CAPSULE

History of life
Several changes in geography happened about 50 million years ago when the landmass that is now India collided with Asia. Now, Princeton University researchers argue that this also resulted in increased oxygen content in the oceans, thereby altering the conditions for life in the region. Their inference comes after a study of the nitrogen cycle.

Hungry black hole
Astronomers may have just identified a black hole devouring a nearby neutron star, if reports from the LIGO-VIRGO collaboration are confirmed. The event, labelled for now as #s190426c, occurred 1.2 billion light years away. Observatories around the world are working to analyse their signals and confirm this, a *Nature* report says.

Jamia team develops ultrasensitive quantum thermometer

The thermometer can measure micro Kelvin changes in temperature and has quick response time

R. PRASAD

Researchers at Jamia Millia Islamia, New Delhi, have developed an ultrasensitive quantum thermometer using graphene quantum dots. The thermometer can precisely measure a wide range of temperature: 27 degree C to -196 degree C. The thermometer has high sensitivity when measuring different temperatures and can measure very minute (micro Kelvin) changes in temperature.

Robust: The thermometer showed excellent repeatability with negligible variation in response when tested for over 50 cycles, says Saikh Islam (centre).

Sensitive device
The thermometer developed by a team led by Saikh S. Islam, Director of the Centre for Nanoscience and Nanotechnology also showed extremely quick response time of just about 300 milliseconds to register a change in temperature from 27 degree C to -196 degree C. And the time taken to return to its initial temperature value was as little as about 800 milliseconds. The results of the study were published in the journal *Nanoscale Advances*.

"The thermometer showed excellent repeatability with negligible variation in sensing response when tested for over 50 cycles during a one-year period. The sensor was stable and responded ultra-fast when we tested it repeatedly," says Prof. Islam.

"The device can find widespread applications in cryogenic temperature sensing. Since the sensor has high sensitivity and ability to measure minute changes in temperature, it will be useful in the pharmaceutical industry, healthcare to measure the incubation temperature of biological cells and molecules and the automobile industry to measure the ignition temperature within the engine," he says.

The sensor can also be used for measuring high temperatures up to 100 degree C. "In the past, we have tested it up to 300 degree C. Compared with low temperature, the high-temperature sensitivity is low but it is still much higher than currently available solidstate thermometers in terms of sensitivity, resolution, response and recovery timings," says Poonam Sehrawat from Jamia Millia Islamia and first author of the paper. "Since the sensor is stable and shows linear sensitivity behaviour, it does not need calibration."

Sensor preparation
The researchers first prepared graphene oxide and chemically made it reduced graphene oxide. "The physical and chemical properties of reduced graphene oxide are very close to monolayer graphene. So by using reduced graphene oxide it is easy to synthesise in large-scale materials having properties similar to graphene," says Prof. Islam. During the reduction process, quantum dots are formed in the graphene oxide. The reduced graphene oxide having quantum dots is mixed with a ceramic (aluminium oxide), to produce the sensor. The sensor does not need any encapsulation as ceramic forms the matrix.

The reduced graphene oxide flakes containing the quantum dots (measuring 3-6 nanometre in size) are dispersed in the ceramic; the ceramic does not interfere with the sensor response but provides rigidity to the film. "The graphene oxide flakes are in contact with each other in the composite. So a continuous network of current path is obtained," he says. The temperature sensors were fabricated from this film by using small piece measuring 1x1 cm and depositing two silver electrodes to it for measuring the sensor response.

"The synthesis process is extremely cost effective, has high yield and batch fabrication is possible. One of the main advantages is that this device can be made to any shape and dimension," Prof. Islam says.

"We are working on making a prototype of this thermometer to be used in electronic devices, as on-chip thermometers that do not even require calibrations. We will now replicate these achievements in single electron transistors (SETs) to miniaturise it for integration in integrated circuits," he adds.

How depression affects memory

ASWATHI PACHA

Forming a memory of people, places, and events is a dynamic process, and many studies have shown that psychiatric disorders such as depression may affect this process.

Now researchers from the National Centre for Biological Sciences (NCBS), Bengaluru, have shown how memories change and get updated over time in people with unipolar and bipolar depression.

The study published in *Neurobiology of Learning and Memory* involved controls, unipolar- and bipolar-depression patients admitted at the National Institute of Mental Health and Neuro-Sciences (NIMHANS). Unipolar patients experience depressive symptoms such as low mood, lack of motivation, etc. whereas bipolar patients alternate between periods of depression and mania. Only bipolar patients in a depressive phase were included in the study.

