

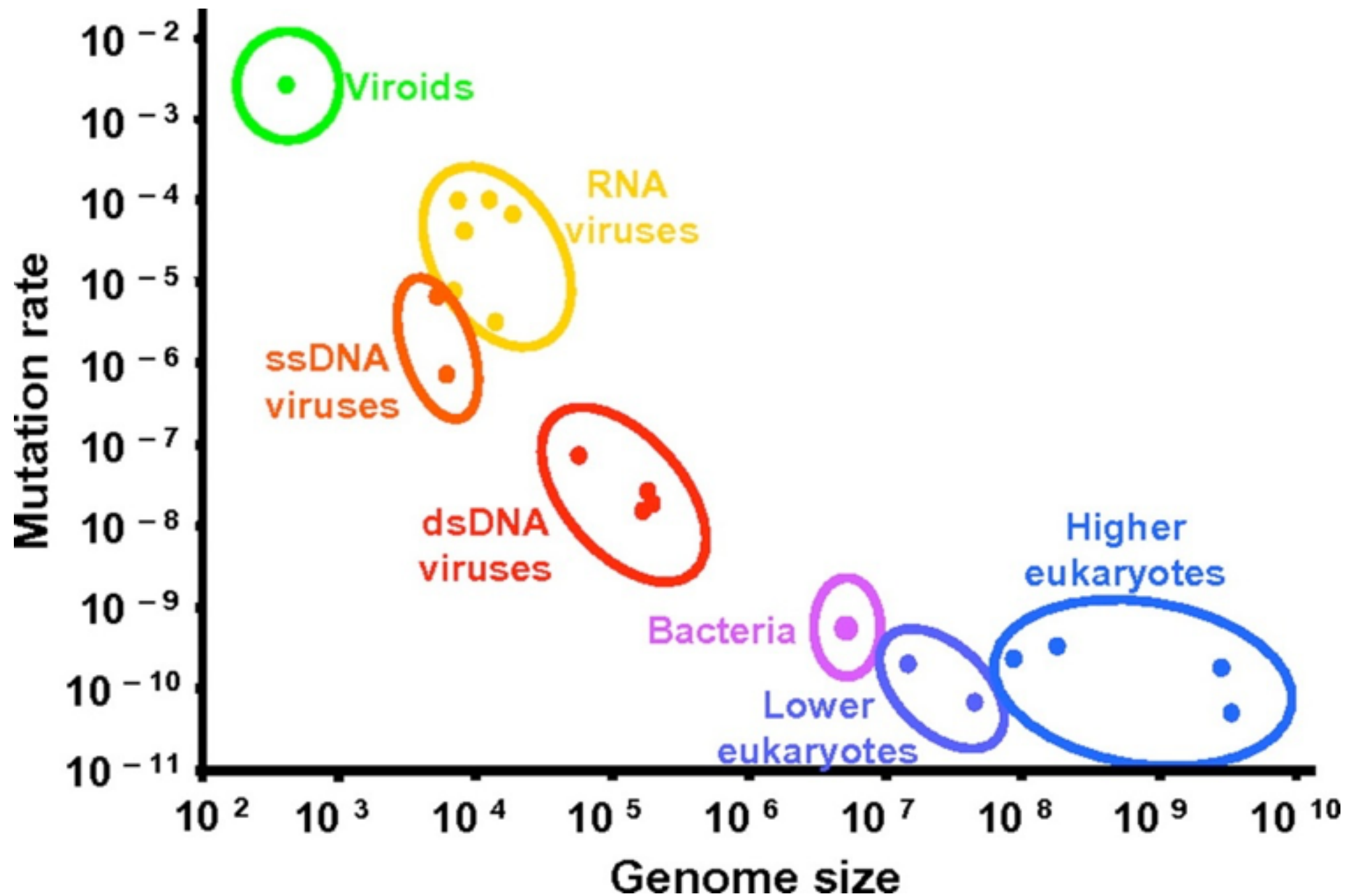
Introduction to infectious disease phylodynamics

Oliver Pybus

What Is Phylodynamics?

“Rapidly evolving pathogens are unique in that their ecological and evolutionary dynamics occur on the same timescale and can therefore potentially interact.”

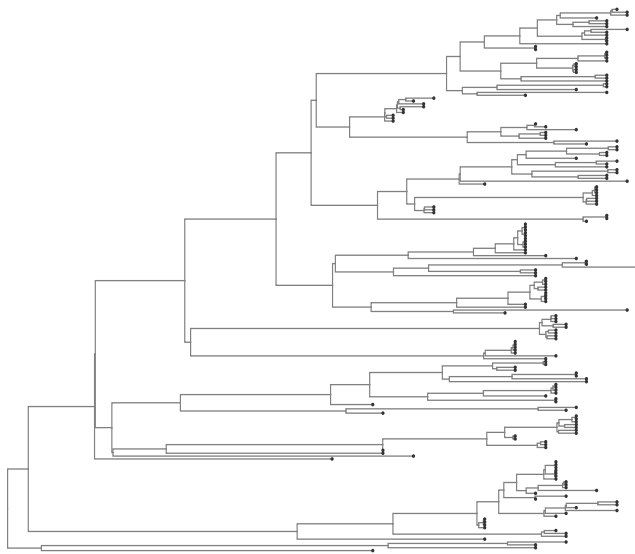
What Is Phylodynamics?



What Is Phylodynamics?

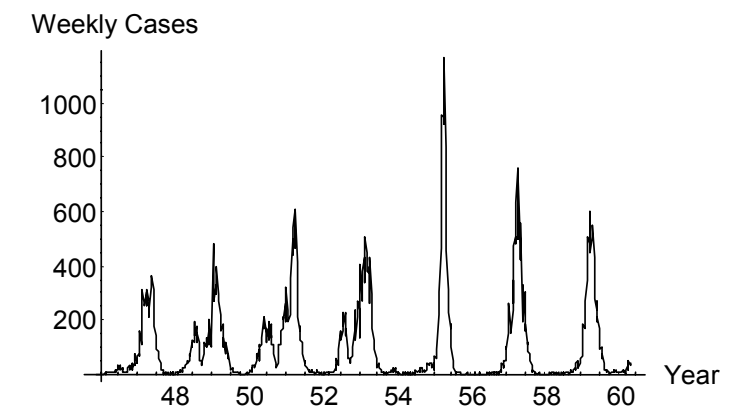
GENETIC DIVERSITY

(phylogenetics & population genetics)



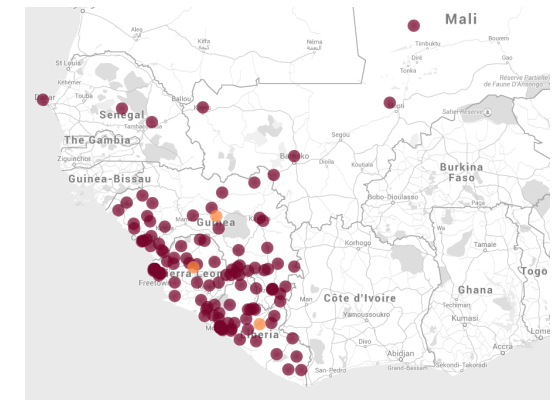
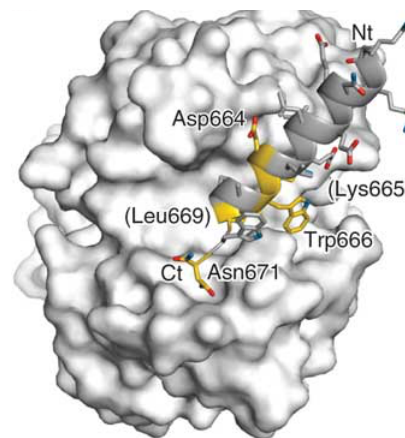
EPIDEMIC DYNAMICS

(mathematical & spatial epidemiology)

