The Boyd Orr Centre
for Population and Ecosystem Health

What can pathogen phylogenetics tell us about cross-species transmission?

Roman Biek
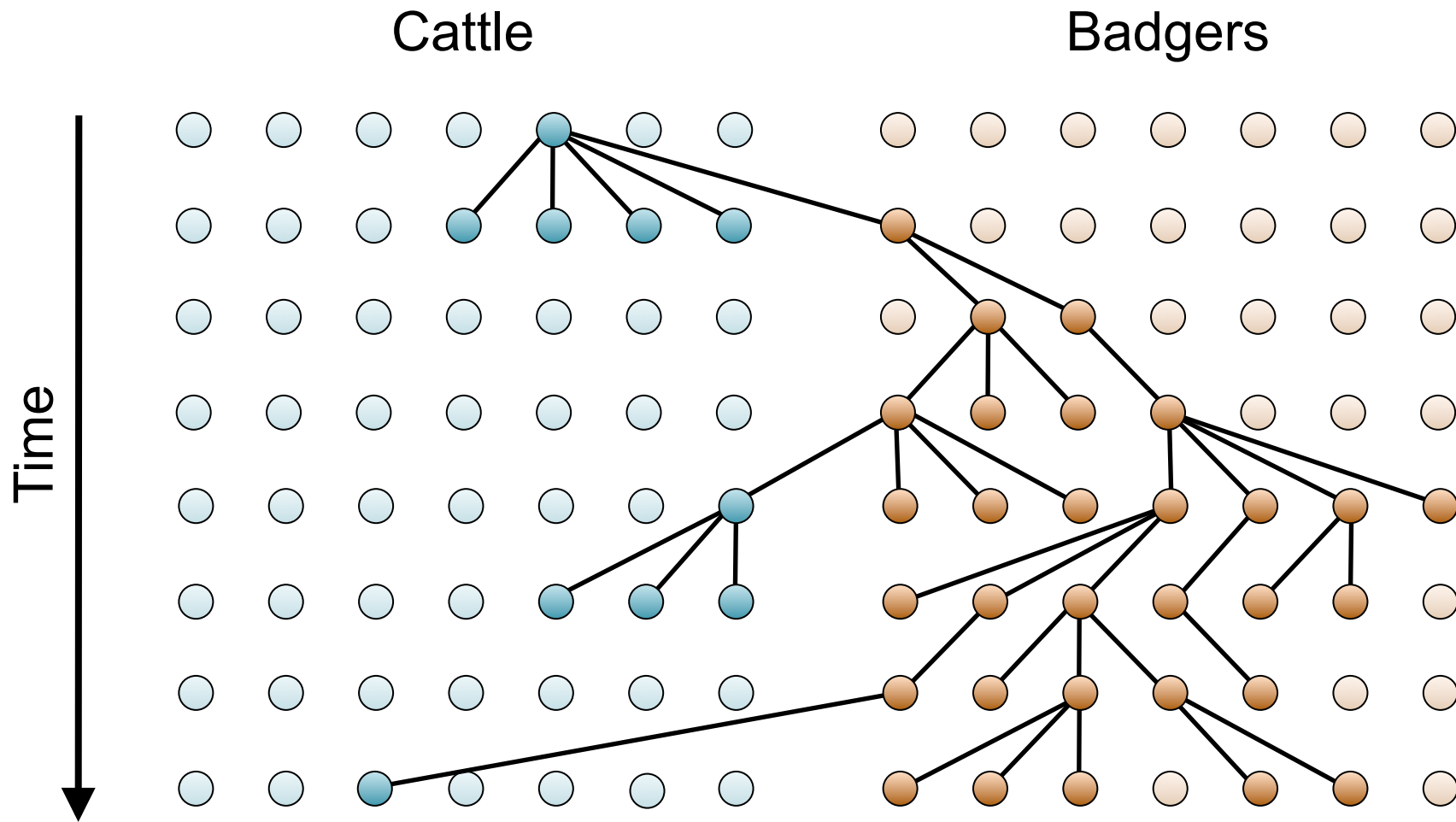
Bovine TB workshop

3 Sep 2015
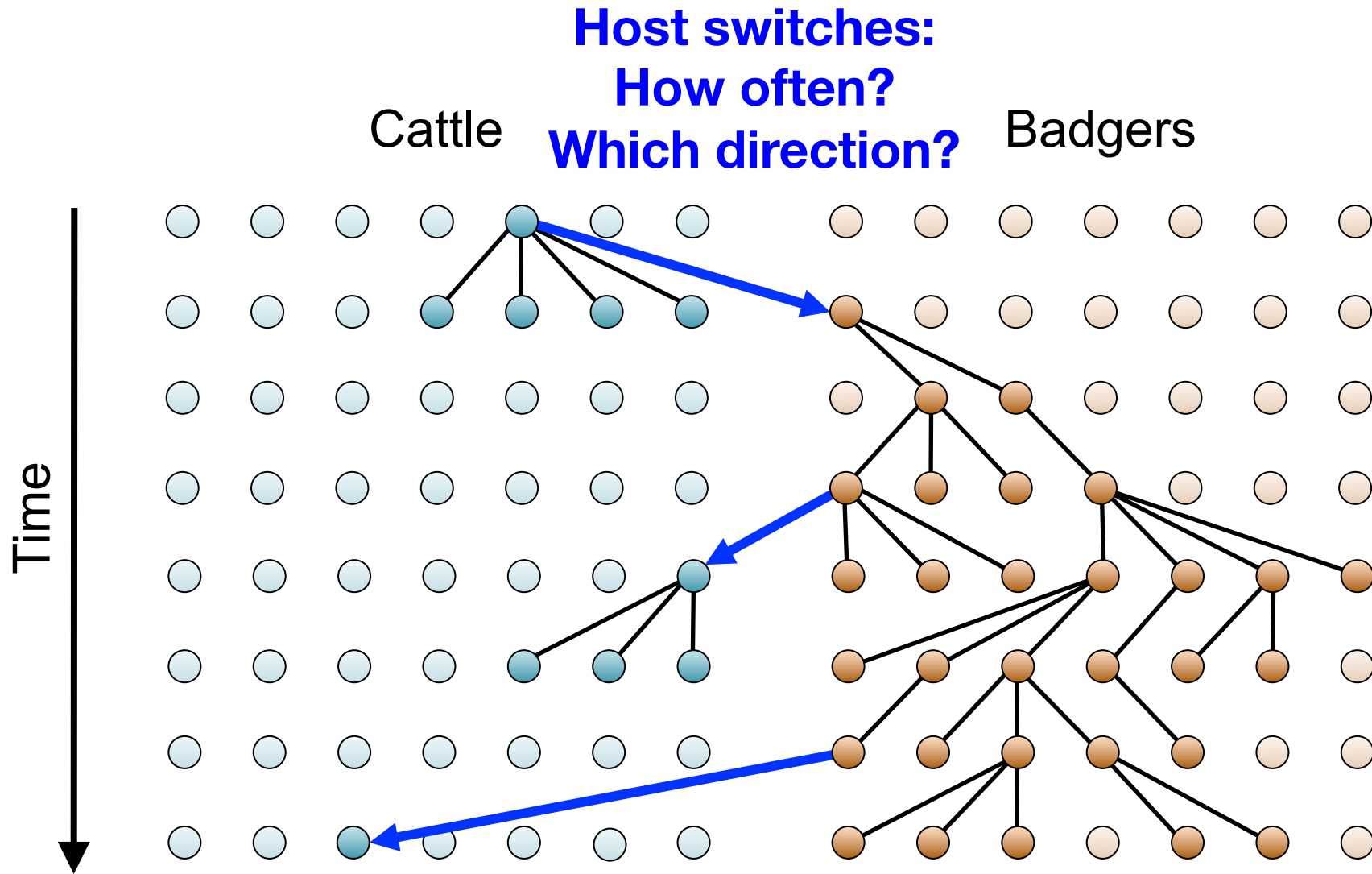
University of Glasgow

Talk outline

- Genetic tracking of pathogen transmission

- Host species as discrete character states

- Analytical challenges
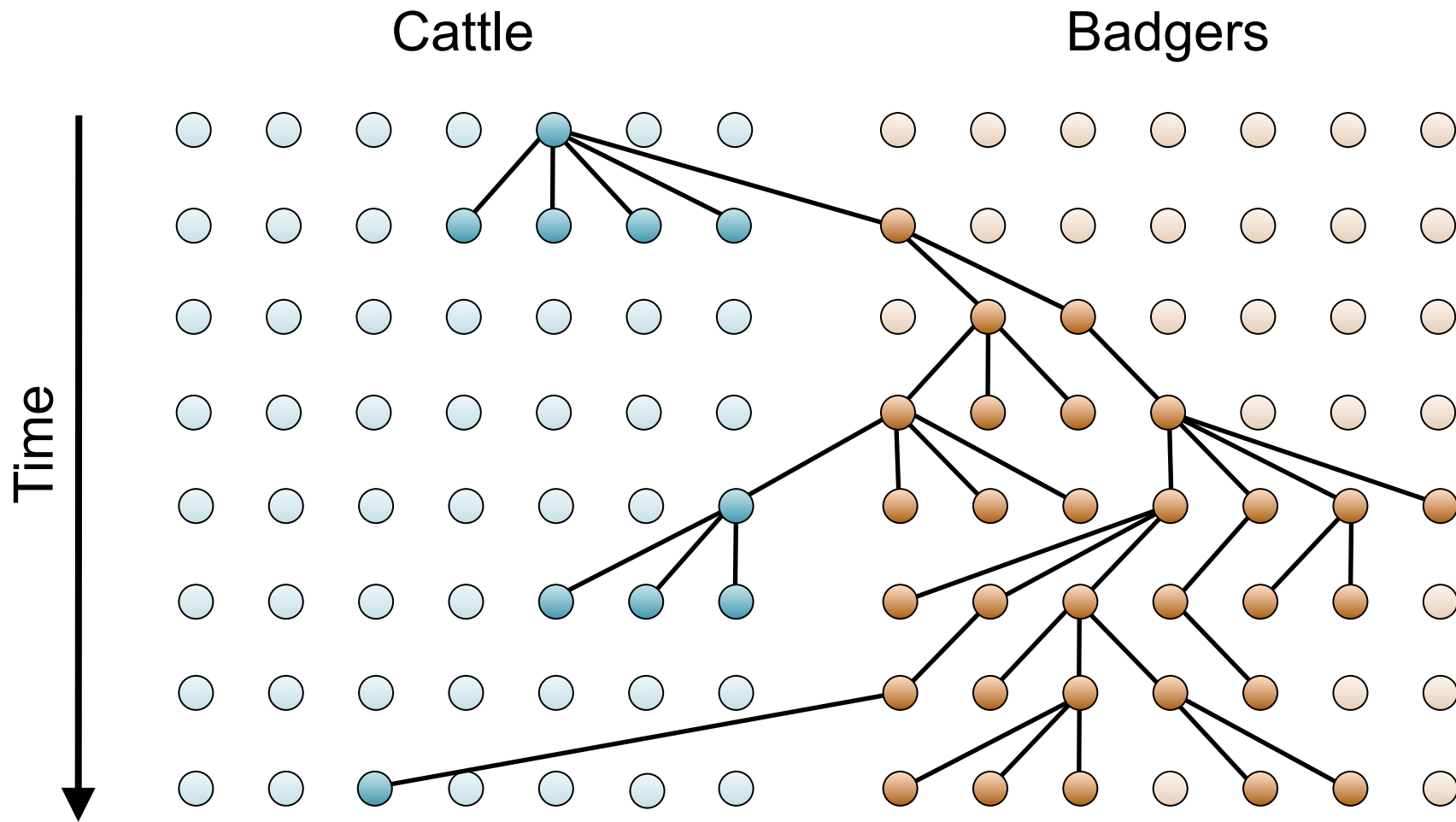
- Case studies: CSF and bTB

