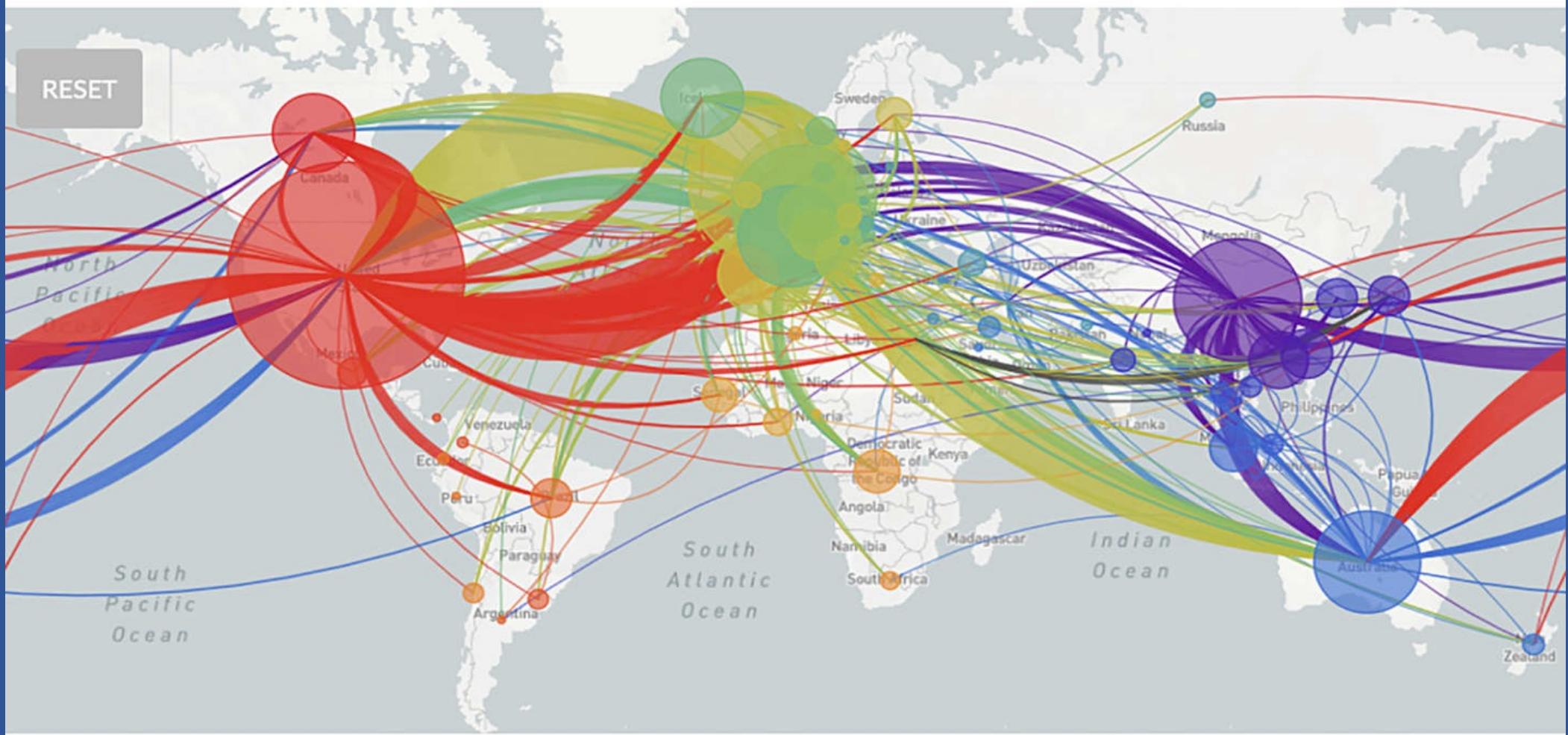


Phyldynamics



Phyldynamics

What can phylogenetic patterns reveal about the underlying population processes?

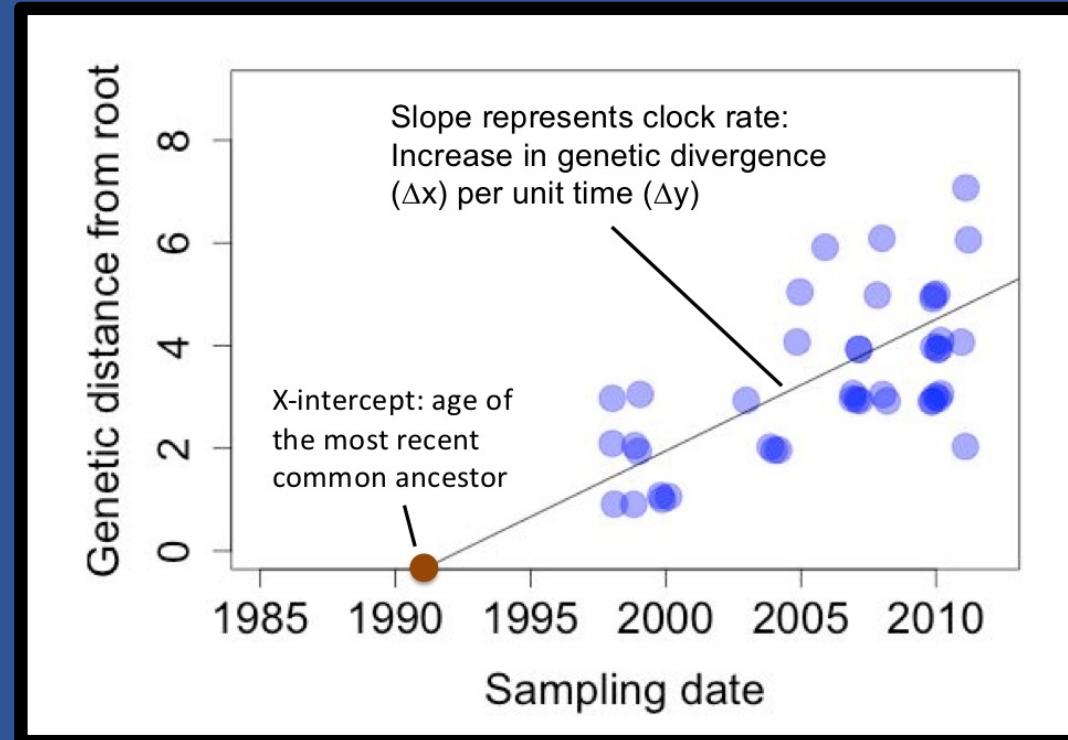
REVIEW

Unifying the Epidemiological and Evolutionary Dynamics of Pathogens

Bryan T. Grenfell,^{1*} Oliver G. Pybus,² Julia R. Gog,¹ James L. N. Wood,³ Janet M. Daly,³ Jenny A. Mumford,³ Edward C. Holmes²

Phyldynamics

- Linking epidemiology with pathogen evolution
- RNA viruses have rapid evolutionary rates



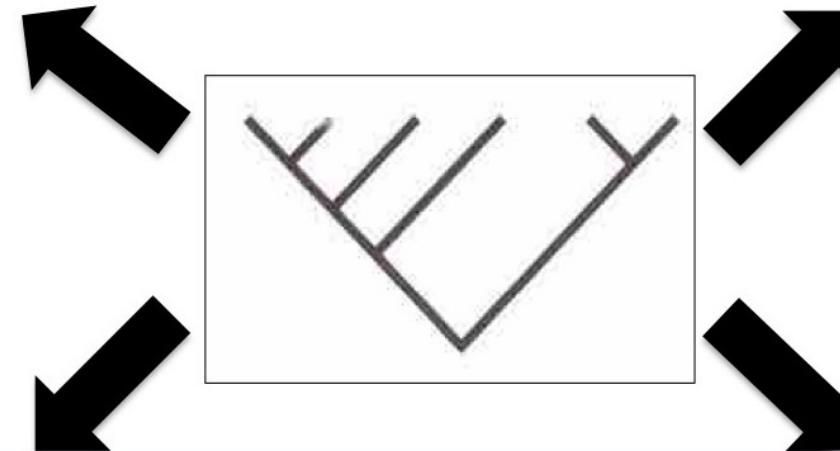
Phylogenies at the center of phylodynamic questions

Molecular clocks

e.g. “*How long ago since two groups split?*”

Selection

e.g. “*Which genes or sites have undergone adaptive change?*”



Ancestral state change

e.g. “*Movement rate between population A and B?*”

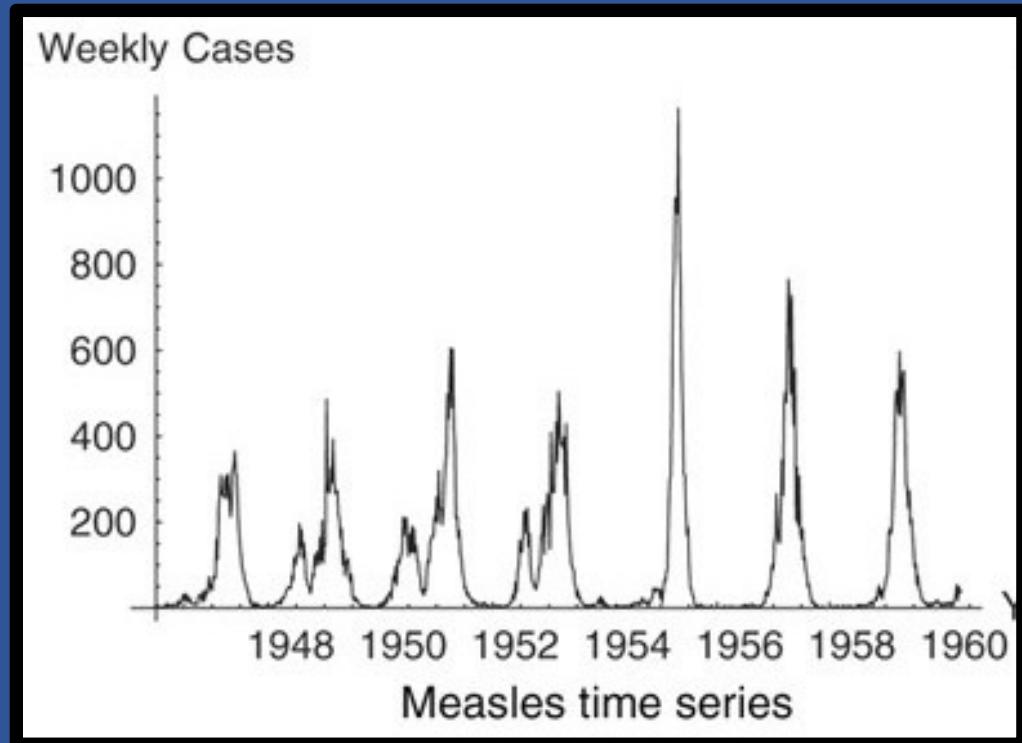
Demographic reconstruction

e.g. “*How has population size changed through time?*”

