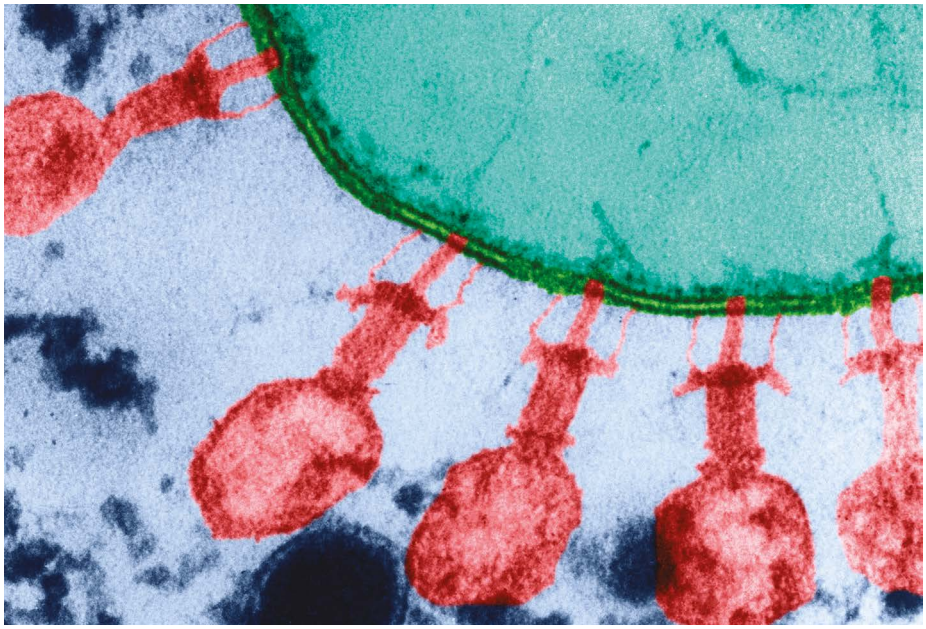

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AI-designed bacteriophages were capable of infecting and killing host bacteria.

AI-DESIGNED VIRUSES ARE A STEP TOWARDS AI-GENERATED LIFE

Scientists used artificial intelligence to write viral genomes, then produced viruses that kill bacteria.

By Katie Kavanagh

Scientists have created the first ever viruses designed by artificial intelligence (AI), and they're capable of hunting down and killing strains of *Escherichia coli* (*E. coli*).

"This is the first time AI systems are able to write coherent genome-scale sequences," says Brian Hie, a computational biologist at Stanford University, California. "The next step is AI-generated life," says Hie, although his colleague Samuel King adds that "a lot of experimental advances need to occur in order to design an entire living organism".

The study, by Hie, King and their colleagues, was posted on the preprint server bioRxiv on 17 September (S. H. King *et al*. Preprint at bioRxiv https://doi.org/p7dj; 2025) and is not yet peer reviewed, but the authors say that it shows the potential of AI to design biotechnological tools and therapies for treating bacterial infections. "Hopefully, a strategy like this can complement existing phage-therapy strategies and someday augment the therapeutics [to] target pathogens of concern," says Hie.

AI models have already been used to generate DNA sequences, single proteins and multi-component complexes (A. Madani *et al*. *Nature Biotechnol.* **41**, 1099–1106; 2023). But designing a whole genome is much more challenging owing to complex interactions between genes and gene replication and regulation processes. These AI systems are now capable of helping scientists to manipulate highly intricate biological systems, such as whole genomes, says Hie. "There are many important biological functions that you can only access if you're able to design complete genomes."

Genomes from the computer

To design the viral genomes, the researchers used Evo 1 and Evo 2, AI models that analyse and generate DNA, RNA and protein sequences. First, they needed a design template, which is a starting sequence that guides the AI model to generate a genome with the desired characteristics. They chose ΦX174, a simple single-stranded DNA virus that contains 5,386 nucleotides in 11 genes, and all the genetic elements required to infect hosts and replicate inside them.

The Evo models had already been trained on more than two million phage genomes, but the researchers further trained the models — using a method called supervised learning — to generate ΦX174-like viral genomes with the specific function of infecting *E. coli* strains, especially those resistant to antibiotics.

The researchers evaluated thousands of AI-generated sequences and narrowed their search down to 302 viable bacteriophages. Most candidates shared more than 40% nucleotide identity with ΦX174, but some had completely different coding sequences. The researchers synthesized DNA from the AI-designed genomes and inserted them into host bacteria to grow phages. These phages were then experimentally tested to see whether they could infect and kill *E. coli*.

Some 16 of the 302 AI-designed bacteriophages showed host specificity for *E. coli* and could infect the bacteria. The researchers found that combinations of AI-designed phages could infect and kill three different *E. coli* strains, which the wild-type ΦX174 was unable to do.

"It was quite a surprising result that was really exciting for us, because it shows that this method might potentially be very useful for therapeutics," says King.

Biosafety concerns

"This study provides a compelling case study of what is possible today and sets the stage for more-ambitious applications in the future," says Peter Koo, a computational biologist at Cold Spring Harbor Laboratory in Laurel Hollow, New York. "It provides a spotlight for an interesting application domain," he adds.

Koo says that the Evo model alone is not yet sufficient to design and generate viruses without intervention, guidance and filtering from the team. "But I think as an overall system, with all the filters in place and the whole system and pipeline they laid out, it shows that it could possibly be an approach that can lead to functional genomes," he adds.

There are ethical concerns over AIs being used to design viruses that can harm humans. But Kerstin Göpfrich, a biophysicist and synthetic biologist at Heidelberg University in Germany, says that this problem — known as the dual-use dilemma — is not unique to AI, but is always a concern in biology. "I think in research in general, you always have a dual-use dilemma. There's nothing specific about AI, and you can always use progress for the better or for the worse," she says.

The authors addressed biosafety concerns in the manuscript. They say that they excluded viruses that affect eukaryotes, including humans, from the Evo models' training data. The ΦX174 phage and *E. coli* host systems they studied were also non-pathogenic and have "a long history of safe use in molecular-biology research", the researchers write.

The researchers hope that their approach could be used to safely generate AI-designed viruses that treat various diseases and address public-health issues, including the growing problem of bacterial resistance.

"I think this will definitely be a growing field and I'm super excited about it," Göpfrich says.