INTERDISCIPLINARY QUICK TALKS

Open Data Open Possibilities

Open Genomic Data for Studying Infectious Diseases

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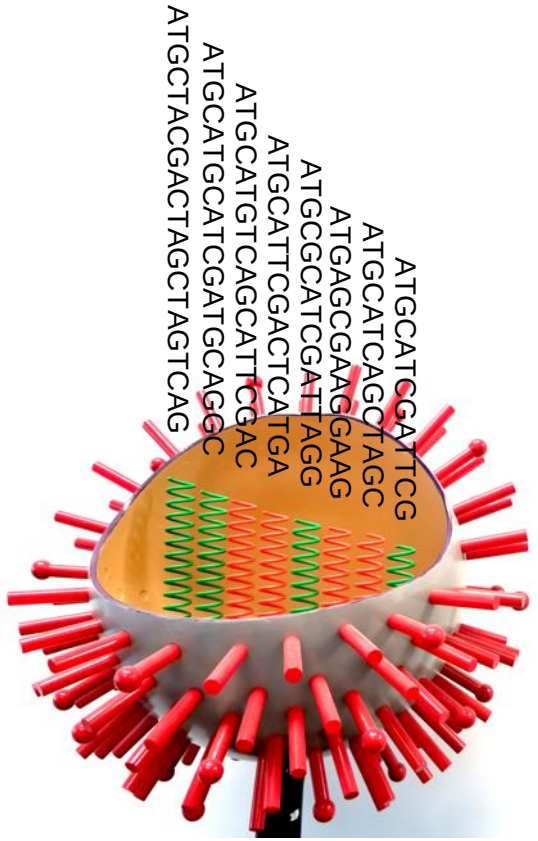
Pathogen genomes for disease investigation

INTERDISCIPLINARY QUICK TALKS

Diagnosis	Precise pathogen identity, genotype, recombinant/reassortant
Predicting phenotype	Predict virulence, pathogenicity, transmissibility
Response to treatment	Antiviral drug resistance, vaccine escape, antimicrobial resistance
Source of infection	Human or animal origin, time and location of source
Transmission / epidemiology	Spatial dissemination pattern, outbreaks linkage, infected population size, transmission drivers

