Sat. Mar 20, 2021

Webiner 1

Award Presentations, Special Lectures | Award Presentations, Special Lectures | Award Presentations, Special Lectures

[S01-2am] Award Presentations, Special Lectures

Chair:Minoru Osada, Takashi Hayashita
9:00 AM - 11:40 AM Webiner 1 (Online Meeting)

[S01-2am-01] Development of Artificial Receptors Based on Assembly of Metal Complex Units and Desymmetrization of Molecular Components

○Takashi Nakamura[1,2] (1. Fac. of Pure and Appl. Sci., Univ. of Tsukuba, 2. TREMS, Univ. of Tsukuba)

9:00 AM - 9:30 AM

[S01-2am-02] Construction of Kinetically Controlled Dynamic Host-Guest Systems

○Yoko Sakata[1] (1. Kanazawa University)

9:30 AM - 10:00 AM

[S01-2am-03] Innovations in Bio-Analytical Chemistry and Biomedical Engineering by Nanobiodevices

○Yoshinobu Baba[1,2] (1. Nagoya University, 2. QST)

10:00 AM - 10:50 AM

[S01-2am-04] Solid electrolytes based on inorganic chemical process and their application to all-solid-state batteries

○Akitoshi Hayashi[1] (1. Osaka Prefecture University)

10:50 AM - 11:40 AM

[S01-2am] Award Presentations, Special Lectures

Chair:Minoru Osada, Takashi Hayashita

Sat. Mar 20, 2021 9:00 AM - 11:40 AM Webiner 1 (Online Meeting)

[S01-2am-01] Development of Artificial Receptors Based on Assembly of Metal Complex Units and Desymmetrization of Molecular Components

○Takashi Nakamura[1,2] (1. Fac. of Pure and Appl. Sci., Univ. of Tsukuba, 2. TREMS, Univ. of Tsukuba)

9:00 AM - 9:30 AM

[S01-2am-02] Construction of Kinetically Controlled Dynamic Host-Guest Systems

○Yoko Sakata[1] (1. Kanazawa University)

9:30 AM - 10:00 AM

[S01-2am-03] Innovations in Bio-Analytical Chemistry and Biomedical Engineering by Nanobiodevices

○Yoshinobu Baba[1,2] (1. Nagoya University, 2. QST)

10:00 AM - 10:50 AM

[S01-2am-04] Solid electrolytes based on inorganic chemical process and their application to all-solid-state batteries

○Akitoshi Hayashi[1] (1. Osaka Prefecture University)

10:50 AM - 11:40 AM

Development of Artificial Receptors Based on Assembly of Metal Complex Units and Desymmetrization of Molecular Components

(*[1]Faculty of Pure and Applied Sciences, University of Tsukuba*, *[2]Tsukuba Research Center for Energy Materials Science (TREMS), University of Tsukuba*) ○Takashi Nakamura[1,2]

Keywords: Supramolecular Chemistry; Molecular Recognition; Metal Complexes; Desymmetrization; Macrocycles

Natural receptor proteins can bind substrates selectively at the pocket surrounded by multiple amino acid residues. Relatively weak intermolecular interactions, such as hydrogen bonds, are synergistically exerted during the recognition events. Meanwhile, it was difficult for synthetic receptors to achieve precise molecular binding by arranging various interaction moieties in an unsymmetrical manner. In this presentation, novel macrocyclic receptors developed based on two concepts, that is, (1) assembly of metal coordination sites (**Fig. 1a**), and (2) desymmetrization of homooligomers (**Fig. 1b**), are reported.

