Drzewa filogenetyczne

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How sequences evolve?

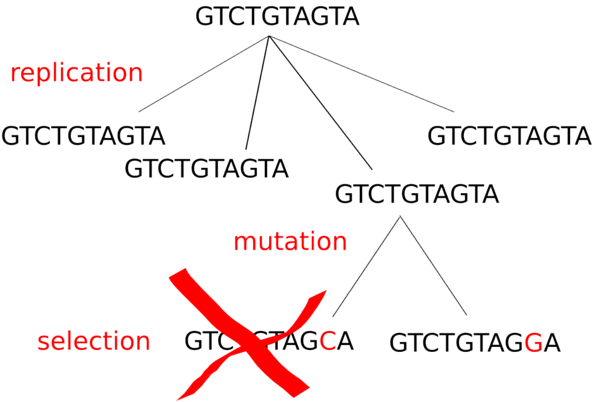


image (c) BW

Tree of life?

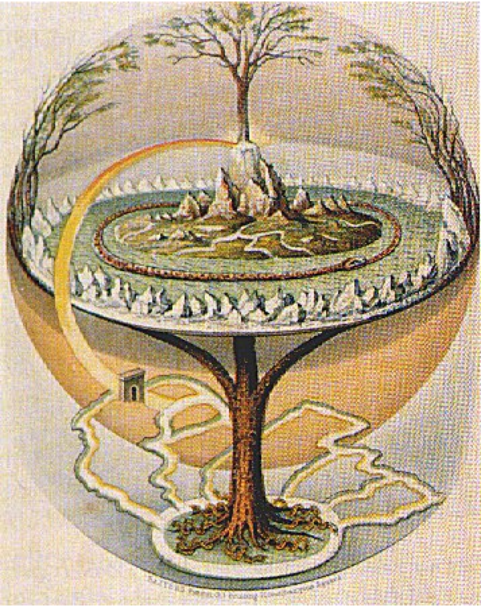


image (c) Wikimedia

Molecular tree of life

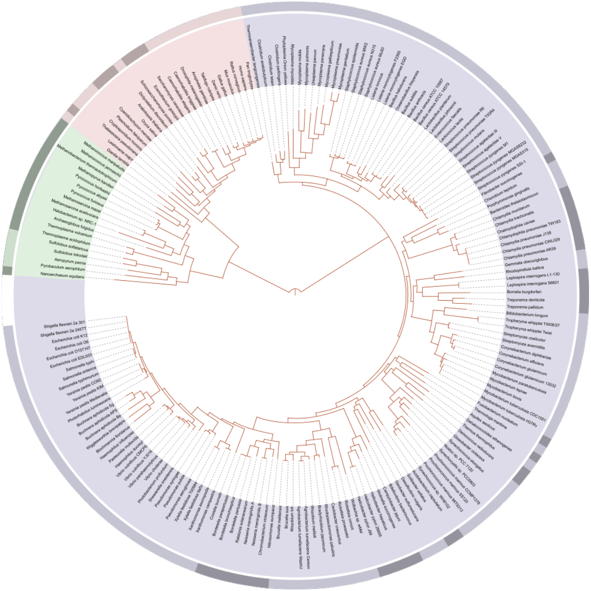


image (c) I. Letunic – itol.org

evolutionary distance vs. similarity

- We are interested in measuring evolutionary distances by looking at molecular sequences
- We expect *distances* to *grow* with **decreasing similarity**
- The sequence alignment problem allows us to find the optimal alignment, however the score of the alignment is a measure of *similarity*, rather than distance
- problem of *maximizing similarity* is similar to *minimizing distance*
- However:
  - We expect $d(x, x) = 0$ while for most a, b , $sim(a, a) \neq sim(b, b)$
  - Distances have triangle inequality, and similarities not

