RESEARCH ACTIVITIES

Theoretical and Computational Molecular Science

The goal of the Department is to predict and elucidate static and dynamic properties, reactions, and functions in condensed phase including biomolecular and heterogeneous catalytic systems by developing novel theories and computational methods based on quantum mechanics, statistical mechanics, and solid state physics.

The Department collaborates with Research Center for Computational Science on researches.

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

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

SAITO, Shinji
Professor
[shinji@ims.ac.jp]

Education
1988 B.S. Keio University
1990 M.E. Kyoto University
1995 Ph.D. The Graduate University for Advanced Studies

Professional Employment
1990 Technical staff, Institute for Molecular Science
1994 Research Associate, Nagoya University
1998 Associate Professor, Nagoya University
2005 Professor, Institute for Molecular Science
2006 Professor, The Graduate University for Advanced Studies

Member
Assistant Professor
  MORI, Toshifumi
  KODA, Shin-ichi
JSPS Post-Doctoral Fellow
  MATSUMURA, Yoshihiro
Post-Doctoral Fellow
  MAURYA, Manish
Graduazte Student
  KALATHINGAL, Mahroof
  ZHU, Zhe
Secretary
  CHIBA, Fumika

Keywords Reactions, Functions, Fluctuations

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 investigate fluctuations and dynamics of liquids by developing computational methods for multi-dimensional nonlinear spectroscopy that can reveal detailed dynamical infomation not available from conventional linear spectroscopy. Consequently, we revealed the molecular origins of 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 temperature of liquid water. We currently investigate how rare but persistent structural relaxation of liquid water proceeds towards the glass transition temperature.

Complex conformational fluctuations and changes can be observed in biomolecular systems. Such 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.

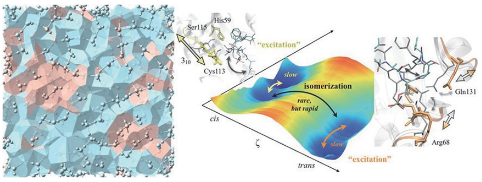

Figure 1. Snapshot of two-state model in supercooled water consisting of high- and low-density liquids (left) and schematic of 2D free energy surface for enzymatic reaction (right).

Selected Publications

- T. Yagasaki and S. Saito, *Annu. Rev. Phys. Chem.* **64**, 55–75 (2013). T. L. C. Jansen, S. Saito, J. Jeon and M. Cho, *J. Chem. Phys.* **150**, 100901 (17 pages) (2019), C. R. Baiz *et al.*, *Chem. Rev.* **120**, 7152–7218 (2020).
- K. Kim and S. Saito, *J. Chem. Phys. (Special Topic on Glass Transition)* **138**, 12A506 (12 pages) (2013).
- S. Saito, B. Bagchi and I. Ohmine, *J. Chem. Phys.* **149**, 124504 (8 pages) (2018), S. Saito and B. Bagchi, *J. Chem. Phys.* **150**, 054502 (14 pages) (2019).
- T. Mori and S. Saito, *J. Phys. Chem. Lett.* **10**, 474–480 (2019).
- S. Saito, M. Higashi and G. R. Fleming, *J. Phys. Chem. B* **123**, 9762–9772 (2019).

1. Dissecting the Dynamics during Enzyme Catalysis: A Case Study of Pin1 Peptidyl-Prolyl Isomerase(1)

Free energy surfaces have played a central role in studying protein conformational changes and enzymatic reactions over decades. Yet, free energy barriers and kinetics are highly dependent on the coordinates chosen to define the surface, and furthermore, the dynamics during the reactions are often overlooked. Our recent study on the Pin1-catalyzed isomerization reaction has indicated that the isomerization transition events remarkably deviate from the free energy path, highlighting the need to understand the reaction dynamics in more detail. To this end, here we investigate the reaction coordinates that describe the transition states of the free energy and transition pathways by minimizing the cross-entropy function. We show that the isomerization transition events can be expressed by the concerted changes in the improper torsion angle ζ and nearby backbone torsional angles of the ligand, whereas the transition state of the free energy surface involves changes in a broad range of coordinates including multiple protein–ligand interactions. The current result supports the previous finding that the isomerization transitions occur quickly from the conformational excited states, which is in sharp contrast to the slow and collective changes suggested from the free energy path. Our results further indicate that the coordinates derived from the transition trajectories are not sufficient for finding the transition states on the free energy surfaces due to the lack of information from conformational excited states.

2. An Alternative Interpretation of the Slow KaiB-KaiC Binding of the Cyanobacterial Clock Proteins(2)

The biological clock of cyanobacteria is composed of three proteins, KaiA, KaiB, and KaiC. The KaiB–KaiC binding brings the slowness into the system, which is essential for the long period of the circadian rhythm. However, there is no consensus as to the origin of the slowness due to the prebinding conformational transition of either KaiB or KaiC. In this study, we propose a simple KaiB–KaiC binding scheme in a hexameric form with an attractive interaction between adjacent bound KaiB monomers, which is independent of KaiB's conformational change. We then show that the present scheme can explain several important experimental results on the binding, including that used as evidence for the slow conformational transition of KaiB. The present result thus indicates that the slowness arises from KaiC rather than KaiB.

3. Site-Dependent Fluctuations Optimize Electronic Energy Transfer in the Fenna-Matthews-Olson Protein(3)

Light absorbed by light-harvesting antennae is transferred to the reaction center (RC). The excitation energy transfer (EET) to the RC is known to proceed with nearly perfect quantum yield. However, understanding of EET is still limited at the molecular level. Here, we examine the dynamics in the Fenna–Matthews–Olson (FMO) protein by developing an efficient molecular dynamics simulation that can properly describe the electronic properties of bacteriochlorophylls. We find that the FMO protein consists of sites with heterogeneous fluctuations extending from fast to slow modulation. We also find that efficient EETs are facilitated by site-dependent fluctuations that enhance the resonance condition between neighboring sites with large site energy differences and circumvent exciton trapping on the pathway to the RC. Knowledge of site-dependent fluctuations is an important component of understanding optimization of EET in photosynthetic systems.

4. Molecular Mechanism of Acceleration and Retardation of Collective Orientation Relaxation of Water Molecules in Aqueous Solutions(4)

The collective orientation relaxation (COR) of water molecules in aqueous solutions is faster or slower with the increase in concentration of the solutions than that in pure water; for example, acceleration (deceleration) of the COR is observed in a solution of sodium chloride (tetramethylammonium 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.

References

1) T. Mori and S. Saito, *J. Chem. Theory Comput.* **16**, 3396–3407 (2020).
2) S.-i. Koda and S. Saito, *Sci. Rep.* **10**, 10439 (7 pages) (2020).
3) S. Saito, M. Higashi and G. R. Fleming, *J. Phys. Chem. B* **123**, 9762–9772 (2019).
4) N. Moritsugu, T. Nara, S.-i. Koda, K. Tominaga and S. Saito, to be submitted.

Theoretical Studies on Novel Physical Properties Arising from Many-Body Interaction

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

MINAMITANI, Emi
Associate Professor
[eminamitani@ims.ac.jp]

Education

2005 B.S. Osaka University
2010 Ph.D. Osaka University

Professional Employment

2010 Postdoctoral Fellow, Osaka University
2011 Special Postdoctral Researcher, RIKEN
2013 Assistant Professor, The University of Tokyoy
2015 Lecturer, Cornell University
2019 Associate Professor, Institute for Molecular Science
Associate Professor, The Graduate University for Advanced Studies

Awards

2008 L'Oréal–UNESCO Japan National Fellowships for Women in Science
2011 Best Poster Award in ISSS-6 Internal Symposium on Surface Science
2017 Young Scientist Award of the Physical Society of Japan
2019 The Commendation for Science and Technology by the Minister of Education, Culture, Sports, Science and Technology
The Young Scientists' Prize

Member

Assistant Professor
SHITADE, Atsuo

Research Fellow
HINODE, Kenji
OKUGAWA, Shinichi

Secretary
AKABA, Atsuko

Keywords Quantum Many-Body Interaction, Density Functional Theory, Quantum Field Theory

Quantum many-body interaction is a source of novel physical properties in the condensed matters. In our group, we develop theoretical methods by combining quantum field theory and density functional theory, and carry out collaborative research with experimental groups. As specific targets, we focus on magnetism in nanostructure and energy dissipation.