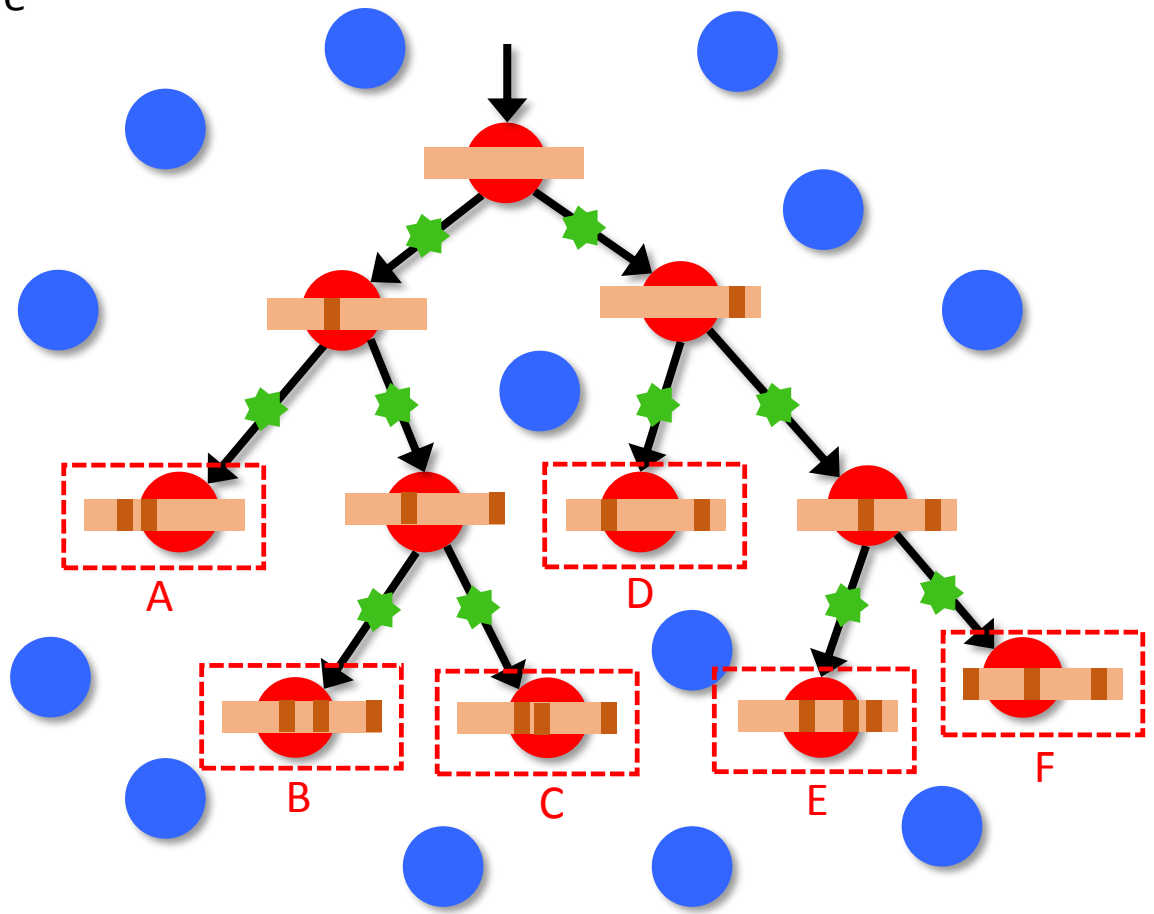


Transmission Imprinted in Pathogen Genome

Susceptible

Infected

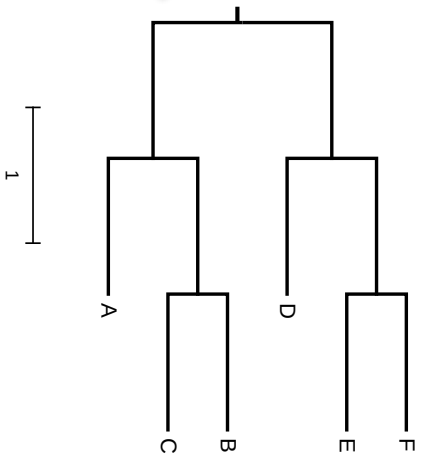
Sampled

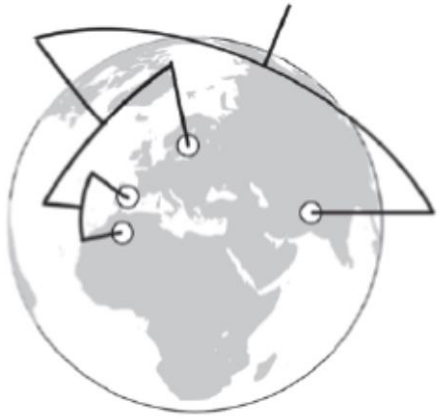


Pathogen genome sequences:

```
A|  AATTAAAAAAA
B|  ATATAAAAAAT
C|  AAATTAAAAAT
D|  AAAAATAATAA
E|  AAAAAATTTAA
F|  TAAAAATATAA
```

