

# Bayesian Inference and MCMC

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(With thanks to Mark Holder and Paul Lewis for slides!)

# Usually there are many parameters...

A 2-parameter example

$$f(\theta, \phi | D) = \frac{f(D | \theta, \phi) f(\theta) f(\phi)}{\int_{\theta} \int_{\phi} f(D | \theta, \phi) f(\theta) f(\phi) d\theta d\phi}$$

Diagram illustrating the components of the Bayesian formula for a 2-parameter example:

- Likelihood**:  $f(D | \theta, \phi)$  (indicated by a double-headed arrow above the numerator)
- Prior probability density**:  $f(\theta) f(\phi)$  (indicated by a double-headed arrow above the numerator)
- Marginal probability of data**:  $\int_{\theta} \int_{\phi} f(D | \theta, \phi) f(\theta) f(\phi) d\theta d\phi$  (indicated by a double-headed arrow below the denominator)
- Posterior probability density**:  $f(\theta, \phi | D)$  (indicated by an upward arrow from the label to the left side of the equation)

An analysis of **100 sequences** under the simplest model (JC69) requires 197 branch length parameters. The denominator is a **197-fold integral** in this case! Now consider summing over **all possible tree topologies**! It would thus be nice to avoid having to calculate the marginal probability of the data...

## Markov Chain Monte Carlo (MCMC)

- ▶ **Monte Carlo** - stochastic
- ▶ **Markovian** - present state depends only on the previous state and no other state

# Markov chain Monte Carlo

- Simulates a walk through parameter/tree space.
- Lets us estimate posterior probabilities for any aspect of the model
- Relies on the *ratio* of posterior densities between two points

$$R = \frac{Pr(\text{Point}_2|\text{Data})}{Pr(\text{Point}_1|\text{Data})}$$

$$R = \frac{\frac{Pr(\text{Point}_2)L(\text{Point}_2)}{Pr(\text{Data})}}{\frac{Pr(\text{Point}_1)L(\text{Point}_1)}{Pr(\text{Data})}}$$

$$R = \frac{Pr(\text{Point}_2)L(\text{Point}_2)}{Pr(\text{Point}_1)L(\text{Point}_1)}$$

We can avoid calculating the prior probability of the data!

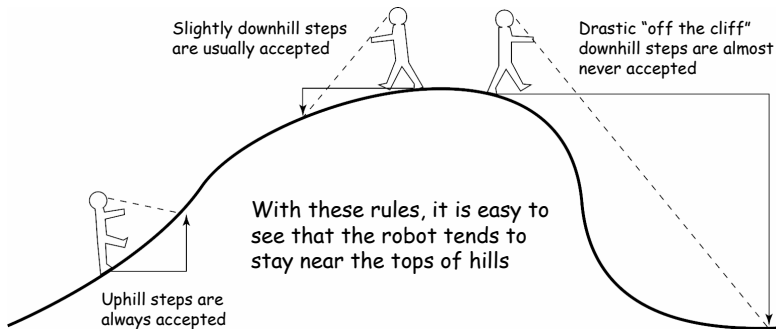
```
CAGCAGGTTACCTGCAAGGGGAAGCCCATCCACCATTCTTGGCAC-
CACCAGATTTACATGCAAGGGCAAACAGTCCACCATTCTTGAACAC-
CAGCAGGTTTACCTGCAAAGGGGAAGCCTATTCTTCACTTCATGGGAAC-
CAGCAGGTTTACCTGCAAAGGGAAAACAGTTTACCATTTCTTGGAAC-
CAGCAGGTTTACCTGCAAGGGGAAATCAATATATCACTTTGGTAATAC-
```

We can avoid calculating the prior probability of the data!

```
CAGCAGGTTACCTGCAGAGGGGAAGCCCATCCACCATTCTTGGCAC-  
CACCAGATTTACATGCAAGGGCAAACCCAGTCCACCATTGATGAACAC-  
CAGCAGGTTTACCTGCAAAAGGGAAGCCTATTCTTCAC TTCATGGGAAC  
CAGCAGGTTTACCTGCAAAAGGAAAAACAGTTTACCATTTCTTTGGAAC-  
CAGCAGGTTTACCTGCAAGGGAAAAATCAATATATCACTTTGGTAATAC-
```

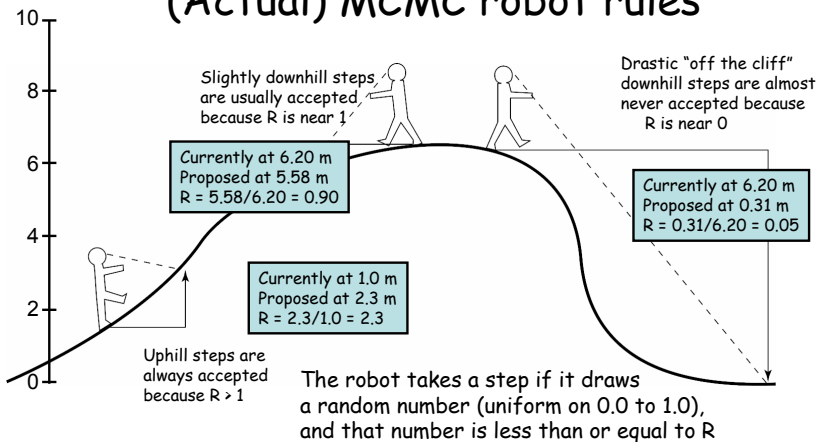
Imagine using a robot to survey a landscape...

