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Spotlights on Recent *JACS* Publications

SEEING INTO AND THROUGH BACTERIAL CELL WALLS WITH NMR

The outer wall of bacterial cells contains a medley of molecules that allow the microorganisms to recognize and stick to hosts, as well as regulate other important cellular functions. Understanding the structure of the bacterial cell wall may help scientists develop novel antibiotics. Solid-state nuclear magnetic resonance spectroscopy (SSNMR) offers a window into cell walls, but it is limited by inherently low sensitivity. Combining multidisciplinary research with the use of dynamic nuclear polarization, Sabine Hediger and colleagues have enhanced the sensitivity of the NMR signals from a bacterial cell wall 24-fold over conventional SSNMR, enough, they say, to contemplate the possibility of atomic-scale studies of cell wall interactions (DOI: 10.1021/ja312501d).

To achieve the sensitivity enhancement, Hediger's team and collaborators mix *Bacillus subtilis* bacterial cells with biradical 1-(TEMPO-4-oxy)-3-(TEMPO-4-amino)propan-2-ol (TOTAPOL), a polarizing agent used to hyperpolarize nearby molecules, boosting NMR signals significantly. The researchers demonstrate that TOTAPOL strongly binds to peptidoglycans, a sugary constituent of bacterial cell walls. Because TOTAPOL only polarizes molecules in close proximity, this binding affinity allows the researchers to selectively enhance signals from the cell wall, or, alternately, to suppress them, leaving only signals originating from inside the cell. The authors say the method could be extended to the study of plant cell walls, which also contain sugars that TOTAPOL may bind. **Erika Gebel, Ph.D.**

TINY ANTENNAS GIVE IR SPECTROSCOPY A BOOST

Molecules are always moving, but like dancers in a nightclub, each vibrates a little differently. To overcome the challenge of weak signals in vibrational spectroscopy techniques like infrared spectroscopy (IR)—a method that uses molecules' characteristic movements to determine structure, composition, and orientation—Naomi J. Halas, Peter Nordlander, and their coworkers rely on the power of geometry (DOI: 10.1021/ja312694g).

Previously, to determine the identity of functional groups in very small numbers of molecules with IR spectroscopy, chemists needed to either zap the molecules with an extremely high energy source or place the molecules on large arrays of metallic nanostructures. Now, the researchers have improved the signal amplification by patterning gold nanoantennas like a cross made up of four fingers pointing inward, rather than using metallic islands or nanorod arrays.

Molecules caught in the gap between the fingers experience electric fields 12 000 times more intense than the best previous methods, according to simulations. The antennas can be tuned to specific vibrational modes simply by varying the finger length, and the researchers demonstrate the technique by identifying two different functional groups in two very different molecules. For the first time, researchers who need detailed information about surface molecules can get enhanced IR spectra from a conventional infrared source without the need for specialized instruments. **Jenny Morber, Ph.D.**

HOW PROTEINS FOLD IN A CROWD

Michael Feig and colleagues use molecular dynamics simulations and NMR studies of highly concentrated protein mixtures to show that increased crowding can destabilize proteins, causing them to partially denature (DOI: 10.1021/ja3126992).

To understand how proteins fold, researchers often study them in dilute solutions. But within cells, proteins inhabit a crowded, highly concentrated environment, and this crowding influences protein structure. Researchers have hypothesized that crowding drives proteins to fold into compact, native states that exclude solvent in an entropically favorable manner.

Feig and co-workers find that the destabilization is caused by changes in protein−protein interactions at higher concentrations. They hypothesize that these interactions make partially unfolded states energetically favorable through enthalpic and solvation contributions. Notably, the crowding-induced denatured state does not resemble a chemically induced one. The results could help researchers make more realistic models of protein folding and interactions in realistic cellular environments. **Deirdre Lockwood**

STRUCTURE AND FUNCTION OF MEMBRANE-TETHERED GTPASE AT ATOMIC LEVEL

GTPases are a large family of hydrolase enzymes that play an important role in many critical biological processes in the cell. The Ras family small GTPases are switch-like proteins that control diverse processes including gene expression, proliferation and differentiation, cell motility, and subcellular trafficking. Mitsuhiko Ikura and co-workers present the first experimental work to directly probe the structures, dynamics, and functions of a GTPase at the atomic level (DOI: 10.1021/ja312508w).

Until now, little was known about how GTPases interact with the cellular membrane or how this environment may affect enzyme function due to the inherent difficulty of studying proteins associated with a membrane bilayer. By using lipid nanodiscs as a model native-like bilayer membrane environment, the researchers enable the study of the membrane-conjugated Rheb (Ras homologue enriched in brain) by solution-state NMR. They find that the GTPase domain interacts transiently with the surface of the bilayer in two distinct preferred orientations, semi-perpendicular and semi-parallel.

This finding allows the authors to propose models of signal regulation by Rheb, shedding light on previously unexplained in vivo properties of this GTPase. The method can be applied to study the regulation of other GTPases. **Lingling Chen, Ph.D.**

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