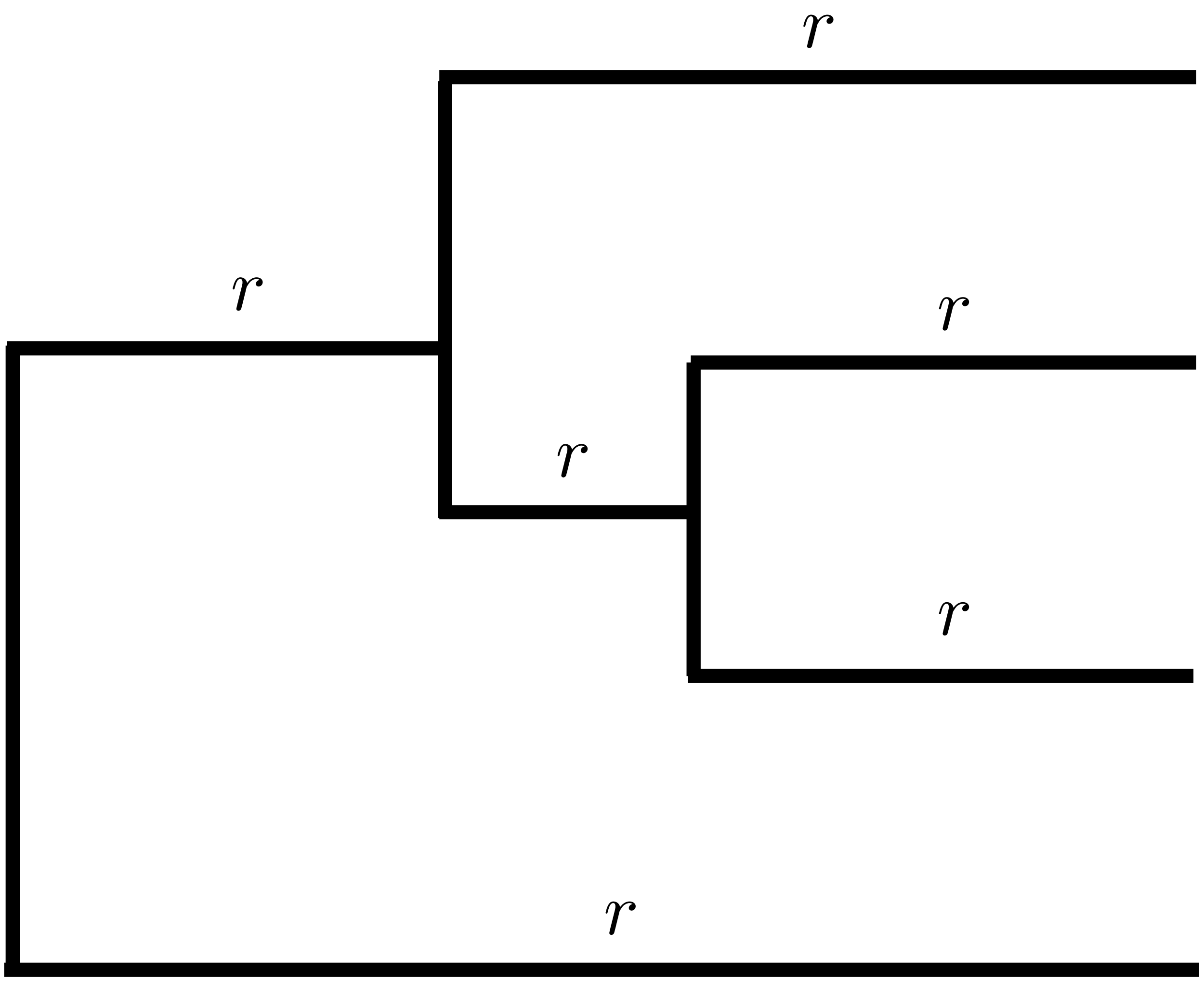
Divergence time estimation

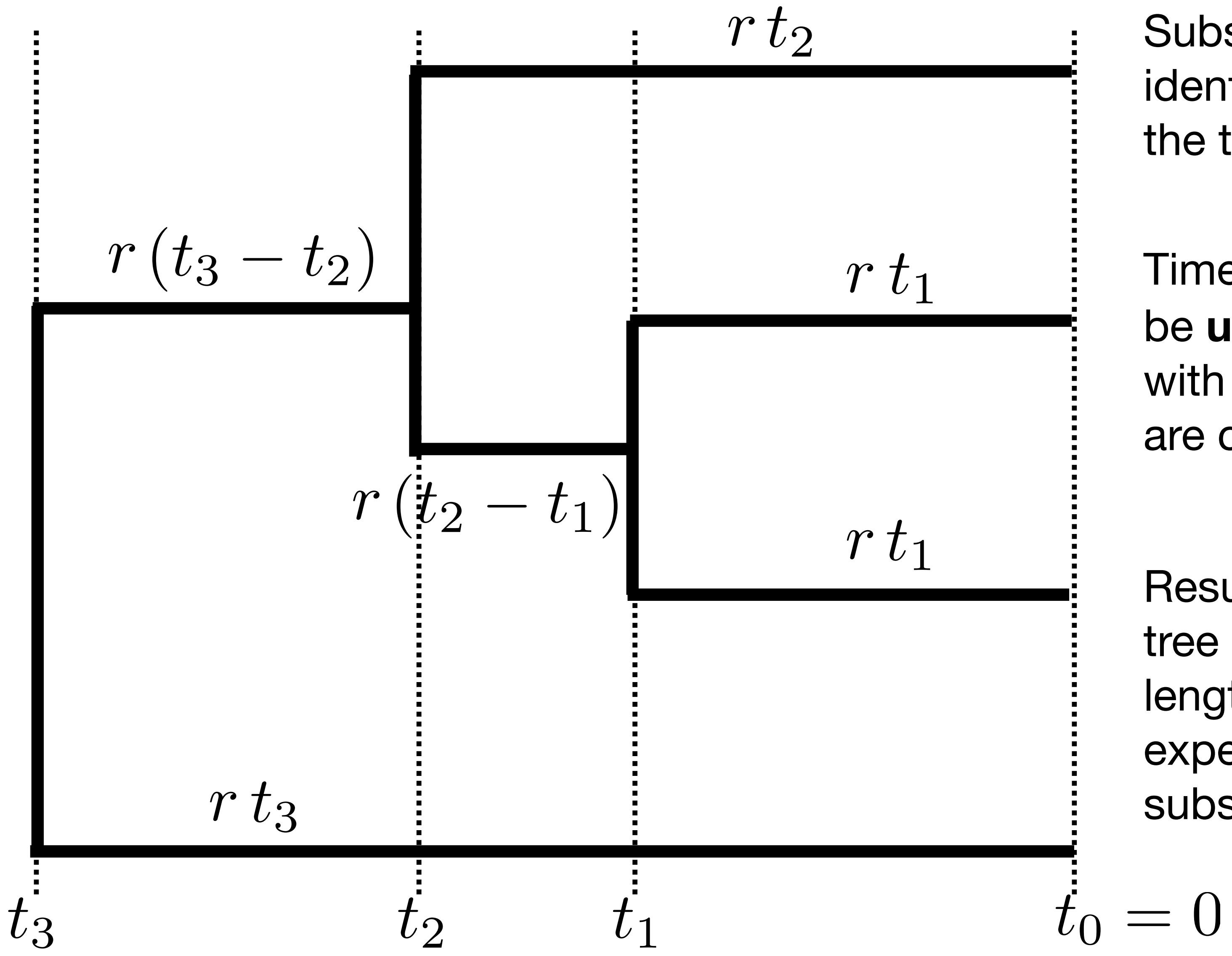
rate × time = expected number of substitutions

Strict Molecular Clock



Substitution rate *r* is identical for every edge in the tree.