For magnetism in nanostructure, we are interested in the Kondo effect and spin–orbit interaction. The Kondo effect arises from the interaction between the localized spin and conduction electrons, which forms a characteristic many-body state so called the Kondo singlet state. The spin–orbit interaction originating from relativistic effect constrains the direction of magnetic moment to specific direction. We investigate the possibility of novel physical phenomena induced by these interactions in the nanostructure and molecules on surfaces.

For energy dissipation, we focus on the effect of electron–phonon interaction. The electron–phonon interaction is one of the most fundamental interactions in the condensed matter physics, and the quantitative evaluation in realistic materials is highly demanding. We adopt the ab-initio calculation to analyze the signal of electron–phonon coupling in surface spectroscopy and thermal properties in various kind of solids.

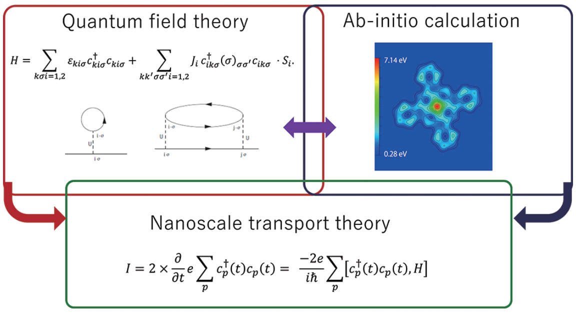

Figure 1. Schematic image of the theoretical method developed in our group.

Selected Publications

- E. Minamitani, N. Tsukahara, D. Matsunaka, Y. Kim, N. Takagi and M. Kawai, "Symmetry-Driven Novel Kondo Effect in a Molecule," *Phys. Rev. Lett.* **109**, 086602 (2012).
- E. Minamitani, R. Arafune, N. Tsukahara, Y. Ohda, S. Watanabe, M. Kawai, H. Ueba and N. Takagi, "Surface Phonon Excitation on Clean Metal Surfaces in Scanning Tunneling Microscopy," *Phys. Rev. B* **93**, 085411 (2016).
- E. Minamitani, N. Takagi and S. Watanabe, "Model Hamiltonian Approach to the Magnetic Anisotropy of Iron Phthalocyanine at Solid Surfaces," *Phys. Rev. B* **94**, 205402 (2016).
- R. Hiraoka, E. Minamitani, R. Arafune, N. Tsukahara, S. Watanabe, M. Kawai and N. Takagi, "Single-Molecule Quantum Dot as a Kondo Simulator," *Nat. Commun.* **8**, 16012 (2017).
- E. Minamitani, R. Arafune, T. Frederiksen, T. Suzuki, S. M. F. Shahed, T. Kobayashi, N. Endo, H. Fukidome, S. Watanabe and T. Komeda, "Atomic-Scale Characterization of the Interfacial Phonon in Graphene/SiC," *Phys. Rev. B* **96**, 155431 (2017).
- E. Minamitani, M. Ogura and S. Watanabe, "Simulating Lattice Thermal Conductivity in Semiconducting Materials Using High-Dimensional Neural Network Potential," *Appl. Phys. Express* **12**, 095001 (2019).

1. Superconductivity in Chemically Doped 2D Materials

Layered materials have been investigated for a long time owing to their tunable features, which enable various applications. Amongst them, superconductivity has recently attracted considerable attention. Although several types of 2D superconductors have been experimentally and/or theoretically investigated, most of them are metallic/semimetallic materials, such as metal atomic layers on semiconductor surfaces, layered materials such as FeSe and $NbSe_2$, and electron-doped graphene. The other class of 2D superconductors is doped 2D semiconductors or insulators.

We focused on hexagonal boron nitride (h-BN) as a candidate for a 2D superconductor. Bulk h-BN has a wide bandgap of approximately 6 eV, and it exists in the monolayer form. Although the application of h-BN as an inert and atomically flat insulating layer to realize novel 2D-material-based electronics has been widely investigated, its possibility as a superconductor has been untapped until recently. In our previous study, we reported that a Li-intercalated h-BN bilayer became a phonon-induced superconductor with a T_c of up to 25 K, thereby indicating that both the phonon properties and electron–phonon coupling (EPC) in doped h-BN are appropriate for realizing superconductivity.1) However, the fabrication of a superconducting Li-intercalated h-BN bilayer is experimentally challenging, as the stacking order of the h-BN sheets must differ from that of the original bulk structure to attain a high T_c. To seek a promising candidate for an h-BN-based superconductor with a more experimentally feasible structure than the bilayer structure, we investigated the properties of doped monolayer h-BN by using ab-initio calculation of electron–phonon interaction.

Consequently, we reveal that Sr- and Ba-doped monolayer h-BN and Ca-doped monolayer h-BN with 3.5% tensile strain are energetically stable and become superconductors.2) The estimated T_{cs} from McMillan–Allen–Dynes formula are approximately 5.83, 1.53, and 10.7 K, respectively. Interestingly, the T_{cs} for the Ca-, Sr-, and Ba doped graphene are lower than 0.5K.

To clarify the difference between h-BN and graphene, we analysed the electronic band structure depicted in Figure 2. The projection of the DOS from the adsorbate s-orbital onto the electronic-band structures indicated the presence of adsorbate bands that crossed the Fermi level in all systems. These bands correspond to the interlayer state reported in previous studies. In doped graphene systems, the interlayer state is crucial for determining T_c. However, the similarity in the interlayer state between doped graphene and h-BN indicates that the T_c in these systems is governed by other factors. Other than the interlayer states, several bands that originated from h-BN and graphene orbitals crossed the Fermi level.

These band structures around the Fermi level resulted in Fermi surfaces of different shapes and positions, as depicted in Figure 3. In both the h-BN and graphene cases, the Fermi surface around the K point originates from the interlayer state, and those around the Γ point correspond to the band from the h-BN or graphene states. The shape of the Fermi surfaces from the interlayer states resembled each another in both the doped h-BN and graphene cases, except for the size of the pocket. However, the shapes of the inner Fermi surfaces around the Γ point between the doped h-BN and graphene cases differed significantly. In the doped h-BN case, the inner Fermi surface exhibited a snowflake-like shape, but it was hexagram-like in the doped graphene case. The projection of the k-resolved EPC (λ_k) shows that the electron–phonon interaction in the inner Fermi surface is crucial for determining T_c. Compared with doped graphene, the doped h-BNs exhibited greater λ_k in general in the Brillouin zone. The most prominent enhancement in λ_k was observed around the Γ point.

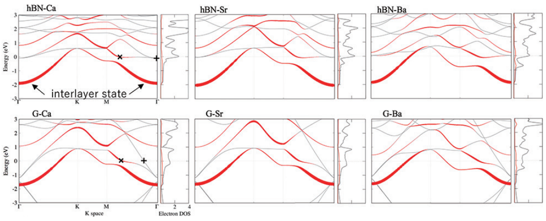

Figure 2. Electronic band dispersions and DOS for doped h-BN and graphene.

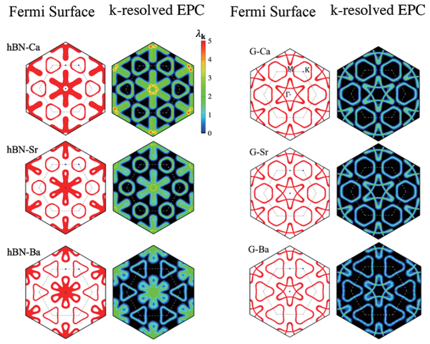

Figure 3. Fermi surfaces and k-resolved EPC projected on Fermi surface in doped h-BN and graphene.