# MCMC robot's rules





# (Actual) MCMC robot rules

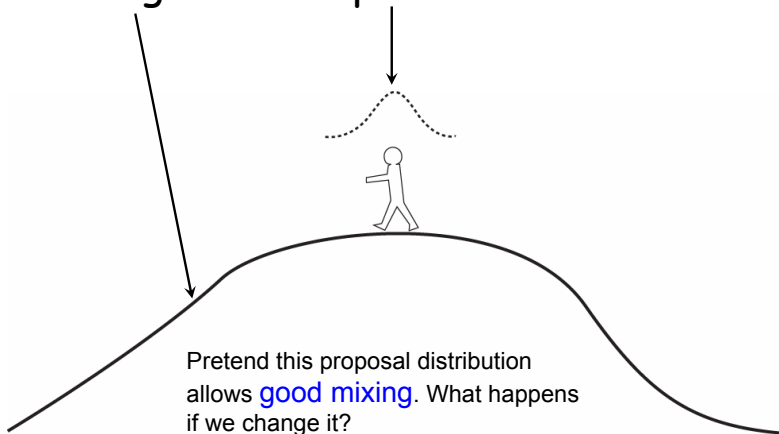


# Target vs. proposal distributions

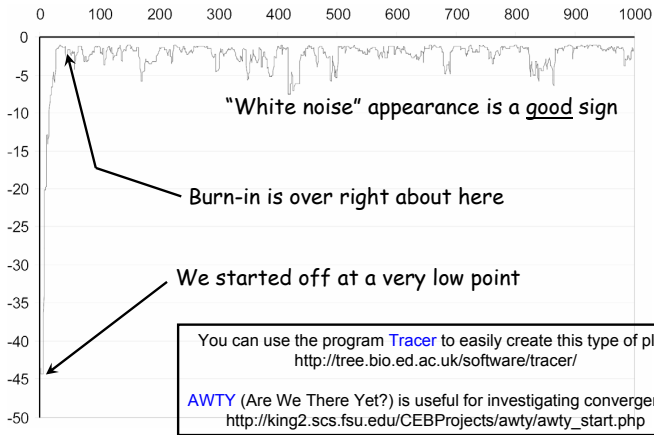
- The target distribution is the posterior distribution of interest
- The proposal distribution is used to decide which point to try next
  - you have much flexibility here, and the choice affects only the **efficiency** of the MCMC algorithm
  - MCMC using a **symmetric** proposal distribution is the Metropolis algorithm (Metropolis et al. 1953)
  - Use of an **asymmetric** proposal distribution requires a modification proposed by Hastings (1970), and is known as the Metropolis-Hastings algorithm

Metropolis, N., A. W. Rosenbluth, M. N. Rosenbluth, A. H. Teller, and E. Teller. 1953. Equation of state calculations by fast computing machines. J. Chem. Phys. 21:1087-1092.

# Target vs. Proposal Distributions



# Trace plots



# Target vs. Proposal Distributions

Proposal distributions  
with **smaller variance**...



**Disadvantage:** robot takes smaller steps, more time required to explore the same area



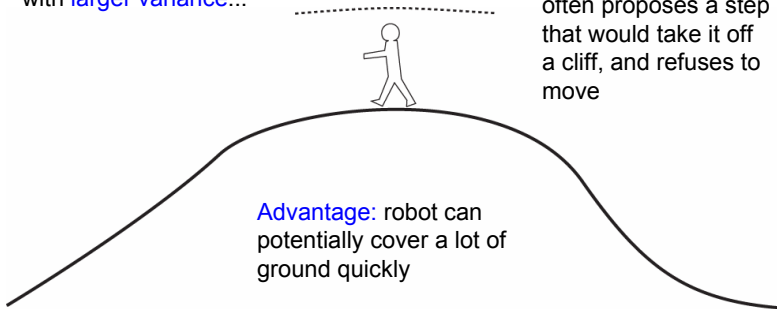
**Advantage:** robot seldom refuses to take proposed steps

# Target vs. Proposal Distributions

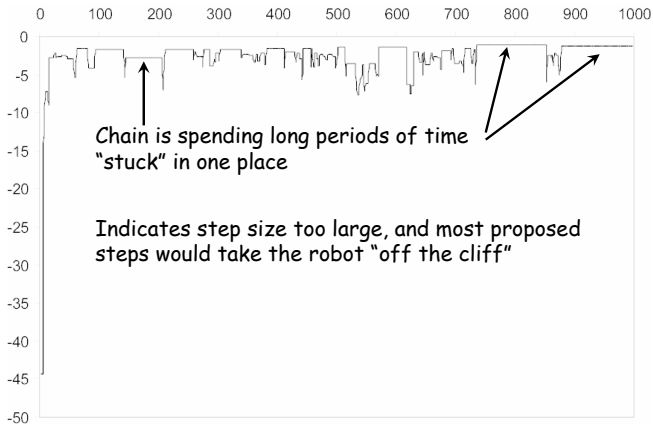
Proposal distributions  
with **larger variance**...

