Bayesian phylogenetics

In ML we choose the hypothesis that maximizes the probability of the data [e.g., L_h = Pr(H|D)]. This makes sense, but the L_h number itself is rather meaningless to us. What we really want to know is the probability of the hypothesis given the data.

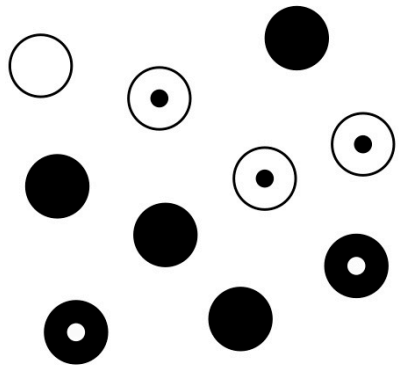
To evaluate this probability we use an equation named after Thomas Bayes (1702-1761), an English mathematician and Presbyterian minister, which shows us how opinions about a hypothesis held prior to the experiment should be modified by the evidence of the experiment:

$P(H_i|E) = P(E|H_i)xP(H_i)/P(E)$ (1)

In this equation $(H_i|E)$ is the posterior probability of the hypothesis *i* after experiment E; $P(E|\ H_i)$ is the likelihood of the hypothesis *i*; and $P(H_i)$ is its prior probability.

To understand this equation, we have to understand the concepts of joint, marginal, and conditional probabilities, which can be explained using an example with marbles (or with girls and their hair color…).

Example with marbles



We also used an example with an unknown paternal genotype to understand the idea behind the posterior probability.

Genotype of a mother: aa
Genotype of a child: Aa
Genotype of the father?

If we know genetics, and the father is biological, we have to consider two possibilities: AA and Aa, hence two hypotheses:

	H1	H2	Row sum
Genotype	AA	Aa	-
Prior probability	0.5	0.5	1
Likelihood	1	0.5	-
Likelihood x Prior	0.5	0.25	0.75
Posterior probability	2/3	1/3	1

So, even if we don't know anything about the frequencies of two alleles in a population (flat prior), but we know that the child is Aa, the probability that the father is AA is 2/3.

Homework problem:

- Suppose that we have a rare genetic disease in the human population, which the occurrence rate 1 in 1000.
- Suppose that you bought one of the fancy genomic screening kits, which includes a test for this disease and the test comes out positive (although you have no symptoms yet!)
- You frantically read the instructions and find out that the test has a 99% hit rate, meaning that if a person has the disease, then the test result is positive 99% of the time.
- You also read that the test has a false alarm rate of 5%
- What is the probability that you have a disease?

So far, we considered discrete characters/parameters. In case of continuous parameters (e.g., rates, branch lengths, frequencies of nucleotides, etc), we need to modify and use probability densities rather than probabilities per se:

$$f(\Theta|D) = \frac{f(D|\Theta)f(\Theta)}{\int_{\Theta} f(D|\Theta) \cdot f(\Theta) d\Theta}$$

where $f(\Theta|D)$ is the posterior probability density; $f(D|\Theta)$ – the likelihood, $f(\Theta)$ – the prior probability density, and the denominator – the marginal probability of the data.

It is practically impossible to do Bayesian calculations analytically because denominator involves summing and integrating over all possible hypotheses. But it is relatively easy to calculate the ratio of posterior probabilities, as two denominators cancel out. Random sampling of parameter space is also impossible (Huge space, most of it with very low probability). Thus posterior probability density is approximated by the Markov Chain Monte Carlo (MCMC) method.

Markov chain Monte Carlo (MCMC) is a general computational technique for evaluating sums and integrals, especially those that arise as probabilities or expectations under complex probability distributions.
Monte Carlo implies that the method is based on using chance.

Markov Chain indicates a dependent sampling scheme with the probability distribution of each sampled point depending on the value of the previous one.

MCMC works by taking a series of steps that form a conceptual chain. The algorithm used to make these steps is known as **Metropolis-Hastings** algorithm. At each iteration, the algorithm picks a candidate for the next sample value based on the current sample value. Then, with some probability, the candidate is either accepted (in which case the candidate value is used in the next iteration) or rejected (in which case the candidate value is discarded, and current value is reused in the next iteration). The probability of acceptance is determined by comparing the likelihoods of the current and candidate sample values.

A related term is **Gibbs sampling** (named after the physicist Josiah Willard Gibbs), which in its basic version, is a special case of the Metropolis–Hastings algorithm but, in its extended versions can be considered a general framework for sampling from a large set of variables by sampling each variable in turn that incorporates the Metropolis–Hastings algorithm. Gibbs sampling is applicable when the joint distribution is not known explicitly, but the conditional distribution of each variable is known and can be sampled from. The Gibbs sampling algorithm generates an instance from the distribution of each variable in turn, conditional on the current values of the other variables. It can be shown that the sequence of samples constitutes a Markov chain, and the stationary distribution of that Markov chain is just the sought-after joint distribution.

Metropolis-coupled Markov chain Monte Carlo (MCMCMC) involves running several chains simultaneously. One is the cold chain, the rest are heated chains. Chain is heated by raising densities to a power less than 1.0. These heated chains increase the acceptance probabilities making it easier to cross the likelihood valleys. Chains are allowed to swap with the cold chain from time to time. Only the cold chain is sampled.

Comparison between Bayesian and ML inference (p. 175-176 of the textbook):

1) Both are model-based methods in which a probabilistic description of the data generation process is assumed;
2) Both involve computing P(data | p) for parameter values p. In Maximum Likelihood, this is the Likelihood function we seek to maximize; in a Bayesian analysis it appears in the process of computing the posterior distribution.
3) A Bayesian analysis requires specifying a prior distribution of the parameters we seek to infer, which expresses our beliefs in what parameter values are likely before the data are considered.
4) Maximum Likelihood produces a single estimate, called a point estimate, of the parameters we infer. A Bayesian analysis produces a distribution of estimates, the posterior distribution, which indicates differing levels of support for different parameter values.