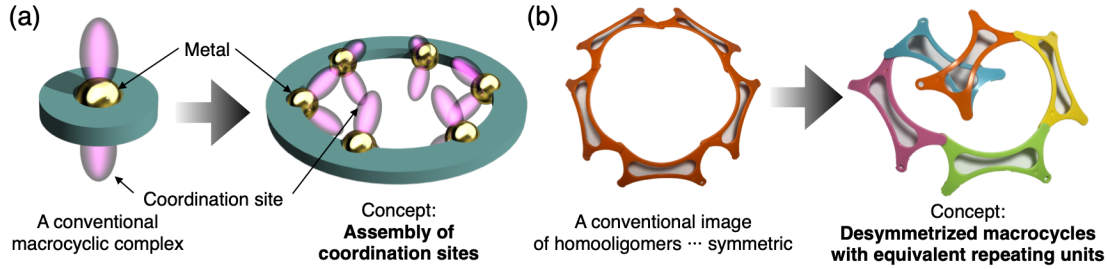


Figure 1. Approaches for macrocyclic receptors with precise molecular recognition. (a) Assembly of metal coordination sites. (b) Desymmetrization of homooligomers.

1. Hexapap[1]: Receptors that capture molecules via multipoint coordination (Fig. 2a)

A macrocyclic ligand with six pap moieties (N_2O tridentate chelate), hexapap, was designed and synthesized. Its hexanuclear zinc complex inwardly arranges multiple labile coordination sites for external molecules. The zinc complex captured two dicarboxylic acid molecules of a specific length in its cavity, and formed a unique wavy-stacked dimeric complex. The saddle-shaped deformation and dimerization realize the desymmetrization, and there are three different Zn-pap units in the dimeric complex. Utilizing this structural feature, the regulation of the guest-binding modes at specific metal coordination sites among the many present has been achieved utilizing acid/base as an external stimuli.

2. Bpytrisalen[2]: Spatial arrangement of different coordination sites (Fig. 2b)

A triangular macrocyclic ligand possessing three units each of the bpy (N_2 bidentate chelate) and salen (N_2O_2 tetradentate chelate), bpytrisalen, has been synthesized. The coordination sites of metals at the bpy are directed inward, while the ones at the salen are vertically pointing out of the macrocyclic plane. Selective anion binding onto the heteronuclear complex has been achieved utilizing the difference in coordination. Furthermore, the orthogonality in coordination has been utilized for the construction of double-decker complex.

3. Saloph-belt[3]: Belt-shaped macrocycles generated from a bis-armed bifunctional monomer (Fig. 2c)

A bis-armed bifunctional monomer bearing two salicylaldehyde units and one *o*-phenylenediamine unit has been designed. Oligomerization of the monomer resulted in the belt-shaped macrocyclic tetramer of saloph (N_2O_2 tetradentate chelate). Its zinc complex exhibited a remarkable selectivity regarding the encapsulation of fullerenes ($K_a(C_{70})/K_a(C_{60}) > 100$). The molecular recognition to distinguish the small difference in size has been realized utilizing the rigid belt-shaped scaffold.

4. Amide-cyclodextrin[4]: Multipoint hydrogen bond utilizing desymmetrized structure (Fig. 2d)

Cyclodextrin derivatives with amide groups directly attached to each pyranose ring were synthesized. The amide cyclodextrins show unique anion recognition properties by multipoint hydrogen bond. Especially, an amide-cyclodextrin derivative possessing seven bipyridyl (bpy) groups forms mononuclear complexes whose specific three bpy groups are linked in the *fac*-Λ configuration, and chiral recognition of amino acid anions has been achieved utilizing the distinctive amide groups arranged on the unsymmetrically fixed scaffold.

