Lecture 2.4:
Infectious disease phylodynamics

Macro-phylogenetics

Years

HIV

Months

Phylodynamics

Rabies virus

Smallpox virus

Days

Influenza A (human H1N1)

Epidemiological processes

Days   Months   Years

Timescale at which novel genomic variation is observed

From Biek et al. 2013 *Trends Ecol Evol*
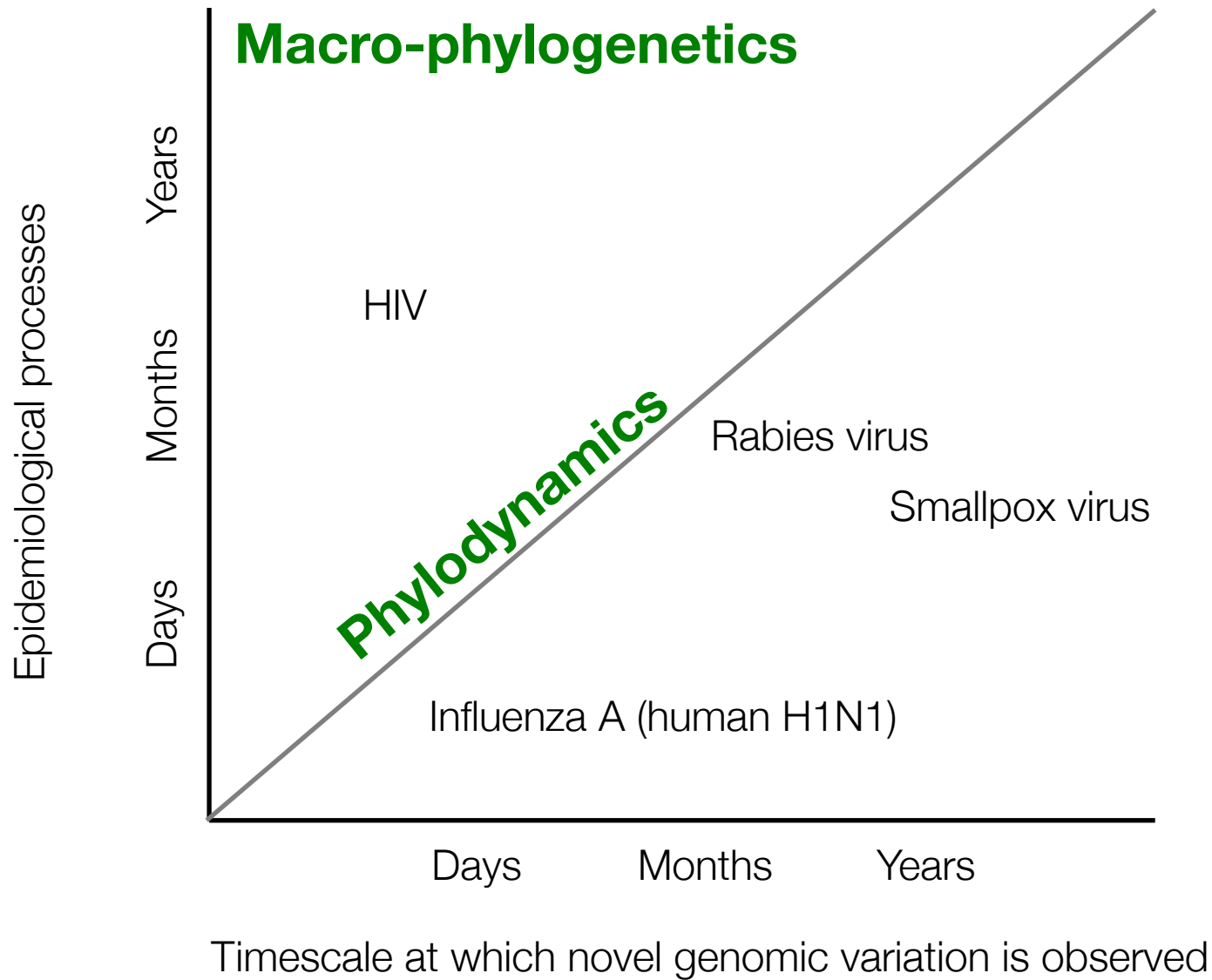
# The basic reproductive number

The basic reproductive number: R_0

R_0 is the average number of secondary infections in a **fully susceptible** population

