallelized computations. By using GCEED, we are currently computationally designing unified photonic and electronic nanodevices.

We also launched a new project of computational design of heterogeneous catalysts to develop efficient and commercially appealing ones, thus reducing the use of expensive rare catalytic metals. The simulations were carried out by using the first-principles, *i.e.*, Car-Parrinello, molecular dynamics simulations. The theoretical approach allows us to treat dynamical chemical reaction processes taking account of the effects of temperature and nonequilibrium interactions between clusters and supports.

Selected Publications

- K. Nobusada and K. Yabana, “Photoinduced Electric Currents in Ring-Shaped Molecules by Circularly Polarized Laser Pulses,” *Phys. Rev. A* **75**, 032518 (7 pages) (2007).
- K. Nobusada and T. Iwasa, “Oligomeric Gold Clusters with Vertex-Sharing Bi- and Tricosahedral Structures,” *J. Phys. Chem. C* **111**, 14279–14282 (2007).
- M. Noda, K. Ishimura, K. Nobusada, K. Yabana and T. Boku, “Massively-Parallel Electron Dynamics Calculations in Real-Time and Real-Space: Toward Applications to Nanostructures of More than Ten-Nanometers in Size,” *J. Comput. Phys.* **265**, 145–155 (2014).
- M. Yamaguchi and K. Nobusada, “Indirect Interband Transition Induced by Optical Near Fields with Large Wave Numbers,” *Phys. Rev. B* **93**, 195111 (2016).

1. Indirect Interband Transition Induced by Optical Near Fields with Large Wave Numbers¹⁾

Optical near fields (ONFs) have Fourier components with large wave numbers that are two or three orders of magnitude larger than those of far-field propagating light owing to their nonuniformity in space. By utilizing these large wave numbers, the ONF is expected to induce an indirect interband transition between Bloch states having different wave numbers and directly generate an electron–hole pair without electron–phonon coupling. We perform time-dependent dynamics calculations of a one-dimensional periodic potential with an indirect band-gap structure and demonstrate that the ONF definitely induces an indirect interband transition. Instead of using the general Bloch boundary condition, which is usually imposed in conventional band structure calculations, we adopt an alternative boundary condition, the Born–von Karman boundary condition¹⁾, to appropriately treat indirect interband transitions. The calculated absorption spectra for the far-field and ONF excitations show different absorption edges and spectral patterns. We argue that this difference can be experimentally measured as evidence of the effects of the large wave numbers of the ONF.

2. Reducing the Cost and Preserving the Reactivity in Noble-Metal-Based Catalysts: Oxidation of CO by Pt and Al–Pt Alloy Clusters Supported on Graphene²⁾

The oxidation mechanisms of CO to CO₂ on graphene-supported Pt and Pt–Al alloy clusters are elucidated by reactive dynamical simulations. The general mechanism evidenced is a Langmuir–Hinshelwood (LH) pathway in which O₂ is adsorbed on the cluster prior to the CO oxidation. The adsorbed O₂ dissociates into two atomic oxygen atoms thus promoting the CO oxidation. Auxiliary simulations on alloy clusters in which other metals (Al, Co, Cr, Cu, Fe, Ni) replace a Pt atom have pointed to the aluminum doped cluster as a special case. In the nanoalloy, the reaction mechanism for CO oxidation is still a LH pathway with an activation barrier sufficiently low to be overcome at room temperature, thus preserving the catalyst efficiency. This provides a generalizable strategy for the design of efficient, yet sustainable, Pt-based catalysts at reduced cost.

3. Interface Electronic Properties Between a Gold Core and Thiolate Ligands: Effects on an Optical Absorption Spectrum in Au₁₃₃(SPh-*t*Bu)₅₂³⁾

We analyze the electronic structures and optical absorption spectrum of Au₁₃₃(SPh-*t*Bu)₅₂, particularly in terms of

interface electronic properties between the Au core and the thiolate ligands. Computations are performed by using the time-dependent density functional theory approach in real-time and real-space that has recently been developed by our group. Local density of states analysis reveals a relationship between an icosahedral Au core and a thiolate-protected Au cluster; Au atoms associated with the edge or surface sites of the icosahedral core anchor the ligands to the core, whereas Au atoms associated with the apex sites bridge two thiols forming –S–Au–S– bonds. We compare the optical absorption spectrum of Au₁₃₃(SPh-*t*Bu)₅₂ with that of an icosahedral Au₁₄₆ bare cluster to clarify effects of the ligands on the optical absorption. The absorption intensity for Au₁₃₃(SPh-*t*Bu)₅₂ is obviously higher than that for the bare cluster. The significant increase in the optical absorption of Au₁₃₃(SPh-*t*Bu)₅₂ is attributed to mutual enhancement of electric polarizations induced both in the Au core and in the thiolate ligands. The effect of the enhancement is computationally visualized by analyzing the electric fields generated in the Au core and the thiolate ligands.

4. Nonlinear Optical Response Induced by a Second-Harmonic Electric-Field Component Concomitant with Optical Near-Field Excitation⁴⁾

Electron dynamics excited by an optical near field (ONF) in a two-dimensional quantum dot model was investigated by solving a time-dependent Schrödinger equation. It was found that the ONF excitation of the electron caused two characteristic phenomena: A two-photon absorption and an induction of a magnetic dipole moment with a strong third-harmonic component. By analyzing the interaction dynamics of the ONF and the electron, we explained that the physical mechanism underlying these phenomena was the second-harmonic electric-field component concomitant with the near-field excitation originating from the nonuniformity of the ONF. Despite a *y*-polarized ONF source, the second-harmonic component of an *x*-polarized electric field was inherently generated. The effect of the second-harmonic electric-field component is not due to usual second-order nonlinear response but appears only when we explicitly consider the electron dynamics interacting with the ONF beyond the conventional optical response assuming the dipole approximation.

References

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- 2) K. Koizumi, K. Nobusada and M. Boero, *Chem. –Eur. J.* **22**, 5181 (2016).
- 3) K. Iida, M. Noda and K. Nobusada, *J. Phys. Chem. C* **120**, 2753 (2016).
- 4) M. Yamaguchi and K. Nobusada, *Phys. Rev. A* **92**, 043809 (2015).

