

# Phylogenetics

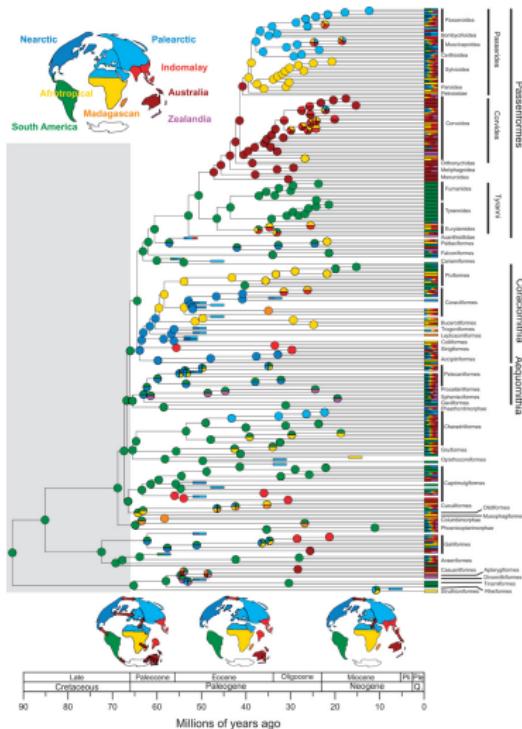
Bayesian timetrees: clock models and node dating

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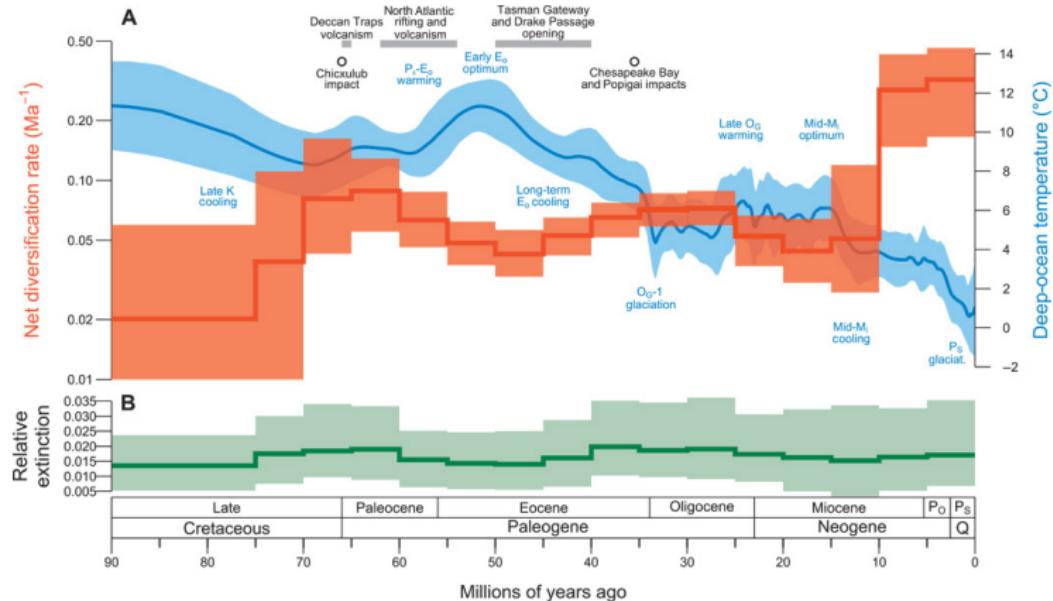
# The molecular clock

# Telling evolutionary time: motivation



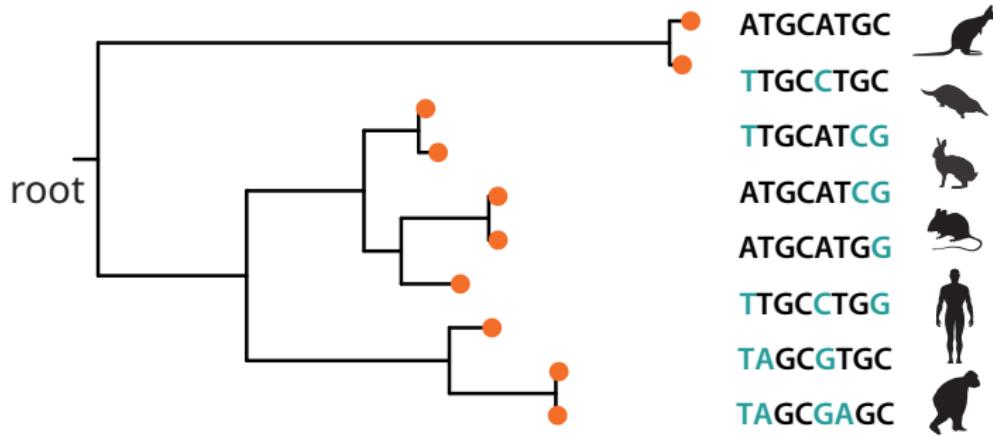
Claramunt et al. 2015 *Science Advances* — A new time tree reveals Earth history's imprint on the evolution of modern birds

# Telling evolutionary time: motivation



Claramunt et al. 2015 *Science Advances* — A new time tree reveals Earth history's imprint on the evolution of modern birds

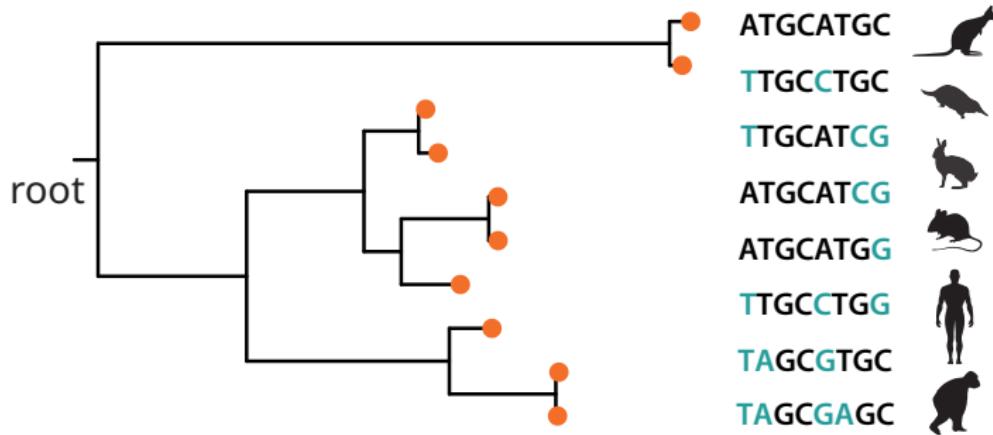
# Molecular (or morphological) characters are not independently informative about time



