

## Applied physics

## To catch a photon

Daniel E. Prober

Astronomers crave a detector sensitive enough to detect a single photon and determine its energy. A new single-pixel device can do this, and could also be built up into a large array suitable for a telescope.

Vision is the richest of the human senses, and detectors of light have long featured in science and technology. In fields as diverse as telecommunications, medicine and astronomy, there is demand for exquisitely sensitive detectors of the quantum of light, the photon. But as yet there is no single commercial device that can simultaneously detect individual visible photons and record the colour (or energy) and arrival time of each photon. If such a detector existed, it should also produce images with many picture elements (pixels) — and be affordable. Day and colleagues<sup>1</sup> now propose a device, based on the principle of kinetic inductance, that could function as an individual pixel in a photon detector (page 817 of this issue). Importantly, they show that the device has the necessary properties to allow the incorporation of

many such pixels into the 'ultimate' photon detector, one that could also be read out with practical, available electronics.

The search for the ultimate photon detector has been driven by astronomers, who are often faced with a limited number of photons to measure, emitted from some object in our Galaxy or beyond, and limited time in which to measure them. At present, astronomy is well served by the charge-coupled detector (CCD), familiar to many people as the CCD sensor in their digital camera or camcorder. Megapixel CCDs are now common. But this detector cannot resolve individual photons, because the noise occurring randomly in its readout electronics is too large to allow it. Moreover, the physics of the detector precludes the measurement of photon colour, unless colour filters are used. These reduce efficiency, but without such

filters a CCD would see only shades of grey.

To record single photons cleanly and to discern their energy and arrival time requires a detector that operates at low temperatures. This gets rid of the thermal agitation in the device that would disrupt a single-photon signal, and also means that materials and techniques can be used that are fundamentally different from those employed in the CCD. The first advance in cryogenic detector technology was the silicon 'microbolometer'<sup>2</sup>, in which a small piece of silicon is held at 0.05 K but heats up when a photon is absorbed. The subsequent rise and fall of the temperature is recorded, to determine the photon energy. These detectors are employed by astronomers for rocket-based observations of photons at X-ray wavelengths, with an energy 100 to 1,000 times that of visible photons. But their sensitivity is not sufficient to record visible photons, with an energy of 1.5 to 3 electronvolts.

Over the past decade, new devices have been developed that are more sensitive and can record visible photons<sup>3–9</sup>. These detectors fall into two classes. The first is the bolometer, which uses the same heating effect as mentioned above to determine photon energy. The thermometer inside such a device, recording the temperature change, is a strip

## Genetics

## Secrets of a porkier porker

Gregor Mendel's remarkable studies of peas revealed a straightforward pattern of genetic inheritance. But since then we've learned that matters are not always so simple: many identifiable traits result from complex interactions between multiple genes and environmental factors. Current work in genetics aims to quantify the contributions of specific variations in each gene to the mix. But pinpointing the right spot in an animal's huge genome can be a nightmare, even in organisms that have had their genome completely sequenced.

The humble pig, meanwhile, has only recently received its own genetic map — a first-generation sketch of what its genome sequence might look like. Imagine, then, how difficult it must have been to find one specific nucleotide that controls 15–30% of the variation in muscle mass seen between pigs. But that's just what Anne-Sophie Van Laere *et al.* report elsewhere in this issue (*Nature* 425, 832–836; 2003).

The authors find that a change from a guanine nucleotide to an adenine at a specific point in the



*IGF2* gene can add 3–4% more meat to a pig. The nucleotide change disrupts the regulation of *IGF2*, increasing its expression threefold in muscle but not at all in liver, another main organ of expression. As the IGF-II protein stimulates muscle growth, the result is a pig with more muscle and less fat — a boon for meat production. And, as the change occurs in part

of the gene that does not actually code for protein, it suggests that researchers should not study just the protein-coding bits when looking for important genetic differences between individuals.

Of course, farmers don't need to know the exact mechanism involved; they spotted this physical trait years ago and selected for it in breeding schemes. Thus, Van Laere

*et al.* show that the muscle-favouring alteration has swept through commercial pig populations, but is not present in Asian or European wild boars tested. Now that the pig is lining up with other farm animals such as cows and chickens to have its genome sequenced, we should be able to find other genetic contributions to bulked-up pigs. **Chris Gunter**

of partly superconducting metal<sup>3,6</sup>, the readout amplifier is also superconducting. As superconductivity — the flow of current without resistance — is a low-temperature property, the entire structure of the device is a cryogenic environment (which is easier to engineer than a device with only some superconducting components).

The second class of detector makes use of the electron excitations created in solids by the energy of an incoming photon<sup>5</sup>. Numerous observations have been made with such detectors developed at the European Space Agency<sup>7–9</sup>, including observations of the Crab nebula and short-period binary systems, known as polars<sup>9</sup>. The readout electronics of these detectors, however, operates at room temperature, with the consequence that the number of channels that can be read out is limited. So far, the number of pixels in an image has been limited to 36. Clever device design might mean that this number of pixels can be expanded by a factor of maybe 10 to 20, but the engineering is proving difficult.

