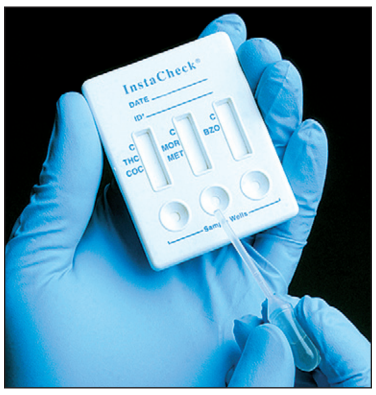
SCIENCE BRIEFS>>

From the American Association for the Advancement of Science's Annual Meeting 2005 in Washington D.C. MIKE GHENU reports on some of the latest ideas



Saliva drug test to come

A credit-card-sized kit that analyzes tiny amounts of saliva may one day replace uncomfortable urine or blood tests as a way to detect drug use, HIV, or agents such as the bacterium *Bacillus cereus*, a cousin of anthrax. This is because the composition of saliva closely mirrors that of blood. Researchers led by Daniel Malamud, of the University of Pennsylvania, have developed a small sponge that collects tiny amounts of saliva from a subject's mouth. The fluid is analyzed in a portable kit through a series of chemical reactions, producing results in about an hour. Malmud's team is now working to integrate the different tests into one device.

We are warming the oceans

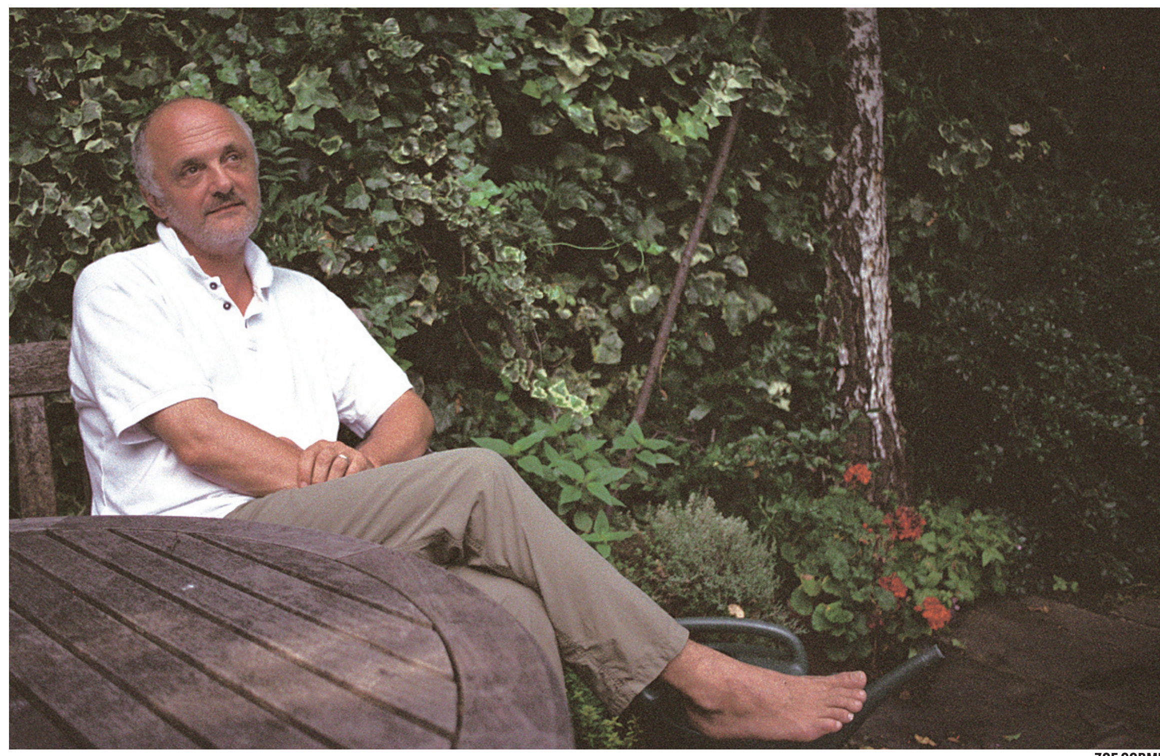
"The debate about whether or not there is a global warming signal here and now is over—at least for rational people," said Tim Barnett, a marine physicist from the University of California in San Diego. Barnett and other researchers fed weather data into computer models of ocean circulation to estimate human-caused warming of the world's oceans. Their predictions confirmed measured ocean temperatures with a confidence level exceeding 95 per cent. Ruth Curry, a researcher at the Woods Hole Oceanographic Institution, added that increasing ocean temperatures and the melting of the Greenland ice sheet is causing global sea levels to rise at a rate of about 20 centimetres per century.

