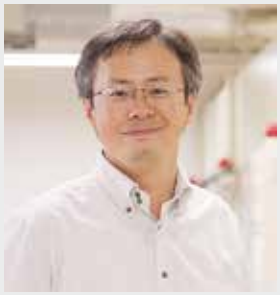
RESEARCH ACTIVITIES

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



AKIYAMA, Shuji
Professor
[akiyamas@ims.ac.jp]

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
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

Member
Assistant Professor
MUKAIYAMA, Atsushi
FURUIKE, Yoshihiko
Post-Doctoral Fellow
OUYANG, Dongyan
Visiting Scientist
TONIOLO, Paul*
MARIE, Vincent*
Graduate Student
SIMON, Damien
Technical Fellow
SHINTANI, Atsuko
HAYAKAWA, Arina
WASHIO, Midori
TAKAYA, Mari
SUGISAKA, Kanae
Secretary
SUZUKI, Hiroko

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 revelas 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 transmural 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

- D. Ouyang, Y. Furuike, A. Mukaiyama, K. Ito-Miwa, T. Kondo and S. Akiyama, *Int. J. Mol. Sci.* **20**, 2789–2800 (2019).
- A. Mukaiyama, D. Ouyang, Y. Furuike and S. Akiyama, *Int. J. Biol. Macromol.* **131**, 67–73 (2019).
- A. Mukaiyama, Y. Furuike, J. Abe, E. Yamashita, T. Kondo and S. Akiyama, *Sci. Rep.* **8**, 8803 (2018).
- 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*: Atomic-Scale Origins of Clock Slowness in Cyanobacterial Circadian Clock System[1)]

TTo identify the structural origins of slowness encoded in KaiC, its N-terminal ATPase domain was analyzed using high-resolution x-ray crystallography.[1)] Water molecules are prevented from attacking into the ideal position (a black dot in Figure 1) for the ATP hydrolysis by a steric hindrance near ATP phosphoryl groups. In addition, this hindrance is surely anchored to a spring-like structure derived from polypeptide isomerization. The ATP hydrolysis, which involves access of a water molecule to the bound ATP and reverse isomerization of the polypeptide, is expected to require a significantly larger amount of free energy than for typical ATP hydrolysis. The atomic structure discovered by us explains why the ATPase activity of KaiC is so much lower (by 100- to 1,000,000-fold) than that of typical ATPase molecules.

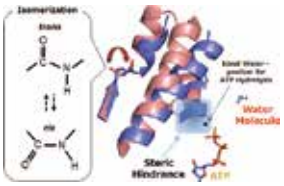


Figure 1. Structural basis for steady slowness. The steric barrier prevents access of a water molecule to the catalytic site (indicated by a black dot).

2. *Rhythm*: Transmural Hierarchy in Cyanobacterial Circadian Clock System[2,3)]

KaiC ATPase is of particular interest here, as it finely correlates to the frequencies of *in vivo* as well as *in vitro* oscillations. This unique property has inspired us to develop an ATPase-based screening for KaiC clock mutants giving short, long, and/or temperature-dependent periods.[2)] A developed HPLC system with a 4-channel temperature controller has reduced approximately 80% of time costs for the overall screening process (Figure 2).

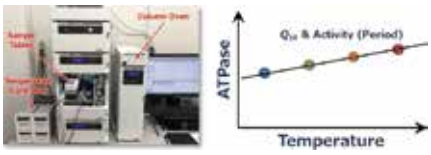


Figure 2. Development of a quick ATPase assay system.

How is the intra-molecular slowness encoded in KaiC (Figure 1) transmitted to the inter-molecular interactions with other Kai proteins? To address this question, a tryptophan residue was introduced in the N-terminal ring of KaiC as the fluorescent probe for KaiBC complex formation.[3)] Our kinetic data indicated that KaiB exclusively selects the post-ATP-hydrolysis state of KaiC to form the KaiBC complex. This process follows a mechanism called conformational selection (CS), in which proteins (KaiC) first undergoes a structural change to form a specific intermediate. Ligands (KaiB) are then recognized specifically through the intermediate state to form a tight ligand-protein complex. The CS mechanism is elegantly designed in KaiC so that the slow intra-molecular ATPase reaction in KaiC can be the rate-liming step of the overall KaiBC complex formation.

