

Science in the new year

THERE IS THE PROMISE OF GOOD THINGS TO COME,
WRITES S ANANTHANARAYANAN

Research in science and sharing of work is greater now than ever before and every day uncovers new discoveries and insights. The progress made in the recent months in many areas suggests that we can expect important results in the course of the coming year. The journal, *Nature*, lists:

- **The Large Hadron Collider:** The facility at Cern, near Geneva, accelerates charged particles to unprecedented energies through a 27-km vacuum tube lined with powerful electromagnets working in unison. The purpose is to collide subatomic particles at near-light speeds and energies of electrons driven by many thousands of billions of volts, and then to examine the products of interactions.

- **The most promising current theory** of the nature of matter, which seeks to explain both the fine-scale interactions of subatomic particles as well as the gravitational forces between planets, predicts the fleeting existence of particles with very high mass. It would be only in the most energetic of reactions, as there might have been at the start of the "Big Bang", that such particles could arise. The first spell of the LHC, from 2008 to 2013, raised energies to 4,000 times a billion electron volts and created a sensation by revealing a particle that resembled



Excavations at Sima de los Huesos a cave site in the Atapuerca Mountains in northern Spain, have revealed a cache of 28 skeletons that were dated at 300,000-600,000 years ago. Work is on to decode the complete genome from the remains and results could throw new light on the mobility and inbreeding of ancient, proto-human species.

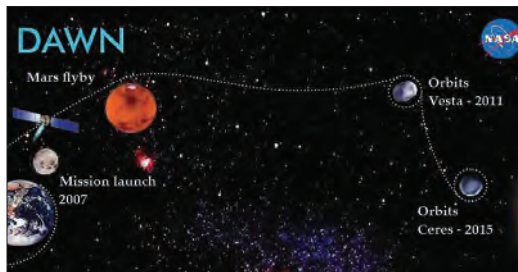
the Higgs Boson. But analyses of the results, including a number of new, high-mass particles created, has raised more questions that it has answered and the current theory, of so-called *supersymmetry*, is itself in question.

- **The LHC was shut down in 2013** for ramping up the capability and is due to reopen in March 2015 with twice the power, rising to about 13,000 times a billion electron volts. The results, once the collider gets going, would uncover new phenomena, which would either confirm and refine current thinking or invite a correction of course!

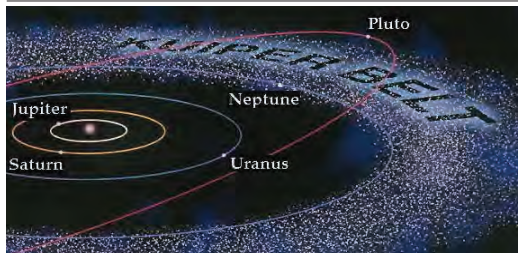
- **Climate change:** For all the proof of climate change due to GHG build-up in the atmosphere, the world's governments and industry have not made concrete progress to contain emissions. In the last international protocol of 2008, the USA, the largest emitter of GHG, stayed out because limits were not imposed on developing countries. While the USA took measures, nevertheless, China embarked on massive industrialisation and surpassed the USA in GHG emissions. The level of GHG in the atmosphere is, hence, poised to cross 400 parts per million, the highest seen since millions of years.

- **In the context,** the recent agreement by the USA and China to contain emission forms a solid basis for the UN conference on Climate Change, scheduled at Paris in December 2015. The expectation of the conference is that all countries in the world could agree on a legally binding set of specific emission limits that may be their last chance to avert ecological disaster.

- **Ebola virus:** The outbreak in Guinea, Sierra Leone, Liberia, Mali and Nigeria, in West Africa, has created a serious scare of spreading worldwide. The disease, which leads to death in 25-90 per cent of the cases, is highly infectious and calls for an advanced level of isolation and community involvement. The world has reacted with testing all entrants at international borders and quaran-



Dawn, a Nasa space probe launched to study objects in the asteroid belt between the orbits of Mars and Jupiter, will reach the 590-km dwarf planet Ceres in April 2015.



Nasa's New Horizons, a spacecraft launched in 2006, is due to reach the dwarf planet Pluto at the outer rim of the Solar System in July 2015.

line of infected persons, but it may be impossible to control a virus that compromises the immune system even while it causes internal bleeding and other symptoms.

- **Resources for rapid detection and isolation,** and also trained personnel have been rushed to the affected areas for the best possible control. Vaccines are to be tried out early in 2015 and results may be in by June. Several drugs are under development, as also the use of the antibody-rich blood of persons who have survived. Ebola will be the focus of science, hopefully successful, for all of 2015.

