

## News in focus

Meta's network, called ESMFold, isn't quite as accurate as AlphaFold, Rives' team reported earlier this year<sup>2</sup>, but it is about 60 times faster at predicting structures for short sequences, he says. "What this means is that we can scale structure prediction to much larger databases."

As a test, the researchers unleashed their model on a database of bulk-sequenced 'metagenomic' DNA from environmental sources such as soil, seawater and the human gut and skin. The vast majority of the entries – which encode potential proteins – come from single-cell organisms that have never been isolated or cultured and are unknown to science.

In total, the team predicted the structures of more than 617 million proteins. The effort took just two weeks (by contrast, AlphaFold can take minutes to generate a single prediction). The structures are freely available for use, as is the code underlying the model, says Rives.

Of the 617 million predictions, the model deemed more than one-third to be high quality, such that researchers can have confidence that the overall protein shape is correct and, in some cases, can discern atomic-level details. Millions of these structures are entirely unlike anything in the databases of protein structures determined experimentally, or any of AlphaFold's predictions from known organisms.

A large chunk of the AlphaFold database is made up of structures that are nearly identical to each other, whereas metagenomic databases "should cover a large part of the previously unseen protein universe", says Martin Steinegger, a computational biologist at Seoul National University. "There's a big opportunity now to unravel more of the darkness."

Sergey Ovchinnikov, an evolutionary biologist at Harvard University in Cambridge, Massachusetts, wonders about the hundreds of millions of predictions that ESMFold made with low confidence. Some might lack a defined structure, at least in isolation, whereas others might be non-coding DNA mistaken for protein-coding material. "It seems there is still more than half of protein space we know nothing about," he says.

### Leaner, simpler, cheaper

Burkhard Rost, a computational biologist at the Technical University of Munich in Germany, is impressed by the combined speed and accuracy of Meta's model. But he questions whether ESMFold really offers an advantage over AlphaFold's precision when it comes to predicting proteins from metagenomic databases. Language-model-based prediction methods – including one developed by his team<sup>3</sup> – are better suited to quickly determining how mutations alter a protein's structure, which is not possible with AlphaFold. "We will see structure prediction become leaner,

simpler, cheaper, and that will open the door for new things," he says.

DeepMind doesn't currently have plans to include metagenomic structural predictions in its database, but hasn't ruled out adding them to future releases, according to a company representative. But Steinegger and his collaborators have used a version of AlphaFold to predict the structures of some 30 million metagenomic proteins. They are hoping to find new kinds of RNA virus by looking for

previously unknown forms of the viruses' genome-copying enzymes.

Steinegger sees trawling biology's dark matter as the obvious next step for such tools. "I do think we will quite soon have an explosion in the analysis of these metagenomic structures."

1. Lin, Z. et al. Preprint at bioRxiv <https://www.biorxiv.org/content/10.1101/2022.07.20.500902v2> (2022).
2. Lin, Z. et al. Preprint at bioRxiv <https://www.biorxiv.org/content/10.1101/2022.07.20.500902v1> (2022).
3. Weissenow, K., Heinzinger, M. & Rost, B. *Structure* **30**, 1169–1177 (2022).

# SCIENTISTS CHEER LULA VICTORY IN BRAZIL ELECTION

## Many hope that the new president will restore research funding and environmental protections.

By Jeff Tollefson

Scientists breathed a sigh of relief on 30 October as Brazil narrowly elected Luiz Inácio Lula da Silva as president, ousting the current leader, who they say disregarded science, weakened environmental policies and disparaged minority groups.

Overcoming the reputational damage of a 19-month stint in prison on corruption charges – which were tossed out in 2021 – Lula received nearly 51% of the vote in a runoff election against the right-wing incumbent,

Jair Bolsonaro. Lula, a leftist labour leader and former president, will take office in January.

"Today is a very hopeful day here in Brazil," says Elisa Orth, a chemist at the Federal University of Paraná in Curitiba. Orth has watched students walk away from science over the past several years, while Bolsonaro slashed research funding and attacked scientists, academics and others. With Lula, Orth says, "we voted for somebody who believes in science, who believes in education".

Many scientists and academics had lined up in favour of Lula, who garnered international fame during his first two terms in office, from



Luiz Inácio Lula da Silva celebrates his victory in the Brazilian presidential election.

ALEXANDRESCHNEIDER/GETTY

2003 to 2010, for promoting sustainable development, lifting millions out of poverty and sharply reducing deforestation in the Amazon. His Workers' Party invested heavily in science, innovation and education.

By contrast, during his presidency, Bolsonaro cut science budgets, curbed the enforcement of environmental laws and promoted misinformation about COVID-19 and vaccines. The pandemic killed more than 685,000 people in Brazil. A former army captain, Bolsonaro repeatedly questioned the legitimacy of Brazil's electoral system in the run-up to the election, leading many to fear that he might attempt a coup. He has not conceded the election, but his chief of staff has said that a transition of power will go ahead.

