direct time-resolved measurement of the enhancement remains a challenge because the total external quantum efficiency, including the out-coupling efficiency, is still quite low ( $\sim 10^{-5}$ ).

Cho *et al.* report that the optical transition originates from phonon-assisted hot-carrier recombination before thermalization to the lowest energy state in the conduction band (Fig. 2b), rather than from the band-edge transition between the lowest energy of the conduction and valance bands<sup>2</sup>. This means that the Purcell effect is effective even for very complex optical transitions. Furthermore, because the energy of hot-carrier transitions is larger than the bandgap of silicon (1.1 eV, infrared), the silicon nanocavity emits visible light, thereby opening up new applications for silicon photonic devices.

Unfortunately, Cho et al. estimate that the internal quantum efficiency<sup>2</sup>  $(\sim 10^{-2})$  will be too low for immediate practical applications. Besides exploring better nanocavity structures, the internal quantum efficiency could be increased by combining this technique with other approaches, such as quantum confinement<sup>4-6</sup> to enhance emission rates and/or surface passivation to suppress non-radiative processes<sup>10</sup>. The development of practical silicon optoelectronic devices such as light-emitting diodes and lasers requires an appropriate current-injection method<sup>11</sup>. In light-emitting diodes, improving the lightextraction efficiency from the device is also important<sup>12</sup>. To achieve lasing, a balance between optical gain and combined losses is needed. Enhancement in the radiative



Figure 2 | Simplified electronic band structure and optical transitions of semiconductors. **a**, Direct-bandgap semiconductors such as GaAs, InP and GaN. **b**, An indirect-bandgap semiconductor, such as silicon.

emission rate could lead to an increase in optical gain<sup>13</sup>. At the same time, it will be critical to reduce cavity losses (that is, increase Q) while maintaining an ultrasmall mode volume V to overcome absorption losses in the metal. Although reducing Vtypically increases losses and thus reduces Q, reducing cavity losses can lower the threshold carrier density required for lasing, thus reducing other serious losses in silicon such as free-carrier absorption and Auger recombination<sup>1</sup>. Pursuing the development of technologies such as silicon nanocavities could brighten the path towards securing the biggest dream of photonics and material scientists — a silicon laser. 

Masayuki Fujita is at the Graduate School of Engineering Science, Osaka University, 1-3 Machikaneyama, Toyonaka 560-8531, Japan and at the Department of Electronic Science and Engineering, Kyoto University, Katsura, Nishikyo-ku, Kyoto 615-8510, Japan. e-mail: fujita@ee.es.osaka-u.ac.jp

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### ACOUSTO-OPTIC IMAGING

# Merging the best of two worlds

The combination of ultrasound and optics, together with statistics, now permits light focusing and imaging deep inside strongly scattering media at the optical diffraction limit.

## Geoffroy Lerosey and Mathias Fink

ethods for focusing light and imaging deep inside strongly scattering media for imaging purposes are strongly desired for applications including biomedical imaging, medical therapy and local drug delivery, to name a few. Biological tissues are inherently inhomogeneous and have microscopic permittivity fluctuations that scatter light as it propagates through them. These characteristics prevent conventional imaging techniques being used at depths greater than a few hundred micrometres.

To resolve this problem, a method based on the principle of time reversal<sup>1</sup>, called time reversal of ultrasonically encoded light (TRUE), was proposed in 2011<sup>2</sup>. TRUE uses ultrasound to focus light inside scattering media onto spots of the size of the ultrasonic focus, which is orders of magnitude larger than the optical diffraction limit<sup>2</sup>. Now, writing in *Nature Photonics*, Benjamin Judkewitz and co-workers report a paradigm shift by proposing the time reversal of variance-encoded light (TROVE) method<sup>3</sup>. Using several random wavefronts and a statistical approach, they demonstrate focusing of ultrasonically frequency-shifted light inside a scattering medium onto spots as small as an optical speckle grain.

When light propagates in a medium and encounters refractive-index

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inhomogeneities, it can be reflected, refracted or more generally scattered. In a typical biological tissue, for instance, a photon experiences a scattering event on average every few hundredths of a micrometre, the so-called scattering mean free path. This multiply scattered light 'loses' the memory of its original propagation direction within a few hundred micrometres, and, owing to the disordered nature of the medium of propagation, generates a random interference pattern or speckle. Hence, conventional imaging methods that rely on ballistic photons those that pass through the medium along a straight path — become useless at depths of the order of a millimetre. Although multiple scattering scrambles the photons in a seemingly indistinguishable wave field, it is a deterministic process. In other words, provided the medium of interest is stationary, a given wavefront entering a strongly scattering medium produces a random but unique speckle.

