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Glimpses from Indian Research 2018-19

CURATED SCIENCE STORIES | IN ASSAMESE, ENGLISH, HINDI, KANNADA & MARATHI

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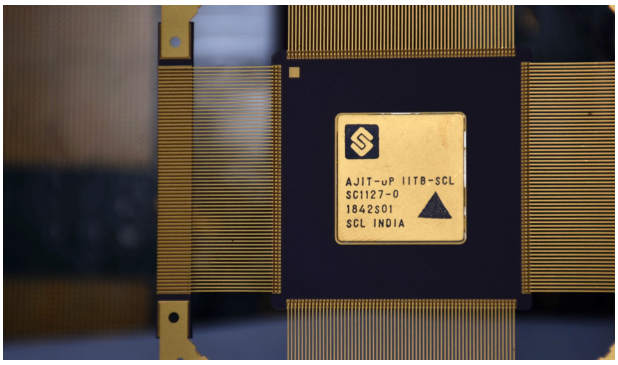

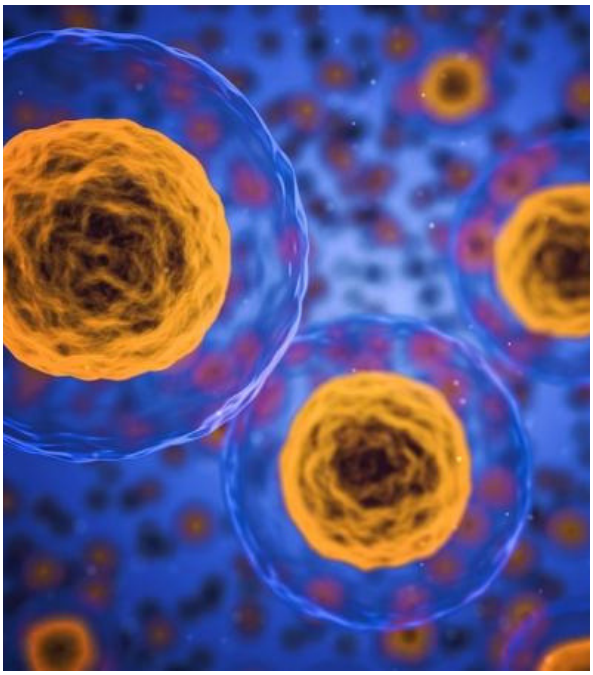

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The Indian Dravidian language family is 4500 years old—What does that mean and how do we know?

By Suma M

India, the land of diversity, is bestowed with several cultures. The vast number of languages spoken here is a testimonial to that fact. While learning these languages is exciting, studying them is fascinating for another reason—they help us understand the little-known history of the Dravidians, who lived in the subcontinent before the speakers of Indo-Aryan languages arrived around 1500 BC. So far, not much is known about their origin and their dispersal across the country. Now, a study by a group of researchers from the Max Planck Institute for Psycholinguistics, the Netherlands, has tried to reconstruct the Dravidian language family tree in an attempt to understand Dravidian history. The results show that these languages are as old as 4500 years! So what does that mean?

The Dravidian language family is one of the world's primary language families. It has 80 varieties, spoken by over 200 million people in south, central and north India. Interestingly, the Kurukh language of Nepal and the Brahui language of Pakistan and Afghanistan belong to the Dravidian family. Certain languages of the Dravidian language family are known to have been written for over 2000 years, and influenced Vedic Sanskrit and modern Indo-Aryan languages, thus playing a significant role in contact between Indo-European and Austroasiatic language families.

Previous linguistic studies have tried to understand the relationship between various Dravidian language subgroups and have recognised four main branches of the

language family. The South Dravidian I subgroup consists of Tamil, Malayalam, Irula, Kodava, Kurumba, Kota, Toda, Badaga, Kannada, Koraga and Tulu, among others. The South Dravidian II subgroup has Telugu, Gondi and Kuvi, and others. The Central Dravidian subgroup comprises Gadaba, Parji and Kolami, and the North Dravidian subgroup has Brahui, Kurukh and Malto languages.

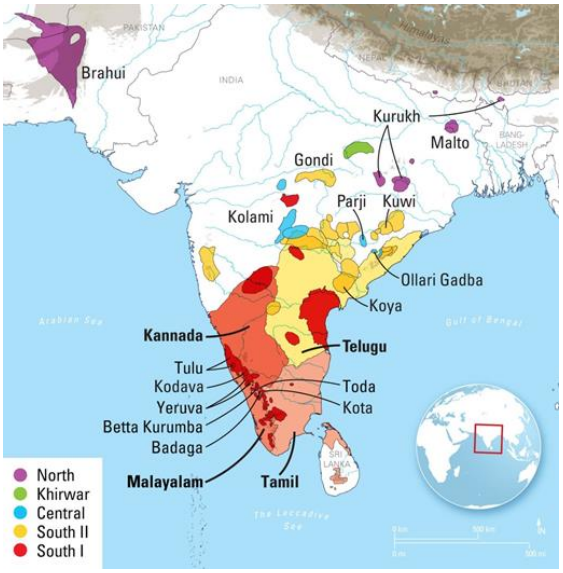
An interesting fact about the Dravidian family of languages is that there many smaller, spoken ones, which are not well-studied. The researchers of this study, published in the journal Royal Society Open Science, focused on a representative sample of languages to reconstruct the Dravidian language family tree by using first-hand data.

"We collected 100 items of basic vocabulary from native speakers of a diverse sample of Dravidian languages", says Dr. Annemarie Verkerk, an author of the study.

They used the Swadesh list, a compilation of primary vocabulary that can help in assessing the relationship between existing languages alongside the changes over time, devised by the linguist Morris Swadesh.

While previous studies on the Dravidian family of languages have used datasets derived from dictionaries, this study combined data collected first-hand with advanced statistical analysis.

"Swadesh's 100-concept elicitation list was used to collect lexical data for 20 languages. Responses were recorded and written down if this was possible. For some spoken languages, informants did not want to write down responses in non-native scripts. Recordings and written transcripts were transcribed to the International Phonetic Alphabet (IPA). Cognate (relatedness) coding of the responses was performed using the Dravidian Etymological Dictionary", explains Dr. Verkerk, talking about the methods used in the study.



Map of the Dravidian languages in India, Pakistan, Afghanistan and Nepal adapted from Ethnologue (Source:rsos.royalsocietypublishing.org R. Soc. Open sci. 5: 171504).

The researchers used a Bayesian phylogenetic inference method, a probability-based statistical approach that estimates the evolutionary history and relationships of a set of species or languages based on some prior data. Commonly used in ecology, this approach deduced a set of highly probable language trees, rather than a single 'best' language tree.

The findings are then compared to a commonly used reference tree namely Krishnamurti's family tree, which classifies the languages into three main groups—South I and South II, Central and North. B. Krishnamurti, a linguist, is one of the most prominent figures in the study of the Dravidian languages as he applied modern comparative linguistic theory to study the diverse Dravidian languages and their relationships. The results of his work are used as a reference in further studies on Dravidian languages.

However, the researchers of this study found that there is a significant split between South I and the three other groups, which is estimated to have happened 2500-3000 years

ago, a little latter than the expansion of the Southern Neolithic civilisation between 4000 and 3000 years ago. The agricultural practices in this period provide external evidence through crop vocabulary for the findings of this study.

The researchers incorporated historical and linguistic data, mostly evidence on when the written Dravidian languages are first attested in inscriptions, in the language tree to estimate the age of the Dravidian language family. Using these data, they found that the Dravidian language tree to be approximately 4500 years old, coinciding with the archaeological findings regarding the Southern Neolithic, a definitive period on the archaeological timescale. The Neolithic period in South India which lasted from 5000 years ago to 3400 years ago, is characterised by man-made artefacts like the ash mounds produced by early agricultural communities.

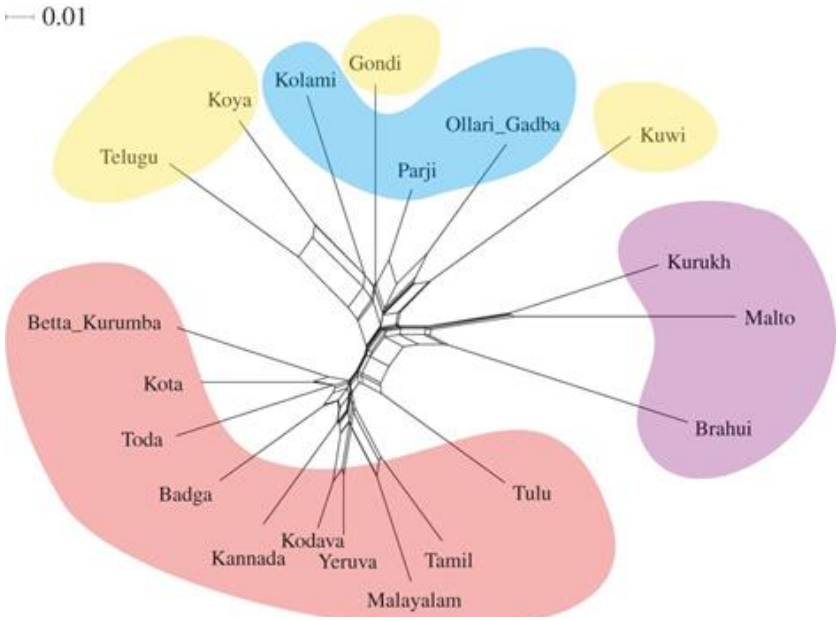
While the analysis is informative about when the Dravidian languages originated and when they diversified, it does not tell us much about where this may have happened.

"The current analysis is an investigation of the genealogy of languages. It does not incorporate information about the current geographical information of languages, nor does it reconstruct where ancestors of the Dravidian languages were spoken in the past. However, this is possible, and this has been done for other language families", says Dr. Verkerk.

The use of a Bayesian phylogenetic technique for linguistics makes the current study an interesting one.

"The methods employed in this study have been started to be used in linguistics from 2000 onwards. They have been met with scepticism by historical linguists, who invented the 'standard' way to study the history of language, the so-called comparative method. The comparative approach makes a feature-by-feature comparison of two or more languages with common descent from a shared ancestor, to extrapolate and infer the properties of the ancestor. However, phylogenetic techniques for linguists build on the comparative method and are gaining more acceptance now", explains Dr. Verkerk.

The study is one of the few based on the best-supported analysis that provides the current best estimate of Dravidian descent, throwing light onto the movement of ancient populations into and through South Asia. It shows that dating languages is one of the critical steps in understanding the history of Eurasia.



