Hearing loss could soon be reversed

VIRUSES CAN BE THE VEHICLE TO CARRY GENETIC MATERIAL TO THE INNER EAR, SAYS **S ANANTHANARAYANAN**

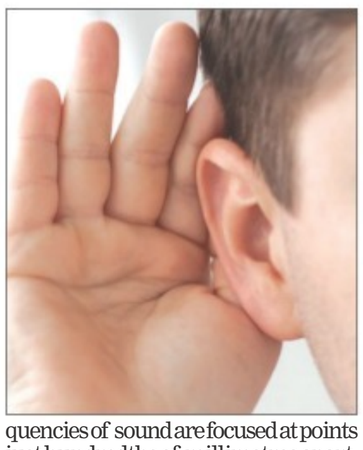
Inherited genetic deficiency is the reason for about half the 250 million cases of hearing loss worldwide. In most of these, the function itself of the organs of the ear is affected and medical intervention is generally not effective. Even devices like hearing aids or implants in the middle and inner ear, which partially restore auditory functions, are not always possible.

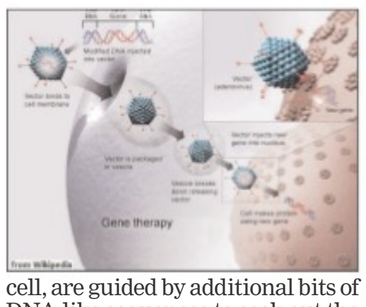
Answers for many medical conditions like haemophilia, leukaemia or Parkinson's disease have been found in gene therapy, where genetic material is introduced into living cells to modify their function. In dealing with hearing loss, however, there have been limitations in the use of gene therapy, because of the different organs involved, particularly the inner and outer hair cells, which act in concert to ensure the remarkable sensitivity of the ears of mammals.

Two groups of researchers, working in institutes in Massachusetts, Chicago, New Orleans, North Carolina, Washington and Vienna, report in the journal, Nature Biotechnology, their success in creating a virus in the laboratory that is able to invade the cells of the inner ear and introduce a scrap of genetic material that sets right the working of both kinds of deficient hair cells. The work has been done with a particular inner ear condition that affects mice, but this is the first time that hearing function has been recovered and it holds promise of being useful to deal with human hearing loss, the authors of the papers say.

While the architecture of the ear provides the framework for capturing and channelling sound waves, it is the fine hair-like structures in the inner ear that translate sound vibrations into nerve signals, to be recognised as sounds. And here, there are different kinds of hair cells, some to sense high and low frequencies and others to help focus different frequencies at specific places.

The complexity is incredible — the tiny, liquid-filled resonating chamber of the ear, the cochlea, has tens of thousands of hair cells and different frequencies of sound are focused at points just hundredths of millimetres apart.





The functioning of physiological systems is orchestrated by the action of proteins, which play different roles of signalling and enabling organs to act in specific ways. Thousands of proteins are synthesised within the cells by joining together chemical units, called amino acids, according to specific patterns. The patterns are spelt out by the units in sequence along the length of the DNA, the giant molecules that code the entire genetic information of the cell. If there is an error or an omission in the code for a protein, which is important for the cell's function, then it is not able to generate that protein and is not able to work correctly.

It is this kind of deficiency that is found to bring about deafness in some 50 per cent of the hearing-impaired people across the world. And more than 300 locations along the length of the DNA have been found to be relevant and over a hundred genes, or bits of DNA that code for the production of particular proteins, have been isolated in people affected by loss of hearing.

Gene therapy seeks to remedy this condition by replacing the deficient gene with a functional, therapeutic version, so that that a genetically deficient cell creates the required proteins and functions normally. Therapeutic genes, once introduced into the cell, are guided by additional bits of DNA-like sequences to seek out the correct place and replace the deficient portion. A difficult part of the operation, however, is the actual insertion of the genes and bits of DNA-like material into the diseased cell.

One successful method of doing this is with the help of viruses. Viruses are "almost" living entities that resemble cells, in so far as they contain DNA, but not any further. Viruses are almost only DNA, contained inside a protein coat, sometimes with a fatty covering. They have no other apparatus to create proteins or even to reproduce. But the special feature is that they are small, most cannot be seen with an optical microscope, and they are able to get through the outer membrane and into the body of specific kinds of cells. It is within such a "host" cell that viruses use the available resources to reproduce, and this is the process, which could lead to failure or death of the cell — this causes diseases arising from viral infections.

This disease-causing capability can also be used for the therapeutic purpose of inserting genes into gene-deficient cells. The viruses used are a category of adeno-associated viruses, which have been found to be present with others of the ilk but cause no disease. AAVs are small, just 20 nanometres, and are able to enter many kinds of cells. And then, they attach to the DNA at a specific place known as AAVS1. This quality makes AAVs safe and convenient to use for gene delivery.

