

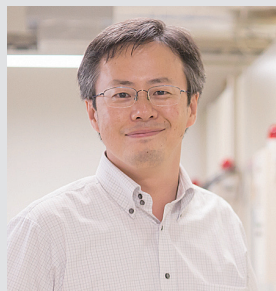
RESEARCH ACTIVITIES

Research Center of Integrative Molecular Systems

The mission of CIMoS is to analyze molecular systems in nature to find the logic behind the sharing and control of information between the different spatiotemporal hierarchies, with the ultimate goal of creating novel molecular systems on the basis of these findings.

Biological Rhythm and Dynamics through Chemistry

Research Center of Integrative Molecular Systems Division of Trans-Hierarchical Molecular Systems



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Education

1997 B.E. Kyoto University
1999 M.E. Kyoto University
2002 Ph.D. Kyoto University

Professional Employment

2001 JSPS Research Fellow
2002 JSPS Postdoctoral Fellow
2003 RIKEN Special Postdoctoral Researcher
2005 JST-PRESTO Researcher
2008 Junior Associate Professor, Nagoya University
2011 Associate Professor, Nagoya University
2012 Professor, Institute for Molecular Science
Professor, The Graduate University for Advanced Studies

Awards

2022 NAGASE Research Promotion Award
2016 The 13th (FY2016) JSPS PRIZE
2008 The Commendation for Science and Technology by the Minister of Education, Culture, Sports, Science and Technology
The Young Scientists' Prize
2007 Young Scientist Prize, The Biophysical Society of Japan
2006 SAS Young Scientist Prize, IUCr Commission on Small-angle Scattering
2002 The Protein Society Annual Poster Board Award

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Keywords

Biological Rhythm, Circadian Clock, Cyanobacteria

Living organisms on Earth evolved over time to adapt to daily environmental alterations, and eventually acquired endogenous time-measuring (biological clock) systems. Various daily activities that we perform subconsciously are controlled by the biological clock systems sharing three characteristics. First, the autonomic rhythm repeats with an approximately 24-hour (circadian) cycle (self-sustainment). Second, the period is unaffected by temperature (temperature compensation). Third, the phase of the clock is synchronized with that of the outer world in response to external stimuli (synchronization). We seek to explain these three characteristics, and consider the biological clock system of cyanobacteria to be an ideal experimental model.

The major reason that cyanobacteria are considered to be the ideal experimental model is that the core oscillator that possesses the three characteristics of the clock can be easily reconstructed within a test tube. When mixing the three clock proteins KaiA, KaiB, and KaiC with ATP, the structure and enzyme activity of KaiC change rhythmically during a circadian cycle. Taking advantage of this test tube experiment, we used an approach combining biology, chemistry, and physics

to elucidate the means by which the clock system extends from the cellular to atomic levels.

Among the three Kai proteins, KaiC is the core protein of the oscillator. In the presence of KaiA and KaiB, KaiC reveals the rhythm of autophosphorylation and dephosphorylation; however, the cycle of this rhythm depends on the ATPase activity of KaiC independent of KaiA or KaiB. For example, when the ATPase activity of KaiC doubles as a result of amino acid mutations, the frequencies of both the *in vitro* oscillator and the intracellular rhythm also double (the cycle period is reduced to half). This mysterious characteristic is called a transmembrane hierarchy, in which the cycle (frequency) and even the temperature compensation both *in vitro* and *in vivo* are greatly affected (controlled) by the function and structure of KaiC.

How are the circadian activities and temperature compensation features encoded in KaiC and then decoded from it to propagate rhythms at the cellular level? We are committed to better understanding biological clocks and other dynamic systems through the chemistry of circadian **rhythm, structure**, and evolutionary **diversity**.

Selected Publications

- Y. Furuike, A. Mukaiyama, S. Koda, D. Simon, D. Ouyang, K. Ito-Miwa, S. Saito, E. Yamashita, T. Nishiwaki, K. Terauchi, T. Kondo and S. Akiyama, *Proc. Natl. Acad. Sci. U. S. A.* **119**, e2119627119 (2022).
- Y. Furuike, A. Mukaiyama, D. Ouyang, K. Ito-Miwa, D. Simon, E. Yamashita, T. Kondo and S. Akiyama, *Sci. Adv.* **8**, eabm8990 (2022).
- Y. Furuike, D. Ouyang, T. Tominaga, T. Matsuo, A. Mukaiyama, Y. Kawakita, S. Fujiwara and S. Akiyama, *Commun. Phys.* **8**, 75 (2022).
- J. Abe, T. B. Hiyama, A. Mukaiyama, S. Son, T. Mori, S. Saito, M. Osako, J. Wolanin, E. Yamashita, T. Kondo and S. Akiyama, *Science* **349**, 312–316 (2015).
- Y. Murayama, A. Mukaiyama, K. Imai, Y. Onoue, A. Tsunoda, A. Nohara, T. Ishida, Y. Maéda, T. Kondo and S. Akiyama, *EMBO J.* **30**, 68–78 (2011).
- S. Akiyama, A. Nohara, K. Ito and Y. Maéda, *Mol. Cell* **29**, 703–716 (2008).