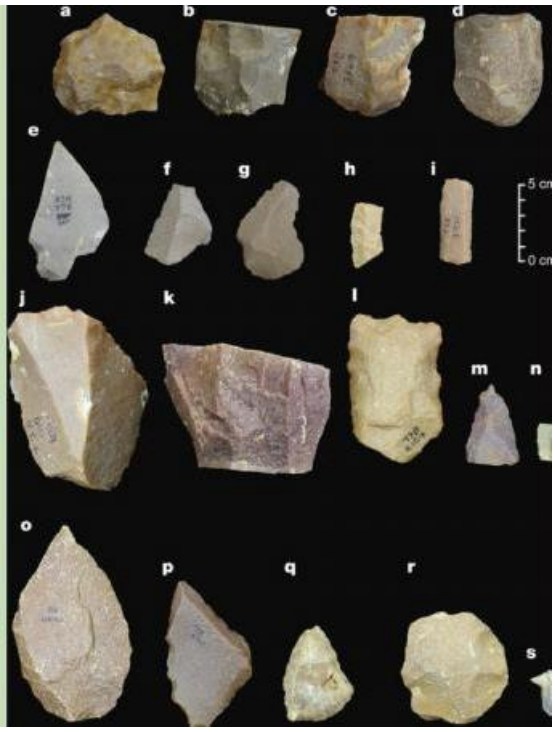
A NeighborNet visualization of differences relating to the vocabulary of languages. Colour-coding gives subgroup affiliation: red, South I; blue, Central; purple, North; yellow, South II. (Source: rsos.royalsocietypublishing.org R. Soc. open sci. 5: 17

Human migration history – what the stone tools in Attirampakkam tell us

By Annie Megan Santamaria

In the story of human origin and migration, many pages have been lost to the sands of time. Now, archaeologists from India and France have found one such coveted page in the sediments of Attirampakkam, a small town near Chennai, India, which is a classic site in the history of Indian archeology, known to be one of the oldest sites to contain stone artifacts.

Among the 7,000 stone tools recovered, the archeologists have observed a progressive change in the tool making technique similar to those used by the precursors to modern humans during the stone age. These tools, the archaeologists believe, are between 3,85,000 to 1,72,000 years old, belonging to the Middle Palaeolithic culture.



3,85,000-year-old stone tools found in India could give insights into the migration of ancient humans from Africa. What other mysteries lie beneath India's sediments? Photo: Dr. Shanti Pappu

The stone tools found in Attirampakkam are special because going by their age, the finding contradicts the previously accepted theory that ancient Homo sapiens migrated to India from Africa some 1,25,000 years ago. The location of the Indian subcontinent actings as a checkpoint in the map of human migration, it is an important evolutionary crossroad. Thus, the findings suggests that the migratory pulse might have happened more than 60,000 years earlier than estimated!

"Several decades of intensive research in India has yielded many rich Palaeolithic complexes with wonderful contributions from many archaeologists. Relatively few have been excavated or dated compared to the wealth that we have", says Dr. Shanti Pappu from the Sharma Centre for Heritage Education, India, who is also the lead researcher of the study published in the journal Nature. "Though it is unlikely to find DNA evidences or fossil evidences at this site or area, owing to the nature of the sediments, several discoveries have been made elsewhere in India and there is a possibility for more fossil finds", she adds.

The researchers of the study used a technique called 'luminescence dating' to calculate the age of the stone implements. This technique measures the amount of light emitted by an artefact depending on the amount of radiation it has been exposed to, from its surrounding environment since the time of it's burial. Since skeletal material this old is relatively scarce, over 7,000 stone implements were dated to study human evolution in Eurasia

according to the types of tools used by these ancient humans.

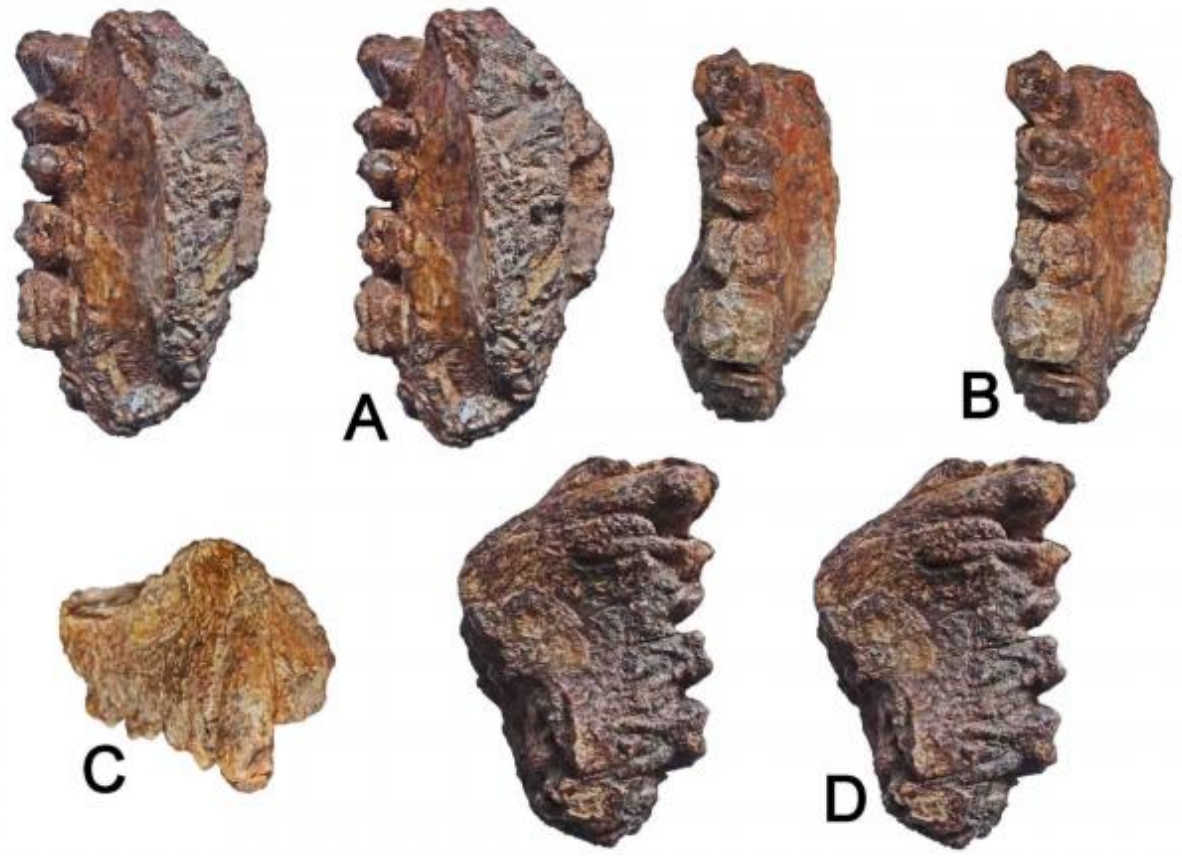
When our hominid ancestors – Homo erectus – left Africa, they carried with them their signature tool-- the large Acheulean axe. The data from this study showed a shift from these biface axe-like tools to much smaller stone tools made in a style called Levallois. The more complex and advanced Levallois flint had a sharp edge and was most likely mounted on a stick, to be used as a spear. The appearance of this type of tool marked the shift from the preceding Acheulian culture to the Middle Palaeolithic culture. This coincides with recent discoveries of hominid remains in Morocco and the United Arab Emirates which put the migratory phase from Africa to Eurasia at around 3,50,000 years ago, thus cementing the belief that the migratory event happened much earlier than once thought.

However, an opposing theory suggests that hominids indigenous to India might have invented this technique of tool making without the influence of hominids that migrated from Africa to India. A study of the transition from Acheulean bi-faced tools to Levallois flake tools undertaken in Armenia, says that this gradual shift is part of a logical progression and that the transitional change occurred many times independently before becoming widespread. As seen with other archaic human and the Neanderthals.

"We do have transitional assemblages that mark the transitions from the preceding Acheulian. We are not speaking only about one technology or tool type, rather a total shift in the overall patterns of making tools. We are very cautious in our paper as regards correlations with species", comments Dr. Pappu on the alternative theory.

The most definitive way to discern who the proprietors of these tools are, would be to unearth the skeletal remains of the ancient human species. However, the lack of skeletal fossil finds make this a daunting task. While we may not really know "who" exactly made these tools, we can now say that it was made by someone who was here before the arrival of Homo sapiens from Africa, as we understand today. This finding might help rewrite the story of human migration, as evidence from across the world gathers towards this.

There are numerous stratified sites like Attirampakkam in many parts of India that have huge potential and could hold the answers to human evolution and dispersion. And researchers are constrained by funds and resources to dig our history. "We need more grants for long-term research projects in prehistory in India", says Dr. Pappu.



Right maxilla preserving Canine-M2 by Ansuya Bhandari et al. (Nov. 2018), PLoS ONE 13(11)

First-ever hominoid ape fossils discovered in Peninsular India

By Jyotsana Dixit

The story of human evolution takes a different twist with each new piece of fossil found. Palaeontologists trace the first human (or human-like) footsteps from the Olduvai Gorge in Tanzania. From there, the story of where our early ancestors set foot becomes a matter of in-depth discussion and debate. It is believed that about 14 million years ago, during the Miocene, ape-like species first originated on earth and gave rise to the present-day taxonomic family called Hominidae. This belief is supported by fossil remains recovered from Africa and beyond, including India, where at least four hominid families are found. Two of them belonged to the larger Indopithecus, and the other two to smaller Sivapithecus. Indopithecus fossils have been reported earlier from Hari Talyangar region of Himachal Pradesh, while those of Sivapithecus from Siwalik regions of India and Pakistan.

In a recent study, palaeontologists from India have discovered fossil evidence of a hominid species at Tapar in the Kutch basin of Gujarat. The study, published in the journal PLoS ONE, involved scientists from the Birbal Sahni Institute of Palaeosciences, Lucknow, Duke University, USA, Wadia Institute of Himalayan Geology, Dehradun, Indian Institute of Technology, Roorkee, and the Northeastern

Ohio Medical University, USA. The Department of Science and Technology partially funded the study as an award of Fellowship to Dr. Ansuya Bhandari.

The study began in 2011 when researchers were in Kutch hunting fossils. Dr Ansuya Bhandari, Scientist at the Birbal Sahni Institute of Palaeosciences, stumbled upon something that looked like a fossilised upper jaw, or the Maxilla, of an ape-like individual. They later took this treasure to the lab and analysed it with X-Rays and computer-based tomography to learn more about it. About a thousand radiographic slices were used to reveal the internal details of the fossil.

The researchers then compared the pattern of the teeth of the fossil with those found earlier in the region. They concluded that the upper jaw was of an adult ape belonging to the genus Sivapithecus, and lived about 11-10.8 million years ago during the Miocene. The researchers could not precisely identify if the individual belonged to either S. sivapithecus or S. hysudricus species because of the poor condition of the fossil.

"Unfortunately, the specimen had much iron in it from being in iron-rich ancient soil. Hence, the radiations did not penetrate very far into the specimen", said Dr Richard F. Kay and Blythe A. Williams from Duke University, who are also the authors of the study.

This discovery is exciting because fossil remains of Sivapithecus have so far been found only in four regions around the Siwalik Hills, a mountain range of the outer Himalayas stretching from the Indus to the Brahmaputra.

This is the first-ever discovery of a Sivapithecus fossil outside the Siwaliks. "This is a landmark discovery which represents a significant southern range extension of Miocene hominoids in the Indian peninsula. It is the farthest south that it has been found. This finding, almost 1000 km south of Siwaliks has increased the geographic range of the genus," says Dr Bhandari, who is also the corresponding author of the study. "This finding fills a time window of approximately 11 million years in the evolutionary history of future hominid remains in India", she adds.

The researchers hope that this finding will draw more attention to the region and more such studies will be carried out in the future.

"Kutch is a paradise for fossils. Many associated mammal fossils belonging to the similar age have been discovered here. Such remains will help us understand in detail about the evolution of great apes and humans," says Prof. Sunil Bajpai from IIT Roorkee, who is also an author of the study.