One group of the researchers, including Lukas D Landegger, Konstantina M Stankovic and Luk H Vandenberghe among others, tried out a number of AAVs and found that the synthetic virus, Anc80L65, was able to efficiently transfer a fluorescent green protein into both the inner as well as outer hair cells. Being effective with outer hair cells was an improvement over existing vectors. Laboratory tests were carried out with human cells and the vector was found to be equally effective.

The second group, Gwenaëlle S Géléoc and colleagues, sought out a genetic condition where the genes involved were found in both types of cochlear hair cells. The Usher's syndrome, which causes severe deafness and also affects balance and leads to blindness, results from the lack of a gene, UCH1C, which encodes the protein, harmonin. A sub-group of gene deficient mice, the c.216AA, were found to show both the hearing and visual defects of human Usher's syndrome. Study of c.216AA mice showed that both types of cochlear hair lost their function after the first week of birth.

As lack of harmonin was the apparent cause, the group investigated whether introducing harmonin in c.216AA hair cells would preserve their function. The known synthetic viral vector called Anc80L65was hence designed to carry the code for harmonin-A1 or harmonin-B1, and introduced into the inner ear by injection.

The results were dramatic — a thousand-fold improvement of hearing, to near normal levels, of otherwise deaf and dizzy c.216AA mice. More than a hundred genes may be implicated in disorders of the human ear. Finding ways to use Anc80L65 with large animals could speed up the discovery of gene therapy methods for disorders of the human ear, authors of the paper say.

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Complexity of hearing

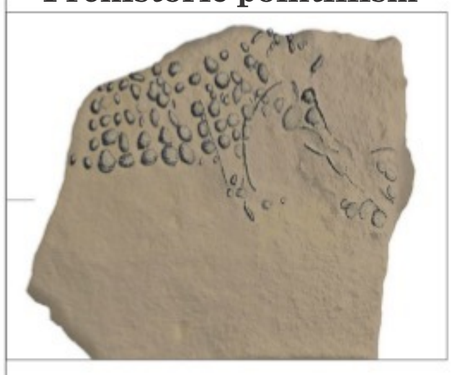
The human ear, which is not the most sensitive among animals, can react to sounds where the pressure difference is less than one billionth of the atmospheric pressure. Such a faint sound corresponds to movement of air by the distance of a tenth of an atomic diameter!

And then, if 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 to 20,000 cycles per second. Dogs can hear up to 40,000 to 60,000 cps, while cats go as high as 79,000 cps and dolphins and bats, which use high pitched sounds for navigation, can hear sounds at 1,00,000 cps. Mice also make and hear sounds as shrill as 79,000 cps, for communication outside the range of normal predators. (The sensitivity of cats is probably an adaptation to get the mice)

But range of frequency apart, the remarkable feature of the ears is the ability to tell the difference of very small changes 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 to 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 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.

PLUS POINTS

Prehistoric pointillism



What could be the oldest images in the world have been discovered in France. And the engravings of mammoths and wild cows known as aurochs were made from individual pixels — essentially the same technique used to produce images on computers and televisions. The pictures are also being compared to the pointillism technique supposedly pioneered in the 1880s by artists like Vincent van Gogh and Georges Seurat.

The 16 decorated stone blocks were discovered during an excavation of a now-collapsed rock overhang in France's Vézère Valley, which was used as a shelter by the Aurignacian people, the earliest modern human culture in Europe. They were radiocarbon dated to 38,000 years old, which could mean they are the oldest pictures ever created.

A painted hand silhouette found in Spain could be about 5,000 years older but its dating has been contested. An ivory sculpture of a female figure from about the same period as the French engravings was also found in southern Germany.

Professor Randall White, a New York University anthropologist, told *The Independent* that the images were certainly "among the very earliest images of things we can actually recognise in the entire archaeological record".

The pictures are fairly basic. But White said it was, "after all, 38,000 years old and the tools that are being used are rather robust .It's not so much the final effect that we found interesting, it's the conception of it — the use of individual points to form the body or the outline of a figure," he said.

White said that they had been excavating the site for 18 months before they found the images. "The engraving was face down and we knew within these sites such things are possible, so we were taking great care," he said. The discovery was reported in the journal, *Quarternary International*.

IAN JOHNSTON/THE INDEPENDENT

WHY DOES THE SKY APPEAR BLUE?

NATIONAL SCIENCE DAY IS OBSERVED ON 28 FEBRUARY IN HONOUR OF CV RAMAN'S DISCOVERY ON THE SCATTERING OF LIGHT. **ANISHA DUTTA** LOOKS BACK AT THE EXTRAORDINARY LIFE OF THE GREAT SCIENTIST AND EXPLAINS THE BASICS OF THE RAMAN EFFECT

Thirty years ago, 28 February was announced as National Science Day in India as the world-renowned Raman Effect was invented on that day in 1928. The object of observing National Science Day is not only to honour CV Raman but also to inspire Indian scientists and technologists.

