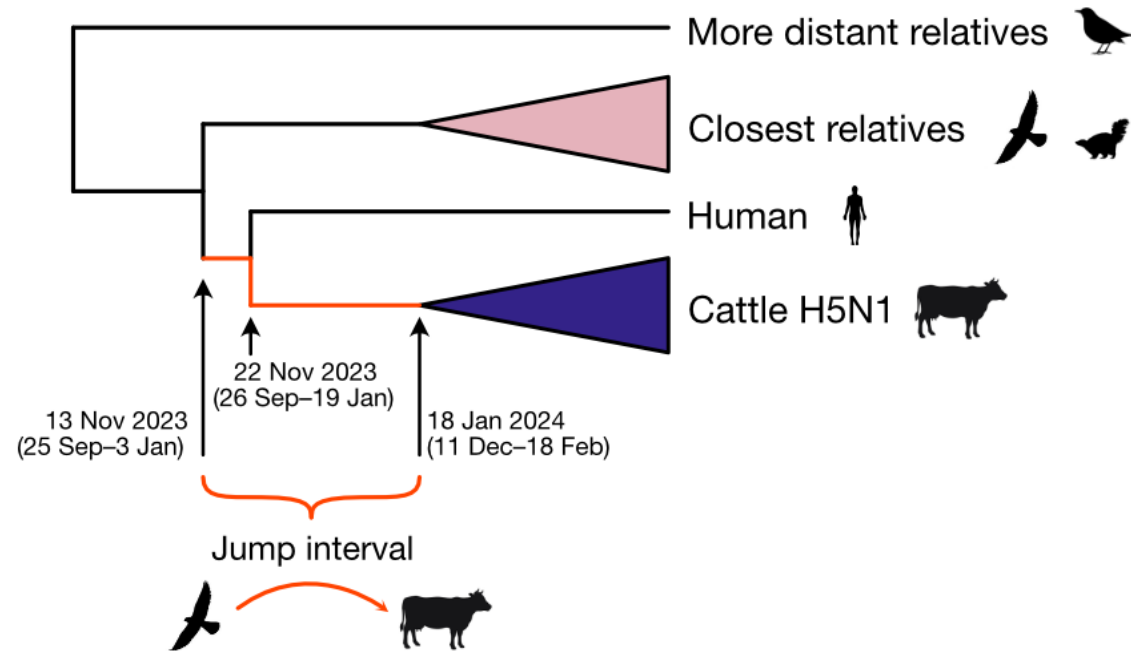


Predicting Human Infectivity of Influenza A Sequences Using Masked Language Modeling