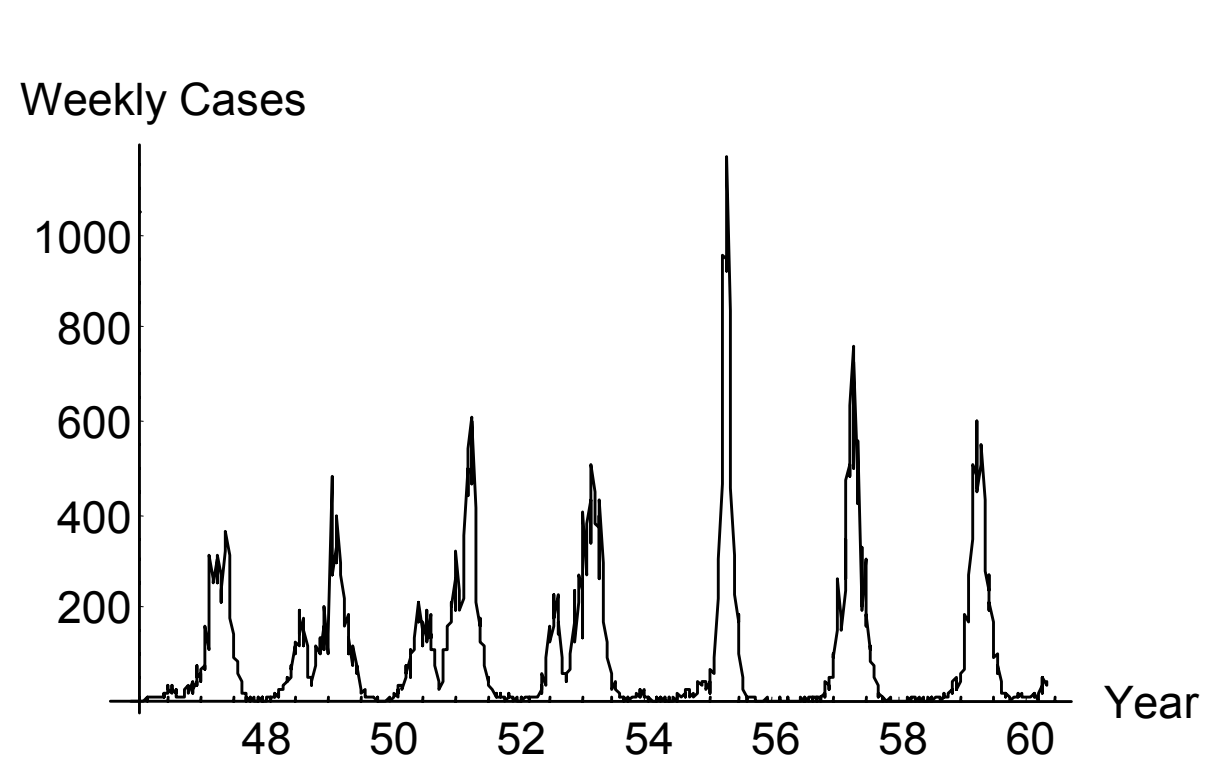


VIRUS PHENOTYPE

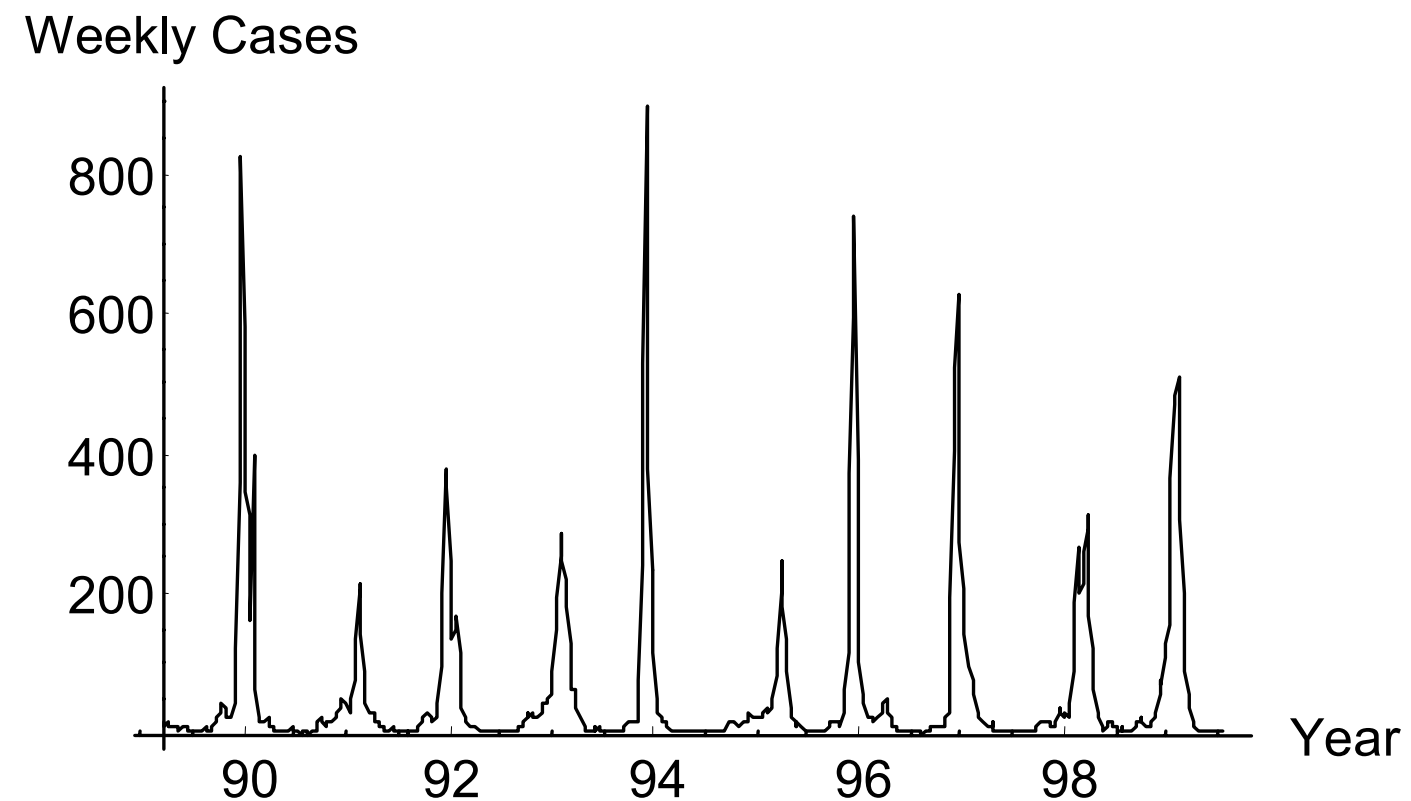
(molecular virology & immunology)



Measles vs Influenza Transmission Dynamics



Pre-vaccination dynamics
(1940-1960, Leeds UK)

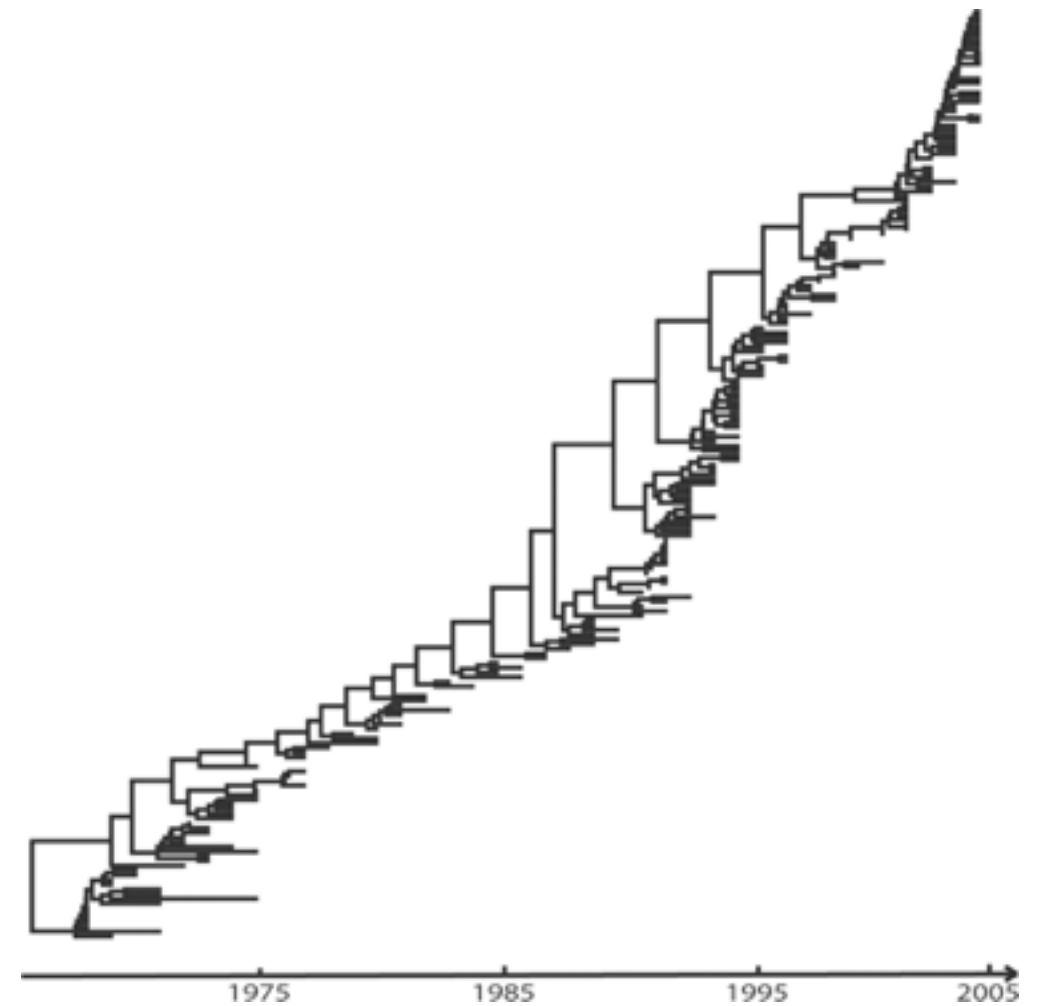


Influenza-like illness
(1989-1999, France)