R_0 for some diseases

| Measles	>12
HIV	$2-5$
Ebola	2.2 (Stadler et al. 2014)
TB	3.4 (Tanaka et al. 2006)
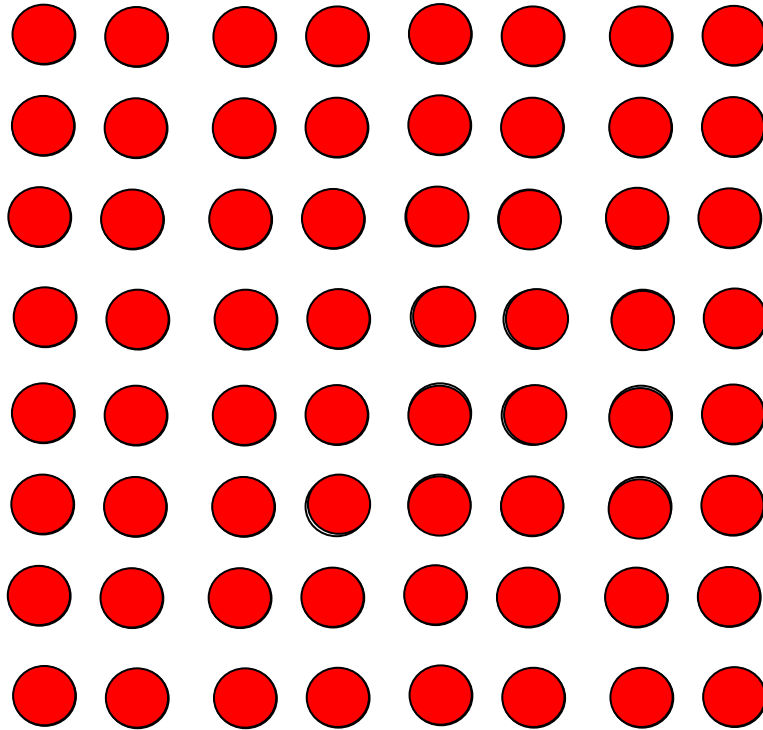
$R_0 > 1$ Infection can spread

$R_0 < 1$ Infection will die out

The basic reproductive number: R_0

- Can depend on many factors:
  - Duration of infection
  - Incubation period
  - Host immunity
  - Behavioral changes
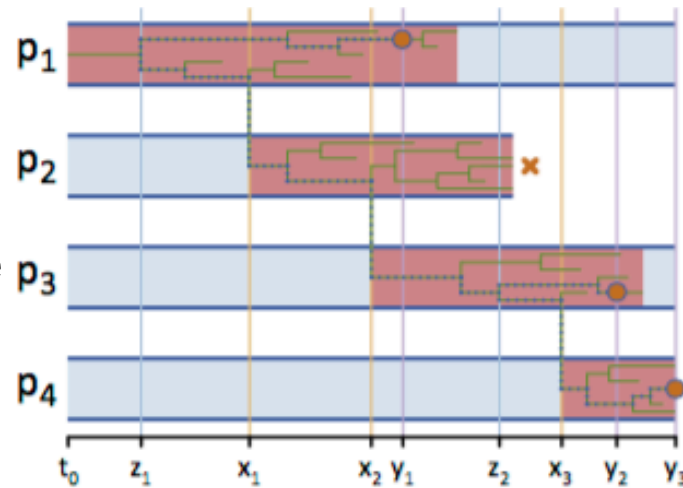- Some of these can be modeled using compartmental models:
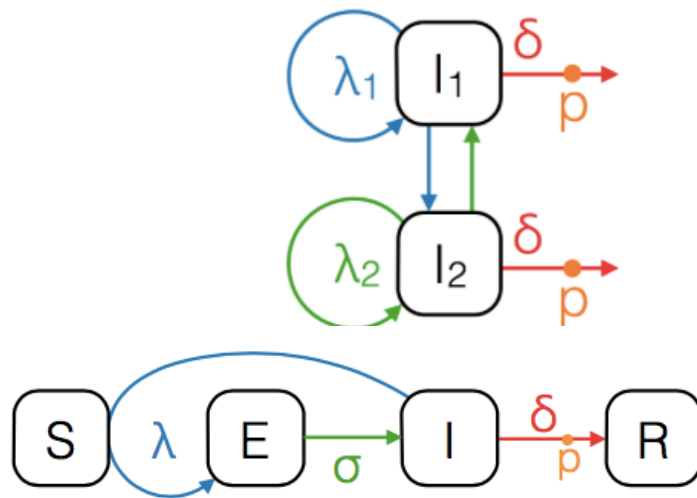
- λ — infection rate
- σ — incubation rate
- δ — becoming-noninfectious rate
- p — sampling probability

From Stadler et al. 2014 *PLOS Current Outbreaks*
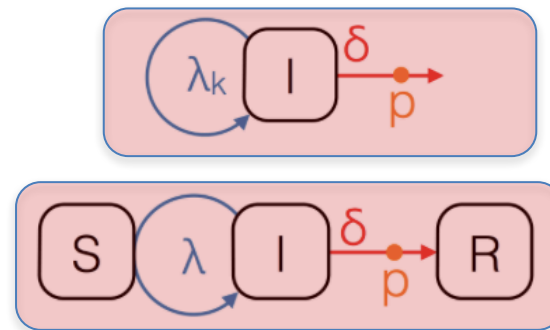
Phylogenetic epidemiology

