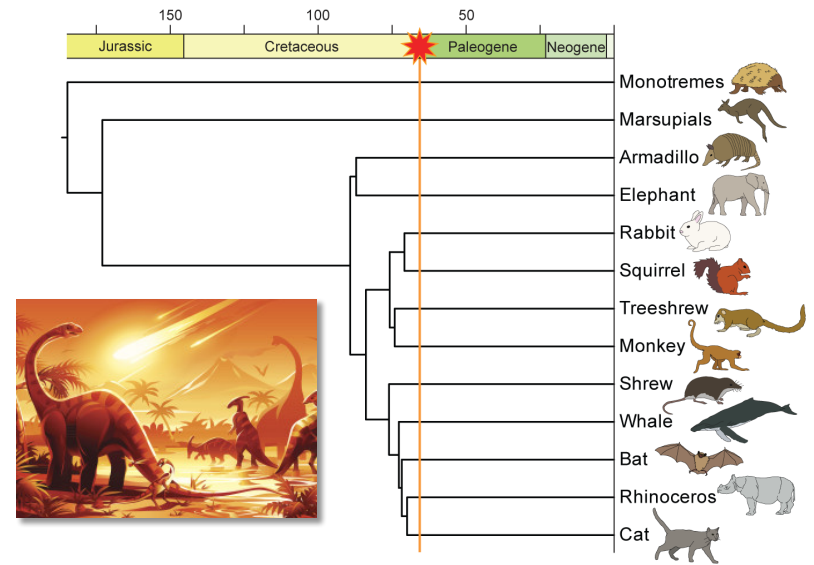


Lecture 2.3

Molecular Dating

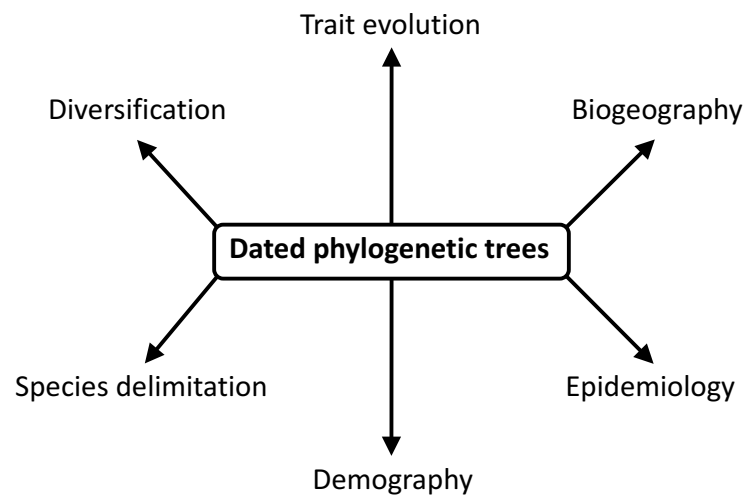
Simon Ho

Evolutionary timescales



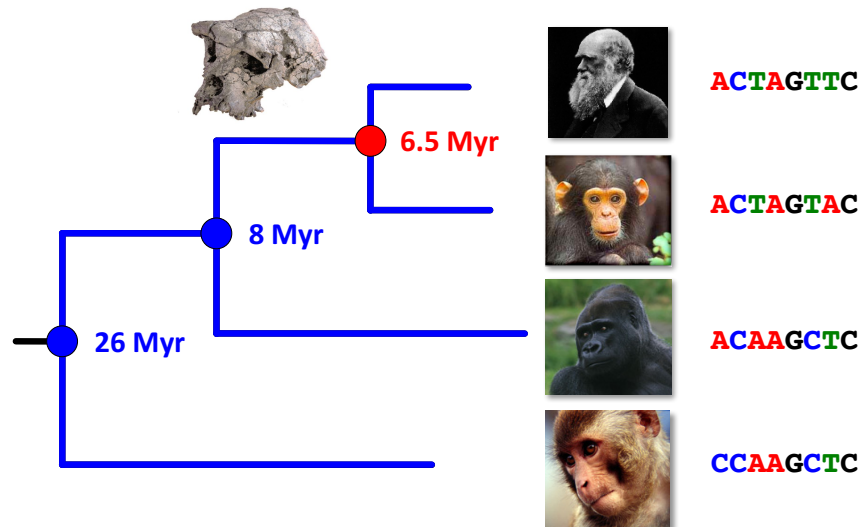
dos Reis et al. (2012) *Proc Roy Soc B* 2

