the entanglement between the two crystals. Using these measurements, Usmani *et al.* were able to demonstrate that their single heralded photon indeed created an entangled state between the two crystals.

Of course, there are plenty of challenges that must be overcome before this system can be used to establish a large quantum network. One of the biggest challenges — one faced by all such probabilistic entangling schemes demonstrated so far — will be increasing the overall efficiency of the system, which limits the rate of entanglement generation and thus the rate of information transfer. Another necessary improvement is increasing the distance between the crystals — Usmani *et al.* employed a spacing of just 1.3 cm to avoid the use of multiple cryostats. Other issues include improving the quality of the entanglement and lengthening the storage duration of the quantum state.

However, researchers have already demonstrated impressive progress towards tackling many of these issues, including demonstrations of long-lived coherences in crystals[6] for potentially storing received information and proposed architectures to increase the distance between crystal quantum memories[7]. Moreover, the intriguing possibility of fabricating structures directly into the crystals to improve the overall efficiency of the system adds to the appeal of these solid-state devices. Combining such advances with the spatial and temporal multiplexing abilities of these crystals, which might also be used to improve the entanglement rate, will make this system a strong contender for the scalable technology needed to implement large quantum networks. ❐

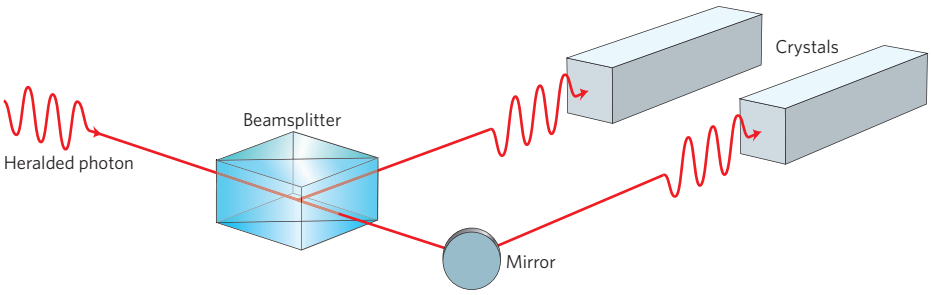

Figure 2 | Creating entanglement between two quantum memories. A heralded single photon (the 'pea') first passes through a beamsplitter. The outputs of the beamsplitter are directed to the two crystals (the 'shells'), where the photon is absorbed to produce a single excitation. The lack of information regarding the path of the photon creates an entangled state between the two crystals.

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VIEW FROM... SPIE PHOTONICS WEST 2012

Photons, neurons and wellbeing

Techniques for the targeted optical stimulation of neurons may offer new ways to tackle medical problems such as heart defects, epilepsy, Parkinson's, blindness and hearing loss.

David Pile

Using light to control biological processes is a relatively new joint research direction of the biological and physical sciences. Yet there is already a great deal of motivation for developing such technologies, as made clear from the "Photons and Neurons" sessions at SPIE Photonics West 2012, held in San Francisco, USA, on 21–26 January 2012.

Over a billion people worldwide suffer from brain disorders such as stroke, depression, migraine, epilepsy, Parkinson's, chronic pain and blindness. According to Edward Boydon, an expert on brain disorders from the Massachusetts Institute of Technology Media Lab, few of these disorders are effectively treatable by drugs or neurosurgical procedures. Furthermore, the treatments that do exist are often partial or present undesirable side effects. Part of the problem is the complexity of the dense neural circuits in the brain.

"Ideally we would be able to hone in on the precise circuits that can best contribute to the remedy of disease, and then use those circuits as drug targets, or as targets for neurosurgeons to implant electrodes to reduce symptoms," Boydon explained. "To do this, we invented a new technology that allows us to control specific cells embedded within dense neural circuits with light. We do this by exploiting the photosynthetic and photosensory proteins found in many biological species, which convert light into electrical energy."

Installing photosensory cells in a particular region of the brain modifies the neuronal cells to respond to light while leaving the surrounding cells unaffected. Boydon's team deliver the genes that encode for these proteins to targeted neurons by employing gene therapy viral vectors currently used for gene therapy trials in humans. They deliver the light by inserting compact optical probes such as optical fibres attached to small LEDs or lasers into the brain. Boydon and colleagues are now working on three-dimensional (3D) light-delivery devices — arrays of waveguides — to achieve improved control over 3D neural circuits. Light delivery methods in the field of optogenetics (the stimulation of nerve cells with light) was one of the key discussion points at the meeting.

Partrick Degenaar from Newcastle University in the UK explained that the rise of optogenetics has many exciting applications to neuroprosthesis. Future developments will require researchers to find ways of efficiently delivering light at the required intensity and depth — particularly because biological tissue is a strong scatterer

of light — while also maintaining low power consumption.

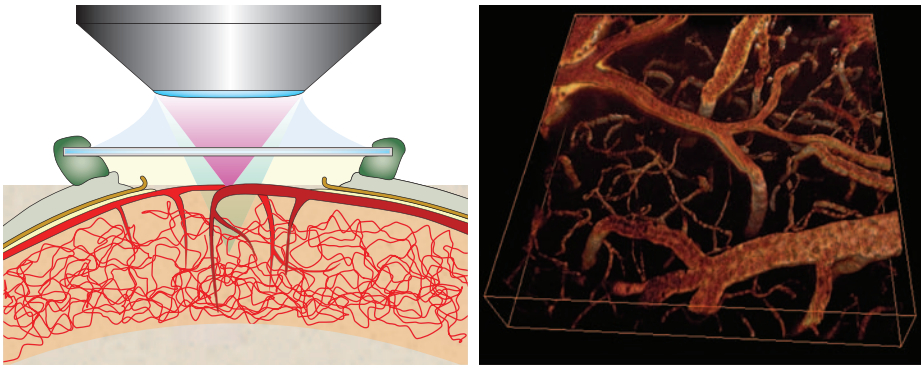
"We have presented simulations of what will be achievable using our micro-LED stimulator arrays coupled to waveguiding optrodes," Degenaar explained. "With the right engineering, we believe it should be possible to stimulate hundreds of points simultaneously, given the power dissipation of the human 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.



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.

"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. ❐

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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.