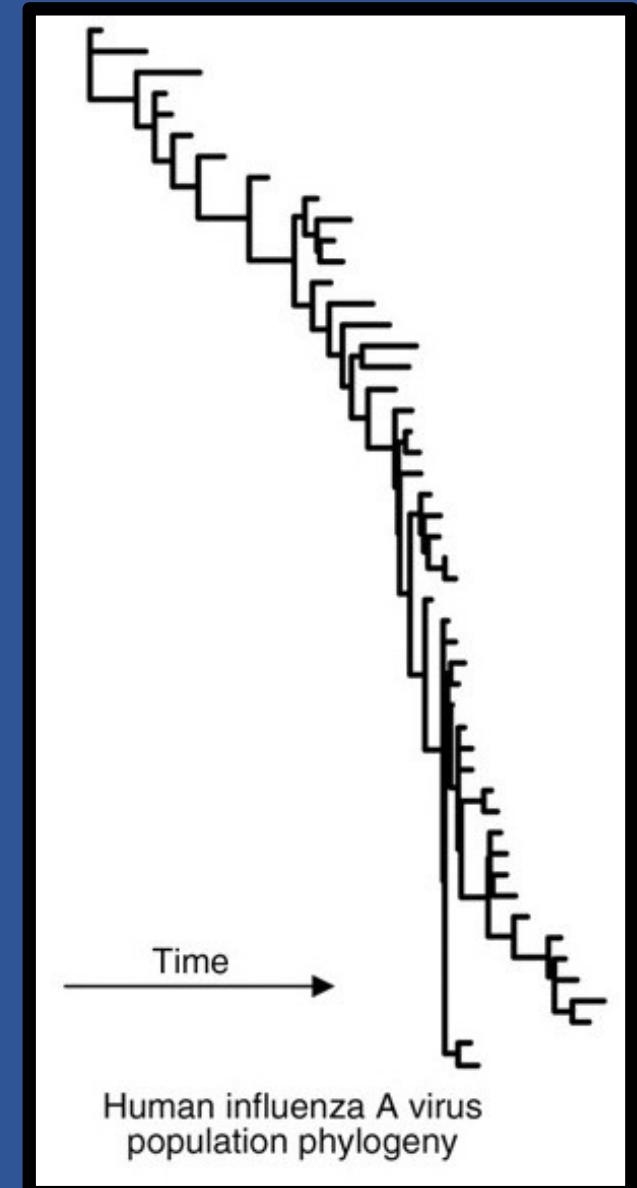
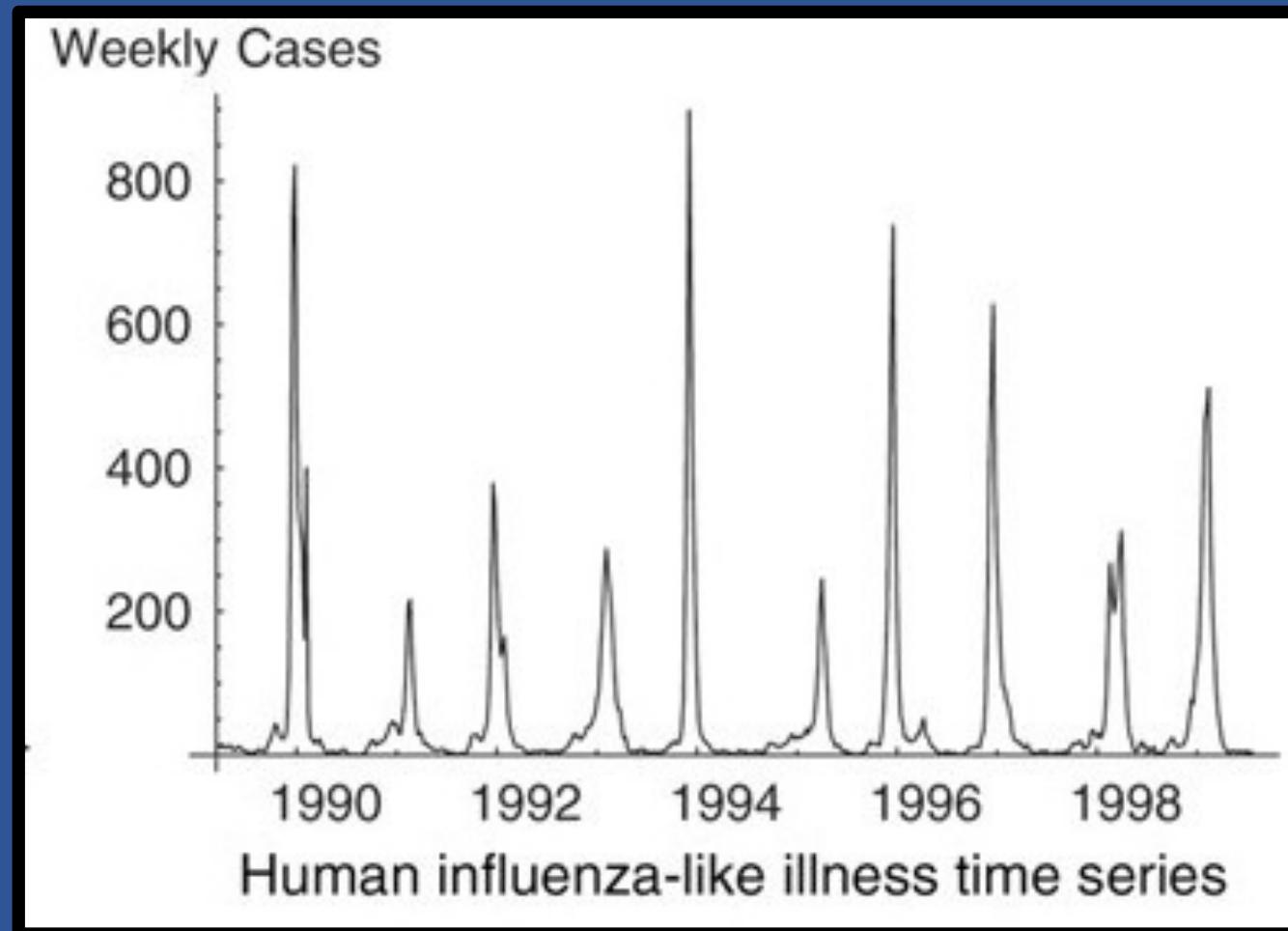
Phyldynamics

- Epidemiological driver – time scale
 - Acute vs. persistent
- Phylogenetic driver
 1. Natural selection
 2. Neutral epidemiological factors (e.g., spatial separation)
- Relies on measurably evolving pathogens
 - **Transmission and mutational events on similar time scales**

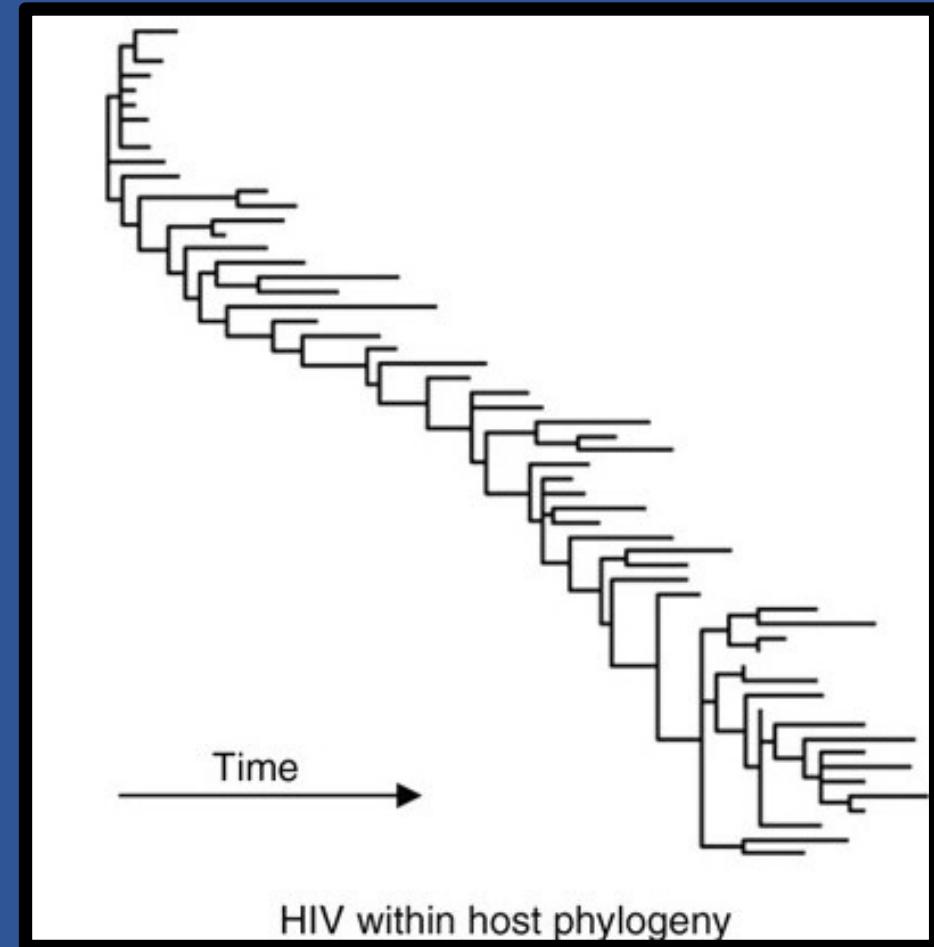
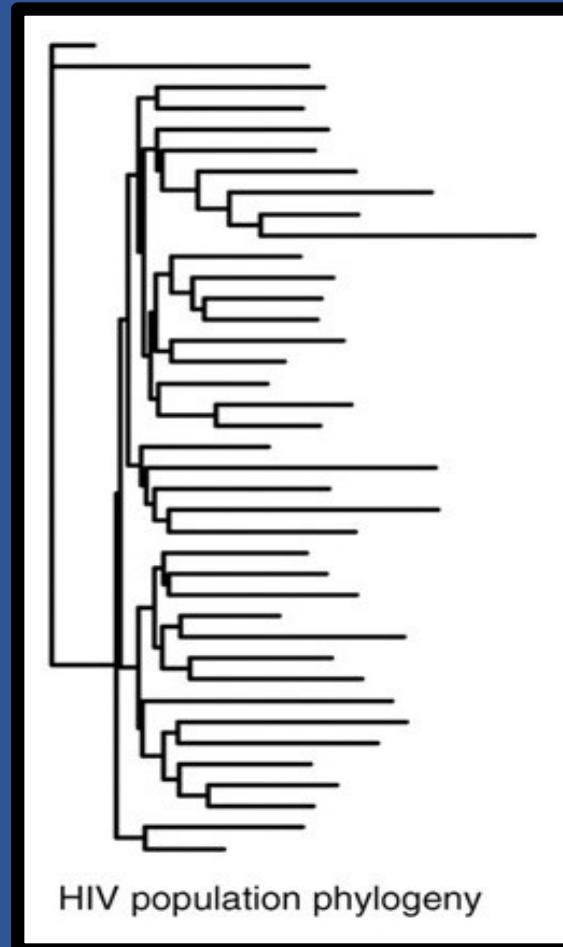
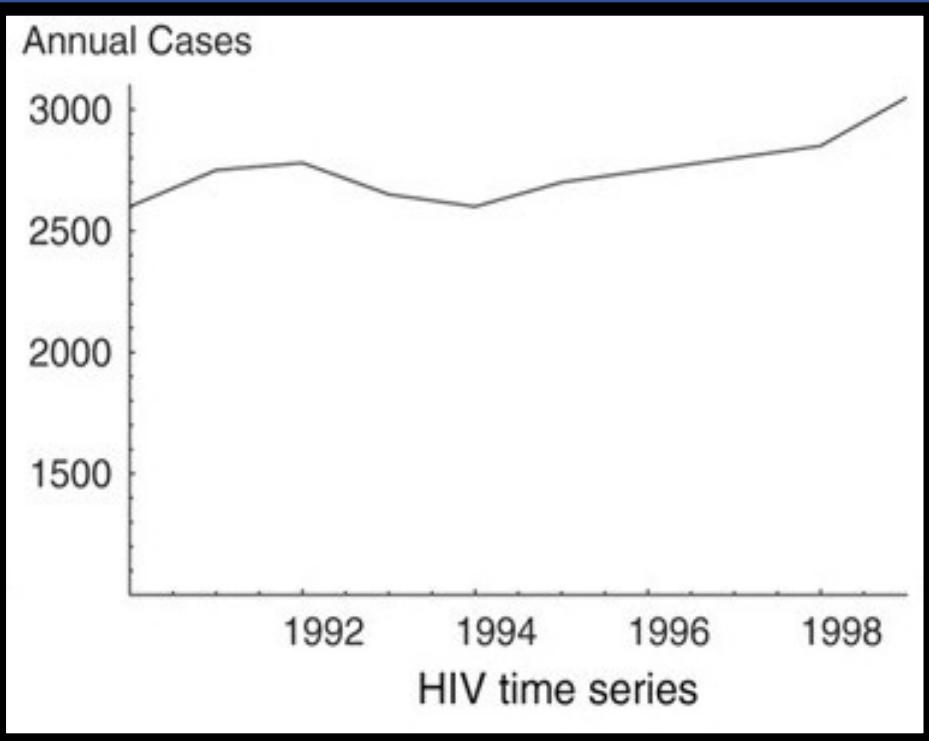
Short infections with strong cross-immunity



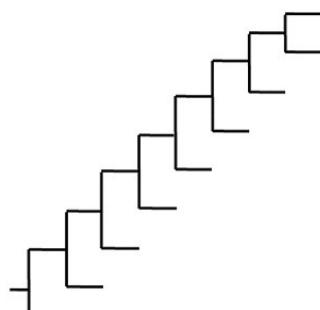
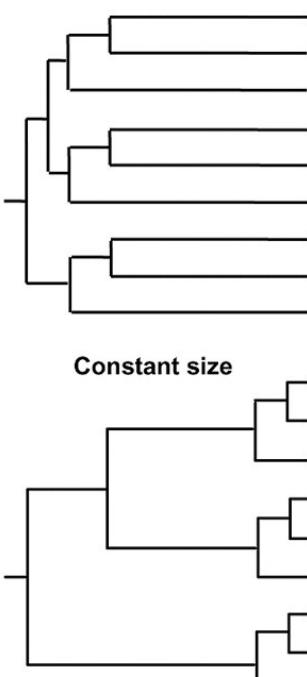
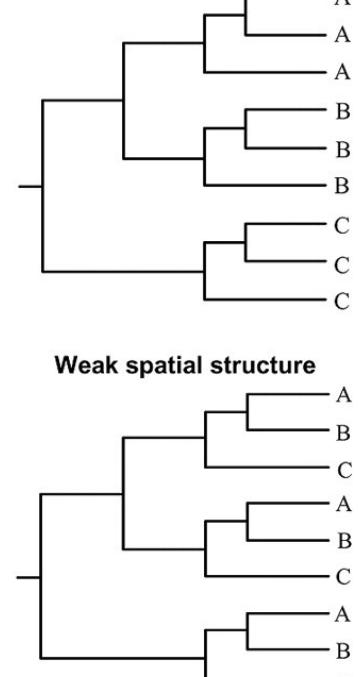
Short infections with partial cross-immunity



