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Spotlights on Recent *JACS* Publications

DIFFERENT STROKES FOR DIFFERENT PROTEINS

Proteins are so much more complex than can be seen in the static crystal and NMR structures often used to portray the macromolecules. Scientists are eagerly pursuing methods that capture protein dynamics, the movements that can be critical to a protein's function. One famous example is a class of proteins that bind to small molecules through a "venus flytrap" mechanism in which the protein goes from an open and empty state to a closed one by clamping down on its substrate. In a new study, Oscar Millet and colleagues analyze the motions of two such proteins and find that, despite sequence and structural similarities, their movements and the mechanism by which they capture a substrate are very different (DOI: 10.1021/ja3092938).

The researchers used nuclear magnetic resonance (NMR) spectroscopy to study glucose/galactose binding protein (GGBP) and ribose binding protein (RBP), solving the proteins' structures and analyzing their motions residue-by-residue. They found that GGBP swings open and shut in its empty form, whereas RBP does not display this segmented motion while unoccupied. Instead, RBP shifts into its closed form upon binding a sugar, in a classic "induced fit" mechanism. The researchers then mutated residues in GGBP's hinge region, which stopped the protein's chomping motion and lowered its affinity for the substrate, demonstrating the importance of protein dynamics for function. **Erika Gebel, Ph.D.**

FINDING OUT ABOUT FOLATE BIOSYNTHESIS

Diverse organisms ranging from bacteria to humans require the B vitamin folate for a variety of biological activities, such as the synthesis and repair of DNA. In turn, the biosynthesis of folate has emerged as a target for numerous diseases, including several types of cancer and infections. For example, dihydroneopterin aldoase (DHNA), an enzyme involved in folate biosynthesis in bacteria but not other organisms, is a promising drug target for various bacteria including *Mycobacterium tuberculosis*, the bacterium that causes tuberculosis.

To gain a better understanding of how DHNA from *M. tuberculosis* works, Clarissa Czekster and John Blanchard undertake a detailed analysis of the kinetics of the enzyme (DOI: 10.1021/ja308350f). They find that it actually efficiently catalyzes three different reactions and generates five distinct products, uncovering an inherent versatility that likely contributes to its function in bacteria. In addition to deepening our appreciation for this sophisticated enzyme, this characterization will facilitate efforts to design DHNA inhibitors, which could lead to new drugs for the treatment of tuberculosis and other bacterial infections. **Eva J. Gordon, Ph.D.**

NEW MECHANISM FOR TRANSFER RNA METHYLATION

RNA molecules are decorated with assorted chemical modifications, such as methyl groups, that contribute to their structure and function. RNA methylation is typically carried out by using *S*-adenosylmethionine or methylene-tetrahydrofolate as the methyl donor. However, an enzyme called TrmFO was recently discovered and shown to methylate transfer RNAs (tRNAs), the RNAs responsible for transporting amino acids to growing peptide chains during protein synthesis, via a different mechanism that is not well understood. Djemel Hamdane and co-workers use a variety of biochemical and spectroscopic techniques to explore just how TrmFO methylates tRNAs (DOI: 10.1021/ja308145p).

The authors find compelling evidence that, unlike other methyltransferases, which require physically separate methyl donors to catalyze methylation reactions, the methylating agent in TrmFO is covalently attached to the enzyme itself, along with another molecule called flavin adenine dinucleotide (FAD). FAD is needed to transfer the methyl group to the tRNA, which is a previously uncharacterized function of this well-studied enzyme cofactor. The elucidation of this novel tRNA methylation mechanism expands our understanding of this important modification in RNA biology. **Eva J. Gordon, Ph.D.**

ORGANIC CHIRAL COMPOUNDS AS SOURCE MATERIAL FOR TWO TYPES OF SEMICONDUCTORS?

Researchers have investigated a large number of organic semiconductor materials for their suitability in organic electronics such as transistors and solar cells. Although p-type semiconductors (with an excess of holes) are readily available, suitable n-type organic semiconductors (with an excess of electrons) are more difficult to develop because of their chemical instability and low efficiency as charge carriers.

Takuji Hatakeyama and co-workers report the synthesis of a new, chiral semiconductor material, azaboradibenzo[6]helicene, a compound based on six fused benzene rings that can assume mirror image left-handed and right-handed stereochemical structures (DOI: 10.1021/ja310372f). When allowed to self-assemble in layers to form a film, a mixture of equal amounts of both left- and right-handed enantiomers forms a racemate, a material in which the two enantiomers alternate. The packing structure of the racemate differs from the packing structure of an enantiopure film, one containing either the right-handed or left-handed enantiomer only. By studying the electrical properties of the racemic and enantiopure films, the researchers found that the racemic material has a high hole mobility and is a p-type semiconductor, while the enantiopure material has an even higher electron mobility and is a n-type semiconductor.

This so-called carrier inversion, in which a semiconductor can be either p-type or n-type based on the packing of enantiomeric molecules, was surprising. "The results indicate the potential of these chiral organic semiconductors in electronic applications", the authors conclude. **Alexander Hellemans**

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