
**100 YEARS AGO**

**Intentional introductions of wild species, however, have almost without exception resulted disastrously .... In 1872 Mr. W. Bancroft Espeut imported four pairs of the Indian mongoose from Calcutta into Jamaica for the purpose of destroying the "cane-piece rat." Ten years later it was estimated that the saving to the colony through the work of this animal amounted to 100,000*l.* annually. Then came a sudden change in the aspect of affairs. It was found that the mongoose destroyed all ground-nesting birds, and that the poultry as well as the insectivorous reptiles and batrachians of the island were being exterminated by it. Injurious insects increased in consequence a thousand-fold; the temporary benefits of the introduction were speedily wiped away, and the mongoose became a pest. Domestic animals, including young pigs, kids, lambs, newly-dropped calves, puppies and kittens, were destroyed by it, while it also ate ripe bananas, pine-apples, young corn, avocado pears, sweet potatoes, cocoas, yams, peas, sugar-cane, meat, and salt provisions and fish. Now, we are told, nature has made another effort to restore the balance. With the increase of insects, due to the destruction by the mongooses of their destroyers, has come an increase of ticks, which are destroying the mongoose, and all Jamaicans rejoice.**
From *Nature* 21 October 1897.

**50 YEARS AGO**

**A project for a Central Library of the World, drawn up during the German occupation of France, with the dual objects of providing more effectively for the preservation of the documents on which human culture rests and making their utilization easier and more widespread, is of interest in relation to the programme of work now contemplated by the United Nations Educational, Scientific and Cultural Organization. ... The preliminary scheme summarized in this pamphlet contemplates the establishment of the organisation, to be called the Bibliothèque Centrale du Monde, by a statute guaranteeing the absolute inviolability of the headquarters of the organisation, which is to be regarded as a world reserve; the territory where it is located should belong to no nation....**
From *Nature* 25 October 1947.

foods by spice lovers is due to death of neuronal pain fibres. Alternatively, the entry of calcium may initiate intracellular regulatory mechanisms (such as phosphorylation of target proteins or transcription) that reduce the cellular response. In any case, capsaicin is known to have analgesic effects against arthritis and post-herpetic neuralgias, and desensitization of the nerve response may be the main mechanism by which it acts.

Rapid increase of temperature to levels that produce pain (noxious heat) is also thought to be sensed by the capsaicin receptors in neurons[8]. Interestingly, the VR1 channel also senses temperature at levels that produce pain, providing a plausible molecular explanation for why we perceive foods that contain capsaicin as hot. Moreover, Julius and colleagues found that rapid increases in temperature — from 22 °C to 48 °C — evoke ion currents from expressed VR1 channels that closely mimic those induced by capsaicin.

The amino-acid sequence of VR1 is most closely related to the transient receptor potential (TRP) class of proteins (reviewed in ref. 9), several subtypes of which have now been cloned in humans. There has been much talk — but no definitive data — to suggest that TRP proteins comprise the class of channels that are activated by depletion of calcium from the intracellular calcium repository. Such 'store-operated' channels might not only replenish intracellular calcium, but they may have other functions. The message that signals the plasma membrane to let in more calcium remains a mystery. Julius and co-workers rule out a store-operated role for VR1 channels: thapsigargin, which stimulates depletion of intracellular calcium by blocking Ca–ATPase pumps, does not activate expressed VR1 channels. Moreover, most of the sequence homology to TRP proteins is in the amino-terminal ankyrin repeats, which probably act to localize and anchor such proteins.