Advanced Electronic Structure Theory in Quantum Chemistry

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Electronic Structure Theory, Quantum Chemistry, Computational Chemistry

Computational quantum chemistry, that is, practicing quantum chemical theory using computers, is now considered to be a powerful means to provide detailed analysis of chemical phenomena. The focus of our group is to develop methods and algorithms of molecular electronic structure calculations, which are capable of supplying electronic-level interpretation and reliable prediction of chemical characters, reactivity, energetics, and spectroscopic properties of molecular systems. Also, we are interested in applying the methods to challenging chemical systems. Recently, we have developed advanced multireference methods to describe highly-correlated many-electron wavefunction, which cannot be qualitatively accounted for with mean-field or one-electron theory (*e.g.*, density functional theory). The multireference wavefunction need be represented with a quantum superposition of multiple electron configurations; however, this gives rise to a high computational expense because the degree of the superposition is in general exponentially dependent on the system size. We approach the multireference problems using the density matrix renormalization group (DMRG), which is originally a method of condensed matter physics to solve strong correlation phenomena in physical models. We developed an efficient implementation for adapting DMRG to quantum chemical calcula-

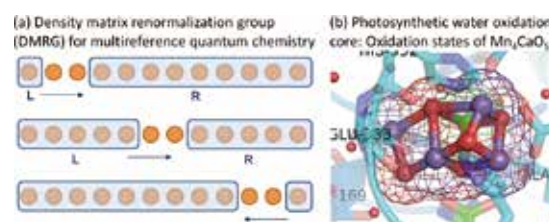


Figure 1. (a) Algorithm of density matrix renormalization group (DMRG) and (b) Its application to manganese cluster.

tion, in which the DMRG is exploited to describe static correlation in combination with the complete active space (CAS) model. Our DMRG-based methods have shown to be capable of handling very large correlation space, which far exceeds the limitation of conventional methods. We have further introduced a scheme to additively account for dynamic correlation on top of active-space DMRG wavefunction. Using these methods, we carried out chemical applications to multireference electronic systems, ranging from organic material molecules, such as radicals of graphene nanoribbons, to transition metal complexes, such as tetranuclear manganese cluster.

Selected Publications

- Y. Kurashige and T. Yanai, "High-Performance *Ab Initio* Density Matrix Renormalization Group Method: Applicability to Large-Scale Multireference Problems for Metal Compounds," *J. Chem. Phys.* **130**, 234114 (21 pages) (2009).
- W. Mizukami, Y. Kurashige and T. Yanai, "More π Electrons Make a Difference: Emergence of Many Radicals on Graphene Nanoribbons Studied by *Ab Initio* DMRG Theory," *J. Chem. Theory Comput.* **9**, 401–407 (2013).
- Y. Kurashige, G. K-L. Chan and T. Yanai, "Entangled Quantum Electronic Wavefunctions of the Mn_4CaO_5 Cluster in Photosystem II," *Nat. Chem.* **5**, 660–666 (2013).

1. Computational Evidence of Inversion of 1L_a and 1L_b -Derived Excited States in Naphthalene Excimer Formation from Highly-Correlated *ab initio* Multireference Theory²⁾

The naphthalene molecule has two important lowest-lying singlet excited states, denoted 1L_a and 1L_b . Association of the excited and ground state monomers yields a metastable excited dimer (*excimer*), which emits characteristic fluorescence. Here, we report a first computational result based on *ab initio* theory to corroborate that the naphthalene excimer fluorescence is 1L_a parentage, resulting from inversion of 1L_a and 1L_b -derived dimer states. This inversion was hypothesized by earlier experimental studies; however, it has not been confirmed rigorously. In this study, the advanced multireference (MR) theory based on density matrix renormalization group that enables using unprecedented large-size active space for describing significant electron correlation effects is used to provide accurate potential energy curves (PECs) of the excited states. The results evidenced the inversion of the PECs and accurately predicted transition energies for excimer fluorescence and monomer absorption. Traditional MR calculations with smaller active spaces and single-reference theory calculations exhibit serious inconsistencies with experimental observations.

The excimer formation is driven by the strong 1L_a 's attractive intermolecular interaction arising from a mixing of excitation resonance (ER) and charge resonance (CR) configurations. At large distance $r(R-R) = 5.2 \text{ \AA}$, $^1L_a^-$ and $^1L_b^-$ states are both characterized by near 100% ER. In $^1L_a^-$, the CR character rises up to 40% for the excimer formation, while it remains negligible in $^1L_b^-$. This near CR-free character in $^1L_b^-$ is an interesting finding; the previous semi-empirical approaches were unable to unveil it. Since the transition dipole moment of the monomer 1L_b is much smaller than that of 1L_a , the attractive interaction in $^1L_b^-$ driven by ER alone should be far weaker than that in $^1L_a^-$. In the presence of the transition dipole-transition dipole interaction, the attractive interaction in $^1L_a^-$ is further pronounced by the growth of its CR character, as modeled by the semi-empirical approach. These imbalanced intermolecular interactions underlie the mechanism of the inversion of the two excitation levels.

2. Theoretical Investigation into Pentanuclear Iron Catalyst Designed for Water Oxidation³⁾

Quantum chemistry calculations were performed on the pentanuclear iron complex and its reaction intermediates using density functional theory (DFT). The catalyst based on the complex was recently developed by Masaoka group; it was

Naphthalene excimer: DMRG-CASPT2 study

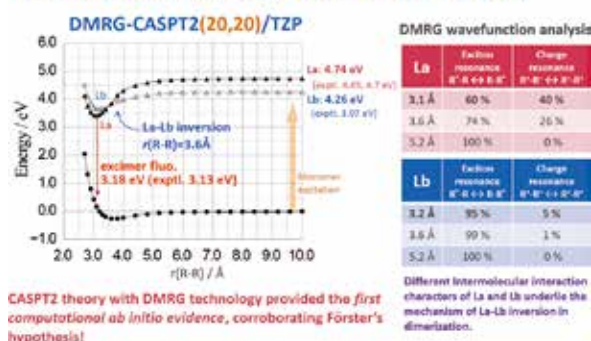


Figure 2. The potential energies of naphthalene dimer of ground, 1L_a and 1L_b excited states as a function of intermolecular distance. DMRG wavefunction analysis showing the weights of exciton and charge resonance characters of the DMRG-CASSCF wavefunction.

revealed that it here has a remarkable ability to catalyze water oxidization with significant efficiency and robustness. We first examined the viability of water attack reaction. Potential energy surface scan calculations were carried out to derive a reaction pathway of the insertion of a single water to the cluster. Our computational model showed that the coordination of water to activation iron site occurs with activation barrier of 14 kcal/mol. Next, we assume that the reaction proceeds to the coordination of another water and sequential or simultaneous deprotonation, affording cofacial Fe=O radical units. It was found that these top and bottom iron sites play a role as oxidants that withdraw two electrons from water-coordinated activation iron sites during deprotonation; so, intramolecular electron rearrangement takes place between central sites and up-down sites, and they assist generation of reactive high-valence iron-oxo species. Importantly, the number of electrons are conserved in the step. This system was found a mixed valence system involving three kinds of valence, Fe^{II} , Fe^{III} , and Fe^{IV} , simultaneously. Such remarkable redox flexibility is perhaps responsible for high efficiency of catalytic core. In addition, our computational investigation indicated that the O-O bond formation proceeds from the mixed-valence $Fe^{II}_2Fe^{III}(Fe^{IV}=O)_2$ intermediate with a reaction barrier of less than 10 kcal mol⁻¹.

