Actually seeing what was so far inferred

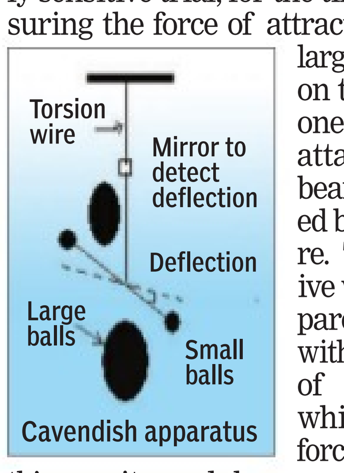
THE FORCES OF GRAVITY ARE EITHER SO FEEBLE OR SO FAR AWAY THAT THEY ARE DIFFICULT TO MEASURE, WRITES **S ANANTHANARAYANAN**

The week just passed has seen the world in jubilation at the detection of gravitational waves. These waves were the prediction of theory hardly in doubt and the confirmation was mainly the culmination of increasing precision of the detection system. While the detection may hence be viewed as inevitable, what has been achieved, by the revamped Laser Interferometer Gravitational-wave Observatory arrangement, located at two ends of the US continent, is an unprecedented measurement of a change, due to the fluctuation in gravity, of a length of just the billionth of a billionth of a metre over a distance of four kilometres!

The force of gravity itself presents great difficulty in being studied because it is so feeble. While all of us are aware of gravity, while we lift loads or drop things, this is only because we have a 6,000-billion billion tonne earth exercising all its gravity right at our feet. But the force of gravity between two objects in our normal experience, or the change in the earth's gravity even in the presence of a large mountain or at the bottom of the shaft of a mine, is difficult to detect. On the other hand, the gravity in black holes is so great that it keeps even light from emerging. But this is to no avail, as these objects are so distant.

The first formal laboratory measurement of gravity was by Henry Cavendish 100 years after the laws of gravity had been formalised by Isaac Newton in the 17th century.

Cavendish performed a remarkably sensitive trial, for the time, of measuring the force of attraction of two larger lead balls on two smaller ones that were attached to a beam suspended by a thin wire. The objective was to compare the force with the weight of the balls, which was the force of the earth's gravity, and, hence, compute the mass and density of the earth.



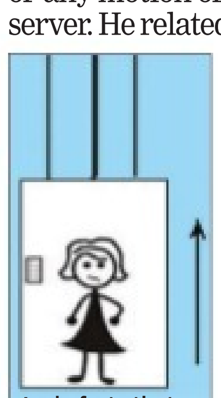
Cavendish apparatus

Newton's main contribution was that massive bodies have *inertia*, or resistance to being moved by a force, more massive bodies showing more inertia. And then there was the law of gravity, that massive bodies attracted each other, proportionate to the masses and inversely to the square of the distance. A little later, the question arose of whether the mass that gave rise to inertia was the same as what caused gravity, and this was answered by the experiment of Eötvös in 1906, where a pair of balls suspended from a torsion balance were subjected to both the inertial forces arising from the rotation of the earth and also the force of gravity.

The early work on detecting gravity due to isolated objects grew in sensitivity and found application in sounding the bottom of lakes, finding underground salt formations and even to help submarines sense the seafloor without using sonar, which would give them away. The actual constant of proportionality in the gravity formula is now known with great accuracy, but is both not a great improvement since the time of Cavendish and also somewhat uncertain even now.

Gravitational wave

Albert Einstein first reformulated the concepts of length and time to account for the observation that light moved at the same speed, regardless of any motion of the source or the observer. He related measurement to the relative source/observer speed, and the speed of light, which led to the mass and energy being related by a factor of the square of the speed of light — the celebrated $E=mc^2$ formula. As a sequel, Einstein examined the observation that the force of gravity is the same as the force felt when a body is accelerated, and the implications of this when related to the equivalence of mass and energy. The result was the discovery that the presence of a mass affected the nature of space and time and brought about curvature of space, which was perceived as acceleration and, hence, as gravity.


Lady frets that she is gaining weight when the elevator speeds upwards.

The backdrop of these discoveries was that the properties of electrical charges and the magnetic effects of moving charges, which had the form of growing weaker with distance, like gravity, had been very elegantly formulated. It had also been shown that periodic movement of charges gave rise to periodic magnetic effects, which, in turn, gave rise to electrical effects, and so on, leading to the original charge losing energy by radiating electromagnetic waves.