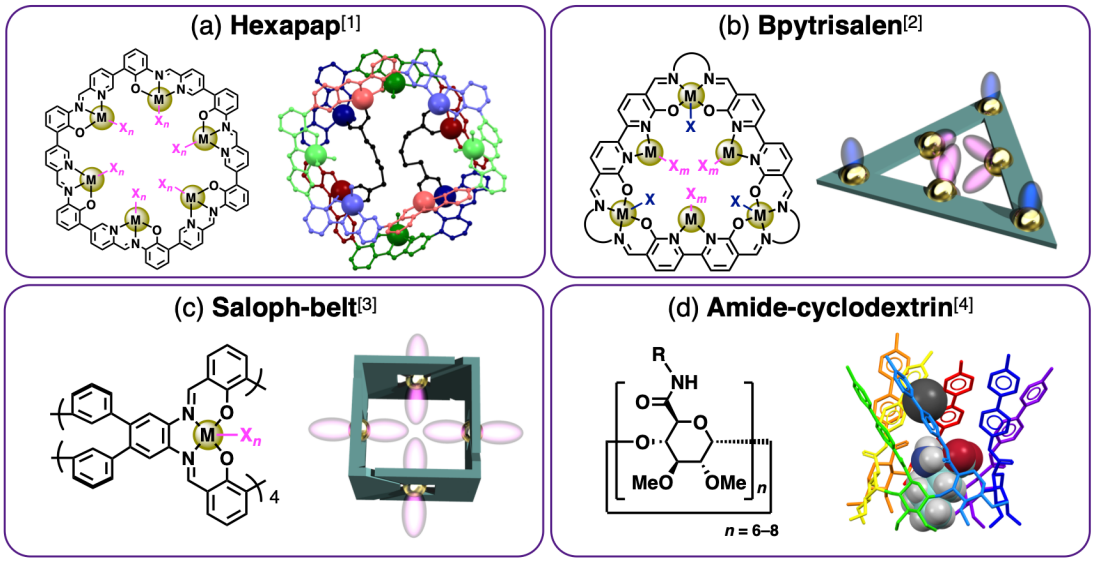


Figure 2. Macrocycles with unique molecular recognition properties developed based on the assembly of metal complex units and the desymmetrization of homooligomers.

References

[1] (a) T. Nakamura, Y. Kaneko, E. Nishibori, T. Nabeshima, *Nat. Commun.* **2017**, *8*, 129.
(b) A. Nagai, T. Nakamura, T. Nabeshima, *Chem. Commun.* **2019**, *55*, 2421.
(c) T. Nakamura, R. Y. Feng, T. Nabeshima, *Eur. J. Inorg. Chem.* DOI: 10.1002/ejic.202000882
[2] T. Nakamura, Y. Kawashima, E. Nishibori, T. Nabeshima, *Inorg. Chem.* **2019**, *58*, 7863.
[3] T. Nakamura, S. Tsukuda, T. Nabeshima, *J. Am. Chem. Soc.* **2019**, *141*, 6462.
[4] (a) T. Nakamura, S. Yonemura, T. Nabeshima, *Chem. Commun.* **2019**, *55*, 3872.
(b) S. Yonemura, T. Nakamura, T. Nabeshima, *Chem. Lett.* **2020**, *49*, 493.
(c) T. Nakamura, S. Yonemura, S. Akatsuka, T. Nabeshima, *Angew. Chem. Int. Ed.* DOI: 10.1002/anie.202011348

Construction of Kinetically Controlled Dynamic Host-Guest Systems

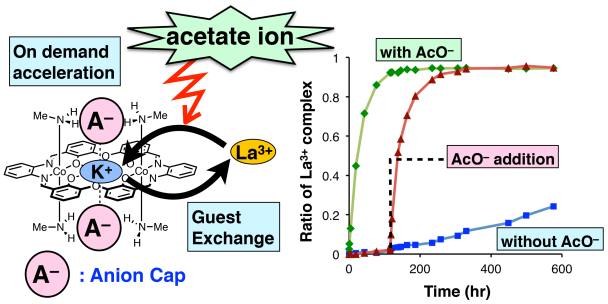
([1]*Graduate School of Natural Science and Technology, Kanazawa University*, [2]*WPI-Nano Life Science Institute, Kanazawa University*) ○Yoko Sakata,[1,2]

Keywords: Supramolecular Chemistry, Metal Coordination, Kinetic Control, Host-Guest Chemistry, Self-Assembly

The recent advances in supramolecular chemistry, which deals with noncovalent interactions between molecules, have allowed numerous studies of molecular recognition behaviors and self-assembly processes. While they are generally thermodynamically controlled events, kinetic control of such processes is essential for the development of new supramolecular functional systems. In this study, we created new responsive systems whose functions can be kinetically controlled[1-6,9] and synthesized a new class of kinetically-stable self-assembled metal complexes.[7-8]

