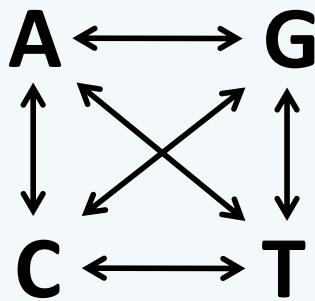

Lecture 2.1

Bayesian Phylogenetic Analysis

Phylogenetic methods

	Algorithm-based	Optimality criterion	Other
No explicit substitution model	Distance-based methods	Maximum parsimony	
	Distance-based methods	Maximum likelihood	Bayesian inference

The Bayesian framework

Bayesian phylogenetic analysis

- Bayesian phylogenetic analysis was developed in the mid 1990s
- Now one of the most widely used methods

MrBayes



BEAST 1



RevBayes



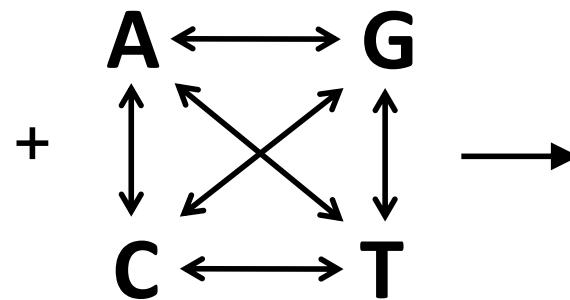
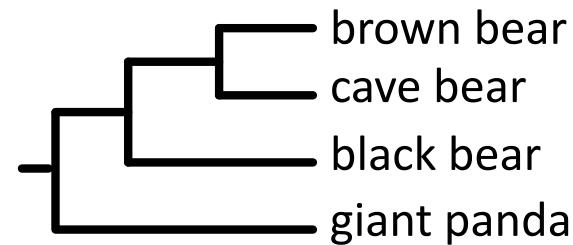
BEAST 2



Bayesian phylogenetic analysis

Maximum likelihood

Given

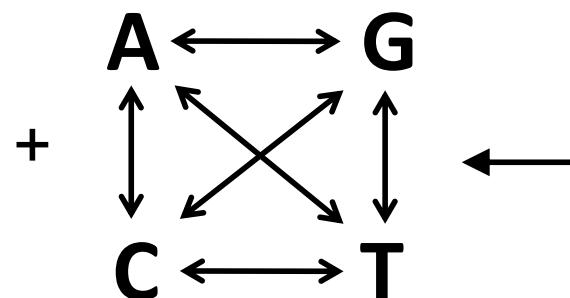
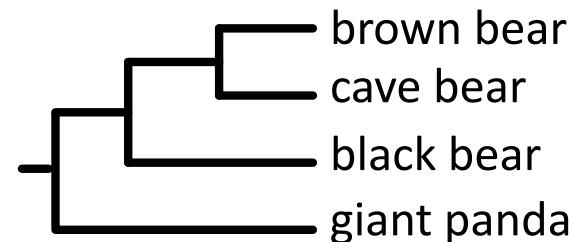


Probability of?

brown bear	CGTTAGTACACT
cave bear	CGATAGTTCACT
black bear	CGTTAGTTTACC
giant panda	CATTGGTTACT

Bayesian inference

Probability of?



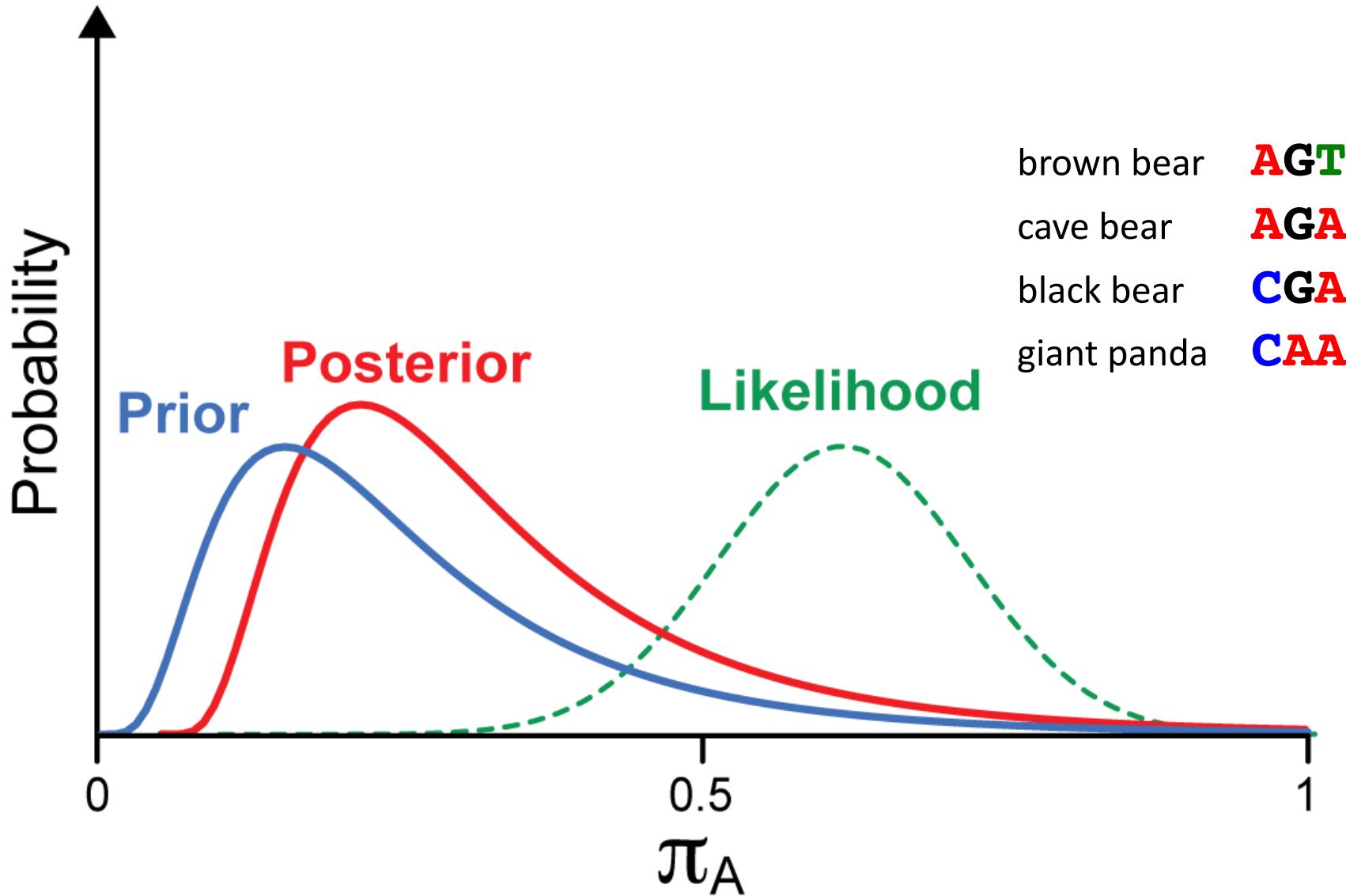
Given

brown bear	CGTTAGTACACT
cave bear	CGATAGTTCACT
black bear	CGTTAGTTTACC
giant panda	CATTGGTTACT

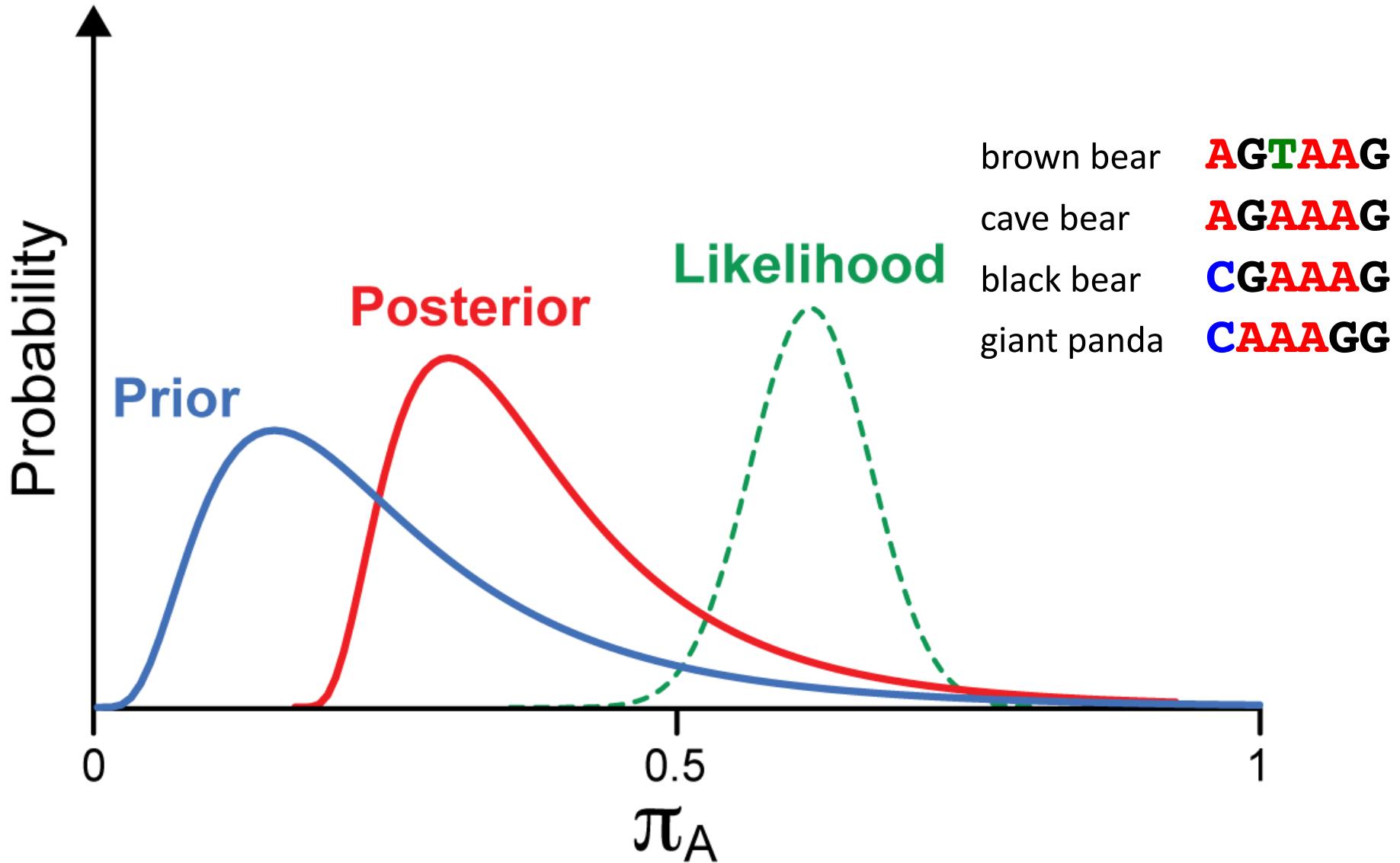
The Bayesian paradigm

- Contrast with frequentist statistics (**likelihood**)
- Parameters have **distributions**
- Before the data are observed, each parameter has a **prior distribution**
- The **likelihood** of the data is computed
- The prior distribution is combined (updated) with the likelihood to yield the **posterior distribution**