branch lengths = genetic distance

$$v = rt$$

# Molecular (or morphological) characters are not independently informative about time

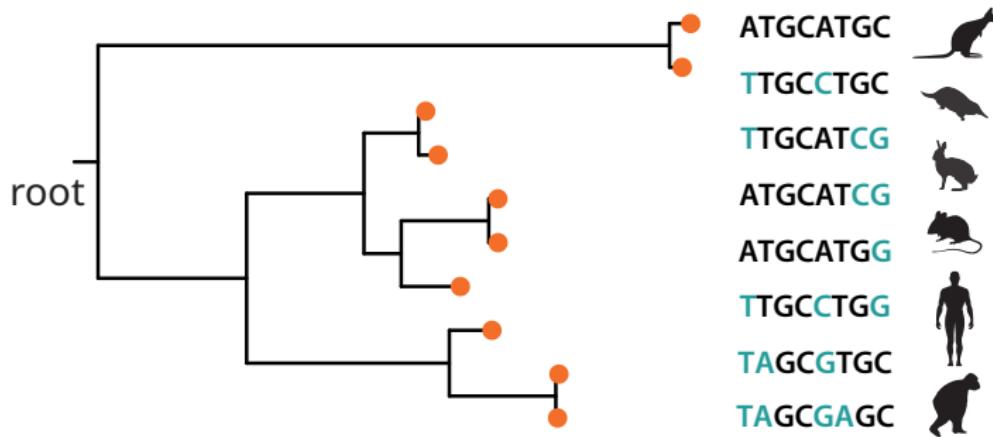


branch lengths = genetic distance

$$v = rt$$

Slow rate, long interval OR fast rate, short interval?

# Molecular (or morphological) characters are not independently informative about time

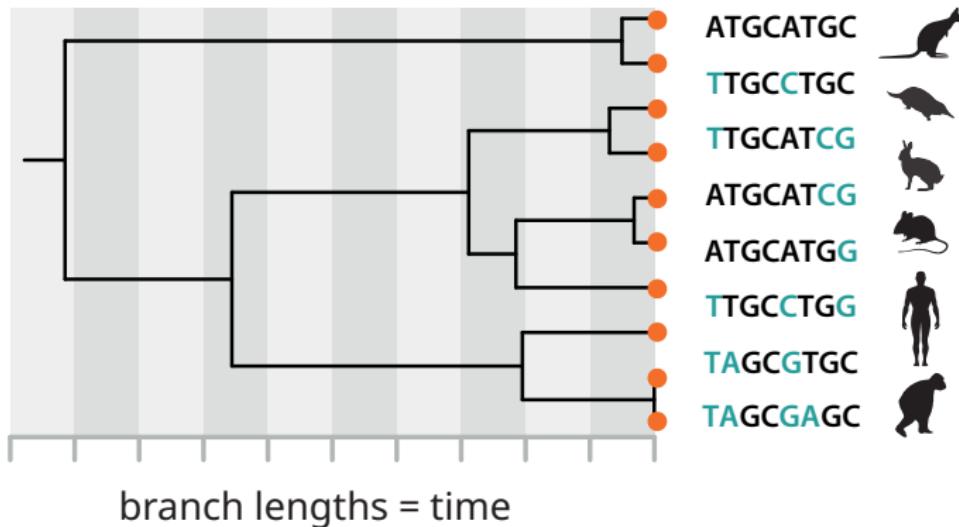


branch lengths = genetic distance

$$v = rt$$

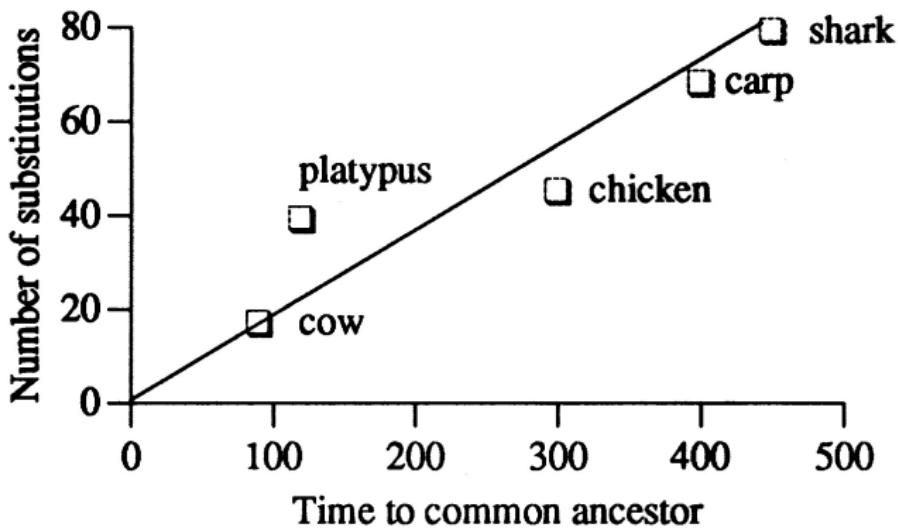
**Goal:** to disentangle evolutionary rate and time.

