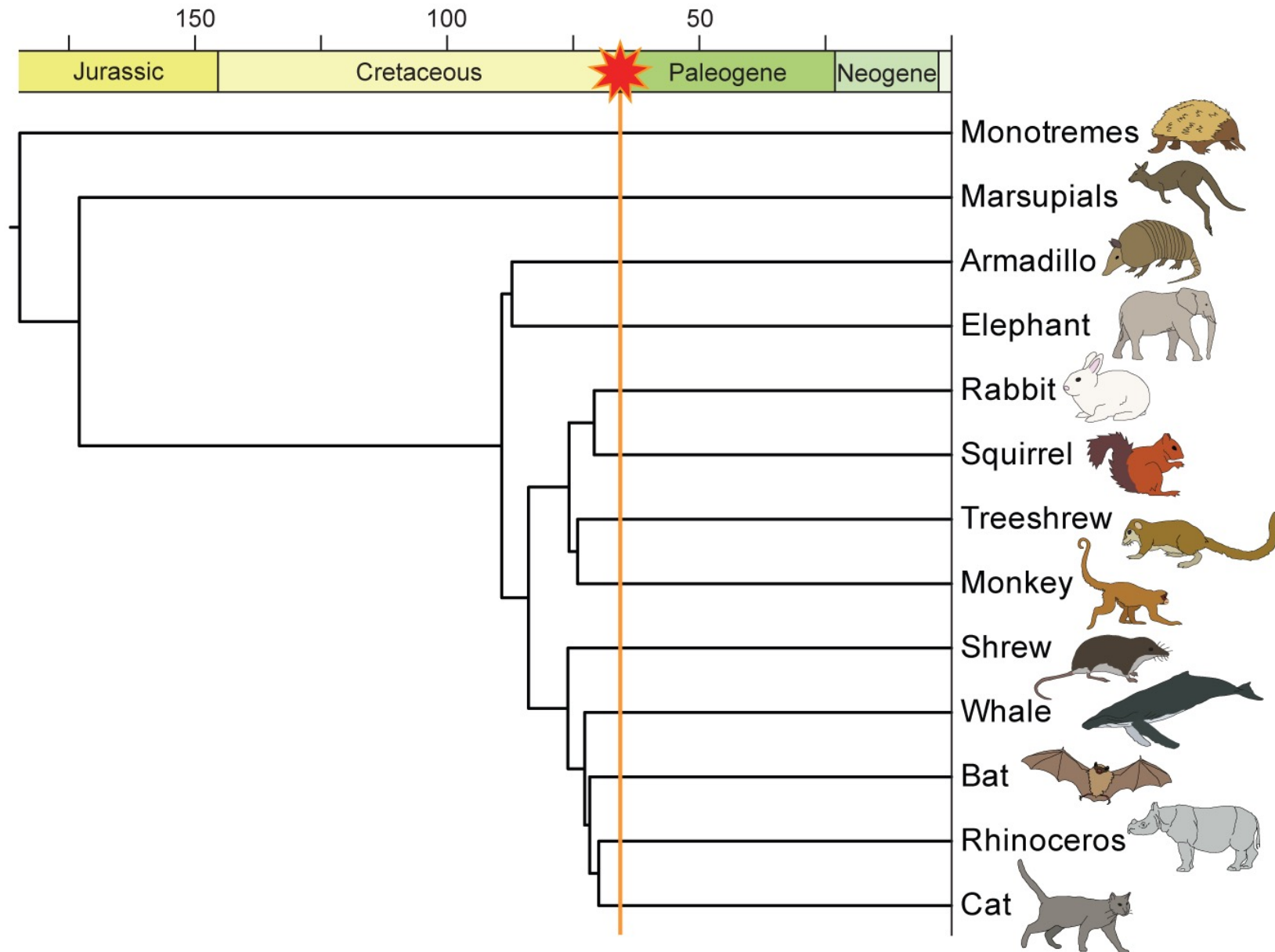

Lecture 2.3

Molecular Dating

Evolutionary timescales

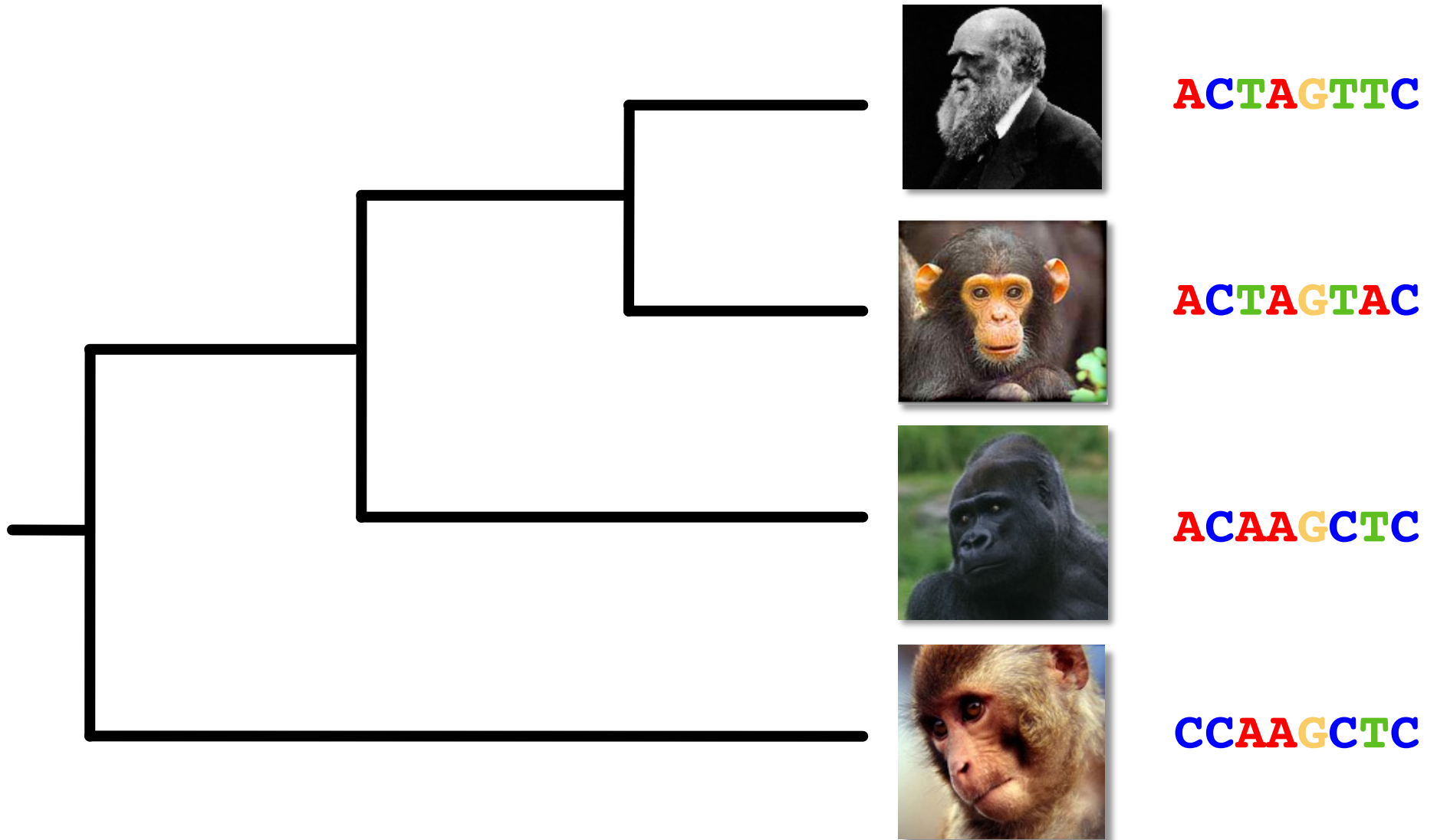


Dated phylogenetic trees

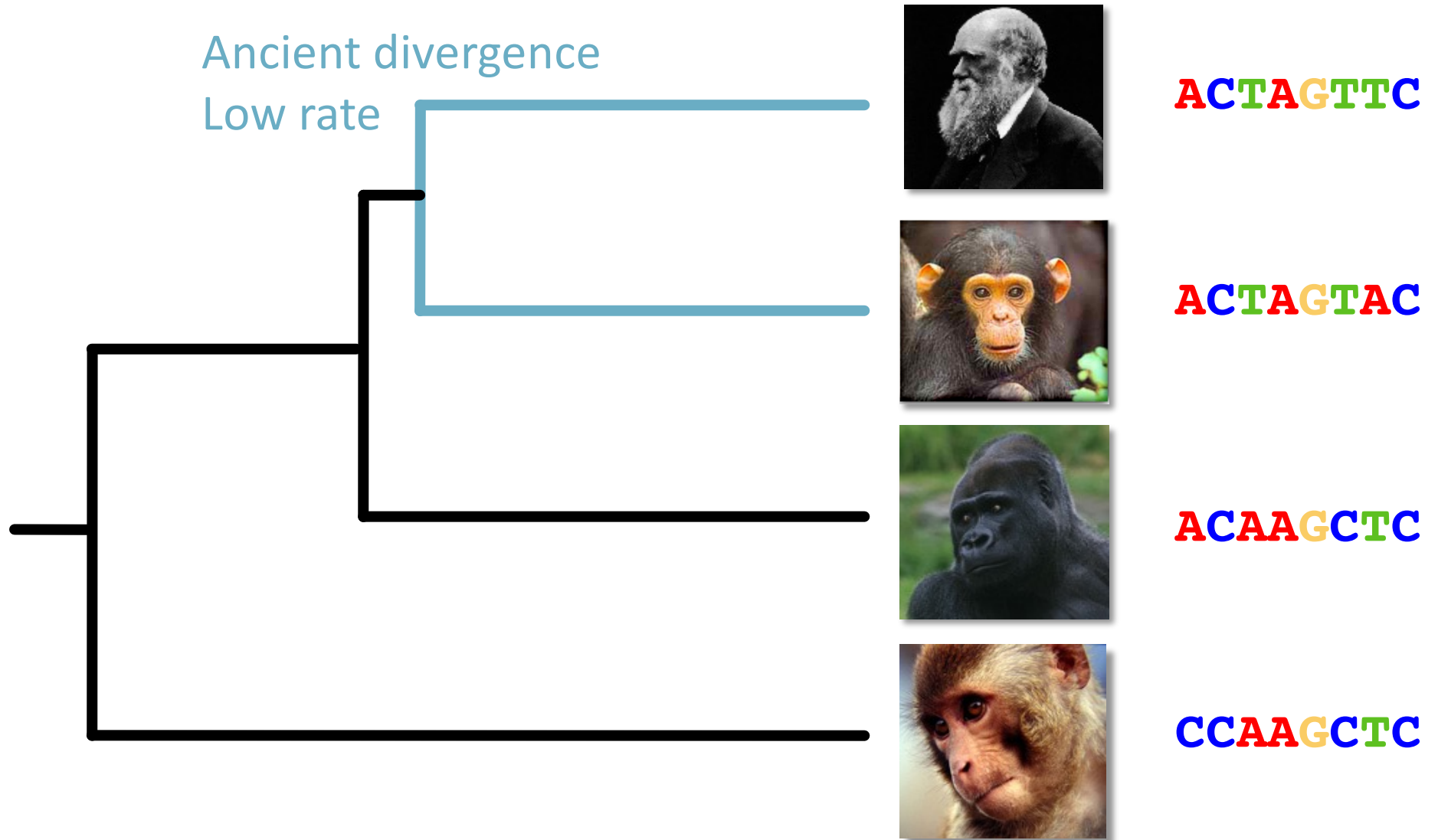
- Species delimitation
- Diversification rates
- Trait evolution
- Biogeography
- Epidemiology
- Demographic history

