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Spotlights on Recent *JACS* Publications

FINDING THE KEY TO ORGANIC-FREE ZEOLITES

Zeolites have many uses in industrial settings, such as adsorbants, catalysts, and ion exchange materials. To be able to tailor their specific properties is highly desirable, as this would broaden their functionality. Most of the work aimed to expand these capabilities employs organic structure-directing agents (SDAs) to customize crystal size and structure. However, SDAs are expensive, and they cannot be recovered and reused. Out of the almost 200 framework types of zeolites, only a small number of crystallize without a SDA, and chemists do not yet understand how the growing conditions influence the specific crystal polymorphs.

Jeffrey Rimer and co-workers have figured out how to easily identify compositions and conditions that can give specific phase-pure zeolite structures (DOI: 10.1021/ja3105939). The researchers create phase diagrams of the synthesis of sodium zeolites without SDAs by examining six parameters: different ratios of silicon, aluminum, and sodium hydroxide, the amount of water, temperature, and time. They find that zeolites form denser structures with higher temperatures and/or longer reaction times, and that using less water can drop the temperature needed to make higher-density frameworks. This work is a significant step toward rational design of zeolites, which could in time lower the cost of creating zeolites specific to desired tasks, leading to cheaper consumer goods in future markets. **Leigh Krietsch Boerner, Ph.D.**

COMPUTER MODELS PROBE MEMBRANE–PROTEIN INSERTION

The vast majority of drug targets are membrane proteins such as hormone receptors, chemical sensors, and ion channels, but just how those proteins actually become embedded into the cell membrane remains a mystery. A new series of molecular modeling experiments suggests a possible mechanism (DOI: 10.1021/ja310777k).

Benoît Roux, Klaus Schulten, and colleagues use kinetic and thermodynamic models, as well as some high-powered computers, to simulate on various time scales the insertion of model hydrophobic and hydrophilic peptides into a cell membrane via the protein, SecY. Among other tests, they model the impact of the nascent peptide's hydrophobicity on the opening of the SecY "lateral gate" (through which a protein passes to enter the membrane), the movement of hydrophobic and hydrophilic peptides toward or away from the channel center, and the probability of membrane insertion as a function of the free energy difference between channel and membrane.

The results "suggest that the membrane-insertion process is not solely thermodynamic, but is rather a competition between kinetic and thermodynamic effects that mimics a two-state partitioning under typical cellular and experimental conditions," the authors conclude. **Jeffrey M. Perkel**

MORE EFFICIENT EVOLUTION

Borrowing from Nature's method of evolution to acquire beneficial traits, scientists have developed a technology called directed evolution to create biomolecules with desired characteristics. In directed evolution of an enzyme, for example, the gene encoding the enzyme is repeatedly subjected to conditions that generate mutations in its sequence. The mutant enzymes are screened, and those that exhibit enhanced activity are selected. While this technology is now well established, variations that increase the efficiency of the process are evolving alongside the biomolecules. In this vein, Manfred Reetz and co-workers report the use of a technique called iterative saturation mutagenesis (ISM) in the directed evolution of *Candida antartica* lipase B (CALB), an enzyme that is widely used both as a research tool and in industrial applications, including in the production of polymers, pharmaceuticals, and pesticides (DOI: 10.1021/ja310455t).

In ISM, the screening process is accelerated by using structural biology data to help strategically generate enzyme mutants and determine synergistic combinations of mutations. Using this approach, the authors generate mutant CALB enzymes capable of reacting with α-substituted carboxylic acid esters, which are poor substrates for the natural enzyme. This method for generating CALB mutants with novel functions and product profiles could have far-reaching effects in the industrial applications of this important enzyme. **Eva J. Gordon, Ph.D.**

FLUORESCENT SENSORS FOR SIMPLER BLOOD SUGAR MONITORING

Diabetics need to regularly check their blood glucose levels, requiring them to draw blood several times a day. To make glucose testing simpler, researchers hope to develop implantable devices that could continuously monitor glucose concentrations using fluorescent chemical sensors. A common class of such sensors, boronic acid derivatives, fluorescently detects glucose with high sensitivity, but they lack selectivity because they also bind and respond to fructose. So far, overcoming this hurdle has involved designing complex molecules bearing multiple boronic acid groups.

To solve this problem with a simpler design, Tony D. James, Yun-Bao Jiang, and colleagues make a monoboronic acid compound with a pyrene fluorophore that responds differently to glucose and fructose in solution (DOI: 10.1021/ja311442x). It binds glucose with a 2:1 stoichiometry, forming complexes that aggregate and emit fluorescence at 510 nm, in proportion to glucose concentration. In contrast, the compound binds fructose with a 1:1 stoichiometry, causing lower aggregation and no fluorescence at this wavelength.

The compound is 4 times more selective for glucose than for fructose. The researchers improve its glucose selectivity by adding phenylboronic acid, which preferentially binds to fructose. The combined simplicity, specificity, and selectivity of this system could bring researchers closer to developing personal, noninvasive glucose monitoring devices. **Deirdre Lockwood**

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MOLECULAR MODELING, MEMBRANES, AND MICELLES

Proteins often carry out their functions through interactions with other proteins, and many of these interactions take place within the cell membrane. Transmembrane interactions are notoriously difficult to characterize, in part due to the unique molecular environment of the membrane. Cell membranes are composed mainly of a lipid bilayer embedded with proteins; micelles, which are also composed of lipid bilayers, are frequently used as cell membrane models to facilitate exploration of membrane biology.

The unique challenges associated with studying transmembrane interactions in the laboratory make computational methods of particular value in their investigation. Satyan Sharma and André Juffer use molecular modeling and simulations to investigate the interactions between two incredibly important proteins in the immune system, the T cell receptor (TCR) and cluster of differentiation 3 (CD3), in both micelles and cell membrane environments (DOI: 10.1021/ja308413e). They find that the interactions between these proteins are significantly different in a membrane environment versus micelles. Based on these findings, they propose a new model for the TCR-CD3 interaction, and they challenge the validity of using micelles to explore protein interactions in cell membranes. **Eva J. Gordon, Ph.D.**

INSECT CELLS HOST HUMAN PROTEIN FOR STUDY BY NMR

The cell is a crowded place, and such close quarters affect the behavior of intracellular proteins. Studying proteins in a realistically crowded environment may not only reveal their biologically relevant structures and actions, but also help drug developers identify promising medications by monitoring their interactions with target molecules inside cells.

In-cell nuclear magnetic resonance (NMR) spectroscopy detects protein structure inside living cells at atomic resolution; however, most of the studies to date have used bacteria. These prokaryotes are incapable of the post-translational modifications required by many human proteins that only a eukaryotic cell can provide. Now Yutaka Ito and colleagues develop a method for expressing and observing proteins inside insect cells with NMR (DOI: 10.1021/ja310928u).

First, the researchers use viruses to insert the protein genes into the insect cells, and then they grow the cells on media containing $^{13}C/^{15}N$ to label the proteins for NMR. As a result, all the proteins in the insect cells become NMR active. To remove background signals, the researchers subtract a spectrum from labeled cells modified to not express the protein of interest. The resulting difference spectrum contains only the target protein's peaks. For the first time, the researchers are able to assign a large majority of the backbone resonances from a protein inside eukaryotic cells, offering new possibilities for the study of human proteins under physiological conditions. **Erika Gebel, Ph.D.**

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