Scientists discover the first Ichthyosaur skeleton from India in Gujarat. [Photos : Prof. Guntupalli]

Catch of the Kachchh – this time, a complete ichthyosaur

By Suma M

Ichthyosaurs were large marine reptiles which once lived in the Earth's oceans. Though considered distant relatives of snakes and lizards, ichthyosaurs were not dinosaurs. So far, scientists have found fossil evidences of these giant 'fish-lizards' in parts of South America, North America and Europe. However, recently, paleontologists from India have discovered one such fossil in the Kachchh basin of Gujarat.

"No ichthyosaur remains have been reported so far from the Triassic rocks of India. From the Jurassic, the skeleton collected by us is the first from India. It is the oldest known occurrence of ichthyosaurs in India and is the only near-complete skeleton of ichthyosaur from India", says Dr. Prasad Guntupalli, one of the authors of the study by a team of researchers from Delhi University, Manipal University, Christian-Albrechts-Universität zu Kiel, Friedrich-Alexander-Universität Erlangen-Nürnberg and Kachchh University. It was published in the journal PLOS ONE.

Ichthyosaurs are believed to have existed since the early Triassic Period (about 250 million years ago) until the Cretaceous period (about 90 million years ago). Their diversity was known to have been greatly affected by the end Triassic mass extinction -- a global extinction event that occurred about 200 million years ago. Though they made a comeback during the Jurassic Period (200-145 million years ago), they were eventually wiped out of the planet in the early Late Cretaceous (90 million years ago).

Explaining the timeline of ichthyosaurs, Dr. Guntupalli says, "Around 250 million years ago, all the continents that we see today, was assembled into a single supercontinent known as Pangaea. This supercontinent broke up in the late Jurassic (160 million years ago) into two major continental blocks known as Gondwanaland (comprising of South America, Africa, Antarctica, Australia, India and Madagascar) and Laurasia (consisting of North America, Europe and Asia)".

Interestingly, most fossil remains so far of ichthyosaurs were found in Laurasian continents with limited occurrences from Gondwanaland. This discovery, one of the rare finds of near complete skeleton from the former Gondwanaland, has hence intrigued many. It was found in the lower Katrol Formation, a type of Jurassic rocks found in Kachchh. "The Upper Jurassic (152 million years) Katrol Formation is predominantly represented by sandstone and shale rocks", says Dr. Guntupalli.

In the recent discovery, the researchers have presented a preliminary description of the ichthyosaur skeleton. The fossil remains at the excavation site included vertebral column, ribs, neural spines, gastralia (bones found between the sternum and the pelvis in reptiles) and two associated fins, alongside a part of the snout, jaws and other bone fragments. Further examination by the researchers revealed that the specimens belong to the family Ophthalmosauridae, which had a graceful dolphin-shaped body as long as 5.5 meters.

The discovery hints at the movement of animals between Indo-Madagascar and Mediterranean faunal provinces, during the Jurassic Period. Does it mean a possible seaway connected the two landmasses? If so, this seaway connected Tethys, an epicontinental sea that existed between Laurasia and Gondwanaland, which could have facilitated faunal exchanges between today's Europe and Madagascar.

But, have you wondered how paleontologists excavate these fossil remains, study them to this depth, and find out who exactly these fossilized remains once were?

"Fossils collected from the field are often embedded in rock matrix, as is the case with the Ichthyosaur skeleton we have collected from Kachchh. The first step we follow is to free the fossil specimen from rock matrix by cleaning with equipments like pneumatic tools and sand blaster, and sometimes by treating with mild acids", explains Dr. Guntupalli, sharing some insights into his skillful work. "Following this, the fossils are treated with consolidants to strengthen fossils and finally deposited in a museum so that they are available for future study by any researcher and for display to the public".

There have been quite a few related fossil discoveries in India. "*Ichthyosaurs remains comprising of a few isolated teeth and fragmentary vertebrae, believed to be 100 million years old, have been discovered in the rocks of the Cauvery basin in South India",* says Dr. Guntupalli, adding that future explorations in remote areas such as Kachchh are expected to lead to more exciting discoveries of palaeontological significance.

India's rising population: Are we heading towards a demographic dividend or a Malthusian catastrophe?

By Vimal Simha

"It's difficult to make predictions, especially about the future", goes a saying, although it is contested as to who said this. The essence of this saying is nowhere more true than in the field of population projections. For example, naively extrapolating the past rate of world population growth into the future starts to give absurd results very quickly. Yet, this has not deterred people from trying to project not only population growth but a host of associated social and economic parameters into the future.

Back in the 19th century, Thomas Malthus, an English scholar in economy and demography, argued that population increases exponentially, while food production can only grow linearly. It meant that eventually there would be too many hungry mouths to feed that our food production cannot match. Ultimately, the world would tend towards a 'Malthusian catastrophe'. However, an increasing population also has its benefits. It can lead to growth in the economy due to the change in the age structure of the population. This positive outcome is called the 'demographic dividend'.

By 2025, India's population is expected to reach 1.5 billion. Will this increase produce a 'demographic dividend' or lead to a 'Malthusian catastrophe'? Different methods for predicting India's future population give radically different results. Now, researchers at the Shanghai University, China and the International Institute for Applied Systems Analysis, Austria, have developed a novel model that takes many other characteristics of the population into account, compared to other models, to make demographic projections.

Conventional models for population projection use the national age and sex distribution for their estimates. But, the population of a country does not consist of identical individuals producing the same number of offspring. The authors of the present study, published in the Proceedings of the National Academy of Sciences (PNAS), argue that such models suffer from two types of difficulties. They do not consider the heterogeneity of the population and do not take into account all possible factors that influence fertility rates.

In a vast country like India, fertility rates show significant regional differences. For instance, in the 1990s, the fertility rate in Kerala was 1.8 per woman while it was 5.1 in Uttar Pradesh. Applying the same model, but at the level of each state rather than nationally, yields a substantially higher national population because the high-fertility states produce a more offspring and hence gain higher weightage over time. This raises the question of the appropriate scale at which the model should be applied.

However, even among individuals of the same age and sex, other factors determine how many offspring they are likely to produce. One such element is the education level of an individual because educated women tend to produce fewer children. Explicitly considering education levels, and its projected increase with time, results in lower projected population growth as the proportion of educated women, with lower fertility rates, increases with time. Hence, the projection model needs to recognise factors whose inclusion will help improve predictions, while not burdening it with superfluous details.

In this study, the researchers propose a multi-dimensional model that projects future trajectories of fertility, mortality and migration based on current data and past trends. Besides, to address the issue of heterogeneity, the researchers consider the urban and rural populations of each of India's states and union territories separately.

The results of the analyses show India's population peaking between 1.66 billion and 1.8 billion by mid-century, before declining after 2070. If education enrollment were to remain constant at today's levels, India would still have a significant population of uneducated people. However, in the last thirty years, the proportion of adult women without school education has fallen from 70% to 46%.

If education enrollment levels continued to increase, one would expect concomitant improvements in human development and economic growth, say the researchers. They also point out that broad-based education has many benefits ranging from poverty eradication and economic growth to health and well-being to quality of institutions and even democracy.

The study provides some insights into the implications of population growth for the future of India, and also for developing other population projection models around the world.

"We have shown how different degrees of accounting for measurable heterogeneity within populations changes the way in which we see the future", say the authors.

Similar studies on population estimations in the past have had distinctly mixed results. One of the most well known is the "Second India" study commissioned by the Ford Foundation in the 1960s to examine the social and economic consequences of a projected doubling of the Indian population from 500 million, which it was then, to 1 billion. In retrospect, projections for food production turned out to be underestimates, whereas projections on education and poverty were too optimistic.

So, what does the future hold for India? How does India compare with its neighbour China, which also has a comparably large population? The researchers note that China is about three to four decades ahead of India because of its massive investment in universal education in the 1950s. The education pyramid of India looks similar to China's in 1980, and the projected education pyramid for India in 2050 looks similar to China's today.

"While cultural and institutional factors may differ between the two countries, and there can be no perfect analogy, this comparison makes it look likely that India will experience similarly rapid human-capital–driven development as China has over the past three to four decades", concludes the study.

Zika surveillance in India: The key to management and control

By Farida Kothari

Beginning in 2015, physicians in Brazil began to notice an outbreak of rashes, fever, red eyes, joint pain and headaches in their patients. Though initially thought to be dengue, the illness was finally identified as an outbreak of the Zika virus. With 2016 olympics scheduled in Brazil, fear about the virus being spread globally began to emerge. As a result, the World Health Organization (WHO) declared the Zika outbreak as a public health emergency of international concern.

Zika is a mosquito-borne virus first identified in monkeys in Uganda. Since then, several human cases of the virus have been documented in various parts of the world. There are various neurological disorders and neonatal malfunctions linked to the virus. In children born to Zika infected mothers, for example, the virus can cause brain damage and microcephaly, as well as other congenital defects. Babies with microcephaly have unusually small heads, often accompanied by intellectual and motor disabilities. In adults, the Zika virus may lead to a disorder called Guillain-Barré syndrome, which is a form of temporary paralysis.

With its large population and conducive climatic conditions, India has the ideal conditions for the transmission and potential outbreak of the Zika virus. The virus is primarily transmitted by the bite of the infected female Aedes mosquito--a widely prominent mosquito in India that also causes dengue and chikungunya. And, there are no available drugs or vaccines effective against the virus.

"India has most of the conditions necessary for the Zika virus to spread. In order to

prevent an outbreak, we need a structured surveillance program in place," urges Dr. Farah Ishtiaq, from the Centre for Ecological Sciences at the Indian Institute of Science (IISc), Bangalore.

In her recent study, Dr. Ishtiaq details how such a program can be developed to include screening before an outbreak arises, collecting baseline data, and researching on the ecology of the disease.

According to a report from WHO, so far, over 80 countries have reported a Zika virus transmission, including India, Thailand, Singapore and Bangladesh. India also has the climatic conditions necessary for a year-round transmission of the virus. Additionally, with over 60,000 air travelers arriving to India every year, the country's 1.2 billion citizens become susceptible to Zika exposure, especially during the rainy season. The media has already reported four cases of Zika in India, though they are not the first.

An important first step to lower the risk of a Zika outbreak in India is screening both humans and mosquitoes for the presence of the virus. According to data from the Indian Council of Medical Research (ICMR), till date, a little over 24,000 Aedes mosquitoes have been screened so far for the virus in India. "This number is too low," says Dr. Ishtiaq. There are significantly more mosquitoes than those screened for the virus. Besides the Aedes mosquito, other species of mosquito, such as the Culex quinquefasciatus, could also potentially transmit the virus and this must be screened too. Controlling the spread of mosquitoes goes a long way in controlling the disease, opines Dr. Ishtiaq.

In addition, other animals, such as birds, horses, bats, and so on, could also be hosts of the Zika virus. Due to a lack of research on how infectious diseases interact and influence the ecosystems they are in, the potential of other animals being hosts of the virus in India has never been considered.

The next step is to screen the transmission of the virus in the case of pregnant mothers to their infants. Children born with microcephaly at birth should be screened too in order to check for the virus in mothers.

Dr. Ishtiaq highlights, "It is important to conduct screenings to identify whether reported microcephaly cases in India are Zika-linked or not. To do this, we need to begin collecting data on microcephaly and other birth defects linked to the Zika infection."

Finally, all these sources of data need to be collated and documented accurately in order to create a comprehensive database. This kind of baseline data can further help to assess the future risk of the disease and monitor potential birth defects across the country. It would also enable the international scientific community to understand the extent of the disease by understanding the strain and genetic data of the Zika virus.

