Bayesian phylogenetic inference

Comparative Genomic Analyses

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Bayesian inference

Bayesian inference: way to reason about probabilities.

- nothing more than a probability analysis
- a mathematical formalization of a decision process
- constitutes a different interpretation of probability

Thomas Bayes (1702-1761)

Bayesian inference

Bayesian approach to probability has some unique aspects.

- prior beliefs
- information from the data
- the idea of updated probability

Bayesian inference

The Bayes' theorem or Bayes' rule is the fundamental formula of Bayesian inference.

$$p(\theta|D) \propto p(\theta)p(D|\theta)$$

- $p(\theta)$: **prior distribution**
- $p(D|\theta)$: **likelihood**
- $p(\theta|D)$: **posterior distribution**

The posterior distribution specifies the the probability after the prior has been updated with the available data.

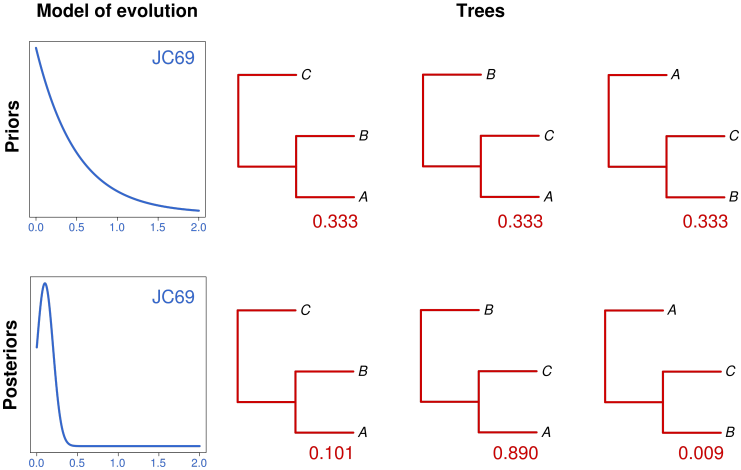
Bayesian phylogenetic inference

The Bayes' theorem translates straightforwardly to tree inference problems.

$$p(\tau, \theta | D) \propto p(\tau, \theta) p(D | \tau, \theta)$$

- D is the molecular sequence alignment
- τ and θ represent the tree and the model of evolution parameters

Bayesian phylogenetic inference



Bayesian phylogenetic inference

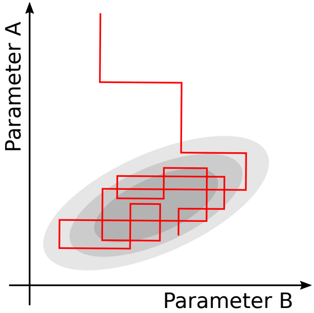
Estimating the posterior distribution in a phylogenetic context can be difficult.

- impossible to derive $p(\tau, \theta|D)$ analytically
- concentrated in a small part of a vast parameter space

Markov chain Monte Carlo

The posterior distribution is estimated using Markov chain Monte Carlo (or **MCMC**) sampling.

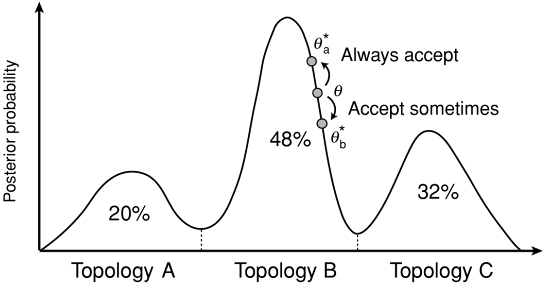
- set up a Markov chain that converges to the posterior probability distribution
- MCMC represents random samples from the posterior



Markov chain Monte Carlo

Metropolis-Hastings algorithm is an MCMC method.

- make small random changes on the parameter values
- accept or reject those changes according to the appropriate probabilities



Markov chain Monte Carlo

An MCMC run is a random sample of the posterior distribution.

- the amount of time it spends sampling a particular region is proportional to the posterior probability of that region given that it converged to the target distribution
- convergence needs to be monitored

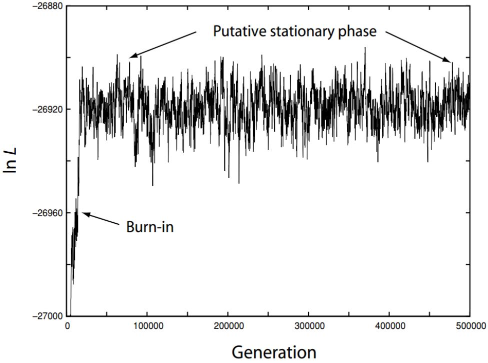
Markov chain Monte Carlo

Burn-in:

- early phase of the run
- heavily influenced by the starting points
- likelihood increases very rapidly

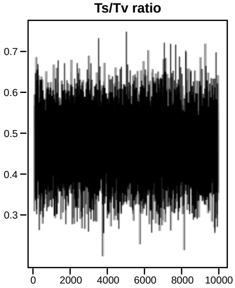
Stationary phase:

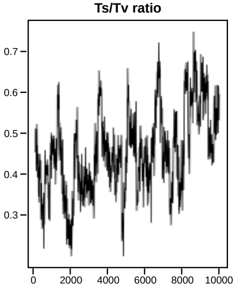
- the chain approaches its stationary distribution
- the likelihood values reach a plateau

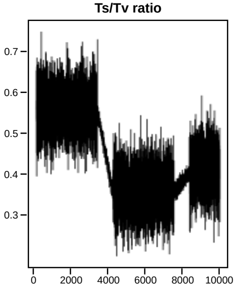


Markov chain Monte Carlo

Checking the convergence of MCMC with trace plots:







Summarizing the posterior distribution

The model parameters and the tree are summarized differently:

- model parameters are usually continuous and can be summarized as any usual statistics: means, median, the credibility interval
- trees are more difficult to summarize
- **posterior clade probabilities**: the sum of the posterior probabilities of all trees that contain that clade

Summarizing the posterior distribution

Exercise
Bayesian phylogenetic inference in a sequence alignment with five species returned the three topologies with the following posterior probabilities (P.p.):

Topology	P.p.
`(((Human,Dog),(Chicken,Lizard)),Frog)`	0.76
`((((Human,Dog),Chicken),Lizard),Frog)`	0.17
`(((Human,Dog),Chicken),(Lizard,Frog))`	0.07

What is the posterior probability of the following clades: (Chicken,Frog), (Chicken lizard), ((Human,Dog),Chicken) and (Human,Dog)?

Bayesian *versus* maximum likelihood trees

Maximum-Likelihood trees

- $p(D|\tau,\theta)$
- Maximum likelihood tree
- ignores pre-existing information
- bootstrapping
- resample characters

Bayesian trees

- $p(\tau,\theta|D)$
- Maximum a-posteriori tree
- considers pre-existing information
- MCMC
- resample parameters

Literature

The Phylogenetic Handbook by Lemey, Salemi and Vandamme (2009)
Cambridge University Press

- Chapter 7: sections 7.1, 7.2 and 7.3, 7.4, 7.6, 7.7 and 7.9