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Spotlights on Recent *JACS* Publications

NMR LINE WIDTHS REVEAL MANAGANESE HYDRATION STATE

Manganese is a key element in a variety of enzymes and life processes. Moreover, the metal's properties make it a valuable magnetic resonance imaging probe, allowing researchers to, for example, assess cell viability in diabetes or spot liver damage, or map neural pathways. However, little is known about how manganese travels—whether as an ion or ion complexes—in the body, a property that is essential to understanding the metal's function. Peter Caravan and colleagues have developed a method using nuclear magnetic resonance spectroscopy that can count how many water molecules are bound to manganese. Understanding this property can provide key structural information regarding the interactions of manganese with biomolecules and deepen our understanding of manganese transport, MRI contrast in vivo and catalysis in metalloenzymes. (DOI: 10.1021/ja4094132).

The researchers exploit the fact that manganese affects the NMR relaxation rates of exchangeable metal-bound water molecules. They demonstrate that the hydration state of manganese can be inferred through the ^{17}O NMR line-width of solvent water when measured in the presence of a manganese coordination complex or a manganese metalloprotein. This simple method for measuring the hydration state may offer new opportunities to study the structure of manganese containing species that is otherwise inaccessible by other techniques.

Erika Gebel Berg, Ph.D.

NMR CLUES THAT MAY STUNT HIV MATURATION

For the human immunodeficiency virus to become infectious, it must first package its RNA genome into a capsid shell made up of viral proteins. Scientists are trying to understand how the capsid forms in hopes of developing drugs that can inhibit viral maturation. The protein that makes up the bulk of the capsid, called CA, starts out as part of a longer polypeptide chain. Gag polyprotein, a precursor of CA, is cleaved into shorter and shorter bits to produce CA through several steps. The final step before 1200 copies of CA join together to form the capsid involves the cleavage of each CA protein from a peptide named SP1.

Scientists continue to debate how the separation of SP1 and CA triggers capsid formation, but Tatyana Polenova and colleagues have added new structural insight by studying the system using magic angle spinning (MAS) nuclear magnetic resonance spectroscopy (DOI: 10.1021/ja406907h). They selected MAS NMR because it can characterize protein structures within large complexes. In solution, CA forms tubules that depict important structural features of the viral capsid. CA-SP1 also forms tubules, capturing a precursor to the mature capsid. Based on the MAS NMR data, the researchers show that SP1 is unstructured inside the CA-SP1 tubule. The researchers conclude that the cleavage of SP1 from CA-SP1 facilitates the disassembly of an immature CA lattice and the assembly of the mature CA capsid.

Erika Gebel Berg, Ph.D.

SURFACE-BOUND POLYMERS WRIGGLE AND HOP

It is well known that polymers interact with surfaces, but the mystery lies in how exactly they move once attached. Polymers have been commonly assumed to move about the two-dimensional plane of the surface to which they are adsorbed, but a new study suggests their behavior is much more dynamic.

Michael Skaug and colleagues use single-molecule tracking experiments to reveal that the widely used polymer, poly(ethylene glycol) (PEG), wriggles and hops along hydrophobic surfaces (DOI: 10.1021/ja407396v). The team uses total internal reflection fluorescence microscopy to observe the movements of individual surface-adsorbed PEG molecules and find mobility is dependent on molecular weight. The results suggest that the interactions between surfaces and molecules in bulk solution may be stronger than previously believed, which could help explain certain previously puzzling phenomena, such as anomalously slow removal of surface-adsorbed polymers and the influence of highly attractive surfaces on the diffusion of polymers in solution. But it remains an open question whether this desorption-mediated mechanism observed for PEG can be assumed for other classes of polymers.

Christine Herman, Ph.D.

HOW A TAILORING PROTEIN GETS READY FOR WORK

Tom W. Muir and co-workers elucidate the assembly mechanism of a valuable class of peptide tools used in protein engineering, the split inteins (DOI: 10.1021/ja4104364).

Inteins are protein domains that act like a fusion of tailor and cloth: they snip themselves out of a polypeptide sequence and then "sew up" the loose ends with a peptide bond in a process called protein splicing. As this technique is a valuable commodity for engineering new proteins, inteins are prized biochemical tools. A particularly efficient set of inteins called split inteins splice proteins in seconds rather than hours.

Now Muir and colleagues have determined for the first time how split inteins assemble by studying a characteristic example, the Dna intein from *Nostoc punctiforme*, using various biophysical techniques together with protein engineering. They find that two fragments of the protein, one disordered and one partly folded, "capture" each other to form an ordered intermediate that then collapses into the protein's canonical fold. The work provides a framework for studying the assembly of other split inteins, and could enhance the use of these tools in protein engineering efforts.

Deirdre Lockwood, Ph.D.

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