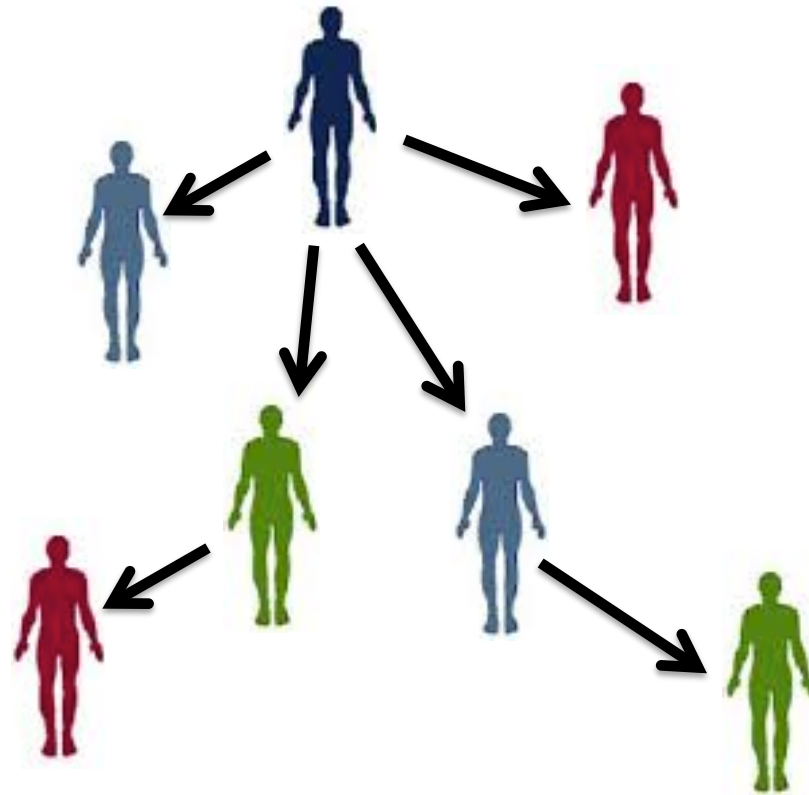


Inferring transmission with the Structured Coalescent

Nicola De Maio



14 Feb 2017



Oxford Biomedical Research Centre

Oxford Radcliffe Hospitals NHS Trust



NHS National Institute for Health Research



wellcome trust



Department of Health



Animal & Plant Health Agency



OXFORD
MARTIN
SCHOOL

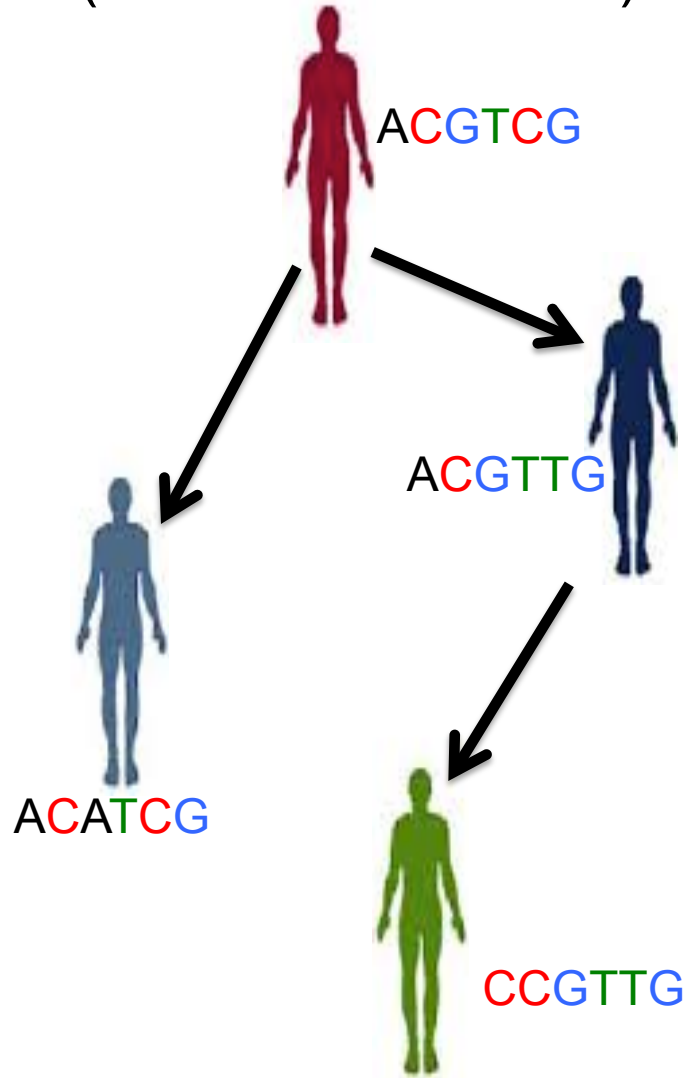
Funded by

NHS

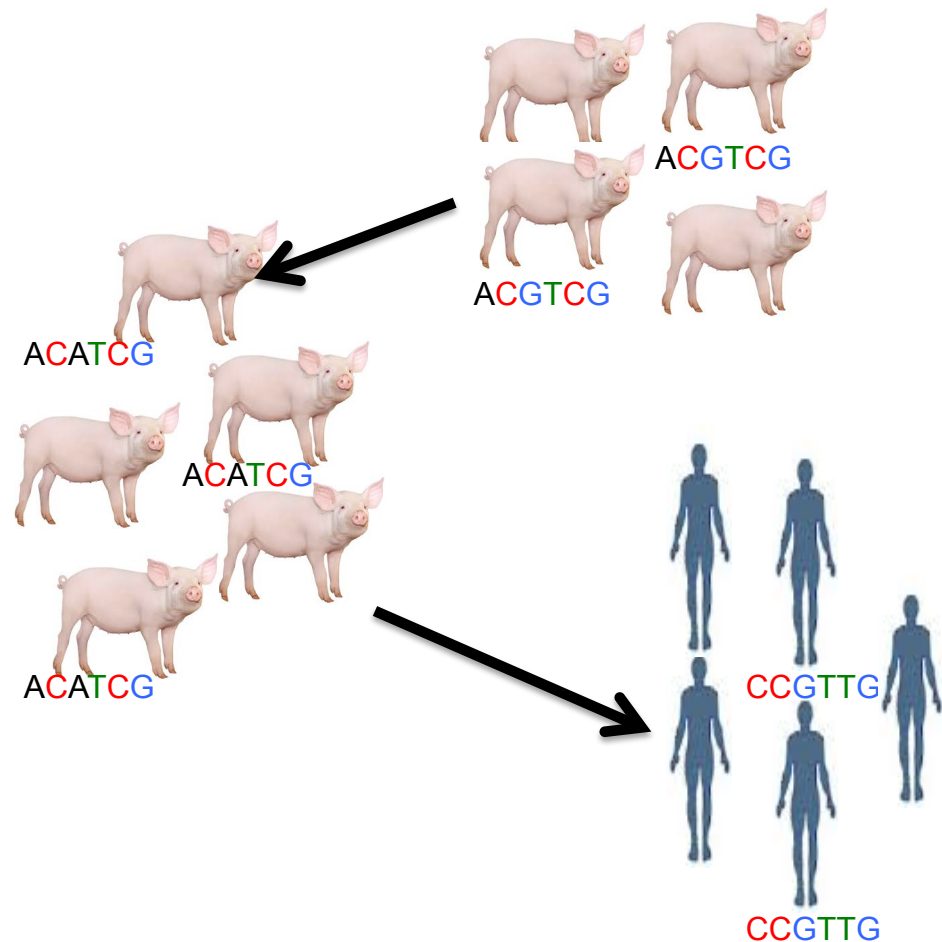
National Institute for Health Research

Objectives:

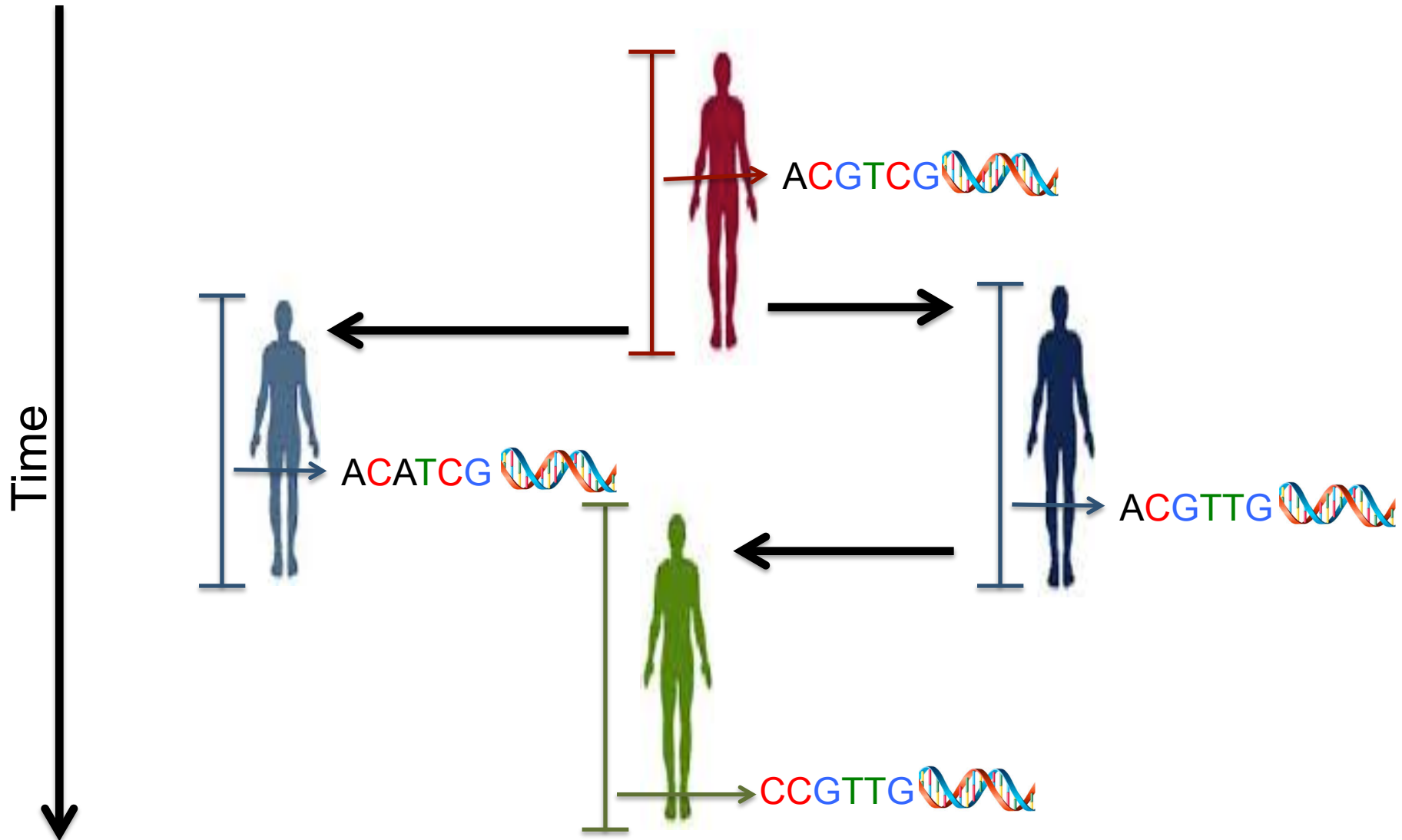
Reconstruct transmission
between patients
(transmission trees)



Reconstruct transmission
between groups
(locations, farms, communities.)

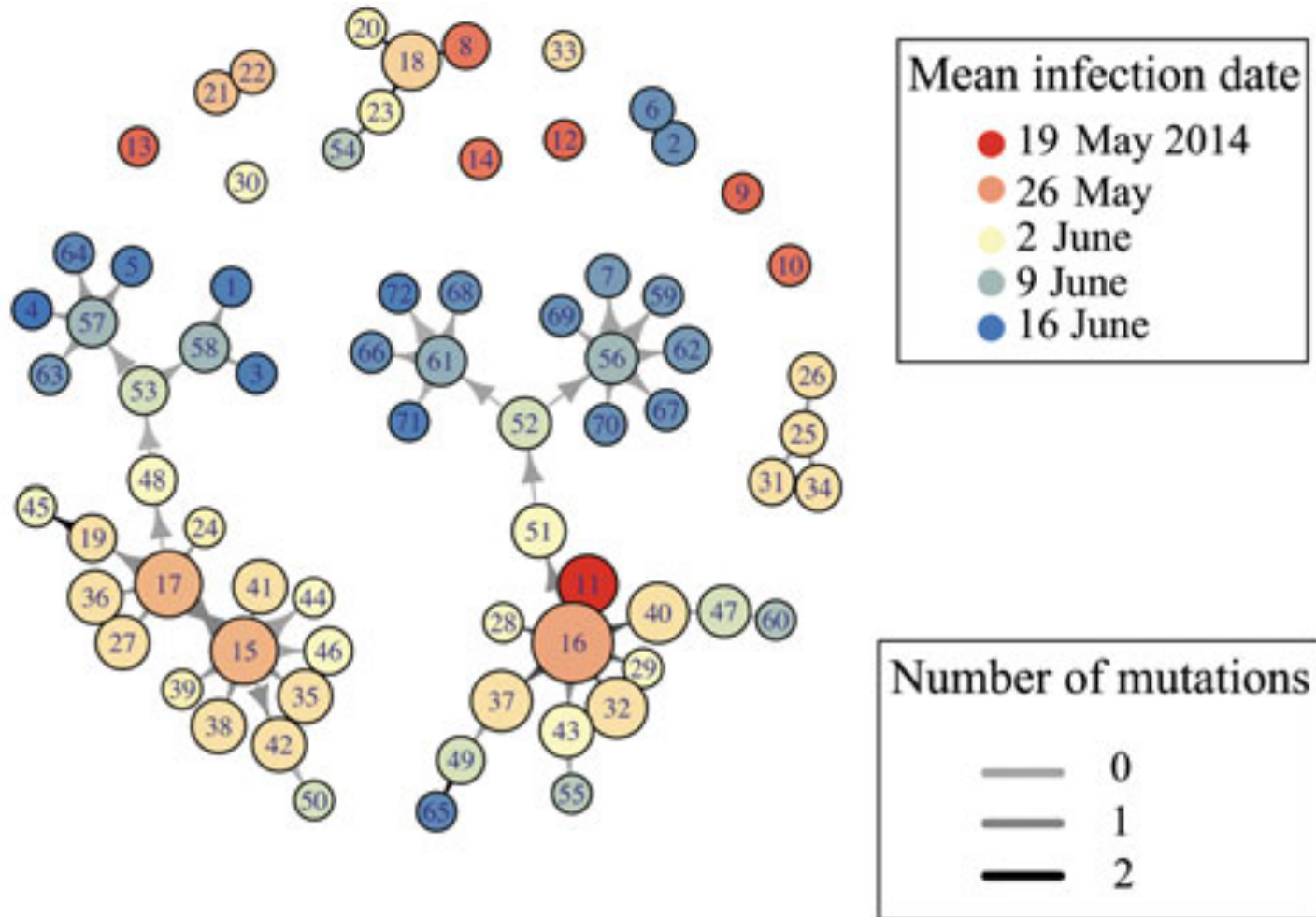


Reconstructing transmission between hosts



Epidemiological examples

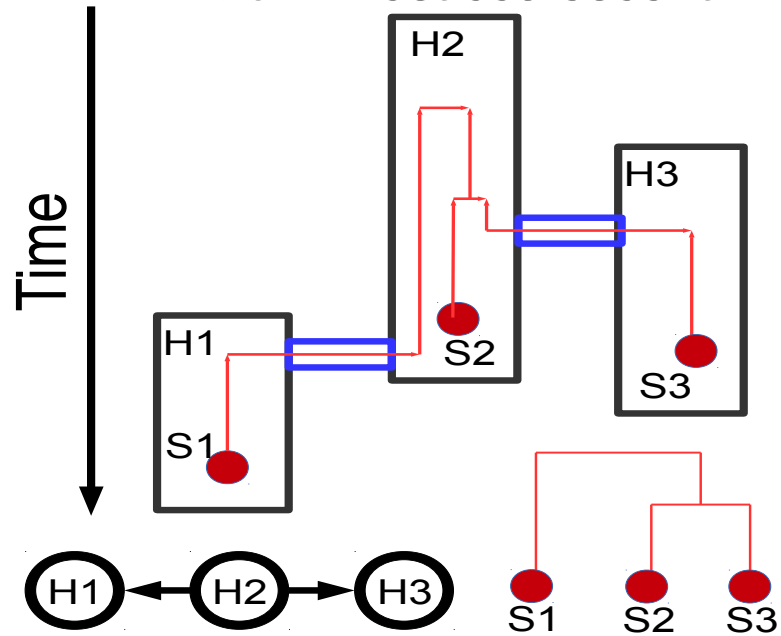
Epidemiological and Viral Genomic Sequence Analysis of the 2014 Ebola Outbreak Reveals Clustered Transmission



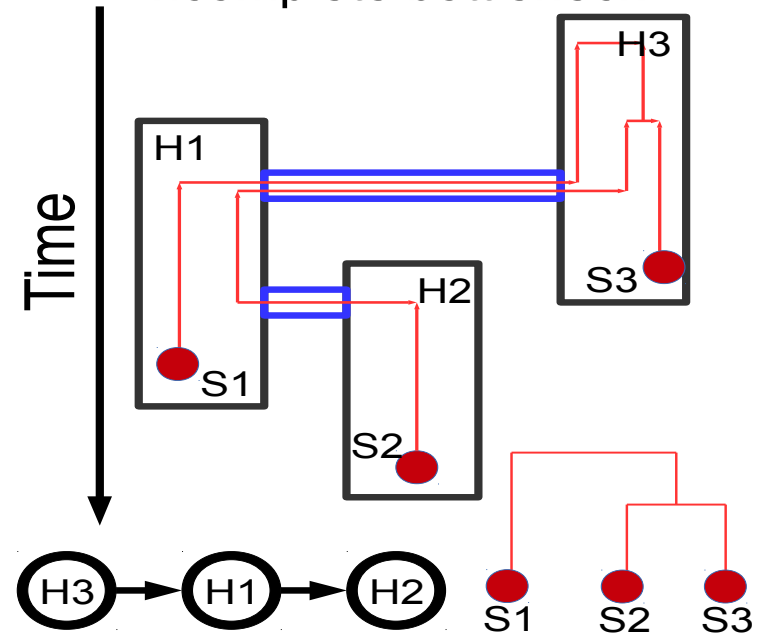
Scarpino et al 2014 Clinical Infectious Diseases