Dr. Ishtiaq believes that Zika surveillance could be enhanced in India through the 'one health' approach, where multiple sectors and stakeholders work together to achieve better public health results. "To assess and manage the risk of future diseases, we need the collaboration of everyone involved – doctors, public officers, and so on. Even researchers, like us, will do our part", she signs off.

Immune Checkpoint Blockade Therapy – Unleashing the immune system in a war against cancer

By Savitha Sekhar Nair

The defence system of the human body is incredible. Given the kind of challenges it faces, from microbes such as bacteria and viruses, on a daily basis, the fact that we are all still alive is nothing short of a miracle. The immune system, that deals with threats from the outside world, can also combat threats from within equally well. This is why scientists are now exploring the possibilities of channelling the immune system to fight cancer. However, the idea that one can harness the immune system to do so is not new.

In the mid-1900s, although not everyone was convinced, immunotherapy was being pursued by quite a number of researchers as an exciting prospect for cancer treatment. But what sounded great on paper simply didn't work as well in practice. The results of studies on treating cancer with immunotherapy were pretty bleak. Towards the later part of the 20th century, the concept of cancer immunotherapy began to lose its appeal, and many scientists gave up. However, few held on, and one among them was Prof. James Allison, the pioneer of the so-called "check-point-blockade" cancer immunotherapy as it stands today. What began in the late 1980s, as a quest to understand the responses of certain immune cells, turned out to be the research that would redefine the face of cancer therapies. By 2011, Ipilimumab, the immunotherapy-based-drug designed by him and his team, was shown to become the first drug ever to improve survival rates among those suffering from advanced cases of skin cancer (melanoma).

Since this discovery, the field of immunotherapy is gaining wide-spread recognition. In fact, in 2016, two of the three groups of scientists predicted by Thomson Reuters as potential Nobel Prize winners, worked in the field of cancer immunotherapy. Recognising the importance of immunotherapy, Prof. James Allison was awarded the 2014 Breakthrough Prize, considered by many as the Russian Nobel, in life sciences. Today, immunotherapy is the approach that holds the highest promise in cancer therapy. It is also touted to be the next big thing in cancer research.

Immunotherapy: How does it work?

The immune system of our body is often likened to the defence sector of a nation for good reasons. It has its own set of cells and molecules, each conferred with specific responsibilities towards protecting the body. They work as a team, discovering and destroying anything that does not belong to our body.

Imagine that you learn of the presence of a group of criminals responsible for heinous criminal acts throughout your city. What would you do? Either you could devise various strategies to take them down yourself, or you could call the security forces, acknowledging their expertise, and assist them in whatever ways to set things straight.

Immunotherapy is when you choose the second option.

In most cases, the immune system can detect and ward off all ominous growths in the body, including cancers. But sometimes, cancerous cells escape the notice of the immune system for various reasons. Either the immune system fails to recognise the cancer due to their constraints, or it may be that the cancer cells over-produce inhibitory signals – signals that were ideally meant to keep the immune cells in check. This ensures that the homicidal immune cells stay away. Regardless of how the cancer cells escape the action of the immune system, the consequence is that the immune system ceases to be effective, and the cancer flourishes.

How does one make the immune system effective in such cases? One could extricate the immune cells from their constraints or quell the inhibitory signals, thereby letting the immune system act on the cancerous cells. And the latter is exactly what is achieved by 'Immune Checkpoint Blockade Therapy'(ICBT). Currently approved ICBT drugs are antibodies that bind to those molecules, which prevent the immune cells from killing the cancerous cells. They work by 'freeing' the immune system so that it can eliminate cancer.

Yervoy – the breakthrough drug

The story of ICBT begins with the success of Ipilimumab, which was dispensed under the trade name 'Yervoy'. The drug activates the immune system by targeting CTLA-4 – a protein receptor that inhibits a class of immune system cells known as Cytotoxic T lymphocytes (CTLs). Although CTLs can recognise and destroy cancer cells, they are blocked by the presence of CTLA-4. Yervoy is an antibody that binds to CTLA-4, thus relieving the lymphocytes, which can drift across the body, detecting and destroying cancerous cells.

The success of Yervoy raised hopes that immunotherapy can work against cancer and sent out a widespread frenzy in the medical and pharmaceutical industry with a new drug out for trial, every couple of months. Although some worked, others did not. While there was plentiful research invested in uncovering new molecules that could fight cancer, some questions remained unanswered.

One, for instance, was how Yervoy, which binds to the inhibitory signal molecule CTLA-4, could be successful in silencing the action of CTLA-4, in spite of other molecules that also interact with CTLA-4. How does Yervoy differentiate CTLA-4 from other molecules that resemble CTLA-4 and bind only to CTLA-4? Scientists could not yet answer them.

Research in India finds answers

Dr Udupi Ramagopal, Associate Professor and structural biologist at Poornaprajna Institute of Scientific Research, Bangalore, has been working on the structural aspects of immune modulators for almost a decade now. In a recent study, Prof. Ramagopal together with a team of scientists from Albert Einstein College of Medicine (USA) and Bristol-Myers Squibb have analysed the interaction between Yervoy and CTLA-4 using X-Ray crystallography, providing crucial insights into the mechanism of action of Yervoy. The results of this study, published in the Proceedings of the National Academy of Sciences (PNAS), not only illustrates the molecular interaction between Yervoy and CTLA-4, but also allows the rational design of drugs that can be more effective.

"The thing with most cancer therapies is that even if you treat 99.999% of the disease,

one cell is good enough for the cancer to relapse. But with Immune Checkpoint Blockade Therapy, you are not working on the cancer cells. You are training the immunological armed forces by eliminating inhibitory signals. And so, you are creating an immunological memory that can fight the cancer", explains Prof. Ramagopal.

And what happens if there is a relapse?

"Post recovery, if the cancer does attempt to strike back, even at a different location in the body, the immune system is equipped to fight it. And that is why the ICBT is said to have changed the face of cancer therapy", he adds.

Although drugs such as Yervoy hold a lot of promise, there are a number of disadvantages. Firstly, it doesn't always work in all the patients that it has been administered to, and we still don't know why. Then, there is the issue of side effects. Since Yervoy inactivates CTLA-4 that serve as brakes controlling the lymphocytes, the lymphocytes are now free to attack without checks and balances, resulting in a number of side effects including stomach pain, bloating, constipation or diarrhoea, fever, breathing or urinating problems. In severe cases, it could lead to neurological complications like paralysis.

Another major drawback with immunotherapy drugs is its production techniques. Antibodies used in medicines like Yervoy are generated using animal systems, rather than from human systems. This might trigger secondary immunological reactions in the body. There is also the high cost associated with the research that translates to equally pricey drugs. Today, a course of immunotherapy with Yervoy costs a whopping ₹77 lakhs!

Prof. Ramagopal and his team members Ms. Swetha Lankipalli and Mr. Shankar Kundapura are currently engaged in pursuing a simpler, cost-effective alternative with a new class of drugs that can be designed using the basics of protein structural biology. Protein molecules – including inhibitors and their interaction partners are huge conglomerations of amino acids, just like a huge bunch of grapes with hundreds of grapes (amino acids) on it. When an inhibitor molecule interacts with any another molecule, not all the amino acids are involved in the interaction.

The strategy followed by Prof. Ramagopal and his team is simple – they determine the structure of inhibitory molecules and its interaction partners. Once they know which amino acids resides where and figure out which amino acids are involved in the interaction, they can effectively design molecules that can bind to the inhibitor. "This way, looking at the structures of the inhibitors and its partners, I know which region is responsible for their interaction. So, I know which amino acid(s) I need to tweak to design an efficient lead molecule against the inhibitor". More importantly, it is derived from our own molecule, so it may not elicit immune response, unlike that expected from most animal-developed antibodies, explains Prof. Ramagopal.

"And the best part is that this approach is way more economical", concludes Prof. Ramagopal enthusiastically, raising hopes for those battered by cancer.

ICUs in hospitals a haven for drug-resistant bacteria, finds study

By Paramananda Barman

A recent study by researchers at the University of Delhi, Vardhman Mahavir Medical College and Safdarjung Hospital, Delhi and the SMiLE Incubator, Sweden have found alarming cases of drug-resistant bacteria in patients admitted to intensive care units (ICUs). The study, published in the journal Antimicrobial Resistance & Infection Control, raises concerns around the safety of ICUs in hospitals, where most patients are already in critical condition.

Bacterial infections during an ICU stay is a significant blow to patients whose immunity are already compromised due to other health complications. The alarming rise in the strains of bacteria that are resistant to different antibiotics makes matters worse. As a result, patients are often recommended a prolonged stay in the hospital and heavy doses of antibiotics. This situation affects not only their health but also their finances as hospital stays are expensive. Hence, identifying these deadly bacteria can help to prevent fatal infections.

In the current study, the researchers studied the prevalence of the bacteria Escherichia coli (E. coli) in patients admitted to ICUs. Although most strains of E. coli are harmless, there are some nasty strains which cause complications like diarrhoea.

"It causes a wide array of disease and is responsible for around 17–37% of both community and hospital-acquired clinically significant bloodstream infections, and a major cause of mortality from these infections", say the researchers about the threat from pathogenic E. coli.

The researchers isolated E. coli strains from the blood of patients admitted to ICU and diagnosed with sepsis—a life-threatening complication of an infection. They also isolated these bacteria from faeces of patients without sepsis. Using molecular techniques, they then identified the different strains of E. coli and studied their response to various antibiotics, including cephalosporins, which are used to treat a wide range of bacterial infections.

The researchers found that a majority of the bacteria found in the patients belonged to two strains of E. coli that were known to cause diarrhoea. When these bacteria were treated with antibiotics, the results were alarming.

"Antibiotic susceptibility results showed that more than 70% of the faecal E. coli isolates and more than 90% of the blood isolates were resistant to all of the cephalosporins tested", report the authors.

They also add that these bacterial strains were mostly resistant to other classes of antibiotics as well.

But, how does E. coli become resistant to drugs? It is by the action of a group of enzymes called extended-spectrum β-lactamase, or ESBLs, which break down antibiotics like penicillin and cephalosporin, rendering them ineffective. The study found that 68% of blood and 44% of the faecal E. coli strains produced these enzymes. The study also found a very high prevalence of ST131, an extensively drug-resistant group of E. coli among the ICU patients.

The findings of the study highlight the grave threat to public health posed by drug-resistant bacteria, even in hospital environments which are otherwise considered safe and sterile.

"Increasing antimicrobial resistance among E.coli to commonly used cephalosporins hinders the decision of the optimal drug therapy for patients. Continuous surveillance and rational use of antibiotics along with effective hygienic measures are urgently needed in our setting", conclude the authors.

Wind turbines—causing more harm than good?

By Paramananda Barman

Hailed as 'clean' energy, wind energy is seen as an affordable solution to satiate the ever-growing global energy demands. However, a new study by researchers at the Indian Institute of Science (IISc), Bengaluru, claims that wind turbines, installed to harness renewable energy from the wind, are instead creating deleterious effects on predatory birds and their prey. The study, published in the journal Nature Ecology & Evolution, has described how anthropogenic disturbances act as apex predators and how they affect the ecosystem of the Western Ghats.

The study was conducted in the lateritic plateaus of the Western Ghats of India where wind turbines have been functioning for the last 16–20 years. The researchers studied the behaviour of predatory birds and their prey, the superb Fan-throated lizard (Sarada superba)—the most common lizard species in the region. They compared the activities of these birds and lizards in areas with and without wind turbines on the same plateau.