1. Structure: Reasons for Seeking Structure and Dynamics of Circadian Clock Components in Cyanobacteria^{1–4)}

A great deal of effort has been devoted to characterizing structural changes in the clock proteins along the circadian reaction coordinate. However, little is known about the mechanism driving the circadian cycle, even for the simple cyanobacterial protein KaiC that has ATPase and dual phosphorylation sites in its N-terminal C1 and C-terminal C2 domains, respectively. Nearly all KaiC structures reported to date share a nearly identical structure, and they do not appear to be suggestive enough to explain the determinants of circadian period length and its temperature compensation. We are studying the structural and dynamical origins in KaiC using high-resolution x-ray crystallography,^{1,2)} real-time fluorescence detection,³⁾ and quasielastic neutron scattering.⁴⁾

2. Rhythm: Cross-Scale Analysis of Cyanobacterial Circadian Clock System^{4–6)}

KaiC ATPase is of particular interest here, as it finely correlates to the frequencies of *in vivo* as well as *in vitro* oscillations and also it is temperature compensated. This unique property has inspired us to develop an ATPase-based screening⁵⁾ for KaiC clock mutants giving short, long, and/or temperature-dependent periods.⁶⁾ A developed HPLC system with a 4-channel temperature controller has reduced approximately 80% of time costs for the overall screening process (Figure 1). Using the developed device, we are screening a number of temperature-dependent mutants of KaiC.^{4,5)}

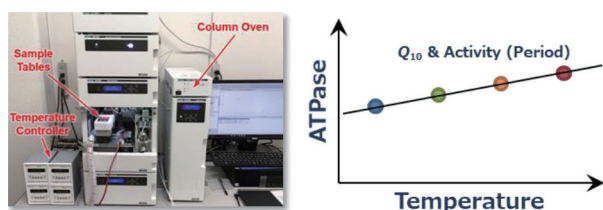


Figure 1. Development of a quick ATPase assay system.

3. beyond Evolutionary Diversity⁷⁾

In the presence of KaiA and KaiB, the ATPase activity of KaiC oscillates on a 24-hour cycle. KaiC is not capable of maintaining a stable rhythm on its own, but its activity was observed to fluctuate with reduced amplitude over time (Figure 2A). We have identified a signal component that is similar to damped oscillation, and propose that it encodes the specific

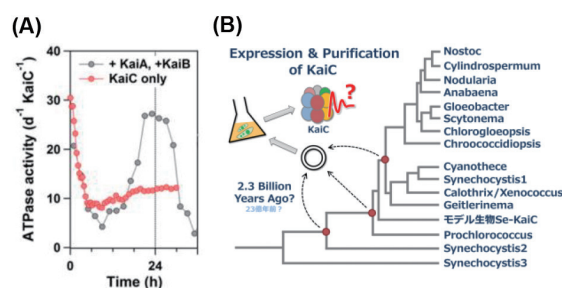


Figure 2. Damped oscillation of KaiC ATPase activity (A) and evolutionary diversity of cyanobacteria (B).

frequency, equivalent to a 24-hour cycle.

The habitats of cyanobacteria are diverse, so the space of their sequence is immense.⁷⁾ Furthermore, some KaiA and KaiB genes are missing in several strains of cyanobacteria. This is understandable to some extent if KaiC possesses the specific frequency. Given this assumption, *what specific frequencies are possessed by KaiC homologues in other species and ancestral cyanobacteria?* (Figure 2B) If you strain your ears, the rhythms of the ancient Earth may be heard from beyond evolutionary diversity.