Complications

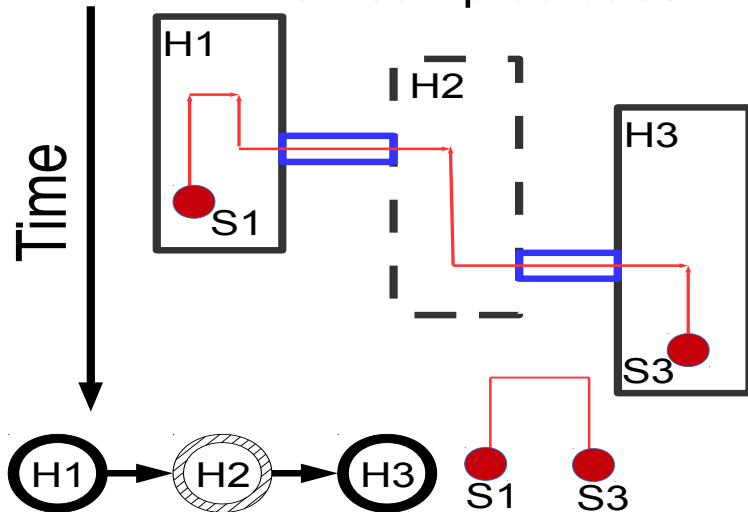
Within-host coalescent



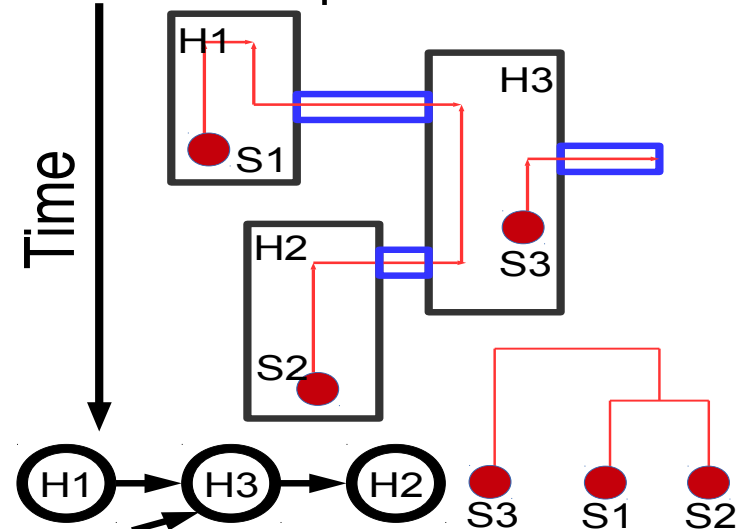
Incomplete bottleneck



Non-sampled case



Multiple infections



Comparison with other methods

Method	Allows multiple samples from same host	Uses exposure data	Uses sampling times	Uses phylogenetic structure	Accounts for tree uncertainty	Allows non-observed hosts	Allows host distance data	Models within-host evolution	Allows mixed infections	Models partial transmission bottlenecks	Allows compartmentalization model	Infers infection times
Cottam et al 2008	✗	✓	✓	✓	✗	✗	✗	✗	✗	✗	✗	✓
Aldrin et al 2011	✗	✓	✗	✗	-	✗	✓	✗	✗	✗	✗	✓
Ypma et al 2011	✗	✓	✗	✗	-	✗	✓	✗	✗	✗	✗	✓
Jombart et al 2011 (SeqTrack)	✗	✗	✓	✗	-	✓	✓	✗	✗	✗	✗	✗
Morelli et al 2012	✗	✓	✓	✗	-	✗	✓	✗	✗	✗	✗	✓
Ypma et al 2013	✗	✓	✓	✓	✓	✗	✗	✓	✗	✗	✗	✓
Jombart et al 2014 (Outbreaker)	✗	✗	✓	✗	-	✓	✓	✗	✗	✗	✗	✓
Didelot et al 2014	✗	✓	✓	✓	✗	✗	✗	✓	✗	✗	✓	✓
Mollentze et al 2014	✗	✓	✓	✗	-	✓	✓	✗	✗	✗	✗	✓
SCOTTI	✓	✓	✓	✓	✓	✓	✗	✓	✓	✗	✗	✗

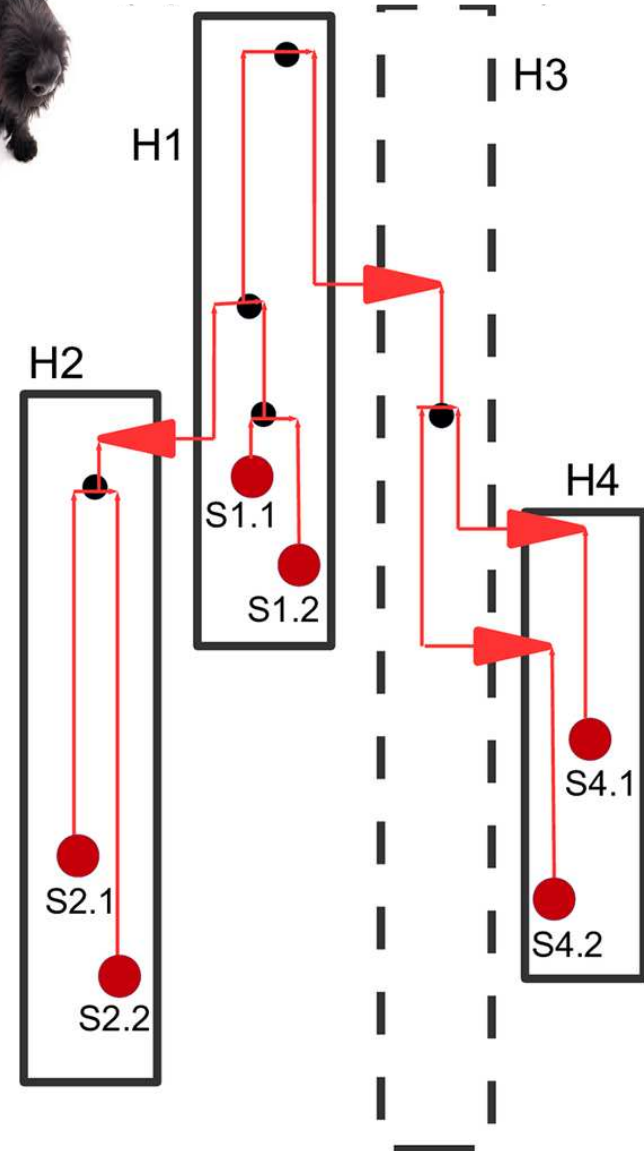
SCOTTI



SCOTTI: Efficient Reconstruction of Transmission within Outbreaks with the Structured Coalescent

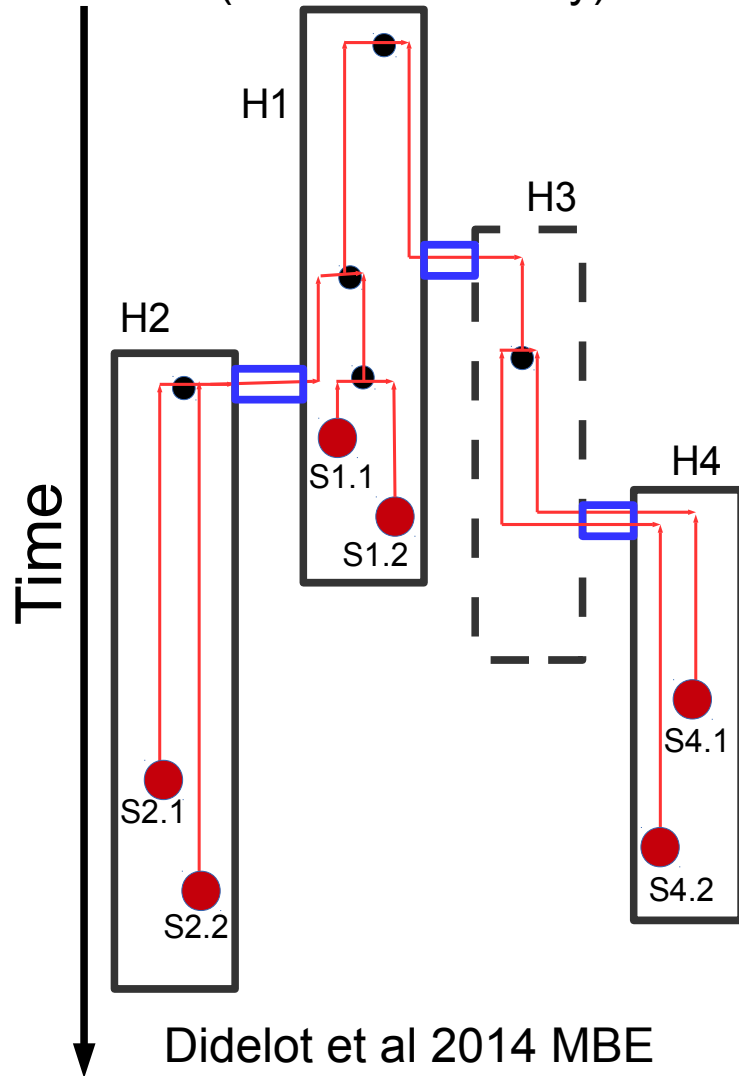
Nicola De Maio^{1,2*}, Chieh-Hsi Wu², Daniel J Wilson^{1,2,3}