Cloning of the noxious-temperature-sensitive capsaicin receptor adds an important member to the list of relatively nonselective ion channels that are gated by ligands. Unlike the purinergic- and glutamate-receptor-channels, the natural ligand — if one exists — is not known. It is possible that the real purpose of the channel is to sense noxious temperature, and that capsaicin is nature's low-energy way of harnessing the sensor. But it would be interesting if there turned out to be related channels and, perhaps, intrinsic agonists that could be used as pharmacological targets. Certainly, clinical management of chronic pain — such as that caused by arthritis, spinal-cord injury or diabetic neuropathy — could use new therapeutic strategies. At the very least, Mexican restaurants might be able to provide antidotes for their jalapeño-challenged clientele. □

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Sensors

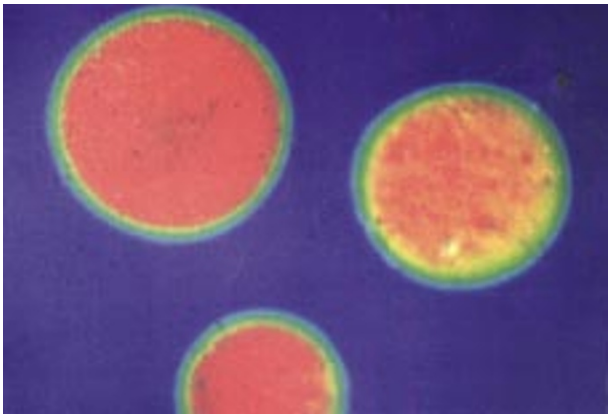
# New age crystals

David G. Grier

How much lead is in your drinking water? How much glucose is in your bloodstream? Assaying trace components in complex solutions usually requires the sophisticated facilities of an analytical laboratory. But a new class of composite materials created by Holtz and Asher at the University of Pittsburgh may revolutionize such measurements, moving them out of the laboratory and into everyday life[1]. The sensors they describe on page 829 of this issue combine sensitivity with specificity in an economical system that is appropriate to a very wide range of applications. Moreover, the sensors are strikingly beautiful, shimmering with the colours of the rainbow (Fig. 1).

The active elements in the new sensors are chemically functionalized gels. These gels are networks of crosslinked polymer strands, saturated like a sponge with a fluid solvent. Small changes in the fluid's composition can lead to dramatic changes in the gel's volume through a combination of processes known collectively as swelling. The degree to which a gel swells is controlled by a delicate balance of interactions between the polymer and its solvent, and between different chemical domains on the polymer itself. Changing the balance, for example by changing the gel's temperature, causes the polymer network to expand or contract.

Chemically functionalized gels can be tailor-made to respond strongly to a specific stimulus, such as the concentration of a particular ion in solution. The trick is to incorporate chemical groups into the polymer whose response to the desired stimulus induces a swelling transition. The functional groups highlighted in Holtz and Asher's study respond to specific chemical species by



J. H. HOLTZ & S. A. ASHER

Figure 1 **Leaded lights: a new gel sensor shows three drops of dilute $Pb^{2+}$ solution, spreading slowly. A chemically functionalized gel fills the space between tiny plastic spheres that form a colloidal crystal. This usually diffracts violet light towards the angle observed here, but when the lead solution diffuses through it the gel swells, increasing the spacing of the crystal so that it diffracts red light.**

developing electrostatic charges whose mutual repulsion causes the gel to swell. Other gels swell in response to light[2] or pH[3]. The response to these stimuli can be calibrated precisely and is highly reproducible.

Until now, gels' utility as sensor materials has been limited by a lack of accurate techniques to gauge their swelling. The Pittsburgh group have solved this problem by encapsulating colloidal crystals within their gels to form composite materials whose optical properties respond strongly to small chemical changes.

Colloidal crystals are regular arrays of small particles, often spheres, suspended in a fluid[4]. Hard spheres experiencing only contact repulsion form rigidly ordered crystals when they fill roughly half of the available volume; charged spheres with longer-range interactions crystallize at much lower concentrations. These crystals have lattice constants that are comparable to the wavelength of light, and so they act like three-dimensional diffraction gratings, resolving incident white light into its component wavelengths. The resulting blaze of pure colours is familiar from peacock feathers, butterfly wings and gem opals, all of which owe their beauty to such ordered microstructures. Changing a crystal's lattice constant changes what colour it scatters into a particular angle, and the Pittsburgh sensors exploit this effect to measure swelling.

