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

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Bovine TB workshop
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Talk outline

- Genetic tracking of pathogen transmission
- Host species as discrete character states
- Analytical challenges
- Case studies: CSF and bTB
Two-host transmission tree

Cattle

Badgers

Time
Two-host transmission tree

Host switches:
How often?
Which direction?

Cattle

Badgers

Time
Actual transmission tree is unknown
Actual transmission tree is unknown

Most hosts are not sampled
Actual transmission tree is unknown

Most hosts are not sampled

Cattle

Badgers

Time

Host switch missed
Actual transmission tree is unknown

Mutations make tree visible

Cattle

Badgers

Time
Rare switches are easy to detect
Only applies to few reservoir systems

Host switches only rare in this zone

Viana et al. 2014, Trends Ecol & Evol
Frequent switches create ambiguous signal

Multiple switches or continuous transmission?
• What is the minimum number of host switches 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

\[ \beta \]

\[ \beta_{i,j} \]  \hspace{1cm} \[ \beta_{j,i} \]
Inferring host state probabilities for internal tree nodes
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

- **Central Europe**
  - From domestic pig: 0.18
  - From wild boar: 0.40

- **SE Europe**
  - From domestic pig: 0.31
  - From wild boar: 0.36

- **Italy**
  - From domestic pig: 0.10
  - From wild boar: 0.33
Effects of sampling bias?

More virus samples available from domestic pigs

- Central Europe
- SE Europe
- Italy
Reduce sampling bias by down-sampling

Randomly remove taxa from tree => repeat 40x

Original model still receives highest support

Central Europe

SE Europe

Italy

Models

ΔAIC
Assessing the effect of biased sampling using simulations

Empirical ratio in CSF study

- 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
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