What the nose knows

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Smell technology: Technology can manipulate and reproduce sight and sound with amazing fidelity. But what about smell?

WHEN it comes to reproducing sights and sounds, technology has made great strides in the past century. It is now possible to buy a high-definition television that produces an image almost indistinguishable from an aquarium or the view through a picture window; the best surround-sound systems can reproduce a concert performance so that it sounds just as it did in real life. While technologists have concentrated on sight and sound, however, smell has been left behind. Perhaps that is not surprising, since smell is, for most people, of lesser importance. But sometimes smell can provide information that other senses cannot. And that potentially opens the door to a range of new technologies.

For decades, scientists have been interested in imitating the way in which the nose detects compounds. Devices that do so are usually called artificial or electronic noses, says Vivek Subramanian, an engineer at the University of California in Berkeley. He has developed a new type of electronic nose that can, among other things, tell when wine has gone stale. The advantage of an electronic nose is that it is far more efficient and versatile than traditional chemical sensors. Developing a sensor to detect a single chemical substance is expensive, says Dr Subramanian, and such sensors then cannot be used to detect anything else. It is as if you had invented a camera that can take pictures only of red objects, or a microphone that picks up words only if they are spoken in French. But a general-purpose electronic nose can be used for all sorts of things, from sniffing food for quality control to detecting explosives at airports.

The inspiration for such general-purpose devices is the human nose itself. Rather than recognising individual chemicals, each of its 300-400 different types of receptor responds to a wide range of volatile compounds. Across the tens of millions of cells that make up the human olfactory system, recognition of a smell appears to emerge from the combination of many such responses, much as the recognition of a face depends on identification of many different characteristics. This distributed approach enables the olfactory system to detect tens of thousands of smells without having to have tens of thousands of different types of receptor.

Today's electronic noses consist of an array of a dozen or so polymer films, each of a slightly different type. The electrical conductivity of these films varies in the presence of different chemicals, so that when the array of films is exposed to a particular odour, the different films respond in a characteristic way.

Dr Subramanian's electronic nose, however, takes a different approach. Instead of polymer films, it uses an array of transistors made out of various organic semiconductor materials. Transistors are ideal for sensing, he says, because they are highly sensitive to very slight changes in charge structure and bond structure, both of which can be induced by bringing them into contact with other compounds. Transistors made of different materials respond differently to different chemicals, so that the array produces a distinctive signal when exposed to an odour. A sensor based on an array of five types of organic transistor is capable of distinguishing between unspoiled and oxidised wine.

Dr Subramanian's new nose is unusual not only in how it works, but also in how it is made. Organic semiconductors can be printed using special inkjet printers, which greatly reduces their cost. This could slash the price of electronic noses from hundreds to just a few dollars. Indeed, Dr Subramanian believes that electronic noses will eventually be so cheap that they will be built into food containers and pharmaceutical packaging, to indicate when a product is past its best. For this to happen, however, the price will have to fall below $1, which is unlikely for at least five years, he says.

Even when cheap sensors do become available, detecting compounds is only half the problem. As with a natural olfactory system, electronic noses must be able to learn and later recognise new smells. Ritaban Dutta at Warwick University in Britain has developed software that can recognise the smell of bacteria, including the deadly superbug MRSA (methicillin-resistant *Staphylococcus aureus*). The project began when his collaborator, David Morgan, who is a surgeon at the Heart of England Hospital in Birmingham, noticed the distinctly different smells given off by abscesses during surgery. He wondered if a machine could be trained to tell these different smells apart.

Armed with a traditional polymer-based electronic nose of the kind used by the food industry to detect rotten ingredients, Dr Dutta trained his software to recognise MRSA by exposing it to samples of the bacteria. This was more difficult than it sounds, since the relative concentrations of the various compounds that correspond to a particular odour can vary from one sample to another. But when it was tested on 150 known samples, the resulting system was able to identify MRSA correctly 96% of the time. Dr Dutta is now seeking backing to extend his system so that it can also detect other dangerous bacteria, such as those that cause Legionnaire's disease. It might ultimately be possible

to install sensors in hospital ventilation systems, he says, to prevent the spread of infections.

Michael Phillips of Menssana Research in Fort Lee, New Jersey, has gone one step further by developing a breathalyser that can detect lung cancer. "We can pick it up very early," says Dr Phillips. His invention, called the Breath Collection Apparatus, has already been approved by America's medical regulator, the Food and Drug Administration, for detecting the early signs of heart-transplant rejection, and he believes it can also be used to detect breast cancer and tuberculosis.

