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Spotlights on Recent *JACS* Publications

TAKING SPECTROSCOPY TO ANOTHER DIMENSION

Ēriks Kupče and Ray Freeman have developed a convenient approach that highlights changes in spectra caused by molecular interactions or external influences such as temperature, solvent, and pressure (DOI: 10.1021/ja310107e). The display of spectra in this new format can help drug developers design medications that bind drug targets with high affinity under the relevant biological conditions. However, current methods for analyzing perturbations of spectroscopic data are tedious, particularly in crowded spectra.

The new method is applicable to a variety of spectroscopic techniques, but this proof-of-principle study focuses on nuclear magnetic resonance spectroscopy. The researchers measure the chemical shifts of hydrogen atoms in an 11-residue peptide while varying temperature in 1 K increments between 292 and 312 K. As a second test, the researchers perform NMR on strychnine while altering the solvent by adding deuterated chloroform. The resulting two-dimensional spectra highlight the chemical shift changes caused by varying the temperature or the solvent.

The method enables observation of the chemical shift perturbations at a glance, and assessment of their rates of change and directions. It may profoundly affect the way spectroscopists use and interpret data about molecular perturbations. **Erika Gebel, Ph.D.**

ENZYMES STEER TOWARD HIGH SUBSTRATE CONCENTRATIONS

Imagine autonomous nanosized devices sailing through the bloodstream, detecting molecular signs of disease or delivering drugs. Such devices will need motors that can drive and steer them through the body. A team led by Peter J. Butler and Ayusman Sen shows that enzymes can act as molecular-sized engines (DOI: 10.1021/ja3091615). They find that as enzymes catalyze reactions, force is produced to set them in motion, with higher reactant concentrations causing greater propulsion. The effect is not observed when the enzymes are inhibited, suggesting that the reactions catalyzed by the protein fuel the movement.

In order to examine if this enzyme motion can be directed, the researchers examine each enzyme's movements in a Y-shaped microfluidic channel. The enzyme solution is introduced through one inlet and the substrate through the other. Both enzymes diffuse across the boundary from the enzyme side to the substrate side in the main channel. In another experiment, the researchers pair the catalase solution with one containing glucose oxidase. Glucose oxidase reacts with glucose to produce hydrogen peroxide, which is catalase's substrate. The team observes that the catalase molecules diffuse toward the glucose oxidase side of the main channel only in the presence of glucose. **Sarah Webb, Ph.D.** *C&EN*

APTAMERS AND DNAZYMES TEAM UP FOR PROTEIN DETECTION

A new technique combines aptamers, DNAzymes, nanoparticles, and surface plasmon resonance imaging to enable the quantitative detection of protein−DNA interactions (DOI: 10.1021/ja311367t).

The approach, developed by researchers led by Robert Corn, involves the creation of a monolayer of single-stranded DNA molecules, which contain a protein-binding aptamer sequence specific for the human protease thrombin, a DNAzyme cleavage site, plus additional nucleic acid sequences that allow for signal enhancement with nanoparticles. When the team introduces a thrombin solution to the surface, it binds to the aptamer, blocking the DNAzyme cleavage site, allowing the reporter sequence to remain tethered, and ultimately resulting in a detectable signal that corresponds with protein concentration.

This technique, termed "DNAzyme footprinting" because of its similarity to the well-known DNase approach to detecting DNA−protein interactions, has the potential to be coupled with other nucleic acid surface amplification techniques, expanded to a multiplexed platform for the simultaneous detection of multiple ligands, and combined with other approaches to surface-based bioaffinity measurements, including fluorescence imaging and microring resonators. **Christine Herman, Ph.D.**

POLYKETIDE SYNTHASE MECHANISM PROBED IN VITRO

Polyketides are secondary metabolites with considerable pharmacological potential. They are constructed by polyketide synthases (PKSs), which build and modify polyketides through multiple rounds of malonyl-CoA addition and reduction steps similar to fatty acid synthesis. The fungal kinase inhibitor hypothemycin is assembled by the PKSs Hpm8 and Hpm3, but the precise mechanism by which these enzymes work is unclear. Now John Vederas, Yi Tang, and colleagues describe a procedure to dissect Hpm8 activity in vitro (DOI: 10.1021/ja4001823).

The team synthesizes a series of proposed Hpm8 intermediates as ^{13}C-labeled *N*-acetylcysteamine thioesters, feeds them to purified Hpm8 and Hpm3, and measures the enzymes' ability to convert those intermediates to dehydrozearalenol, a hypothemycin precursor. They also test four "unnatural" precursors, which could be used to produce hypothemycin variants.

Using their in vitro method, the authors deduce several of the structural intermediates and chemical selectivities governing PKS behavior, noting that their analysis "represents the first example of incorporation of a labeled advanced intermediate by a purified iterative [highly reducing PKS—Hpm8]."

Perhaps more significantly, the study could also expand pharmaceutical libraries. "Our findings not only further support the processive nature of polyketide biosynthesis but also

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provide guidelines for precursor-directed biosynthesis to generate novel polyketides with improved biological profiles," the authors say. **Jeffrey M. Perkel**

PEEKING INSIDE HOLLOW NANOPARTICLES

Elena Shevchenko and her team have found a way to characterize the voids inside hollow nanoparticles (DOI: 10.1021/ja311926r). With diameters between 1 and 100 nm, nanoparticles (NPs) bridge a middle ground between molecules and bulk materials. Hollow NPs are especially interesting to researchers because of their unique properties and because they can be used to carry cargo in applications such as controllable drug release. A major hurdle in research on these hollow NPs has been determining whether they are truly hollow.

The authors combine a variety of techniques to analyze the composition of voids in differently sized hollow iron oxide (Fe_3O_4) NPs. The analysis reveals more than just a vacuum: the voids appear to contain small fragments of iron and/or iron oxide, and the authors are able to rule out environmental contamination as a source. Further experiments demonstrate that the polycrystalline particle shells do not contain pores that would allow diffusion of liquids or gases into the inner core.

Knowledge of the composition of hollow NPs and the interior space is critical for many of their most enticing applications. "We believe that our approach toward analysis of the void composition of hollow Fe_3O_4 NPs can be used to study penetrability of any type of nanoshells and allows compositional analysis of the inner voids of any hollow nanostructures," the authors conclude. **Jenny Morber, Ph.D.**

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