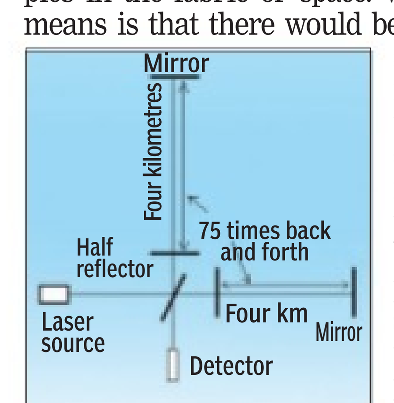
Ligo consists of two identical arrangements -- one at Hanford, near the west coast of the USA, and the other at Livingston, 3,000 km to the southeast.

Einstein, hence, went after a formulation of gravity along the lines of what had been done with electricity, with the difference, however, that gravitational force is only attractive and also that there is no equivalent of magnetism in gravity. But still, as the presence of a mass was seen as affecting the state of energy of the surrounding space, which would then affect the space further afield, the periodic movement of a mass also led to the spreading of a disturbance, in a wave-like way, with the moving mass gradually radiating and losing energy.

The effect of gravity, however, is so much feebler than those of electric charges that the actual "curving" of space and then of waves is not detectable except when dealing with the masses of stars and galaxies. The curvature of space was verified in the celebrated experiment of Arthur Stanley Eddington, where stars that should have been hidden by the sun became visible when the glare of the sun was blocked in a solar eclipse. In the case of gravity waves, however, their amplitude becomes perceptible only with very fast acceleration of very large masses, which exist only at great distances, so that they grow weak and are scarcely detectable when they reach us.

The Ligo arrangement

The way we detect feeble optical, infra-red or radio waves is with large, chemical or electronic collectors and amplifying systems. These collectors, however, do not respond to gravity waves, which manifest in the forms of ripples in the fabric of space. What this means is that there would be minute, and this is really minute, changes in distances between points in space as the wave passes through. Fortunately, we do have the means of measuring changes in distances, using a measuring scale of the dimensions of the wavelength of light.



Schematic of Ligo

The interferometer is such an instrument, which splits a beam of light into two at a partially reflecting surface, as shown in the picture. The two halves of the beam then traverse the two arms of the arrangement before they recombine, to be viewed through the telescope. These two halves now behave like the waves at the seaside, where returning waves meet the next set of incoming waves. We may have noticed that the waves sometimes meet with both crests together, when they get amplified, or, if a crest meets a trough, they are extinguished. The two halves of the light beam in the interferometer similarly rejoin, at the same stage of wave motion or otherwise, depending on the distance they traverse along the two arms, and this is sensitive at the level of the wavelength of light.

The Ligo has two arms, encased in high vacuum tubes that are four kilometres long and the laser beam that is used goes back and forth 75 times, or a distance of 600 km before recombining. The mirrors are adjusted so that the two beams extinguish and the field is normally dark. Now, if a gravity wave were to pass through, it would alter the distance of the arms and cause a rise and fall in the length, which would cause the field of view to grow bright and dark at the frequency of the wave!

Now, as the change in distance that is to be detected is so exceedingly small, there has to be a way of knowing that any fluttering of the light is not due to vibrations in any part of the four-kilometre arms or the detectors. To take care of this, apart from the best insulation from vibrations, Ligo consists of two identical arrangements — one at Hanford, near the west coast of the USA, and the other at Livingston, 3,000 km to the southeast. Now, an event is counted only if it takes place at both the sites, separated by the 10 milliseconds that the wave takes to cover the distance. As it is highly unlikely that there would be chance disturbances that caused a signal at both sites at the same time, this makes sure that false alarms are discarded.

Ligo was first set up in 1992, with hundreds of scientists the world over collaborating. Thousands of computers were also drafted to continuously monitor the signals recorded at the two sites but no results were recorded till 2011, after which Ligo went in for overhaul and enhancement. It may be fortunate that as soon as it was back in action in mid-September 2015, it was able to record a series of events that were matched at the two sites, and have been attributed to the spiralling and coming together, a 350-km orbit, over 100 times a second, at nearly the speed of light, of two black holes, each over 30 times the mass of the sun and a billion light years away.

Black holes, by definition, emit no light and cannot be observed. To detect gravity waves that mark the interaction of these bodies is, hence, to see directly what was so far only inferred. Gravity waves are also the means to observe events so ancient and so far that no other signals can survive the distance, maybe the earliest split seconds of the Big Bang, which was opaque to other radiation!

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PLUS POINTS

Live longer

Taking part in social activities such as book clubs or religious groups after retirement makes people live longer and appears to be as important to health as exercise, according to new research.