- **In the solar system:** Two mission of exploration would reach their destinations in 2015. The first is *Dawn*, the space probe launched by the National Aeronautics and Space Administration in 2007 to study objects in the asteroid belt between the orbits of Mars and Jupiter. Dawn

surveyed the 525-km *Vesta*, the second most massive asteroid, in 2012 and would reach the 590-km dwarf planet *Ceres* in April 2015, which is believed to consist of a rocky core covered by a 100-km thick mantle of ice, with 200 million cubic kilometers of water.

The second mission is *Nasa's New Horizons*, a spacecraft launched in 2006, and is due to reach the dwarf planet Pluto at the outer rim of the Solar System in July 2015. Pluto had at first been classified as the ninth planet but lost this status when the scattered disc object, *Eris*, which is 27 per cent more massive, was discovered. Pluto is now known as the largest object of the *Kuiper belt*, a region beyond the orbit of Neptune, and extending nearly as far beyond. *New Horizons* would fly past Pluto and take pictures of it and its five moons, and then fly on to probe one or two other Kuiper belt objects, depend-

ing on positions. Since passing Jupiter in 2007, *New Horizons* has been kept "hibernating" for 10 months of the years, to conserve fuel.

- **Space-time waves:** Einstein's General Theory of Relativity describes the force of gravity as curvature in space-time. A consequence of the theory is that great acceleration of masses should cause waves that would be reflected as instantaneous changes in distances in space. But the extent of variation is of the order of fractions of dimensions of atomic particles and is, hence, yet to be directly detected. The *Laser Interferometer Gravitational-wave Observatory* is an arrangement of two four-kilometre long light paths that may be able to detect such fleeting variations. A laser beam is split in two and passed down each arm of the "L" 75 times, back and forth, and then recombined. Slight variations in the length of either path would show up as an interference effect of the light beams. To eliminate physical, for example, seismic causes of change in length, the experiment is done simultaneously at places that are far apart and events are counted as valid only if they occur at both places.

- **While there have been indirect ways to confirm Einstein's prediction,** Ligo, which is looking for direct evidence, was not able to record anything of significance from 2002 to 2010. But the arrangement is being upgraded to be more sensitive, as "Advanced Ligo", and is to become operational in 2015.

- **The origins of humans:** Excavations at *Sima de los Huesos*, or the *Pit of Bones* — a cave site in the Atapuerca Mountains in northern Spain — have revealed a cache of 28 skeletons that were dated at 300,000-600,000 years ago. The Spanish paleontologists teamed up with the Max Planck Institute and an analysis of a part of the DNA, called the mitochondrial DNA, showed similarity with a stream of human species called *Denisovans*, found in ranges from Siberia to South-east Asia. This fact, although the physical features are akin to Neanderthal Man who was found more to the north, suggests that the skeletons are of a common ancestor.

- **But work is on to decode the complete,** or the nuclear genome from the ancient skeletal remains and results expected in 2015 could throw new light on the mobility and inbreeding of ancient, proto-human species.

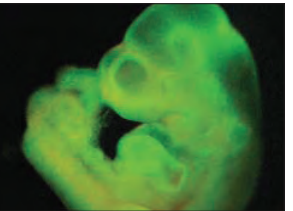
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PLUS POINTS

Science scandals

As always, in addition to the scientific breakthroughs that make headlines throughout the year, there is also a dark side to science. From misconduct to human error, there is always the possibility for something to go wrong. This year saw the announcement and retraction of a new method of cellular reprogramming; a lawsuit against users of an anonymous post-publication peer review website; and multiple biosecurity breakdowns at US federal facilities.

- **The Stap saga:** In January this year, Haruko Obokata of the Riken Center for Developmental Biology in Kobe, Japan, along with her colleagues published two papers in



Nature that described pluripotent stem cells that had been derived simply by applying a physical stressor to adult cells.

- **Known as Stimulus-Triggered Acquisition of Pluripotency,** or *Stap*, the findings attracted the attention of the scientific community and media. But it didn't take long for some researchers to raise questions. Scientist bloggers led the way, posting the results of their attempts to replicate the study in real time. Users of the post-publication peer review website *PubPeer* also raised concerns. By February, Riken had launched its own investigation, which led to a finding of scientific misconduct against Obokata. In July, *Nature* retracted both papers. Sadly, in August, Obokata's supervisor Yoshiki Saiji committed suicide, after having been hospitalised for stress and exhaustion.

- ***PubPeer's* legal woes:** The post-publication peer review forum found itself in hot water this October when Wayne State

PREPARING FOR STRESS

TAPAN KUMAR MAITRA
EXPLAINS SIGNAL TRANSDUCTION
MECHANISMS THAT INVOLVE
MESSENGERS AND RECEPTORS

Most cells respond to hormones, growth factors and other substances present in the extracellular fluid. Such responses are mediated by receptor proteins, either at the cell surface or inside the cell. Each receptor protein has a binding site that is specific for its particular ligand. In the case of membrane receptors, ligand binding is followed by transmission of the signal to the interior of the cell, thereby regulating specific intracellular events.