4. Bio-SAXS Activity in IMS⁸⁾

We have supported SAXS users so that they can complete experiments smoothly and publish their results.⁸⁾

References

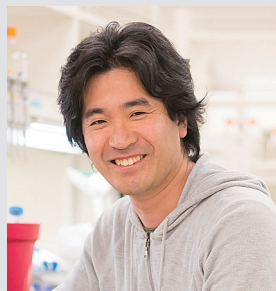
- 1) Y. Furuike, A. Mukaiyama, D. Ouyang, K. Ito-Miwa, D. Simon, E. Yamashita, T. Kondo and S. Akiyama, *Sci. Adv.* **8**, eabm8990 (2022).
- 2) Y. Furuike, A. Mukaiyama, S. Koda, D. Simon, D. Ouyang, K. Ito-Miwa, S. Saito, E. Yamashita, T. Nishiwaki-Ohkawa, K. Terauchi, T. Kondo and S. Akiyama, *Proc. Natl. Acad. Sci. U. S. A.* **119**, e2119627119 (2022).
- 3) A. Mukaiyama, Y. Furuike, E. Yamashita and S. Akiyama, *Biochem. J.* **479**, 1505–1515 (2022).
- 4) Y. Furuike, D. Ouyang, T. Tominaga, T. Matsuo, A. Mukaiyama, Y. Kawakita, S. Fujiwara and S. Akiyama, *Commun. Phys.* **5**, 75 (2022).
- 5) D. Ouyang, Y. Furuike, A. Mukaiyama, K. Ito-Miwa, T. Kondo and S. Akiyama, *Int. J. Mol. Sci.* **20**, 2789–2800 (2019).
- 6) D. Simon, A. Mukaiyama, Y. Furuike and S. Akiyama, *Biophys. Physicobiol.* **19**, e190008 (2022).
- 7) A. Mukaiyama, D. Ouyang, Y. Furuike and S. Akiyama, *Int. J. Biol. Macromol.* **131**, 67–73 (2019).
- 8) M. Okumura, S. Kanemura, M. Matsusaki, Y. H. Lee, S. Akiyama and K. Inaba, *Structure* **29**, 1–14 (2021).

Awards

AKIYAMA, Shuji; NAGASE Research Promotion Award (2022).
 FURUIKE, Yoshihiko; The Early Career Award in Biophysics (2022).
 FURUIKE, Yoshihiko; SPRUC 2022 Young Scientist Award (2022).

Protein Design Using Computational and Experimental Approaches

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Education

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Professional Employment

2003 JSPS Research Fellow
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2007 Postdoctoral Fellow, Kyoto University
2007 JSPS Postdoctoral Fellow for Research Abroad
2009 Postdoctoral Fellow, University of Washington
2014 Associate Professor, Institute for Molecular Science
Associate Professor, The Graduate University for Advanced Studies
2014 JST-PRESTO Researcher (additional post) (–2017)
2018 Associate Professor, Exploratory Research Center on Life and Living Systems (ExCELLS)
2022 Professor, Osaka University

Awards

2013 Young Scientist Award, The 13th Annual Meeting of the Protein Science Society of Japan
2013 Young Scientist Award, The 51st Annual Meeting of the Biophysical Society of Japan
2018 Morino Foundation for Molecular Science

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Keywords

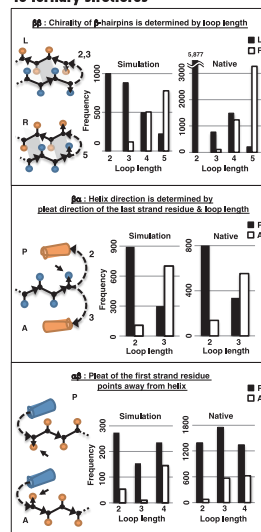
Protein Design for Structure and Function, Protein Folding, Structural Biology

Protein molecules spontaneously fold into unique three-dimensional structures specified by their amino acid sequences from random coils to carry out their functions. Many of protein studies have been performed by analyzing naturally occurring proteins. However, it is difficult to reach fundamental working principles of protein molecules only by analyzing naturally occurring proteins, since they evolved in their particular environments spending billions of years. In our lab, we explore the principles by computationally designing protein molecules completely from scratch and experimentally assessing how they behave.

Protein design holds promise for applications ranging from catalysis to therapeutics. There has been considerable recent progress in computationally designing new proteins. Many of protein design studies have been conducted using naturally occurring protein structures as design scaffolds. However, since naturally occurring proteins have evolutionally optimized their structures for their functions, implementing new functions into the structures of naturally occurring proteins is difficult for most of cases. Rational methods for building any arbitrary protein structures completely from scratch provide us opportunities for creating new functional proteins. In our lab, we tackle to establish theories and tech-

nologies for designing any arbitrary protein structures precisely from scratch. The established methods will open up an avenue of rational design for novel functional proteins that will contribute to industry and therapeutics.