Day *et al.*<sup>1</sup> now present a new approach to the problem of photon detection. Their device contains a superconducting film held at low temperature. Inside the film, resistanceless current flows in the form of electron pairs. If a photon hits the device, it can break up some of these pairs, with the result that the supercurrent becomes more 'sluggish'<sup>10</sup>. That increase in sluggishness can be detected in the surrounding microwave circuitry. The nature of the measurement is akin to watching an object on a spring, vibrating at the natural oscillation rate: the rate of the spring's vibration reveals the mass ('sluggishness') of the object.

The authors also show that cryogenic electronics systems already available are adequate for the readout of the signal from their device. Device and readout together make the desired single-photon detector. Moreover, the method of readout used can be rather easily generalized to accommodate hundreds, and perhaps thousands, of pixels. Other fields of science, such as fluorescence microscopy studies of single molecules, should also benefit from this new detector technology.

The ultimate photon detector, however, is not yet at hand. Some challenges remain for Day and colleagues' design<sup>1</sup>: for example, although there is very little noise in the readout system, the detector itself has not yet achieved that low level of noise. Whether the noise source is intrinsic or extrinsic is not clear, but I am optimistic that it can be remedied. Meanwhile, in the race to produce the ultimate photon detector, the other candidates (mentioned above) are advancing<sup>11–13</sup>. The winner — or winners — of this race will be determined in part by issues that go beyond performance, such as cost and ease of use. Practical engineering factors hold sway in astronomy, just as in regular life. ■

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## Stem cells

# Interactive niches

Ihor R. Lemischka and Kateri A. Moore

The microenvironment, or niche, in which stem cells reside controls their renewal and maturation. The niche that regulates blood-forming stem cells in adult animals has eluded researchers — until now.

Cell-fate decisions in the developing embryo are governed by a complex interplay between cell-autonomous signals and stimuli from the surrounding tissue — the microenvironment. Similar processes control the birth and maturation of stem cells that replenish mature cell populations in adults<sup>1,2</sup>. But where are the stem-cell microenvironments located in adult tissues? And what other cell types contribute to these 'niches'? In mammals, the niches for gut and certain skin stem cells have been pinpointed, and in several cases the molecular signals that emanate from them have been identified<sup>3–6</sup>. Somewhat ironically, however, the niches that interact with the best-characterized mammalian stem cells, the haematopoietic stem cells (HSCs), which replenish at least ten blood-cell lineages, have been much more elusive. In this issue, Zhang *et al.*<sup>7</sup> and Calvi *et al.*<sup>8</sup> now provide insights into the nature of HSC niches in adult animals. These authors demonstrate that osteoblasts — cells that reside in the bone marrow and secrete the calcified bone matrix — have a crucial role in HSC regulation.

Several studies have suggested that primitive HSCs reside next to the inner surface of bone and that they migrate towards the blood vessels at the centre of the bone marrow cavity as they mature and 'differentiate'<sup>9,10</sup>. Since the 1970s, efforts to characterize the HSC niche have involved developing systems *in vitro* that might mimic some of the features of stem cell–niche interactions *in vivo*<sup>11</sup>. Indeed, single clones of 'stromal' cells can support HSC self-renewal and differentiation in culture<sup>12</sup>. And some of these stromal cell clones are part of the bone-forming 'osteoblastic' lineage, which is consistent with the idea that osteoblasts might be a component of the HSC niche *in vivo*<sup>13</sup>.

Zhang *et al.*<sup>7</sup> and Calvi *et al.*<sup>8</sup> have now confirmed that osteoblasts have a function in stem-cell regulation in animals. Both groups employed genetic strategies to increase the

size of the osteoblast population in specific regions of bone. They then looked at how this affected the HSC population. In essence, they found that increasing the number of osteoblasts causes parallel increases in the HSC population.

Zhang *et al.*<sup>7</sup> looked at the involvement of signalling by bone morphogenetic protein (BMP) in HSC regulation. The activity of BMP is crucial to the development of blood-forming tissue in embryos. The authors show that mutant mice depleted of a cellular receptor for BMP develop bone abnormalities — calcified 'trabecular bone-like areas' form within long bones. And the numbers of primitive long-term (LT) HSCs are approximately doubled in these animals. The authors go to considerable lengths to demonstrate that the HSC pool is specifically increased without concomitant increases in other primitive progenitor cell populations. Such a specific increase in only the LT-HSC population is consistent with very local effects; in other words, it suggests that a very specific niche is functionally enhanced.

To gain further insight, the authors employed a more elaborate genetic strategy in which a fluorescent green protein marker was activated in cells that were depleted of the BMP receptor. Only the osteoblasts that lined the surface of the bone-like area fluoresced. Using a combination of cell markers to label the LT-HSCs, Zhang *et al.* found that the stem cells co-localized with spindle-shaped osteoblasts lining the bone surface. And a doubling of this osteoblast population mirrored the increase in the LT-HSC population in the mutant mice. These osteoblasts, and a subpopulation of the HSCs, expressed N-cadherin, a cell-surface molecule that helps cells adhere to one another. The authors suggest that N-cadherin and a protein that forms a complex with it,  $\beta$ -catenin, might form important components of the interaction between the stem cell and its niche. To prove this, it will be necessary to