Evolutionary timescales



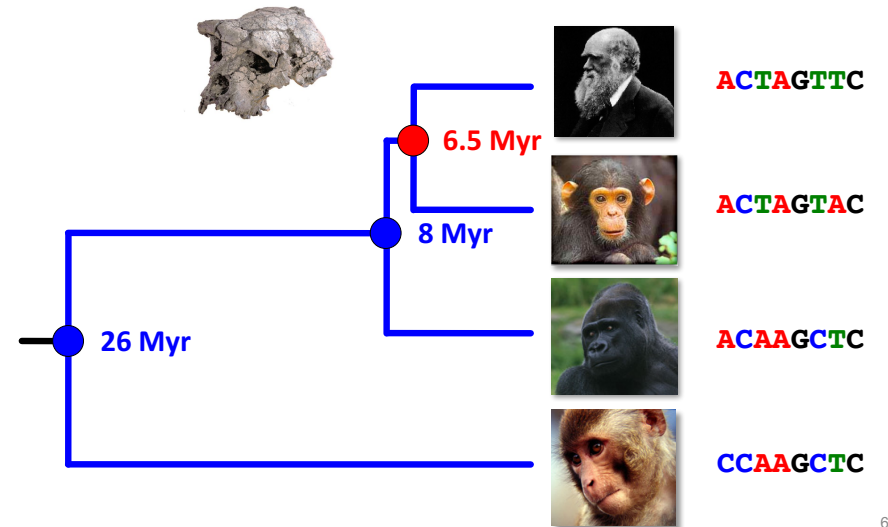
The Molecular Clock

The molecular clock



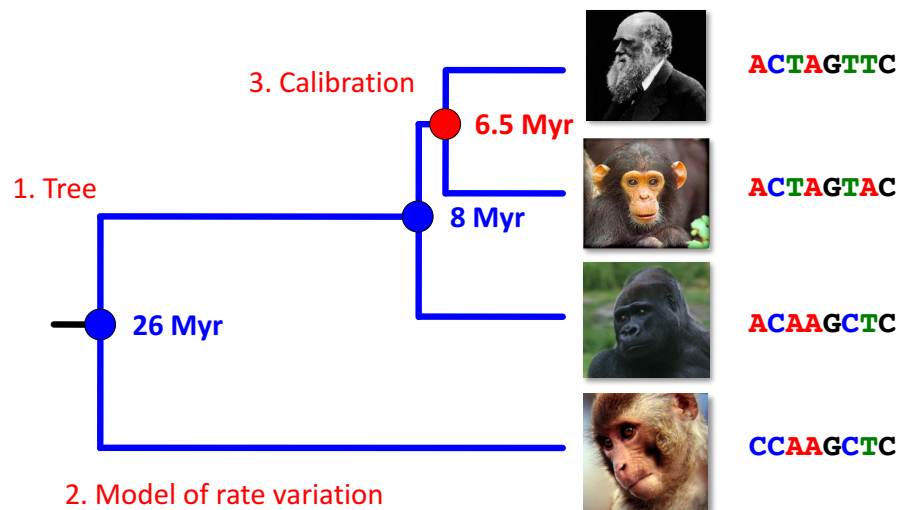
5

The molecular clock



6

Sources of error



7

A brief history

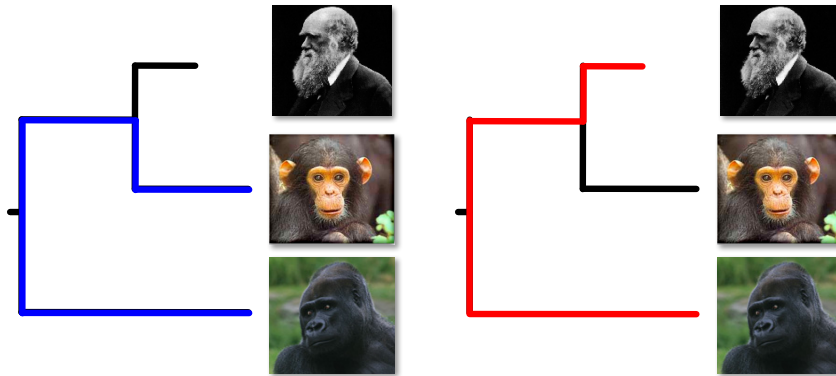
- Emile Zuckerkandl and Linus Pauling
- 1962** Assumed constant rate among species to estimate timing of globin gene duplications
- 1965** Introduced the term 'molecular evolutionary clock'



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Testing for clocklike evolution

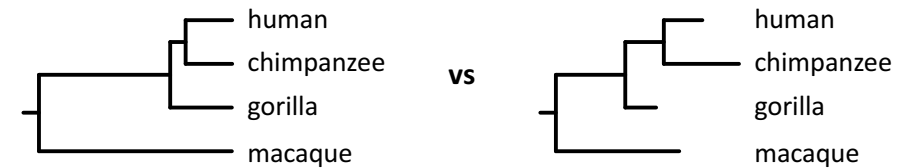
- Relative-rates test (Fitch, 1976)



9

Testing for clocklike evolution

- Whole-tree methods (*e.g.*, likelihood-ratio test)

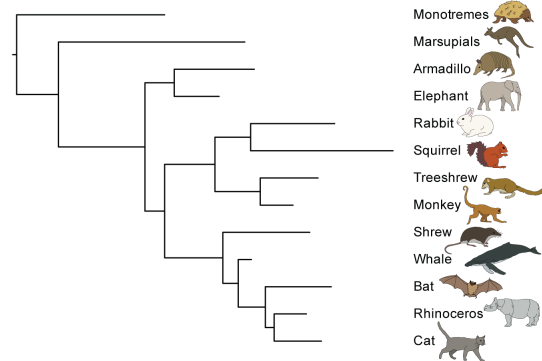


- Limitations
 - Cannot identify instances in which all lineages experience simultaneous rate shift