Phylogenetics trees and infection

Complete transmission tree

Sampled transmission tree

Reconstructed genealogy

Account for sampling fraction
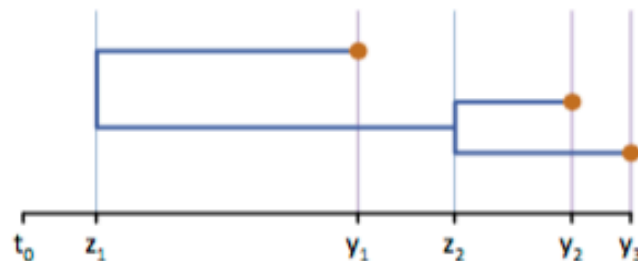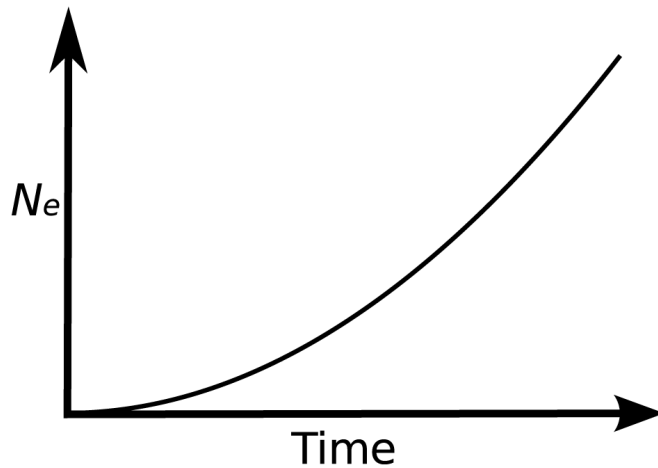
Assume that the sampled tree and reconstructed genealogy are equal
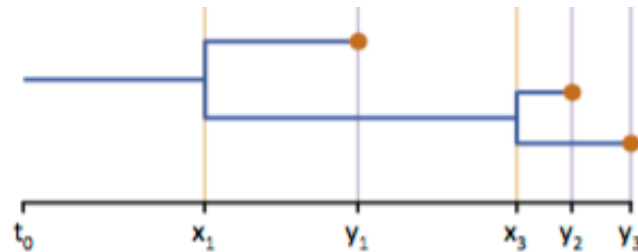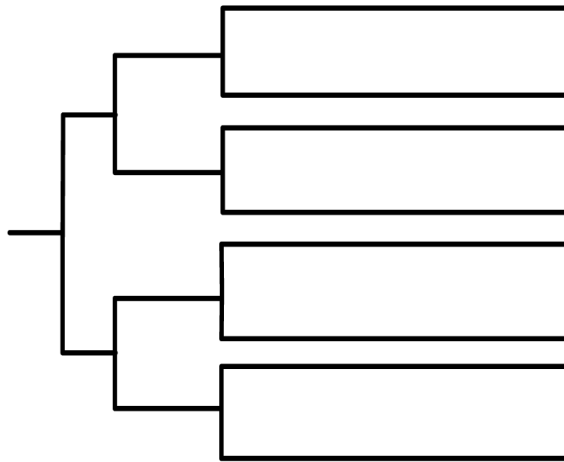
The genealogies have no information about who infected whom
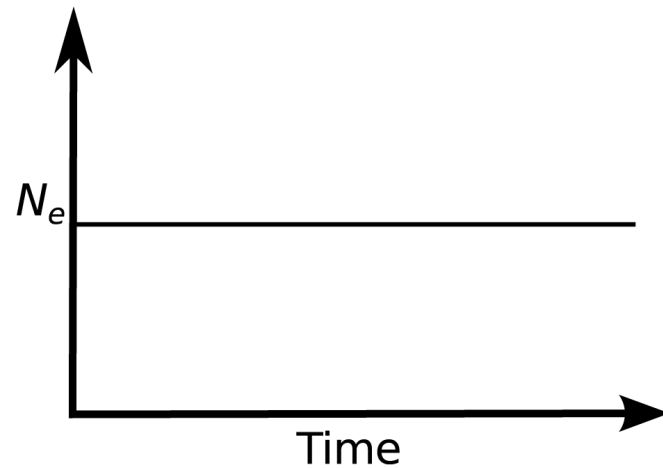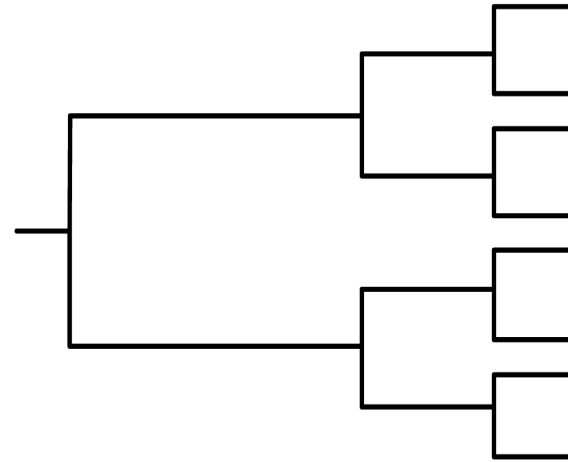
Estimating population size: the coalescent