3. beyond Evolutionary *Diversity*[1,4)]

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 3A). We have identified a signal component that is similar to damped oscillation, and propose that it encodes the specific frequency, equivalent to a 24-hour cycle.[1)]

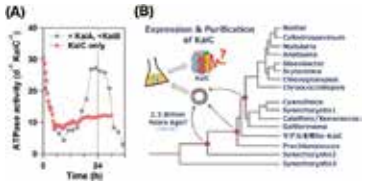


Figure 3. Damped oscillation of KaiC ATPase activity (**A**) and evolutionary diversity of cyanobacteria (**B**).

As this proposal is further discussed and verified, development of new studies is expected. 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 our current understanding of this phenomenon, *what specific frequencies are possessed by KaiCs and their homologues in other species and ancestral cyanobacteria?* (Figure 3B) The habitats of cyanobacteria are diverse, so the space of their sequence is immense.[4)] If you strain your ears, the rhythms of the ancient Earth may be heard from beyond evolutionary diversity.

4. Bio-SAXS Activity in IMS[5,6)]

We have supported SAXS users so that they can complete experiments smoothly and publish their results.[5,6)]

References

1) 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).
2) D. Ouyang, Y. Furuike, A. Mukaiyama, K. Ito-Miwa, T. Kondo and S. Akiyama, *Int. J. Mol. Sci.* **20**, 2789–2800 (2019).
3) A. Mukaiyama, Y. Furuike, J. Abe, E. Yamashita, T. Kondo and S. Akiyama, *Sci. Rep.* **8**, 8803 (2018).
4) A. Mukaiyama, D. Ouyang, Y. Furuike and S. Akiyama, *Int. J. Biol. Macromol.* **131**, 67–73 (2019).
5) M. Okumura, K. Noi, S. Kanemura, M. Kinoshita, T. Saio, Y. Inoue, T. Hikima, S. Akiyama, Y. Ogura and K. Inaba, *Nat. Chem. Biol.* **15**, 499–509 (2019).
6) Y. Furukawa, C. Lim, T. Tosha, K. Yoshida, T. Hagai, S. Akiyama, S. Watanabe, K. Nakagome and Y. Shiro, *PLoS One* **13**, e0204355 (2018).

* IMS International Internship Program

Protein Design Using Computational and Experimental Approaches

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

KOGA, Nobuyasu
Associate Professor
[nkoga@ims.ac.jp]

Education
2001 B.S. Kobe University
2006 Ph.D. Kobe University

Professional Employment
2003 JSPS Research Fellow
2006 Postdoctoral Fellow, Kobe University
2007 Postdoctoral Fellow, Kyoto Universtiy
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

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

Member
Assistant Professor
KOSUGI, Takahiro
Research Fellow
KOGA, Rie
KONDO, Minako
MINAMI, Shintaro
KOBAYASHI, Naoya
Graduate Student
SAKUMA, Kouya
MITSUMOTO, Masaya
YAMADA, Hiroko
Secretary
SUZUKI, Hiroko

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

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 proteins with new functions. 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 technologies 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.

Selected Publications

- N. Koga, R. Tatsumi-Koga, G. Liu, R. Xiao, T. B. Acton, G. T. Montelione and D. Baker, "Principles for Designing Ideal Protein Structures," *Nature* **491**, 222–227 (2012).
- Y.-R. Lin, N. Koga*, R. Tatsumi-Koga, G. Liu, A. F. Clouser, G. T. Montelione and D. Baker*, "Control over Overall Shape and Size in De Novo Designed Proteins," *Proc. Natl. Acad. Sci. U. S. A.* **112**, E5478–E5485 (2015).

1. Principles for Designing Ideal Protein Structures

Understanding the principles for protein folding is complicated by energetically unfavorable non-ideal features—for example kinked α-helices, bulged β-strands, strained loops and buried polar groups—that arise in proteins from evolutionary selection for biological function or from neutral drift. Here, we uncovered the principles for protein folding by designing "ideal" protein structures, which are stabilized by completely consistent local and non-local interactions. We discovered a set of rules relating local backbone structures (secondary structure patterns) to tertiary motifs (Figure 1 left), which were identified using a combination of folding simulations and analyses of naturally occurring proteins. Building backbone structures according to the rules (Figure 1 top right), and placing side chains stabilizing the backbone structures, we can readily design the proteins which have funnel-shaped folding energy landscapes leading into the target folded state.

