

Lecture 3.3

Tip-Dating Analysis

David Duchêne

Heterochronous data

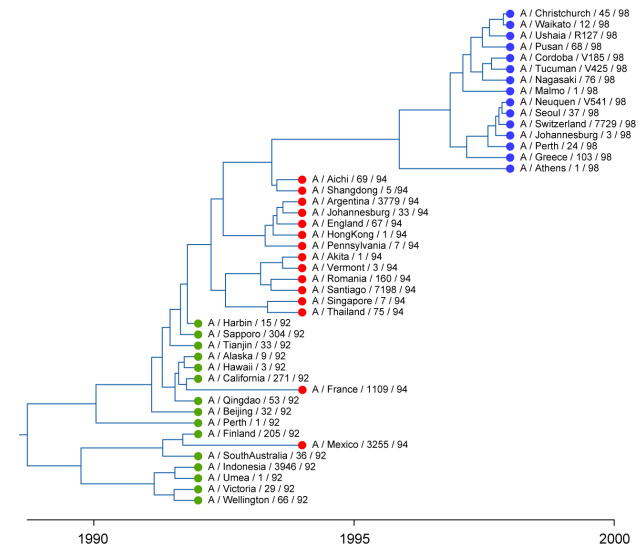
- Biological samples with different ages
 - RNA/DNA from rapidly evolving pathogens
 - Ancient DNA
- Fossils
 - Morphological characters



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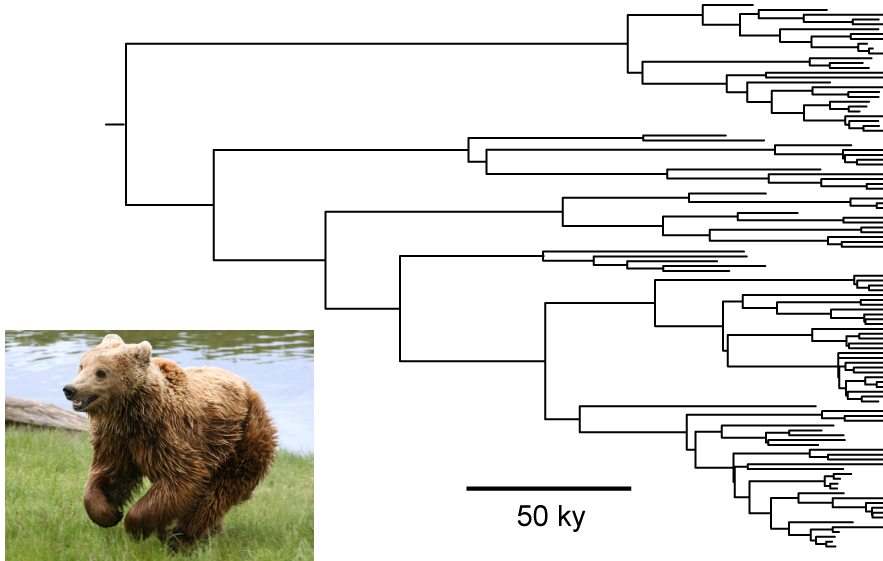
Time-structured Sequence Data

Rapidly evolving pathogens



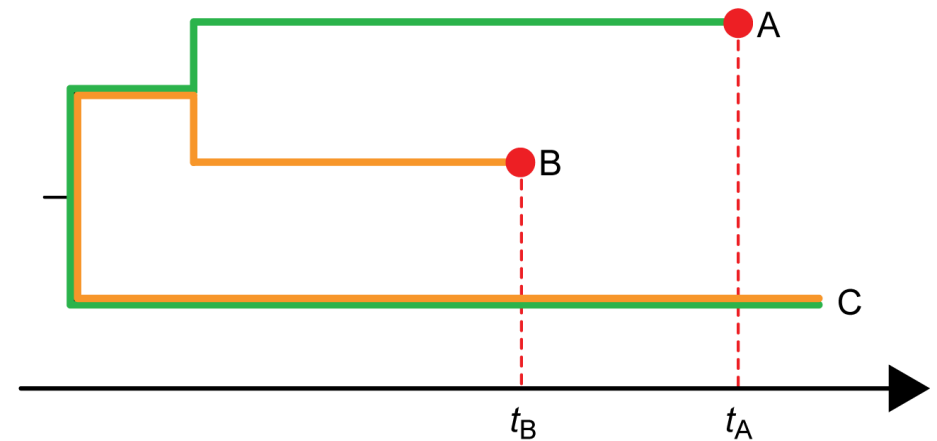
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Ancient DNA