The Molecular Clock

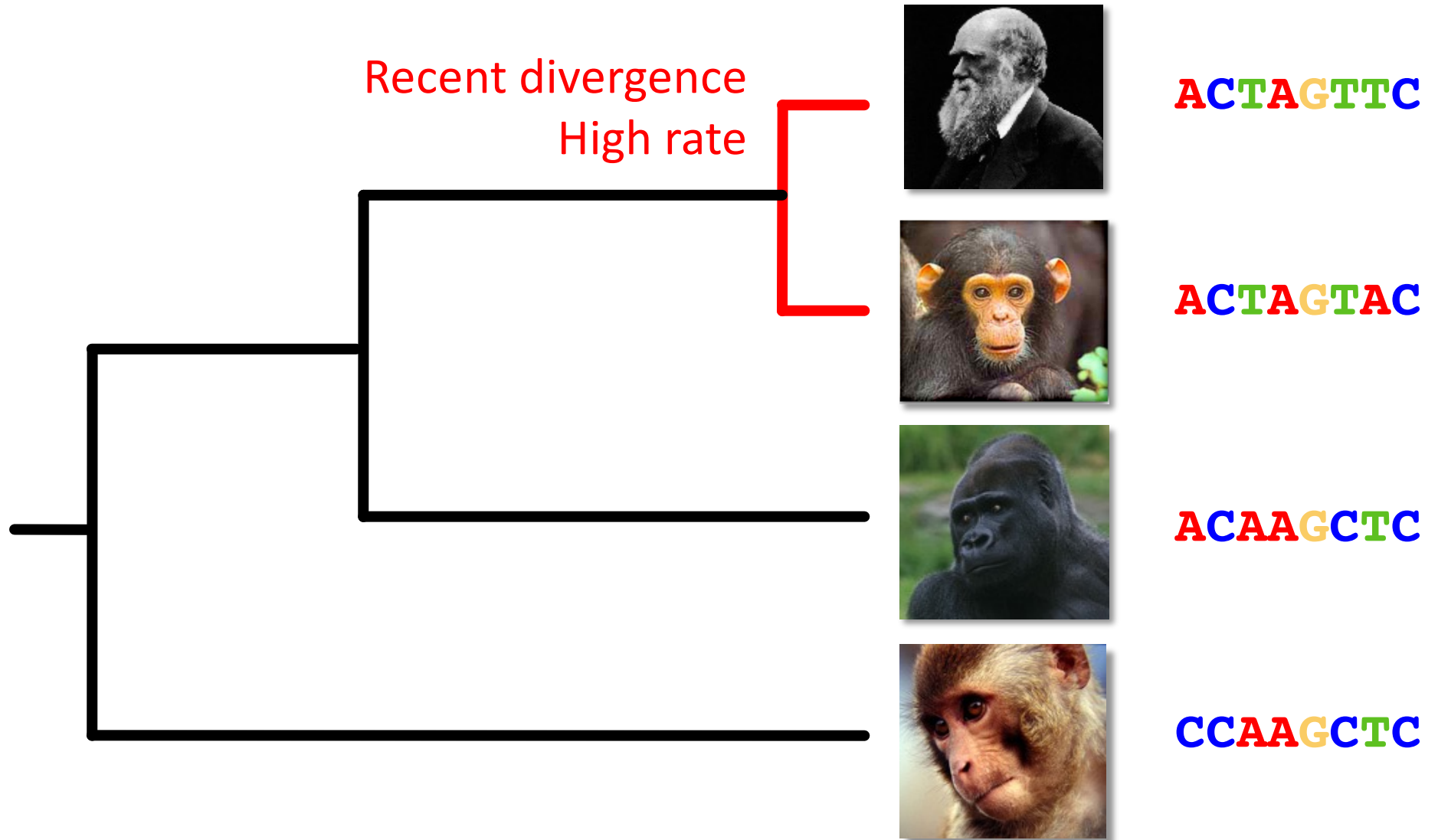
Rates and times



Rates and times



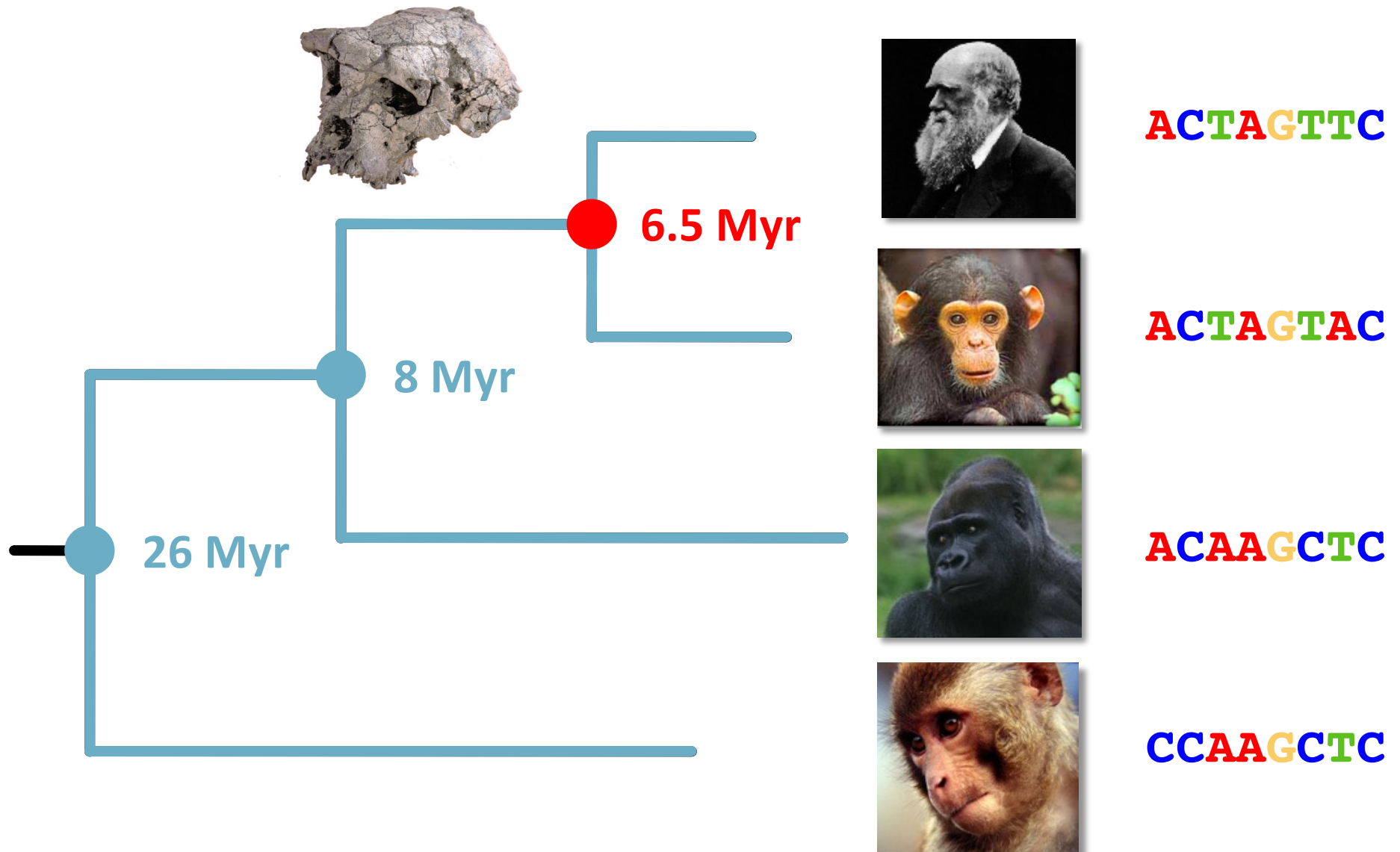
Rates and times



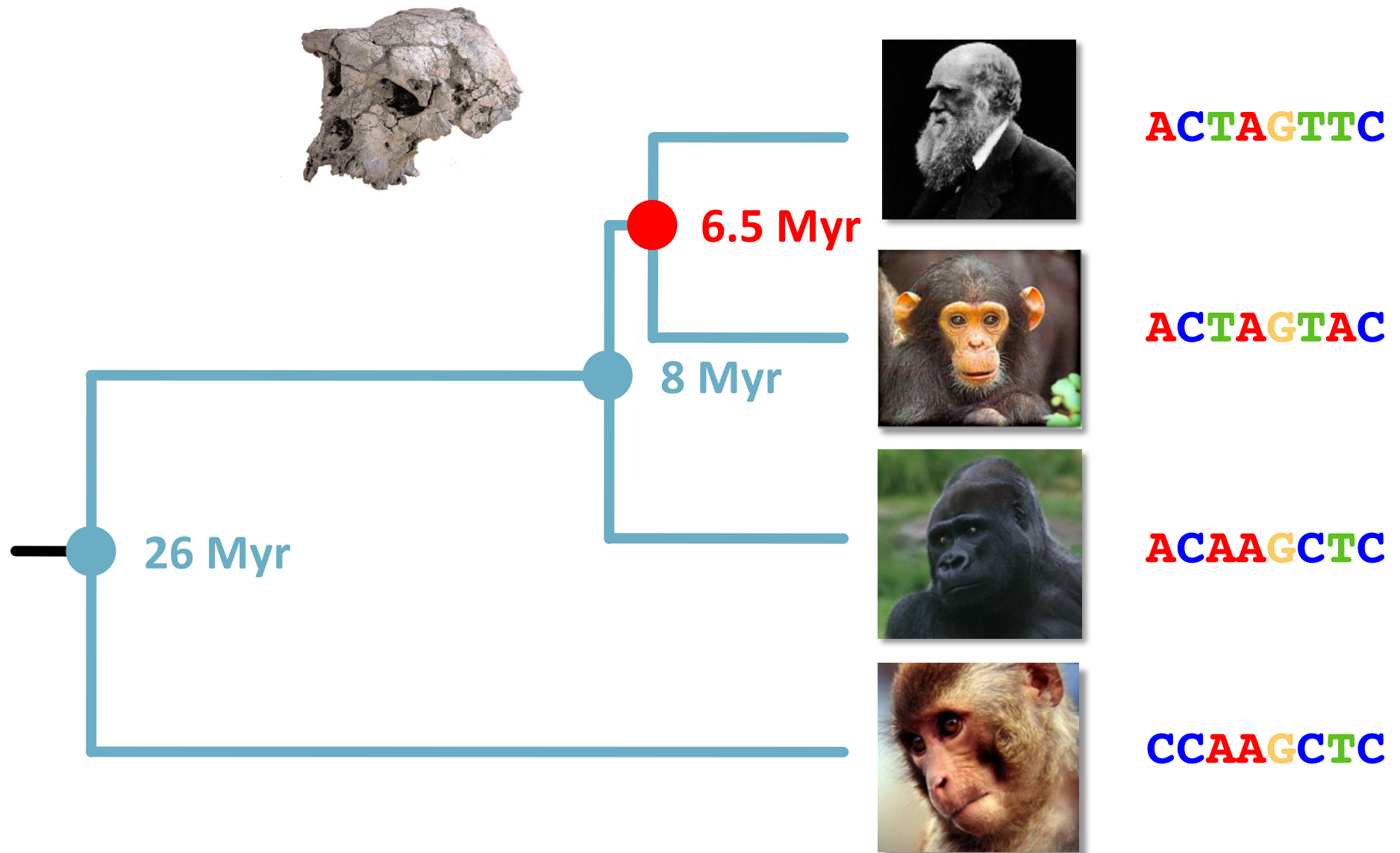
Rates and times

- 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