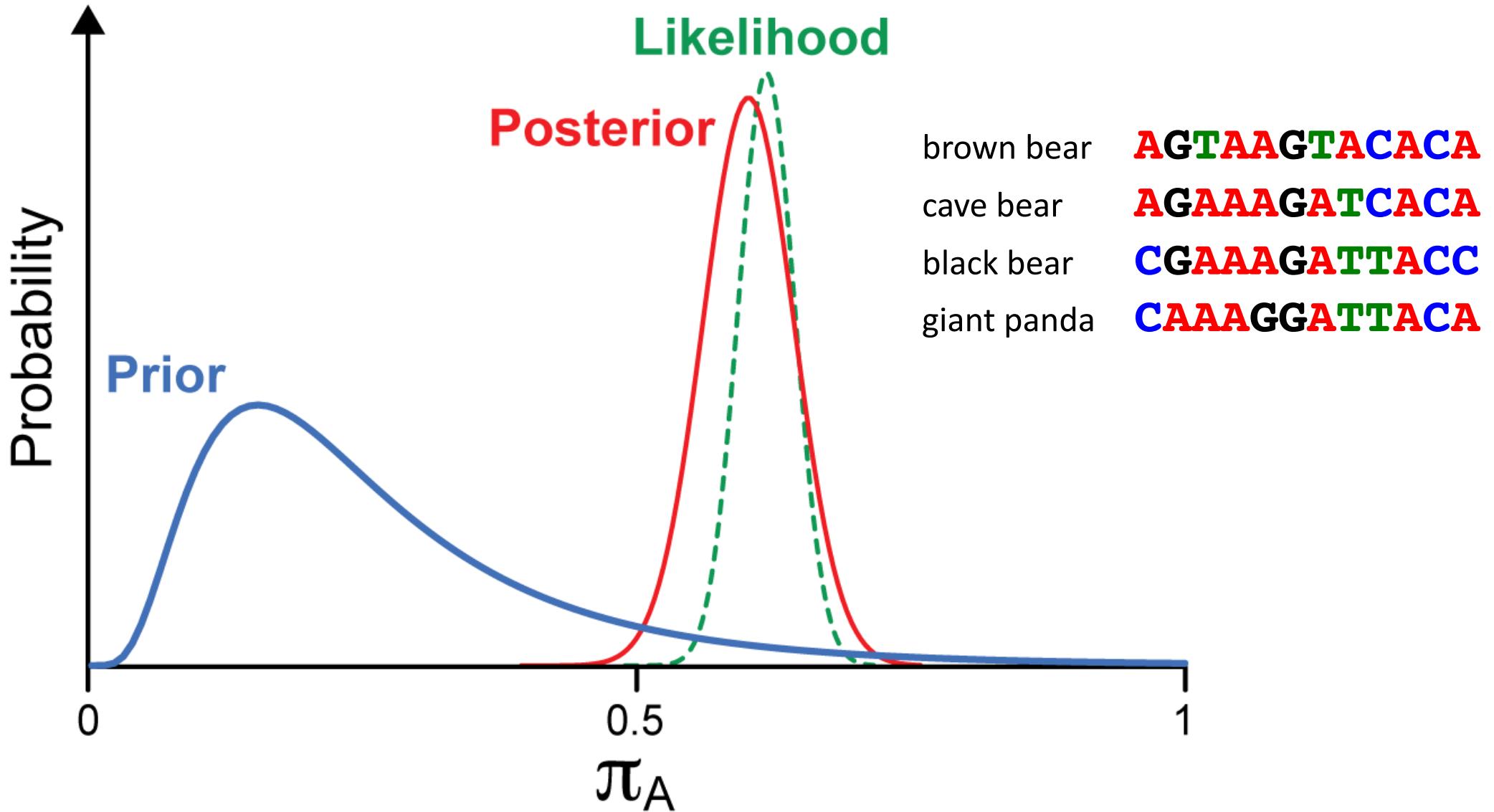
Simple example



Simple example



Simple example



Bayesian inference

Prior

Specified by user,
independent of data

Likelihood

Calculated from data

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

Posterior

This is what we
want to estimate

normalising constant
marginal likelihood of the data
model likelihood

Bayesian inference

$$\Pr(\tau, M, r \mid D) = \frac{\Pr(\tau) \Pr(M) (\Pr(r)) \Pr(D \mid \tau, M, r)}{\Pr(D)}$$

Prior prob of tree
Topology
Branch lengths

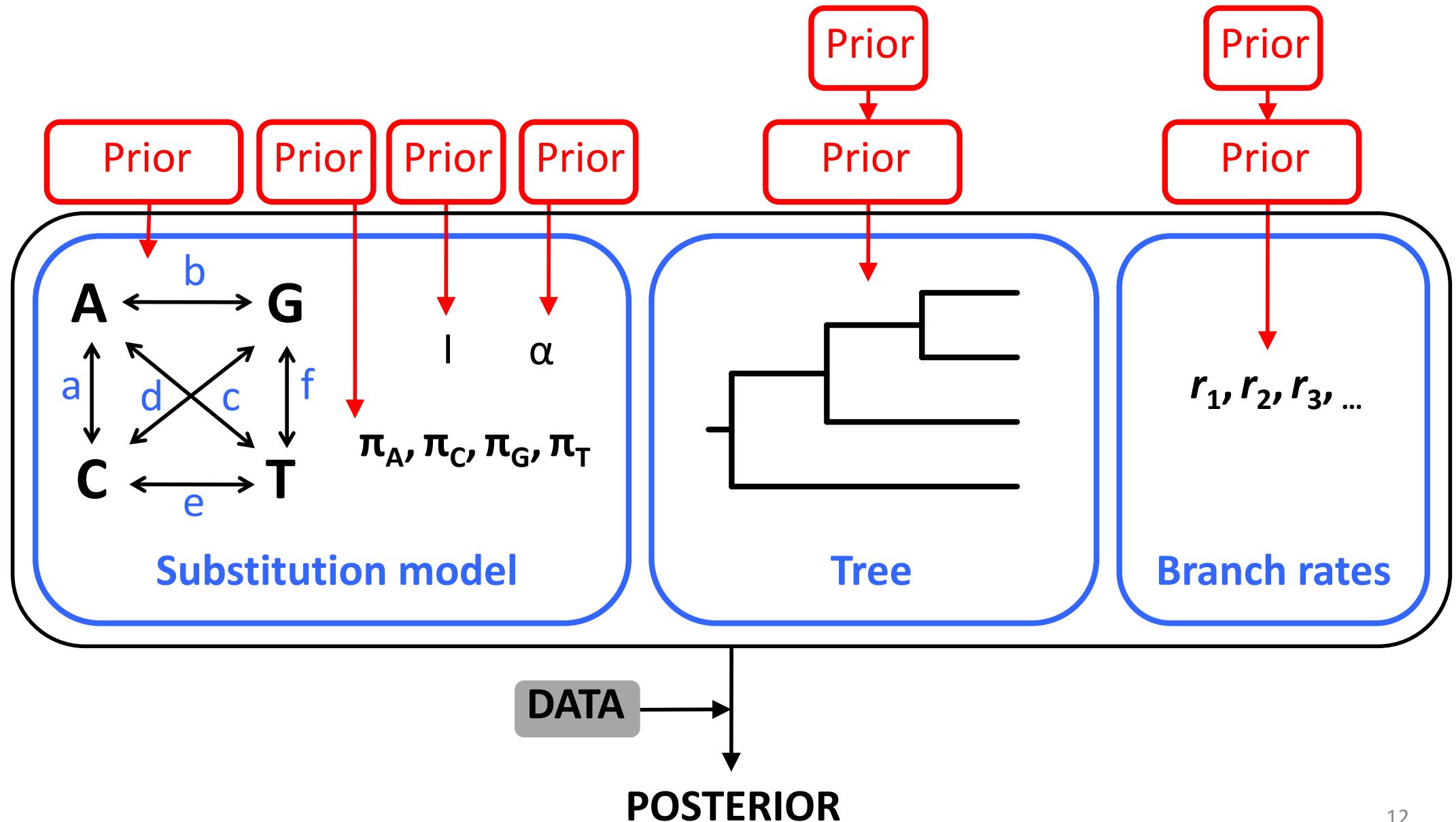
Prior prob of substitution model parameters
Rate parameters
Base frequencies

Prior prob of branch rates

Posterior
This is what we want to estimate

Likelihood
Calculated from data

Bayesian hierarchical model



Priors

- Priors are chosen in the form of probability distributions
- Reflect our prior expectations (and uncertainty) about values of parameters (without knowledge of the data)
 - Past observations
 - Personal beliefs
 - Use of a biological model
- Uninformative priors

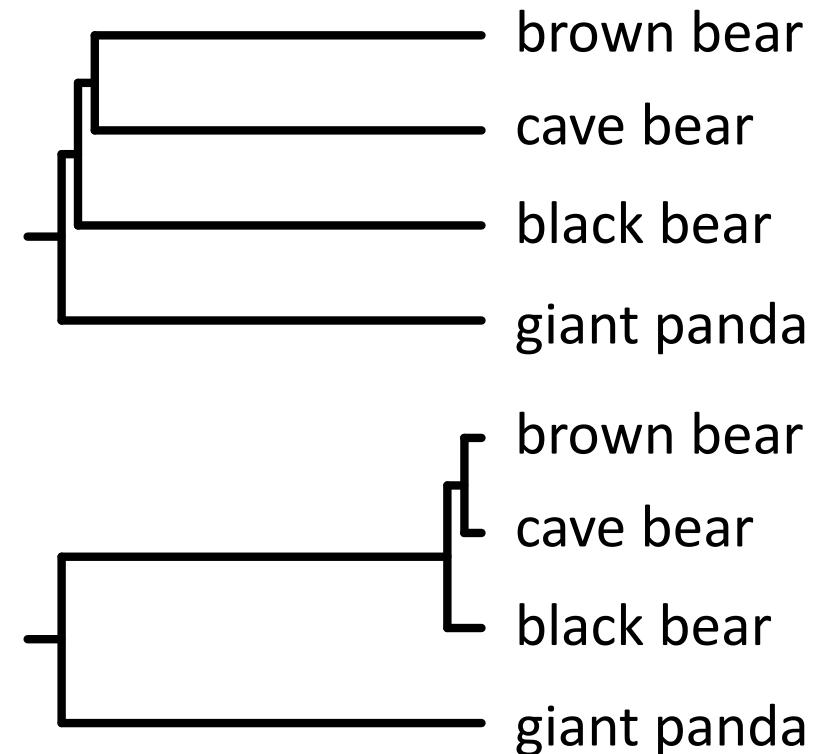
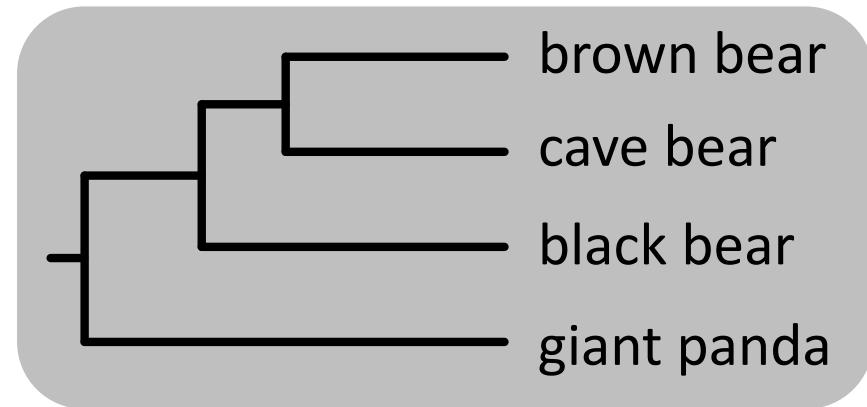
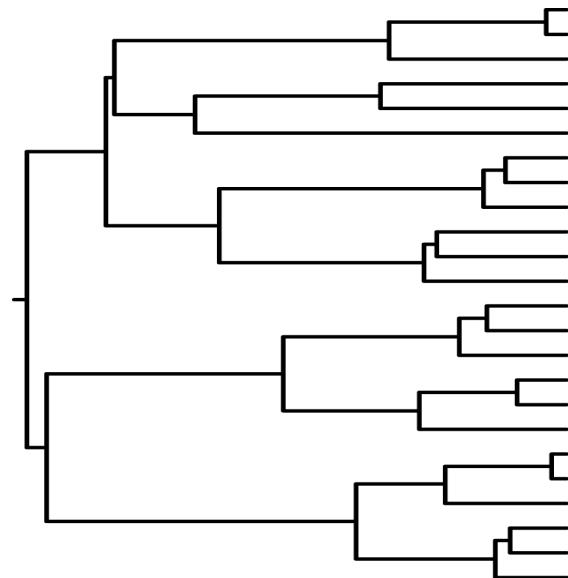
Priors