A retired person's risk of death is dramatically lowered if he/she takes part in such groups in the first few years after stopping working, the study found — suggesting that future retirees should pay as much attention to keeping active socially as they do to planning their finances and maintaining their physical health.

Researchers at the University of Queensland in Australia tracked the health of more than 400 over-50s living in England for six years after they retired, comparing their results with people of a similar age who were still working. They found that every social group membership people lost after retirement resulted in a 10 per cent drop in their quality of life rating six years later.

If a person belonged to two social groups before retirement and kept this up over the following six years, their risk of death was just two per cent, the study found. However, the risk rose to five per cent if they gave up one membership and 12 per cent if they gave up membership of both. The researchers said social groups could be defined as anything that a person sees as "an important part of their identity", from book clubs to religious groups through to tennis club memberships or involvement in trade unions.

"Retirement has an important bearing on health and quality of life because it typically involves relinquishing social group memberships that have been a key focus for people's self-definition for years or decades," they wrote.

The study also examined how changes in exercise levels after retirement affected a person's risk of death – and found that the impact was the same as giving up membership of social groups. Those who exercised vigorously once a week before retirement and continued to do so afterwards had a three per cent risk of death, rising to six per cent if they exercised less than once a week and 11 per cent if they stopped altogether.

CHRIS GREEN/THE INDEPENDENT

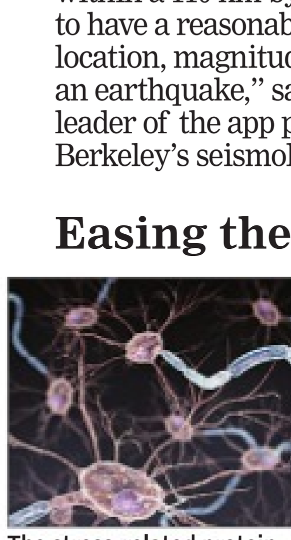
'Quake detectors

US researchers have developed an app that uses networks of smartphones to detect earthquakes and could send out life-saving alerts. The free app, called MyShake and released on 12 February for Android users, could be useful in countries without conventional warning systems, say the developers at the University of California, Berkeley.

MyShake uses movement sensors in smartphones, known as accelerometers, to detect tremors. It then sends the information in real-time, together with satellite-based position data, to a central system that compiles data from other mobiles in the area and could alert the regions likely to be hit next.

"We need at least 300 smartphones within a 110-km-by-110-km area in order to have a reasonable estimate of the location, magnitude and origin time of an earthquake," says Richard Allen, leader of the app project and director of Berkeley's seismological laboratory.

Easing the pain


The stress-related protein, FKBP51, expressed in parts of the spinal cord, can drive chronic pain.

Through glucorticoid signalling, the protein FKBP51 can regulate the perception of chronic but not acute pain in mice, scientists from University College London and their colleagues have found. Stress and chronic pain can go hand in hand, yet much of how stress and chronic pain-related signalling are connected remains a mystery. Previously shown to be involved in responses to stress in humans and rodents, FKBP51 now appears to be a factor common to both processes. The results, published on 10 February in *Science Translational Medicine*, point to FKBP51 as a potential therapeutic target to alleviate long-term, persistent pain.

"(The work) suggests that stress signalling, through the secretion of glucocorticoids, is an important regulator of chronic pain," wrote Jaclyn Schwarz, a neuroimmunologist at the University of Delaware who was not involved in the study, in an email to *The Scientist*. "The authors also confirm quite well... what has long been suspected: that the mechanisms underlying acute pain versus chronic pain are distinct."

