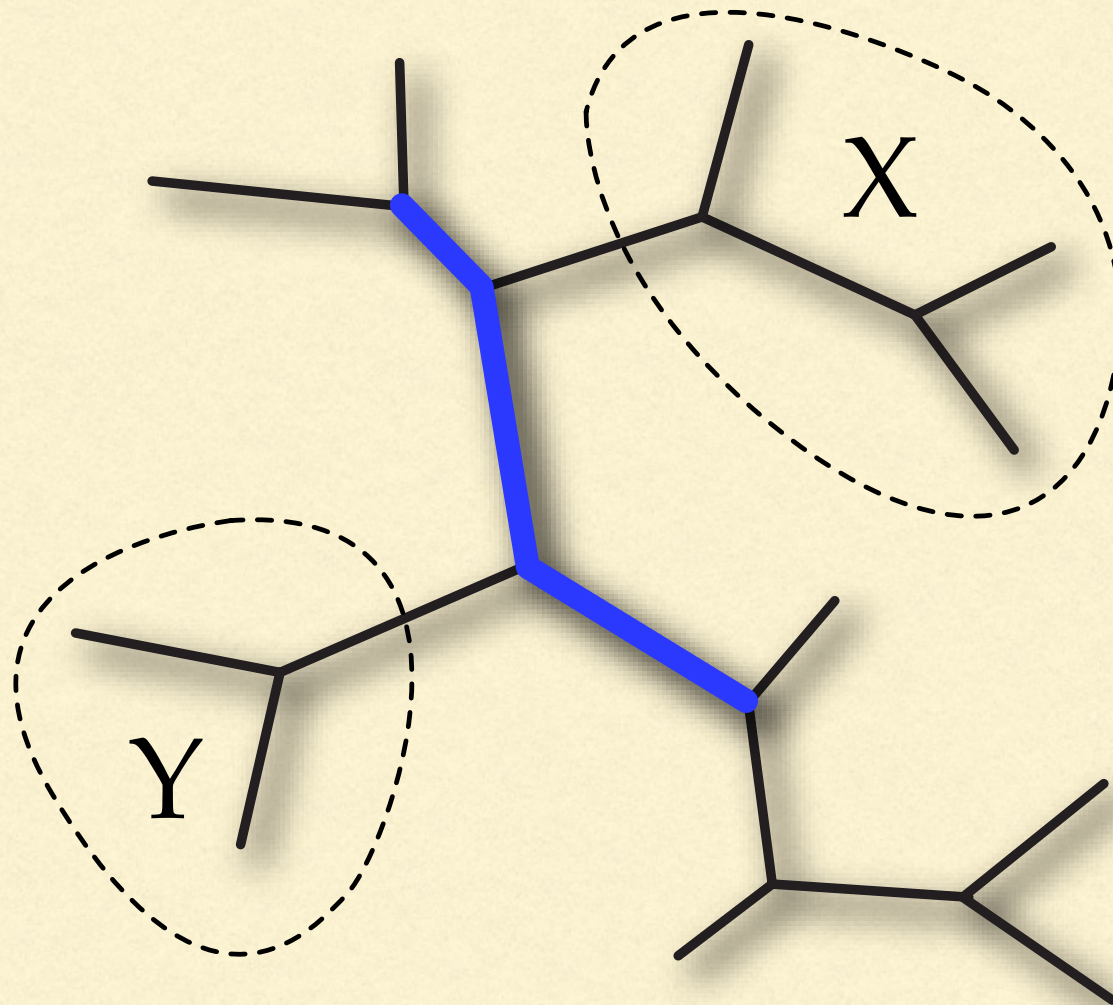

MCMC proposals

Moving through treespace



The Target-Simon move

Step 1:

Pick 3 contiguous edges randomly, defining two subtrees, X and Y

Larget, B., and D. L. Simon. 1999. Mol. Biol. Evol. 16: 750-759.
See also: Holder et al. 2005. Syst. Biol. 54: 961-965.

Moving through treespace

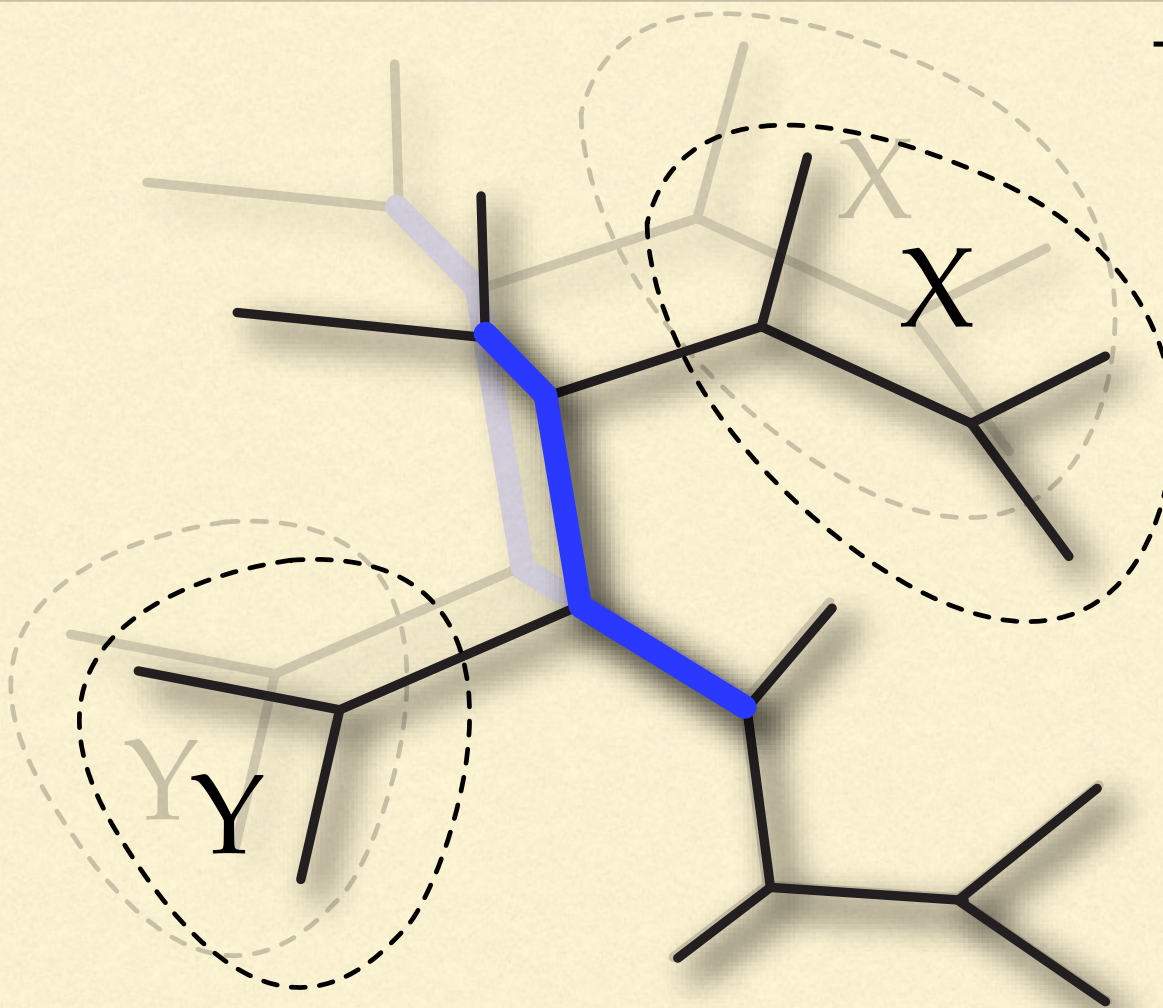
The Larget-Simon move

Step 1:

Pick 3 contiguous edges randomly, defining two subtrees, X and Y

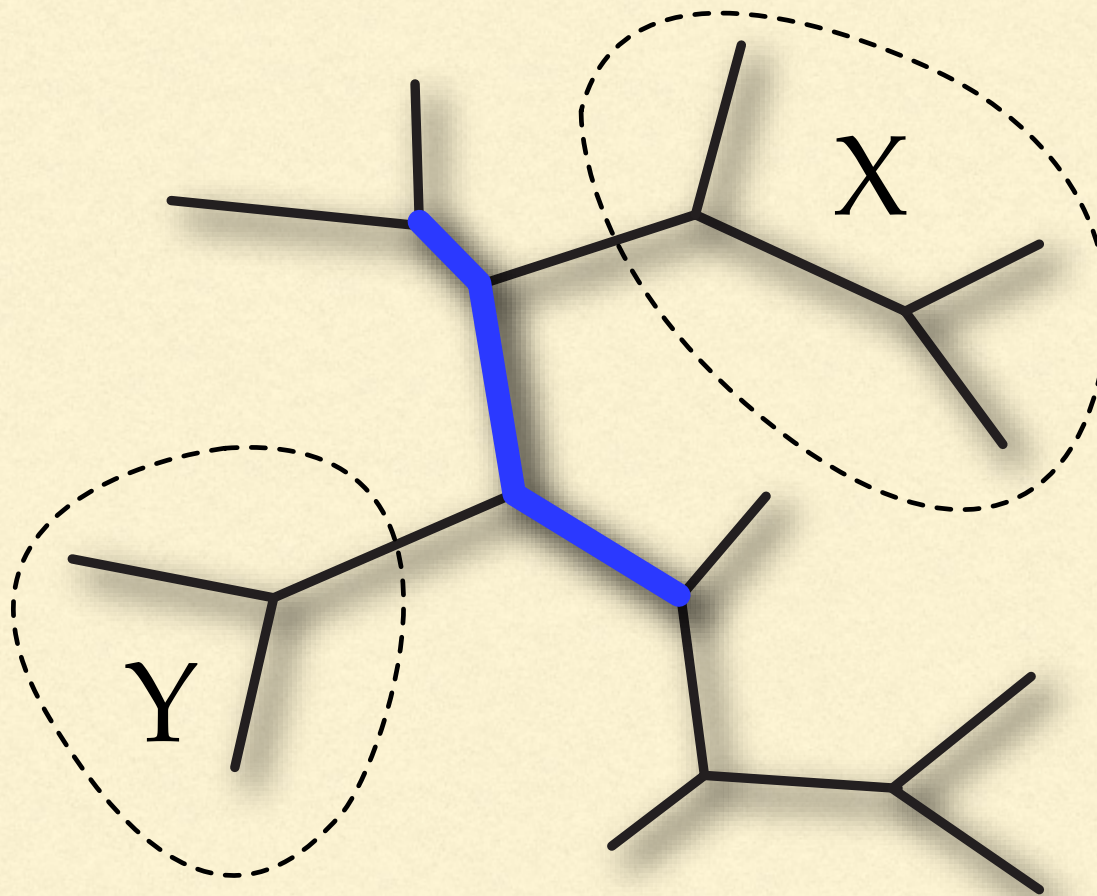
Step 2:

Shrink or grow selected 3-edge segment by a random amount



Moving through treespace

The Larget-Simon move



Step 1:

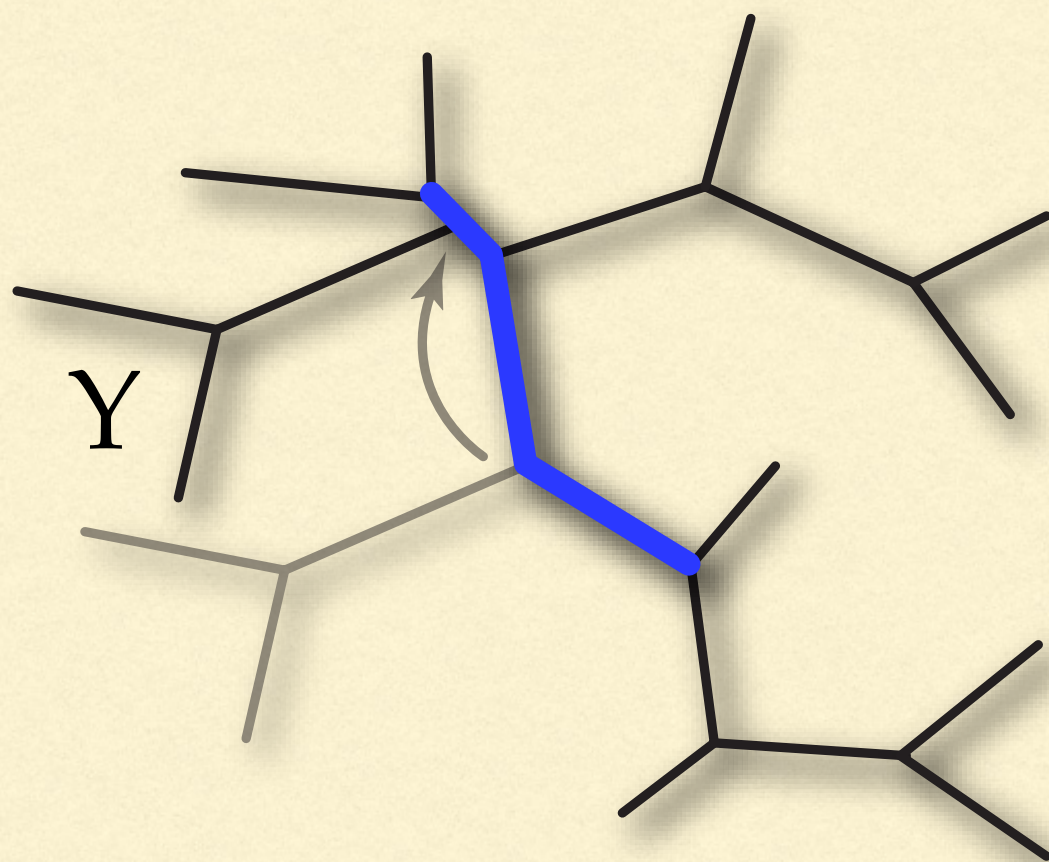
Pick 3 contiguous edges randomly, defining two subtrees, X and Y

Step 2:

Shrink or grow selected 3-edge segment by a random amount

Moving through treespace

The Larget-Simon move



Step 1:

Pick 3 contiguous edges randomly, defining two subtrees, X and Y

Step 2:

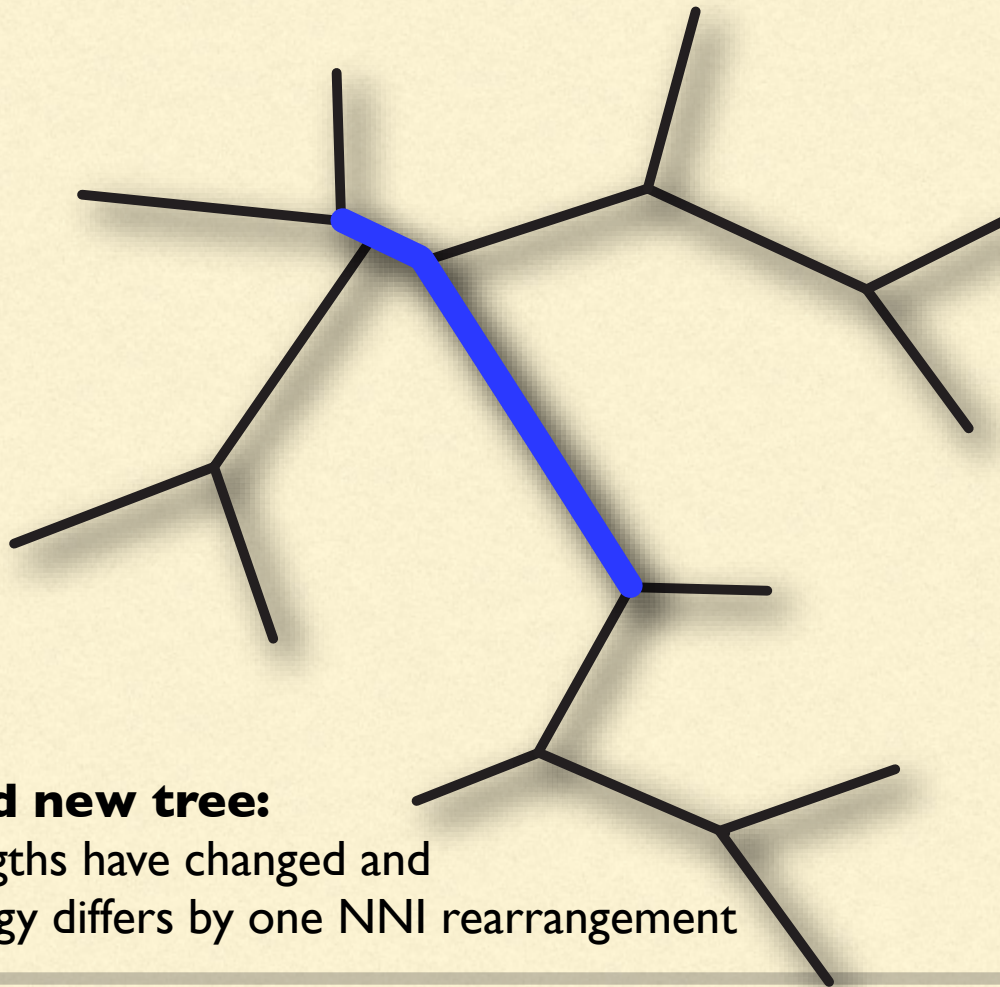
Shrink or grow selected 3-edge segment by a random amount