Rules relating local backbone structures to tertiary structures



Selected Publications

- R. Koga*, M. Yamamoto, T. Kosugi, N. Kobayashi, T. Sugiki, T. Fujiwara and N. Koga*, "Robust Folding of a De Novo Designed Ideal Protein Even with Most of the Core Mutated to Valine," *Proc. Natl. Acad. Sci. U. S. A.* **117**(49), 31149–31156 (2020).
- N. Koga*, R. Koga, G. Liu, J. Castellanos, G. T. Montelione and D. Baker*, "Role of Backbone Strain in De Novo Design of Complex α/β Protein Structures," *Nat. Commun.* **12**, 3921 (12 pages) (2021).

1. State-Targeting Stabilization of Adenosine A_{2A} Receptor by Fusing a Custom-Made De Novo Designed α -Helical Protein

G-protein coupled receptors (GPCRs) are known for their low stability and large conformational changes upon transitions between multiple states. A widely used method for stabilizing these receptors is to make chimeric receptors by fusing soluble proteins (*i.e.*, fusion partner proteins) into the intracellular loop 3 (ICL3) connecting the transmembrane helices 5 and 6 (TM5 and TM6). However, this fusion approach requires experimental trial and error to identify appropriate soluble proteins, residue positions, and linker lengths for making the fusion. Moreover, this approach has not provided state-targeting stabilization of GPCRs.

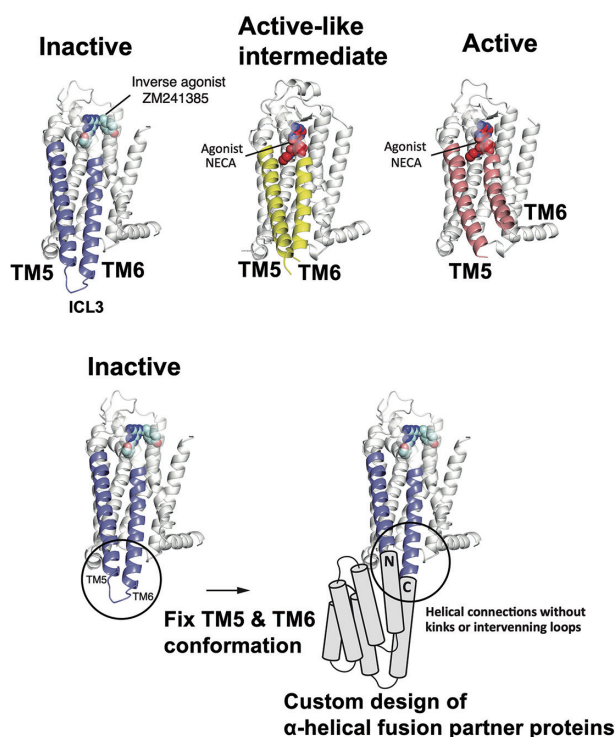


Figure 1. Strategy for state-targeting stabilization of GPCR, using de novo designed fusion partner proteins.

We designed fusion partner proteins customized for stabilizing one of the class A GPCRs, adenosine A_{2A} receptor (A_{2A}R), in an inactive state. Class A GPCRs are the largest subfamily of GPCRs, and the receptors in the class have been suggested to undergo large conformational changes in TM6

associated with TM5 upon the state transitions. We assumed that the TM5 and TM6 conformation could be fixed in a specific state through straight helical connections between a fusion partner protein and A_{2A}R. Therefore, we sought to design α -helical protein structures de novo, of which the N- and C-terminal helices are, respectively, connected to TM5 and TM6 of an inactive state A_{2A}R structure without any kinks or intervening loops.

The chimeric A_{2A}R fused with one of the designs (FiX1) exhibited increased thermal stability. We studied the stability of A_{2A}R–FiX1 by measuring the apparent melting temperatures in the clear-native polyacrylamide gel electrophoresis (CN–PAGE) method. The melting temperature was found to be significantly increased. For comparison, the melting temperature for A_{2A}R–BRIL (BRIL is one of the major fusion partner proteins) was also measured; the value was comparable to those of A_{2A}R–FiX1. Moreover, compared with the wild type, the binding affinity of the chimera against the agonist NECA was significantly decreased, whereas that against the inverse agonist ZM241385 was similar, indicating that the inactive state was selectively stabilized. Our strategy contributes to the rational state-targeting stabilization of GPCRs.

