Daily News Juice 13th Oct, 2024

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1. India's Absence from Letter Supporting UN Secretary-General

Introduction

India was notably absent from a letter signed by 104 countries, including many from Europe, Africa, and the Global South. The letter condemned Israel for banning United Nations Secretary-General António Guterres from entering Israeli territory. The ban came after Israeli officials criticized Guterres for not strongly condemning Iranian missile strikes on Israel.

India's Consistent Position on Israel

India has abstained from several UN resolutions that are critical of Israel in recent years. However, not signing this letter is seen as more significant because it was viewed as a defense of the UN Secretary-General and the United Nations as a whole, rather than supporting one side of the Israeli-Palestinian conflict.

International Response

Most countries from South Asia, West Asia, South America, and Africa signed the letter. The signatories expressed "deep concern and condemnation" of Israel's decision to declare Guterres persona non grata (PNG). The letter emphasized that such actions undermine the UN's ability to mediate conflicts and provide humanitarian aid.

Israel's Stance

Israel issued the PNG order against Guterres on October 2. Israeli Foreign Minister Israel Katz said that Guterres did not deserve to visit Israel because he failed to strongly condemn Iranian missile strikes on Israel. Although Guterres had commented on the strikes before and after the ban, Israel accused him of not being firm enough in his criticism.

No Official Comment from India

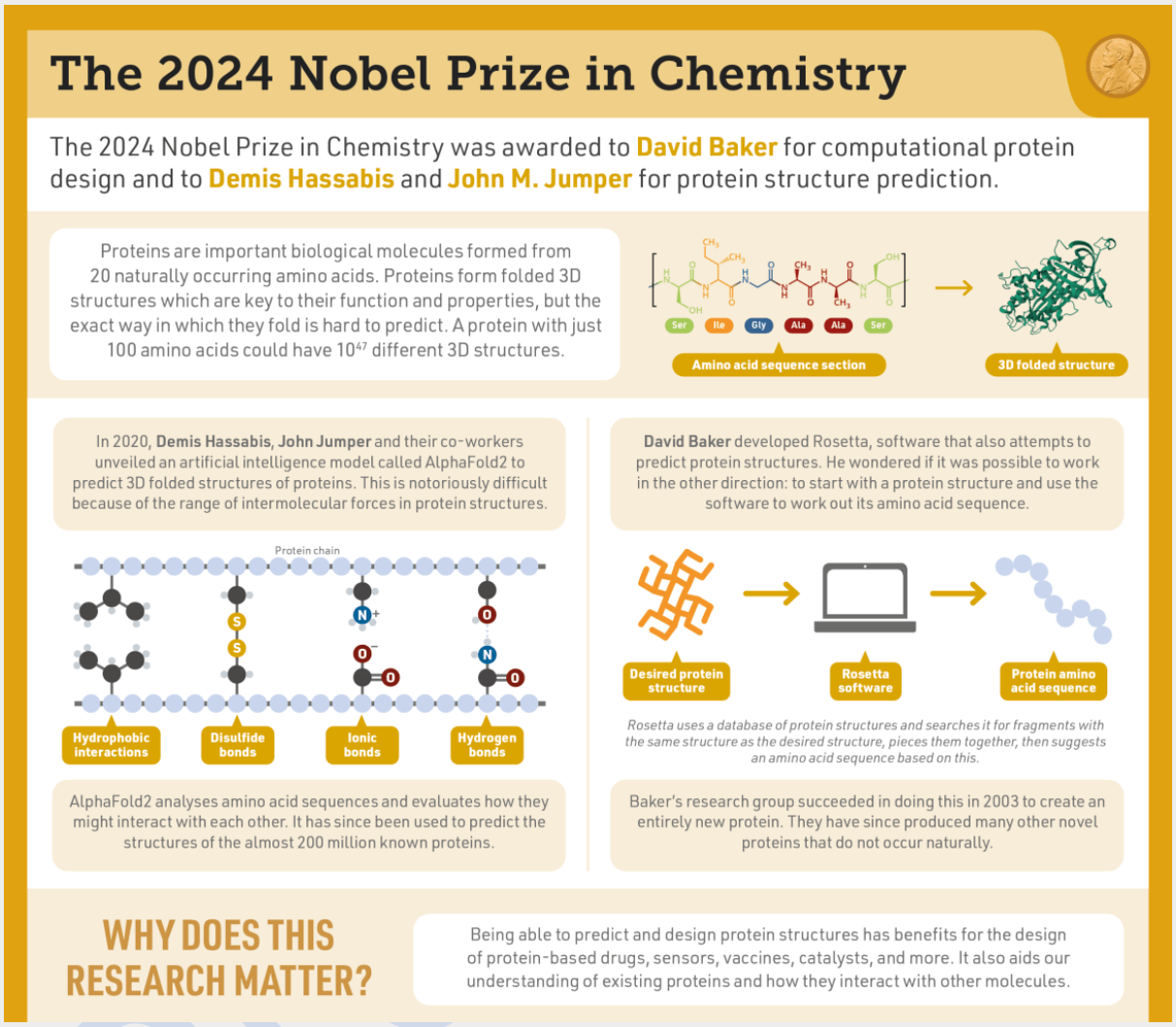
India's Ministry of External Affairs (MEA) has not provided a reason for why the country chose not to sign the letter, maintaining its silence on the issue.

