Self-assembled dodecahedral nanostructure features 60 metal ions and peptide ligands

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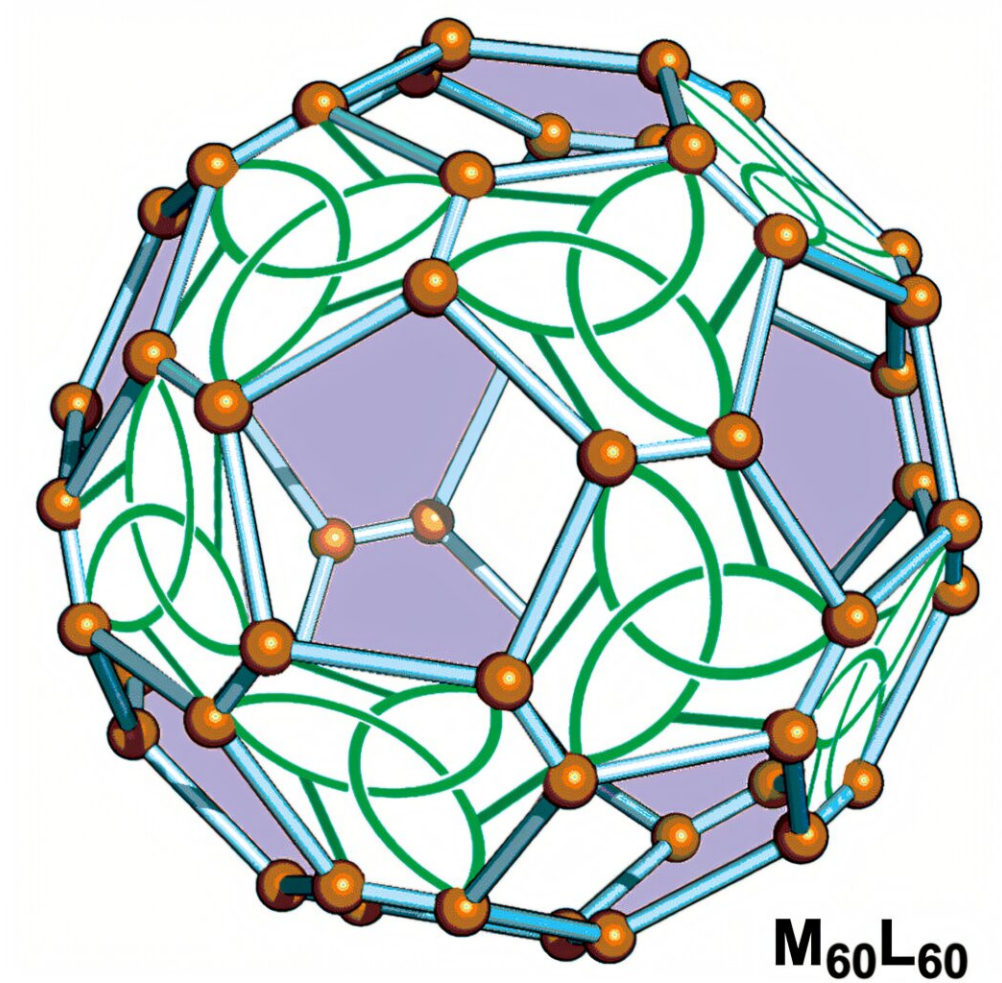


- **Dodecahedral spatial graph** (60-crossings)
- **Goldberg polyhedron** ($T = 3$)

Graphical abstract. Credit: *Chem* (2025). DOI: 10.1016/j.chempr.2025.102555

Controlling the topology and structure of entangled molecular strands is a key challenge in molecular engineering, particularly when attempting to create large nanostructures that mimic biological systems. Examples found in nature, such as virus capsids and cargo proteins, demonstrate the remarkable potential of such architectures. However, methods for constructing large hollow nanostructures with precise geometric control have remained elusive—until now.

A research team led by Associate Professor Tomohisa Sawada from the Institute of Science Tokyo, Japan, has successfully constructed a molecular spherical shell structure with the geometric topology of a regular dodecahedron.

This groundbreaking work, which was published online in the journal *Chem*, describes how the researchers created this large structure, bearing an outer diameter of 6.3 nanometers, through the entanglement of peptides with metal ions.

