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JOURNAL OF THE AMERICAN CHEMICAL SOCIETY
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Spotlights on Recent *JACS* Publications

HOW FLEXIBLE CRYSTALS TAKE A BREATH

Metal−organic frameworks (MOFs) are porous crystalline solids made up of metal corners and organic linking molecules. Some MOFs exhibit a 'breathing' behavior, in which the material's pores expand and contract in response to a stimulus. Often, atoms or small molecules may enter and exit these spaces as it breathes. One prototypical breathing MOF is a flexible material called MIL-53(Sc), which looks like a fish net with the transition-metal scandium at each corner.

Tina Dueren and her team explore how MIL-53(Sc) bends and flexes in response to changes in temperature and carbon dioxide adsorption (DOI: 10.1021/ja403453g). The authors use computer simulations based on first-principles electronic interactions (ab initio molecular dynamics) to predict the structural transformations and then use X-ray diffraction experiments to verify these predictions with extraordinary accuracy.

Researchers are currently scurrying to find robust and efficient ways to capture carbon dioxide to help slow climate change and ocean acidification. Potential applications of breathing MOFs include gas storage and separation, drug encapsulation, and drug delivery. The simulation method should also help researchers to probe other flexible MOFs in which the structure is known, but the material's flexibility in response to a guest molecule is still undetermined. **Jenny Morber, Ph.D.**

NOVEL ARRAY FOR DETECTING ABUSE OF OVER-THE-COUNTER MEDICATIONS

In the past few years, many of us have been startled to find some over-the-counter medications under lock and key at the drugstore. The reason is that these medications, mostly for colds and allergies, contain ingredients that people can become addicted to and abuse. There is a need for an easy and unambiguous test that clinicians and law enforcement officers can do to see how much of a particular component a person has consumed. Existing quantitative measurements of these ingredients after ingestion are labor-intensive, time-consuming, and prone to false-positive readings because of structural similarities.

Now Lyle Isaacs, Pavel Anzenbacher, and colleagues have developed an array sensor that uses two fluorescent probes that have complementary reactivities with several ingredients found in cold and allergy medications (DOI: 10.1021/ja407722a). By using samples of water spiked with mixtures of the ingredients and urine collected from people who had taken a cold medication, the investigators demonstrate that the array clearly distinguishes between different ingredients, such as the antihistamine doxylamine and the decongestants pseudoephedrine and phenylephrine. The array also quantitatively measures these ingredients. Furthermore, unlike current methods, the samples do not need to be purified prior to detection and quantification.

The authors suggest the array can be useful for high-throughput screening of a variety of drugs in clinical settings. **Rajendrani Mukhopadhyay, Ph.D.**

HOW DOES WATER START TO FREEZE?

The transition of liquid water to ice is one of the most important crystallization transitions on Earth, affecting everything from ice formation in atmospheric clouds to cryopreservation of biological tissues. Still, the freezing transition remains a mystery. For example, water can be cooled well below its freezing point without ice formation by carefully controlling the experimental conditions to avoid nucleation events. Freezing can either be induced by a foreign seed (heterogeneous nucleation) or by a small nucleus formed within the bulk metastable liquid water (homogeneous nucleation).

Eduardo Sanz, Chantal Valeriani, and co-workers describe computer simulation results where they explore homogeneous nucleation of supercooled water—liquid water cooled below the freezing point (DOI: 10.1021/ja4028814). The size of the critical ice nuclei is found to vary between ∼8000 water molecules (4 nm radius) at −15 °C to ∼600 water molecules (1.7 nm radius) at −35 °C. These simulations agree with experimental measurements of the homogeneous nucleation rate and predict that this freezing mechanism is impossible for temperatures higher than −20 °C. This work begins to fill the gap in our understanding of water freezing aspects that experiments cannot probe due to the small and short-lived character of ice nuclei. **Dalia Yablon, Ph.D.**

UNCOVERING LONG-TERM STABILITY OF MEMBRANE PROTEINS

More than just strings of amino acids, proteins fold into complex three-dimensional structures that are intricately linked to their function. The process by which proteins fold, unfold, and misfold is an area of intense research, both to gain a better fundamental understanding of protein biology and to guide therapeutic strategies for diseases caused by improperly folded proteins. James Bowie and co-workers explore an intriguing aspect of protein folding by examining the unfolding kinetics of a particularly challenging class of proteins, those that reside in the cell membrane (DOI: 10.1021/ja407232b).

While a number of soluble, nonmembrane bound proteins are kinetically stable, i.e., they unfold slowly with half-lives ranging from weeks to billions of years, little is known about whether membrane proteins can exhibit such behavior. Using the bacterial membrane protein diacylglycerol kinase as a model system and two experimental approaches called steric trapping and subunit exchange measurements, the authors demonstrate that diacylglycerol kinase unfolds with a half-life of at least several weeks.

The results suggest that kinetic stability may be a mechanism used by cells to regulate membrane protein function. These insights could help direct engineering efforts toward the creation of novel, kinetically stable membrane proteins. **Eva J. Gordon, Ph.D.**

Received: October 18, 2013
Published: October 22, 2013

   dx.doi.org/10.1021/ja410682n | *J. Am. Chem. Soc.* 2013, 135, 15965−15965