 - Failure to reject clock can be due to lack of power or lack of information

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Departures from the clock

- Rates vary among lineages because of differences in:
 - Exposure to mutagens
 - Metabolic rate
 - Generation time
 - Population size
 - Strength and direction of selection



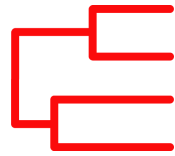
The assumption of rate constancy can be relaxed

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Molecular-Clock Models

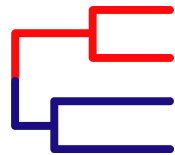
Molecular-clock models

Strict or 'global' molecular clock



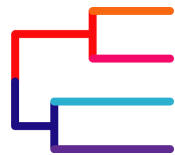
$$k = 1$$

Multi-rate clocks



$$1 < k < n$$

Relaxed clocks



$$k = n$$

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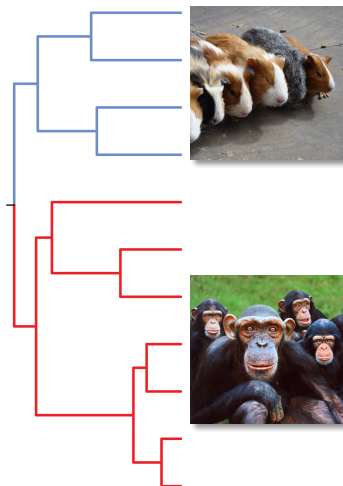
Multi-rate clocks

