of light — while also maintaining low power consumption.

"We have presented simulations of what will be achievable using our micro-LED stimulator arrays coupled to waveguiding optrodes," Degenaar explained. "With the right engineering, we believe it should be possible to stimulate hundreds of points simultaneously, given the power dissipation of the human brain. This would prove to be a major advance over existing electrical forms of neural prosthesis. It is now our intention to move towards the fabrication and testing of such optrode arrays."

Spatial light modulators (SLMs) are another option for controlling illumination in a sophisticated manner. Rafael Yuste's group at Columbia University in the USA presented a talk on the use of an SLM to control both the imaging and the two-photon photo-activation of neurons in three dimensions. Yuste said that one aim of their work is to preserve the single-cell resolution of two-photon imaging when performing experiments in highly scattering media such as the mammalian brain, *in vivo*.

"SLMs provide the ultimate flexibility for microscopy because they can be used to mimic most arbitrary optical transfer functions," explained Yuste. "In our talk we demonstrated the use of SLMs for two-photon calcium imaging and photo-activation using RuBi-Glutamate, a novel caged glutamate compound that we developed together with our collaborator Roberto Etchenique, and a new optogenetic construct, in partnership with the Deisseroth lab."

Yuste and colleagues have also developed the PocketScope, a handheld SLM microscope that can be used to perform sophisticated imaging and uncaging experiments. This device, which is similar in performance to much more complex and expensive laser scanning microscopes, was demonstrated at the meeting in the booth of Boulder Nonlinear Systems, a manufacturer of high-performance SLMs. Yuste explained that the PocketScope can shape an incoming two-photon laser beam into nearly arbitrary excitation patterns, thus allowing for the simultaneous imaging or photostimulation of different regions of a sample with three-dimensional precision at high frame rates. They also demonstrated the functionality of this system for imaging brain slices by activating multiple neurons simultaneously in two and three dimensions.

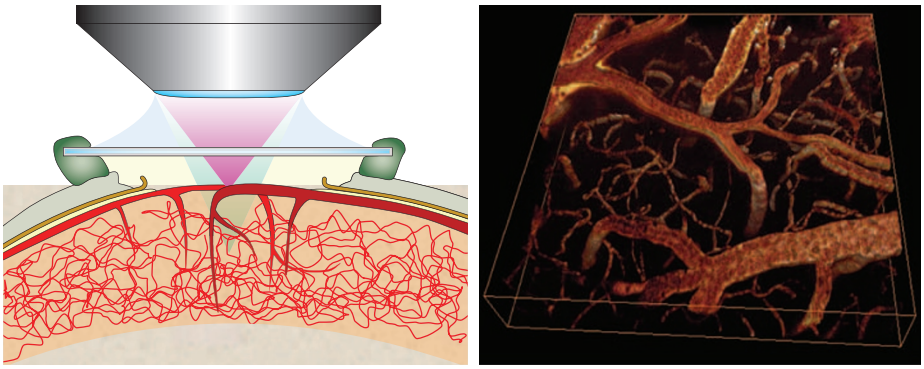
Poor 3D imaging speeds are a major hurdle when monitoring complex networks of vessels and neurons. According to Elizabeth Hillman from Columbia University in the USA, most approaches that increase the acquisition speed of scanning microscopes do so at the expense of spatial resolution or penetration depth. However, Hillman and colleagues have now developed an approach to two-photon microscopy that allows two or more layers of the living brain to be imaged simultaneously without a drop in image integrity. The technique relies on spectral multiplexing, in which excitation beams of different wavelengths simultaneously scan different regions of the sample. Spectral demultiplexing is used to extract images from each of the targeted regions and the fluorescence emissions are separated using a combination of two spectrally distinct fluorophores.

"We have demonstrated the power of this technique by imaging resting-state fluctuations in vascular tone through two layers of *in vivo* rat somatosensory cortex to determine the direction of vasodilation propagation," explained Hillman. "Using this technique with second- or third-harmonic generation contrast would allow broadband multiplexing of 3D volumes. The technique can be easily implemented in any nonlinear microscopy system that has two or more available laser wavelengths, and requires no modification to the detector configurations or electronics."

Light is also being used to stimulate neurons in individuals with hearing loss. According to Agnella Izzo Matic from North Western University in the USA, today's cochlear implants are limited partly by the spread of electric current in the cochlea, and therefore struggle to operate correctly in noisy environments. Lasers can stimulate more discrete populations of neurons than conventional electrical stimulation, thus potentially improving the user's hearing.

"We are working towards a cochlear implant built on optical technology. Our talk presented results from infrared neural stimulation in a chronically deafened animal model, which considers the hair cell loss and neural degeneration that is present in cochlear implant users," Matic reported. "The data showed small, discrete areas of stimulation in the chronically deafened cochlea, as well as the ability of the neurons to follow a stimulus of up to 120 Hz. These data show the feasibility of using lasers to stimulate remaining neurons at a rate that is biologically relevant to the auditory system."

Michael Jenkins' group from Case Western Reserve University in the USA discussed the use of pulsed 1.851 μm infrared light to non-invasively synchronize a beating heart to the pulse frequency of the laser without the use of exogenous agents. The researchers are now using this technique to investigate the potential causes of heart defects. Samarendra Mohanty's group from the University of Texas-Arlington in the USA discussed all-optical techniques for combining the light-mediated delivery of opsins (light-sensitive protein-coupled receptors found in the retina) in spatially targeted regions of neural tissue with optical identification of expression using yellow fluorescent protein imaging, followed by optical activation for the detection of neural activity. Mohanty and colleagues used an ultrafast near-infrared laser for the delivery and nonlinear activation of opsins in neuronal cells, both in *in vitro* and *in vivo*. We look forward to further innovations in photon–neuron interactions at next year's SPIE Photonics West, which will be held on 2–7 February 2013 in San Francisco, USA. ❐



LAUREN GROSBERG AND ELIZABETH HILLMAN

The use of light to stimulate neurons was a highlight topic at SPIE Photonics West 2012. Left, schematic for the 3D two-photon stack rendering of a vasculature. Right, resulting image acquired from a living rat brain.

David Pile is a senior editor at Nature Photonics, *225 Bush Street, Suite 1453, San Francisco, California 94104, USA.*
e-mail: d.pile@us.nature.com

Correction

The print version of the Research Highlight "Fibre 'black light'" (*Nature Photon.* **6,** 138; 2012) contained incorrect information regarding the emission wavelength range of the source.

The HTML and PDF versions of this Research Highlight are correct.