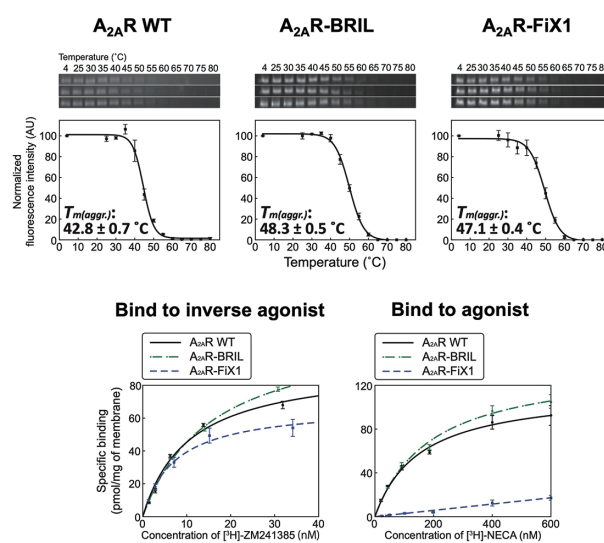


Figure 2. Experimental characteristics of A_{2A}R fused with or without fusion partner proteins.

Reference

- 1) M. Mitsumoto, K. Sugaya, K. Kazama, R. Nakano, T. Kosugi, T. Murata and N. Koga*, *Int. J. Mol. Sci.* **22**, 12906, 13 pages (2022).

Awards

MITSUMOTO, Masaya; The Student Presentation Award of Biophysical Society of Japan (BSJ) (2021).
KAIDA, Shingo; The Student Presentation Award of Biophysical Society of Japan (BSJ) (2021).
MITSUMOTO, Masaya; The SOKENDAI Award from Dean of School of Physical Sciences (2022).
KAIDA, Shingo; The Chemical Society of Japan Tokai Branch Award (2022).

Elucidation of Function, Structure, and Dynamics of Condensed-Phase Molecular Systems by Advanced Ultrafast Laser Spectroscopy

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Education

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Professional Employment

2013 Special Postdoctoral Researcher, RIKEN
2016 Research Scientist, RIKEN
2017 JST-PRESTO Researcher
2020 Associate Professor, Institute for Molecular Science
Associate Professor, The Graduate University for Advanced Studies

Awards

2017 The 8th Research Incentive Award of RIKEN
2017 The Spectroscopical Society of Japan Award for Young Scientists
2019 RSC PCCP Prize
2020 The Commendation for Science and Technology by the Minister of Education, Culture, Sports, Science and Technology
The Young Scientists' Award
2020 Morino Foundation for Molecular Science
2020 The 13th Young Scientist Awards of the Japan Society for Molecular Science
2021 The 13th Inoue Science Research Award

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YONEDA, Yusuke
Secretary
ITO, Atsuko

Keywords

Ultrafast Spectroscopy, Nonlinear Spectroscopy, Chemical Reaction Dynamics

We develop and apply advanced ultrafast laser spectroscopy based on state-of-the-art optical technology to study the chemical reaction dynamics of the condensed-phase molecules. In particular, we focus on exploiting unique methodologies based on few-cycle ultrashort pulses (e.g., time-domain impulsive vibrational spectroscopy and multidimensional spectroscopy) and tracking molecular dynamics from electronic and structural viewpoints throughout the chemical reaction with exquisite temporal resolution. We also develop a novel methodology and light source to probe ultrafast dynamics of single molecules in the condensed phase at room temperature, with the aim to understand chemical reaction dynamics at the single-molecule level. Our particular interest rests on elucidating sophisticated molecular mechanisms that underlie the reactions of functional molecular systems such as proteins,

molecular assemblies, and metal complexes. On the basis of new insights that can be gained from our advanced spectroscopic approaches, we aim to establish a new avenue for the study of chemical reaction dynamics.

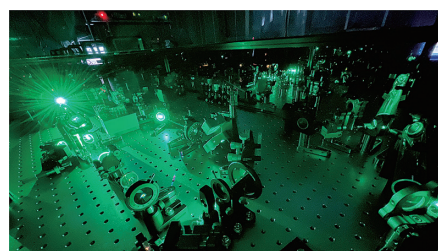


Figure 1. Setup for advanced ultrafast spectroscopy based on sub-10-fs pulses.