Strict Molecular Clock

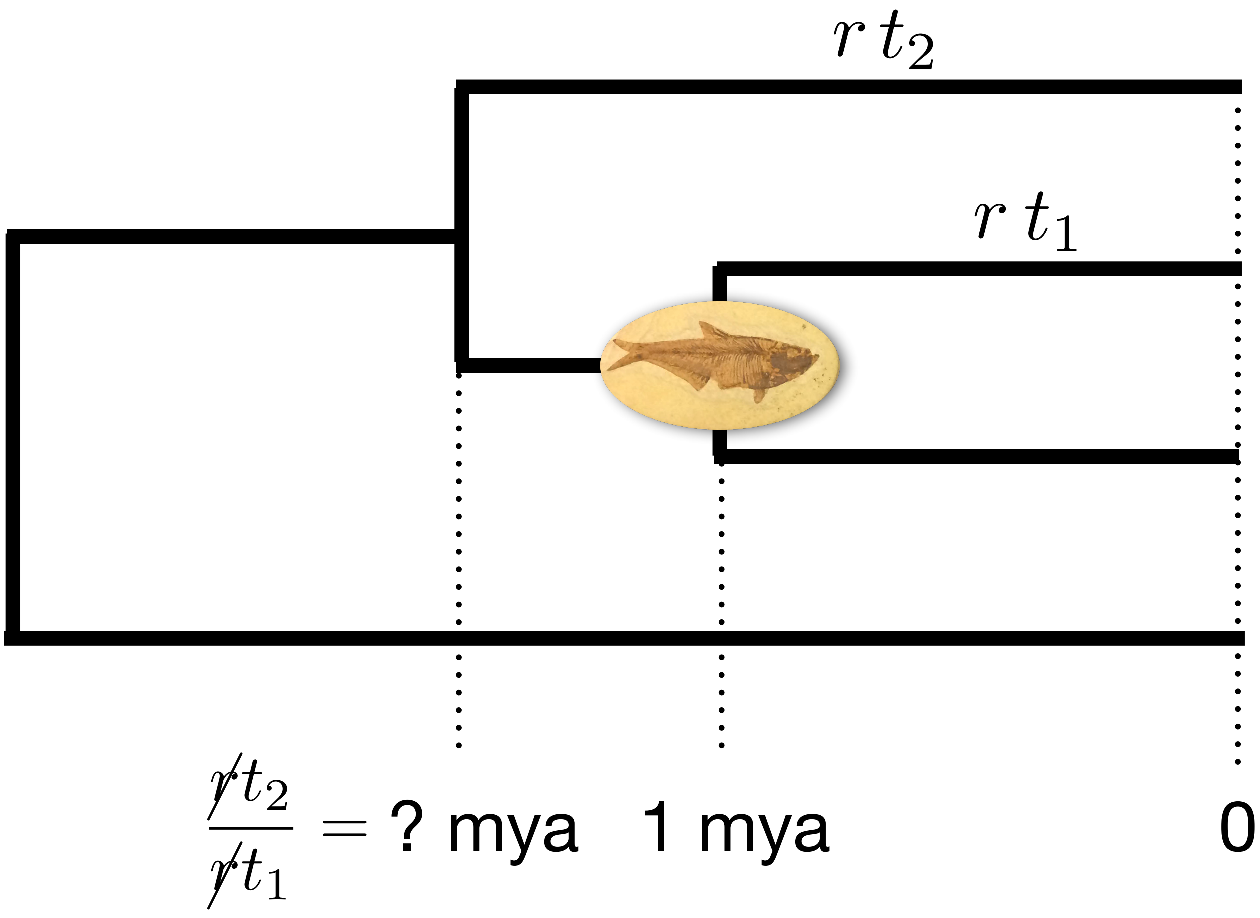


Substitution rate *r* is identical for every edge in the tree.

Times are constrained to be **ultrametric**, consistent with the fact that all tips are contemporary

Result is an ultrametric tree even when edge lengths are measured in expected number of substitutions per site (*rt*)