Specifically, a source placed in front of a slab of multiple-scattering medium generates a random wave field at its output; if this wave field is then propagated backwards by phase conjugation or time reversal, it will focus on the original source position. Over the past two decades, this property has been used with various types of waves to focus energy or to image through random media by using time reversal, phase conjugation, digital phase conjugation or iterative algorithms<sup>1,4-7</sup>. However, all these methods necessitate measuring the optical field on both sides of the sample. The problem of focusing and imaging inside a strongly scattering medium is more complicated because it requires either locally probing the field or placing a source inside the medium. Both methods can be achieved by, for example, embedding particles that have a nonlinear response (such as metallic nanoparticles) in the medium, and measuring the nonlinear wavefront originating from these particles after it propagates through the scattering medium<sup>8</sup>. Because this method requires depositing particles inside the medium, it is too invasive for most biomedical applications.

The TRUE<sup>2</sup> method was proposed by the group of Lihong Wang to overcome this limitation. The method is based on the acousto-optic effect: an ultrasonic beam is focused onto a spot in a medium that is highly scattering for light but almost homogeneous for sound. Photons generated by a laser source and propagating through the highly scattering medium undergo multiple reflections in the ultrasonic spot and hence reflect off the



Figure 1 | Experimental set-up and results by Judkewitz *et al.* **a**, Schematic of the experimental set-up. **b-e**, Epifluorescence images of two beads used for the demonstration without diffusers (**b**), between the diffusers using direct imaging (**c**), TRUE (**d**) and TROVE (**e**).

medium inhomogeneities, which vibrate at the ultrasonic frequency. As a result, the frequencies of some of the photons crossing the ultrasonic beam are Doppler-shifted by the ultrasound frequency<sup>9</sup>. Viewed from outside the medium, this volume of tagged photons thus functions as a virtual source that emits light of a slightly different wavelength from within the multiplescattering medium. In their demonstration, Wang and co-workers then phase conjugate the wavefront exiting the medium at this wavelength, which focuses light back inside the medium onto the ultrasonic focal spot<sup>2</sup>. This use of ultrasound eliminates the scattering nature of the medium, but at a cost: the resolution of the focal spot is determined by the ultrasonic diffraction limit, which is orders of magnitude larger than the optical one.

The question that arises next is how to overcome this acoustic diffraction barrier? Judkewitz and colleagues tackle this issue in a very clever way<sup>3</sup>. They start with a very simple consideration. The statistical properties of a random multiplescattering medium are such that if one could measure the total light intensity exciting each speckle grain at a given depth in a slab, one would obtain a constant value. The virtual source created by the acousto-optic effect in TRUE consists of an ensemble of such speckle grains, each of which is associated with an optical mode in the medium. Depending on the optical wavefront incident on the slab, these modes may be excited by light with random phases and amplitudes, but the intensity of those speckle grains averaged over many statistically independent wavefronts will be constant. Consequently, averaged over many incident wavefronts, the total output intensity from a given optical mode that

has been acousto-optically excited follows the spatial distribution of the ultrasonic focus. Simply stated, the position of a given optical mode inside the acoustic focus is coded by the amount of light it emits through the random medium, notwithstanding the symmetric nature of the ultrasonic focal spot.

To obtain the optical wavefront corresponding to a given speckle grain, Judkewitz and colleagues shine several random wavefronts on the scattering sample and use interferometry to record the corresponding output optical fields<sup>3</sup>. They then use a statistical procedure that selects a linear combination of all those wave fields whose total energy equals that of the desired speckle grain. This wavefront permits light to be focused at a specified location inside the strongly scattering medium onto a focal spot the size of a speckle grain, hence reaching the optical diffraction limit.

This breakthrough result is first demonstrated in a focusing scheme using the set-up shown in Fig. 1a. The sample under study consists of an opentop agarose-gel-filled quartz cuvette flanked on two opposite lateral sides by strong diffusers, which eliminate all ballistic photons. An ultrasound beam with a frequency of 50 MHz is focused in the cuvette from the top. The random wavefronts with a wavelength of 532 nm are generated on the left side using a rotating glass diffuser and the wavefronts are measured on the right side using an interferometric set-up. After performing an acquisition and calculating the searched wavefront, the wavefront is displayed on the measurement side using a spatial light modulator. To image the resulting focusing, a thin sheet containing fluorescent beads

is inserted between the diffusers and a conventional camera whose imaging plane is normal to the thin sheet is focused onto the sheet; the camera then detects the photons generated by the beads. Judkewitz et al. obtained results for plane-wave illumination, which was generated by displaying a constant-phase matrix on the spatial light modulator, thereby producing a very broad diffuse halo with a Rayleigh distribution. The TRUE method achieved a 30-µm-wide focal spot (the acoustic diffraction limit), whereas the TROVE method of Judkewitz et al. gave an optical focal spot that is about 5 µm wide. In this way, they demonstrated focusing of light in a scattering medium at a resolution limited only by the size of the optical speckle grain.

