TOOLS IN BRIEF

SENSORS AND PROBES

A new fluorophore for super-resolution imaging

Various localization-based super-resolution microscopy techniques exist, but the general mechanism of how they work is common to all: only a small subset of fluorophores is switched on and detected at any given time. By repeating this process, microscopists can construct a super-resolution image from a large number of snapshots. In order to switch fluorophores on and off, however, high laser powers and additives such as thiols must typically be applied. Uno *et al.* describe a rhodamine-based small-molecule fluorophore that blinks spontaneously without high-power laser irradiation or additives, by way of an intramolecule spirocyclization reaction between nucleophilic and electrophilic moieties in the same molecule. This new fluorophore has advantages particularly for time-lapse super-resolution imaging of structures in live cells.

Uno, S.N. *et al. Nat. Chem.* **6**, 681–689 (2014).

NEUROSCIENCE

Automated analysis of fly feeding

There are several methods used to monitor the feeding behavior of *Drosophila melanogaster*, but most are difficult to scale up, implement over long periods or quantify. Two independent groups now report setups in which they use simple electronic circuits to monitor, in an automated fashion and with high temporal resolution, the interaction of tens to thousands of fruit flies with food. Ro *et al.* demonstrate the power of their approach for long-term experiments by profiling fly feeding over multiple circadian cycles. Itskov *et al.* combine their method with sensitive measurements of bioluminescent food uptake to estimate the volume in a single fly 'sip'. Both groups validate their results by comparison to manual monitoring of proboscis extension as well as by correlation with standard approaches.

Itskov, P.M. *et al. Nat. Commun.* **5**, 4560 (2014).

Ro, J. *et al. PLoS One* **9**, e101107 (2014).

STRUCTURAL BIOLOGY

The structural basis of Spinach

Analogously to the use of GFP and its rainbow of derivatives to label proteins with a fluorescent tag, Spinach is a useful tool for fluorescently labeling RNA via genetic encoding. Spinach is made up of an RNA aptamer and a small-molecule analog of the GFP chromophore, which only fluoresces upon binding to the aptamer. Now Warner *et al.* provide a detailed investigation into the structural basis of Spinach fluorescence by solving the cocrystal structure of the aptamer bound to its chromophore. They found that a G-quadruplex architecture was crucial for generating fluorescence. The structural results allowed them to design a miniaturized 'Baby Spinach' that is half the size of Spinach but retains 95% of its fluorescence intensity; such a miniature version may reduce imaging artifacts.

Warner, K.D. *et al. Nat. Struct. Mol. Biol.* **21**, 658–663 (2014).

SENSORS AND PROBES

Colorful voltage sensors

Expanding the color range of genetically encoded sensors for neuronal activity enables combinatorial expression of different sensors and thus more flexibility in the types of experiments that can be performed. Zou *et al.* developed a series of voltage sensors whose emissions cover the visible spectrum. These voltage sensors are based on electrochromic fluorescence resonance energy transfer, meaning that the brightness of a fluorescent protein is influenced by the fluorescent voltage sensor to which it is fused. The most sensitive versions of this type of sensor are fusions between QuasAr2 and Citrine, mOrange2 or mRuby2. They allow the detection of action potentials in cultured hippocampal neurons and show fluorescence changes of 8–13% per 100 millivolts. It will be interesting to see their performance *in vivo* and in combination with other optogenetic tools.

Zou, P. *et al. Nat. Commun.* **5**, 4625 (2014).