Selected Publications

- H. Kuramochi and T. Tahara, "Tracking Ultrafast Structural Dynamics by Time-Domain Raman Spectroscopy," *J. Am. Chem. Soc.* **143**, 9699–9717 (2021).
- H. Kuramochi, S. Takeuchi, M. Iwamura, K. Nozaki and T. Tahara, "Tracking Photoinduced Au–Au Bond Formation through Transient Terahertz Vibrations Observed by Femtosecond Time-Domain Raman Spectroscopy," *J. Am. Chem. Soc.* **141**, 19296–19303 (2019).
- H. Kuramochi, S. Takeuchi, H. Kamikubo, M. Kataoka and T. Tahara, "Fifth-Order Time-Domain Raman Spectroscopy of Photoactive Yellow Protein for Visualizing Vibrational Coupling in Its Excited State," *Sci. Adv.* **5**, eaau4490 (2019).
- H. Kuramochi, S. Takeuchi, K. Yonezawa, H. Kamikubo, M. Kataoka and T. Tahara, "Probing the Early Stages of Photoreception in Photoactive Yellow Protein with Ultrafast Time-Domain Raman Spectroscopy," *Nat. Chem.* **9**, 660–666 (2017).
- T. Fujisawa, H. Kuramochi, H. Hosoi, S. Takeuchi and T. Tahara, "Role of Coherent Low-Frequency Motion in Excited-State Proton Transfer of Green Fluorescent Protein Studied by Time-Resolved Impulsive Stimulated Raman Spectroscopy," *J. Am. Chem. Soc.* **138**, 3942–3945 (2016).
- H. Kuramochi, S. Takeuchi and T. Tahara, "Femtosecond Time-Resolved Impulsive Stimulated Raman Spectroscopy Using Sub-7-fs Pulses: Apparatus and Applications," *Rev. Sci. Instrum.* **87**, 043107 (2016).

1. Towards Sub-10-fs Time-Resolved Spectroscopy of Single Molecules at Room Temperature

In complex biological molecular systems, the slow (μ s), large-amplitude structural fluctuation significantly modulates the molecular environment inside/outside the molecule, affecting the reactivity at the relevant local sites. Elucidating how such a fluctuation modulates and regulates particular “fast” local chemical reaction dynamics is vital to interrogating the sophisticated molecular mechanisms behind the functions. Nevertheless, the relevant information cannot be accessed by conventional time-resolved spectroscopy because it only provides statistically averaged information about the ensemble. Unraveling how the slow spontaneous fluctuation regulates the chemical reaction inevitably requires observation of the dynamics at the single-molecule level. To this end, we have been developing ultrafast spectroscopy that can track the reaction dynamics of single molecules at room temperature with a temporal resolution as high as <10 fs. Recently, we constructed a confocal microscope as a platform to perform single-molecule ultrafast spectroscopy, and successfully verified that we could detect single molecules. Using a newly developed high-repetition-rate ultrashort laser, ultrafast spectroscopy with single-molecule sensitivity is now underway.

2. Generation of Wavelength-Tunable Sub-10-fs Pulses at a Multi-MHz Repetition Rate

Time-resolved spectroscopy at the single-molecule level inevitably requires extremely high sensitivity, so the light source having high stability and repetition rate is essential. Typically, an optical parametric oscillator (OPO) or a supercontinuum laser is employed as a light source, which offers stable, tunable outputs with a $>$ MHz repetition rate. However, measurements using OPO have a limitation in the temporal resolution (~ 200 fs) and lack spectral information of detected transients due to the narrow bandwidth. Supercontinuum laser offers broad bandwidth, but its pulse duration is limited to a few ps due to nontrivial phase structure. To realize ultrafast spectroscopy of various complex molecules with single-molecule sensitivity, we need a light source having wavelength tunability, high repetition rate, ultrashort pulse duration, and high stability. We developed a light source for generating sub-10-fs pulses at a multi-MHz repetition rate. Using a ytterbium fiber chirped-pulse-amplification system, we generated pulses tunable from 500–950 nm with broad bandwidths. The outputs were dispersion-compensated,¹⁾ and the typical pulse duration of the compressed output was <10 fs, as shown in Figure 2. Shot-to-shot and long-term ($>$ hours) fluctuations were evaluated to be $<0.3\%$ rms. This high stability holds promise for the application to single-molecule spectroscopy. We will use this high repetition-rate ultrashort light source for ultrafast spectroscopy of single molecules under the microscope and aim to investigate primary events in photoactive proteins with single-molecule sensitivity.

Awards

YONEDA, Yusuke; Best Presentation Award at The 15th Annual Meeting of Japan Society for Molecular Science (2021).
YONEDA, Yusuke; The Early Career Award in Biophysics (2022).

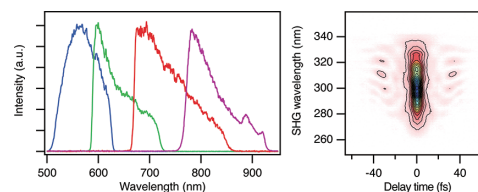


Figure 2. (Left) Typical spectra of the broadband pulses that support Fourier transform limit pulse duration of <10 fs. (Right) Typical FROG trace of the broadband pulse. The pulse duration was evaluated as 6.8 fs.