Build a **phylogenetic tree**





Pathogen & its genome

Mutation

Transmission history ≈ Evolutionary history

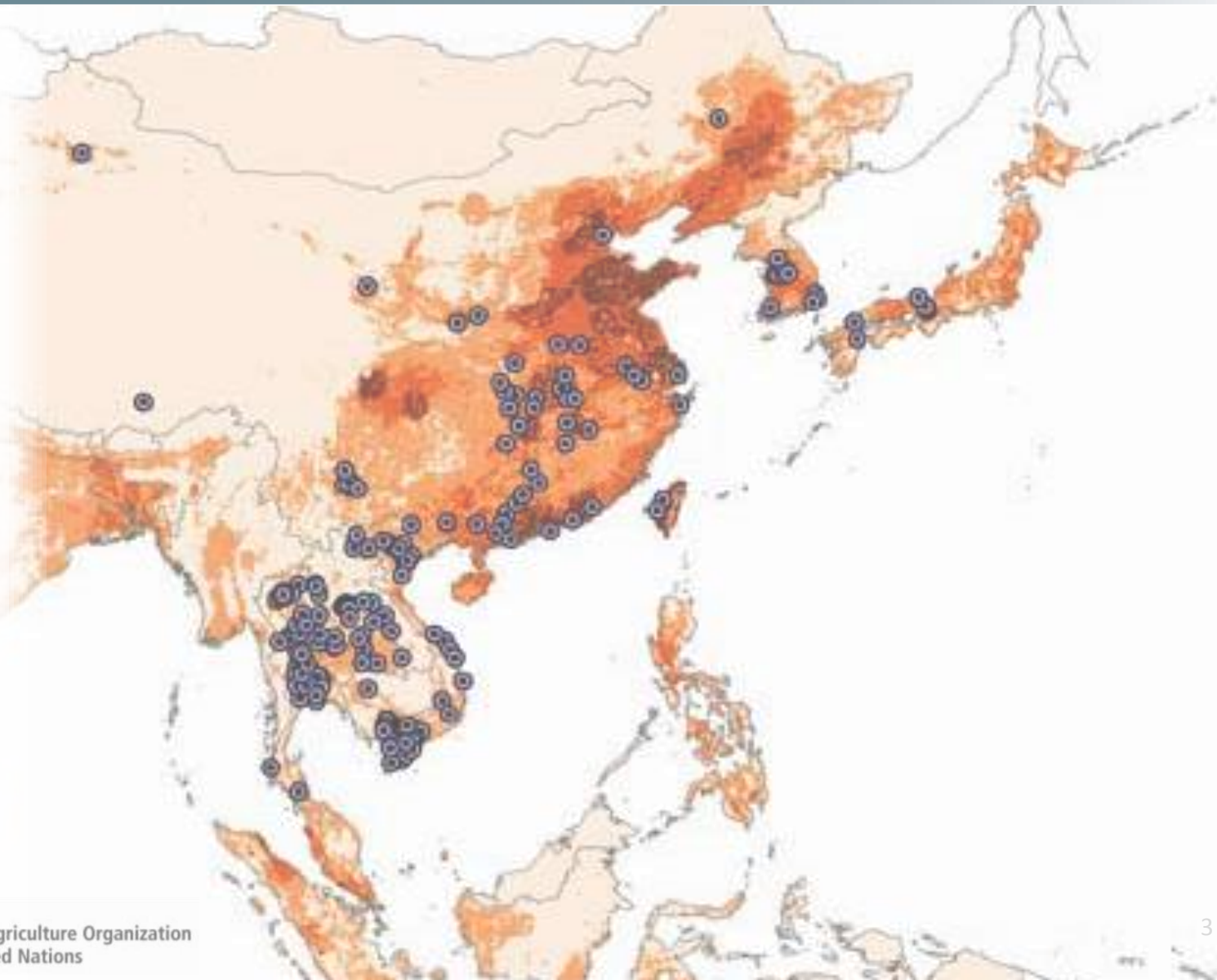
Spatial spread of infectious disease

Data: disease reports – geospatial data

Analysis methods:

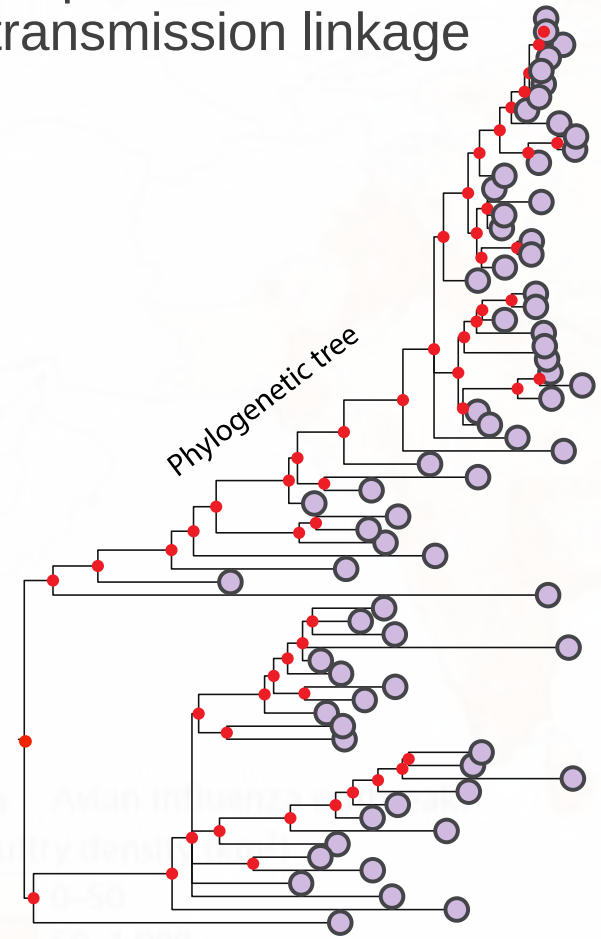
- Spatial clustering (Moran's I, Geary's c, Ripley's K, EMM, etc)
- Risk factor modeling (regression, discriminant analyses)
- Simulation (spatial-epidemic models)