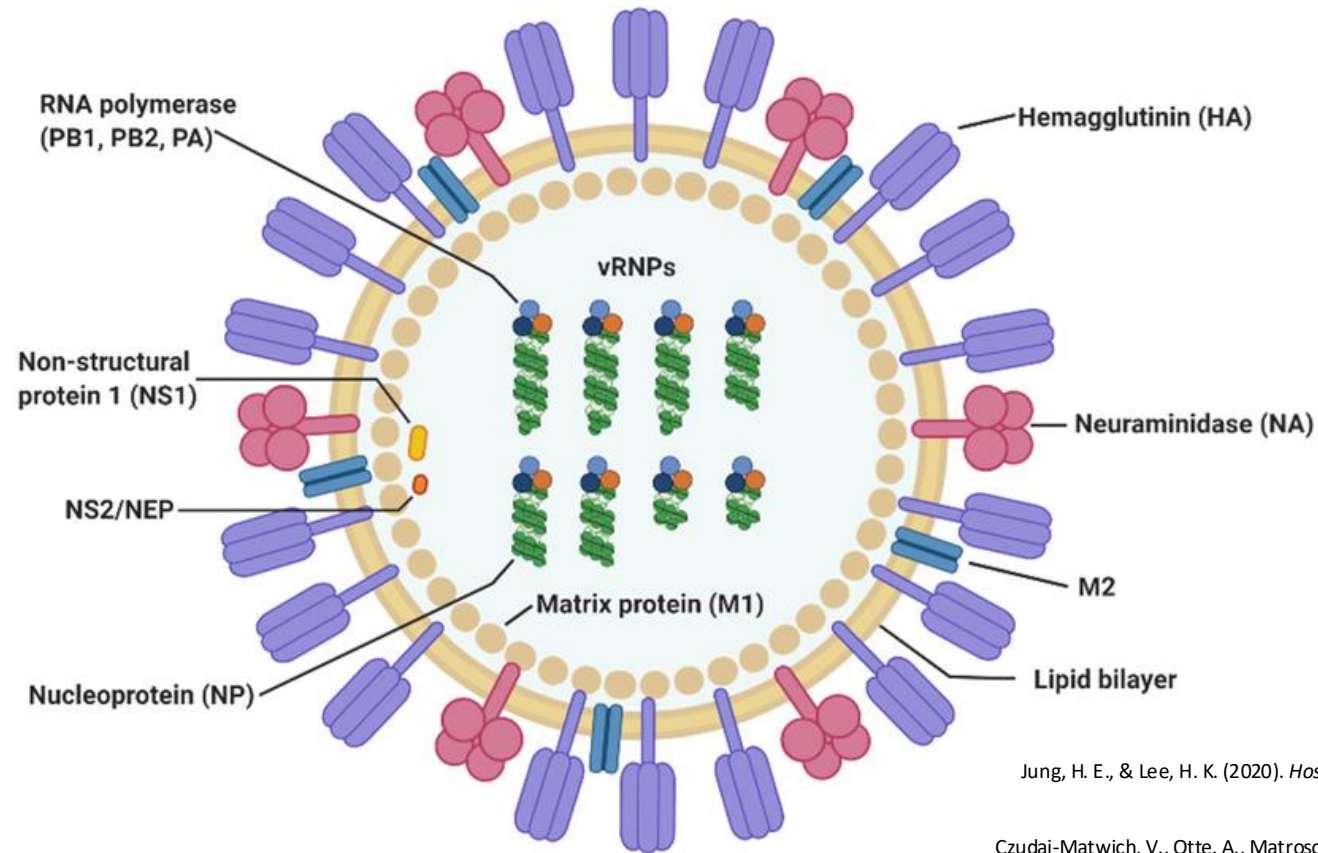
Vedant Hathalia; Praneeth Gangavarapu; Karthik Gangavarapu, PhD; Kristian Andersen, PhD

Avian Influenza is Adapting to Mammals



Worobey, M., Gangavarapu, K., Pekar, J. E., Joy, J. B., Monda, L., Kraemer, M. U. G., Dudas, G., Goldhill, D., Ruis, C., Malpica Serrano, L., Ji, X., Andersen, K. G., Wertheim, J. O., Lemey, P., Suchard, M. A., Rasmussen, A. L., Chand, M., Groves, N., Pybus, O. G., Peacock, T. P., Rambaut, A., & Nelson, M. I. (2024). *Preliminary report on genomic epidemiology of the 2024 H5N1 influenza A virus outbreak in U.S. cattle (Part 1)* [Report]. *Virological.org*.