The researchers found that wind turbines leads to many deaths of birds and bats, and restrict their movements. "We found that both the abundance of predatory birds and the frequency of predation attempts (dive attacks) by raptors on ground-dwelling prey were almost four times lower in sites with wind turbines", say the authors about their findings.

The lack of predators has resulted in a rise in the number of lizards. The density of the superb Fan-throated lizards in sites with wind turbines was found to be three times higher than regions without those turbines. "By reducing the activity of predatory birds in the area, wind turbines effectively create a predation-free environment that causes a cascade of effects on a lower trophic level", explain the researchers on the effect of wind turbines on the food chain.

The researchers also point out the direct and indirect consequences of the killing of the predatory birds by the wind turbines. Apart from the increase in the lizard density, the changes in the predation pressure have caused a reduction in the amount of the stress hormone, corticosterone, in the lizards.

"Changing predation pressure can affect the local density of prey through direct consumption, but predation risk can also cause non-consumptive effects by altering the behaviour, physiology, and morphology of prey that survives", remark the authors.

Although the lizards in areas with wind turbines led a stress-free life, all was not well in the absence of their predators. One would expect the lizards to be healthy as they can now freely roam around collecting enough food without the fear of being eaten. However, the researchers found that the lizards were thinner in areas with wind turbines. The researchers explain that the increased density of the lizards, in the absence of their predators, could have lead to an enhanced competition for resources, resulting in the lizards being thin. The increased density also led to the reduction in sexual ornamentation or colouration in the male lizards, the study found.

The study emphasises the need for a thorough analysis of the consequences of such anthropogenic activities in ecologically sensitive areas. "Since the locations of wind farms are mainly determined based on economic rather than environmental considerations, we stress that the consequences of wind farms are greatly underestimated. There is thus a strong need for an ecosystem-wide view when aligning green-energy goals with environment protection", conclude the researchers.

Can classroom lighting conditions affect your child's learning?

By Purabi Deshpande

Learning in schools depends heavily on visual inputs. Without the writing on a blackboard, or more recently presentation slides, listening to a teacher talk for the better part of an hour can be a huge demand on a child's attention span. If the environment of the classroom, like the amount of light, is not sufficient, students are likely to strain their eyes. In a recent study, researchers from Sankara Nethralaya, Chennai, Shanmugha Arts, Science, Technology & Research Academy (SASTRA) University, Thanjavur and Elite School of Optometry, Chennai have studied how the environmental factors of a classroom affect a student's clarity of vision.

Children spend one-third of their day in school performing tasks like reading and writing which are heavily sight dependent. Environmental factors like light, sound, temperature, and age of school building have been known to affect the performance of students. Stressful environmental conditions, like less light in classrooms, can hamper a students ability to learn. Hence it is important to identify optimal conditions to aid classroom performance.

In an attempt to identify these optimal conditions, the researchers looked at eight schools in their study. They studied 29 classrooms; randomly selecting one class of each grade in each school. They observed the contrast of the chalk and board, the angle made between letters in lowercase on the board and how the students viewed them.

They also calculated the minimum distance for visual acuity or clarity based on the smallest letter size and longest viewing distance in a classroom. The researchers conducted experiments where students were allowed to read letters written on a blackboard at a certain light intensity and made to move closer to the board until the letters became clear. They gathered additional information through a questionnaire answered by the students on their perception of the classroom environment.

The study shows that 62% of the observed classrooms had poor lighting and calls for better classroom design to allow more light. Looking at the position of seating in a classroom, the study showed that the proportion of children under visual stress increased from 23% on the first desk to 56% on the middle desk and finally 73% at the last desks implying that the students on the desks at the back of the room had more strain on their eyes.

The researchers underline the need to ensure better seating arrangements in classrooms. In a case where seating arrangements cannot be improved the study shows that other factors like the contrast of the chalk colour on the board colour and size of letters could reduce the visual stress on students. They suggest auditing of the classroom environment and eye check-up of the students on a regular basis.

Welcome AJIT, a 'Made in India' Microprocessor

By Arati Halbe

Researchers at IIT Bombay develop the country's first indigenously designed and fabricated microprocessor.

India's electronics market is in its biggest boom ever. Fuelled by the demand for electronic devices, it is expected to reach a whopping $400 billion by 2020. Most of the electronic devices we use are imported; only a quarter of the devices are produced in the country. According to statistics, electronic goods in India account for more than 10% of total imports, second only to petroleum products! One electronic equipment that is almost always imported is the microprocessor—the 'brain' of an electronic device.

A microprocessor is an integrated circuit (IC) that contains a few millions of transistors (semiconductor-based electronic devices) fused on a semiconductor chip. It is just a few millimetres in dimension and is used in almost every electronic device—from the microwave and washing machine in homes to advanced supercomputers of a space station. However, developing and manufacturing a microprocessor is not easy—it is expensive,

risky and needs much skill. Hence, only a handful of companies across the world have been able to manufacture and sell microprocessors successfully.

In an attempt to make a mark in the highly competitive segment of microprocessor manufacturing, engineers from the Indian Institute of Technology Bombay (IIT Bombay) have developed a new microprocessor called AJIT—the first ever microprocessor to be conceptualised, designed, developed and manufactured in India. This innovation could not only reduce the country's imports but also make India self-reliant in electronics.

AJIT marks the first time in the country's history where the industry, academia and the government have come together. Prof. Madhav Desai and his team of about nine researchers from IIT Bombay have designed and developed the processor entirely at the institute. The project was funded by the Ministry of Electronics and Information Technology (MeitY) and IIT Bombay. Powai Labs, a Mumbai-based company, has also invested in the venture and will own, market and support the product. "I am thankful to Dr Debashish Dutta of MeitY for championing this project and to Reapan Tikoo of Powai Labs for supporting the project financially and as industry partner," says Prof Desai acknowledging the contributions of the partner institutions.

"We have been working on this processor design for more than two years now. The design has been tested on programmable semiconductor chips before we began our effort towards fabricating the processor," says Prof. Desai.

AJIT - Packed with features

Akin to most microprocessors available today, AJIT comes with an arithmetic logic unit that can do basic arithmetic and logical operations like addition, subtraction and comparison, and a memory management unit that stores and retrieves data from memory. There is also a floating point unit designed to handle calculations with non-integer numbers efficiently. For those who would like to program the microprocessor, there is a hardware debugger unit to help them monitor and control the processor.

AJIT's features can be compared to many of the microprocessors of its size available in today's market. Unlike the ones used in the desktops like the Intel's Xeon, AJIT is a medium-sized processor. It can be used inside a set-top box, as a control panel for automation systems, in a traffic light controller or even robotic systems. What's more, the researchers expect that AJIT will cost as less as ₹100 when it is produced en-masse! AJIT can run one instruction per clock cycle and can operate at clock speeds between 70-120MHz, comparable to its competitors in the market.

The researchers have made the software tools associated with AJIT freely available to everyone. The processor is also available as a 'softcore', where vendors can buy a license to use the design of the microprocessor and fabricate it to use it in their system. The researchers also offer to customise the processor for specific applications.

"The design of the processor is modular, and at some extra cost, vendors can get a processor design with a feature set suitable for the system they are designing", says Prof. Desai.

The 'Made-in-India' advantage

Prof Desai and his team of students---C. Arun, M. Sharath, Neha Karanjkar, Piyush Soni, Titto Anbadan, Ashfaque Ahmed, Aswin Jith, Ch. Kalyani, Nanditha Rao---used a tool set called AHIR-V2, that can convert an algorithm to hardware and which was developed completely at IIT Bombay to design the microprocessor circuit. Prof Desai mentioned that many fruitful discussions with his colleagues in IIT Bombay, Prof V. R. Sule, Prof M. Shojaei-Baghini and Prof M. Chandorkar helped the project and he acknowledged the contribution of H. Jattana, Pooja Dhanker and Shubham of Semiconductor Labs, Chandigarh towards fabrication of the processor.

In the first stage, AJIT has been manufactured in the government-owned Semiconductor Laboratory (SCL), Chandigarh, with a technology that offers the smallest building block of the size 180 nanometers. The researchers also plan to commercially manufacture the processor using more

advanced techniques that provide the smallest building block of size 65 nm or 45 nm, which is the current state of the art.

"Fabricating this using 180nm technology is the first step. Although this may not be the state of the art technology, it is enough for most of the targeted applications. Using advanced technology for large manufacturing quantities—tens of lakhs—would bring the cost per piece down", remarks Prof. Desai.

A processor made in India offers more than just the cost benefits. It provides the country with autonomy and self-reliance in the electronics sector and reduces our dependence on technology imported from other parts of the world. It also ensures a secure system with no opportunity for any backdoor entry, thus preventing digital sabotage by other countries or malicious organisations. So far, though we have had Indian teams design complete processors in India, no Indian company owns a commercially available microprocessor product. AJIT hopes to change that soon.

A home-grown processor is also likely to reduce the burden of imports. Manufacturers of electronics devices could benefit from the ready availability and competitive price of an Indian device with an added advantage of having the design and support team nearby. If an equipment manufacturer needs any modification or customisation, the design and support team would be accessible.

"Geographical proximity could easily make it possible to get something done in say two weeks time, instead of three months required otherwise", says Prof. Desai.

The challenges and the roadmap

The feat of building the indigenous microprocessor was not without challenges. Prof. Desai had only a small group very talented and passionate but inexperienced graduate students, and they worked on a shoestring budget to ensure a sound design before the processor was fabricated. "The challenge was to structure and partition the design in a way suitable to be implemented in this setup. To enable early testing, we created a computer-based model of the processor that could simulate the functionality of the processor in detail. This made testing the processor possible, much before it was fabricated," recalls Prof. Desai.

It's not done yet; there are tougher challenges ahead for the team to make the processor commercially viable to make this a grand success story. "For AJIT, we need to get more people to use it. Primary tests have indicated that the specifications of the processor match many in the competition and the new processor would also be cost-competitive. If the business community at large would own this processor, build systems around it so that users, as well as supporters, see value in this and can make money from the effort, then this effort can remain sustainable", says Prof. Desai.

The researchers hope that since AJIT compares well with other imported processors, it could see many early adopters. They also plan to introduce AJIT to the academia to expand its reach and provide graduating students a hands-on experience. "We could push the usage of this new microprocessor by introducing it as a part of the syllabus in engineering colleges. A well-designed single-board computer system could be made available at a low cost for students and other enthusiasts to experiment with", suggests Prof. Desai.

On the government's part, MeitY has extended its funding to enhance the processor and deploy it in government-initiated projects. SAMEER (Society for Applied Microwave Electronics Engineering & Research), an independent lab under MeitY, Government if India is planning to use AJIT in the receivers being developed for NAVIC or IRNNS (The Indian Regional Navigation Satellite System), an indigenous navigation system for the Indian subcontinent.

"We are hoping that people use AJIT and plan and build equipment using it. We are ready and prepared to support them. We have a seed, and we need people to grow it", signs off Prof. Desai.

Throwing light on dark matter

By Vimal Simha

All the matter that we see around us is ultimately made up of atoms, which in turn is made up of protons and neutrons. Surprisingly, such ordinary matter constitutes less than 15% of the total matter in the Universe. Most of the Universe is made up of dark matter - matter that does not emit any light but interacts with other objects only through gravity. Although we know dark matter exists, we do not know what exactly it is. Now, a study by researchers from Bengaluru has tried to understand the dark matter better.