The enhancement in λ_k around the Γ point in the Ca-doped h-BN is attributed to the spatial distribution of the wavefunction of the electronic states induced by the lower symmetry compared to the graphene case. These results indicate that instead of tuning the interlayer state, reducing the symmetry and introducing strong adsorbate–substrate interactions are alternative strategies to increase the T_c of doped 2D semiconductors/insulators.

Other Ongoing Projects:

- Geometric Spin–Orbit Coupling and Chirality-Induced Spin Selectivity

- Ab-Initio Calculation of Heat Generation in Semiconductors

References

1) N. H. Shimada, E. Minamitani and S. Watanabe, *Appl. Phys. Express* **10**, 9 (2017).

2) N. H. Shimada, E. Minamitani and S. Watanabe, *J. Phys.: Condens. Matter* **32**, 435002 (2020).

Theoretical Studies of Chemical Dynamics in Condensed and Biomolecular Systems

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

ISHIZAKI, Akihito
Professor
[ishizaki@ims.ac.jp]

Education

2008	D.S. Kyoto University

Professional Employment

2006	JPSP Research Fellow, Kyoto University
2008	JPSP Postdoctoral Fellow for Research Abroad, University of California, Berkeley
2010	Postdoctoral Fellow, Lawrence Berkeley National Laboratory
2012	Research Associate Professor, Institute for Molecular Science
2013	Fellow 2012–2013, Wissenschaftskolleg zu Berlin
2016	Professor, Institute for Molecular Science Professor, The Graduate University for Advanced Studies Visiting professor, Nagoya University

Awards

2015	10th Condensed-Matter Science Prize, Japan
2016	10th Young Scientist Award of the Physical Society of Japan
2016	18th Sir Martin Wood Prize
2017	The Commendation for Science and Technology by the Minister of Education, Culture, Sports, Science and Technology The Young Scientists' Prize
2020	JSPS Prize
2020	Japan Academy Medal

Member
Assistant Professor
NGUYEN, Thanh Phuc
Post-Doctoral Fellow
FUJIHASHI, Yuta
Secretary
AKABA, Atsuko

Keywords Quantum Dissipative Systems in Complex Molecular Systems, Quantum Optics, Light-Matter Interaction

Quantum dynamic phenomena are ubiquitous in molecular processes, and yet remain a challenge for experimental and theoretical investigations. On the experimental side, it has become possible to explore molecules on a time scale down to a few femtoseconds. This progress in ultrafast spectroscopy has opened up real-time observation of dynamic processes in complex chemical and biological systems and has provided a strong impetus to theoretical studies of condensed phase quantum dynamics.

Essentially, any quantum systems can never be regarded as "isolated systems." Quantum systems are always in contact with "the outside world," and hence their quantum natures are sometimes sustained and sometimes destroyed. In condensed phase molecular systems, especially, quantum systems are affected by the huge amount of dynamic degrees of freedom such as solvent molecules, amino acid residues in proteins, and so forth. Balance between robustness and fragility of the quantum natures may dramatically alter behaviors of chemical dynamics and spectroscopic signals. Therefore, theoretical tools to adequately describe (1) dynamical behaviors of quantum systems affected by the huge amount of dynamic degrees of freedom and (2) the interaction with radiation fields should be developed.

For this purpose, our research group has been tackling the following subjects:

(1) Developments of condensed phase quantum dynamic theories
(2) Quantum theories to describe dynamical and transport processes in materials and biological systems
(3) Theoretical investigations on measurement and control with the use of atomic-molecular-optical (AMO) physics approaches.

In recent years, specifically, special attention is devoted to the subject (3). We have been examining whether ideas and concepts in the field of quantum science and technology would provide novel control knobs that supplement classical parameters in conventional spectroscopic tools such as frequencies and time delays.

Selected Publications

- A. Ishizaki and G. R. Fleming, "Quantum Coherence in Photosynthetic Light Harvesting," *Annu. Rev. Condens. Matter Phys.* **3**, 333–361 (2012). [Invited review article]
- G. D. Scholes *et al.*, "Using Coherence to Enhance Function in Chemical and Biophysical Systems," *Nature* **543**, 647–656 (2017).
- T. P. Nguyen and A. Ishizaki, "Control of Excitation Energy Transfer in Condensed Phase Molecular Systems by Floquet Engineering," *J. Phys. Chem. Lett.* **9**, 1243 (2018).
- A. Kato and A. Ishizaki, "Non-Markovian Quantum-Classical Ratchet for Ultrafast Long-Range Electron–Hole Separation in Condensed Phases," *Phys. Rev. Lett.* **121**, 647 (2018).
- Y. Fujihashi, R. Shimizu and A. Ishizaki, "Generation of Pseudo-Sunlight via Quantum Entangled Photons and the Interaction with Molecules," *Phys. Rev. Res.* **2**, 023256 (2020).
- A. Ishizaki, "Probing Excited-State Dynamics with Quantum Entangled Photons: Correspondence to Coherent Multidimensional Spectroscopy," *J. Chem. Phys.* **153**, 051102 (2020). [Editor's Pick]

1. Precise Determination of Excitation Energies Based on Exciton-Polariton Measurements

The precise determination of the excitation energies in condensed-phase molecular systems is important for understanding system-environment interactions as well as for the prerequisite input data of theoretical models used to study the dynamics of the system. The excitation energies are usually determined by fitting of the measured optical spectra that contain broad and unresolved peaks as a result of the thermally random dynamics of the environment. Herein, we proposed a method for precise energy determination by strongly coupling the molecular system to an optical cavity and measuring the energy of the resulting polariton. The effect of thermal fluctuations induced by the environment on the polariton was also investigated, from which a power scaling law relating the polariton's linewidth to the number of molecules was obtained.1)

2. Controlling the Nonadiabatic Electron Transfer Reaction Rate through Molecular Vibration Polaritons

Recent experiments showed that the chemical reaction rate is modified by strongly coupling a nuclear vibration mode to the single mode of an optical cavity. Herein we investigated how the rate of an electron-transfer reaction depends on the molecule-cavity coupling. We found two main factors that determine the modification of the reaction rate: The relative shifts of the energy levels induced by the coupling and the mixing of the ground and excited states of molecular vibration in the ground state of the hybrid molecule-plus-cavity system through which the Franck-Condon factor between the initial and final states of the transition is altered. The effect of the mixing of molecular vibrational states on the reaction rate is, however, suppressed in a system containing a large number of molecules due to the collective nature of the resulting polariton, and thus should be observed in a system containing a small number of molecules. In contrast, the effect of the relative shifts of the energy levels should be essentially independent of the number of molecules coupled to the cavity.3)

3. Generation of Pseudo-Sunlight via Quantum Entangled Photons and the Interaction with Molecules

Light incident upon molecules triggers fundamental processes in diverse systems present in nature. However, under natural conditions such as sunlight illumination, it is impossible to assign known times for photon arrival due to continuous pumping, and therefore the photoinduced processes cannot be easily investigated. In this work, we demonstrated theoretically that the characteristics of sunlight photons, such as photon number statistics and spectral distribution, can be emulated through a quantum entangled photon pair generated with parametric down-conversion (PDC). We showed that the average photon number of sunlight in a specific frequency spectrum, *e.g.*, the visible light, could be reconstructed by adjusting the PDC crystal length and pump frequency, and thereby the molecular dynamics induced by the pseudo-sunlight could be investigated. The entanglement time, which is the hallmark of quantum entangled photons, can serve as a control knob to resolve the photon arrival times, enabling investigations on real-time dynamics triggered by pseudo-sunlight photons.4)