Two-host transmission tree

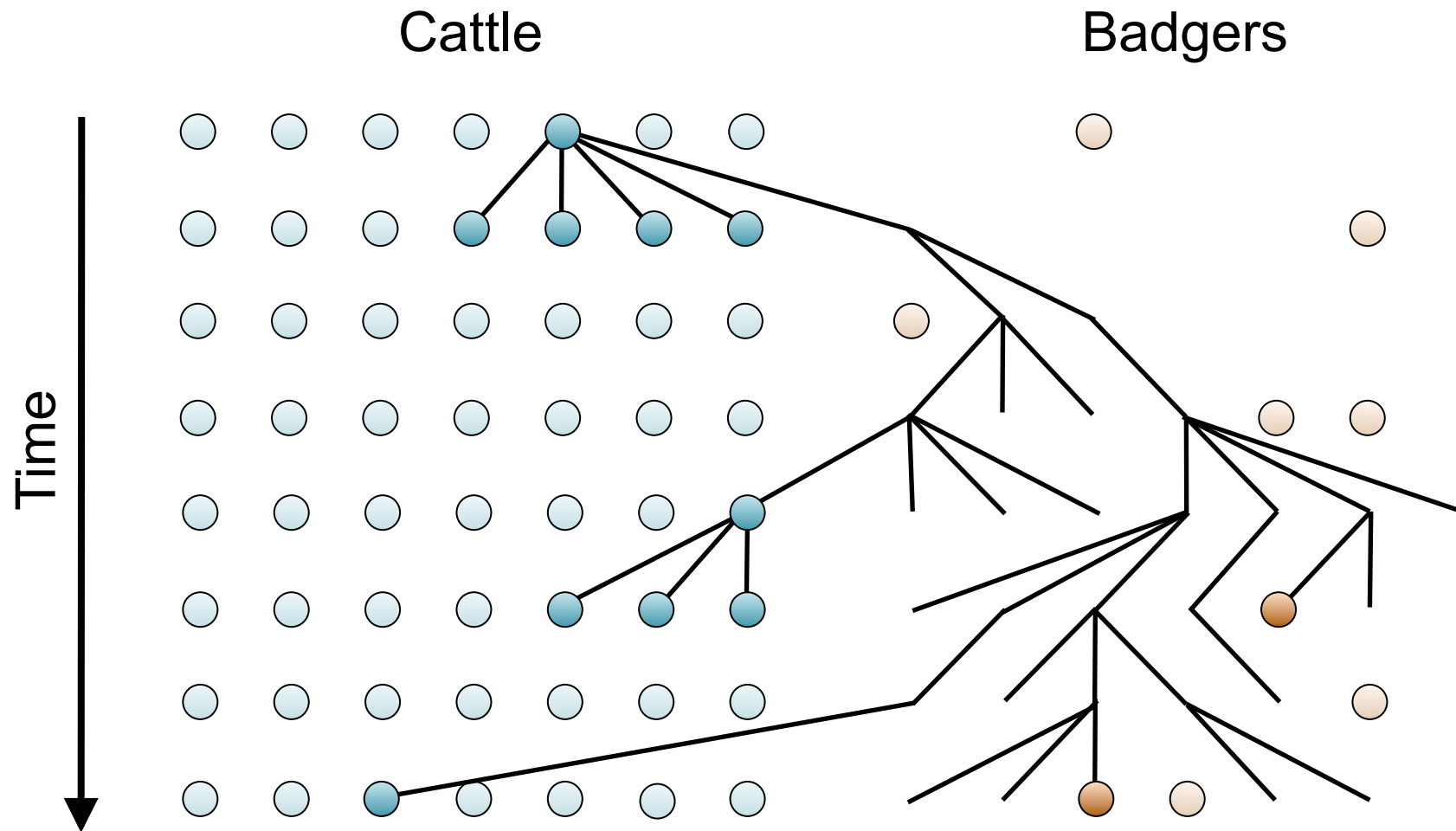# Two-host transmission tree

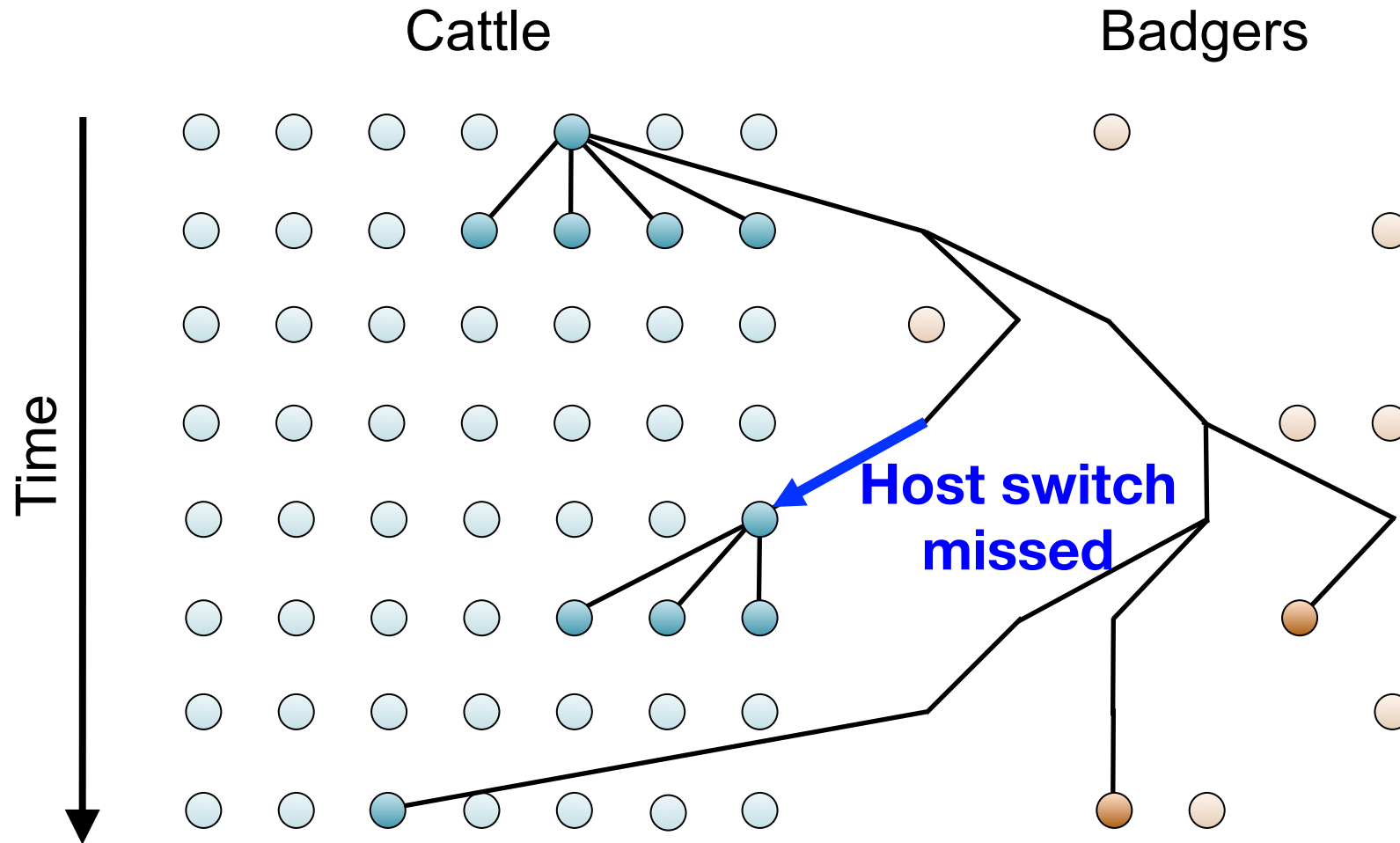# Actual transmission tree is unknown

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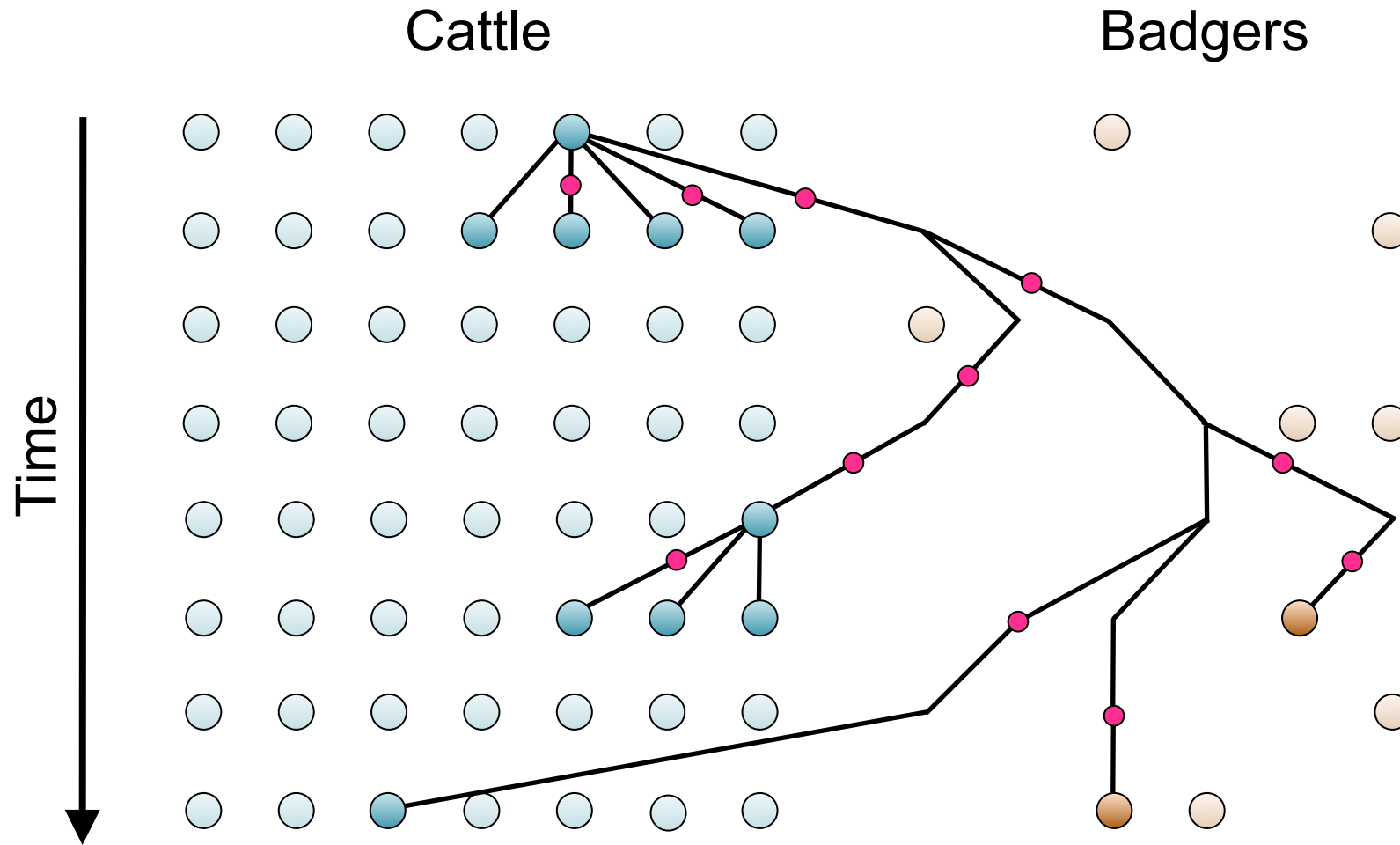
Most hosts are not sampled