3. Development of Ultrabroadband Two-Dimensional Electronic Spectrometer

Two-dimensional electronic spectroscopy (2D-ES) is a powerful tool for studying the dynamics and structure of molecules having multiple chromophores with high temporal and frequency resolution. 2D-ES disentangles and visualizes how the optical transitions of each chromophore are coupled and how the excitation energy transfers among them. The technique has been successfully utilized to elucidate the primary energy transfer dynamics in photosynthetic systems and various other biological and materials systems. When the technique is applied to the transients, it is even possible to visualize the migration of wavepackets and/or dynamic heterogeneity. While its success, the spectral range of most of the previous 2D-ES measurements has been limited to <100 nm, hampering us from gaining full insights into the intricate electronic dynamics of condensed-phase complex molecular systems. Aiming to broaden the spectral coverage of 2D-ES and enable investigating electronic and nuclear dynamics comprehensively, we constructed an ultrabroadband 2D-ES setup covering >200 nm for the excitation axis and >400 nm for the detection axis. As shown in Figure 3, the typical data measured for a molecular thin film fully resolve auto- and cross-correlations of the electronic transitions of the ground and excited states over the broad spectral region.

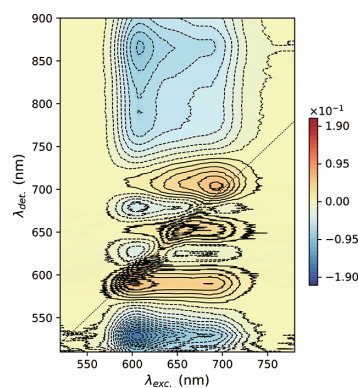


Figure 3. Ultrabroadband two-dimensional electronic spectrum of a molecular thin film measured with <8 -fs pulses.

Reference

- 1) H. Kuramochi, S. Takeuchi and T. Tahara, *Rev. Sci. Instrum.* **87**, 043107 (2016).

Open up Future Electronics by Organic Molecules

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Education

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Professional Employment

1998 Research Associate, Gakushuin University
1999 Special Postdoctoral Fellow, RIKEN
2000 Research Scientist, RIKEN
2007 Senior Research Scientist, RIKEN
2012 Professor, Institute for Molecular Science
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Awards

2009 RSC Publishing CrystEngComm Prize
2009 Young Scientist Awards, Japan Society for Molecular Science
2010 RIKEN-ASI Award for the Young Scientist
2019 The CSJ Award for Creative Work
2020 NAGAI Foundation for Science & Technology Academic Award

Member

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Secretary
SUZUKI, Ai
ISHIKAWA, Yuko

Keywords

Organic Spintronics, Chirality, Organic Superconductor

Spintronics is a new ingredient of electronics in which a magnetic moment of an electron is utilized as an information carrier together with its charge. Spin-polarized current is one of the most important resources in spintronics, because it can drive devices such as ferromagnetic memory with spin angular momentum. In conventional spintronics, such a spin-polarized current is generated by passing a charge current through ferromagnetic metals. However, recently, researchers are finding other ways of spin-polarized current generation by using topological insulators and non-collinear antiferromagnets, which can sometimes be more efficient than those with ferromagnets.

Chiral molecules are attracting recent attention as a new source of spin-polarized current. Chirality-Induced Spin Selectivity (CISS) effect generates spin polarization parallel to or antiparallel to the electron's velocity depending on the handedness of the chiral molecule that is being passed through by a tunneling electron (Figure 1). Although the mechanism of CISS effect is still under debate, it seems to create spin-polarization higher than those of ferromagnets, which is surprisingly large when the small spin-orbit coupling energy of organic molecules is considered. In order to rationalize such a large effect, some microscopic hypotheses are proposed based on experimental results, whose proofs are being waited for.

Our group is trying to unveil such mechanisms that drive CISS effect by using chiral crystalline materials.

The use of crystalline materials has several advantages. For example, one can employ theoretical framework with well-defined wave number of electrons. Another advantage is the size of the chiral material which allows direct attachment of detection electrodes in different positions. With these merits in mind, we are fabricating spintronic devices suitable for the CISS investigations.

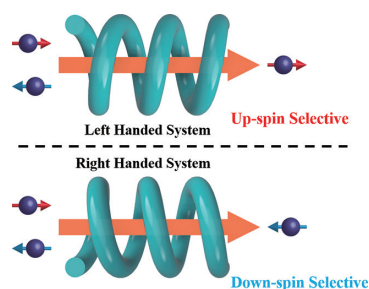


Figure 1. Conceptual schematic for CISS effect. P-helix molecule (lower panel) can transmit more electrons with spins antiparallel to the velocity (negative helicity electrons) than the other, while M-helix molecule (upper panel) favors transmission of electrons with parallel spin (positive helicity electrons).