De Maio et al 2016



Models used

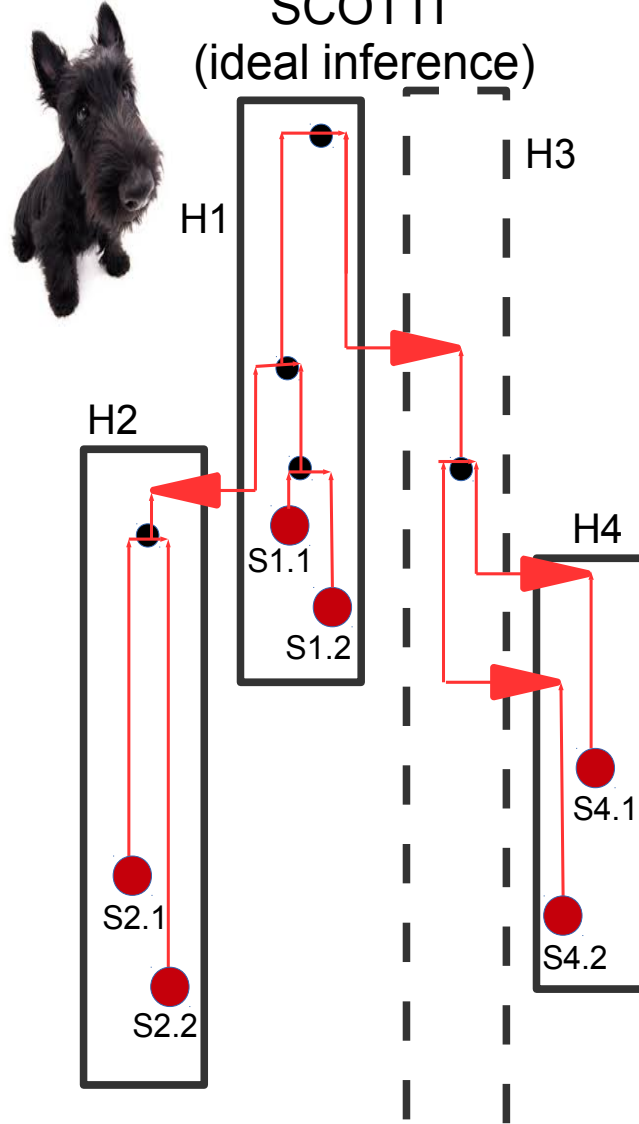
Multispecies
(simulated history)



Didelot et al 2014 MBE

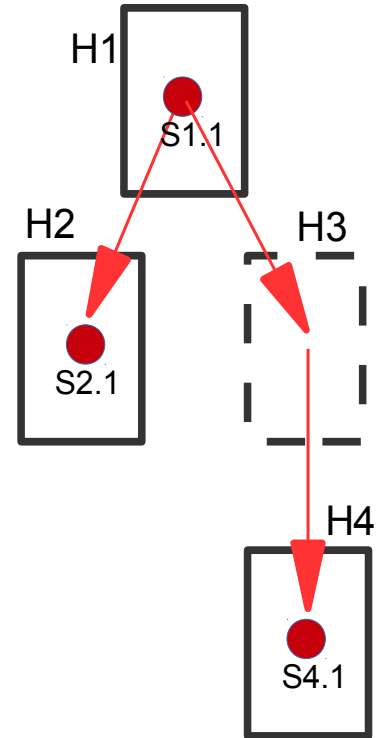
Hall et al 2015 PLOS Comput Biol

SCOTTI
(ideal inference)



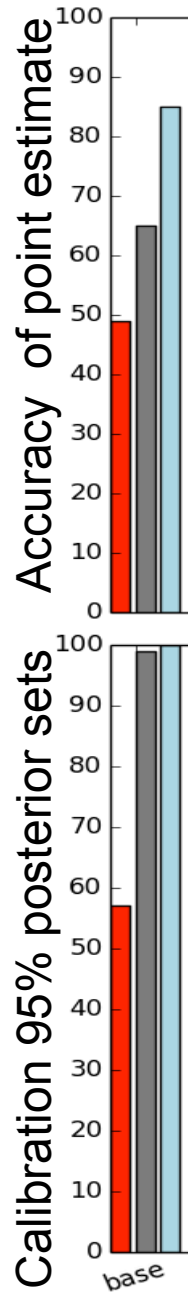
De Maio et al 2016
PLOS Comput Biol

Outbreaker
(ideal inference)