Mind matters: We studied how depression affects aspects of factual memories, say Sumantra Chattarji (right) and Bhaktee Dongaonkar.

Memory test
On the first day, all the participants memorised a list of 20 everyday objects. Two days later, controls, unipolar and bipolar patients were split into two groups, and the first group was prompted to remember what happened on the first day while the other group did not get this reminder. All the participants were then made to memorise a different list of everyday objects.

On the fifth day, all participants were asked to recollect the objects from the list shown on the first day.

Unipolar and bipolar patients remembered fewer objects than controls. The controls who were reminded recalled objects from the second list in addition to the first list. Such recall is a form of memory updation where new learning updates older memories, but only when the old memory is activated by a reminder. Controls who were not reminded did not recall objects from the second list.

In unipolar patients, this ability to update memories with a reminder was not affected and was similar to controls.

However, bipolar patients appeared to be mixing the objects from two lists during recall, irrespective of the reminder manipulation. "Though we asked only for objects from the first list, they also named items from the second list. Basically, they remembered the objects but had difficulty in remembering which list the object belonged to – a phenomenon known as source confusion in psychology. This mixing was not seen in unipolar or the control group," explains Bhaktee Dongaonkar, a postdoctoral fellow at NCBS and first author of the paper.

"This is the first such study aiming to understand how depression affects a more nuanced aspect of factual memories – how information learned first is influenced by information acquired later. Importantly, this study explores this important question for the first time in Indian patient populations," says Sumantra Chattarji from NCBS, the head of the research team. He is also the Director at the Centre for Brain Development and Repair, Bengaluru.

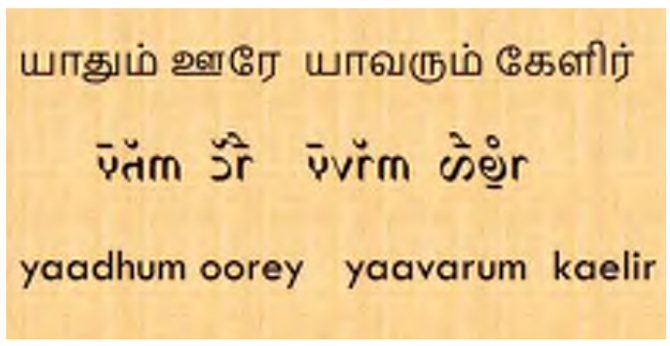
"Future studies can build upon these findings to examine potential changes in brain structure and function, using neuroimaging techniques such as MRI," says Prof. Chattarji.

IIT Madras: Easy OCR system for nine Indian languages

The Bharati script unifies nine Indian languages

SHUBASHREE DESIKAN

Taking a cue from European languages, several of which have the same (Roman letter-based) script, Srinivasa Chakravathy's team at IIT Madras has, over the last decade, developed a unified script for nine Indian languages, named the Bharati script. The team has now gone a step further since developing the script: it has developed a method for reading documents in Bharati script using a multi-lingual optical character recognition (OCR) scheme. The team has also created a finger-spelling method that can be used to generate a sign language for hearing-impaired persons. In collaboration with TCS Mumbai, the researchers have found a way for persons with hearing disability to generate signatures using this finger-spelling technique.



Transliteration: Tamil verse from Sangam literature written in Bharati script (centre) and English. ▪ SRINIVASA CHAKRAVARTHY

The scripts that have been integrated include Devnagari, Bengali, Gurmukhi, Gujarati, Oriya, Telugu, Kannada, Malayalam and Tamil. English and Urdu have not been integrated so far. Dr Chakravarthy says, "Urdu and English alphabet systems have a very different phonetic organisation. But that does not mean a mapping is not possible. It is quite possible and can be done."

In general, optical character recognition schemes involve first separating (or segmenting) the document into text and non-text. The text is then segmented into paragraphs, sentences words and letters. Each letter has to be recognised as a character in some recognisable format such as ASCII or Unicode. The letter has various components such as the basic consonant, consonant modifiers, vowels etc.

Easy to read
The scripts of Indian languages pose a problem for such a character recognition because the vowel and consonant-modifier components are attached to the main consonant part. This difficulty is removed in the Bharati script which can be easily read. "In Bharati characters, these different components are segmentable by design. So OCR works quite accurately. Our OCR engines gives almost 100% accuracy even with mild noise added," says Dr Chakravarthy.