**Disadvantage:** robot  
often proposes a step  
that would take it off  
a cliff, and refuses to  
move

**Advantage:** robot can  
potentially cover a lot of  
ground quickly

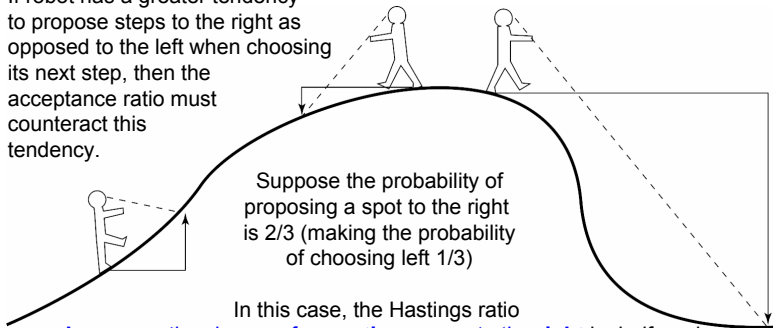


# Poor mixing



# The Hastings ratio

If robot has a greater tendency to propose steps to the right as opposed to the left when choosing its next step, then the acceptance ratio must counteract this tendency.



Suppose the probability of proposing a spot to the right is  $2/3$  (making the probability of choosing left  $1/3$ )

In this case, the Hastings ratio **decreases the chance of accepting moves to the right** by half, and **increases the chance of accepting moves to the left** (by a factor of 2), thus **exactly compensating** for the asymmetry in the proposal distribution.

Hastings, W. K. 1970. Monte Carlo sampling methods using Markov chains and their applications. *Biometrika* 57:97-109.



Paul Lewis' MCMC robot demo

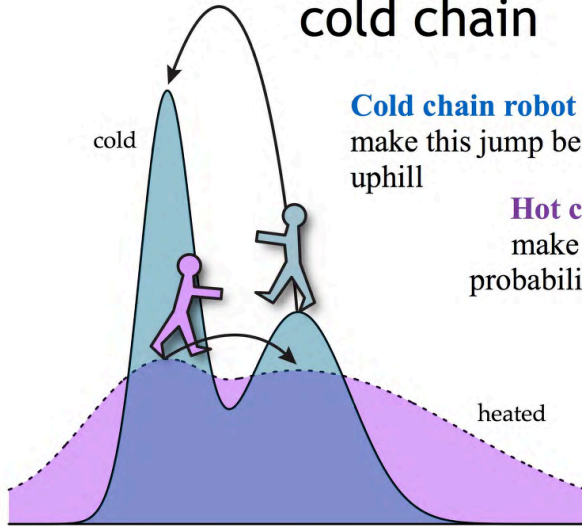
<http://phylogeny.uconn.edu/mcmc-robot/>

# Metropolis-coupled Markov chain Monte Carlo (MCMCMC)

- MCMCMC involves running **several chains simultaneously**
- The **cold chain** is the one that counts, the rest are **heated chains**
- Chain is heated by raising densities to a power less than 1.0 (values closer to 0.0 are warmer)

Geyer, C. J. 1991. Markov chain Monte Carlo maximum likelihood for dependent data. Pages 156-163 *in* Computing Science and Statistics (E. Keramidas, ed.).

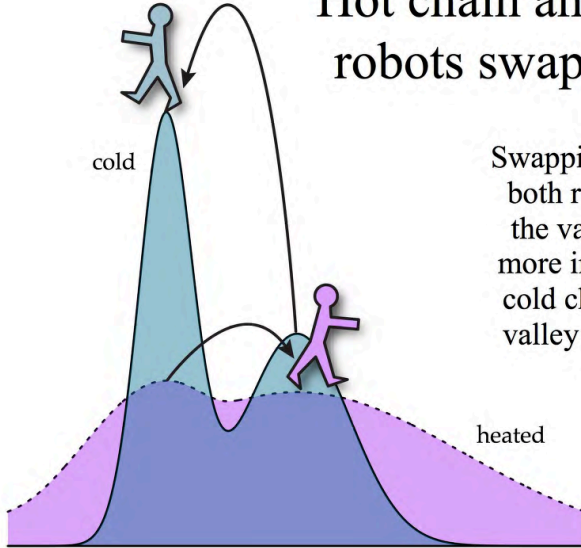
# Heated chains act as scouts for the cold chain



**Cold chain robot** can easily make this jump because it is uphill

**Hot chain robot** can also make this jump with high probability because it is only slightly downhill

# Hot chain and cold chain robots swapping places



Swapping places means both robots can cross the valley, but this is more important for the cold chain because its valley is much deeper

# Back to MCRobot...

Paul Lewis' MCMC robot demo, with poor mixing  
<http://phylogeny.uconn.edu/mcmc-robot/>

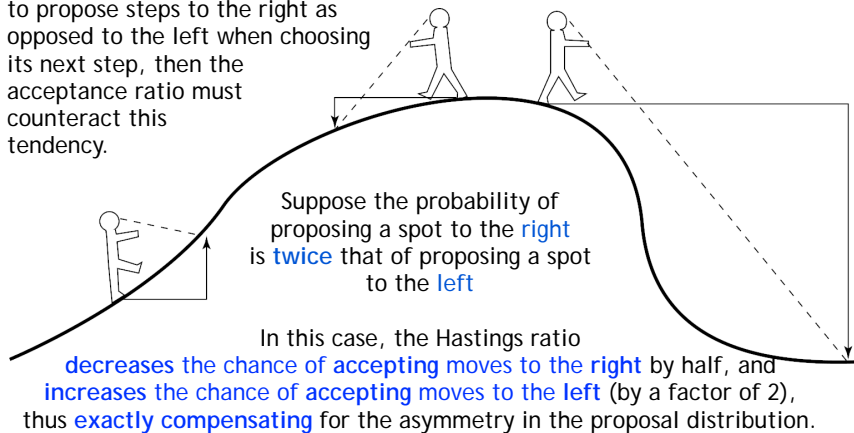
“Metropolis algorithm will produce a precise and accurate approximation of the posterior distribution if run long enough”. - Paul Lewis

“Metropolis algorithm will produce a precise and accurate approximation of the posterior distribution if run long enough”. - Paul Lewis “People always forget how long of a time infinity really is” - paraphrased from Dave Swofford



# The Hastings ratio

If robot has a greater tendency to propose steps to the right as opposed to the left when choosing its next step, then the acceptance ratio must counteract this tendency.

