

## News in focus

experiments can explain a lot of viral evolution, but not all of it.

The arrival of AI-based protein-structure prediction tools – such as AlphaFold, created by London-based AI company DeepMind, as well as ESM-2 (ref. 3) and ESMFold, both created by Meta (formerly Facebook, headquartered in Menlo Park, California) – has brought new energy to the field, says David Robertson, a virologist at the University of Glasgow, UK.

**“It’s a really exciting and very useful area for research.”**

AI models require vast amounts of data to be able to predict viral evolution. The mass sequencing of SARS-CoV-2, the virus that causes COVID-19, has made this possible, says Junpei Ito, a bioinformatician at the University of Tokyo. Researchers have close to 17 million sequences they can use to train their models.

One model, called EVEscape, which was developed by Debora Marks at Harvard Medical School in Boston, Massachusetts, and her team, has been used to engineer 83 possible versions of the SARS-CoV-2 spike protein, which the virus uses to infect cells. These spike avatars can evade antibodies from people who have been vaccinated or infected with currently circulating variants<sup>4</sup>, and could test the effectiveness of future COVID-19 vaccines.

Ito’s group is focusing on a broader characteristic of viral fitness – the ability of variants to spread rapidly in a population, and eventually dominate. The researchers used ESM-2 to create a model called CoVFit, which can predict the relative fitness of SARS-CoV-2 variants. CoVFit is trained on 13,643 SARS-CoV-2 spike-protein variants, and also uses experimental data from Cao’s group about how individual mutations affect the virus’s ability to evade antibodies. Ito’s team created a restricted model trained using variant data up to August 2022, and found that it successfully predicted the improved fitness of certain variants after that cut-off – including XBB (ref. 5), a variant that took hold later that year.

By March 2024, the dominant SARS-CoV-2 variant was one named JN.1. Using CoVFit, Ito’s group identified three single-amino-acid changes that would help JN.1 to gain fitness. These mutations have since been seen in variants that are rapidly expanding globally.

### More data needed

To make AI models more accurate, researchers will need more than five years of data on viral evolution, says Cao. Combining surveillance sequencing data with experimental data helps to overcome some data challenges, he says.

Several other groups are also developing models using combined data<sup>6</sup>. In work that has

not yet been published, the group of University of Tokyo evolutionary virologist Shusuke Kawakubo is looking at the influenza virus’s ability to induce an immune response in its host. If influenza’s haemagglutinin protein (its spike-protein equivalent) changes enough, it might not be recognized by the body’s immune response, at which point, the world’s vaccine makers need to adjust the next season’s flu jabs.

### Big leaps

Most of these models are restricted to understanding the effects of small changes but, in theory, viruses have almost infinite room to evolve, says Ito. For example, the Omicron variant arrived with more than 50 mutations, looking like nothing researchers had seen before.

These sudden evolutionary leaps are hard to predict. Robertson and his colleagues are trying to find ways of using AI models to

understand these vast evolutionary trajectories and determine their limits. They found that if they gave ESM-2 a single spike sequence, it could identify regions where changes could occur, and how those changes might affect other parts of the protein<sup>7</sup>. “It kind of feels like dark magic,” says Robertson. The goal, he says, is to be able to work out how much scope a virus has to evolve, very soon after its detection in people.

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2. Jian, F. *et al. Nature* <https://doi.org/10.1038/s41586-024-08315-x> (2024).
3. Lin, Z. *et al. Science* **379**, 1123–1130 (2023).
4. Youssef, N. *et al. Preprint at bioRxiv* <https://doi.org/10.1101/2023.10.08.561389> (2024).
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6. Han, W. *et al. Nature Commun.* **14**, 3478 (2023).
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# NASA STILL HAS NO PLAN FOR HOW IT WILL BRING MARS ROCKS TO EARTH

The Perseverance rover collected the precious samples, looking for evidence of past life.

By Alexandra Witze

**N**ASA has again put off deciding how to accomplish one of its highest-profile missions in decades: bringing rocks back from Mars.

After years of ballooning cost estimates, the agency promised last April that it would develop a cheaper method for Mars

sample return. But during a mission update on 7 January, it kicked the can down the road, saying it would continue to explore two options: one using well-tested NASA technology and the other relying on systems being developed by private aerospace companies.

The final decision isn’t expected until next year. The earliest the NASA spacecraft could launch would be 2031, with the samples coming to Earth no earlier than 2035. Costs for both options range from around US\$6 billion to \$7 billion – less than earlier estimates of up to \$11 billion, but still a major challenge for the cash-strapped agency.

“I’m disappointed we don’t have an entirely clear path forward yet,” says Victoria Hamilton, a planetary geologist at the Southwest Research Institute in Boulder, Colorado, who chairs a group that provides NASA with community input on its Mars exploration plans. She notes that Mars sample return has been a top priority for US planetary science for decades and the community is keen for it to get under way.

### Challenging delivery

No nation has yet delivered Mars samples to Earth, although China is working on plans to do so as early as 2031. Studying Martian rocks in person would allow scientists to conduct



A rock sampled in Jezero Crater on Mars.

analyses much more sophisticated than those that rovers can do on the red planet. Keeping both design options for now “will help us achieve delivering this science for everybody”, said Nicola Fox, NASA’s associate administrator for science, during the media briefing.

NASA’s goal is to bring back 30 of the tubes of Martian rock, dust and air that the agency’s Perseverance rover has collected over the past few years from a variety of geological environments in Jezero Crater, where it landed. The rover has travelled across an ancient river delta and last year left the crater, entering a realm of ancient rocks that have never been explored.

NASA put its Mars sample-return plans on hold last year while it solicited fresh ideas from businesses and the public about how to do it for less than \$11 billion. On the basis of the feedback, NASA administrator Bill Nelson chose the two-option approach.