4. Probing Excited-State Dynamics with Quantum Entangled Photons

Quantum light is a key resource for promoting quantum technology. One such class of technology aims to improve the precision of optical measurements using engineered quantum states of light. In this study, we investigate transmission measurement of frequency-entangled broadband photon pairs generated via parametric down-conversion with a monochromatic laser. It is observed that state-to-state dynamics in the system under study are temporally resolved by adjusting the path difference between the entangled twin beams when the entanglement time is sufficiently short. The non-classical photon correlation enables time-resolved spectroscopy with monochromatic pumping. It is further demonstrated that the signal corresponds to the spectral information along anti-diagonal lines of, for example, two-dimensional Fourier-transformed photon echo spectra. This correspondence inspires us to anticipate that more elaborately engineered photon states would broaden the availability of quantum light spectroscopy.5)

5. Prerequisites for Relevant Spectral Density and Convergence of Reduced Density Matrices at Low Temperatures

Hierarchical equations of motion approach with the Drude–Lorentz spectral density has been widely employed in investigating quantum dissipative phenomena. However, it is often computationally costly for low-temperature systems because a number of Matsubara frequencies are involved. In this work, we examined a prerequisite required for spectral density, and demonstrated that relevant spectral density significantly reduced the number of Matsubara terms to obtain convergent results for low temperatures.2)

References

1) T. P. Nguyen and A. Ishizaki, *Phys. Rev. Res.* **1**, 033019 (2019).
2) T. P. Nguyen, Q. T. Pham and A. Ishizaki, *Sci. Rep.* **10**, 7318 (2020).
3) Y. Fujihashi, R. Shimizu and A. Ishizaki, *Phys. Rev. Res.* **2**, 023256 (2020).
4) A. Ishizaki, *J. Chem. Phys.* **153**, 051102 (2020). [Editor's Pick]
5) A. Ishizaki, *J. Phys. Soc. Jpn.* **89**, 015001 (2020).

Awards

ISHIZAKI, Akihito; 16th JSPS Prize (2020).
ISHIZAKI, Akihito; 16th Japan Academy Medal (2020).

Theoretical Studies of Functional Molecular Systems and Heterogeneous Catalysts

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

EHARA, Masahiro
Professor
[ehara@ims.ac.jp]

Education

1988	B.E. Kyoto University
1990	M.E. Kyoto University
1993	Ph.D. Kyoto University

Professional Employment

1993	Postdctral Fellow, Institute for Fundamental Chemistry
1994	JSPS Postdoctoral Fellow
1994	Visiting Researcher, Heidelberg University (–1995)
1995	Assistant Professor, Kyoto University
2002	Associate Professor, Kyoto University
2006	Theoretical Research Division Supervisor, Kyoto University (–2008)
2008	Professor, Institute for Molecular Science Professor, The Graduate University for Advanced Studies
2012	Professor, Elements Strategy Initiative for Catalysts and Batteries (ESICB), Kyoto University (additional post)

Awards

2009	APATCC Pople Medal
2009	QSCP Prize CMOA

Member

- Post-Doctoral Fellow
  - ZHAO, Pei
  - VIGNESH, K. R.
- Visiting Scientist
  - ZHAO, Xiang
  - PRIYAKUMAR, Deva U
  - BOBUATONG, Karan
- Graduate Student
  - KANAZAWA, Yuki
  - SHIRAOGAWA, Takafumi
- Secretary
  - KAWAGUCHI, Ritsuko
  - SUGIMOTO, Yukari

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 heterojunction of Ag nanocluster supported by alumina surface in terms of H_2 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 H_2 Activation at Ag Cluster/θ-Al_2O_3 Dual Perimeter Sites: A DFT Study,” *J. Phys. Chem. C* **118**, 7996–8006 (2014).

1. Theoretical Design of Photofunctional Molecular Aggregates for Optical Properties: An Inverse Design Approach1)

Properties of molecular aggregates are defined by their composition and structure. It is becoming possible to control these elements via advances in experimental techniques, and therefore the design guidelines are demanded for developing efficient optical materials. Here we propose a theoretical design approach for photofunctional molecular aggregates using an inverse design framework, the linear combination of atomic potentials (LCAP). The Frenkel exciton model coupled with the LCAP is introduced for designing systems with desired optical properties by gradient-guided optimization searches in terms of constituent molecules in chemical space of molecular aggregates. We have applied this approach to design one-dimensional molecular aggregates having locally maximized absorption and/or circular dichroism (CD) intensities as an example. By exploring a small fraction of the vast chemical space of 10^{26} possible systems varying in composition and structure, we successfully obtained the optimal aggregates. The optimal structure–photofunction relationships were investigated from the designed systems. The present method is useful to design photofunctional molecular aggregates and accelerate optical material discoveries.

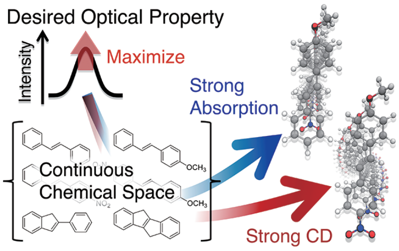

Figure 1. Schematic representation of the inverse design of photofunctional molecular aggregates with desired optical properties.

2. Importance of the Pd and Surrounding Site in Hydrosilylation of Internal Alkynes by Pd-Au Alloy Catalyst2)

Hydrosilylation is one of the key reactions in the formation of carbon−silicon bonds, where the addition of Si−H bonds occurs across the unsaturated bond in organic compounds. The Pd−Au alloy catalyst has been developed for the hydrosilylation of internal alkynes as well as α, β-unsaturated ketones under mild conditions. Herein, density functional theory calculations were utilized to study the mechanism of the hydrosilylation reaction of internal alkynes on the Pd−Au catalyst. The calculated energy profiles show that the reaction follows the Chalk−Harrod mechanism. The Pd site acts as the adsorption site and the reactive center as observed in experiments. The surrounding Pd−Au bridge and Au sites are also relevant for the bond activation and accepting the substrates or intermediates during the reaction, which is characteristic in the Pd−Au alloy catalysts and not available in the homogeneous catalyst. The present picture of the relevance of the Pd atomic site and its surrounding Pd−Au bridge or Au sites will be useful for developing the alloy catalysts for the related catalytic reactions.

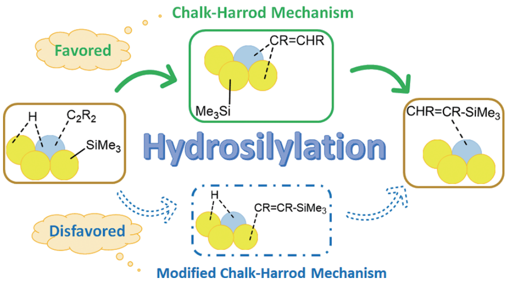

Figure 2. Hydrosilylation on the Pd-Au Alloy Catalyst.

3. Theoretical Study on ^{31}P NMR Chemical Shifts of P-Modified CHA Zeolites3)

The modification of zeolites with phosphorus is a widely adopted method to tune the acidity and consequently the catalytic properties in terms of activity, shape selectivity, and hydrothermal stability. The ^{31}P MAS NMR spectra of phosphorus-modified chabazite (P-CHA) zeolites have been observed during the hydrothermal treatment to probe the structural changes of phosphorus species in zeolites. Theoretical calculations on the ^{31}P and ^{27}Al NMR chemical shifts have been systematically performed to disclose the possible phosphorus species of intra- and extra-framework and the structural changes during the hydrothermal treatment. The present theoretical results provide useful information regarding the ^{31}P NMR chemical shifts in P-CHA, which will significantly improve the ^{31}P NMR assignments in future experiments.

