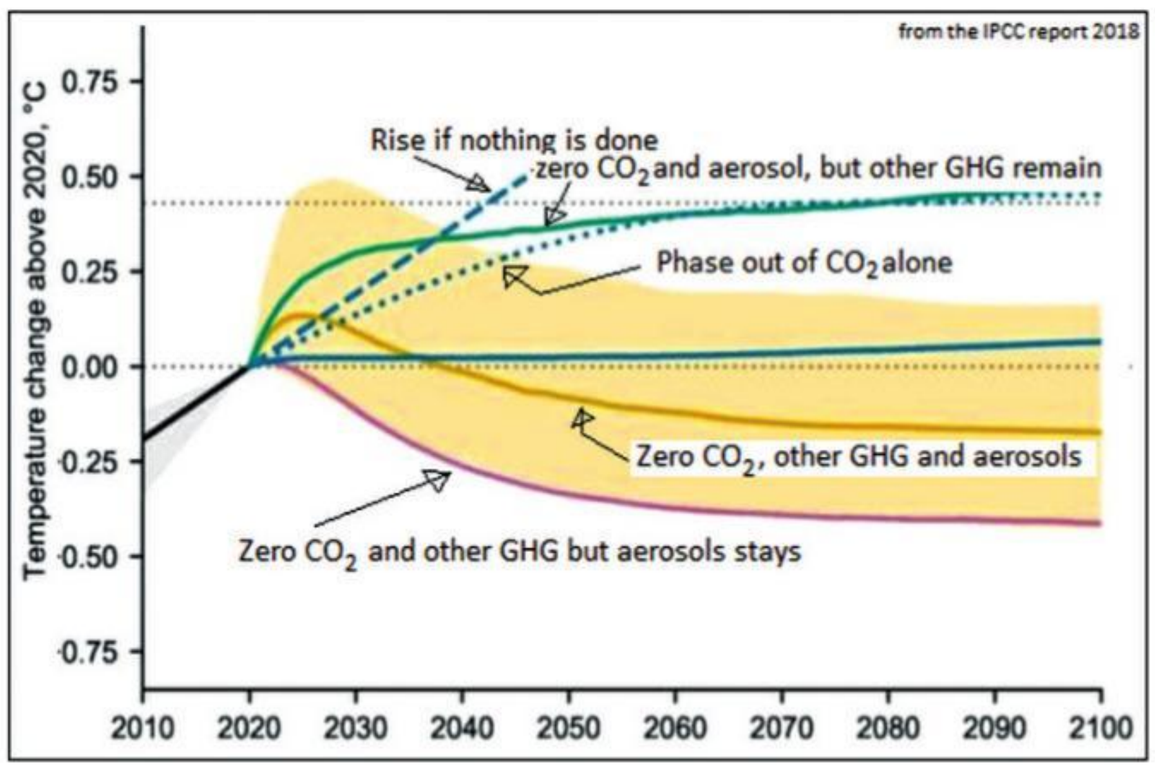
Is 1.5°C within reach?

Would global warming continue even after emissions are controlled?

S ANANTHANARAYANAN



It took a century for the Earth to warm. Would it take as long for warming to stop? Early last month, Mark Hertsgaard, director of the media support group, Covering Climate Now, and Laura Helmuth, editor-in-chief of *Scientific American*, interviewed Michael E Mann, director of Penn State Earth System Science Center, United States, and Saleemul Huq, director of the International Centre for Climate Change and Development in Dhaka. The subject of the interview was a mention in the sixth Assessment Report of the Inter-governmental Panel on Climate Change, or IPCC, issued in August 2021, that the global temperature would stabilise "rapidly", as opposed to "slowly", once the pace of greenhouse gas emission was controlled.

Hertsgaard started off with the note that all climate modelling, so far, has considered that carbon dioxide in the atmosphere, once it builds up, "persists", or stays there for decades, even centuries. Hence, even after the world manages to stop adding carbon dioxide to the atmosphere, it has been understood that global warming would continue for 30-40 years. While there was limited progress after the COP21, Paris in 2015, and disappointment in COP26 at Glasgow in 2021, the idea that warming does not end when emissions are controlled has been another damper. And the feeling has spread that holding the warming to 1.5°C or even 2°C may not be possible.

Except, Hertsgaard said, that the IPCC report of August 2021, even before the Glasgow meet, had put forward a new understanding -- that warming does not continue once emissions are controlled, but stabilises within three years. The trouble, however, is that this important information is tucked away, virtually buried, within the report. The whole report is nearly 4,000 pages long and the technical summary is 159 pages. Even a technical person studying the report would very likely miss this information. The 24-page "summary for policymakers" also follows the pattern of the reports, only omitting details, and is not a reader-friendly rendition of the report.

