tackled in this study. The experiment was designed to look at a single major pathogen, the fungus that causes rice blast. But, because the same principles apply to many plant pathogens[4], it is possible to show that several diseases can be restricted in one crop mixture. For example, during studies for the Elm Farm Research Centre, Hamstead Marshall, Berkshire, UK (see ref. 5), I have recorded the simultaneous restriction of at least three observable diseases in mixtures of wheat varieties relative to single components of the mixtures. There is also evidence that mixtures can buffer against unpredictable abiotic variables, such as cold winter temperatures[6]. Indeed, it is likely that the stability of yields from variety mixtures over different environments[5], compared with yields from their components grown as monocultures, results partly from combined restriction of biotic and abiotic stresses.

So why is the mixture approach not used widely? Is it just too simple, not making enough use of high technology? One reason has been concern among farmers and end-users about the quality of the product of the mixtures relative to that of pure varieties: mixtures are said to be unpredictable in terms of quality and ease of harvesting. In practice, such concerns appear to either evaporate or be easily dealt with, as Zhu *et al.* show. In their case, for example, harvesting by hand — a practice common among rice farmers in Yunnan Province — ensured that rice varieties with different qualities could easily be separated and retained for their individual markets. There is also evidence[7] that mixtures can be designed not only to provide significant disease restriction, but also to improve product quality by combining complementary characters and providing stability.

Variety mixtures may not provide all the answers to the problems of controlling diseases and producing stable yields in modern agriculture. But their performance so far in experimental situations merits their wider uptake. More research is needed to find the best packages for different purposes and to breed varieties specifically for use in mixtures. And so far researchers have looked only at mixtures of varieties. Mixtures of species provide another layer of crop diversity, with half-forgotten advantages waiting to be exploited in contemporary approaches[8,9]. It is widely recognized, for example, that high-yielding mixtures of grains and legumes (grass plus clover, maize plus beans, and many other combinations) can restrict the spread of diseases, pests and weeds[10]. At the same time, such mixtures can provide near-complete nutrition for animals and humans alike, without recourse to expensive and uncertain forays into genetic engineering. ■

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Artificial noses

Picture the smell

Ingemar Lundström

There is a growing interest in 'soft' measurement techniques that measure a particular quality of a sample rather than the quantities of individual properties making up this quality. This type of information gathering mimics the human senses, and has led to the development of 'electronic noses' for environmental monitoring, medical testing, and food and drink production. In the most sophisticated systems a unique chemical fingerprint can be generated by an array of sensors and then identified by pattern-recognition techniques as the smell of a rose, for example. On page 710 of this issue[1], Rakow and Suslick suggest that human vision may soon become an important part of what is now known as artificial olfaction.

Attempts to measure odours with electronic instruments[2] were made as early as the 1950s, but the modern field of artificial olfaction began in 1982 with the work of Persaud and Dodd[3], who used a small array of gas-sensitive metal-oxide devices to classify odours. There has since been a steady increase in the number of systems using chemical sensor arrays. The success of artificial olfaction depends not only on the development of new sensor technologies, but also on the availability of powerful pattern-recognition software. This is particularly important for sensor arrays that produce a composite response.

Human vision is probably the most efficient pattern-recognition system available in terms of versatility and speed. Its ability to quickly observe and draw conclusions from changes in the observed images has not been superseded by man-made pattern-recognition systems. It has long been recognized that the most natural way to represent large amounts of data is as an image.

Data from chemical sensor arrays are often presented as images of various types. The most common approach is to cluster data into a two-dimensional image using statistical methods for data reduction and interpretation, such as principal-component analysis. Several ways of creating a visual signature from complex gas mixtures have been suggested — for example, a plot of the different sensor responses in a polar diagram (Fig. 1a).

Ten years ago, our group developed a device in which the properties of a surface coated with catalytic metals change when the surface interacts with different gases[4,5]. A light pulse scanned across this surface converts the chemical responses into electrical currents, which are then used to generate pixelated images that are quite different for different smells.

