

Spotlights on Recent JACS Publications

■ POLYMERASES MAY PROGRESS WITH THE HELP OF HYDROGEN BONDING

Building, replicating, and repairing the genetic code carried by living organisms relies on DNA and RNA polymerases, enzymes that catalyze the addition of new nucleic acids along a strand of DNA or RNA. Despite extensive study of these polymerases, researchers are still debating their mechanistic details.

Now Marco De Vivo, Paolo Carloni, and colleagues propose that a previously unrecognized hydrogen bond may be the key to how the enzymes do their work (DOI: [10.1021/jacs.6b05475](https://doi.org/10.1021/jacs.6b05475)). Through bioinformatic analysis of all available structures of DNA and RNA polymerases in complex with their substrates, they identify a hydrogen bond between the nucleophilic 3'-OH of the 3'-end deoxyribose and a phosphate of the incoming nucleotide. This hydrogen bond is conserved among all domains of life and only present in the enzyme-substrate complex. With quantum mechanics/molecular mechanics simulations of human DNA polymerase- η , the researchers show that this hydrogen bond activates the 3'-OH through deprotonation, facilitating addition of the nucleotide and DNA translocation. They note that this "self-activated mechanism" for nucleic acid elongation may be found in all DNA and RNA polymerases given the conservation of this motif.

Deirdre Lockwood, Ph.D.

■ DYE-SENSITIZED MOLECULAR-SEMICONDUCTOR HYBRIDS FOR SOLAR FUELS

Artificial photosynthesis, a chemical process that replicates the natural process of photosynthesis, converts solar energy to storable chemical energy by producing hydrogen from water splitting or carbon-based fuels from CO₂ reduction. Current research in artificial photosynthesis focuses on one promising approach: dye-sensitized photoelectrosynthesis cells. The photovoltaic electrodes of these electrolytic cells integrate semiconductor oxides with chromophore-catalyst assemblies that combine light-absorbing and catalytic properties.

In a new Perspective, Thomas Meyer and colleagues describe work done, to date, in this rapidly advancing field and future directions aimed at achieving higher solar efficiencies and long-term stabilities for the cells (DOI: [10.1021/jacs.6b06466](https://doi.org/10.1021/jacs.6b06466)). They report progress in integrating light absorption and electron-transfer dynamics between different components of the cell with multi-electron and multi-photon catalysis of water oxidation and CO₂ reduction.

The authors identify several research challenges, such as extending light absorption into wider visible and near-IR regions, stabilizing oxidized and reduced chromophores, improving long-term stability under operating conditions, and developing tandem designs for integrating water oxidation and CO₂ reduction. They conclude their report with an account of research targets: an overall device efficiency of 15%, and 95% retention in photoreactivity.

Alexander Hellemans

■ UNIQUE OXO-IRON COMPLEX AS SIMPLE SYSTEM FOR REACTIVITY STUDY

Selective functionalization of unactivated C-H bonds is an important industrial process. In Nature, heme and non-heme proteins accomplish this challenging task with ease via enzymatic catalysis, and high-valent oxo-iron(IV) species have been identified as pivotal intermediates in the catalytic cycles. Investigations on the reactivity of these intermediates may provide vital insights into the enzymatic reaction mechanism, which, in turn, may facilitate the design of biomimetic metal complexes that can efficiently mimic what Nature does. Shengfa Ye, Mihail Atanasov, Eckhard Bill, Jana Roithová, Franc Meyer, Frank Neese, and co-workers present a unique tetracarbene oxo-iron(IV) complex to serve as a simple model system for investigations into the reactivity of these intermediates (DOI: [10.1021/jacs.6b07708](https://doi.org/10.1021/jacs.6b07708)).

By coupling experimental data with theoretical calculations, the authors are able to look into the electronic structure of the oxo-iron(IV) complex in detail, and they find that the tetracarbene ligand causes a large energy gap between the quintet and triplet states of the complex. Thus, the hydrogen atom transfer reaction with the complex is more likely to occur only via the low-energy triplet state. This finding allows a fair evaluation of the reactivity of a triplet oxo-iron(IV) complex, because the reactions with the majority of oxo-iron(IV) model complexes follow a two-state model involving both the quintet and triplet states.