Dark matter has never been directly observed or created in a lab. Its existence and properties are inferred from its gravitational effects on objects that we can see. In this study, published in the Journal of Cosmology and Astroparticle Physics, researchers from the Raman Research Institute (RRI), Indian Institute of Science (IISc), and the Indian Institute of Astrophysics (IIA), have examined what future experiments can reveal about the nature of dark matter.

"The first partial evidence for dark matter was seen long ago, in the 1930s. But the main evidence came in the 1970s. It was observed that galaxies are rotating too fast to be held together by the gravity of the visible matter alone. Hence the existence of additional invisible, dark matter was postulated. By the late 1980s, additional lines of evidence had emerged from observations of clusters of galaxies, and from even larger cosmological scales", says Prof. Shiv Sethi from RRI, who is also an author of the study, talking about our quest to understand dark matter.

Although the exact nature of dark matter is unknown, there are several different models of what the dark matter particle could be,

most of them motivated by different particle physics models. The most popular model is "cold dark matter", where cold refers to the velocity of the dark matter particles in the early Universe. If dark matter particles were 'hot', travelling at high speeds, they would rush from high density to low-density regions in the early Universe, thereby wiping out these density differences. In contrast, 'cold' dark matter, which moves slowly, would allow density differences in the early Universe to grow into galaxies. Since we can observe galaxies in the present Universe, hot dark matter model is now ruled out.

Scientists probe the nature of dark matter in several ways, including experiments that hope to detect dark matter particles directly. But in this study, the researchers focus on observations of the cosmic microwave background (CMB) -- relic radiation left over from the Big Bang.

"CMB is the most precise measurement in almost all of astrophysics. Moreover, the physics that goes into it is extremely clean. So when we want to look for something in an experiment, we want to manage these two aspects," explains Prof. Sethi.

The cosmic microwave background is nearly uniform, but there are small differences in temperature and density. The pattern of variations in temperature and density depends on what particles are present in the early Universe, and their properties. Hence each type of particle leaves behind a distinct signature in the spectrum of temperature and density fluctuations in the CMB.

In this study, the researchers calculate the effects of different dark matter particle models on the CMB spectrum.

"We have considered a whole range of models that exhaust nearly all possibilities that are still consistent with current experimental constraints," says Prof. Sethi.

The researchers have tried to answer the question -- 'If dark matter changes its nature below a certain scale, how well can we probe it with future experiments? What kind of constraints can we put on these models?'

The study finds that previous and current observations of the CMB are not sensitive enough to distinguish between these dark matter particle models. However, many experiments are being proposed in the next decade to observe the CMB, such as the space-based PIXIE (Primordial Inflation Explorer) mission by NASA and the ground-based CMB S-4 (Stage 4) experiment at the South Pole. Based on the expected sensitivity of PIXIE, the researchers expect these experiments to be able to distinguish between at least some of the dark matter particle models, thereby shedding light on the enduring mystery of what dark matter is.

New Spectrograph at Ladakh Reveals Composition of Ancient Stars

By Vimal Simha

Our body is principally made up of carbon and oxygen, while also containing small quantities of nearly 30 other elements. It might come as a surprise to learn that all the atoms that make up our body were once in stars! In fact, all of them, other than the lightest three (hydrogen, helium and lithium), were made by nuclear reactions in stars, and during many supernovae which are exploding stars. In a new collaborative study, scientists from the Indian Institute of Astrophysics (IIA), Bangalore, University of Notre Dame, USA and Universidad de La Laguna, Spain have attempted to trace out how these elements form by analysing the spectra of ancient stars to determine their chemical composition.

Astronomers study the chemical composition of stars by analysing the light originating from these stars. They examine the spectrum of light using a spectrograph—an instrument which splits light into its constituent colours or wavelengths. Each element produces a characteristic feature in this spectrum, as an increase or decrease in the light put out at a specific wavelength. The strength of each feature tells us how much of the element there is.

Previously, scientists believed that all stars have a similar chemical composition as the Sun. However, in the 1940s, astronomers were able to obtain spectra of a large number of stars and found that many of them had minimal quantities of metals compared to the Sun; metals in this context refers to all elements other than hydrogen and helium.

Since metals are created in stars and supernovae, the stars that formed the earliest have smaller quantities of metals compared to stars like the Sun that formed much later from gas that had already been processed by previous generations of stars. Hence, these metal-poor stars are a relic from the early Universe. Determination of their chemical

composition sheds light on how they were formed, the nature of the environment in the early Universe when they formed and various other related questions in the theory of galaxy formation.

In this study, published in the Astrophysical Journal, the researchers have used data from the Sloan Digital Sky Survey (SDSS) dataset, which contains data from 15 years of observations made by an automated telescope that scans the sky, to identify exciting candidates that could be metal-poor stars. They then took spectra using the High-Resolution Spectrograph (HESP) at the Indian Astronomical Observatory at Hanle in Ladakh.

"These are the first scientific results from HESP. We have undertaken a study of the most ancient population of stars in the Universe. This could lead us to the knowledge of the physical processes of the early Universe like the births, deaths and evolution of the first stars," explains Mr. Avrajit Bandyopadhyay, a doctoral student at IIA who is the lead author of the study.

The researchers analysed the spectra of two classes of stars—Carbon enhanced metal poor (CEMP) stars and extremely metal poor (EMP) stars. CEMP stars are low-metallicity stars that have a high carbon content for reasons that are not well understood. EMP stars, on the other hand, are thought to be the immediate successors of the very first stars in the Universe that formed when the Universe was only a few hundred million years old, a hundredth of its current age.

Surprisingly, the researchers found that these two types of stars have a strikingly similar chemical composition. However, the CEMP and EMP stars they observed have different levels of iron-peak elements—elements close to iron in the periodic table that are only produced during supernovae. This evidence allows the researchers to conclude that these two classes of stars must have different types of ancestors.

While this study sheds some light on the question of where the elements come from, many puzzles remain. Mr. Bandopadhyay's team intends to step up the effort to unravel them. "Nucleosynthesis (formation of elements) in the primordial and subsequent population of stars is also being investigated. We plan to do subsequent studies in the future with additional details," signs off Prof. Bandyopadhyay.

Decoding the pattern of winter rainfall over South Peninsular India

By Spoorthy Raman

The word monsoon may bring to mind the incessant downpours, the lush green surroundings and the sweet smell of earth. Did you know that India, and South Asia, has two monsoons during the year? Yes, the summer or southwest monsoon from June to September, and the winter or northeast monsoon from October to December. In a recent study, researchers from the Indian Institute of Technology Bhubaneswar have tried to understand the pattern of winter rainfall over the last century.

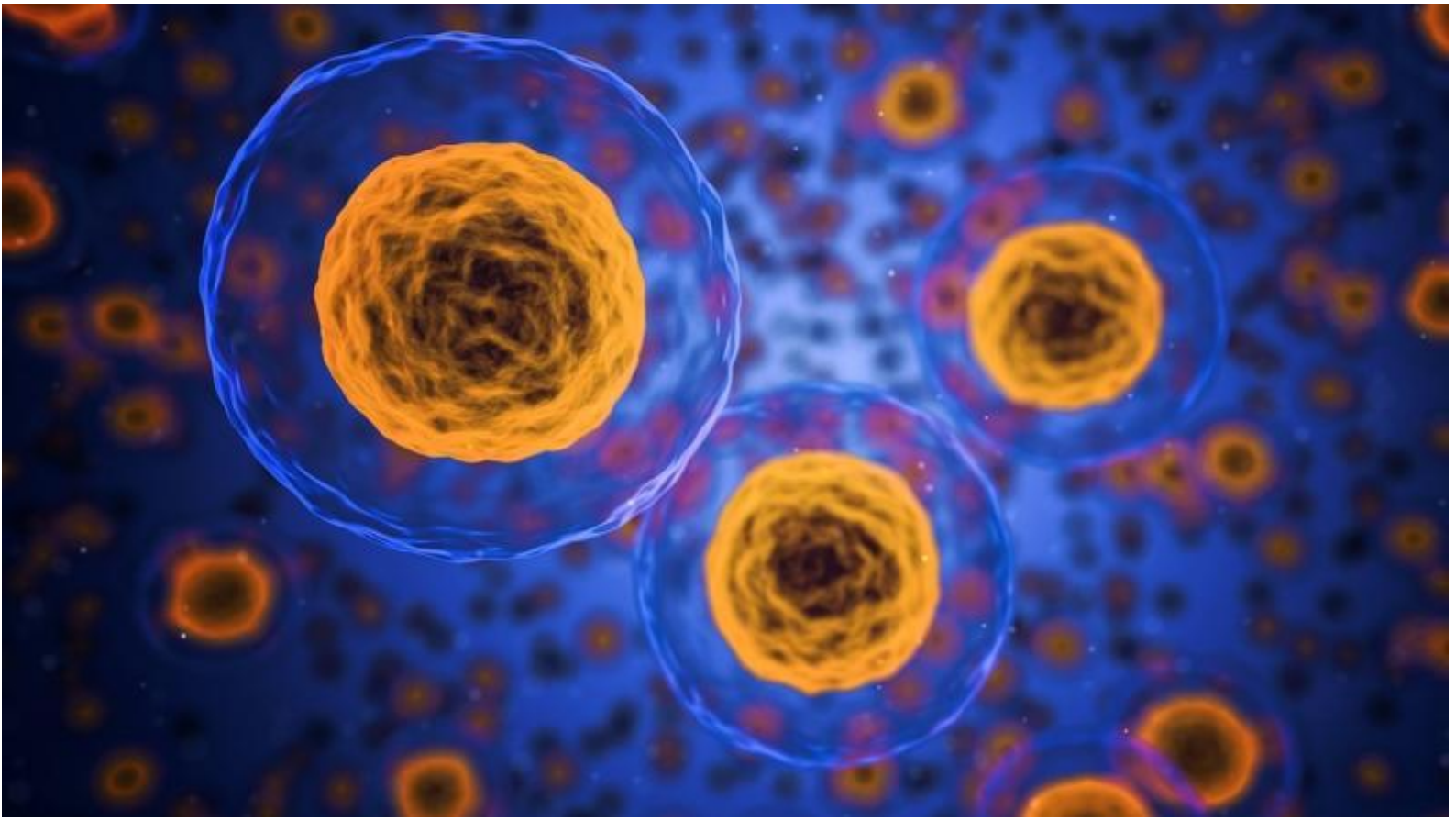
Although the summer monsoon contributes to a significant part of the rainfall received in India, the winter monsoon brings rain to many parts of South India and adds to about 11% of the total annual precipitation. Parts of coastal Andhra Pradesh, Rayalaseema, south interior Karnataka, coastal Karnataka, Tamil Nadu and Kerala receive about 30-60% of the annual rainfall during this time. These monsoon rains also regulate the agricultural production in these areas.

In this study, the researchers have tried to understand the winter rainfall pattern in these areas and how they are affected by global warming. The study, funded by the Department of Agriculture, Cooperation & Farmers Welfare (DAC&FW), was published in the journal Theoretical and Applied Climatology. The researchers studied various aspects of winter monsoon, like the changes in the rainfall amounts in the region, also called variability of rainfall, and the changes in the local climate, in the southern parts of Peninsular India. They used data of 116 years, from 1901–2016, about the winter monsoon obtained from India Meteorological Department.