Measles vs Influenza Genetic Dynamics



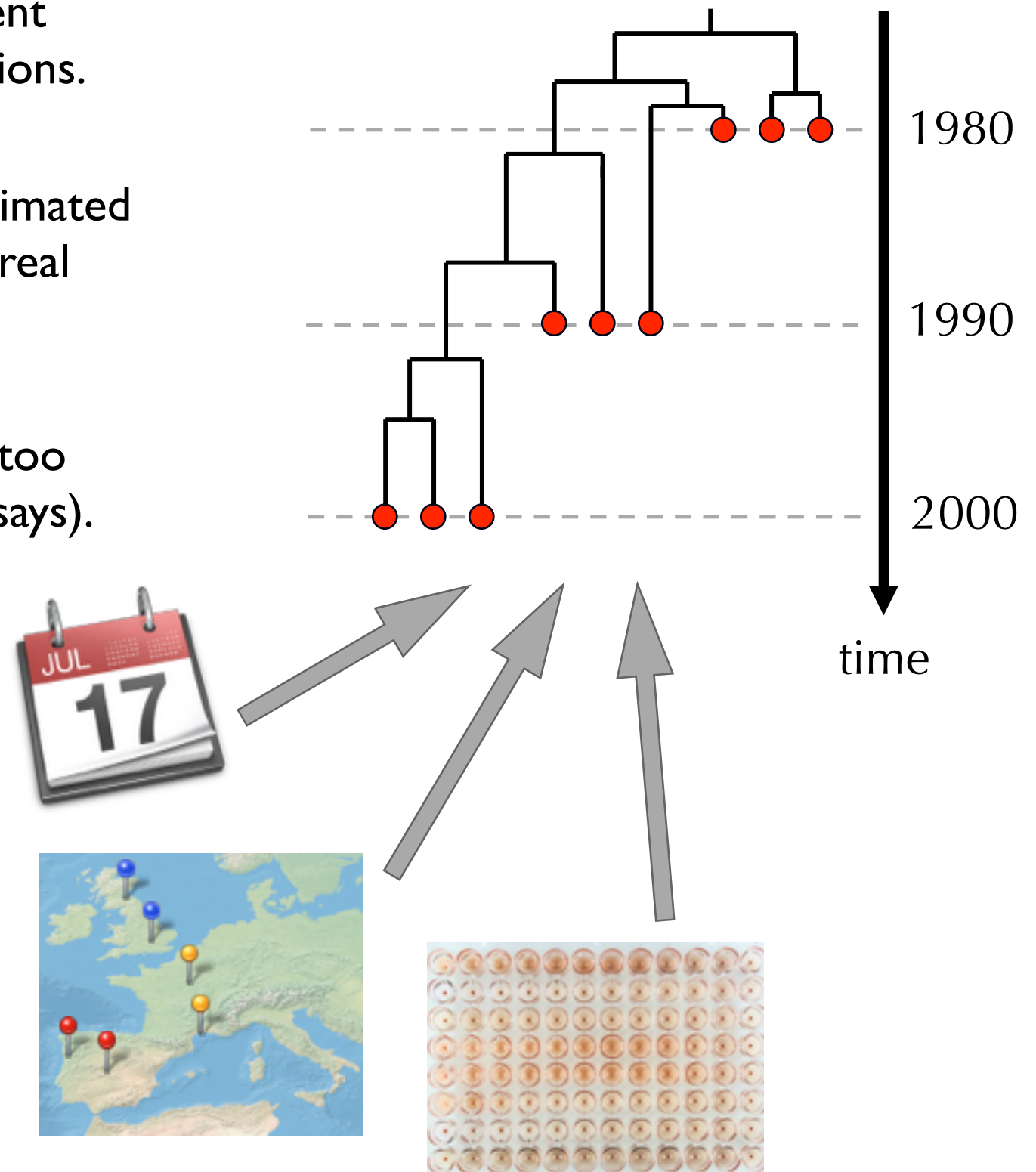
Global measles virus genetic diversity



Global human influenza A H3N2 genetic diversity

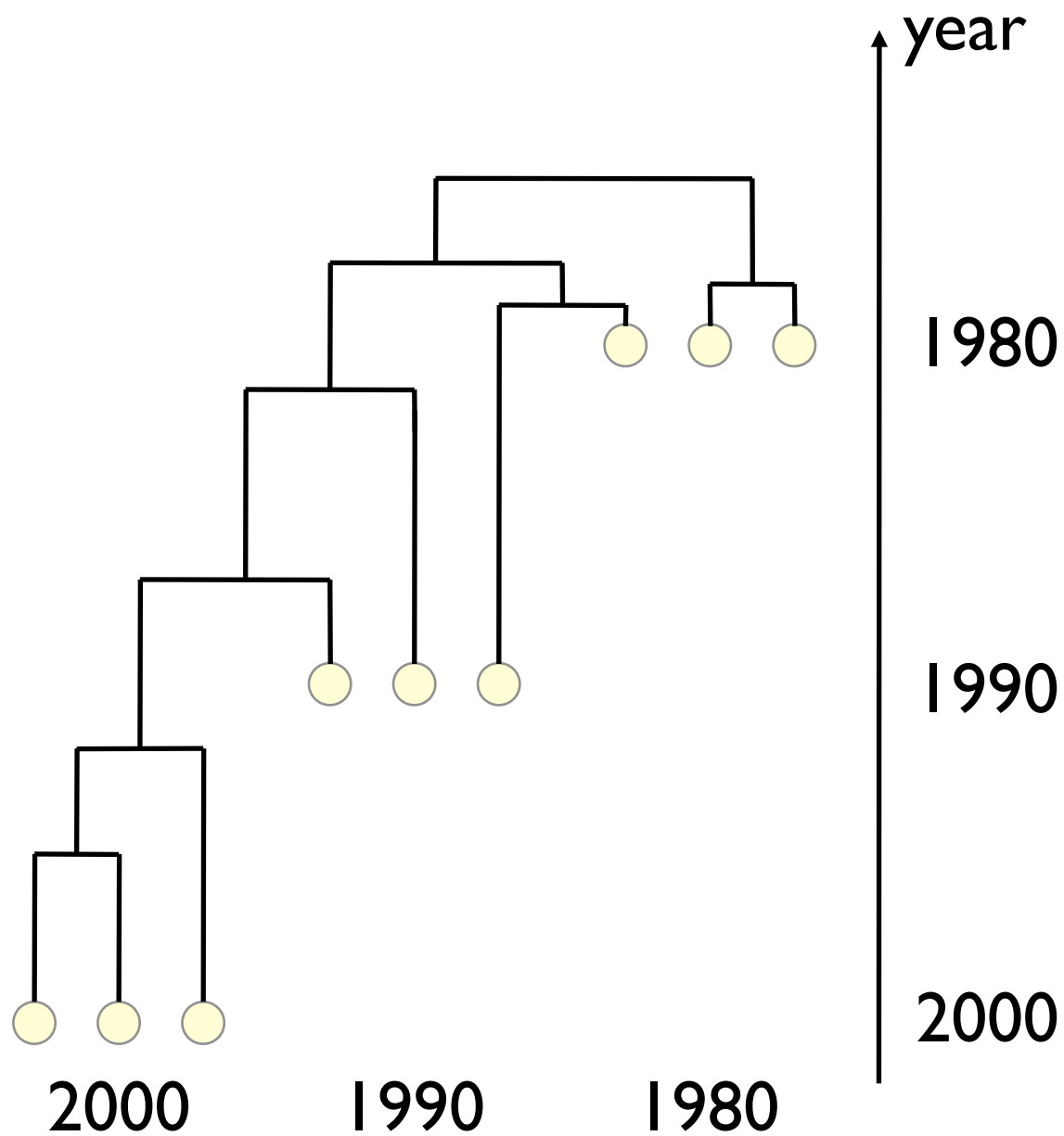
Phylogenetic Data

- Gene sequences are sampled at different points in time and from different locations.
- Hence transmission history can be estimated on a real time-scale (e.g. years) and in real space (e.g. countries, cities).
- Phenotypic trait data may be available too (e.g. drug resistance, immunological assays).