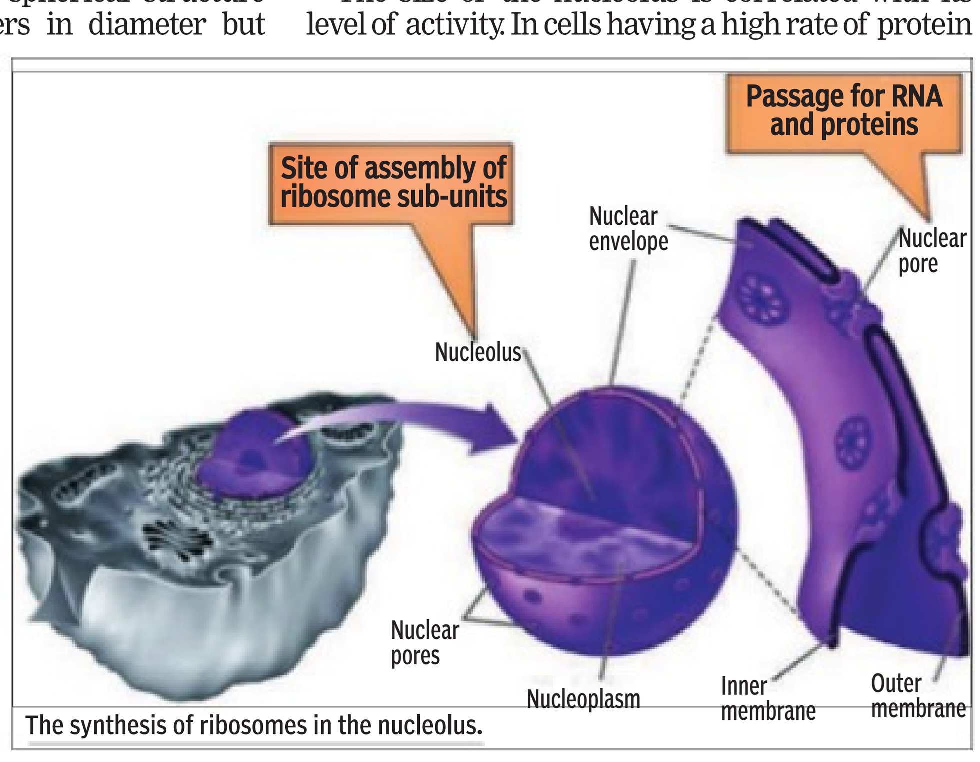
THE SCIENTIST

GRANULAR COMPONENTS

THE NUCLEOLUS IS INVOLVED IN RIBOSOME FORMATION, SAYS **TAPAN KUMAR MAITRA**

A prominent structural component of the eukaryotic nucleus is the nucleolus — the ribosome factory of the cell. Typical eukaryotic cells contain one or two nucleoli, but the occurrence of several more is not uncommon as in certain situations, hundreds or even thousands may be present.

The nucleolus is usually a spherical structure measuring several micrometers in diameter but wide variations in size and shape are observed. Because of their relatively large size, nucleoli are easily seen with the light microscope and were first observed more than 200 years ago. However, it was not until the advent of electron microscopy in the 1950s that the structural components of the nucleolus were clearly identified. In thin-section electron micrographs, each nucleolus appears as a membrane-free organelle consisting of fibrils and granules. The fibrils contain DNA that is transcribed into ribosomal RNA. The granules are rRNA molecules being packaged with proteins (imported from the cytoplasm) to form ribosomal subunits, which are subsequently exported back through the nuclear pores to the cytoplasm. Because of their role in synthesising RNA, nucleoli become heavily radio-labeled when the cell is exposed to radioactive precursors of RNA.



The synthesis of ribosomes in the nucleolus.

The earliest evidence associating the nucleolus with ribosome formation was provided in the early 1960s by Robert Perry, who employed a micro beam of ultraviolet light to destroy the nucleoli of living cells. Such cells lost their ability to synthesise rRNA, suggesting that the nucleolus is involved in manufacturing ribosomes. Additional evidence emerged from studies carried out by Donald Brown and John Gurdon on the African clawed frog, Xenopus laevis. Through genetic crosses, it is possible to produce Xenopus embryos whose cells lack nucleoli. Brown and Gurdon discovered that such embryos, termed anucleolate mutants, cannot synthesise rRNA and therefore die during early development, again implicating the nucleolus in ribosome formation.

If rRNA is synthesised in the nucleolus, then the DNA sequences coding for this RNA must reside in the nucleolus as well. This prediction has been verified by showing that isolated nucleoli contain the nucleolus organiser region — a stretch of DNA carrying multiple copies of rRNA genes. These multiple rRNA genes occur in all genomes and are thus an important example of repeated DNA that carries genetic information. The number of copies of the rRNA genes varies greatly from species to species but animal cells often contain hundreds and plant cells, thousands. The multiple copies are grouped into one or more NORs, which may reside on more than one chromosome — in each NOR, the multiple gene copies are arranged in tandem. A single nucleolus may contain rRNA genes derived from more than one NOR, like in the case of the human genome.

The size of the nucleolus is correlated with its level of activity. In cells having a high rate of protein synthesis and hence a need for many ribosomes, nucleoli tend to be large and can account for 20-25 per cent of the total volume of the nucleus. The main difference is the amount of granular component present. Cells that are producing many ribosomes transcribe, process, and package larger quantities of rRNA and have higher steady-state levels of partially complete ribosomal subunits on hand in the nucleolus, thus accounting for the prominent granular component.