Exponential Growth

Constant Population Size

From Volz et al. 2013 *PLOS Comp Biol*

Estimating R_0: coalescent phylodynamics

Death / Become non-infectious

Transmission event
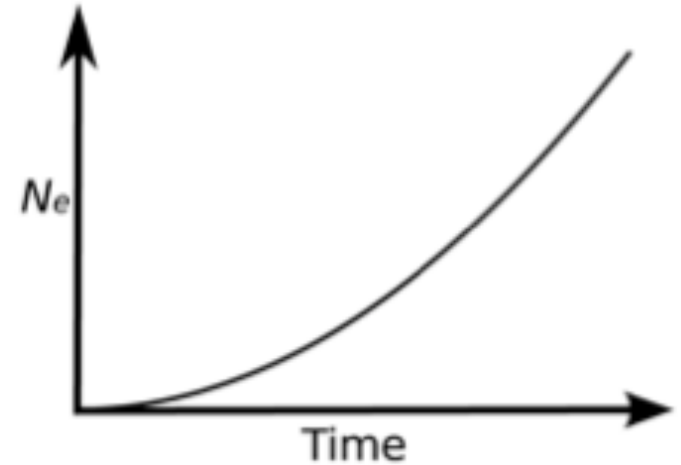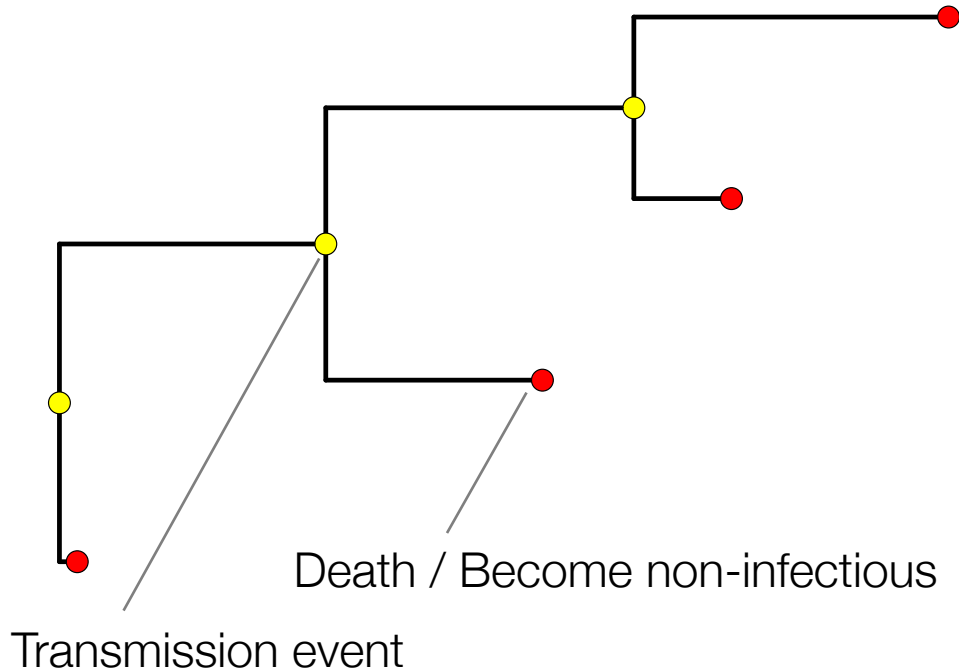
$N(t) = N_0 \, e^{-rt}$

$r = (R_0 - 1) / D$

r: exponential growth rate
N_0: initial population size
N(t): population size at time t

R_0: basic reproductive ratio
D: duration of infection

Estimating R0 using the exponential coalescent model in BEAST

r: growth rate

Φ: scaled population size

λ: birth rate (transmission)

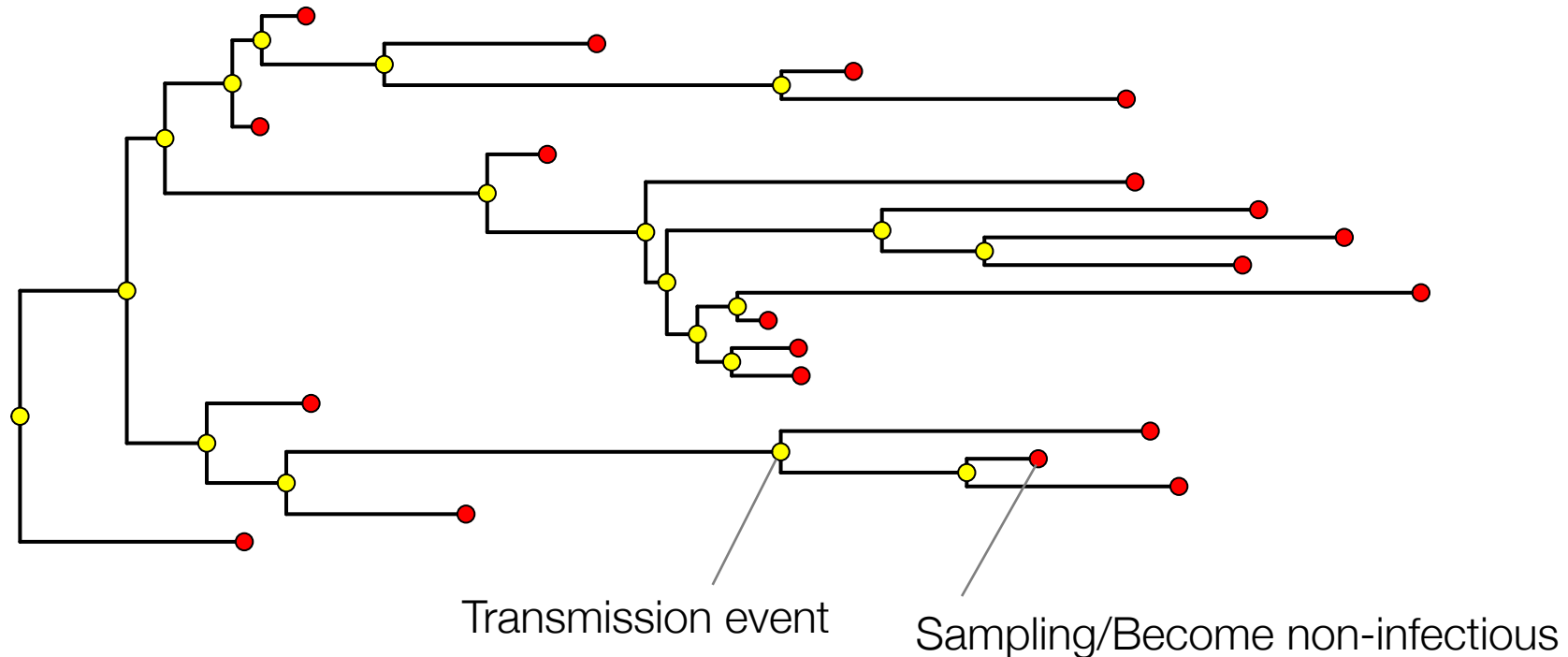δ: become uninfectious rate → $1/\delta$: duration of infection