# Molecular (or morphological) characters are not independently informative about time



**Goal:** to disentangle evolutionary rate and time.

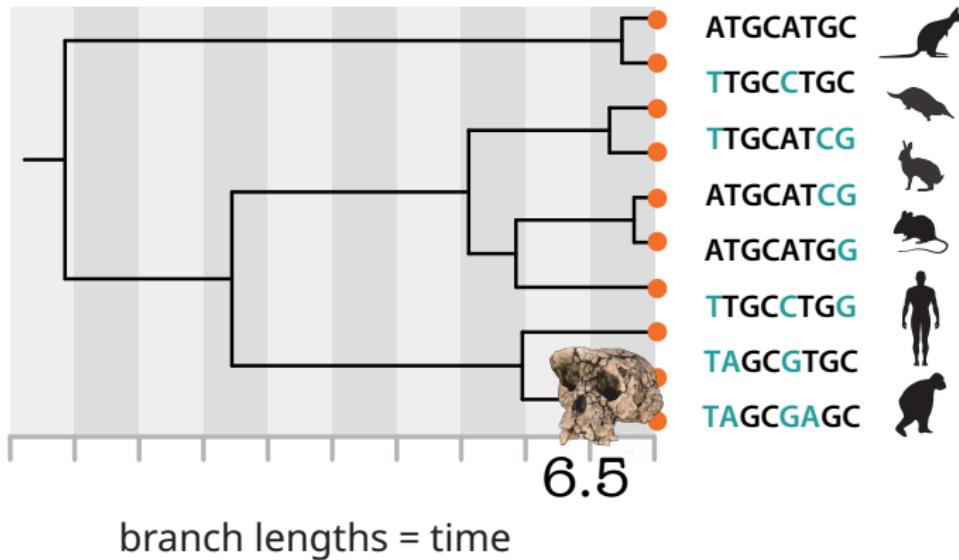
## The molecular clock hypothesis



Zuckerkandl & Pauling (1965) — Molecules as documents of evolutionary history.

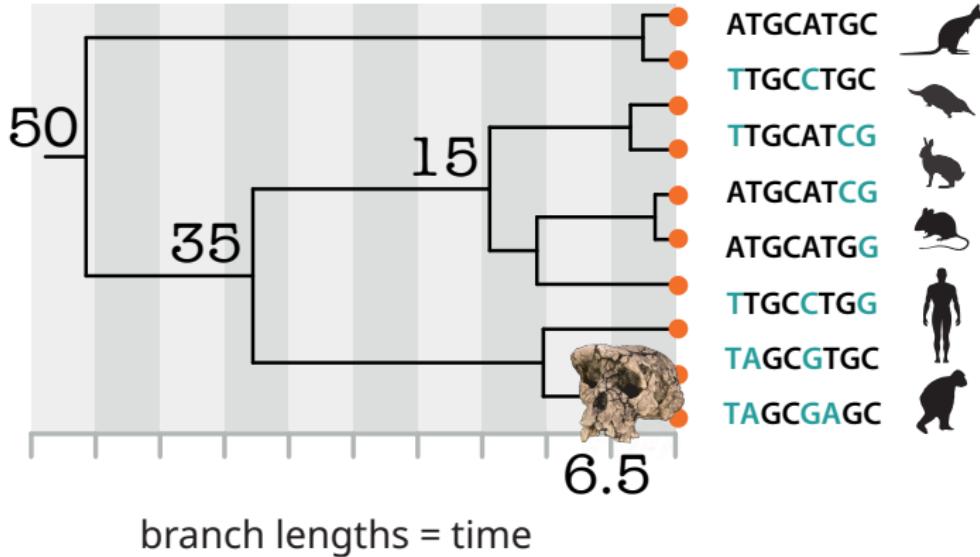
Morgan (1998) — A history of the molecular clock.

If we have independent evidence of time, we can calibrate the substitution rate



Temporal evidence of divergence for one species pair let's us calibrate the average rate of molecular evolution...

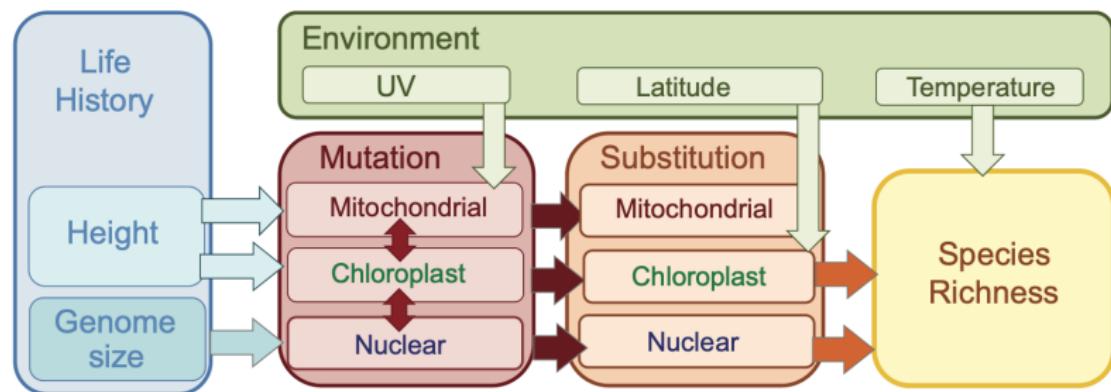
If we have independent evidence of time, we can calibrate the substitution rate



...and use this to extrapolate the divergence times for other species pairs.

# The molecular clock: challenges

Many variables contribute to variation in the substitution rate.



Bromham et al. (2015).

# The molecular clock: challenges

The molecular clock is not constant over time.

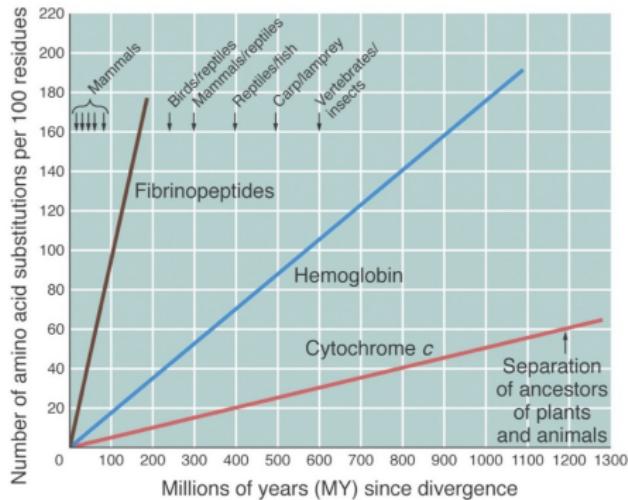
- Rates vary across taxa / time / genes / sites within the same gene



# The molecular clock: challenges

The molecular clock is not constant over time.

- Rates vary across taxa / time / genes / sites within the same gene



Variation in rate makes different genes useful for different timescales.

