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RESEARCH NEWS STORY

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Cooperative Intermolecular Interactions Regulate Supramolecular Polymer Assembly

This study reports the concerted action of distinct noncovalent interactions in the cooperative self-assembly of higher-order supramolecular polymers

Biological supramolecular structures exhibit both lateral and longitudinal interactions, rendering the structure responsive to changes. Thus far, lateral interactions of synthetically assembled supramolecular polymers have only been elucidated. Inspired by microtubules, this study reports cooperative self-assembly of aryl barbiturate molecules into helical coils, driven by the concerted action of noncovalent lateral and longitudinal interactions. These synthetic polymers uniquely alter with changes in temperature. This conceptual advancement will influence future material designs of next-generation polymers.

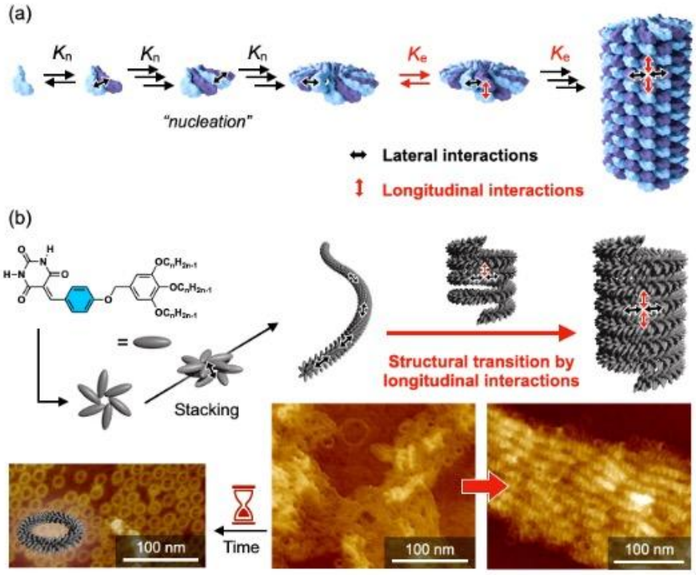

Image title: Self-assembly guided by cooperativity arising from helix structure and structural transition in response to solution temperature
Image caption: (a) Cooperative self-assembly of biological supramolecular polymers. (b) Schematic illustration of cooperative self-assembly in this system.
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Supramolecular chemistry involves the study of self-assembly of discrete molecules that are used to build functional large structures. Often, these molecules are allowed to self-assemble into one-dimensional polymeric structures (supramolecular polymers or SPs) in a suitable environment, and the dynamic molecular interactions are noted for tweaking the environment and improving the features of the resulting SPs. They are being explored as the next-generation polymeric materials with applications in electronics, soft-robotics, nanofabrication, and biomedical fields.

In living systems, biological supramolecules, such as microtubules that form the cytoskeleton, play essential roles. Microtubules assemble in a helical fashion, which allows lateral (circumferential) interactions between neighboring proteins as well as longitudinal (helical axis) interactions between non-neighboring protein molecules, when one helical turn comes in contact with the next. The cooperativity between these lateral and longitudinal interactions enables the efficient regulation of assembly and disassembly, allowing for a rapid response to external stimuli. Such helical self-assembly, reminiscent of biomolecular architectures, remains largely unexplored in material science at the mesoscopic scale (intermediate between nanometer and micrometer).

Deciding to explore this less-developed domain, Assistant Professor Hiroki Hanayama, along with Professor Shiki Yagai from the Graduate School of Science and Engineering, Chiba University, Japan, set out to tweak intermolecular interactions between aryl barbiturate molecules. They teamed up with colleagues Mr. Itsuki Tajima, Mr. Shuhei Yamashita, and Dr. Takumi Aizawa, all from the Graduate School of Engineering, Chiba University. This study, made available online on November 06, 2025, and published in Volume 147, Issue 46 of *Journal of the American Chemical Society* on November 19, 2025, reveals helicoidal SPs of aryl barbiturate molecules that exhibit cooperative self-assembly, driven by two distinct noncovalent interactions.

Explaining the premise of their study, Dr. Hanayama says, *"So far, one-dimensional assemblies of synthetic molecules have reported SPs held together only by lateral interactions that do not exhibit cooperative assembly based on higher order structures, similar to those seen in microtubules."* Prof. Yagai's team has long studied synthetic π-conjugated aryl barbiturate monomers that rely on the π-component and/or hydrogen bonding for the construction of SPs. These monomers also have peripheral alkyl chains that enhance the solubility of the resulting SPs and build interchain interactions, aiding bundling and polymerization.

Prior studies have shown that barbiturate-based hydrogen-bonded monomers can acquire rosettes, cyclic hexamers. Further, the rosettes could intrinsically curve to stack into helicoidal SPs or supramolecular ring structures. Based on this finding, the team set out to mimic the microtubule assembly by prompting longitudinal interactions between non-neighboring molecules of the helicoidal chain. Interestingly, a counterintuitive approach of deliberately weakening the lateral interactions between neighboring molecules resulted in activating the desired cooperative longitudinal interactions.

It is the concerted action of two distinct noncovalent interactions, namely, the π–π stacking between adjacent molecules and the alkyl side-chain interaction between adjacent helicoidal loops, that drives the cooperative self-assembly of SP. The key finding of this study is that the intentional minimizing of the π-conjugated core in the monomer lowers the strength of the π–π stacking interactions, promoting the alkyl−alkyl interactions, thus favoring the formation of extended helicoidal structures. The authors of this study used atomic force microscopy to show that the self-assembly of SP and its structural characteristics altered in response to changes in temperature and concentration.

Notably, the interloop alkyl−alkyl interaction weakened at high temperatures, inducing a transition from helicoidal structures to linear fibers. The fibers, when maintained for an extended period, gradually convert into a ring structure. Such unique assembly and disassembly behavior is fundamentally different from those of conventional SPs and will be useful in the design of highly sensitive materials that respond to subtle environmental changes.

Sharing his vision for the future, Dr. Hanayama notes, *"This concept has the potential to fundamentally transform how molecular materials are designed. Rather than simply assembling molecules to form structures, future design strategies will focus on programming interactions across multiple dimensions to achieve cooperativity. In other words, this discovery may lay the technological foundation for next-generation soft robotics and precise nanofabrication technologies."*

With the rapid advances in computational chemistry, the incorporation of the sophisticated cooperativity used by living systems into the design principles of polymer materials will enable the realization of SPs with multidimensional intermolecular interactions. This conceptual leap is set to revolutionize material design at the mesoscale.

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About Assistant Professor Hiroki Hanayama from Chiba University, Japan

Dr. Hiroki Hanayama received his Ph.D. in Chemistry in 2021 from the Department of Chemistry, The University of Tokyo, Japan. In 2023, he joined the Graduate School of Engineering, Chiba University, Japan, as an Assistant Professor. His research interests range from supramolecular chemistry, transmission electron microscopy, nanotechnology, and nanostructural chemistry. He has published over 20 research articles in leading scientific journals and has been awarded multiple JSPS grants towards his research.

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