Step 3:

Choose X or Y randomly, then reposition randomly

Moving through treespace

The Target-Simon move



Proposed new tree:

3 edge lengths have changed and the topology differs by one NNI rearrangement

Step 1:

Pick 3 contiguous edges randomly, defining two subtrees, X and Y

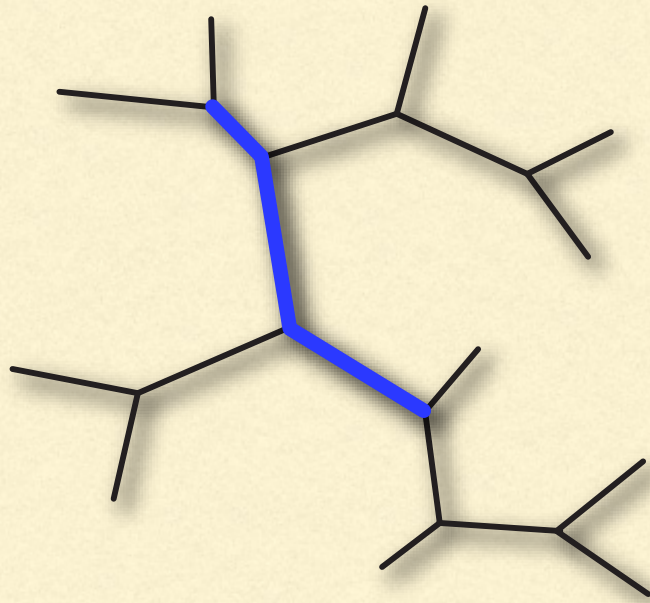
Step 2:

Shrink or grow selected 3-edge segment by a random amount

Step 3:

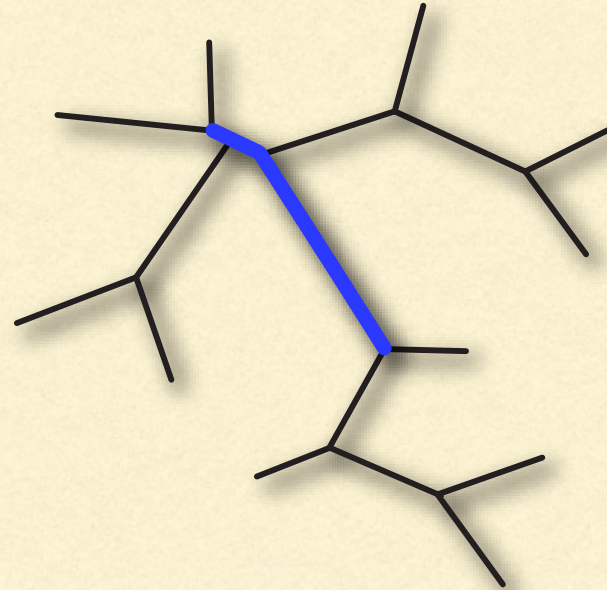
Choose X or Y randomly, then reposition randomly

Moving through treespace



Current tree

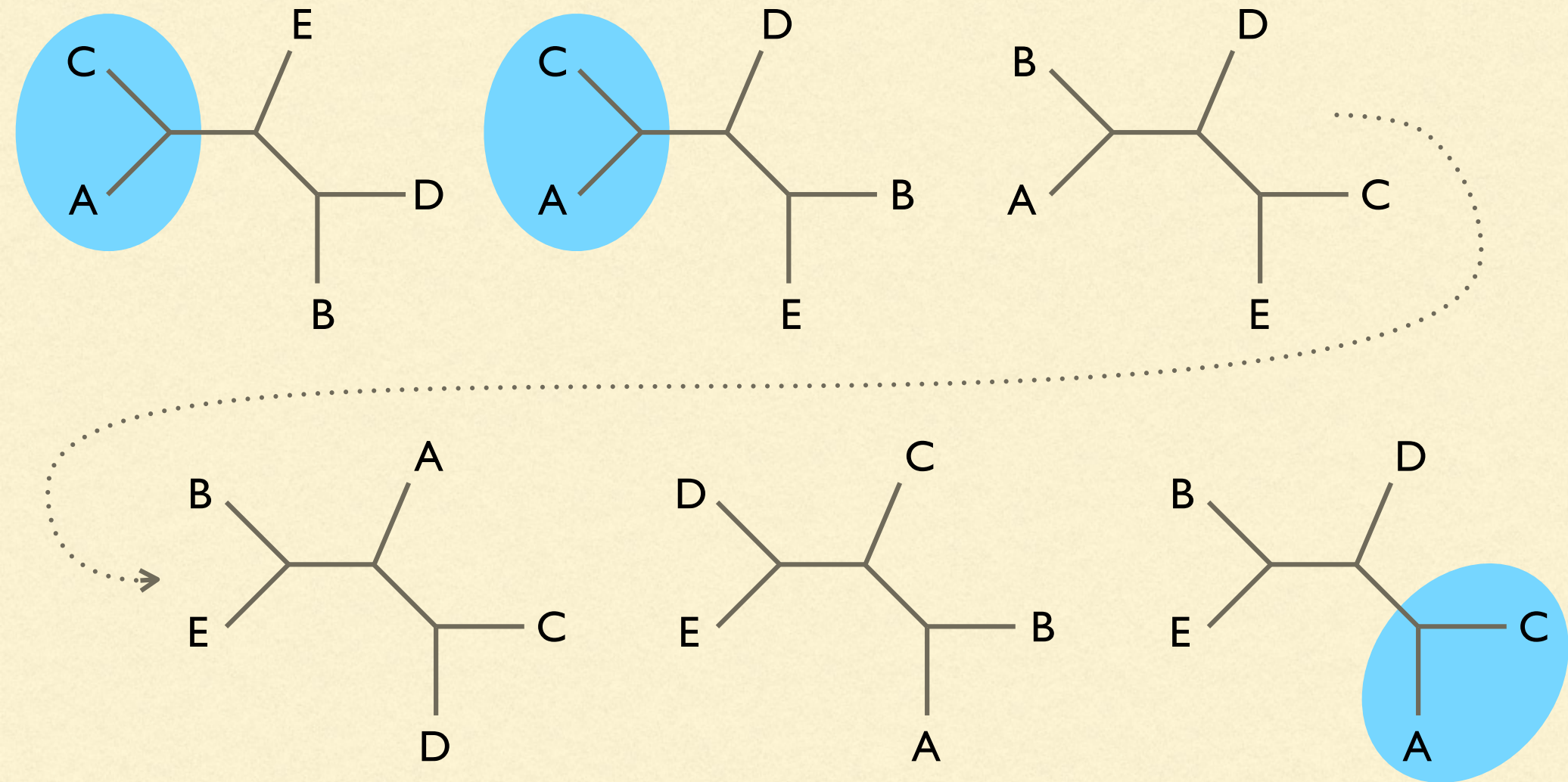
log-posterior = -34256



Proposed tree

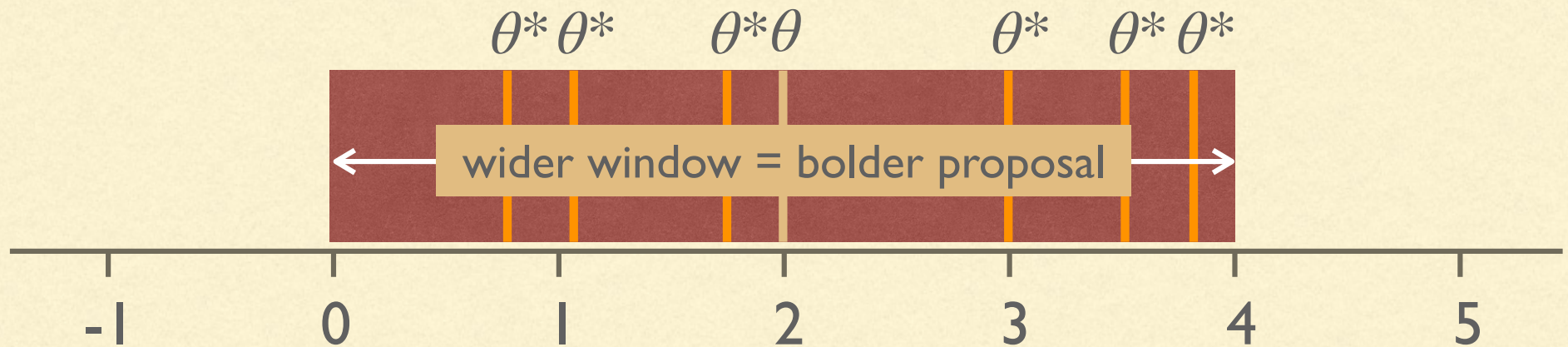
log-posterior = -32519
(better, so accept)

Marginal split posterior probabilities



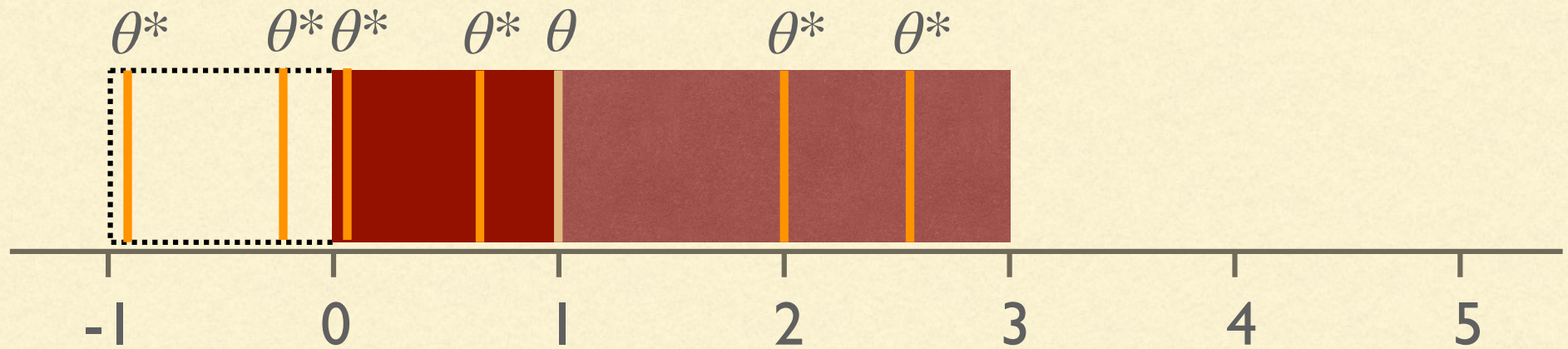
Sliding window proposal

propose new values (θ^*) uniformly
within a proposal window
centered at current value (θ)