Persistent infections



Idealized examples

	Continual Immune Selection	Weak or Absent Immune Selection	
Idealized Phylogeny Shapes		Tree shape controlled by non-selective population dynamic processes	
	 Time →	Population size dynamics  Exponential growth Constant size	Spatial dynamics  Strong spatial structure Weak spatial structure
Examples	Human influenza A virus intra-host HIV	inter-host HIV inter-host HCV	Measles, rabies inter-host HIV
Tree Inferences	Detection of antigenic escape mutations	Estimation of population growth rates	Estimation of population migration rates

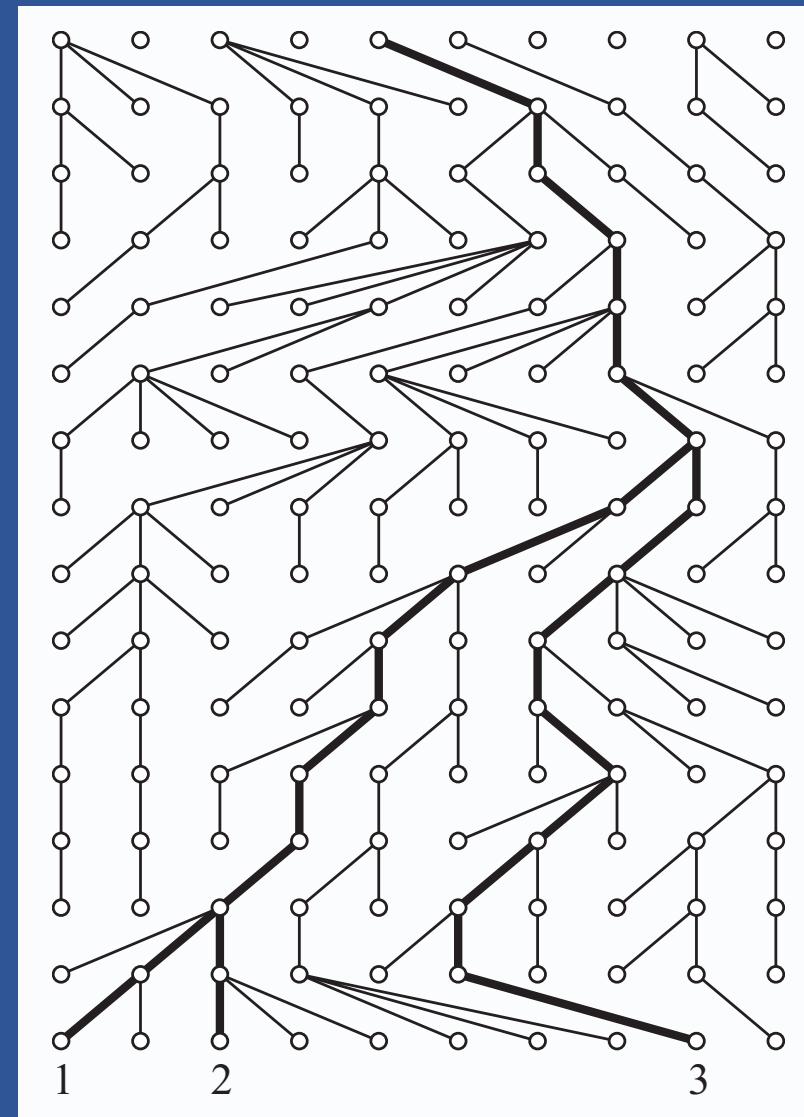
Grenfell et al. 2004
Science

Coalescent theory

Based upon coalescent theory

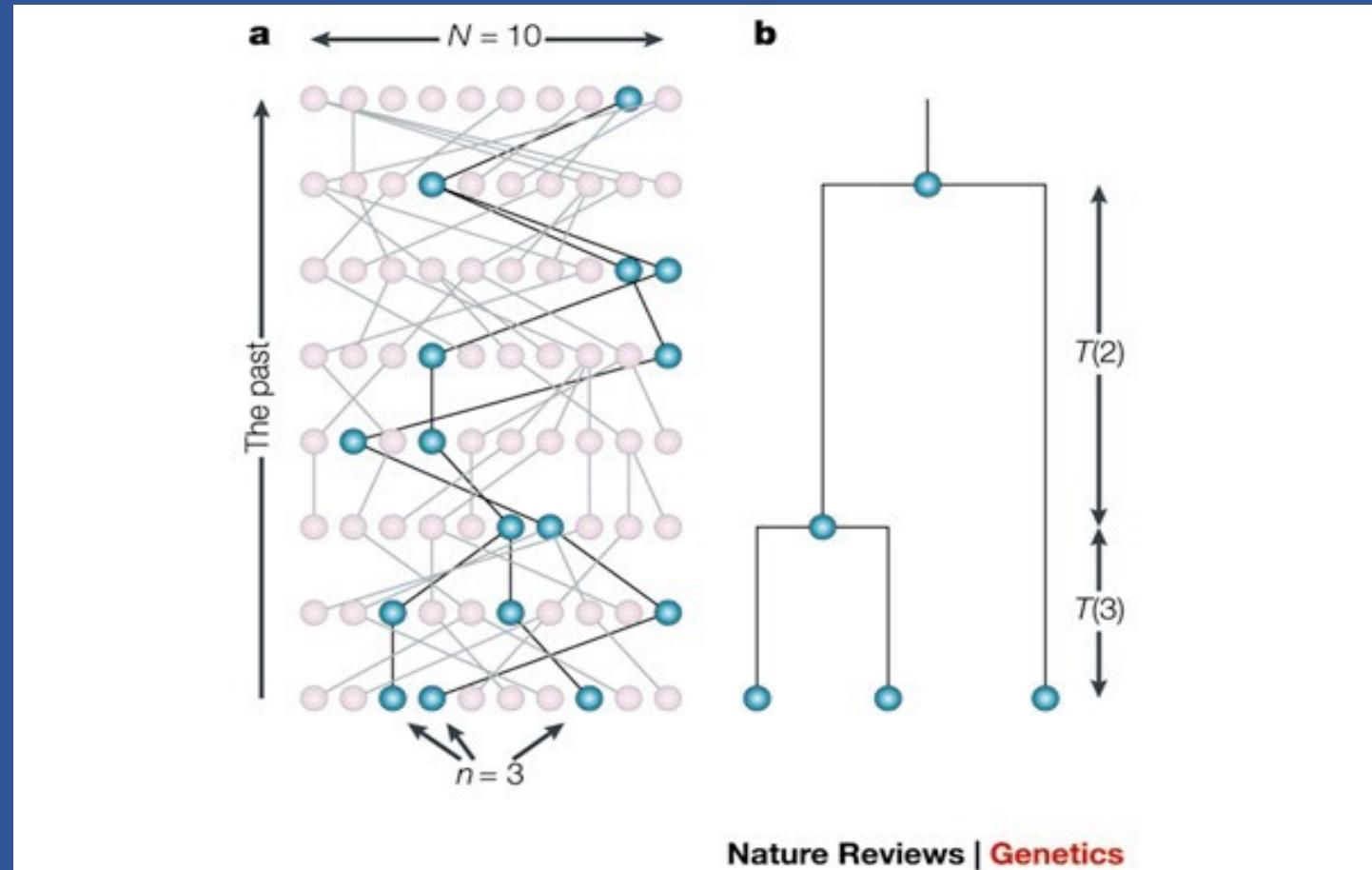
Probabilistic model underlying gene genealogies within a population or populations.

Coalescent theory provides the statistical framework to build virtually any arbitrary complex historical demographic model with parameters such as migration rates, population sizes, divergence times, recombination and selection.



Coalescent theory

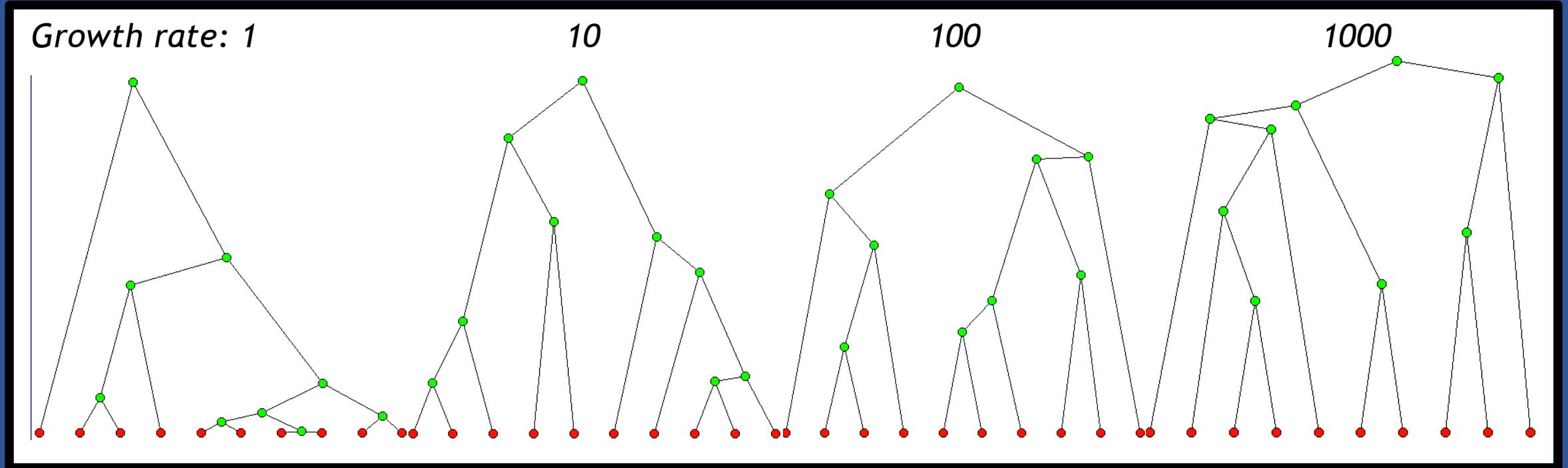
- Going back in time, a coalescent event is when two lineages share the same parent
- Continues until all lineages coalesce at the most recent common ancestor



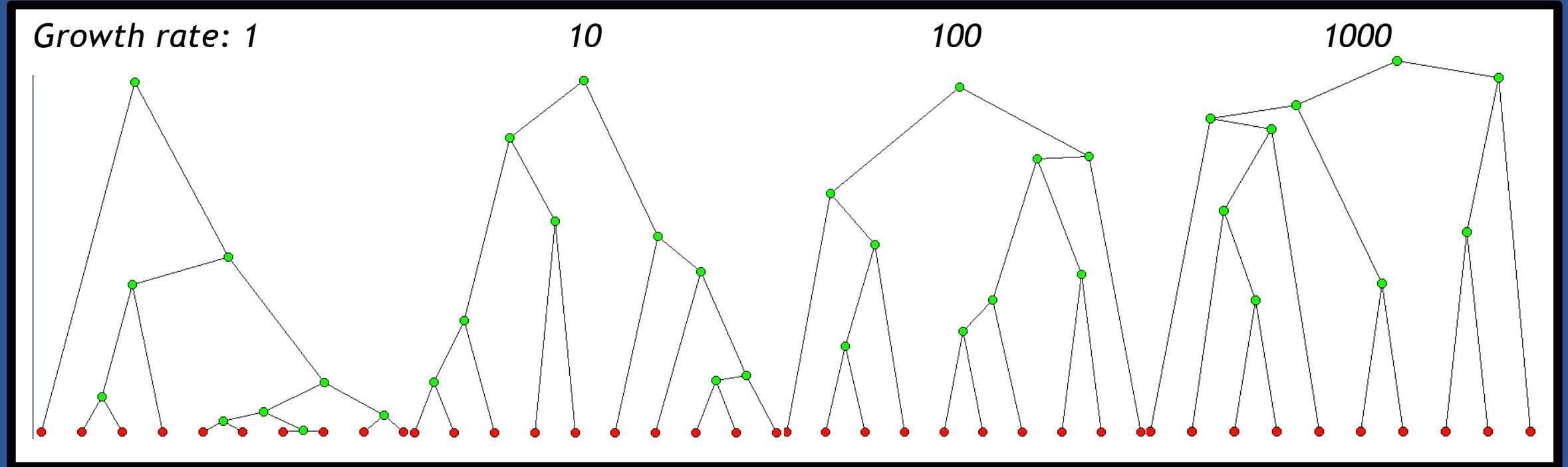
Nature Reviews | Genetics

Rosenberg and Nordborg
2002, Nature Reviews
Genetics

Effect of exponential growth on the coalescent



Effect of exponential growth on the coalescent



Time between coalescent event depends on population size!

