Staying in tune

THE EARS OF ANIMALS DEVELOP IN THE WAY FINE MUSICAL INSTRUMENTS ARE BUILT, WRITES **S ANANTHANARAYANAN**

Musical instruments are built to produce a series of tones of exact pitch. The piano, for instance, has 88 keys that can produce notes of a frequency as low as 27 cycles a second (cps) to as high as 4,186 cps. The strings, which are struck when the keys are pressed, however, need to be tuned just right so that the relationship between notes is always the same — and even the untrained ear can tell the difference of just one cps in the middle range.

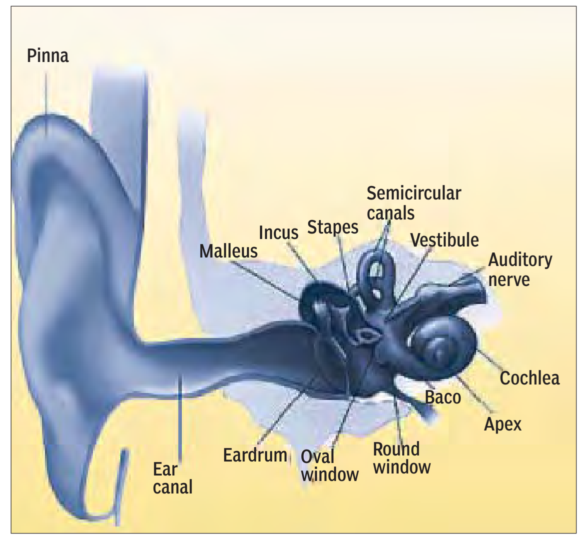
The ears of vertebrates have a complex internal structure to tell such fine differences of pitch apart over a very wide range, from 20 cps to nearly 100,000 cps. Zoe F Mann, Benjamin R Thiede, Weise Chang, Jung-Bum Shin, Helen L May-Simera, Michael Lovett, Jeffrey T Corwin and Matthew W Kelley, of Maryland, Virginia and London, report in the journal *Nature Communications* that they have pinned down the genetic bases of this enormous sensitivity of the hearing organs of animals. They identify the role of a genetic agent, *Bone Morphogentic Protein 7*, which leads to the production of a protein and then regulates the growth of minute organs that react to the closely separated pitch of sounds entering the ear.

The structure of the ear is basically an arrangement to collect and amplify waves, to separate them according to pitch and then to detect sounds of different pitch and cause electrical signals to flow to the brain. The first two functions are of the outer ear and middle ear, while the last functions are of the inner ear. The middle ear has an elastic membrane, the ear drum, which is set vibrating to transmit its movement to the inner ear with the help of three bones, the *hammer*, the *anvil* and the *stirrup*, with an amplification of the sound by nearly 30 times. The inner ear has a fluid in a long and spiral shaped container, the *cochlea*, where the sounds of different pitch concentrate at different parts, where there are fine, hair-like cells that respond and set off chemical changes that affect nerves that carry signals to the brain. As sound is transmitted to a liquid, the same frequency has a much shorter wavelength and the inner ear remains compact.

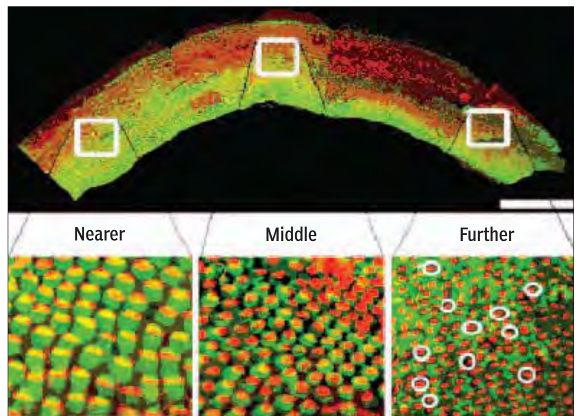
The arrangement has incredible sensitivity. Even the human ear, which, among animals, is not the most sensitive, can react to sounds where the pressure difference is *less than one billionth of the atmospheric pressure*. Such a faint sound corresponds to the movement of air by the distance of a tenth of an atomic diameter! And then the arrangement is incredibly sturdy, the sounds can get so loud as corresponding, for an instant, to 10,000 times the atmospheric pressure. This sensitivity in the human ear is over the range of frequency, or pitch, from 20 cps to 20,000 cps. Dogs can hear up to 40,000-60,000cps, while cats go as high as 79,000 cps and dolphins and bats, which use high-pitched sound for navigation, can hear sounds at 100,000 cps. Mice also make and hear sounds as shrill as 79,000 cps for communication outside the range of normal predators, and the sensitivity of cats is probably an adaptation to get the mice, anyway.