The journal, *Scientific American*, however, had spotted this nugget. And in October 2021, before the Glasgow meet, an article by Mark Fischetti, senior editor, said, "Climate models consistently show that 'committed' (baked-in) warming does not happen. As soon as carbon dioxide emissions stop rising, the atmospheric concentration of carbon dioxide levels off and starts to slowly fall because the oceans, soils and vegetation keep absorbing carbon dioxide, as they always do."

Michael Mann said the slowing down of warming is implicit in the idea of the "carbon budget", that there is an extent of carbon dioxide that we can still push into the atmosphere, before we hit 1.5 °C of warming. If we speak of a budget, it means warming will stop if we stop emissions when the limit is reached, he said. That said, the reason we still thought warming would continue is because there is warming of the sea, a great "heat sink", that also takes place, and the sea is slower to warm. But the understanding which has surfaced over the last decade is that there are other processes, that draw carbon dioxide out of the atmosphere, that continue after we stop pumping carbon dioxide into the atmosphere, and the carbon dioxide content begins to drop.

This, however, only applies to the surface temperature, not the temperature of the sea, which continues to absorb heat. Warming of the sea would hence continue, with effects like the melt of sea ice, and the sea-level would rise. The sea-level is now about a foot higher than at pre-industrial times, and would rise by another foot, even if we do contain carbon dioxide, by half within this decade, and completely by mid-century. But this we must, Mann said, "so that this foot does not become a metre!"

Hertsgaard came in to say that this science, that warming is going to stop very soon after (and if) we arrest emissions, creates a paradigm shift -- it psychologically encourages people, young people who have the largest stakes, to believe that working to reduce carbon would positively benefit them. And thinking like this would affect politics, the kind of leaders we elect, and then government policy.

Huq, from Bangladesh, was introduced as the person who had trained diplomats from the global South and influenced insertion of the 1.5 °C target into the Paris agreement of 2015. In Bangladesh, Huq said, effects of the current 1.1 °C global warming were already part of daily life. His country had been dealing with extreme weather and increased flooding for a decade and common people had found ways to adapt to global warming, he said.

The affluent West was yet to understand, Huq said. During the Glasgow conference, countries most at risk had pressed for the outcome of the conference to be called the "Glasgow Climate Emergency Pact". But the U S, United Kingdom, and other affluent countries, watered it down to the "Glasgow Climate Pact". But warming will catch up and they will understand, or their children will, Huq said.

Global warming was common understanding in Bangladesh, Huq said, and a subject that the local press actively covered. The world's press was present in strength during the inauguration and start of COP26, when dignitaries were there, but they did not stay for the proceedings. It was a television channel called *Bangladesh TV* that was there till the end, Huq said.

The reports of IPCC have been criticised, in the past, for being difficult to understand, if not unreadable. There was a defence that the "summary for policymakers" is the "most widely read" part of the report. This really says nothing, and a glance at the "summary" would show that it is scarcely helpful even to a technical person. And we see that the part of the 2021 report that the *Scientific American* considered the most important was missed by the world's press, to say nothing of policymakers.

Hertsgaard observed that if the press reported the whole news, not just the gloomier parts, but also the information that taking steps could turn things around, there could be more attention paid to what is said.

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Other pollutants

The other greenhouse gas we emit is methane, Mann said. But methane is a gas that decomposes relatively quickly, unlike carbon dioxide, which sticks around for long periods. The methane that we emit is hence not all an addition to the load in the atmosphere.

But there is another pollutant that acts the other way. These are sulphate aerosols that arise from sulphur impurity in coal. Aerosols actually block or reflect some of the sunlight, an effect we call "aerosol masking", which offsets a part of global warming. Now, when we stop burning coal, we do reduce carbon dioxide emission, but we also lose out on a bit of "global dimming" that aerosols bring about.

Improving success rates

Ninety per cent drugs fail clinical trials -- here's a way in which researchers can select better drug candidates

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It takes 10 to 15 years and around $ (United States) one billion to develop one successful drug. Despite these significant investments in time and money, 90 per cent of drug candidates in clinical trials fail. Whether because they don't adequately treat the condition they're meant to target or the side effects are too strong, many drug candidates never advance to the approval stage.

As a pharmaceutical scientist working in drug development, I have been frustrated by this high failure rate. Over the last 20 years, my lab has been investigating ways to improve this process. We believe that starting from the very early stages of development and changing how researchers select potential drug candidates could lead to better success rates and ultimately better drugs.