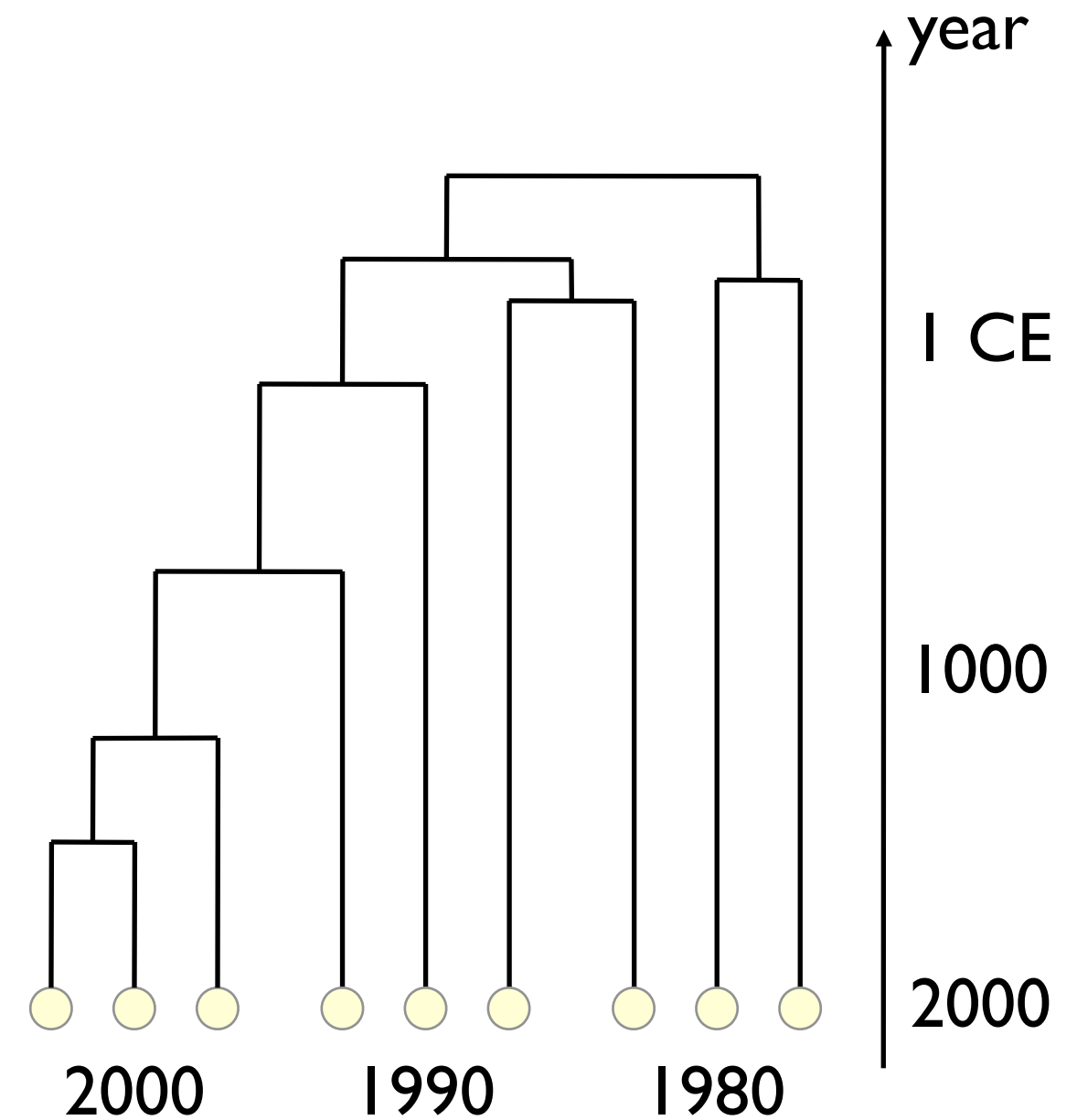


Same sampling times, different rates of evolution

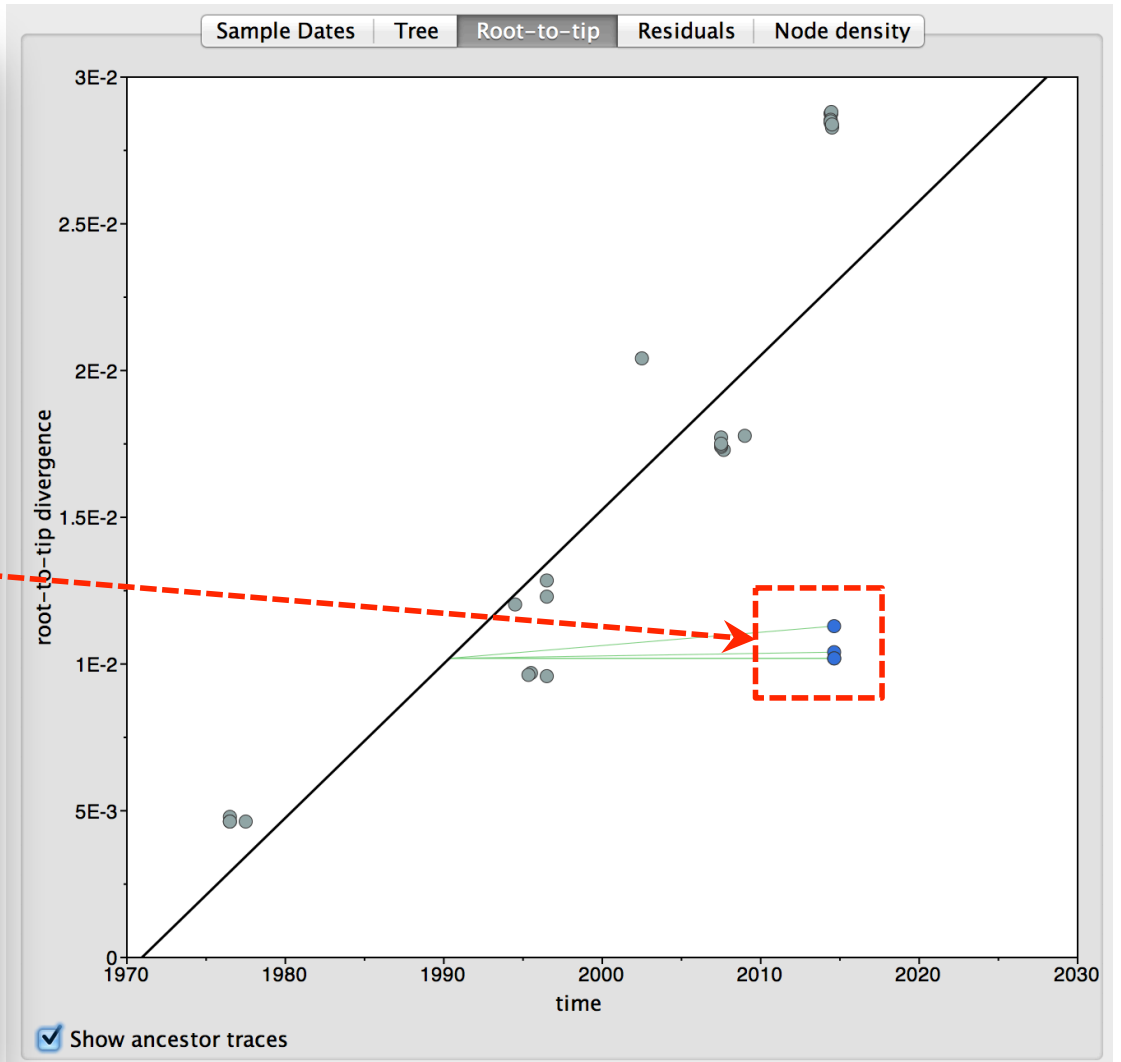
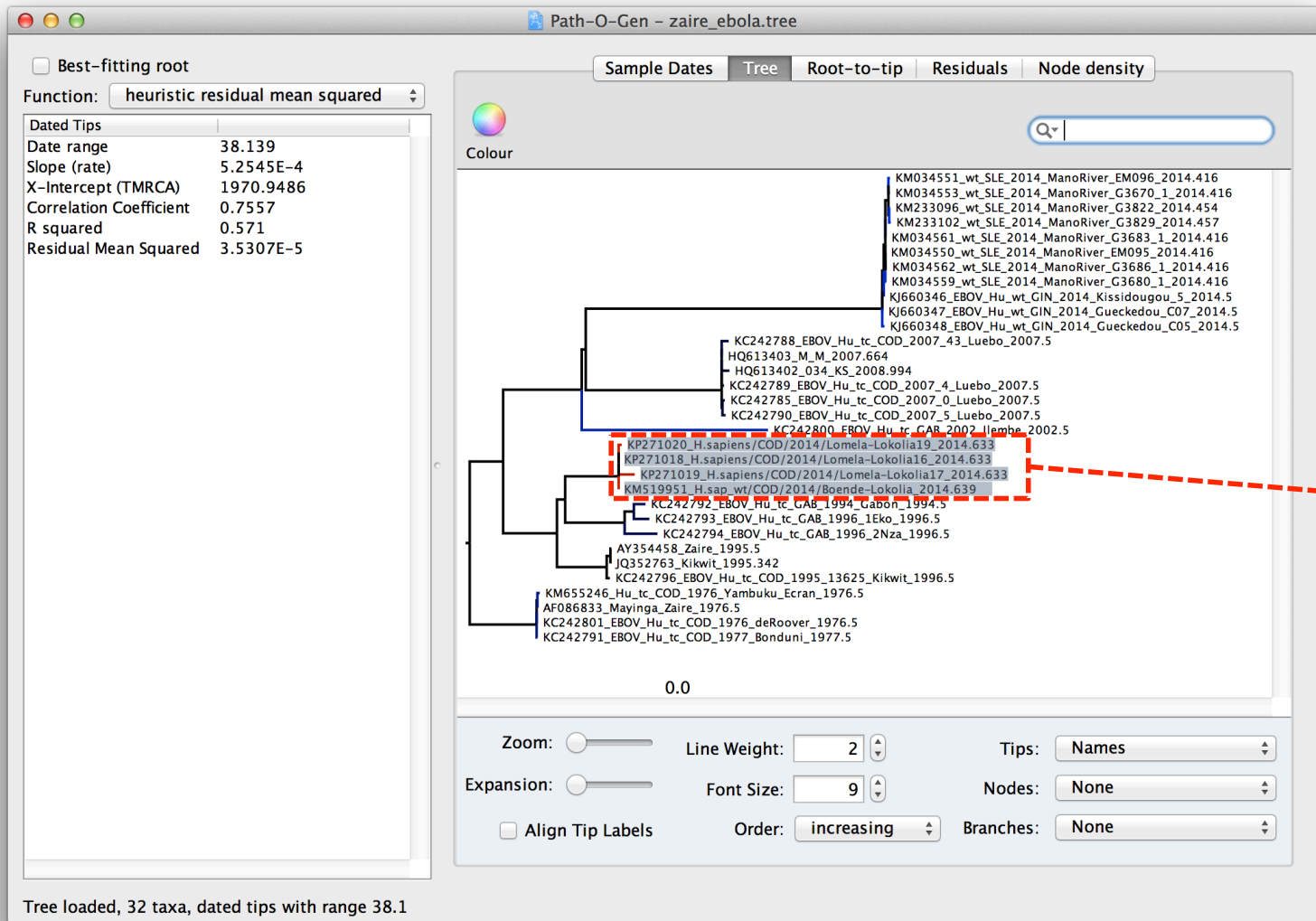
Measurably-evolving population
("heterochronous" or
"serially-sampled")



Not measurably-evolving
("isochronous" or
"contemporaneous sampling")