But the range of frequency apart, the remarkable feature of the ears is the ability to tell the difference of a very small change in frequency. The spiral of the cochlea is only about 3.2 cm long but it is able to separate about 1,500 different frequencies, using 16,000-20,000 hair cells. This amounts to a separate frequency being focused every 0.002 cm. Even with just a dozen or so hair cells assigned to each frequency, such a high resolution would need some form of *sharpening* of the response to pitch along the length of the cochlea, a mechanism that is still not understood.

But the question that the group at Maryland, Virginia and London addressed was of how the hair cells positioned themselves along the length of the cochlea so that they could separately respond to such closely separated frequencies of sound. In the standard piano, there are 230 strings that need to be tuned, in groups, to 88 specific frequencies. This would take a skilled piano tuner a few hours to complete, usually with the help of an electronic device to provide the reference note while adjusting the tension of the strings. The construction of the cochlea may correspond to setting the position of 1,500 frets along the neck of single-stringed guitar!



As a model of their study, the researchers used the hair cells, which are actually cells of the nature of skin, known as *Basilar Palilae* that are found in the sound sensitive part of the ear of a developing chicken. These cells, which are found in birds, lizards and amphibians, correspond to the organs in the cochlea of mammals, and eggs, unlike foetus, permit intervention and study of the course of development. The fertilised eggs of white Leghorn chickens were incubated for study at different stages of growth of the embryo, between Day 6 to Day 14. The embryos were extracted from the eggs and the BPs were extracted, those at the start of the hearing channel being kept separate from those at the far end. The genetic signalling material, which directs the formation of specific proteins, was then extracted and classified to create a map of the variation of the nature of the BPs along the length of the hearing channel.



BPs change along the length of the channel

The study revealed that there was a gradient or a rising slope in the population of Bmp7, the progenitor of the protein that modifies BPs, as one passed along the axis of the hearing sensitive channel. To make sure that this was the factor that controlled frequency response, trials were made with an engineered disruption of the distribution of Bmp7 along the channel, whether after extraction of the BPs or while they were still in the egg.

This action was found to correspondingly affect the nature of the hair cells formed, and their sensitivity to frequencies. The role of Bmp7 was tested in different settings and it was clear that it was the level of the BMP7 protein that led to tone sensitivity of the ear. A further examination of how Bmp7 levels varied and how they communicated to affect cell growth showed a pathway that involved an enzyme called TAK1, whose activation decided how hair cells would respond to frequencies along the sound sensitive channel.

A specific placing of different forms of cells along an axis arises in other organs as well, like along the axes of the body, in parts of the embryo that develop into the central nervous system in the hind and fore limbs. Here again, it is a rising slope in the presence of agents that affect cells that regulate cell growth along axes. The role of Bmps is found in many of these mechanisms and the manner of their action seems to be related to the way hair cells in the ear are positioned.