I(0): Number of infected individuals at present

$$r = \lambda - \delta$$

$$\Phi = I(0) / (2*\lambda)$$

$$R_0 = \lambda / \delta$$

Estimating R_0: Birth-Death models

Transmission event

Sampling/Become non-infectious

λ: transmission rate (birth)

δ = **sampling** + death/recovered

$R_0 = \lambda / \delta$

Estimating R0 using
the birth-death model in BEAST

λ: birth rate (transmission)

δ: become uninfectious rate $\rightarrow$ $1/\delta$: duration of infection

Ψ: sampling rate

μ: death rate

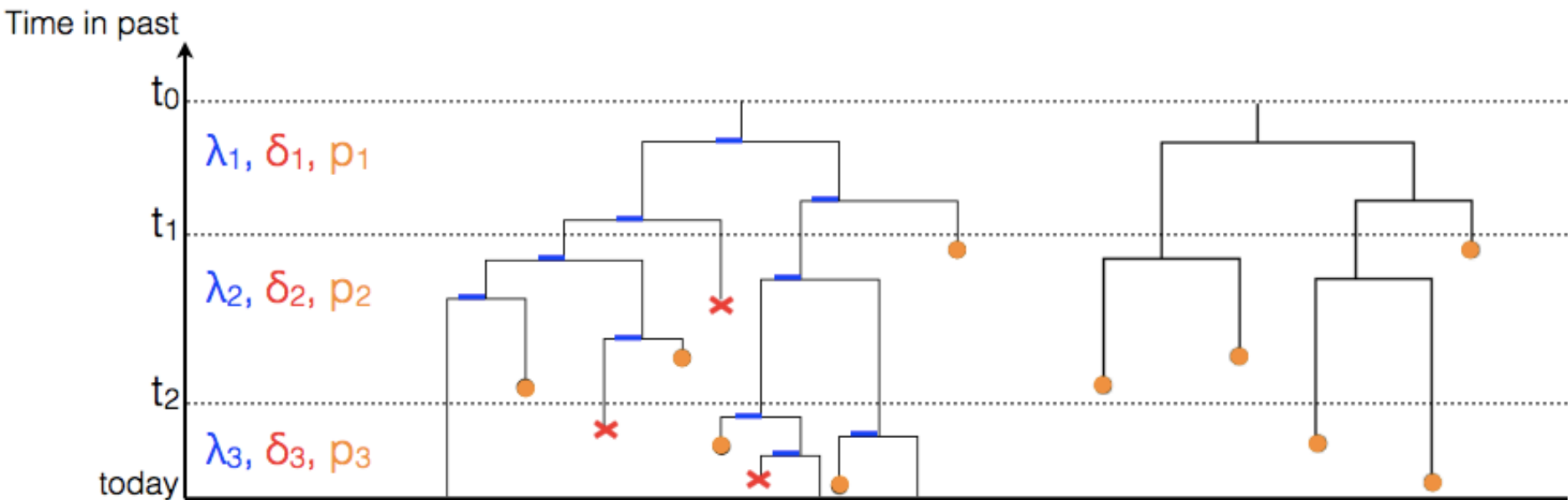p: sampling proportion = $\Psi / (\Psi + \mu)$