Relevance: GS Prelims & Mains Paper II; International Issues
Source: The Hindu

2. How will tech reshape protein studies? Why is the work of the chemistry laureates, David Baker, Demis Hassabis, and John Jumper, significant?

Introduction

The 2024 Nobel Prize for Chemistry was jointly awarded to David Baker for his work on computational protein design and to Demis Hassabis and John Jumper for developing technologies to predict the structure of proteins.



Why are proteins important?
The chemistry prize concerns two areas in the field of protein research: design and structure.

All life (as is known) requires proteins and all proteins are made of amino acids. While there are many types of amino acids in nature, only 20 of them in different combinations make up all the proteins in the human body and in most life forms. Amino acids are found in tissues that provide structural support; they are catalysts in biochemical reactions; move molecules across biological membranes; control muscle contraction that lets us move around and have our hearts beat; and help cells communicate to perform their tasks.

What is the protein-folding problem?
A protein has many identities and one of them depends on the arrangement of its amino acids in the three dimensions of space — in other words, its 3D structure. In 1962, University of Cambridge researchers John Kendrew and Max Perutz won the Chemistry Nobel Prize for

elucidating the first 3D models of hemoglobin and myoglobin, both proteins, using X-ray crystallography.

One breakthrough arrived in 1969 when scientists found that a protein does not try to bend into different shapes. It somehow knows the shape it needs to have and rapidly folds itself to acquire it. The mysterious nature of this 'knowledge' of the protein is called the protein-folding problem.

By the late 2010s, scientists had worked out the structures of around 1.7 lakh proteins — a large number yet still small compared to the roughly 200 million proteins in nature. This situation changed drastically around 2018.

What is AlphaFold?

Hassabis co-founded DeepMind in 2010 which Google acquired in 2014. Here, Hassabis and his colleagues unveiled AlphaFold in 2018. AlphaFold is a deep-learning model to predict the structures of almost all proteins. DeepMind launched its successor AlphaFold 2 in 2020, when it was able to predict the structure of proteins with an accuracy comparable to that of X-ray crystallography.

Jumper led the work on AlphaFold 3, which can predict the structures of various proteins and how two proteins and/or a protein and another molecule might interact. These models are capable of deducing the 3D shapes of most proteins in a matter of hours. However, they have not been able to say why a protein prefers a particular structure. Scientists have thus said it can help them test their hypotheses; making sense of them is still the task of humans.

As Derek Lowe, a pharmaceutical researcher and author of a column in Science, put it to The Hindu in June 2024, "If the protein folding problem was set to us by God to teach us how to learn molecular interactions from first principles, we cheated."

What is protein design?

Baker developed tools scientists use to design new proteins with specific shapes and functions. His first notable work was in 2003 when he led a team to create a novel protein and determined its structure using a bespoke computer program they had developed in 1999 called 'Rosetta'. The researchers compared Rosetta's output with that obtained from X-ray crystallography studies and found them remarkably similar.

According to the Nobel Committee for Chemistry, "Rosetta was designed to be a general program both for protein structure prediction and design, and it has continuously been developed since its inception, with a large cadre of users and co-developers."

