The Next One

Can Artificial Intelligence predict pandemic risk?

The next viral pandemic is on its way; we just don't know where or when to expect it. What the world needs is a NATO-style early warning radar to alert us to these incoming threats. Ideally, the radar must distinguish between the viral majority that pose no risk to human health and the very few that do. And one more thing, it should warn us of this potential pandemic pest before it spills over into humans.

Is that too much to ask? Apparently not.

by Cliff Dominy PhD

A multi-institutional team of scientists led by the University of Glasgow may have come up with a solution. Under the guidance of senior author Dr Liam Brierley, the group developed a machine learning (AI) model capable of predicting which strains of avian influenza, circulating in animals, have the potential to jump into humans. Their research paper is currently undergoing peer-review (which may result in revisions) - but the results look promising.

Brierley and colleagues' AI model represents a significant step forward in computational biology. The novel program analyzes not just the genetic sequence of the viruses in the database, but also the predicted 3D structure of the viral proteins. The team hoped that with this added layer of complexity they could gain a better understanding of the "host-jumping" risk factors at play.

AI
can do that !

This is not a drill

Avian flu has been around for centuries, but is a relatively new pathogen in humans. The first confirmed human case carrying the bird flu signature proteins, H5 and N1, was reported in 1997. This new human-friendly virus has since spread rapidly through the world's bird population.

So far, there has been no human-to-human spread, but viruses do not respect boundaries. The question is not if, but when a new variant spills over and spreads amongst us- it could be just a farmyard cough away from reality.

H5N1 has impacted other mammals, though. In 2023, it decimated the sea lion and elephant seal populations in Peru.

To date, over 600 cases have been reported in humans- mostly farmworkers exposed to their livestock. So far there has been just one confirmed human fatality and no proof of human-to-human transmission - yet.

AI on defense

Brierley and colleagues chose the H5N1 influenza virus for their analysis because it was a credible future pandemic threat. Another advantage for the number crunchers was the extensive avian influenza genetic database at their disposal. Currently, nearly 19000 distinct sequences are available covering 120 different viral subtypes. What is more, 618 of the samples had been isolated from humans.

The research team trained their AI model on a subset of the database and then tested it against the remaining data. They were seeking a connection between the virus sequences combined with the 3 dimensional protein structure predictions identified by their model, and the samples taken from human beings.

Key findings

The results showed the model had a 90% chance of correctly identifying a virus at risk of spillover into humans. Of note, this unparalleled precision was achieved with first-generation protein modelling software on a database that can only get bigger and better.

Whilst many regions of the influenza virus genome have similarities with each other, adding the 3D structural protein predictions narrowed the spillover regions down to just a few key areas. These regions were small, often just two or three base pairs long, but mutations in these regions were critical to allow a bird virus to be recognised by human cells.

The AI model could cut through the noise generated from thousands of viral base pairs and highlight just a few regions that mattered. They were ...

- RNA Polymerase complex: 9 regions across the PA, PB1 and PB2 subunit genes, whose proteins are essential for the virus to replicate, were top of the list.
- Virus binding: 1 region within the haemagglutinin (HA) gene. The “H” in the H5N1 virus family is involved in binding to the host cells. Mutations here could allow the virus to recognize and infect a new host.
- Replication: areas of the nucleoprotein NP- a chaperone responsible for ensuring the host replicates the viral genes correctly and packages them for export.
- Immune evasion: 10 regions within a nonstructural gene NS1. The gene is involved in dampening the host cell's immune response after infection.

The model has already shown potential for use with other influenza viruses outside of the bird family. It flagged rare influenza viruses like H10N8 as well as the H4 subtypes - pathogens not detected in humans - yet. This technology may well have widespread applications.

Next steps

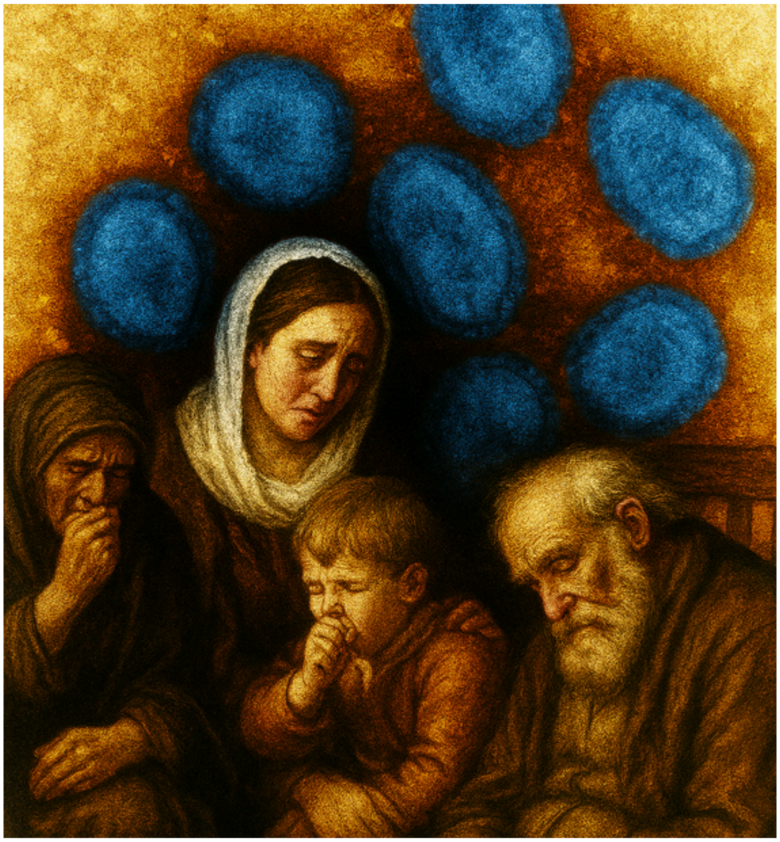
Future priorities for this approach would include expanding the database, especially with viruses that cause asymptomatic infections. The strength of this approach will be centred on the continuous routine screening for viruses by laboratories around the world. Waiting until a problem arises may be too late.

AI will become an important tool in the public health armoury. Despite the clear benefits reported in the study, machine learning can never offer a complete solution. The authors identified some limitations of the approach, which include ...

- Directionality - AI can only analyse samples taken at a single point in time- it cannot gauge the direction of viral spread.
- Modifications - the influenza virus, is subject to modification by its hosts which may affect its virulence and transmissibility. For example, the addition of sugar and phosphate molecules on the mature virus can alter its pathogenicity - a feature that AI would miss.

AI on the offense

This technology is not just an effective defence against viral threats. The information can be used on the offensive to protect us from circulating flu viruses too. The annual flu shot would benefit from the superior predictive power of AI over the traditional genetic approach. Looking beyond influenza, the technology could be readily adapted to other respiratory pathogens like the famous coronaviruses and the infamous common cold.



One thing is clear: as databases grow and protein structural predictions improve, the Brierley group's model could become the centrepiece in the ongoing battle between humanity and the microbial world.

Reference

Brierley L, Mould-Quevedo J, Baylis M. *An AI for an AI: identifying zoonotic potential of avian influenza viruses via genomic machine learning.* bioRxiv. Preprint posted Sep 16, 2025.