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Spotlights on Recent *JACS* Publications

LIGHT FLIPS OPEN A SNAP-TOP SILICA NANOCONTAINER

When designing a drug to be used in the body, such as a chemotherapy drug, releasing the medicine at the right place and time is very important. However, there are few systems that have a convenient or selective trigger. Jeffrey Zink and colleagues have found a way to use light to release drug molecules from a nanoparticle "bottle" (DOI: 10.1021/ja407331n).

Light is an effective trigger for selective drug release—biological tissue is transparent to red wavelengths—and molecules exhibiting two-photon absorption are particularly good candidates, because these compounds absorb red wavelengths. In earlier studies, scientists tried to construct prodrugs, attaching the active molecule to a carrier by a photolabile connection. However, this type of synthesis can be difficult, time-consuming, and expensive.

Another approach is to encapsulate drug molecules inside nontoxic mesoporous silica nanoparticles. Here, Zink and co-workers cap the ends of these silicia drug "bottles" with a molecule that can be photoactivated to move on demand. The "snap-top" is a bulky β-cyclodextrin molecule that is attached to the silica nanoparticle with a photo-cleavable stalk. The researchers find they can break this bond with either one photon or two, releasing both the cap and the cargo inside. This discovery may lead to cancer drug treatment that is more targeted and has fewer side effects. **Leigh Krietsch Boerner, Ph.D.**

PULLING ON A PROTEIN TO MAP ITS UNFOLDING PATHWAYS

Unfolded polypeptide chains are remarkable in their ability to quickly and efficiently fold into the native and active protein. Given the incredibly large number of possible conformations at each step in the folding process, the ultimate protein folding pathway involves retention of partially correct intermediates. Probing the protein energy landscape—the mapping of these protein conformations—is critical to understanding protein folding mechanisms that play an important role in the final structure and biochemical function of the protein.

Now, Sri Rama Koti Ainavarapu and co-workers have directly probed protein unfolding to gain insights into the energy landscape of a multidomain protein that translocates across bacterial membranes (DOI: 10.1021/ja406238q). Using an atomic force microscopy tip as a very small and accurate finger, the authors pull on a leucine binding protein (LBP) to measure tiny mechanical forces as a function of protein unraveling. These experiments reveal discrete force peaks, signifying structural intermediates, along the protein's unfolding path, showing that LBP follows multiple parallel unfolding pathways, more complex than previously thought. Our understanding of protein shape and function can be advanced by mapping the forces that govern peptide chain folding/unfolding. **Dalia Yablon, Ph.D.**

NOROVIRUS PUTS ON ITS COAT WITH A TWO-STEP

Guillaume Tresset, Stéphane Bressanelli, and colleagues show that noroviruses use a different strategy to assemble their protective protein coats than has been seen in other viruses that infect humans, such as hepatitis B (DOI: 10.1021/ja403550f).

Noroviruses are highly infectious in humans, causing about 250 million cases of gastrointestinal distress and over 200,000 deaths each year. Because the viruses are difficult to grow in cell culture, researchers have struggled to uncover how they efficiently package their genetic material into their protective protein coat, or capsid. Tresset and colleagues use a technique rarely used to study viruses, time-resolved small-angle X-ray scattering, to determine the kinetics of how a norovirus assembles its capsid.

They find that capsid self-assembly occurs in two steps. In the first step, which takes seconds, some ten dimers combine to form elongated intermediates. In the following, slower step, which takes hours, these intermediates interlock into a capsid. In contrast, in many other viruses such as hepatitis B, capsids form by sequential addition of dimers.

In clarifying the kinetics involved in norovirus assembly, the work could advance efforts to treat or prevent these infections. It could also be applied to engineer viral nanoparticles to make diagnostic agents and tailored therapeutics. **Deirdre Lockwood, Ph.D.**

CATALYST CALLS THE SHOTS

Paul Gormisky and M. Christina White have developed a new catalyst that accelerates oxidation of C−H bonds selectively in nonaromatic compounds such as terpenes, rather than relying on the inherent properties of the reactant molecules (DOI: 10.1021/ja407388y). The catalyst could boost the versatility with which organic compounds can be synthesized for drug discovery and other applications.

In 2007, researchers in the same laboratory discovered an inexpensive iron-based catalyst, called Fe(PDP), that selectively oxidizes specific C−H bonds in aliphatic compounds (*Science*, DOI: 10.1126/science.1148597). This type of selectivity is difficult to achieve: C−H bonds are strong and relatively unreactive, and their ubiquity in organic molecules makes them difficult for catalysts to distinguish. A drawback of Fe(PDP) is that there is little control over exactly which of the C−H bonds in a molecule are oxidized.

By tweaking Fe(PDP)'s structure with four trifluoromethyl groups, Gormisky and White have now produced a catalyst that shows substrates who's boss. The added groups block substrate access to the catalyst's iron-based active site so only specific C−H bonds conforming to the catalyst's nonnegotiable steric and electronic demands get oxidized there. The researchers demonstrate that Fe(CF_3-PDP) oxidizes substrates at C−H bonds that were before inaccessible to chemical oxidation. **Stu Borman,** *C&EN*

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