The options have the same basic architecture: a spacecraft launches from Earth and delivers a lander near Perseverance. The rover transfers sample tubes to the lander, which blasts them into Martian orbit using a small rocket. Another spacecraft, built and launched by the European Space Agency, captures the samples in Mars orbit and takes them to Earth.

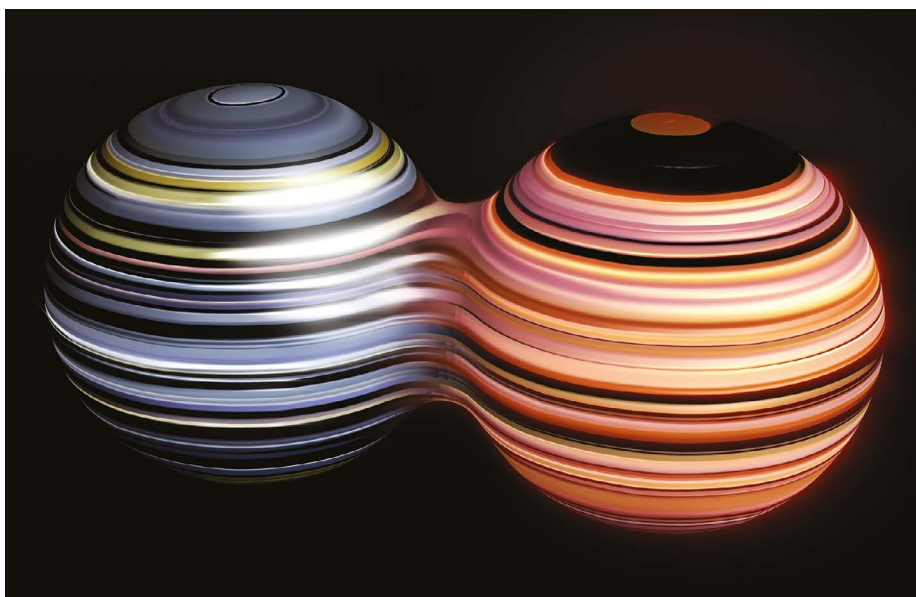
Where the options differ is in how the lander gets to the surface of Mars. One candidate is the well-tested ‘sky crane’ developed by NASA’s Jet Propulsion Laboratory in Pasadena, California, and used to lower Perseverance to the Martian surface in 2021. The commercial option would be a system of large rockets and landing mechanisms, with details of how the lander would be delivered to the surface as-yet unknown. Possible suppliers include Blue Origin of Kent, Washington, and SpaceX in Hawthorne, California, which is headed by incoming US president Donald Trump’s close adviser Elon Musk.

### Money matters

Under both options, the mission is cheaper than earlier proposals because the rocket that ferries the samples from surface to orbit is smaller and cheaper to transport. To make the surface lander more robust, the agency proposes to use radioisotope power to keep the surface lander powered and warm, rather than relying on solar panels as originally planned.

Nelson said at the briefing that it will be up to Congress and the next US presidential administration to decide whether to fund the Mars sample-return mission, and at what level. Trump has nominated billionaire businessman Jared Isaacman to lead NASA. Isaacman, who has paid SpaceX to fly him to space, is an advocate for science but has not spoken publicly about his views on Mars sample return.

The Trump administration and the incoming Republican-led Congress have both proposed slashing budgets across the federal government.



Particles known as fermions (illustration) can’t share the same state.

## EXOTIC ‘PARAPARTICLES’ DEFY CATEGORIZATION BY CONVENTIONAL PHYSICS

Study predicts particles that are neither bosons nor fermions – and hints at uses in quantum computing.

By Davide Castelvecchi

**T**heoretical physicists have proposed the existence of a new type of particle that doesn’t fit into the conventional classifications of fermions and bosons. Their ‘paraparticle’, described in *Nature* this month<sup>1</sup>, is not the first to be suggested, but the detailed mathematical model characterizing it could lead to experiments in which it is created using a quantum computer. The research also suggests that undiscovered elementary paraparticles might exist in nature.

In a separate development published late last year in *Science*<sup>2</sup>, physicists experimentally demonstrated another kind of particle that is neither a boson nor a fermion – an ‘anyon’ – in a virtual one-dimensional universe for the first time. Anyons had previously been created only in 2D systems.

Their unusual behaviour means that both paraparticles and anyons could one day play a part in making quantum computers less error-prone.

### Particle properties

Around the time when physicists began to understand the structure of atoms, a century ago, Austrian-born theorist Wolfgang Pauli suggested that no two electrons can occupy

the same state – and that if two electrons are pushed close to being in the same state, a repulsive force arises between them. This ‘Pauli exclusion principle’ is crucial to the way electrons orbiting an atomic nucleus arrange themselves in shells, instead of all falling to the lowest possible energy state.

Pauli and others soon realized that this empirical rule applied not only to electrons but to a broader class of particles, including protons and neutrons, which they called fermions. Conversely, particles that do like to share the same state – such as the photons in a laser beam – became known as bosons.

Mathematically, the fundamental property of fermions is that when two of them switch positions, the ‘wavefunction’ that represents their collective quantum state changes sign, meaning that it gets multiplied by  $-1$ . For bosons, the wavefunction remains unaltered. Early quantum theorists knew that there could be other kinds of particle whose wavefunctions changed in more complicated ways when they swapped positions. In the 1970s, researchers discovered anyons, which can exist only in universes of one or two dimensions.

Physicists Zhiyuan Wang, now at the Max Planck Institute for Quantum Optics in Garching, Germany, and Kaden Hazzard at Rice University in Houston, Texas, have now