

Spotlights on Recent JACS Publications

■ SECRETS OF PROTEIN–POLYSACCHARIDE INTERACTIONS REVEALED

Textbook descriptions of protein–ligand interactions generally feature high affinities and rigid substrates. But not all macromolecular complexes form that way. Case in point: the bacteriophage Sf6 tailspike protein (Sf6TSP), a trimeric enzyme that binds and cleaves long, floppy O-antigen polysaccharide chains on the surface of its bacterial host.

Stefanie Barbirz, Mark Santer, and colleagues blend X-ray crystallography, NMR spectroscopy, surface plasmon resonance, and a new approach to model ligand interaction obtained from NMR spectroscopy called CORCEMA-ST-CSD, to study the interaction of the Sf6TSP complex with its ligands, including an octasaccharide, dodecasaccharide, and longer lipopolysaccharides (DOI: [10.1021/jacs.6b00240](https://doi.org/10.1021/jacs.6b00240)). The researchers' analysis suggests that O-polysaccharides bind Sf6TSP via a long, shallow binding pocket capable of simultaneously holding up to eight sugar residues (two tetrameric repeats) via key hydrogen bonds, hydration, and hydrophobic interactions, with additional residues draped outside the pocket. The ligand is tightly bound and relatively rigid at one end of the catalytic site, but more dynamic near the other, reducing end.

This multidisciplinary approach, the authors conclude, “could be a valuable scheme in other cases of weakly binding polysaccharide–protein complexes, where the extrapolation toward long polysaccharide fragments with computational methods is desired.”

Jeffrey M. Perkel

■ NEW ZIRCONIUM MOFs “PORE” THEMSELVES INTO THEIR WORK

Metal–organic frameworks (MOFs), which are cage-like crystalline materials made of inorganic metal clusters joined together by organic linker molecules, have promise in a variety of applications, including gas storage and separation, catalysis, chemical sensing, and drug delivery. In efforts to avoid the moisture sensitivity and thermal instability of most MOFs, considerable research has focused on the more stable zirconium-based MOFs. Researchers are actively working on creating novel designs to explore connections between structure and performance of these relatively new materials.

To expand this field, Jian Zhang and co-workers have developed two new zirconium MOFs using tetrahedral ligands as linkers (DOI: [10.1021/jacs.6b04608](https://doi.org/10.1021/jacs.6b04608)). Both MOFs exhibit a topology never before seen in MOFs. The first MOF, NPF-200, shows excellent thermal stability and readily adsorbs nitrogen even after submersion in water. NPF-200 displays the largest surface area, pore size, and solvent-accessible volume among all MOFs constructed with tetrahedral ligands. The second MOF, NPF-201, uses a boron-centered tetrahedral ligand, giving it the ability to adsorb cationic guest molecules. The authors suggest that these new materials further expand the field of zirconium-based MOFs with unusual functional topologies.

Christen Brownlee

■ CHIRAL 1,1-DIARYLALKANES BY SYNERGISTIC COPPER–PALLADIUM CO-CATALYSIS

Transition-metal-catalyzed cross-coupling reactions are commonly used to construct new bonds, especially carbon–carbon bonds, in organic synthesis. The rational combination of two such existing catalytic processes may lead to new reactions with unparalleled advantages.

Inspired by recently published reports on the synergy between copper and palladium catalysis, Stephen Buchwald and co-workers have devised CuH/Pd co-catalyzed enantioselective hydroarylation of vinylarenes, affording in one step synthetically versatile chiral 1,1-diarylalkanes (DOI: [10.1021/jacs.6b04566](https://doi.org/10.1021/jacs.6b04566)). With a carefully chosen ligand pair, stereoselectively generated Cu(I) intermediates from styrenes via hydrocupration can undergo oxidative addition to aryl halides, furnishing final products through Pd catalysis.

The merged Cu/Pd catalysis provides much easier asymmetric access to 1,1-diarylalkanes, motifs widely seen in pharmaceuticals and natural products yet conventionally challenging to prepare. From the perspective of methodology development, this study sets an example of taking advantage of co-catalysis synergy to design creative and convenient transformations.