Generalisations of the standard coalescent model

- Variable population size - coalescences occur more rapidly when the population size is small
- Longer time between Coalescences with more population subdivision and less migration
- Positive selection and/or population expansion – coalescences tend to occur at the time of expansion/selection

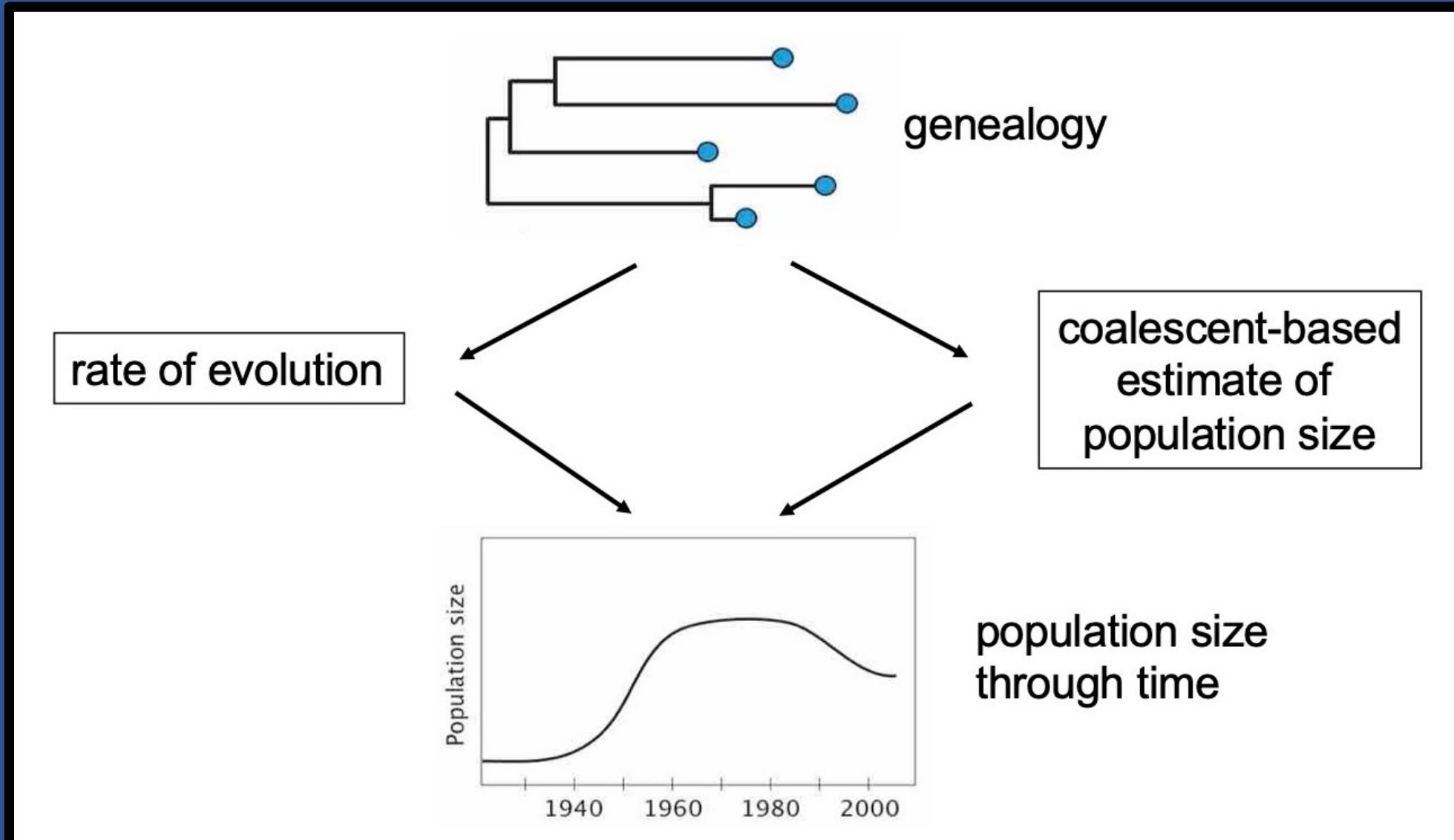
Assumptions

- $N \gg n$ – not more than one coalescent event in the same generation
- No selection
- No recombination
- No population structure

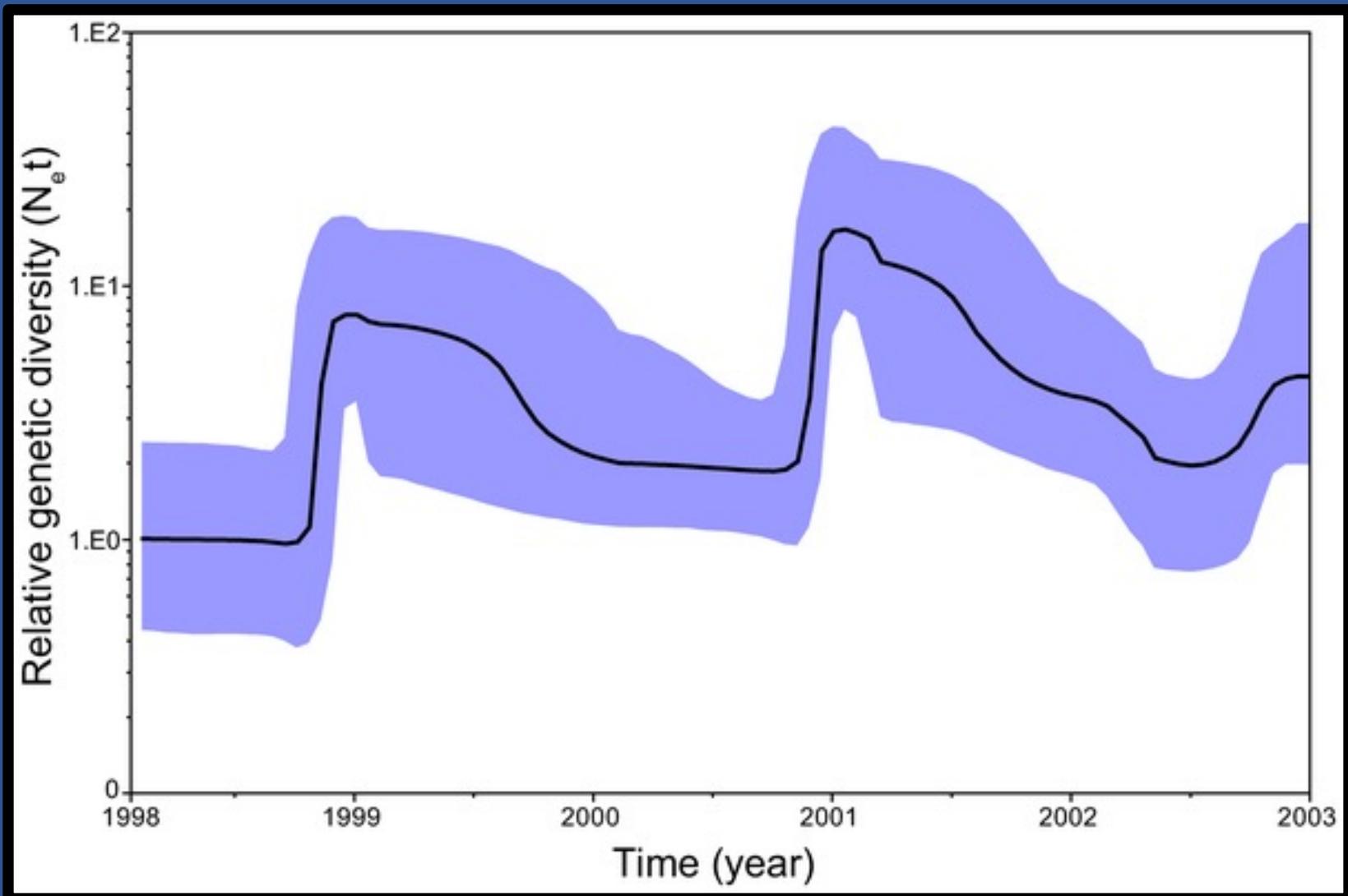
Population size N

- Not the census population size but the effective population size (N_e)
- N_e accounts for variance in numbers of offspring across individuals
- For pathogen transmission, the estimate refers to the effective number of infections