References

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Photosynthesis provides the energy source for essentially all living things on Earth, and its functionality has been one of the most fascinating mysteries of life. Photosynthetic conversion of the energy of sunlight into its chemical form suitable for cellular processes involves a variety of physicochemical mechanisms. The conversion starts with the absorption of a photon of sunlight by one of the light-harvesting pigments, followed by transfer of electronic excitation energy to the reaction center, where charge separation is initiated. At low light intensities, surprisingly, the quantum efficiency of the transfer is near unity. A longstanding question in photosynthesis has been the following: How does light harvesting

deliver such high efficiency in the presence of disordered and fluctuating dissipative environments? Why does not energy get lost? At high light intensities, on the other hand, the reaction center is protected by regulation mechanisms that lead to quenching of excess excitation energy in light harvesting proteins. The precise mechanisms of these initial steps of photosynthesis are not yet fully elucidated from the standpoint of molecular science. Particularly, recent observations of long-lived beating phenomena in two-dimensional electronic spectra of photosynthetic pigment-protein complexes stimulated a huge burst of activity in an interdisciplinary community of molecular science and quantum physics.

Selected Publications

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- A. Ishizaki and G. R. Fleming, "Unified Treatment of Quantum Coherent and Incoherent Hopping Dynamics in Electronic Energy Transfer: Reduced Hierarchy Equation Approach," *J. Chem. Phys.* **130**, 234111 (10 pages) (2009).
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- A. Ishizaki and G. R. Fleming, "Quantum Coherence in Photosynthetic Light Harvesting," *Annu. Rev. Condens. Matter Phys.* **3**, 333–361 (2012). [Invited review article]
- Y. Fujihashi, G. R. Fleming and A. Ishizaki, "Impact of Environmentally Induced Fluctuations on Quantum Mechanically Mixed Electronic and Vibrational Pigment States in Photosynthetic Energy Transfer and 2D Electronic Spectra," *J. Chem. Phys.* **142**, 212403 (12 pages) (2015).

1. Influences of Quantum Mechanically Mixed Electronic and Vibrational Pigment States in 2D Electronic Spectra of Photosynthetic Systems: Strong Electronic Coupling Cases

In 2D electronic spectroscopy studies, long-lived quantum beats have recently been observed in photosynthetic systems, and several theoretical studies have suggested that the beats are produced by quantum mechanically mixed electronic and vibrational states. Concerning the electronic-vibrational quantum mixtures, the impact of protein-induced fluctuations was examined by calculating the 2D electronic spectra of a weakly coupled dimer with the Franck-Condon active vibrational modes in the resonant condition [Fujihashi *et al.*, *J. Chem. Phys.* **142**, 212403 (2015)]. This analysis demonstrated that quantum mixtures of the vibronic resonance are rather robust under the influence of the fluctuations at cryogenic temperatures, whereas the mixtures are eradicated by the fluctuations at physiological temperatures. However, this conclusion cannot be generalized because the magnitude of the coupling inducing the quantum mixtures is proportional to the inter-pigment electronic coupling. In this study, we explore the impact of the fluctuations on electronic-vibrational quantum mixtures in a strongly coupled dimer with an off-resonant vibrational mode. Toward this end, we calculate energy transfer dynamics and 2D electronic spectra of a model dimer that corresponds to the most strongly coupled bacteriochlorophyll molecules in the Fenna-Matthews-Olson complex in a numerically accurate manner. The quantum mixtures are found to be robust under the exposure of protein-induced fluctuations at cryogenic temperatures, irrespective of the resonance. At 300 K, however, the quantum mixing is disturbed more strongly by the fluctuations, and therefore, the beats in the 2D spectra become obscure even in a strongly coupled dimer with a resonant vibrational mode. Further, the overall behaviors of the energy transfer dynamics are demonstrated to be dominated by the environment and coupling between the 0–0 vibronic transitions as long as the Huang-Rhys factor of the vibrational mode is small. The electronic-vibrational quantum mixtures do not necessarily play a significant role in electronic energy transfer dynamics despite contributing to the enhancement of long-lived quantum beating in the 2D spectra.¹⁾

2. Fluctuations in Electronic Energy Affecting Singlet Fission Dynamics and Mixing with Charge Transfer State: Quantum Dynamics Study

Singlet fission is a spin-allowed process by which a singlet excited state is converted to two triplet states. To understand

mechanisms of the ultrafast fission via a charge transfer (CT) state, one has investigated the dynamics through quantum-dynamical calculations with the uncorrelated fluctuation model; however, the electronic states are expected to experience the same fluctuations induced by the surrounding molecules because the electronic structure of the triplet pair state is similar to that of the singlet state except for the spin configuration. Therefore, the fluctuations in the electronic energies could be correlated, and the 1D reaction coordinate model may adequately describe the fission dynamics. In this work we develop a model for describing the fission dynamics to explain the experimentally observed behaviors. We also explore impacts of fluctuations in the energy of the CT state on the fission dynamics and the mixing with the CT state. The overall behavior of the dynamics is insensitive to values of the reorganization energy associated with the transition from the singlet state to the CT state, although the coherent oscillation is affected by the fluctuations. This result indicates that the mixing with the CT state is rather robust under the fluctuations in the energy of the CT state as well as the high-lying CT state.²⁾

3. A Variational Master Equation Approach to Quantum Dynamics with Off-Diagonal Coupling in a Sub-Ohmic Environment

A master equation approach based on an optimized polaron transformation is adopted for dynamics simulation with simultaneous diagonal and off-diagonal spin–boson coupling. Two types of bath spectral density functions are considered, the Ohmic and the sub-Ohmic. The off-diagonal coupling leads asymptotically to a thermal equilibrium with a nonzero population difference $P_z(t \rightarrow \infty) \neq 0$, which implies localization of the system, and it also plays a role in restraining coherent dynamics for the sub-Ohmic case. Since the new method can extend to the stronger coupling regime, we can investigate the coherent–incoherent transition in the sub-Ohmic environment. Relevant phase diagrams are obtained for different temperatures. It is found that the sub-Ohmic environment allows coherent dynamics at a higher temperature than the Ohmic environment.³⁾

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Awards

ISHIZAKI, Akihito; 10th Condensed-Matter Science Prize, Japan (2015).

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Theoretical Study on Photochemistry and Catalysis

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Keywords

Quantum Chemistry, Photophysical Chemistry, Heterogeneous Catalysis

We develop the accurate electronic structure theories and investigate the photochemistry and catalysis theoretically. Currently, our focuses are following research subjects.

(1) Coupled cluster theory for excited states of large system

We develop the coupled cluster theories and their efficient computational algorithm aiming at large-scale calculations of molecular excited states. We also develop the basic theories and methodologies that are useful for fundamental chemistry and applied chemistry; for example, PCM SAC-CI method for effectively describing the solvent effects on excited states, CAP/SAC-CI method for locating metastable resonance states, general-R method for multiple excited states, and active-space method for efficiently describing complex electronic states.

(2) Heterogeneous catalysis

Metal nanoclusters supported by metal oxides or polymers achieve highly efficient catalytic reactions. We study the catalytic activity of these complex systems by means of quantum chemical calculations and informatics theories. We have elucidated the importance of the perimeter sites at hetero-junction of Ag nanocluster supported by alumina surface in terms of H₂ activation, the mechanism of methanol oxidation on Au:PVP and the unique coupling reactions on Au/Pd:PVP. We proceed these works in the project of Elements Strategy

Initiative for Catalysts and Batteries (ESICB).