1. Development of Kinetically Controlled On-Demand Molecular Recognition System

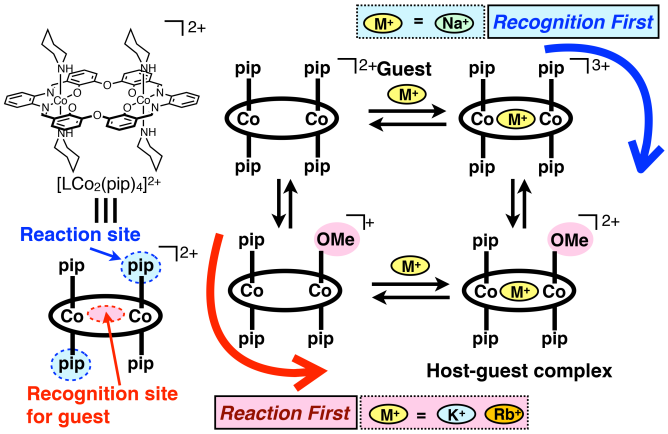
The control of kinetic parameters such as guest inclusion/exchange rate is important for the development of new host-guest system in which a desired function is driven by guest recognition. However, the strategies for the precise control of these kinetic processes have rarely been reported. Here we succeeded in on-demand acceleration of guest exchange rates of a cationic cobalt(III) dinuclear macrocyclic metallohost by the replacement of the counteranions. The newly synthesized cationic cobalt(III) macrocyclic metallohost, $[LCo_2(CH_3NH_2)_4](OTf)_2$ encapsulated alkali metal, alkaline-earth metal, and lanthanide cations in such a way that the counteranions capped the cavity openings. The guest inclusion rates highly depended on the guest cations or anion caps. We also found that the replacement of the triflate anions by acetate anions drastically accelerated the guest exchange rates.



2. Unveiling the Molecular Recognition Mechanism of Multinuclear Metallohosts

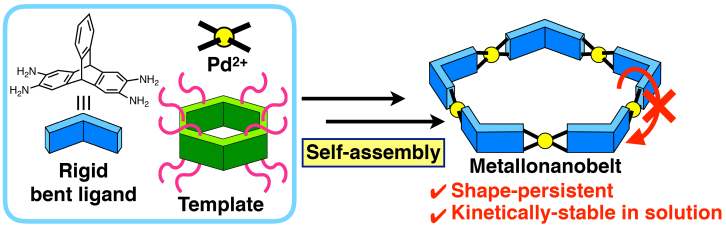
Molecular recognition processes coupled to conformational changes in biomolecules are generally classified into two types of mechanisms, “induced fit” and “conformational selection”. Even for artificial host-guest system, host-guest binding sometimes triggers the subsequent chemical reactions of the host framework. Although it is sometimes difficult to differentiate the mechanisms from the alternative one in which the guest binding occurs after the reaction, it is important to distinguish the two mechanisms when we develop new molecules based on time-dependent functions. Here we investigate the molecular

recognition mechanism of a new macrocyclic dinuclear cobalt(III) metallohost, $[LCo_2(pip)_4](OTf)_2$, (pip = piperidine), which can take up a guest cation (Na^+, K^+, and Rb^+) into its cavity causing concomitant exchange of the axial piperidine Detailed kinetic analysis revealed that the recognition pathway can be switched by changing the guest cations. Control of molecular recognition behaviors by ligand exchange on cobalt(III) ions will be also presented.



3. Construction of Kinetically Stable Metallonanobelt Prepared by Template-Directed Self-Assembly Process

Shape-persistent belt-shaped macrocyclic compounds, which have no rotatable single bond, have attracted much interest due to their unique structural and electronic features. However, there are only a limited number of such macrocyclic complexes. Here we constructed new sufficiently inert shape-persistent molecular belt, prepared by reversible metal-assisted self-assembly processes. The shape-persistent belt-shaped metallomacrocycle, metallonanobelt, was synthesized by the self-assembly of a triptycene-based rigid bent ligand **L** and square planar Pd^{2+}. Particularly, the pentamer metallonanobelt was selectively formed by the complexation of **L** with Pd^{2+} in the presence of pillar[6]arene derivative **P6** having triethylene glycol chains as a template. The guest free pentamer was also successfully isolated and it was found to be remarkably stable towards size-conversion in solution. We also succeeded in the functionalization of metallonanobelt using quinoxaline formation.