The ability to design proteins has far-reaching implications. For example, in 2022, Baker's team developed an antiviral nasal spray to treat COVID-19. At its heart were proteins the team designed using computational methods in the laboratory to stick to vulnerable sites on the viral surface and target the spike protein.

Teams involving Baker have also designed new enzymes to support organic chemistry reactions of commercial value, including the aldol reaction (used to make atorvastatin) and the

Diers-Alder reaction (to make vitamin B6). Recently, scientists have been exploring novel protein designs for use as biosensors to monitor, say, blood glucose levels in people with diabetes.

Relevance: GS Prelims & Mains Paper III; Science & Technology
Source: The Hindu

3. Why is microRNA discovery a big leap?

Introduction

The Nobel Committee announced on October 7 that the Nobel Prize for Medicine or Physiology would be shared by Victor Ambros and Gary Ruvkun "for the discovery of microRNA and its role in post-transcriptional gene regulation," thereby unlocking a secret on how different types of cells develop.

What is microRNA?

The human body is probably the most complex puzzle that humans are still trying to make sense of. Every time there is a better understanding and a piece slides into place with a resounding click, then it is an occasion for celebration. For a Nobel Prize too perhaps. This year's awardees of the Nobel Prize for Medicine — Ambros and Ruvkun — did slide in a couple of pieces into the right slots in the massive puzzle that suddenly opened our eyes to understanding how different cell types develop.

Consider this: Every cell in the body contains the same chromosome, so every cell contains exactly the same set of genes and presumably, the same instructions. But different cell types have different, unique characteristics. It confounded the imagination until Ambros and Ruvkun came along. Their discovery offered a plausible explanation for the conundrum. The piece of the puzzle was called microRNA, a new class of tiny RNA molecules that play a crucial role in gene regulation. As the Nobel announcement statement said, their groundbreaking discovery revealed a completely new principle of gene regulation essential for multicellular organisms, including humans.

It is now known that the human genome codes for over one thousand microRNAs. Genetic information flows from DNA to messenger RNA (mRNA), via a process called transcription, and then on to the cell for production of protein. There, mRNAs are translated so that proteins are made according to the genetic instructions stored in DNA.

The key is in the precise regulation of gene activity so that only the correct set of genes is active in each specific cell type. Additionally, gene activity must be continually fine-tuned to adapt cellular functions to changing conditions in our bodies and environment. If gene regulation goes awry, it can lead to serious diseases. Therefore, understanding the regulation of gene activity has been an important goal for many decades.

What is the work that led to the Nobel prize?

Ambros and Ruvkun, both American biologists, were together in their post-doctoral period at the H. Robert Horvitz lab in the 1980s, and their interest in cell development probably had its spark there. "It was the moment," Ruvkun said later, "when recombinant DNA was just starting to take off and it was obvious that it was a revolution and I wanted to be part of that." As they say, great achievements have humble beginnings, and this duo started appropriately enough with a humble 1 mm long roundworm. This creature was not an odd choice though: it possessed many specialised types of cells, such as nerve and muscle cells, making it a convenient model to study a complex genetic regulation process across species, one that was conserved throughout evolution.

After that, both scientists branched off on their own, though they remained focused on the same theme, obsessively, as great scientists are wont to, but exchanging data with each other, a task assigned great value in the modern scientific world.

The study of mutant strains that disrupt cellular processes offers great insights into gene function, and Ambros and Ruvkun took this path. They studied two mutant strains of worms, lin-4, and lin-14, that displayed defects in the timing of activation of genetic programmes during development.

After his post-doctoral research, Ambros analysed the lin-4 mutant in his laboratory. He managed to clone the gene which revealed that the lin-4 gene produced an unusually short RNA molecule that lacked a code for protein production. This suggested that the small RNA from lin-4 was responsible for inhibiting lin-14.

Concurrently, Ruvkun investigated the regulation of the lin-14 gene at Massachusetts General Hospital and Harvard Medical School. Ruvkun showed that the inhibition occurred at a later stage in the process of gene expression, through the shutdown of protein production. Experiments also revealed a segment in lin-14 mRNA necessary for its inhibition by lin-4. There were therefore complementary sequences in lin-4 and lin-14 mRNA, and the former binds to such sequences in the latter, blocking protein production in lin-14.