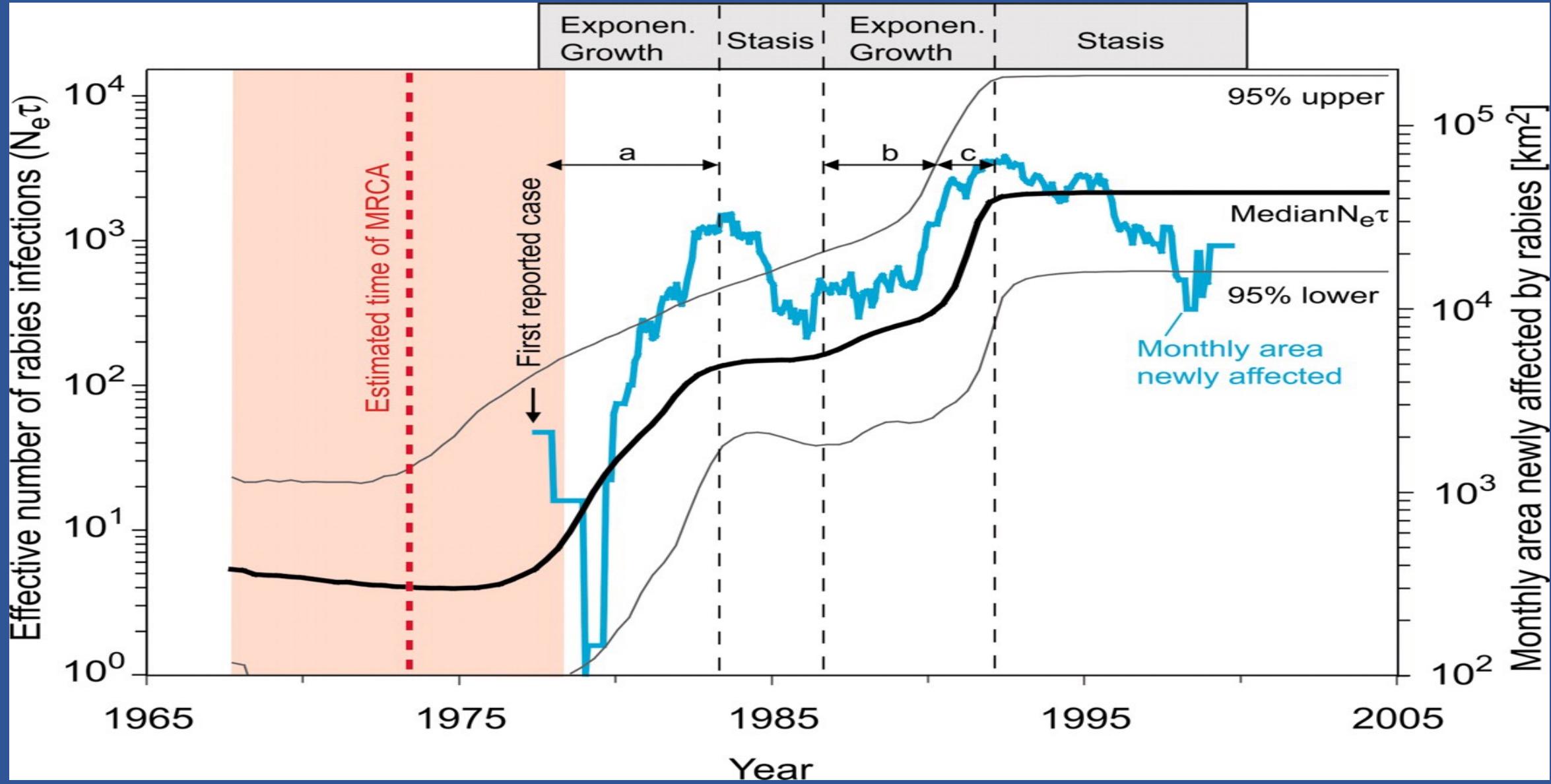
Combining clocks and demography



Population Size Dynamics



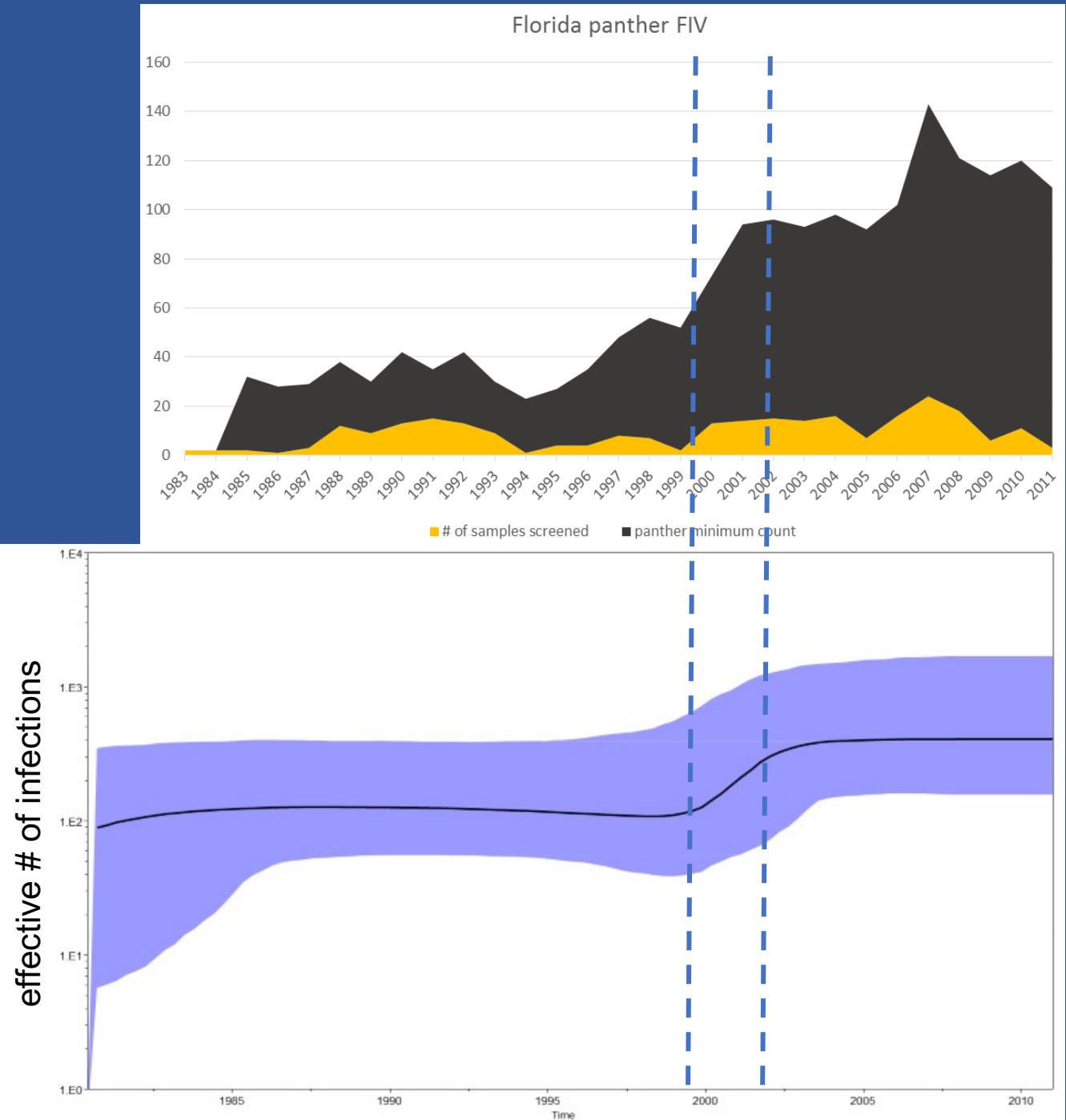
Ross River Virus



Biek et al 2007, PNAS

Florida panther population expansion

Increase in FIVpco infections



Again...

These are not models of transmission and the effective population size is a concept developed for animals that does not translate clearly to pathogens.

But the models are easy to run an interpreting trends by eye can be informative.

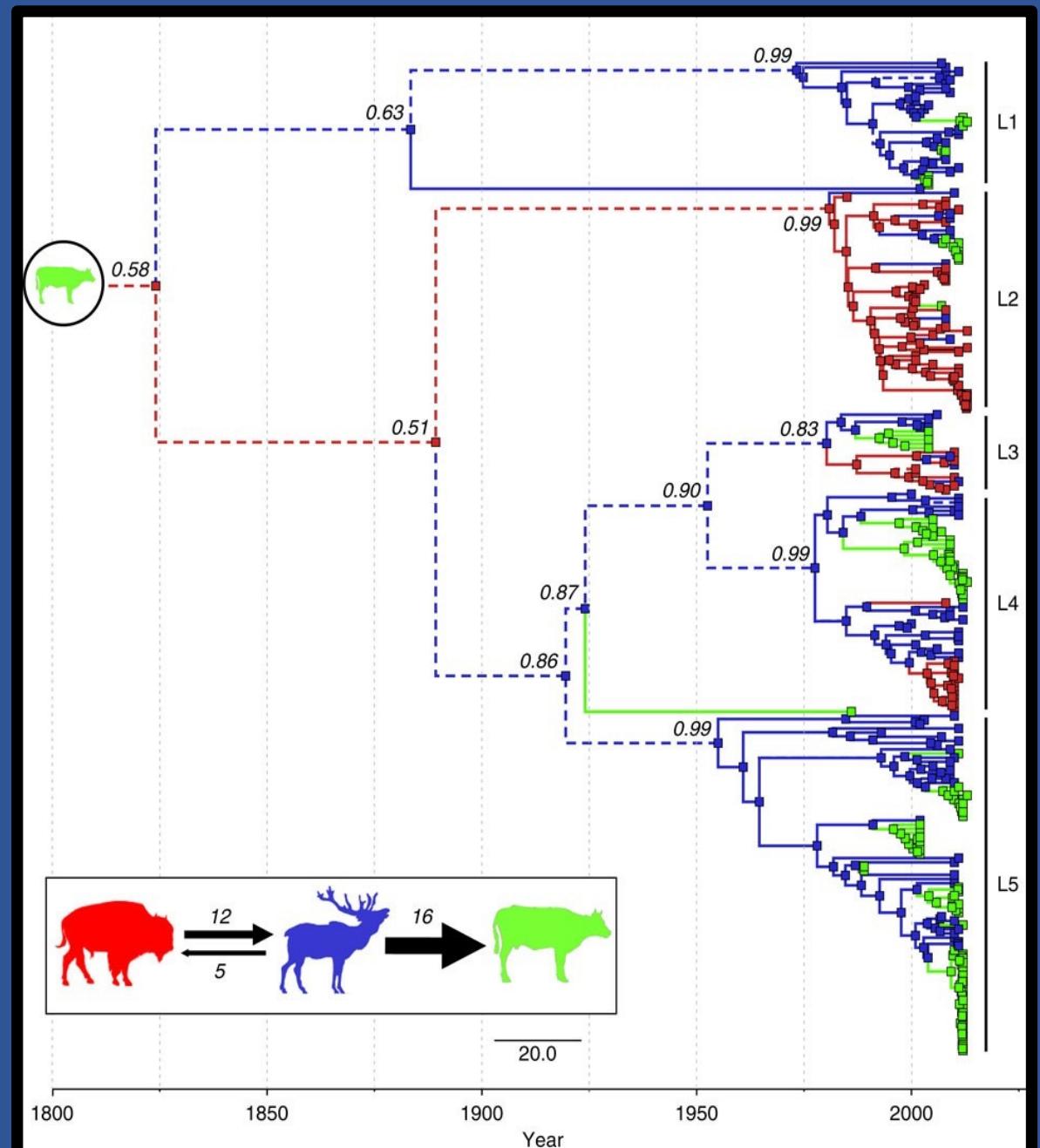
Between species transmission

- There can be a variety of discrete states
- Cross-species transmission an important one

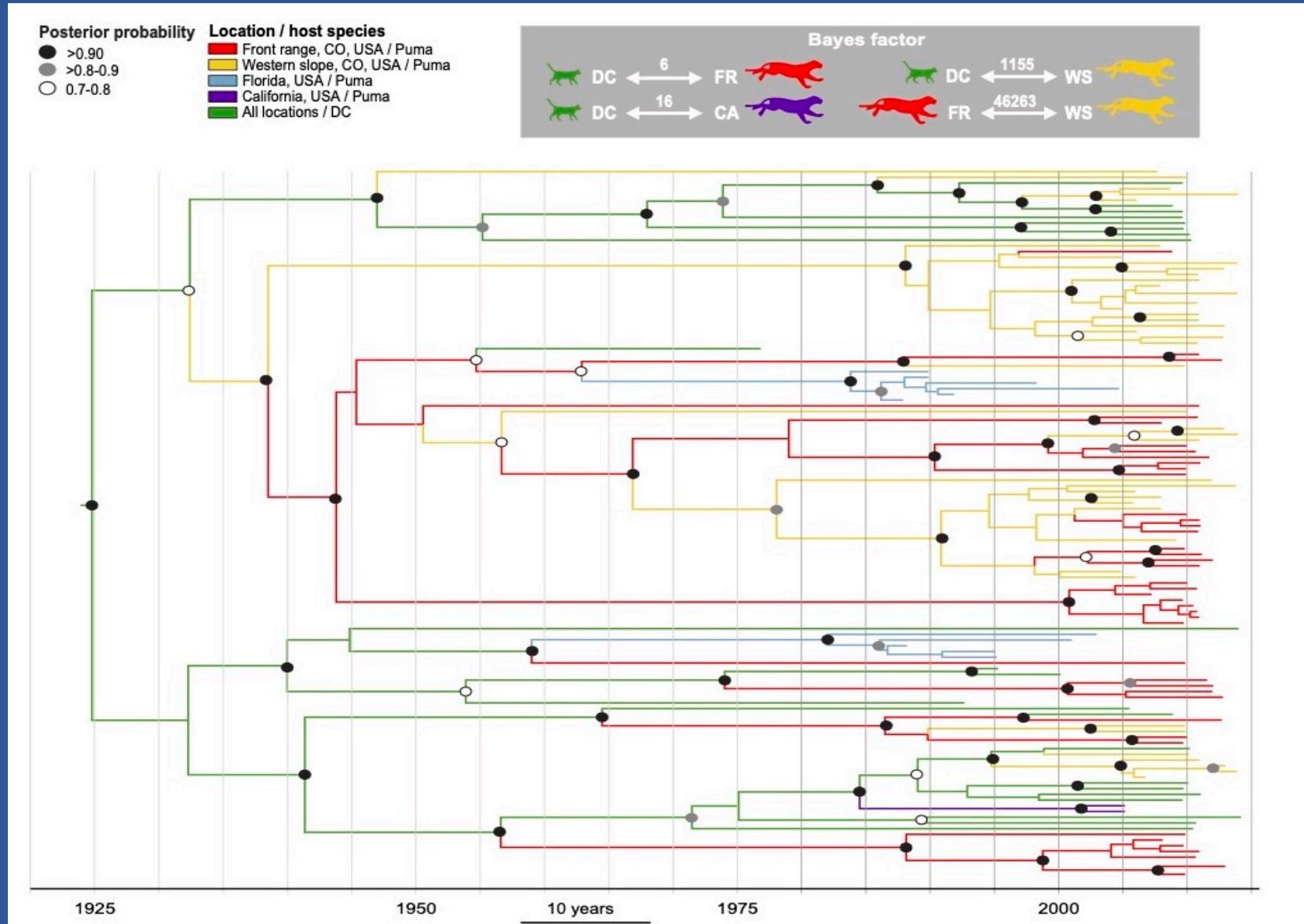


Identification of infection reservoir

- *Brucella abortus* in the Greater Yellowstone Ecosystem
- GDW alumni!