"I'm feeling relieved," says Luis Sánchez, an environmental engineer at the University of São Paulo. Lula's election provides hope that Brazil can move forward with new policies to protect the environment, reduce poverty and promote a more sustainable and equitable route for economic development, Sánchez says, "but it won't be easy".

### A new regime

In his acceptance speech, Lula announced that the environment is one of his top priorities, alongside addressing hunger and poverty. He also welcomed international cooperation to help him end deforestation in the Amazon, which has been driven mainly by the clearing of land for cattle pasture. Scientists, environmentalists and many world leaders keen to curb carbon emissions from deforestation and conserve biodiversity welcomed the news after 4 years of Bolsonaro, under whom forest loss in the Amazon hit its highest level in 15 years.

"The incoming administration is well positioned to turn the tide of deforestation," says Holly Gibbs, a geographer at the University of Wisconsin–Madison. Lula has promised to restore enforcement of environmental laws, but Gibbs says the incoming administration should also focus on transparency.

Brazil was once a global leader in making agricultural data publicly available, she says, and scientists and businesses can use those data to monitor land use and cattle movements (T. A. P. West *et al.* *Conserv. Lett.* <https://doi.org/gq3b3v>; 2022). The Bolsonaro government, however, has restricted access to such information. Gibbs says that being able to track cattle movements in Brazil, the world's largest beef exporter, "is a key to reducing deforestation in the Amazon".

Although Lula came out on top in the presidential election, Bolsonaro's supporters prevailed in many of the congressional elections that took place on 2 October. This means the Lula administration will face extra hurdles implementing its agenda.

Conservatives in the Brazilian Congress

could continue to push legislation that has drawn opposition from scientists and environmentalists, Sánchez says, including a bill aimed at making it easier to approve new infrastructure such as roads, dams and mines by reducing regulatory protections for the environment, communities and Indigenous peoples. Such efforts could put the Lula administration on the defensive, and it remains unclear whether the government will be able to halt this legislation or negotiate a compromise. "No one knows," Sánchez says.

Nonetheless, many scientists remain optimistic. Lula's government will face challenges building support for a new sustainable-development agenda, but his record on tackling deforestation gives reason

for hope, says Aline Soterroni, an environmental scientist at the University of Oxford, UK. "Today, Brazil is a global pariah," she says, but Lula will probably re-engage at the international level and submit an ambitious new commitment to reduce the country's greenhouse-gas emissions under the United Nations climate convention. "We have reasons to believe," she says.

Lula was the only presidential candidate who mentioned science during his campaign – another reason for hope, says Luiz Davidovich, a physicist at the Federal University of Rio de Janeiro and former president of the Brazilian Academy of Sciences. More importantly, Davidovich says, Lula has shown an ability to listen, learn and bring people together.

"That should make a difference," he says.

## COVID 'VARIANT SOUP' IS MAKING WINTER SURGES HARD TO PREDICT

Descendants of Omicron are proliferating worldwide – many with the same mutations.

By Ewen Callaway

Some call it a swarm of variants – others refer to it as variant soup. Whatever it's called, the current crop of immunity-dodging offshoots of the Omicron variant of SARS-CoV-2 is unprecedented in its diversity. This complexity makes it harder to predict coming waves of infection. It might even lead to a 'double wave' in some places, as first one variant and then another overtakes a population.

But amid the chaos, patterns are emerging. The swarm has helped scientists to pinpoint a handful of immunity-evading mutations that power a variant's spread. Globally, a few heavyweight variants have emerged, yielding different outcomes in different regions – at least, so far.

In Europe, North America and Africa, the prevalence of Omicron offshoots in the BQ.1 family is rising quickly, even as overall cases seem to fall. In Asian countries including Singapore, Bangladesh and India, a lineage called XBB has already set off fresh waves of infection. Scientists are closely watching several regions where both are circulating, to see which has the edge.

"In the end, probably, some variants are going to dominate, but it's less decisive than it was in the past," says Cornelius Roemer, a computational biologist at the University of

Basel in Switzerland.

The variants that have driven past waves, such as Alpha and Delta, all arose from distinct branches of the SARS-CoV-2 family tree. But since Omicron emerged in late 2021, it has spawned a series of subvariants, including BA.2 and BA.5, that have sparked global waves of infection. Many countries put their BA.5-led surges in the rear-view mirror in mid-2022, but most scientists thought it was only a matter of time before another sublineage came to the fore.

For the past few months, variant trackers have been combing through global SARS-CoV-2 sequencing data to identify candidates. But instead of one or two fast-rising lineages, they have identified more than a dozen to watch.

"It's a collection or swarm or soup of variants together – not as we have seen before," says Yunlong Richard Cao, an immunologist at Peking University in Beijing, whose team has been studying the variants' immune-evading capacities.

### One big family

The members of the swarm come from various parts of the Omicron family tree. But their rise seems to be due to a handful of shared genetic mutations, most of which lead to amino acid changes in a portion of the viral spike protein called the receptor binding domain (RBD).