The nucleolus disappears during mitosis, at least in the cells of higher plants and animals. As the cell approaches division, chromatin condenses into compact chromosomes accompanied by the shrinkage and then disappearance of the nucleoli. With our current knowledge of the nucleolus' composition and function, this makes perfect sense — the extended chromatin loops of the nucleolus cease being transcribed as they are coiled and folded, and any remaining rRNA and ribosomal protein molecules disperse or get degraded.

Then, as mitosis is ending, the chromatin uncoils, the NORs loop out again and rRNA synthesis resumes. In human cells, this is the only time when the ten NORs of the diploid nucleus are apparent as rRNA synthesis begins again, ten tiny nucleoli become visible, one near the tip of each chromosome. As these nucleoli enlarge, they quickly fuse into the single large nucleolus found in human cells.

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Telling T-cell therapy

STEVE CONNOR REPORTS ON 'EXTRAORDINARY' RESULTS THAT LEAD TO A PARADIGM SHIFT IN CANCER TREATMENT

A revolutionary cancer therapy that uses the body's own immune cells to attack metastatic tumours that have spread is being hailed as a "paradigm shift" in treatment of the disease. Patients with advanced blood cancers who were not expected to live beyond five months have shown complete remission after 18 months of follow-up checks with no signs of the disease returning, scientists have revealed.

In one trial of a patient's own T-cells — a type of white blood cell — that were engineered in the laboratory to identify and attack tumour cells, more than 90 per cent of the 35 patients with acute lymphoblastic leukaemia went into complete remission. In two other clinical trials involving about 40 patients with either non-Hodgkin's lymphoma or chronic lymphocyte leukaemia, more than 80 per cent of patients responded to the treatment. About half of them have been in complete remission for up to 18 months, scientists said.

Detailed findings of the clinical trials are to be published later this year, but summary results were discussed at the American Association for the Advancement of Science, whose annual meeting in Washington DC ended on Monday.

Cancer specialists urged caution over the early trials of T-cell therapy, saying that it did not work for everyone and some patients experienced toxic side-reactions and died. However, they said the improvements seen in some patients who had failed every other course of treatment were unprecedented.

"In the laboratory and in clinical trials, we are seeing dramatic responses in patients with tumours that are resistant to conventional high-dose chemotherapy," said Dr Stanley Riddell, of the Fred Hutchinson Cancer Research Centre in Seattle. "These are in patients who have failed everything. Most of the patients in our trial would be projected to have two to five months to live. This is extraordinary. This is unprecedented in medicine, to be honest — to get response rates in this range in these very advanced patients.


Lymphoblast cells eventually become lymphocytes, cells that are responsible for fighting infection, such as T-cells.

"We have a long way to go. The response is not always durable. Some of these patients do relapse, we are cognisant of that. But the early data is unprecedented. This is potentially paradigm-shifting in terms of how we treat them. I think this is a significant breakthrough, but we have a way to go. We have to understand how we bring it forward earlier into the treatment course of these diseases. We don't want to wait until patients have failed everything else."

T-cells form an important arsenal in the body's immune defences. They help to identify invading viruses and bacteria and can keep a "memory" of previous infections in order to launch a rapid immune response when the body comes under a repeat attack. Scientists have found ways of commandeering the natural killing capacity of T-cells to identify, memorise and attack tumour cells. One approach uses a Chimaeric Antigen Receptor with two sticky ends. One attaches to the T-cell and the other to a tumour cell.

Dr Riddell's team has developed a method of making Car T-cells that are highly stable and consistent, which lowers the risk of a toxic reaction, known as a cytokine storm, which can result in fatal fevers and falls in blood pressure. "Our approach has been to try to formulate a T-cell product of defined composition in every patient, so it is the same in every patient. It removes a big variable," Dr Riddell said. "These cells have the capacity to proliferate.

They have the capacity to survive long term as memory cells, and they have the capacity to differentiate to the effective lineages that are necessary to mediate anti-tumour activity."

T-cell therapy works best on the "liquid" tumours of the blood and bone marrow. Scientists believe its strength lies in the fact that T-cells can live and proliferate within the body for months or even years after they have been transfused back into patients.

One clinical trial involving another kind of modified T-cell found that they were still in circulation within the bloodstreams of patients 14 years after being transfused, according to Dr Chiara Bonini of the University Vita-Salute and San Raffaele Scientific Institute in Milan, Italy. "The last time (I saw) a change in remission rates like this must have been in 2000. This is really a revolution. I think we are at the beginning of a road. I think the first products will be available very soon," Dr Bonini said. "T cells are a living drug and, in particular, they have the potential to persist in our body for our whole lives."

THE INDEPENDENT