- Small number of rates
 - More than 1 rate (*i.e.*, not a strict clock)
 - Fewer than number of branches (*i.e.*, not a relaxed clock)
- **Local clock**
 - Same rate shared by neighbouring branches
- **Discrete clock**
 - Small number of branch rates, distributed across tree

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Local clocks

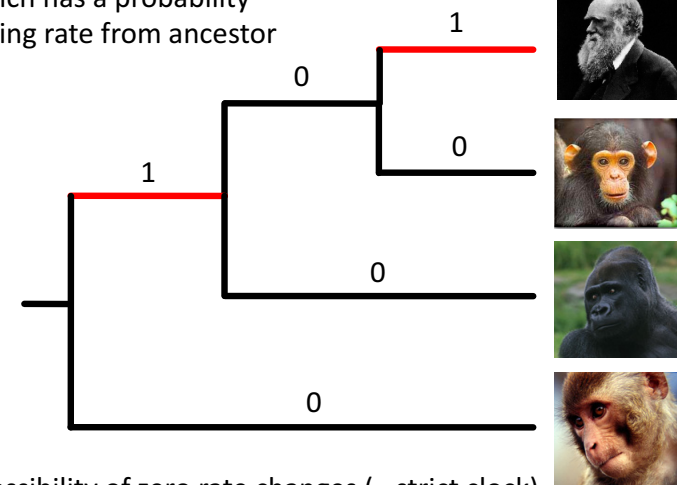
- **User-defined local clock**
 - Fixed tree topology
- **Random local clock**
 - Each branch has a probability of inheriting rate from ancestor
 - Tree estimated



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Random local clock

Each branch has a probability of inheriting rate from ancestor

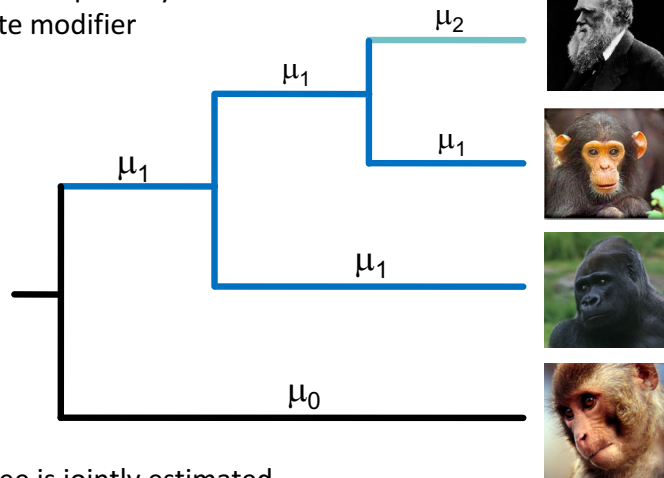


Includes possibility of zero rate changes (= strict clock)

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Random local clock

Otherwise multiplied by a relative rate modifier



Note that tree is jointly estimated

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Relaxed clocks

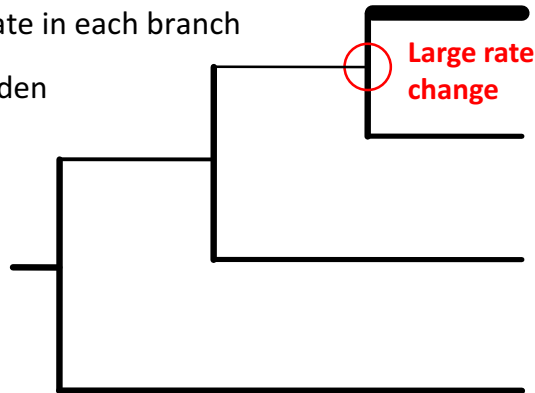
- We know that life-history characteristics:
 - Have effects on rates of molecular evolution
 - Are usually heritable to some degree
- Treat molecular rate as a heritable trait
- Relaxed clocks generally assume that closely related species share similar rates