Lingling Chen, Ph.D.

■ SUBSTOICHIOMETRIC MOLYBDENUM SULFIDE: DOING MORE WITH LESS

Molybdenum-sulfur compounds, an important class of non-noble-metal catalysts, have received considerable attention for applications in hydrogen evolution, microelectronics, and photonics. Researchers are interested in understanding their fascinating electrical and chemical properties, and the complexity of the process underscores the desire for model systems that are suitable for mechanistic studies. Kian Ping Loh and co-workers create a new molybdenum sulfide phase that can serve as a simple model system for fundamental catalytic studies (DOI: [10.1021/jacs.6b09042](https://doi.org/10.1021/jacs.6b09042)).

Several studies in recent years have suggested that uncoordinated sites on the edges of molybdenum disulfide crystals have higher catalytic activity than those without these sulfur defects. However, no model system has been available to study this phenomenon on a basal plane. To fill the gap, the researchers create substoichiometric layers of molybdenum sulfide on sulfur-enriched copper substrate, affording a model system for investigating metal-centered catalysis. Experimental results suggest that the surface contains uncoordinated molybdenum atoms that can dynamically adsorb and desorb hydrogen, indicating that this material could be useful for catalysis in hydrogen-transfer reactions. The authors suggest

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that substoichiometric phases of other transition metal chalcogenides could also offer rich physical and chemical properties.

Christen Brownlee

■ FIGURING OUT HOW TO PUT MOLECULES UNDER STRAIN

Enzymes in Nature produce a wide range of strained molecules, which have increased internal energy arising from abnormal bond angles or other sources of structural stress. Due to their unique three-dimensional structures, strained molecules have potent biological activity, serving as antibiotics, anticoagulants, and antivirals, among other functions. Scientists are interested in synthesizing strained molecules with medical, industrial, or other uses, but such synthesis is challenging in the laboratory. Kendall Houk, Yi Tang, and colleagues focus on what they could learn from Nature about making strained molecules (DOI: [10.1021/jacs.6b09464](https://doi.org/10.1021/jacs.6b09464)).

The researchers target the biosynthesis of fungal natural product, herquiline A. This molecule is a highly strained and reduced piperazine alkaloid with a multicyclic core. Using both experimental and computational methods, they elucidate the complex biosynthetic pathway of herquiline A. The synthesis starts with the formation of a dityrosine. The pathway relies on a P450 enzyme to catalyze phenyl coupling, but it also contains steps that do not require enzyme catalysis at all. The stereochemical outcomes of the nonenzymatic steps depend on the methylated piperazine core. This insight may help scientists synthesize herquiline A in the laboratory for the first time, and get the stereochemistry right.

Erika Gebel Berg, Ph.D.

■ RAPID, QUANTITATIVE STEREOCHEMICAL ANALYSIS OF CRUDE ASYMMETRIC REACTION MIXTURE

On the road to creating asymmetric compounds, one of the major bottlenecks occurs during the characterization of the final product. In order to determine the absolute configuration, enantiomeric excess, and yield, several traditional analytical techniques can be employed. But these techniques often require a cumbersome workup of the crude reaction mixture, which can be time-consuming and costly. Now, Christian Wolf and a co-worker report a so-called “chiroptical” screening method that can be performed rapidly on crude reaction mixtures using circular dichroism and UV analysis (DOI: [10.1021/jacs.6b08892](https://doi.org/10.1021/jacs.6b08892)).

The team carries out the asymmetric hydrogenation of an iminium salt to yield a chiral molecule that self-assembles with a phosphine ligand and Pd(II) in solution. The supramolecular complex created by self-assembly generates characteristic UV and CD signals, which are used to perform the quantitative stereochemical analysis, with only 1 mg of the crude reaction mixture required. The researchers demonstrate that the technique can be exploited for the quantitative stereochemical analysis of a variety of compounds, including amino acids, amino alcohols, and amines. The strategy will help synthetic chemists save time and resources in the process of optimizing reaction conditions for creating asymmetric compounds.

Christine Herman, Ph.D.