How does drug development work?

Over the last few decades, drug development has followed what's called a classical process. Researchers start by finding a molecular target that causes disease -- for instance, an overproduced protein that, if blocked, could help stop cancer cells from growing. They then screen a library of chemical compounds to find potential drug candidates that act on that target. Once they pinpoint a promising compound, researchers optimise it in the lab.

Drug optimisation primarily focuses on two aspects of a drug candidate. First, it has to be able to strongly block its molecular target without affecting irrelevant ones. To optimise for potency and specificity, researchers focus on its structure-activity relationship, or how the compound's chemical structure determines its activity in the body. Second, it has to be "drug-like", meaning it must be able to be absorbed and transported through the blood to act on its intended target in affected organs.

Once a drug candidate meets the researcher's optimisation benchmarks, it goes on to efficacy and safety testing, first in animals, then in clinical trials with people.

Why does 90 per cent of clinical drug development fail?

Only one out of 10 drug candidates successfully pass clinical trial testing and regulatory approval. A 2016 analysis identified four possible reasons for this low success rate.

The researchers found between 40 and 50 per cent of failures were due to a lack of clinical efficacy, meaning the drug wasn't able to produce its intended effect in people. Around 30 per cent were due to unmanageable toxicity or side effects, and 10-15 per cent were due to poor pharmacokinetic properties, or how well a drug is absorbed by and excreted from the body. Lastly, 10 per cent of failures were attributed to lack of commercial interest and poor strategic planning.

This high failure rate raises the question of whether there are other aspects of drug development that are being overlooked. On the one hand, it is challenging to truly confirm whether a chosen molecular target is the best marker to screen drugs against. On the other hand, it's possible that the current drug optimisation process hasn't been leading to the best candidates to select for further testing.

Drug candidates that reach clinical trials need to achieve a delicate balance of giving just enough drug so it has the intended effect on the body without causing harm. Optimising a drug's ability to pinpoint and act strongly on its intended target is clearly important in how well it's able to strike that balance. But my research team and I believe that this aspect of drug performance has been overemphasised. Optimising a drug's ability to reach diseased body parts in adequate levels while avoiding healthy body parts -- its tissue exposure and selectivity -- is just as important.

For instance, scientists may spend many years trying to optimise the potency and specificity of drug candidates so that they affect their targets at very low concentrations. But this might be at the expense of ensuring that enough drug is reaching the right body parts and not causing harm to healthy tissue. My research team and I believe that this unbalanced drug optimisation process may skew drug candidate selection and affect how it ultimately performs in clinical trials.

Improving the drug development process

Over the last few decades, scientists have developed and implemented many successful tools and improvement strategies for each step of the drug development process. These include high-throughput screening that uses robots to automate millions of tests in the lab, speeding up the process of identifying potential candidates; Artificial Intelligence-based drug design; new approaches to predict and test for toxicity; and more precise patient selection in clinical trials. Despite these strategies, however, the success rate still hasn't changed by much.

My team and I believe that exploring new strategies focusing on the earliest stages of drug development when researchers are selecting potential compounds may help increase success. This could be done with new technology, like the gene editing tool CRISPR (an acronym for clustered regularly interspaced short palindromic repeats), that can more rigorously confirm the correct molecular target that causes disease and whether a drug is actually targeting it. And it could also be done through a new "Star" system my research team and I devised to help researchers better strategise how to balance the many factors that make an optimal drug. Our "Star" system gives the overlooked tissue exposure and selectivity aspect of a drug equal importance to its potency and specificity. This means that a drug's ability to reach diseased body parts at adequate levels will be optimised just as much as how precisely it's able to affect its target. To do this, the system groups drugs into four classes based on these two aspects, along with recommended dosing. Different classes would require different optimisation strategies before a drug goes on to further testing.

A Class I drug candidate, for instance, would have high potency/specificity as well as high tissue exposure/selectivity. This means it would need only a low dose to maximise its efficacy and safety and would be the most desirable candidate to move forward. A Class IV drug candidate, on the other hand, would have low potency/specificity as well as low tissue exposure/selectivity. This means it likely has inadequate efficacy and high toxicity, so further testing should be terminated.

Class II drug candidates have high specificity/potency and low tissue exposure/selectivity, which would require a high dose to achieve adequate efficacy but may have unmanageable toxicity. These candidates would require more cautious evaluation before moving forward.

Finally, Class III drug candidates have relatively low specificity/potency but high tissue exposure/selectivity, which may require a low to medium dose to achieve adequate efficacy with manageable toxicity. These candidates may have a high clinical success rate but are often overlooked.