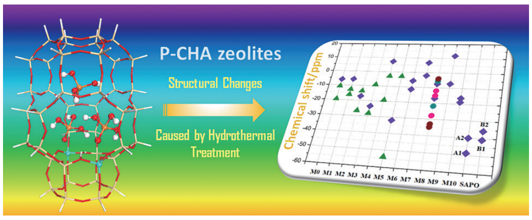

Figure 3. ^{31}P NMR chemical shifts of P-CHA zeolites.

References

1) T. Shiraogawa and M. Ehara, *J. Phys. Chem. C* **124**, 13329–13337 (2020). (Supplemental Cover)

2) T. Sadhukhan, A. Junkaew, P. Zhao, H. Miura, T. Shishido and M. Ehara, *Organometallics* **39**, 528–537 (2020). (Supplemental Cover)

3) P. Zhao, B. Boekfa, T. Nishitoba, N. Tsunoji, T. Sano, T. Yokoi, M. Ogura and M. Ehara, *Microporous Mesoporous Mater.* **294**, 109908 (2020).

Award

SHIRAOGAWA, Takafumi; Poster Award, The 13th Annual Meeting of Japan Society for Molecular Science (2019).

Development of New Simulation Algorithms and its Application to Protein Aggregates

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

OKUMURA, Hisashi
Associate Professor
[hokumura@ims.ac.jp]

Education

1998	B.S. Keio University
2002	Ph.D. Keio University

Professional Employment

2002	Postdoctoral Fellow, The University of Tokyo
2002	Research Associate, Institute for Molecular Science
2004	Research Associate, The Graduate University for Advanced Studies
2006	Research Lecturer, Nagoya University
2008	Research Assistant, Rutgers University
2009	Assistant Research Professor, Rutgers University
2009	Associate Professor, Institute for Molecular Science Associate Professor, The Graduate University for Advanced Studies
2018	Associate Professor, Exploratory Research Center on Life and Living Systems (ExCELLS)

Award

2014	Academic Award of the Molecular Simulation Society of Japan

Member
Assistant Professor
ITOH, Satoru G.
Post-Doctoral Fellow
TANIMOTO, Shoichi
Graduate Student
YAMAUCHI, Masataka
MIYAZAWA, Kazuhisa
FUKUHARA, Daiki
Secretary
KAWAGUCHI, Ritsuko

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.

We are also interested in protein aggregates such as spherical substances called oligomers and acicular substances called amyloid fibrils (Figure 2). These protein aggregates cause more than 30 kinds of diseases. For example, Alzheimer's disease is thought to be caused by aggregated amyloid-β (Aβ) peptides. To overcome these diseases, it is essential to understand the aggregate genesis and disruption of Aβ peptides. We perform such MD simulations of oligomers and amyloid fibrils.

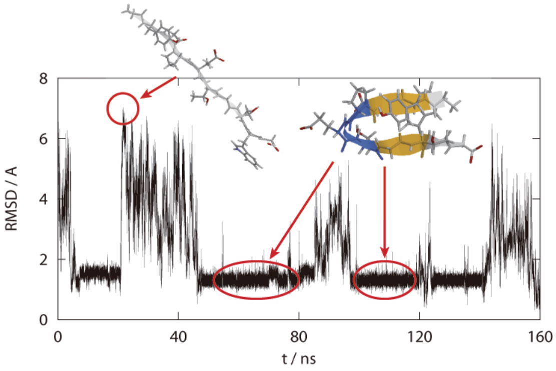

Figure 1. Time series of protein folding simulation.

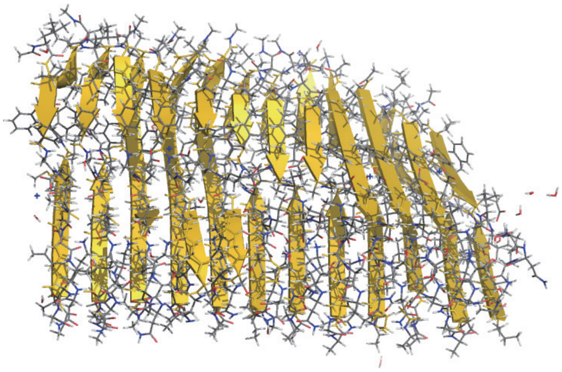

Figure 2. Snapshot of an Aβ amyloid fibril.

Selected Publications

- H. Okumura and S. G. Itoh, "Amyloid Fibril Disruption by Ultrasonic Cavitation: Nonequilibrium Molecular Dynamics Simulations," *J. Am. Chem. Soc.* **136**, 10549–10552 (2014).
- H. Okumura and S. G. Itoh, "Structural and Fluctuational Difference between Two Ends of Aβ Amyloid Fibril: MD Simulation Predicts Only One End Has Open Conformations," *Sci. Rep.* **6**, 38422 (9 pages) (2016).
- 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).
- 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. Molecular Dynamics Simulations of Amyloid-β(16-22) Peptide Aggregation at Air–Water Interfaces

The formation of Aβ oligomers is accelerated at hydrophilic–hydrophobic interfaces, such as the cell membrane surface and air–water interface. To understand the effects of the interface on oligomerization at the atomic level, we performed MD simulations of aggregation of Aβ(16–22) peptides at air–water interfaces.[1] First, 100 randomly distributed Aβ(16–22) peptides (Figure 3(a)) moved to the interface (Figure 3(b)). The high concentration of peptides then accelerated their aggregation and formation of antiparallel β-sheets. Two layers of oligomers were observed near the interface. In the first layer from the interface, the oligomer with less β-bridges exposed the hydrophobic residues to the air. The second layer consisted of oligomers with more β-bridges that protruded into water. They are more soluble in water because the hydrophobic residues are covered by N- and C-terminal hydrophilic residues that are aligned well along the oligomer edge. These results indicate that amyloid protofibril formation mainly occurs in the second layer.

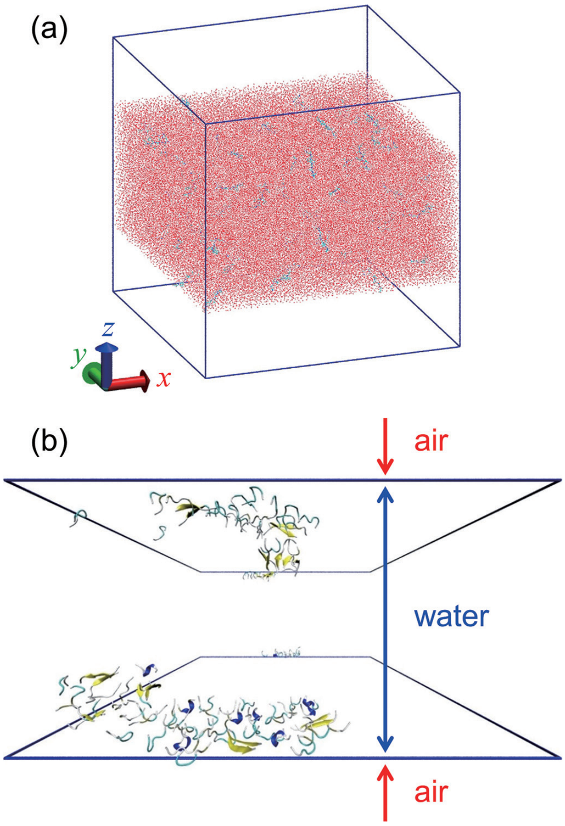

Figure 3. (a) Initial conformation of 100 Aβ(16–22) peptides (blue) and water molecules (red) with air–water interfaces. (b) Side view of the final conformation of Aβ(16–22) peptides. The water molecules are not shown here. The blue frames indicate the air–water interfaces.