A few years ago, another breakthrough in the imaging of smells came with the development of optical-fibre bundles as chemical sensor arrays[6,7]. In this system, each fibre is coated with a combination of a dye and one of several polymers to give different fluores-

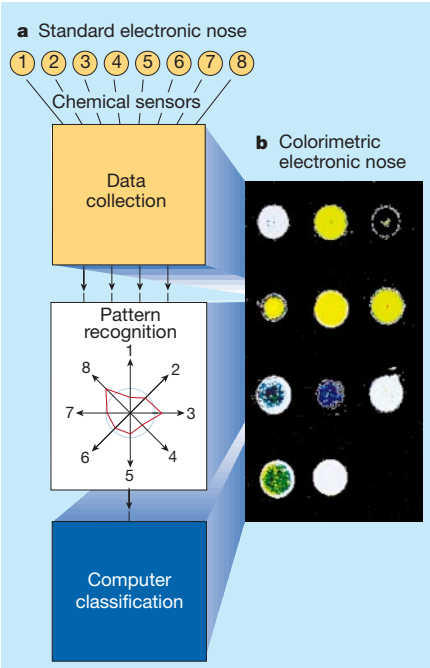

Figure 1 **Smelling by colour.** a, **A typical 'electronic nose' consists of an array of chemical sensors with overlapping selectivity profiles for the smells (gas mixtures) to be measured. This is followed by data collection, a pattern-recognition routine (such as the polar diagram shown), and eventually a computer-based decision.** b, **According to Rakow and Suslick[1] the colorimetric changes of an array of metalloporphyrins upon exposure to organic vapours can replace, with the help of the eye and brain, the various systems used for odour classification. The image here shows an example response from their device to a mixture of 2-methylpyridine and trimethylphosphite vapours.**

cent responses to a gas mixture, thereby producing a pattern of coloured circles at the other end of the fibre bundle. This pattern can be further processed to yield a computer-generated 'olfactory image' of the gas mixture. Such 'olfactory cameras' work in a similar way to biological olfaction in that thousands of odours are detected by a much smaller set of receptor cells (or sensors), which then send signals to the brain, producing a spatially resolved 'neuronal fingerprint'. In this way the natural olfactory system combines high selectivity (for many different odours) with high sensitivity (for trace levels of certain odours).

The 'smell-seeing' device of Rakow and Suslick[1] is based on the colour changes that occur in gas-sensitive metalloporphyrin dyes. Many odour sensors are not able to detect the most toxic vapours, but these compounds bind easily to metalloporphyrins, causing a simple colour change. By fixing an array of different metalloporphyrins in silica gel, the authors are able to produce unique, directly visible, colour patterns when the arrays are exposed to organic vapours, such as ethers (Fig. 1b). They obtain unique 'colour fingerprints' of vapours down to concentrations of a few hundred parts per billion. Although this is competitive with most other chemical sensors, it is still not as sensitive as a natural nose. The commercial viability of this and other devices will also depend on their sensitivity to the background level of humidity, which disrupts many sensors. Rakow and Suslick report that their device is not affected by water vapour.

It is intriguing to be able to identify different smells by eye. Such a system could be used to monitor levels of insecticides in the environment or to sniff out bacteria causing infections. The replacement of pattern-recognition routines and computer-made decisions with the eyes and brain of an experienced (trained) operator will have advantages in many other situations. For example, the screening of antimicrobial peptides to identify replacements for existing antibiotic drugs may soon benefit from a colorimetric sensor array based on lipid vesicles[8]. We have not yet seen the last development in systems to detect specific chemical interactions and, in particular, to 'see the smell'. ■

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Microbiology

Lipid lunch for persistent pathogen

William Bishai

The bacterium *Mycobacterium tuberculosis* is a bit of an oddity among microorganisms that invade the human respiratory tract. Most of them, such as *Streptococcus pneumoniae*, enter their host by colonizing the unsterile upper respiratory tract, waiting for a breach in host defences, and then mounting a burst of replication. In contrast, *M. tuberculosis* invades the sterile lungs, avoiding the clearance mechanisms there, and establishes a niche within lung tissue. It then slows or stops multiplying while waiting for the opportunity — afforded by a weakening of the immune system — to produce disease. In this poorly understood state, known as latent *M. tuberculosis* infection[1] (Fig. 1), living *M. tuberculosis* may remain in the body for decades without causing the symptoms of tuberculosis. Defining this unique host–pathogen relationship is a pressing challenge: one in three individuals worldwide have latent *M. tuberculosis* infection, with its 5–10% lifetime risk of progression to active disease.