(3) Photophysical chemistry

Our accurate electronic structure theories are applied to wide varieties of theoretical studies and sometimes in cooperation with experiments on the photophysical properties and excited-state dynamics of nano-bio systems like photo-electronic devices, photofunctional molecules, and biosensors. Target molecules include nanocarbons like fullerenes, near-IR absorbing phthalocyanine congeners, dye-sensitized solar cells, organometallic compounds for artificial photosynthesis, biological chemosensors, and bio-imaging probes.

(4) Theoretical spectroscopy

New quantum states, single-site and two-site double-core hole states, have been observed owing to the recent development of free electron laser and coincidence spectroscopy. We have proposed new chemical concept regarding the physical properties or relaxation processes of these quantum states in cooperation with experiments. We also perform accurate theoretical analysis for the state-of-the-art molecular spectroscopy; for example, the electronic transitions in the FUV region by ATR-FUV spectroscopy and the excited-state relaxation processes by pump-probe spectroscopy.

Selected Publications

- R. Cammi, R. Fukuda, M. Ehara and H. Nakatsuji, "SAC-CI Method in the Polarizable Continuum Model-Theory for Solvent Effect on Electronic Excitation of Molecules in Solution," *J. Chem. Phys.* **133**, 024104 (24 pages) (2010).
- N. Berrah, M. Tashiro, M. Ehara *et al.*, "Double Core-Hole Spectroscopy for Chemical Analysis with an Intense X-Ray Femtosecond Laser," *Proc. Natl. Acad. Sci. U.S.A.* **108**, 16912–16915 (2011).
- M. Ehara and T. Sommerfeld, "CAP/SAC-CI Method for Calculating Resonance States of Metastable Anions," *Chem. Phys. Lett.* **537**, 107–112 (2012).
- P. Hirunsit, K. Shimizu, R. Fukuda, S. Namuangruk, Y. Morikawa and M. Ehara, "Cooperative H₂ Activation at Ag Cluster/θ-Al₂O₃ Dual Perimeter Sites: A DFT Study," *J. Phys. Chem. C* **118**, 7996–8006 (2014).

1. Low-Lying Resonances of Standard and Rare DNA and RNA Bases

The character and efficiency of electron transfer or electron injection in DNA and RNA play a crucial role in various biological processes. This process is relevant to the more general question of charge transfer in DNA, and much experimental and theoretical effort has been devoted to the study of electron attachment to the vacant π^* molecular orbitals (MOs) of DNA bases. In low-energy (< 3 eV) electron-induced processes, so-called transient or temporary negative ions, also referred to as resonance states, are early key intermediates in the damage of DNA strands.

We have investigated low-lying π^* resonance states of DNA and RNA bases by the recently developed projected complex absorbing potential (CAP)/SAC-CI method using a smooth Voronoi potential as CAP.¹⁾ In addition to these standard bases, three modified forms of cytosine, which serve as epigenetic or biomarkers, were investigated. A strong correlation between the computed positions and the observed ETS values is demonstrated, clearly suggesting that the present computational protocol should be useful for predicting the π^* resonances of DNA and RNA bases (Figure 1).

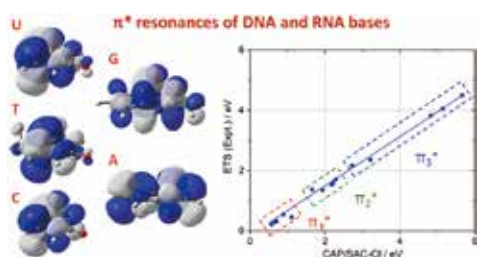


Figure 1. Correlation between calculated resonance energy and observed energy.

2. Donor- π -Acceptor Organic Dyes for a Dye-Sensitized Solar Cell

The electronic structure and photophysical properties of five coumarin-based donor- π -acceptor (D- π -A)-type organic dyes for a dye-sensitized solar cell (DSSC) have been investigated using the TDDFT and SAC-CI methods.²⁾ Theoretical calculations including the solvent effect in state-specific and linear-response scheme reproduced the experimental UV/Vis absorption spectra of these dyes satisfactorily. The π -spacers, thiophene and thiophene-phenylene mixed units, affect the planarity of the molecular structures which is relevant to the photophysical properties and charge polarization. Energy levels of the frontier orbitals and charge separation were analyzed and the thiophene linker was found to be effective for the electron injection in DSSC. The adsorption of these dyes on the TiO₂ anatase (101) surface and the electron injection mechanism were also investigated using a dye-(TiO₂)₃₈ cluster model employing PBE and TD-CAM-B3LYP calculations, respectively. The possible direct electron injection

mechanism was suggested in the present coumarin-based D- π -A dyes in a dye-TiO₂ interacting system.

3. Bond Activation on Bimetallic Alloy Nanoclusters

Bimetallic nanoparticles (NP) have been shown to exhibit certain advantages over pure NPs in catalysis due to synergistic effect. It is common to disperse NPs in polymer matrix such as polyvinylpyrrolidone (PVP) to prevent flocculation, which imparts considerable electronic effects on the NPs.

In this work, interactions between aqueous solutions of N-ethylpyrrolidone (EP, system chosen to model the monomeric form of PVP) and Au/Pd bimetallic NPs, which are relevant in catalysis,³⁾ have been investigated using molecular dynamics simulations and density functional theory (DFT) method.⁴⁾ The interactions of NP with the environment were studied at various concentrations of aqueous solutions of EP to examine the strength of NP-EP and NP-water interactions. Free energy calculations show that the EP adsorption on NP is preferred over the adsorption of water (Figure 2). Extensive analysis of the interactions of the NPs with various concentrations of aqueous EP suggests existence of isolated water molecules that may take part in reactions. Adsorption of unexpectedly large numbers of EP molecules was found to be possible leading to accumulation of the electron density on the Au/Pd NPs, which have previously been shown to enhance the catalytic activity of NPs.

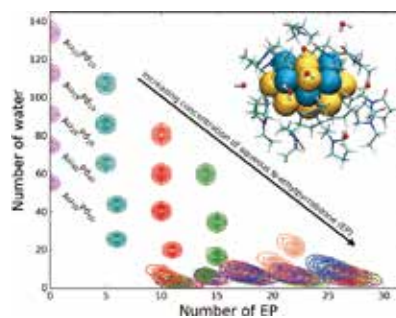


Figure 2. Number of EP and water molecules adsorbed on Au/Pd NC depending on the concentration of EP.

References

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- 3) R. N. Dhital, C. Kamonsatikul, E. Somsook, K. Bobuatong, M. Ehara, S. Karanjit and H. Sakurai, *J. Am. Chem. Soc.* **134**, 20250–20253 (2012).
- 4) A. Gupta, B. Boekfa, H. Sakurai, M. Ehara and U. Deva Priyakumar, *J. Phys. Chem. C* **120**, 17454–17464 (2016).