2. Development of Replica Sub-Permutation Method for Efficient Molecular Dynamics Simulations

We proposed an improvement of the replica-exchange and replica-permutation methods, which we call the replica sub-permutation method (RSPM).[2] Instead of considering all permutations, this method uses a new algorithm referred to as sub-permutation to perform parameter transition, as in Figure 4. The RSPM succeeds in reducing the number of combinations between replicas and parameters without the loss of sampling efficiency. For comparison, we applied the replica sub-permutation, replica-permutation, and replica-exchange methods to a β-hairpin mini protein, chignolin, in explicit water. We calculated the transition ratio and number of tunneling events in the parameter space, the number of folding–unfolding events, the autocorrelation function, and the autocorrelation time as measures of sampling efficiency. The results indicate that among the three methods, the proposed RSPM is the most efficient in both parameter and conformational spaces.

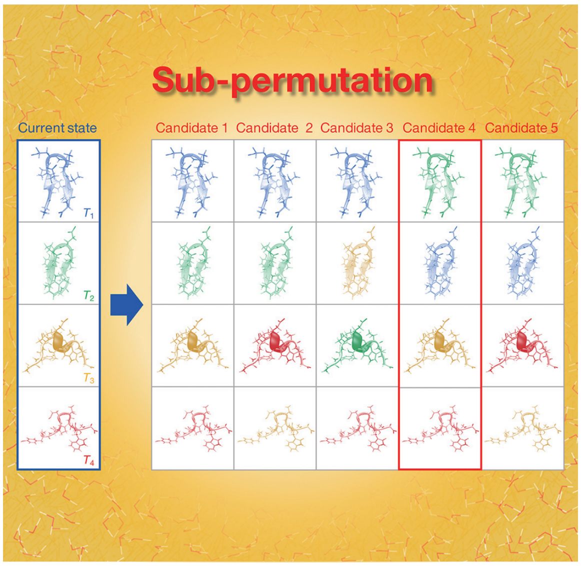

Figure 4. This image shows sub-permutation candidates for a four-replica system. The replica sub-permutation method succeeds in improving sampling efficiency both in parameter and conformational spaces.

References

1) H. Okumura and S. G. Itoh, *J. Chem. Phys.* **151**, 095101 (12 pages) (2020).
2) M. Yamauchi and H. Okumura, *J. Comput. Chem.* **40**, 2694–2711 (2019).

Theoretical Studies on Molecular Aggregates

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

FUJITA, Takatoshi
Research Associate Professor
[tfujita@ims.ac.jp]

Education
2006 B.H.D. Kobe University
2008 M.S. Kobe University
2011 Ph.D. Kobe University

Professional Employment
2010 JSPS Research Fellow (DC2)
2011 JSPS Postdoctoral Fellow (PD)
2012 Postdoctral Fellow, Harvard University
2015 Postdoctral Fellow, Kyoto University
2016 Research Associate Professor, Institute for Molecular Science

Member
Secretary
CHIBA, Fumika

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 can exhibit remarkable optical and electronic properties that are not observed in isolated molecules. 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. Our research also include the developments of theoretical and computational methods.

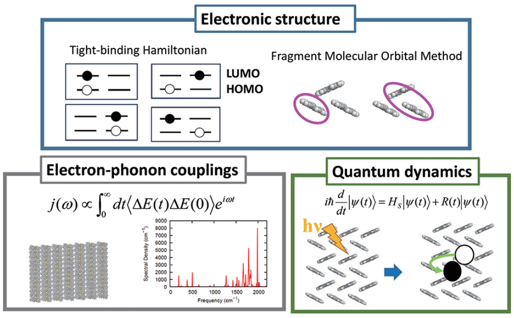

Figure 1. A combine approach to quantum dynamics in molecular aggregates.

It is still challenging to simulate quantum dynamics of energy or charge transfer in condensed systems. An exciton or electron wave functions can be delocalized over many molecules by intermolecular electronic couplings. By contrast, the wave functions can be localized because of the static disorder and interactions with nuclear degree of freedom. Therefore, successful theoretical descriptions require the inclusions of electronic couplings, static disorder, and electron-phonon or electron-vibration interaction. 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. Electronic states of an aggregate are obtained from a large-scale electronic structure calculation, and the model Hamiltonian for an exciton or a charge carrier is derived. The model Hamiltonian is used for simulating energy or charge dynamics by a quantum dynamics method, which incorporates finite-temperature effects and electron-vibration interactions. The combined computational approach allows for bottom-up descriptions of energy or charge transfer dynamics in realistic molecular aggregates.

We currently investigate electronic states and quantum dynamics at organic interfaces. We also develop the many-body perturbation theory to predict electronic levels at higher accuracy.

Selected Publications

- T. Fujita, S. Atahan-Evrenk, N. P. D. Sawaya and A. Aspuru-Guzik, "Coherent Dynamics of Mixed Frenkel and Charge Transfer Excitons in Dinaphtho[2,3-*b*:2'3'-*f*]thieno[3,2-*b*]-thiophene Thin Films: The Importance of Hole Delocalization," *J. Phys. Chem. Lett.* **7**, 1374–1380 (2016).
- T. Fujita and Y. Mochizuki, "Development of the Fragment Molecular Orbital Method for Calculating Nonlocal Excitations in Large Molecular Systems," *J. Phys. Chem. A* **122**, 3886–3898 (2018).

1. Development of FMO-Based Exciton Model within GW/BSE[1)]

Organic optoelectronic devices based on π-conjugated molecules or polymers have attracted considerable attention due to their attractive features. Predicting the electronically excited states is essential for understanding the optoelectronic processes governing the device operation and for rationally designing novel materials. However, accurate calculations of electronic states of organic materials which contain a lot of organic molecules or polymers are still challenging task. Successful theoretical descriptions require an accurate quantum mechanical method. In addition, the effects of polarizable environment must be appropriately taken into account.

In this study, we present the large-scale GW/Bethe-Salpeter equation (BSE) method that enables the computations of delocalized excited states in large molecular assemblies. The many-body Green's function method within the GW approximation can offer practical schemes to calculate electronic states within reasonable accuracy. However, the applications of GW and GW/BSE to large systems were difficult because of their considerable computational times. Here, we develop large-scale GW/BSE method for large systems based on the fragment molecular orbital methods. We have proposed the fragmentation approximations of total polarization functions and ΔCOHSEX approximation that neglects the dynamical polarization of surrounding fragments. We have confirmed that the FMO-GW/BSE method enables accurate calculations of localized electronic states in large systems. Furthermore, the FMO-GW/BSE method was combined with the exciton model to calculate delocalized excited states in molecular aggregates. In the exciton model, the excited-state Hamiltonian for an entire system is calculated in the diabatic basis and then diagonalized to approximate the adiabatic excited states. The FMO-based exciton model utilizes the fragment configuration state functions (CSFs) for intrafragment excited states and for interfragment charge-transfer states, and the excited-state Hamiltonian at the GW/BSE level is calculated in the basis of fragment CSFs. We have shown that the results of unfragmented calculations can be reasonably reproduced; thus, the present FMO-GW/BSE method can offer efficient and practical schemes for investigating realistic molecular aggregates.

2. Revisiting the Electronic Structure of PEN/C_{60} Bilayer Heterojunctions[2)]

Molecular orientations and interfacial morphologies have critical effects on the electronic states of donor/acceptor interfaces and thus on the performance of organic photovoltaic devices. Here, we investigate the charge-transfer (CT) states in pentacene(PEN)/C_{60} interfaces as model systems and highlight the polarization and delocalization effects. The effects of polarization and delocalization on the interfacial CT states are schematically represented in Figure 2. In a gas phase (Figure 2 (a)), the energy of the CT state is given by the highest-occupied molecular orbital (HOMO) energy of a donor molecule, the lowest-unoccupied molecular orbital (LUMO) energy of an acceptor molecule, and the Coulomb interaction between the electron and the hole. The solid-state polarization effects reduce the energy gap between the donor HOMO and the acceptor LUMO (Figure 2 (b)) and weakens the e–h interaction. In a solid phase, the electron or hole wave function can be delocalized over multiple acceptor or donor molecules, and delocalized CT states can be formed (Figure 2 (c)). This charge delocalization can further shift the energy gap and possibly weaken the e–h interaction.