The researchers found that the variability of rainfall during the northeast monsoon has increased in the period between 1959–2016. They also observed that the seasonal rainfall has increased over Tamil Nadu, Rayalaseema, as well as south peninsular India because of an increase in the number of high-intensity rainfall events in the recent period compared to that between 1901–1958. However, in the other parts of south peninsular India, the seasonal rainfall has decreased. The study also found that the relationships between the winter monsoon and other climatic phenomena like the El-Niño Southern Oscillations (ENSO), the Indian Ocean Dipole or Indian Niño, and the summer monsoon have weakened in the recent decades after 1988.

The findings of the study could help design strategies for managing the odds associated with the winter monsoon rainfall, say the researchers.

"This study is very useful in determining the effects on various sectors due to the variability of heavy rainfall events over south peninsular India during this season and assists the risk management sectors in adapting advanced technologies for a sustainable future in the present global warming era", they conclude.



It's not love, but the tension in your cells that governs life

By Nagashree Avabhrath

When we talk of force, most of us go back to our physics lessons and think of gravitational force or electromagnetic force. However, there is one vital force that holds life together—the force in our cells! If you are wondering what that is, let's start with understanding the cell. Our body is made up of trillions of tiny little units called cells that come in many shapes and sizes and perform a myriad of functions. They come together to form structures like tissues, and interact with one another through their cell membranes—the outer boundary of the cell. Anything that needs to go in or out of the cell needs to knock on this membrane.

Substances that cannot pass through the cell membrane get into the cell through a process called endocytosis. The cell membrane invaginates or bends inside, and forms a vesicle or a bag like structure enclosing the entering substance. In another process called exocytosis, those that are inside the cell are transported outside by a similar mechanism.

"Imagine each time you enter a room, you take in the door and a portion of the wall with you. If the membrane is not carefully put back each time through exocytosis, the cell will shrink or enlarge", says Joseph Jose Thottacherry, a graduate student with Dr. Satyajit Mayor at National Centre for Biological Sciences (NCBS), Bengaluru, who has been working on understanding different cellular mechanics since the last five years.

In a recent study, Mr Thottacherry, along with his collaborators from other Indian and Spanish institutes, has tried to understand how cells maintain their shapes in spite of expelling material from their membrane. Published in the journal Nature Communications, the study was partly supported by fellowships from the Council for Scientific and Industrial Research, Department of Science and Technology, and the Wellcome Trust-DBT India Alliance.

The study found that the answer to what makes the cell stay stable lies in a force called membrane tension. "We found that endo-exocytic processes are intimately connected to membrane tension", reveals Thottacherry. The researchers have also identified a particular pathway, called the CLIC/GEEC pathway that can quickly sense and respond to changes in the membrane tension. Increased membrane tension decreases the endocytic pathways, making it difficult for substances to enter into the cell while reducing the membrane tension causes an increase in endocytosis.

The researchers used a 'cell stretcher'—a silicon-based circular membrane—and attached cells to this. Akin to how a pattern on the balloon expands when you blow it, the cells on the membrane also stretch when the membrane stretches, thus altering the membrane tension of the cells.

"This silicon membrane is divided into two concentric circles and cells are added to the inner circle. To stretch it, we apply precisely calibrated vacuum to the outer concentric circle, sucking the membrane in and thus causing the membrane in the inner circle to stretch", explains Mr Thottacherry.

The researchers then tested the process of endocytosis by using fluorescent material and measuring how much the cells would take in for a given amount of time. The fluorescent material helped them image the cells and understand how endocytosis changes with the tension of a cell. They then used a laser-based 'optical tweezer' to hold a bead and pull a thin membrane from the cell. "If the cell applies a higher force, it will pull the bead closer to it. If the force is less, the bead will move less", says Thottacherry, detailing the experiment.

The researchers also identified a critical molecule called vinculin that helps to translate the physics in the membrane tension to a biochemical process in the cell to facilitate movement of particles. "Vinculin remains closed under low forces while on higher forces, it changes its conformation and opens up like a hairpin that is being pried open under force", says Thottacherry. When vinculin opens up, it inhibits the CLIC/GEEC pathway, thus regulating the response to membrane tension and maintaining homeostasis—a steady state inside the cell.

What now appears as a solved problem had its challenges during the making. From building the necessary equipment, like the cell stretcher and the optical tweezer, to learning to use them, the researchers fought all odds. "I think the biggest challenge was setting this up here since many other components were needed for day to day working of this. We had to figure out ways and modify protocols to fit with the equipment we had here", recalls Thottacherry. In the end, collaborating with Raman Research Institute, Bengaluru, paid off their efforts.

The findings of the study reveal how every moment, our cells are continually measuring and responding to changes in the force within them, to sustain what we call as life. As a next step, the researchers are trying to determine the importance of the relationship between membrane tension and the processes of endocytosis and exocytosis, which could play a role in cell migration during metastasis, or the entry of viruses into the cell.

"This study shows the importance of understanding forces in regulating these processes and thus would be important for fighting them effectively," remarks Thottacherry.

Now you know when General Dodonna of Star Wars says, "May the Force be with you", he means it literally.

The Yin and Yang of ecology and evolution

By Annie Megan Santamaria

The lifecycle of organisms, from birth to death, revolves around two things—reproduction and the struggle to survive. It has to beat all odds, including outsmarting predators, for survival and propagation. Through the process of evolution, most organisms seem to have perfected this art. An incredible example is the caterpillar of the swallowtail butterflies, which changes its appearance and colour at various stages of its elaborate life cycle, to escape predators. But, how exactly do they do this? A new study by researchers at the National Centre for Biological Sciences (NCBS), Bengaluru, answers some of these questions. This study was published in the journal Ecology and Evolution.

Swallowtail butterflies are large, colourful butterflies belonging to the family Papilionidae. They are found on every continent except Antarctica and are famous for their dazzling colours and prominent tails on their hindwings. Because of their global distribution, the caterpillars use a wide variety of plants as food, in different habitats. The current study retraces the evolutionary history of these butterflies to understand how their interactions with plants and predators have led to the evolution of colour change through various developmental stages. These changes are also called ontogenic colour changes. Swallowtail butterflies are used as classic models to understand insect colouration since the time of Alfred Russel Wallace, who conceptualised natural selection.

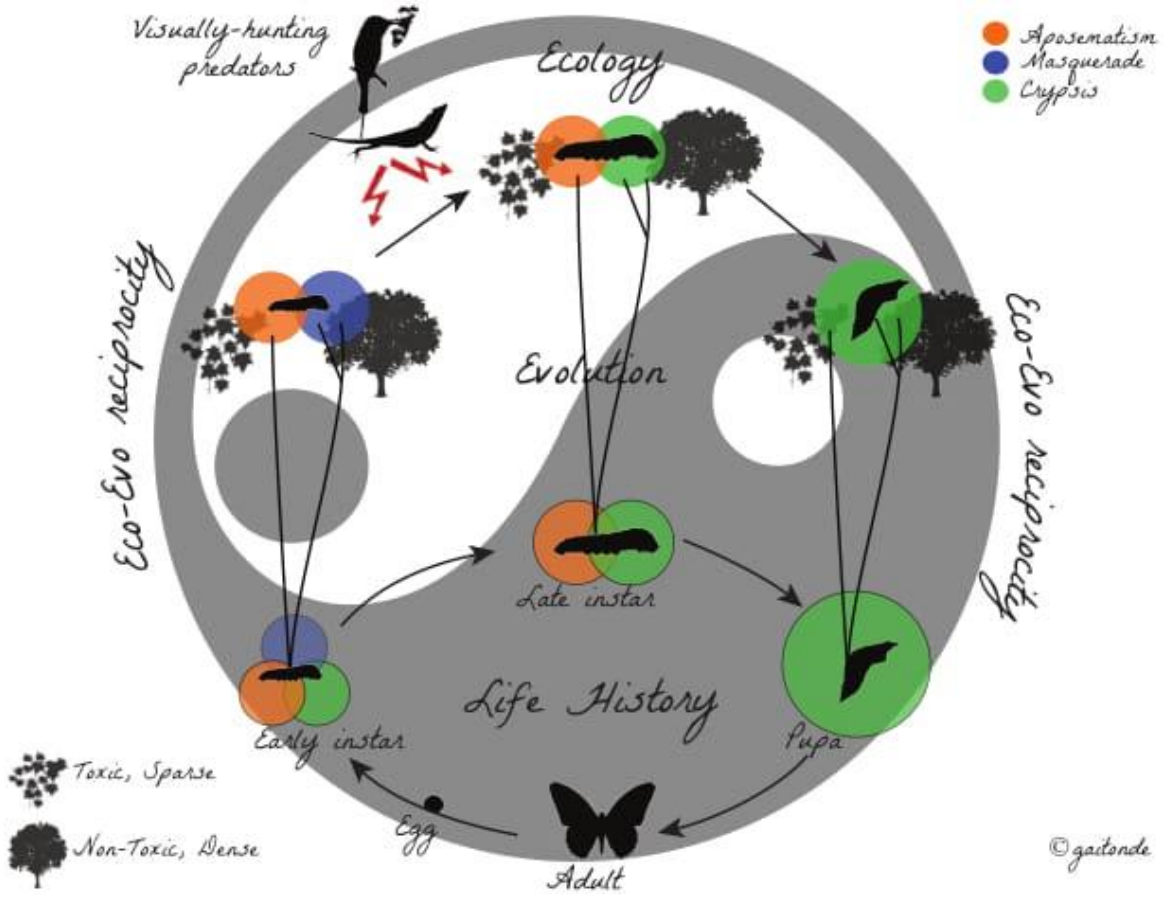
The study shows that the ontogenic colour change depends on the complex interaction between the size and the level of motion associated with the different life stages of the

caterpillar, the characteristics of its host plants, and its ancestry. The researchers quantitatively classified the various colours of the caterpillars into three types of colour defence strategies—aposematism, crypsis and masquerade. A wide variety of organisms use these strategies to escape from predators.

The researchers observed that swallowtail caterpillars at specific life stages opt for the most effective strategy depending on the risks they face and the resources the host plant provides. For instance, caterpillars feeding on toxic plants store these toxins in their bodies and use bright colours and striking patterns to advertise that they are unpalatable. Their predators, like reptiles, birds and small mammals, thus through trial and error, learn to avoid eating them.

If the host plants, on the other hand, are devoid of toxins, the caterpillars opt to resemble some inedible or aversive object, like bird droppings, when they are small in size. This technique is called masquerade. However, when they grow big and have to move more frequently to feed or to become a pupa, they switch to crypsis, where they blend in with their background. When these caterpillars become pupae, they all turn cryptic as a majority of predators detect prey using motion, and hence become less vulnerable.

"This is a very interesting study as it provides a rare example from the natural world of how the evolution of alternative variants of certain traits is driven by ecology", says Prof. Amitabh Joshi, a renowned evolutionary biologist and a Professor at the Jawaharlal Nehru Centre for Advanced Scientific Research (JNCASR), Bengaluru. "Given that adaptive evolution is a historical process, it is always of interest to tease apart the relative role of ancestry, as a constraint to adaptive evolution, and ongoing selection imposed by



The reciprocal relationship between Ecology and Evolution

ecological challenges such as predation or competition, in shaping the adaptations shown by different species or populations", he adds.

The researchers of the study analysed many pictures of different developmental stages of the swallowtail and quantified their colours. This data was then used to retrace the evolutionary history of colour defences using an evolutionary tree of these butterflies to unravel why the colours change through the lifecycle. This analysis revealed some interesting outcomes; it linked the form and colour and of the caterpillars to their host plant, connecting behavioural and sensory ecology with life history theory.