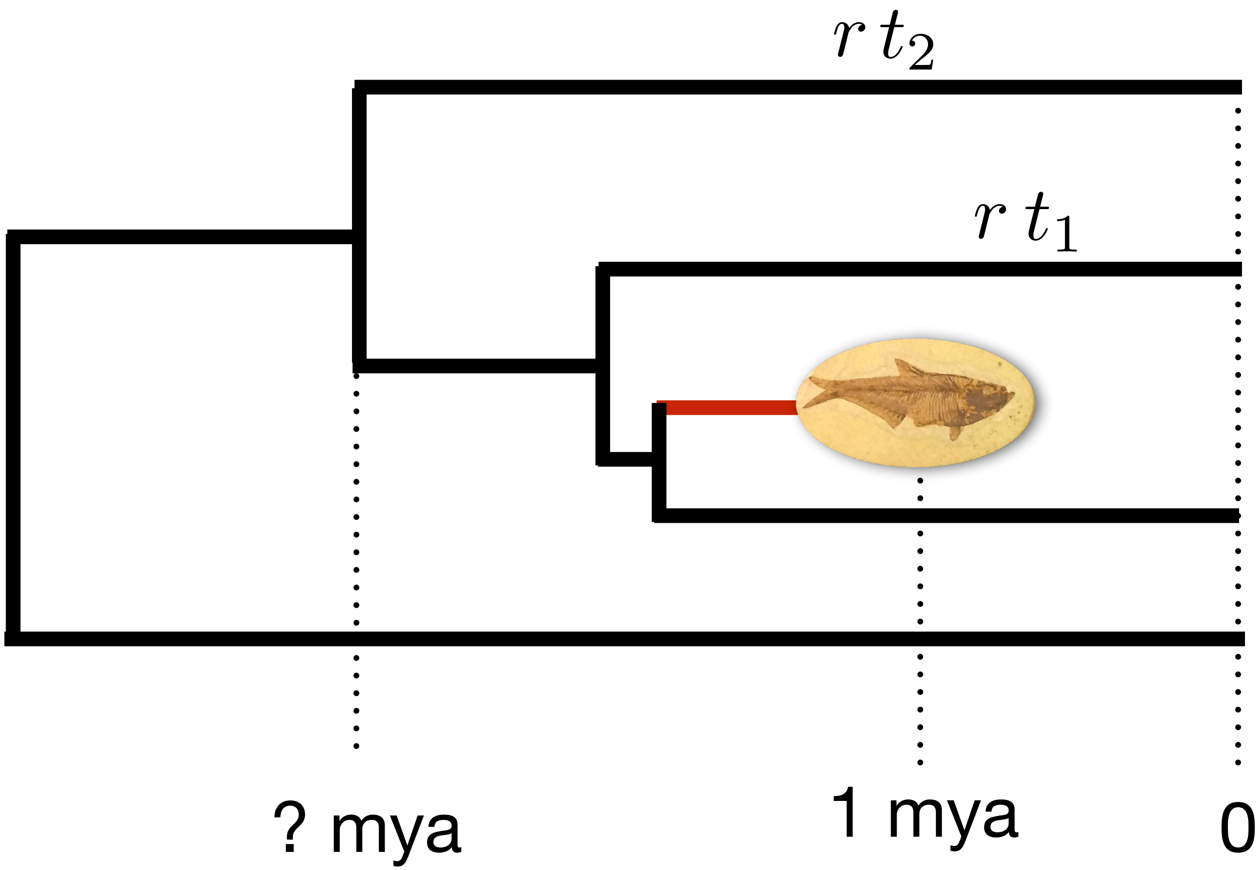
Calibrated Strict Clock



$$\frac{\cancel{r}t_2}{\cancel{r}t_1} = ?\text{ mya}$$

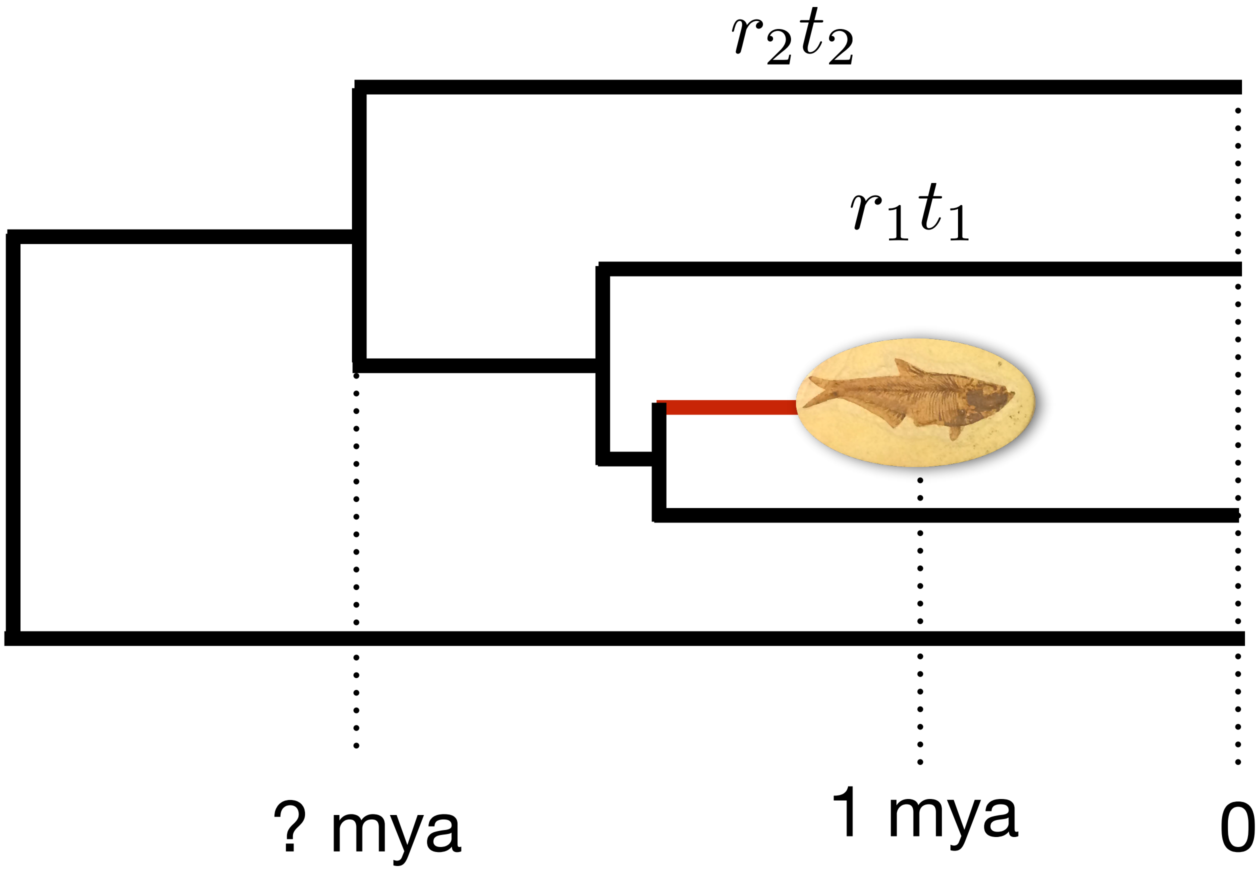
Not the best method, even if rates are constant because…

Calibrated Strict Clock



…fossils seldom represent a direct ancestor, so there is a branch of unknown length throwing a wrench into the works.

Strict clock questionable

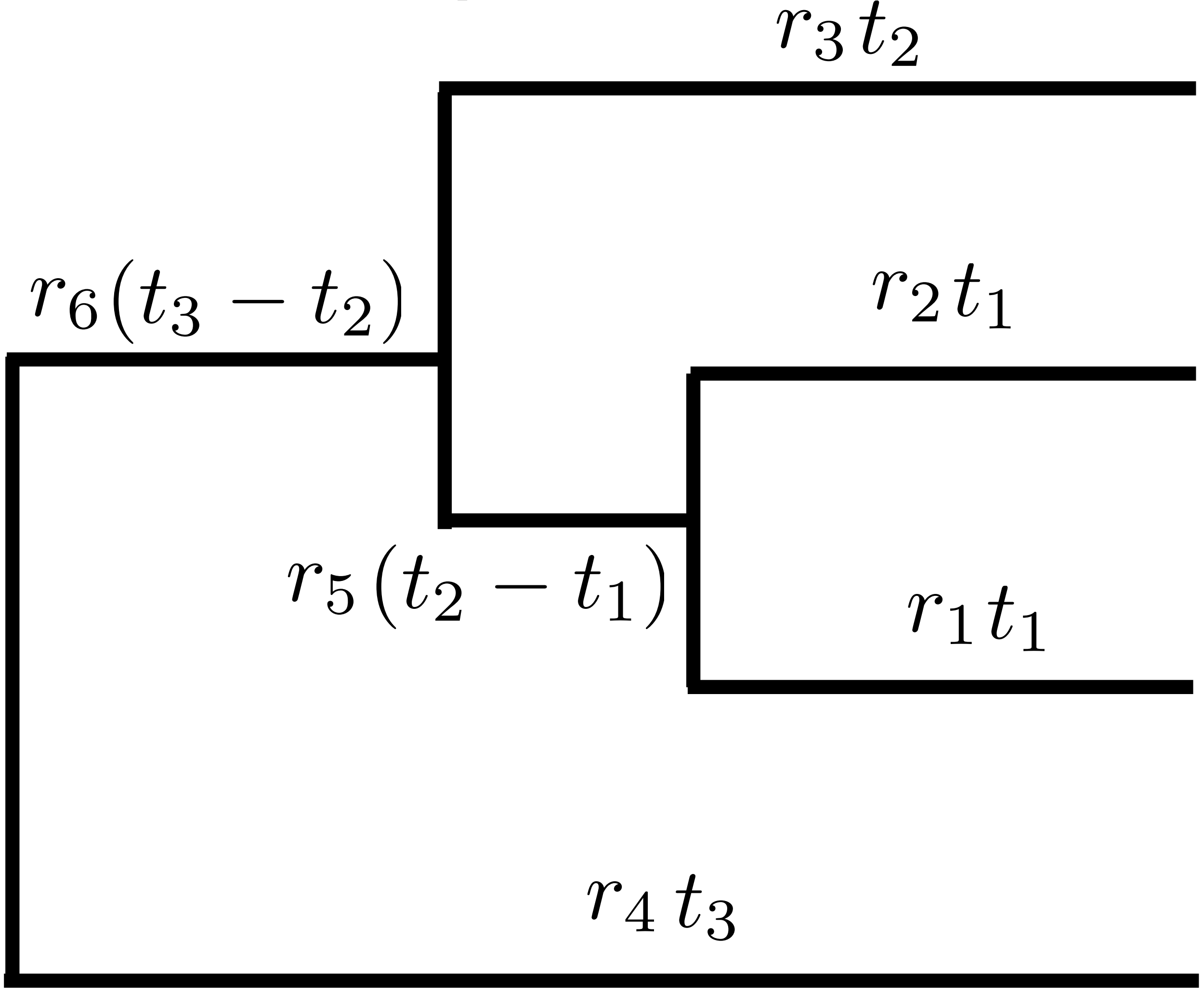


But perhaps even worse is that for most data sets a strict molecular clock can be ruled out, so $r_1 \neq r_2$.

