METHODS IN BRIEF

IMAGING

Fast and easy super-resolution microscopy

A range of optical and computational approaches have been developed to enable super-resolution imaging of biological samples; most of these use sophisticated microscopes and/or specialized fluorophores. Gustafsson *et al.* have developed an algorithmic approach to achieve super-resolution imaging of samples labeled with conventional fluorophores and imaged on standard widefield, confocal or total internal reflection fluorescence microscopes. Their approach, called super-resolution radial fluctuations (SRRF), extracts super-resolution information from a sequence of images without detection and localization of individual fluorophores based on radial symmetry of the imaged fluorophores. They show that their method can achieve 50-nm lateral resolution and can be used to image structures at a wide range of labeling densities. They also demonstrate that the method is valuable for imaging under conditions with low signal-to-noise ratios, as well as for imaging live cells.

Gustafsson, N. *et al. Nat. Commun.* **7**, 12471 (2016).

GENOMICS

A single-cell screen for genetic drivers of leukemia

Mutations that underlie cancers are often obscured by genetic heterogeneity, and sequencing-based approaches typically recover many 'passenger' loci that are not responsible for cancer progression. Starting with a mouse model of acute myeloid leukemia (AML), Mann *et al.* have developed Sleeping Beauty capture hybridization sequencing (SBCapSeq), a functional screening method that couples mutagenesis from an active Sleeping Beauty transposon with sequencing. SBCapSeq uses random fragmentation, size selection and liquid-phase hybridization capture of active transposon sequences (and blocking of unmobilized transposon sequences) to sequence insertions in bulk or single mouse tumor cells. The researchers show that the method recovered AML genes in a semiquantitative manner, allowing them to identify major clonal populations and combinations of driver genes from as few as 26 cells.

Mann, K.M. *et al. Nat. Biotechnol.* **34**, 962–972 (2016).

STRUCTURAL BIOLOGY

Faster spinning for better structure resolution

Magic angle spinning (MAS) solid-state nuclear magnetic resonance (ssNMR) spectroscopy is a useful technique for structure determination, especially of membrane proteins. This method typically requires that protons in proteins be largely replaced with deuterium to reduce spectral overlap. As a result, the method has low sensitivity, and most side chain structures cannot be resolved. Andreas *et al.* discovered that spinning a sample at a substantially higher speed—that is, 100 kHz or more, as opposed to the more usual ~50 kHz—greatly reduces the problem of spectral overlap of fully protonated proteins. This allowed them to resolve the structures (including side chains) of two proteins—the model protein GB1 and a viral coat protein—in a relatively short amount of experimental time and using a very small sample.

Andreas, L.B. *et al. Proc. Natl. Acad. Sci. USA* **113**, 9187–9192 (2016).

IMAGING

Label-free histopathology

Histopathology is widely used both in the laboratory and in the clinic. Although powerful conventional methods exist for fixing and staining tissues for imaging, they are time-consuming and can introduce artifacts. Label-free imaging methods such as multiphoton microscopy can overcome some of these issues, as they can be used to image fresh, unstained tissues. Tu *et al.* introduce a user-friendly approach for label-free histopathology that allows for fresh tissues to be imaged with a combination of two-photon autofluorescence, three-photon autofluorescence, second-harmonic generation, third-harmonic generation and coherent anti-Stokes Raman scattering or stimulated Raman scattering. This combination is enabled by a light-delivery system that could easily be programmed for optimal contrast in the different imaging modalities, and it was used to visualize microstructures in tissues that are not easily seen with conventional methods.

Tu, H. *et al. Nat. Photonics* **10**, 534–540 (2016).