features without stereo viewing or virtual reality hardware. There are two options. First, while viewing the 3D image, a user can mouse-click on a region of interest, rotate the image and click on the same region from another angle. The two clicks define rays that intersect at the desired 3D location and create a marker position there. Alternatively, the software will determine the most likely 3D position the user intended to mark using only a single mouse-click by examining the intensity information along the single ray. Peng says that although it is possible to create image data that fools the latter method, with real data the method is surprisingly accurate. And because the user can always rotate the image and quickly adjust the location, it is very fast.

"The most important part of the 3D pinpointing is that once you have the 3D marker information, you can directly measure it or use it as prior knowledge in computer algorithms," says Peng. His team used this approach in their neuron tracing tool V3D-Neuron. Instead of relying on manual tracing or automated tracing followed by manual correction, V3D-Neuron allows the user to quickly pinpoint markers only at the terminals of the neuronal branches in three dimensions, and then an algorithm finds the optimal connecting paths. "This produced much better performance," says Peng.

Work on V3D is continuing. 3D curve drawing has been implemented, other people are designing plugins, and a V3D hackathon is scheduled for this summer at Janelia Farm. It may not be as fun as 3D gaming but V3D promises to make working with 3D image data in the lab much more enjoyable.

Daniel Evanko

RESEARCH PAPERS

Peng, H. *et al.* V3D enables real-time 3D visualization and quantitative analysis of large-scale biological image data sets. *Nat. Biotechnol.* **28**, 348–353 (2010).

of tissue type. In other words, the interactions themselves might function as tissue 'biomarkers'.

To look into this, the researchers classified transcription factor expression profiles from multiple human tissues. They did this either based on quantitative mRNA levels alone or by adding information from the physical interaction network. By focusing on interacting pairs of factors for which the expression levels were highly correlated in one tissue but not in others, they identified interactions that could quite accurately classify tissue type according to embryonic germ layer. "We think this is a major advance of our paper because it shows how protein networks can serve as powerful biomarkers of cell state," says Ideker, though one challenge will be to identify which biomarkers are actually causal for tissue type. Encouragingly, the best predictive network is enriched for homeobox transcription factors, which are known regulators of development.

And the atlas will probably be expanded in the near future, says Suzuki. The researchers are hoping to compare disease transcription factor networks to normal ones, to identify factors involved in these diseases and to pinpoint interactions that may offer novel targets for therapy. As Ideker sums it up, "it's not about the proteins; it's about the networks."

Natalie de Souza

RESEARCH PAPERS

Ravasi, T. *et al.* An atlas of combinatorial transcriptional regulation in mouse and man. *Cell* **140**, 744–752 (2010).

NEWS IN BRIEF

NEUROSCIENCE

Imaging dopamine with MRI

Magnetic resonance imaging (MRI) is a powerful, noninvasive technology for studying the brain. But neurotransmitters such as dopamine have not been directly observed by MRI. Shapiro *et al.* now report the directed evolution of a MRI contrast agent specific for dopamine, based on the heme domain from a bacterial cytochrome. The probe allowed the researchers to image depolarization-triggered dopamine release in live animal brains.

Shapiro, M.G. *et al. Nat. Biotechnol.* **28**, 264–270 (2010).

CHEMICAL BIOLOGY

More potent CALI reagents

Tools for inactivating protein function in cells, chromophore-assisted light inactivation (CALI) reagents, contain a protein-targeting moiety and a chromophore that generates singlet oxygen when irradiated with light. These tools, however, generally suffer from poor targeting efficiency and poor singlet oxygen generation. Lee *et al.* describe highly potent CALI reagents made by tacking a Ru(II)(tris-bipyridyl)$^{2+}$ derivative, a very efficient photocatalyst for generating singlet oxygen, to a highly selective protein-targeting peptoid.

Lee, J. *et al. Nat. Chem. Biol.* **6**, 258–260 (2010).

SPECTROSCOPY

Introducing SHINERS

Surface-enhanced Raman scattering (SERS) is a useful approach for enhancing Raman signals by distributing metal nanoparticles over a surface, but the nanoparticles often stick to each other and to the material being studied. Li *et al.* now introduce shell-isolated, nanoparticle-enhanced Raman spectroscopy, or SHINERS. Gold nanoparticles are coated with an ultrathin alumina or silica shell; the nanoparticles are spread over the surface without sticking, yet they conform to the surface contours and facilitate single-molecule detection.

Li, J.F. *et al. Nature* **464**, 392–395 (2010).

IMAGING AND VISUALIZATION

New red fluorescent proteins

The titanium-sapphire lasers used in two-photon microscopy have low power output in the excitation wavelength range for red fluorescent proteins, limiting their application. Piatkevich *et al.* introduce two new monomeric red fluorescent proteins, named LSS-mKate1 and LSS-mKate2. These proteins have large Stokes shifts, allowing efficient excitation by titanium-sapphire lasers, in addition to high pH stability, photostability and rapid chromophore maturation, making them useful for multicolor intravital imaging.

Piatkevich, K.D. *et al. Proc. Natl. Acad. Sci. USA* **107**, 5369–5374 (2010).

CELL BIOLOGY

Levitating cell cultures

Souza *et al.* describe a method for three-dimensional tissue culture by magnetic cell levitation. The cells are incubated with a hydrogel made up of gold, magnetic iron oxide nanoparticles and bacteriophages. By controlling the magnetic field, the researchers can manipulate the three-dimensional geometry of the cell culture to better represent the *in vivo* tissue structure.

Souza, G.R. *et al. Nat. Nanotechnol.* **5**, 291–296 (2010).