Using this approach, we designed sequences predicted to fold into ideal protein structures consisting of α-helices, β-strands and minimal loops, using the Rosetta program. Designs for five different topologies were found to be monomeric and very stable and to adopt structures in solution nearly identical to the computational models (Figure 1 bottom right). These results suggest that the local backbone structures determine the tertiary folded structures rather than the details of amino acid sequences.

2. Control over Overall Shape and Size in De Novo Designed Proteins

To achieve fine control over protein shape and size within a particular topology, we have extended the design rules by systematically analyzing the codependences between the lengths and packing geometry of successive secondary structure elements and the backbone torsion angles of the loop linking them. We demonstrate the control afforded by the resulting extended rule set by designing a series of protein with the same fold but considerable variation in secondary structure length, loop geometry, β-strand registry, and overall shape. Solution NMR structures of four designed proteins for two different folds show that protein shape and size can be precisely controlled within a given fold. These extended design principles provide the foundation for custom design of protein structures performing desired functions.

References

1) S. J. Fleishman, S. D. Khare, N. Koga and D. Baker*, *Protein Sci.* **20**, 753–757 (2011).
2) N. Koga, R. Tatsumi-Koga, G. Liu, R. Xiao, T. B. Acton, G. T. Montelione and D. Baker*, *Nature* **491**, 222–227 (2012).
3) J. Fang, A. Mehlich, N. Koga, J. Huang, R. Koga, M. Rief, J. Kast, D. Baker and H. Li*, *Nat. Commun.* **4**, 2974 (2013).
4) Y.-R. Lin, N. Koga*, R. Tatsumi-Koga, G. Liu, A. F. Clouser, G. T. Montelione and D. Baker*, *Proc. Natl. Acad. Sci. U. S. A.* **112**, E5478–E5485 (2015).
5) Y.-R. Lin, N. Koga, S. M. Vorobiev and D. Baker*, *Protein Sci.* **26**, 2187–2194 (2017).
6) S. Basak, R. P. Nobrega, D. Tavella, L. M. Deveau, N. Koga, R. Tatsumi-Koga, D. Baker, F. Massi* and C. R. Matthews*, *Proc. Natl. Acad. Sci. U. S. A.* **116**, 6806–6811 (2019).