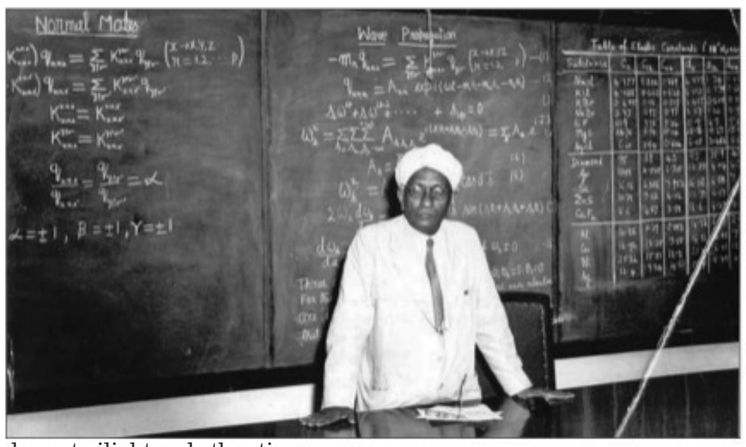
Raman's father Chandra Sekhar Ayer was a professor of physics and mathematics while his mother came from a conservative Sanskrit family. An exceptionally high intellect was inherited from his parents and Raman graduated at 16. At that time, there was hardly any scope for scientific research and so he appeared for a competitive examination for entry into the finance department. As usual, he secured the top position and was selected as assistant accountant general, finance, Government of India. He was only 19 and took up the job in Calcutta where he stayed for the next 10 years.

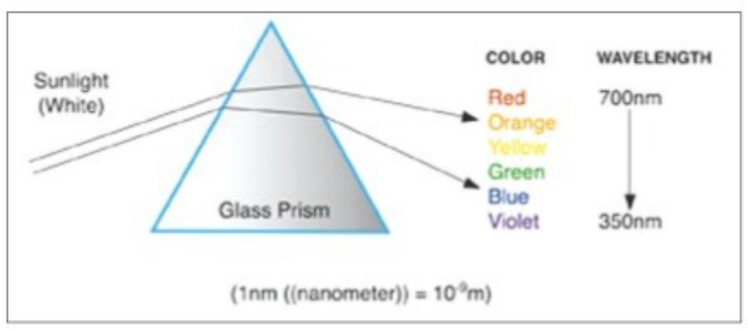
Once on his way to office, Raman noticed the Board of Indian Association for Cultivation of Science. He expressed his desire to conduct research to Amritalal Sarker, then director of the institution, which was established in 1878. It was decided that only Indian scientists would be accepted and Raman was cordially invited to start his research work — he continued that from 1907 to 1917. Next, he became the departmental head of physics at the University of Calcutta.

In 1921, Raman received his first invitation from Europe. In those times, ship was the only mode of transport to travel long distances and on that long sea voyage, he got curious as to why various shades of blue were spread in the sky and sea. The sky is a void and water is colourless, but why do they appear blue? This curiosity made him begin research work on the scattering of light waves through different media like solid, liquid and gas.

The great scientist Lord Raleigh had the idea that scattering of light waves through air particles makes the sky azure and the greenish blue colour of sea water is caused by reflection of that sky in sea water.

Raman did not accept the theory. He conducted research about different colours of the sky — at dawn, twilight and other times throughout the day and concluded that same theory is applicable to both sea water and the sky. In both cases, sun rays are scattered in different wave lengths through air and water particles. Through various experiments Raman concluded that any liquid contains minute particles and because of them blue colour is scattered. The seven visible colours of the spectrum are commonly known as "Vibgyor" and are set from smaller to larger wave lengths. After scattering, rays of smaller wave lengths like violet, indigo, blue and green are spread more widely than yellow, orange and red, which have larger wave lengths.





Though violet has the shortest wave length, the sky looks blue, not violet. This is because, the rays penetrating through the atmosphere and reaching Earth contain mostly blue colour. Also, our eyes are attracted more to wave lengths of blue. During sunrise or sunset, the sun lies close to the horizon and at those times, the "yor" portions are scattered more. As the density of air becomes lesser, the scattering of Vibgyor lessens and sky turns dark.

In oceans, sun rays are scattered through water particles almost at an angle of 30 degrees. In that range, scattering of sun rays through air particles (omitting dust particles). Therefore ocean water does not look like the sky but appears as greenish blue.