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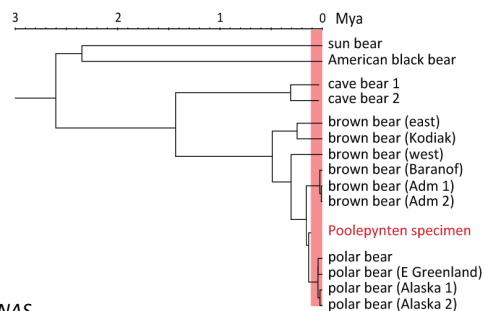
Estimating rates



Rambaut (2000) *Bioinformatics* 6

Measurably evolving populations

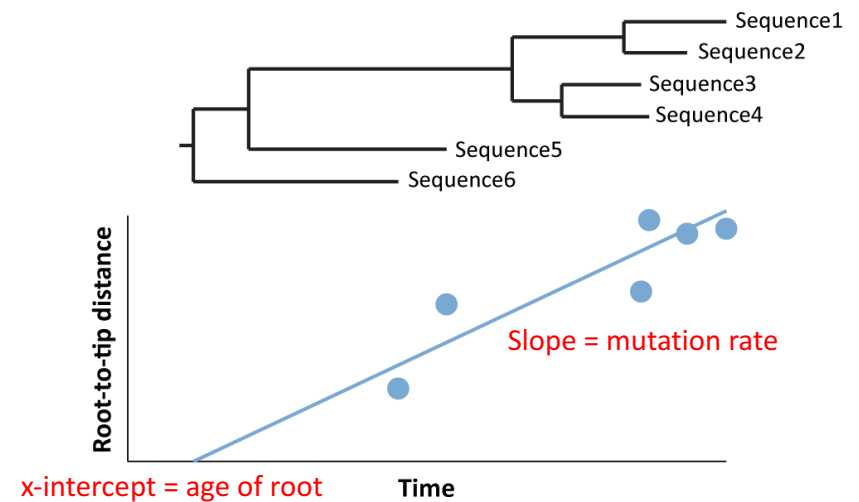
- Can perform tip-dating on **measurably evolving populations**
 - Substantial genetic change during the sampling window
 - High rate (pathogens) or wide window (ancient DNA)
- Sampling window represents large fraction of the tree height



Lindqvist *et al.* (2010) *PNAS*

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TempEst



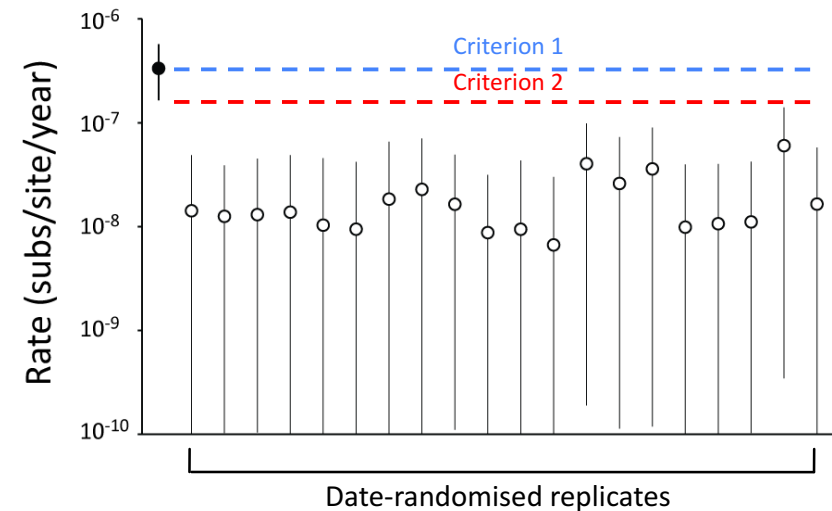
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Date-randomisation test

- Test for temporal signal in the sampling times
- **Date-randomisation test**
 1. Estimate rate from original data set
 2. Estimate rate from replicate data sets in which the sampling times have been randomly reassigned to the sequences
 3. Compare rate estimates from original and replicate data sets