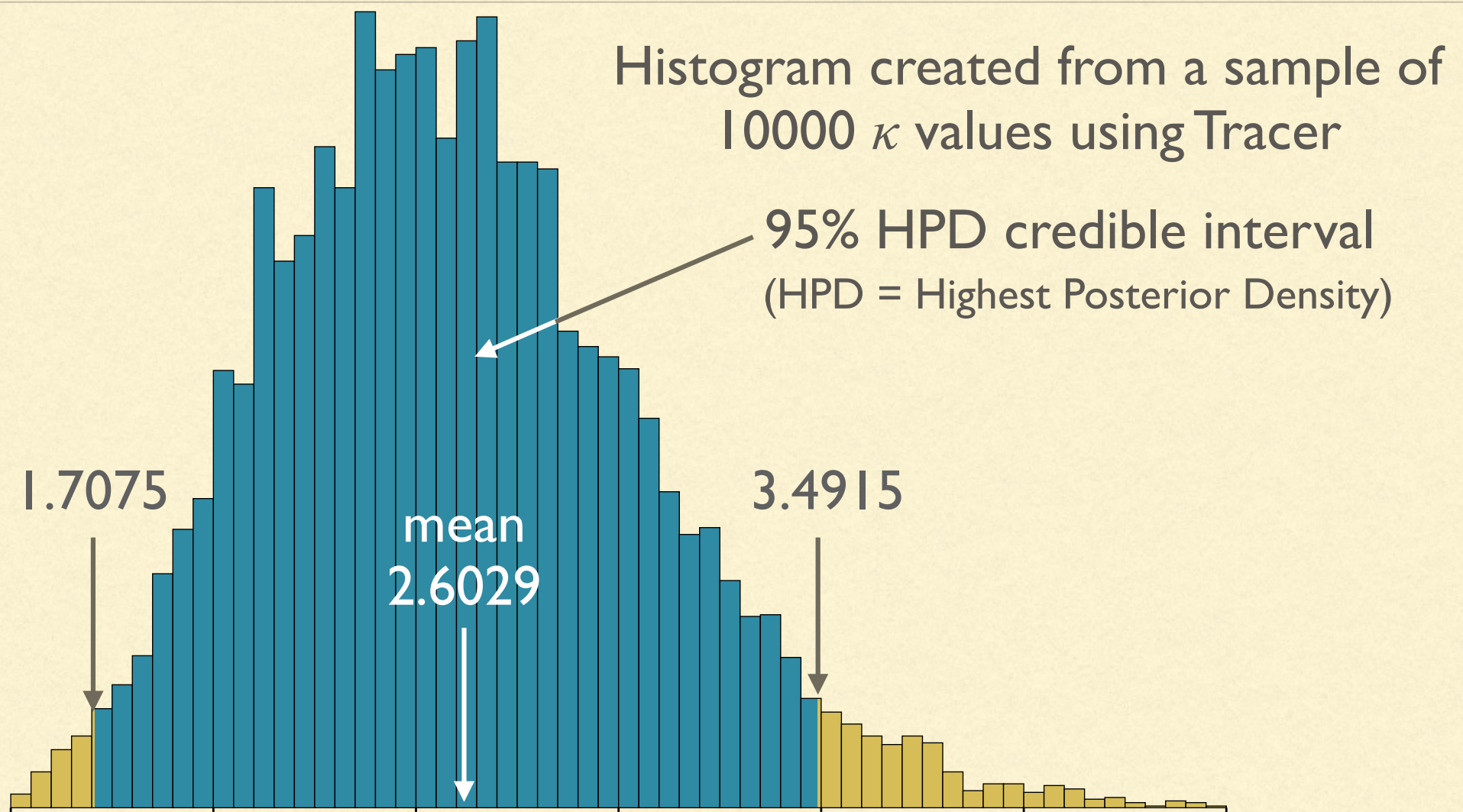
Sliding window proposal

If proposed value is out of bounds,
reflect it back in bounds



Surprisingly, this is a symmetric
proposal, so the Hastings ratio = 1.0

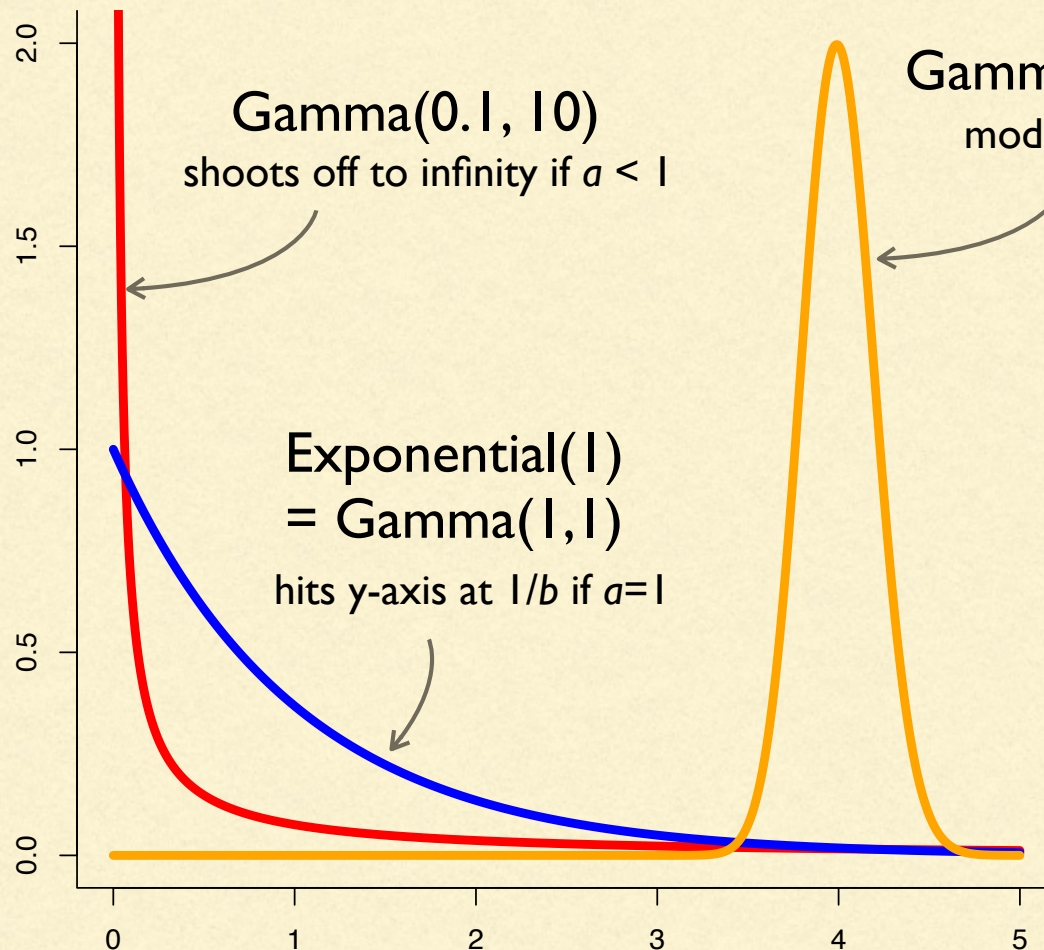
Marginal distributions and credible intervals



Prior distributions

$$p(\theta | D) = \frac{p(D | \theta) p(\theta)}{p(D)}$$

Gamma(a, b) distribution



Gamma(a, b)

distributions are appropriate for parameters that range from 0 to infinity (e.g. branch lengths)

a = shape

b = scale*

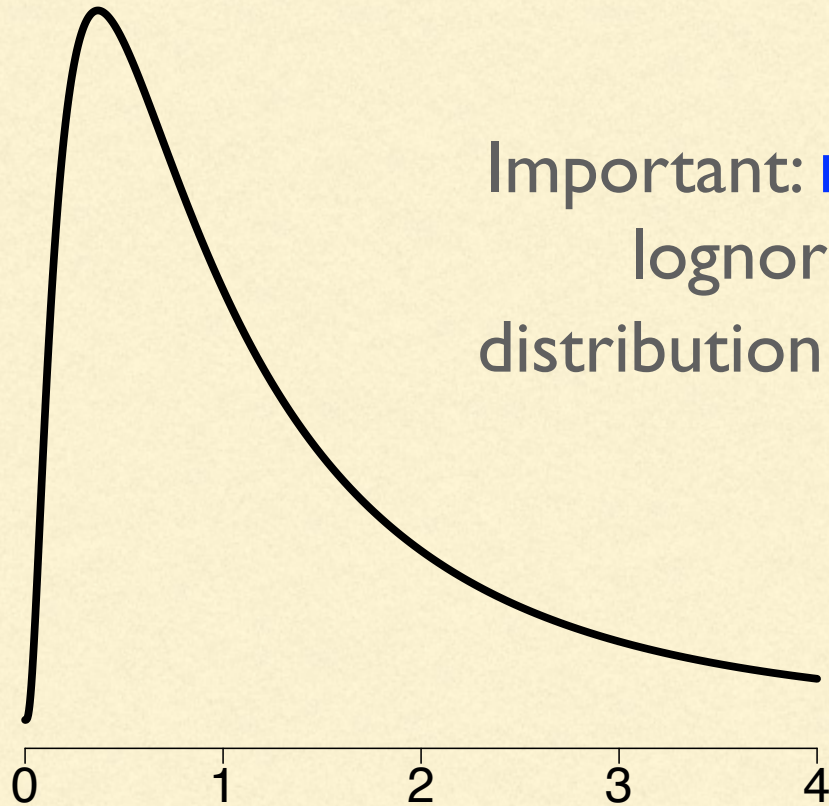
mean = ab

variance = ab^2

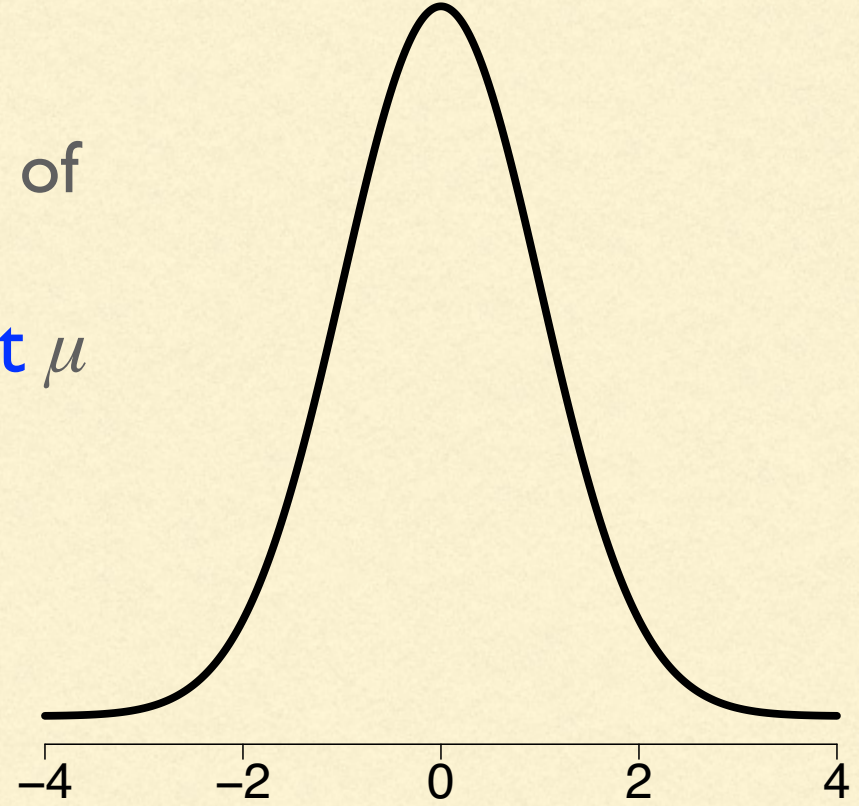
*Note: be aware that in many papers the Gamma distribution is defined such that the second parameter is the rate (*inverse* of the scale b used in this slide) rather than the scale! In this case, the mean and variance would be a/b and a/b^2 , respectively.

Lognormal(μ, σ) distribution

Lognormal($\mu = 0, \sigma = 1$)

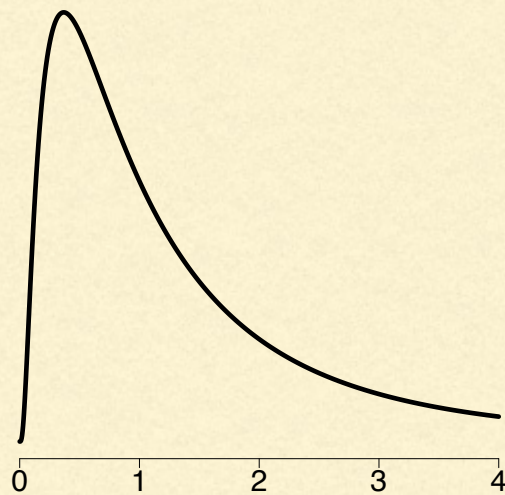


Normal($\mu = 0, \sigma = 1$)



Important: **mean** of
lognormal
distribution is **not** μ

Lognormal(μ, σ) distribution



$$\mu = 0, \sigma = 1$$

$$1.65$$

$$4.67$$

$$0.37$$

$$1.0$$

$$\text{mean} = e^{\mu + \sigma^2/2}$$

$$\text{variance} = e^{2\mu + \sigma^2}(e^{\sigma^2} - 1)$$

$$\text{mode} = e^{\mu - \sigma^2}$$

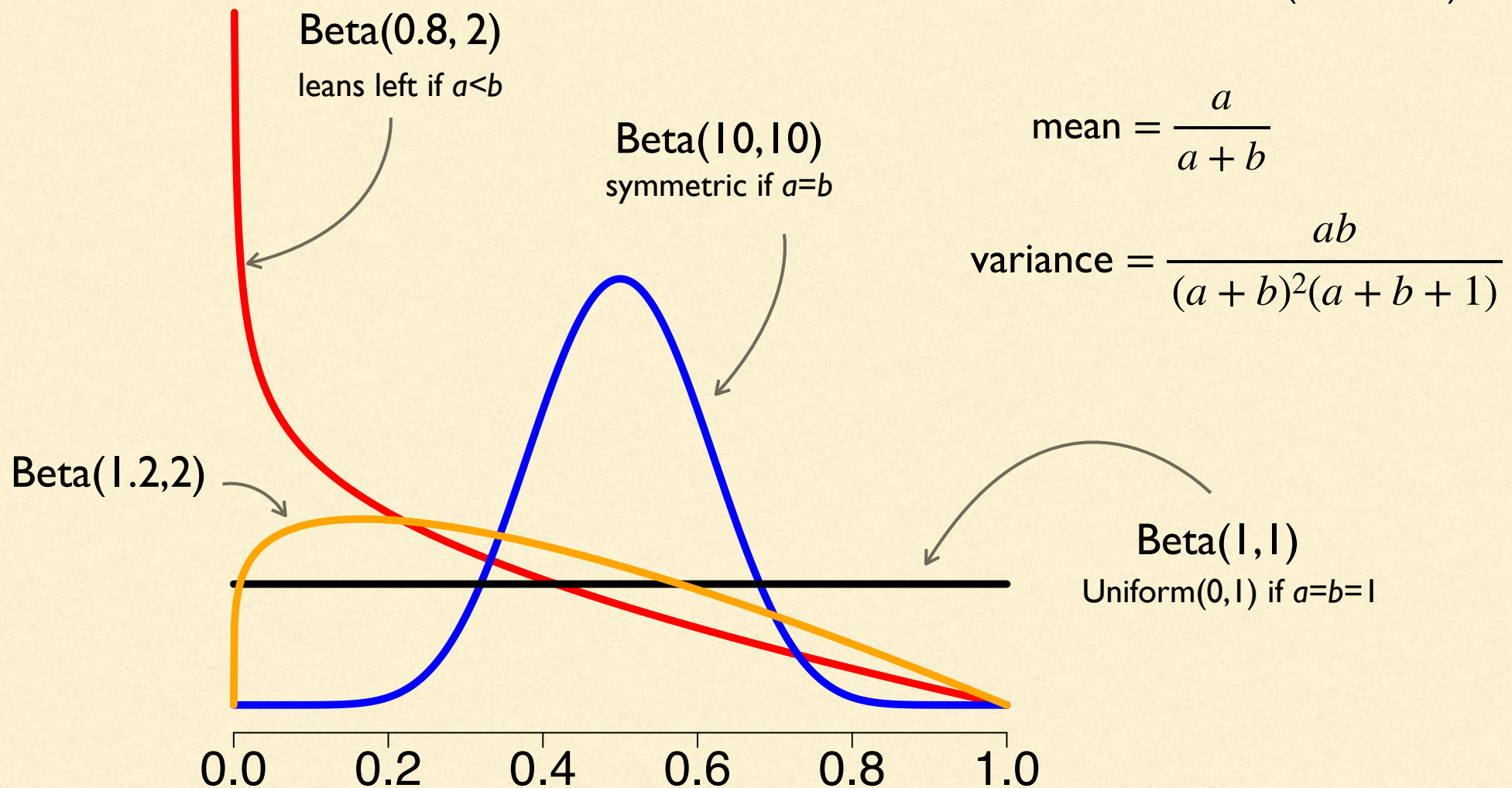
$$\text{median} = e^{\mu}$$

To choose μ and σ to yield a particular mean (m) and variance (v) for a lognormal prior, use these formulas (log is natural logarithm):

$$\sigma^2 = \log \left(1 + \frac{v}{m^2} \right) \quad \mu = \log(m) - \sigma^2/2$$

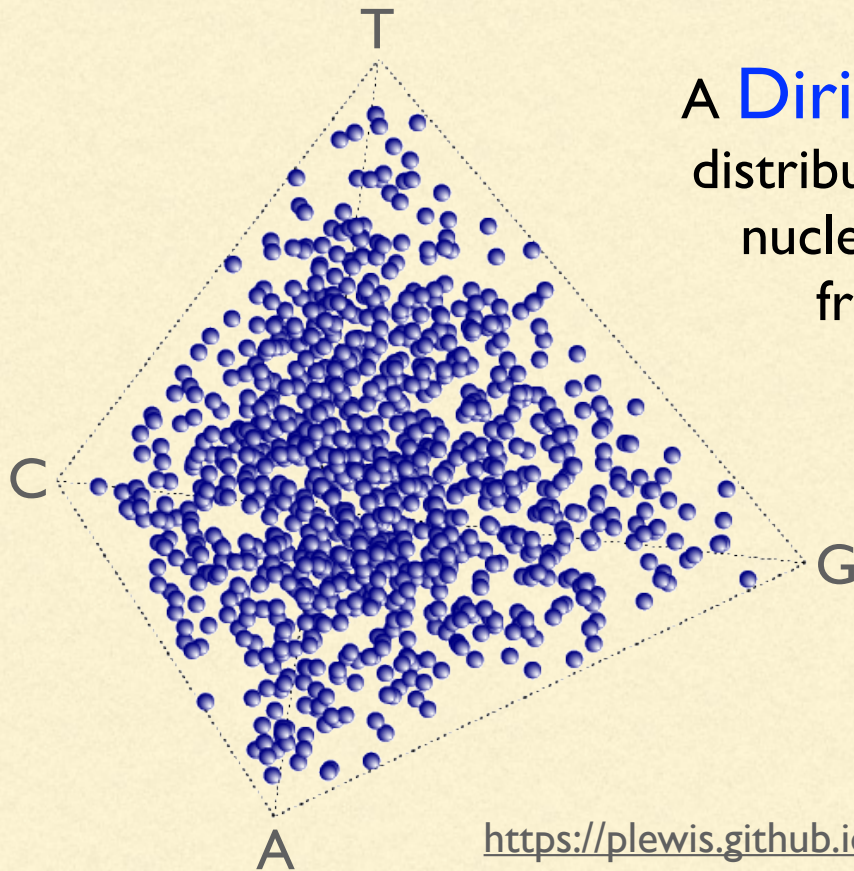
Beta(a,b) distribution

Beta(a,b) distributions are appropriate for proportions, which must lie between 0 and 1 (inclusive).

