Phase-sensitive imaging on a chip

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Scientists in California claim to have created a chip-based device that can perform two-dimensional differential phase imaging of an incident light field with a signal-to-noise ratio of greater than 16 dB and a sensitivity of one degree per micrometre. Developed by researchers at Caltech, the device could aid applications such as laser beam profiling, phase microscopy and optical wavefront sensing. The device works by measuring the interference pattern formed by four-holes (600-nm diameter with 1.2-μm spacing), that are arranged in a 'plus' shape above a CMOS image sensor. The design consists of a 15 × 15 pixel sensor that is coated with an 80-μm-thick layer of SU-8 photoresist and a 100-nm-thick silver film coating the holes. Light transmitted through the holes forms an interference pattern on the sensor and the pattern shifts position depending on the differential phase of the incident light. According to the Caltech team, the advantages of this approach are that the device can be fabricated with existing lithographic techniques, does not contain any optical elements and is potentially inexpensive. The team also says that in principle a microfluidic channel could be fabricated on top of the holes to form a phase-sensitive optofluidic microscope that can efficiently scan biological cells.

Simultaneous proton and X-ray imaging

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A laser-based scheme that can simultaneously generate protons and X-rays has been developed by scientists in Japan and Korea. The source, which emits a proton beam with a maximum energy of a few megaelectronvolts and an X-ray beam on the kiloelectronvolt scale, could prove useful for imaging microstructures. The emissions are generated from the laser–matter interaction that results when a high-intensity femtosecond beam from a chirped-pulse amplification Ti:sapphire laser is focused onto a target of copper tape. The researchers, from Kyoto, Nagasaka and Gwangju, successfully performed high-resolution shadow-graph imaging of miniature metal grid meshes with a resolution of 10 μm, an indication of the source's usefulness. They report that the difference in probing times between the X-rays and protons were of the order of a few hundred picoseconds when using a CR-39 track detector and imaging plate to detect the protons and X-rays, respectively. The team also suggest that the image quality could be improved further by using appropriate X-ray optics.

Multiple channels enhance fluorescent capture

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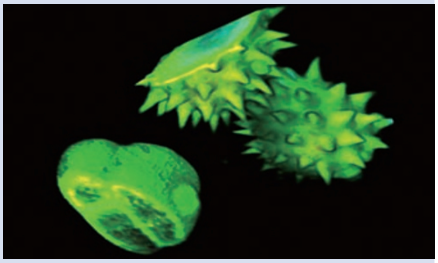
Three-dimensional fluorescence lifetime imaging (FLIM) has had a significant boost in speed thanks to the use of a scheme that uses multiple excitation beams, a multiple-channel detector and time-correlated single-photon counting (TCSPC) electronics. The result is the first multifocal, multiphoton TCSPC–FLIM microscope, according to its developers, a collaboration of scientists from London and Harlow in the UK. Their system uses a 16-channel photomultiplier tube detector and 16 excitation beams to either speed up the imaging process or enhance its sensitivity. The team has successfully imaged pollen grains: three-dimensional FLIM images were produced from an image stack of 150 optically sectioned images taken within 50 minutes. The potential for imaging live cells was also demonstrated, with the researchers concluding that count rates of up to 50 MHz can be achieved with bright fluorescent samples. In addition, when analysing weakly fluorescent samples, the multifocal excitation approach gives a 16-fold increase in fluorescence signal compared with a traditional single-channel system.



Probes provide multicolour capability

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Super-resolution, multicolour imaging is highly desirable for visualizing biological molecular interactions on the nanoscale, but has remained a challenging task so far. Now, the development of a family of fluorescent probes that have customizable properties could help. The approach taken by Mark Bates and colleagues from Harvard University, USA, is based on so-called stochastic optical reconstruction microscopy (STORM). The technique relies on the imaging of fluorescent probe-pairs and their corresponding locations with great precision. The probes consist of a photo-switchable 'reporter' and 'activator' pair of dyes. The reporter is a dye that can be cycled between fluorescent and dark states and the activator is a dye that 'switches on' the reporter. By tailoring the colour of the reporter and activator, it is possible to achieve multicolour imaging. For example, the team says that combinational pairing of three activators and three reporters could generate up to nine distinct fluorescent probes. To demonstrate the potential of the technique, Bates and co-workers performed multicolour imaging of DNA model samples and mammalian cells with a resolution of 20–30 nm. The team says that the resulting images clearly revealed fine structural detail that was not discernible in conventional fluorescent images.

Frequency-encoding boosts operation range

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A technique for increasing the range of optical-frequency-domain imaging (OFDI) has been demonstrated by scientists from the Harvard Medical School and Wellman Center for Photomedicine in the USA. Based on a similar principle to optical coherence tomography, OFDI is becoming a popular technique for applications in medical imaging. The wavelength of a high-speed tunable laser is 'swept' over the sample and an image is created by combining and analysing light from the sample and a reference path. In a conventional configuration, the depth range of the imaging is limited to about half the coherence length of the laser source. As this imposes undesirable constraints on the separation between the probe and the surface of a sample, scientists have been searching for ways to improve the range. Now Reza Motaghian Nezam and co-workers have extended the range of an OFDI system by a factor of three (to 7 mm) by using two independent reference paths of different lengths, each containing a frequency shifter. By using acousto–optic frequency shifters operating at 25 MHz and 50 MHz and a laser tuning range of 117 nm (from 1,240 nm to 1,357 nm) the team have achieved imaging with a signal-to-noise ratio of more than 100 dB. The benefits of the technique have been demonstrated through *ex vivo* imaging of a human aorta .