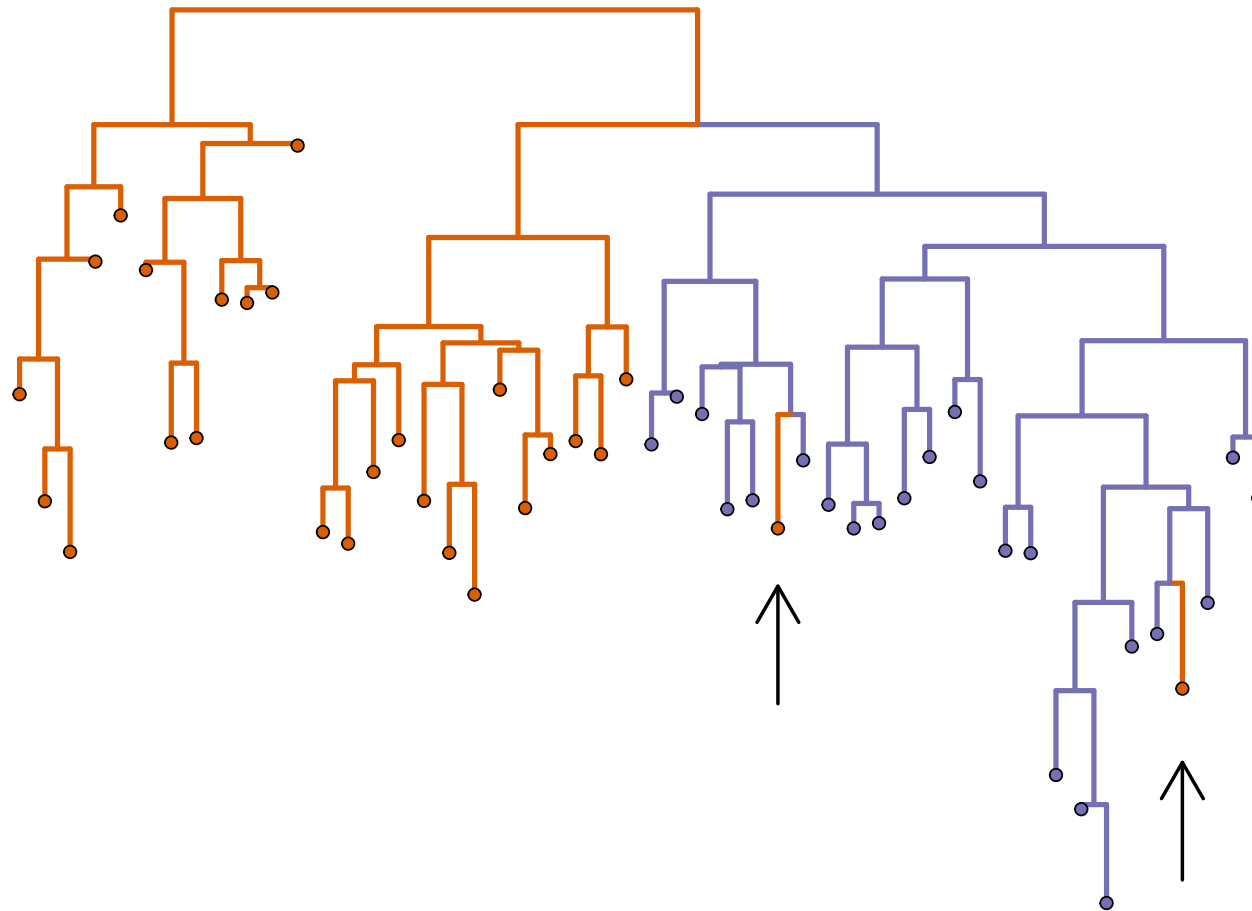# Actual transmission tree is unknown

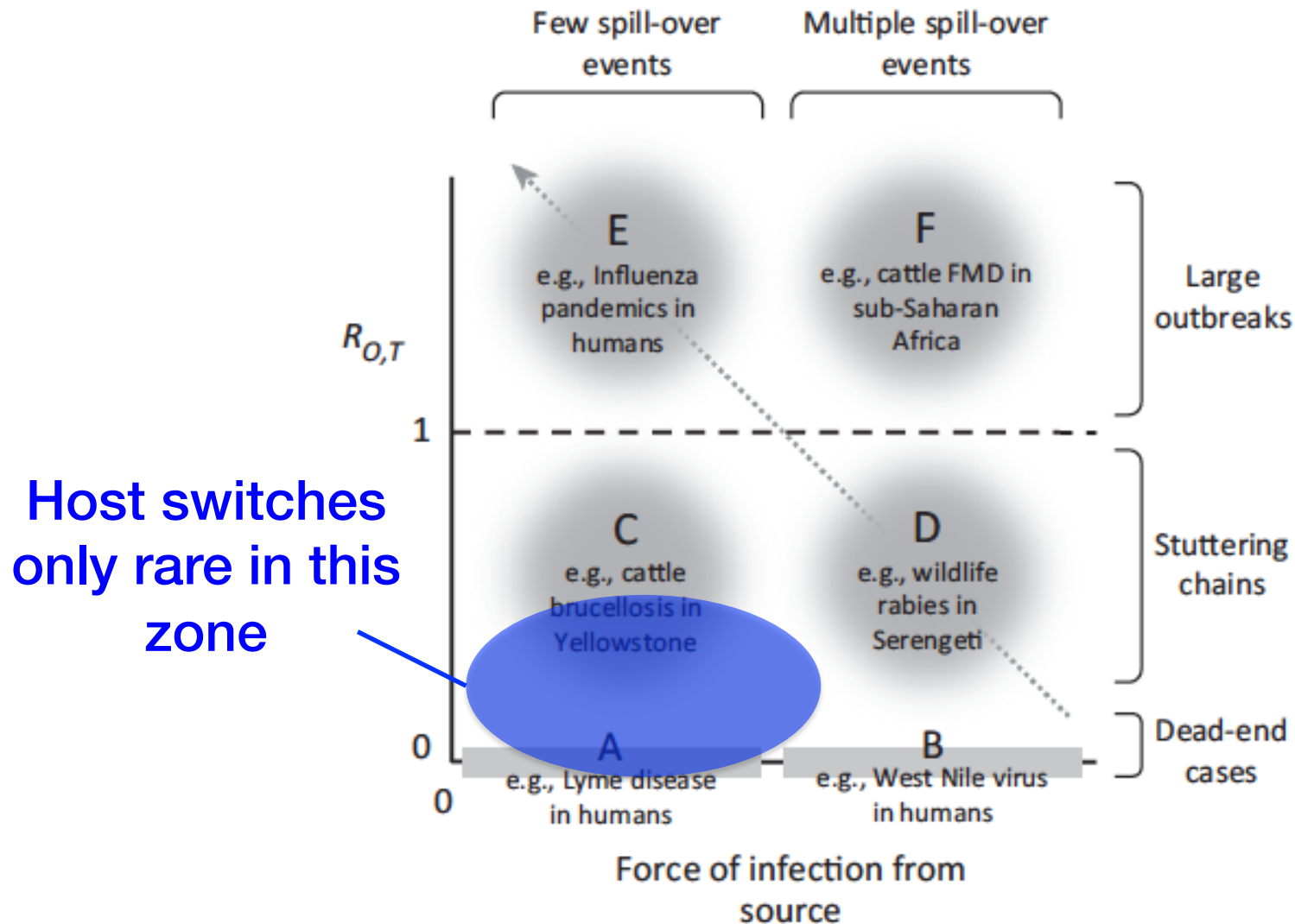Most hosts are not sampled

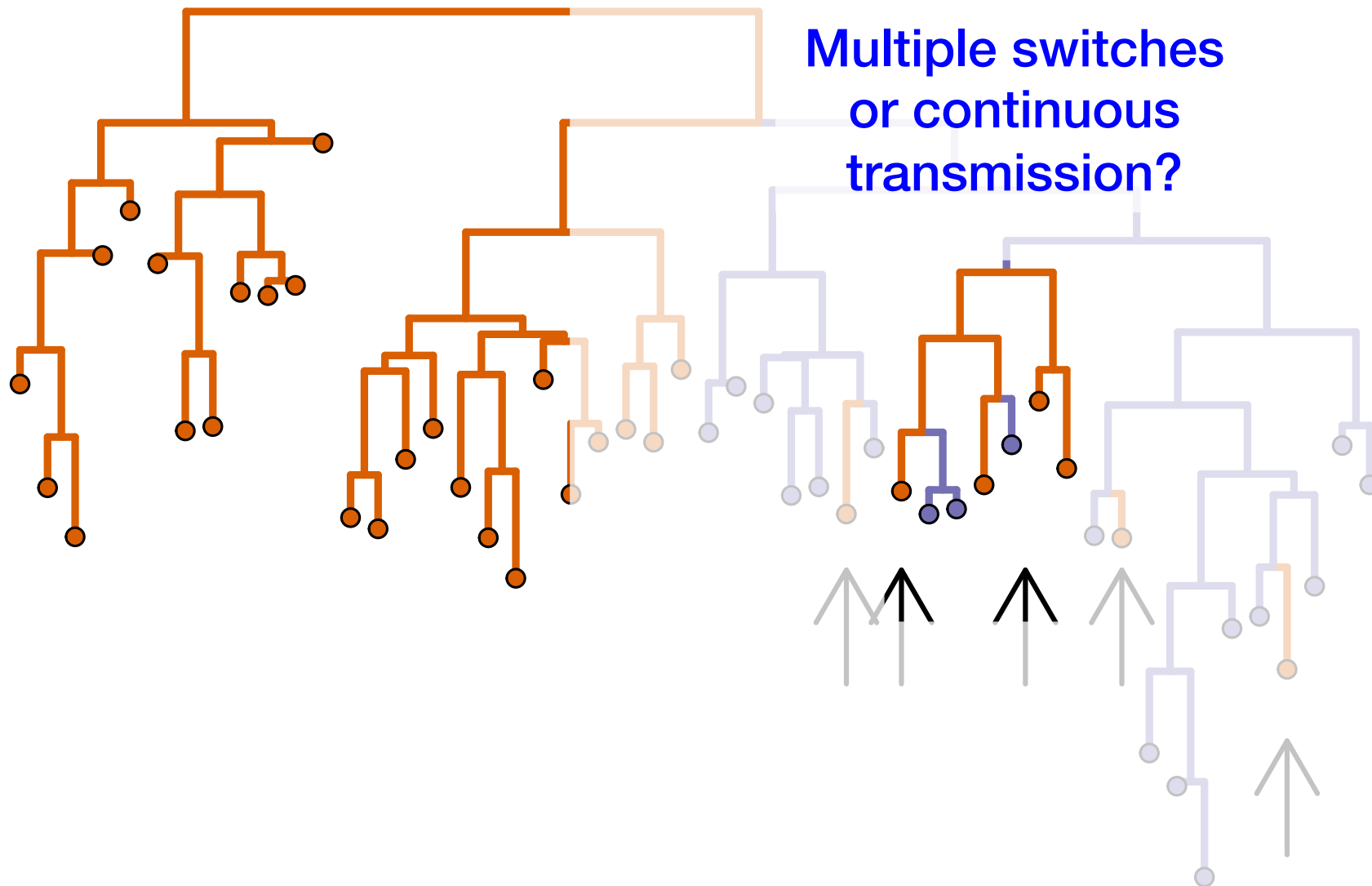# Actual transmission tree is unknown

Mutations make tree visible

Rare switches are easy to detect

Only applies to few reservoir systems

Host switches only rare in this zone

Few spill-over events · Multiple spill-over events

$R_{O,T}$

E — e.g., Influenza pandemics in humans
F — e.g., cattle FMD in sub-Saharan Africa
Large outbreaks

