

## **PRESS RELEASE**

Source: Kanazawa University, Institute for Molecular Science, SOKENDAI

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Kanazawa University research: Watching Molecules Change Shape in Slow Motion

(Kanazawa, 7 July 2026) Researchers at the Nano Life Science Institute (WPI-NanoLSI) at Kanazawa University, Institute for Molecular Science and SOKENDAI have uncovered the hidden mechanism behind a molecular switch—a molecule that can change between different structural states in response to a chemical signal. Their study, published in the *Journal of the American Chemical Society*, reveals how molecules can gradually switch between alternative states, a process that could help scientists design future molecular machines, smart materials, and molecular information technologies.

To make the discovery, Shigehisa Akine and colleagues created a specially designed molecular cage that changes shape unusually slowly. This allowed them to observe, for the first time, the sequence of molecular events that occurs after the molecule receives a chemical input. The study provides one of the clearest views yet of how molecular recognition triggers structural change and demonstrates that the response speed of a molecular system can itself be engineered through molecular design.

### **Building smarter molecular systems**

Responsive molecular materials are attracting increasing attention for their potential to sense, process, and respond to changes in their environment. Such systems are considered important building blocks for future molecular machines, molecular information technologies, and other next-generation nanoscale devices.

A key challenge in designing these systems is understanding exactly how molecular switching occurs. Many molecules can exist in multiple stable states and change between them when exposed to external stimuli such as light, heat, or chemical signals. However, the triggering event is often so rapid that only the initial and final states can be observed, leaving the molecular pathway connecting them hidden from view.

To overcome this challenge, the Kanazawa University team designed a molecular cage in which both guest uptake and structural rearrangement occur unusually slowly, allowing the entire switching process to be followed in real time.

### **A molecular cage that changes its handedness**

The researchers synthesized a triple-helical cobalt metallocryptand—a cage-shaped molecule formed from three intertwined molecular strands surrounding an internal cavity.

The molecule exists in two mirror-image forms, known as right-handed (*P*) and left-handed (*M*) structures. In solution, these forms slowly interconvert, with the right-handed form normally being the more abundant.

The molecular cage was specifically designed with flexible bridging ligands that partially seal its entrances. This closed-cage architecture dramatically slows the movement of guest ions into and out of the cavity, transforming a normally rapid process into one that unfolds over several hours.

### **Watching molecular switching in real time**

When cesium ions were added to the solution, the researchers observed a remarkable transformation.

Over time, the molecular population gradually shifted from predominantly right-handed forms to predominantly left-handed forms. Because the switching process occurred slowly, the researchers were able to monitor the intermediate stages using nuclear magnetic resonance (NMR) and circular dichroism (CD) spectroscopy. X-ray crystallography and theoretical calculations were used to characterize the initial and final molecular states. Together, these complementary approaches allowed the team to follow the switching process in real time, capture structural snapshots of the molecular cage, and explain why the guest ion preferentially stabilized one molecular state over another.

### **A surprising mechanism**

Chemists have long debated how guest-induced structural changes occur. In one model, known as the induced-fit model, a guest molecule first binds to a host structure, triggering a conformational change. In the alternative conformational selection model, multiple structural states already exist, and the guest selectively binds to the state it prefers.

The Kanazawa University team was able to resolve this question directly. Rather than binding to the dominant right-handed form and then triggering a structural change, cesium ions were found to preferentially bind to the less abundant left-handed form already present in solution. The results demonstrate that the switching process

proceeds primarily through a conformational-selection mechanism rather than a classical induced-fit pathway.

### **The hidden pathway behind the switch**

Once the cesium ion is trapped inside the molecular cage, the left-handed form becomes significantly more stable. This progressively shifts the molecular population toward the new state, ultimately reversing the balance between right-handed and left-handed structures. The overall switching process, therefore, emerges from a subtle interplay between guest recognition, structural dynamics, and molecular equilibrium.

### **Opposite signals, opposite responses**

While cesium ions drive the system toward the left-handed state, chloride ions favor the right-handed form by interacting with binding sites on the exterior of the molecular cage. This ability to generate distinct responses to distinct chemical signals highlights the potential of such systems as intelligent, responsive materials capable of processing environmental information.

### **Toward smart molecular architectures**

“Most molecular switches operate too quickly for us to see how they actually work,” says Professor Shigehisa Akine. “By designing a system in which guest uptake and structural switching occur on similar time scales, we were able to uncover the hidden pathway that connects them. We believe these principles will be valuable for the rational design of future smart molecular architectures, including responsive materials, molecular machines, and systems capable of storing and processing molecular information.”

Beyond revealing a previously hidden switching pathway, the study demonstrates that the response speed of a molecular system can itself be engineered through molecular design—a capability that may prove important in the development of future smart molecular architectures.

### **Key Concepts and Methods**

Chirality – the property of existing in right- and left-handed forms.

Conformational selection – a mechanism in which a guest binds preferentially to one of several pre-existing molecular structures.

Nuclear magnetic resonance (NMR) spectroscopy and circular dichroism (CD) spectroscopy – complementary techniques used to monitor the intermediate stages of the molecular switching process.

X-ray crystallography, spectroscopy, and theoretical modeling – complementary techniques used to reveal how the molecular switching process occurs.