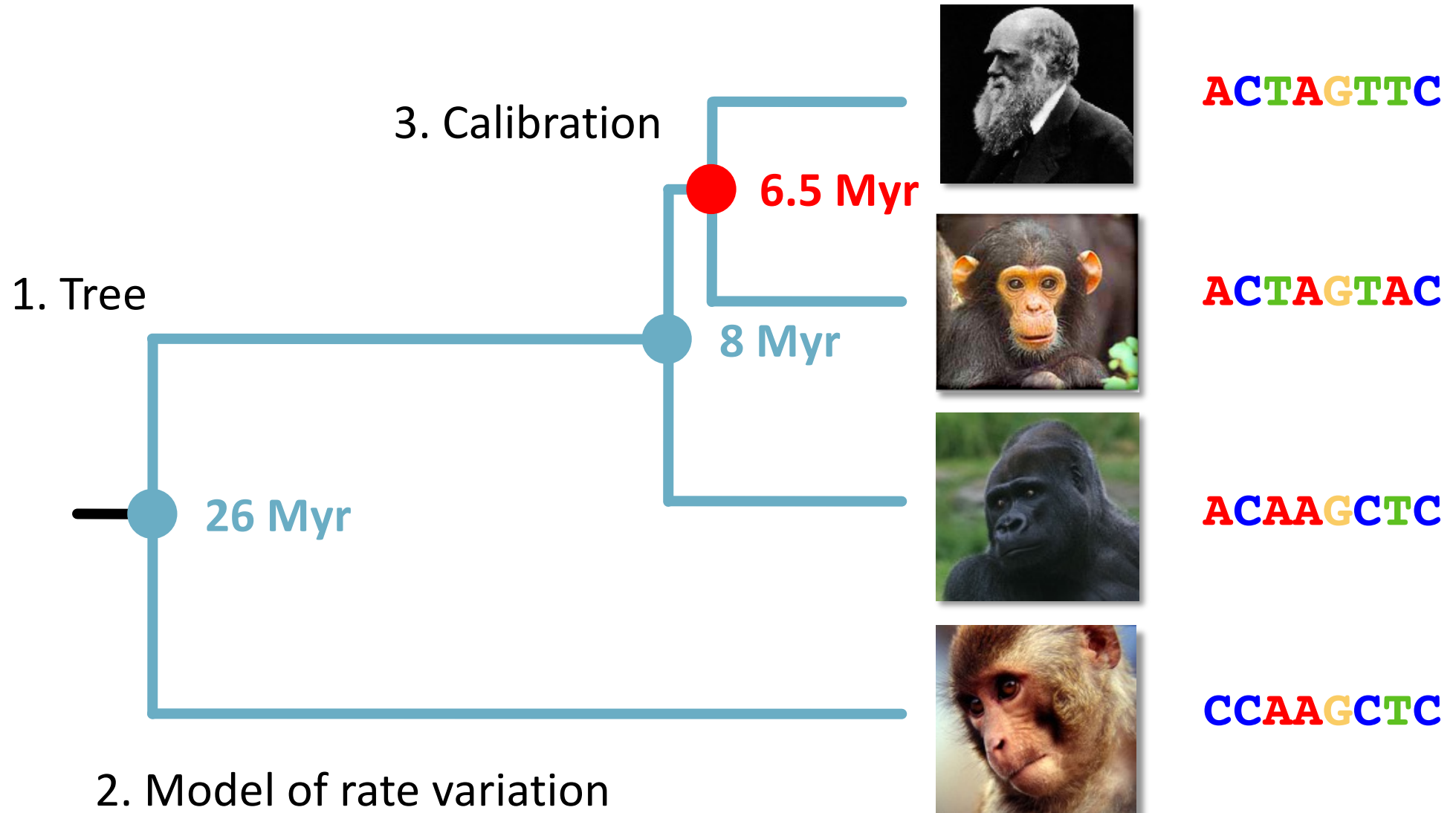
The molecular clock



The molecular clock



Sources of error



A brief history

- Emile Zuckerkandl and Linus Pauling

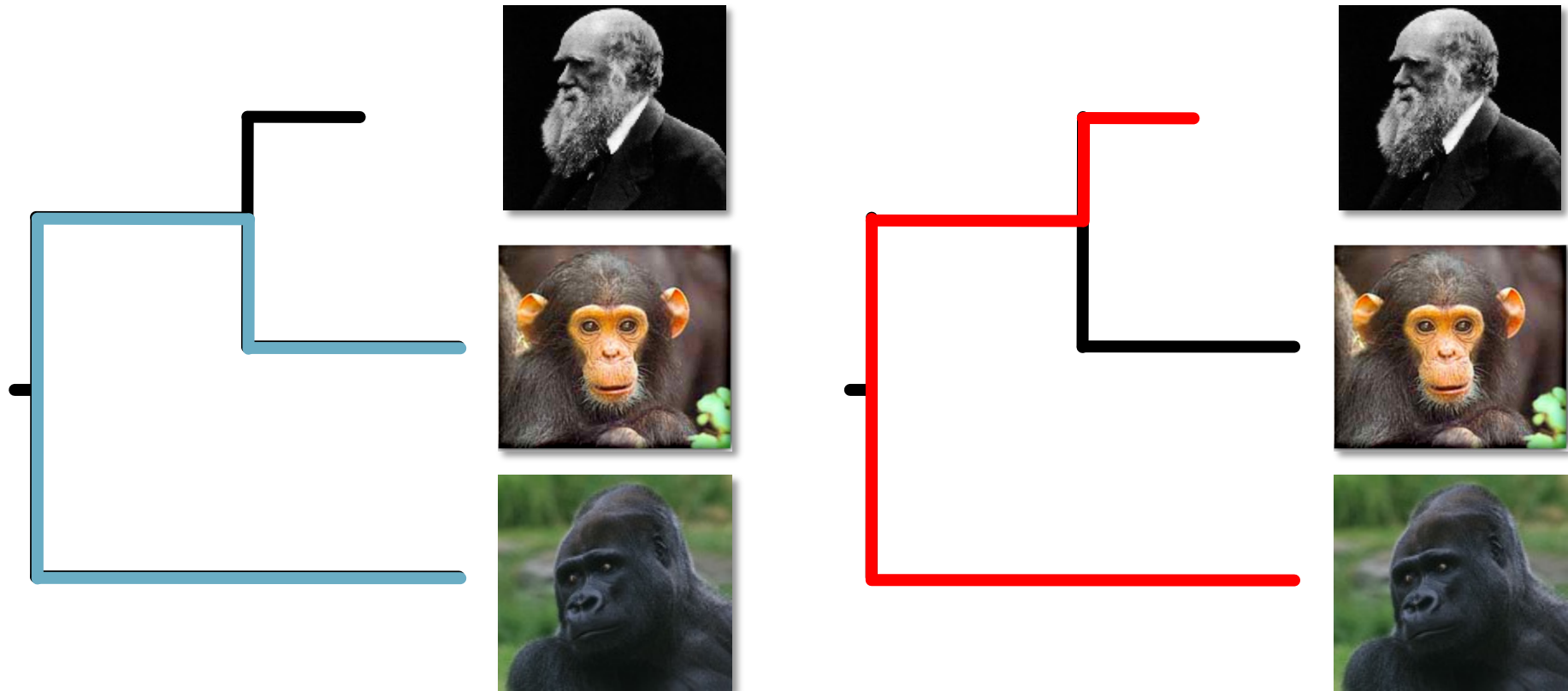
1962 Assumed constant rate among species to estimate timing of globin gene duplications