1. Use a **flat prior** for tree topology (*MrBayes*)
 - All trees have equal probability
 - Also need a prior for branch lengths or node times

2. Use a **biological model** to generate prior distribution (*BEAST* and *MrBayes*)
 - Among species: speciation model
 - Within species: coalescent model

Tree prior: Among species

- Tree shape described by a stochastic branching process
- Yule process
 - Lineages split at a constant rate
 - Simulates speciation process

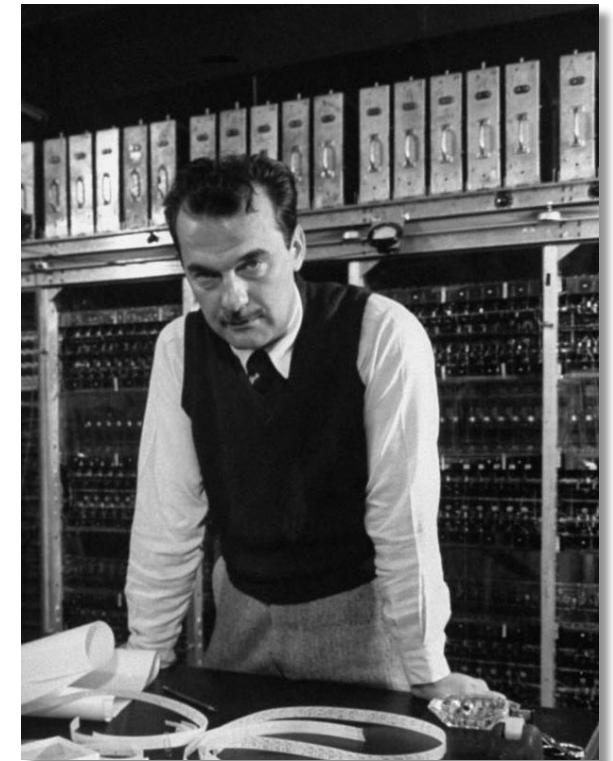


Markov Chain Monte Carlo Sampling

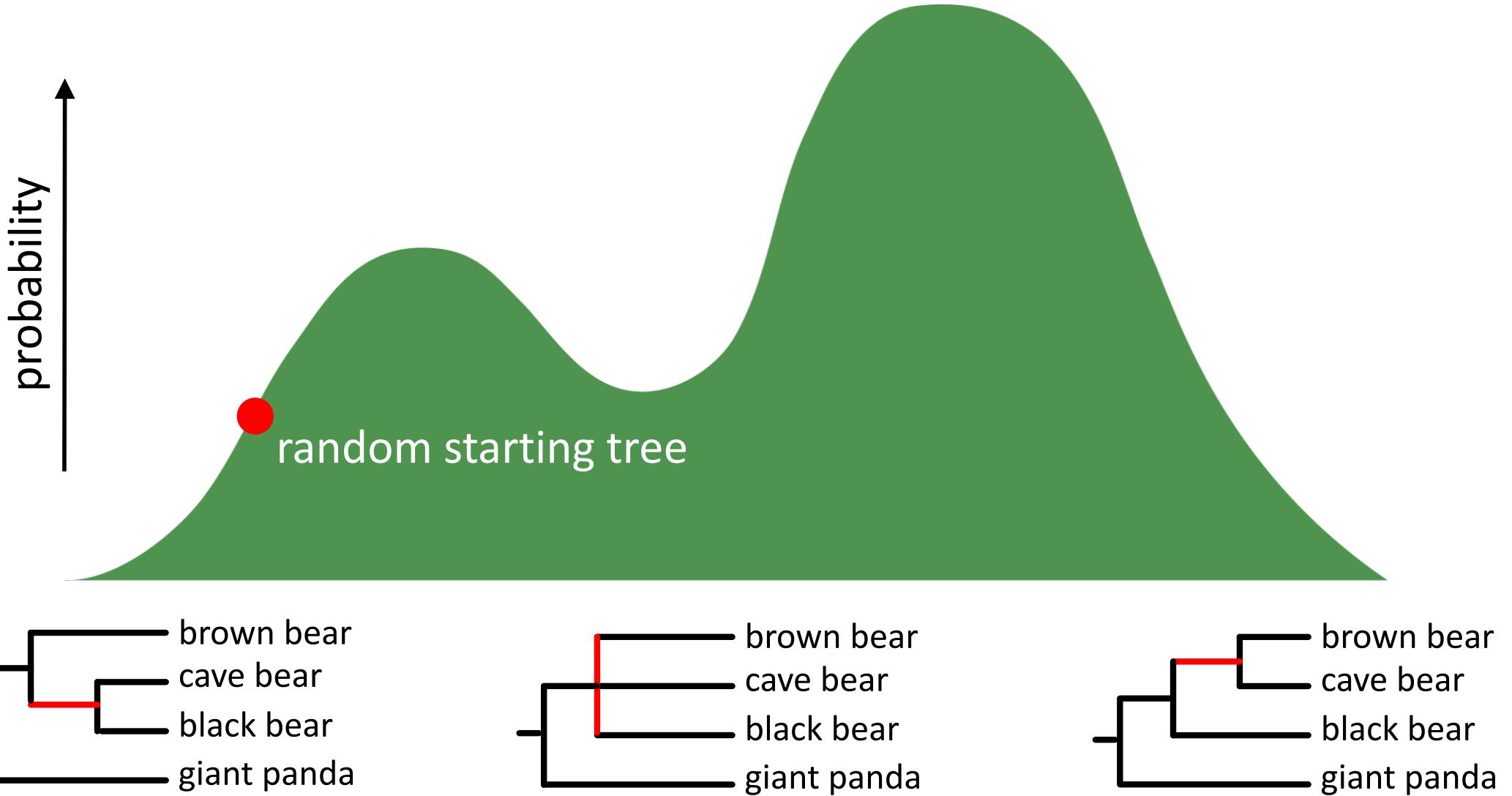
Estimating the posterior

- Impossible to obtain the posterior directly
- Instead, the posterior can be estimated using
Markov chain Monte Carlo simulation
- This is usually done using the
Metropolis-Hastings algorithm