C — e.g., cattle brucellosis in Yellowstone
D — e.g., wildlife rabies in Serengeti
Stuttering chains

A — e.g., Lyme disease in humans
B — e.g., West Nile virus in humans
Dead-end cases

Force of infection from source

Viana et al. 2014, Trends Ecol & Evol

Frequent switches create ambiguous signal

Multiple switches or continuous transmission?
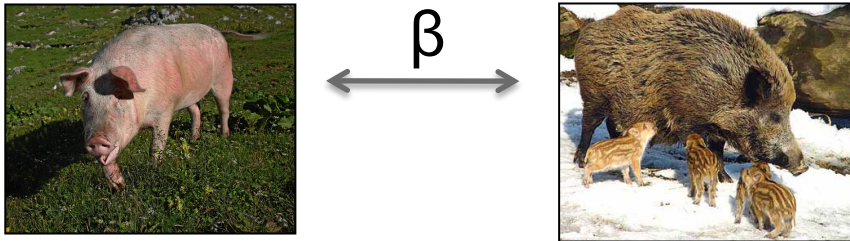
Quantifying cross-species transmission

- What is the <u>minimum number of host switches</u> needed to explain phylogenetic patterns?

  => **parsimony** principle

- Alternative: model host switches over time using Markovian rate matrix (Pagel 1994, Proc Royal Soc B)

  – allows for undetected changes

  – probabilistic model => can be fit using likelihood

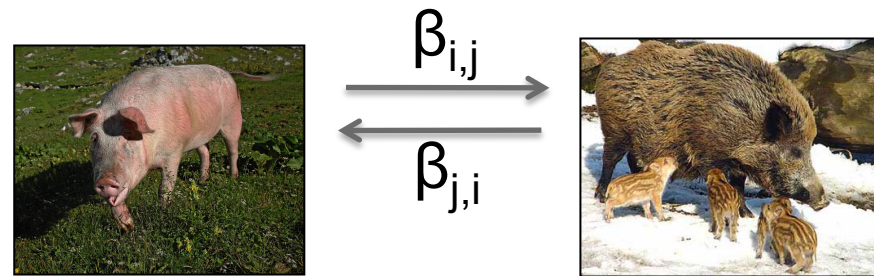 – general method for **discrete character evolution**

Example: classical swine fever virus (CSF)

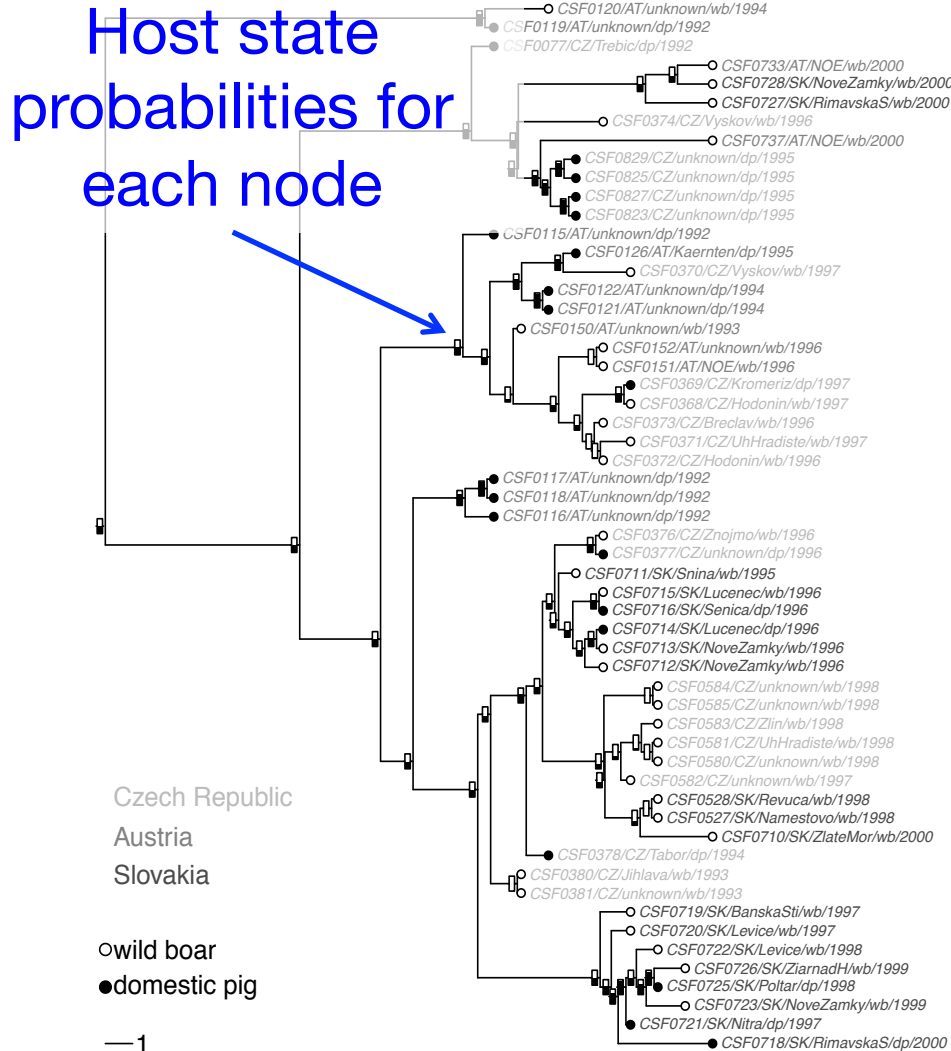Cross species transmission parameters
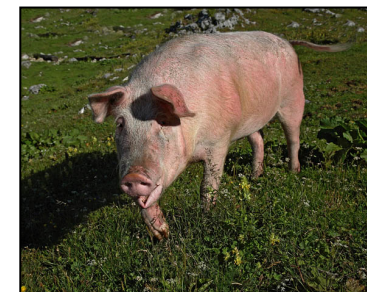
Symmetrical | Asymmetrical

Inferring host state probabilities for internal tree nodes

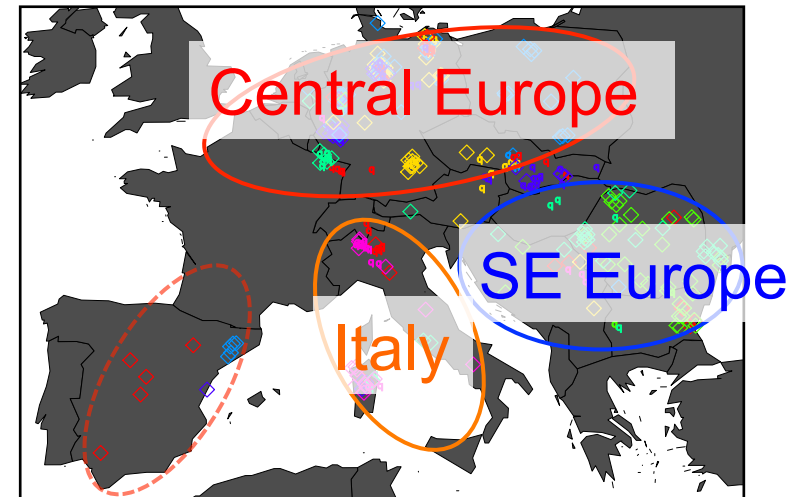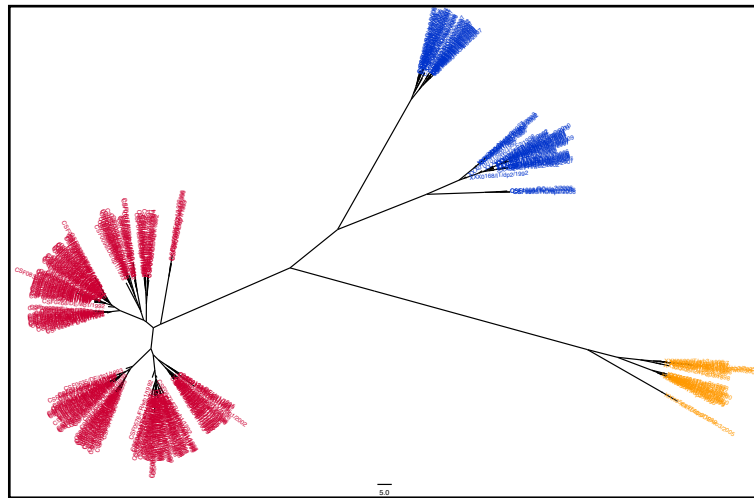Host state probabilities for each node