Combining traits

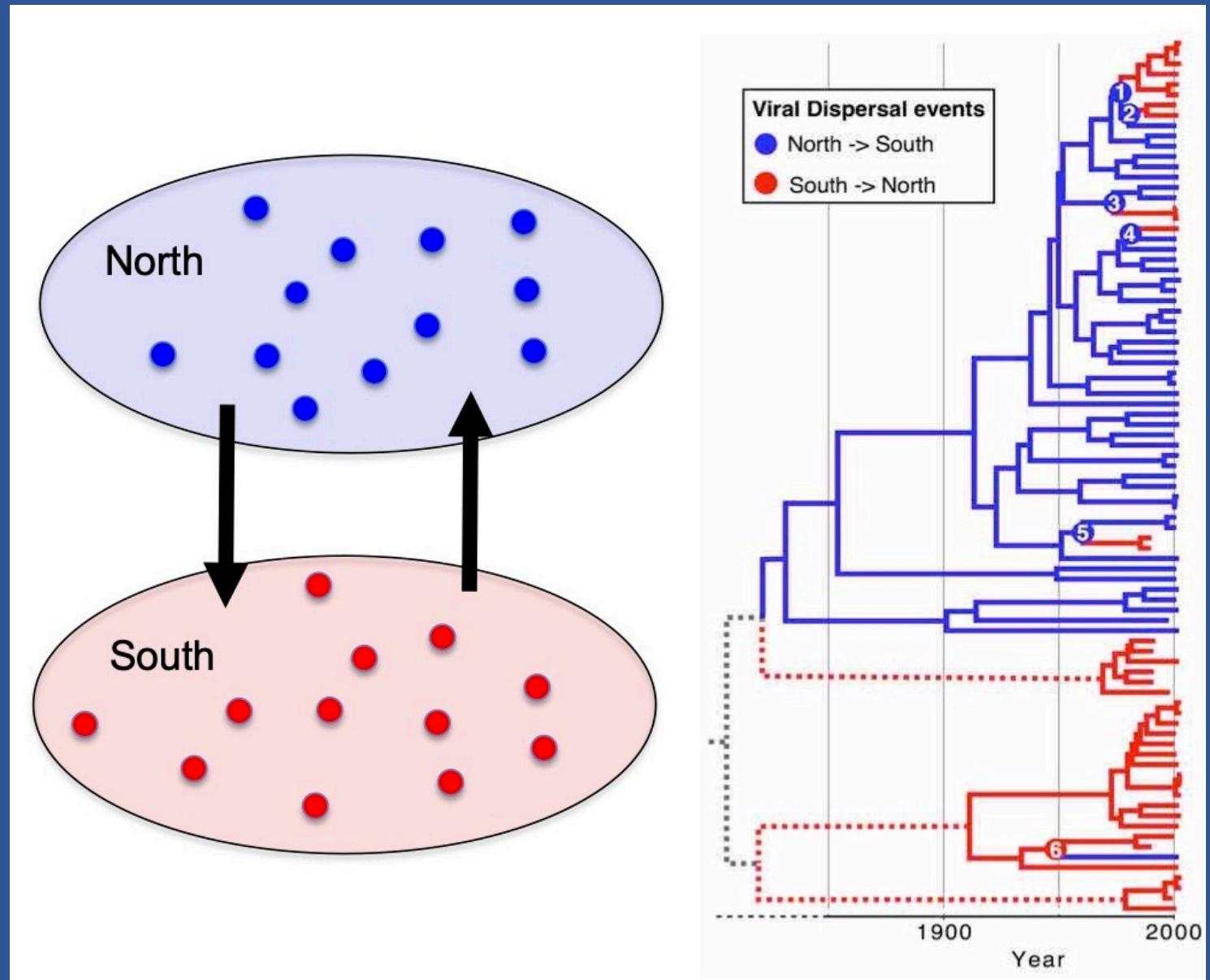


Geographically separated host populations



Estimating pathogen movement

- Dispersal between two host populations



Nextstrain

Real-time tracking of pathogen evolution

Nextstrain is an open-source project to harness the scientific and public health potential of pathogen genome data. We provide a continually-updated view of publicly available data alongside powerful analytic and visualization tools for use by the community. Our goal is to aid epidemiological understanding and improve outbreak response. If you have any questions, or simply want to say hi, please give us a shout at hello@nextstrain.org.

[READ MORE](#)

SARS-CoV-2 (COVID-19)

We are incorporating SARS-CoV-2 genomes as soon as they are shared and providing analyses and situation reports. In addition we have developed a number of resources and tools, and are facilitating independent groups to run their own analyses. Please see the [SARS-CoV-2 resources page](#) for more information.