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Development of New Molecular Dynamics Algorithms for Biomolecular Systems

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Keywords Molecular Dynamics Simulation, Protein, Amyloid

Biomolecules such as proteins and peptides have complicated free-energy landscape with many local minima. The conventional canonical-ensemble molecular dynamics (MD) simulations tend to get trapped in a few of the local-minimum states. To overcome these difficulties, we have proposed new generalized-ensemble algorithms, such as replica-permutation method. We apply these methods to proteins and peptides and try to predict the native structures of proteins as in Figure 1.

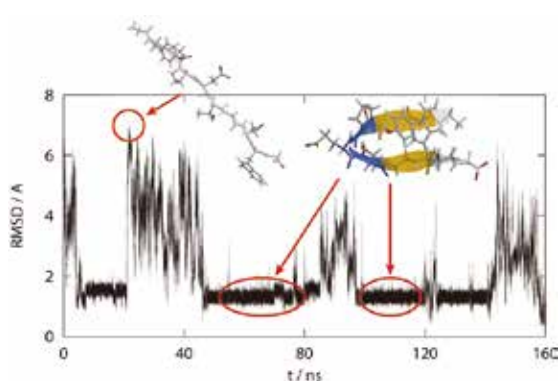


Figure 1. Time series of protein folding simulation.

We are also interested in amyloid fibrils, which are insoluble aggregates of misfolded fibrous proteins and associated with more than 20 human neurodegenerative diseases (Figure 2). For example, Alzheimer's disease is related to amyloid- β ($A\beta$) peptides. To overcome these diseases, it is essential to understand amyloid genesis and disruption. We perform such MD simulations of amyloid fibrils.

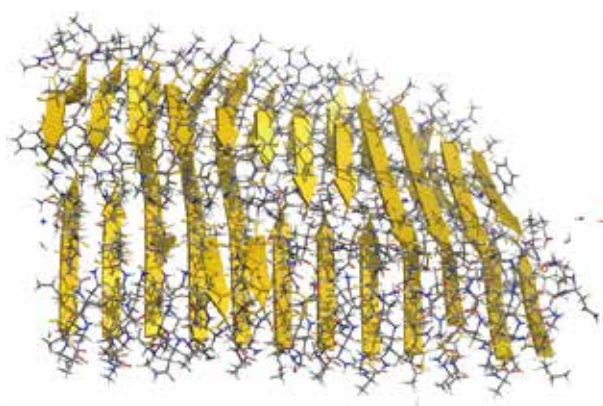


Figure 2. Snapshot of amyloid fibril.

Selected Publications

- Y. Mori and H. Okumura, "Pressure-Induced Helical Structure of a Peptide Studied by Simulated Tempering Molecular Dynamics Simulations," *J. Phys. Chem. Lett.* **4**, 2079–2083 (2013).
- S. G. Itoh and H. Okumura, "Replica-Permutation Method with the Suwa-Todo Algorithm beyond the Replica-Exchange Method," *J. Chem. Theory Comput.* **9**, 570–581 (2013).
- H. Okumura and S. G. Itoh, "Amyloid Fibril Disruption by Ultrasonic Cavitation: Nonequilibrium Molecular Dynamics Simulations," *J. Am. Chem. Soc.* **136**, 10549–10552 (2014).
- S. G. Itoh and H. Okumura, "Oligomer Formation of Amyloid- β (29-42) from Its Monomers Using the Hamiltonian Replica-Permutation Molecular Dynamics Simulation," *J. Phys. Chem. B* **120**, 6555–6561 (2016).

1. Oligomer Formation of Amyloid- β (29-42) from Its Monomers Using the Hamiltonian Replica-Permutation Molecular Dynamics Simulation

Oligomers of amyloid- β peptides ($A\beta$) are formed during the early stage of the amyloidogenesis process and exhibit neurotoxicity. The oligomer formation process of $A\beta$ and even that of $A\beta$ fragments are still poorly understood, though understanding of these processes is essential for remedying Alzheimer's disease. In order to better understand the oligomerization process of the C-terminal $A\beta$ fragment $A\beta$ (29-42) at the atomic level, we performed the Hamiltonian replica-permutation molecular dynamics simulation with $A\beta$ (29-42) molecules using the explicit water solvent model.¹⁾ We observed that oligomers increased in size through the sequential addition of monomers to the oligomer, rather than through the assembly of small oligomers. Moreover, solvent effects played an important role in this oligomerization process.

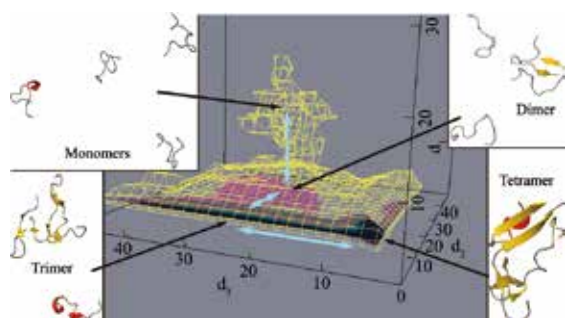


Figure 3. Free-energy surface and typical conformations of four $A\beta$ (29-42) molecules.

2. Simulated Tempering Based on Global Balance or Detailed Balance Conditions: Suwa-Todo, Heat Bath, and Metropolis Algorithms

Simulated tempering (ST) is a useful method to enhance sampling of molecular simulations. When ST is used, the Metropolis algorithm, which satisfies the detailed balance condition, is usually applied to calculate the transition probability. Recently, an alternative method that satisfies the global balance condition instead of the detailed balance condition has been proposed by Suwa and Todo. In this study, ST method with the Suwa- Todo algorithm is proposed.²⁾ Molecular dynamics simulations with ST are performed with three algorithms (the Metropolis, heat bath, and Suwa- Todo algorithms) to calculate the transition probability. Among the three algorithms, the Suwa- Todo algorithm yields the highest acceptance ratio and the shortest autocorrelation time. These suggest

that sampling by a ST simulation with the Suwa- Todo algorithm is most efficient. In addition, because the acceptance ratio of the Suwa- Todo algorithm is higher than that of the Metropolis algorithm, the number of temperature states can be reduced by 25% for the Suwa- Todo algorithm when compared with the Metropolis algorithm.