1) Y. Sakata, C. Murata, S. Akine, *Nature Commun.* **2017**, *8*, 16005. 2) Y. Sakata, M. Tamiya, M. Okada, S. Akine, *J. Am. Chem. Soc.* **2019**, *141,* 15597-15604. 3) Y. Sakata, M. Okada, M. Tamiya, S. Akine, *Chem. Eur. J.* **2020**, *26*, 7595-7601. 4) Y. Sakata, M. Okada, S. Akine, *Chem. Eur. J. in press*. 5) Y. Sakata, S. Chiba, M. Miyashita, T. Nabeshima, S. Akine, *Chem. Eur. J.* **2019**, *25*, 2962-2966. 6) Y. Sakata, S. Kobayashi, S. Akine, *Chem. Commun.* **2017**, *53*, 6363-6366. 7) Y. Sakata, R. Yamamoto, D. Saito, Y. Tamura, K. Maruyama, T. Ogoshi, S. Akine, *Inorg. Chem.* **2018**, *57*, 15500-15506. 8) Y. Sakata, Y. Furukawa, S. Akine, *Tetrahedron Lett.* **2019**, *60,* 2049-2053. 9) Y. Sakata, T. Ogura, S. Akine, *Chem. Commun.* **2020**, *56*, 8735-8738. 10) For a review on kinetic control of host-guest binding, see: S. Akine, Y. Sakata, *Chem. Lett.* **2020**, *49*, 428-441.

Innovations in Bio-Analytical Chemistry and Biomedical Engineering by Nanobiodevices

([1]*Institute for Nano-Life-Systems, Institutes of Innovation for Future Society, Nagoya University,* [2]*Institute of Quantum Life Science, National Institutes for Quantum and Radiological Science and Technology(QST)*) ○Yoshinobu Baba[1,2]
Keywords: Nanobiodevices; Bio-Analytical Chemistry; Biomedical Engineering

The development of biomolecular analytical technology for omics research is highly required to realize a healthy and long-lived society and additionally we need to develop the analytical technologies for cells, bacteria, viruses, exosomes, organs, small animals, and humans.

We succeeded in developing nanostructures of about 1 nm to several tens of nm that can be applied to bio-analytical chemistry. In particular, we constructed a new nanostructure that can experimentally achieve the nonequilibrium transfer and entropy barrier transfer of biomolecules in nanostructures, which was theoretically predicted to be essential for ultrahigh speed biomolecule analysis. By using these nanostructures, the fastest DNA analysis was achieved in 1 to 100 milliseconds and millions to 10 million times faster than before. Furthermore, we developed three-dimensional nanowires for ultrafast separation of not only DNA but also RNA and protein molecules.

We have developed nanobiodevices that can analyze cells, bacteria, viruses, exosomes, and bioaerosols as well. With the development of micro- and nanopores, millisecond level analysis for a single virus, bacterium, and cell was realized by measuring the pA level ultrasmall current when a single virus, bacterium, and cell passes through the micro- and nanopores. Furthermore, we developed separation technologies for cancer cells, bacteria, viruses and exosomes from body fluids (blood, urine, saliva, etc.) with ultra-high efficiency by precisely controlling and constructing the nanowire structure.

We succeeded in developing a nanowire structure that can interact with exosome surface membranes with high efficiency in order to realize early-stage diagnosis of diseases. About several hundred million to one billion nanowires were fabricated on a small chip and adsorbed 10 to 100 exosomes on each nanowire. With this nanowire device, 99% or more of 1 billion to 100 billion exosomes present in 1 mL of body fluid such as urine can be isolated, and all about 2,500 types of human miRNA contained in exosomes can be detected with high sensitivity. In addition, clinical studies conducted large-scale analysis of urinary exosome miRNA in hundreds of healthy individuals and patients with cancer and lifestyle-related diseases. Big data analysis by machine learning resulted in minimally invasive early-stage diagnosis of 6 types of cancer, diabetes, dementia, and arrhythmia.