To further demonstrate the potential of their method, Judkewitz *et al.* perform an imaging experiment. Two 1-µm-diameter fluorescent beads are placed 15 µm apart between the strong diffusers (Fig. 1b). In the first experiment, the two beads are imaged from the right side and a typical speckle image is recorded (Fig. 1c), indicating the random and scattering nature of the diffuser located between the fluorescent beads and the camera. The researchers then use the TRUE and TROVE methods to scan the optical focus around the fluorescent beads, while collecting the fluorescent light exiting the system. Figure 1d clearly shows that the two beads cannot be resolved using TRUE<sup>2</sup>, whereas TROVE<sup>3</sup> achieves very good imaging of the beads with a resolution of the order of 5  $\mu$ m (Fig. 1e), which is again the size of a speckle grain.

This exciting demonstration proves that it is possible to image and focus deep within strongly scattering media. This has many potential implications for fundamental physics; for instance, it could allow one to capture the physics deep within exotic scattering media such as Lévy glasses or Anderson localized media. Moreover, these results show that the ability to image and focus deep inside living biological tissues is not far away.

Of course, many hurdles still need to be overcome before such amazing outcomes can be realized. For instance, for practical reasons, the work by Judkewitz *et al.* showed focusing and imaging between two strong diffusers. A demonstration of the approach within a thick scattering medium would greatly enhance its potential usefulness. Indeed, the amount of light collected would be much lower as a result of scattering deep inside the sample, which would reduce the sensitivity of the method. Furthermore, the technique currently takes two hours to image a  $30 \ \mu m \times 30 \ \mu m$  field of view, making it unsuitable for *in vivo* applications, as living tissues decorrelate on a timescale that is orders of magnitude shorter. The emergence of microelectromechanicalbased ultrafast spatial light modulators and high-speed cameras should enable this type of experiment to be performed in less than a second.

Finally, and most importantly, this work shows that applying statistical approaches to optical experiments is incredibly useful for studying and using scattering media, as has very recently been demonstrated in a related publication<sup>10</sup>.

Geoffroy Lerosey and Mathias Fink are at the Institut Langevin, CNRS and ESPCI ParisTech, 1 rue Jussieu, 75005 Paris, France. e-mail: geoffroy.lerosey@espci.fr

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# BIOIMAGING

# Lab on a DVD

Scientists based in Europe have succeeded in converting a commercial DVD drive into a laser scanning microscope that can analyse blood and perform cellular imaging with onemicrometre resolution (*Lab Chip*, doi: 10.1039/C3LC41360H; 2013). Harisha Ramachandraiah and the team from KTH Royal Institute of Technology in Sweden and the companies, Plarion in the UK and Lingvitae in Norway, say that their 'labon-a-DVD' system offers affordable and convenient cellular diagnostic testing for diseases such as HIV.

The approach makes two important modifications to the DVD drive and standard DVD media. First, an extra photodiode is added to the drive to detect transmitted and forward-scattered light through the disk. Second, the DVD media is replaced with a disposable, multilayer, semi-transparent polymer disk that contains fluidic microchannels



in addition to the usual 0.74- $\mu m$ -wide spiral track.

Before performing experiments, the inner surfaces of the fluidic channels are functionalized to allow surface attachment of the desired cells or particles. Samples of blood or another liquid of interest are then pumped into the channels and the DVD drive is switched on. The added photodiode records the amount of light from the drive's 658-nm semiconductor laser that is transmitted through the disk as it spins. The result is a two-dimensional image, which is saved to a computer hard drive for analysis. Cells or particles that have been successfully bound to the treated channels show up in the resulting images. To date, the team has tested their system by using it to image polymer beads of various sizes (1, 2.8 and 5  $\mu$ m) suspended in a solution as well as CD4<sup>+</sup> cells in blood, which are an important marker for the HIV virus.

The researchers are now working on extending the system to handle larger sample volumes so that lowconcentration species such as circulating tumour cells can be analysed in a fully integrated approach that automates the tasks of channel surface modification, washing and sample preparation.

#### **OLIVER GRAYDON**