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Spotlights on Recent *JACS* Publications

FLUORESCENT LANTHANIDES TRIGGERED BY NEW TARGETS

K. Eszter Borbas and co-workers have designed a new lanthanide probe that can be easily modified to detect ions, metals, enzymes, and oxidizing radicals (DOI: 10.1021/ja3004045). Most earlier probes are specifically designed for one analyte, which limits the broad utility of lanthanide metal-containing fluorescent probes that can be sensors for pH, citrate in urine, or singlet oxygen inside cells.

The new probe contains a lanthanide complex bound to a precursor of the light-absorbing molecule coumarin, and a caging, or masking, group prevents the precursor from forming the coumarin structure. This masking group is selected so that it will be unmasked in the presence of the desired analyte; the analyte causes the precursor to react to form coumarin and in turn causes the lanthanide probe to luminesce. For example, palladium is detected by using an allyl ester masking group, and the β-galactosidase enzyme is detected as it cleaves a galactose linkage.

Because the probe's luminescence is activated by a chemical reaction rather than simply a binding event, the researchers are able to monitor analytes that have been difficult to detect using binding-based, supramolecular probes. These new customizable probes detect a broad range of analyte molecules at nanomolar to micromolar concentrations. **Melissae Fellet**

A COMPUTATIONAL APPROACH TO INTERPRETING INTERCALATION

Molecules capable of wedging themselves between the Watson–Crick base pairs of a DNA double helix, or so-called DNA intercalators, are an important class of anticancer agents. Many intercalators, such as the chemotherapy drug daunomycin, function by inhibiting an enzyme called topoisomerase, which in turn prevents DNA replication and ultimately leads to cell death. Despite the profound therapeutic implications of DNA intercalation, the interactions and energetics that guide the process are not well understood.

Toward gaining a better understanding of DNA intercalation, Richard Lavery and co-workers use two distinct computational approaches to examine the energetic pathway leading to the intercalation of daunomycin (DOI: 10.1021/ja301649k). Based on their analysis, the authors describe the intercalation process in three stages: an initial binding interaction in the minor groove of the helix, followed by rotation of the drug and DNA bending via the formation of a wedge-angle between two base pairs, and finally intercalation with the drug fully inserted in the double helix.

This study demonstrates how computational analysis can provide a valuable perspective into specific structural and energetic features of drug binding, notably how daunomycin transitions from the groove-bound to the intercalated state, and the identity of intermediates in the process, that are difficult to access using experimental methods. These insights may help guide the design of improved intercalating agents for therapeutic applications. **Eva J. Gordon, Ph.D.**

RATCHETING UP TO A MOLECULAR MOTOR

Molecular machines that turn chemical reactions into mechanical work are common in biology. These examples have inspired scientists to develop their own set of tiny gadgets for use in computers and other devices. To make a molecular motor, scientists need a ratchet, which, unlike a molecular switch, can repetitively and progressively do work. In this study, David A. Leigh and colleagues developed a molecular ratchet that moves a ring-shaped molecule along a chemical track in one direction at a time (DOI: 10.1021/ja302711z).

The researchers synthesized a rotaxane that consists of a thread—the chemical track—and a macrocyclic ring. The ring slides along the thread, which is bulky at the ends so the ring cannot fall off, and has three compartments: left, middle, and right. To move the ring to the center or right compartments, the researchers mix the rotaxane with a catalyst that facilitates the attachment of a benzoyl group to the left side of the thread, pushing the ring out of that compartment. The same catalyst then favors benzoylation of the middle compartment when it is empty, trapping the ring in the right compartment and preventing any backslide. NMR confirms the ring's position at each step, and the direction of the movement is controlled by the chirality of the catalyst used. **Erika Gebel, Ph.D.**

FIXING NITROGENASE TO PROBE NITROGEN FIXATION

Nitrogen fixation, the process of converting molecular nitrogen (N_2) into ammonia, is essential for the biosynthesis of the basic building blocks of life, such as the nucleotides that make up DNA and RNA and the amino acids that make up proteins. The inherent strength of the nitrogen–nitrogen triple bond makes the conversion an energetically costly and mechanistically complex process. These intricate protein–protein interactions and catalytic mechanisms are challenging to study, in part because of the continual ATP dependence of the reaction.

To facilitate investigation of one of the enzymes involved in the nitrogen fixation process, the catalytic iron–molybdenum protein (MoFeP), Lauren Roth and F. Akif Tezcan devised a clever method for uncoupling MoFeP activity from ATP hydrolysis (DOI: 10.1021/ja303265m). They made a variant of MoFeP that contains a photosensitizer, so that light instead of ATP could be used to drive the electron-transfer process. They show that the light-responsive MoFeP variant can convert hydrogen cyanide, which like N_2 has a triple bond, to methane and possibly ammonia.

This approach paves the way for examining numerous thus-far elusive aspects of the mechanism of nitrogenase and the important role it plays in the biological life cycle of most organisms. **Eva J. Gordon, Ph.D.**

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GETTING PHOSPHATE FROM PHOSPHONATE

Inorganic phosphate, a molecule composed of a phosphorus atom bonded to four oxygen atoms, is an integral component of many important biomolecules, such as the genetic workhorses DNA and RNA and the energy transporter adenosine triphosphate, or ATP. In environments with a limited supply of inorganic phosphate, an important source is thought to be a compound called 2-aminoethylphosphonic acid, which is found in the cell membranes of many plants and animals. Conversion of 2-aminoethylphosphonic acid to inorganic phosphate involves breaking its carbon−phosphorus bond and replacing it with an oxygen−phosphorus bond, but the mechanism of this transformation is not well characterized.

To better understand how phosphonates like 2-aminoethylphosphonic acid are converted to inorganic phosphate, David Zechel and co-workers investigate two enzymes that were discovered in marine microorganisms, called PhnY and PhnZ (DOI: 10.1021/ja302072f). They discover that PhnY and PhnZ work sequentially to break 2-aminoethylphosphonic acid into two molecules, inorganic phosphate and the amino acid glycine.

This report illuminates how inorganic phosphate, a critical component of many biological compounds, might be procured in low-phosphate environments. Further characterization of the enzymes responsible for this process, PhnY and PhnZ, will contribute to our understanding of how organisms adapt to and thrive in various environments. **Eva J. Gordon, Ph.D.**

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