1965 Introduced the term 'molecular evolutionary clock'



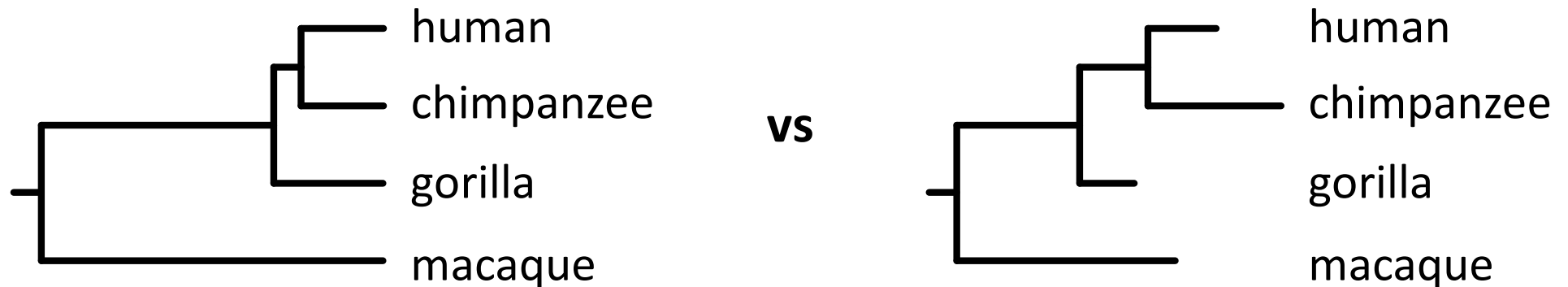
Testing for clocklike evolution

- Relative-rates test (Fitch, 1976)



Testing for clocklike evolution

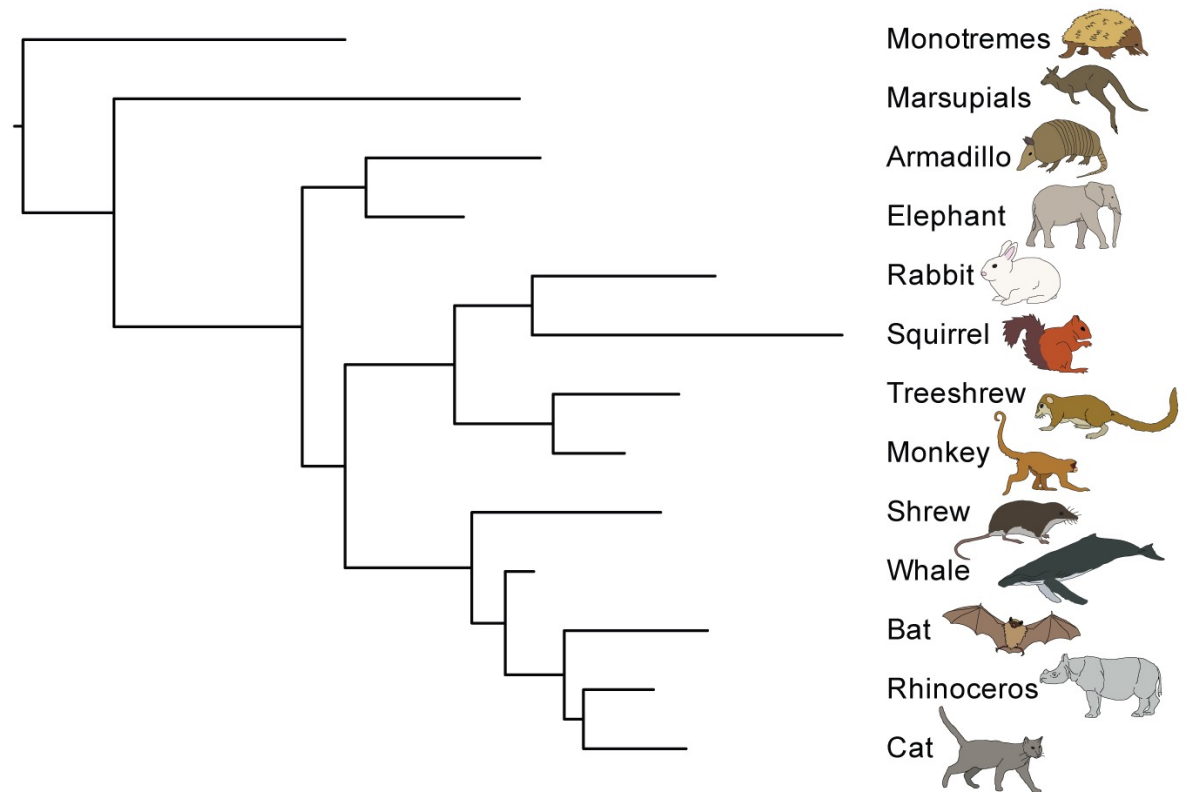
- Whole-tree methods (*e.g.*, likelihood-ratio test)



