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Using Avian Influenza genome sequences to infer the spatial-temporal spread of zoonotic H5N1 and H7N9 viruses in China

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Social media: using #phylogeography to estimate routes of #H5N1 #H7N9 transmission in China

INTRODUCTION

Avian influenza viruses H5N1 and H7N9 can infect humans and cause severe disease and fatalities. H5N1 has spread globally, however the incidence of H7N9 has been largely limited to mainland China. Understanding how these viruses spread across China is important for developing targeted control measures. The poultry production and marketing system in China consists of a complex network made up of traditional farming systems mixed with commercial operations. Live bird movements along broiler and layer poultry supply chains (breeding, hatching, fattening, feeding, slaughter, wholesale and retail markets) is considered to be too complex to be characterised on both national and provincial scales. We aim to characterize the spatial-temporal spread of H5N1 and H7N9 in China using sequence data.

METHODS

H5N1 and H7N9 virus sequences from China, from 1996 to 2016, were downloaded from the Global Initiative on Sharing All Influenza Data. Only sequences annotated with a spatially disaggregate location were used. Phylogenetic trees were inferred using the Bayesian Markov chain Monte Carlo (MCMC) approach. We used a relaxed uncorrelated log normal molecular clock, a flexible Bayesian Skygrid coalescent demographic model, and the Hasegawa-Kishino-Yano model of nucleotide substitution with gamma-distributed rate variation among sites (with four rate categories). A MCMC method to sample trees and evolutionary parameters was run for 10^8 generations (with 10% burn-in) with subsampling every 10^4 iterations. Convergence was assessed by high ESS values using Tracer v1.6. For each virus, we obtained a total of 1,000 trees from which the maximum clade credibility tree was summarized in TreeAnnotator v1.8.3.

RESULTS

We used 170 hemagglutinin (HA) H5N1 sequences and 339 HA H7N9 sequences for separate phylogeography model construction. H5N1 sequences showed more sequence diversity, with H5N1 sequences having 953 identical sites (54.1%) and pairwise identity of 93.9%, whereas H7N9 sequences had 1,299 identical sites (74.6%) and pairwise identity of 98.9%. We developed dynamic visual representations of the spatial-temporal spread of H5N1 and H7N9 in China (**Figure 1**).

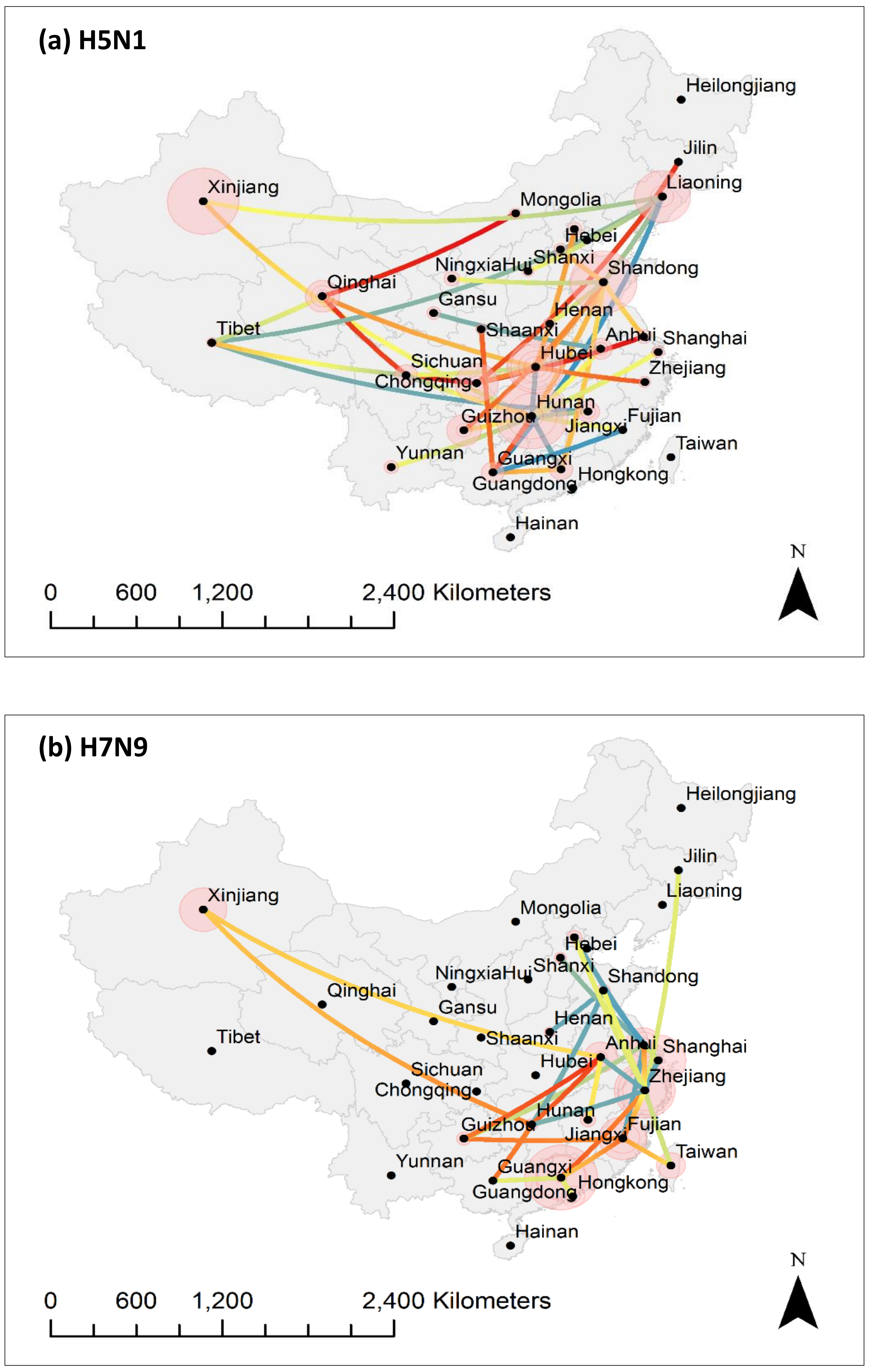

Figure 1. **Representation of H5N1 and H7N9 transmission routes in China**

Panel (a) represents H5N1. Panel (b) represents H7N9. Lines represent likely transmission routes, and line colours represent graded date variations from blue to yellow to red. For H5N1, the dates range from 2000 to 2015, and for H7N9 from 2013 to 2015. The size of the red circles around each province is proportional to the number of lineages that are maintained in that location. Base maps were obtained from the database of Global Administrative Areas. Maps were built using ArcMap 10.2, Beast packages and SpreaD3.

CONCLUSION

This network inferred using Bayesian phylogeography methods can be used to identify important routes to target surveillance and control measures, or used in further modelling applications such as network SIR models. A more complete poultry trading network can be developed by incorporating phylogeography models of other major circulating avian influenza viruses (such as H9N2, H5N6), as well as information on poultry production and sales, major transportation routes, as well as population data.