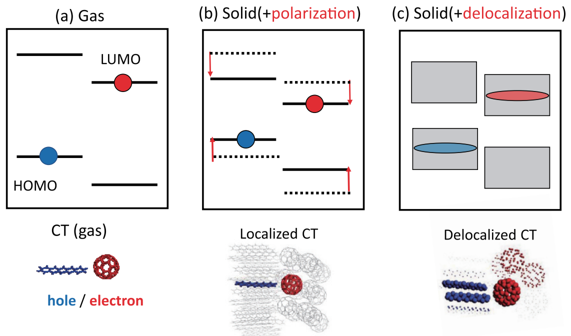

Figure 2. Schematics of solid-state effects on the interfacial charge-transfer states.

In this study, we explore the energy levels and CT states at the organic donor/acceptor interfaces on the basis of the fragment-based GW/BSE approach. The face-on and edge-on orientations of pentacene/C_{60} bilayer heterojunctions have employed as model systems. The FMO-GW/BSE calculations were performed for the local interface structures in the face-on and edge-on bilayer heterojunctions, which contain approximately 2,000 atoms. Calculated energy levels and CT state absorption spectra are in reasonable agreements with those obtained from experimental measurements. We found that the dependence of the energy levels on interfacial morphology is predominantly determined by the electrostatic contribution of polarization energy, while the effects of induction contribution in the edge-on interface are similar to those in the face-on. Moreover, the delocalized CT states contribute to the main absorption peak in the edge-on interface, while the face-on interface features relatively localized CT states in the main absorption peak. The impact of the interfacial morphologies on the polarization and charge delocalization effects is analyzed in detail.

References

1) T. Fujita and Y. Noguchi, in preparation.
2) T. Fujita, Y. Noguchi and T. Hoshi, *Materials* **13**, 2728 (2020).

Functional Dynamics of Biomolecular Machines Revealed by Theoretical Methods

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

OKAZAKI, Kei-ichi
Research Associate Professor
[keokazaki@ims.ac.jp]

Education

2004	B.S. Kyoto University
2006	M.S. Kobe University
2009	Ph.D. Kobe University

Professional Employment

2007	JSPS Research Fellow (DC2), Kobe University
2009	JSPS Postdoctoral Fellow (PD), Waseda University
2010	Part-time Lecturer, Waseda University
2012	JSPS Postdoctoral Fellow for Research Abroad, National Institutes of Health, U.S.A.
2014	Postdoctoral Fellow, Max Planck Institute of Biophysics, Germany
2016	Research Associate Professor, Institute for Molecular Science

Award

2014	Early Career Award in Biophysics, Biophysical Society of Japan

Member
Post-Doctoral Fellow
MAHMOOD, Md Iqbal
JAUNET-LAHARY, Titouan
Secretary
CHIBA, Fumika

Keywords Theoretical Biophysics, Molecular Motors, Transporter

Functional dynamics plays an important role when biomolecular machines fulfill their functions. Motor proteins move on the rail or rotate relative to the stator unidirectionally by using chemical energy. Transporter proteins transport their substrates across the membrane by changing their conformation between the inward-open and outward-open states. We aim to clarify molecular mechanism 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 (MD) simulations alone cannot cover millisecond-long (or even longer) functional dynamics, especially for a large system like typical biomolecular machines. Thus, we use techniques like importance sampling, coarse-graining, and statistical/kinetic modeling to tackle this problem.

We have been working on biomolecular motors such as ATP synthase and chitinase. ATP synthase is a rotary motor that produces most of ATP required in the cell. It is composed of two rotary motors: F_o and F_1. F_o motor is embedded in the membrane driven by proton gradient, while F_1 motor is driven by ATP hydrolysis reaction. We studied how rotation of F_1 is caused by elementary steps such as product release from the catalytic site. Chitinase is a new type of molecular motor that uses hydrolysis energy of single chitin chain, a polysaccharide, for its unidirectional motion. The sliding motion of chitin chain into the catalytic site of chitinase was studied by atomistic simulations. We also developed a novel framework to estimate chemical-state-dependent free energy profile and diffusion coefficient from single-molecule trajectories.

Transporters are membrane proteins that transport their substrates across the membrane. We have studied Na^+/H^+ antiporter that exchanges sodium ions and protons inside and outside the cell. The ion-transport cycle was simulated in atomic detail with the transition path sampling technique. The simulations predicted the mutation that can speed up the ion transport, which was confirmed by experiments. Another membrane-associated protein, F-BAR protein Pacsin1 that remodels the membrane, is our interest too. The curvature induction and sensing of Pacsin1 on the membrane was studied by multiscale MD simulations using both all-atom and coarse-grained models.

Selected Publications

- K. Okazaki and G. Hummer, “Phosphate Release Coupled to Rotary Motion of F_1-ATPase,” *Proc. Natl. Acad. Sci. U.S.A.* **110**, 16468–16473 (2013).
- K. Okazaki and G. Hummer, “Elasticity, Friction, and Pathway of γ-Subunit Rotation in F_oF_1-ATP Synthase,” *Proc. Natl. Acad. Sci. U.S.A.* **112**, 10720–10725 (2015).
- K. Okazaki, D. Wöhlert, J. Warnau, H. Jung, Ö. Yildiz, W. Kühlbrandt and G. Hummer, “Mechanism of the Electroneutral Sodium/Proton Antiporter PaNhaP from Transition-Path Shooting,” *Nat. Commun.* **10**, 1742 (2019).
- M. I. Mahmood, H. Noguchi and K. Okazaki “Curvature Induction and Sensing of the F-BAR Protein Pacsin1 on Lipid Membranes via Molecular Dynamics Simulations,” *Sci. Rep.* **9**, 14557 (2019).

1. Mechanism of Unidirectional Motions of Chitinase

Processive cellulase and chitinase recently have been cast new light as a different type of biomolecular motors that use hydrolysis energy of polysaccharides for their unidirectional movements. We used single-molecule trajectories to estimate an underlying diffusion model with chemical-state-dependent free energy profile.1) To consider nonequilibrium trajectories driven by the chemical energy consumed by biomolecular motors, we developed a novel framework based on a hidden Markov model, wherein switching among multiple energy profiles occurs reflecting the chemical state changes in motors. The chemical-state-dependent free energy profile underlying the burnt-bridge Brownian ratchet mechanism of processive chitinase was determined.1)

2. Mechanism of Na$^+$/H$^+$ Antiporter and Engineering of a Faster Transporter

Na$^+$/H$^+$ antiporters control pH and Na$^+$ concentration in the cell by exchanging sodium ions and protons across lipid membranes. They belong to the cation/proton antiporter (CPA) superfamily, and prevail in all domains of life. The archaeal Na$^+$/H$^+$ antiporters PaNhaP from *Pyrococcus abyssi* and MjNhaP1 from *Methanocaldococcus jannaschii* as well as human NHE1, which is linked to a wide spectrum of diseases from heart failure to autism and has no structure solved yet, are electroneutral antiporters of the CPA1 family, exchanging one proton against one sodium ion. As a model system in mechanistic studies of electroneutral Na$^+$/H$^+$ exchange, we studied the transport mechanism of PaNhaP.2)

Na$^+$/H$^+$ antiporters use the gradient of either sodium ion or proton to drive the uphill transport of the other ion (Figure 1A). The conformational transition of the transporter makes the ion-binding site accessible from either side of the membrane in the alternating manner. For PaNhaP, the inward-open conformation was obtained by X-ray crystallography, while the outward-open conformation is not known experimentally. We modelled the outward-open conformation by MDFF flexible fitting to the low-resolution outward-open structure of the homologous MjNhaP1 from cryo-EM, followed by the long equilibrium MD simulations. It was shown that the transporter domain moves ~3.5 Å in the direction normal to the membrane to take the outward-open state (Figure 1B).