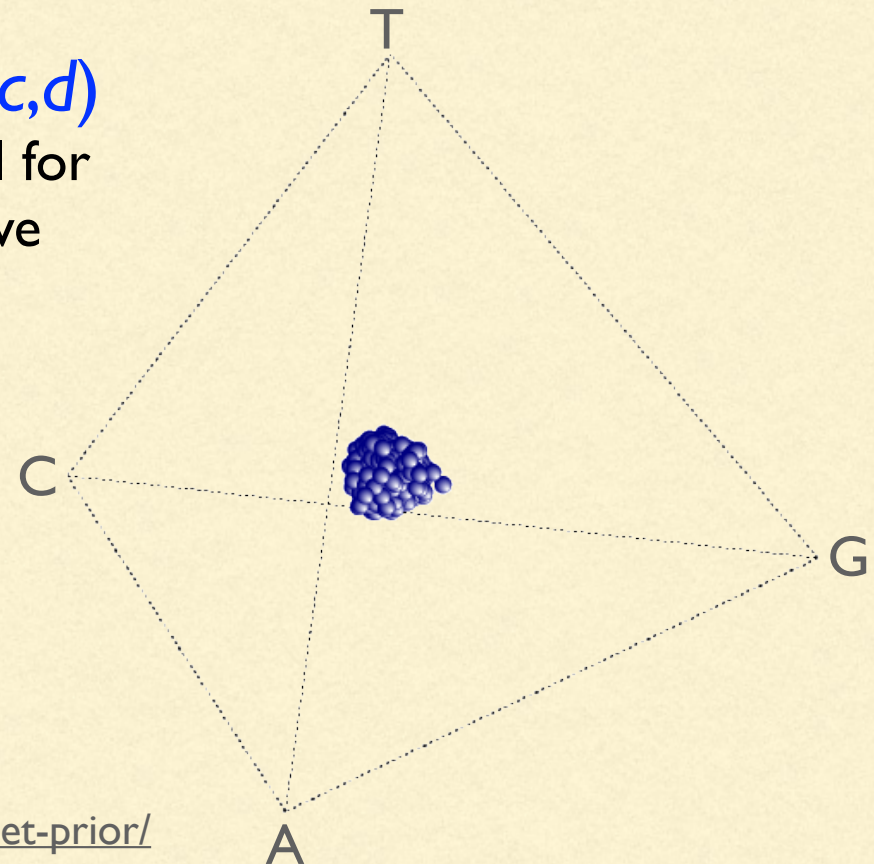


Dirichlet(a, b, c, d) distribution

Flat: $a = b = c = d = 1$
(every combination equally probable)



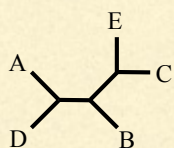
Informative: $a = b = c = d = 100$
(frequencies tend to be nearly equal)



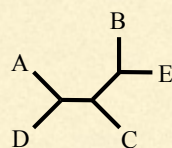
A **Dirichlet(a, b, c, d)** distribution is ideal for nucleotide relative frequencies.