Bifurcating vs. multifurcating trees

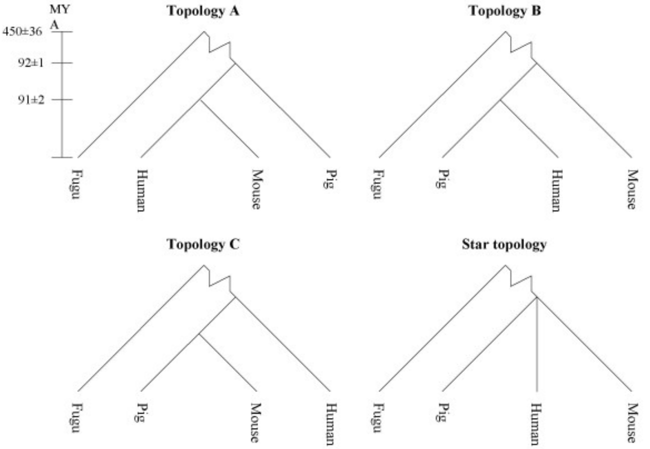
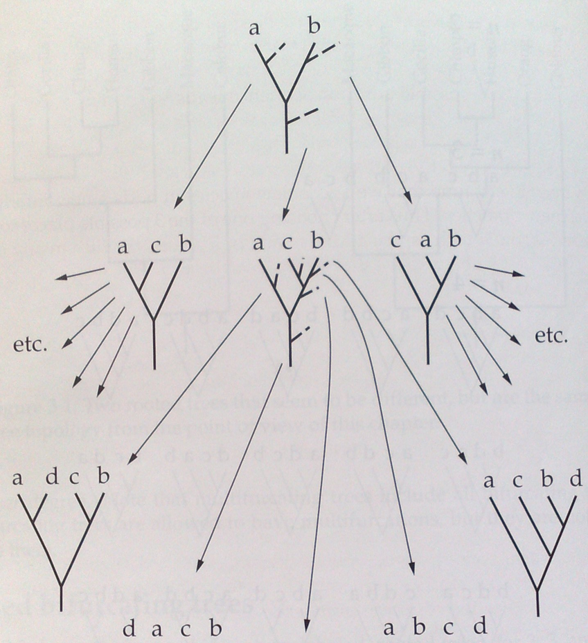
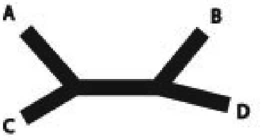


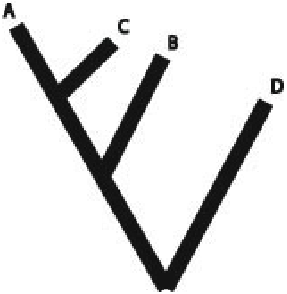
image (c) Jorgensen et al. 2005

How many binary trees are there



Rooted vs. unrooted trees





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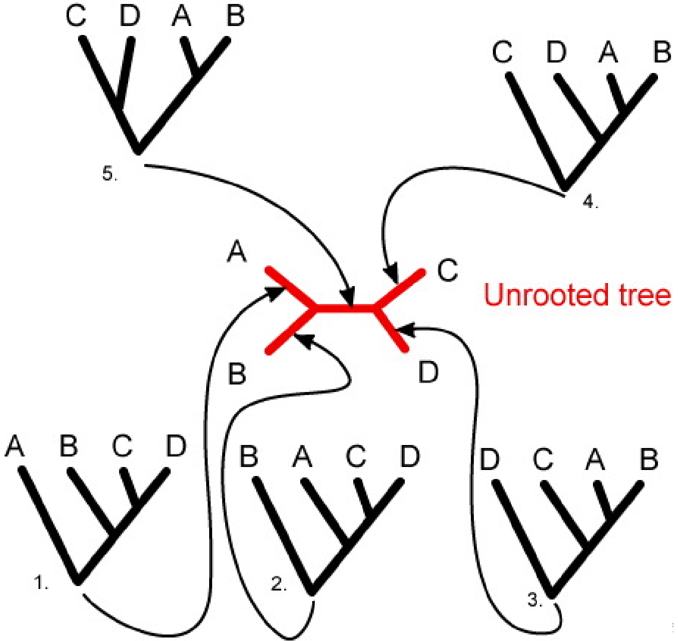
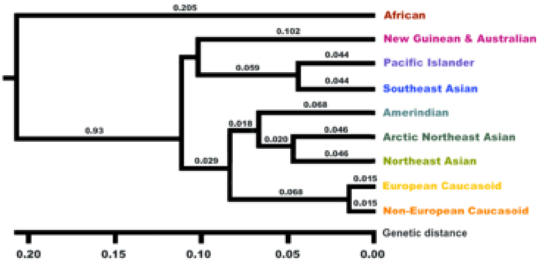
Rooting an unrooted tree

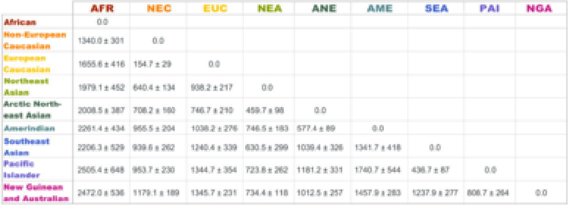


Trees vs. distance matrices

Linkage tree for 9 population clusters showing genetic distances (F_{ST})
(Cavalli-Sforza *et al.*, 1994:80)