- 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

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

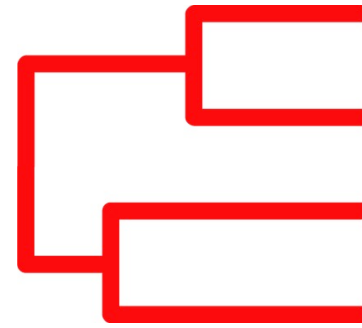


The assumption of rate constancy can be relaxed

Molecular-Clock Models

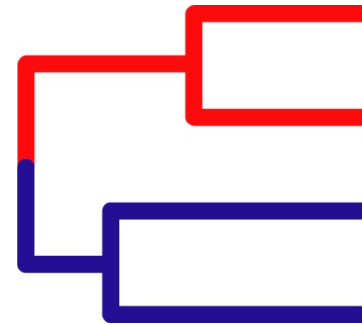
Molecular-clock models

Strict or 'global' molecular clock



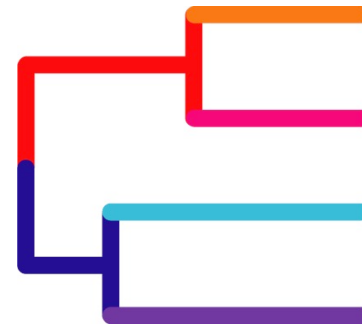
$$k = 1$$

Multi-rate clocks



$$1 < k < n$$