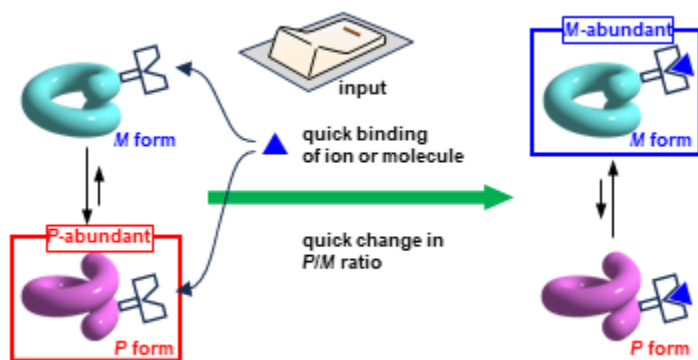


Fig. 1. Typical guest-induced inversion between the right-handed (P) and left-handed (M) forms. Guest molecules or ions bind rapidly, making the chirality inversion appear instantaneously. As a result, the intermediate processes have been difficult to observe and remain poorly understood.

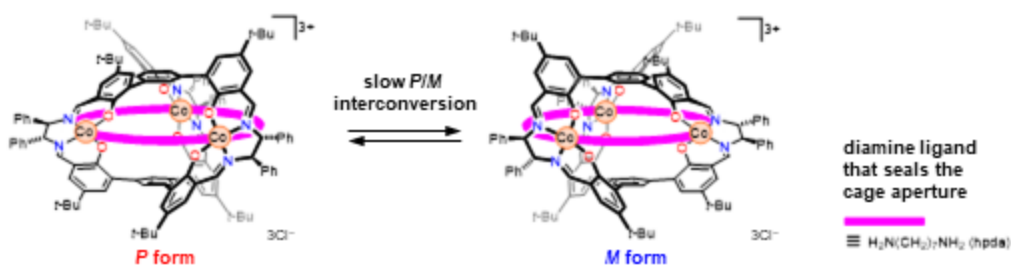


Fig. 2. Structure of the triple-helical closed-cage molecule. Slow uptake of cesium ions ( $\text{Cs}^+$ ) into the internal cavity is accompanied by a gradual shift in the ratio of the right-handed (P) and left-handed (M) forms.

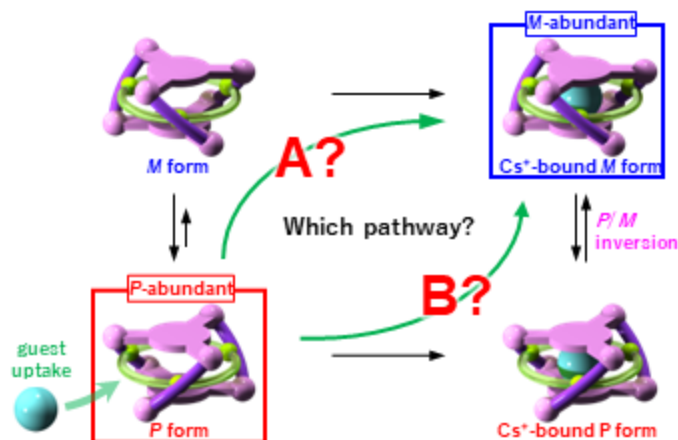


Fig. 3. Changes in the ratio of the right-handed (*P*) and left-handed (*M*) forms of the triple-helical closed-cage molecule during guest uptake. Because of the closed-cage structure, guest binding (the “input”) occurs slowly, and the *P/M* interconversion is also slow. This allows the intermediate states to be analyzed, enabling distinction between the two possible pathways (A and B). Kinetic analysis revealed that, in the present system, the pathway proceeds via initial guest uptake by the less abundant *M* form (pathway A).

## Reference

Interplay between Slow Chirality Inversion and Slow Guest Uptake in a Triple-Helical Closed-Cage Metallocryptand, Sk Asif Ikbal, Masahiro Ehara, and Shigehisa Akine, *J. Am. Chem. Soc.*, published online on 29 June 2026.

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## **Contact**

Motoko YASUHARA

Project Planning and Outreach, NanoLSI Administration Office

Nano Life Science Institute, Kanazawa University

Email: [nanokoho@adm.kanazawa-u.ac.jp](mailto:nanokoho@adm.kanazawa-u.ac.jp)

Kakuma-machi, Kanazawa 920-1192, Japan

National Institutes of Natural Sciences, Institute for Molecular Science, Research  
Enhancement Strategy Office, Public Relations

Email: [press@ims.ac.jp](mailto:press@ims.ac.jp)

## **Nano Life Science Institute (WPI-NanoLSI), Kanazawa University**

Understanding nanoscale mechanisms of life phenomena by exploring “uncharted nano-realms.” Cells are the basic units of life. At NanoLSI, researchers develop nanoprobe technologies that enable direct imaging, analysis, and manipulation of biomolecules such as proteins and nucleic acids inside living cells. By visualizing these processes at the nanoscale, the institute seeks to uncover fundamental principles of life and disease.

<https://nanolsi.kanazawa-u.ac.jp/en/>

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The WPI program was launched in 2007 by Japan’s Ministry of Education, Culture, Sports, Science and Technology (MEXT) to foster world-class research centers with outstanding research environments. WPI centers enjoy a high degree of autonomy, enabling innovative management and global collaboration. The program is administered by the Japan Society for the Promotion of Science (JSPS).

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### **About Kanazawa University**

Founded in 1862 in Ishikawa Prefecture, Kanazawa University is one of Japan's leading comprehensive national universities with a history spanning more than 160 years. With campuses at Kakuma and Takaramachi-Tsuruma, the university upholds its guiding principle of being "a research university dedicated to education, while opening its doors to both local and global society."

Internationally recognized for its research institutes, including the Nano Life Science Institute (WPI-NanoLSI) and the Cancer Research Institute, Kanazawa University promotes interdisciplinary research and global collaboration, driving progress in health, sustainability, and culture.

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