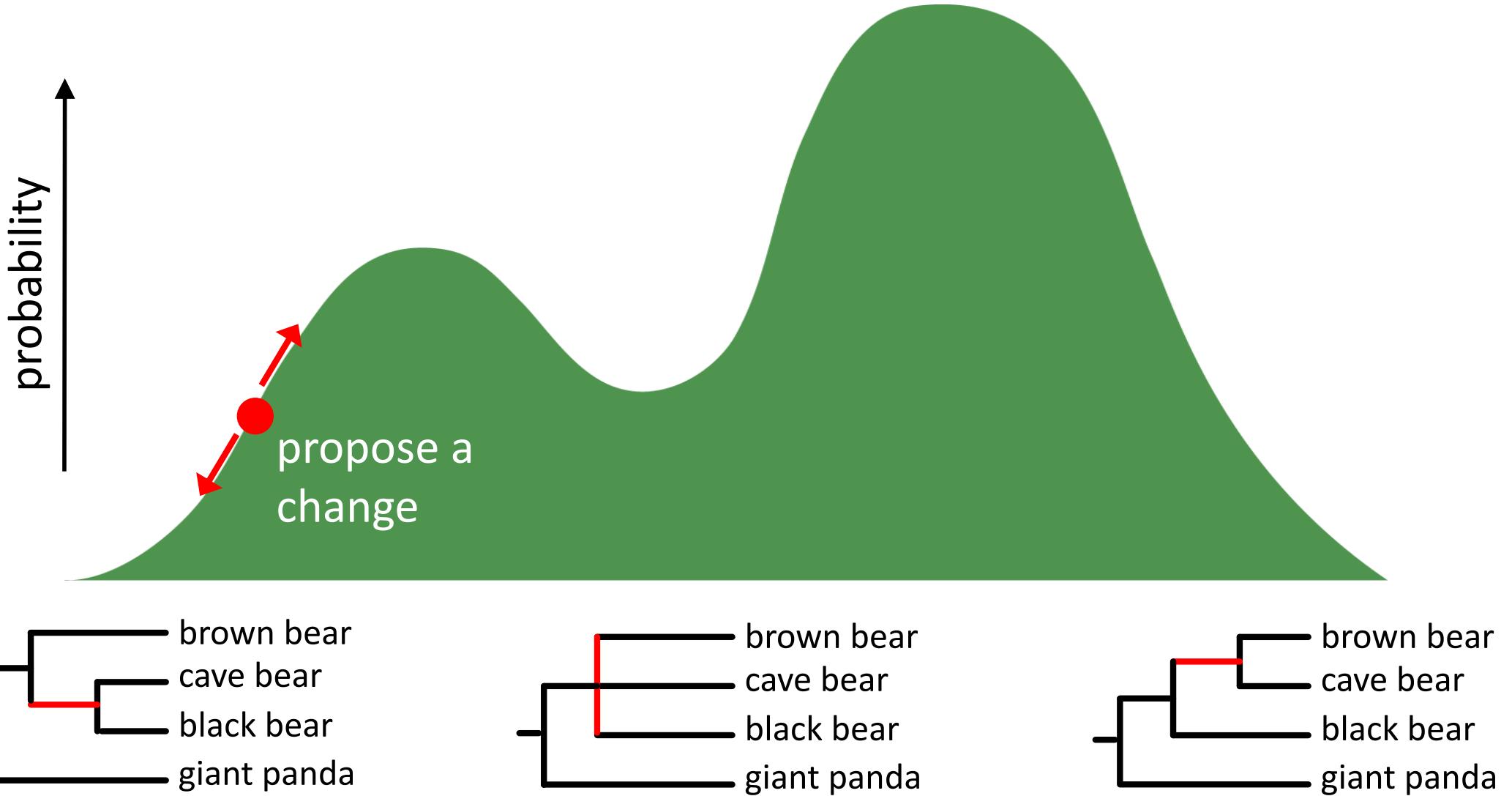
Nicholas Metropolis
Los Alamos, 1953



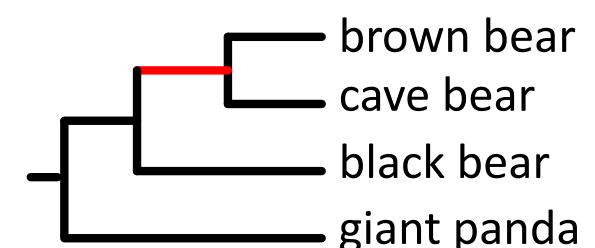
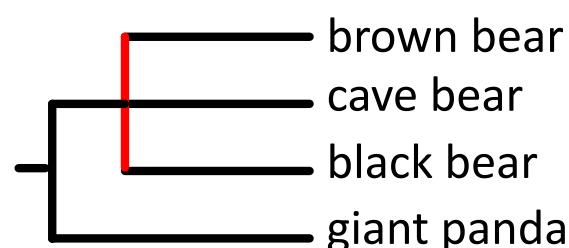
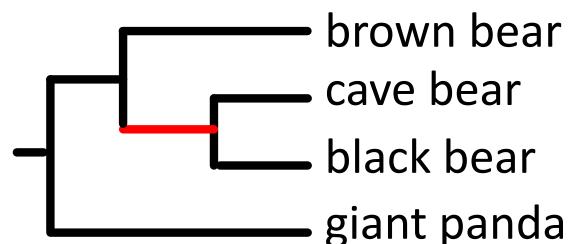
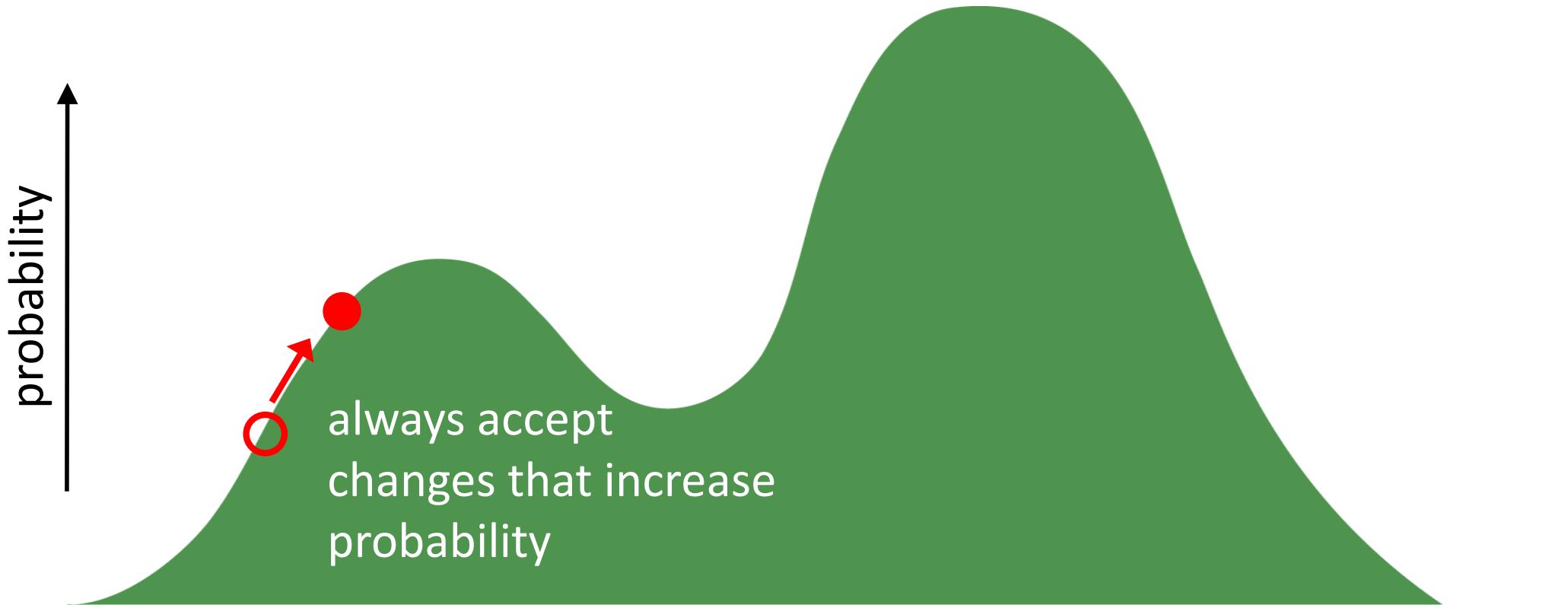
MCMC simulation



