TOOLS IN BRIEF

STRUCTURAL BIOLOGY

Channelrhodopsin's crystal structure

The neuroscience community has enthusiastically embraced channelrhodopsin 2 (ChR2)—and its now many variants—as a tool with unique capability to control neuron activity using light with high temporal and spatial precision. Properties of the original ChR2 have been tailored and improved by targeted mutagenesis, but mutations have so far been largely chosen based on the well-studied bateriorhodopsin, a relative of ChR2. Unfortunately, the two proteins are only partially homologous. Now Kato *et al.* resolve the crystal structure of a channelrhodopsin chimera (chimera of ChR1 and ChR2) at 2.3-angstrom resolution. The structure revealed the unique architecture of channelrhodopsins and will be a very valuable tool for the design of new optogenetic tools.

Kato, H.E. *et al. Nature* **482**, 369–374 (2012).

IMAGING

Exploding nanodroplets

Photoacoustics—the use of light to generate acoustic signals inside a material—is garnering increased attention for *in vivo* tissue imaging. Of the available methods for creating a photoacoustic signal, thermal expansion has so far been the only one suitable for living organisms, and unfortunately the thermal expansion signal is very small. Exogenous contrast agents such as nanoparticles or liquid droplets of perfluorocarbons can increase the signal, but each has limitations. Wilson *et al.* now combine these two methods by creating photoacoustic nanodroplets composed of nanoscale perfluorocarbon droplets containing optically absorbing nanoparticles. The droplets are small enough to exit the bloodstream to reach target tissues, and light absorption by the nanoparticles heats and vaporizes the droplets. The resulting acoustic signals are an order of magnitude higher than the signals obtained from nanoparticles alone.

Wilson, K. *et al. Nat. Commun.* **3**, 618 (2012).

SINGLE MOLECULE

Timing DNA repair

DNA-binding proteins find their individual target sites in a process known as facilitated transport, during which the dimensionality of the search space on the DNA is reduced. The mechanism involves either one-dimensional sliding along the DNA molecule or three-dimensional hopping on and off the DNA. To separately study these events with a DNA-repair enzyme, Schonhoft & Strivers used a molecular clock, a small molecule that acts as a weak active-site inhibitor of the enzyme with a known time constant and only traps enzymes that come off the DNA, leaving the sliding ones unperturbed. Using this tool, the researchers found that the enzyme was sliding over distances of fewer than 10 base pairs, whereas they saw short and fast hops for sites at a distance of 10 or more base pairs from the original binding site. This combination of slower sliding and fast hopping ensures that the enzyme rapidly surveys the DNA and locates any site of damage.

Schonhoft, J.D. & Strivers, J.T. *Nat. Chem. Biol.* **8**, 205–210 (2012).

SMALL RNAs

Screening for potent viral RNA interference

RNA interference is an effective way to knock down gene expression, but the secondary structure and mutability of viral RNA genomes make for challenging targets. Tan *et al.* applied a high-throughput screening system for silencing short hairpin RNA (shRNA) to all possible target sites of hepatitis C, H1N1 influenza A, and two human immunodeficiency virus genomes. They used over 40,000 barcoded probes to make a library of sensors with a targeting shRNA under inducible control and a target site–bearing fluorescent reporter to report knockdown activity. Screening the pooled library in cells by fluorescence-activated cell sorting and microarray hybridization allowed identification of highly effective shRNAs. Potency was dependent on distinct target sequence features, secondary structure and G+C content.

Tan, X. *et al. Proc. Natl. Acad. Sci. USA* **109**, 869–874 (2012).