Jombart et al 2014
PLOS Comput Biol

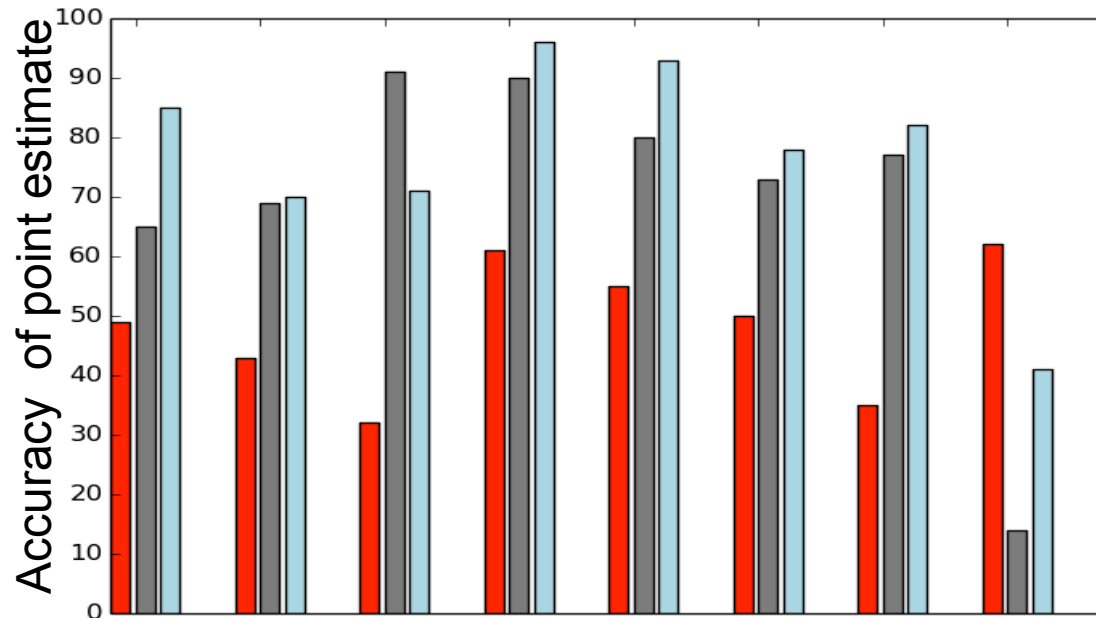
Simulations



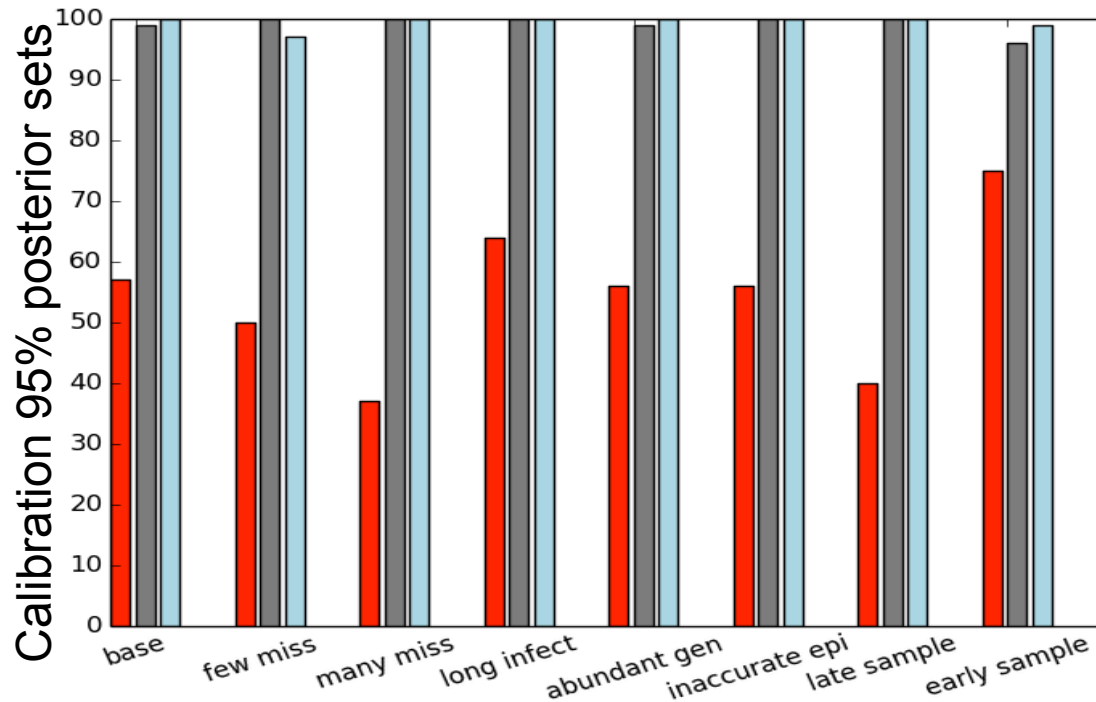
 Outbreaker



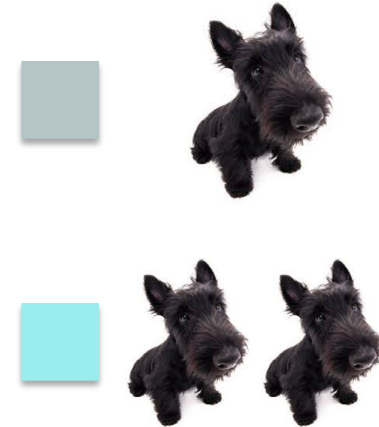
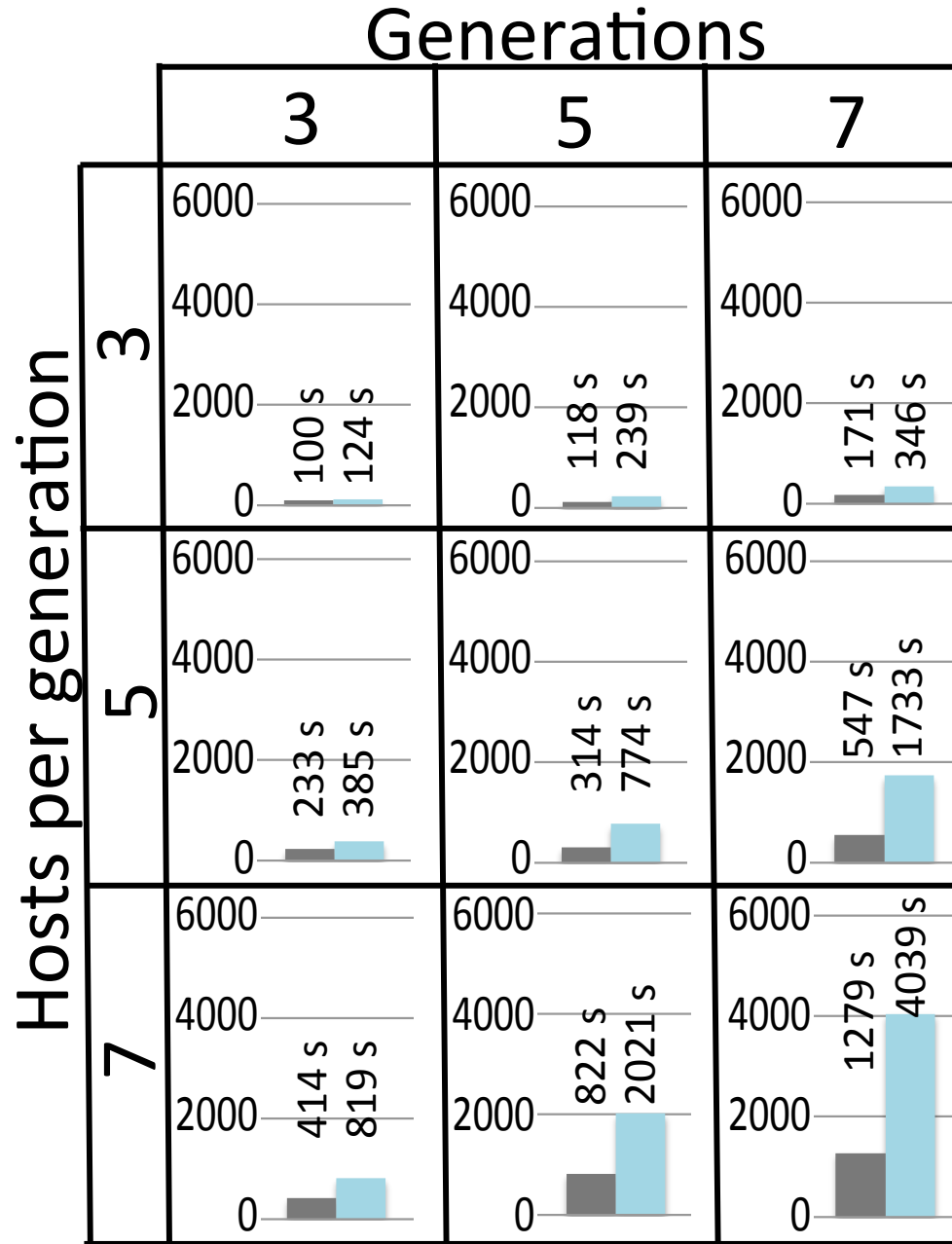
Simulations



 Outbreaker



Simulations – Running time

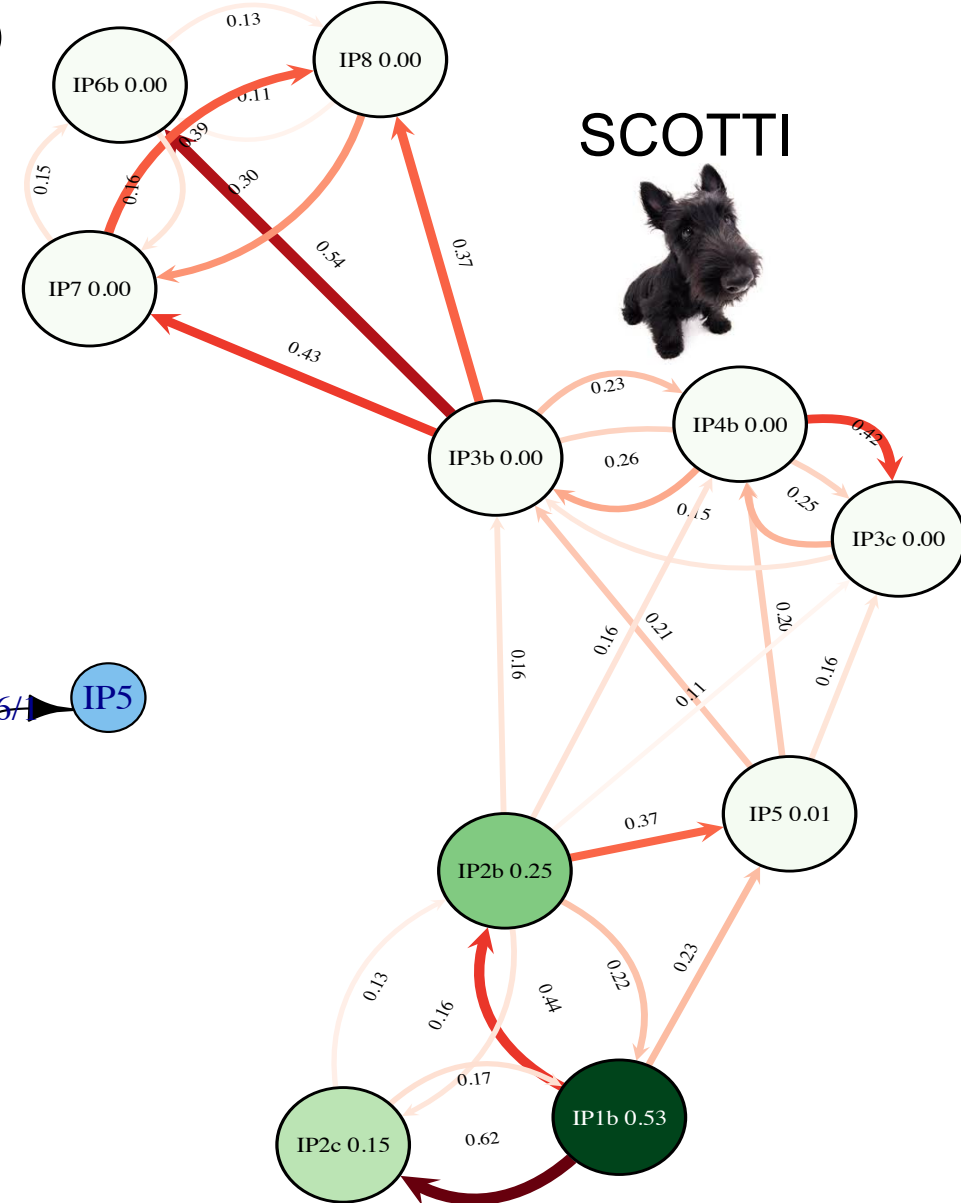
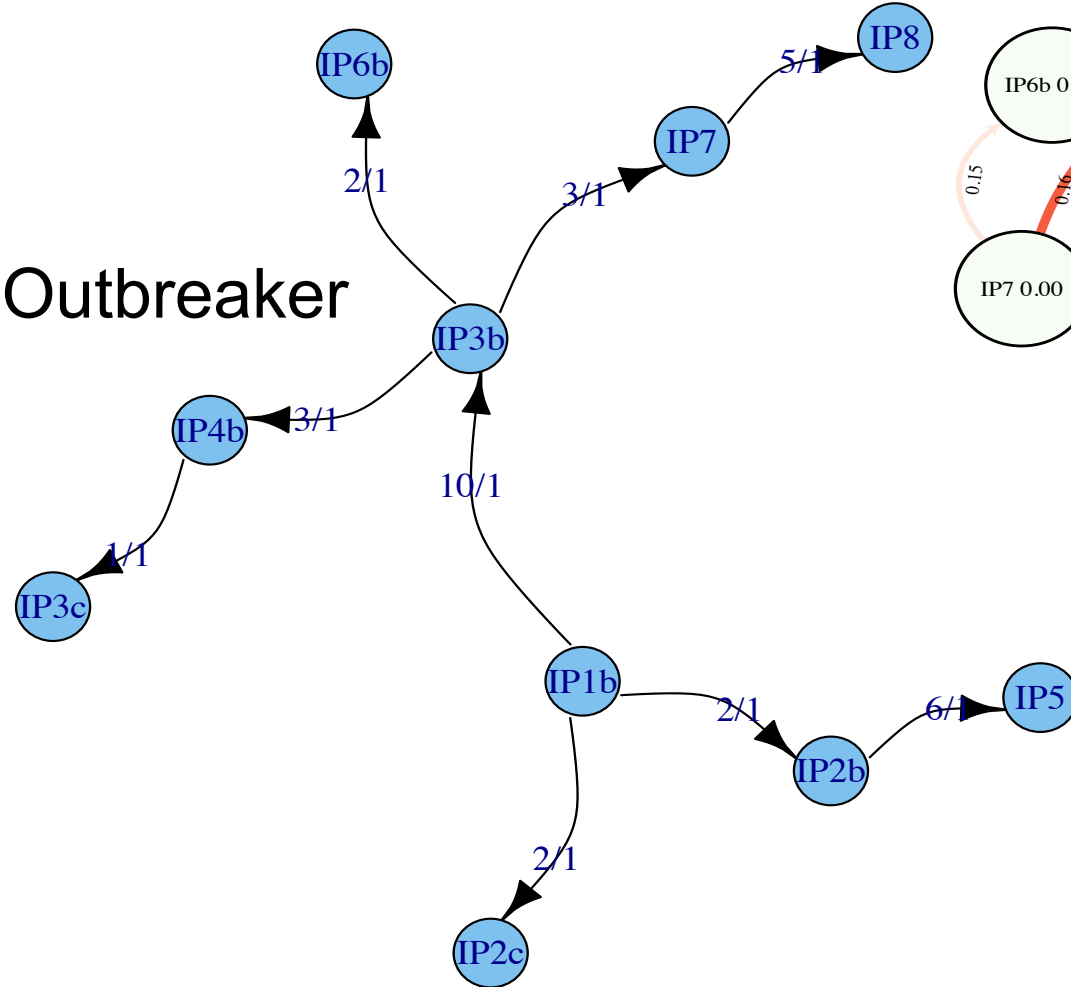