## The molecular clock: challenges

The molecular clock is not constant over time.

- Rates vary across taxa / time / genes / sites within the same gene

Calibrations are rarely known precisely.

## The molecular clock: challenges

The molecular clock is not constant over time.

- Rates vary across taxa / time / genes / sites within the same gene

Calibrations are rarely known precisely.

→ we need a flexible statistical framework that deals well with uncertainty.

# Bayesian inference

# Bayes' theorem

$$P(\text{parameters} | \text{data, model}) =$$

posterior

likelihood

priors

$$\frac{P(\text{data} | \text{parameters, model}) P(\text{parameters} | \text{model})}{P(\text{data} | \text{model})}$$

P ( data | model )

marginal probability of the data

## Bayes' theorem

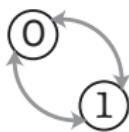
$P(\text{data} \mid \text{parameters, model})$  ← the model used to calculate the **likelihood**.

$P(\text{parameters} \mid \text{model})$  ← this represents our **prior knowledge** of the model parameters.

$P(\text{parameters} \mid \text{data, model})$  ← the **posterior** reflects our combined knowledge based on the likelihood and the priors.

# Bayesian phylogenetic dating requires three model components

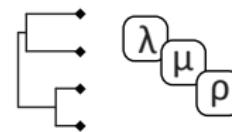
- The **substitution model** ← describes how sites evolve over time.
- The **clock model** ← describes how evolutionary rates vary across the tree.
- The **tree model** ← describes how trees grow over time. Temporal evidence is included here.



Substitution model



Clock model



Tree and tree model

# Bayesian phylogenetic dating

## The data

AND/OR  
0101... ATTG...  
1101... TTGC...  
0100... ATTC...



Characters

Fossil ages

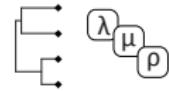
## The model



Substitution  
model



Clock  
model



Tree and tree  
model

## Bayesian phylogenetic dating

## The data

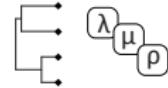
**AND/OR**  
0101... ATTG...  
1101... TTGC...  
0100... ATTC...



## Characters

## Fossil ages

## The model



## Substitution model

Clock  
model

## Tree and tree model

$$P(\text{posterior} \mid \text{evidence}) =$$

probability of the character  
data given everything else\*

probability of the timetree  
given the timetree model

priors on model parameters

$P(0101\dots | \square^{\lambda}_{\mu}, \circ, \circ_1, \text{clock}) P(\square^{\star} | \star^{\lambda}_{\mu}) P(\lambda_{\mu}) P(\circ) P(\circ_1)$

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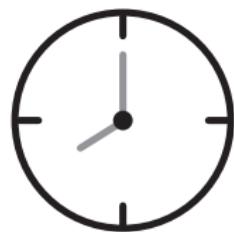
$P(0101\dots | \star^{\lambda}_{\mu})$

marginal probability of the data

\*the timetree, the parameters and the tripartite model

## Molecular clock models

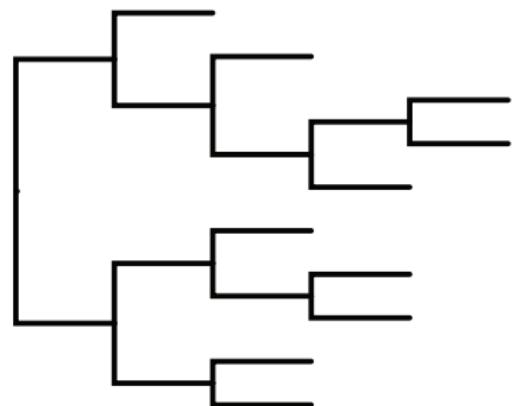
The **clock model** ← describes how evolutionary rates vary across the tree.



# The strict / constant molecular clock model

Assumptions:

- The substitution rate is constant over time.
- All lineages share the same rate.

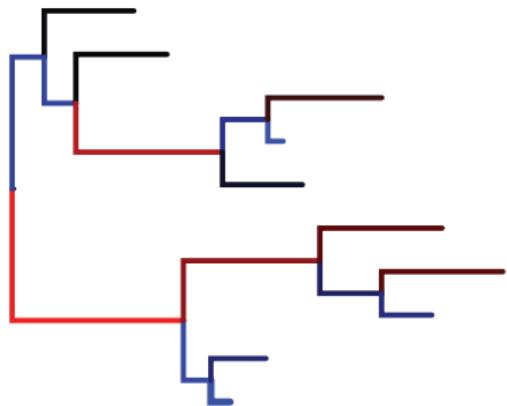


branch length = substitution rate  
low  high

## Relaxed clock models

Assumptions:

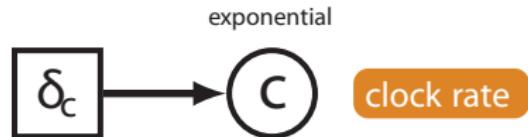
- Lineage-specific rates are independent (i.e., uncorrelated).
- The rate assigned to each branch is drawn independently from the underlying distribution.



branch length = substitution rate  
low high

## Graphical models: strict clock model

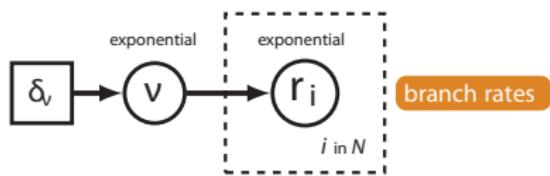
- a) Constant node
- b) Stochastic node
- c) Deterministic node
- d) Clamped node  
(observed)



Höhna et al. (2014)

# Graphical models: relaxed clock model

- a) Constant node
- b) Stochastic node
- c) Deterministic node
- d) Clamped node  
(observed)
- e) Plate



