# Technology watch

## SUPER-RESOLUTION IMAGING

Recent advances in the development of super-resolution imaging techniques and fluorescent probe technology have improved spatial and temporal resolution, bringing us closer to the ideal of imaging individual cellular features in real time with molecular resolution. Two studies now report significant advances in multicolour three-dimensional (3D) stochastic optical reconstruction microscopy (STORM) and 4D imaging in ultrafast electron microscopy (UEM).

Huang *et al.* generated photoswitchable probes in several distinct colours by covalently linking a photoswitchable cyanine reporter and an activator molecule to assist bioconjugation, and obtained whole-cell images with a spatial resolution of 20–30 nm and 60–70 nm in the lateral and axial dimensions, respectively. The 3D STORM images resolved mitochondrial morphologies and mitochondria–microtubule contacts that were obscured in conventional fluorescence images.

Barwick *et al.* report 4D imaging, with *in situ* spatiotemporal resolutions, in UEM. The ability to capture selected-area image dynamics with pixel resolution and to control the time separation between pulses for temporal cooling of the specimen made possible studies of fleeting structures and morphologies using gold or graphite. The success of this study demonstrates the promise of UEM in real-space imaging of cell dynamics.

**ORIGINAL RESEARCH PAPERS** Barwick, B. *et al.* 4D imaging of transient structures and morphologies in ultrafast electron microscopy. *Science* **322**, 1227–1231 (2008) | Huang, B. *et al.* Whole-cell 3D STORM reveals interactions between cellular structures with nanometer-scale resolution. *Nature Methods* **5**, 1047–1052 (2008)

## MAXQUANT FOR PROTEOMICS

Efficient analysis of large amounts of raw data for peptide identification and protein quantitation remains a main challenge in mass spectrometry (MS)-based proteomics. Cox and Mann now describe a set of algorithms that efficiently and robustly extract information from raw MS data and allow very high peptide identification rates as well as high accuracy protein quantitation for several thousand proteins in complex proteomes. This integrated platform of algorithms, which the authors named MaxQuant, detects peaks, isotope clusters and stable isotope labelling with amino acids in cell culture (SILAC) peptide pairs at three-dimensional objects in mass/charge, elution time and signal intensity space. By integrating multiple mass measurements and correcting for linear and non-linear mass offsets, this method achieved a sixfold increase in mass accuracy over standard techniques. MaxQuant has already been applied to quantify the yeast proteome and more than 5,000 proteins in the mouse stem cell proteome. The authors propose that "with further advances in instrumentation, proteomics should be suitable for routine functional genomics experiments, for which microarrays have so far been the only option".

**ORIGINAL RESEARCH PAPER** Cox, J. & Mann, M. High peptide identification rates, individualized ppb-range mass accuracies and proteome-wide quantitation via novel computational strategies. *Nature Biotech.* 30 Nov 2008 (doi:10.1038/nbt.1511)