TOOLS IN BRIEF

SENSORS AND PROBES

Super-resolution FlAsH

The binding of fluorescein arsenical helix binder (FlAsH) to small tetracysteine tags in proteins has not quite lived up to its early promises of nonperturbative fluorescence labeling of proteins in living cells, but it has proven useful for labeling proteins that mediate bacterial and viral infection. These proteins are sensitive to fusion tags, and immunolabeling is unsuitable for crucial live-cell imaging studies. Now Lelek *et al*. show that FlAsH can be converted between excited and dark states for switching-based super-resolution imaging. They labeled the integrase enzyme of human immunodeficiency virus (HIV) with FlAsH and used its switching ability to image HIV intracellular complexes at ~30-nanometer resolution during infection. This allowed them to measure the size and shape of the viral complex as it transited the cell. They observed the presence of intact capsids in the cytoplasm and much smaller complexes in the nucleus.

Lelek, M. *et al. Proc. Natl. Acad. Sci. USA* **109**, 8564–8569 (2012).

SYNTHETIC BIOLOGY

Assemble-on-a-chip

Imitating nature's assembly lines would help researchers make effective biodevices, but too much is still unknown about the process by which proteins and nucleic acids come together to form active complexes. Heyman *et al*. took a step toward a better understanding of the assembly process by designing a nanoscale platform that allows for molecule synthesis, assembly and imaging. On a transmission electron microscopy chip, they immobilized DNA, which was then transcribed and translated; protein-specific antibodies, immobilized on the chip next to the DNA, subsequently captured the protein. The researchers observed the correct folding of GFP and that of a more complex nanotube-forming protein, and they assembled two separate proteins in a specific pattern. The next step could be a more complex assembly starting from a set of structural genes.

Heyman, Y. *et al. Nat. Nanotechnol*. **7**, 374–378 (2012).

MICROSCOPY

Metallic electron microscopy

A genetically encoded tag for protein identification in transmission electron microscopy would be useful for studying cellular ultrastructure. Some such approaches have been previously reported, but tags that are robust, nonperturbative and enable high-resolution imaging are still needed. Risco *et al.* built on previous work *in vitro* and in bacteria to show that the 61–amino acid metal-binding protein metallothionein can serve as such a tag in mammalian cells. They incubated cells expressing a tagged protein with gold salts, which yielded an approximately 1-nanometer gold cluster around each tag. The authors demonstrated that gold, in amounts sufficient for labeling, can enter BHK-21 cells without obvious toxicity and that endogenous cellular metallothionein does not give a detectable signal. They applied the approach to detect rubella virus particles at multiple locations in the cell.

Risco, C. *et al. Structure* **20**, 759–766 (2012).

SIGNAL TRANSDUCTION

Functional glycoarrays

Natural sugars come in many varieties, which makes it difficult to sort out their biological activity. Puvirajesinghe *et al*. took the concept of a glycoarray, in which glycan libraries are spotted on a slide to screen for glycan-protein interactions, and adapted it to detect a functional readout of cell signaling. The group immobilized oriented glycans on aminosilane-coated glass slides and overlaid them with sulfate-deficient mouse fibroblasts in the presence of FGF2 ligand. Subsequent antibody staining and conventional imaging identified a downstream phosphorylation event that revealed which glycans promote FGF signaling. Using this functional glycomics approach, the group confirmed that two known heparin saccharides can activate the signaling pathway.

Puvirajesinghe, T.M. *et al. Chem. Biol.* **19**, 553–558 (2012).