Maximum Likelihood and the Bootstrap

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Principle of Maximum Likelihood

- Given parameters θ and data X
- The function $f(X \mid \theta)$ is the probability of observing data X given parameter θ. (Both X and θ can be multi-dimensional.)
- Keeping θ fixed, and treating f as a function of X, the total probability is one.

Principle of Maximum Likelihood

- The function $L(\theta) = f(X \mid \theta)$ with X fixed and θ unknown is called the *likelihood function*.
- The *principle of maximum likelihood* is to estimate θ with the value $\hat{\theta}$ that maximizes $L(\theta)$.
- In practice, it is common to maximize the log-likelihood, $\ell(\theta) = \ln L(\theta)$.
- This is because X often takes the form of an independent sample so that

$$L(X) = \prod_{i=1}^{n} f(X_i \mid \theta), \qquad \ell(\theta) = \sum_{i=1}^{n} \ln f(X_i \mid \theta)$$

Coin-tossing Example

- A coin has a probability θ of being a head.
- Consider tossing the coin 100 times. The probability of each single sequence with exactly x heads is $f(x \mid \theta) = p^x(1-p)^{100-x}$.
- Say we observe the sequence

$$HHTHTHHT \dots TTH$$

  where heads appear 57 times.
- The maximum likelihood estimate is the value $\hat{\theta}$ that maximizes the function

$$L(\theta) = \theta^{57}(1-\theta)^{43},$$

  or, equivalently that maximizes

$$\ell(\theta) = 57(\ln \theta) + 43(\ln(1-\theta)) \; .$$

  Simple calculus and common sense lead to the estimate $\hat{\theta} = 0.57$.

Maximum-likelihood edge lengths

- For the Jukes-Cantor model, a pair of sequences have x sites with observed differences and $n - x$ sites with the same base.
- The probability of any given sequence pair is

$$L(d) = \left(\frac{1}{4}\right)^n \times \left(\frac{1}{4} - \frac{1}{4}\mathrm{e}^{-\frac{4}{3}d}\right)^x \times \left(\frac{1}{4} + \frac{3}{4}\mathrm{e}^{-\frac{4}{3}d}\right)^{n-x}$$

which has the form

$$L(\theta) = C \times \theta^x (1 - 3\theta)^{n-x}$$

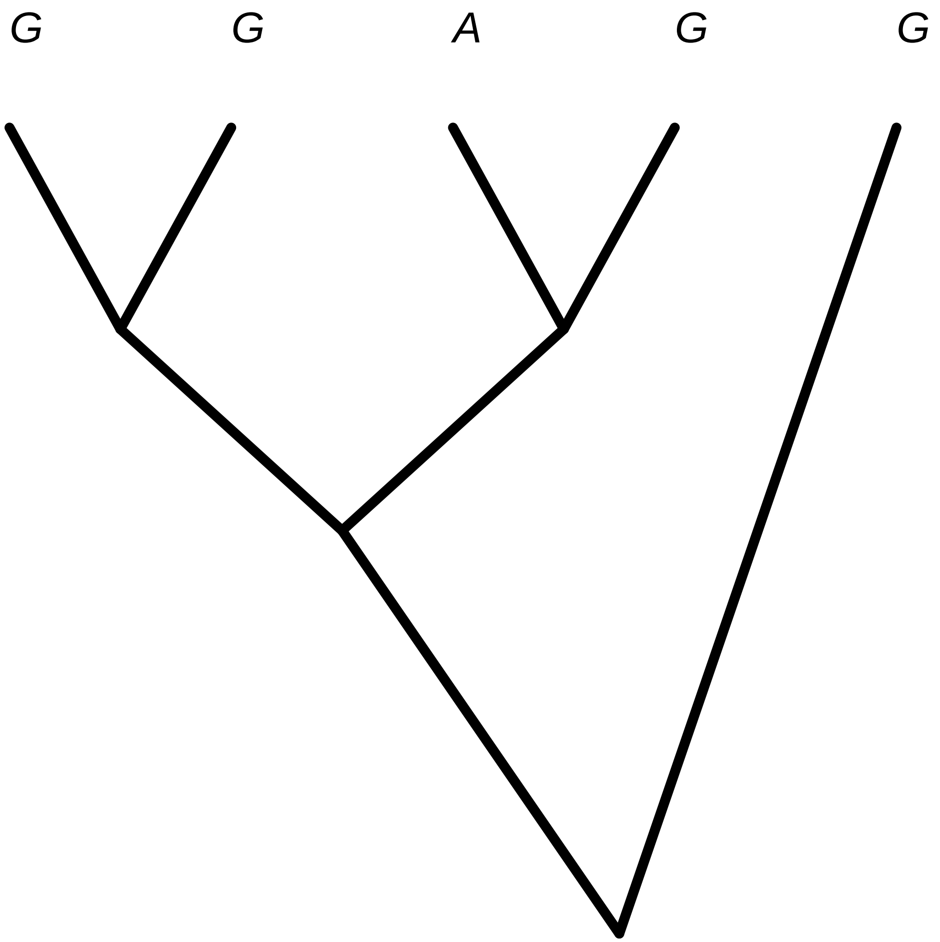
where

$$\theta = \frac{1}{4} - \frac{1}{4}\mathrm{e}^{-\frac{4}{3}d} \ .$$

- Solving the calculus problem yields $\hat{\theta} = \frac{x}{3n}$.
- Plugging in and solving for d gives