$$\delta = \Psi + \mu$$
$$R_0 = \lambda / \delta$$

Likelihood depends on $\lambda*\delta*p$ and $\lambda-\delta$ in both models (BD or CE)
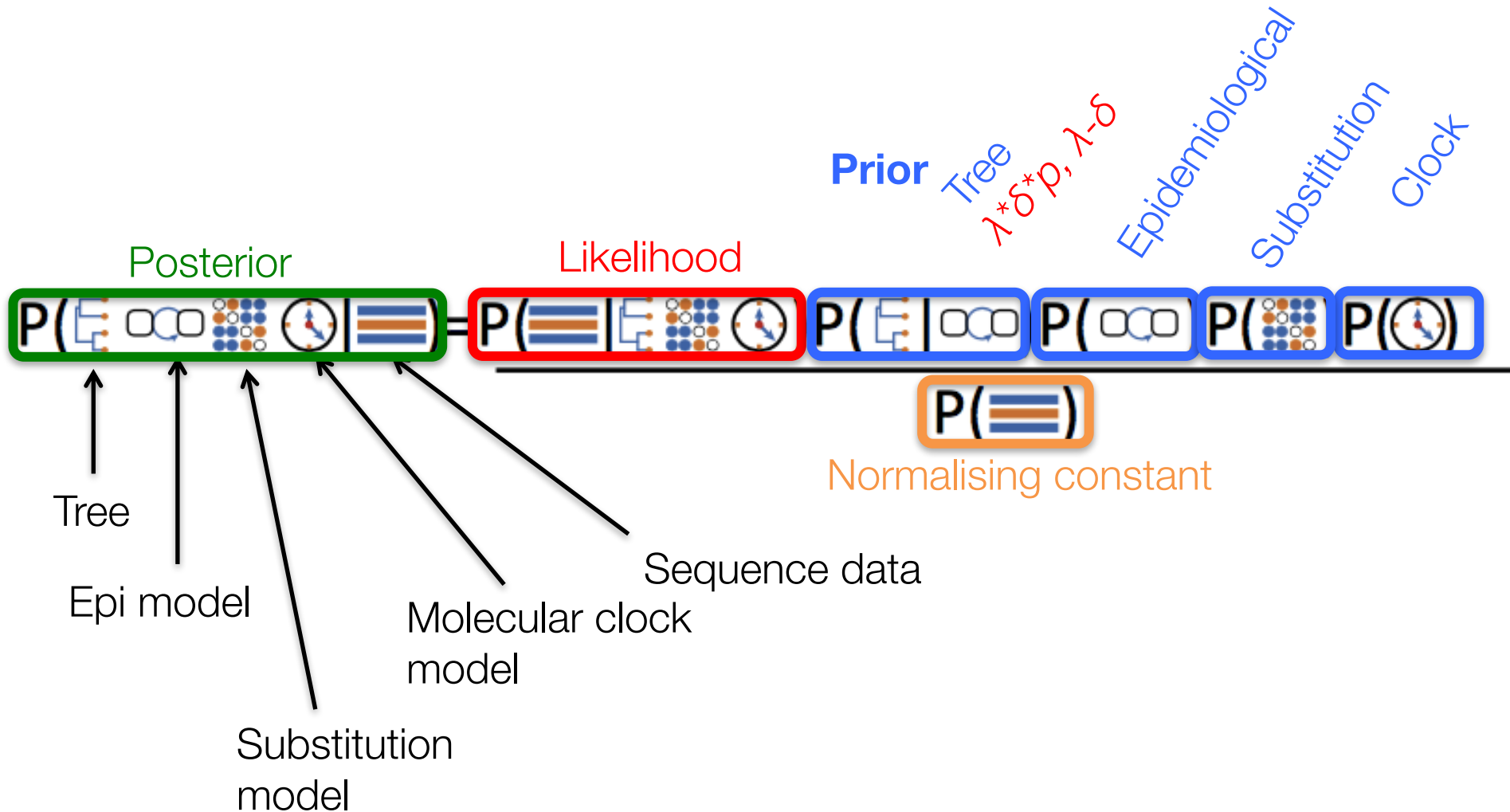
Skyline methods

- Coalescent and Birth-Death methods assume constant parameters
- This assumption can be relaxed
  - Birth Death Skyline
  - Coalescent Skyline

$$R_e(t)$$
$$R_e(0) = R_0$$

Image modified from Tanja Stadler's slides
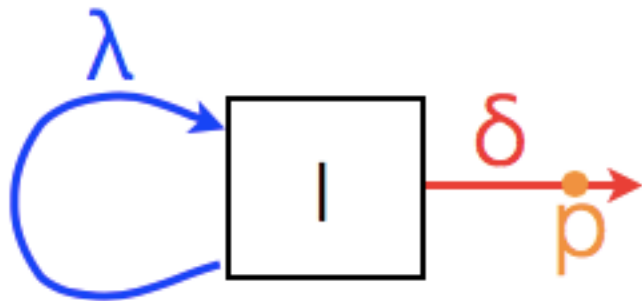
Modelling framework

Bayesian approach

Prior

Tree

λ*δ*ρ, λ-δ

Epidemiological

Substitution

Clock

Posterior

Likelihood

Normalising constant

Tree

Epi model

Substitution model

Molecular clock model

Sequence data

Compartmental models

Birth-Death

$$R_0 = \lambda / (\delta)$$

λ = transmission rate
δ = becoming non-infectious rate
ρ = sampling

From Stadler et al. 2014 *PLOS Current Outbreaks*

Compartmental models

Birth-Death Susceptible-infected-recovered
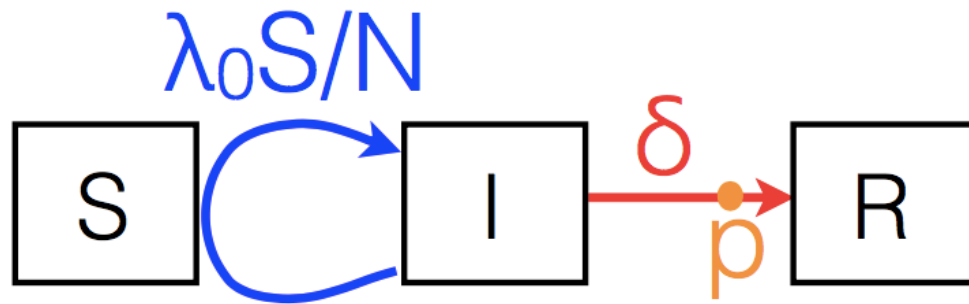
λ = transmission rate
δ = becoming non-infectious rate
ρ = sampling