<https://plewis.github.io/applets/dirichlet-prior/>

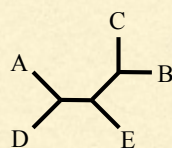
Topology: discrete uniform



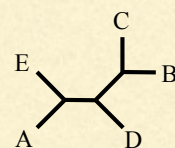
$$\frac{1}{15}$$



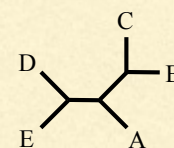
$$\frac{1}{15}$$



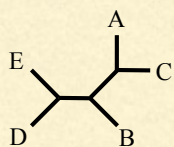
$$\frac{1}{15}$$



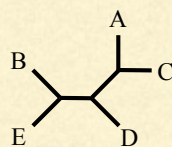
$$\frac{1}{15}$$



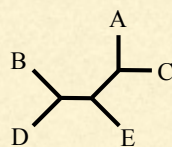
$$\frac{1}{15}$$



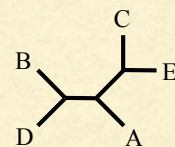
$$\frac{1}{15}$$



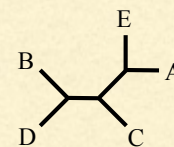
$$\frac{1}{15}$$



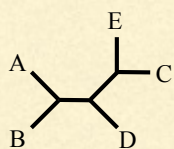
$$\frac{1}{15}$$



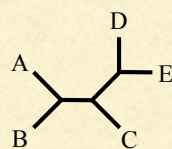
$$\frac{1}{15}$$



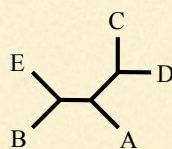
$$\frac{1}{15}$$



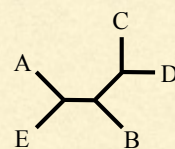
$$\frac{1}{15}$$



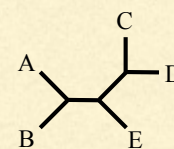
$$\frac{1}{15}$$



$$\frac{1}{15}$$

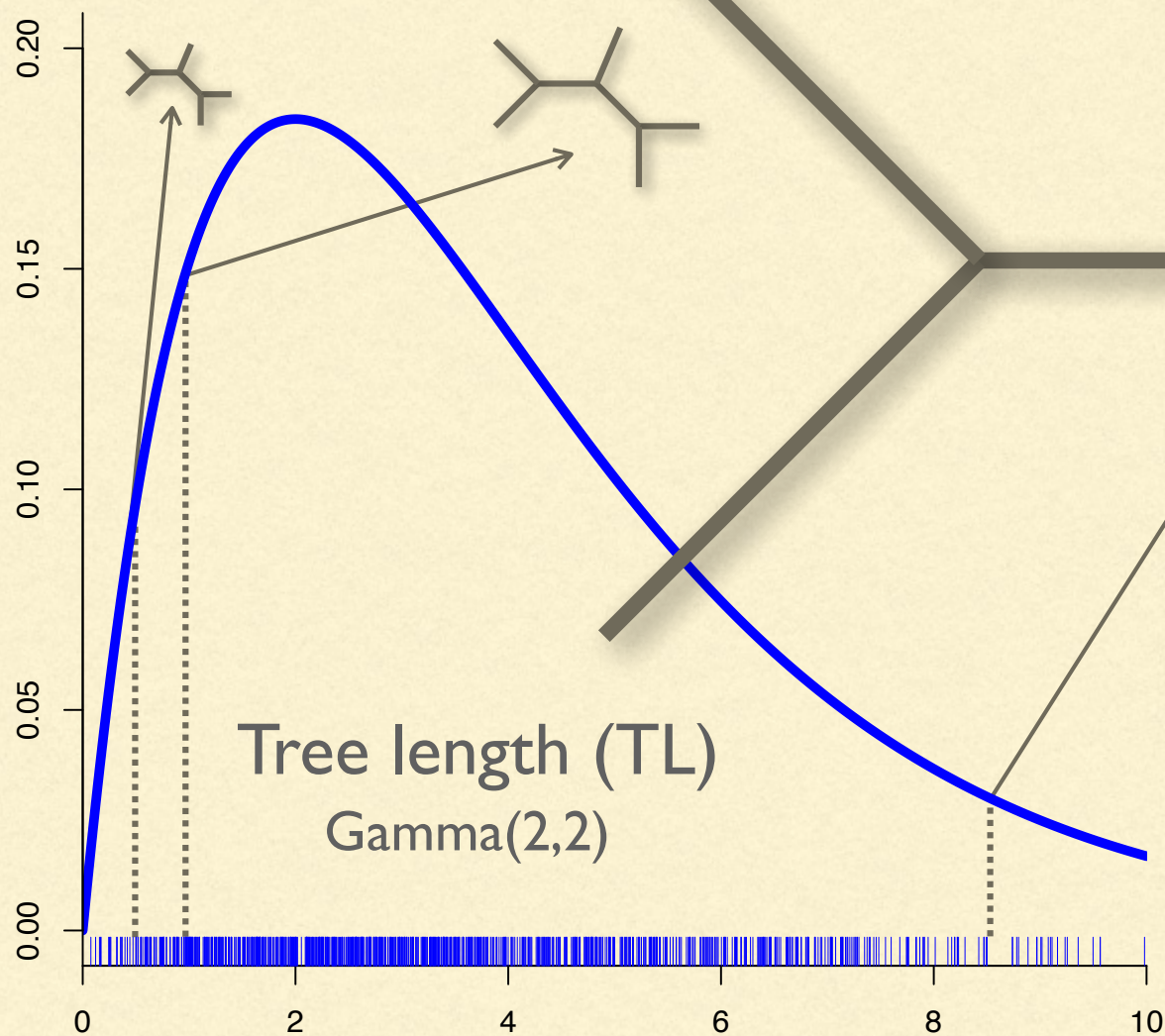


$$\frac{1}{15}$$

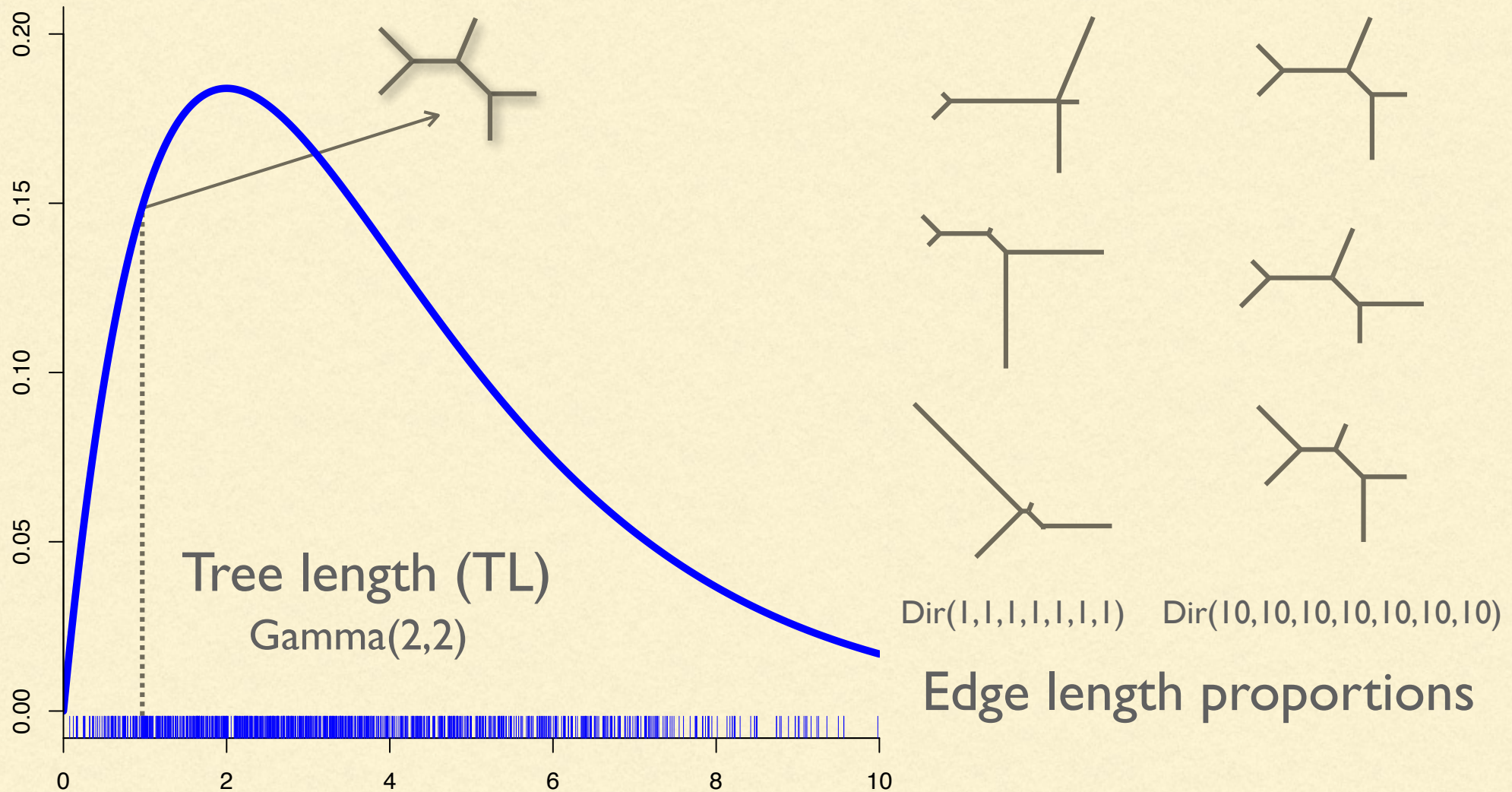


$$\frac{1}{15}$$

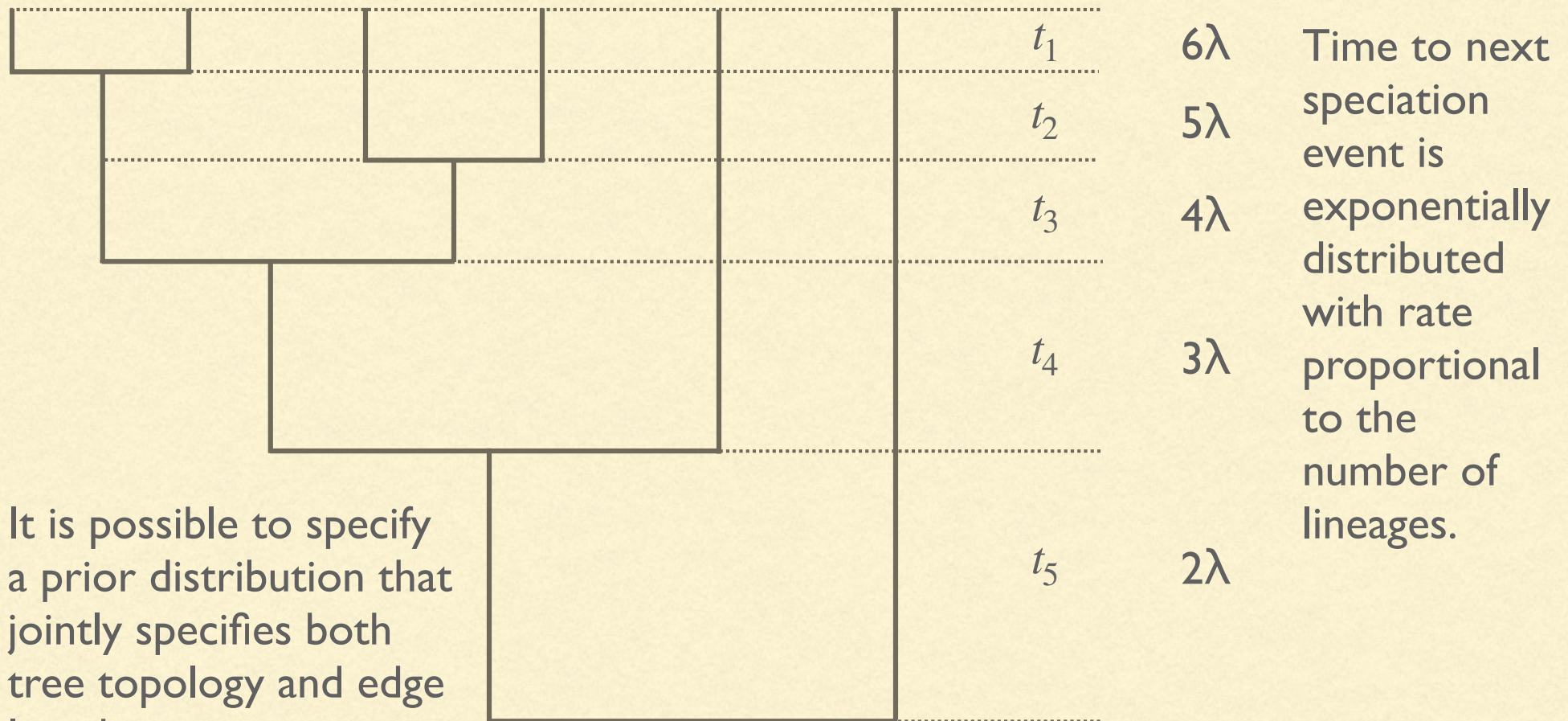
Edge lengths: Gamma-Dirichlet



Edge lengths: Gamma-Dirichlet



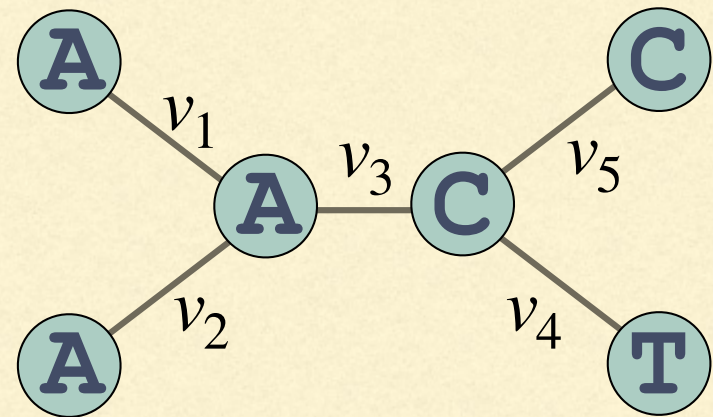
Yule (pure birth) prior



Hierarchical models

Non-hierarchical model

All model parameters can be found in the likelihood function



Prior mean 0.1

$$L_k = \frac{1}{4} \left(\frac{1}{4} + \frac{3}{4} e^{-4v_1/3} \right) \left(\frac{1}{4} + \frac{3}{4} e^{-4v_2/3} \right) \left(\frac{1}{4} - \frac{1}{4} e^{-4v_3/3} \right) \left(\frac{1}{4} - \frac{1}{4} e^{-4v_4/3} \right) \left(\frac{1}{4} + \frac{3}{4} e^{-4v_5/3} \right)$$

JC69 likelihood for site k

Hierarchical model

A prior for a hyperparameter is a hyperprior

μ is a hyperparameter

Hyperprior



Prior mean μ

Some model parameters (hyperparameters) are **outside** the likelihood function

$$L_k = \frac{1}{4} \left(\frac{1}{4} + \frac{3}{4} e^{-4v_1/3} \right) \left(\frac{1}{4} + \frac{3}{4} e^{-4v_2/3} \right) \left(\frac{1}{4} - \frac{1}{4} e^{-4v_3/3} \right) \left(\frac{1}{4} - \frac{1}{4} e^{-4v_4/3} \right) \left(\frac{1}{4} + \frac{3}{4} e^{-4v_5/3} \right)$$

JC69 likelihood for site k

Empirical Bayes

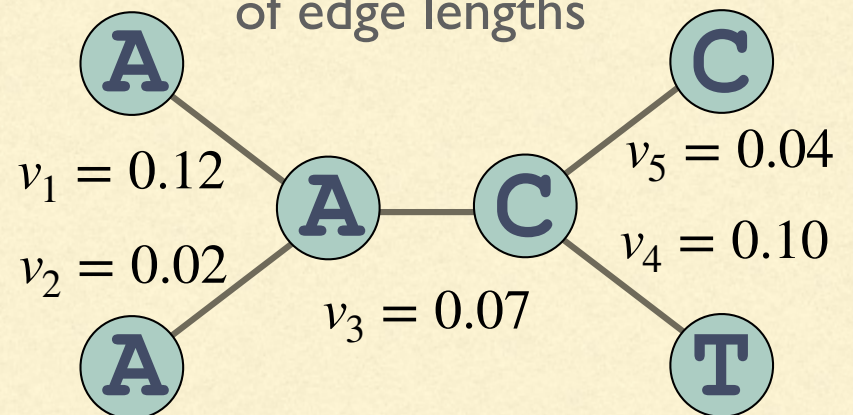
Empirical Bayes approach

Average edge length MLE used as the mean of the prior.

$$0.07 = (0.12 + 0.02 + 0.07 + 0.04 + 0.10) / 5$$

Prior mean = 0.07

Maximum likelihood estimates (MLEs) of edge lengths



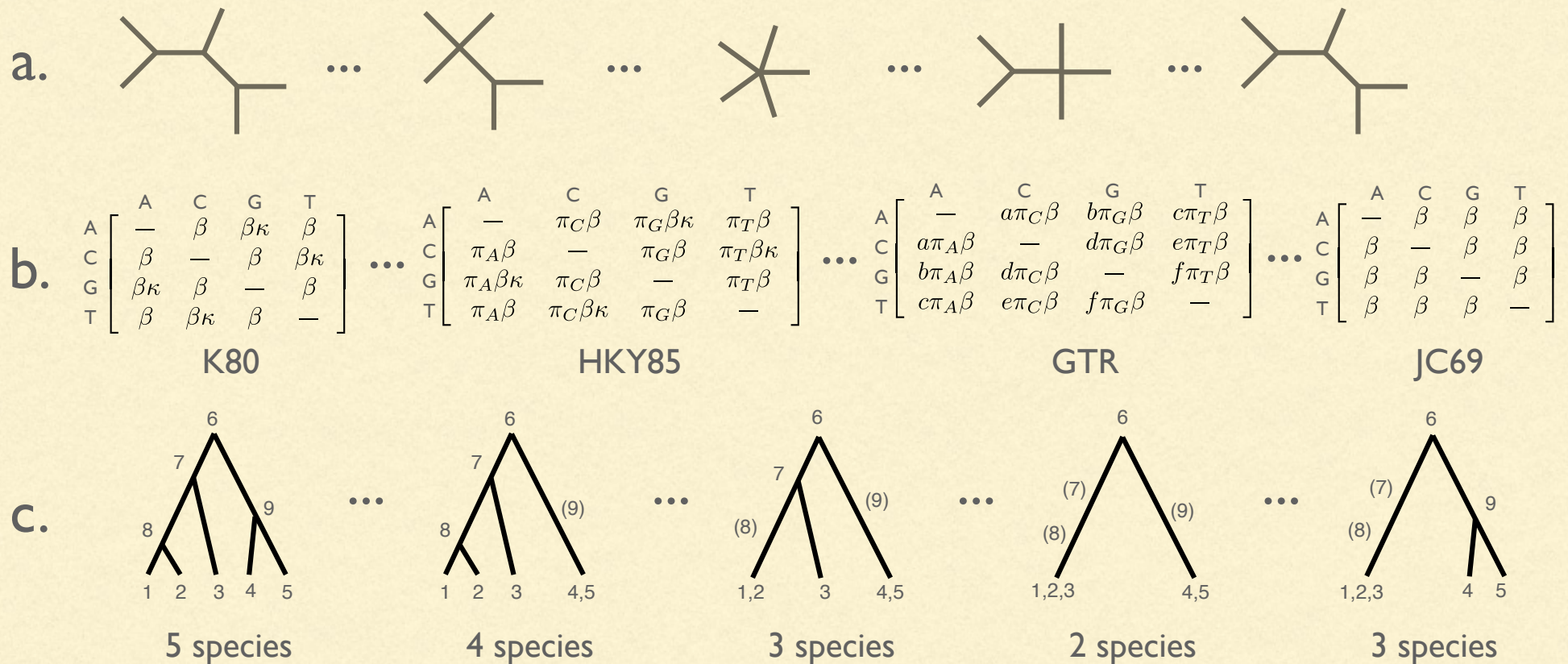
$$L_k = \frac{1}{4} \left(\frac{1}{4} + \frac{3}{4} e^{-4v_1/3} \right) \left(\frac{1}{4} + \frac{3}{4} e^{-4v_2/3} \right) \left(\frac{1}{4} - \frac{1}{4} e^{-4v_3/3} \right) \left(\frac{1}{4} - \frac{1}{4} e^{-4v_4/3} \right) \left(\frac{1}{4} + \frac{3}{4} e^{-4v_5/3} \right)$$

JC69 likelihood for site k

rjMCMC

(reversible-jump MCMC)

Examples of rjMCMC analyses

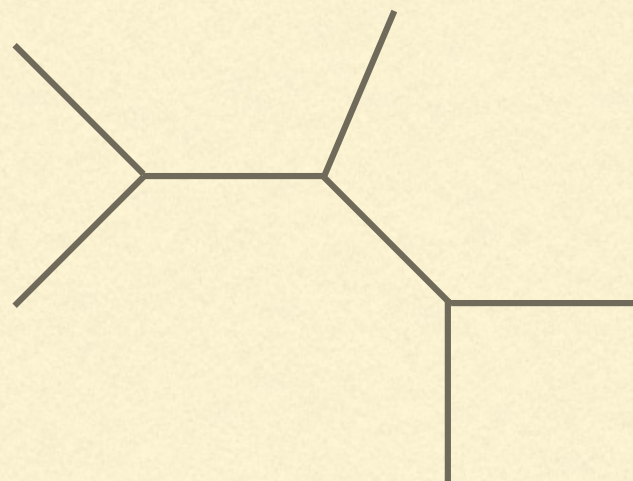


a. Lewis, Holder, & Holsinger. 2005.
Systematic Biology 54:241–253.

b. Huelsenbeck, Larget, & Alfaro. 2004.
Molecular Biology and Evolution 21:1123–1133.

c. Rannala & Yang. 2013.
Genetics 194:245–253.

rjMCMC polytomy model



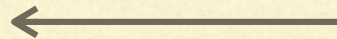
7 edge lengths

a. choose 1 of 2 edges
to delete

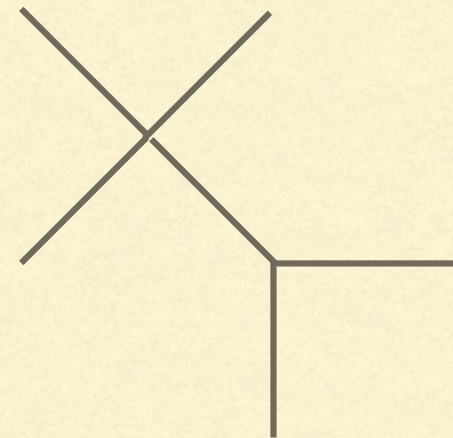


forward

reverse



a. choose 1 of 1 polytomies
in which to insert an edge
b. invent a new edge length
to go with the new edge



6 edge lengths

The probability of accepting the forward proposal must take into account the proposal that exactly reverses it to ensure that at equilibrium the chain visits each model with the appropriate frequency

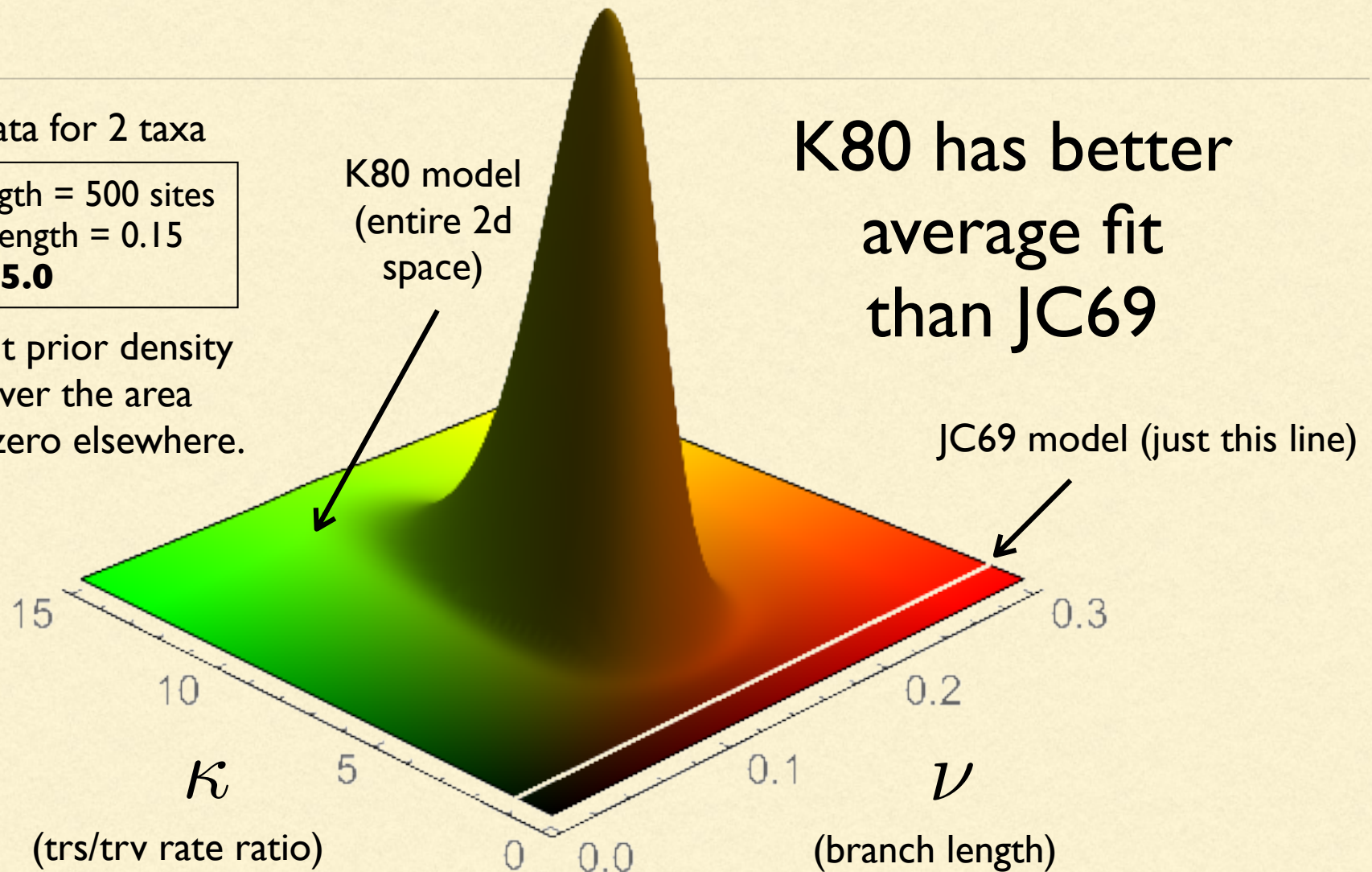
Bayes' factors

Likelihood surface when K80 true

Simulated data for 2 taxa

sequence length = 500 sites
true branch length = 0.15
true kappa = **5.0**

Assume joint prior density
is uniform over the area
shown and zero elsewhere.