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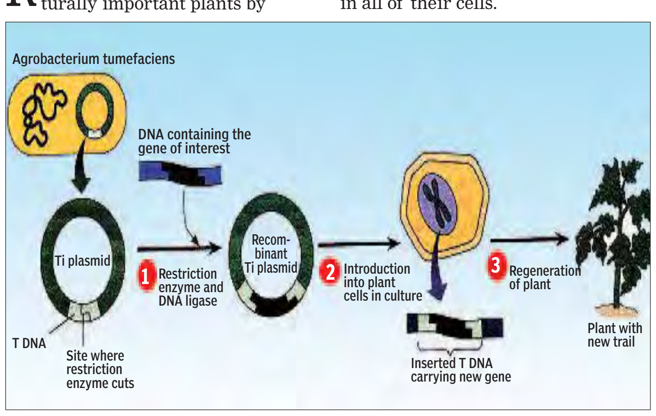
LEARNING FROM NATURE

THE TI PLASMID IS A USEFUL VECTOR FOR INTRODUCING FOREIGN GENES INTO PLANTS, SAYS **TAPAN KUMAR MAITRA**

Recombinant DNA technology may be used to modify agriculturally important plants by inserting genes designed to introduce traits such asresistance to insects, herbicides, or viral disease, or to improve a plant's nitrogen-fixing ability, photosynthetic efficiency, nutritional value, or ability to grow under adverse conditions. Cloned genes are transferred into plants by inserting them first into the Ti plasmid, a naturally occurring DNA molecule carried by the bacterium *Agrobacterium tumefaciens*.

In nature, infection of plant cells by this bacterium leads to the insertion of a small part of the plasmid DNA, called the T DNA region, into the plant cell's chromosomal DNA; expression of the inserted DNA then triggers the formation of an uncontrolled growth of tissue called a crown gall tumor. In the laboratory, the DNA sequences that trigger tumor formation can be removed from the Ti plasmid without stopping the transfer of DNA from the plasmid to the host cell chromosome.
Inserting genes of interest into such modified plasmids produces vectors that can transfer foreign genes into plant cells.
The desired foreign gene is first inserted into the T DNA region of the isolated plasmid using standard recombinant DNA techniques, the plasmid is put back into the Agrobacterium bacteria, and these genetically engineered bacteria are then used to infect plant cells growing in culture. When the recombinant plasmid enters the plant cell, its T DNA becomes stably integrated into the plant genome and is passed on to both daughter cells at every cell division. Such cells are subsequently used to regenerate plants that contain the recombinant T DNA – and, therefore, the desired foreign gene — in all of their cells.



Using the Ti plasmid to transfer genes into plants: Most genetic engineering in plants uses the Ti plasmid as a vector. (1) The Ti plasmid is isolated from the bacterium Agrobacterium tumefaciens, and a DNA fragment containing a gene of interest is inserted into a restriction site located in the T DNA region of the plasmid. (2) When the recombinant plasmid is introduced into plant cells, the T DNA region becomes integrated into the plant cell's chromosomal DNA. (3) The plant cell is then allowed to divide and regenerate a new plant containing the recombinant T DNA stably incorporated into the genome of every cell.

The foreign gene will now be inherited by progeny plants just like any other gene.

Such plants are said to be transgenic, a general term that refers to any type of organism, plant or animal that carries one or more genes from another organism in all of its cells, including its reproductive cells.

Transgenic plants are also commonly referred to as *GM* (genetically modified) plants.

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Tiny plastic timebombs

YOU PROBABLY DIDN'T KNOW THEY WERE THERE IN YOUR COSMETICS, BUT MILLIONS OF TONS OF MICROBEADS ARE BEING WASHED INTO RIVERS AND SEAS, UP THE FOOD CHAIN AND HEADING FOR THE FISH ON YOUR PLATE. **STEVE CONNOR** REPORTS

Millions of people unwittingly pour hundreds of tons of tiny plastic beads down the drain. These can persist in the environment for more than 100 years, and have been found to contaminate a wide variety of freshwater and marine wildlife. Few consumers realise that many cosmetic products, such as facial scrubs, toothpastes and shower gels, now contain many thousands of microplastic beads that have been deliberately added by the manufacturers of more than 100 consumer products over the past two decades.