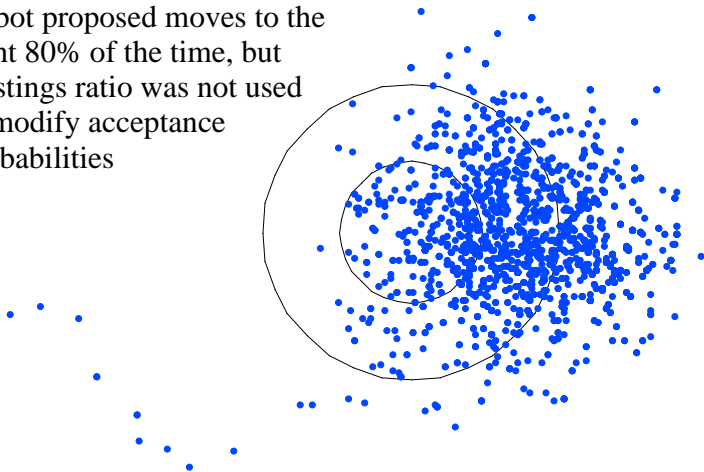


Hastings, W. K. 1970. Monte Carlo sampling methods using Markov chains and their applications. Biometrika 57:97-109.

# The Hastings ratio

Example where MCMC

Robot proposed moves to the right 80% of the time, but Hastings ratio was not used to modify acceptance probabilities



# Hastings Ratio

$$R = \left[ \frac{f(D|\theta^*) f(\theta^*)}{f(D|\theta) f(\theta)} \right] \left[ \frac{q(\theta|\theta^*)}{q(\theta^*|\theta)} \right]$$

Acceptance  
ratio

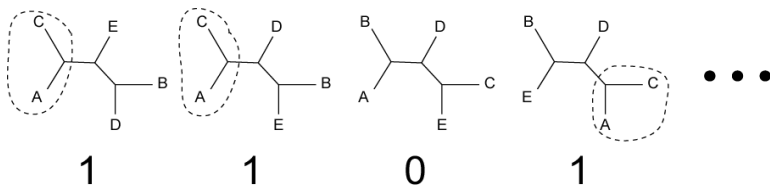
Posterior ratio

Hastings ratio

Note that if  $q(\theta|\theta^*) = q(\theta^*|\theta)$ , the Hastings ratio is 1

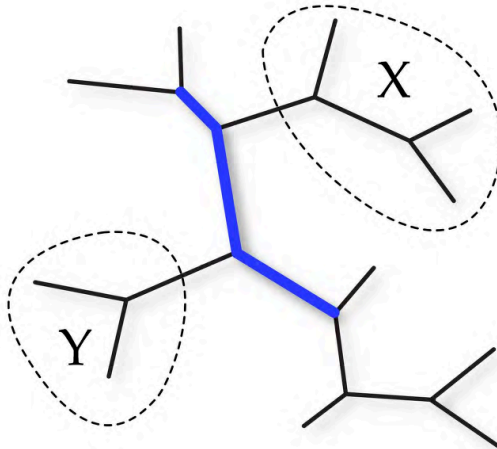
# III. Bayesian phylogenetics

# So, what's all this got to do with phylogenetics?



The posterior probability of the split  $AC|BDE$  may be approximated by the fraction of trees sampled from the posterior that contain that split.

# Moving through treespace



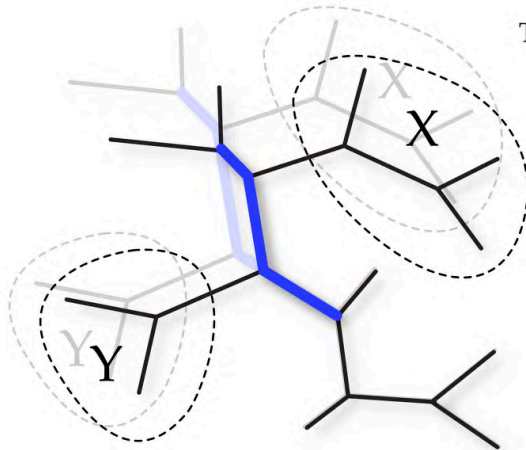
The Larget-Simon move

## Step 1:

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

\*Larget, B., and D. L. Simon. 1999. Markov chain monte carlo algorithms for the Bayesian analysis of phylogenetic trees. *Molecular Biology and Evolution* 16: 750-759. See also: Holder et al. 2005. *Syst. Biol.* 54: 961-965.