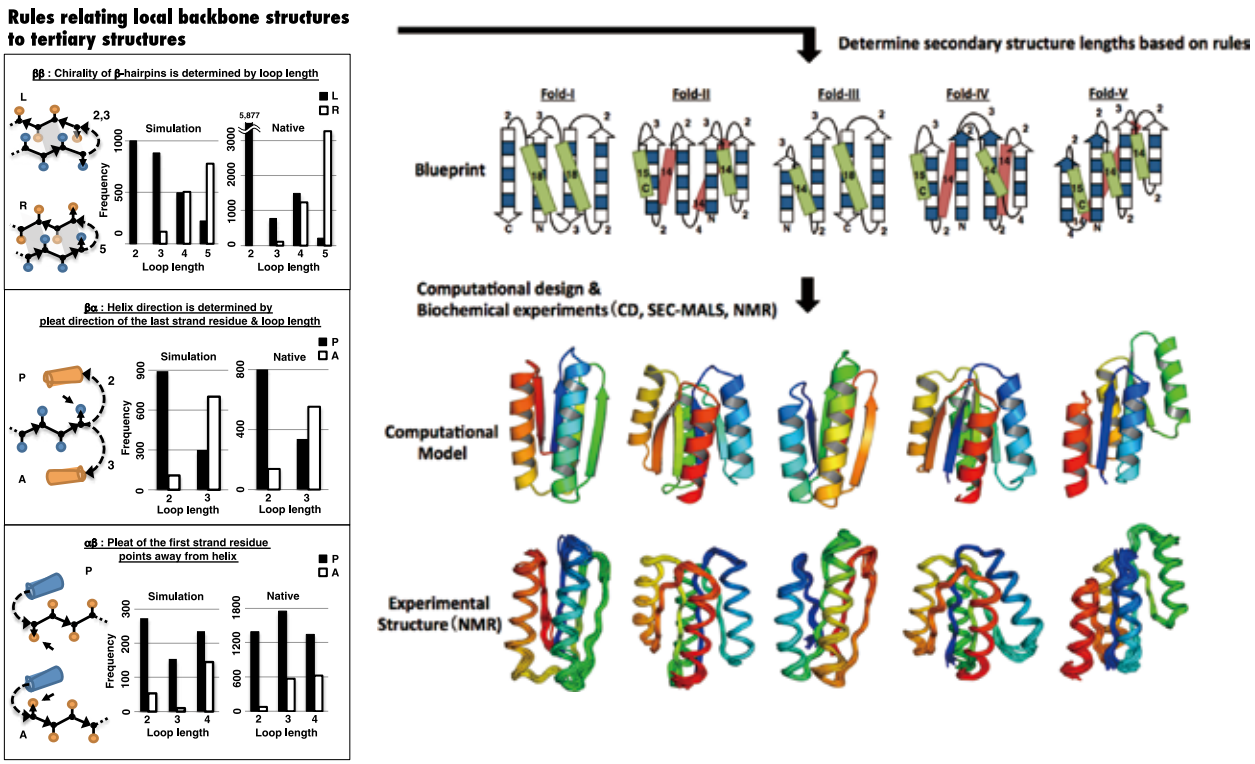


Figure 1. Left: Rules relating local backbone structures to tertiary motifs. Right: De novo designed protein structures.

Open up Future Electronics by Organic Molecules

Research Center of Integrative Molecular Systems
Division of Functional Molecular Systems

YAMAMOTO, Hiroshi
Professor
[yhiroshi@ims.ac.jp]

Education
1993 B.S. The University of Tokyo
1998 Ph.D. The University of Tokyo

Professional Employment
1998 Research Associate, Gakushuin University
1999 Special Postdoctral Fellow, RIKEN
2000 Research Scientist, RIKEN
2007 Senior Research Scientist, RIKEN
2012 Professor, Institute for Molecular Science
Professor, The Graduate University for Advanced Studies
2015 Visiting Professor, Tohoku University

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

Member
Assistant Professor
SUDA, Masayuki
HIROBE, Daichi
IMS Research Assistant Professor
KAWAGUCHI, Genta
Technical Associate
URUICHI, Mikio
Visiting Scientist
SAENNAWA, Wiyada*
Graduate Student
CHOOPPAWA, Tianchai
MORISHIMA, Masaki
AIZAWA, Hiroki
NABEI, Yoji
Technical Fellow
MURATA, Ryosuke
Secretary
SUZUKI, Ai

Keywords Organic Mott Insulator, Field Effect Transistors, Organic Spintronics

Organic molecules are attracting recent attention as new ingredients of electronic circuits. Our group focuses on the development of organic electronics in the next era by providing new mechanism and concepts of the device operation and fabrication. For example, an electronic phase transition is utilized for the ON/OFF switching of our field-effect-transistor (FET). This special FET is called an organic Mott-FET, where the conduction electrons in the organic semiconductor are solidified at the OFF state because of Coulomb repulsion among carriers. In the operation, these solidified electrons can be melted by applying a gate voltage, and show an insulator-to-metal transition so-called Mott-transition to be switched to the ON state. Because of this phase transition, a large electric response of the device can be achieved, resulting in the highest device mobility ever observed for organic FETs. In addition to this high performance, the Mott-FET is interesting in terms of superconductivity. Because the Mott-transition sometimes accompanies superconducting phase in between metal and insulator, modulation of gate electric field at low temperature may induce superconductivity. In fact, we have achieved first example of field-induced superconductivity in an organic FET. By combining a strain effect that can tune the bandwidth, this type of electric-field-induced superconducting transition can be utilized for mapping the phase diagram around the Mott-insulator as shown in Figure 1.

Another approach to the future electronics is the development of spintronic devices based on chirality of organic material. We aim to implement chirality-induced spin selectivity (CISS) effect into molecular devices that can generate spin-polarized current. This type of device is expected to realize spintronics devices without magnet or topological insulator.