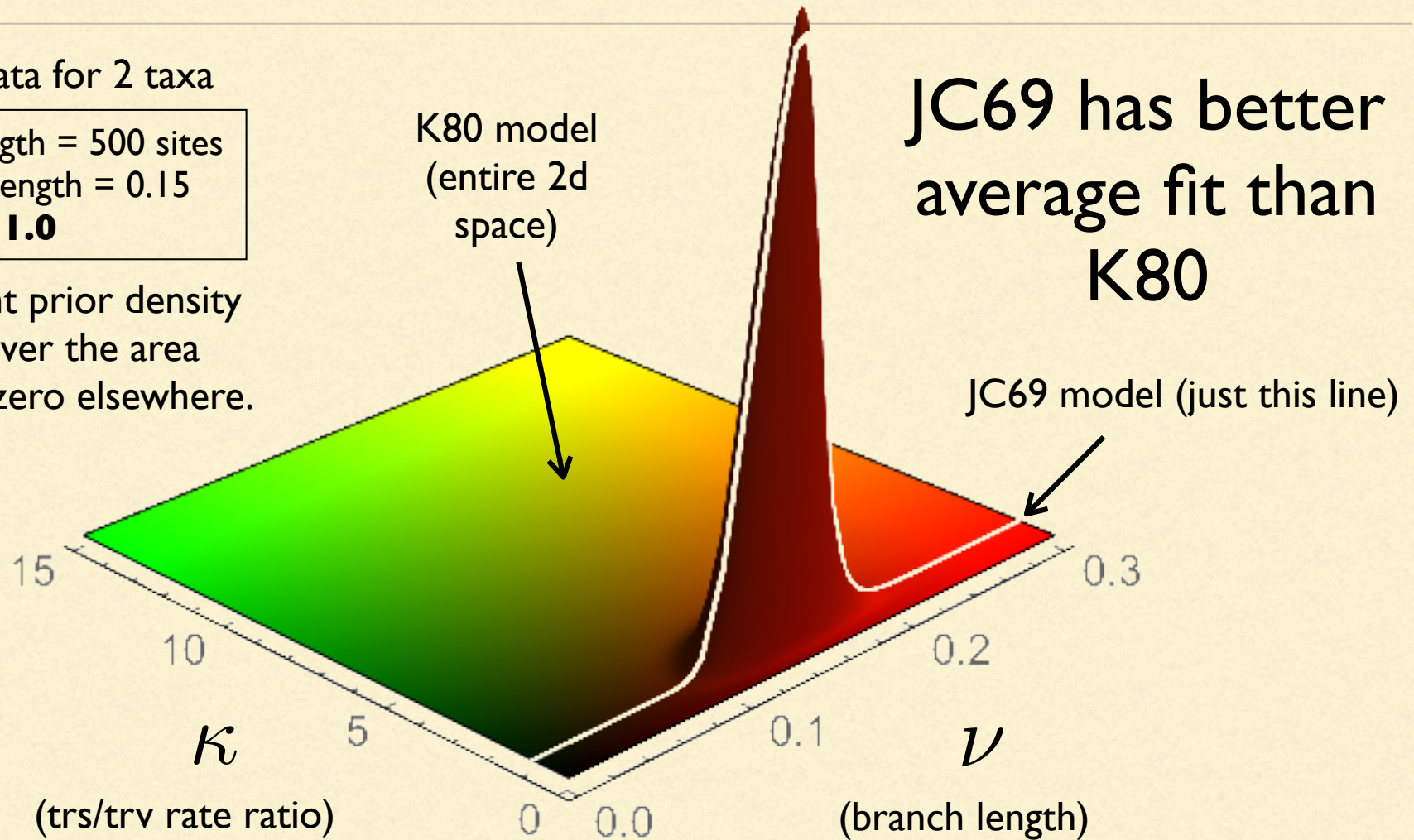


Likelihood surface when JC69 true

Simulated data for 2 taxa

sequence length = 500 sites
true branch length = 0.15
true kappa = **1.0**

Assume joint prior density
is uniform over the area
shown and zero elsewhere.



Marginal likelihood and model fit

Bayes' rule:
$$p(\theta | D, M) = \frac{p(D | \theta, M) p(\theta | M)}{p(D | M)}$$

MCMC does not require $p(D|M)$.

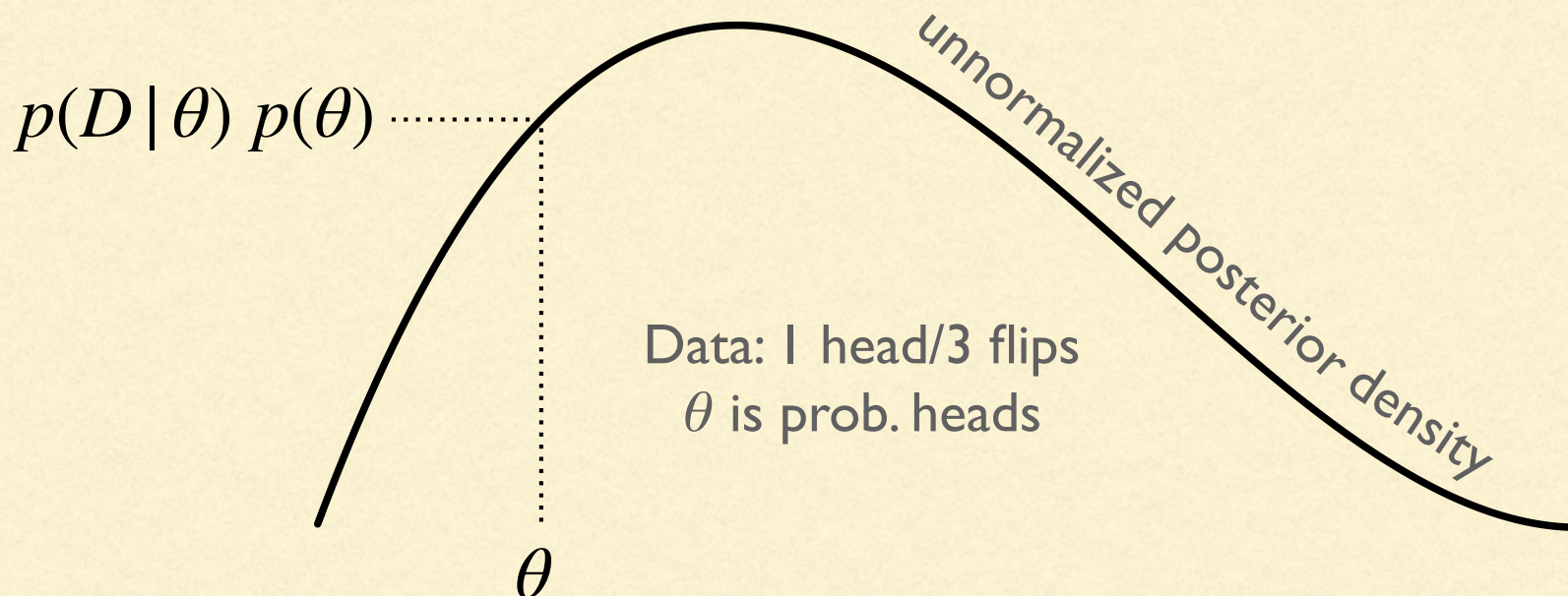
$p(D|M)$ measures the average fit of model M to data D and is thus very useful for model choice.

So we need to estimate $p(D|M)$ after all in order to choose amongst competing models.

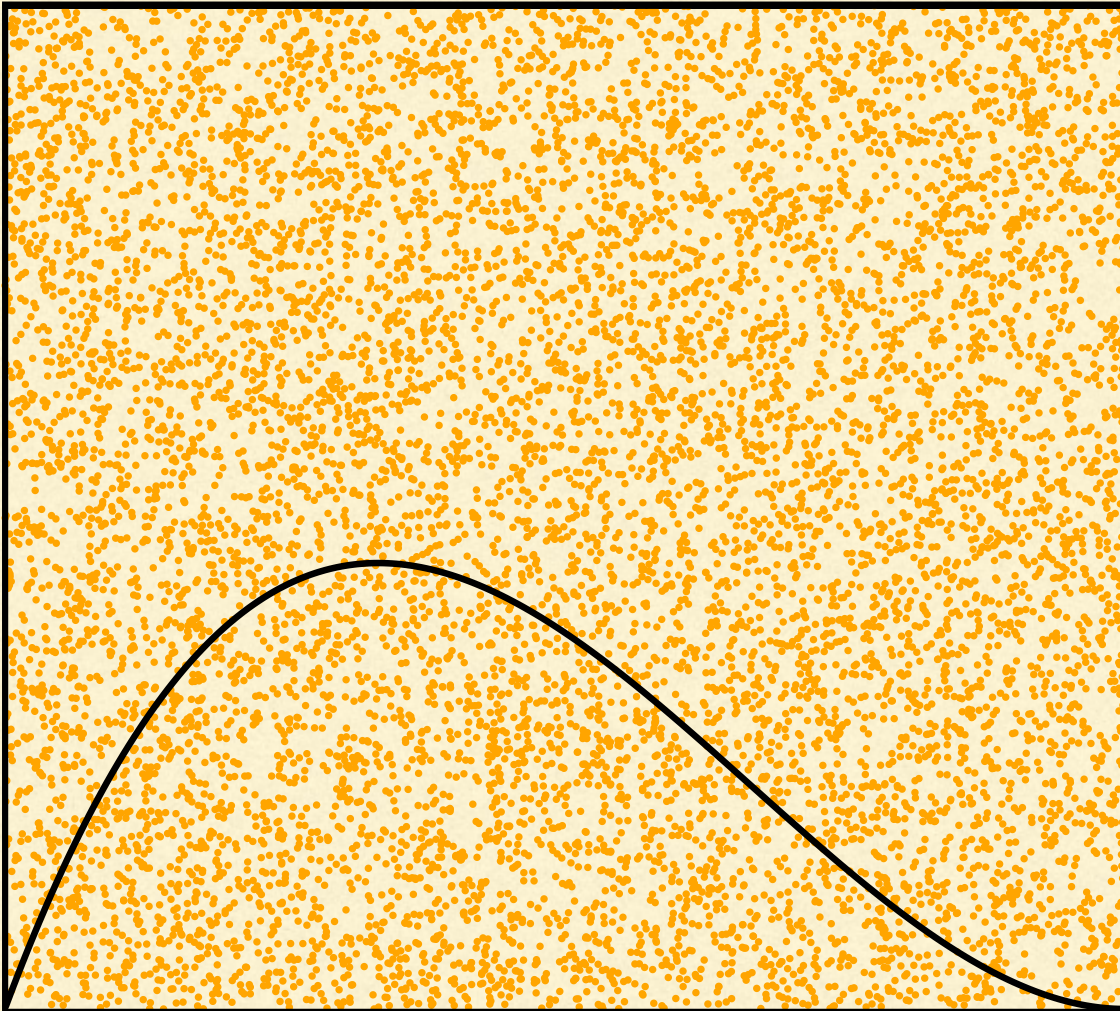
Marginal likelihood estimation

$$p(D) = \int p(D | \theta) p(\theta) d\theta$$

Estimating $p(D)$ is equivalent to estimating the area under the curve whose height is, for every value of θ , equal to $p(D|\theta) p(\theta)$



Simplest method



Sample evenly from a box with known area A that completely encloses the curve.

Area under the curve is just A times the fraction of sampled points that lie under the curve.

2567 = under curve

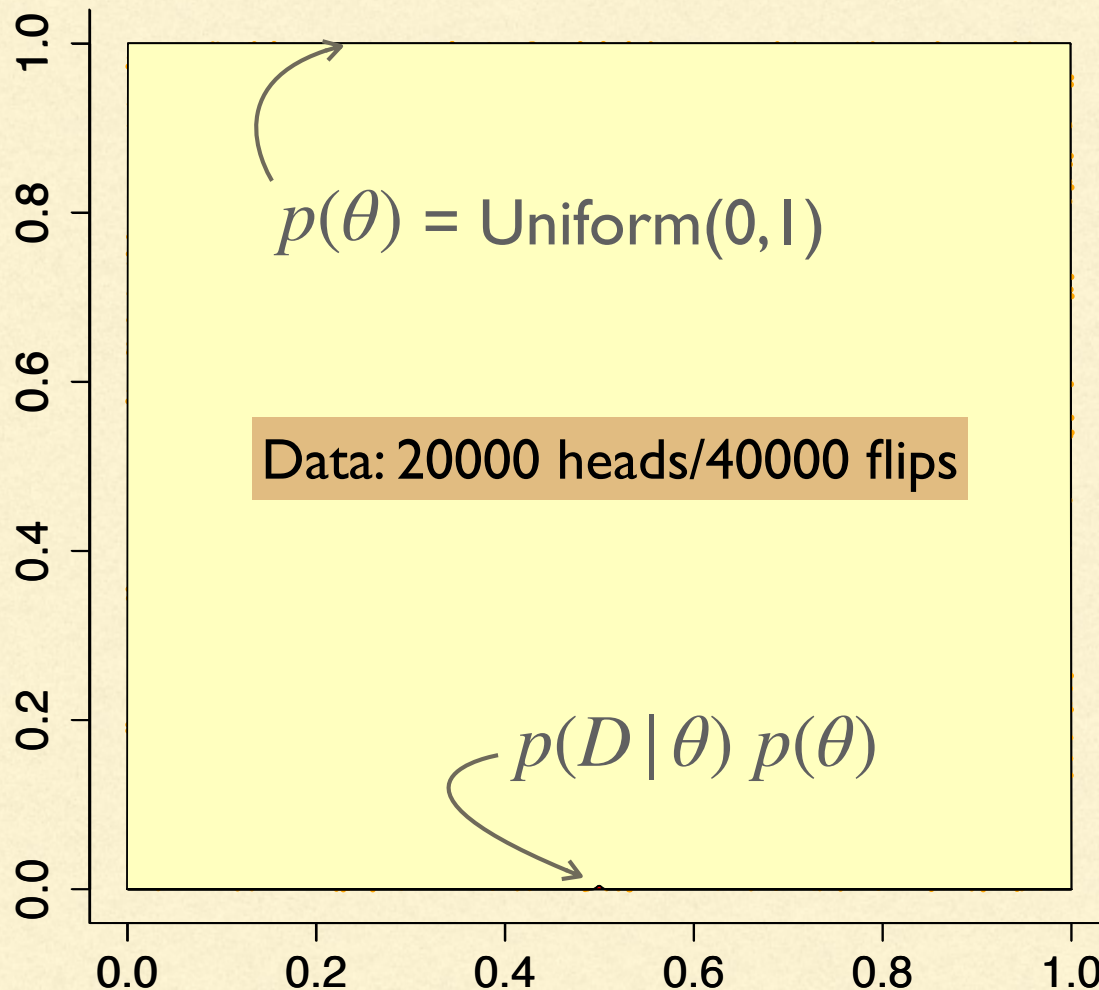
10000 = inside box

1.0 = area of box

0.2567 = estimated value

0.2500 = true value

With much more data, things get complicated

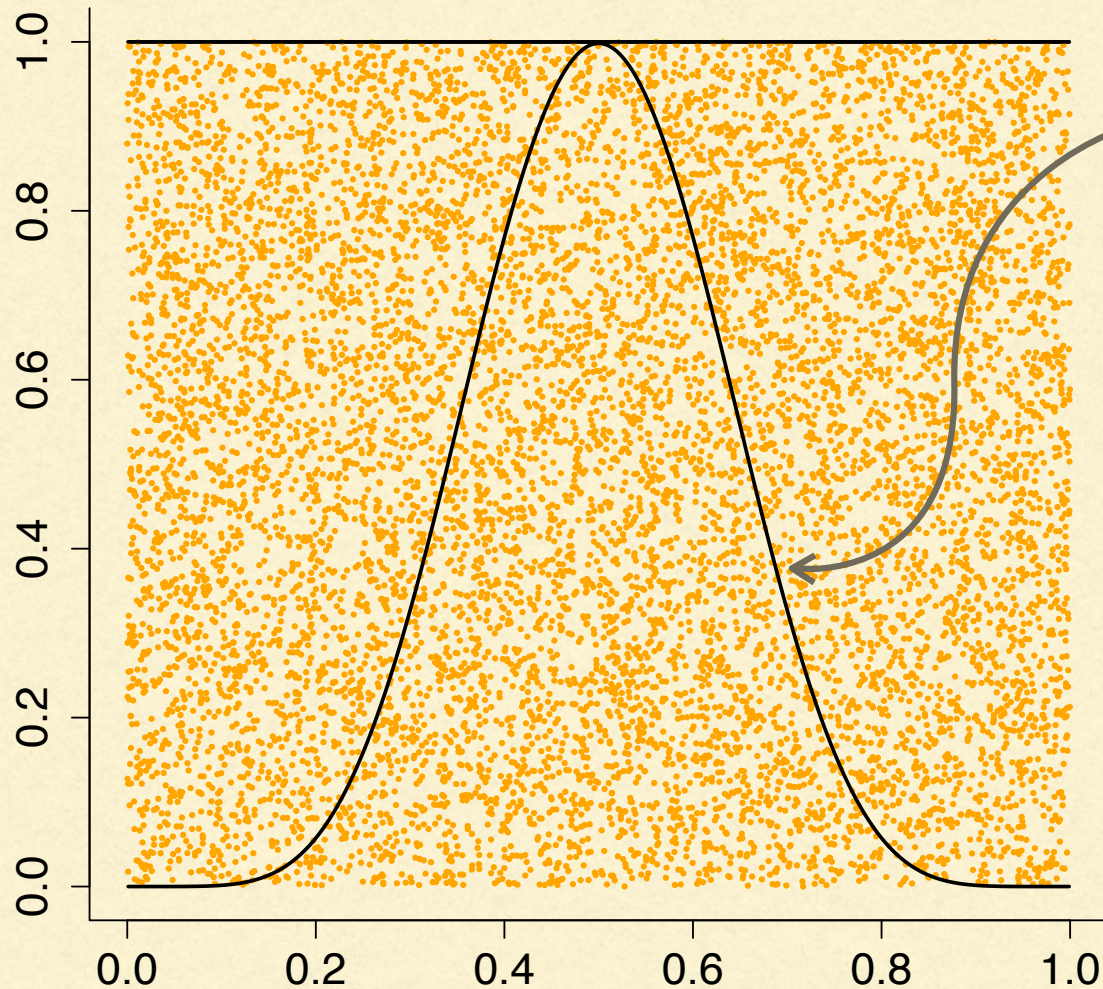


The prior density can serve as our box. It has area 1.0 and is everywhere higher than the posterior *kernel* (likelihood times prior density).