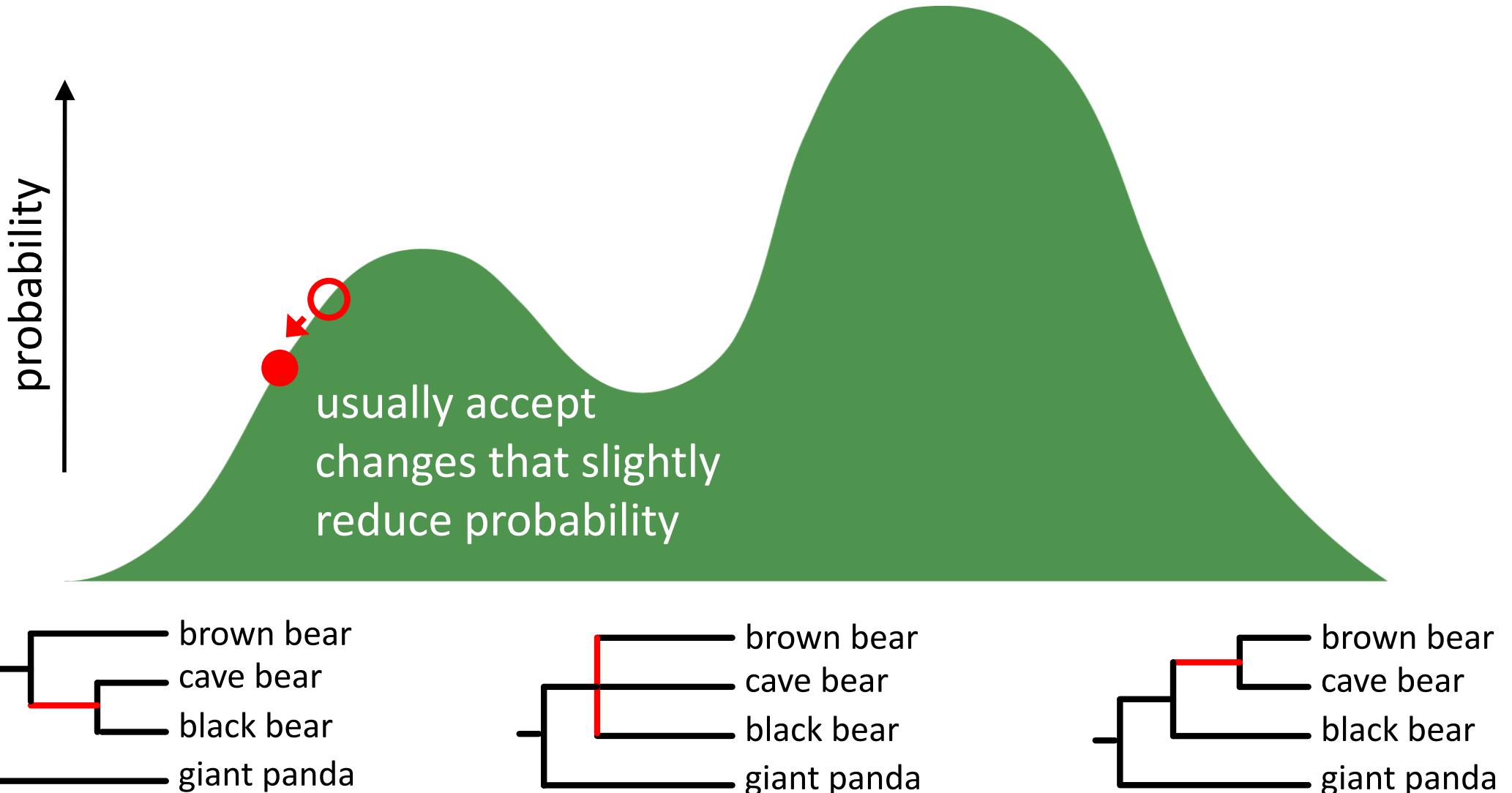
MCMC simulation



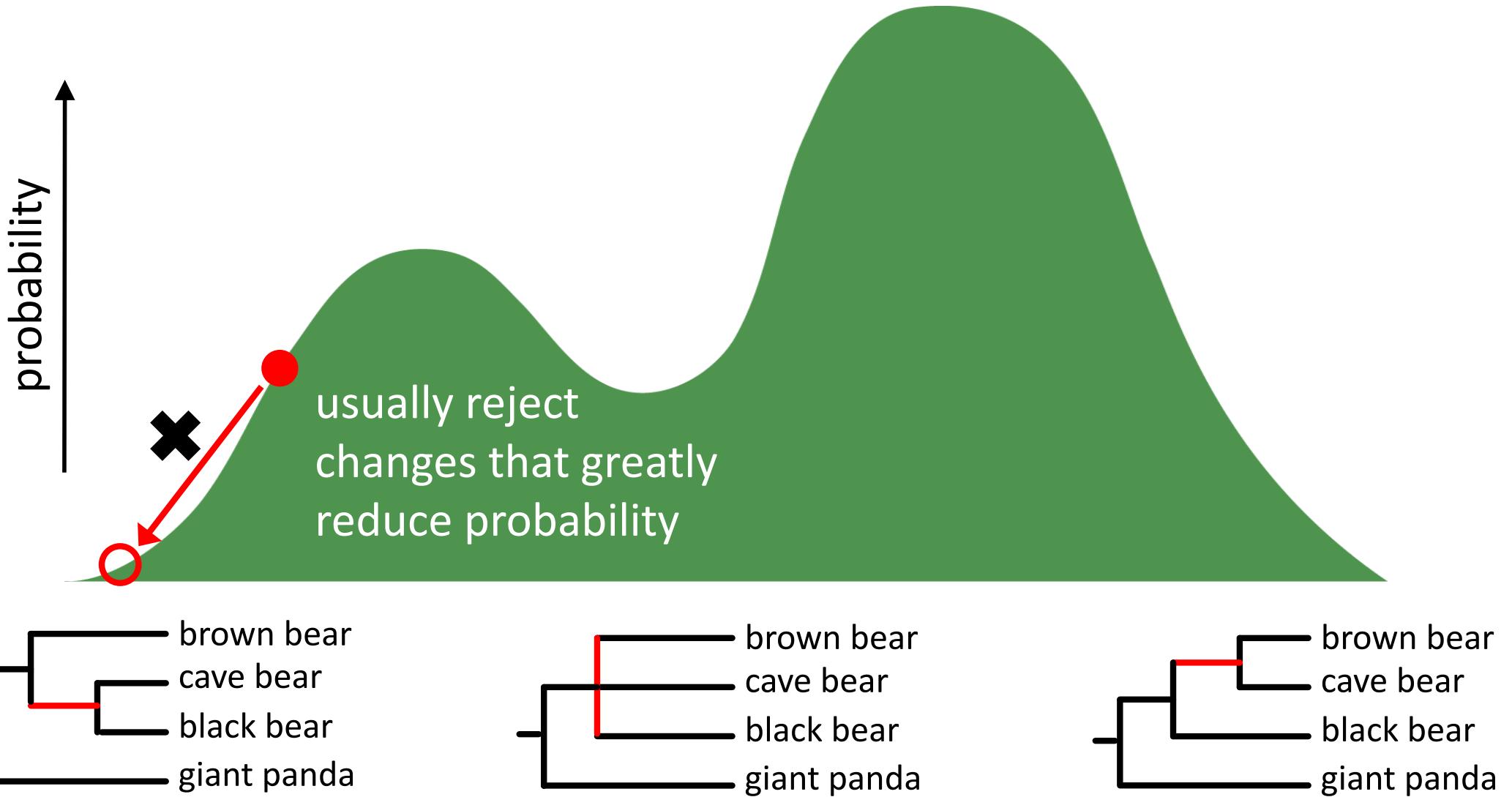
MCMC simulation



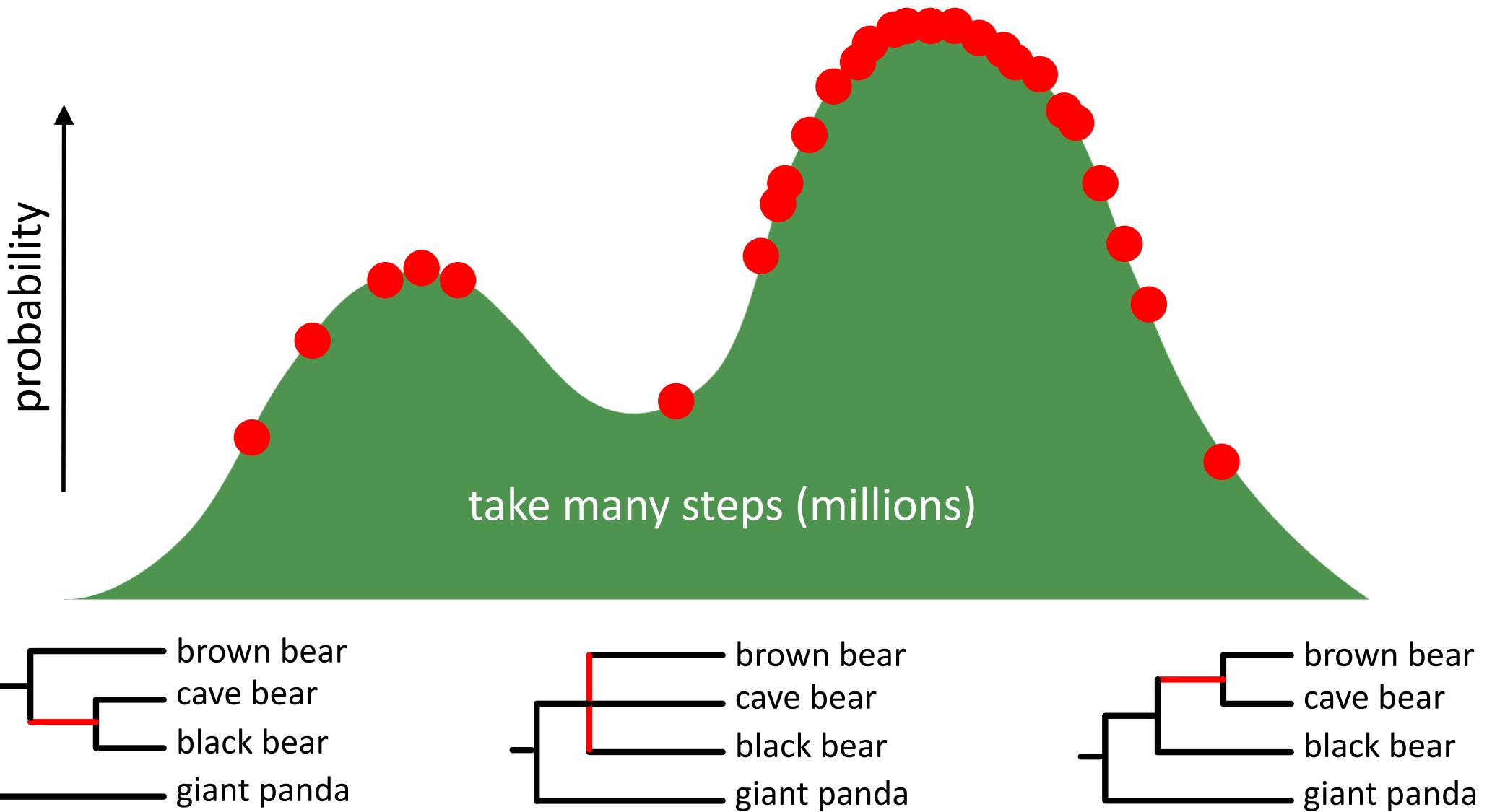
MCMC simulation



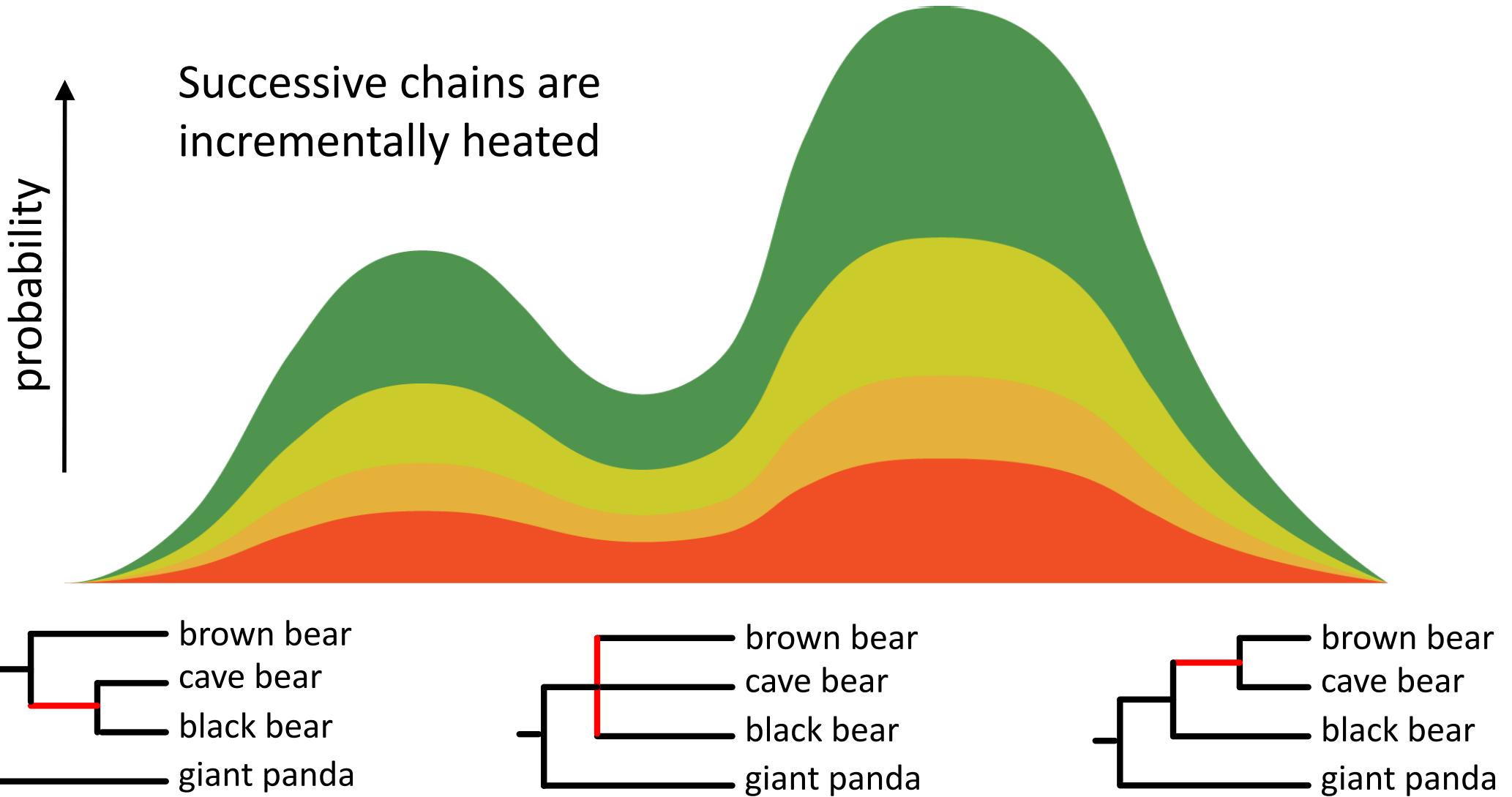
MCMC simulation



MCMC simulation



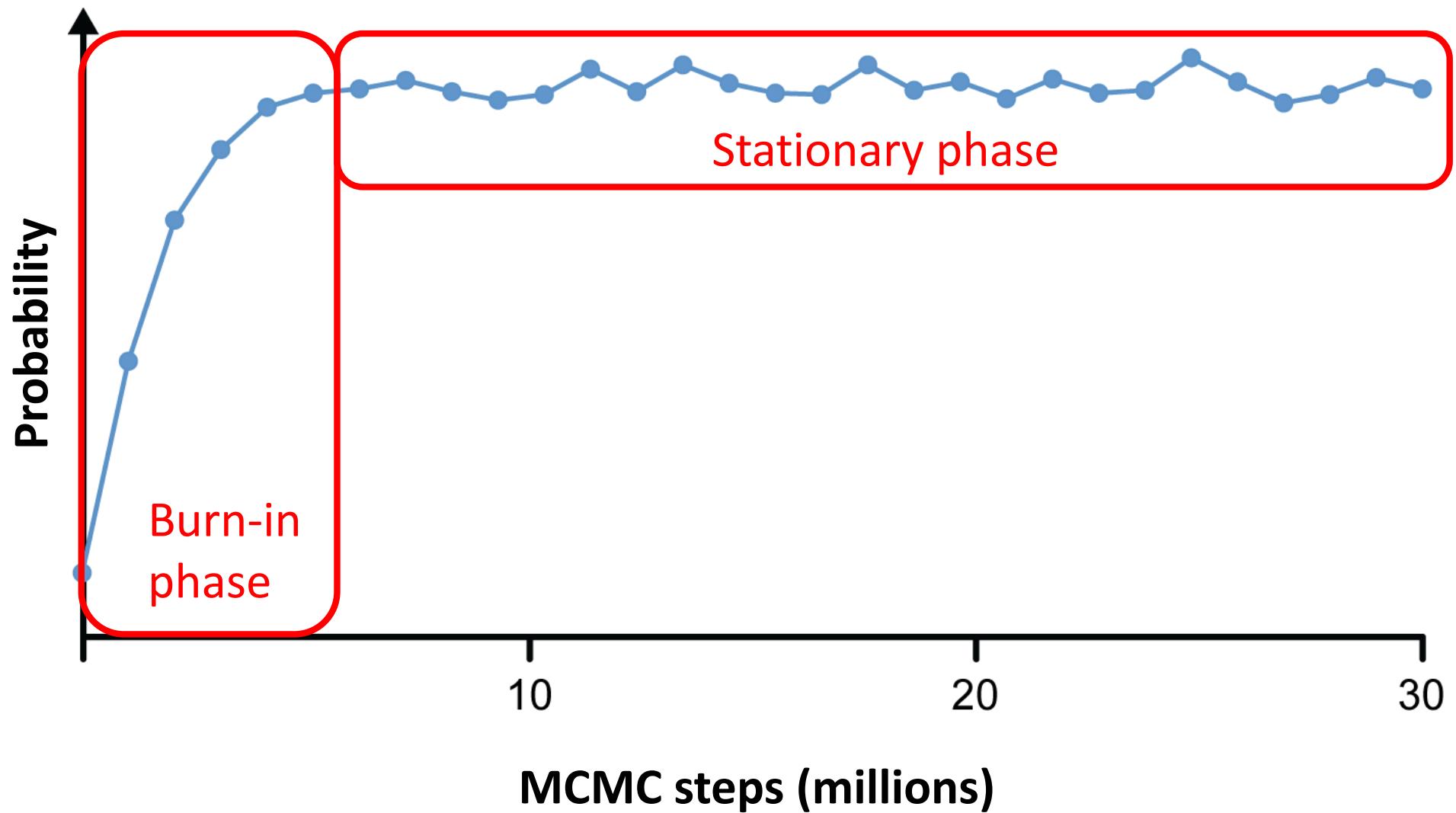
Metropolis-coupled MCMC



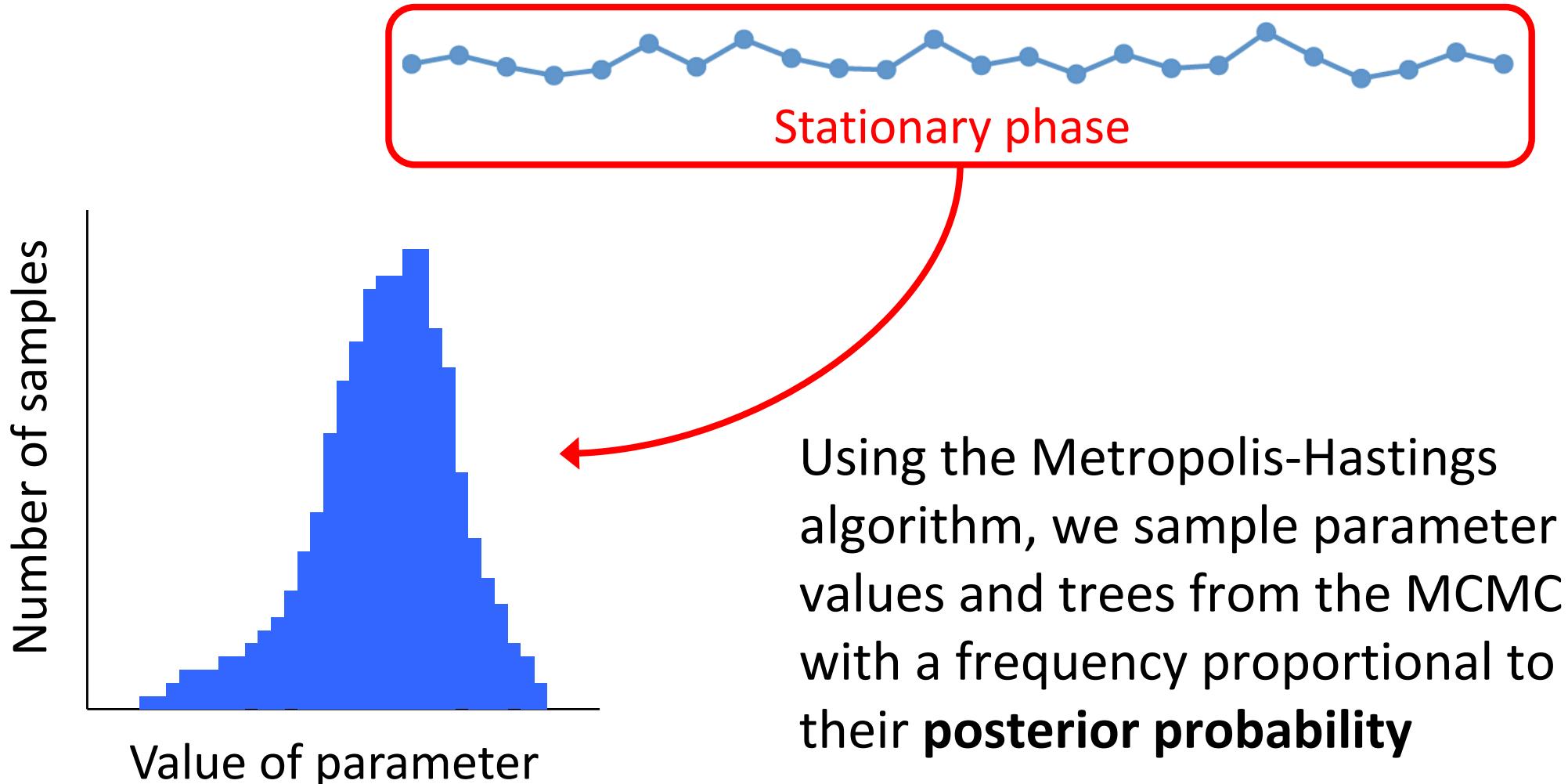
Samples from the MCMC

- Output from a Bayesian phylogenetic analysis:
 - A list of the **parameter values** visited by the Markov chain (.p file in *MrBayes*, .log file in *BEAST*)