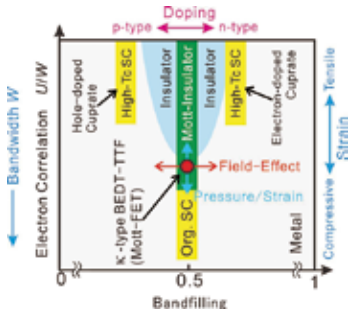


Figure 1. Phase diagram surrounding a Mott-insulator. SC denotes superconductor, while *U* and *W* are on-site Coulomb repulsion and bandwidth, respectively.

Selected Publications

- H. M. Yamamoto, M. Suda and Y. Kawasugi, "Organic Phase-Transition Transistor with Strongly Correlated Electrons," *Jpn. J. Appl. Phys.* **57**, 03EA02 (7 pages) (2018).
- Y. Kawasugi, K. Seki, Y. Edagawa, Y. Sato, J. Pu, T. Takenobu, S. Yunoki, H. M. Yamamoto and R. Kato, "Electron–Hole Doping Asymmetry of Fermi Surface Reconstructed in a Simple Mott Insulator," *Nat. Commun.* **7**, 12356 (8 pages) (2016).
- M. Suda, R. Kato and H. M. Yamamoto, "Light-Induced Superconductivity Using a Photo-Active Electric Double Layer," *Science* **347**, 743–746 (2015).
- H. M. Yamamoto, M. Nakano, M. Suda, Y. Iwasa, M. Kawasaki and R. Kato, "A Strained Organic Field-Effect Transistor with a Gate-Tunable Superconducting Channel," *Nat. Commun.* **4**, 2379 (7 pages) (2013).

1. Light-Driven Spin Switching Device Using an Artificial Molecular Motor[1)]

Artificial molecular switches and machines that enable the directional movements of molecular components by external stimuli have undergone rapid advances over the past several decades. Particularly, overcrowded alkene-based artificial molecular motors are highly attractive from the viewpoint of chirality switching during rotational steps. However, the integration of these molecular switches into solid-state devices is still challenging. In this study, solid-state spin-filtering devices that can switch the spin polarization direction by light irradiation or thermal treatment have been examined. We measured magnetoresistance of a device, in which M-cis form (Figure 2) of the motor is sandwiched by two electrodes as tunnelling layer, before and after photo irradiation. The magnetoresistance showed switching of spin polarization from up-spin selective to down-spin selective by the irradiation of light. This result indicates that the M to P chirality conversion by light is switching the spin of electrons that tunnel through the motor molecule because of CISS effect. We also confirmed that spin direction switching is possible in the next step, too, where heat treatment inverts the molecular chirality from P to M. During this study we found that the flexibility at the molecular scale is essential for the electrodes in solid-state devices using molecular machines. The same device operation was also confirmed by conductive AFM (atomic force microscope) measurement with magnetized tip. We also evaluated the strength of spin–orbit interaction by quantum chemical calculation, and found that state transitions between σ and π electron states are good to enhance the interaction. This result demonstrates a possibility of novel spintronics based on solid-state functionalities emerging from nano-sized motions of molecular switches.

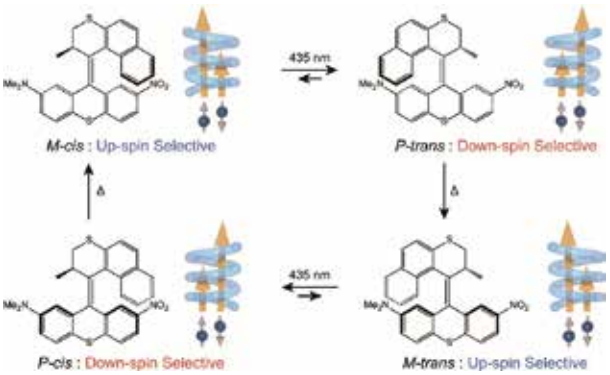


Figure 2. Spin selectivity switching by light irradiation and heat. The molecular motor has four steps for the 360 degree rotation, during which the four times chirality switching and associated spin switching occurs.