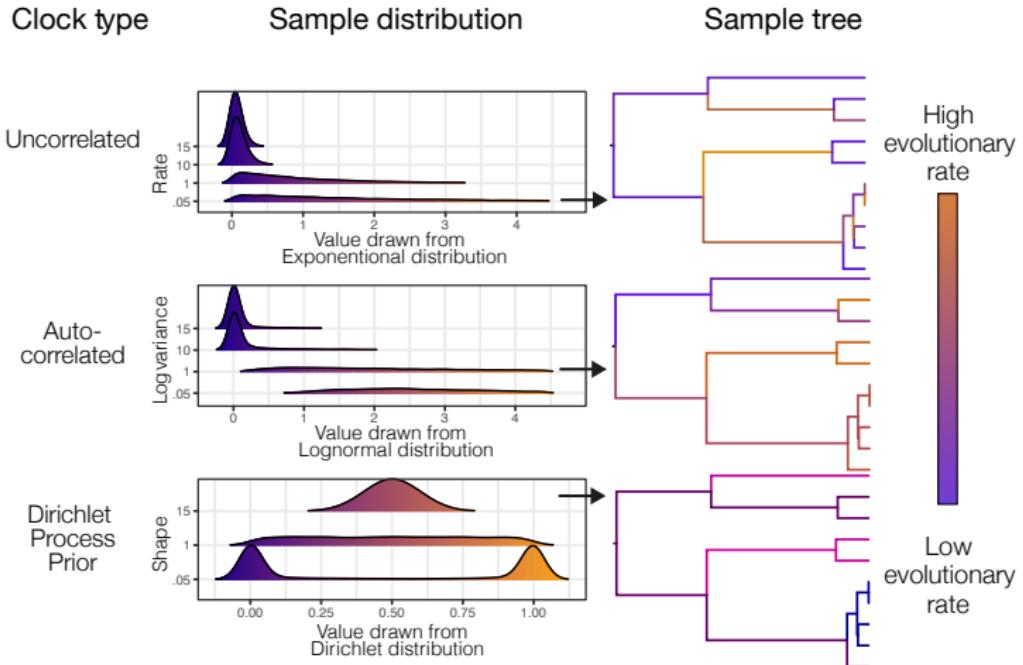
Höhna et al. (2014)

## Many different clock models

- Strict clock
- Uncorrelated clock (= the favourite)
- Autocorrelated clock
- Local clocks
- Mixture models

See Warnock & Wright (2020) for an overview.

# Many different clock models



Warnock & Wright (2020)

# Tree models and node dating

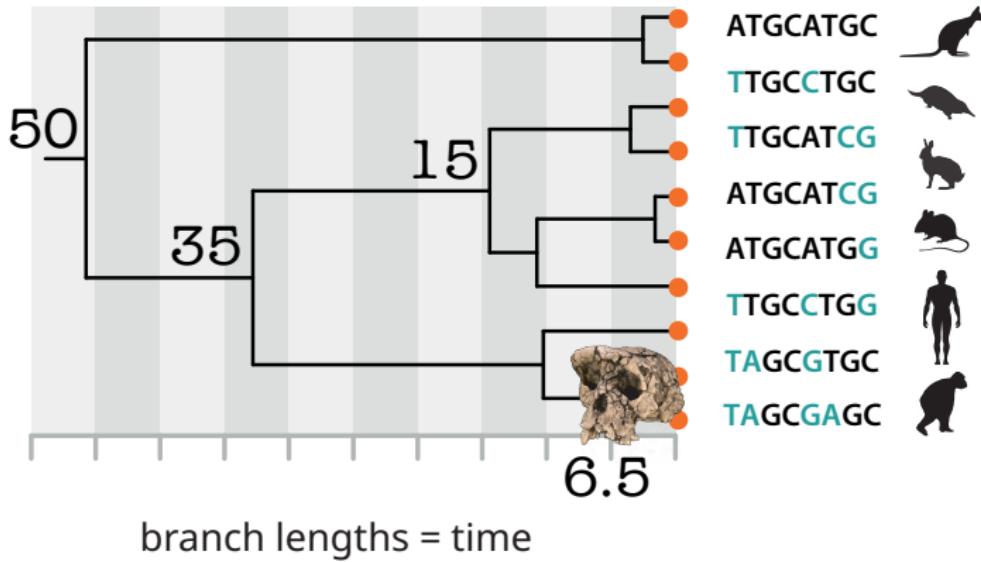
## The tree model

- Describes the dynamics (speciation / transmission / replication) of the tree generating process over time.
- Gives rise to the **tree prior**:

$$P(\text{Tree} \mid \star, \lambda, \mu, \rho)$$

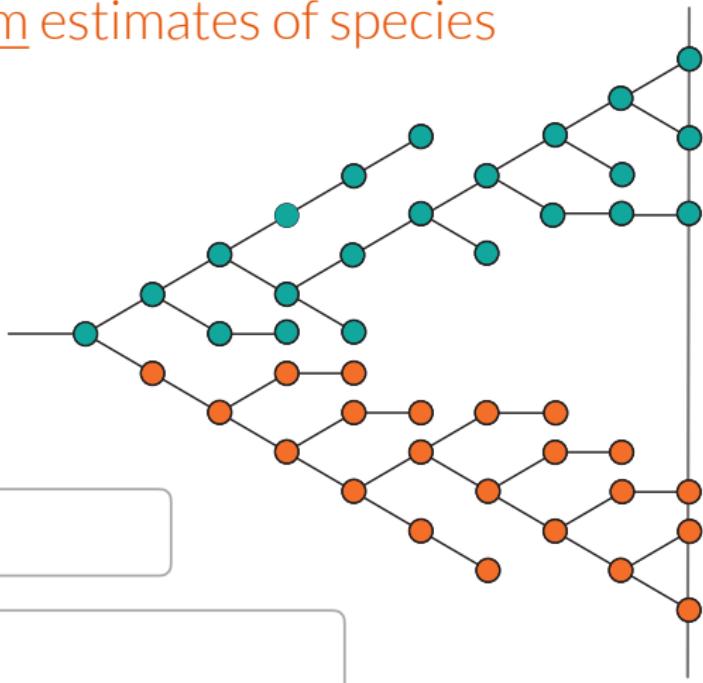
- How likely is the phylogeny given the tree model?
- Calibration information is either combined with or incorporated into the tree model.