○ Wild boar

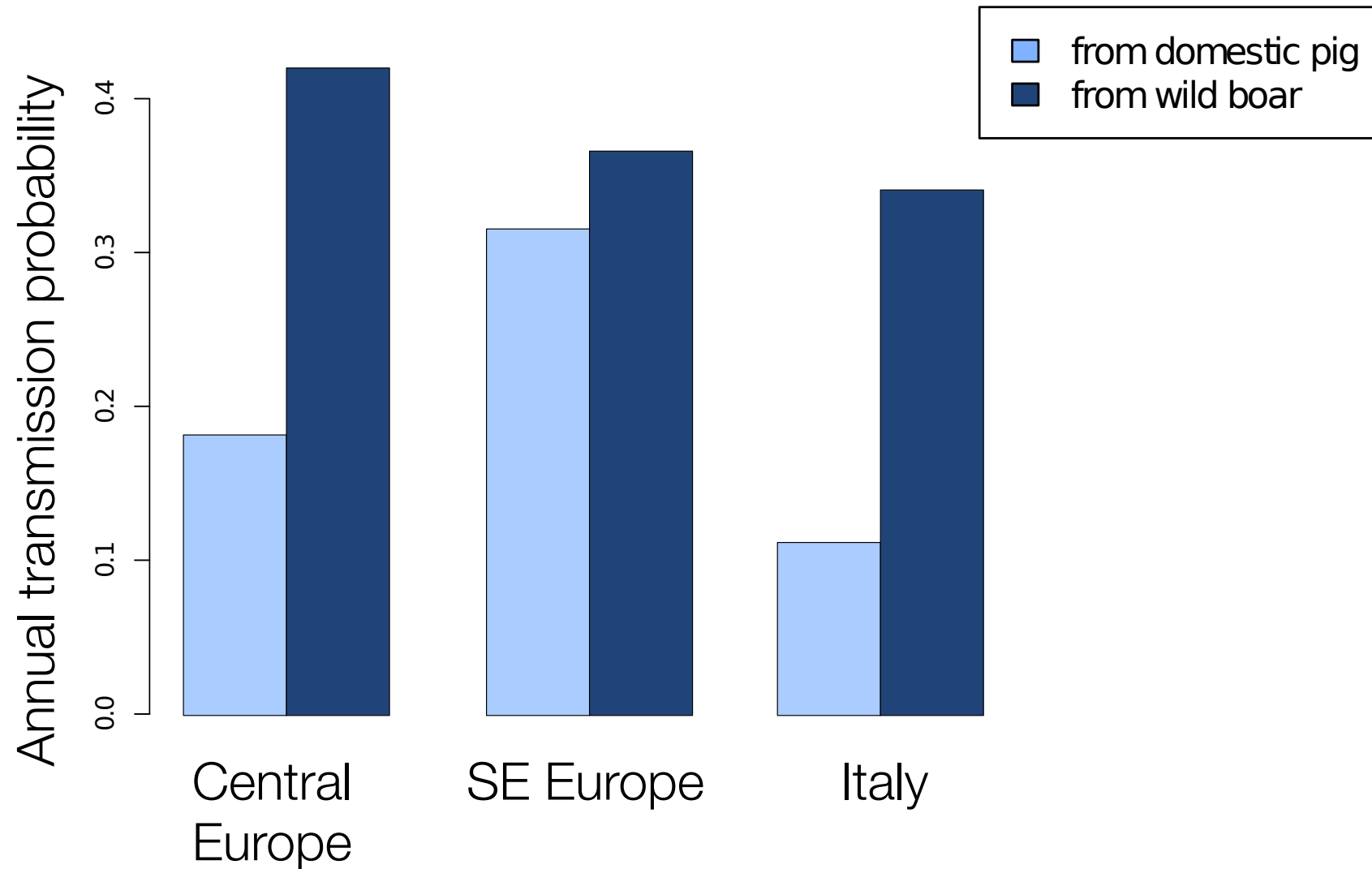● Domestic pig

Spatial population structure
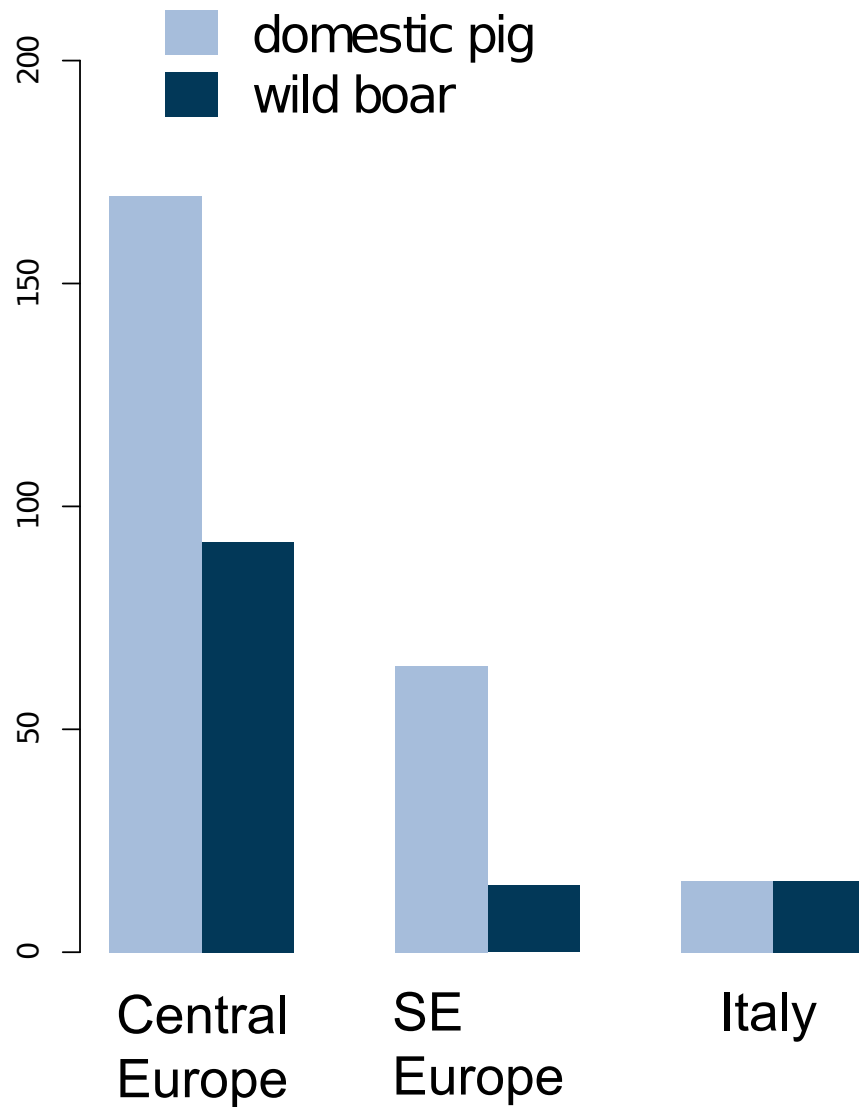
Three spatially distinct clades of CSF

How do patterns of cross-species transmission compare between different parts of Europe?