We have developed a microfluidic bridge circuit that can measure extremely small currents to identify pathogens and drug-resistant bacteria by micro- and nanopores. This circuit efficiently reduced background noise to about 1/10,000 of the conventional level and

realized all detection with the same device, from viruses of about 100 nm to bacteria cells of about 10 μm. Furthermore, we machine-learned clinical strains owned by Nagoya University School of Medicine as teacher data, and demonstrated that pathogens can be identified with an accuracy of 90% or more. By applying an electric field to the micro- and nanopores, the cell wall of the bacterium is punctured, and the ions inside the bacterium are released into the pores, resulting in changes in the measured current values. We have demonstrated that even drug-resistant bacteria, which were extremely difficult to identify in the past, can be identified with high accuracy.

We have developed a new nanoparticle synthesis technology for quantum dots and quantum sensors, which have high cell safety for iPS cells and other types of cells, in order to realize iPS cell regenerative medicine. These nanoparticles have extremely high light transmission in the living body, since they emit fluorescence in the near-infrared light region. We have also developed a new method for introducing these nanoparticles into cells with high efficiency and safety. With these quantum dots and quantum sensors, we have succeeded in labeling stem cells with high efficiency and in real-time *in vivo* imaging of single cells in live animal organs using a multi-photon microscope. Furthermore, we were the first in the world to succeed in imaging the regenerative ability of stem cells using a quantum sensor.

In addition to *in vivo* imaging of human iPS cells, we realized *in vivo* imaging of iPS cell differentiated cells, such as nerve cells for Parkinson's disease treatment, pituitary hormone-producing cells, corneal endothelial/corneal epithelial cells for ophthalmic treatment, knee joint chondrocytes, and lung cells for bioengineered lung. This technology is accelerating the practical application of regenerative medicine by succeeding in developing an *in vivo* safety evaluation technology for iPS cell differentiated cells, which is indispensable for obtaining approval for regenerative medicine.

In collaboration with NIH and Nagoya University School of Medicine, we have developed a fusion technology of quantum materials and photoimmunotherapy in order to improve the effect of cancer photoimmunotherapy. This technique was applied to photoimmunotherapy for small cell lung cancer and malignant pleural mesothelioma.

1)T. Yasui, et al., *ACS Nano,* 2013, 7, 3029-3035. 2) T. Yasui, et al., *Nano Lett.*, 2015, 15, 3445- 3451. 3) T. Yasui, et al., *Scientific Reports,* 2016, 6, 31642. 4) H. Yasaki, et al. *J. Am. Chem. Soc*., 2017, 139, 14137-14142. 5) T. Yasui, et al., *Science Advances,* 2017, 3, e1701133. 6) Y. Ogihara, et al., *Scientific Reports,* 2017, 7, 40047. 7) Q. Wu, et al., *Scientific Reports,* 2017, 7, 43877. 8) H. Yasaki, et al., *ACS Sensors*, 2018, 3, 574-579. 9) T. Yasui, et al., *ACS Nano*, 2019, 13, 2262–2273. 10) C. Wang, et al., *Nano Lett.*, 2019, 19, 2443-2449. 11) M.F. Serag, et al., *ACS Nano*, 2019, 13, 8155-8168. 12) Y. Isobe, et al., *EBioMedicine*(Published by THE LANCET), 2020, 52, 102632. 13) H. Yukawa, et al., *Nanoscale Advances,* 2020, 2, 1859-1868. 14) Z. Xixi, et al., *Nano Lett.*, 2020, 20, 599-605. 15) Y. Nishinaga, et al., *Cells,* 2020, 9, 1019. 16) J. Liu, et al., *Comm. Mat.,* 2020, 1, 58. 17) A. Arima, et al., *ACS Sensors,* 2020, 5, 3398-3403.