FMDV

SCOTTI



Outbreaker



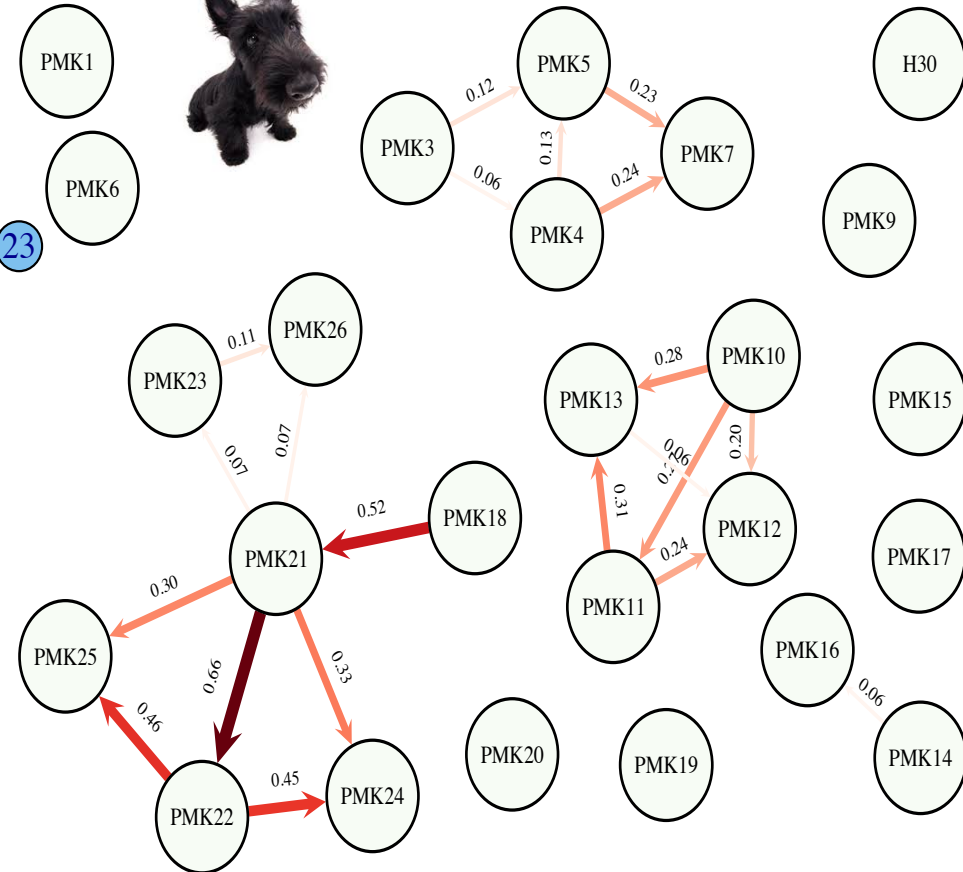
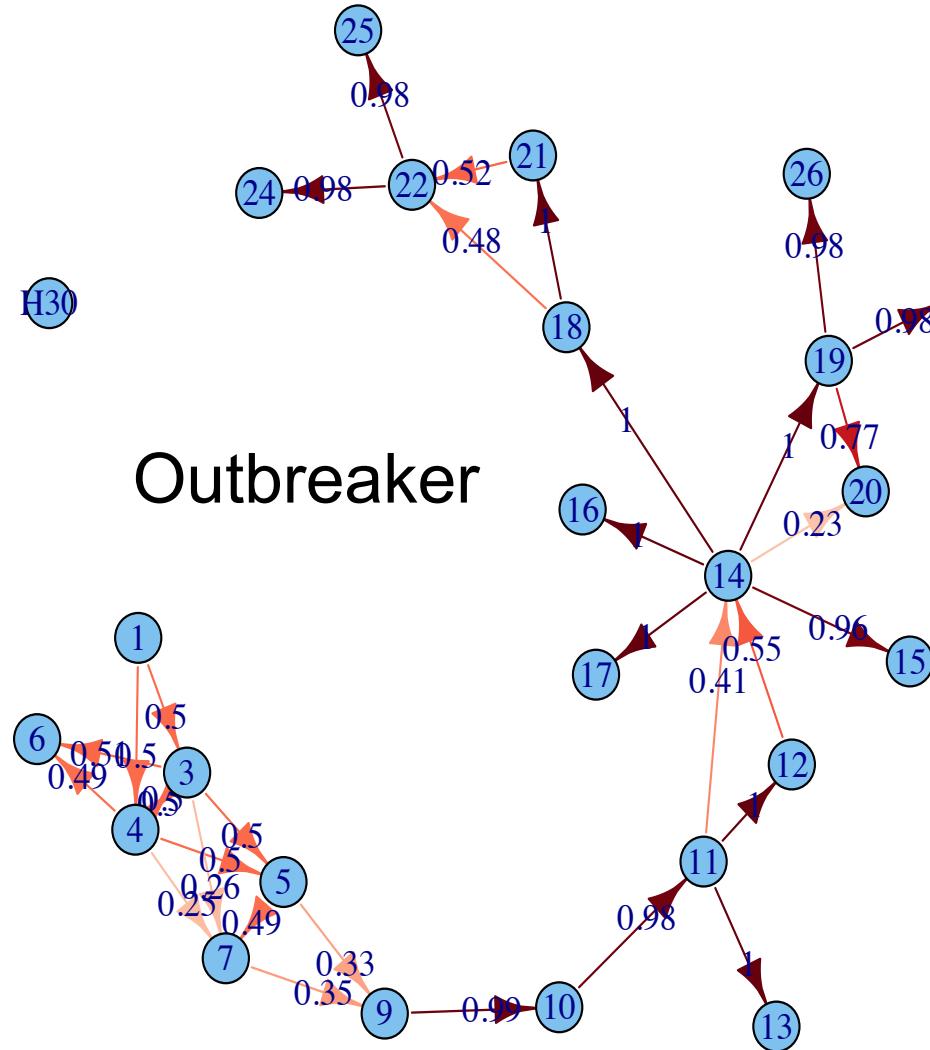
Cottam et al. 2008 PLOS Pathogens