F_{ST} distance matrix for the 9 clusters shown above
(x10,000 with standard errors obtained by bootstrap analysis)



	AFR	NEC	EUC	NEA	ANE	AME	SEA	PAI	NGA
African	0.0								
Non-European Caucasian	1340.0 ± 301	0.0							
European Caucasian	1655.6 ± 416	154.7 ± 29	0.0						
Northeast Asian	1979.1 ± 452	640.4 ± 134	938.2 ± 217	0.0					
Arctic Northeast Asian	2008.5 ± 387	708.2 ± 160	746.7 ± 210	459.7 ± 98	0.0				
Amerindian	2261.4 ± 434	955.5 ± 204	1038.2 ± 276	746.5 ± 183	577.4 ± 89	0.0			
Southeast Asian	2206.3 ± 529	939.6 ± 262	1240.4 ± 339	630.5 ± 299	1039.4 ± 326	1341.7 ± 418	0.0		
Pacific Islander	2505.4 ± 648	953.7 ± 230	1344.7 ± 354	723.8 ± 262	1181.2 ± 331	1740.7 ± 544	436.7 ± 87	0.0	
New Guinean and Australian	2472.0 ± 536	1179.1 ± 189	1345.7 ± 231	734.4 ± 118	1012.5 ± 257	1457.9 ± 283	1237.9 ± 277	808.7 ± 264	0.0

image (c) Cavalli-Sforza 1994

Finding an optimal tree

- Given a tree with branch lengths T, we can easily generate distance matrix d_{ij}
- Can we solve the reverse problem, and how does it relate to the original problem?
- Formally, for a given distance matrix D, we want to find a labelled tree T, optimizing the least squares criterion:

$$Q = \sum_{i=1}^{n} \sum_{j=1}^{n} w_{ij} (D_{ij} - d_{ij})^2$$

- In general, it is equivalent to solving the Steiner tree problem – one of the the original NP-complete problems
- Can we find any approximate or specialized solutions?

ultrametric trees: “Evolutionary clock”

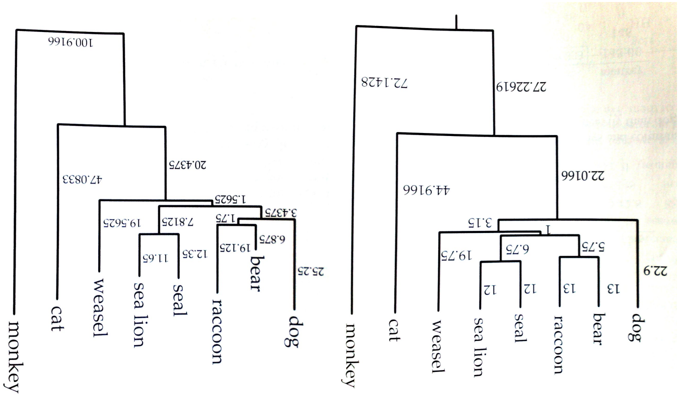


image (c) J. Felsenstein

ultrametric trees: properties

metric requirements

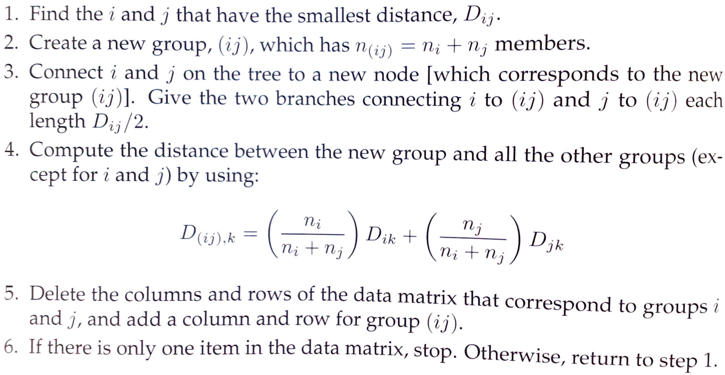
$$\begin{array}{rcll} d(x,y) & > & 0 & \mathit{for}\ x \neq y \\ d(x,y) & = & 0 & \mathit{for}\ x = y \\ d(x,y) & = & d(y,x) & \forall\ x,y \\ d(x,y) & \leq & d(x,z) + d(y,z) & \forall\ x,y,z \quad \text{(triangle inequality)} \end{array}$$

ultrametric – any three nodes can be relabelled so, that

$$d(x,y) \leq d(x,z) = d(y,z)$$

If you have a distance matrix induced from a tree, is it ultrametric?