Bayesian uncorrelated lognormal model

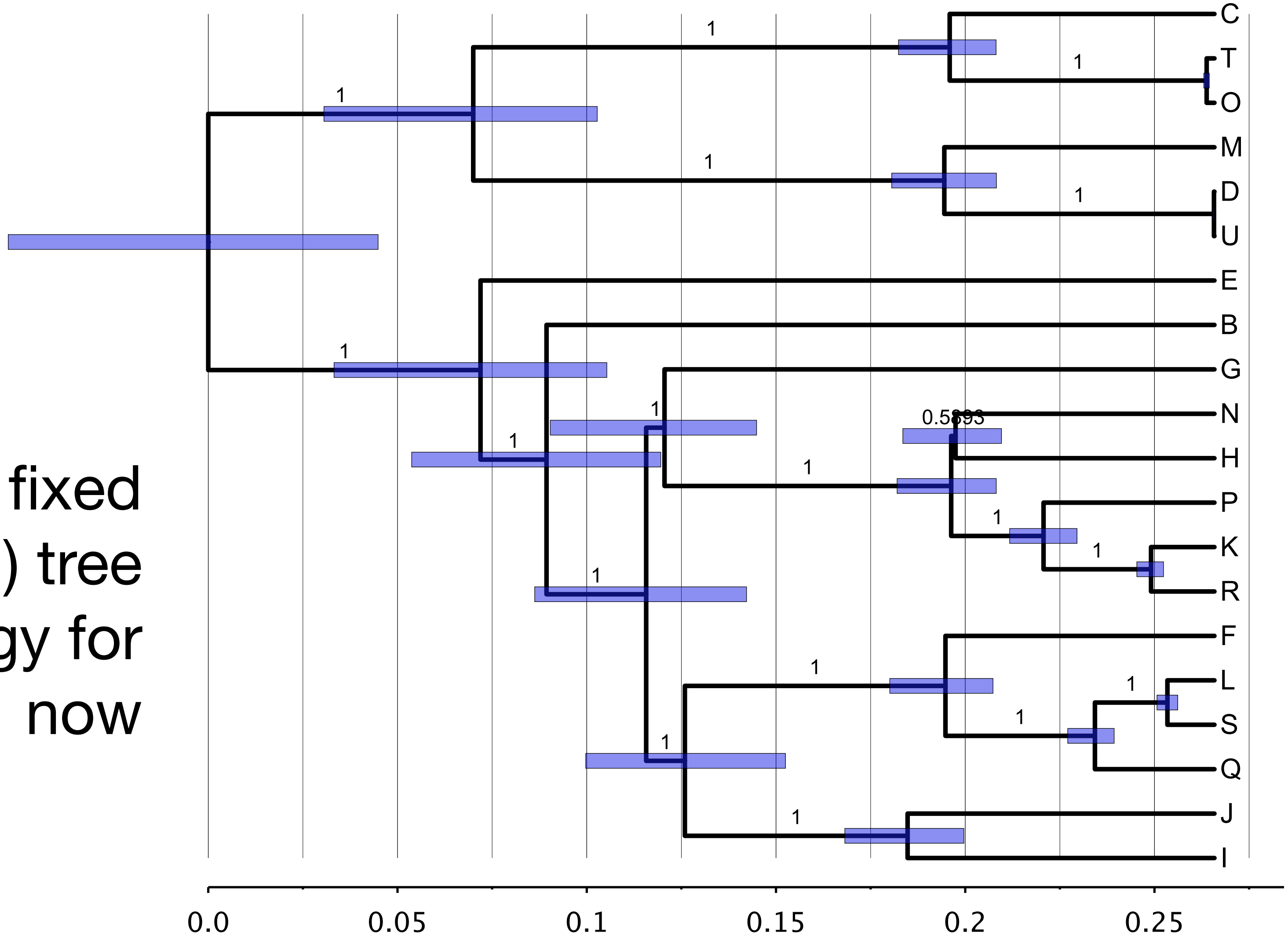
Drummond et al. 2006

Must know rates and times to compute likelihood



The goal: credible intervals for divergence times

Assume fixed (rooted) tree topology for now



Posterior density for times ***t*** given data ***y***

$$p(\mathbf{t}|\mathbf{y}) = \int p(\mathbf{t},\mathbf{r}|\mathbf{y})d\mathbf{r}$$

Bold symbols denote vector quantities.
That is, ***t*** represents a vector of ancestral node times.

Marginalize over rates ***r***: we are only interested in the distribution of times.

You must have known that Bayes' rule was coming sooner or later…

$$p(\mathbf{t}|\mathbf{y}) = \int p(\mathbf{t},\mathbf{r}|\mathbf{y}) d\mathbf{r}$$

posterior

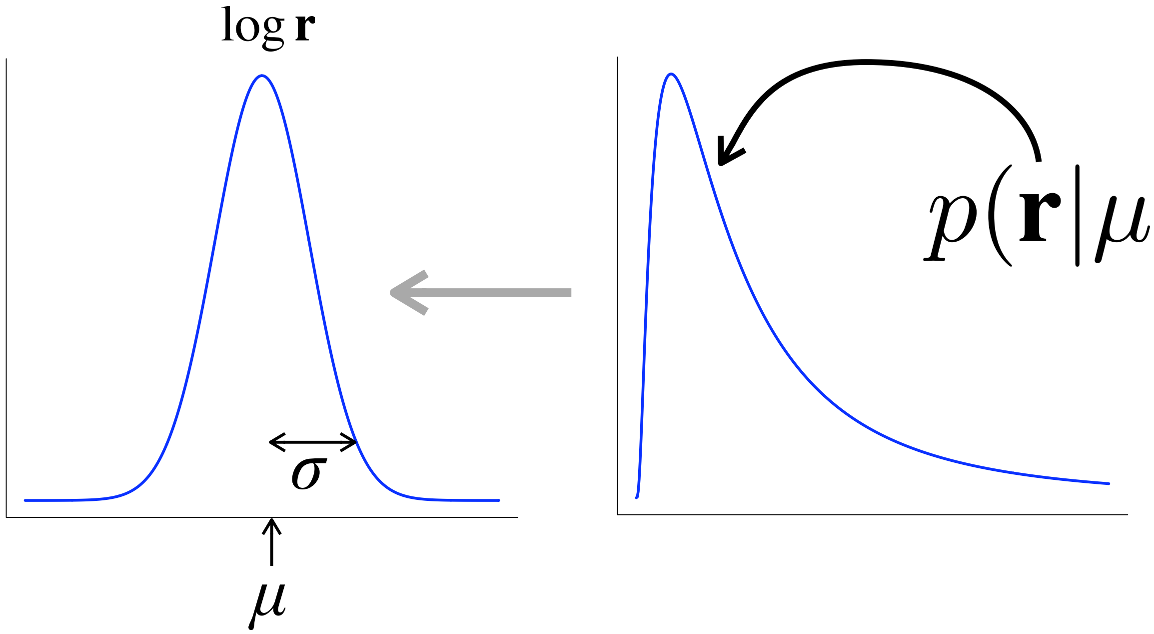
↓

likelihood ← prior →

$$\frac{p(\mathbf{y}|\mathbf{t},\mathbf{r})\ p(\mathbf{r})\ p(\mathbf{t})}{p(\mathbf{y})}$$