=> Potential for sampling bias: Has relative sampling effort with respect to pigs and boar been the same across these areas?
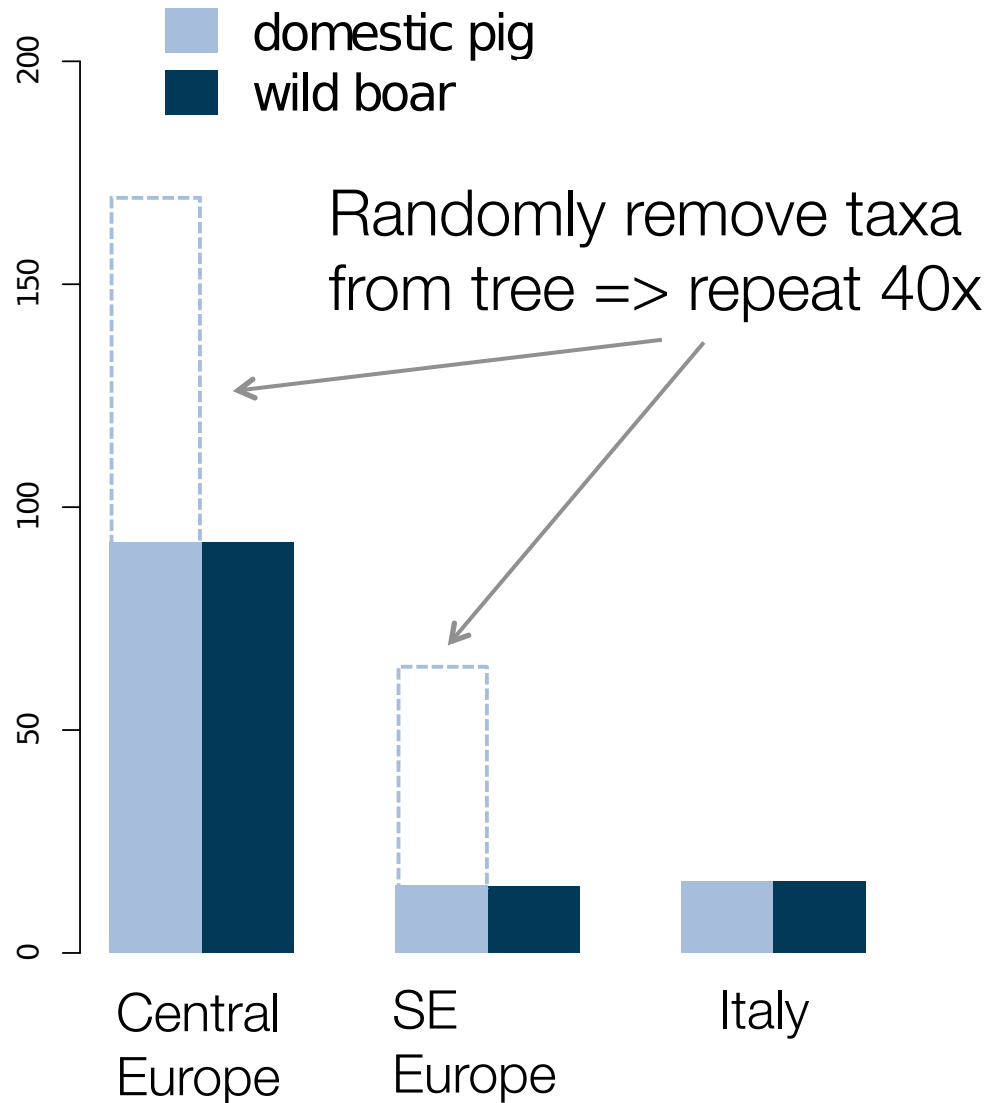
Estimated rates of cross species transmission

Effects of sampling bias?