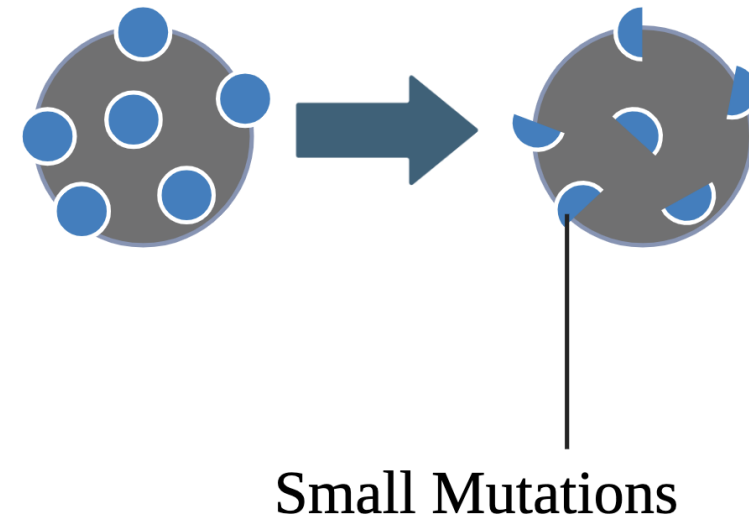
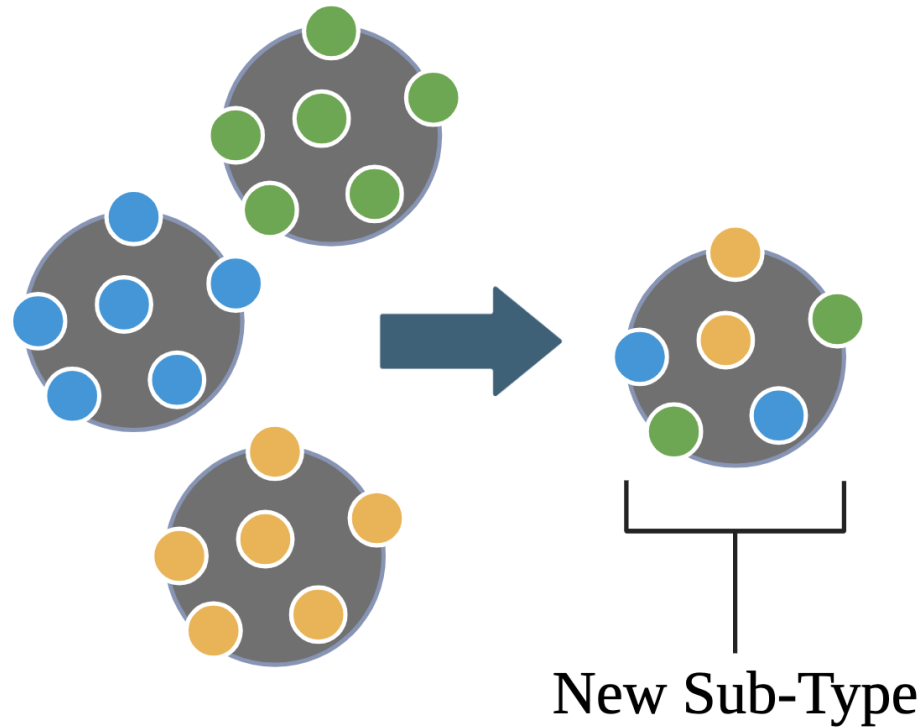
Segmented Genome Enables Complex Viral Strategy



Jung, H. E., & Lee, H. K. (2020). *Host protective immune responses against Influenza A virus infection* [Diagram]. *Viruses*, 12(5), 504. Retrieved July 16, 2025

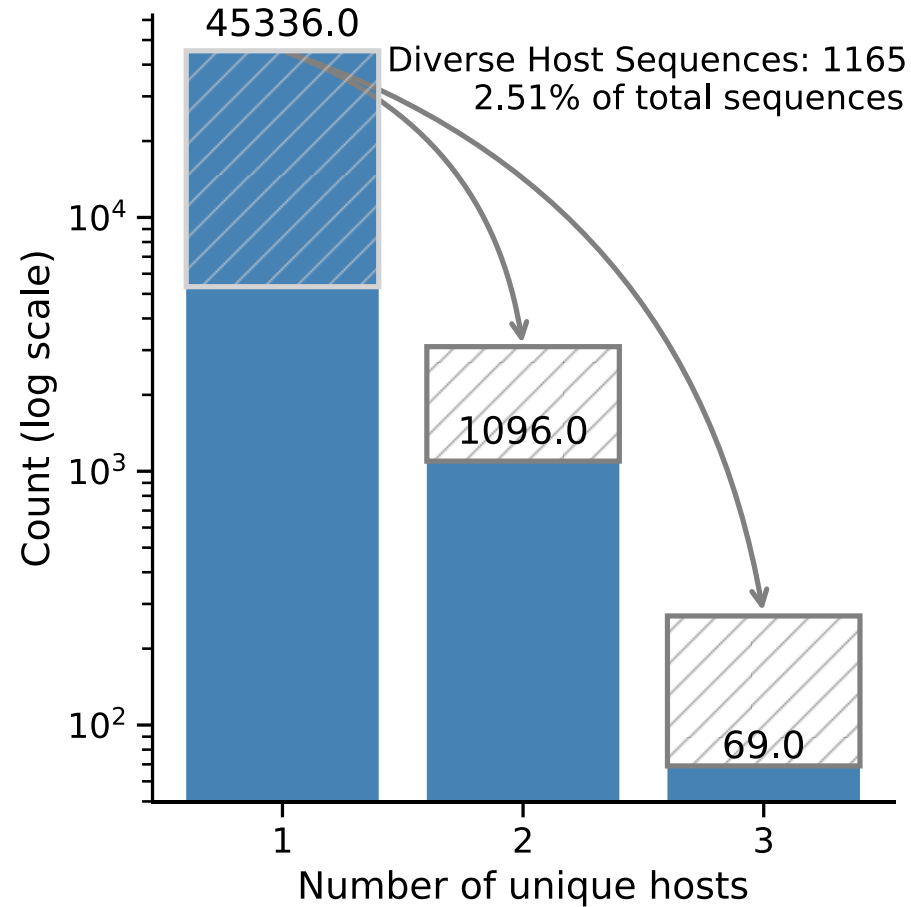
Czudai-Matwich, V., Otte, A., Matrosovich, M., Gabriel, G., & Klenk, H.-D. (2014). PB2 mutations D701N and S714R promote adaptation of an influenza H5N1 virus to a mammalian host. *Journal of Virology*, 88(16), 8735–8742.