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Date-randomisation test



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Date-randomisation test

- Test is misleading if many sequences are clustered into a few sampling times
- Randomisation should be done by randomly reassigning dates among clusters rather than among individual sequences

The Performance of the Date-Randomization Test in Phylogenetic Analyses of Time-Structured Virus Data

Sebastián Duchêne^{*,1}, David Duchêne², Edward C. Holmes^{1,3} and Simon Y.W. Ho¹

Methods in Ecology and Evolution

Methods in Ecology and Evolution 2016, 7, 80–89

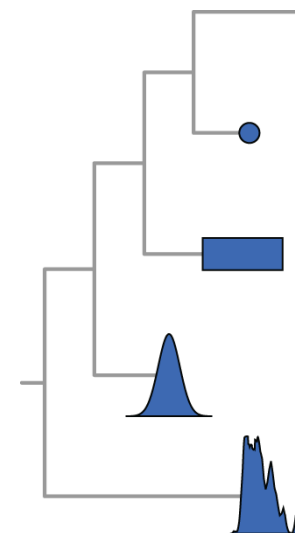
doi: 10.1111/2041-210X.12466

The effect of genetic structure on molecular dating and tests for temporal signal

Gemma G. R. Murray^{1*}, Fang Wang¹, Ewan M. Harrison², Gavin K. Paterson^{2,3}, Alison E. Mather^{2,4}, Simon R. Harris¹, Mark A. Holmes², Andrew Rambaut⁵ and John J. Welch¹

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Calibration priors

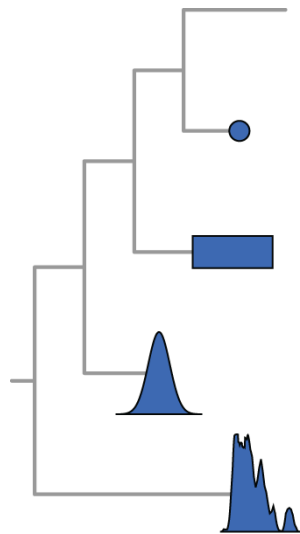


Point calibration

- Ignores uncertainty due to preservational biases, isotopic dating errors, *etc.*

Ho & Duchêne (2014) *Mol Ecol* 12

Calibration priors

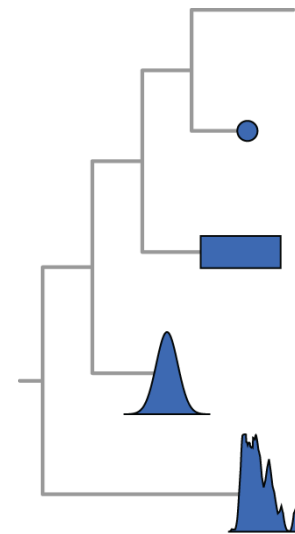


Uniform calibration

- Layer-dated samples
- Uninformative sampling records

Ho & Duchêne (2014) *Mol Ecol* 13

Calibration priors



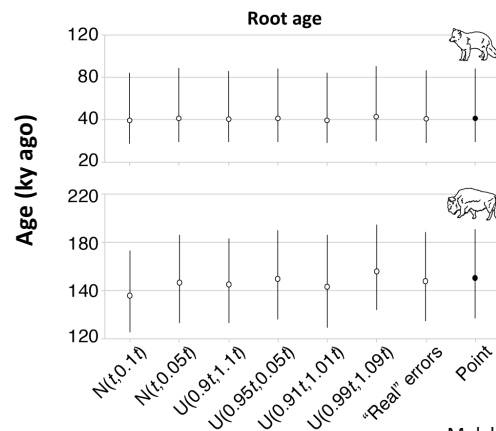
Empirical radiocarbon sampler

- Models uncertainty in radiocarbon dating

Molak et al. (2015) *Mol Ecol Resour* 14

Calibration priors

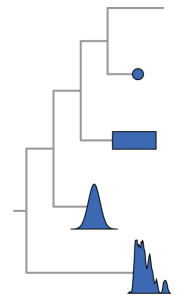
- In practice, accounting for uncertainty in sampling times does not have much impact on estimates of rates and dates



Molak et al. (2013) *Mol Biol Evol* 15

Estimating sample ages

- Some sequences have unknown sampling times
- Normally treated as nuisance parameters