More virus samples available from domestic pigs

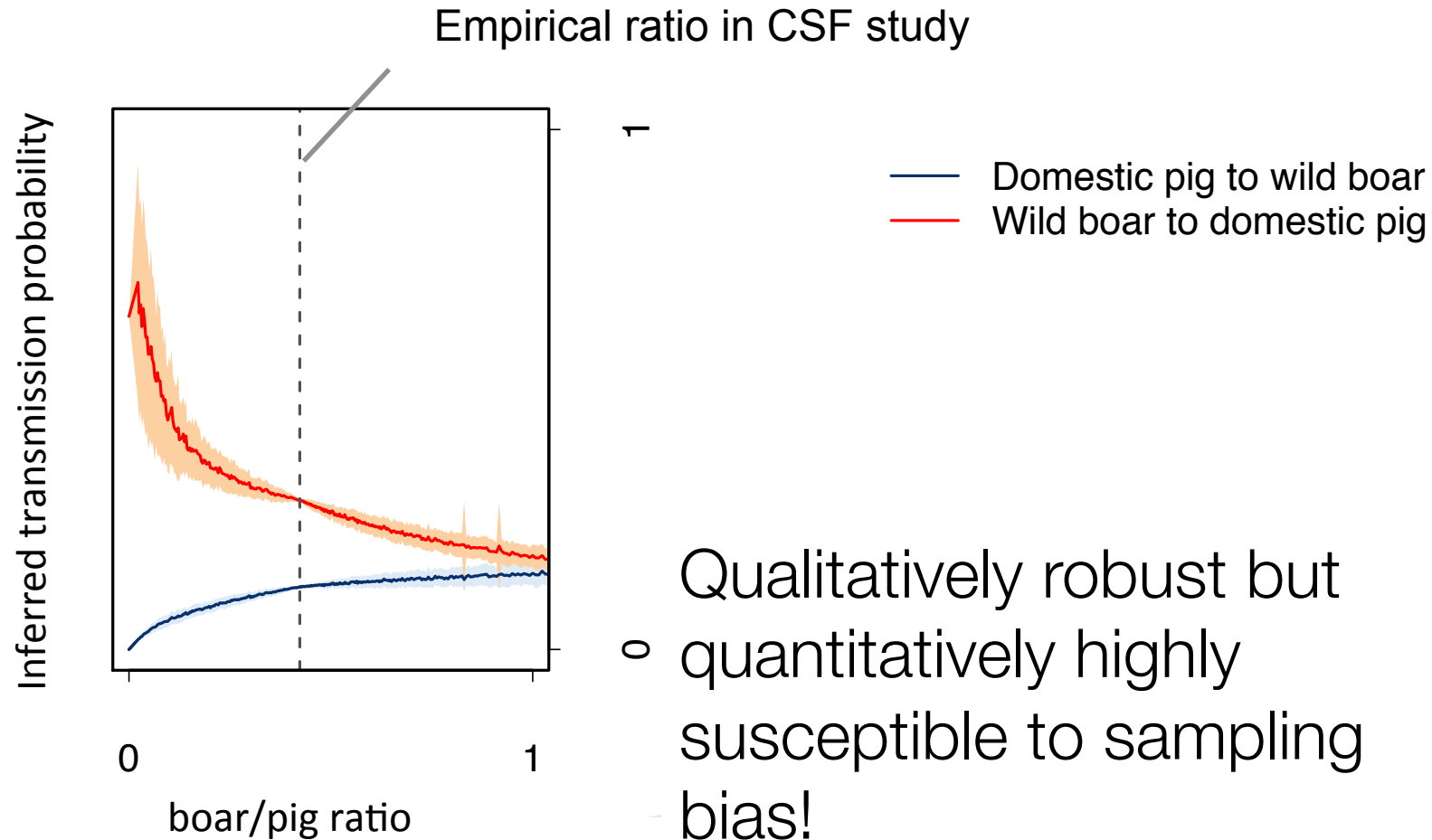# Reduce sampling bias by down-sampling

domestic pig
wild boar

Randomly remove taxa
from tree => repeat 40x

Central Europe   SE Europe   Italy

Original model
still receives
highest support

ΔAIC

mod1 mod2 mod3 mod4 mod5 mod6
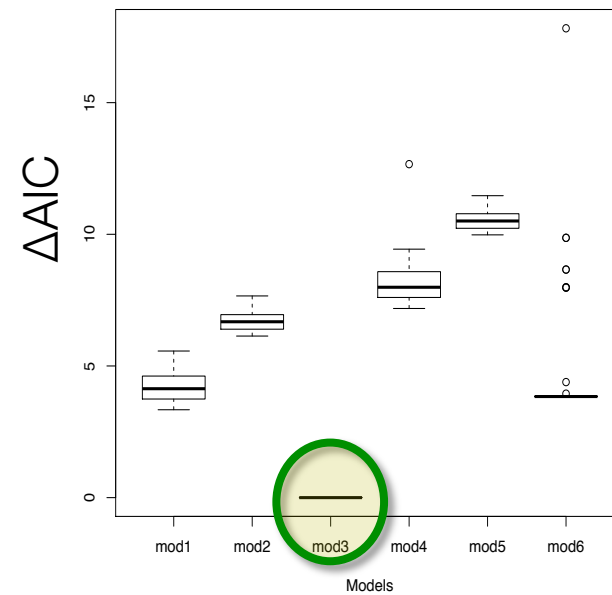
Models

Models

Assessing the effect of biased sampling using simulations

Empirical ratio in CSF study

Inferred transmission probability

— Domestic pig to wild boar
— Wild boar to domestic pig

0   boar/pig ratio   1

Qualitatively robust but quantitatively highly susceptible to sampling bias!
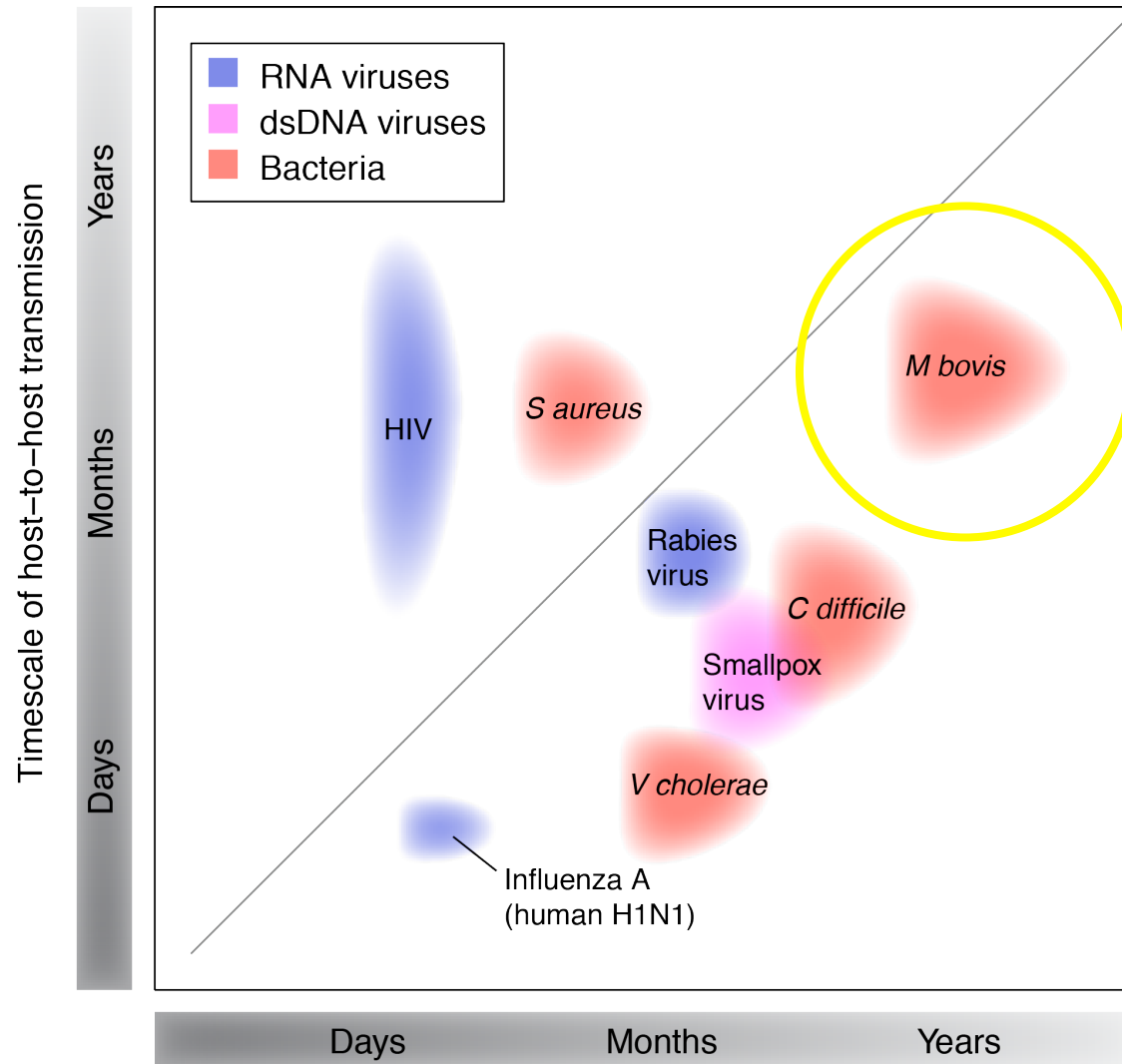
Lessons from *M bovis* genome data

Trewby et al., in review
