METHODS IN BRIEF

SEQUENCING

A dilution solution to haplotyping

Next-generation sequencing and genotyping arrays do not distinguish which chromosomal copy alleles belong to. One approach that has been used to resolve haplotypes involves first diluting samples into aliquots that each contain no more than a fragment from a single chromosome copy. Kaper *et al*. applied this principle on the Illumina sequencing platform by amplifying diluted aliquots with multiple displacement amplification and then preparing barcoded libraries for multiplexed sequencing. They demonstrated targeted haplotype-resolved sequencing of a 1-megabase Duchenne muscular dystrophy region with high accuracy and then produced two long-range haplotype-phased human genomes.

Kaper, F. *et al. Proc. Natl. Acad. Sci. USA* **110**, 5552–5557 (2013).

SENSORS AND PROBES

Probing cells with lots of dots

On top of being stable and bright, quantum dots also feature narrow emission spectra, leading advocates to champion their potential for multiplexed probing. In reality, however, multiplexed immunolabeling with quantum dots has been limited by technical issues. Zrazhevskiy and Gao introduce multicycle multicolor molecular profiling (dubbed M3P), showing that five staining cycles with five antibodies each can be applied to a single sample. They first create a library of quantum dots conjugated to protein A and then simply mix each with a different antibody at high concentration to produce quantum dot–linked antibodies. Each staining cycle is imaged with a hyperspectral camera and followed by destaining. The researchers demonstrate probing with minimal aggregation, probe cross-talk and sample degradation and provide preliminary evidence to suggest that the method could be used to image 100 targets.

Zrazhevskiy, P. & Gao, X. *Nat. Commun*. **4**, 1619 (2013).

STRUCTURAL BIOLOGY

Observing a maturing protein

The unique technique of in-cell nuclear magnetic resonance (NMR) allows proteins to be observed at atomic resolution under close-to-physiological conditions. In contrast to the highly artificial environment of a purified protein (as is typical for structural studies), in-cell NMR can yield a more realistic picture of how a protein actually behaves in the cell. Banci *et al.* report improvements to the in-cell NMR technique that allowed them to follow the complete post-translational maturation process of human protein superoxide dismutase 1 (SOD1), which defends the cell against oxidative stress. These improvements included expressing the protein in human cells at near-physiological concentrations, optimizing conditions to maintain cell viability in the NMR tube and increasing the sensitivity of the NMR measurements. The authors observed the processes of zinc and copper binding in SOD1 and found that the copper chaperone for SOD1 promotes disulfide bond oxidation.

Banci, L. *et al. Nat. Chem. Biol.* doi:10.1038/nchembio.1202 (3 March 2013).

NANOBIOTECHNOLOGY

Building DNA gridirons

A wide variety of DNA nanostructures, ranging from the merely cute to the cleverly useful, have been made using so-called DNA origami folding techniques. However, it has remained a challenge to build gridiron-like structures using the DNA origami approach, in which a long scaffold strand is folded by interactions with many 'staple' strands. Han *et al.* now describe a design approach that utilizes a set of immobile four-arm Holliday junction analogs as the basic structural unit to create gridiron nanostructures. They further show that by adding DNA segments of different lengths between the individual joints, they could create a variety of two- and three-dimensional nanostructures, from simple lattices to multilayer gridirons to wire-frame spheres and screws.

Han, D. *et al. Science* **339**, 1412–1415 (2013).