Empirical evidence of transmission linkage between infections



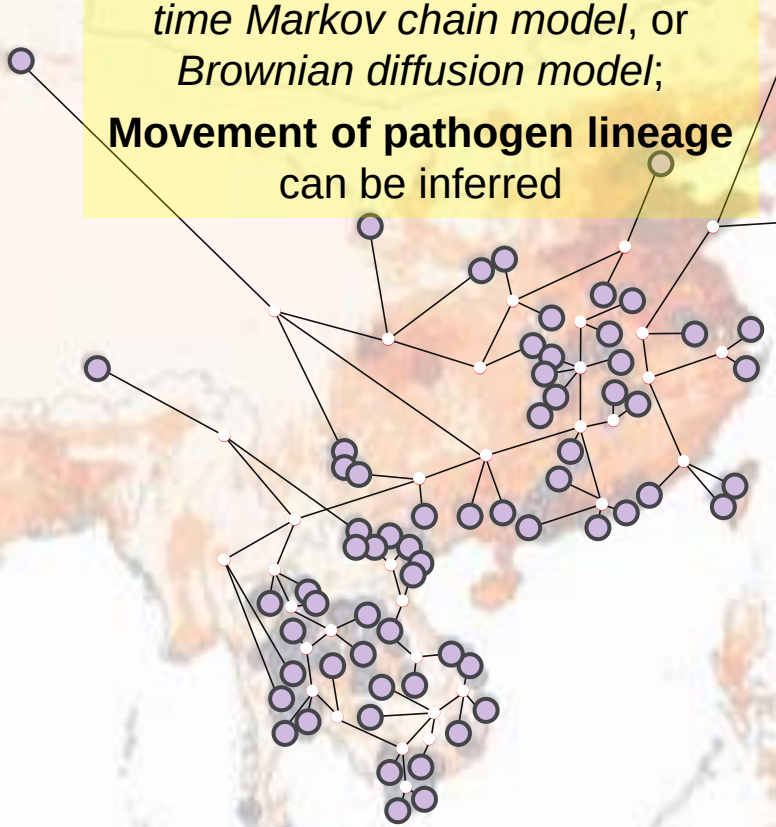
Phylogeographic inference

Phylogenetic tree provides empirical evidence of transmission linkage



Ancestral geographic locations are estimated with *continuous-time Markov chain model*, or *Brownian diffusion model*;

Movement of pathogen lineage can be inferred



Lemmon et al. Syst. Biol (2008)57

$$\delta_i = 2\,R \arcsin \times \left[\sqrt{\sin^2\left(\frac{\phi_k^r-\phi_j^r}{2}\right)+\cos(\phi_j^r)\cos(\phi_k^r)\sin^2\left(\frac{\lambda_k^r-\lambda_j^r}{2}\right)}\right],$$

$$L(\phi_e, \lambda_e, \psi|\phi_o, \lambda_o) = \prod\left(\frac{\delta_i}{b_i\psi^2}e^{-\delta_i^2/(2b_i\psi^2)}\right)$$

$$\frac{\partial}{\partial\psi}L(\phi_e, \lambda_e, \psi|\phi_o, \lambda_o) = \frac{(\xi-2)e^{-\frac{1}{2}\xi}}{\psi^{2n+1}}\prod\frac{\delta_i}{b_i}$$

Lemey et al. MBE (2010)27:8

$$f(g,\Theta,\Phi,\Omega|D) = \frac{1}{Z}\Pr\{D|g,\Phi,\Omega\}f_G(g|\Theta)f_{\Theta\Omega\Phi}(\Theta,\Omega,\Phi).$$

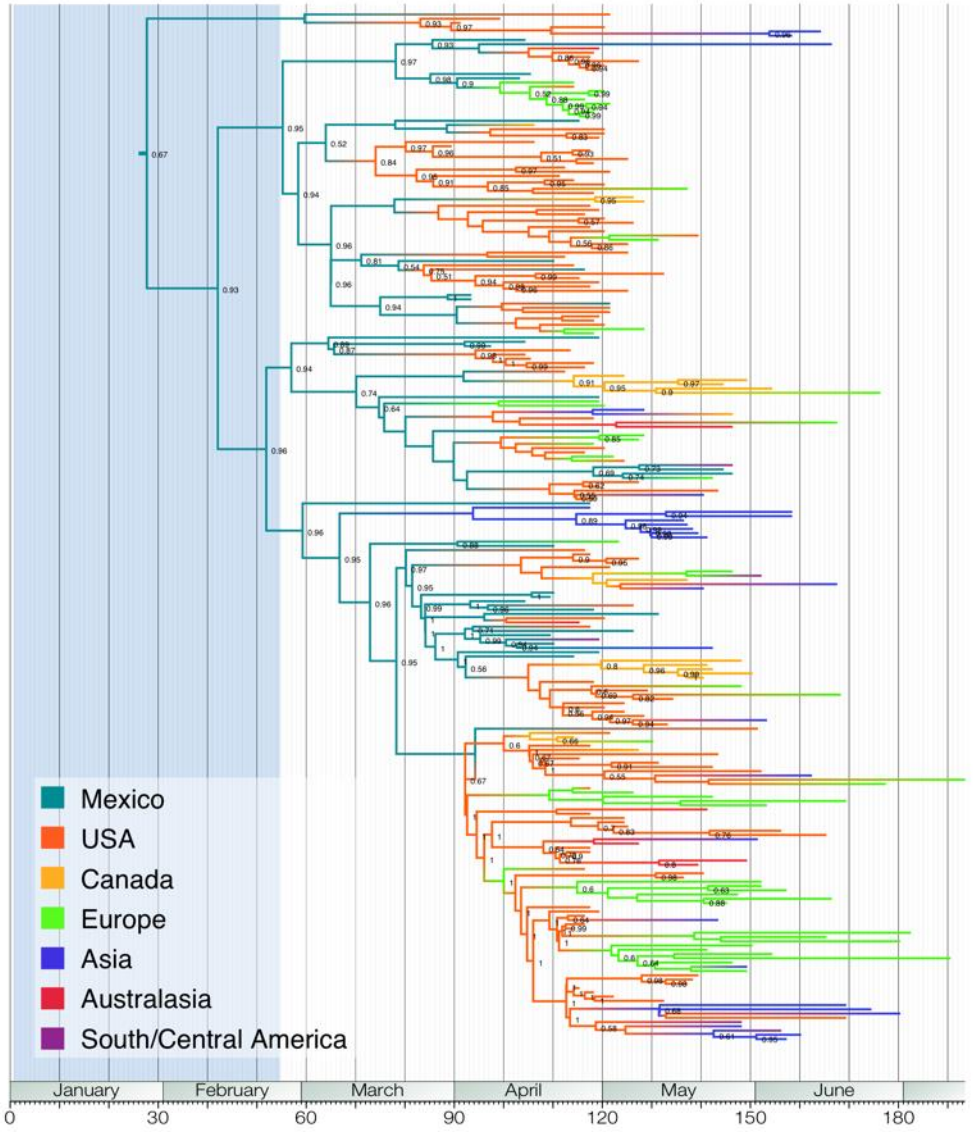
$$\phi_b \overset{\text{i.i.d.}}{\sim} \text{Gamma}(\nu/2,\nu/2)$$