From Stadler et al. 2014 *PLOS Current Outbreaks*
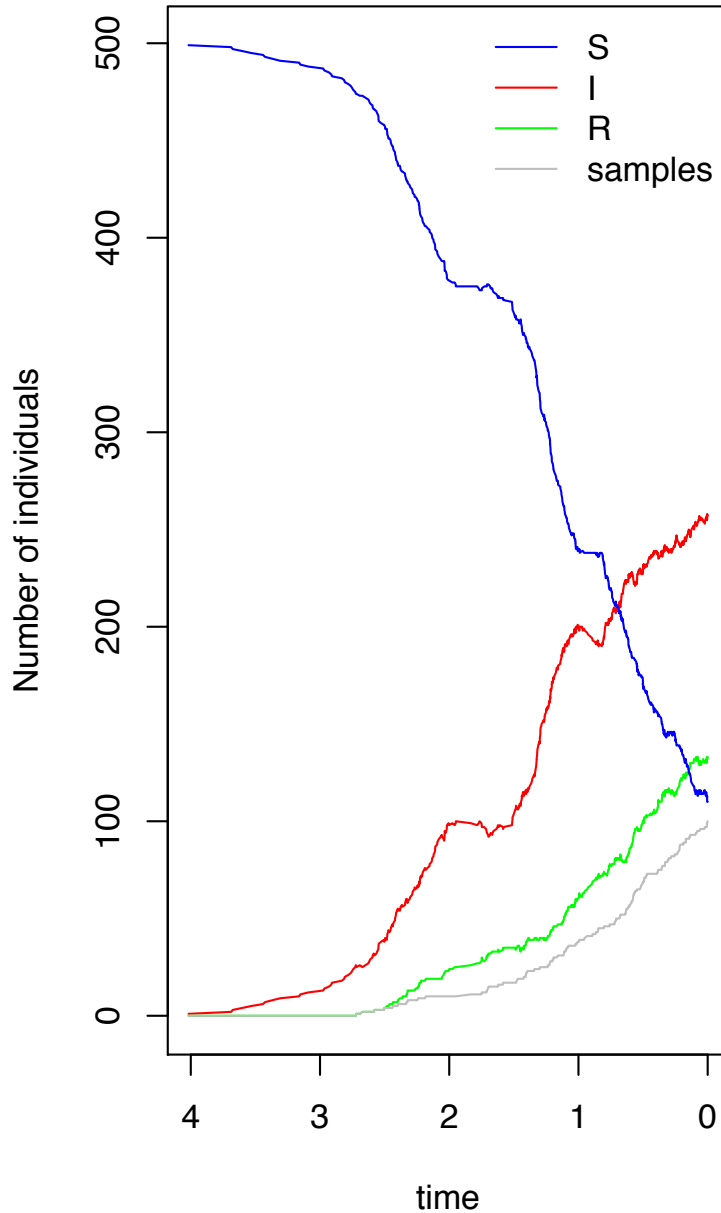
Transmission rate (birth): β

Become uninfectious rate: γ

Susceptible pop. size: n_s
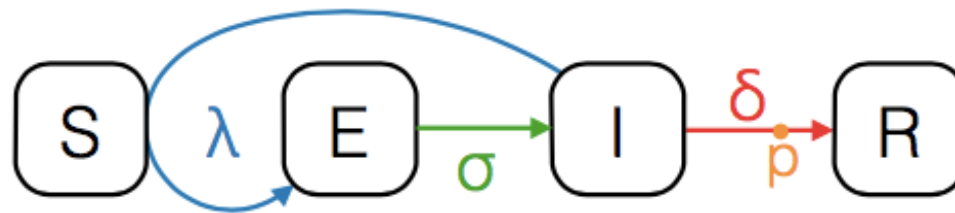
$R_e = \beta * n_s / \gamma$

$R_0 = \beta * n_s(0) / \gamma$

SIR and BD are equivalent when S → N

Compartmental models

Birth-Death Exposed-infected-recovered

λ = transmission rate
δ = becoming non-infectious rate
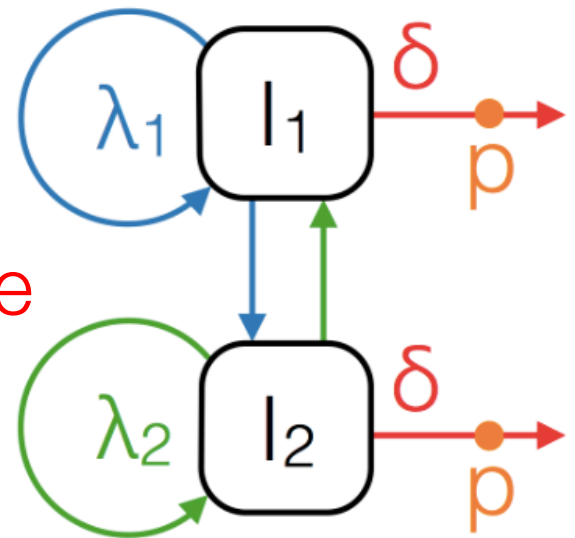ρ = sampling probability
σ = incubation rate