Greedy approach 1 – hierarchical clustering



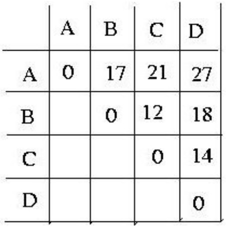
1. Find the i and j that have the smallest distance, D_{ij}.
2. Create a new group, (ij), which has $n_{(ij)} = n_i + n_j$ members.
3. Connect i and j on the tree to a new node [which corresponds to the new group (ij)]. Give the two branches connecting i to (ij) and j to (ij) each length $D_{ij}/2$.
4. Compute the distance between the new group and all the other groups (except for i and j) by using:

$$D_{(ij),k} = \left(\frac{n_i}{n_i + n_j}\right) D_{ik} + \left(\frac{n_j}{n_i + n_j}\right) D_{jk}$$

5. Delete the columns and rows of the data matrix that correspond to groups i and j, and add a column and row for group (ij).
6. If there is only one item in the data matrix, stop. Otherwise, return to step 1.

image (c) J. Felsenstein

Greedy approach 1 – example



	A	B	C	D
A	0	17	21	27
B		0	12	18
C			0	14
D				0

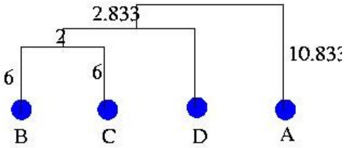
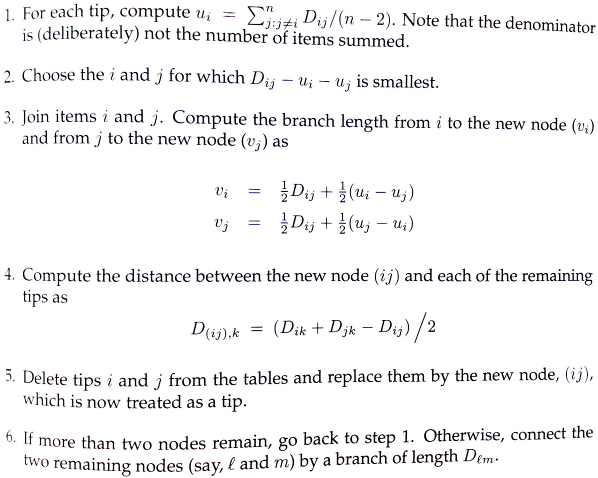


image (c) P. Winter

Greedy approach 2 – Neighbor-joining



1. For each tip, compute $u_i = \sum_{j:j \neq i}^{n} D_{ij}/(n-2)$. Note that the denominator is (deliberately) not the number of items summed.
2. Choose the i and j for which $D_{ij} - u_i - u_j$ is smallest.
3. Join items i and j. Compute the branch length from i to the new node (v_i) and from j to the new node (v_j) as

$$
\begin{aligned}
v_i &= \tfrac{1}{2}D_{ij} + \tfrac{1}{2}(u_i - u_j) \\
v_j &= \tfrac{1}{2}D_{ij} + \tfrac{1}{2}(u_j - u_i)
\end{aligned}
$$

4. Compute the distance between the new node (ij) and each of the remaining tips as

$$D_{(ij),k} = (D_{ik} + D_{jk} - D_{ij}) \Big/ 2$$

5. Delete tips i and j from the tables and replace them by the new node, (ij), which is now treated as a tip.
6. If more than two nodes remain, go back to step 1. Otherwise, connect the two remaining nodes (say, ℓ and m) by a branch of length $D_{\ell m}$.

image (c) J. Felsenstein

Properties of Neighbor-Joining

- The same complexity as average linkage hierarchical clustering $\mathcal{O}(n^3)$
- Guaranteed to return the correct answer if the distance matrix D originates from a tree
- Works also for non-ultrametric trees

Further links

- More information: *Inferring phylogenies* J. Felsenstein
- More advanced methods based on probabilistic approaches (Maximum likelihood, Bayesian approaches)
- Tree reconstruction might give different results for different genes, we will discuss this issue later
- Pairwise distances might lead to "unrealistic" phylogenies, We will discuss this problem next week.