 - A list of the **trees** visited by the Markov chain (.t file in *MrBayes*, .trees file in *BEAST*)

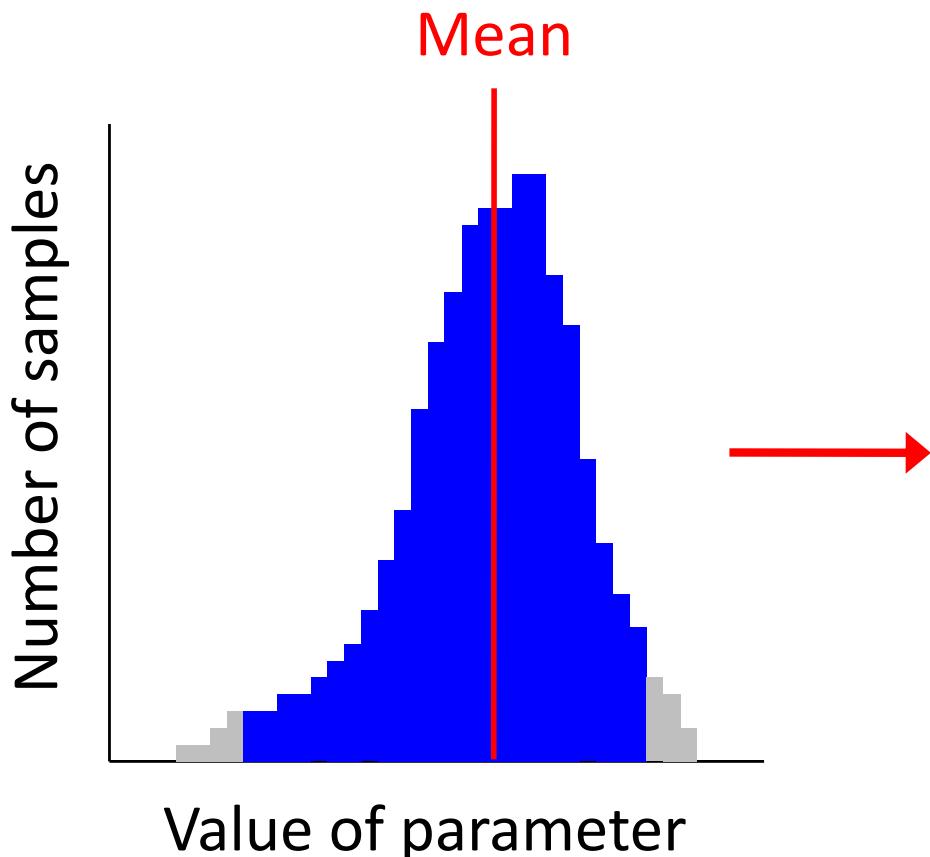
Samples from the MCMC



Samples from the MCMC



Samples from the MCMC



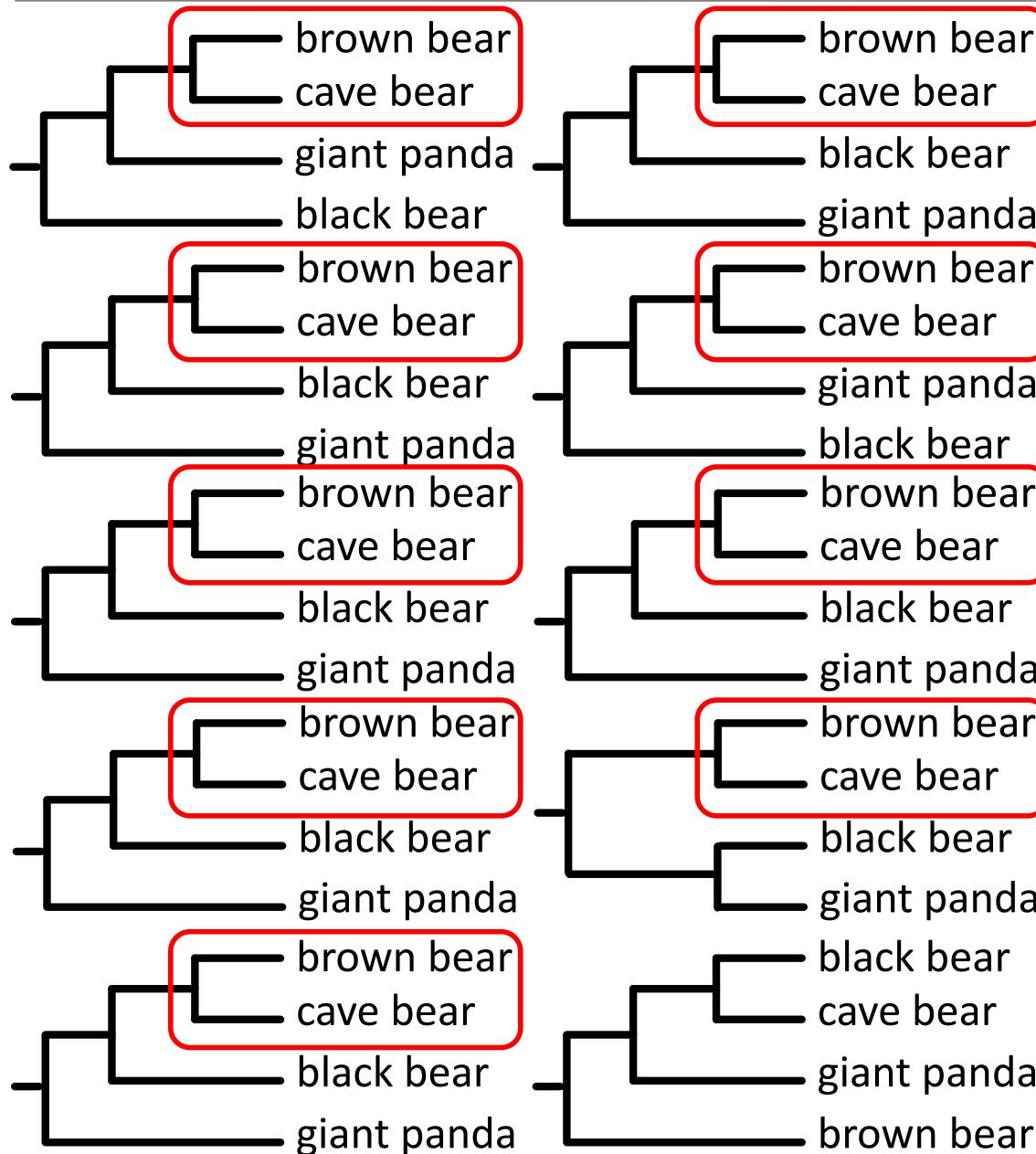
- Take the mean of the sampled values

Mean posterior estimate

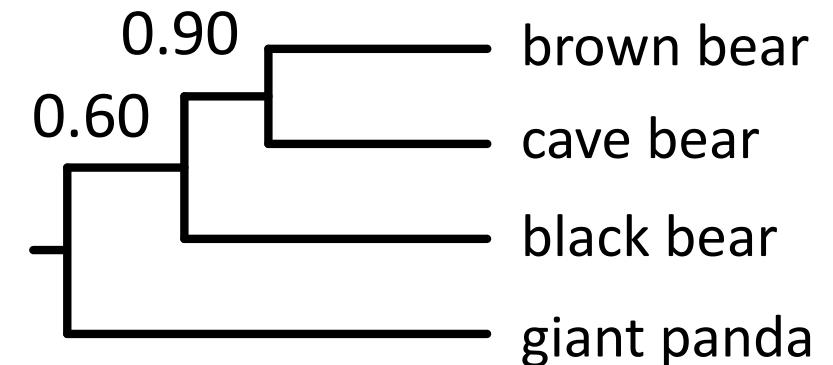
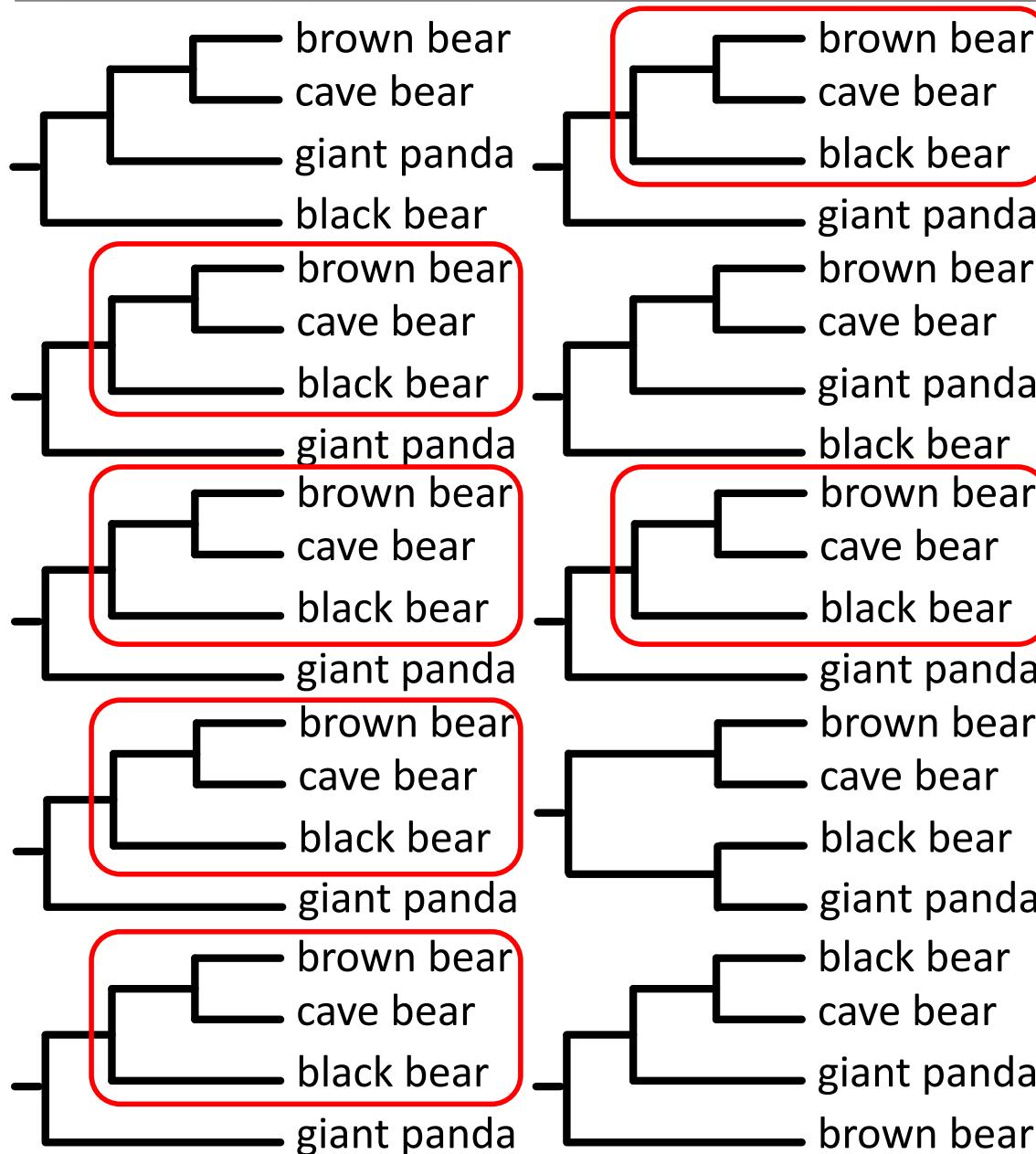
- Take the central 95% of the sampled values