Selected Publications

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1. Spin Current Generation in a Chiral Organic Superconductor

Although *s*- and *d*-wave superconductors are in a spin singlet state at its ground state, a superconductor with broken mirror symmetry is expected to show spin triplet state when supercurrent is flowing, according to a theory developed by Edelstein.¹⁾ This means spin polarization can be generated by applying supercurrent in a chiral superconductor. The magnetization direction that depends on the lattice symmetry has been recently calculated by group theory.²⁾ We have tested this idea by employing κ -(BEDT-TTF)₂Cu(NCS)₂ (hereafter, κ -NCS) which is an organic superconductor with chiral and polar crystal lattice. The space group of this crystal is $P2_1$, and its handedness is defined by the relative arrangement between the anionic Cu(NCS)₂ and cationic BEDT-TTF. This handedness can be experimentally determined by X-ray diffraction or circular dichroism (CD).

After confirming pure enantiomeric lattice system with CD microscope, a thin crystal of κ -NCS has been laminated onto a resin substrate with prepatterned gold and nickel electrodes. At temperature lower than superconducting T_c , an a.c. electrical excitation was applied to induce spin polarization (Figure 2). The spin polarization accumulated at the interface between κ -NCS and the magnetic electrode was detected as a built-up voltage that is dependent on the relative angle between the accumulated and ferromagnetic spins. We have compared the observed voltage with theoretical estimation and found that it exceeds the value predicted by Edelstein effect more than 1000 times. This surprising result suggests that there is a spin enhancement effect other than Edelstein effect, implying existence of an effect analogous to CISS for a chiral superconductor.

By measuring the angle dependency of this magneto-voltaic signal, the direction of accumulated spin could be determined. The observed spin polarization direction was dependent on the location of the detection electrode inside the crystal, and its arrangement was consistent with a magnetic monopole structure which has been hypothesized in a chiral molecule under non-equilibrium state with CISS effect. More specifically, the spin accumulation was forming an antiparallel pair on the upper and lower sides of the κ -NCS crystal. With a right-handed crystal, the accumulated spins showed outward spin pairs.

To our surprise, this spin accumulation could be observed in nonlocal measurements where the excitation and detection electrodes are separated by 600 μm . We have also fabricated a nonlocal detection device with a crystal possessing two chirality domains where right- and left-handed crystal structures are spatially separated. By exciting this crystal at two different positions with opposite handednesses, we have observed a switching of spin pairing mode from outward to inward. This corresponds to the sign reversal of magnetic monopole in the language of multipole expression.³⁾ An interesting point here is that the sign of magnetic monopole, which shows time-

reversal-odd (*T*-odd) characteristics, is connected to the chirality of underlying crystal lattice so that representing *T*-odd chirality. Although this *T*-odd chirality is a metastable state and disappears at ground state, its relevance to the enantio-separation experiments in CISS effect is directly implied in this experiment. If one accepts the fact that a sign of such a metastable magnetic monopole at excitation can represent the sign of chirality (electric toroidal monopole) at ground state lattice, both the large enhancement of spin polarization and the enantio-separation of chiral molecules at non-equilibrium state observed in CISS experiments can be naturally understood, because such a monopole can interact with magnetic substrate in a handedness-specific manner. In this sense, this experiment provides the first direct observation of spin pair (or magnetic monopole) formation from coherent chiral system and provides proof of concept for microscopic CISS mechanism. Although the Hamiltonians describing the chiral superconductor and chiral molecules are quite different, there are many common features such as singlet ground state, chiral lattice and quantum coherence over the entire body. Therefore, we believe the present result provides a lot of stimulating insights for microscopic understanding of CISS. Since the conversion from *T*-even spin current to *T*-odd spin accumulation requires time integration with an existence of spin reservoir, the spin carriers in chiral molecules and superconductors should be identified in future studies. We also expect emergence of superconducting spintronics once a sourcing of spin-polarized current in superconductor is established by chiral superconductors.

(BEDT-TTF = bis(ethylenedithio)tetrathiafulvalene)

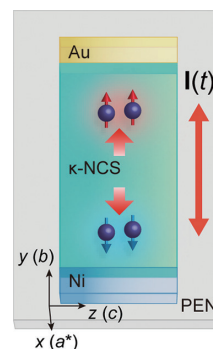


Figure 2. Device schematic for the detection of spin polarization in a chiral superconductor κ -NCS. By applying electrical current, electron spins are polarized along the current direction by CISS-like effect which can be detected as voltage across the κ -NCS/Ni interface. The amplitude of the signal is proportional to the accumulated spins at the interface.

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