marginal likelihood

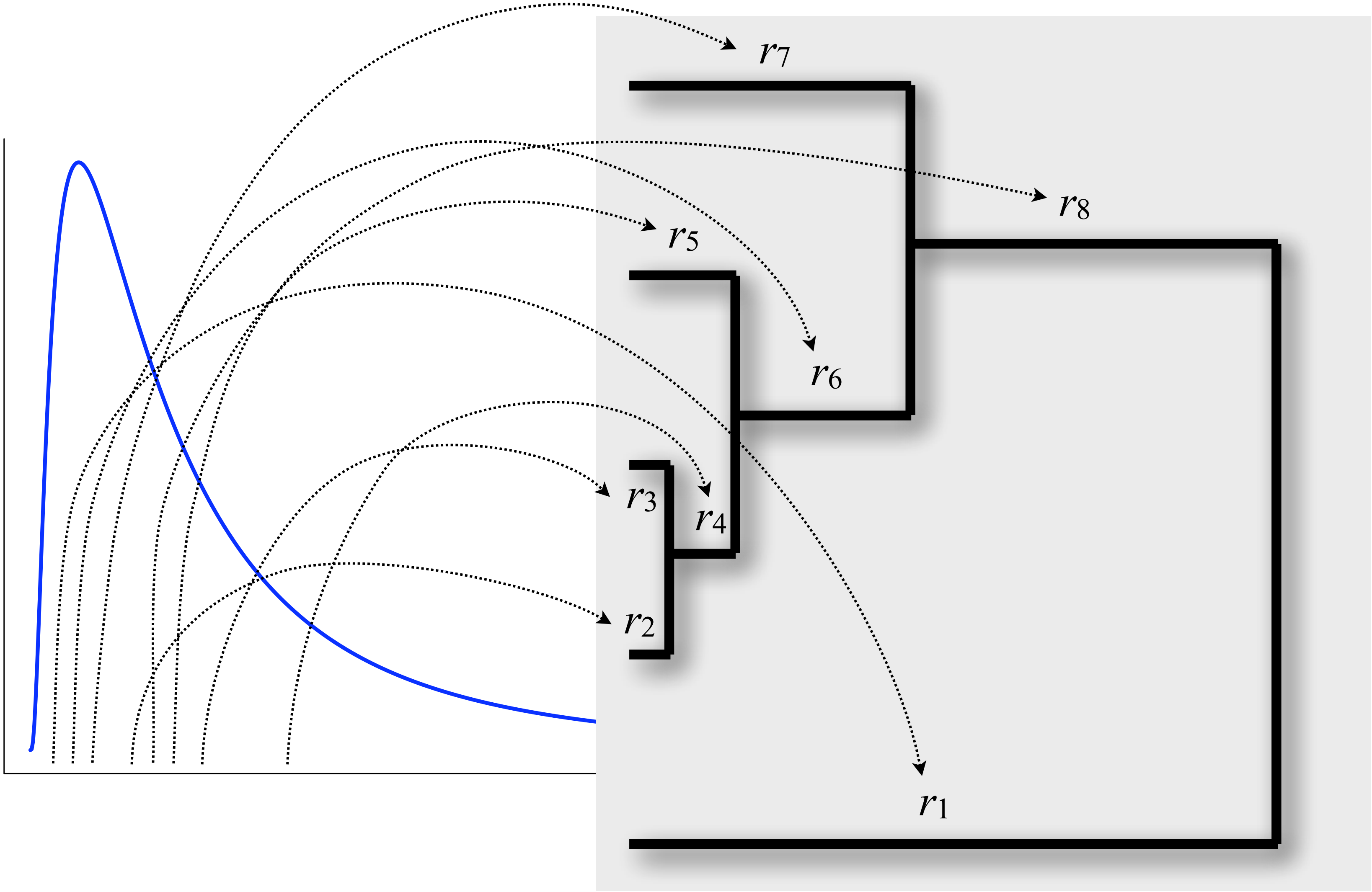
Rate prior is lognormal



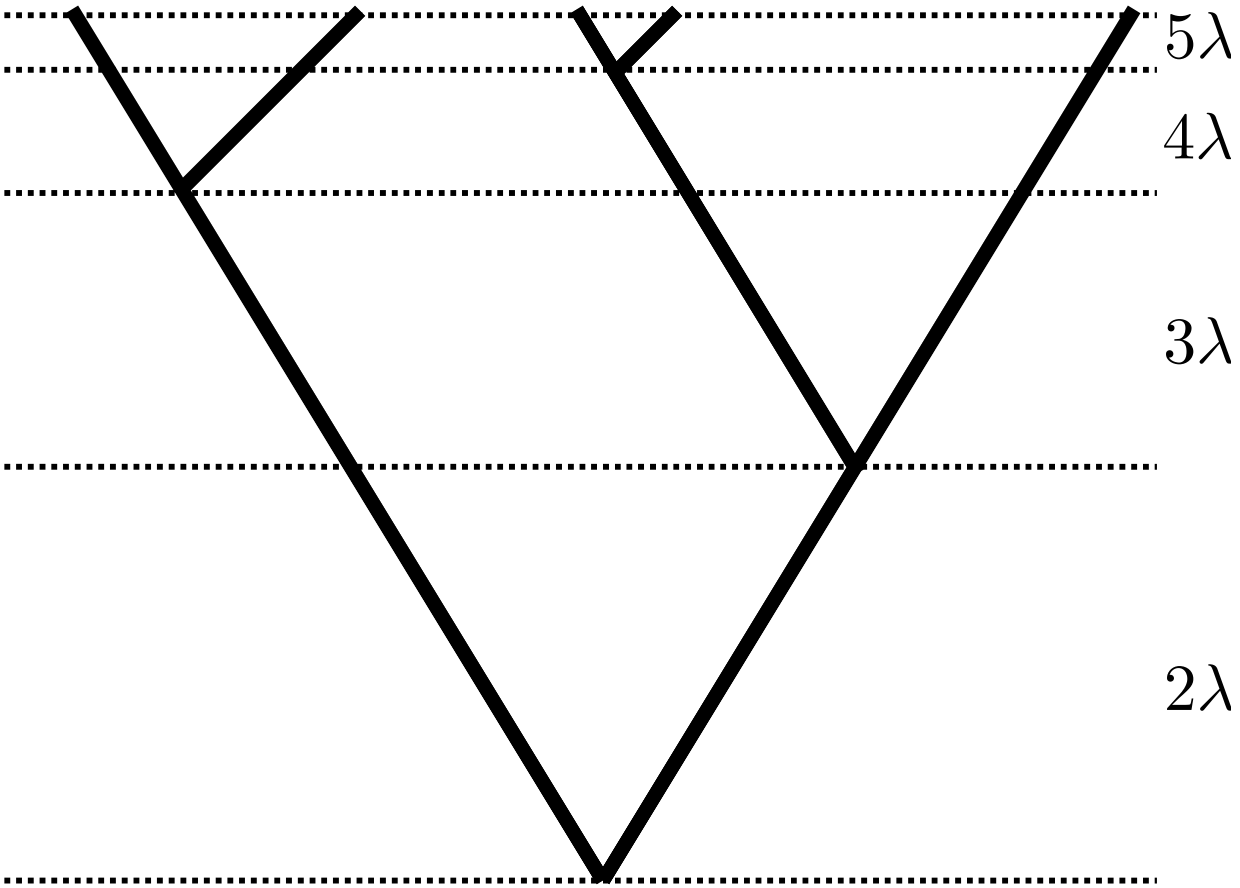
$$p(\mathbf{r}|\mu,\sigma)\;p(\mu)\;p(\sigma)$$

$$p(\mathbf{t},\mathbf{r}|\mathbf{y}) = \frac{p(\mathbf{y}|\mathbf{t},\mathbf{r})\;p(\mathbf{r})\;p(\mathbf{t})}{p(\mathbf{y})}$$

Rates are **conditionally independent** - any correlation between rates is due only to the fact that they all share the same lognormal prior distribution.



Time prior provided by birth-death model



Yule model (pure birth):
exponential sojourn
times between
speciation events

$$p(\mathbf{t}|\lambda)\ p(\lambda)$$

↑

$$\frac{p(\mathbf{y}|\mathbf{t},\mathbf{r})\ p(\mathbf{r}|\mu,\sigma)\ p(\mu)\ p(\sigma)\ p(\mathbf{t})}{p(\mathbf{y})}$$

Full uncorrelated lognormal relaxed clock model

$$p(\mathbf{t}, \mathbf{r}, \mu, \sigma, \lambda | \mathbf{y})$$

$$= \frac{p(\mathbf{y}|\mathbf{t}, \mathbf{r})\ p(\mathbf{r}|\mu, \sigma)\ p(\mu)\ p(\sigma)\ p(\mathbf{t}|\lambda)\ p(\lambda)}{p(\mathbf{y})}$$

This uses the JC69 model (the likelihood involves only branch lengths).

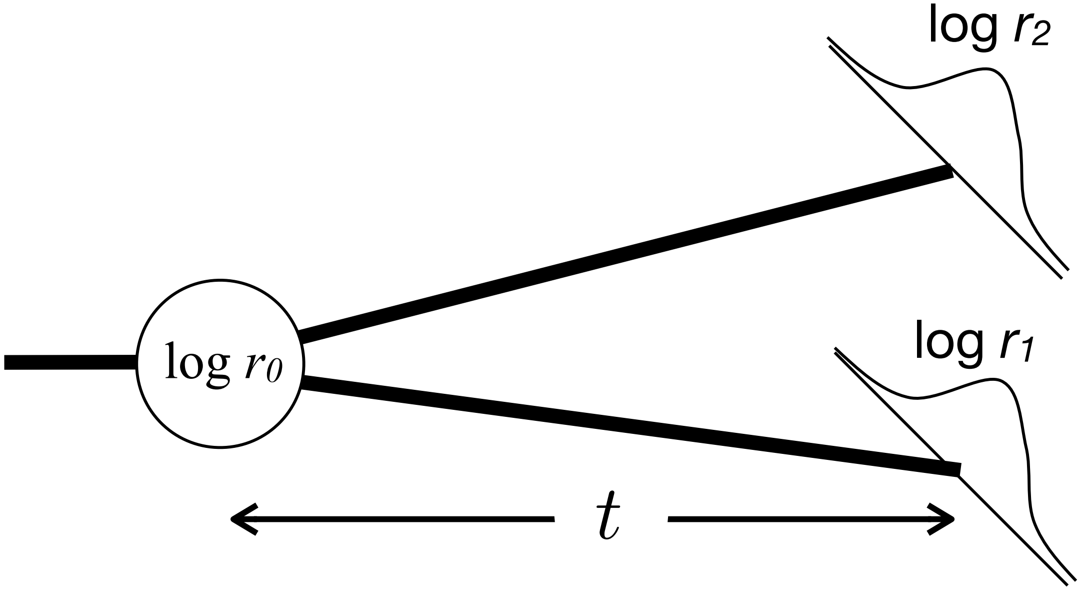
Is this a hierarchical model?

Bayesian correlated relaxed clock model

Thorne et al. (1998); Kishino et al. (2001)

Thorne/Kishino model

Each node in the tree has its own rate.