The study found that the appearance of caterpillars was shaped primarily by their development, their predators and the host plants. The plants try to avoid being eaten up by the caterpillars and other herbivores; the caterpillars aim to grow fast and survive to adulthood; and the predators are always on the lookout for a juicy worm. The researchers found that the swallowtail lineages that stuck to their ancestral host plants, which are toxic and sparsely vegetated, had striking warning colouration. Those that frequently shifted host plants, used hues depending on the characteristics of the new host. Flashy warning colours were seen in caterpillars that fed on toxic sparsely vegetated plants, while those that ate non-toxic, densely-vegetated plants used camouflage to hide on their host plant and escape from predators.

This evolution of protective colouration in swallowtails elegantly illustrates the reciprocal yin yang-like relationship between ecology and evolution. Here, the evolutionary shifts from one family of host plants onto another altered the ecology of the swallowtail caterpillars, which then influenced the evolutionary trajectory of their colour defences. "Although several factors influencing animal colouration such as visual backgrounds, chemical nature of their diet, and lifestage vulnerability were individually identified, their interaction effects on the evolution of ontogenic shifts in colouration, which a wide variety of organisms exhibit, was largely missing. The study attempted to fill in those gaps", explains Nikhil Gaitonde, a researcher at NCBS and the lead author of the study.

"Such detailed support for the overriding effect of ecology compared to ancestry has rarely been reported for a natural system", remarks Prof. Joshi adding that the study is an excellent example of the power of the classic 'comparative method' in evolution, which is the principal way of deciding whether some trait variant is an adaptation in a set of naturally occurring species.

"Experimental evolution in the lab can help one explore with exemplary rigour what "can" evolve, but only studies on natural populations of related species, like this study, can address the question of what "did" evolve as an adaptation to a specific ecological challenge", he adds.

This study is also the first of its kind to quantify colour in caterpillars of a globally distributed family of butterflies. "In a tropical and biodiverse country like India, there are several excellent natural systems capable of providing novel insights in ecology and evolution using natural history observations and simple but well-designed experiments. But curiosity and a passion for the natural world is utmost necessary", points out Gaitonde.

The authors stress that citizen science initiatives, like iNaturalist and ifoundbutterflies that curates valuable natural history information through pictures contributed by ordinary citizens, are treasure troves of biodiversity knowledge and played a vital role in this research.

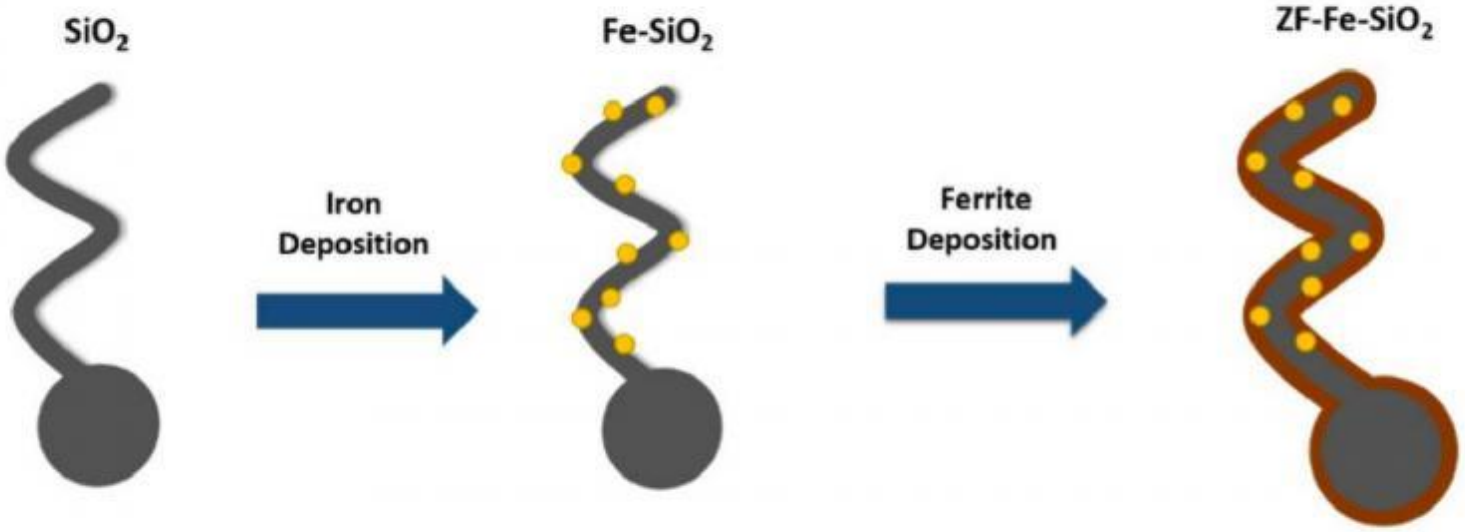


Photo :Pooyath Lekshmy Venugopalan, Shilpee Jain, Srinivasrao Shivashankar and Ambarish Ghosh, Single coating of zinc ferrite renders magnetic nanomotors therapeutic and stable against agglomeration, Nanoscale, 10.1039/C7NR08291F, 2018

IISc Researchers design multifunctional nanomotors to fight cancer

By Farida Kothari

Researchers from the Indian Institute of Science (IISc), Bengaluru, have demonstrated the integration of therapeutic modalities to "magnetic nanomotors", which may be of significance in cancer therapy.

Advances in the field of nanotechnology – the science that deals with structures whose sizes are a few nanometers (a billionth of a meter) – have proliferated into many areas of science, including biology and medicine. Scientists across the world are looking at ways in which these tiny systems can help improve disease diagnosis, detection and drug delivery. In an interdisciplinary study, researchers from the Indian Institute of Science (IISc), Bengaluru, have demonstrated the integration of therapeutic modalities to "magnetic nanomotors", which may be of significance in cancer therapy.

Nanomotors are nanosystems capable of motion through an external force; magnetic field in the case of magnetic nanomotors. They have the potential to be steered and localized within the human body.

"There is tremendous current interest to use nanomotors for targeted therapeutics and the present work is a major step in this direction", says Prof. Ambarish Ghosh, from Centre for Nano Science and Engineering, IISc, who spearheaded this study.

Recent studies have explored the possibilities of using magnetic nanomotors for various biomedical applications because they can be maneuvered inside the body remotely, and also because these motors need no chemicals to move. In a previous study, Prof. Ghosh, Dr. Lekshmy, and their group had reported the first successful voyage of these magnetic nanomotors in human blood. In general, the magnetic nanomotors tend to form agglomerates due to magnetic attraction, which severely limits their applications. In the present study, researchers have circumvented this problem by providing a ferrite layer on the magnetic nanomotors, which renders these nanomotors stable against agglomeration, making it possible to store them in a suspension for more than six months.

But how do these nanomotors kill cancerous tumours? It is through a phenomenon called 'magnetic hyperthermia' where application of high frequency magnetic fields increases the temperature of the nanomotor, which could kill cancer cells.

"This is the first demonstration of integration of hyperthermia potential to nanomotors," explains Dr. Pooyath Lekshmy Venugopalan, a research associate in Prof. Ghosh's lab, who led the experiments.

The hyperthermia potential of the zinc ferrite coated nanomotors was demonstrated on cervical cancer cells – HeLa cells. The nanomotors showed an increase in temperature over time when subjected to high frequency alternating magnetic fields. This rate of increase was greater for higher magnetic field strengths.

"The observed rise was enough to reach cell death temperatures, of around 43^{0}C, within 20 minutes," says Venugopalan, adding "this means that the heat generated was enough to cause cell death in cancer cells."

These magnetic nanomotors are helical in structure and are made of silica (SiO_2). Over the helical structure, a layer of magnetic material (here, iron) is deposited. This makes the nanomotors magnetic in nature. These iron-coated helical structures are then coated with a 150 nanometer thick layer of zinc ferrite.

The application of a single ferrite coating allows researchers to achieve a dense, stable suspension of magnetic nanomotors, which would otherwise agglomerate and become unusable. It also provides a therapeutic potential to these nanomotors. "The two functionalities are interrelated since for higher therapeutic value, a denser suspension is necessary," explains Prof. Ghosh.

This interesting research demonstrates a single step method to fabricate magnetic nanomotors in a scalable manner that are highly stable and also provide therapeutic potential via magnetic hyperthermia which could have implications in cancer therapeutics. The researchers are now working towards improving the heating efficiency of these nanomotors, as well as methods to attach drugs to these nanomotors to carry out in vivo experiments. Their experiments are being carried out in close collaboration with biologists and doctors.

How knowing helps in searching

By Mira Murali

We search for things all the time often with highly variable demands. For instance, at the supermarket snacks aisle you might look for a particular brand of chocolate, any chocolate or a different-looking chocolate. How does knowing what to look for help in finding it? A study by researchers at the Indian Institute of Science (IISc), Bangalore has now revealed a novel insight into how knowing helps you in searching.

To perform this study, Prof. S. P. Arun and his student Sricharan Sunder at the Centre for Neuroscience at IISc devised a task where human volunteers had to find an odd item among a field of identical other distractors. They compared two conditions: trials in which the subjects saw a preview of the odd item before seeing the full field of items, with ones where they saw an unrelated white square. As expected from previous studies, subjects were able to find the odd item faster if they knew what to look for, and they benefited more if this was a hard search to begin with. All this suggested that somehow knowing benefits hard searches more than easy searches, which seemed paradoxical, since this meant the brain needed to know in advance which search was easy or hard.

But on carefully analyzing a variety of searches, Arun & Sricharan discovered something unexpectedly far simpler.

If the same data was taken in terms of the reciprocal of the time taken to find the odd item, hard and easy searches were benefited to the same extent. In other words, knowing what to look for makes searching easier, but this benefit accumulates for a longer time in a hard search.

"This brings a new perspective to how people have been thinking about previewing in visual search. We have shown, contrary to earlier research, that the benefit because of preview is a fixed constant irrespective of search difficulty", adds Sricharan while talking about the research.

"An interesting experiment that we conducted was to look at whether previewing the distractor actually benefited the search and to our surprise it did albeit only weakly! This led to an insight that even knowing what's irrelevant helps you search" says Sricharan.

"This study demonstrates a simple and elegant insight about how knowing what to look for benefits visual search. It has been gratifying to see such a simple insight hold up to detailed scrutiny", says Prof Arun who wants to push this finding more to gain better insights into how knowledge influences how we act and perceive.

Glimpses from Indian Research

2018-19

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Gubbi Labs is a private research collective with strong foundations in research and the underpinnings of a social enterprise. About five years ago, at Gubbi Labs, a division was carved out, called Research Media Services, with the aim of bridging the gap between research institutes and the general public, from whose money science is funded. The larger goal is to raise the bar of scientific literacy across the country.

For academic research to reach the public, the availability of up to date information about the latest research is critical. Busy journalists looking for science-based stories, students looking for prospective research groups, even an interested layperson browsing the web, all gain from clear summaries of current research. In 2014, in association with the Indian Institute of Science (IISc) we set up a Science Media Center at IISc. By 2016, as we expanded covering research from other leading institutions in the country, we now put all our content under '*Research Matters*'. Research Matters is now our one-stop destination for all content forms: Feature Articles, Deep-dives, News, SciQs, Podcasts, and Sci-toons.

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