Three-tiered structure
The ease in design comes about because the Bharati characters are made up of three tiers stacked vertically. The consonant at the root of the letter is placed in the centre and the modifiers are in the top and bottom tiers.

In collaboration with Sunil Kopparappu of Innovation Labs, TCS, Mumbai, the team has developed a universal finger-spelling language for the nine Indian languages. They are working on a system that can help people sign documents using a finger-spelling method, and future plans include developing a new Braille system with the Bharati script.

'Address the innovation deficit in neglected diseases'

The thrust in funding research should be followed up with policies that incentivise industry in drug development

ZAKIR THOMAS

It is encouraging that India was reported to be the fourth largest funder of research and development (R&D) in neglected diseases as per the G Finder Survey which tracks global investments in R&D for the neglected diseases *(The Hindu,* January 24). This reflects the government's commitment towards addressing the innovation problem in neglected diseases.

Neglected diseases are mostly tropical infectious diseases, and the market size for drugs for such diseases is small due to their limited geographical incidence. To highlight the common problem of lack of innovation for drugs, diagnostics and vaccines for this basket of diseases, WHO started addressing these as neglected diseases from late 1980s. Some examples of neglected diseases are malaria, tuberculosis, leishmaniasis (kala azar), dengue, leprosy, lymphatic filariasis and diarrhoeal diseases.

These diseases face an innovation deficit as they are neglected in R&D efforts of the pharmaceutical industry. However, it is not just the neglected diseases in the developing world that face this innovation deficit. Several rare diseases that affect the developed markets are called "orphan diseases." These are called orphans because the pharmaceutical industry does not find it profitable to develop and market products intended for only a small number of patients suffering from rare diseases.

Geography: Neglected diseases are mostly tropical infectious diseases, and the market size for drugs for such diseases is small. ▪ K. R. DEEPAK

Innovation model
This innovation deficit is caused by the prevailing model of pharmaceutical innovation. Drug discovery came about as a key component of modern medicine towards the end of the 19th century. Till mid-20th century, this was mostly carried out in academic settings. By the middle of the 20th century it became an endeavour that was largely driven by pharmaceutical companies. The second half of the 20th century saw consolidation of pharmaceutical entities leading to multinational pharmaceutical companies who drive innovation in the pharmaceutical sector. The business model of pharmaceutical innovation is market driven, and the governments have adopted a hands-off policy letting the market forces to work. However, the outcome of this process, namely, new drugs, diagnostics or vaccines are subject to strict regulatory control by the governments.

Orphan diseases comprise both rare diseases and neglected diseases. They are orphans of research focus, market interest and even public health policies. The reasons why these diseases have been ignored for so long are better understood today. The industry-led model works well in cases of diseases with markets that ensure adequate return on investment. If the market size is not attractive, industry will not invest in such cases. This leads to market failures resulting innovation deficit.

When market fails, public policies must be put in place to address the issue. For this reason, governments and patient organisations in the developed markets have emphasised the need for providing policy incentives to encourage innovation to develop solutions for the "orphaned" rare disease patients. Both the U.S. and European Union have policies to support drug development for orphan diseases. The U.S., the U.K., Denmark, France, Italy, Sweden and Spain have public policies for treatment of rare diseases. The policy approach has been to treat such diseases as a class and tailor suitable policies.

India may learn from the above global examples treating neglected diseases as a class requiring special policy intervention to address the innovation deficit. A comprehensive policy supporting research, development and marketing and treatment of neglected disease aiming at their elimination is required if India aims to meet the Sustainable Development Goals.

Incentives
The thrust in funding research should be followed up with policies that incentivise industry to take up drug development. The Orphan Drugs Act of the U.S. has a basket of policies from drug development grants to tax credits, fast track approvals by regulatory agencies, seven-year market exclusivity, fee reductions for regulatory approvals to priority review vouchers.

Establishing a biomedical observatory which records and monitors the ongoing R&D in neglected diseases will help the government to ensure effective disbursal of the limited resources, identify research gaps and take corrective measures. The current thrust in internal resource generation in the national laboratories have the unintended effect of diverting research to diseases with market. A sustained and long-term funding commitment to neglected diseases will address this issue. If the Prime Minister's slogan of 'Jai Anusandhan' has to reach its benefits to the poor and neglected patients, there should be a comprehensive policy to address the innovation deficit in neglected diseases.

(The author is an IRS officer who was earlier with CSIR's Open Source Drug Discovery programme. Views expressed are personal.)