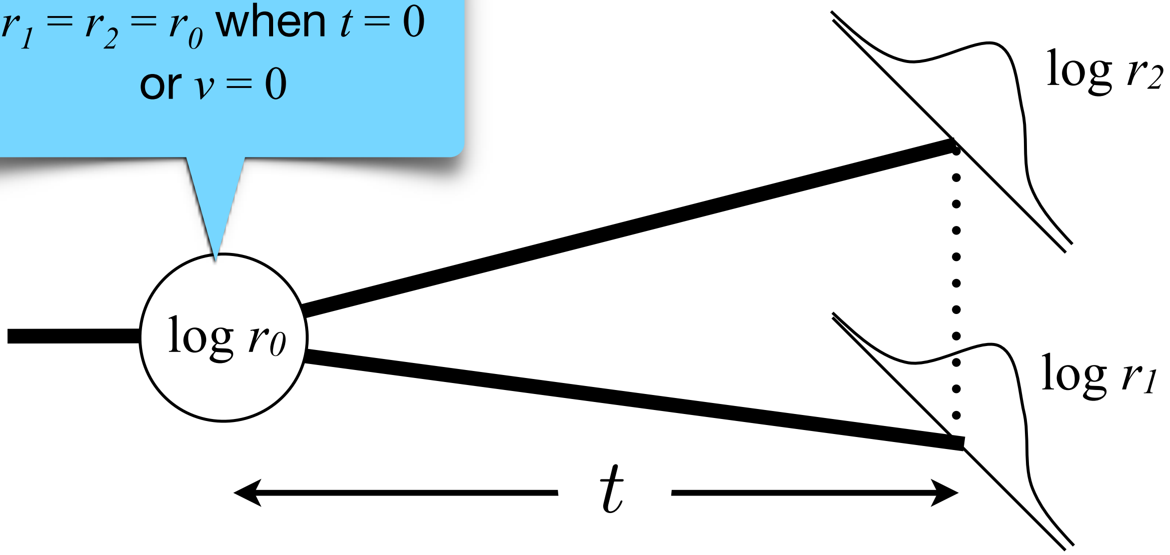


Both $\log r_1$ and $\log r_2$ are normally distributed with:

mean = $\log r_0$
variance = vt

Thorne/Kishino model

$r_1 = r_2 = r_0$ when $t = 0$
or $v = 0$

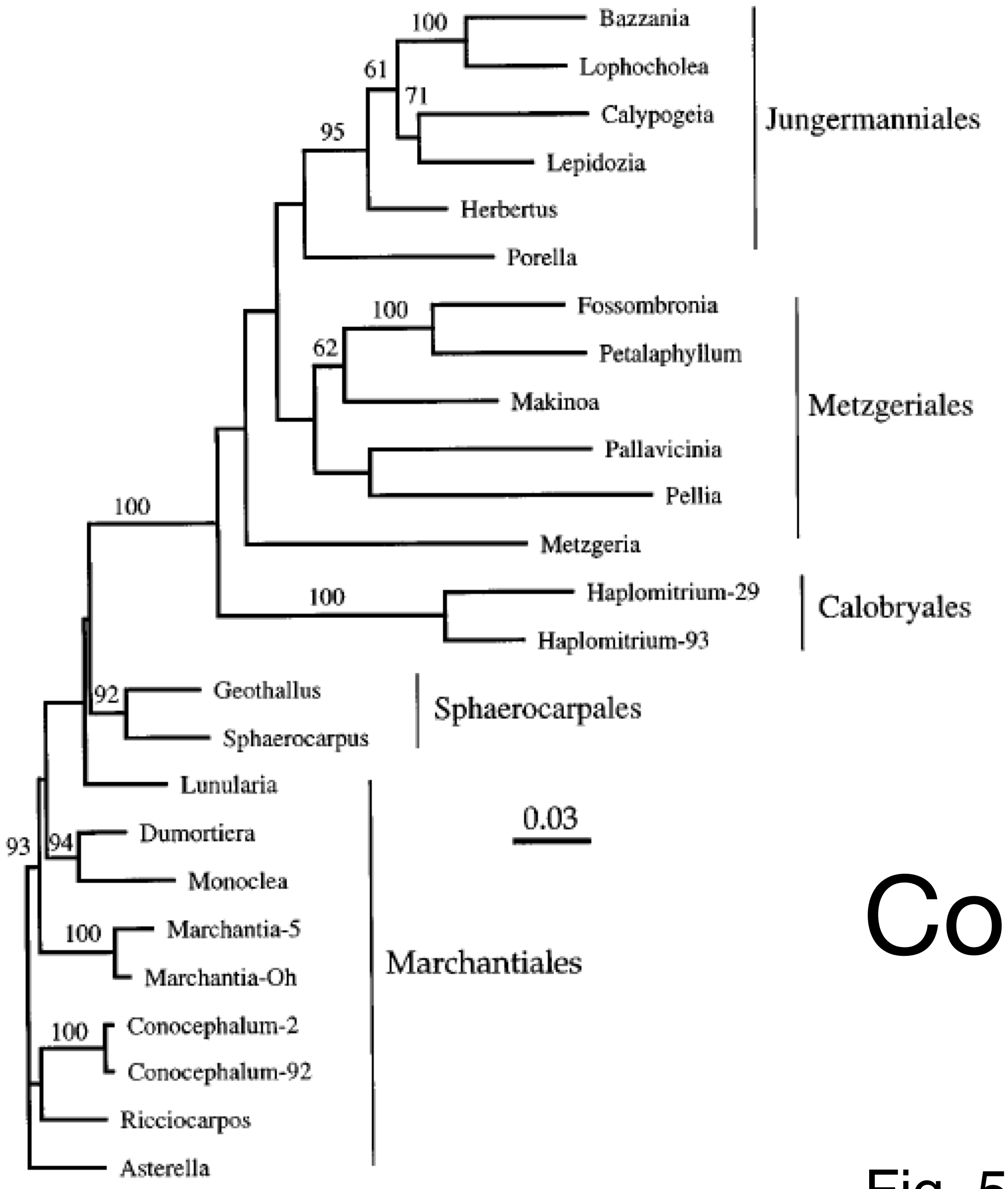


v is a parameter of the model that determines how **correlated** descendant rates are with their parental rates.

v = 0 corresponds to a strict molecular clock

large values of *v* mean less constrained
rates (and correspondingly less certainty about
divergence times)

Correlated Rates



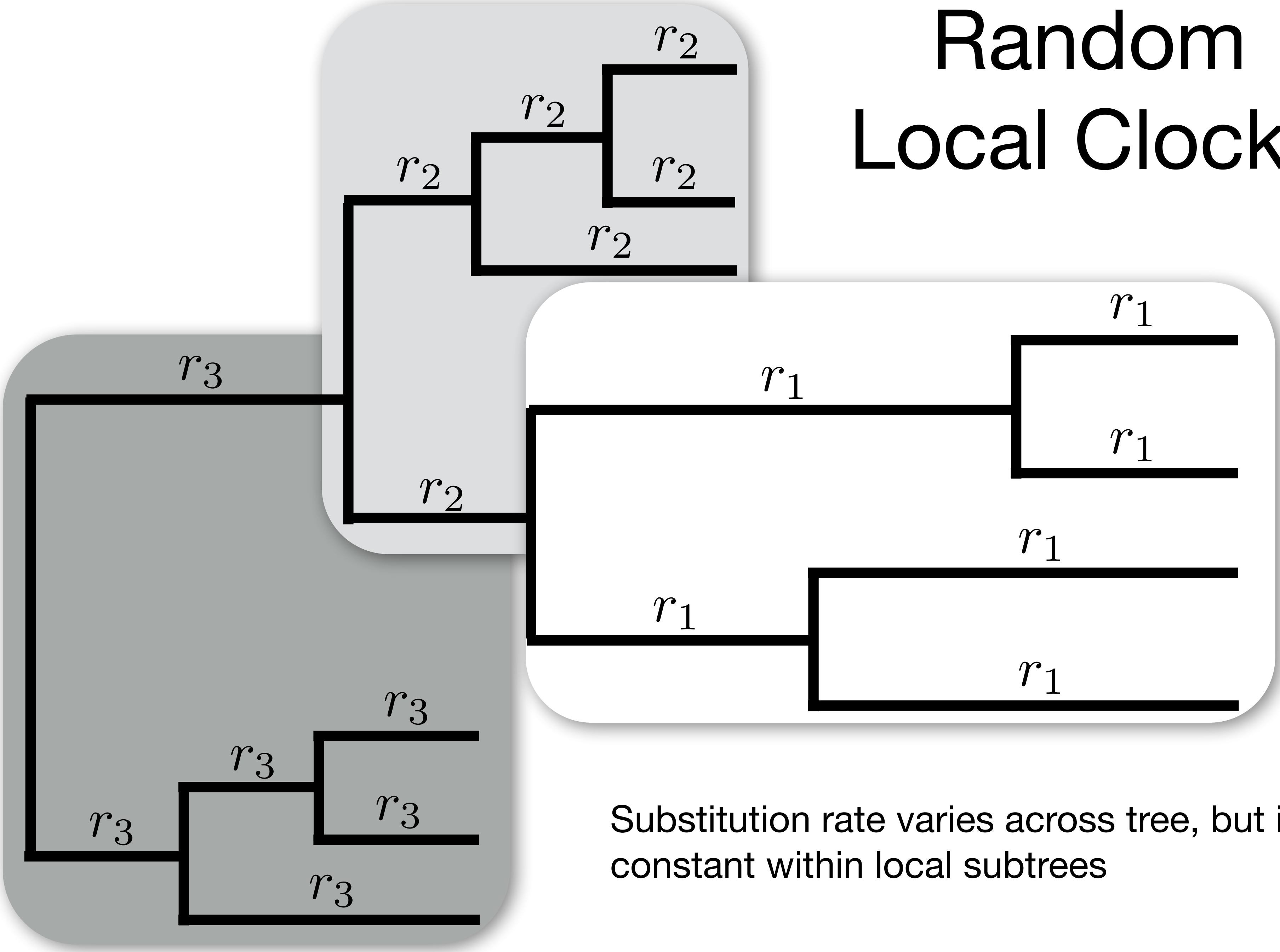
Almost all rates in this tree are predicted well by the rate of their parent, so a correlated rates or local clock model would work well.