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Likelihood-based relaxed clocks

- Allow a different rate in each branch
- Penalise large, sudden changes in rates



$$\text{Penalised likelihood} = \ln L - \lambda \Phi(r)$$

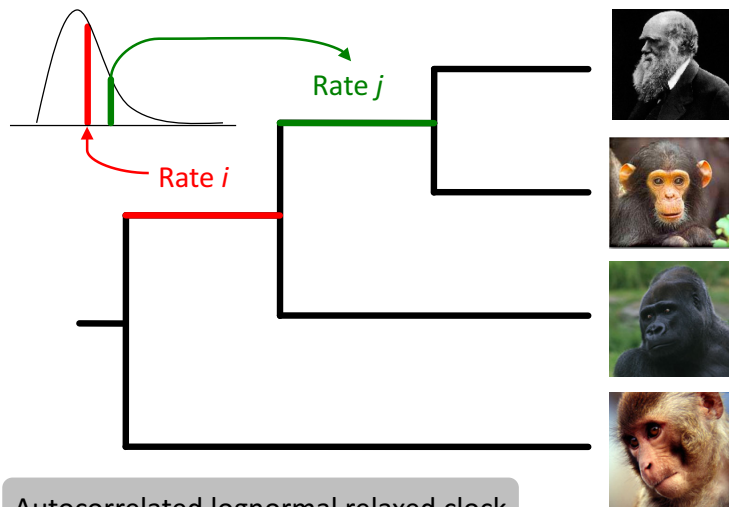
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Bayesian relaxed clocks

- Allow a different rate in each branch
- Statistical models of rates among branches
- Rates can be autocorrelated or uncorrelated
 - **Autocorrelated**
rates in neighbouring branches are related
 - **Uncorrelated**
rates identically and independently distributed among branches

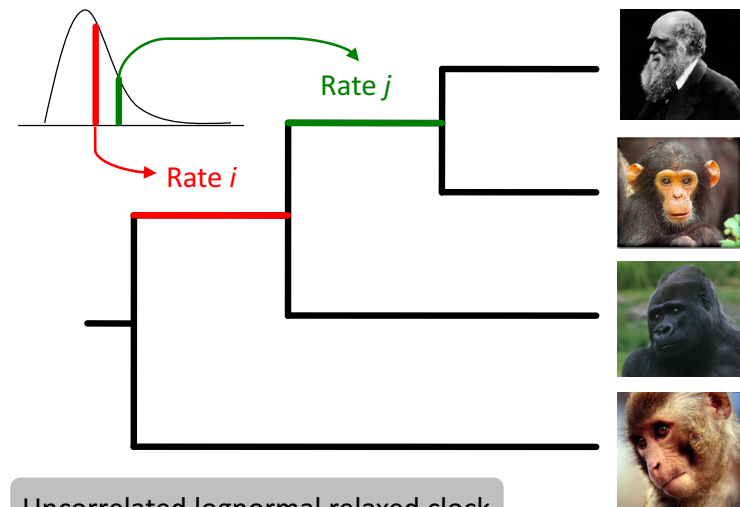
20

Bayesian relaxed clocks



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Bayesian relaxed clocks



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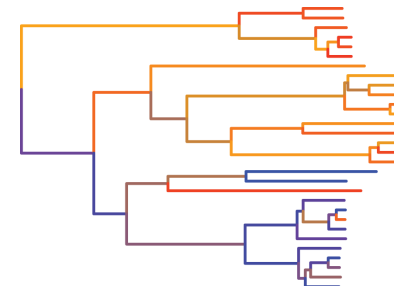
Bayesian relaxed clocks