K. Pneumoniae outbreak in Nepal

SCOTTI



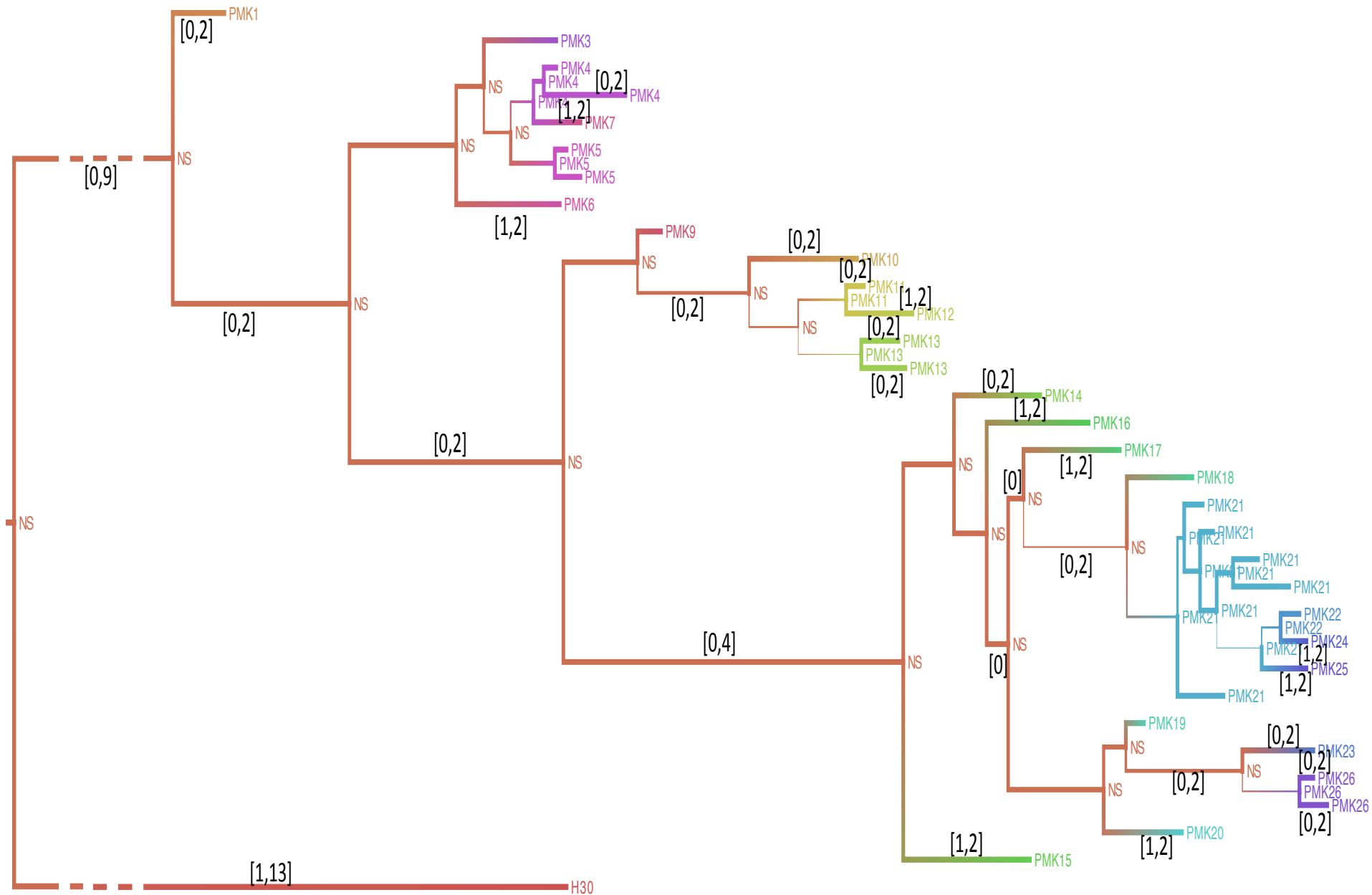
Outbreaker



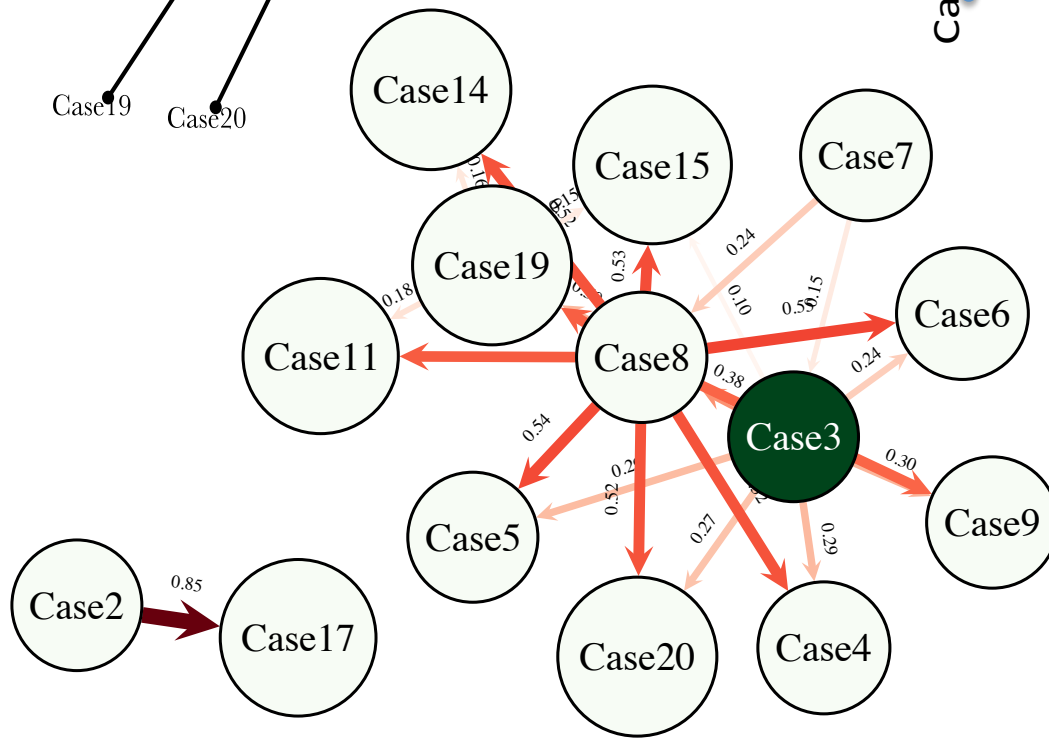
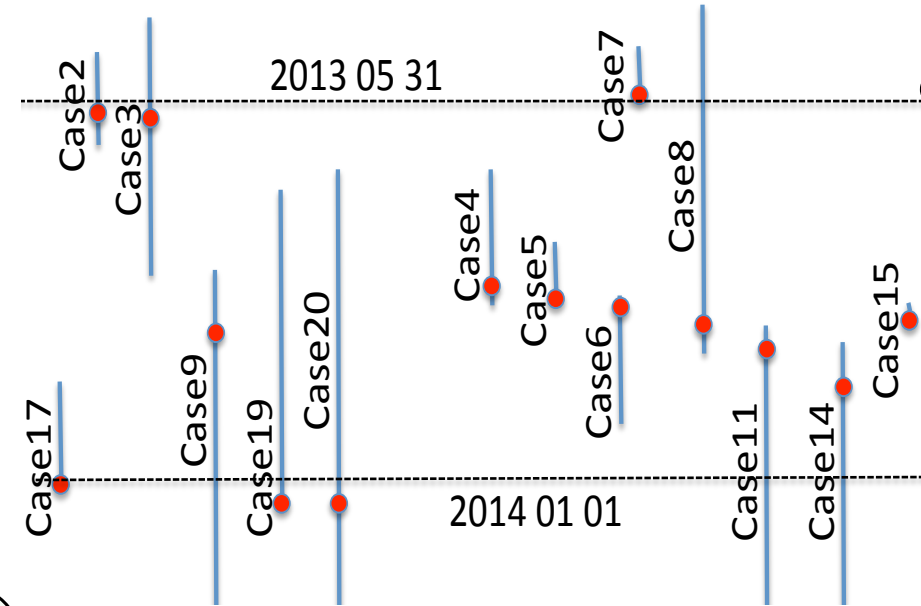
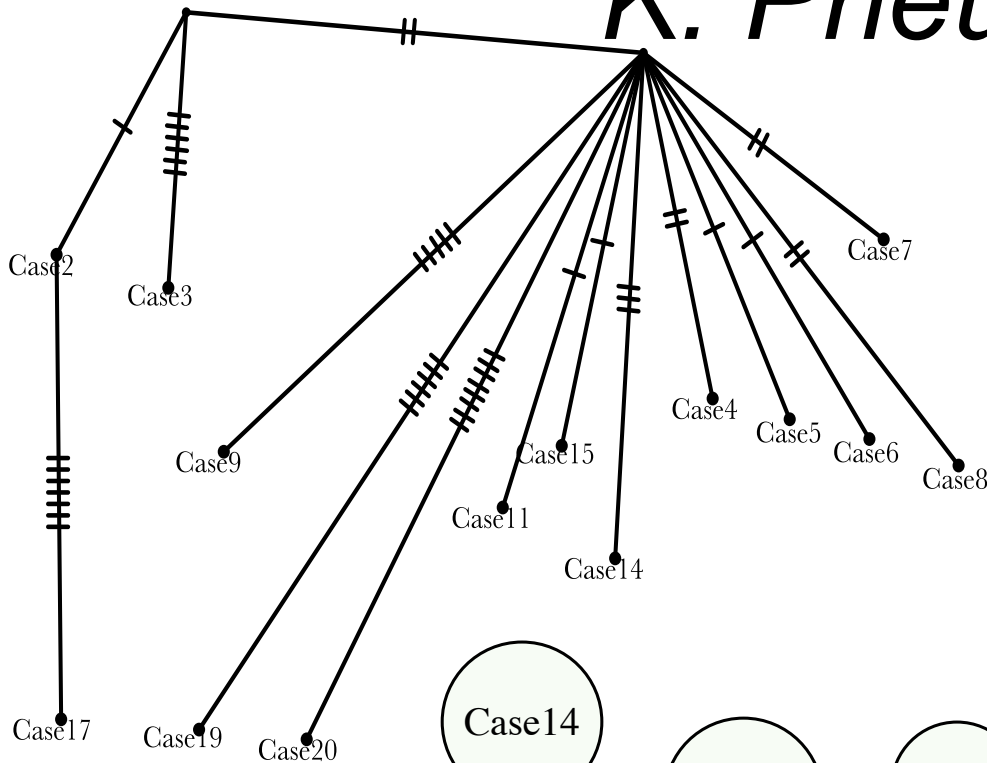
Stoesser et al. 2014

Antimicrobial agents and chemotherapy

K. Pneumoniae



K. Pneumoniae in Leeds



Martin et al, J. Antimicrobial Chemotherapy, accepted

Summary

Accounting for complexities is important.

SCOTTI can infer transmission tree from genetic and epi data in many scenarios, accounting for within-host evolution and non-sampled hosts.