Creating a functionalized gel around a colloidal crystal is not much more complicated than adding fruit to a gelatin dessert. Colloidal spheres can be dispersed in a solution of reagents used to make a functionalized gel. Once the spheres have assembled themselves into a crystal, the gel can be polymerized around it. Individual spheres either become chemically bound to the polymer network, or else become tangled within the web. Then, as the gel swells, the crystal's lattice constant changes by an amount that can be measured optically.

A practical sensor might consist of a small chunk of composite gel, probably smaller than a cubic millimetre, attached to the end of an optical fibre. This end would be dipped into a test solution whose constituents would diffuse into the gel, coming into equilibrium with the chemically-specific binding sites. A spectrophotometer at the dry end of the fibre would then gauge the gel's response to its target stimulus by measuring its optical reflectivity.

Different gels would be needed to measure different stimuli. The necessary volume of gel is so small, however, that each optical probe should be very cheap. Moreover, because gels can be sensitized to a wide range of stimuli, many different tests could take advantage of the same optical read-out equipment. Indeed, an array of such sensors could be devised to perform highly efficient combinatorial assays along the lines pioneered by Peter Schultz and co-workers at Berkeley[5]. This flexibility and generality contrasts with conventional techniques, such as conductivity probes for pH and ionic concentration, which tend to be highly specialized, delicate and expensive.

In addition to their practical applications, gelled colloidal crystals are likely to be interesting in their own right. For instance, they might help to resolve a heated controversy regarding interactions between charged colloidal spheres[6,7]. Experiments and theoretical considerations imply that within a colloidal crystal, like-charged spheres may attract one another, contrary to conventional understanding. Optically measured structural changes in gelled crystals might provide new insights into the anomalous attraction's mechanism. Conversely, the spheres might serve as useful tracers[8] with which to probe the structure and dynamics of the gels, neither of which is particularly well understood. Both as sensors and as subjects for fundamental research, functionalized gelled colloidal crystals have a bright future. □

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Genomic imprinting

# Disomy and disease resolved?

Nicholas Hastie

Why is it that babies with two doses of chromosome 11p15 from their father — instead of one from each parent — have disproportionate overgrowth of organs such as tongue, muscles, kidney, liver and heart[1,2]? This is the so-called Beckwith–Wiedemann syndrome (BWS)[3], and other symptoms include omphalocele (an abdominal-wall defect), thickening of long bones, renal dysplasia (abnormal growth), adrenal cytomegaly and polyhydramnios (excess amniotic fluid).

On page 809 of this issue, Sun *et al.*[4] report that they have used a transgenic-mouse approach to provide convincing evidence that some, but not all, of these problems arise because the children have double the normal dose of insulin-like growth factor-2 (IGF2). The *IGF2* gene on chromosome 11p15 is remarkable in that it is imprinted — in other words, only one of the two parental copies is normally active. In this case, the paternal copy is active whereas the maternal gene is silent in most tissues. So a baby with a paternal duplication of chromosome 11 would be expected to have a double dose of the protein.

IGF2 has long been a front runner for a BWS factor. It is expressed at highest levels in the tissues that are most affected in BWS. Moreover, mutations in mice that lead to increased (indirectly) or decreased expression of *Igf2* result in overgrowth or undergrowth, respectively[5,6]. Most compelling is the fact that *IGF2* imprinting is lost in 80% of BWS cases, so the maternal allele is also expressed[7]. But all of the evidence so far has been circumstantial, the problem being that there is a cluster of imprinted genes on chromosome 11, and no chromosome rearrangements or mutations that affect expression of *IGF2* alone[3] have been identified in BWS patients.

To sort things out, many researchers have asked whether mice with additional functional copies of the *Igf2* gene would develop BWS symptoms. But it has been impossible to obtain transgenic mouse lines expressing increased doses of Igf2. So Sun *et al.*[4] have taken an alternative route. They introduced