- In the uncorrelated lognormal relaxed clock, two statistics can be obtained:
 - Coefficient of variation of rates**
Measures the rate variation among branches
A value of 0 indicates clocklike evolution
 - Covariance of rates**
Measures autocorrelation of rates between adjacent branches

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Rate autocorrelation

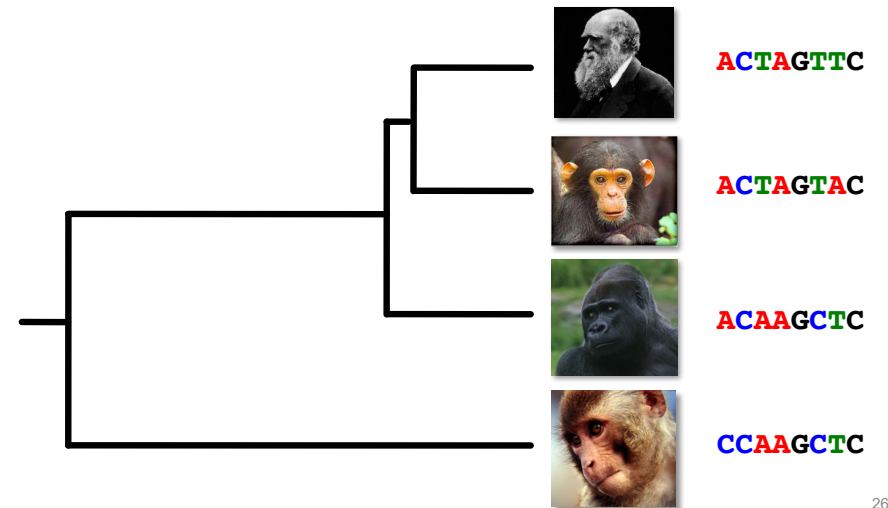
- Little evidence of rate autocorrelation in real data
- Uncorrelated relaxed clock probably appropriate in most cases
- Compare estimates from auto- and uncorrelated relaxed clocks