$$\phi_b \overset{\text{i.i.d.}}{\sim} \text{Lognormal}(1,\sigma),$$

Pandemic (H1N1) 2009 influenza

- A **novel** influenza A (H1N1) infection started in **California, 15th April 2009**
- Soon **spread to the world** within months
- Many **virological labs** sequenced the viruses, and deposited to **public databases**
- Analyzed the disease emergence and spread using **242 open viral sequences** (40 locations; Mar-Jul 2009), with **geographic labels**; using *relaxed molecular clock models* and *discrete continuous-time Markov chain* as the spatial diffusion model
- Need **bioinformatics specialist**

Lemey et al. PLoS Currents Influenza. (2009) doi: 10.1371/currents.RRN1031



Pandemic (H1N1) 2009 influenza

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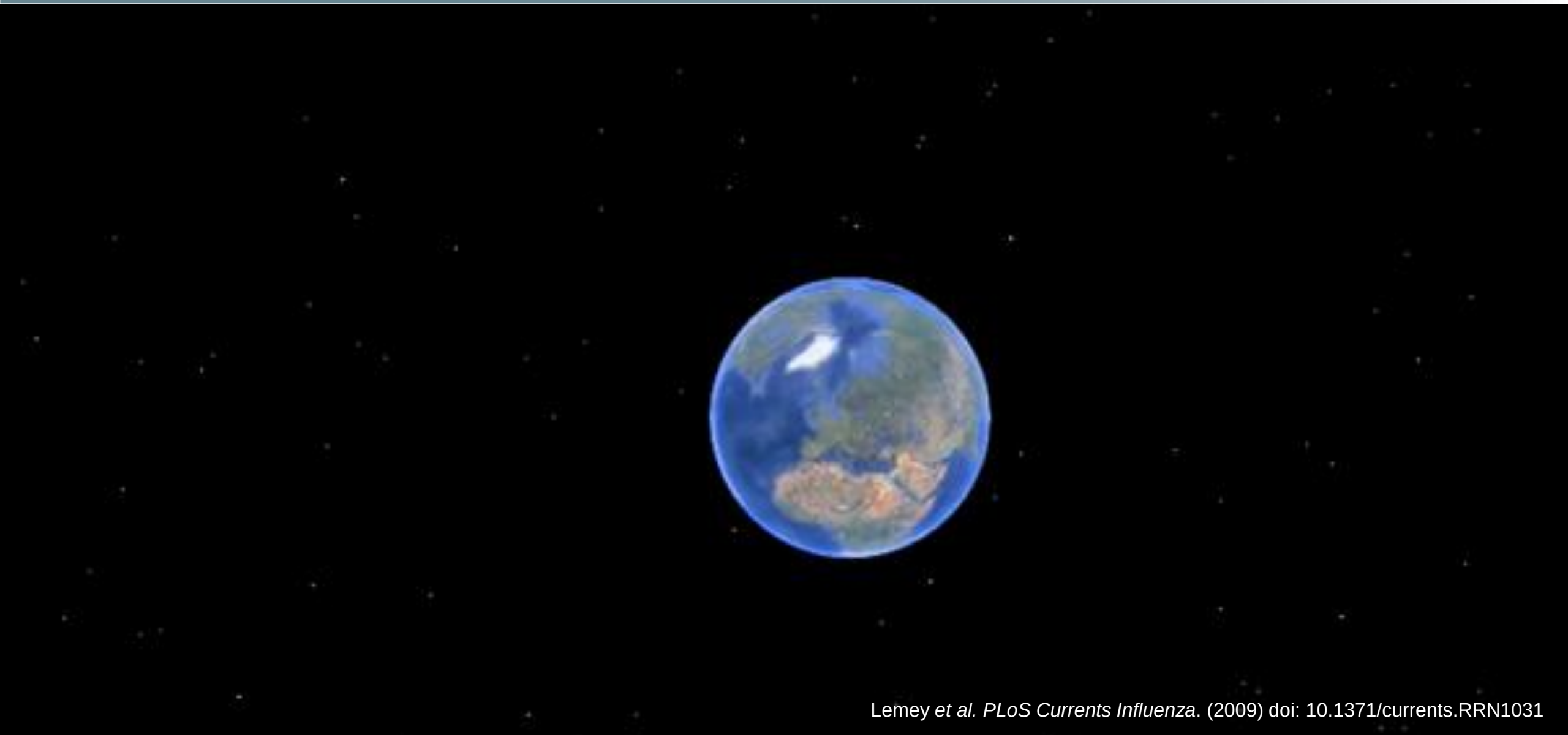
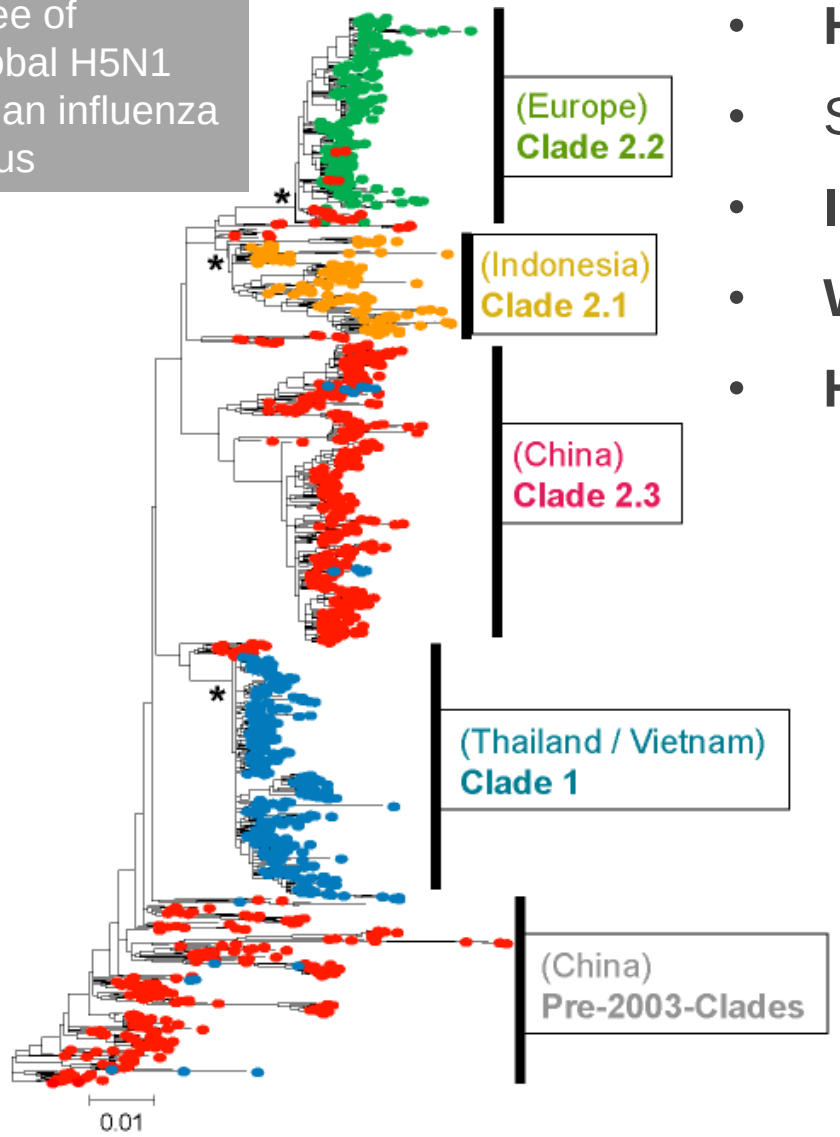


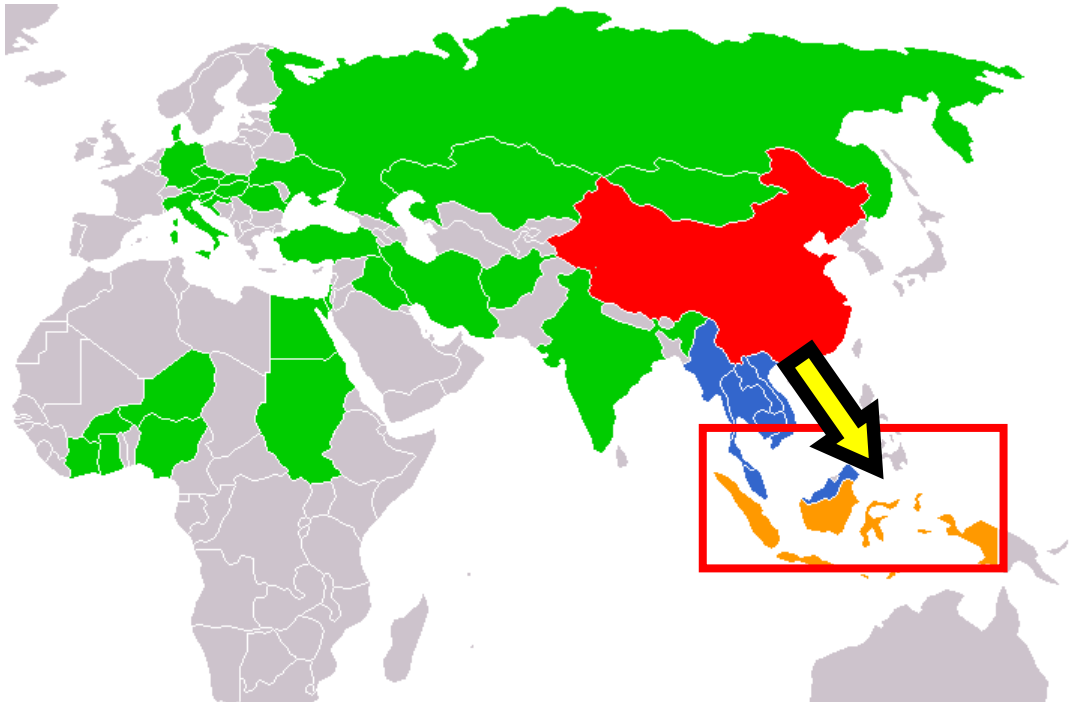
Lemey *et al. PLoS Currents Influenza*. (2009) doi: 10.1371/currents.RRN1031