Fixing our fisheries

New research shows that overfishing harms fish stocks in two ways. First, it eliminates the highly-productive larger and older fish from the population, which produce up to ten times as many larvae as the smaller youngsters. Second, it gives an evolutionary advantage to smaller and slower-growing fish, permanently altering the genetic diversity of fish stocks. Larry Crowder, marine biologist at Duke University, suggested zoning oceans to create marine reserves to protect the larger individuals from fishermen's nets. That is the approach taken by Australia to protect the Great Barrier Reef—a third of which is permanently out-of-bounds to fishing and other human activities.

Making sense of smell

by ZOE CORMIER
SCIENCE EDITOR



ZOE CORMIER

Biophysicist Dr. Luca Turin, at his home in London, has a "radical" theory about how smell works.

"Here, smell this, tell me what you think it smells like," said biophysicist Dr. Luca Turin, seated in his garden in London, England, offering a scent sample on a slender, white stick.

Definitely smells fruity. Orange? But there's something else there, something almost bitter, I can't tell what. Everyone knows that feeling, when you recognize a smell, you know you've smelled it before, but you just can't quite put your finger on it.

Everyone, that is, except perhaps Turin, who has spent the better part of his life thinking, writing, and philosophizing about smell. "How about carrot?" he asks. And that's exactly what it smells like—orangey carrot. But the scent does not come from orange and carrot extracts—it comes from a synthetic chemical that Turin created in his basement, using simple machinery and a radical idea.

Since childhood Turin has been fascinated by smell. "I've always loved perfume with a passion," said Turin, born to Argentinean-Italian parents and raised in France. In 1992 he authored France's best-selling perfume guide, *Parfum: Le Guide*, a gigantic tome listing and critiquing almost every perfume ever created—the Guerlains, the Yves Saint Laurents, *Chanel no. 5, White Linen*, and all manner of obscure, nineteenth-century antiques he dug up in the dusty perfume stores of Nice.

This book brought Turin into contact with the perfume giants, and permanently changed the course of his academic career.

Only six companies, who collectively generate about $20 billion a year in economic activity, make virtually all the synthetic scents you can buy, from the smell of Tide detergent to *Cool Water.* And after reading his perfume guide, who wanted to know what Turin thought of their new scents.

It was while exploring the labs of the perfume giants that Turin realized one extremely important thing about smell: we do not understand how it works.

The perfume giants employ thousands of chemists (each at a sizable salary) to create new molecules that they can patent. A successful molecule will net tens of millions of dollars in profit. But, in order to produce even 20 good molecules, chemists have to produce anywhere between 500 and 2,000 molecules. They take the appropriate chemical building blocks, rearrange them into hundreds of new molecules, and then sift through them one by one to find the precious few that smell good.

Why go through such a wasteful, time-consuming process? "Because they don't have a clue [about how smell works,]" said Turin. "They readily admit they don't have a theory—otherwise they wouldn't be making thousands of molecules."

Scientists figured out decades ago how vision and hearing work. They know which wavelengths of light look like which colours; they know which frequencies generate vibrations in which parts of the ear and what that sounds like; any standard physiology text will have detailed descriptions of the eye and the ear, but will contain little information on the nose.

Why have scientists taken so long to crack the sense of smell?

"One reason is that 'real men' don't smell things," says Turin. "And, science being chiefly male, it's always been considered a field where you could not rely on your sensation. I'm always struck by this—even professionals in the field do not understand that when perfumists say something smells musky, or woody, or ambery, it means something *very* precise. They think these are just words that wine experts might say, like 'I'm getting strawberry,' or some such bullshit. They just don't think that the sensation of smell has the same legitimacy as vision, or hearing."

Classical biological thinking assumed that smell must work the same way that most other biological systems work: by recognizing molecular shape. Enzymes in your stomach, for example, will recognize specific molecules, like lactose, by their shape. The lactose molecule fits into the enzyme like a key in a lock, and the enzyme breaks it down. If you don't have the enzyme for lactose, you can't digest it.

The human body can only digest about a hundred different molecules, so we have only about a hundred different enzymes. Most biological systems, like the neurotransmitters and hormones, work by shape. It was assumed smell worked the same way.

But there's a problem. You can smell *anything*—any molecule that fits the appropriate chemical criteria you can smell. You can even smell perfumes that were invented last year, that our ancestors were never exposed to. You can digest glucose because your ancestors evolved the appropriate enzymes. But if ancient humans never smelled *Tommy Girl*, why can you?

To date, scientists have identified at least 10,000 molecules that we can smell. If smell works by shape recognition, should we not then have at least 10,000 different kinds of odour receptors in our noses?

In 1991 Linda Buck and Richard Axel made history when they identified the genes for olfactory receptors in rats, a feat for which they were jointly awarded the Nobel Prize this year. It turns out humans have about 1,000 different kinds of olfactory receptors. An impressive number for sure, but not enough to suggest that shape is the only thing determining a molecule's smell.