Light appears in two features — waves and photon particles. When a monochromatic ray passes through pure matter, most photon particles will pass directly. A little portion will be scattered in different directions after interaction with the particles of the medium. Raleigh came to the conclusion that in a liquid medium, a tiny portion of the scattered ray travels in the same wave length as the incident ray but only changes direction. Later, more investigations showed that the scattered ray contains photon particles of frequencies varied than incident ray. This variation in frequency is manifested due to the specific nature of the medium's particles.

When a photon particle is incident on a molecule of the medium, it can interact with an electron either in the ground state or high levels. Number of electrons in the ground state always exceeds the number of electrons in higher energy levels. Therefore the possibility of interaction with electrons in the ground state is always higher. For this reason, electrons gain energy from photon particles and increase their energy levels. This restless condition of electrons persists for a very short interval and therefore there are greater possibilities for repeated scattering of photon particles in same energy and same frequency levels. This is known as Raleigh Scattering.

On the other hand, in every medium, a limited number of electrons always exist in high energy levels. An electron in the ground state gains the energy of the incident photon particle and rises to a higher energy level. Then the energy of the scattered photon particle will have the difference of the energy of the electron and the energy of the incident photon. Similarly, if an electron in high energy levels gains energy of the incident photon then the scattered photon will possess the sum of the energy of both. This is the simplest way to understand the Raman Effect.

This transfer of energy is dependent on the vibration of particles and temperature. When the temperature diminishes, particles of the medium will absorb energy from the incident photon and energy of the scattered beam diminishes. Therefore frequency diminishes and wavelength increases. As temperature rises, the particles of the medium supply energy to the incident photon. The frequency increases, thereby causing a decrease in wave length. In either case, the wave length of the scattered beam differs from that of the incident beam.

The funniest thing is that the apparatus in this illustrious invention by Raman contained a mirror to reflect the sun's ray, a lens; a pair of complementary glass filters to obstruct the selected paths of rays, a flask full of benzene and a pocket spectroscope. At the time, the total cost was barely Rs 200! And he was awarded the Nobel Prize in Physics in 1930.

Its full name is the Raman-Krishnan Effect as his brilliant student KS Krishnan helped him by laboriously conducting research over several years. In 1933, Raman became the director of the Indian Institute of Science in Bangalore and the next year, he established the Indian Academy of Science. From 1940, he started research on the scattering of light in crystals, gem stones, pearls, corals and diamonds. He was awarded the Bharat Ratna in 1950. Owing to his affinity for roses, Raman maintained a rose garden where he was buried in 1970.

Raman never went abroad for higher education and conducted all his research in India — he tried to motivate scholars in the same way. Of course, now the scenario differs greatly owing to globalisation and as such is quite necessary. But one only wishes that National Science Day is observed every year in a big way as a mark of respect to CV Raman and the ideals he lived by.

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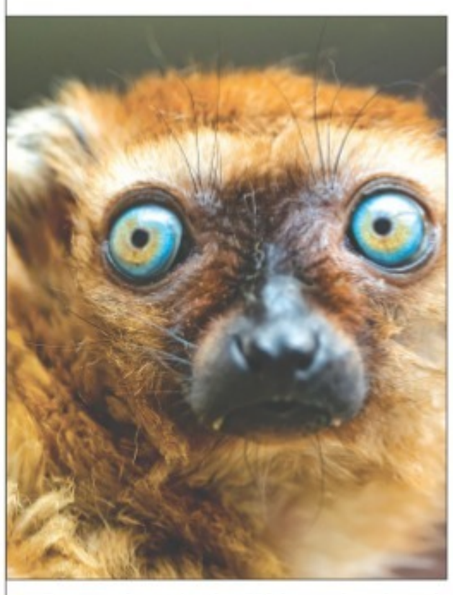
Tracking lemurs



Researchers in the US have developed a computer-assisted recognition system that can identify individual lemurs in the wild through their facial characteristics.

LemurFaceID, which identifies individuals based on photos, allows researchers to build a database for long-term research on the species.

Rachel Jacobs, a biological anthropologist at the George Washington University's Centre for the Advanced Study of Human Paleobiology and who was involved in the system's development, said the method could aid in evolutionary studies and conservation efforts.

The software could help to create records of how many individual lemurs there are in populations and what kind of social system they live in. It could also help to track trafficked lemurs if they are taken from the wild, said Jacobs, in a statement by George Washington University.

Traditional methods require researchers to trap and physically tag them, but LemurFaceID is non-invasive, fast, cost-effective and accurate, she said. The researchers hope the software can serve as a model for tracking other species and, in some cases, potentially replace physically tagging animals.

"We think this method could be applied to studies of species that have similar variation in hair and skin patterns, such as red pandas and some bears, among others," Jacobs said. Lemurs were named the world's most endangered group of mammals in 2012.

SAMANTHA BOH/THE STRAITS TIMES