On page 735 of this issue[2], McKinney *et al.* show that a biochemical pathway called the glyoxylate shunt is important for the long-term survival of *M. tuberculosis* within mouse tissues. Their results may have implications for the treatment of, and vaccination against, this persistent disease.

Like all bacterial pathogens, *M. tuberculosis* needs to adapt during infection. Years ago, important biochemical changes were identified in mouse-grown *M. tuberculosis*[3,4]. After developing an *in vitro* model of latency that involves gradual oxygen withdrawal, Wayne[5,6] noted that 'glyoxylate shunt' enzymes were activated during the metabolic downshift that accompanies oxygen withdrawal[7]. This model was based on two ideas: that lung granulomas — nodular scars containing bacteria and host-cell debris at their centres surrounded by a ring of immune cells — are the sanctuary for latent *M. tuberculosis*, and that oxygen depletion may trigger bacterial adaptation to the latent state.

Isocitrate lyase, the subject of the study by McKinney *et al.*[2], is one of the glyoxylate-shunt enzymes activated in Wayne's model. Isocitrate lyase and malate synthase together form the glyoxylate shunt, which bypasses the CO_2-generating steps of the tricarboxylic acid (TCA) cycle — the metabolic pathway by which acetate is oxidized to generate ATP. The net result of the glyoxylate shunt is the consumption of two molecules of acetyl CoA to generate one molecule of succinate. Lipids are a source of acetyl CoA; succinate is a precursor for the synthesis of glucose. So the glyoxylate shunt allows *M. tuberculosis*

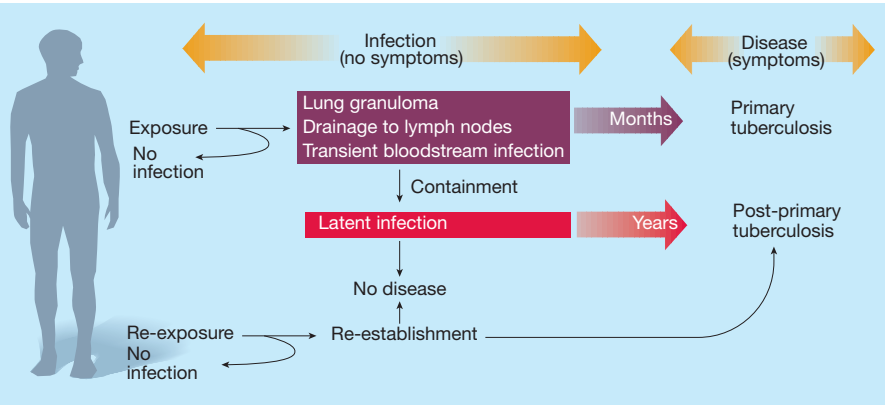

Figure 1 **Tuberculosis in humans. This complex disease has several steps, with two forms of progression to active disease — primary and post-primary. *Mycobacterium tuberculosis* infects the lungs, where it grows within macrophages (immune cells that ingest foreign material) during acute infection. An immune response follows, characterized by lung granulomas — nodules containing bacteria and host-cell debris, surrounded by a ring of immune cells. Before full immunity and containment occur, the bacteria probably drain into the regional lymph nodes and the bloodstream. Primary tuberculosis results when acquired immunity fails to contain this initial infection. Successful containment is associated with a failure to eradicate all viable bacteria; this results in a state of latent infection. The location of bacteria during latent infection remains controversial, but old lung granulomas, lymph nodes or remote body sites are possibilities. The results of McKinney *et al.*[2] indicate that late-stage *M. tuberculosis* may convert lipids into carbohydrates through the glyoxylate-shunt pathway. So the latent bacteria may reside in an environment — perhaps lung granulomas — in which carbohydrates are limited but lipids are available.**