Thanks for listening!



Daniel J Wilson

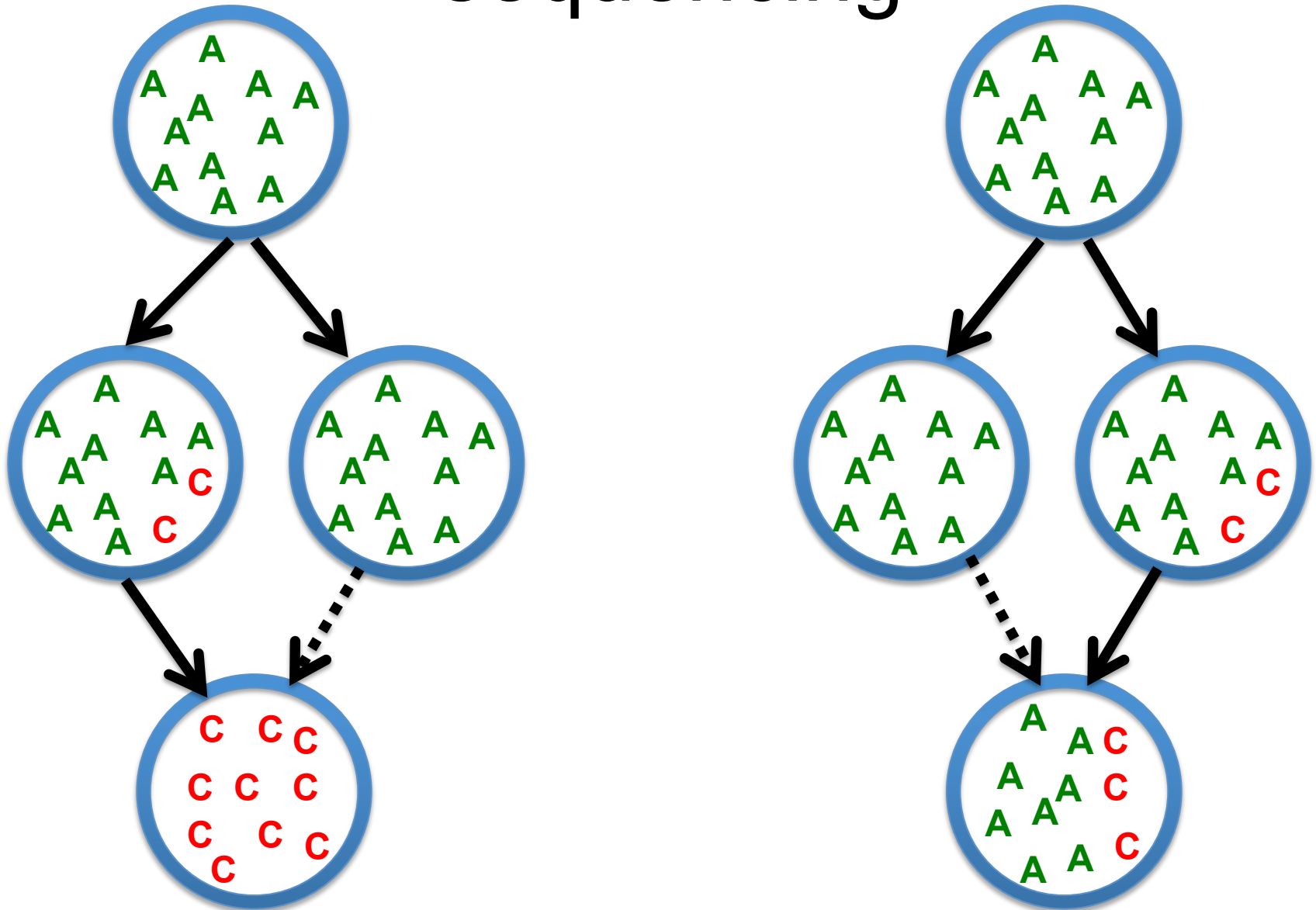


Chieh-Hsi Wu

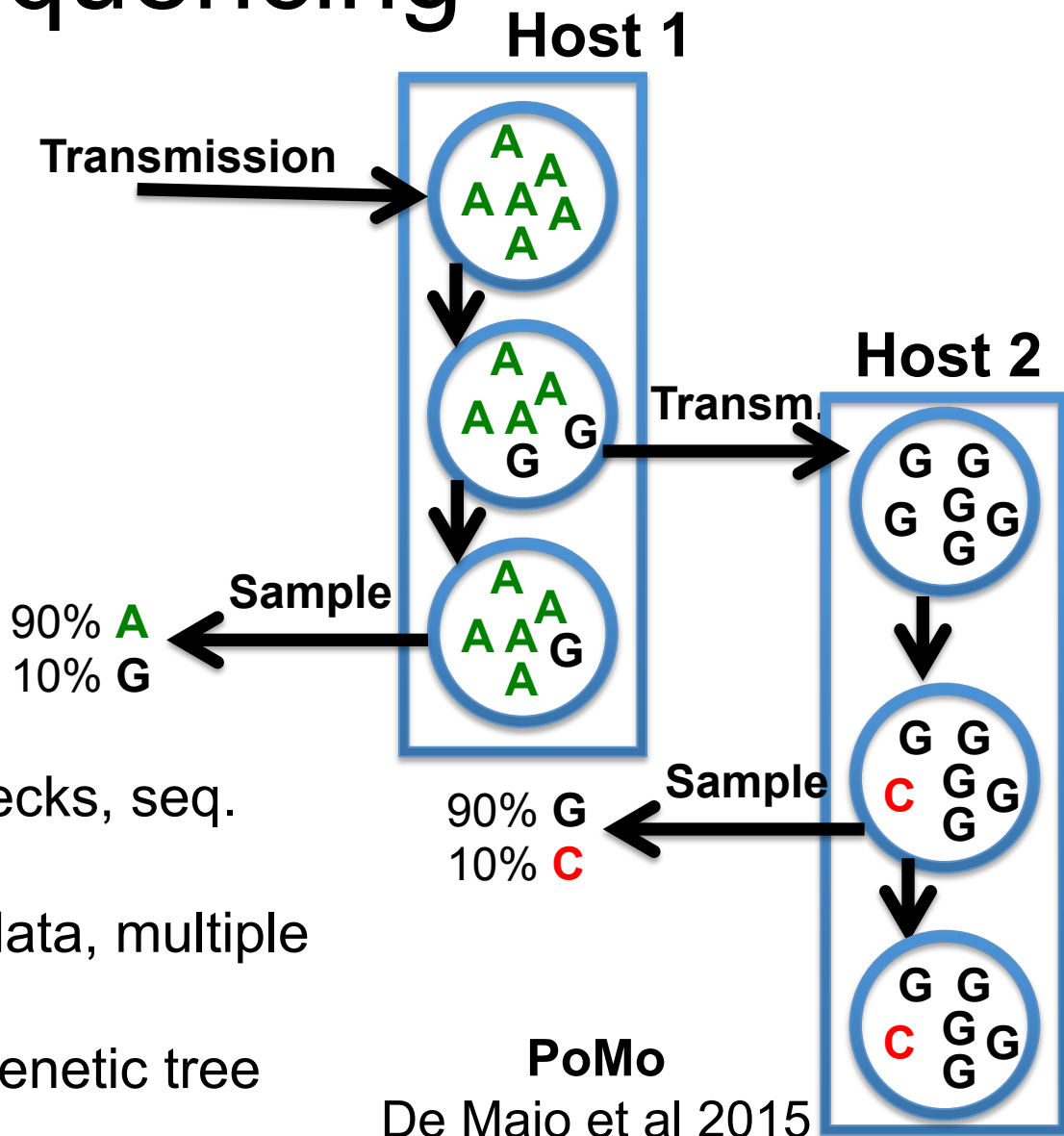
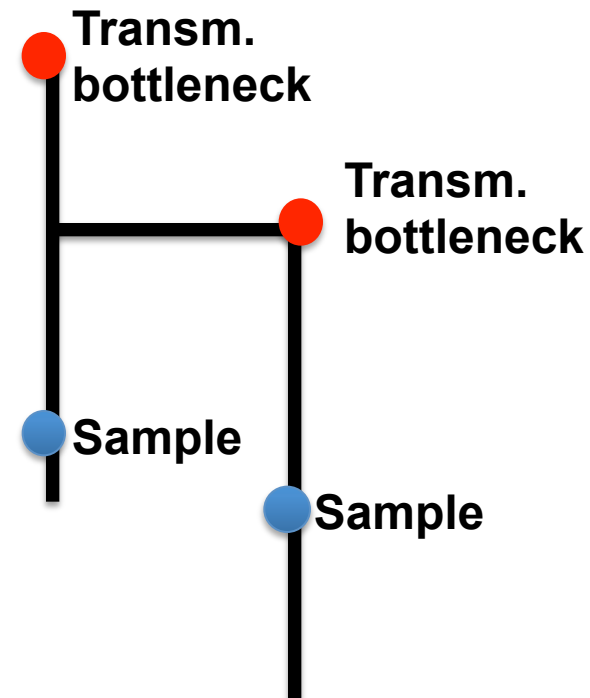
Nicole Stoesser, Hang Phan,
Derrick Crook group (NDM Microbiology)



Inferring transmission from deep sequencing



Inferring transmission from deep sequencing



Advantages:

- 1) Can model transm. bottlenecks, seq. error, within-host evolution.
- 2) Allows recombination, epi data, multiple samples.
- 3) Transmission tree = phylogenetic tree