$$\hat{d} = -\frac{3}{4} \ln\left(1 - \frac{4}{3}\frac{x}{n}\right)$$

Computing Likelihood on a Tree



Transition Probabilities

$$P(0.1) = \begin{bmatrix} 0.90 & 0.04 & 0.04 & 0.03 \\ 0.03 & 0.91 & 0.04 & 0.03 \\ 0.03 & 0.04 & 0.91 & 0.03 \\ 0.03 & 0.04 & 0.04 & 0.90 \end{bmatrix} \qquad P(0.2) = \begin{bmatrix} 0.81 & 0.07 & 0.07 & 0.05 \\ 0.05 & 0.83 & 0.07 & 0.05 \\ 0.05 & 0.07 & 0.83 & 0.05 \\ 0.05 & 0.07 & 0.07 & 0.81 \end{bmatrix}$$

$$P(0.4) = \begin{bmatrix} 0.67 & 0.13 & 0.13 & 0.08 \\ 0.08 & 0.71 & 0.13 & 0.08 \\ 0.08 & 0.13 & 0.71 & 0.08 \\ 0.08 & 0.13 & 0.13 & 0.67 \end{bmatrix}$$

Model Selection

12 *rbcL* genes from 12 plant species

Model	p	ℓ
JC69	21	-6262.01
K80	22	-6113.86
HKY85	25	-6101.76
HKY85 + Γ_5	26	-5764.26
HKY85 + C	35	-5624.70

- The AIC criterion is to select the model with the lowest AIC score, which is

$$\text{AIC} = -2\ln(\text{likelihood}) + 2 \times (\#\text{ of parameters})$$

- AIC balances the competing goals to fit the data well (likelihood high) and keep the model simple (few parameters).
- For this data, the HKY85+C model is the best among those compared; using 9 more parameters yielded an improvement in loglikelihood of over 139, which lowered the AIC by about 130.

The Bootstrap: A brief history

- The bootstrap was introduced to the world by Brad Efron, chair of the Department of Statistics at Stanford University, in 1979.
- The bootstrap is one of the most widely used new method in statistics that was invented within the past 50 years.
- In a special issue of *Statistical Science* that celebrates the 25th anniversary of the bootstrap, Brad Efron uses its application to phylogenetics as one of a small number of examples to illustrate its use and importance.

The General Bootstrap Framework

- We have a sample $x_1, \ldots, x_n$ drawn from a distribution F from which we wish to estimate a parameter θ using a statistic $\hat{\theta} = T(x_1, \ldots, x_n)$. (We might think of θ as being the median of the distribution, for example, and $\hat{\theta} = T(x_1, \ldots, x_n)$ as the sample median.)
- If we wanted to compute the standard error of the estimate, we would ideally compute the standard deviation of $T(X_1, \ldots, X_n)$ where $X_i \sim \mathrm{iid}\ F$.
- We could estimate this to any desired degree of accuracy by generating a large enough number (say B) of random samples $X_1, \ldots, X_n$, computing $\hat{\theta}_i = T(X_1, \ldots, X_n)$ for the ith such sample, and then computing the standard deviation of these estimates.

$$\sqrt{\frac{\sum_{i=1}^{B}(\hat{\theta}_i - \theta)^2}{B}}$$

The Key Idea

- Unfortunately, we cannot take multiple samples from F.
- However, our original sample $x_1, \ldots, x_n$ *is an estimate of the distribution F*.
- Instead of taking samples from F, we could sample from the estimated distribution $\hat{F}$ by sampling from our original sample *with replacement*.

The Procedure

- We sample n values $x_1^*, \ldots, x_n^*$ with replacement from $x_1, \ldots, x_n$.
- It is very likely that some of the original x values will be sampled multiple times and others will not be sampled at all.
- For each sample, compute the estimate of θ using the original statistic.
- The ith estimate is $\hat{\theta}_i^* = T(x_1^*, \ldots, x_n^*)$.
- Repeat this B times and compute the standard deviation of the bootstrap estimates around the estimate from the original sample.