# Moving through treespace



## The Target-Simon move

### Step 1:

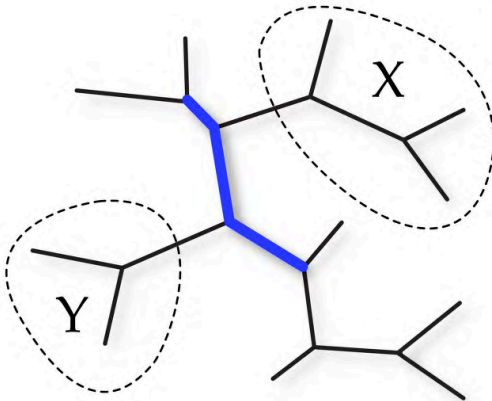
Pick 3 contiguous edges randomly, defining two subtrees, X and Y

### Step 2:

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

# Moving through treespace

## The Target-Simon move



### Step 1:

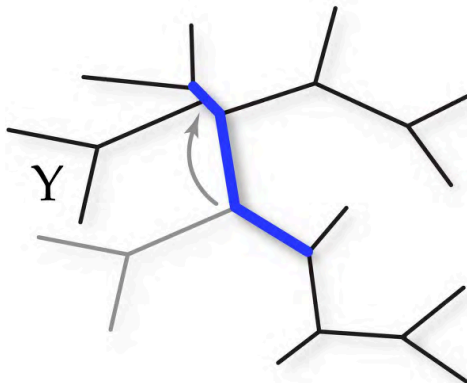
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# Moving through treespace



## The Target-Simon move

### Step 1:

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

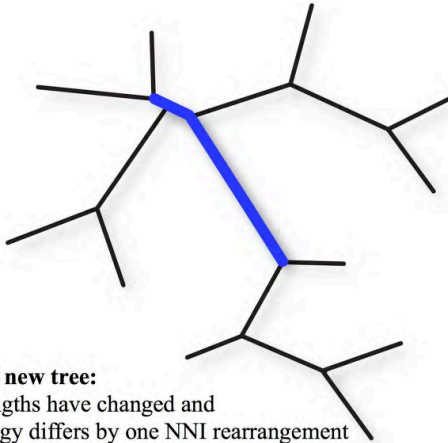
### Step 2:

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

### Step 3:

Choose X or Y randomly, then reposition randomly

# Moving through treespace



**Proposed new tree:**  
3 edge lengths have changed and  
the topology differs by one NNI rearrangement

## The Target-Simon move

### Step 1:

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

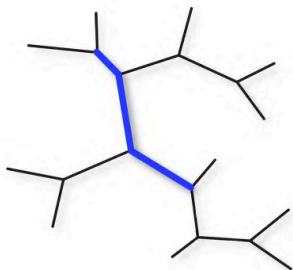
### Step 2:

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

### Step 3:

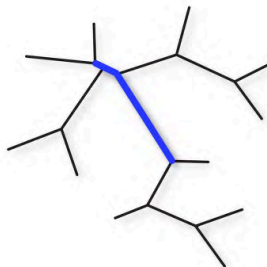
Choose X or Y randomly,  
then reposition  
randomly

# Moving through treespace



Current tree

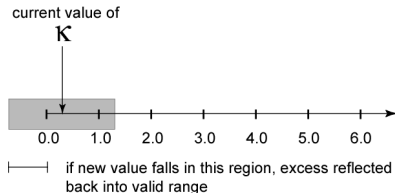
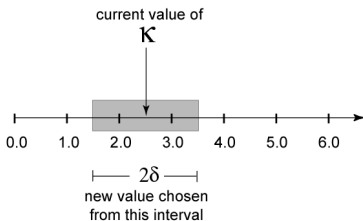
log-posterior = -34256



Proposed tree

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

# Moving through parameter space



Using  $\kappa$  (ratio of the transition rate to the transversion rate) as an example of a model parameter.

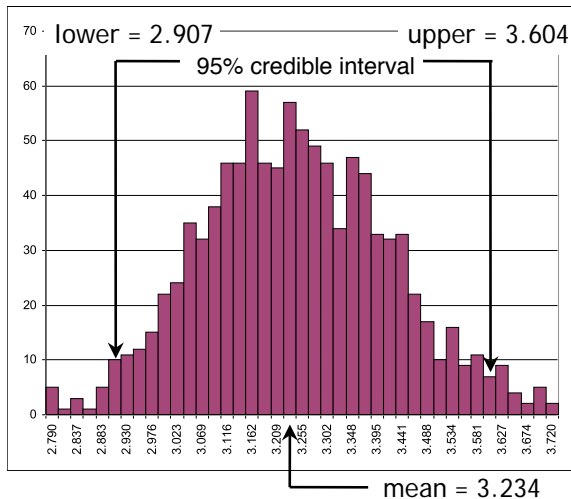
Proposal distribution is the uniform distribution on the interval  $(\kappa - \delta, \kappa + \delta)$

The “step size” of the MCMC robot is defined by  $\delta$ : a larger  $\delta$  means that the robot will attempt to make larger jumps on average.

# Putting it all together

- **Start with** random tree and arbitrary initial values for branch lengths and model parameters
- **Each generation** consists of one of these (chosen at random):
  - Propose a **new tree** (e.g. Target-Simon move) and either accept or reject the move
  - Propose (and either accept or reject) a **new model parameter value**
- Every  $k$  generations, save tree topology, branch lengths and all model parameters (i.e. **sample the chain**)
- After  $n$  generations, **summarize sample** using histograms, means, credible intervals, etc.