2. Ambipolar Superconductivity in Organic Field-Effect Devices[2,3)]

Because Mott-FET shows ambipolar operation, field-induced superconductivity in both p-type and n-type regimes is expected. This idea coincides with the fact that both hole-doped and electron-doped cuprates show superconductivity in the vicinity of Mott-insulator. We performed both FET and EDLT (electric double-layer transistor) measurement with organic Mott-insulator at low temperature. In the EDLT experiment, a flexible substrate was employed to tune not only the gate voltage but also the strain. With such a device, we could perform the scanning of bandwidth and bandfilling simultaneously. The phase diagram thus obtained at 5.5 K is shown in Figure 3.[2)] This is the first experimental example of a phase diagram in which ambipolar superconductivity and strain-induced superconductivity are continuously surrounding the Mott-insulator. From theoretical insights, a p/n asymmetry evident in this diagram seems to originate in the band structure calculated without correlation. A similar ambipolar switching of superconductivity was also observed in Mott-FET with κ-$(BEDT\text{-}TTF)_2Cu(NCS)_2$.[3)]

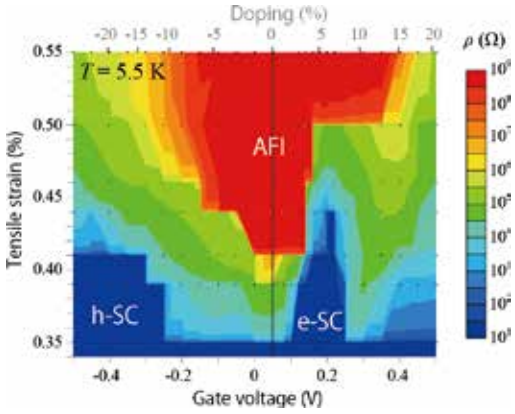


Figure 3. Emergence of both p-type (h-SC) and n-type (e-SC) superconductivity by gate voltage at various tensile strain. The strain is controlling electron correlation *U*/*W* while gate voltage controls bandfilling (see also Figure 1). AFI denotes antiferromagnetic insulator, meaning a Mott-insulating phase.

References

1) M. Suda, Y. Thathong, V. Promarak, H. Kojima, M. Nakamura, T. Shiraogawa, M. Ehara and H. M. Yamamoto, *Nat. Commun.* **10**, 2455 (2019).
2) Y. Kawasugi, K. Seki, S. Tajima, J. Pu, T. Takenobu, S. Yunoki, H. M. Yamamoto and R. Kato, *Sci. Adv.* **5**, eaav7282 (2019).
3) G. Kawaguchi, A. A. Bardin, M. Suda, M. Uruichi and H. M. Yamamoto, *Adv. Mater.* **31**, 1805715 (2019).

Award

YAMAMOTO, Hiroshi; The CSJ Award for Creative Work (2019).

* IMS International Internship Program

Development of Graphene Molecules as Organic Semiconductors

Research Center of Integrative Molecular Systems
Division of Functional Molecular Systems

SUZUKI, Toshiyasu
Associate Professor
(–March, 2019)
[toshy@ims.ac.jp]

Education
1985 B.S. Nagoya University
1992 Ph.D. University of California, Santa Barbara

Professional Employment
1992 Assistant Professor, Institute for Molecular Science
1998 Associate Professor, Institute for Molecular Science
Associate Professor, The Graduate University for Advanced Studies

Member
Secretary
WATANABE, Yoko

Keywords Organic Synthesis, Organic Semiconductor, Graphene Molecule

Graphene and curved graphenes have been extensively investigated by both chemists and physicists because of their unique structures and properties. C_{60} fullerene is spherical and has the positive Gaussian curvature. Carbon nanotubes (CNTs) have the cylindrical structures with the zero Gaussian curvature. The introduction of curvatures to graphene changes the dimensionality and electronic properties. For example, graphene is a two-dimensional zero-gap semiconductor with the ambipolar character (both p- and n-types). C_{60} is a zero-dimensional n-type semiconductor, and CNTs are one-dimensional p-type semiconductors or metals. Three-dimensional graphenes with the negative Gaussian curvature were proposed as shown in Figure 1. It is interesting to see how the curvature influences the structure and properties of the graphene molecule.

Perfluorination is a simple method to prepare an n-type semiconductor with the same molecular symmetry. It is important to understand the impact of perfluorination on the solid-state structures and charge transport properties. We are currently working on the synthesis of new perfluorinated aromatic compounds.