$$\sqrt{\frac{\sum_{i=1}^{B}(\hat{\theta}_i^* - \hat{\theta})^2}{B}}$$

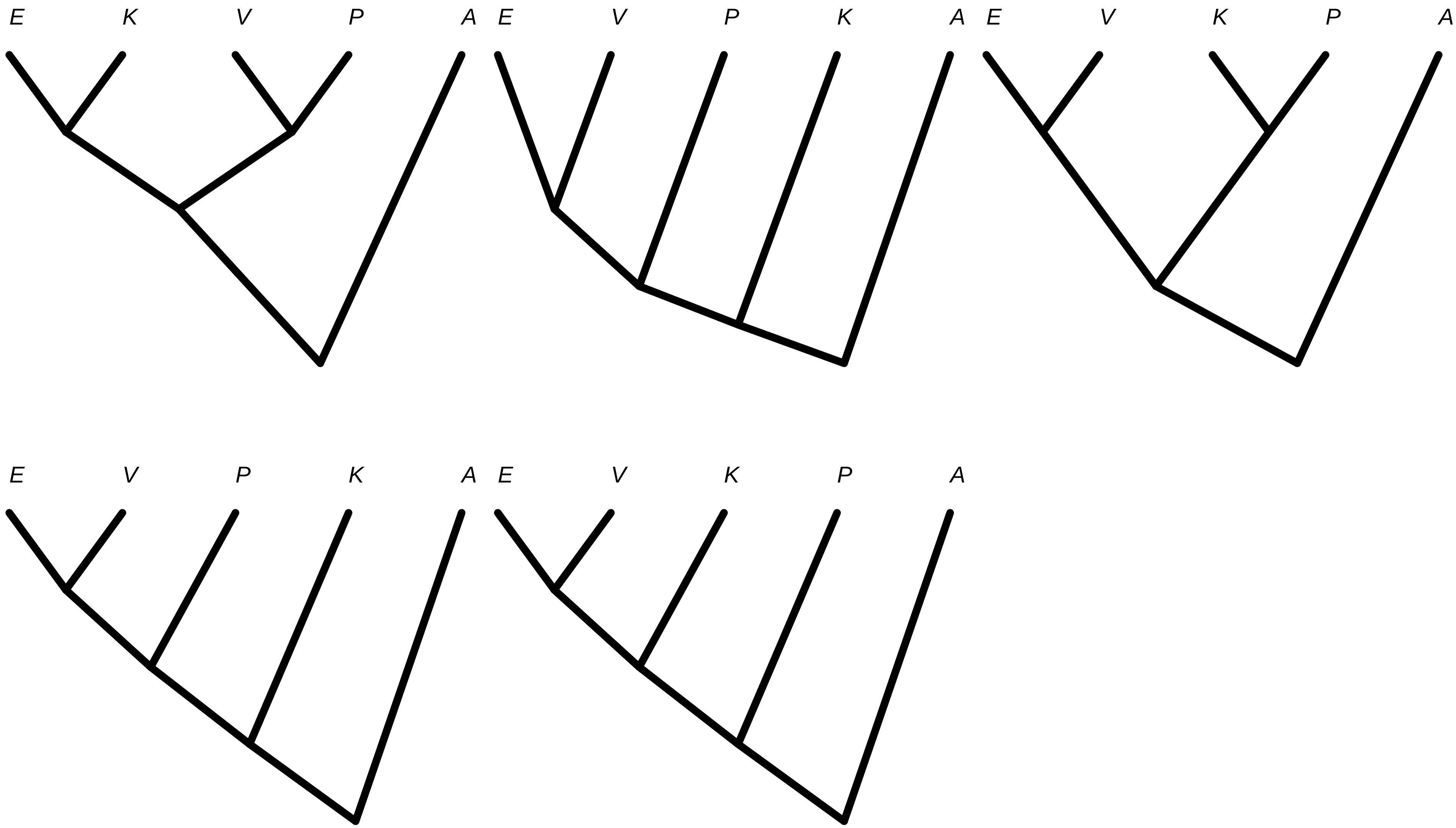
Why it works

- If the sampling distribution of the bootstrap sample estimate $\hat{\theta}^*$ around the estimate $\hat{\theta}$ is similar to the sampling distribution of the estimate $\hat{\theta}$ around the true value θ, then the boostrap standard error will be a good estimate of the real standard error.
- The bootstrap can be used to estimate bias, variance, for confidence intervals, and for hypothesis testing in many situations.
- It does depend critically on the assumption of independence of the original sample.

Consensus Trees

- A *strict consensus tree* shows only those clades that appear in every sampled tree.
- A *majority rule consensus tree* shows all clades that appear in more than half the sample of trees.
- (Notice that two clades that each appear in more than half the sampled trees must appear in at least one tree together, implying that they are compatible with one another.)
- A *priority consensus tree* adds clades to the majority rule consensus tree in order of decreasing frequency in the sample provided that these clades do not conflict with a clade with higher frequency.

Example



Dynamic Exploration of Tree Samples

- Show off Mark Derthick's **Summary Tree Explorer**.
- Software is free and available at `http://cityscape.inf.cs.cmu.edu/phylogeny/` .

Interpretation of Bootstrap Proportions

What does a bootstrap porportion mean? Let me count the ways.

- *Confidence* that the clade is in the true tree.
- Bayesian posterior probability that the clade is in the true tree.
- One minus p-value for a formal hypothesis test that the clade is in the true tree.
- Rough measure of method robustness.
- Measure of repeatability of the inferences for the method at hand.
- Others?