Realistic expectations for drug development

Having a drug candidate reach the clinical trial stage is a big deal for any pharmaceutical company or academic institution developing new drugs. It's disappointing when the years of effort and resources spent to push a drug candidate to patients so often lead to failure.

Improving the drug optimisation and selection processes may significantly improve success of a given candidate. Although the nature of drug development may not make reaching a 90 per cent success rate easily achievable, we believe that even moderate improvements can significantly reduce the cost and time it takes to find a cure for many human diseases.

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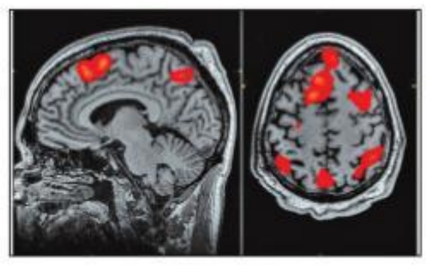
PLUS POINTS

Life recalled



A landmark study involving a dying person's brain activity could provide an explanation for reports of people vividly recalling their lives in near-death experiences.

The study has revealed patterns around the time of death similar to those during dreaming and memory recall, and challenge our understanding of when exactly life ends. The findings, published last week in the journal *Frontiers in Ageing Neuroscience*, also raise important questions related to the timing of organ donation.

Neuroscientists, including Raul Vicente of the University of Tartu, Estonia, were initially studying the brain waves of an 87-year-old epilepsy patient for seizures using an electroencephalography, or EEG, device, but in the middle of the study, the patient had a heart attack and died. The EEG recording shed light on about 900 seconds of the person's brain activity as they died, and the scientists attempted to investigate what specifically happened in the 30 seconds before and after the heart stopped beating.

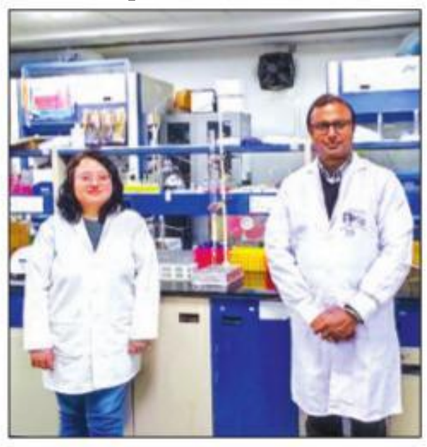
The findings revealed that as the person was dying, there was an increase in brain waves known as gamma oscillations that typically occur during dreaming and memory retrieval, as well as others such as delta, theta, alpha, and beta oscillations. Brain waves are rhythmic electrical activity in normal living human brains, and different types of these waves are linked to different states.

Citing an example, researchers said gamma oscillations are linked to high-cognitive functions like concentrating, dreaming, meditation, memory retrieval and conscious perception, like those linked to memory flashbacks. And studies have also shown that alpha waves, which oscillate in the frequency of eight-12 Hertz, could play a role in filtering out distracting sensory information and helping pay attention.

Based on existing knowledge of the activities associated with different brain waves, scientists speculate the dying 87-year-old person may have been making a "last recall of life ". That said, since the new research is based on a single patient who had also suffered injury, seizures and swelling, researchers said that interpretation of the data may be complicated, adding that there is a need to investigate more cases and see the latest results as a "source of hope".

The independent

Conversion catalyst



Researchers at the Indian Institute of Technology-Mandi have used hydrochar, made from orange peels, as a catalyst to convert biomass-derived chemicals into biofuel precursors. The research will help develop biomass-based fuel to overcome socio-political instabilities associated with dwindling petroleum reserves.

The findings of the research team have been recently published in the journal *Green Chemistry*. The research was led by Venkata Krishnan, associate professor, School of Basic Sciences, IIT-Mandi, and co-authored by his students Tripti Chhabra and Prachi Dwivedi.

Biomass-derived products from naturally occurring materials is currently the fourth-most significant energy source after coal, oil, and natural gas, in the country. Lignocellulosic biomass obtained from forestry and agricultural waste, for example, can potentially be converted into a variety of useful chemicals by various methods.

Of these methods, the use of catalysts for the conversion is particularly useful because such processes can be carried out with minimal energy input and the type of product obtained from the biomass can be controlled through the right choice of catalysts and reaction conditions.

The simplest and most low-cost catalyst that has been studied by the researchers for biomass conversion reactions is hydrochar. It is typically obtained by heating the biomass waste (orange peels in this case) in the presence of water through hydrothermal carbonisation process. The use of hydrochar as a catalyst for biomass conversion is attractive because it is renewable and its chemical and physical structures can be altered for better catalytic efficiencies.