If we have independent evidence of time, we can calibrate the substitution rate



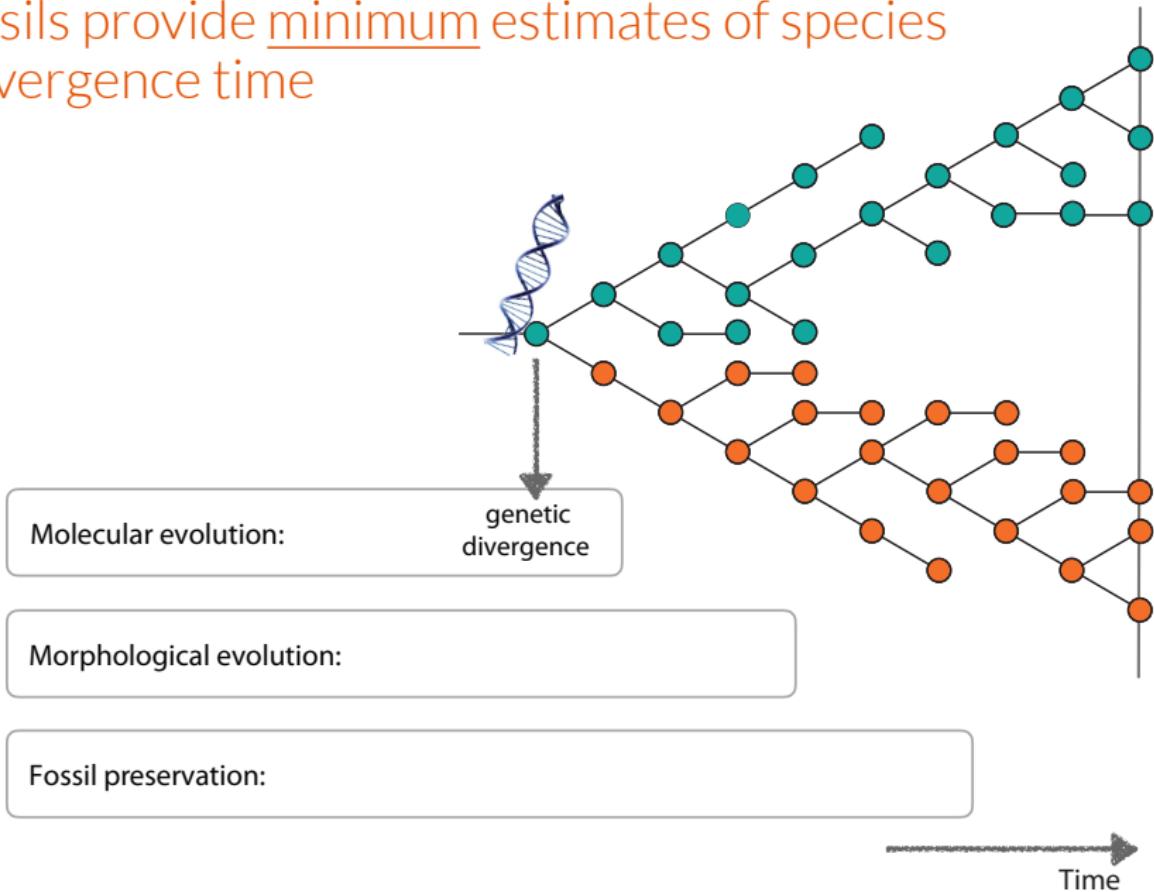
What evidence are we really able to recover from the fossil record?