Relaxed clocks



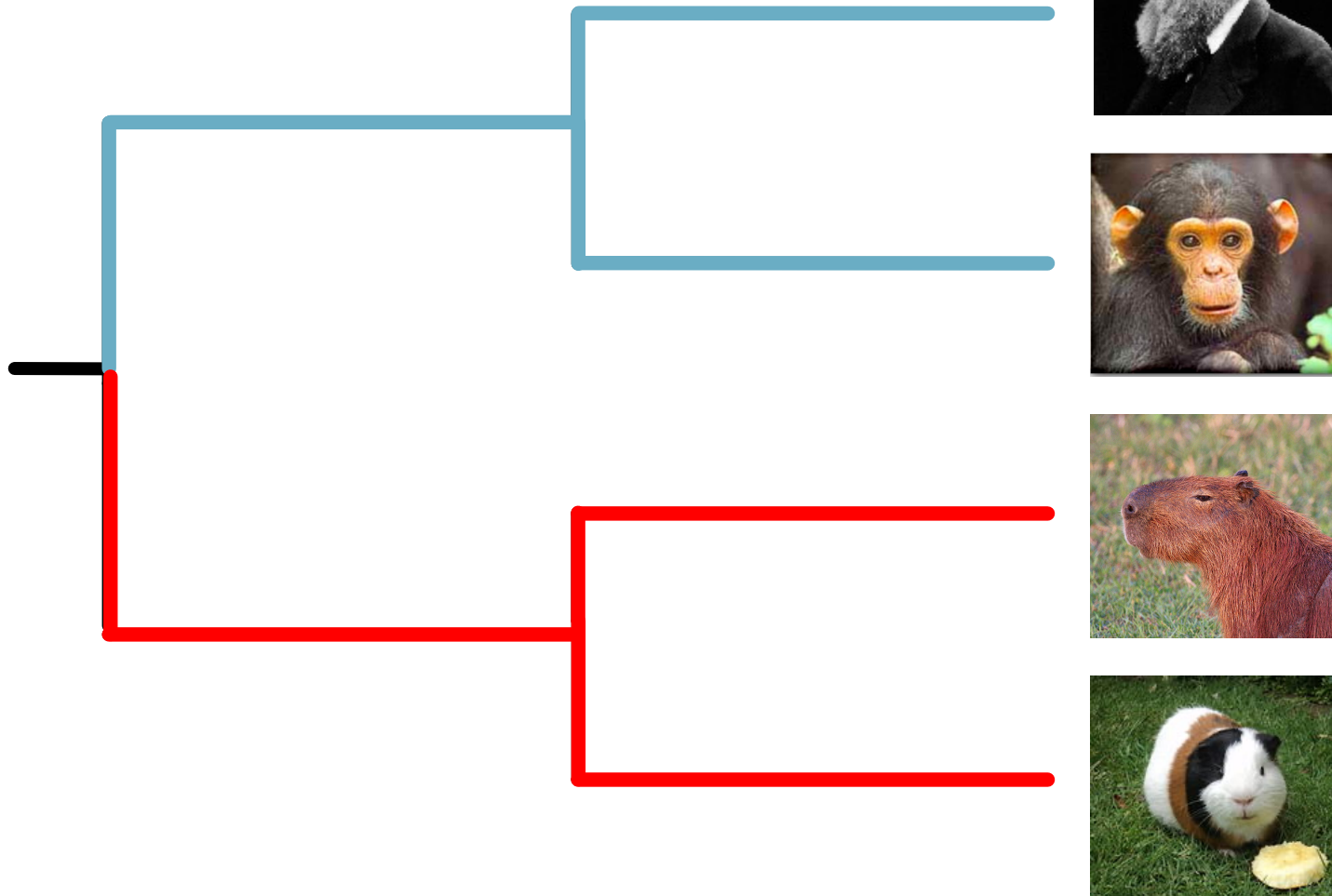
$$k = n$$

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

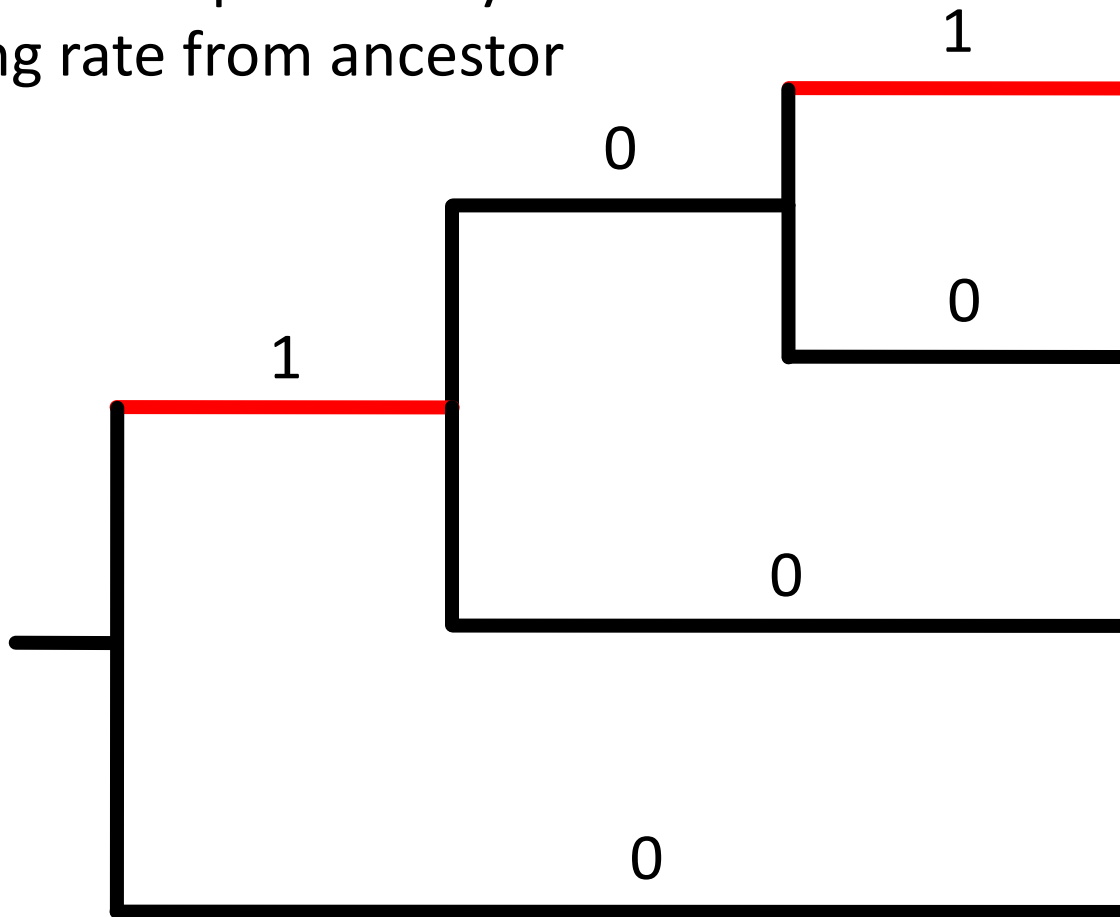
User-defined local clock

Fixed tree topology



Random local clock

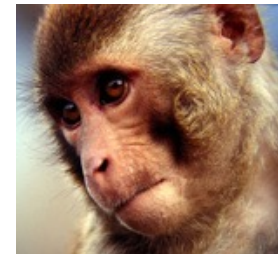
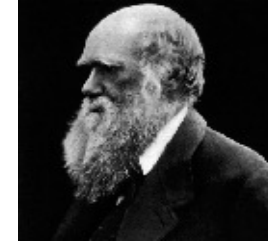
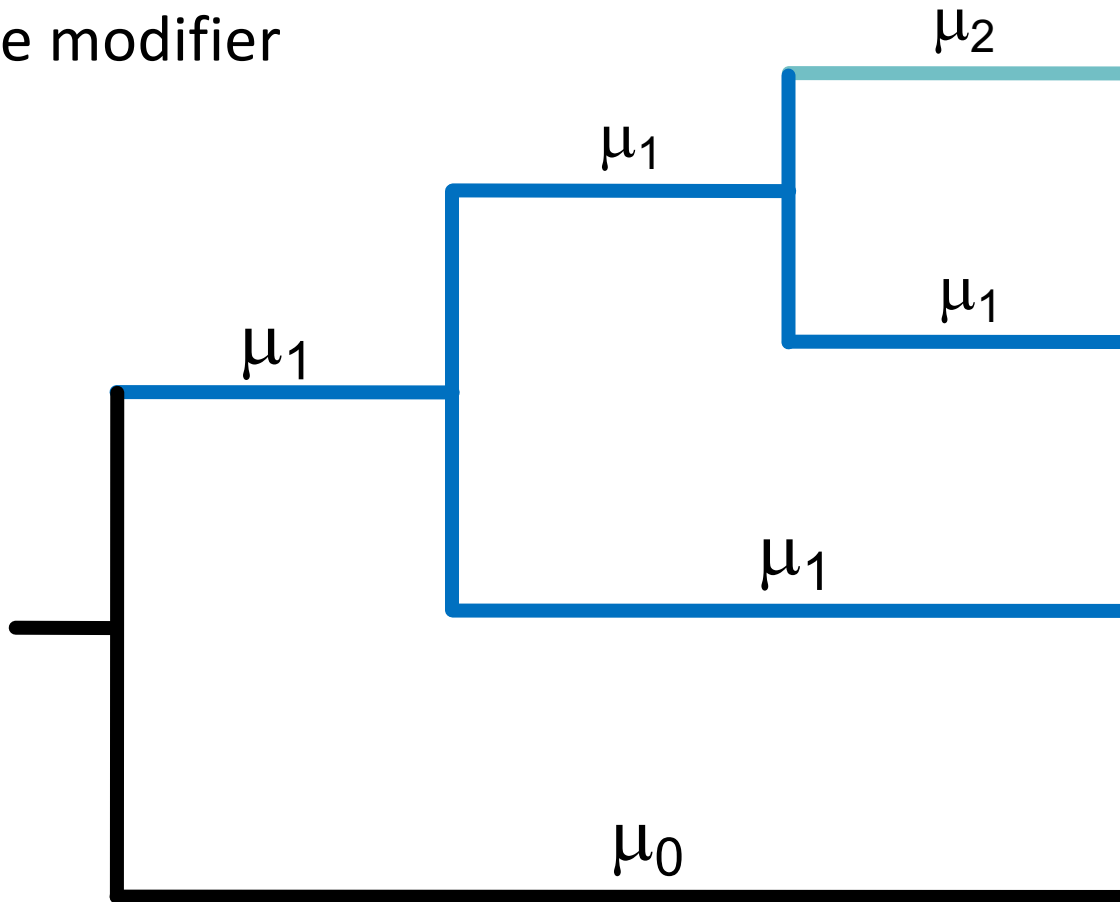
Each branch has a probability of inheriting rate from ancestor