Explore pathogens

Genomic analyses of specific pathogens kept up-to-date by the Nextstrain team

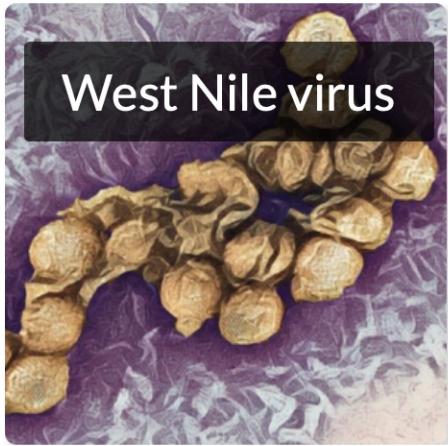
SARS-CoV-2



Seasonal influenza



West Nile virus



Mumps



Zika



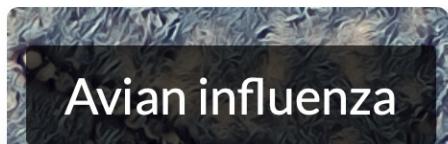
West African Ebola 2013-16



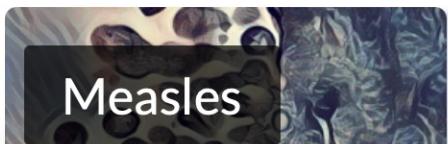
Dengue



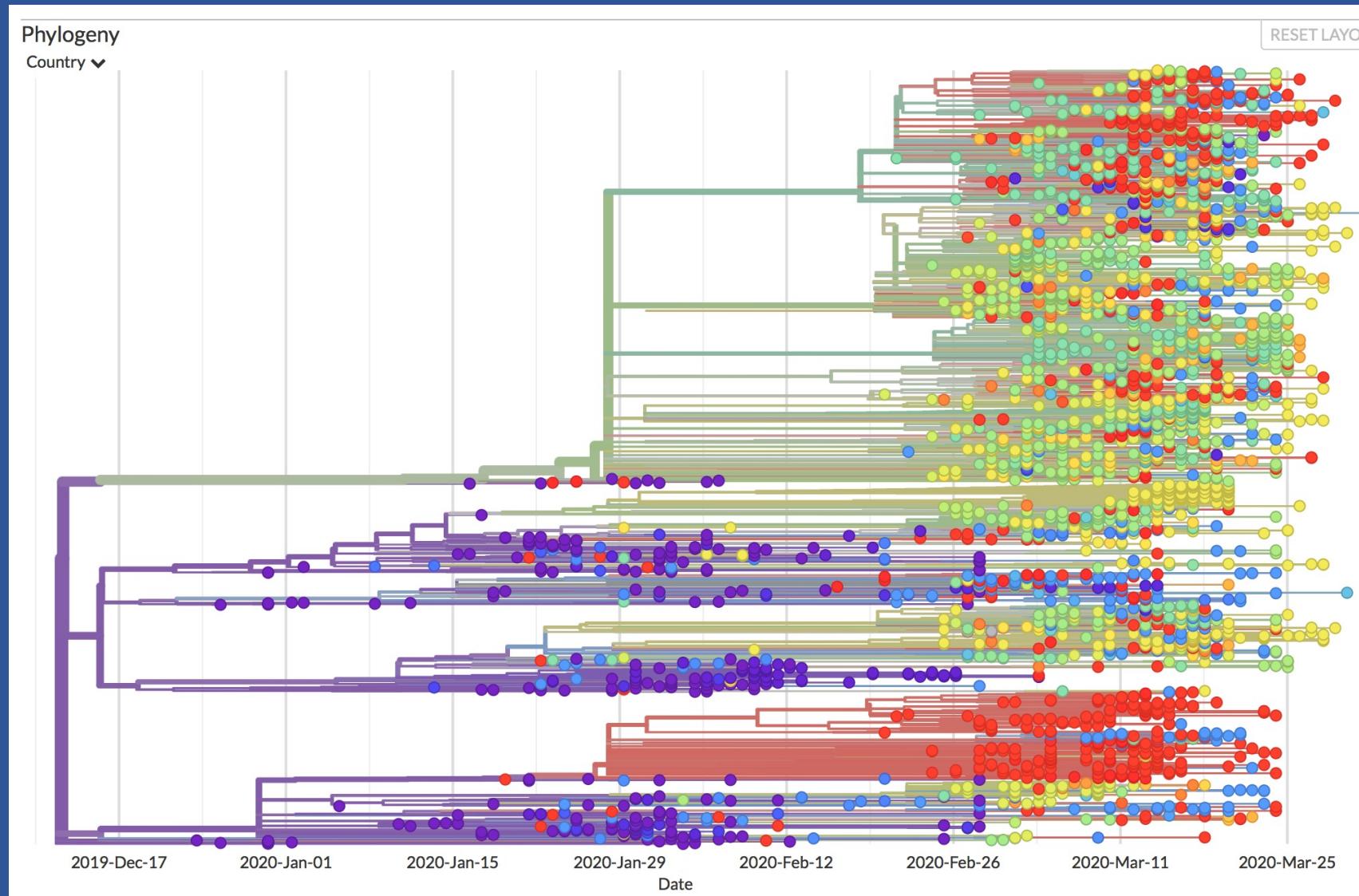
Avian influenza



Measles

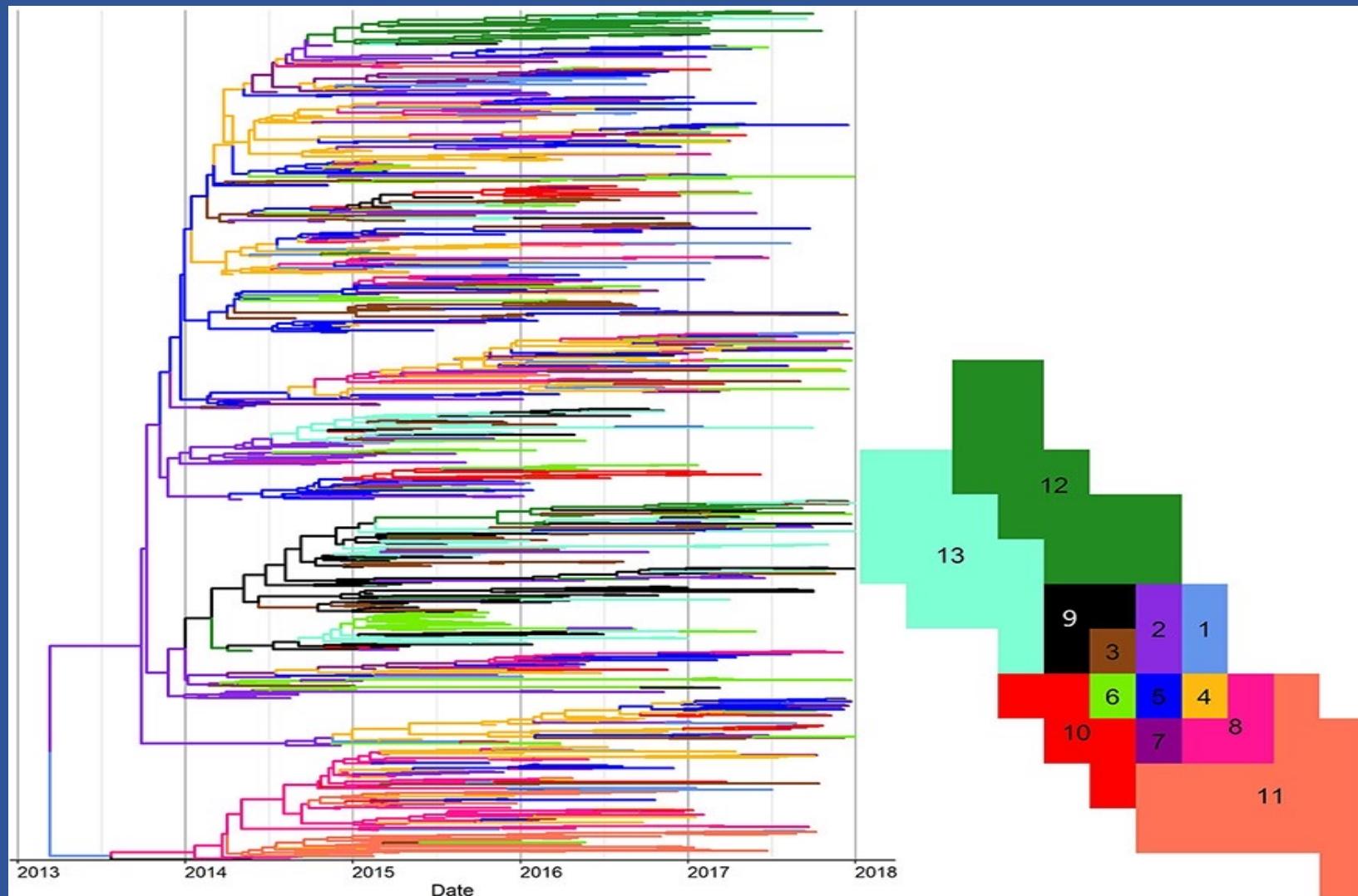


SARS-CoV-2 early international spread

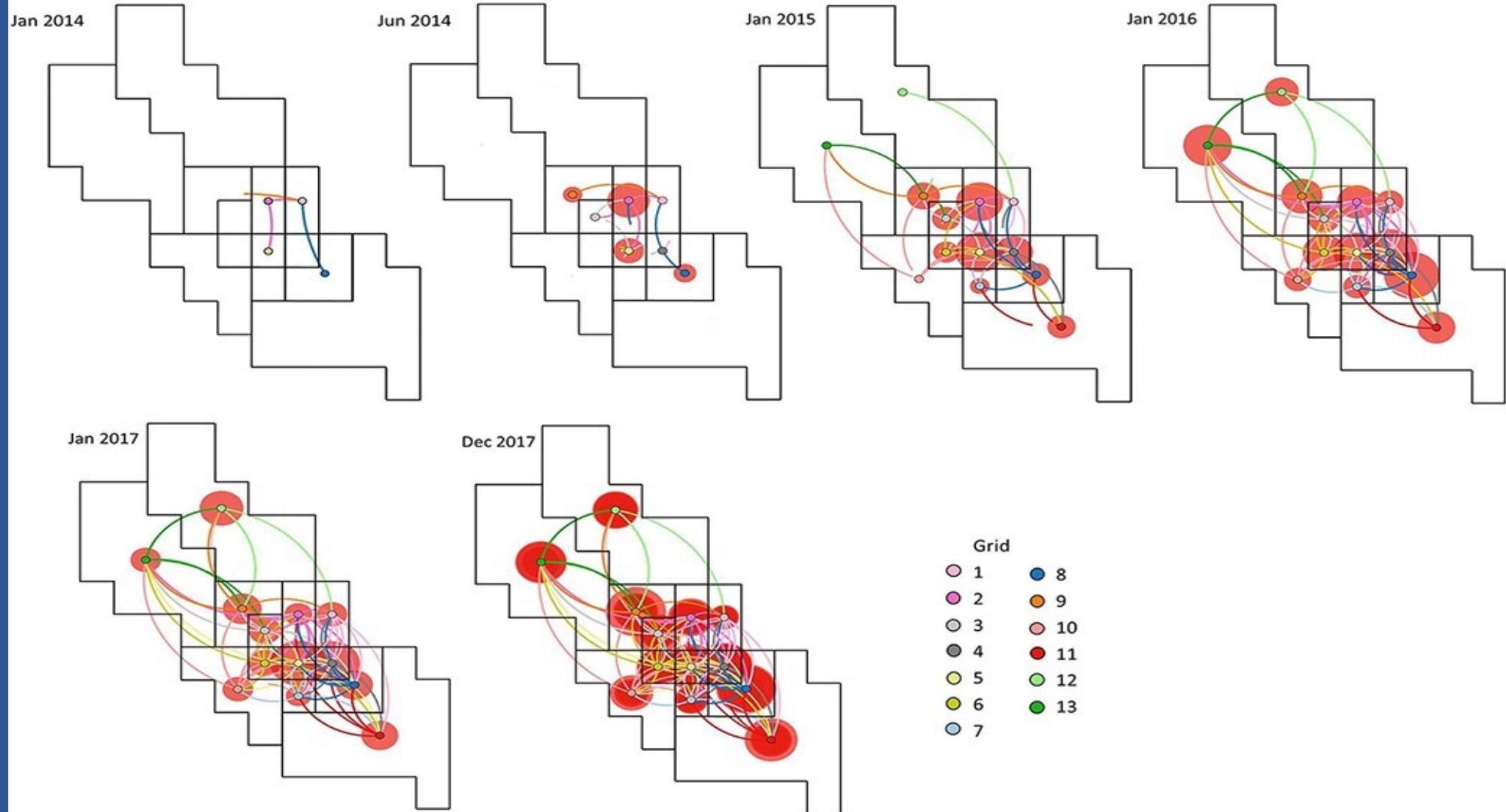


Nextstrain

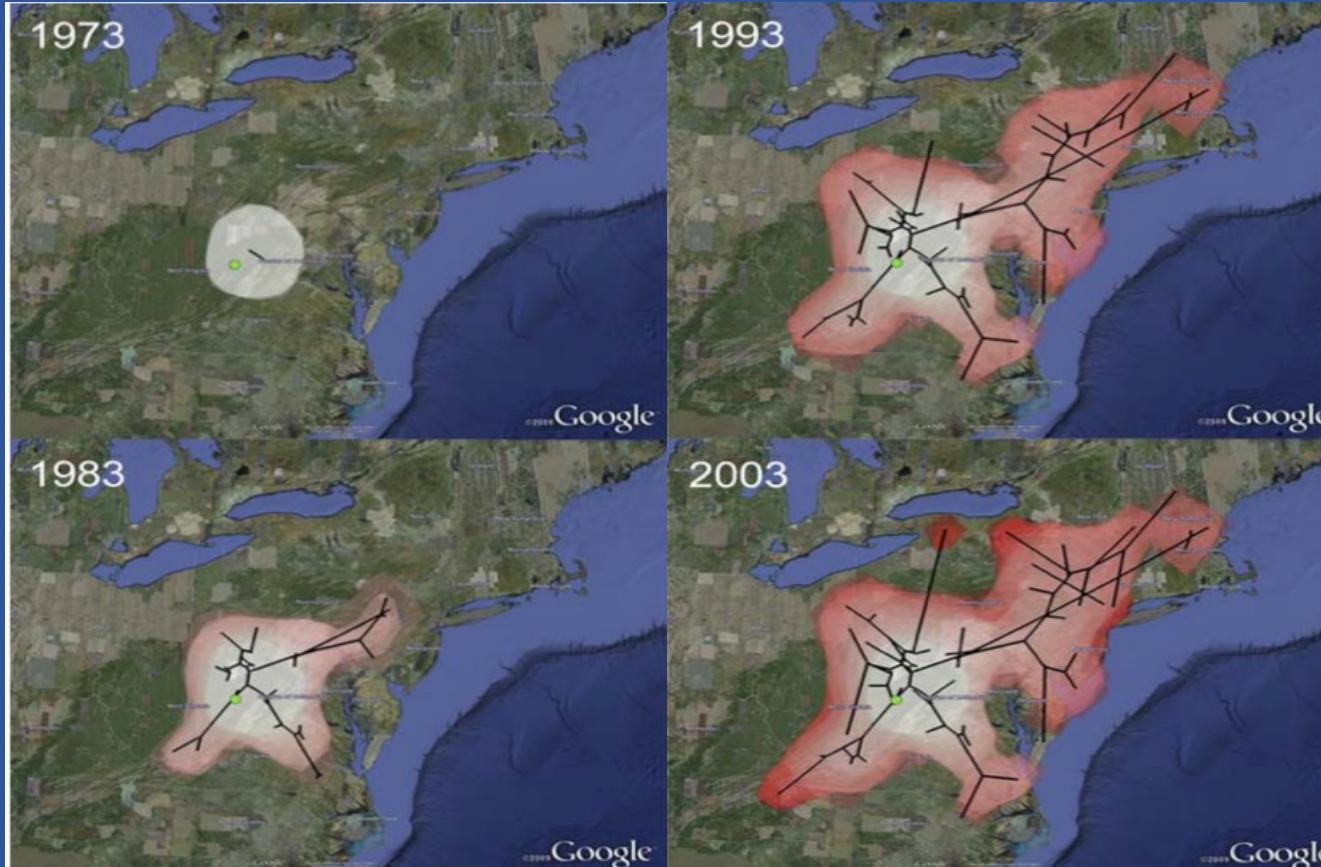
PRRSV spread in US



Phylogeny to a map

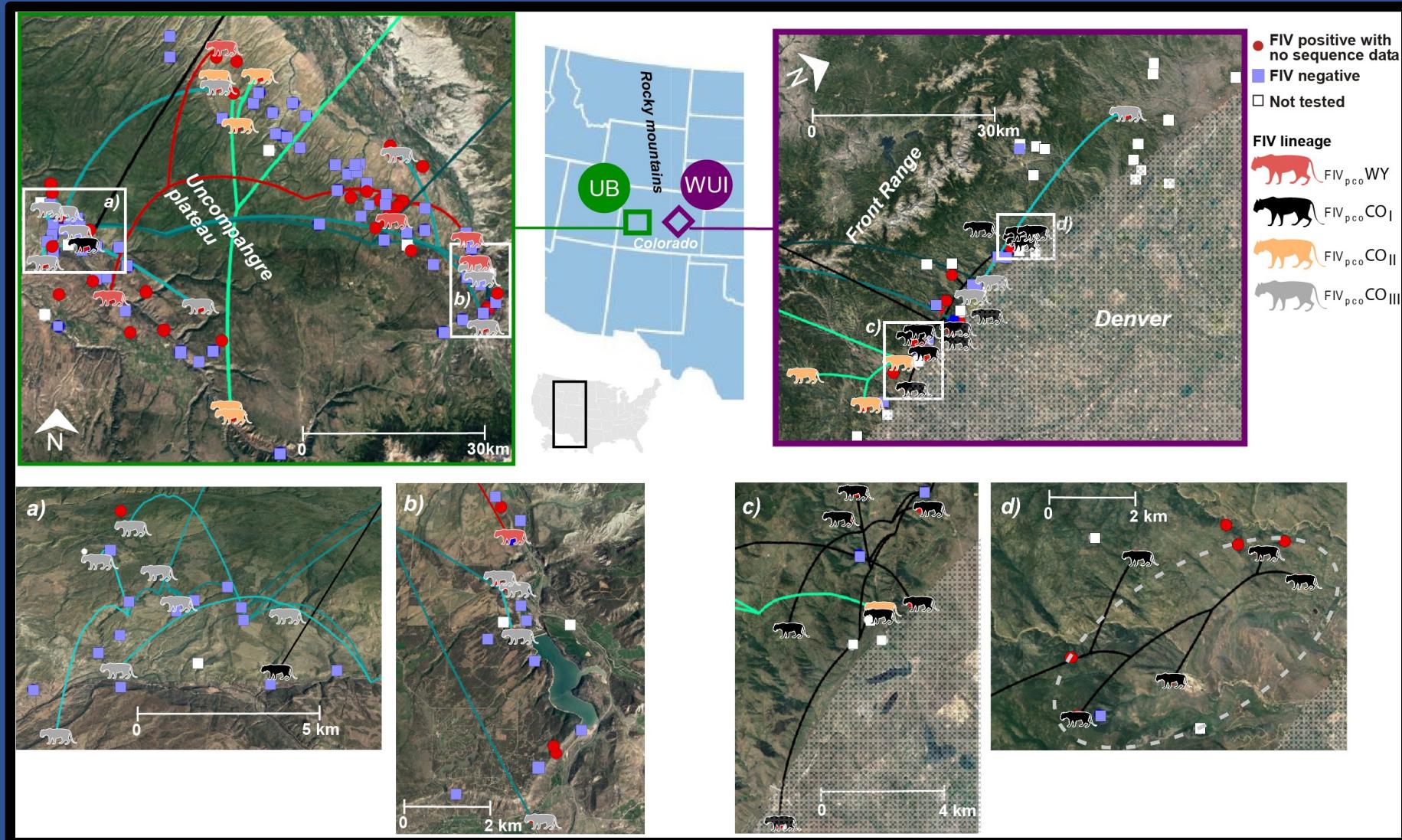


Incorporating spatial data

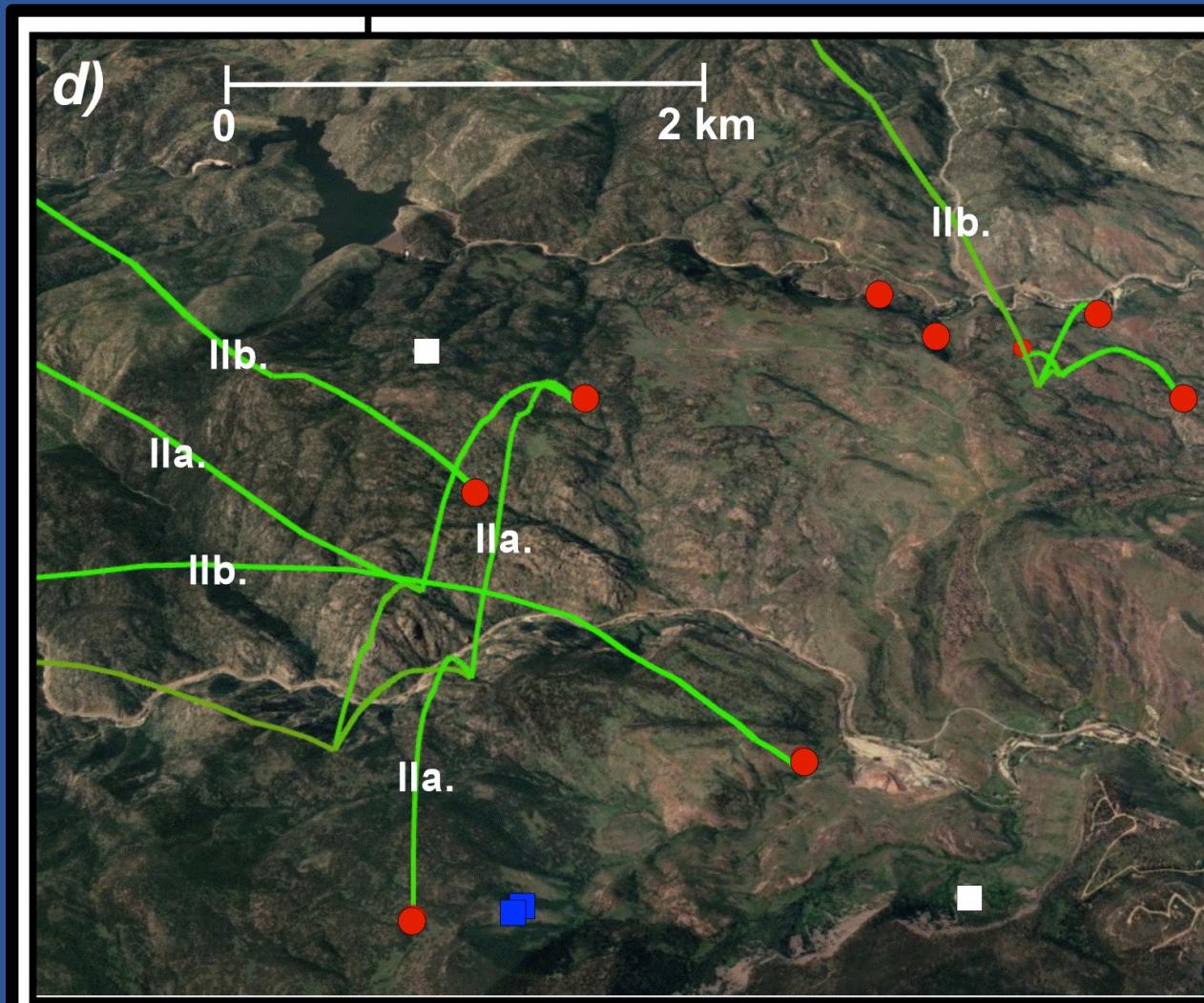


Lemey 2010 Mol. Bio. Evol.

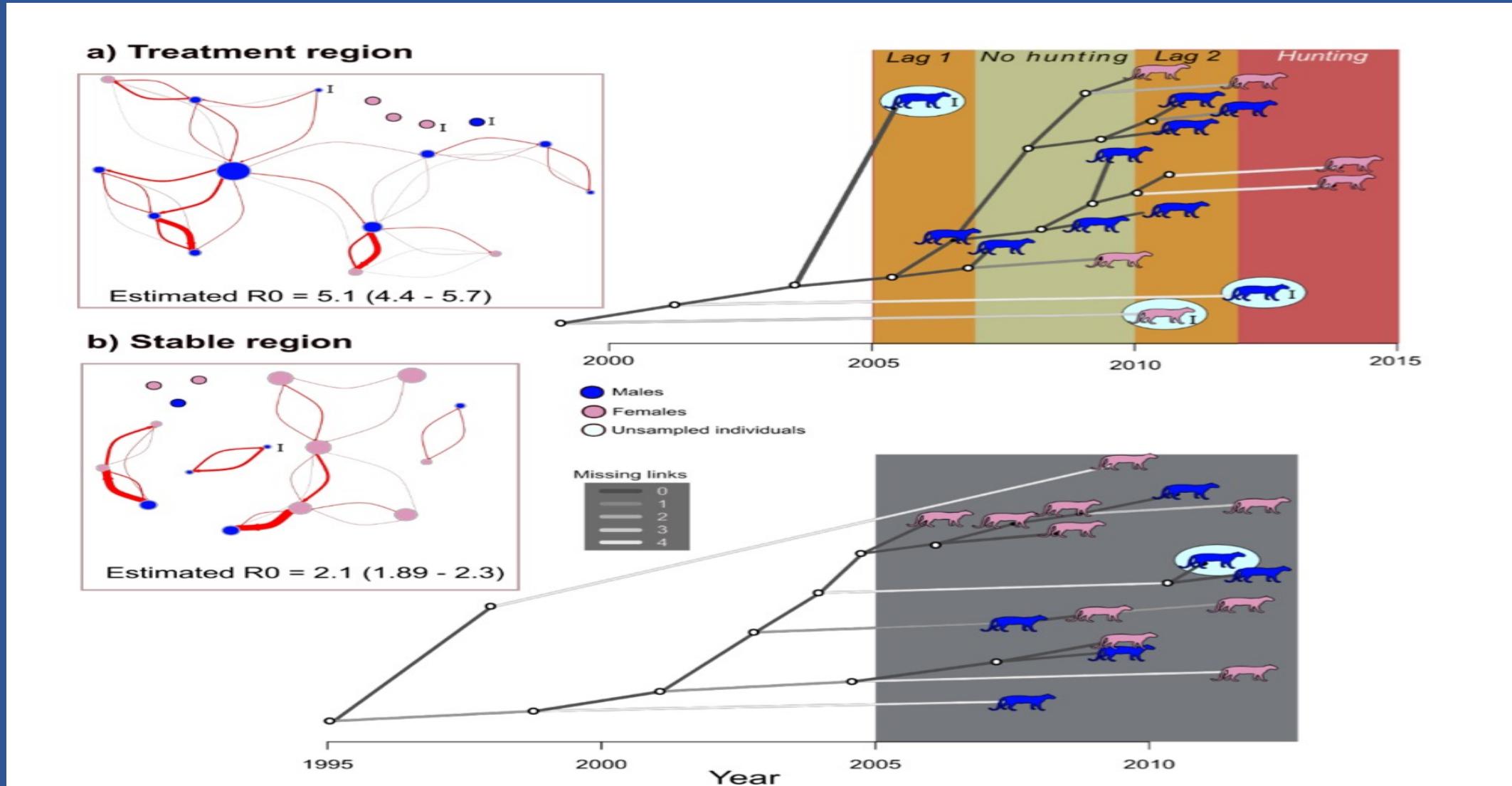
Inferring Viral Spread



Inferring Viral Spread



Within population spread



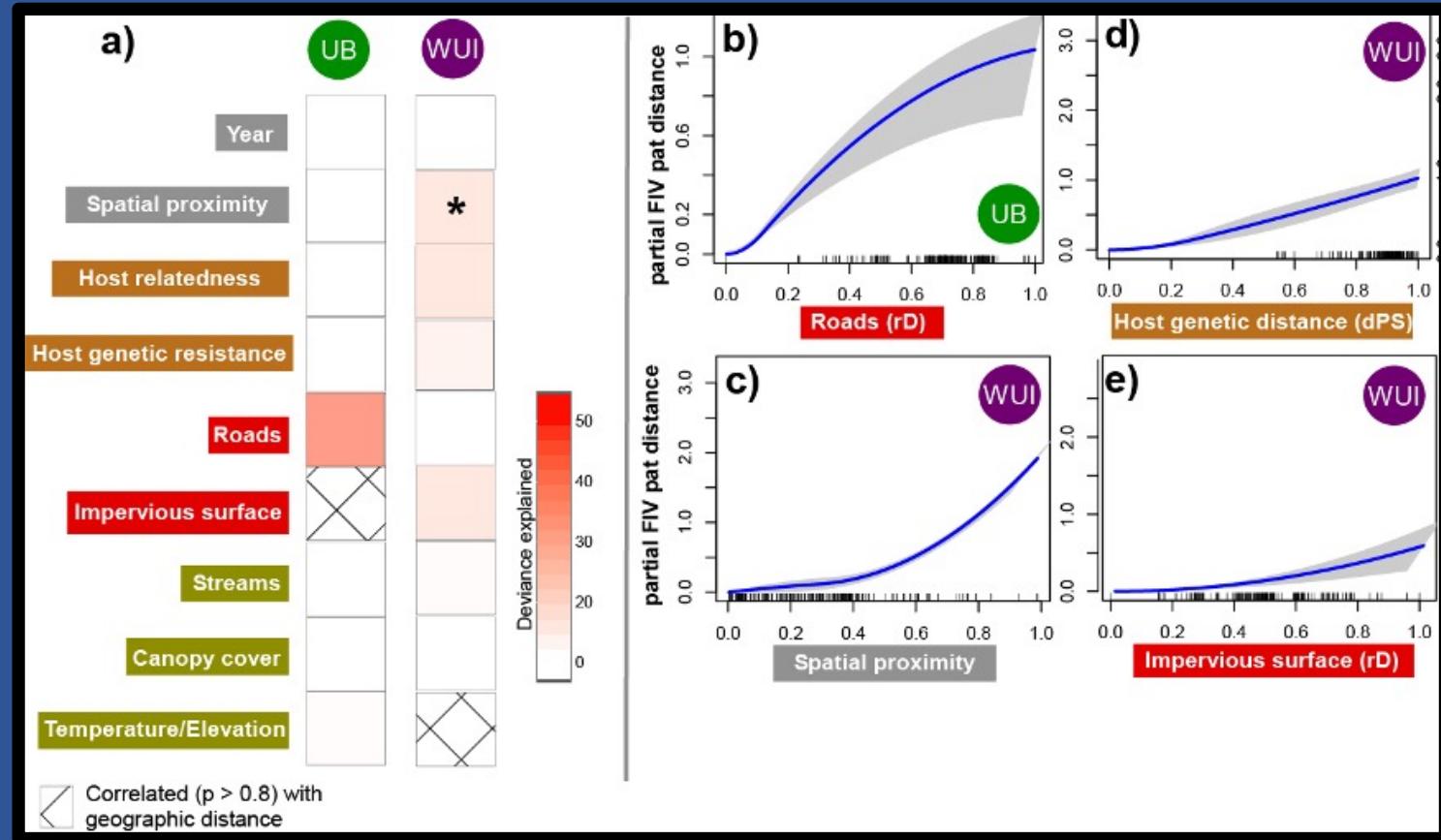
Dealing with sampling bias

Types of inference	Importance of bias	Recommended practice
Molecular clock	Usually more robust	Sample evenly across time, maximize date range
Demographic inference (i.e. change in population size through time)	High	Define target population, sample evenly across space AND time
Ancestral states (e.g. cross species transmission)	High	Sample evenly across space AND species AND time

Where can we go with this...

Rapidly advancing field
with increasing ability to
understand disease