There are other problems with the shape theory. Some molecules that are shaped very similarly have different smells. Vanillin smells like a rich vanilla, and isovanillin smells richer and spicer, "somewhat phenolic," says Turin.

And some molecules that have completely different shapes smell exactly the same; Osyrol and betasantalol, for instance, both smell like sandalwood.

Turin came to believe that smell works not by shape, like digestion, but by vibration, like hearing. We can only hear sounds within a given range (we can't hear the high pitches of echolocating bats, for example), but we can hear *every* sound in our range.

So if you think of molecules in musical terms, the theory is easier to understand. A molecule is made up of a collection of atoms, and each bond between those atoms has a particular energy. If you think of one bond as being like a note on a keyboard, you can think of every molecule as being like a "miniature musical instrument," having its own particular chord, or combination of notes, says Turin.

A laboratory spectroscope works by this principle—it shoots light at a sample, "plays" the notes, and figures out what a molecule is made of. Turin argued that the nose works like a spectroscope, and that these notes correspond to smell.

This, he said, explains how two molecules, ferrocene and nickelocene, both shaped like "burgers," smell different, because buried in their interiors they contain different metal atoms, iron and nickel, with different bond energies. And he said this also explained how hydrogen cyanide, made of three atoms, and benzaldehyde, a ring-shaped molecule, both smell like bitter almonds, because although they are made of different atoms, their bonds have the same energies, the same notes.

This idea is not new. An English scientist, Malcolm Dyson, first proposed a vibrational theory of olfaction in 1938, and a Canadian, R.H. Wright, revived the idea in 1977. But neither scientist could explain how the human nose could accomplish what a piece of laboratory equipment made of metal and glass and lights can do.

Turin, however, did have an idea about how a nose made of flesh could perform spectroscopy: electron-tunnelling. It is possible to read the bond energies in a molecule not by shooting photons of light at it, but by shooting electricity at it.

In 1989 Turin became the first person to show that proteins can conduct electricity. He created a diode that used albumin (egg white protein) to conduct electricity.

So he thought it was possible that a protein could channel electrons like a battery, and probe odorous molecules for their chords. Using the code for the receptors that Axel and Buck had found, Turin came up with a model of how the nose receptors could channel electrons into a molecule.

He took his model, his same-shape different-smell molecules and same-bond energy same-smell molecules, and submitted a paper to the prestigious journal *Nature*.

The editors deliberated for a year on the paper, and eventually rejected it. "It seemed to them an unnecessary gamble," said Turin. So Turin had to settle for publication in 1996 in a less notable journal, *Chemical Senses*.

Turin's vibration theory was not well received by other smell scientists; he says that not only did most smell scientists reject his theory outright, they did so without even reading his paper.

"I don't think any scientist has any

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Ocean tides created massive icebergs

by MIKE GHENU
VARSITY STAFF

On six separate occasions during the past 60,000 years iceberg armadas streamed forth into the North Atlantic from the Labrador Sea. The icebergs carted boulders and rubble from Eastern Canada, which were deposited on the ocean bottom as they melted. The flood of meltwater in the North Atlantic was so great that it disrupted the circulation of the ocean, which affected climate globally. All this happened in only about 500 years.

Rest assured though: it's only a theory, and these events occur only during ice ages. It was put forth by a German scientist named Heinrich, who fit together pieces of evidence from the climate record and from the bottom of the Atlantic Ocean. So-called "Heinrich events" occur when large icebergs drift down from the poles and disrupt the global climate.

But until now, no one could explain why most of the icebergs 60,000 years ago seemed to have come from the Labrador Sea.

In a paper recently published in the journal *Nature*, Dr. Brian Arbic, a research oceanographer at Princeton University, and a team of researchers that included Prof. Jerry Mitrovica in the department of physics at U of T, believe they have done just that.

"Big tides may explain why the ice came from that spot," Arbic told *The Varsity* in a telephone interview. Ocean tides are Arbic's area of expertise: he has developed a simulation that predicts the height of tides throughout the world with 92 per cent accuracy.

Tides are caused by the Moon's force of gravity pulling on the Earth. "The part of the Earth facing the Moon is closer to it," explained Arbic. "So it feels a stronger pull, whereas the opposite side of the Earth feels a weaker pull." This difference in forces produces a wave on the side of the Earth that is being pulled more strongly—the ocean is literally pulled towards the Moon. This is known as high tide. On the opposite side of the Earth the opposite of a wave is produced—low tide. Since the Moon and Earth rotate around each other, the high tide constantly circles the globe as it follows the pull of the Moon.