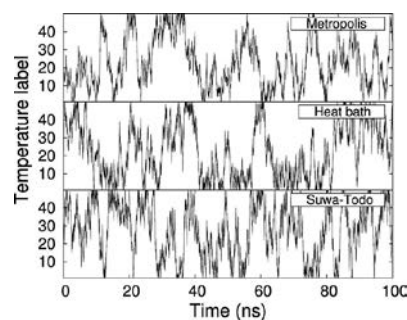


Figure 4. Time series of the temperature label in the simulations with the Metropolis, heat bath, and Suwa- Todo algorithms

3. Conformation Study of ϵ -Cyclodextrin: Replica-Exchange Molecular Dynamics Simulations

There is growing interest in large-ring cyclodextrins (LR-CDs) which are known to be good host molecules for larger ligands. The isolation of a defined size LR-CD is an essential prerequisite for studying their structural properties. Unfortunately the purification procedure of these substances turned out to be very laborious. Finally the problem could be circumvented by a theoretical consideration: The replica exchange molecular dynamics (REMD) simulation offers an ideal approach for studying the conformational change of ϵ -cyclodextrin (CD10), a smaller representative of LR-CDs. Three carbohydrate force fields and three solvent models were tested.³⁾ The conformational behavior of CD10 was analyzed in terms of the flip (turn) of the glucose subunits within the macrocyclic ring. In addition a ranking of conformations with various numbers of turns was performed. Our findings might be also helpful in the temperature controlled synthesis of LR-CDs as well as other experimental conditions, in particular for the host-guest reaction.

References

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- 2) Y. Mori and H. Okumura, *J. Comput. Chem.* **36**, 2344–2349 (2015).
- 3) W. Khuntawee, T. Rungrotmongkol, P. Wolschann, P. Pongsawasdi, N. Kungwan, H. Okumura and S. Hannongbua, *Carbohydr. Polym.* **141**, 99–105 (2016).

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Theoretical Studies on Molecular Aggregates

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Keywords Exciton, Energy and Charge Transfer, Organic Semiconductors

Organic molecules can assemble into an ordered structure by non-covalent interactions, forming various types of aggregates. Molecular aggregates exhibit characteristic optical and electronic properties that are not observed in isolated molecules. For example, their photophysical processes include electronic energy transfer and charge separations, which are desirable for low-cost electronic devices.

We study optoelectronic properties and quantum dynamics of molecular aggregates. More specifically, we focus on energy and charge transfer dynamics, energy conversions, and structure-property relationship.

It is still challenging to simulate quantum dynamics in condensed systems. An exciton or electron wave function can be delocalized by electronic couplings due to molecular interactions; it is modulated by molecular vibrations. It is thus essential to consider electronic couplings and electron-phonon couplings on the same footing. We develop a method to simulate quantum dynamics in condensed phase by combining molecular dynamics simulations, electronic structure theories, and quantum dynamics methods, as shown in Figure 1. An electronic structure of an aggregate is described as tight-binding Hamiltonian with electronic couplings obtained from the fragment molecular orbital method. The energy or charge dynamics is described by quantum dynamics methods with

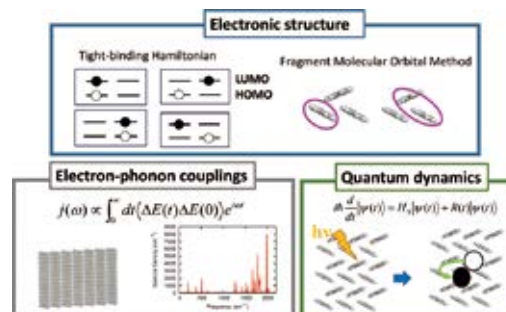


Figure 1. A combine approach to quantum dynamics in molecular aggregates.

incorporating finite-temperature effects and electron-phonon couplings. The combine computational approach allows for bottom-up descriptions of energy or charge transfer dynamics in molecular aggregates.

We currently investigate exciton dynamics in organic semiconductors, and structure-property relationships in ion-based π -conjugated molecular systems. We also study statistical-mechanics theories for predicting supramolecular structures in solution, and a many-body approach for excited-state calculations.

Selected Publications

- T. Fujita, J. C. Brookes, S. K. Saikin and A. Aspuru-Guzik, "Memory-Assisted Exciton Diffusion in the Chlorosome Light-Harvesting Antenna of Green Sulfur Bacteria," *J. Phys. Chem. Lett.* **3**, 2357–2361 (2012).
- T. Fujita, J. Huh, S. K. Saikin, J. C. Brookes and A. Aspuru-Guzik, "Theoretical Characterization of Excitation Energy Transfer in Chlorosome Light-Harvesting Antennae from Green Sulfur Bacteria," *Photosynth. Res.* **120**, 273–289 (2014).

1. Coherent Dynamics of Mixed Frenkel and Charge-Transfer Excitons¹⁾

There has been a growing interest in electronic properties in organic semiconductors due to their broad applications for electronic devices. Optical properties of organic molecular aggregates have been traditionally explained in terms of Frenkel exciton model, which describes an electronic excited state as a bound electron–hole pair. In recent years, great attention has been focused on charge-transfer excitons—a state where electron and hole can be located in separate regions. The CT excitons play essential roles in singlet fission and charge separations at donor/acceptor interfaces.

In this study, we focus on a p-type organic semiconductor, dinaphtho[2,3-b:2'3'-f]thieno[3,2-b]-thiophene (DNTT). A time-resolved spectroscopy study suggests that mixed Frenkel and CT excitons are formed in DNTT thin films after the optical excitation. Although the degree of CT characters in excited states has been discussed, its role in excitation dynamics has remained unclear. We investigate optical properties and exciton dynamics in the DNTT. The excited states of DNTT aggregates are described by tight-binding Hamiltonian combined with electronic couplings. Exciton dynamics coupled to molecular vibrations is modeled by a stochastic Schrödinger equation with spectral densities derived from molecular dynamics simulations and excited-state calculations.

The calculated absorption spectrum is in qualitative agreement with the experimental one. Our theory predicts that the low-energy Frenkel exciton band consists of 8 to 47% of CT character. The obtained excitonic Hamiltonian was used to simulate real-time quantum dynamics with incorporating exciton–phonon interactions in atomistic details. We observe the mixing of CT excitons with Frenkel state in 50 fs after the excitation. Accordingly, an electron–hole separation increases and shows an oscillation pattern as a result of delocalization of electron and hole and electron–hole Coulomb interactions.

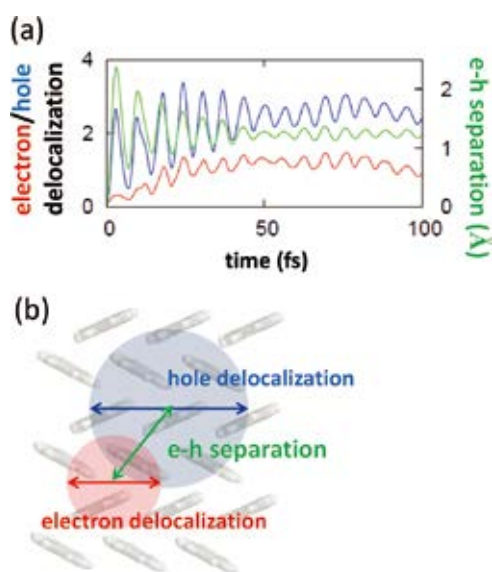


Figure 2. Ultrafast dynamics of mixed Frenkel-CT excitons in DNTT. (a) Electron and hole delocalization lengths, and electron–hole separations. (b) A schematic picture.