Plastic microbeads, which are typically less than a millimetre wide and are too small to be filtered by sewage-treatment plants, are able to carry deadly toxins into the animals that ingest them, including those in the human food chain such as fish, mussels and crabs, according to scientists. While many people have assiduously tried to recycle their plastic waste, cosmetics companies have at the same time been quietly adding hundreds of cubic metres of plastics such as polyethylene to products that are deliberately designed to be washed into waste-water systems — one estimate suggests that in the USA alone up to 1,200 cubic metres of microplastic beads are washed down the drains each year.

Scientists and environmentalists have started lobbying the industry to stop using plastic microbeads in exfoliant skin creams and washes, but with limited success — a relatively small number of firms have publicly agreed to phase them out, and even then have given themselves several years to do so.

Britain, along with the rest of the European Union, is being urged to follow the lead of New York state, which last week became the first place in the world to prohibit the use of plastic micropellets in cosmetic products after a failure by the vast majority of personal-care companies to agree to an immediate voluntary ban. The state assembly decided to act after scientists found disturbing levels of microplastic beads in the Great Lakes of North America. The researchers said the beads arrived in wastewater contaminated with the microplastic residues of more than 100 consumer products, including facial scrubs, soaps, shampoos and toothpaste. "People are unwilling to sacrifice water quality just to continue to use products with plastic microbeads. I never met anyone who has wanted plastic on their face or in their fish," said Robert Sweeney, chair of the assembly's conservation committee, after last week's unanimous vote to ban the use of microbeads in personal-care products.

The House of Commons Science and Technology Committee last year heard evidence of the serious impact that microplastic waste could be having on Britain's aquatic environments. Some members of the committee are calling for tougher legislation if the cosmetics industry continues to prevaricate. "There is no reason for these microplastics in cosmetic products and I think they should be phased out. If they are not taken out voluntarily, then there should be legislation to ban their use," said Graham Stringer, member of Parliament and member of the Commons committee. The committee is due to meet next month to review its work on water quality, and some members want to press the cosmetics industry further on what it intends to do about phasing out plastic microbeads in personal-care products, Stringer said.

Originally, the cosmetics industry used natural ingredients such as ground-up apricot kernels, crushed walnut shells and dried coconut as skin exfoliants – gentle abrasives that can remove dirt and dead layers of cells. However, at some point in the late 1990s some companies quietly switched to plastic microbeads and the practice quickly spread to other firms and now includes most skin scrubs, polishes and soaps, even when they are not sold as skin exfoliants.

When you scrub your face and brush your teeth, the tiny microbeads wash down the drain into the sea where they can be eaten by marine life.

Microbeads up close.

Microbeads, which are often simply labelled "PE", "PP" or "PMMA" in the product ingredients, are now found in more than 100 toiletries and cosmetics. They are made by companies ranging from the big chemicals giants such as Johnson & Johnson, Procter & Gamble and Unilever, and supermarket chains such as Sainsbury's, Tesco and Marks and Spencer, to high-end cosmetics firms such as Clarins and L'Oréal.

Richard Thompson, professor of marine biology at Plymouth University, said plastic microbeads washed into waste water were a needless source of contamination given that there were viable alternatives that had already been used to do much the same job in terms of skin exfoliation. "These small particles, or microplastics, may produce a different sort of problem than larger fragments of plastic debris. We know that a range of organisms will eat these microplastics and the prevalence in populations of some species may reach 80 per cent," Professor Thompson said.

"Microplastic beads may also lead to the transfer of chemical contaminants into the animals that ingest the plastic. This is in addition to the physical damage done by the plastic itself. Our work, for instance, has shown that mussels will retain ingested plastic particles for more than 48 days. Hence, there is potential for harm from both the physical presence of the plastic and any contaminants that may be transported with it," he said. Professor Callum Roberts of the University of York said, "As plastics fragment into smaller pieces, they concentrate toxins. Microbeads are highly potent concentrators, feeding toxins into plankton at the bottom of the food web. These chemicals then biomagnify up the food web, and it ends up meaning the top predators have the highest concentration of this stuff, and the top predators are precisely the things we like to eat, like tuna and swordfish. It really is a case of what goes around comes around.