Several different mechanisms for signal transduction are known and an important one involves receptors linked to G proteins, which are activated when the binding of a ligand to a neighbouring receptor causes a conformational change in the G protein, resulting in the displacement of GDP by GTP. The G protein then activates an enzyme system that produces intracellular chemical signals called second messengers, one of the most common of which is cyclic AMP, synthesised when the enzyme adenylyl cyclase is activated by a G protein. In an alternative pathway, the second messengers are inositol trisphosphate and diacylglycerol, which are produced from phosphatidylinositol bisphosphate when a G protein activates the enzyme phospholipase C. Regardless of the pathway, second messengers mediate specific intracellular responses by activating specific enzymes or enzyme cascades.

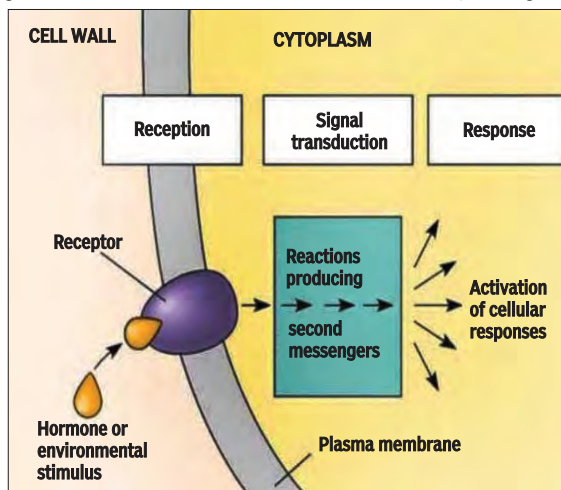
Calcium ions play a central role in cellular activation processes and can be considered second messengers as well. Calcium effects are often mediated by calmodulin, a protein that is activated when calcium ions bind to it. Depending on the target cell, the calcium-calmodulin complex can activate any of a variety of enzymes, thereby modulating enzyme activity in response to the cytosolic calcium concentration. Release of calcium from internal stores within the endoplasmic reticulum, triggered by IP₃, is an important step in many signalling processes, including fertilisation of animal eggs.

Receptor protein kinases, such as receptor tyrosine kinases, act via a third category of signal transduction mechanisms. Upon binding of the appropriate

ligand, such receptors become phosphorylated on specific tyrosines. The phosphorylated receptor becomes a binding site for other proteins, which contain SH2 domains. When these proteins bind to the receptor, they are activated either by the binding itself or by subsequent phosphorylation. SH2 domain-containing proteins activate major signal transduction pathways, including the Ras and phospholipase C pathways.

Growth factors are messengers that play a specific role in regulating cell growth and behaviour. Many growth factors bind receptor tyrosine kinases; other growth factor receptors have serine/threonine kinase activity. In these and other cases, signal transduction events result in alterations in phosphorylation of cytosolic proteins, ultimately resulting in changes in the function of proteins that enter the nucleus to affect the expression of genes.

The signal transduction pathways initiated by these different types of receptors provide an important link to our understanding of embryonic development. Mutations can lead to unregulated activity or lack of function of the receptor or of components of the signal transduction pathway. As a result, cells may experience changes in the stimuli they perceive, which can lead to abnormal function, including can-



Signal transduction pathways.

cer. Hormones are messengers that regulate the activities of body tissues distant from the tissues that secrete them. Hormones can be endocrine or paracrine, depending on the mode of delivery. The adrenergic hormones secreted by the adrenal medulla are examples of endocrine hormones. Adrenergic hormone receptors can be classified as α - and β -adrenergic receptors. The β -adrenergic receptors are linked to a G protein that stimulates the formation of cAMP, whereas the α -adrenergic receptors stimulate phospholipase C, resulting in elevation of the intracellular calcium concentration. The different receptors mediate opposite effects in different smooth muscles but work together to coordinate changes in blood flow and other activities, thereby preparing the body for stressful situations.

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A mystery explained

TIA GHOSE REPORTS ON AN ANALYSIS OF AN
ANCIENT CHINESE CIVILISATION'S DISAPPEARANCE

An earthquake nearly 3,000 years ago may be the culprit in the mysterious disappearance of one of China's ancient civilisations, according to new research. The massive upheaval may have caused catastrophic landslides, damming up the Sanxingdui culture's main water source and diverting it to a new location.

That, in turn, may have spurred the ancient Chinese culture to move closer to the new river flow, study co-author Niannian Fan, a river sciences researcher at Tsinghua University in Chengdu, China, told the 47th annual meeting of the American Geophysical Union in San Francisco on 18 December.