The two laureates compared their findings, which resulted in a breakthrough discovery. A new principle of gene regulation, mediated by a previously unknown type of RNA, microRNA, had been discovered. The results were published in 1993 in two articles in the journal Cell. Incidentally, Ambros' wife Rosalind Lee was his colleague and the first author of the Cell paper cited by the Nobel Committee. As Iorio and Croce wrote in their paper Causes and consequences of microRNA dysregulation, in the Cancer Journal, "microRNAs represent indeed an entire novel level of gene regulation that forced scientists to revise and somehow reorganise their view of the molecular biology."

While these results were met with initial silence from the scientific community, perception changed and euphoria took over, after Ruvkun's research group published their discovery of another microRNA encoded by the let-7 gene, seven years later. This gene was highly conserved and present throughout the animal kingdom, unlike lin-4. Over the following years, different microRNAs were identified. As a result of this work, researchers are today aware of the presence of more than 1,000 genes for different microRNAs and that gene regulation for microRNA is present in all multicellular organisms.

What are the applications for the future?

As Iorio and Croce list, since the first discovery, there have been remarkable advances in the understanding of microRNA biology. These include the identification of hundreds of microRNA genes; the dissection of microRNA biogenesis pathways; the identification of numerous microRNA targets and the establishment of principles of target regulation; and more importantly, there have been vigorous studies of their biological functions in physiological and pathological conditions.

Researchers found that a single microRNA can regulate the expression of many different genes, and conversely, a single gene can be regulated by multiple microRNAs, thereby coordinating and fine-tuning entire networks of genes. Extensive research has also yielded knowledge that cells and tissues do not develop normally without microRNAs. Abnormal regulation by microRNA can contribute to cancer, and mutations in genes coding for microRNAs have been found in humans, causing conditions such as congenital hearing loss, eye and skeletal disorders. Mutations in one of the proteins required for microRNA production result in the DICER1 syndrome, a rare but severe syndrome linked to cancer in various organs and tissues.

Relevance: GS Prelims & Mains Paper III; Science & Technology
Source: Indian Express

4. How are the physics laureates impacting AI?

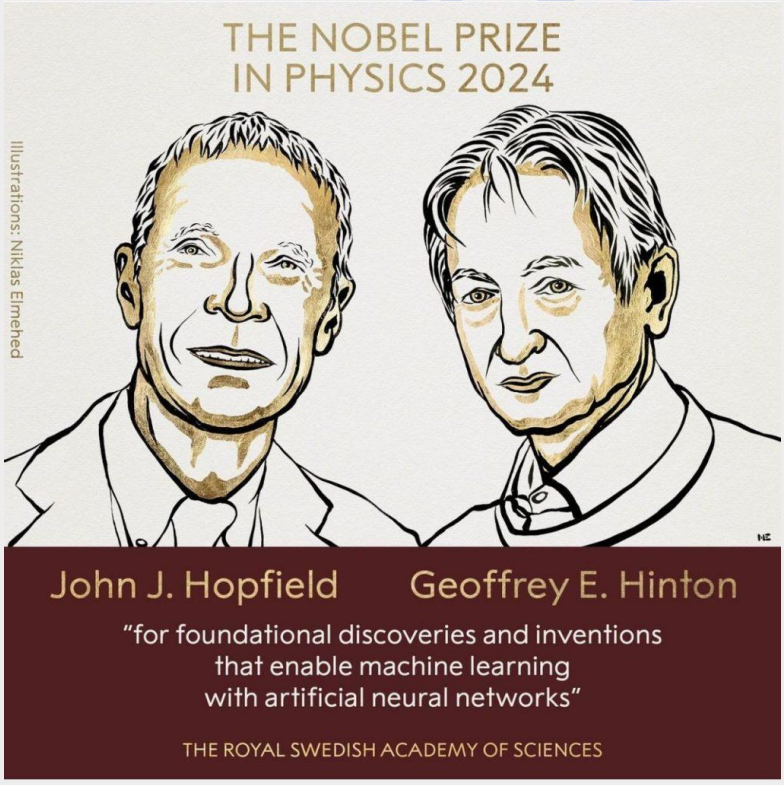
Introduction

On October 8, John Hopfield and Geoffrey Hinton won the 2024 Nobel Prize for Physics "for foundational discoveries and inventions that enable machine learning with artificial neural networks". Their work lies at the roots of a large tree of work, the newest branches of which are seen today as apps like ChatGPT.