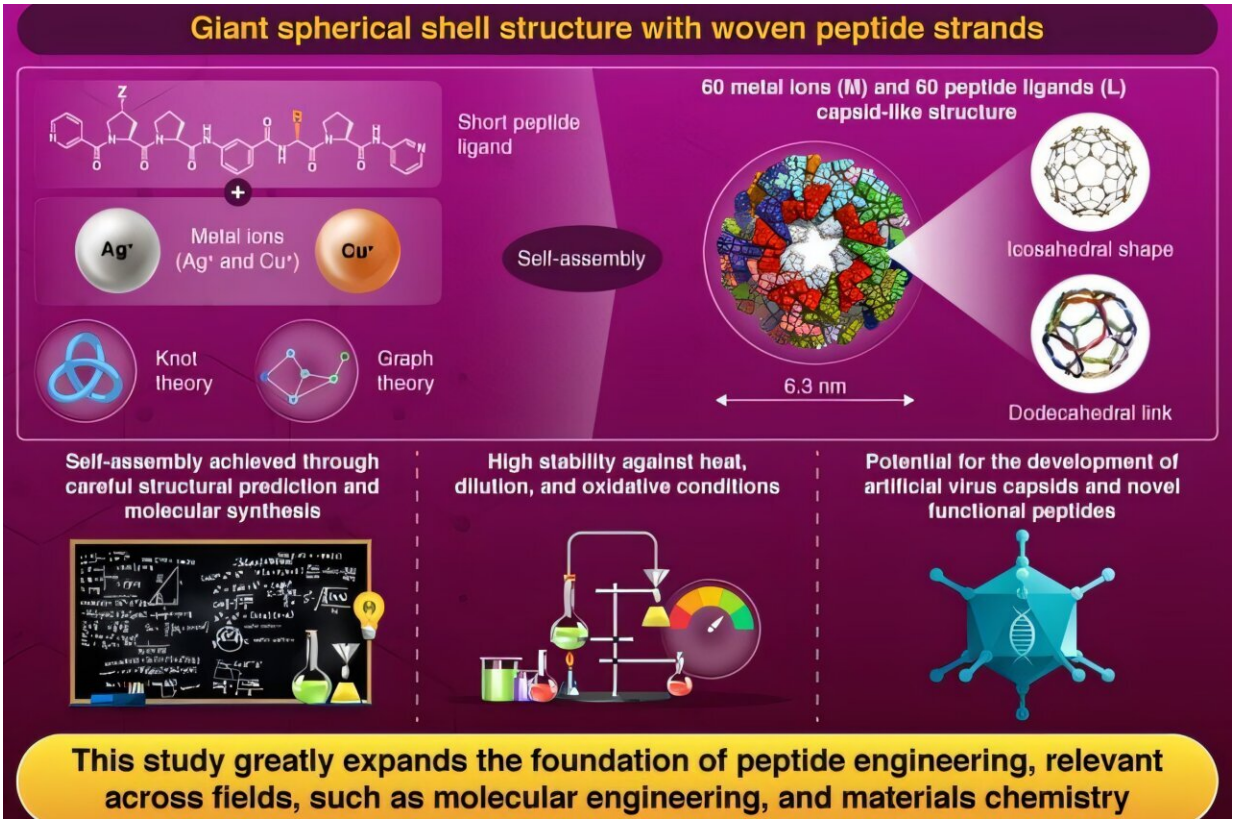
"The synthesis of this highly complex structure was based on geometric considerations and predictions, leading to the proposal of a new concept: the geometric control of chemical structures," explains Sawada.

The team's approach combined two distinct mathematical frameworks, namely knot theory and graph theory, to predict and then achieve the self-assembly of an unprecedented dodecahedral link with an entanglement of 60 crossings, composed of 60 metal ions and 60 peptide ligands (or $M_{60}L_{60}$).

The researchers had previously created smaller structures with

tetrahedral and cubic links. However, a more complex dodecahedral link emerged after they introduced further modifications to the peptide sequence during attempts to functionalize $M_{24}L_{24}$, a smaller cubic link.

X-ray crystallographic analysis revealed that the resulting $M_{60}L_{60}$ metal-peptide shell contains an inner cavity of approximately 4.0 nanometers (approximately 34,000 $Å^3$), which is large enough to encapsulate macromolecules such as proteins or nanomaterials.



Researchers develop a large dodecahedral structure through the self- assembly of metal ions and peptides, with potential implications in drug delivery systems and molecular transportation. Credit: Dr. Tomohisa Sawada / Institute of Science Tokyo, Japan

Beyond its impressive structural complexity, the $M_{60}L_{60}$ shell exhibited remarkable stability against heat, dilution, and oxidative conditions, which the researchers attributed to its unique entangled network structure.

The team also demonstrated that the capsid's surface could be modified with various functional groups while maintaining its structural integrity, opening pathways for customization based on specific needs.

These features make $M_{60}L_{60}$ a promising platform for various applications, including drug delivery systems and molecular transportation.

"Considering the diversity and modifiability of peptide structures, our method is overwhelmingly advantageous compared to DNA origami technology in terms of functionalizing structures," highlights Sawada.

"Moreover, since our approach involves theoretical prediction and trial-and-error experiments, sometimes astonishing structures far beyond our expectations are obtained—this is the essence of chemistry."

Overall, this research represents a significant step forward in understanding how to construct artificial virus capsid-like structures.

"Our findings significantly expand the foundation of peptide engineering and are anticipated to have immense effects across various fields, including molecular self-assembly, materials chemistry, and mathematical theories," concludes Sawada.

The researchers are now aiming for even more ambitious structures, envisioning $M_{180}L_{180}$ and $M_{240}L_{240}$ assemblies with 180 and 240 crossings, respectively, as their next challenges.

More information: Yuuki Inomata et al, An M60L60 metal-peptide capsid with a 60-crossing woven network, *Chem* (2025). DOI: 10.1016/j.chempr.2025.102555

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