95% credibility interval

Samples from the MCMC



Samples from the MCMC



Samples from the MCMC

- **Majority-rule consensus tree (*MrBayes*)**
Shows all nodes with posterior probability >0.50
- **Maximum a posteriori (MAP) tree**
Sampled tree with highest posterior probability
- **Maximum clade credibility (MCC) tree (*BEAST/TreeAnnotator*)**
Sampled tree with highest sum or product of posterior node probabilities

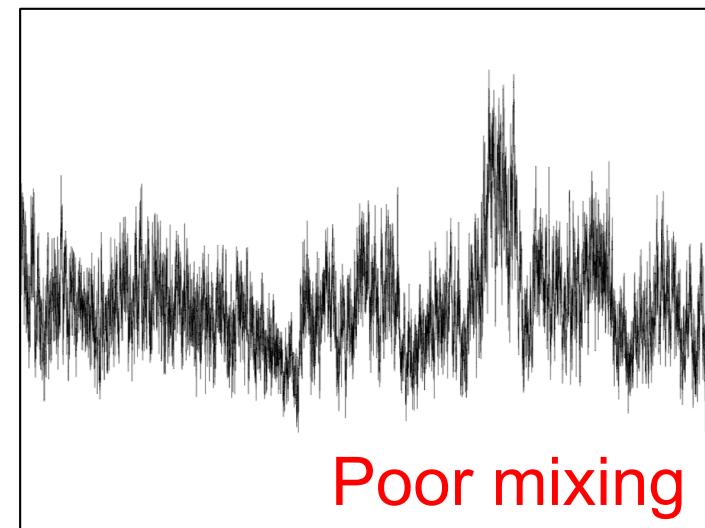
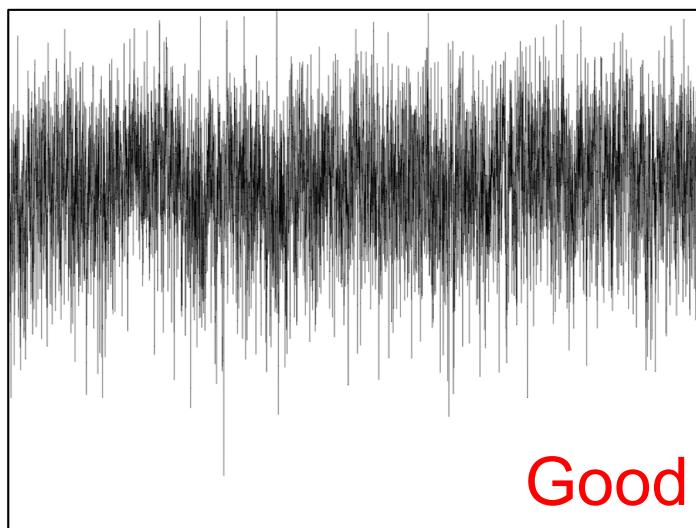
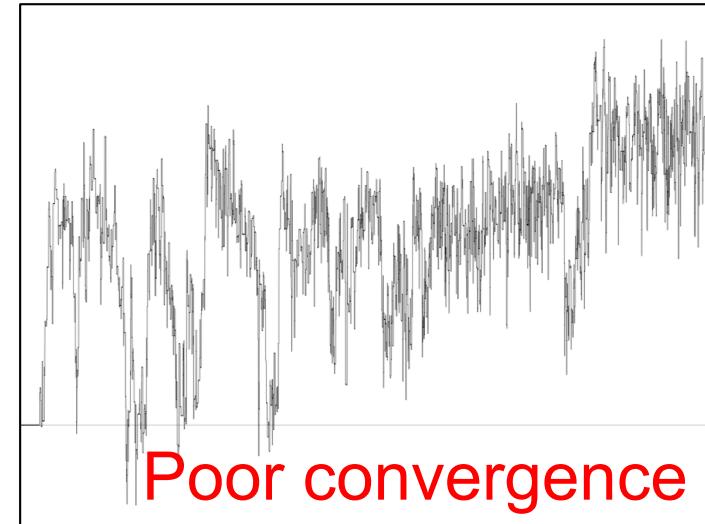
Diagnostics

1. Convergence

Are we drawing samples from the stationary distribution?

2. Sufficient sampling

Have we drawn enough samples to allow a reliable estimate of the posterior distribution?



Convergence

- Run at least 2 independent chains
- Posterior probabilities and likelihoods should be similar
- **Model parameters**
 - Check if estimates of model parameters are similar between runs

Sufficient sampling

- **Effective sample size (ESS)**
 - Have we drawn enough independent samples to produce a reliable estimate of the posterior distribution?
- ESS is preferably **>200** for each parameter
- ESS can be increased by:
 - Increasing the length of the MCMC
(and decreasing the frequency of sampling)
 - Modifying the MCMC proposals

Advantages and Problems

Advantages

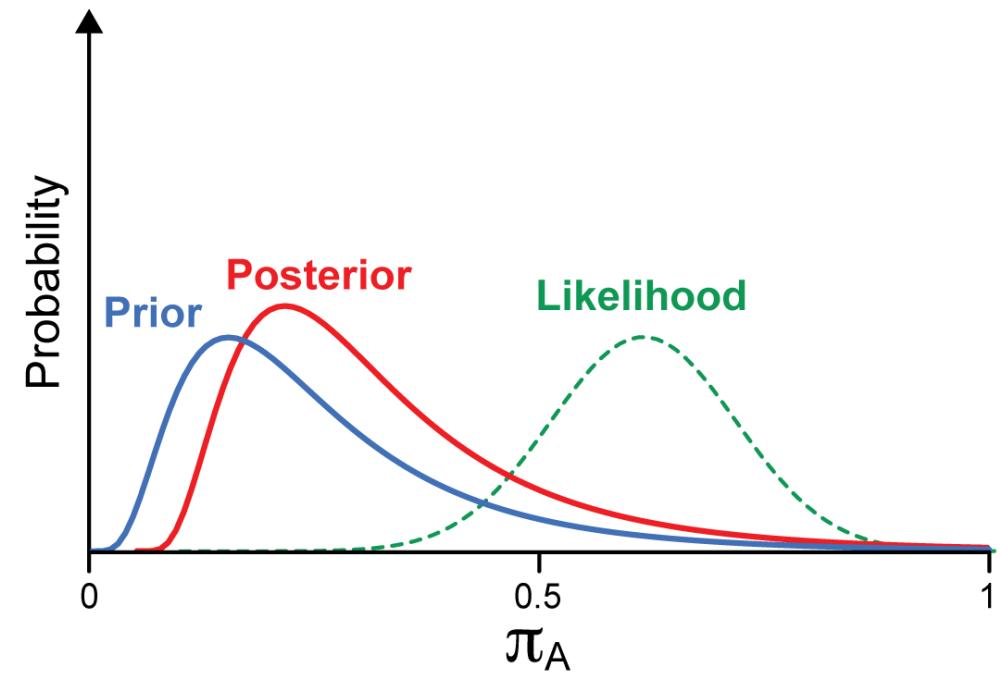
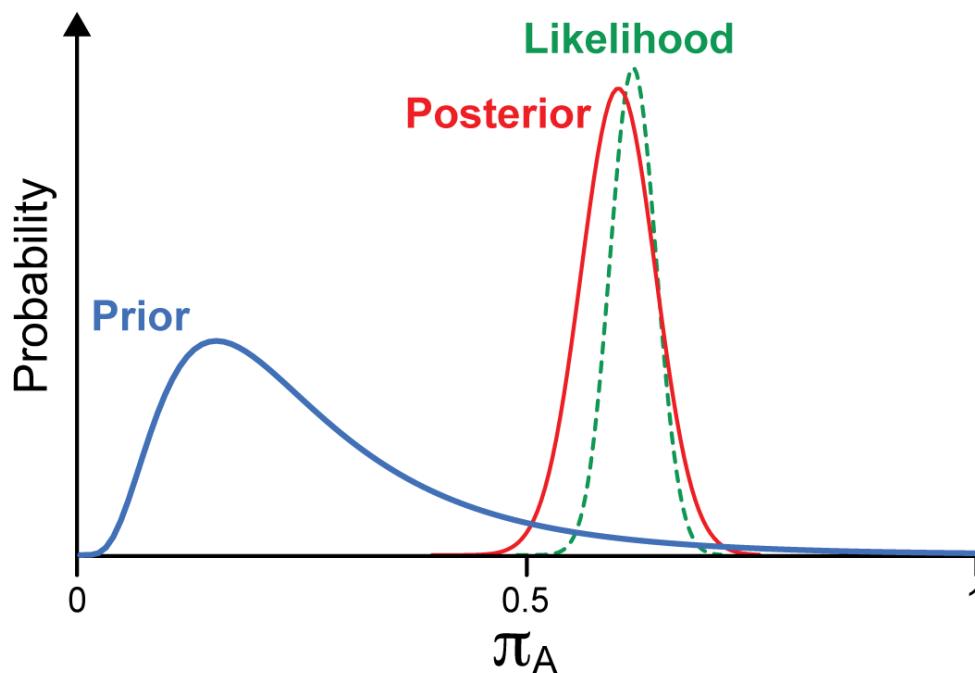
- Able to **implement highly parameterised models**
- **Estimating tree uncertainty** is straightforward
 - Can only do this indirectly in likelihood (via bootstrapping)
- **Posterior probabilities** have an intuitive interpretation
- Can incorporate **independent information** (in the prior)