固体電解質創製にむけた無機化学プロセスと全固体電池への応用

（阪府大院工）○林　晃敏

Solid electrolytes based on inorganic chemical process and their application to all-solid-state batteries (*Graduate School of Engineering, Osaka Prefecture University*) ○Akitoshi Hayashi

The development of an all-solid-state battery is eagerly desired for the realization of a carbon-free society. Formation of solid-solid interfaces in all-solid-state batteries and synthesis of solid electrolytes with both high Li^+ or Na^+ conductivity and good formability are important. By using various inorganic chemical processes including solid-phase, gas-phase, and liquid-phase ones, sulfide, oxide, and nitride solid electrolytes suitable for all-solid-state batteries have been synthesized. In particular, the sulfide $Na_{2.88}Sb_{0.88}W_{0.12}S_4$ electrolyte exhibits a high Na^+ conductivity of 3.2×10^{-2} S cm^{-1} at room temperature. In addition, sulfide electrolytes are prepared via a liquid-phase process and their precursor solutions are useful for close contact with active material particles. All-solid-state Na/S cells with the Na_3SbS_4 electrolyte shows an almost full reversible capacity at 25ºC. The Li_3BN_2 nitride and the Li_3BO_3-Li_2SO_4-Li_2CO_3 oxide electrolytes, which have the same excellent formability as sulfide electrolytes, are mechanochemically prepared. All-solid-state cells with amorphous $LiCoO_2$-Li_2SO_4 positive electrodes with good formability and mixed conductivity show better capacity retention.

Keywords : Solid Electrolyte; All-Solid-State Battery; Inorganic Chemical Process; Glass

脱炭素社会の実現に向けて、次世代蓄電池の一つである全固体電池の開発が切望されている。この電池を実現するためには、アルカリ金属イオン(Li^+, Na^+)が高速に伝導できる優れた固体電解質の創製と、電極活物質との広く、密接した固体界面の形成プロセスの開発が重要である[1]。固相法や気相法、液相法などの様々な無機化学プロセスを用いることによって、全固体電池に適した硫化物、酸化物、窒化物固体電解質を作製することができる。固体電解質の最有力候補として、高い導電率と優れた成形性を併せ持つ硫化物材料が挙げられるが、例えば固相法の一つであるメカノケミカル法を用いて作製した $Na_{2.88}Sb_{0.88}W_{0.12}S_4$ が、室温で 3.2×10^{-2} S cm^{-1} の極めて高い Na^+伝導度を示すことを見いだした[2]。この電解質は水分に曝しても硫化水素がほとんど発生しないため、安全性の観点からも優れている。また Na_3SbS_4 をベースとする電解質は水を溶媒とした液相法を用いて合成できる[3]。この電解質の水溶液で表面コーティングして得られた硫黄正極を用いた全固体 Na/S 電池は室温で二次電池として作動し、高容量と優れたサイクル特性を示した[4]。またメカノケミカル法により作製した Li_3BN_2 窒化物電解質[5]や Li_3BO_3-Li_2SO_4-Li_2CO_3 系酸化物電解質[6]は、硫化物に類似した優れた成形性をもつことを明らかにした。さらに $LiCoO_2$ などの正極活物質と Li_2SO_4 をメカノケミカル処理することによって、優れた成形性と混合伝導性をもつアモルファス正極活物質が得られ、酸化物型全固体電池へ適用できることを示した[7]。

1) A. Hayashi *et al., Front. Energy Res*. **2016**, 4, 25; 2) A. Hayashi *et al.*, *Nat. Commun*. **2019**, 10, 5266; 3) S. Yubuchi *et al., J. Mater. Chem. A* **2020**, 8, 1947; 4）T. Ando *et al., Electrochem. Commun.* **2020**, 116, 106741; 5) M. Shigeno *et al., Solid State Ionics* **2019**, 339, 114985; 6）K. Nagao *et al., J. Power Sources* **2019**, 424, 215; 7) K. Nagao *et al, Adv. Mater. Interfaces* **2019**, 6, 1802016.