# Marginal Posterior Distribution of $\kappa$



Histogram created from a sample of 1000 kappa values.

## IV. Prior distributions

# Common Priors

- **Discrete uniform** for topologies
  - exceptions becoming more common
- **Beta** for proportions
- **Gamma** or **Log-normal** for branch lengths and other parameters with support  $[0, \infty)$ 
  - Exponential is common special case of the gamma distribution
- **Dirichlet** for state frequencies and GTR relative rates



While we often motivate Bayesian analysis by integrating prior information, setting up accurate, informative priors for phylogenetic inference is hard to do.

# Common Priors

- **Discrete uniform** for topologies
  - exceptions becoming more common
- **Beta** for proportions
- **Gamma** or **Log-normal** for branch lengths and other parameters with support  $[0, \infty)$ 
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- **Dirichlet** for state frequencies and GTR relative rates

# Discrete Uniform distribution for topologies



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



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



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



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



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



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



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



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



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



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



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



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



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

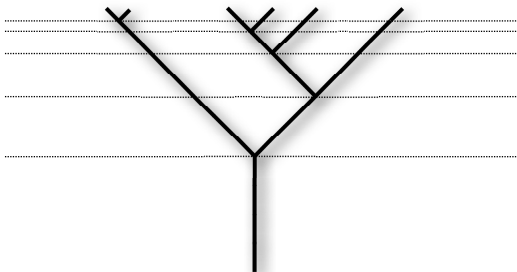


$$\frac{1}{15}$$



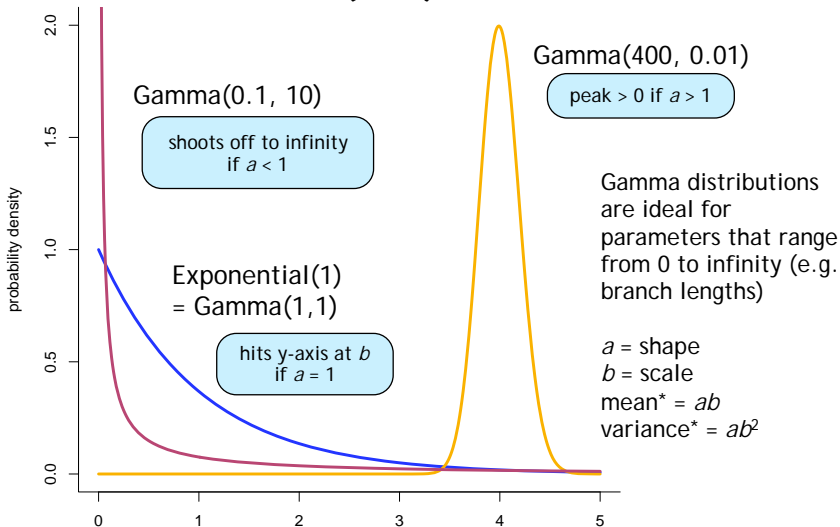
$$\frac{1}{15}$$

# Yule model provides joint prior for both topology and divergence times



The rate of speciation under the Yule model ( $\lambda$ ) is constant and applies equally and independently to each lineage. Thus, speciation events get closer together in time as the tree grows because more lineages are available to speciate.

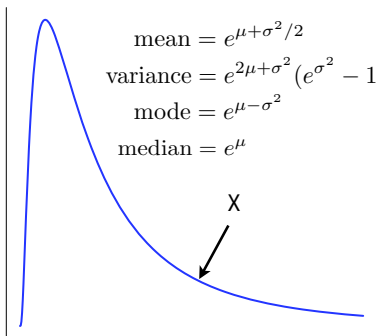
# Gamma( $a, b$ ) distributions



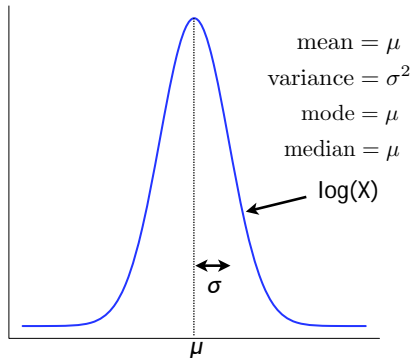
\*Note: be aware that in many papers the Gamma distribution is defined such that the second (scale) parameter is the *inverse* of the value  $b$  used in this slide! In this case, the mean and variance would be  $a/b$  and  $a/b^2$ , respectively.

# Log-normal distribution

If  $X$  is log-normal with *parameters*  $\mu$  and  $\sigma$ ...



...then  $\log(X)$  is normal with *mean*  $\mu$  and *standard deviation*  $\sigma$ .



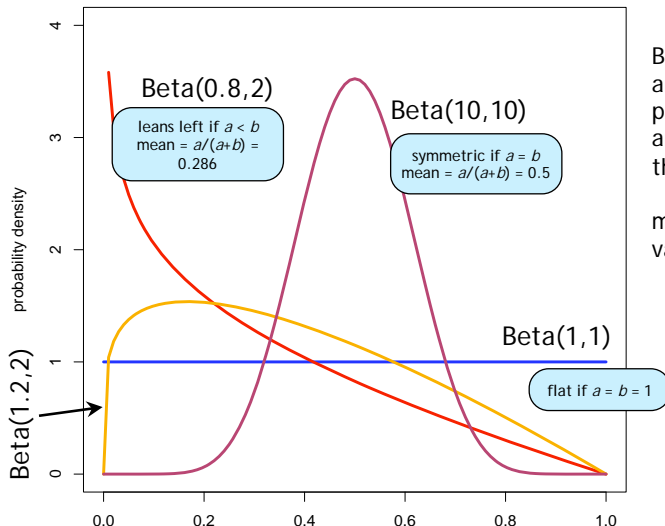
**Important:**  $\mu$  and  $\sigma$  do not represent the mean and standard deviation of  $X$ : they are the mean and standard deviation of  $\log(X)$ !