Using estimates of global sea levels from Mitrovica, Arbic simulated the global height of tides during the times Heinrich events are known to have occurred. His simulation indicated that tides in the Labrador Sea were much higher than they are now, ranging from 2.7 to 3.9 meters. Presently, their height is only about 1.5 metres. Arbic believes these higher tides weakened the ice shelf —a tongue of ice on the surface of the ocean hundreds of metres thick—that covered the Labrador Sea.

The researchers were most surprised when they superimposed global tide levels onto a map. "You get this bulls-eye of incredibly large tides just over the area people had surmised was the source of the iceberg armadas," said Mitrovica. "Those tides just pounded," he said, and most likely broke off huge icebergs.

The important role ocean tides play in Heinrich events may lead scientists to consider the effect of tides in other climate enigmas, according to Mitrovica. "This is the first time, I think, that tides have been implicated in a climate story."

A more complete understanding of Heinrich events is important as well. "It will help us understand what natural climate cycles the Earth can go through," he said.

Researchers developing drug "patch"

by MARY TURNER

Imagine that your doctor has just given you a drug injection. The drug will take some time to travel through your blood to its destination, say your liver. The drug must eventually reach a concentration in your organ where it won't be so high that it will harm you, but will be sufficiently high enough to pack punch. Ideally, you'd like your medicine delivered to the right cells at a constant rate so as to achieve the right concentration.

Kai Landskron and Geoffrey Ozin of the Materials Chemistry Research Group at the U of T Department of Chemistry are hoping to develop a system that may help deliver medicine in such a way. In a paper published in *Science,* they describe how they produced a highly organized porous material with holes that could potentially be shaped to fit certain drug molecules.

By manipulating the pores, drug molecules of various sizes and chemical makeups may be fit into and released from the pores in a controlled fashion. This way the drug can be released at a constant and appropriate rate. The aim is to design a material that could allow drugs to be absorbed through the skin, not unlike how nicotine patches work.

According to Landskron, "no special precautions are required in the lab during synthesis of these compounds." He adds, "To my knowledge, there is no danger in applying such compounds to the skin."

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business dismissing an interesting paper as crap unless they've read it. No scientist worth a damn should ever do such a thing," he said.

But while other olfactory scientists were not interested in his idea, the popular press was; the BBC produced a documentary on him, and American journalist Chandler Burr wrote a book about him—which did not go over well with the scientific community. As one recent anonymous editorial in *Nature Neuroscience* complains, Turin's theory, "while provocative, has almost no credence in scientific circles…[but has received an] extraordinary—and inappropriate—degree of publicity from uncritical journalists."

Indeed, many smell scientists are not fond of Turin's idea. Columbia's Dr. Stuart Firestein, "who thinks I'm less than shit," commented Turin, responded to initial emails from *The Varsity*, but ceased replying after he was asked for his opinion of Luca Turin.

But not every scientist thinks the vibrational theory should be cast aside. U of T's Dr. David Lovejoy, who has spent a large part of his career studying the same kinds of proteins that comprise the nose receptors, had not heard of the idea in November, 2004. But when asked about it two months later he replied, "Every time I think about it, the idea makes more sense."

Dr. Zach Mainen, who works in Coldsprings Harbour, New York, had enough interest in Turin's idea to test it. He and his team tried to see if rats could smell the difference between isotopes, molecules that differ not in shape but in weight (and hence bond energies).

"And indeed they can discriminate them," he said. "But we also found that they could discriminate different *batches* of the same isotope," said Mainen, which meant that maybe the rats were simply smelling the impurities in the mixtures.

"One of the problems with the theory is that it's based on sort of hearsay," commented Mainen. Turin's descriptions about what things smelled like were largely based on what he alone thought, "so all these claims about what smells similar to what are actually not so clear," said Mainen.

"Turin's theory is sort of weird, but it's conceivable. I wouldn't say this idea is dead in the water, but there isn't much evidence for it yet," said Mainen. "[But] can you absolutely rule his theory out? Not yet. Ultimately we still don't really know how these receptors work."

While most of academia continues to ignore the vibrational theory, Turin has left academia. He is now the CTO for a startup company, Flexitral, which creates scent molecules based on his theory.

But unlike all the other major scent producers, Flexitral employs only one fragrance chemist: Turin. After all, if you have a theory that allows you to make molecules that smell like whatever you wish, what do you need hundreds of chemists for? And, if Turin is right, his theory will make him a very, very rich man—he won't have to split the profits with hundreds of other chemists.

And so far, it seems that his idea is working. "I thought an orange-carrot smell would go nice with an orange-coloured soap," said Turin, so he made it.

Although Turin hopes that his idea will, within his lifetime, be accepted, he concedes that understanding how the receptors work is just one tiny part of the smell puzzle. Not all the nerves in the nose are activated by the same odorants, and it seems like the patterns of which nerves are activated at which times are important in determining what you perceive something to smell like.

"The real miracle is the work done by the brain," says Turin.