This matrix displays pairwise distances among three species.

	A	B	C
A	0	4	6
B	4	0	8
C	6	8	0

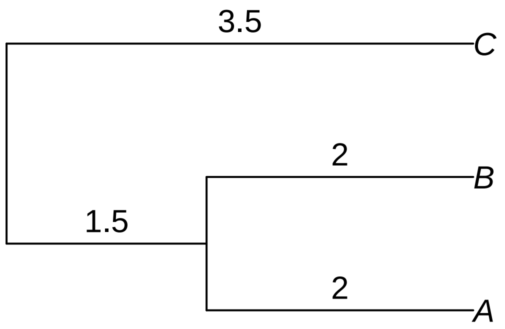
1. (10 points) Find the UPGMA tree and neighbor-joining trees associated with the distance matrix. Draw each tree to scale and indicate branch lengths with numbers. Indicate in your drawing if each tree is rooted or not.

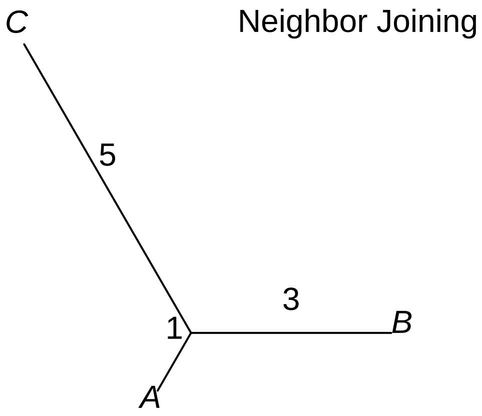
Solution:

UPGMA tree: ((A:2,B:2):1.5,C:3.5);
First join A and B at a depth of $4/2 = 2$. New distance from A/B to C is $(6+8)/2 = 7$. Depth of MRCA of A/B and C is $7/2 = 3.5$, so A/B MRCA is 1.5 from the root and C is 3.5 from the root.

NJ tree: (A:1,B:3,C:5);
Adjusted matrix has all off-diagonal values -18; so can join any pair. $u_A = 10$, $u_B = 12$, $u_C = 14$. Length of edge to A is $(4+10-12)/2 = 1$. Length of edge to B is $(4+12-10)/2 = 3$. New distance from A/B root to C is $(6+8-4)/2 = 5$. As this is the last pair, just connect with this distance.

UPGMA





2. (4 points) Many studies have shown that in a wide variety of settings for generating simulated molecular sequences, distance methods are less accurate (have smaller probabilities of estimating the correct tree) than alternatives including maximum parsimony and maximum likelihood. Provide one possible explanation for this.

   Solution: Distance methods begin by reducing the full sequence matrix to pairwise distances, which loses information.

3. (4 points) Distance methods do have one substantial practical advantage over maximum parsimony and maximum likelihood when the number of taxa in the estimation problem is very large. What is this advantage?

   Solution: They are very fast, even for large numbers of taxa.

The following table summarizes the maximum log-likelihood values for each of three possible tree topologies in a four-taxon molecular data set for an alignment of 1200 nucleotide bases under a variety of likelihood models. The parameters are include those associated with branch lengths of the tree and those associated with the substitution model of molecular evolution. The modifier Γ_4 means that the model included the 4-category discrete Gamma distribution for rate variation among sites and the modifier C means that the model partitioned sites by codon position.

	Tree Topology			
Model	1	2	3	# of Parameters
JC69	$\underline{-2400}$	-2420	-2403	5
K80	-2350	-2365	$\underline{-2348}$	6
HKY95	$\underline{-2160}$	-2177	-2163	9
HKY95+Γ_4	$\underline{-2092}$	-2105	-2094	10
HKY95+Γ_4+C	$\underline{-1880}$	-1897	-1881	22
GTR	$\underline{-2140}$	-2159	-2142	14
GTR+Γ_4	$\underline{-2070}$	-2093	-2074	15
GTR+Γ_4+C	$\underline{-1865}$	-1885	-1867	37

4. (8 points) For each model, find the tree topology that is the maximum likelihood estimate.

   Solution: Highest loglikelihood in each case. Look at underlined values.

5. (4 points) On the basis of AIC, which of these models would be the best to use? Support your answer with a brief numerical calculation.

   Solution: Actually, there is a tie. Models HKY95+Γ_4+C and GTR+Γ_4+C each have the same AIC values (rounded). $2(1880) + 2(22) = 2(1865) + 2(37) = 3804$.

6. (4 points) Briefly explain in concept how one would use the bootstrap to assess the confidence in the maximum likelihood estimate tree topology using the best model from the previous problem by the AIC criterion.

   Solution: For B times (say $B = 1000$), create a new data set by resampling sites with replacement from the original data. For each new data set, find the maximum likelihood tree using the same model as before (say, GTR $+ \Gamma +$ C). For each clade in the maximum likelihood tree from the original data, find the proportion of bootstrap trees that contain the clade.

7. (2 points) The bootstrap and Bayesian inference use different methods to produce collections of trees, which are then summarized. In one case, each tree is associated with a different data set. In the other, each tree is associated with a different set of parameter values for the same data set. Which is which?

   Solution: Bootstrap trees are found form different data sets. Bayesian trees are found for different parameter values.

8. (10 points) Bayesian phylogenetic inference is typically implemented by sampling trees using Markov chain Monte Carlo, but an alternative possibility would be to calculate the probability of the data for each tree topology (averaging over other parameters) and compute the posterior probability for each tree topology using Bayes' Theorem. If one assumed a uniform probability distribution over the three possible tree topologies and the average log-likelihoods (natural log) using the GTR+Γ_4+C model above were -1900, -1918, and -1903, what would be the posterior probability of the first tree topology?

   Solution: The posterior probability of the first tree would be

$$\frac{\exp(-1900)}{\exp(-1900) + \exp(-1918) + \exp(-1903)} = \frac{1}{1 + \exp(-18) + \exp(-3)} = 0.9526.$$