Avian influenza (H5N1)

Tree of global H5N1 avian influenza virus



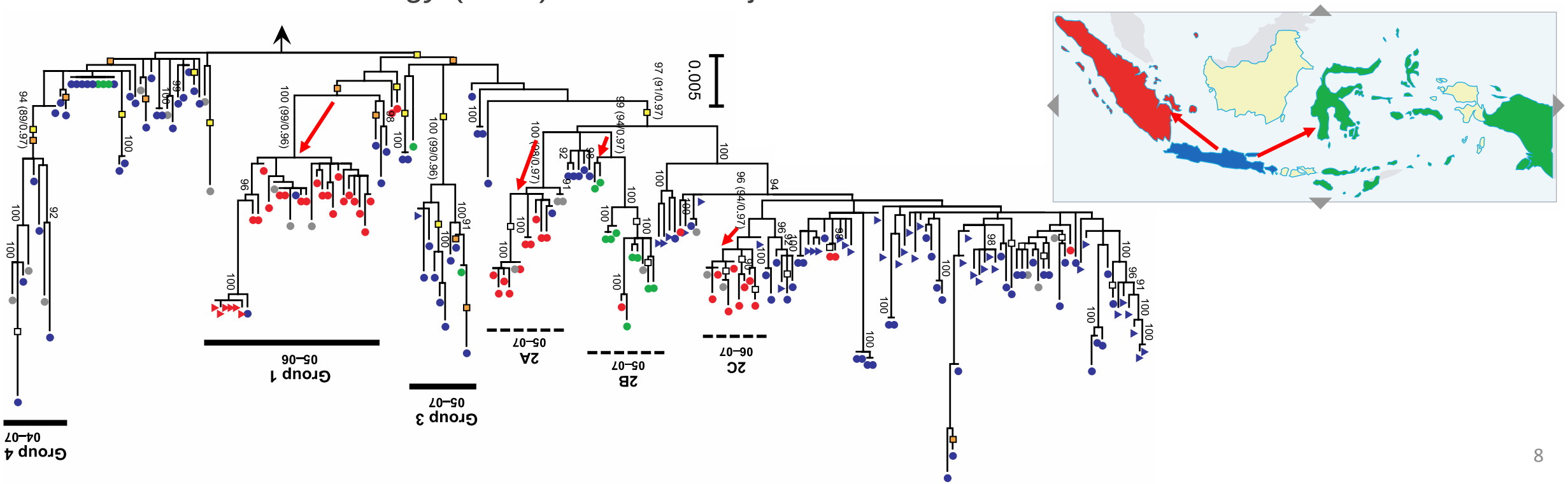
- **H5N1 highly pathogenic avian influenza** emerged in China, 1996.
- Spread to **Southeast Asia, including Indonesia** in 2003.
- **Indonesia** - caused big economic and health burden
- **Where** was it first introduced?
- **How** did it spread across the Indonesian islands?