Problem: with lot of data, posterior kernel is minuscule compared to prior.

In fact, of 10000 darts thrown at the prior, 0 fell beneath the posterior kernel (that little bump along the bottom)

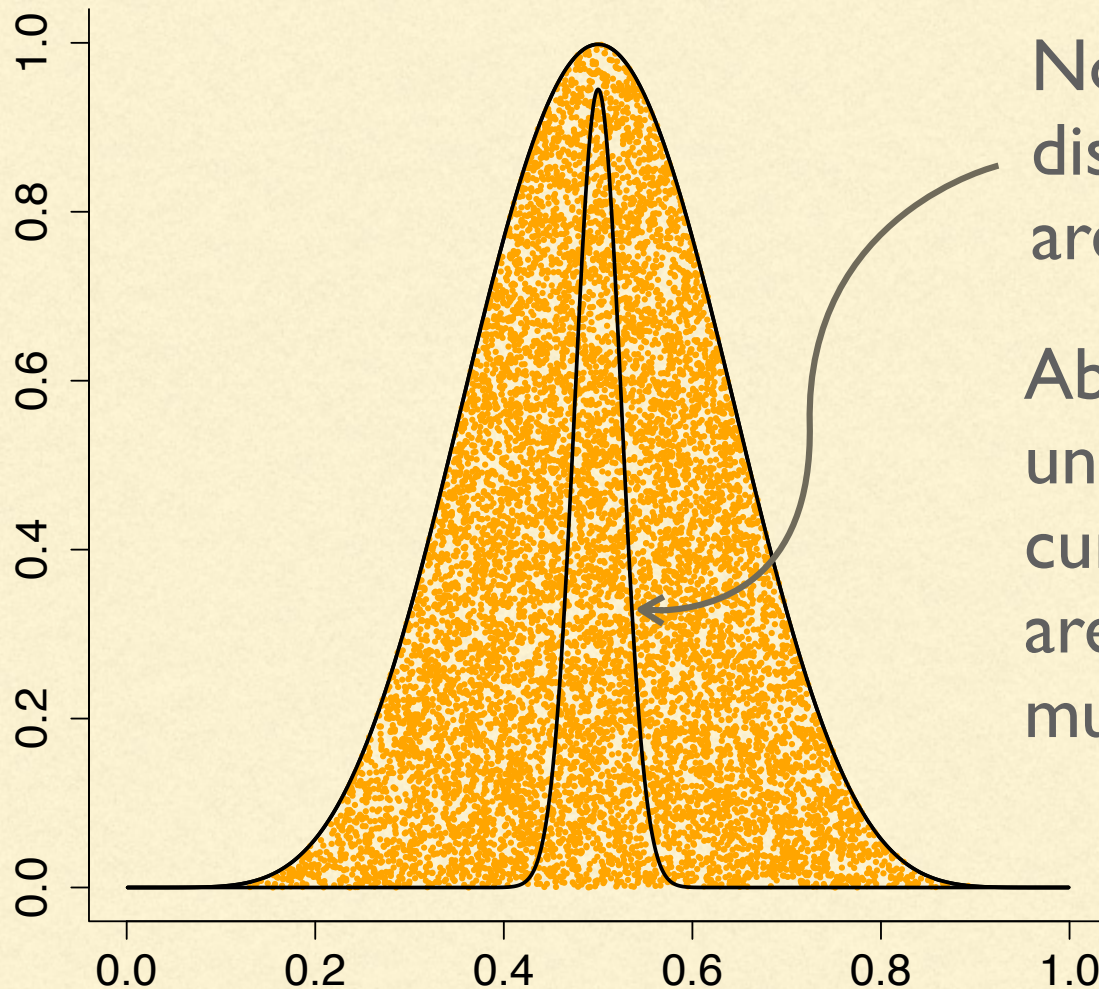
Solution, create stepping stones



Start by estimating the area under this curve (also everywhere higher than the posterior kernel).

About 33% of the darts thrown at the larger box (which has area 1.0) fall under the inner curve, so the area under the inner curve must be about 0.33

Solution, create stepping stones

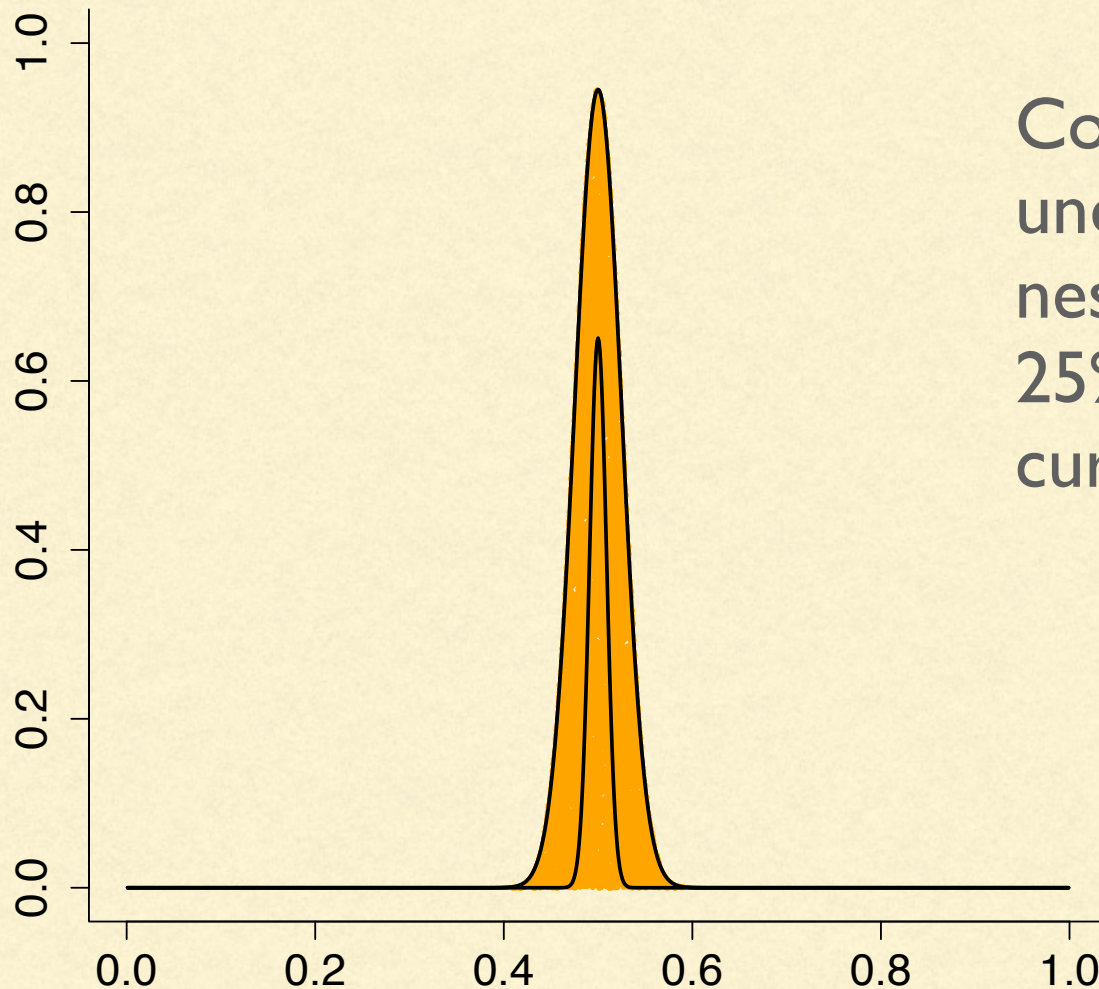


Now throw darts at the inner distribution and estimate the area under this curve

About 5.8% of the points fall under the inner, nested curve, so we know that the area under that nested curve must be

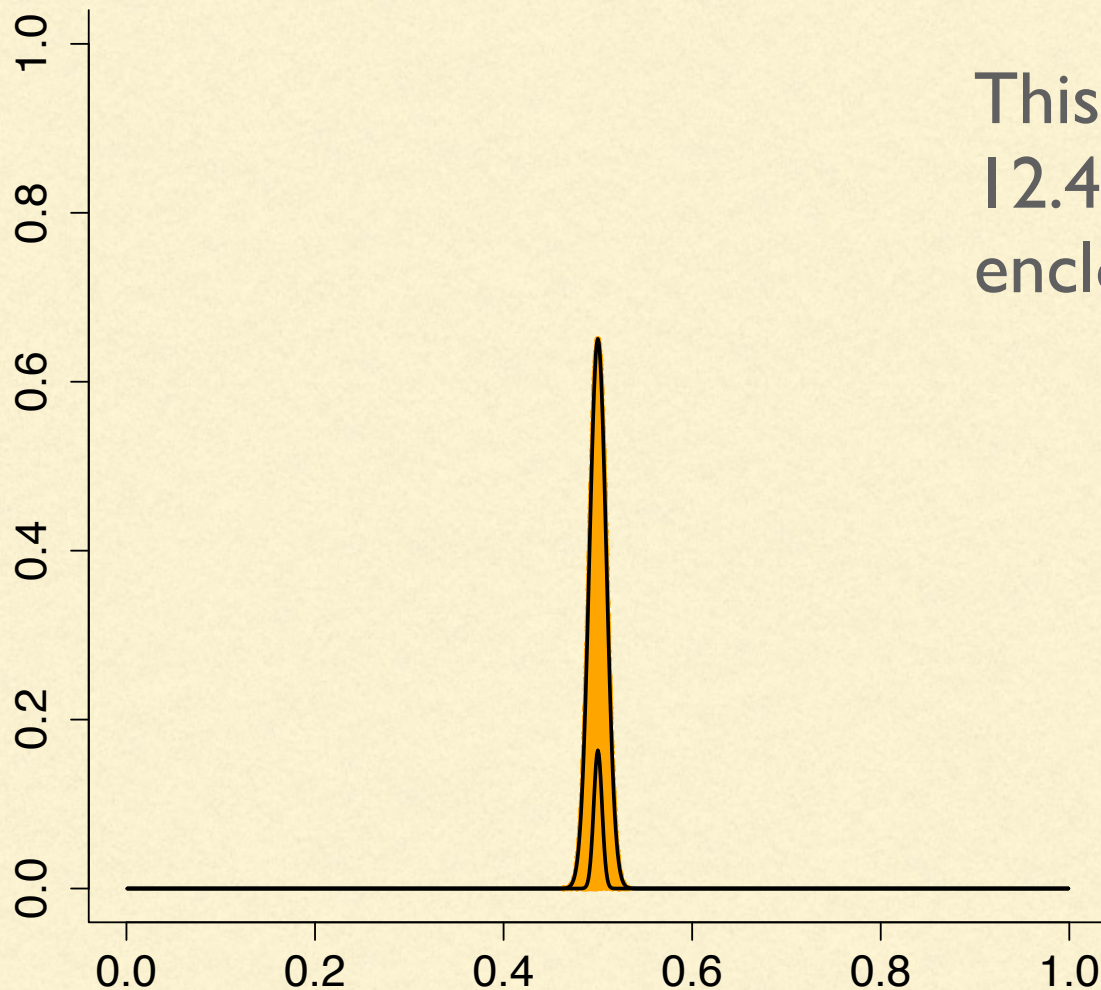
$$(1.0)(0.330)(0.058) = 0.019$$

Solution, create stepping stones



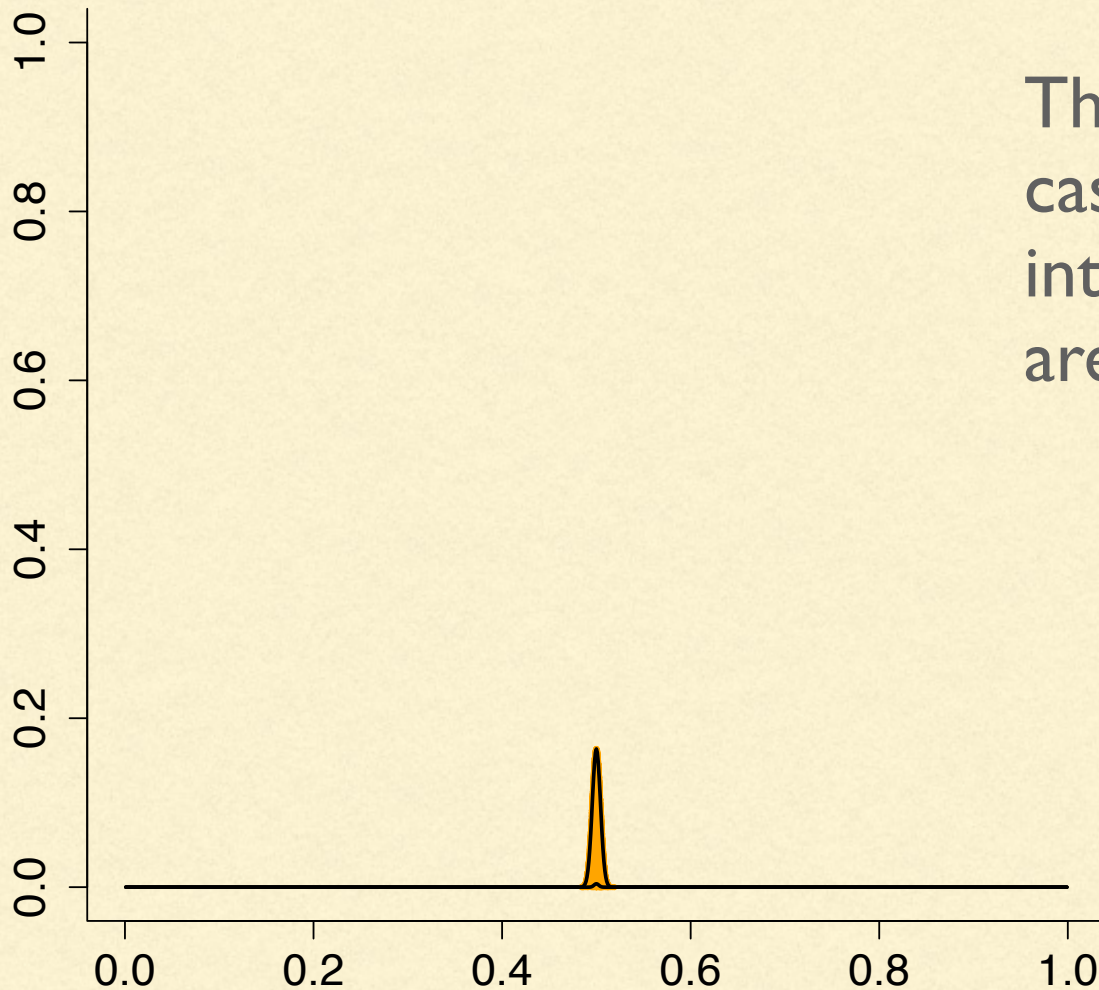
Continue estimating the area under nested curves. The nested one here has about 25% of the area of the outer curve.