Influenza Evolves Through Gradual Drift and Sudden Shift

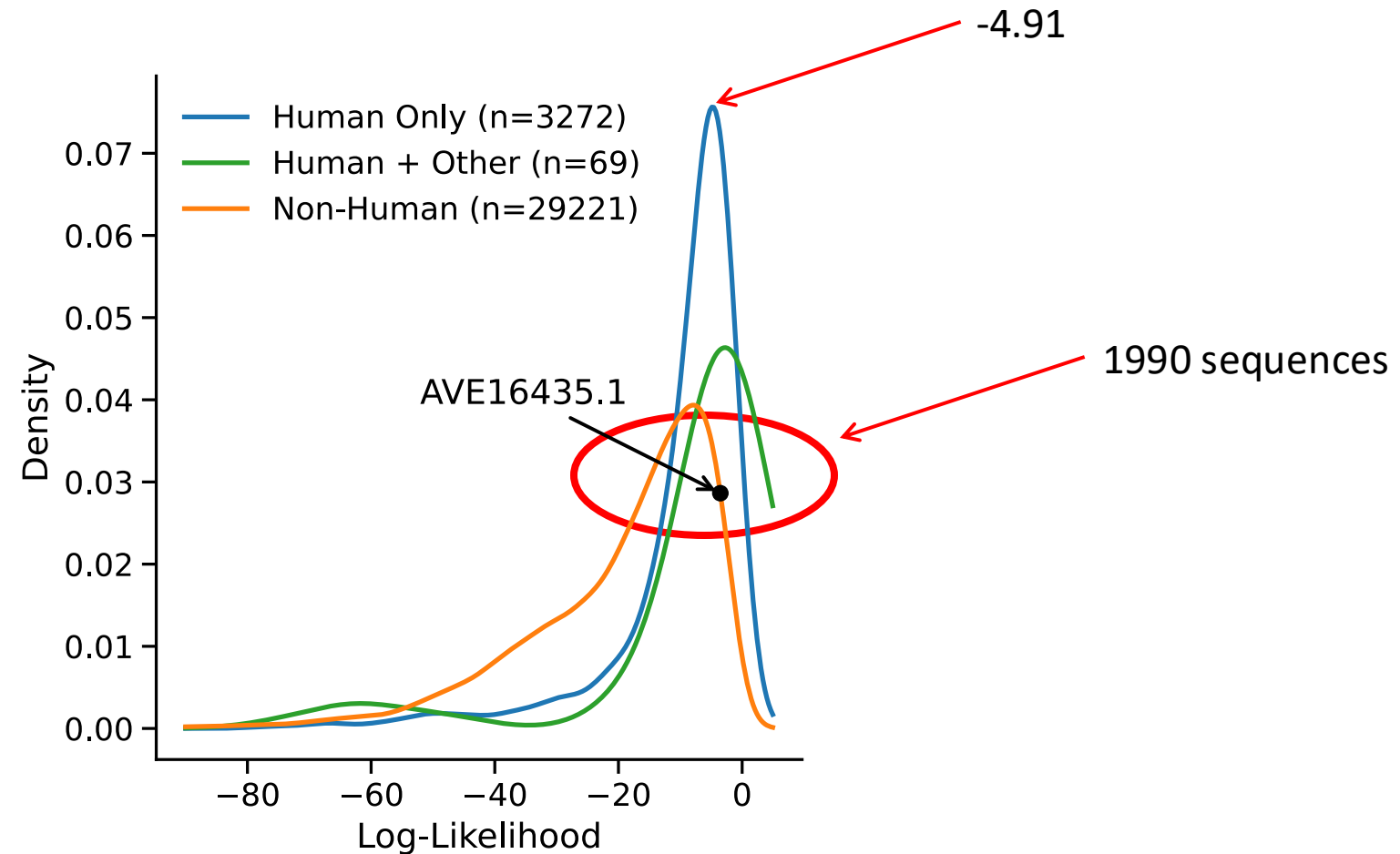


Aryal, S. (2022, August 10). *Antigenic shift and antigenic