The researchers used simulations to model the decay of the light at the tip and the sides of the nanopillars (the light emerges mostly from the sides). They estimate the observation volume to be 10^{-16} litres, an order of magnitude smaller than that achieved with two-photon excitation. They have grown cortical neurons, hippocampal neurons, cardiomyocytes and a variety of mammalian cell lines on these pillars, and in all cases the cells seem to thrive. "Because of the small dimensions of the pillar, the cell seems to treat it as some sort of cellular organelle, to recognize those dimensions," Bianxiao Cui says. The researchers continue to investigate the best dimensions and interpillar distances for various applications.

Although others have in the past used nanopillars to deliver molecules to cells, the data at this stage are not entirely conclusive about whether the pillars are topologically inside or outside the cell (that is, whether they access the cytosol or not). Scanning electron micrographs show that the cells seem to engulf the pillars, but the resolution is insufficient to tell whether or not there is a membrane between the pillar and cytoplasm. This will affect the types of experiments that can be done: for instance, recruiting cytosolic molecules to the pillars will only be possible if they are actually inside the cell.

Irrespective of the topology, the pillars can still be used to optically excite molecules in a very small volume. Bianxiao Cui and her lab members are pursuing experiments in which they use the nanopillars to either locally photo-uncage a neurotransmitter or to excite a small number of photoactivatable fluorescent proteins so that the behavior of single molecules can then be studied as they diffuse to dark areas in the cell.

Natalie de Souza

RESEARCH PAPERS

Xie, C. *et al.* Vertical nanopillars for highly localized fluorescence imaging. *Proc. Natl. Acad. Sci. USA* **108**, 3894–3899 (2011).

before the proteins will translocate into the nucleus to activate transcription factors. Although stimulation of the whole network has been found to result in a lag phase before ERK accumulation in the nucleus, the elementary kinetic steps of this process had not been previously resolved. By photo-uncaging the primed MEK1 and then using time-lapse microscopy to follow the fate of EGFP-tagged ERK in the cells, the researchers confirmed that the diphosphorylation step determined the rate of the appearance of ERK in the nucleus.

When they stimulated the whole network, they observed that ERK accumulated in the nucleus, reaching a peak, but then rapidly dissipated. They did not see this with the photocaged MEK1, which is only regulated by light and not by Raf. This suggests that a negative feedback mechanism is at play.

The method could be especially powerful for determining the kinetics of each of the elementary steps in a signaling pathway. This could be achieved by photocaging each of the kinases in the pathway in turn, which should be relatively straightforward to do because of the conserved lysine in the ATP-binding pocket. "By comparing the kinetics when you activate at different points in the pathway," says Chin, "you'll be able to say something about the rate of potentially every step in the pathway and make quantitative models."

Allison Doerr

RESEARCH PAPERS

Gautier, A. *et al.* Light-activated kinases enable temporal dissection of signaling networks in living cells. *J. Am. Chem. Soc.* **133**, 2124–2127 (2011).

NEWS IN BRIEF

NEUROSCIENCE

Dissecting neural networks with Brainbow

Neurotropic viruses—which replicate in neurons and can cross synapses—are useful as neural circuit tracing tools. Card *et al.* combine this technology with the Brainbow approach to highlight neuronal connections within a larger network. They inserted the Brainbow cassette into the genome of an engineered pseudorabies virus, which resulted in the expression of either yellow or cyan fluorescent reporters in response to Cre recombinase–mediated recombination, allowing synaptic connections to be traced.

Card, J.P. *et al. Proc. Natl. Acad. Sci. USA* **108**, 3377–3382 (2011).

IMAGING

A label for electron cryotomography

Electron cryotomography allows cells, organelles and macromolecular assemblies to be imaged at high resolution in a near-native state. A major challenge, however, is the identification of cellular structures of interest. Wang *et al.* describe the use of a ferritin protein as a clonable fusion label for electron cryotomography. Ferritin consists of a protein shell with a central cavity that can be loaded with iron, providing an electron-dense tag for image contrast.

Wang, Q. *et al. Structure* **19**, 147–154 (2011).

GENOMICS

A population-scale variation map

Mills *et al.* applied different methods, including paired-end mapping, depth-of-coverage analysis, split-read mapping and sequence assembly, to detect structural variants on a population scale. The resulting variant map encompasses deletions, insertions and tandem duplications, more than 50% of which could be mapped at base-pair resolution. This resource will be valuable for the understanding of the origin of variants, their genotyping in large cohorts and for disease-association studies.

Mills, R.E. *et al. Nature* **470**, 59–65 (2011).

SENSORS AND PROBES

Oligodeoxyfluorosides for imaging

Guo *et al.* present oligodeoxyfluoroside (ODF) fluorophores, made up of a DNA backbone in which fluorophores replace the DNA bases; energy transfer between the fluorophores allows a wide variety of emission colors to be generated with a single excitation wavelength. The authors conjugated the ODF fluorophores to antibodies and showed that they could be used for multicolor cellular imaging.

Guo, J. *et al. Proc. Natl. Acad. Sci. USA* **108**, 3493–3498 (2011).

NEUROSCIENCE

Optogenetics toolkit for primates

With optogenetics, light is harnessed to control specific neurons in the brain. Beyond basic neuroscience research applications, optogenetics has the potential to treat brain injury and disease. Diester *et al.* now present a set of optogenetics tools for experiments in nonhuman primates. They characterized the safety and efficiency of opsin expression in the rhesus monkey cortex. They also describe a fiber-optic device for making minimally invasive, repeated *in vivo* fluorescence measurements over time.

Diester, I. *et al. Nat. Neurosci.* **14**, 387–397 (2011).