

sequences that bind to part of the barcodes. For each antibody–PSA sandwich complex, hundreds of DNA barcodes are detected on the glass array, thereby giving a large signal for a small amount of PSA.

Controversy surrounds the use of PSA in population screening for prostate cancer<sup>3</sup> because PSA is not a truly cancer-specific marker and other non-cancerous diseases of the prostate, such as benign prostatic hyperplasia, can also lead to increased levels of PSA in the blood<sup>4</sup>. However, the fact that it can predict the recurrence of prostate cancer following surgery is largely undisputed, with the risk of recurrence increasing with elevating PSA concentrations<sup>5</sup>. The bio-barcode assay would seem to validate the role of PSA metrics in this context. Accordingly, patients with low but detectable PSA could

be reassured that they are not at risk of recurrence if they show a non-rising profile, and patients with rising PSA levels will more promptly receive appropriate treatment.

Where this ultrasensitive assay may have significant benefit is in tracking PSA levels in patients who have undergone secondary treatment. The obvious question is how low is too low or where does ultrasensitivity actually become insignificant? There is need for a similar retrospective study with a larger cohort of patients and, more importantly, a prospective study to validate the exact clinical utility of the ultrasensitive monitoring of PSA levels (and to study the influence of other factors such as family history, age and ethnicity).

Just as ambrosia was the elixir of immortality for the Greek gods, the Norse

equivalent was golden apples. Although bio-barcoded gold nanoparticles may not confer immortality, they have demonstrated potential promise for improving prostate cancer outcomes. □

*Stephen Hearty, Paul Leonard and Richard O'Kennedy are in the School of Biotechnology and Biomedical Diagnostics Institute, National Centre for Sensor Research, Dublin City University, Dublin 9, Ireland. e-mail: stephen.hearty@dcu.ie; paul.leonard@dcu.ie; richard.okennedy@dcu.ie*

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## PHOTONIC-PLASMONIC DEVICES

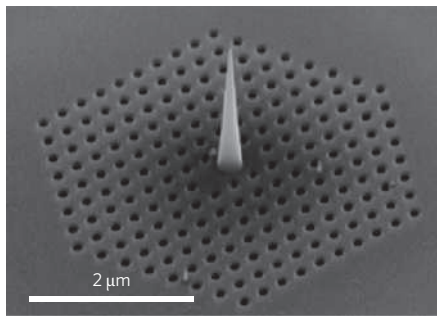
# A 7-nm light pen makes its mark

An optical probe has been developed for the chemical mapping of materials at the nanoscale by combining plasmonics, Raman spectroscopy and atomic force microscopy.

Nikolay I. Zheludev

When an electronic engineer examines a complex circuit, such as an old-style radio set, they often probe it with a sharp metal tip that is attached to an oscilloscope or spectrum analyser with a coaxial cable. By bringing the probe into proximity of the circuit (the near-field) or, better still, in contact with the wires of the circuit, the engineer hopes to learn how the individual elements perform. This cannot be done without a local near-field probe because, at a distance, signals from different components within the circuit will have been mixed up, and many of the components are specifically designed not to emit signals into the far-field.

For a circuit operating at a certain main clock frequency — an oscillating signal that is used to coordinate the processes of a circuit — the near-field probe can identify areas where electric fields oscillate with high and low amplitudes, thus testing the integrity of connections and identifying broken links. Furthermore, sophisticated circuitry containing active signal-processing components such as diodes, nonlinear capacitors (varactors) or resistors can be examined further. These components may give signature signals at frequencies different from that of the main clock, and their amplitudes could be used to judge whether the active elements are operating in the



**Figure 1** | The ‘light pen’ created by Di Fabrizio and co-workers consists of a sharp silver tip on a thin semiconductor membrane that contains an array of nanoscale holes. When illuminated from below, the membrane harvests the incident light and converts it into plasmon polaritons that propagate along the silver tip to produce an energy hotspot with a diameter of 7 nm at the end of the tip. This hotspot can be used to obtain topographic and chemical information about samples through the Raman effect.

correct regime. The signals will typically be at harmonic frequencies that are multiples of that of the clock.

Circuits operating with several frequencies may also show a more complex behaviour. A resonant circuit containing a nonlinear component, such as a lump inductance in

parallel with a varactor, can give a signature response with a frequency corresponding to the difference between that of the clock and the tuned resonance of the circuit. This signal can be used to determine the frequency that the resonant circuit is tuned to. The response will also be sensitive to the environment surrounding the circuit.

Imagine now that we scale the circuit down in size a hundred million times. What was a radio resonator will become a molecule with its own characteristic frequencies of vibrations. What was previously a radiofrequency signal will now have a wavelength between the visible and the infrared parts of the spectrum. What was previously the process of differential frequency generation will become Raman scattering which, as the basis of Raman spectroscopy, allows us to identify molecules by how they scatter light. It is also extremely sensitive to intermolecular interactions.

But do we have a sharp optical probe to match the engineer’s electric probe? This probe needs to be capable of facilitating Raman spectroscopy with extremely high lateral resolution. To achieve this, the dimensions of the probe have to be comparable to the size of a molecule. Writing in *Nature Nanotechnology*, Enzo Di Fabrizio of NanoBioScience Laboratory and the University of Magna Graecia and colleagues

at five Italian laboratories report the development of such an optical probe<sup>1</sup>.