Fossils provide minimum estimates of species divergence time

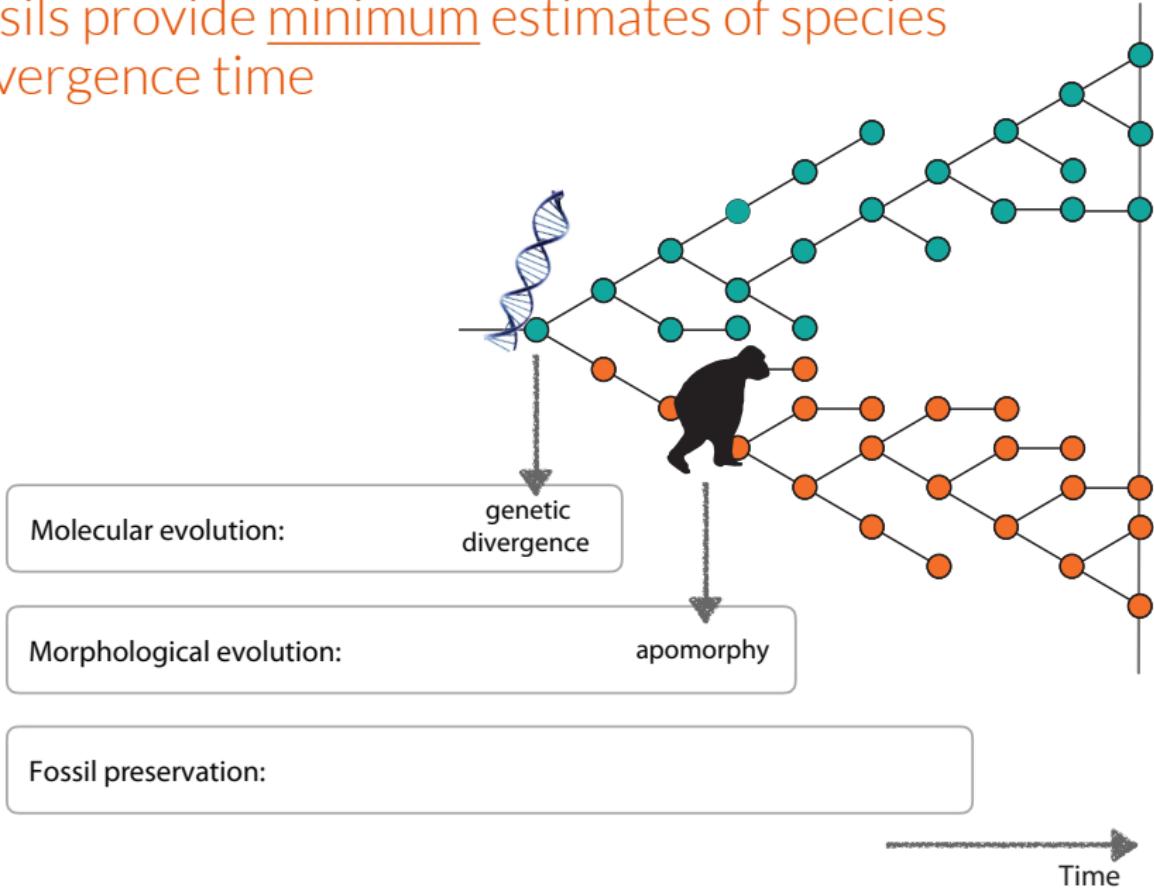


Time →

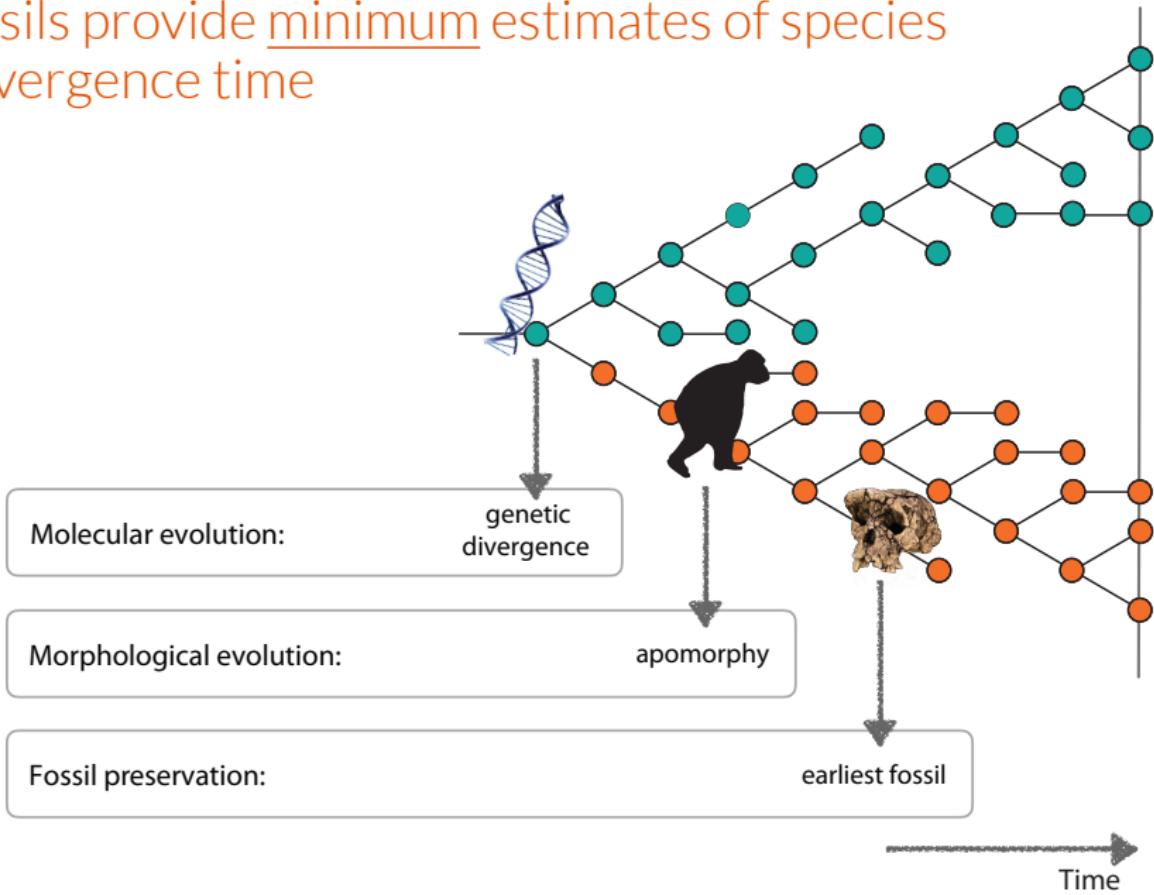
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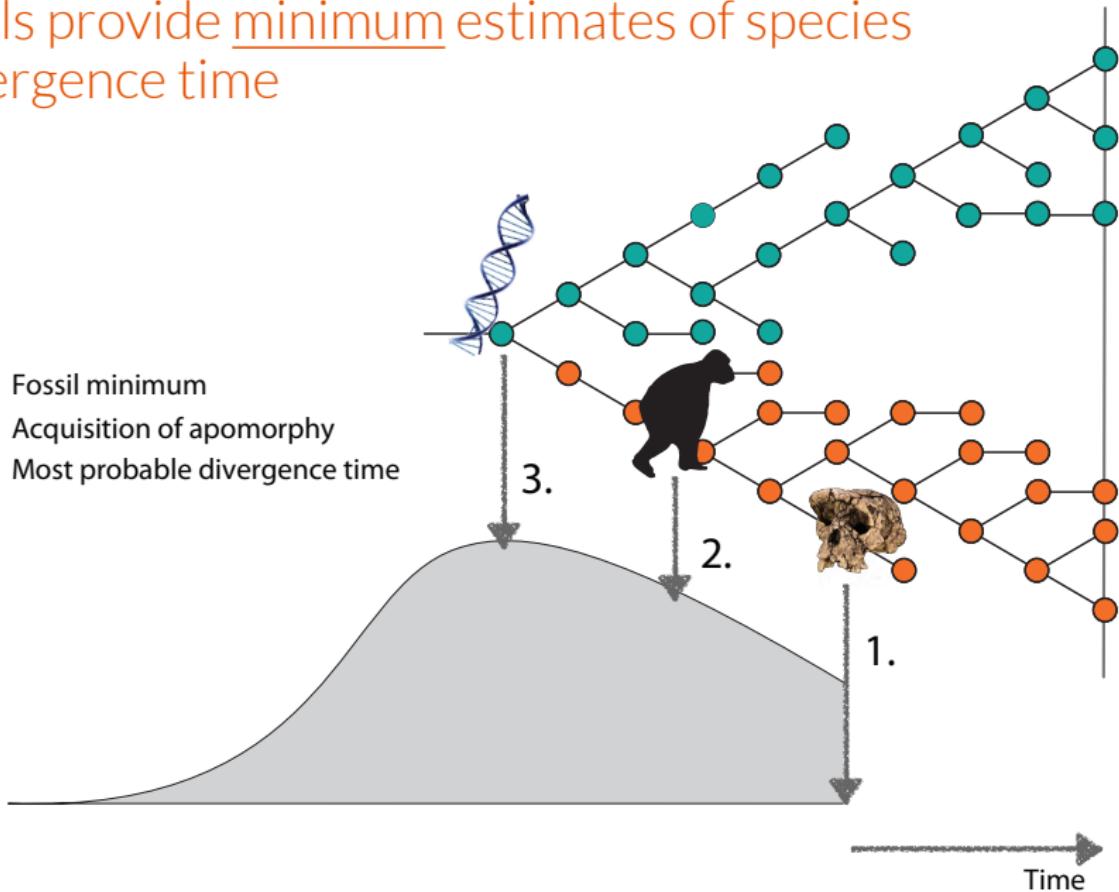


