

## Spotlights on Recent JACS Publications

### ■ ONE BEAD, TWO CAPTURE SEQUENCES

Next-generation DNA sequencing typically reports population-level data for a group of cells. But some questions require probing cell-to-cell variability. One such strategy is Drop-seq, which uses barcoded beads to tag sequences from each individual cell before sequencing. These beads act as unique identifiers, targeting generic mRNA; however, one limitation is that the beads can carry only a single capture sequence. Now, Jennifer Heemstra, John Phillips, and colleagues describe a method for capturing multiple sequences at the same time while retaining that critical barcode identifier (DOI: [10.1021/jacs.6b04465](https://doi.org/10.1021/jacs.6b04465)).

The researchers produce a barcoded bead containing two different capture sequences. To create such a bifunctional bead, they protect the chain ends using a mixture of nucleotides having orthogonal protecting groups. They then selectively remove one protecting group, synthesize and attach the first oligonucleotide capture sequence, and repeat the deprotection and synthesis step on the other oligonucleotide chain. Beads created using this strategy are capable of capturing both the T-cell receptor  $\alpha$  and  $\beta$  genes from a single cell simultaneously. The method is of significant value in obtaining paired sequence information for antigen receptors, which could drive research into human pathologies and autoimmune diseases.

Jeffrey M. Perkel

### ■ ZINC OXIDE NANOCRYSTALS SHOWCASE THEIR TRUE POTENTIAL

A variety of applications, including quantum dot solar cells, light-emitting diodes, photodetectors, and photocatalysts, all rely fundamentally on electron transfer across semiconductor–dielectric interfaces at nanocrystal surfaces. Thus, tailoring nanocrystals for specific applications requires understanding the energetics of electrons in these materials, that is to say, their redox potentials. However, finding the right method to measure redox potentials of freestanding colloidal nanocrystals has been a challenge. In a recent study, Daniel Gamelin and co-workers show that these properties can be ascertained for zinc oxide nanocrystals charged with excess electrons using simple potentiometric titrations (DOI: [10.1021/jacs.6b05848](https://doi.org/10.1021/jacs.6b05848)).

By using various titrants, including one that removes electrons, one that removes protons, and a third that removes both, the researchers are able to alter specific microscopic properties of the nanocrystals while measuring the corresponding changes in their charging potentials. These potentiometric titrations in turn allow them to quantify the nanocrystals' ability to store an electric charge, or capacitance, much like pH titrations can reveal a molecule's ability to bind protons. The authors suggest that potentiometric titration could offer a useful way to characterize electron energetics for many other types of semiconductor nanocrystals.

Christen Brownlee

### ■ SEMICONDUCTING POLYMERS TURN TO FLUORINE FOR A PERFORMANCE BOOST

Polymer solar cells coated with an active layer comprising semiconducting polymers and fullerene derivatives have garnered attention in recent years owing to their low cost and moderate environmental impact. Compared with solar cells made of inorganic materials, polymer solar cells have the potential to be lightweight, flexible, and semi-transparent while maintaining high power conversion efficiencies.

Now, Hideo Ohkita, Itaru Osaka, and co-workers report that the introduction of fluorine atoms can lead to further improvements in power conversion efficiencies for some semiconducting polymers (DOI: [10.1021/jacs.6b05418](https://doi.org/10.1021/jacs.6b05418)). The modified polymers have a higher open-circuit voltage in solar cells than their non-fluorinated counterpart, owing to their deeper HOMO energy level. The new semiconducting polymers demonstrate outstanding device performance with power conversion efficiencies as high as 10.5%. The authors further investigate the effects of fluorine substitution on the charge generation and recombination and other photovoltaic properties, and find correlations between the polymer structure, ordering structure, and photovoltaic performance. The results shed new light on the design of semiconducting polymers and suggest that there is still much room for improving polymer solar cell efficiency.

Christine Herman, Ph.D.