2. Polymorphism and Optoelectronic Properties of Anion-Responsible Molecules

π -conjugated molecules, especially aromatic hydrocarbons, show characteristic electronic and optical properties. The planar geometries are useful for constructions of stacking assemblies. Maeda and co-workers have proposed ion-based π -conjugated systems based on dipyrrolyldiketone difluoroboron (BF_2) complexes. Mixed with anion and cationic π -conjugated molecules, they form ion-based molecular assemblies.

Here, we consider the dipyrrolyldiketone BF_2 . This molecule shows the polymorphism of solid-state assemblies with different stacking modes. They have distinct optical and charge transport properties, which depend on their molecular stacking and interactions. In this study, we calculate charge mobility based on fragment molecular orbital calculations for transfer integrals and Marcus theory for charge transfer. Charge mobility is obtained from diffusion constants by Master equation with the hopping rates. Calculated hole mobility correlates well with time-resolved microwave conductivity measurements, suggesting that hole transport is responsible for the photoconductivity.

3. Solution Theories for Nano-Sized Hydrophobic Molecules

Solvation free energy (SFE) is most important thermodynamics quantities in solution chemistry. Molecular dynamics simulations combined with thermodynamic integration or free energy perturbation can offer exact computations of SFEs within statistical error and force fields employed. However, it requires large computational time especially for nano-sized molecular systems. Accurate and efficient estimations of SFEs is still challenging.

Here, we investigate the accuracy of approximate solution theories for calculating hydration free energies (HFEs) of nano-sized hydrophobic molecules. Energy representation and three-dimensional reference interaction site model (3D-RISM) with different closures were compared with molecular dynamics simulations with the Bennett acceptance ratio. The HFEs from approximate theories are in reasonable agreement for relatively small hydrophobic solutes. However, they show considerable errors in HFEs of large hydrophobic solutes and predict artificial solute-size dependence of the HFEs. A recently-proposed empirical correction based on a partial molar volume (PMV) of a solute significantly improves the 3D-RISM results in such a way that they become qualitatively agreement with the BAR. The success of the PMV correction is discussed in terms of asymptotic behaviors of HFEs in a limit of large solute size.

Reference

- 1) T. Fujita, S. Atahan-Evrenk, N. P. D. Sawaya and A. Aspuru-Guzik, *J. Phys. Chem. Lett.* **7**, 1374–1380 (2016).

Functional Dynamics of Biomolecular Machines Revealed by Theoretical Methods

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Keywords Theoretical Biophysics, Molecular Motors, Molecular Simulations

Functional dynamics plays an important role when biomolecular machines fulfill their functions. For example, motor proteins walk on the rail or rotate relative to the stator by using ATP hydrolysis energy. Transporter proteins transport their substrates across the membrane by changing their conformation between inward-open and outward-open conformations. We aim to understand design principles of these precise, yet dynamic nano-machines developed by nature.

Functional dynamics of biomolecular machines involve wide spectrum of intricate motions and reactions. In order to understand such dynamics, we need a multiscale approach to cover full range of these motions and reactions. Conventional atomistic molecular dynamics simulations alone cannot cover millisecond-long (or even longer) functional dynamics, especially for a large system like typical biomolecular machines with more than hundreds of thousand atoms including water

molecules. Thus, we use both atomistic and coarse-grained molecular simulations, as well as kinetic models based on statistical mechanics, to tackle this problem.

We have been particularly focusing on ATP synthase that produces most of ATP required for living activities. The ATP synthase is composed of two rotary motors, F_0 and F_1 . The F_0 motor is embedded in membrane and its rotation is driven by proton gradient. The F_1 motor is a catalytic part that produces ATP from ADP and P_i . However, the F_1 motor by itself (F_1 -ATPase) rotates the central stalk, γ -subunit, in the opposite direction by hydrolyzing ATP. Thus, the two motors are driven by different energy sources and rotate in the opposite directions. In order to understand how ATP synthase works, we have to look into both individual motors and ATP synthase as a whole.

Selected Publications

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- K. Okazaki and G. Hummer, "Elasticity, Friction, and Pathway of γ -Subunit Rotation in F_0F_1 -ATP Synthase," *Proc. Natl. Acad. Sci. U.S.A.* **112**, 10720–10725 (2015).
- M. Sugawa, K. Okazaki, M. Kobayashi, T. Matsui, G. Hummer, T. Masaike and T. Nishizaka, " F_1 -ATPase Conformational Cycle from Simultaneous Single-Molecule FRET and Rotation Measurements," *Proc. Natl. Acad. Sci. U.S.A.* **113**, E2916–E2924 (2016).

1. Mechanochemical Coupling Mechanism of F₁-ATPase

Many single-molecule studies as well as crystallographic studies have clarified how the γ -subunit rotation is coupled to ATP hydrolysis reactions at three catalytic sites of F₁. As summarized in Figure 1B, main points are, 1) 120° step inferred from three-fold symmetry is further divided into 80° and 40° substeps, 2) the 80° substep is driven by ATP binding and ADP release, 3) the 40° substep is driven by P_i release and ATP hydrolysis reaction, 4) typical crystal structures correspond to catalytic dwell (before 40° substep). There are still some remaining questions, though. What is the timing of P_i release: Just after the hydrolysis reaction or after ADP release? What conformation does it take in ATP-binding dwell (before 80° substep)?

We resolved the timing of P_i release by using atomistic molecular dynamics simulations.¹⁾ The question is, essentially, from which catalytic site, DP-site or E-site, P_i is released. Since the P_i release takes ~millisecond, a biasing method called metadynamics was employed to facilitate the functional dynamics. Different pathways were observed depending on the site P_i was released. From the E-site it went through P-loop toward outside of the ring structure, while from the DP-site it went through switch II toward inside of the ring structure (Figure 1C). We estimated mean first-passage time from free energy profile (Figure 1D) and diffusion coefficient and concluded that P_i is released from the E-site. That is, P_i is released after ADP release, which is unique among other members of ATPases.

We also identified conformational state of the ATP-binding dwell by combining single-molecule FRET measurements and systematic structural analysis.²⁾ We found that an ϵ -inhibited *E. Coli* structure that has half-closed β_{DP} and loose $\alpha\beta_E$ interface is consistent with the conformation taken in the ATP-binding dwell.

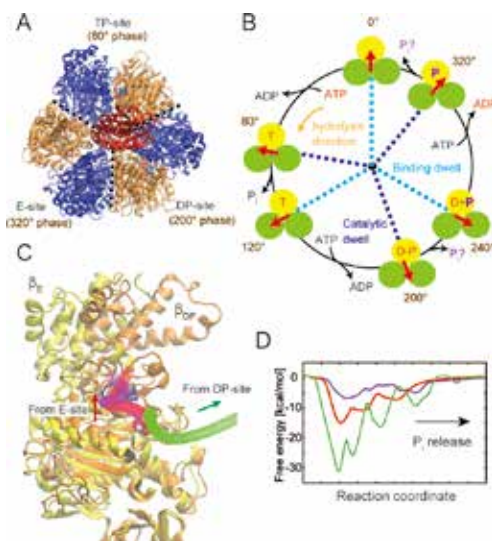


Figure 1. Mechanochemical coupling scheme and P_i release in F₁-ATPase.