Fig. 5 in Lewis et al. (1997)

Bayesian random local clocks model

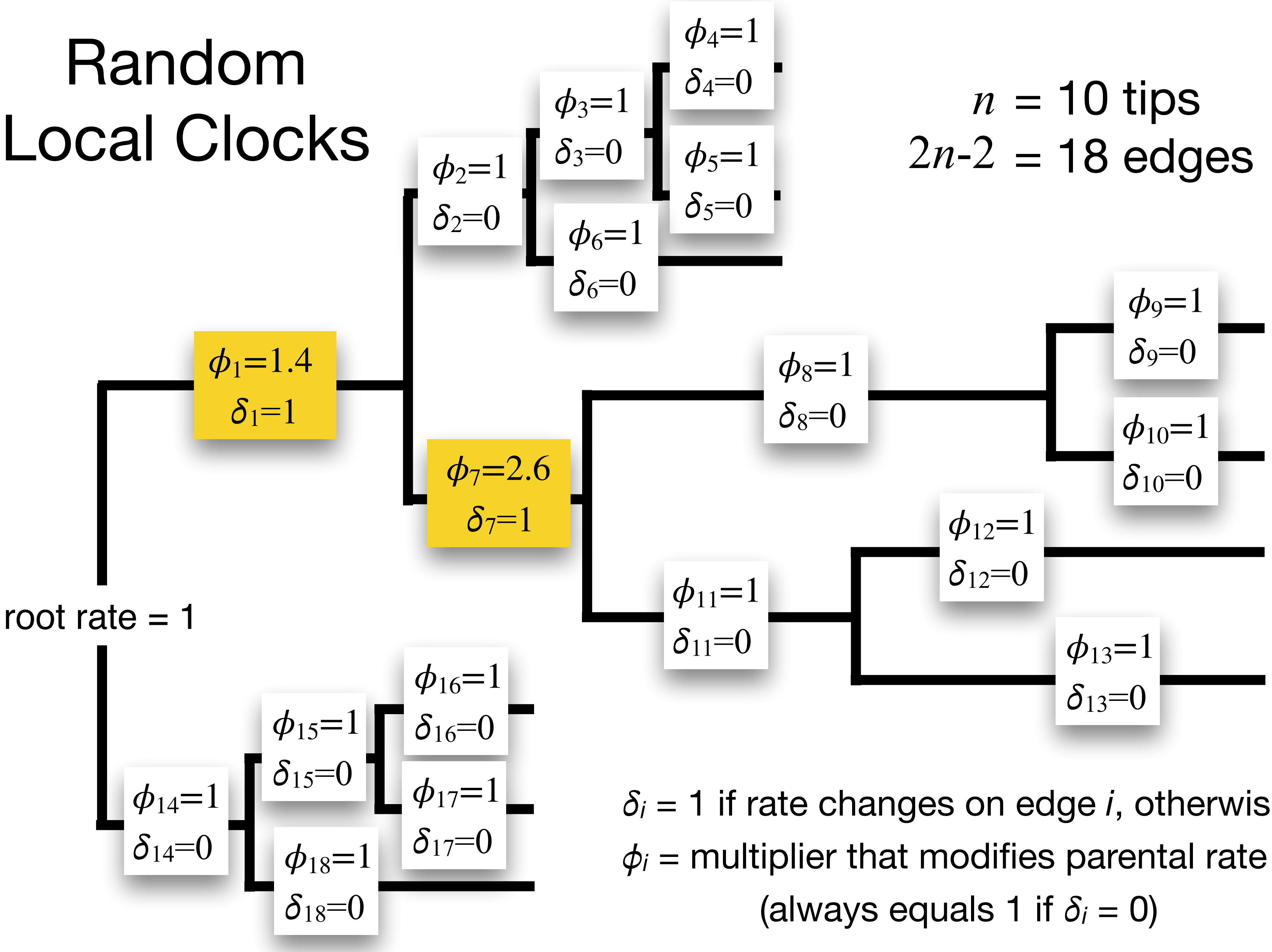
Drummond and Suchard (2010)

Random Local Clocks



Substitution rate varies across tree, but is constant within local subtrees

Random Local Clocks



n = 10 tips

$2n\text{-}2$ = 18 edges

δ_i = 1 if rate changes on edge i, otherwise 0

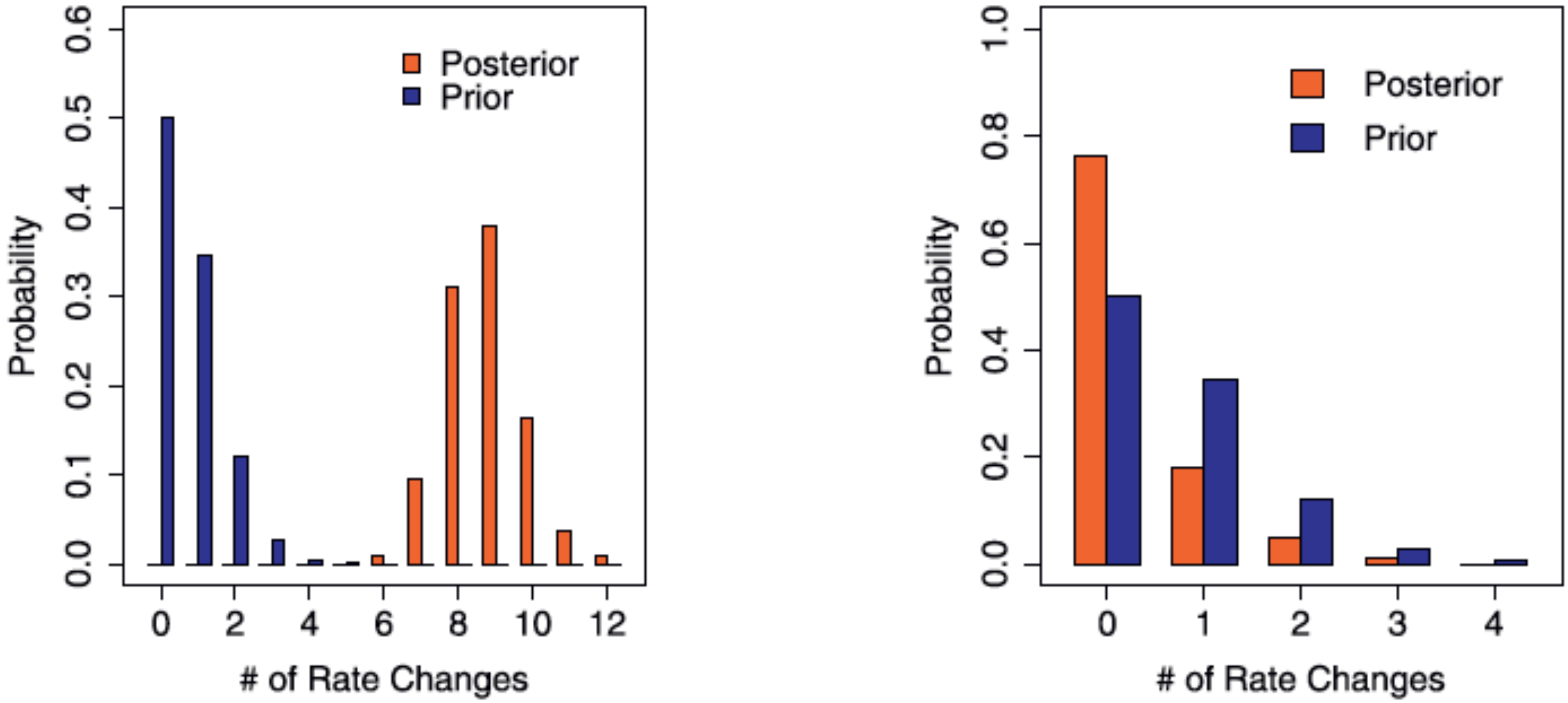
ϕ_i = multiplier that modifies parental rate