### ■ ELUSIVE PARENT MONOCHLOROSILYLENE FINALLY CAUGHT IN A PUSH–PULL TRAP

Silylenes—silicon analogues of carbenes—are composed of a silicon atom with two chemical groups attached ( $:\text{SiR}_2$ ). They have drawn great attention since their discovery as transient species nearly a half-century ago. Some stable silylenes have served as potent ligands in transition metal complexes. However, the parent silylene ( $:\text{SiH}_2$ ) and simple chlorosilylenes ( $:\text{SiCl}_2$  and  $:\text{SiHCl}$ ) have only been observed as reaction intermediates, and trapping these species has been a long-standing challenge.

Recently, Gregory Robinson and co-workers have developed a strategy for stabilizing the elusive parent monochlorosilylene  $[:\text{SiHCl}]$  species (DOI: [10.1021/jacs.6b06726](https://doi.org/10.1021/jacs.6b06726)). Pairs of  $[:\text{SiHCl}]$ , each with their own carbene ligand, are attached by a bridging  $\text{Fe}(\text{CO})_3$  unit. In this “push–pull” setup each silicon atom accepts a pair of electrons from the carbene ligand while also donating an electron pair to the  $\text{Fe}(\text{CO})_3$  unit. Crystallographic studies reveal the structure of this unusual molecule, and spectroscopic studies show that in solution it exists as two diastereoisomers. The authors suggest that this molecule represents the first experimental realization of  $[:\text{SiHCl}]$  under ambient conditions.

Christen Brownlee

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## ■ MULLING A MOLDY BIOSYNTHESIS YIELDS A NOVEL TERPENOID

By exploring a fungal biosynthetic pathway, Ikuro Abe and colleagues have isolated a novel sesterterpenoid with an unprecedented scaffold and mechanism of synthesis (DOI: [10.1021/jacs.6b05799](https://doi.org/10.1021/jacs.6b05799)).

Sesterterpenoids, molecules derived from five five-carbon terpene units, are one class of terpenoid natural products. Many terpenoids have been exploited as pharmaceuticals—for example, the anticancer drug Taxol and the antimalarial artemisinin. Yet, sesterterpenoids have been less studied than other classes of terpenoids. In an effort to find undiscovered yet intriguing sesterterpenoid scaffolds with potentially valuable uses, Abe and co-workers use a genome mining approach to explore enzymes involved in sesterterpenoid biosynthesis. The team first identified and isolated a fungal sesterterpenoid synthase, EvQS. Expression of EvQS in a strain of the fungus *Aspergillus oryzae* generates a novel sesterterpene, quiannulatene, which has an unusual molecular structure with a complex fused five-ring system.

Using an isotopic labeling strategy, the researchers also show that synthesis of quiannulatene proceeds through a new cyclization mechanism involving three rounds of hydride shifts and two successive carbon–carbon bond migrations. The work could lead to the discovery of other new terpenoids and may also help inspire synthetic strategies for potential new medicines.

**Deirdre Lockwood**, Ph.D.

## ■ “GLYCO-SEEK” METHOD DETECTS TARGET GLYCOPROTEIN WITH OUTSTANDING SENSITIVITY

Glycosylation is a post-translational modification that attaches carbohydrates to proteins, enabling so-called glycoproteins to carry out their unique cellular functions. Many human illnesses—including breast cancer, diabetes, and cardiovascular disease—are marked by errors in glycosylation. Therefore, being able to spot faulty glycoproteins in cells could have implications in diagnostics and lead to a better understanding of the role of glycosylation in disease.

Now, Peter Robinson, Cheng-ting Tsai, Carolyn Bertozzi, and co-workers describe a new method for detecting glycoproteins in cell lysate with sensitivity several orders of magnitude higher than that of current techniques such as traditional Western blotting (DOI: [10.1021/jacs.6b03861](https://doi.org/10.1021/jacs.6b03861)). The non-destructive biochemical technique is termed “Glyco-seek” and is used for the analysis of proteins with a specific form of glycosylation known as O-GlcNAc. By converting the glycosylated protein into a detectable PCR product, the method allows detection of low-abundance glycoproteins from complex samples, including serum. Unlike mass spectrometry-based assay, which relies on protein digestion and fragmentation and is better suited for the discovery of new glycoproteins, “Glyco-seek” is the directed approach to sensitive and convenient glycoprotein analysis. The authors envision that the method will be complementary to other techniques like protein microarrays for assay of targeted candidate glycoproteins without isolation or enrichment.

**Christine Herman**, Ph.D.