drift [Infographic]*. *MicrobiologyInfo*. Retrieved July 16, 2025.

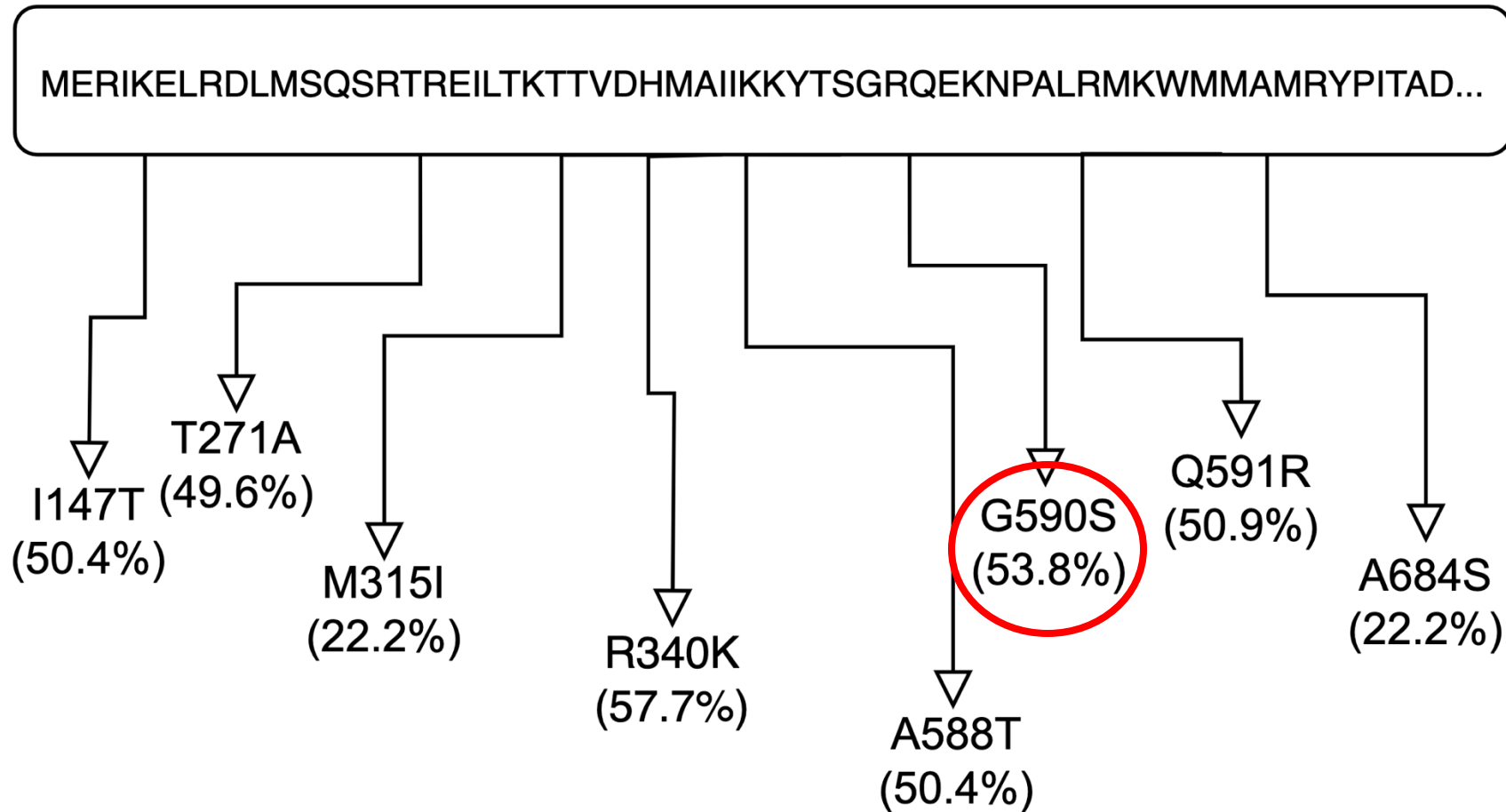
Sequences May Infect More Hosts than Detected



