

Spotlights on Recent JACS Publications

■ A SYNTHETIC TOM AND JERRY TO POWER MOLECULAR MACHINES

André Estévez-Torres, Yannick Rondelez, and colleagues have synthesized a chemical system that reproduces traveling waves observed in predator–prey interactions (DOI: 10.1021/ja403584p).

It is a dance we have all seen first-hand or at least in cartoons: cat chases mouse; mouse runs away. But from a physical perspective, interactions between predator and prey generate spatial patterns such as oscillations, waves, and spirals. The patterns are observed in populations of bacteria, plants, and marine phytoplankton. Researchers want to reproduce such biological patterns using synthetic chemical reactions so that they can incorporate them into molecular machines.

Now the team has synthetically generated for the first time a traveling wave based upon a predator-prey-like interaction by mixing small DNA fragments with enzymes. They determine the wave velocity and propose a reaction–diffusion model to explain the observations. As the oligonucleotide components of the system can be tuned to control its physical performance, the research could help build self-organizing molecular machines. **Deirdre Lockwood, Ph.D.**

■ HOW TO MAKE A PROTEIN LOOK LIKE A TADPOLE

Cells are very good at making proteins that are just the right size, have just the right components, and fold just the right way. But the peptide sequence must almost always be linear. Bags of cells called polymer engineers do the opposite: chemical polymerization provides limited control in other areas, but these large molecules can have any number of shapes. David Tirrell, Frances Arnold, and co-workers have married the strength of each with a versatile technique that creates proteins with nonlinear shapes (DOI: 10.1021/ja4076452).

The researchers modify genes to encode artificial proteins with specially placed chemical units. These units attract and bind to each other somewhat like a lock and key. Here, the key is called SpyTag, and the lock is SpyCatcher. With careful attention to where genes place SpyTag and SpyCatcher on each molecule, the researchers create proteins in the shape of a circle, a star, an H, and even a tadpole.

Though artificial, the “elastin-like proteins” used here are similar to elastins found in connective tissues. When combined with the precision of cellular protein synthesis, this technique allows a protein engineer to control all of the fundamental properties of long-chain molecules, with no fundamental limit on molecular weight. **Jenny Morber, Ph.D.**

■ PSEUDOPERICYCLIC ACYL MIGRATION: A VALID VIOLATION OF THE WOODWARD–HOFFMANN RULES

For decades, the Woodward–Hoffmann rules have been used by organic chemists to predict products of pericyclic reactions based on the conservation of orbital symmetry. However, reactions forbidden by the Woodward–Hoffmann rules may proceed via orbital symmetry allowed pseudopericyclic pathways without the

presence of cyclic orbital overlap as is required for pericyclic pathways. Pseudopericyclic reactions usually involve planar transition states with lower barriers than their pericyclic alternatives.

Combining experimental and computational efforts, David M. Birney and co-workers elucidate the mechanism for ester rearrangements of three *o*-quinol acetate derivatives (DOI: 10.1021/ja4077364). They first identify that the dominant [3,5]-sigmatropic rearrangements, predicted forbidden as pericyclic reactions, occur in a cyclic, concerted pseudopericyclic fashion. The increased selectivity for [3,5] rearrangements at higher temperatures leads to the proposal of key intermediates which are confirmed computationally.

This study recognizes the pseudopericyclic pathway as an important complement to the more common pericyclic one, yet free of the limitations of orbital symmetry rules. Moreover, the proposed mechanism may have a general scope for acyl migration. **Xin Su**

■ CLOSE PROTEIN ENCOUNTERS OF THE WEAK ATTRACTION KIND

Packed within the crowded confines of intracellular space, proteins can behave differently than they do in the sparse environment of most test tube experiments. In-cell NMR spectroscopy allows researchers to study proteins in a living cell, offering an opportunity to tease out precisely how molecular crowding exerts its effects on proteins.

In this study, Volker Dötsch and colleagues have studied the protein Pin1—an enzyme that is inactivated by phosphorylation—inside frog egg cells (DOI: 10.1021/ja405244v). The in-cell NMR spectra of the inactivated enzyme have sharp lines, indicating the protein was behaving as a monomer. The spectra from the active enzyme, on the other hand, show considerable line broadening. This suggests that the protein’s active site sticks to other molecules under crowded conditions. The broader implication is that crowding can affect the active state of a protein and thus its function.

For the next experiment, the researchers attempt to assess the forces behind protein sticking by mixing Pin1 with a series of substances commonly used to mimic cellular crowding. The only medium that generates NMR spectra matching those taken in cells was a high concentration of ovalbumin, suggesting that weak attractive forces between neutral proteins compels Pin1 to form complexes. These findings also demonstrate that common crowding agents, such as Ficoll 70, do not adequately mimic the intracellular environment. **Erika Gebel Berg, Ph.D.**

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