

## **PATHOGEN PHYLODYNAMICS, PHYLOGEOGRAPHY AND VIRAL FITNESS IN MULTI-HOST AND MULTI-STRAIN SYSTEMS**

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Pathogen genomes collected from populations over months or several years can be used in phylodynamic and phylogeographic models to infer viral effective population sizes over time and spatial or between host transmission patterns. To illustrate how sequence data and models can provide insight into epidemic situations involving complex systems of multiple host species, I will describe recent work on the highly pathogenic avian influenza global epizootic using time-resolved Bayesian phylogenies.

Highly Pathogenic Avian Influenza H5N1 (clade 2.3.4.4b) is responsible for major outbreaks in poultry and wild birds in recent years. Phylogenetic analyses shows that the virus has undergone additional reassortments with internal protein coding segments from other co-circulating low pathogenic strains, and we track the intercontinental spread from Europe to the Americas using continuous space phylogeographic diffusion models.

To predict which strains may become dominant, the fitnesses of different reassortments in host species strata were estimated as a function of time from the trees using a local branching index. There have also been multiple spill-overs into mammals in both Europe and the Americas, and very unusually for Influenza A, this has also resulted in outbreaks in dairy cattle in multiple States of the USA. Work is ongoing to understand how these spill overs occurred and genomic signatures predictive of spill over risk and mammal adaptation. To conclude I will discuss how mutational signatures and drivers of spread such as wild bird movements and environmental spatial data can be used as predictors for future outbreaks.