Includes possibility of zero rate changes (= strict clock)

Random local clock

Otherwise multiplied by a
relative rate modifier



Note that tree is jointly estimated

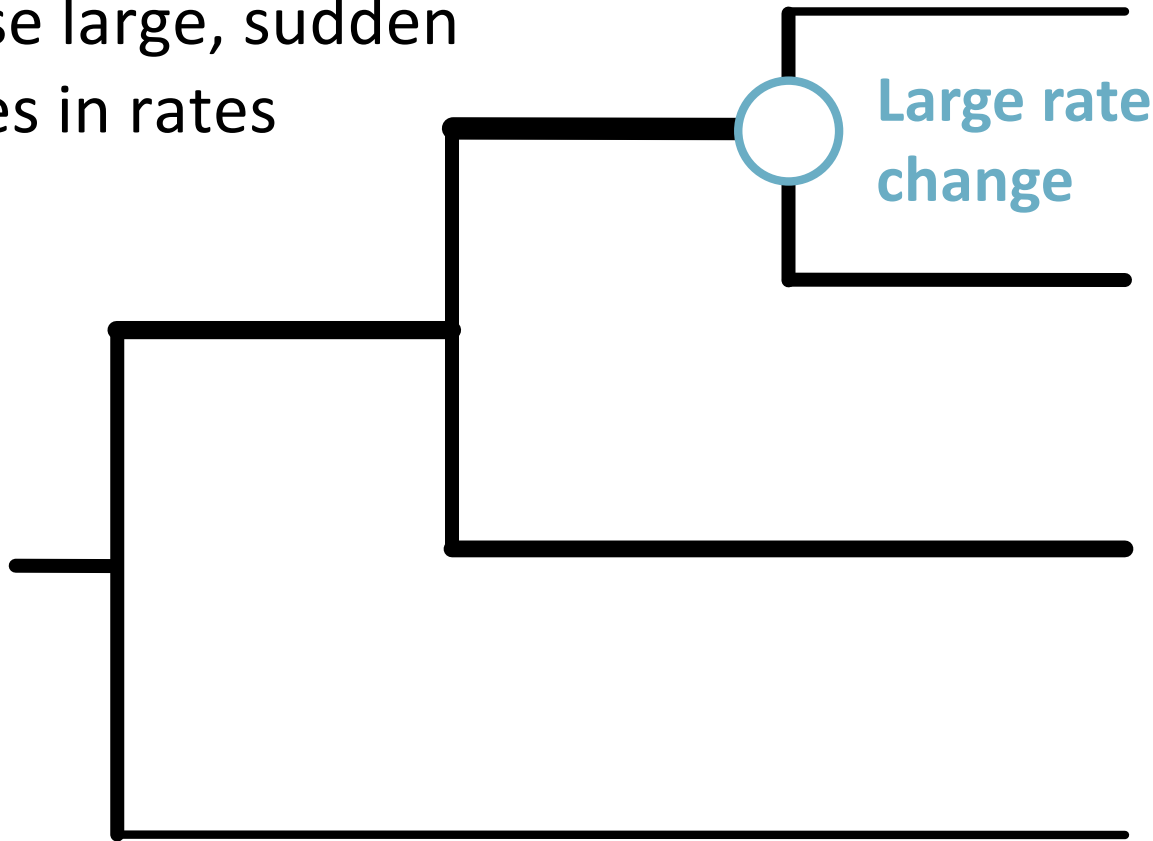
Relaxed clocks

- 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



Likelihood-based relaxed clocks

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

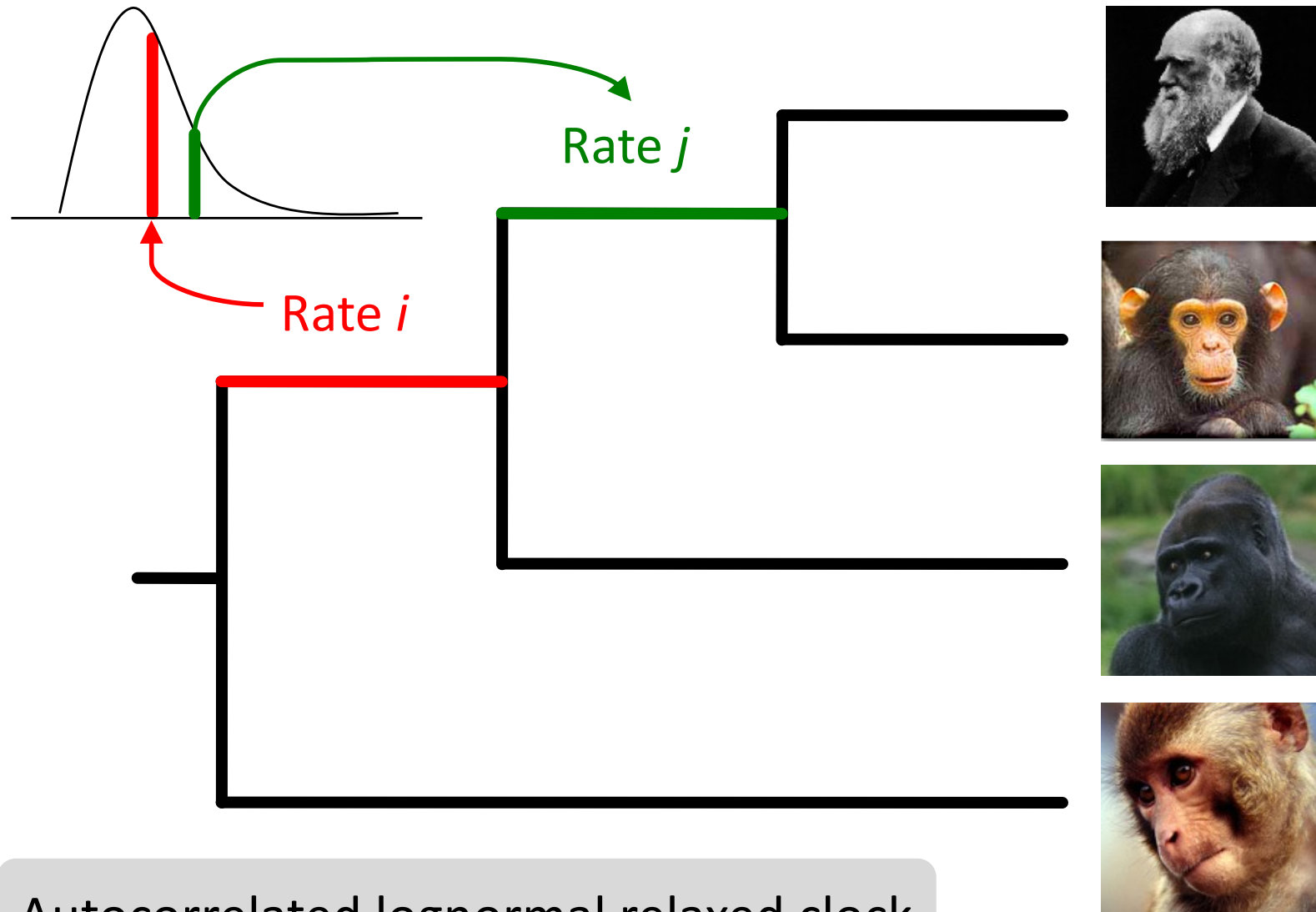


$$\text{Penalised likelihood} = \ln L - \lambda \Phi(r)$$

Bayesian relaxed clocks

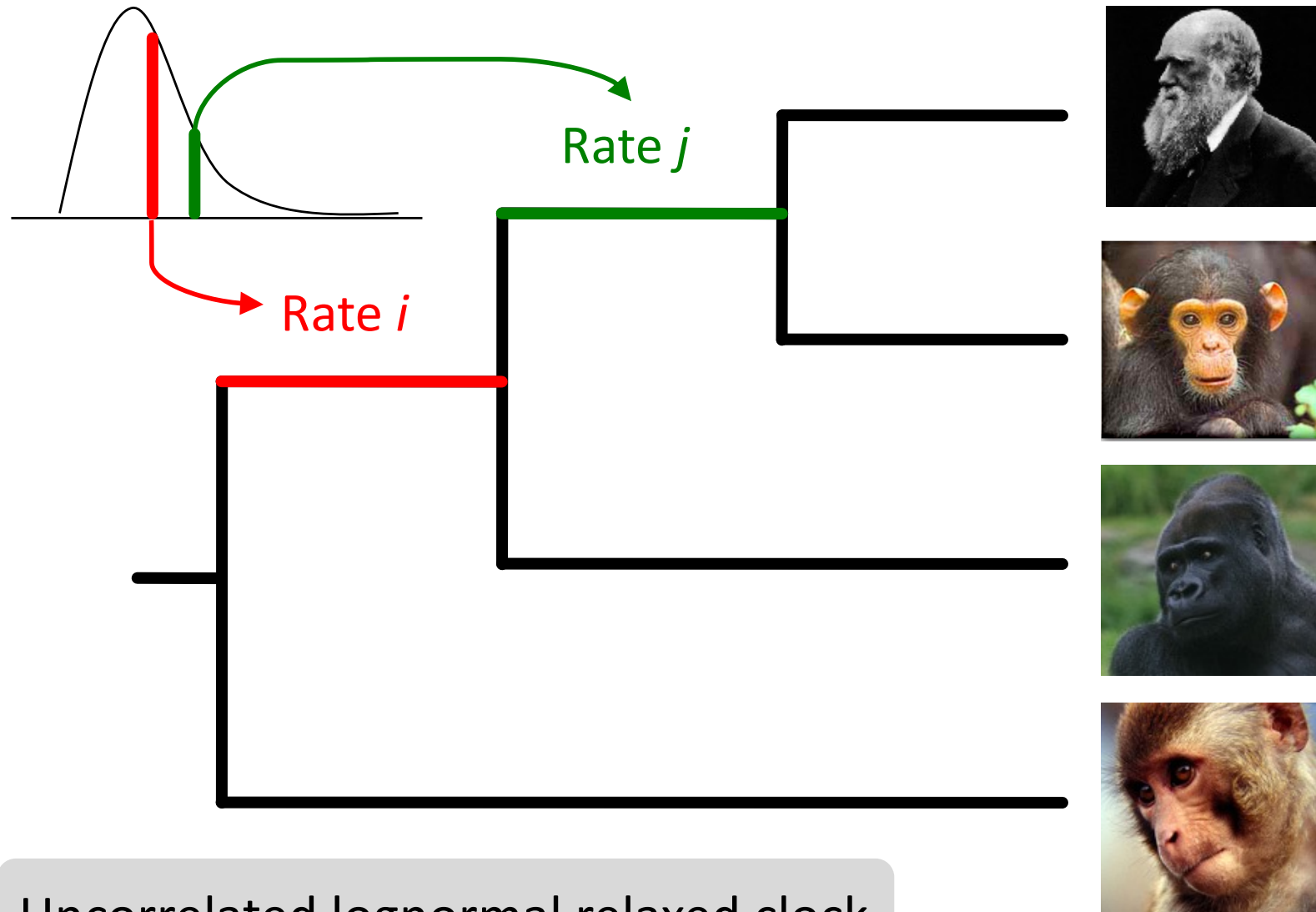
- Allow a different rate in each branch
- Statistical models of rates among branches
- Rates can be autocorrelated or uncorrelated
 - **Autocorrelated**
rates in neighbouring branches are related
 - **Uncorrelated**
rates identically and independently distributed among branches

Bayesian relaxed clocks