Avian influenza (H5N1) - Indonesia

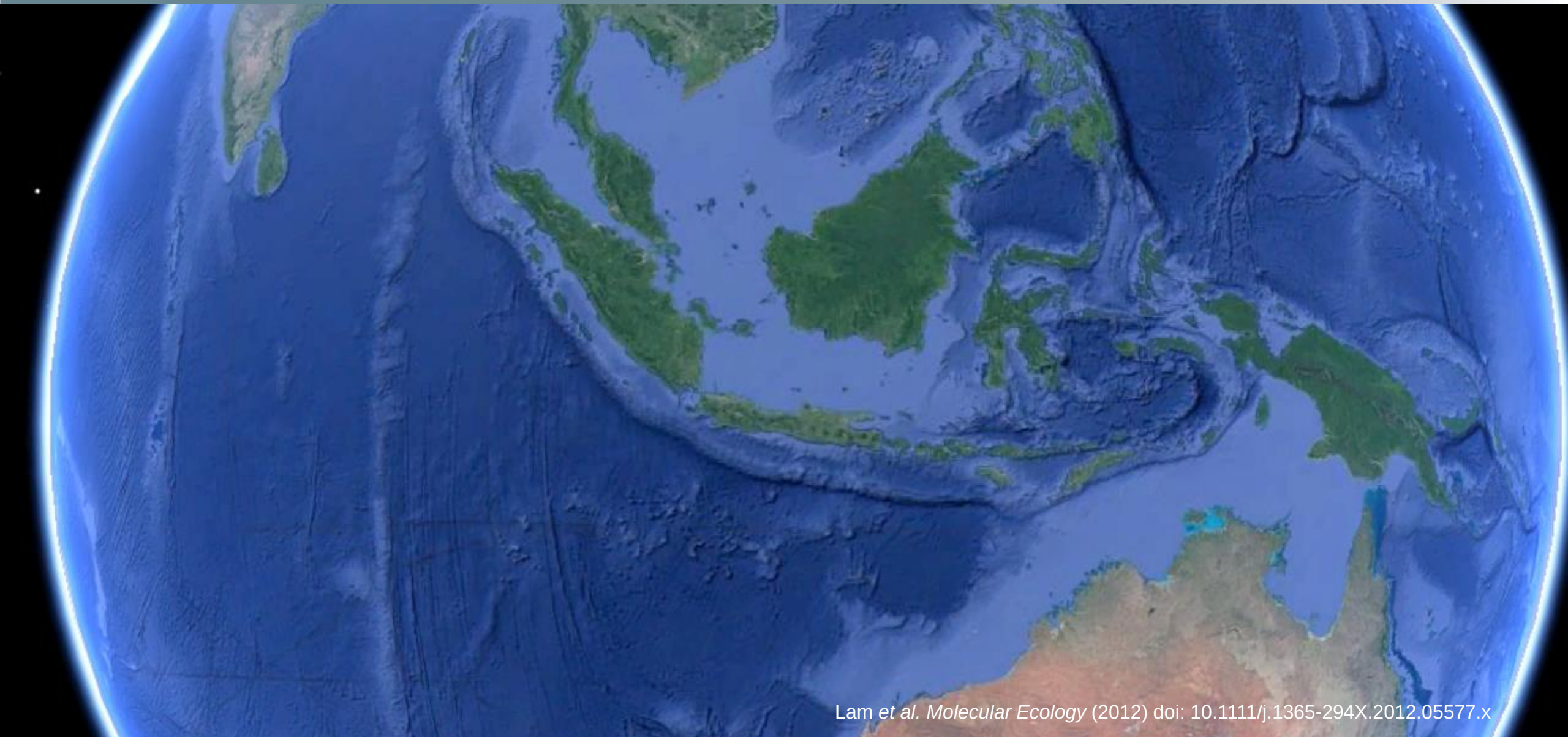
- Analyzed **213** open Indonesian H5N1 avian influenza gene sequences, with time and location information
- Introduced to **Java Island** and spread to other islands
- How did it **spread inside** Java Island?

Lam *et al. Molecular Ecology* (2012) doi: 10.1111/j.1365-294X.2012.05577.x



Avian influenza (H5N1) - Indonesia

INTERDISCIPLINARY QUICK TALKS



Lam *et al. Molecular Ecology* (2012) doi: 10.1111/j.1365-294X.2012.05577.x

Benefits of Open Genomic Data

- Encourage **Multidisciplinary** Collaboration, **Full Use** of Data
  - Microbiologist and Bioinformatician
- Allow **Massive Analyses**
  - First Swine Flu genome released on 24th April 2009, many analyses published in personal blogs
- Increase **Completeness** in Analyses
  - Genetic data from every region are important for powerful analytics and interpretations

More Insights, Better Prevention & Control, Healthier City

Open Genomic Data for Hong Kong

- There were pathogen genome sequences published by HK Gov Labs (e.g. influenza, norovirus) - Are all data open?
- Time is key for infectious disease control and prevention
- Less / solvable privacy issue for pathogen data
- E.g. Dengue virus genome sequences
  - Determine local transmission or foreign introductions
  - Source of introductions
  - Time of local transmission started

Links to Further Information

Analysis on open *Swine Flu* genome data:

- Lemey *et al.* PLoS Currents Influenza. (2009) http://currents.plos.org/influenza/index.html%3Fp=4725.html

Analysis on open Indonesian *Avian Flu* genome data:

- Lam *et al.* PLoS Pathogen (2008) 4 https://journals.plos.org/plospathogens/article?id=10.1371/journal.ppat.1000130
- Lam *et al.* Molecular Ecology (2012) 12 https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1365-294X.2012.05577.x

Figure Credits

- Slide#2: https://www.cell.com/trends/ecology-evolution/pdf/S0169-5347(11)00354-5.pdf
- Slide#3,4: http://www.fao.org/docrep/007/y5537e/y5537e03.htm

THANK YOU