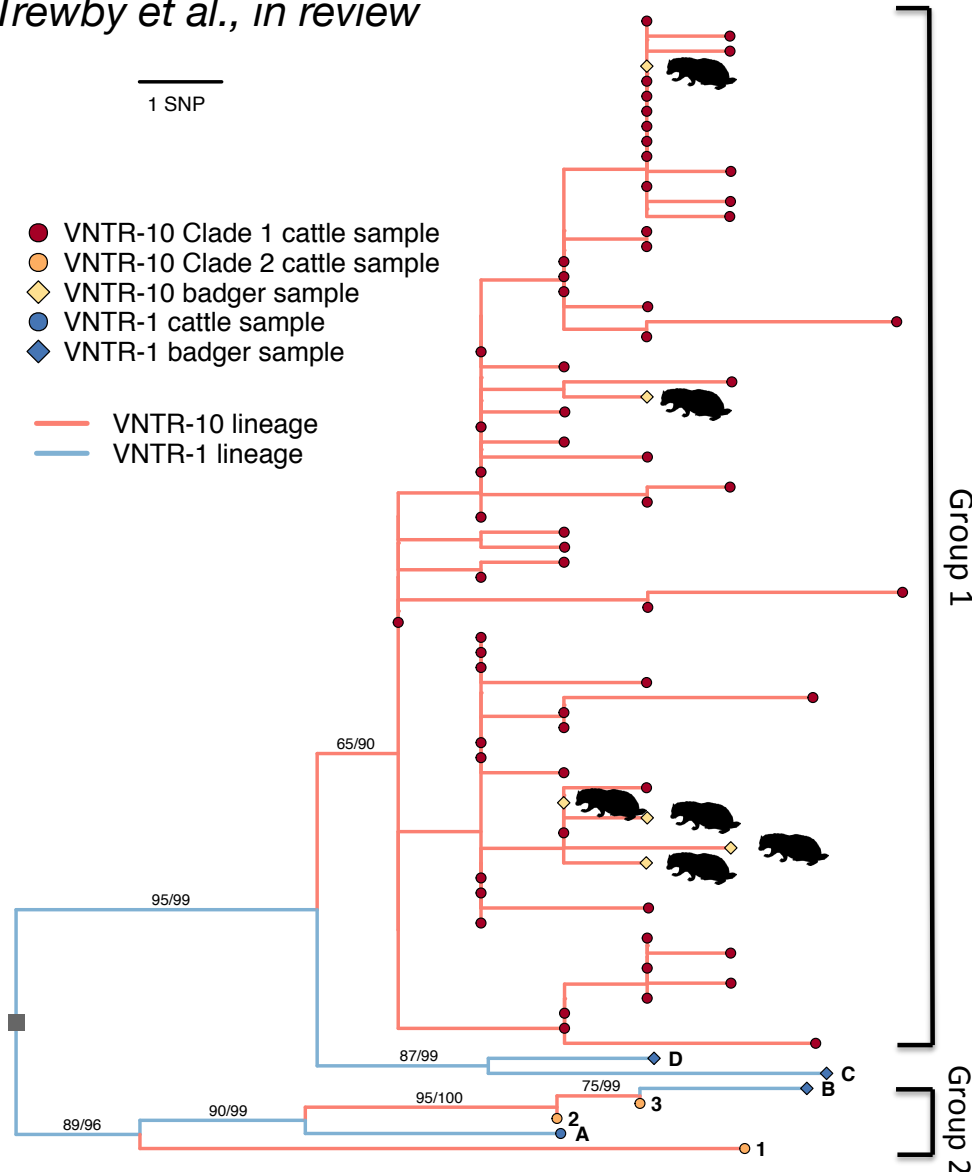
- Limited phylogenetic resolution

- No badger-associated clades

- VNTR-type switching

- Evolution measurable but slow: on average one mutation every 4-5 years

Evolution & epidemiology: relative time scales

Biek et al. 2015, Trends Ecol Evol

Conclusions

- Cross-species transmission can be inferred using discrete character state approach

- Inference rarely straight forward, especially with respect to quantitative answers

- Sampling biases may drive results - difficult to avoid but important to assess

- Additional challenges in the case of *M. bovis* => sequence data alone will be insufficient to reveal transmission patterns

Acknowledgements

- bTB - Rowland Kao, Hannah Trewby, Robin Skuce and team at AFBI
- CSF – Thibaud Boutin