Nanoscale tips are already used in the scanning tunnelling microscope and the atomic force microscope, which are capable of atomic-scale visualization and manipulation. Nanoscale tips are also used, in combination with a light source, in scanning near-field optical microscopes. However, Di Fabrizio and co-workers have gone further. They have developed a sub-10-nm light concentrator that works simultaneously as an atomic force microscope tip and as a probe for the optical-range spectrum analyser (Fig. 1).

The Italian team show that by converting light into surface plasmon polaritons — a form of coupled oscillations of electromagnetic fields and electrons in a metal — the optical energy can be focused into a region just a few nanometres wide. This is achieved through an adiabatic compression process, which was proposed

by Mark Stockman in 2004 (ref. 2). In the process, plasmon polaritons travelling towards the tip of a metallic tapered waveguide will slow down and the amplitudes of the electric-field oscillation will increase. This concentration and field enhancement cannot continue *ad infinitum*: solid-state physics tells us that the tip loses the metallic characteristics needed to support plasmons when its taper shrinks to a size of about 5 nm. Di Fabrizio and co-workers go extremely close to this fundamental limit — their plasmonic tapered probe can concentrate signals to an area of about 7 nm in diameter.

The team demonstrate the capabilities of this 'light pen' by using it to deliver a 'clock' optical frequency to silicon molecules in nanocrystals and detecting the Raman signals that are of the same nature as the differential frequency signals created by the lump electronic resonators. As the probe can function as an atomic force microscope tip, as

well as a nanoscale light source for near-field Raman excitation, the researchers are able to scan the silicon sample at the same time as acquiring Raman data. As a result, they can obtain topographic, chemical and structural information about the silicon nanocrystals.

Di Fabrizio and colleagues<sup>1</sup> have succeeded in developing a close optical analogue to the electrical probe used by countless electronic engineers, thus placing a new and potentially useful tool into the hands of researchers working on nanoscience and technology. □

Nikolay I. Zheludev is with the Optoelectronics Research Centre, University of Southampton, Southampton SO17 1BJ, UK.  
e-mail: niz@orc.soton.ac.uk

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## QUANTUM DEVICES

# Towards entangled electrons

A new method has been developed for extracting Cooper pairs from a superconductor and splitting them. The next challenge is to show that these unpaired electrons are entangled.

Christoph Strunk

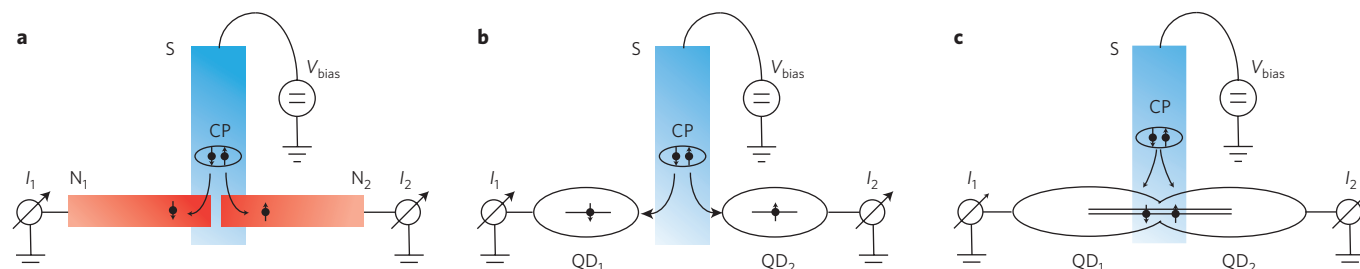
Quantum mechanics describes physical properties such as polarization or spin in terms of quantum states. Two particles are said to be entangled if the measurement or manipulation of the quantum state of one particle affects that of the other particle. Entanglement forms the basis of the famous Einstein–Podolsky–Rosen paradox, in which very distant particles seem to exchange information instantaneously, in apparent conflict with special relativity. Although the entanglement of the polarization of photons has been

demonstrated<sup>1</sup> and applied in quantum cryptography, other applications — such as solid-state quantum computers and other new electronic devices — would benefit from a reliable source of entangled electrons<sup>2</sup>.

Spin-entangled electrons can be produced by splitting apart the pairs of electrons (Cooper pairs) that are found in superconductors<sup>3–6</sup>. Cooper pairs have a well-defined total spin of zero, but the orientations of the spin of each electron are entirely undetermined at any given time. It is this combination of the known and unknown

that makes pairs of entangled electrons so potentially useful for quantum computers.

One approach to splitting Cooper pairs involves placing two normal metallic output leads adjacent to a superconductor. Only Cooper pairs with an energy below the superconducting energy gap can enter or leave the superconductor. As a result, at low temperature and voltage bias (Fig. 1a), electron extraction into the leads can be restricted to consist entirely of Cooper pairs, leading to entanglement and other non-local quantum effects. In the normal metal, the



**Figure 1** | Three types of Cooper pair (CP) splitter. In each case, a bias voltage ( $V_{\text{bias}}$ ) is applied to a superconducting contact (S), and the currents ( $I_1$  and  $I_2$ ) from the two output channels are measured. **a**, An all-metallic device with two normal metal terminals ( $N_1$  and  $N_2$ )<sup>5–7</sup>. **b**, A device with two weakly coupled quantum dots ( $QD_1$  and  $QD_2$ ): splitting occurs when the Cooper pair tunnels out of the superconductor<sup>8</sup>. **c**, A device with two strongly coupled quantum dots: entanglement is maintained on the double dot, and splitting occurs when the Cooper pair leaves the double dot through different terminals<sup>9</sup>.