# Fossils provide minimum estimates of species divergence time

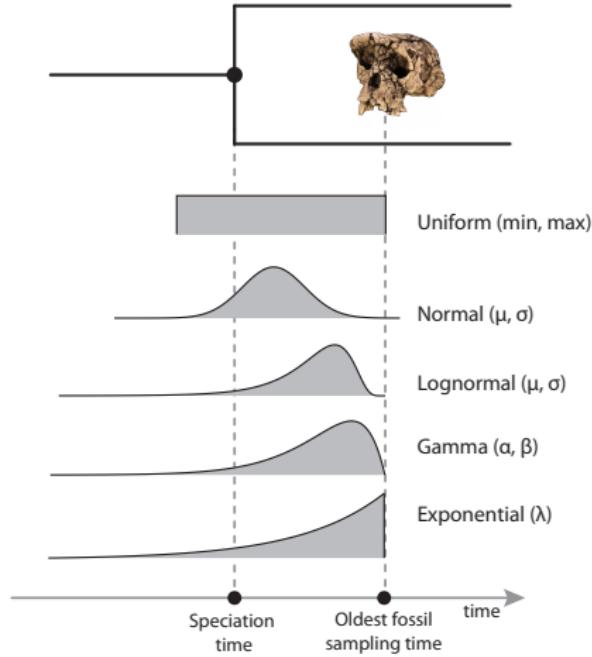


# Fossils provide minimum estimates of species divergence time

1. Fossil minimum
2. Acquisition of apomorphy
3. Most probable divergence time



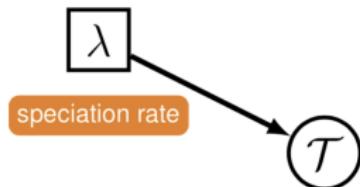
# Node dating



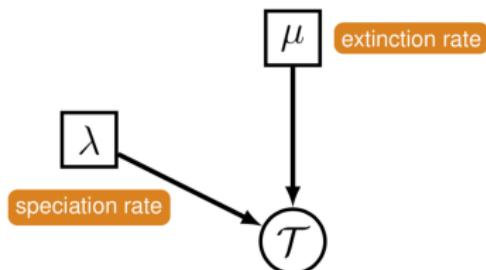
- We used a birth-death model to describe the tree generating process, given we only observe extant species.
- Then we separately apply a calibration density to constrain internal node ages.

Image adapted from Heath (2012) *Systematic Biology*

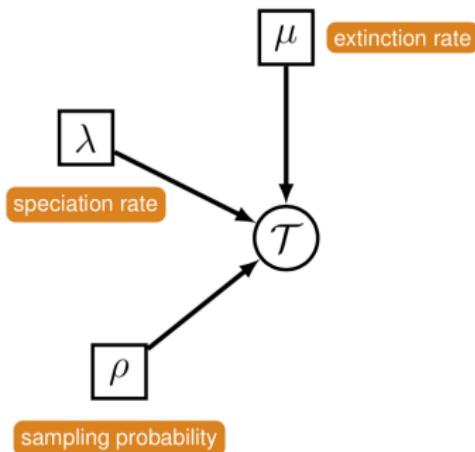
# The tree prior (for the non-fossil calibrated nodes)



Pure birth process  
i.e. no extinction



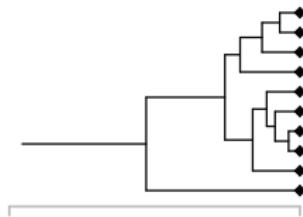
Birth-death process



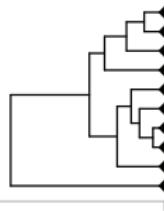
Birth-death sampling process

# Complete versus reconstructed tree

The complete outcome of the diversification and sampling processes



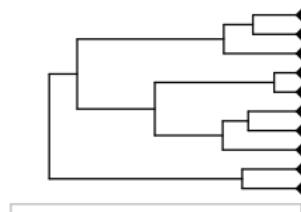
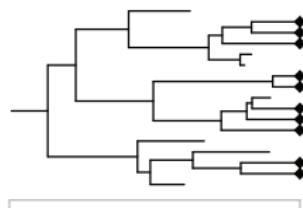
The reconstructed tree



Model parameters

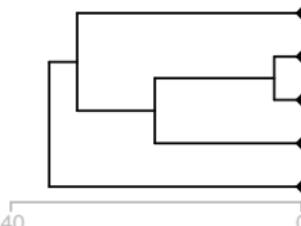
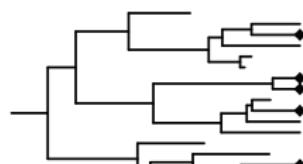
speciation ( $\lambda$ ) = 0.1

Pure birth process



speciation ( $\lambda$ ) = 0.1  
extinction ( $\mu$ ) = 0.05

Birth-death process



speciation ( $\lambda$ ) = 0.1  
extinction ( $\mu$ ) = 0.05  
extant sampling ( $p$ ) = 0.6

Birth-death sampling process

40 0 40 0

## Take homes

Sequences do not directly contain information about time.  
To date phylogenetic trees we need to separate rate and time.

The molecular clock hypotheses allows us calibrate the substitution rate and to date phylogenetic trees.

Bayesian inference is a flexible statistical framework that allows us to integrate prior knowledge with models that describe evolutionary processes.

## Suggested reading

*Understanding the tripartite approach to Bayesian divergence time estimation* — Warnock, Wright (2020) → the goal of this review was to provide an accessible introduction to the substitution, clock and tree models.

# Exercise