To choose  $\mu$  and  $\sigma$  to yield a particular mean ( $m$ ) and variance ( $v$ ) for  $X$ , use these formulas:

$$\mu = \log(m^2) - \log(m) - \frac{\log(v + m^2) - \log(m^2)}{2}$$

$$\sigma^2 = \log(v + m^2) - \log(m^2)$$


# Beta( $a, b$ ) gallery



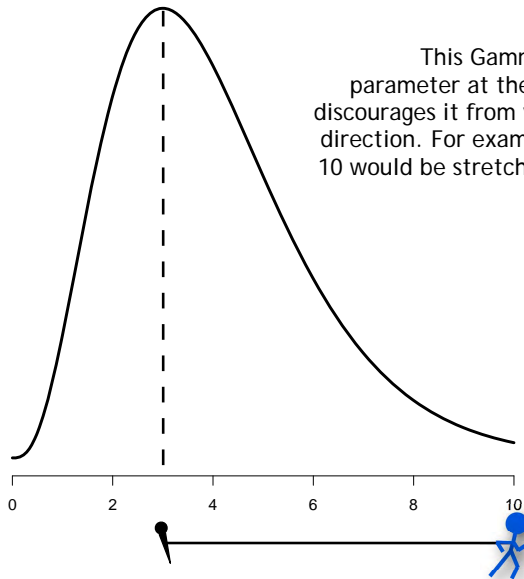
Beta distributions are appropriate for proportions, which are constrained to the interval  $[0, 1]$ .

$$\text{mean} = a/(a+b)$$
$$\text{variance} = ab/[(a+b)^2(a+b+1)]$$

# Prior Miscellany

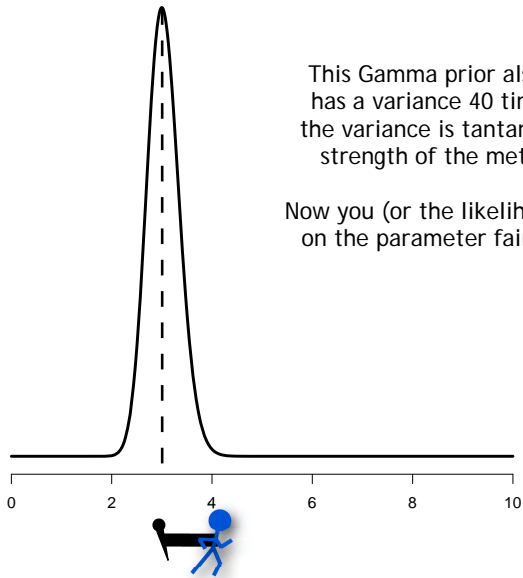
- priors as rubber bands 
- running on empty
- hierarchical models
- empirical bayes





This Gamma(4,1) prior ties down its parameter at the mode, which is at 3, and discourages it from venturing too far in either direction. For example, a parameter value of 10 would be stretching the rubber band fairly tightly

The mode of a Gamma( $a, b$ ) distribution is  $(a-1)b$  (assuming  $a > 1$ )

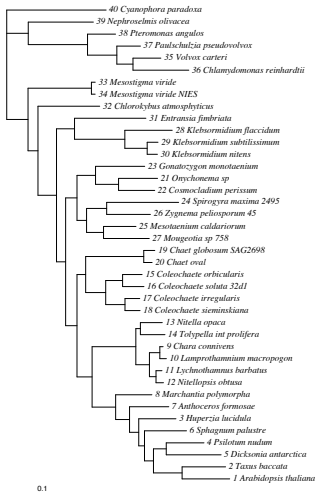


This Gamma prior also has a mode at 3, but has a variance 40 times smaller. Decreasing the variance is tantamount to increasing the strength of the metaphorical rubber band.

Now you (or the likelihood) would have to tug on the parameter fairly hard for it to have a value as large as 4.

This gamma distribution has shape 91.989 and scale 0.032971

# Example: Internal Branch Length Priors

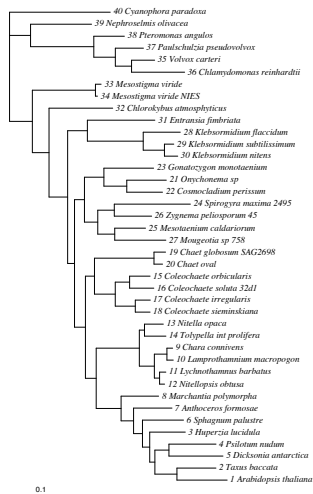


Separate priors applied to  
internal and external branches

External branch length prior is  
exponential with mean 0.1

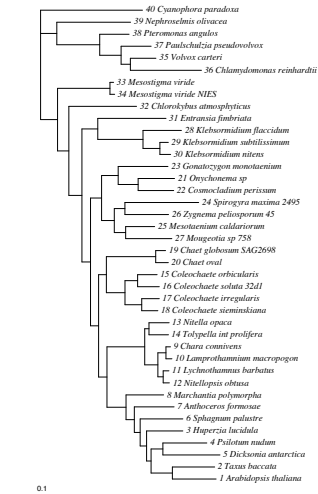
Internal branch length prior is  
exponential with mean 0.1