Phylogenetic Data

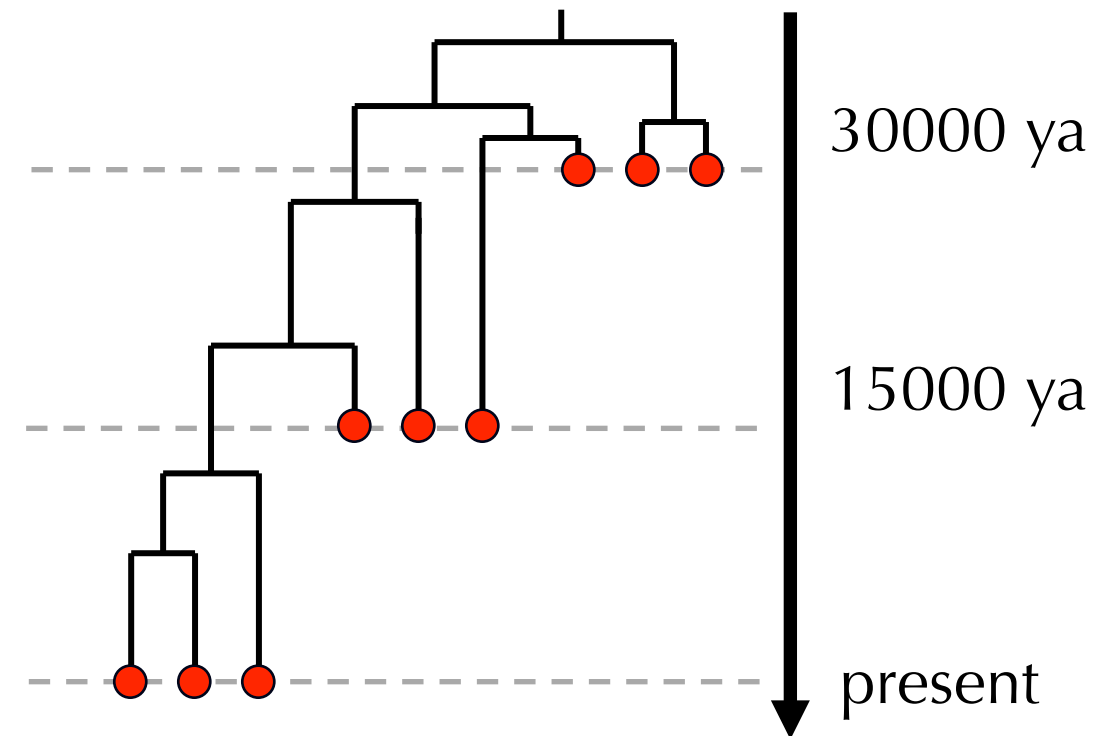


Use TempEst to determine if your sequences are **heterochronous**. Do they exhibit a correlation between genetic divergence and time?

Phylogenetic Data

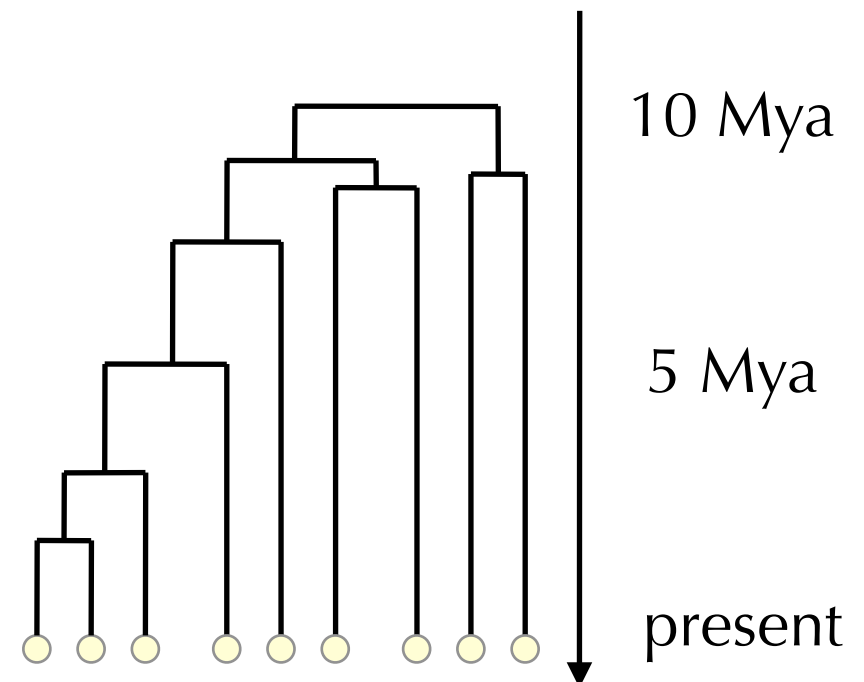
- Are rapidly-evolving pathogens the only source of heterochronous data?

No. Ancient DNA can be recovered from biological material that is >100,000 years old.



- Can phylodynamics be applied to isochronous data?

Yes, although statistical power is weaker. For example, estimating speciation and extinction rates, or investigating the creation and deletion of genes within gene families.



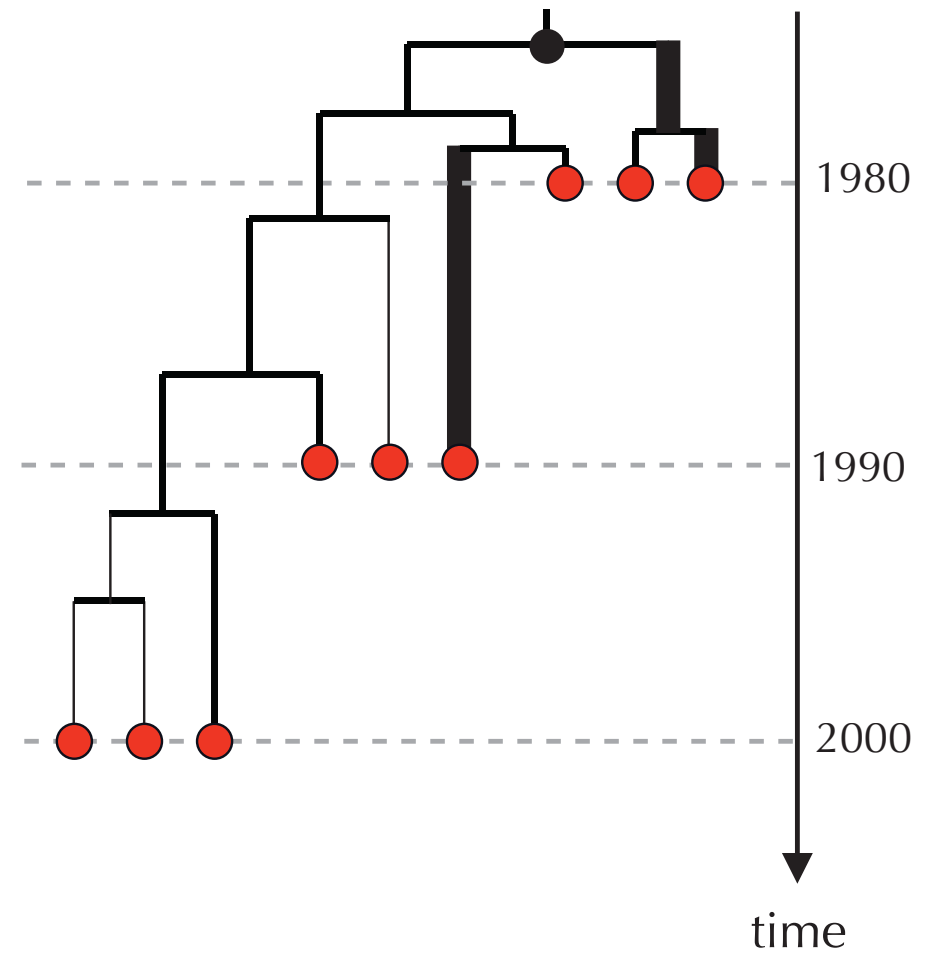
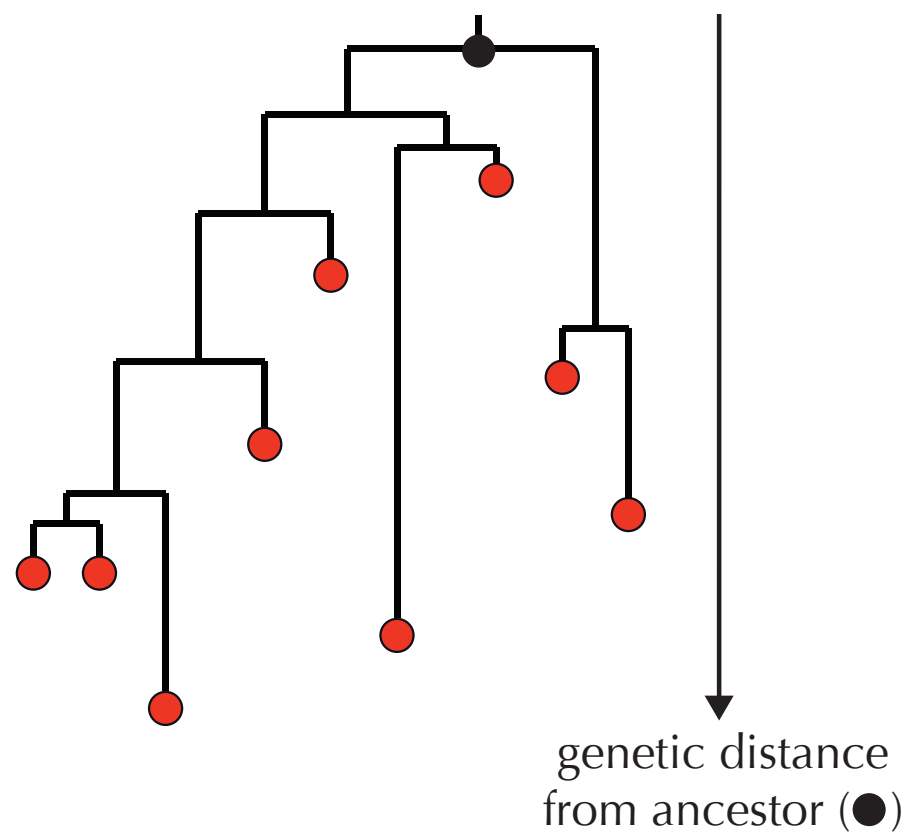
Phylodynamic Questions

- How genetically diverse is a pathogen population?
- How do pathogen genomes change through time?
- How does pathogen genetic diversity vary through space?
- What processes or events determine these changes?
- When did an epidemic start?
- Where did it come from?
- How fast is it transmitting?
- In what direction is it spreading?
- Are hosts X,Y & Z epidemiologically linked?