dynamics in wildlife

However, it is incredibly
complex and requires
careful consideration of the
way data is being analyzed
AND the biology



Fountain-Jones et al. 2021



COMMUNICATIONS BIOLOGY

ARTICLE



Check for updates

<https://doi.org/10.1038/s42003-020-01548-2>

OPEN

Host relatedness and landscape connectivity shape pathogen spread in the puma, a large secretive carnivore

Nicholas M. Fountain-Jones ^{1,2}✉, Simona Kraberger³, Roderick B. Gagne ³, Daryl R. Trumbo⁴, Patricia E. Salerno^{4,5}, W. Chris Funk ⁴, Kevin Crooks⁶, Roman Biek ⁷, Mathew Alldredge⁸, Ken Logan⁹, Guy Baele¹⁰, Simon Dellicour ^{10,11}, Holly B. Ernest¹², Sue VandeWoude ³, Scott Carver ² & Meggan E. Craft ¹

Where are we?

- From data generation to complex applied outcomes
- Increasingly applying pathogen genomics to addressing complex epidemiological questions
- Moving toward multi step process.
 1. Generate a phylogeny with informative branch lengths (ML)
 2. Estimate molecular clock and fit tree to the timeline
 3. Use dated phylogeny to fit phylodynamic model

Summary

- Strong, continual selection, results in temporal pathogen phylogenetic structure
- Limited selection pathogen phylogenies reflect other epidemiological processes
 - Such as population dynamics and spatial change
- Sampling biases often unavoidable
 - Well-documented effects on demographic and diffusion models
 - Less effects on molecular clock
 - Proactive alteration of sampling