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Spotlights on Recent *JACS* Publications

EYEING NANOPARTICLE SURFACES WITH A LITTLE MAGIC

Siloxane-grafted nanoparticles serve as valuable tools with potential applications ranging from biomedicine to industrial coatings. Modification of SiO_2 nanoparticles begins with a silanization reaction to yield a functionalized surface, the chemical architecture of which can be difficult to characterize. 2D $^{29}Si-^{29}Si$ solid-state NMR could be employed for nanoparticle surface analysis; however, it has been deemed impractical for routine use because of long acquisition times caused by the low natural abundance of ^{29}Si and the challenges associated with isotopic labeling. But a new study led by Gaël De Paëpe shows that it is possible to readily characterize surface grafting networks with the help of a technique known as dynamic nuclear polarization under magic angle spinning (DOI: 10.1021/ja506688m).

Using this signal-enhancing technique, the team finds that the reaction conditions they use to create organosiloxane-modified nanoparticles yield surfaces with laterally self-condensed functionalizing groups that appear to have formed via domain growth. They report the results of through-space and through-bond 2D $^{29}Si-^{29}Si$ correlation experiments that also allow them to estimate interatomic distances. The results show that the technique can be used to routinely characterize the polymerization path and polymer structures on surface-modified nanoparticles, which can help in the effort to design materials with improved chemical and physical properties.

Christine Herman, Ph.D.

NEW APPROACH TO MAP PROTEIN STRUCTURE IN THE GAS PHASE

Determining the structures of proteins is critical for understanding how they function. Mass spectrometry is a key way to study protein structure, but the technique analyzes molecules in the gas phase. Researchers often struggle to transform proteins into gaseous molecules without affecting their structure. Even if they manage to get the proteins into the gas phase, researchers run into difficulties in finding important structural details.

Now Ryan Julian and colleagues have come up with a gas-phase approach that allows them to determine a significant detail about protein structure, specifically the distance between critical points on the protein (DOI: 10.1021/ja507215q). The investigators apply energy excitation transfer to gas-phase peptides and demonstrate that they can map the distances between a disulfide bond and one of two amino acids, tryptophan or tyrosine. When either tryptophan or tyrosine is excited by ultraviolet light, the amino acid transfers energy to the disulfide bond in a distance-dependent manner to break it. The investigators establish that tryptophan could break disulfide bonds up to ~15 Å away, but tyrosine could only break disulfide bonds within 6 Å.

The authors suggest that, when combined with site-directed mutagenesis, which makes proteins with known changes in amino acid sequence, the distance-dependent nature of their new approach can be used to reveal notable details about protein structure.

Rajendrani Mukhopadhyay, Ph.D.

NOVEL PEPTIDE "GATEKEEPERS" CONTROL DRUG RELEASE FROM SILICA NANOPARTICLES

Mesoporous silica nanoparticles (MSNs) are drug-delivery vehicles that can work via two strategies. Drug molecules may be either coupled to the MSN surface or encapsulated within MSN pores. The latter method is preferable, as it requires no chemical modification of the drug compound. The trick is "gating" the drug so it can be released when and where it is needed. Here, Chulhee Kim, Keun-Hyeung Lee, and colleagues at Inha University (Korea) describe peptide "gatekeepers" that can do just that (DOI: 10.1021/ja507767h).

The team couples two tetrapeptides to MSN surfaces and loads the particles with a fluorescent dye. One peptide (Fmoc-CGGC) assumes a random structure, the other (Fmoc-CPGC) an orderly turn. When they test these peptides' gatekeeping abilities, they find that while the former continually leaks its fluorophore cargo, the other does not.

They then modify the Fmoc-CGGC peptide to be responsive to either a reducing agent (glutathione) or metal ion chelation—a strategy they can exploit to create drug-delivery agents sensitive to biological conditions that trigger the conformational conversion of the peptide gatekeeper.

"These results provide valuable information for the optimized design of stimuli-responsive multifunctional peptide gatekeepers which would be useful delivery vehicles with on-demand release characteristics," the authors conclude.

Jeffrey M. Perkel

SELF-STARTING PEPTIDE DELIVERS DRUGS TO COLON CELLS

Bastien Castagner, Jean-Christophe Leroux, and colleagues introduce a new cell-penetrating peptide platform for delivering nucleic acid drugs to the colon mucosa, the mucus layer that lines the intestines, also commonly referred to as the large intestine (DOI: 10.1021/ja507547w).

Cell-penetrating peptides have great potential for delivering drugs, such as nucleic acids, that are challenging to transfer across cell membranes. Researchers have struggled to exploit such peptides, however, because they can cause toxicity and may lack specificity for individual target tissues.

The researchers have developed a new cell-penetrating peptide platform that can deliver a nucleic acid specifically to the colon. The peptide, which is conjugated to a peptide nucleic acid cargo, is delivered in an inactive form: the construct is protected from interaction with the mucosa of the upper part of the gastrointestinal tract by the attachment of an azobenzene with poly(ethylene glycol) chains. Once inside the colon mucosa, the reduction of the azobenzene causes the

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construct to self-immolate, and in turn releases the active nucleic acid conjugate.

The new concept could eventually be applied to deliver nucleic acid drugs for the treatment of diseases such as colon cancer, ulcerative colitis, and Crohn's disease.

Deirdre Lockwood, Ph.D.

LIGHTING A NEW PATH FOR ARTIFICIAL PHOTOSYNTHESIS

Fraser A. Armstrong and co-workers advance the artificial photosynthesis frontier with the development of a platform in which visible light and a biosynthetic enzyme drive a fuel-forming hydrogenation reaction (DOI: 10.1021/ja507733j). To attract investment, artificial photosynthesis, which strives to convert solar energy to storable chemical energy, needs to be efficient, scalable, and cost-effective; i.e., it must show promise for competing economically with established industries. To date, however, artificial photosynthesis has been focused on production of hydrogen and C1 compounds that are obtained very cheaply from fossil reserves using existing technology.

Toward the generation of more sophisticated compounds, the authors exploit the functionality of the enzyme flavocytochrome c_3, which catalyzes the conversion of fumarate to succinate via the reduction of a central carbon−carbon double bond. To construct an artificial photosynthesis system, they immobilize the enzyme on dye-sensitized titanium oxide nanoparticles. When incorporated into a photoelectrochemical cell with water as the oxidant, the light-driven catalytic system can achieve a full photosynthetic cycle, producing succinate from fumarate and demonstrating the coupling of water splitting to hydrogenation of an alkene functionality.

These results represent a significant advance in the development of artificial photosynthesis and highlight its potential for the synthesis of organic chemicals other than simple fuels.

Eva J. Gordon, Ph.D.

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