What is AI?

An accessible AI today is likely to be an implementation of an artificial neural network (ANN) — a collection of nodes designed to operate like networks of neurons in animal brains. Each node is a site where some input data is processed according to fixed rules to produce an output. A connection between nodes allows them to transfer input and output signals to each other. Stacking multiple layers of nodes, with each layer performing a specific task with great attention to detail, creates a machine capable of deep learning.

The foundations of contemporary AI, for which Hopfield and Hinton received this year's physics Nobel Prize, are in machines that started off doing things humans were better at — pattern recognition — and based on ideas in statistical physics, neurobiology, and cognitive psychology.



What is the Hopfield network?

In 1949, Canadian psychologist Donald Hebb introduced a neuropsychological theory of learning to explain the ability of connections between neurons to strengthen or weaken. Hebb posited that the connection between two neurons becomes more efficient if the neurons constantly talk to each other. In 1983, Hopfield developed an ANN whose nodes used Hebb's postulate to learn by association. For example, if a node is exposed to many texts, one set in English and the other its Tamil translation, it could use Hebbian learning to conclude "hand" and "kai" are synonymous because they appear together most often.

Another feature of Hopfield network is information storage. When the network is 'taught' an image, it stores the visual in a 'low-energy state' created by adjusting the strengths of the nodes' connections. When it encounters a noisy version of the image, it produces the denoised version by progressively moving it to the same low-energy state. The use of 'energy' here is an echo of the fact that the Hopfield network is similar in form and function to models researchers have used to understand materials called spin glasses. A low-energy state of a Hopfield network — which corresponds to its output — could map to the low-energy state of a spin glass modelled by the same rules. Hopfield's mapping was a considerable feat because it allowed researchers to translate ideas from statistical physics, neuro-psychology, and biology to a form of cognition.

What is a Boltzmann machine?

Hinton's share of the Nobel Prize is due to his hand in developing the first deep-learning machines. In 1872, Austrian physicist Ludwig Boltzmann published an equation to predict, say, the possible behaviours of a tub of fluid with one end hotter than the other. Whereas the first guess of a simple logic would be that all the possible states this system can take would be equally probable, Boltzmann's equation predicts that some states are more probable than others because the system's energy prefers them.

In the mid-1980s, Hinton and his peers developed an ANN with a tendency to move towards some outcomes over others by using Boltzmann's equation to process its inputs. Their network had visible nodes, which could input and output information, and a set of hidden nodes that only interacted with other nodes. The visible nodes worked like a Hopfield network whereas the hidden nodes modelled new possibilities using Boltzmann's equation. This was the dawn of generative AI. In another breakthrough in the 2000s, Hinton and others devised a form of the Boltzmann machine where the hidden nodes were connected only to visible nodes, and vice versa. These restricted Boltzmann machines (RBMs) could learn more efficiently, using the contrastive divergence algorithm Hinton et al. developed. Hinton, Simon Osindero, and Yee-Whye Teh also found that 'layers' of ANNs could be trained using RBMs and then stacked to create a deep learning model.

Where are ANNs today?

Technologies evolve through successive levels of abstraction. The individual computer of the late 1980s is today part of the cloud, a distributed network of computing sites linked by data networks and managed using software and hardware controls. ANNs are the product of a similar abstraction, which Hopfield and Hinton helped achieve, and have further transformed. Thus they are within the reach of millions of people but also less resemble their ancestors.

Advances in this area have benefited from the work of multiple teams and ideas, so much so that drawing a straight line from Hopfield's and Hinton's work to ChatGPT is impossible. One new form of ANN is the transformer, a two-part neural network that encodes and then decodes information, with valuable applications in object detection and recognition. Other developments include back-propagation, a technique that allows ANNs to upgrade themselves as they learn, and the long short-term memory that enables ANNs to 'remember' some information for a fixed number of steps.

ANNs are also on our minds. Hinton has said he is "worried the overall consequence… might be systems more intelligent than us that eventually take control." He left Google in 2023 to spread awareness of AI's risks. Hopfield has expressed similar sentiments. Why do it then? Presumably because the tree is big and it is impossible to see the branches sitting at the roots.

Relevance: GS Prelims & Mains Paper III; Science & Technology
Source: The Hindu