This is a reasonably vague  
internal branch length prior

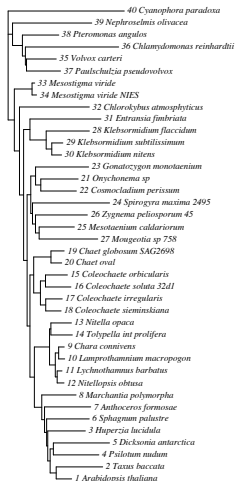


Internal branch length prior mean 0.01

(external branch length prior mean always 0.1)

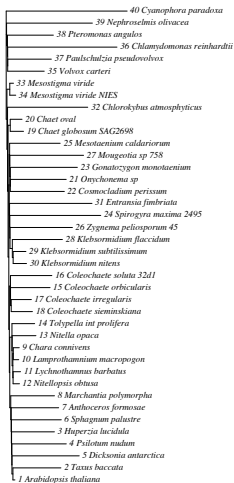


Internal branch length prior mean  
0.001

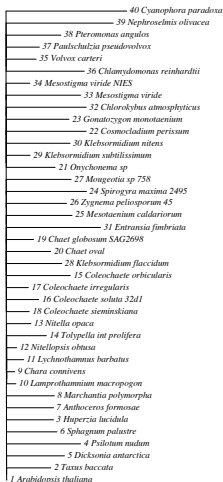


Internal branch length prior mean  
0.0001

0.1



Internal branch length prior mean  
0.00001



Internal branch length prior mean  
0.000001

The internal branch length prior is  
calling the shots now, and the  
likelihood must obey.

0.1

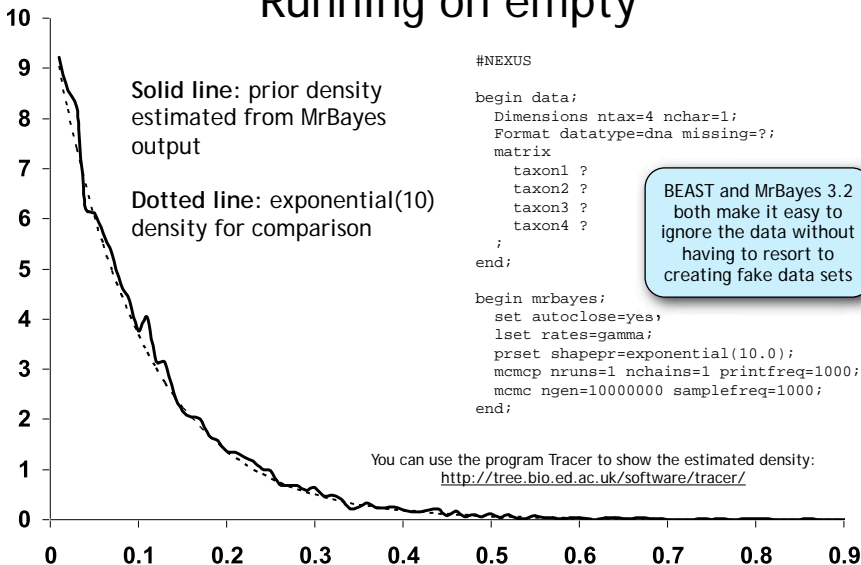


# Prior Miscellany

- priors as rubber bands
- running on empty
- hierarchical models
- empirical bayes



# Running on empty



# Prior Miscellany

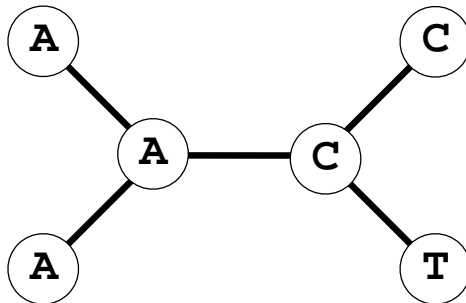
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In a **non-hierarchical** model, all parameters are present in the likelihood function

Prior: Exponential, mean=0.1

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



## Hierarchical models add *hyperparameters* not present in the likelihood function

$\mu$  is a *hyperparameter* governing the mean of the edge length prior

hyperprior



Prior: Exponential, mean  $\mu$

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

During an MCMC analysis,  $\mu$  will hover around a reasonable value, sparing you from having to decide what value is appropriate. You still have to specify a hyperprior, however.

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- priors as rubber bands
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# Empirical Bayes

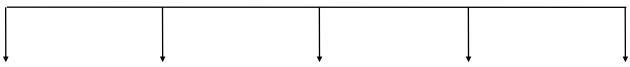
Empirical Bayes uses the data to determine some aspects of the prior, such as the prior mean.

Pure Bayesian approaches choose priors without reference to the data.

An empirical Bayesian would use the maximum likelihood estimate (MLE) of the length of an average branch here



Prior: Exponential, mean=MLE


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

Demo:

Using revbayes to set up an MCMC analysis.

We will rerun the “Basic Introduction to Markov chain Monte Carlo.”  
tutorial from <http://revbayes.github.io/tutorials.html>

Use 'qssh' on the cluster, and call RevBayes using 'revbayes'

Files are in /home/courses/ejmctavish/qsb244/revbayeslab