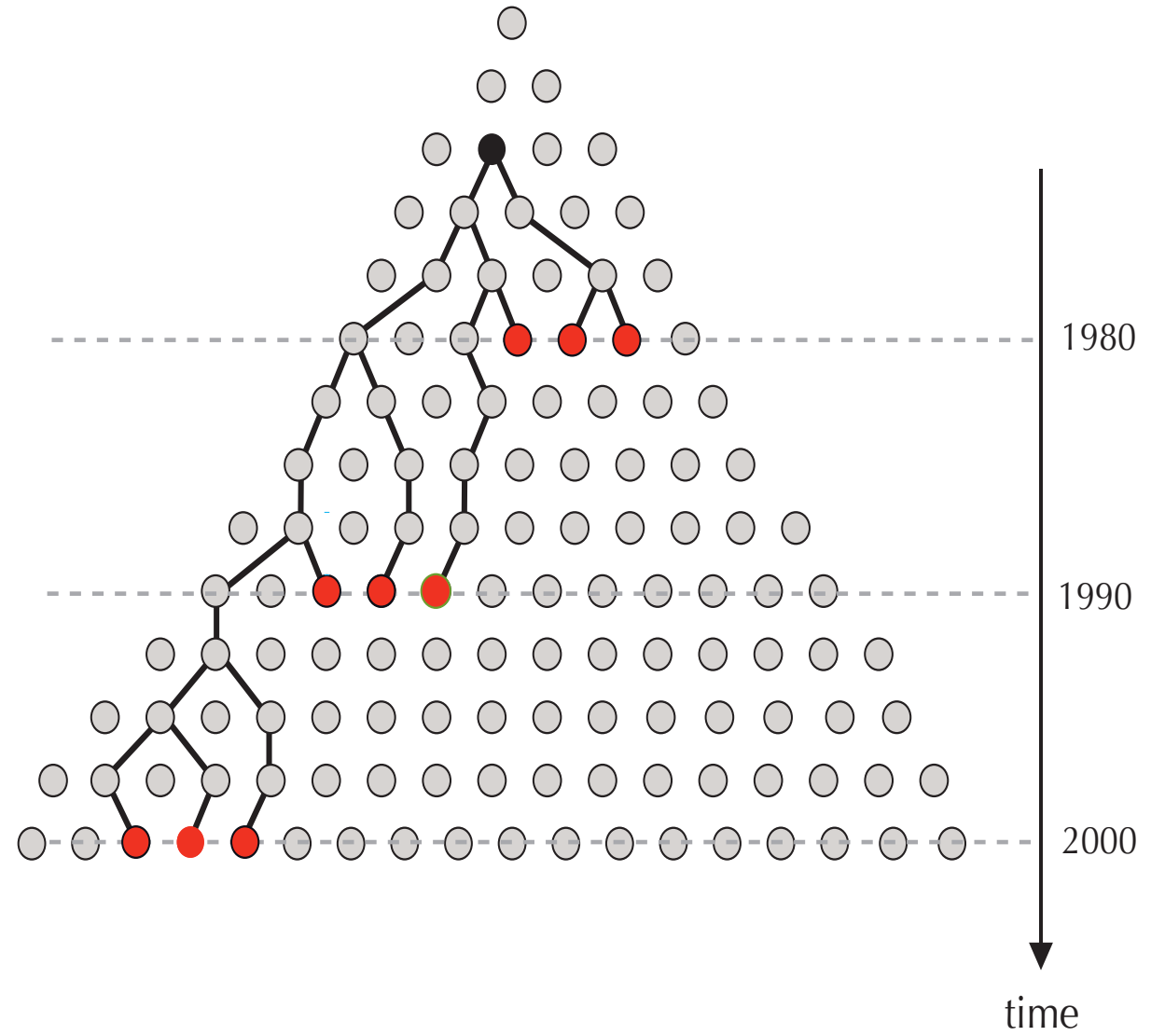
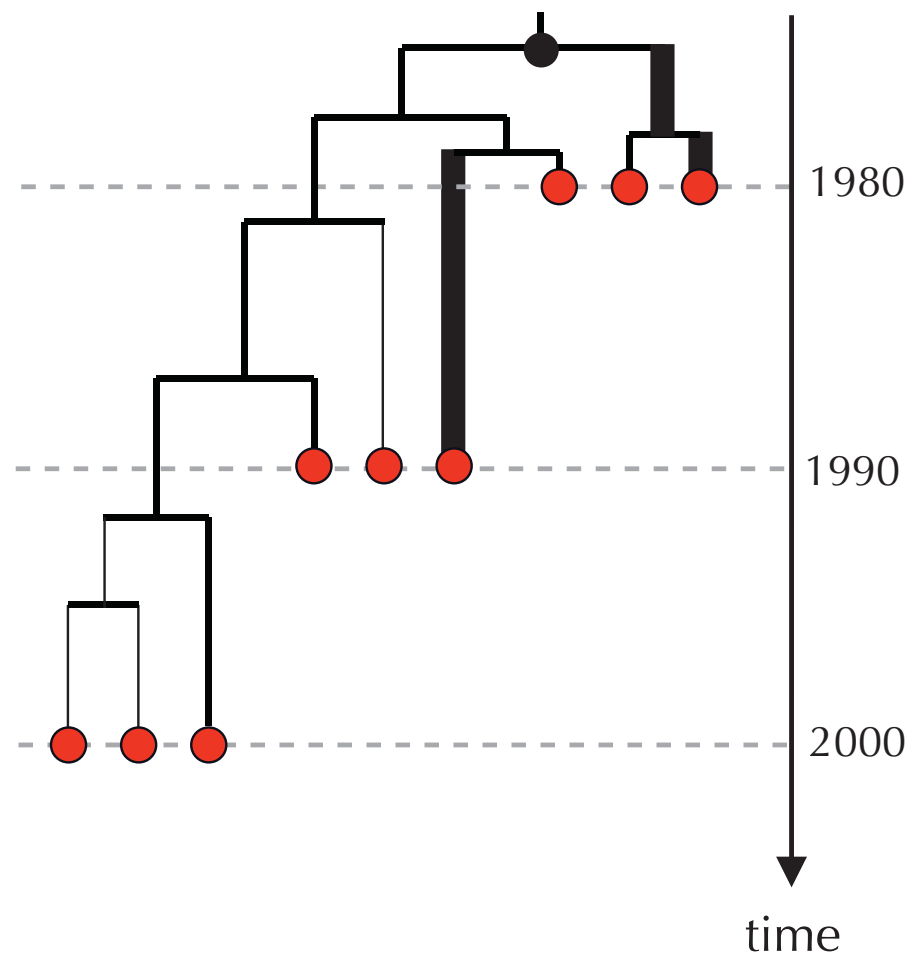
Commonly-used methods for the evolutionary analysis of rapidly-evolving pathogens

- Molecular clocks
- Coalescent theory
- Phylogeography
- Selection analysis
- Recombination analysis