The trick is to get a big sample of breath, says Dr Phillips. The patient breathes into the device for two minutes and an absorbent trap captures volatile organic compounds (VOCs), which are found in the bloodstream and pass into the breath in minute quantities. The levels of VOCs are then measured using gas chromatography, and compared with those in a sample of ambient air taken at the same time. The system can detect very minute concentrations of VOCs—as low as a few parts per trillion. A pilot study found that the presence of a combination of 22 VOCs was an accurate indication of lung cancer, and a larger study is now under way. In the first stages of lung cancer, patients have an 80% chance of surviving for another five years, compared with a 5% chance when at stage four, says Dr Phillips. "We can detect lung cancer at stage one," he says.

So much for devices that detect smells; what about systems that emit them? These turn out to have therapeutic uses, such as in the treatment of war veterans suffering from post-traumatic stress disorder (PTSD). Skip Rizzo, a psychologist at the Institute of Creative Technology at the University of Southern California in Los Angeles, has been using virtual reality, in the form of video games, to treat PTSD. The idea is gradually to reintroduce the patient to the environment that caused the stress and trauma in the first place, steadily increasing the realism of the experience until it no longer causes them suffering, he says.

To make the treatment even more realistic, Dr Rizzo has taken to using a box of tricks that squirts out a range of odours, including the smells of cordite, diesel, body odour, gunpowder and even rubbish, intended to make soldiers feel as though they are back in Iraq. It is an old but effective trick: real-estate agents often recommend making coffee before potential buyers visit a home, because the smell makes them feel relaxed and at ease. Similarly, shopping centres often have cookie shops, which pump out warm chocolatey smells. "The olfactory system is linked to the limbic system, which controls memory," says Dr Rizzo, and that explains why such tricks are so effective.

Towards smellyvision

These smell boxes are remarkably simple, but might eventually lead to the ultimate in olfactory output technology: smellyvision. According to Doron Lancet, a scientist at the Weizmann Institute in Israel, just about any kind of smell can be bottled, from burnt tyres to candy-floss. But he believes it will be possible to make devices that can produce just about any kind of smell without having to have samples of each and every one. "We have mathematical algorithms that could streamline the process of mixing the odours," he says. These formulae could be used to mix compounds from a palette of smells to

produce a range of different odours. In conjunction with an electronic nose, it would then be possible to sample a smell in one place, and synthesise it at another.

This was the dream of DigiScent, an American company that Dr Lancet joined in 2000. DigiScent had the ambitious goal of odourising the internet with digital scents in this way. "We were trying to make odour generators which could be controlled electrically," he says. But even though their prototype machines could indeed produce a few dozen smells, smellyvision was sadly not to be. "People told us this was a technology ahead of its time," says Dr Lancet.

A third type of smell technology does not detect or reproduce smells, but prevents the sense of smell from working—providing the olfactory equivalent, in other words, of a blindfold or earplugs. Overcoming horrendous smells can be one of the biggest obstacles in clean-up operations such as those that followed the Asian tsunami of 2004 and Hurricane Katrina in New Orleans last year. The stench of decaying flesh from bodies floating in the water or hidden inside buildings, combined with the reek of overflowing sewers, is enough to turn even the strongest stomach.

Besides making the conditions for relief workers unimaginably difficult, it can also leave them with memories that haunt them for years. Such an experience can be so unpleasant and powerful that the smell seems to etch itself into the olfactory senses, in what is sometimes called the "barbecue effect"—so named because the smell of burning meat can trigger horrific memories of burned bodies in fire-fighters or soldiers years later.

Yet when clearing up in the aftermath of Katrina, many of the relief workers avoided this possibility by smearing a novel gel under their noses. Called OdorScreen, the gel looks and smells deceptively simple, but is quite unlike other odour-neutralising agents. While the mentholated petroleum jelly that pathologists and crime-scene workers sometimes use is designed to overpower unpleasant smells, OdorScreen interferes with the sense of smell itself. "OdorScreen is a completely different concept," says Dr Lancet, who acts as a consultant for Patus, the Israeli company that developed the gel.

OdorScreen works by releasing into the nose harmless compounds that interfere with receptor proteins involved in controlling the perception of the intensity of malodours. These mechanisms serve a similar purpose to the iris, which controls how much light enters the eye. Without such mechanisms, our senses would be overwhelmed, says Dr Lancet. The effect lasts for about two hours, after which fresh gel can be applied without fear of an overdose. And unlike a nose clip, the gel does not interfere with breathing.

Since it seems to be capable of concealing all kinds of malodours, the gel could have a wide range of uses beyond disaster-recovery, says Dr Lancet. It could be used in operating theatres, for example, and might even find its way into household products such as nappies. A trivial application, perhaps—but one that is not to be sniffed at.