The inward-open and outward-open conformations described above only provides the end points of the ion-transport. The transition dynamics between the two states is central to the transport mechanism, revealing at once rate-limiting steps, substrate pathways, and the opening and closing of the gate preventing ion leakage. However, with ion exchange occurring on a timescale of seconds at ambient conditions, regular MD simulations are far too slow to resolve transitions. Instead, we can resort to importance sampling of transition dynamics. To sample unbiased transition paths between the inward- and outward-open states, we used techniques from the transition path sampling.

In analysis of the transition paths, we found hydrophobic gates above and below the ion-binding site, which open and close in response to the domain motions (Figure 1C). From the reaction coordinate analysis, it was shown that open-close motion of the outside gate (Ile163-Tyr255) is a rate-limiting step of the alternating-access conformational change. Based on this result, we weakened the outside gate by mutating the residues to both alanine. It was expected that this mutation lowers the barrier and makes the ion transport faster. It was confirmed by experiments that the ion-transport speed of the mutant is indeed twice faster than the wild-type transporter.

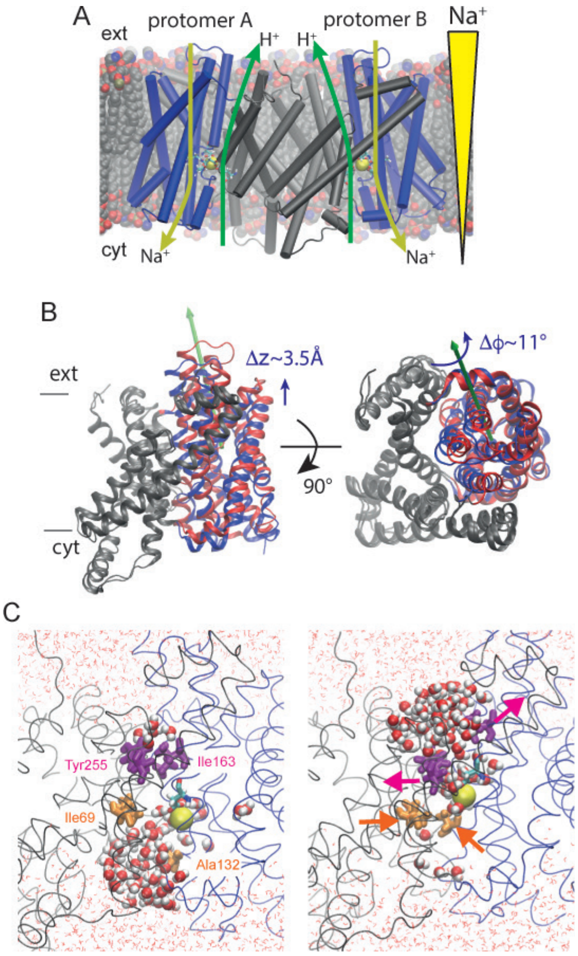

Figure 1. (A) PaNhaP dimer structure. (B) Comparison of the transporter domain between the inward-open (blue) and outward-open (red) states. (C) The outside (purple) and inside (orange) gates found in the transition paths.

References

1) K. Okazaki, A. Nakamura and R. Iino *J. Phys. Chem. B* **124**, 6475–6487 (2020).

2) K. Okazaki, D. Wöhlert, J. Warnau, H. Jung, Ö. Yildiz, W. Kühlbrandt and G. Hummer, *Nat. Commun.* **10**, 1742 (2019).

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 on ionic liquids (ILs). ILs' projects are focused on the unique dissolution process of cellulose polysaccharides, and the investigation of statical and dynamical properties on ionic liquids including temperature effects.

1. Investigations of Dissolution and Decomposition Mechanisms of a Cellulose Fiber in Ionic Liquids1) with Molecular Dynamics Simulation

We studied dissolution and decomposition mechanisms of cellulose (I_β) polymers in ILs. In order to investigate motion of cellulose fibers and intermolecular interactions between cellulose molecules and cationic and anionic species in ILs, we carried out molecular dynamics simulation. We employed the 1-ethyl-3-methylimidazolium acetate IL solvent for target system. It was found out that the intermolecular interaction energy between cellulose polymers in the IL are reduced, comparing with that in water. Also, our results suggest that the enhancement of the flexibility of rigid cellulose chains triggered by the breakage of intrachain H-bonds due to anions starts decomposition processes accompanied by dissolution processes due to the intercalation of cations, synergistically, and, then, both dissolution and decomposition processes are executed simultaneously.

2. Researches on Statical and Dynamical Properties of Ionic Liquids: Molecular Origin of Low-k Peak of ILs and Dynamical Heterogeneity

We have investigated the molecular level origin of low-k peak (< 0.5 Ang.$^{-1}$) in the structure factor in ILs. In particular, we found out that the structure factor of heterocyclic ring parts in cations largely contribute to low-k peak in ILs. Also, we are going to carry out the study of dynamical properties of ILs, dynamical heterogeneity in ILs at room temperature with molecular dynamics simulation procedure.

Reference

1) T. Ishida, *J. Phys. Chem. B* **124**, 3090–3102 (2020).

Visiting Professors

Visiting Professor
MORI, Hirotoshi *(from Chuo University)*

Electronic Structure Informatics for Designing Functional Liquid Materials

Mixed liquids exhibit various chemical functions depending on their composition and mixing ratio. Contrary to its fundamental scientific importance, however, the chemistry of mixing is an area where molecular level knowledge is not still enough. With the backgrounds, we have been challenging the predictive chemistry of functional liquid materials by developing a novel *ab initio* molecular simulation method with conventional computational cost (Effective fragment potential molecular dynamics; EFP-MD) and a data science approach. In fiscal 2020, we worked on the prediction of Henry's constant values related to the absorption of various industrial exhaust gases for non-aqueous mixed solutions (mixed ionic liquids, ionic liquids/organic solvent mixtures) which supports environmental chemical engineers shortly. We will proceed with our research aiming at the construction of statistical thermodynamic theory for real systems that predict mixed thermodynamics.

Visiting Professor
YANASE, Youichi *(from Kyoto University)*

Theoretical Study of Exotic Quantum Phases

We are working on theoretical studies of exotic quantum phases such as unconventional superconductivity, parity-violating antiferromagnet, quantum liquid crystal, and topological state of matter. In particular, my recent interest focuses on quantum phases lacking global or local space inversion symmetry. For instance, we classified such quantum phases in terms of multipole moment with the use of group theory, and explored emergent electromagnetic responses, such as magnetopiezoelectric effect and chiral photocurrent. Furthermore, a rigorous and gauge-invariant formulation of multipole moment was given by the thermodynamic definition, which is directly related to the magnetoelectric effect. Superconductivity induced by multipole fluctuations was clarified. To develop the functionality of superconductors, we showed a giant superconducting Edelstein effect in topological superconductors. By considering a light-matter interaction, we proposed laser-induced topological superconductivity in TMD.

Visiting Associate Professor
HIGASHI, Masahiro *(from Kyoto University)*

Theoretical Study on the Excited-State Reactions in Condensed Phases

We are theoretically investigating chemical reactions and physical properties in condensed phases such as solutions and proteins. In particular, we are focusing on the excited-state reaction dynamics in condensed phases. Theoretical studies on the excited-state reaction dynamics of large systems is still one of most challenging tasks due to the high computational cost of electronic structure calculations for excited states and adequate statistical samplings required for molecular dynamics simulations. To overcome this difficulty, we have been developing several efficient methods combining electronic structure calculations and molecular dynamics simulations. Recently, we analyzed the excitation energy transfer in a light-harvesting complex by using our developed methods. The calculated excitation energies of pigments and their fluctuations are in quantitative agreement with the experimental ones. It is found that the fluctuations of pigments are largely affected by the individual protein environments and that the efficient excitation energy transfer is achieved by the site-dependent fluctuations.