Autocorrelated lognormal relaxed clock

Bayesian relaxed clocks



Uncorrelated lognormal relaxed clock

Bayesian relaxed clocks

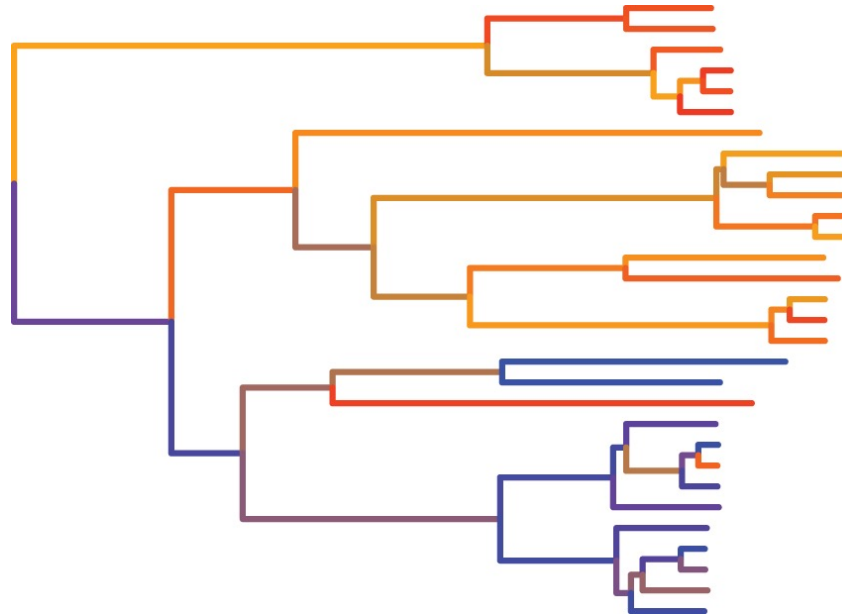
- In the uncorrelated lognormal relaxed clock, two statistics can be obtained:
 1. **Coefficient of variation of rates**
Measures the rate variation among branches
A value of 0 indicates clocklike evolution
 2. **Covariance of rates**
Measures autocorrelation of rates between adjacent branches

Bayesian relaxed clocks

- Autocorrelated rates
 - Autocorrelated lognormal
 - Autocorrelated gamma
 - Autocorrelated exponential
 - Ornstein-Uhlenbeck process
 - Cox-Ingersoll-Ross
- Uncorrelated rates
 - Uncorrelated lognormal
 - Uncorrelated exponential
 - Uncorrelated gamma
 - White noise

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



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.