In 1929, a peasant in Sichuan province uncovered jade and stone artifacts while repairing a sewage ditch located about 24 miles from Chengdu. But their significance wasn't understood until 1986, when archaeologists unearthed two pits of Bronze Age treasures, such as jade, about 100 elephant tusks and stunning eight-foot high bronze sculptures that suggested an impressive technical ability that was present nowhere else in the world at the time, said Peter Keller, a geologist and president of the Bowers Museum in Santa Ana, California, which is currently hosting an exhibit of some of these treasures.

The treasures, which had been broken and buried as if they were sacrificed, came from a lost civilisation now known as the Sanxingdui, a walled city on the banks of the Minjiang river. "It's a big mystery," said Keller, who was not involved in the current study.

Archaeologists now believe that the culture willfully dismantled itself sometime between 3,000-2,800 years ago, Fan said. "The current explanations for why it disappeared are war and flood, but both are not very convincing."

But about 14 years ago, archaeologists found the remains of another ancient city called Jinsha near Chengdu. This site, though it contained none of the impressive bronzes of Sanxingdui, did have a gold crown with a similar engraved motif of fish, arrows and birds as a golden staff found at Sanxingdui, Keller said. That has led some scholars to believe that the people from Sanxingdui may have relocated to Jinsha. But why has remained a mystery.



Fan and his colleagues wondered whether an earthquake may have caused landslides that dammed the river high up in the mountains and rerouted it to Jinsha. That catastrophe may have reduced Sanxingdui's water supply, spurring its inhabitants to move. The valley where Sanxingdui sits has a large floodplain, with 4.3 miles of high terraced walls that were unlikely to have been cut by the small river that now flows through it, said Fan.

And some historical records support their hypothesis. In 1099 BC, ancient writers recorded an earthquake in the capital of the Zhou dynasty in Shaanxi province, Fan said. Though that spot is roughly 250 miles from the historic Sanxingdui site, the latter culture didn't have writing at the time, so it's possible the earthquake epicentre was actually close to Sanxingdui — but it just wasn't recorded there, he said. Geological evidence also suggests that an earthquake occurred in the general region between 3,300-2,200 years ago, he added.

Around the same time, geological sediments suggest massive flooding occurred, and the later Han dynasty document, *The Chronicles of the Kings of Shu*, records ancient floods pouring from a mountain in a spot that suggests the flow being rerouted, said Fan. (Around 600 years later, Jinsha residents built a wall to prevent flooding.)

Together, the findings hint that a major earthquake triggered a landslide that dammed the river, rerouting its flow and reducing water flow to Sanxingdui, Fan said. But if so, where did the river get rerouted? The team found clues high up in the mountains in the deep and wide Yamen ravine, at about 12,460 feet above sea level. The modern river cuts through the ravine, which was carved by glaciers about 12,000 years ago. Yet the telltale signs of that glacial erosion — bowl-shaped basins known as cirques — are mysteriously absent for a long stretch of the ravine. The team hypothesises that an earthquake spurred an avalanche that then wiped out some of the cirques about 3,000 years ago.

At this point, the theory is still very speculative and additional geological data was needed to buttress it, said Fan.

But while the geological story is possible, Keller said it didn't answer the basic question, "What would motivate people to destroy their entire culture?"



University pathologist Fazlul Sarkar bought a lawsuit against the site's users for allegedly making defamatory comments questioning some of Sarkar's publications. According to Sarkar, the comments cost him a job at the University of Mississippi. He and his lawyer subpoenaed identifying information about the users, but *PubPeer* has refused to turn it over.

On 10 December, the site filed a motion to quash the subpoena.

- **Containment issues at federal agencies:** US government labs also ran into some trouble this year. In June, as many as 75 scientists at the Centers for Disease Control and Prevention (CDC) were exposed to live *Bacillus anthracis* when anthrax-causing microbes were shipped to laboratories not equipped to handle the pathogen



safely. Then in July, Food and Drug Administration employees packing up an old storage unit run stumbled upon 16 forgotten vials of smallpox. Later that same month, researchers at the CDC's influenza lab reported that a shipment of benign avian influenza virus sent to a Department of Agriculture facility was contaminated with the highly pathogenic H5N1.

In the wake of these safety breaches, the CDC called for a moratorium on movement of biological materials from biosafety level 3 (BSL-3) and BSL-4 facilities in July, the head of the CDC Bioterror Rapid Response and Advanced Technology Laboratory resigned, and the National Science Advisory Board for Biosecurity was overhauled.

"These are wake-up calls. These are events that tell us we have a problem," CDC director Thomas Frieden said during a July press briefing. "We're going to fix them."

JEFF AKST/THE SCIENTIST