Nuisance parameters

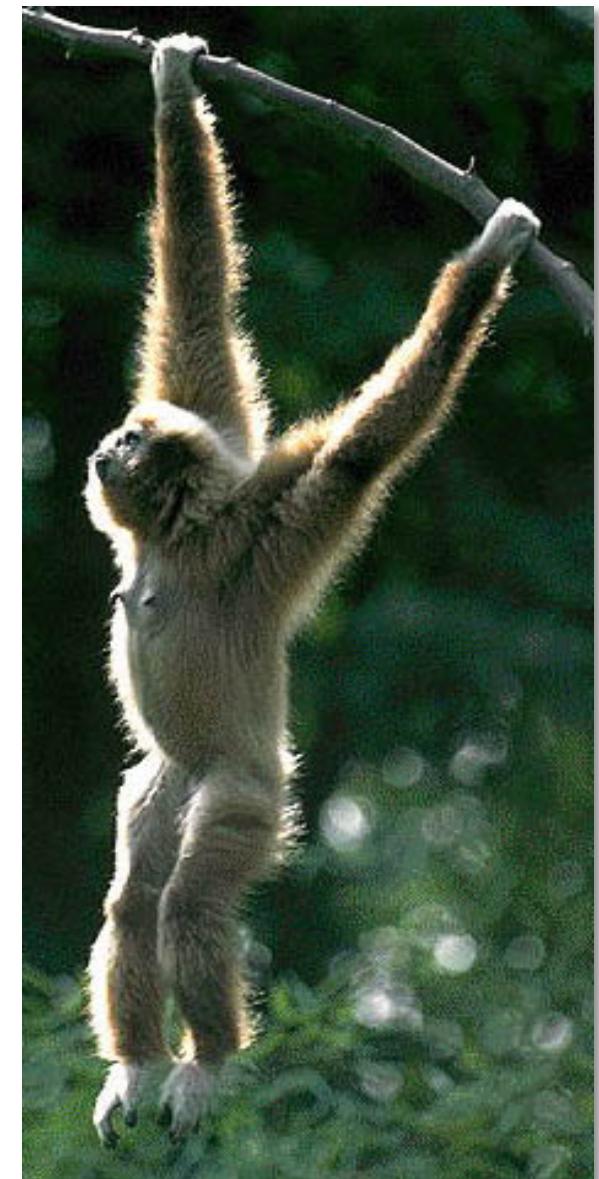
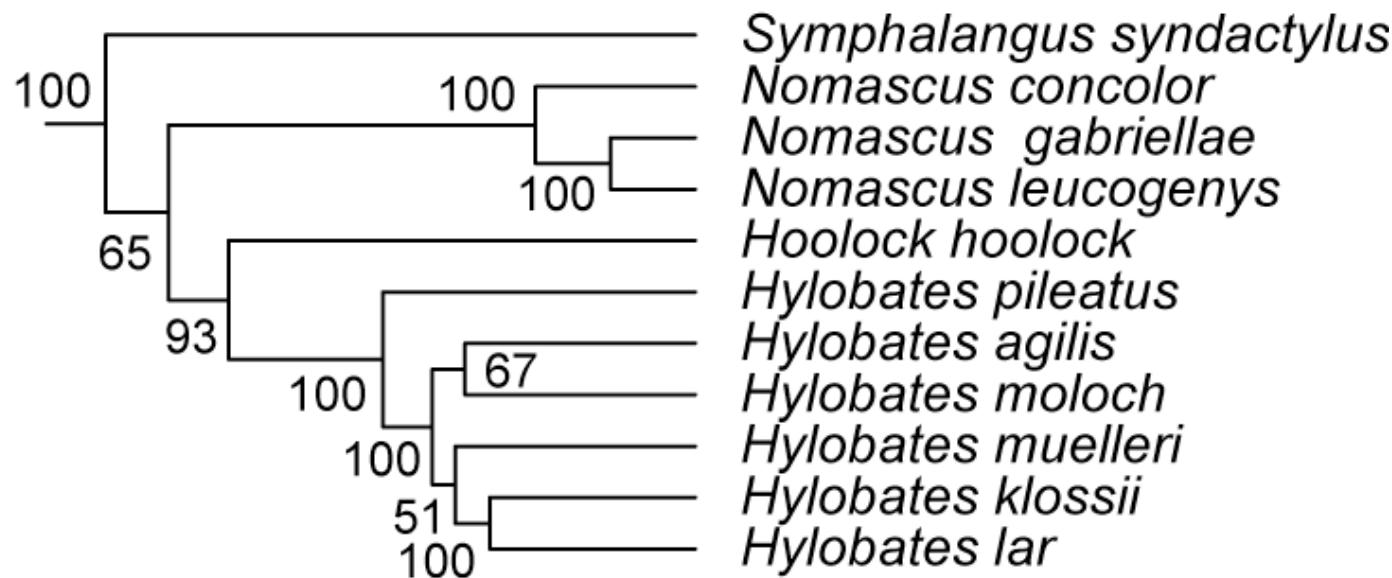
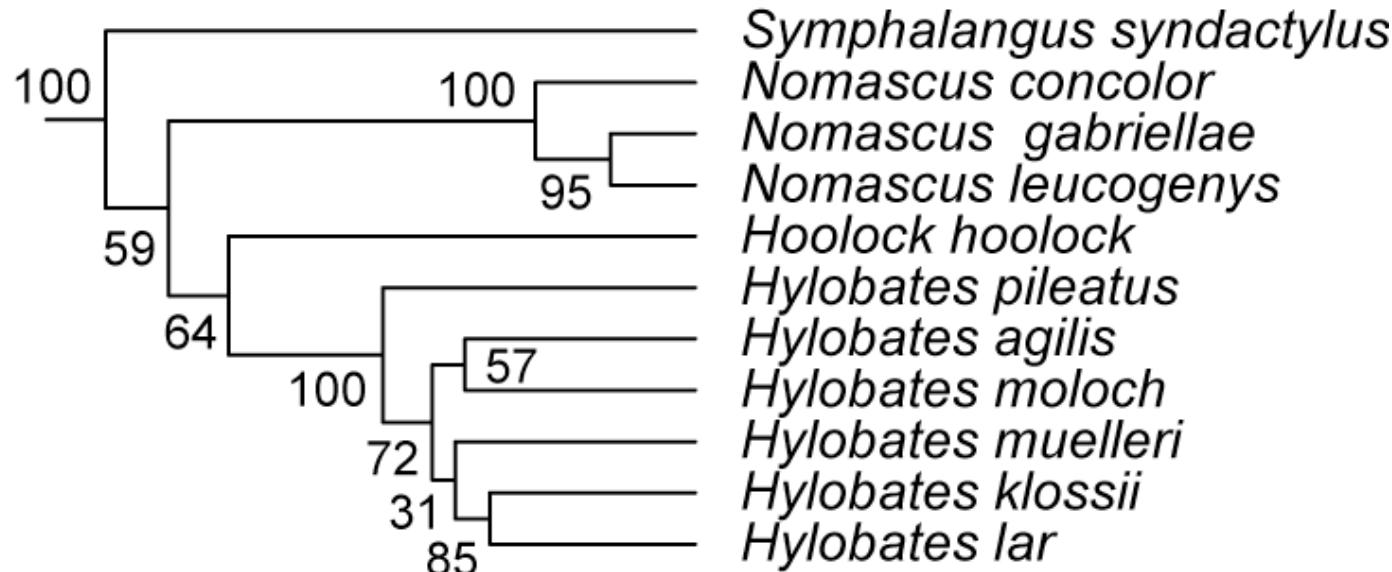
- Integrate over ‘nuisance’ parameters
- Marginal distribution of a parameter of interest

Influence of priors

- Sensitivity of the posterior to the prior
- This problem can occur if the data are uninformative, the prior is strong, or both



Problems: Inflated support values?



BEAST 1

- Bayesian Evolutionary Analysis by Sampling Trees
- Analyse population- or species-level data
- Simultaneous estimation of tree and node times
- Range of clock models
- Range of tree priors and demographic models





- Re-write of *BEAST* to increase modularity
- Users can extend *BEAST* by adding packages
- Additional tree priors not available in *BEAST* 1
- Capacity to perform simulations

For a comparison of *BEAST* 1 and 2:
www.beast2.org/beast-features

MrBayes

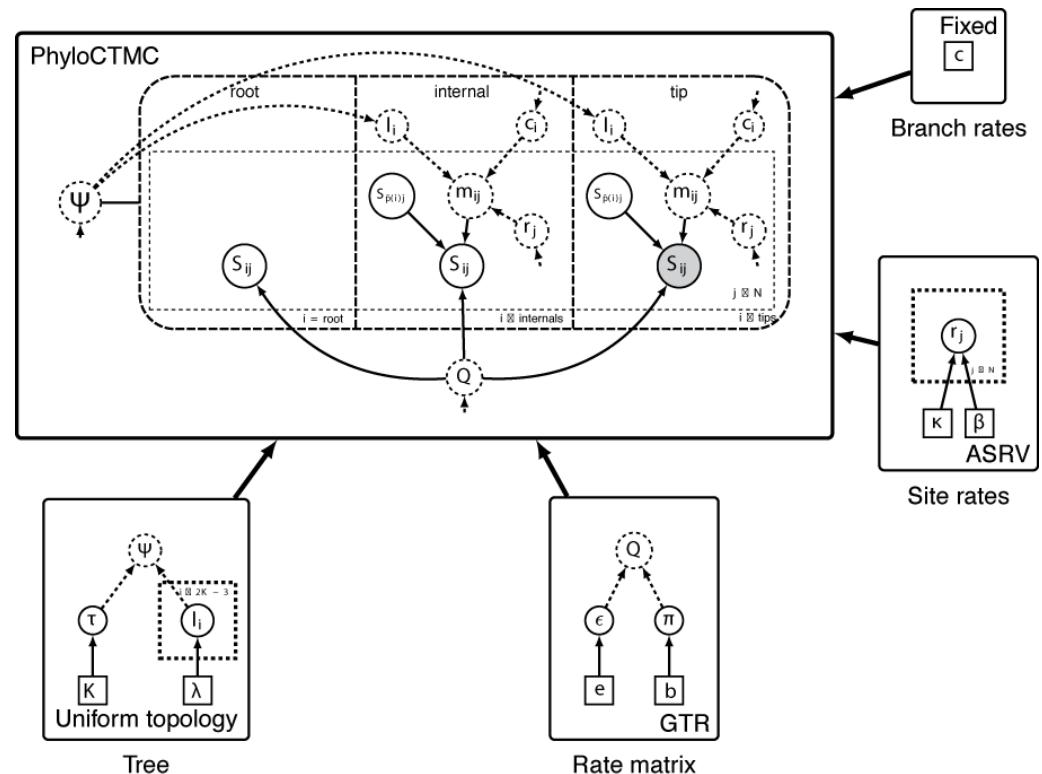
- Primarily designed for species-level data
- Simultaneous estimation of tree and node times
- Range of clock models
- Range of tree priors
- Multiple chains and MCMC diagnostics



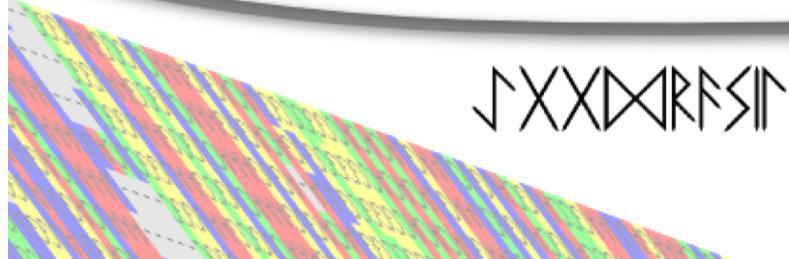
RevBayes



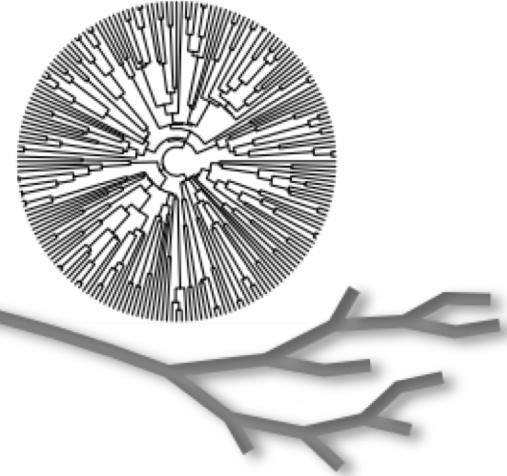
- Uses its own R-like language, Rev
- Interactive construction of graphical model
- Flexible and can be used for simulation and inference
- Ongoing development



EXABAYES



XXDREFSII



- Analyses of large data sets on computing clusters
- Available priors similar to those in older versions of *MrBayes*
- Limited options, no molecular dating
- Likelihood component adapted from *RAXML*

Useful references