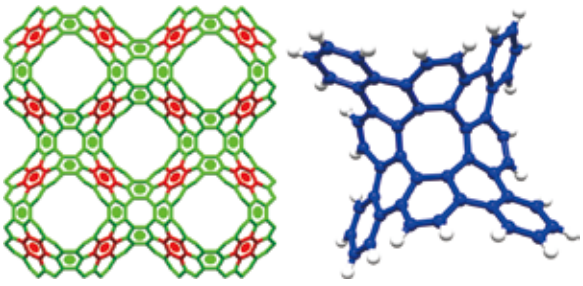


Figure 1. Schwarzite P192 (left) as a hypothetical 3D graphene with the negative Gaussian curvature. Tetrabenzo[8]circulene (right) as a repeating molecular unit for Schwarzite P192.

Selected Publications

- T. Iwamoto, Y. Watanabe, Y. Sakamoto, T. Suzuki and S. Yamago, "Selective and Random Syntheses of [*n*]Cycloparaphenylenes (*n* = 8–13) and Size Dependence of their Electronic Properties," *J. Am. Chem. Soc.* **133**, 8354–8361 (2011).
- Y. Sakamoto and T. Suzuki, "Tetrabenzo[8]circulene: Aromatic Saddles from Negatively Curved Graphene," *J. Am. Chem. Soc.* **135**, 14074–14077 (2013).
- Y. Kuroda, Y. Sakamoto, T. Suzuki, E. Kayahara and S. Yamago, "Tetracyclo(2,7-carbazole)s: Diatropicity and Paratropicity of Inner Regions of Nanohoops," *J. Org. Chem.* **81**, 3356–3363 (2016).
- Y. Sakamoto and T. Suzuki, "Perfluorinated and Half-Fluorinated Rubrenes: Synthesis and Crystal Packing Arrangement," *J. Org. Chem.* **82**, 8111–8116 (2017).

1. Brønsted Acid-Initiated Formal [1,3]-Rearrangement Dictated by β-Substituted Ene-Aldimines[1)]

The rearrangement of ene-aldimines is a useful reaction for affording homoallylic amines. Despite their utilities in synthetic chemistry, the rearrangement for accessing homoallylic amines substituted at the 2-position remains elusive. In this study, the Brønsted acid-initiated formal [1,3]-rearrangement of ene-aldimines was developed to synthesize 2,4,4-substituted homoallylic amines that were otherwise inaccessible previously. Our study reveals an intermolecular pathway in which the rearrangement proceeds via a protonation-mediated 2-azaallenium cation.

2. Widely Dispersed Intermolecular Valence Bands of Epitaxially Grown Perfluoropentacene on Pentacene Single Crystals[2)]

Strong intermolecular electronic coupling and well-ordered molecular arrangements enable efficient transport of both charge carriers and excitons in semiconducting π-conjugated molecular solids. Thus, molecular heteroepitaxy to form crystallized donor–acceptor molecular interfaces potentially leads to a novel strategy for creating efficient organic optoelectronic devices via the concomitance of these two requirements. In the present study, the crystallographic and electronic structures of a heteroepitaxial molecular interface, perfluoropentacene (PFP, $C_{22}F_{14}$) grown on pentacene single crystals (Pn-SCs, $C_{22}H_{14}$), were determined by means of grazing-incidence X-ray diffraction (GIXD) and angle-resolved ultraviolet photoelectron spectroscopy (ARUPS), respectively. GIXD revealed that PFP uniquely aligned its primary axis along the $[1\bar{1}0]$ axis of crystalline pentacene to form well-crystallized overlayers. Valence band dispersion (at least 0.49 eV wide) was successfully resolved by ARUPS. This indicated a significant transfer integral between the frontier molecular orbitals of the nearest-neighbor PFP molecules.

References

1) C. Jongwohan, Y. Honda, T. Suzuki, T. Fujinami, K. Adachi and N. Momiyama, *Org. Lett.* **21**, 4991–4995 (2019).
2) Y. Nakayama, R. Tsuruta, N. Moriya, M. Hikasa, M. Meissner, T. Yamaguchi, Y. Mizuno, T. Suzuki, T. Koganezawa, T. Hosokai, T. Ueba and S. Kera, *J. Phys. Chem. Lett.* **10**, 1312–1318 (2019).