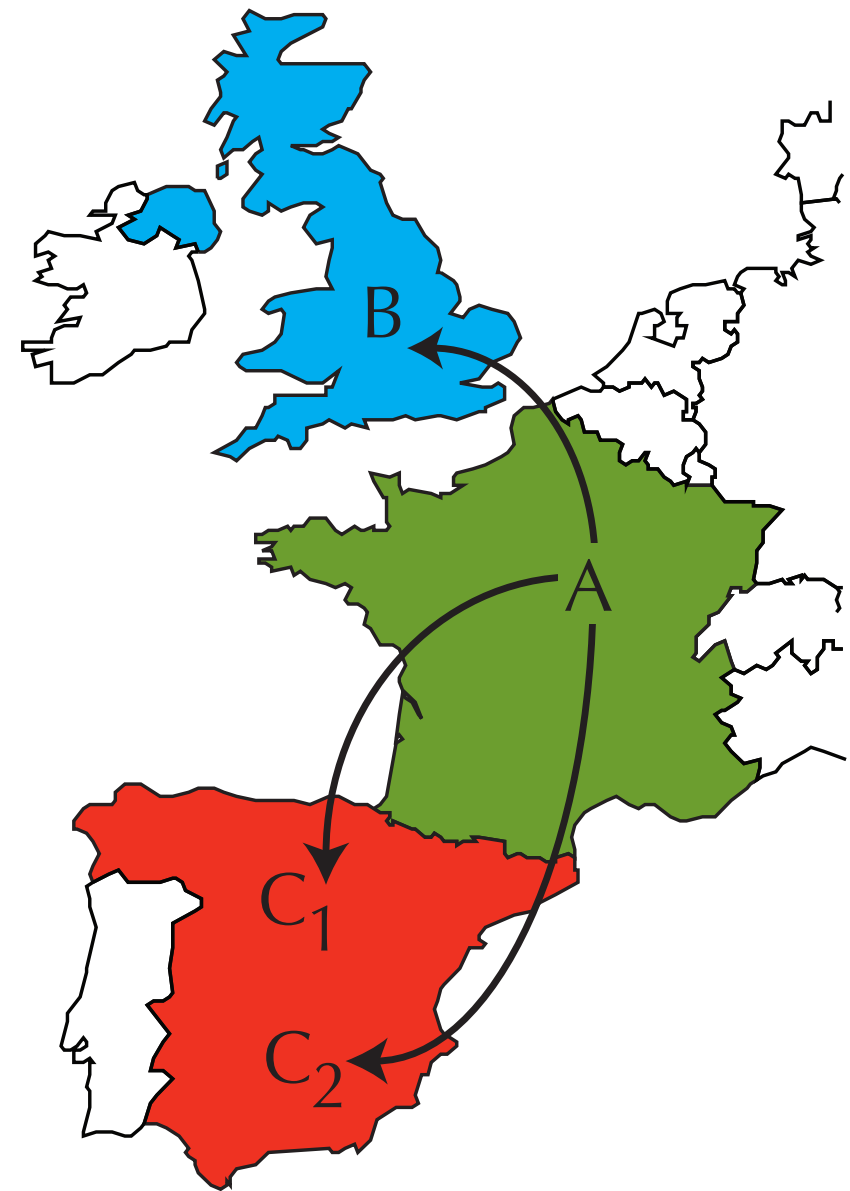
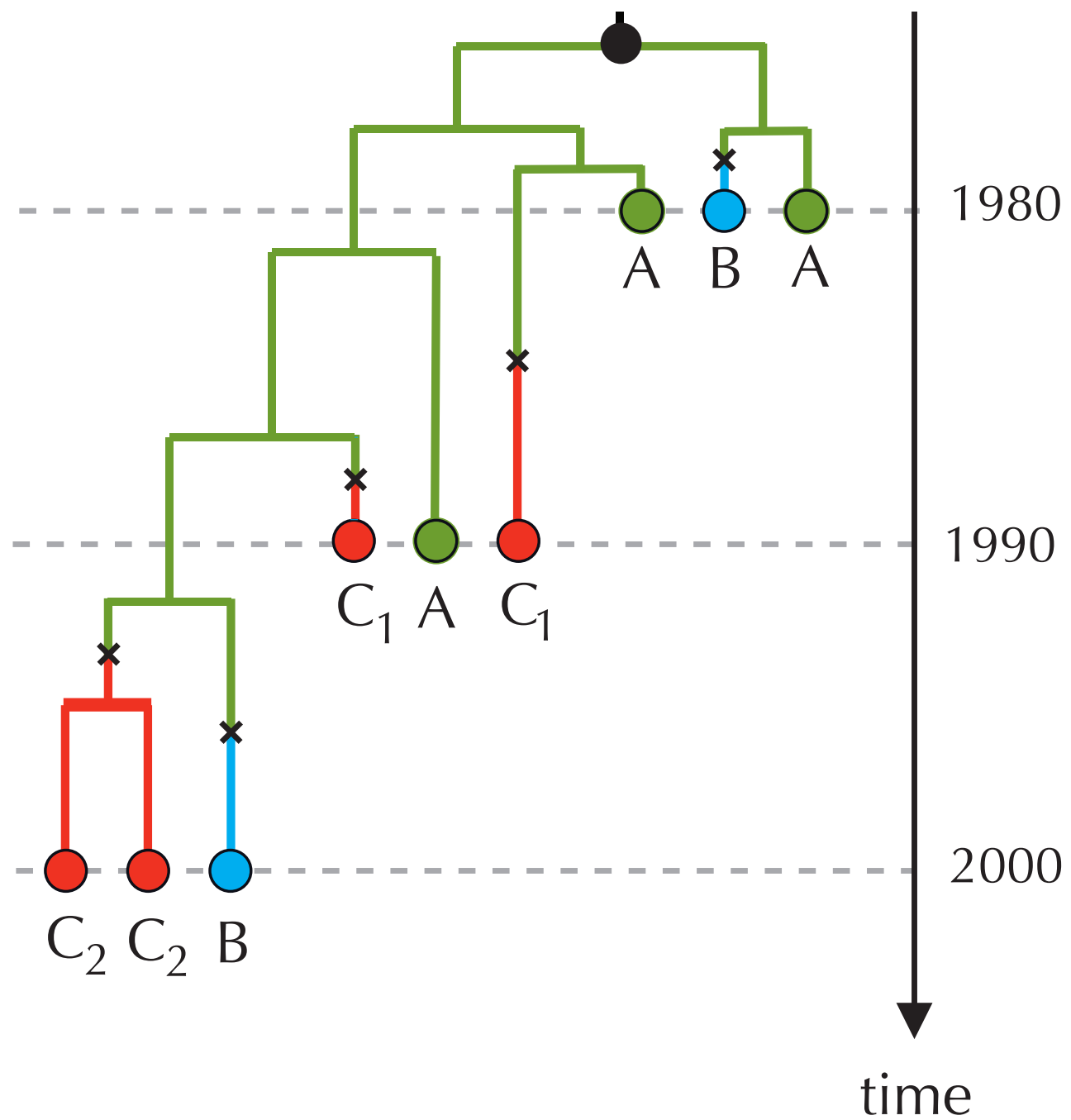
(I) The Molecular Clock



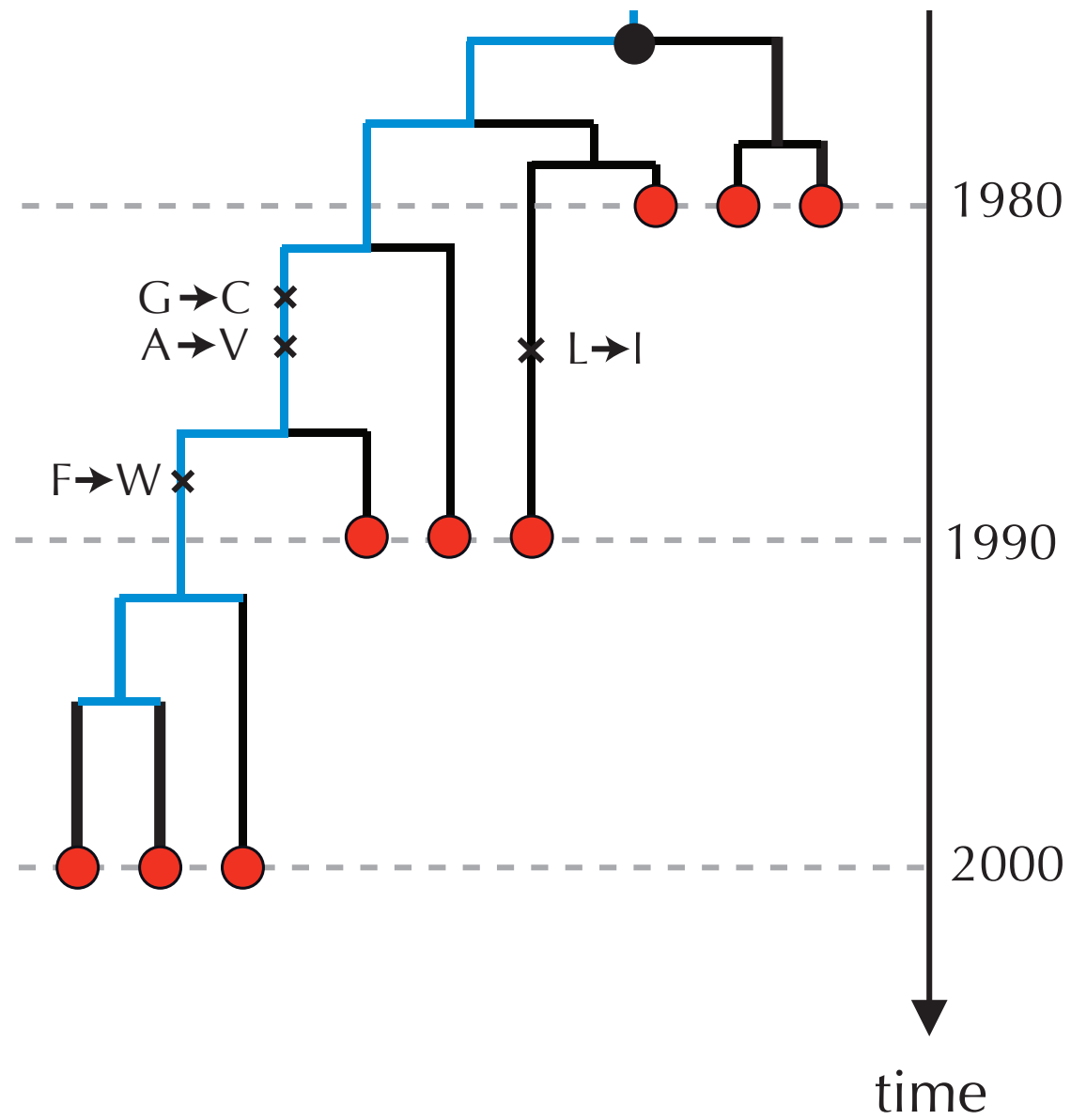
(2) Coalescent Theory / Birth Death Models



