TOOLS IN BRIEF

SENSORS AND PROBES

Imaging protein interactions in living cells

Methods to study protein-protein interactions in their native context, that is, the living cell, are needed to understand protein function and signal transduction. Two groups recently described new tools for this application and demonstrated their use in living cells. Slavoff *et al.* report the use of a mutant lipoic acid ligase to catalyze the attachment of a coumarin fluorophore to a short acceptor peptide. By fusing the ligase to one protein of interest and the acceptor peptide to its putative binding partner, the researchers ensured that coumarin labeling would only occur if the two proteins specifically interact. Rutkowska *et al.* report a dimeric biarsenic derivative of carboxy-fluorescein, called xCrAsH, which lights up only when it is covalently bound simultaneously to two interacting proteins, each containing tetracysteine peptide motifs.

Slavoff, S.A. *et al. J. Am. Chem. Soc.* advance online publication (18 November 2011).

Rutkowska, A. *et al. Angew. Chem.* advance online publication (16 November 2011).

NEUROSCIENCE

Neurophysiology on the move

Studying brain physiology in freely moving rodents is steadily replacing neuroscience practices in which animals are anesthetized or restrained to study their brains. Multi-unit electrode-based neural recording systems can be combined with optical hardware for optogenetic control, but so far these setups have not been small and light enough to be easily carried by behaving mice. Anikeeva *et al.* attached 16 electrodes (four 'tetrode' units) to an optical fiber shaft and generated a lightweight and compact device, the 'optetrode', that enables delivery of both the light source and recording electrodes together in multiple regions of the animal's brain. The optetrode can be used to perform optical stimulation or inhibition of brain activity and simultaneous multichannel electrophysiological recordings in mice during open-field exploration.

Anikeeva, P. *et al. Nat. Neurosci.* advance online publication (4 December 2011).

PROTEOMICS

Optimizing protein identification

In shotgun proteomics analyses, proteins are identified by comparing the experimental peptide mass spectra to theoretical peptide mass spectra generated from sequence databases. A crucial step in this approach is inferring the identity of the protein from these peptide-spectrum matches. The false discovery rate is typically controlled at the peptide but not protein level, which can result in error inflation. Spivak *et al.* describe a software tool, Barista, designed to identify proteins from shotgun mass spectrometry data with high confidence. Barista is based on a machine-learning algorithm that maximizes the number of proteins that can be confidently accepted as correct and minimizes the number of incorrect identifications. Barista outperformed current popular software tools including ProteinProphet and IDPicker, especially for identifying short proteins and proteins with only one detected peptide.

Spivak, M. *et al. Mol. Cell. Proteomics* advance online publication (3 November 2011).

SENSORS AND PROBES

A fluorescent protein with many faces

Increased interest in super-resolution microscopy methods that require fluorophore switching is stimulating the development of more varieties of photoactivatable and photoswitchable fluorescent proteins. Recently, tetrameric and monomeric IrisFP fluorescent proteins that combine the properties of both irreversible green-to-red photoconversion and reversible photoswitching of both colors were reported. Adam *et al.* report a new member of this fluorescent protein family called NijiFP that displays both types of phototransformations and has some improved characteristics. They demonstrate the flexibility afforded by the multiple phototransformations available and perform photoactivated localization microscopy using both the red and green forms of the protein. This new member of this flexible class of fluorescent proteins should help stimulate creative labeling and imaging applications by biologists.

Adam, V. *et al. Chem. Biol.* **18**, 1241–1251 (2011).