Xin Su, Ph.D.

■ ONE-SHOT REACTION FOR THE PREPARATION OF HIGH-MOLECULAR-WEIGHT POLYMERS

In the field of polymer synthesis, there is a growing interest in developing strategies for preparing complex, multifunctional macromolecules as easily as possible. Graft and dendronized polymers have attracted much attention, but the production of these high-molecular-weight polymers while maintaining high selectivity remains a significant challenge.

Now, researchers led by Tae-Lim Choi report the synthesis of a library of graft and dendronized polymers by using a technique known as copper-catalyzed multicomponent polymerization (MCP) (DOI: [10.1021/jacs.6b04695](https://doi.org/10.1021/jacs.6b04695)). The team uses three types of bench-stable, readily accessible monomers and applies them in a diversity-oriented synthesis approach that results in the preparation of 54 high-molecular-weight graft and dendronized polymers. The method allows the researchers to manipulate the structures of both the main chains and the side chains, and they use analytical techniques to visualize the extended conformations that many of the polymers adopt in the solid state. The new one-step multicomponent polymerization is an important stride toward the tunable synthesis of this special class of molecules containing side chains composed of linear polymers or dendrons for applications in nanoscale electronics and biomaterials.

Christine Herman, Ph.D.

Published: July 27, 2016

■ SYNTHETIC BUCKYBOWL IS A SUBUNIT OF C₇₀

Xinliang Feng, Klaus Müllen, and their colleagues have synthesized a new buckybowl containing 34 carbon atoms (DOI: [10.1021/jacs.6b04426](https://doi.org/10.1021/jacs.6b04426)). Buckybowls are bowl-shaped polycyclic aromatic hydrocarbons with interesting electronic properties, like conductivity, as well as structural features like chirality, inversion, and supramolecular assembly.

Researchers have combined buckybowls to make a C₆₀ buckyball, or fullerene, but synthesizing a bowl subunit to make C₇₀ and larger fullerenes is challenging because it needs to contain five different types of carbon atoms and eight different types of carbon–carbon bonds. To build a C₃₄ buckybowl in five steps, the researchers elongate a halogenated linear triaryl system with additional aromatic rings and cyclize the molecule to form a bowl-shaped structure. Then they characterize its structure and optoelectronic properties and find that the bowl inverts at room temperature. Because this C₃₄ buckybowl contains all the carbon atoms and carbon–carbon bonds in C₇₀, it can serve as subunit for the construction of C₇₀ and higher fullerenes.

Melissae Fellet, Ph.D.

■ METALLOPROTEIN MIMICRY WITH BIOTIN–STREPTAVIDIN

Metalloproteins play a vital role in a wide range of biochemical processes; their importance cannot be overstated. Researchers would like to capture and extend those properties in designed or synthetic systems, but metalloprotein engineering is not easy. Now, A. S. Borovik, Thomas Ward, and colleagues describe a strategy to circumvent such issues for the class of copper-containing enzymes called cupredoxins (DOI: [10.1021/jacs.6b05428](https://doi.org/10.1021/jacs.6b05428)).

The researchers build cupredoxin analogues using the bacterial protein streptavidin, which tightly binds the small molecule, biotin. The team adds a tridentate metal-ion chelator composed of two pyridyl rings and an amine that is connected to biotin through a variable-length carbon linker. These biotinylated complexes are anchored in either wild-type streptavidin or a serine-to-cysteine mutant designed to resemble the active sites of native cupredoxins.

They then characterize the artificial copper proteins using absorbance and EPR spectroscopies, X-ray diffraction, and voltammetry, showing that, by varying the length of the carbon linker, the position of the copper center within the protein can be adjusted, dramatically altering both structural and physical properties of the copper complexes confined with the protein.

“These results further highlight the benefits of this approach in modulating the structure and properties of an immobilized metal complex to obtain new structures,” the authors conclude.

Jeffrey M. Perkel