Ho, Duchêne, & Duchêne (2015) *Mol Ecol Resour* 24

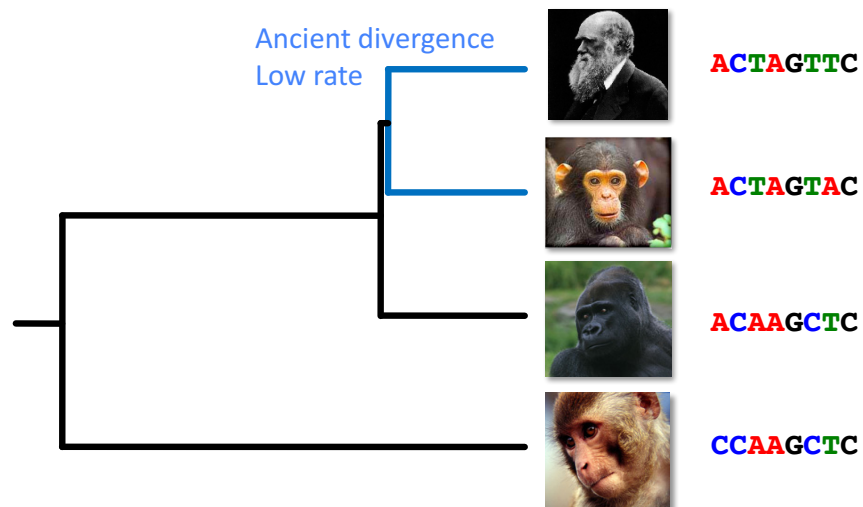
Calibrating the Molecular Clock

Calibrating the molecular clock



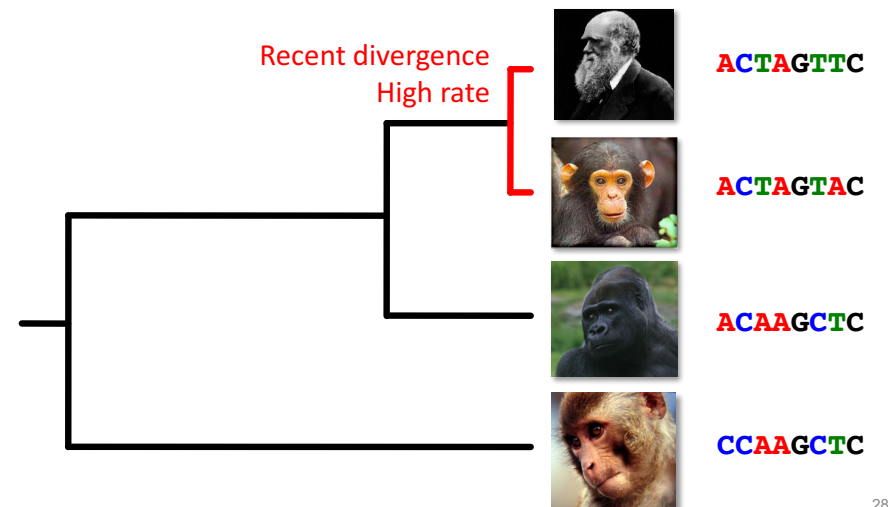
26

Calibrating the molecular clock



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Calibrating the molecular clock



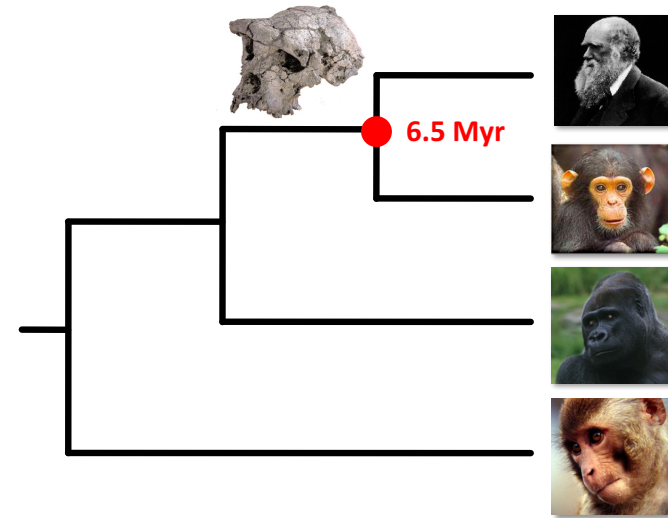
28

Calibrating the molecular clock

- Rates and times are **non-identifiable**
- Likelihood only depends on their product
 - Branch lengths in substitutions per site
- To separate rate and time, we need (prior) information about one or the other

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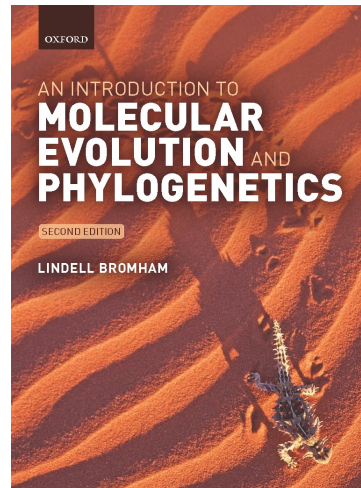
Calibration: Fossil record



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Useful references

- **A practical guide to molecular dating**
Sauquet (2013) *Comptes Rendus Palevol*, 12: 355–367.
- **Bayesian molecular clock dating of species divergences in the genomics era**
dos Reis, Donoghue, & Yang (2016) *Nature Reviews Genetics*, 17: 71–80.
- **Molecular-clock methods for estimating evolutionary rates and timescales**
Ho & Duchêne (2014) *Molecular Ecology*, 23: 5947–5965.



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