"The waste chemicals we thought we had gotten rid of are coming back to haunt us, and it won't be long before the fish we like to eat will be subject to health warnings for compounds like PCBs (polychlorinated biphenyl) or pesticides, as they already are for mercury. It's not just harmless roughage, there's a toxic load added." Studies have shown that persistent organic pollutants, among them fat-soluble chemicals such as DDT and PCBs, stick to polyethylene microbeads, where they can become super-concentrated.

THE INDEPENDENT

PLUS POINTS

Undersea odyssey

A team of 12 researchers is hoping to discover new species of gelatinous zooplankton in a three-year underwater journey through the world's oceans. They are hoping to find out more about the creatures that form the basis of the marine food chain but remain largely undiscovered.

Only around 1,000 species of gelata are known to science, estimated to be about 20 per cent of the world's total. It is exceptionally difficult to study the creatures in a laboratory. Expedition Aquatilis will cover 35,000 miles spanning the Atlantic, Pacific and Indian Oceans and will be led by marine biologist and underwater photographer Alexander Semenov. The team, will travel in a 70-ft custom-built, self-sufficient expedition vessel and is scheduled to depart from Marmaris in Turkey in the summer of 2015. The expedition's route is specifically designed around poorly explored diving locations and will focus on the study of gelatinous zooplankton. They hope to use funding to bankroll their expedition and are hoping to raise Rs 8.7 crore.

Olga Grum-Grzhimaylo, a member of the Aquatilis team, dives beneath the ice to collect scientific samples in the White Sea, Russia. Scientists currently know of only about 1,000 species of gelatinous zooplankton, the basis of the marine food chain – an estimated 20 per cent of the world's total.

The places they will visit include the Azores, the Caribbean, Brazil, Argentina, Cape Horn, Chile, Peru, California, Hawaii, New Zealand, the Great Barrier Reef, Papua New Guinea, the Philippines, Indonesia, Sri Lanka, the Indian Ocean, Madagascar and Cape Town.

Combing operation

Traditionally, Urinary Tract Infections have been treated with antibiotics, but despite the treatment bacteria can sometimes hide in the bladder and form a dormant reservoir of pathogens. These reservoirs can later release a burst of infecting pathogens and cause recurring infections. A group of scientists from the USA and Slovenia? claim to have found a way to get rid of these hard-to-reach bacteria. Working with mice, the team found that in the presence of a chemical called *chitosan* these hiding bacteria can be forced to come out in the open, inside the bladder. This makes them amenable to an antibiotic treatment.

The team started with testing the effects of chitosan on the growth and survival of a common UTI-causing bacteria. They found that chitosan affected the way bacteria attached itself to the inner walls of the urinary tract. Armed with this piece of information, they decided to test the effects of chitosan in the bladder of mice.

The study was led by Matthew Blango from the Division of Microbiology and Immunology, University of Utah. He says, "Chitosan causes a release of the bacteria from the cells lining the bladder wall because it provokes the host cell to divide. We found that coupling a chitosan treatment with an antibiotic treatment of sparfloxacin or ciprofloxacin for seven days helped clear the majority of the bacteria from the bladder."

Matthew Blango

The team is now trying to fine-tune their chitosan and antibiotic method of treating UTIs. But there are experts who do not share Blango's optimism. Vivekanand Jha, professor of nephrology, Post Graduate Institute of Medical Education and Research, Chandigarh, and secretary of the Indian Society of Nephrology, says, "The method is very far from any clinical application and, in fact, may never come to that stage because there are a number of issues in terms of clinical delivery and applicability in the approach."

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