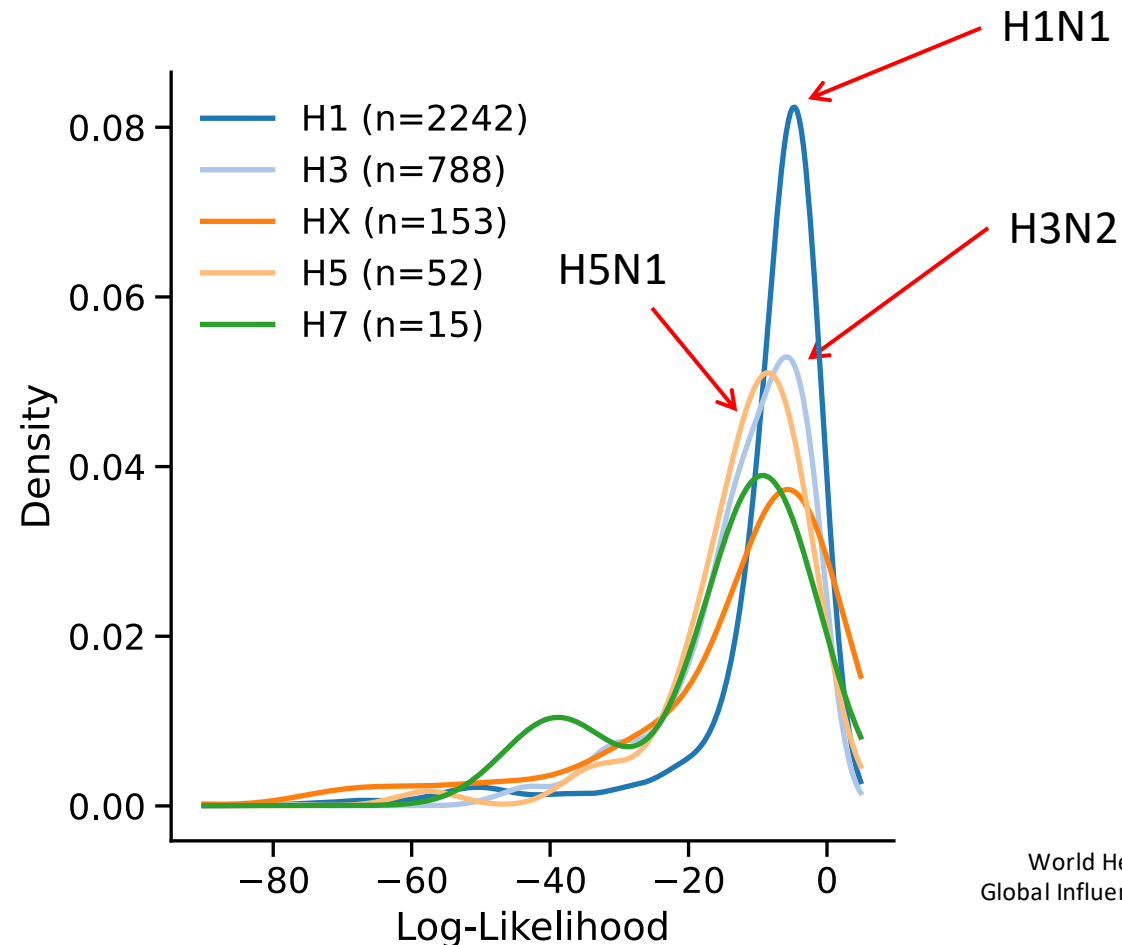
Non-human sequences with overlapping log-likelihoods may infect humans