From Stadler et al. 2014 *PLOS Current Outbreaks*

Compartmental models

Birth-Death super-spreading

λ_1 = transmission rate 1
λ_2 = transmission rate 2
δ = becoming non-infectious rate
ρ = sampling probability
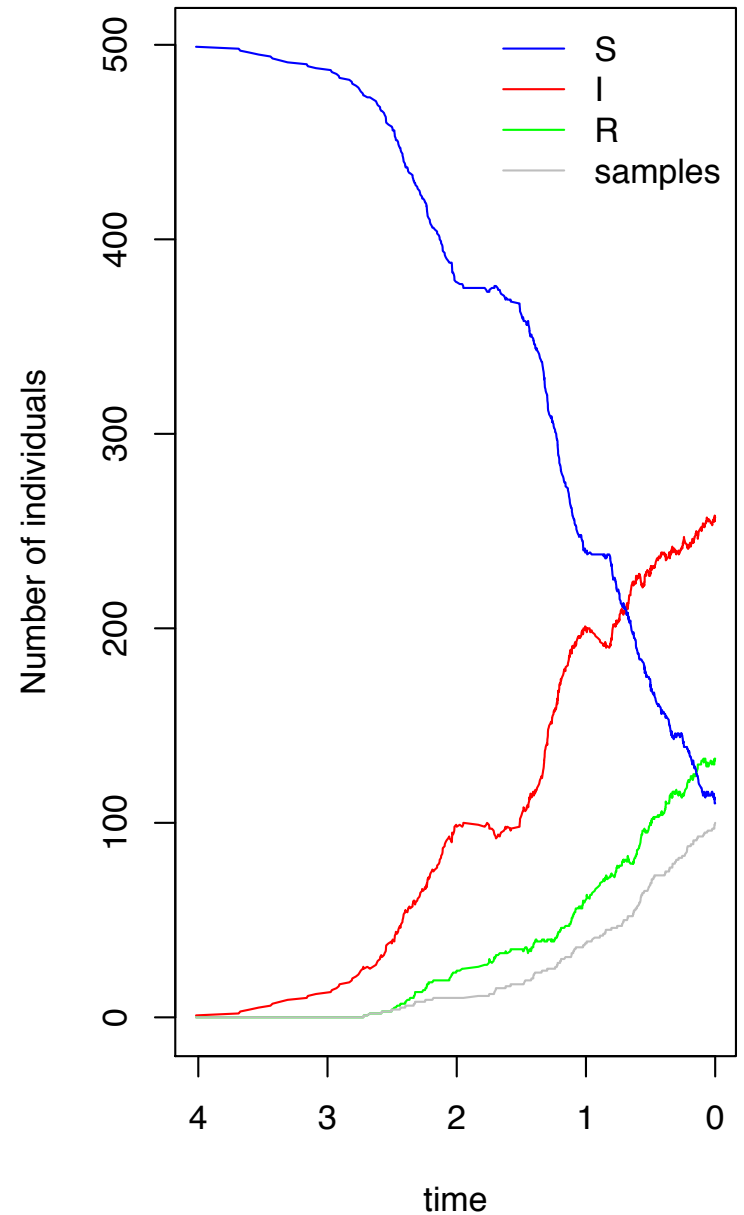
From Stadler et al. 2014 *PLOS Current Outbreaks*

Simulating trajectories
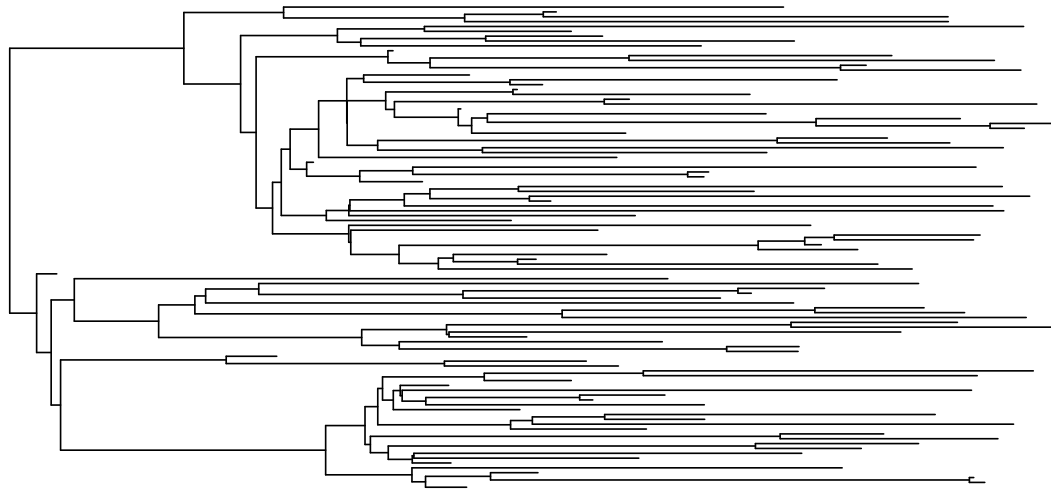
MASTER (BEAST2)
   (Vaughan and Drummond 2013)
TreeSim (Stadler 2011)

Useful references

Kühnert, Denise, et al. "Simultaneous reconstruction of evolutionary history and epidemiological dynamics from viral sequences with the birth–death SIR model." *Journal of the Royal Society Interface* 11.94 (2014): 20131106.

du Plessis, Louis, and Tanja Stadler. "Getting to the root of epidemic spread with phylodynamic analysis of genomic data." *Trends in microbiology* 23.7 (2015): 383-386.

Boskova, Veronika, Sebastian Bonhoeffer, and Tanja Stadler. "Inference of epidemiological dynamics based on simulated phylogenies using birth-death and coalescent models." PLoS computational biology 10, no. 11 (2014): e1003913.

Go to **Practical: Phylogenetic epidemiology in BEAST**