Solution, create stepping stones



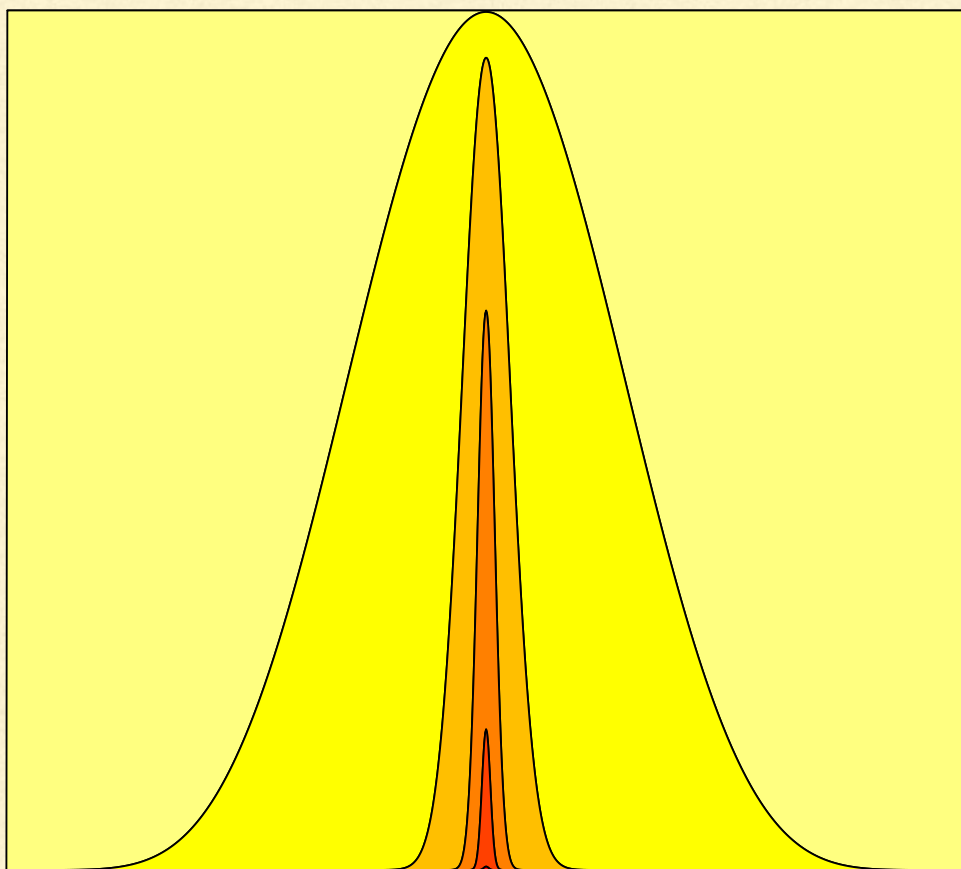
This nested curve has about 12.4% of the area of its enclosing curve

Solution, create stepping stones



The nested curve is, in this case, equal to the curve of interest, and has 1.4% of the area of its enclosing curve

Solution, create stepping stones



We've broken up the estimation of the area under the posterior kernel into a series of 5 area estimations:

$$\frac{a}{g} = \left(\frac{a}{\cancel{b}} \right) \left(\frac{\cancel{b}}{\cancel{c}} \right) \left(\frac{\cancel{c}}{\cancel{d}} \right) \left(\frac{\cancel{d}}{\cancel{f}} \right) \left(\frac{\cancel{f}}{g} \right)$$

a = area under posterior kernel

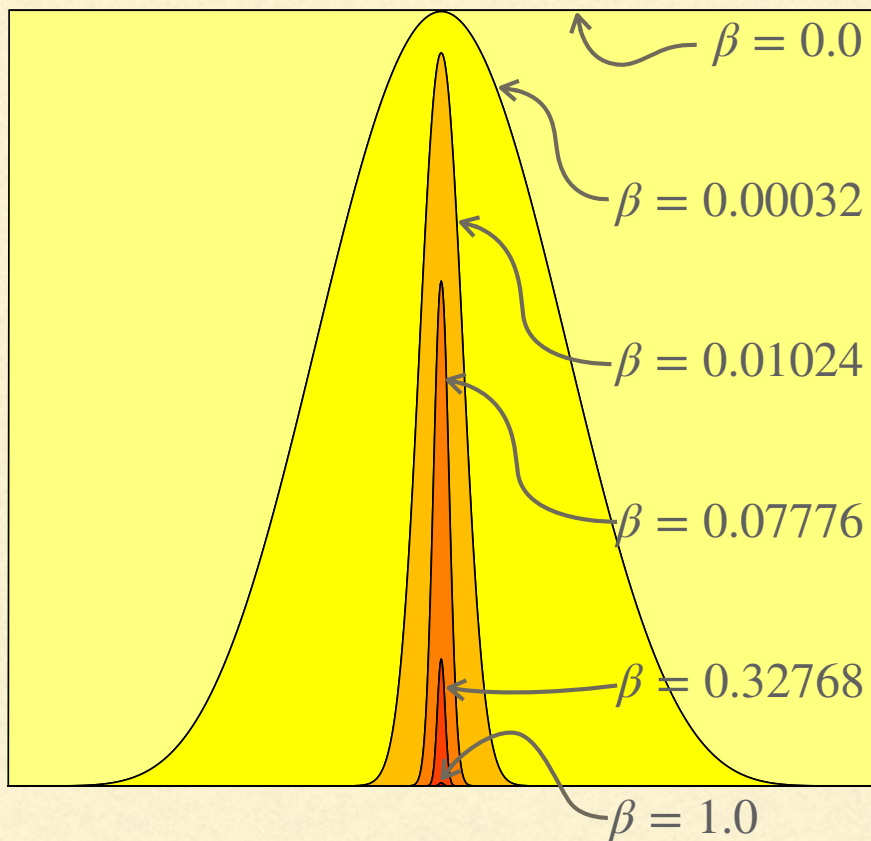
g = area under the prior = 1.0

0.000025 | estimated

0.0000250 true

Stepping-stone method

How can we choose the intermediate density functions that serve as stepping stones?



Power posterior kernel:

$$p(D | \theta)^\beta p(\theta)$$

$\beta = 1$ posterior kernel

$0 < \beta < 1$ intermediate

$\beta = 0$ prior density

Bayes factor for M_0 against M_1

$$B_{01} = \frac{p(D | M_0)}{p(D | M_1)} = \frac{\text{marginal likelihood for model } M_0}{\text{marginal likelihood for model } M_1}$$

Normally, both marginal likelihoods are on the log scale, so usually it is the (natural) log Bayes factor that is reported:

$$\log B_{01} = \log p(D | M_0) - \log p(D | M_1)$$

Dirichlet process (DP) prior

all genes share same tree topology

ABCD

ABC

D

ABD

C

AB

CD

AB

C

D

ACD

B

AC

BD

AC

B

D

AD

BC

A

BCD

A

BC

D

AD

B

C

A

BD

C

A

B

CD

A

B

C

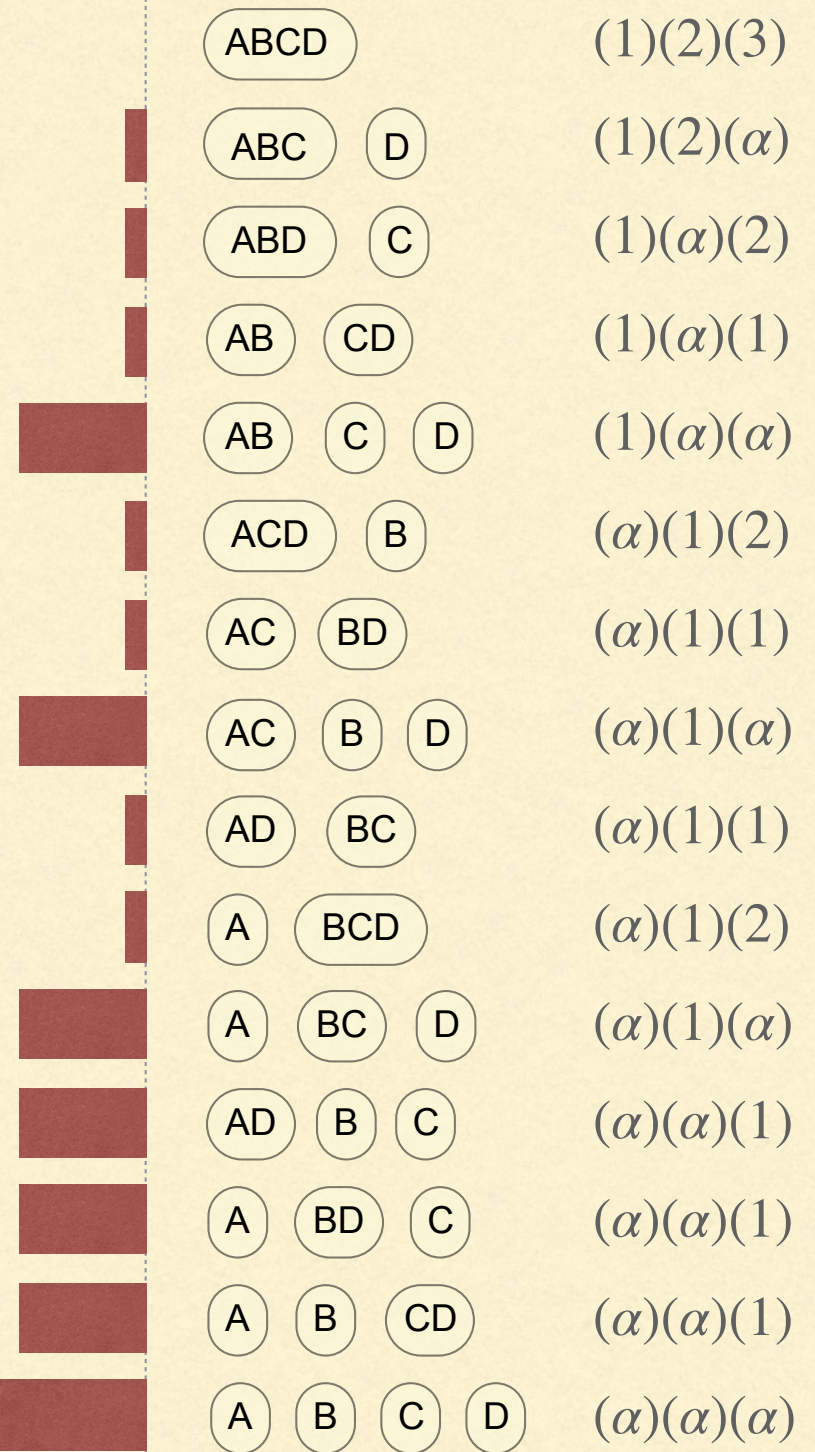
D

Suppose we have data for 4 genes:
A, B, C, D

Would like a prior that
encourages concordance (i.e.
genes have same tree topology)
but allows discordance

each gene has a different tree topology

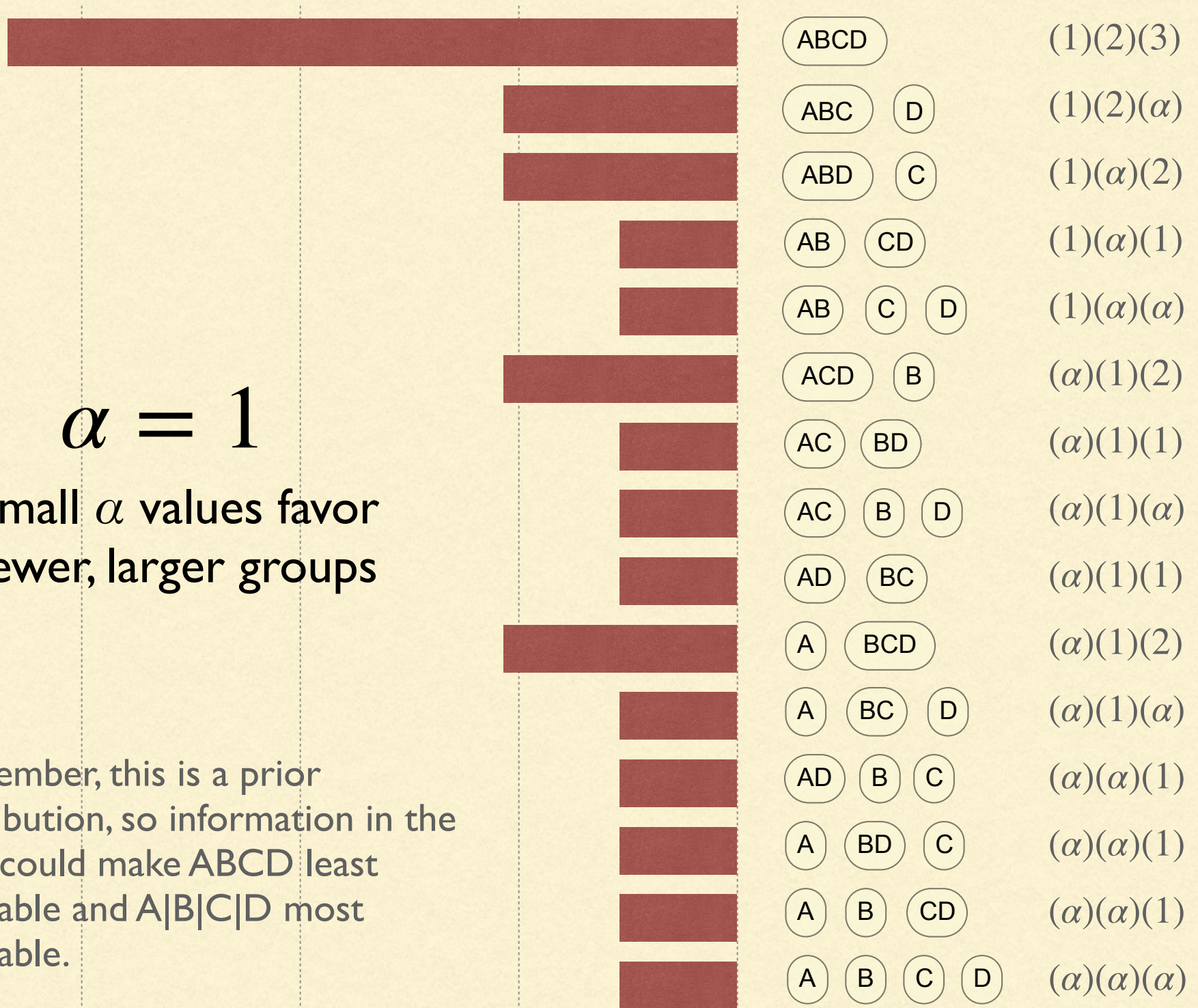
$\alpha = 10$
 Large α values favor
 more, smaller groups



$$\alpha = 1$$

Small α values favor fewer, larger groups

Remember, this is a prior distribution, so information in the data could make ABCD least probable and A|B|C|D most probable.



Dirichlet Process Prior applet

<https://plewis.github.io/applets/dpp/>