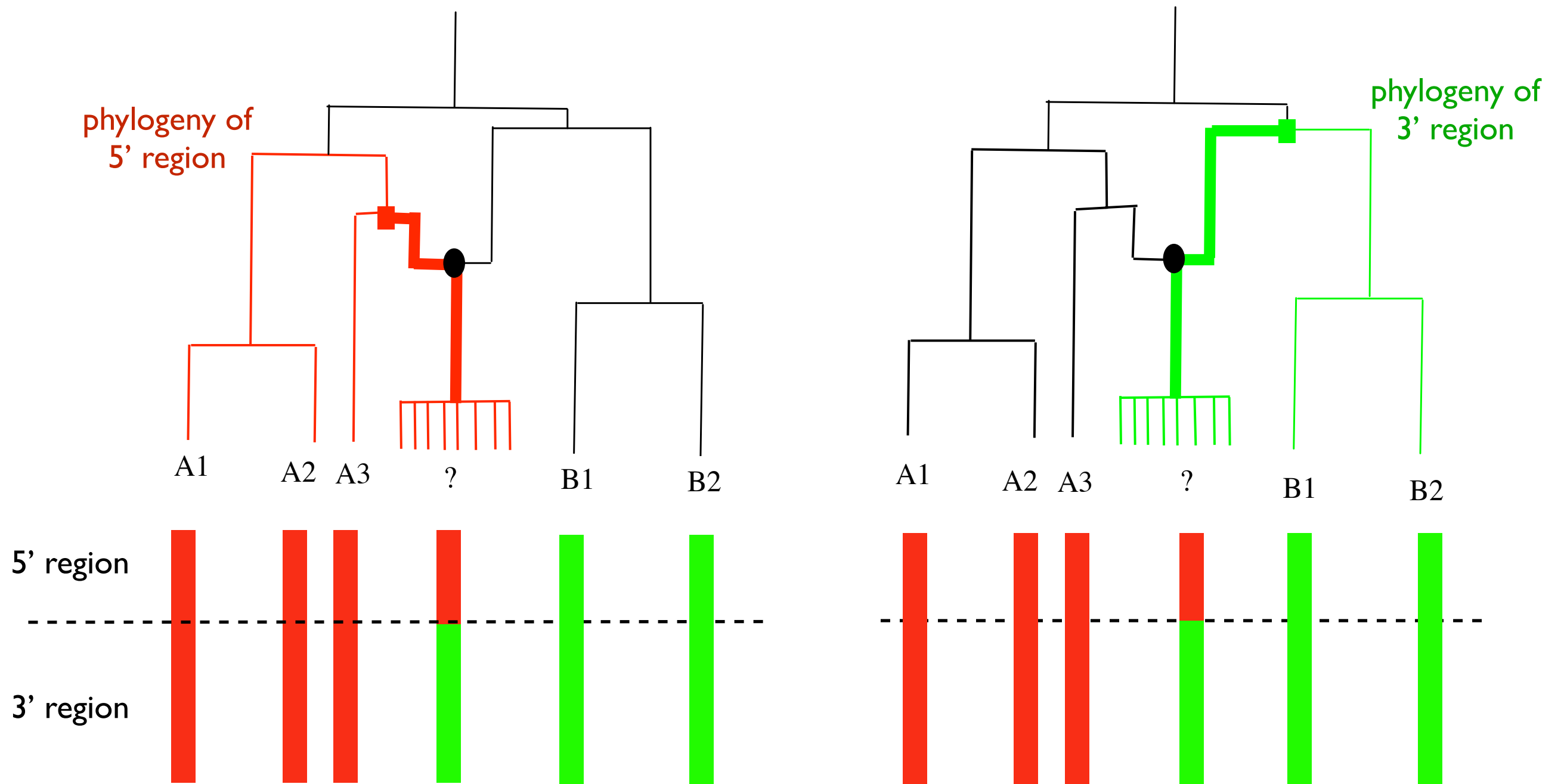
(3) Trait evolution



(4) Selection Analysis



(5) Recombination Analysis



SAMPLES FROM INFECTED INDIVIDUALS

*Clinical Virology
Genomics*



PATHOGEN GENOME SEQUENCES

*Alignment Methods
Sequence Evolution Models*



GENETIC DISTANCES



*Recombination
Analysis*

Phylogenetic Methods



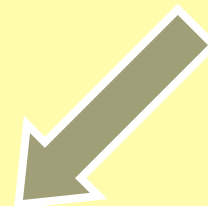
PHYLOGENY (time scale = genetic distance)

*TempEst
Molecular Clocks*



PHYLOGENY (time scale = years)

*Coalescent Theory
Birth/Death Models*



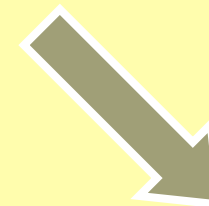
POPULATION DYNAMICS

*Adaptation
Analysis*



ADAPTATION DYNAMICS

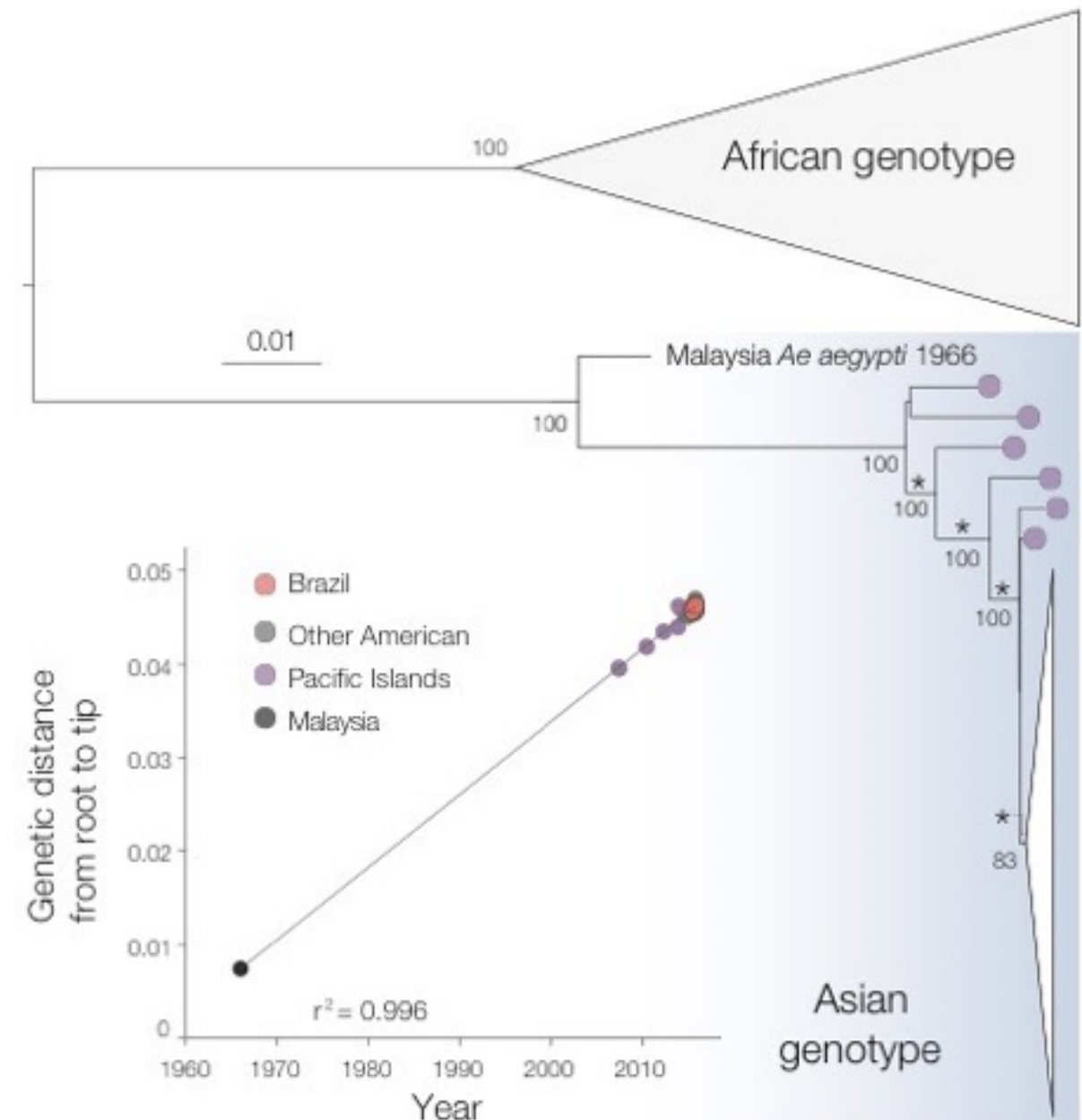
Trait evolution models



PHENOTYPE EVOLUTION

Zika virus in the Americas

- Zika virus isolated in Uganda in 1947
- Transmitted via *Aedes aegypti* that is also the main vector of DENV, CHIKV and YFV
- Flavivirus with single stranded RNA genome of 11kb
- Two phylogenetic genotypes: African and Asian
- Yap Islands (2007), French Polynesia (2013-14), New Caledonia (2014), Easter Island (2014), Samoa (2015)
- Circulation of the ZIKV Asian genotype in Bahia, northeast Brazil confirmed in March 2015
- Increase in microcephaly cases noted in October 2015



Single introduction of Zika into the Americas

Large scale mobility patterns and the arrival of ZIKV in Brazil