(always equals 1 if $\delta_i = 0$)

Random Local Clocks

Definitely not a strict clock

May be a strict clock



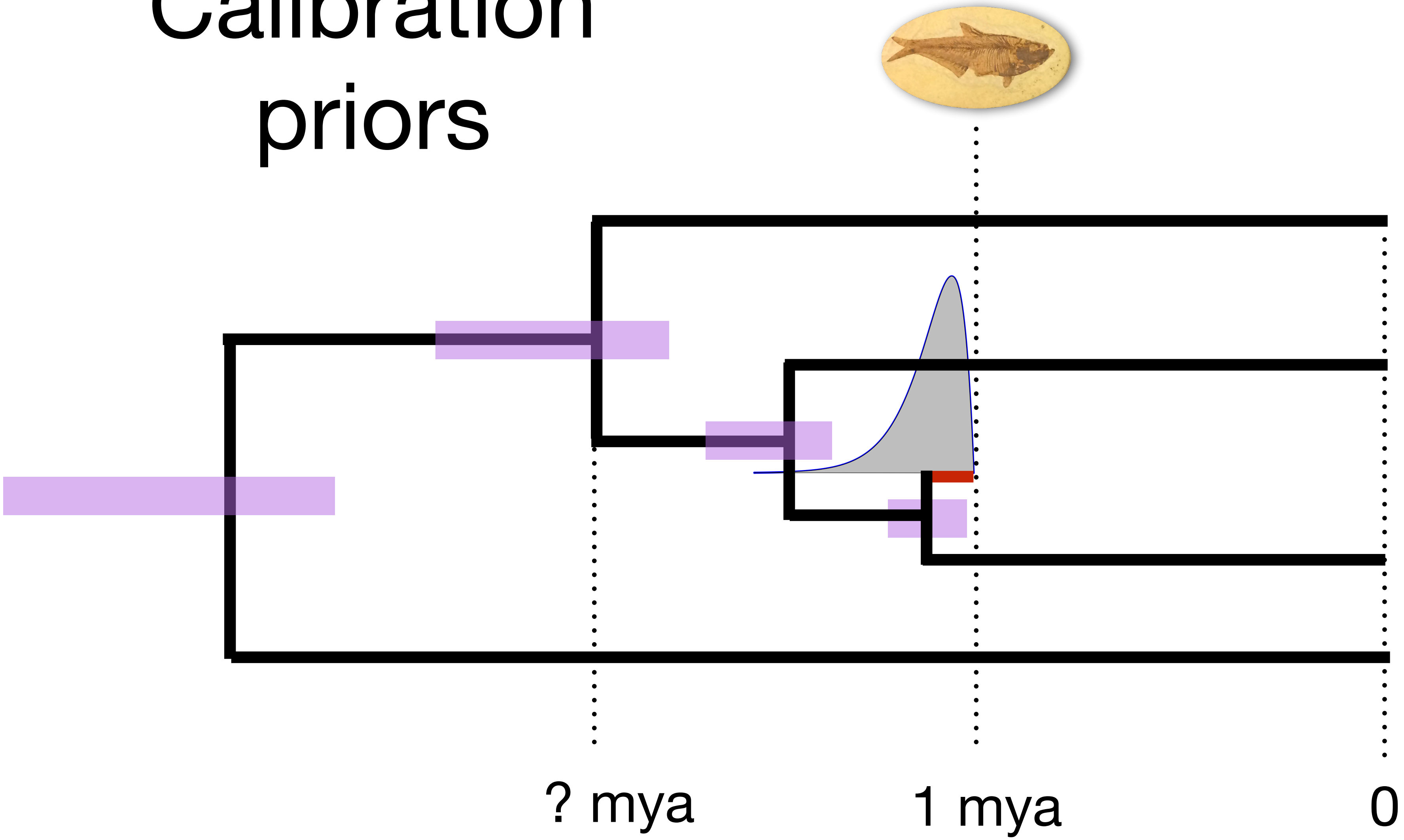
(a) 3 nuclear genes from 42 mammals

(b) mtDNA from 7 primates

Fig. 2 from Drummond and Suchard (2010)

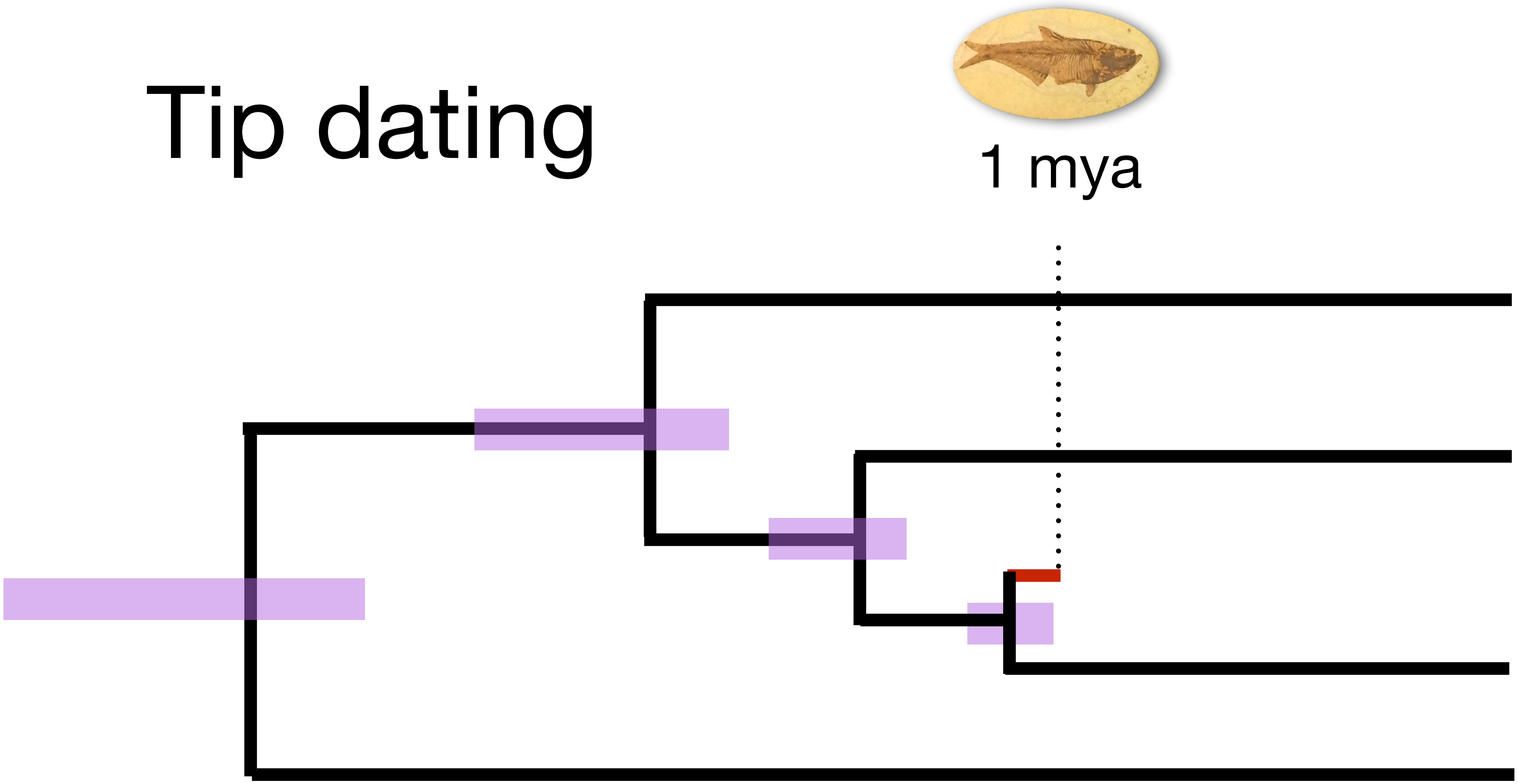
Calibrating the clock

Calibration priors



Calibration priors provide a plausible time frame for when the fossil branch joins the main tree

Tip dating



Tip dating uses morphology to place the fossils in the tree. The morphological data thus determines the length of the edge leading to the fossil.

Ronquist et al. (2012)