Human Adaptive Mutations Found in Non-Human Sequences

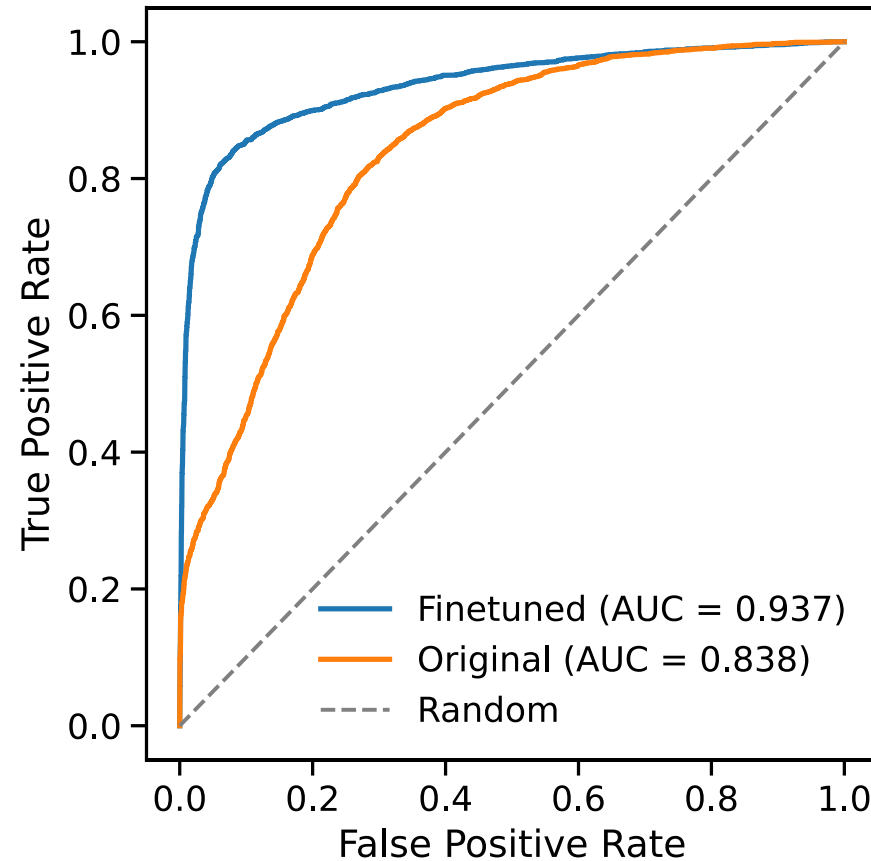


Less Seen HA Subtypes Perform Worse than Common Human-Infecting Subtypes



World Health Organization. (2025, July). *Influenza update N° 535*. WHO Global Influenza Surveillance and Response System. Retrieved July 16, 2025

Model Better Distinguishes Human-Infecting Sequences through Fine-Tuning



Future Directions



- Train on segments besides PB2
- Causal LM
- Longer Sequence Length
- Nucleotides

References

- 1) Worobey, M., Gangavarapu, K., Pekar, J. E., Joy, J. B., Moncla, L., Kraemer, M. U. G., Dudas, G., Goldhill, D., Ruis, C., Malpica Serrano, L., Ji, X., Andersen, K. G., Wertheim, J. O., Lemey, P., Suchard, M. A., Rasmussen, A. L., Chand, M., Groves, N., Pybus, O. G., Peacock, T. P., Rambaut, A., & Nelson, M. I. (2024). *Preliminary report on genomic epidemiology of the 2024 H5N1 influenza A virus outbreak in U.S. cattle (Part 1)* [Report]. *Virological.org*.
- 2) Jung, H. E., & Lee, H. K. (2020). *Host protective immune responses against Influenza A virus infection* [Diagram]. *Viruses*, 12(5), 504. Retrieved July 16, 2025
- 3) Czudai-Matwich, V., Otte, A., Matrosovich, M., Gabriel, G., & Klenk, H.-D. (2014). PB2 mutations D701N and S714R promote adaptation of an influenza H5N1 virus to a mammalian host. *Journal of Virology*, 88(16), 8735–8742.
- 4) Aryal, S. (2022, August 10). *Antigenic shift and antigenic drift* [Infographic]. *MicrobiologyInfo*. Retrieved July 16, 2025.
- 5) World Health Organization. (2025, July). *Influenza update N° 535*. WHO Global Influenza Surveillance and Response System. Retrieved July 16, 2025