A Bayesian Phylogenetic Method to Estimate Unknown Sequence Ages

Beth Shapiro,^{*1} Simon Y. W. Ho,² Alexei J. Drummond,³ Marc A. Suchard,⁴ Oliver G. Pybus,⁵ and Andrew Rambaut^{6,7}

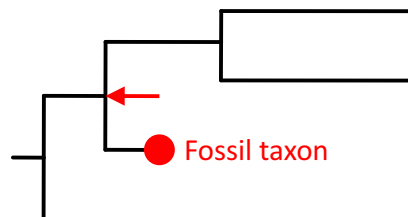
Total-Evidence Dating

- Combined morphological and molecular data set
- Fossil taxa included
 - Phylogenetic placement estimated using morphological data
 - Age acts as a calibration by constraining the age of parent node
- Birth-death tree prior

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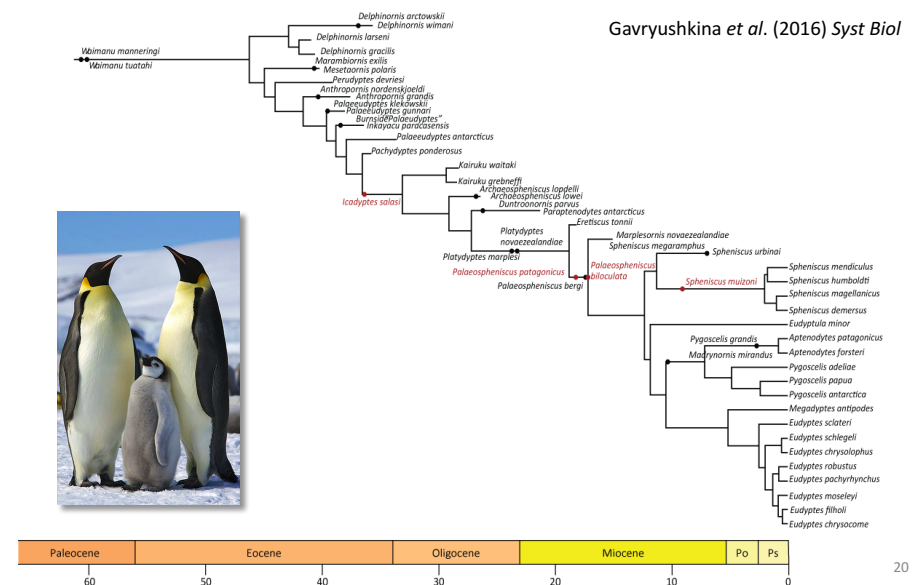
Total-evidence dating

- Avoids the need to construct priors for ages of internal nodes
- Can include fossil taxa with uncertain phylogenetic position
- Can provide sufficient calibration without the need to include maximum age constraints



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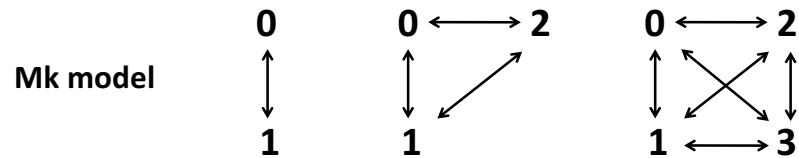
Total-evidence dating



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Morphological character evolution

- Morphological characters as discrete states



- Correction for ascertainment bias: **Mkv model**
 - Morphological characters usually chosen for variability
- Can apply gamma-distributed rates across characters

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Outstanding questions

1. How adequate is the Mk model of morphological evolution?
2. What is the best method for modelling the relationship between molecular and morphological rate?
3. Are the induced time priors consistent with the fossil record?
4. Are morphological data better treated as categorical or continuous characters?

O'Reilly *et al.* (2015) *Trends Genet* 22

Useful references

- Measurably evolving pathogens in the genomic era**
Biek *et al.* (2015) *Trends Ecol Evol*, 30: 306–313.
- Inferences from tip-calibrated phylogenies: a review and practical guide**
Rieux & Balloux (2016) *Mol Ecol*, 25: 1911–1924.
- Estimating evolutionary rates using time-structured data: a general comparison of phylogenetic methods**
Duchene *et al.* (2016) *Bioinformatics*, 32: 3375–3379.
- Dating tips for divergence-time estimation**
O'Reilly *et al.* (2015) *Trends Genet*, 31: 637–650.

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