2. Torsional Elasticity and Friction of Rotor in F_oF₁-ATP Synthase

It has been known that there is a symmetry mismatch between F_o c-ring and F₁ $\alpha_3\beta_3$ ring. The F₁ $\alpha_3\beta_3$ ring has (pseudo) three-fold symmetry, while the F_o c-ring in animal mitochondria has 8-fold symmetry. Thus, the common rotor, γ -subunit, has to rotate by 120° steps (or 80°+40° substeps) in F₁ part, while it has to rotate by 45° steps in F_o part. Therefore, it has to have torsional elasticity to solve the mismatch. In order to estimate torsional elasticity as well as viscosity of the γ -rotation, we built a simple viscoelastic model (Figure 2B) and fitted it against atomistic simulation trajectories in which external torque was applied on γ .³⁾

The estimated torsional elasticity is consistent with values from single-molecule experiments. By using this elasticity, we identified pathways and associated free energies of the coupled F_oF₁ rotation (Figure 2C). It turned out that with the two-substep F₁ the pathway is blocked by high-energy states. To solve this situation, F₁ needs three substeps as was measured for human mitochondrial F₁ recently. From the estimated torsional friction, we predict that γ -rotation can be as fast as 1 MHz and this fast rotation can be observed with an attached bead as small as 20 nanometer diameter.

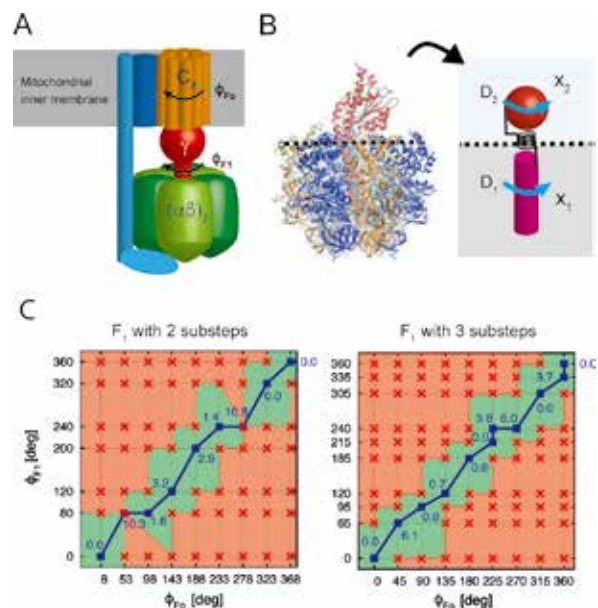


Figure 2. Viscoelastic model of F_oF₁-ATP synthase.

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Theory and Computation of Reactions and Properties in Solutions and Liquids

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



ISHIDA, Tateki
Assistant Professor

We are interested in the projects both on ultrafast photoinduced electron energy transfer in the excited state in solution and on ionic liquids (ILs). The project on photoinduced electron energy transfer processes in the excited state in solution is aimed at the development of a theoretical method to study electron energy transfer. On the other hand, ILs' projects are focused on the investigation of dynamical properties on ionic liquids and the unique dissolution process of cellulose polysaccharides using molecular dynamics simulation technique.

1. The Theoretical Investigation of Photoinduced Electron Energy Transfer Processes in the Excited State in Solution¹⁾

We have developed a procedure for capturing the time-dependent evolution of the electronic structure of a solute molecule in solution, coupling an electronic structure theory with solvent motion. It is indicated that the coupling between

solvation processes and a fast intramolecular electron energy transfer is likely to play an important role in the emergence of photoinduced unique functionalities in biochemical and metal complex systems.

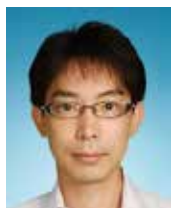
2. Investigations of Ionic Liquids¹⁻²⁾ with Molecular Dynamics Simulation

We focus on the dynamical properties on ionic liquids (ILs). With molecular dynamics simulation procedure, it has been found out that ILs show unique collective dynamics. We have investigated interesting dynamical heterogeneity in ILs at room temperature. Also, we have studied the solvation process of cellulose polymer in ILs.

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Visiting Professors



Visiting Professor

SHIGETA, Yasuteru (from *University of Tsukuba*)

Computational Analyses on Biological Functions at the Atomic Scale

Life is a system that converts a variety of energy (mechanical, electrostatic, thermal, chemical, information, and so forth) into each other to maintain itself. For the understanding and controlling phenomena in the life, elucidation of the relationship between the three-dimensional conformational changes and biological functions of proteins at the atomic scale has become one of the most important issues. However, these conformational changes are induced as slow dynamics upon collective motions, including biologically relevant large-amplitude fluctuations of proteins. Our group develops an efficient conformational search method using molecular dynamics simulations and investigates dynamics of proteins that drive specific biological functions on the basis of quantum mechanical and statistical physics-based methods.



Visiting Associate Professor

NAGATA, Yuki (from *Max Planck Institute for Polymer Research*)

Combined Simulation and Experiment Reveals Physics of Aqueous Interface

Our group aims at obtaining molecular-level understanding of the structure and dynamics of aqueous liquid interfaces, with particular emphasis on water. To this end, by using molecular dynamics (MD) simulations, we have made a direct connection to experiments using 'theoretical sum-frequency generation (SFG) spectroscopy'—both in aiding the interpretation of experimental results, as well as designing novel experiments and experimental schemes. We have interrogated the molecular conformation of water at the water-air and water-lipid interface as well as the effects of surface-active molecules on the conformation of the interfacial water molecules. One research highlights that the water's O–H group near zwitterionic lipids orients *up* toward lipid uniformly, although zwitterionic lipids can be, in principle, electronegative/positive. Having established an excellent agreement between SFG simulation and experiment, we also predicted the molecular mechanism of water evaporation from MD simulation. It turned out that the evaporation is not stochastic process, but has certain pathway for transferring the momentum of water.



Visiting Associate Professor

KATO, Tsuyoshi (from *The University of Tokyo*)

Development of Quantal Dynamical Theory and Its Application to Molecular Dynamics

I am studying in the area of quantal molecular dynamics mainly focusing on the developments of new methods to calculate the electronic and nuclear dynamics in molecules interacting with strong laser field. Currently, I am constructing a time-dependent effective potential theory that could be used to calculate the exact time-dependent wave function of a many-electron system. During the development of the effective potential theory, I found a solution algorithm for the time-independent/dependent Kohn-Sham problem, and presently I am analyzing the relations among some exact wave function theories and density functional theory. Given the exact time-dependent wave function describing quantal many-particle dynamics, my final goal is to establish a method to derive an exact effective single- and two-particle potentials out of the many-particle wave function. Consequently, we are able to use the notions, that are deduced from the analysis of the properties of the exact effective potentials, within the quantum optimal control theory as well as to analyze the chemical reactions.

