394C, Spring 2012

Jan 23, 2012

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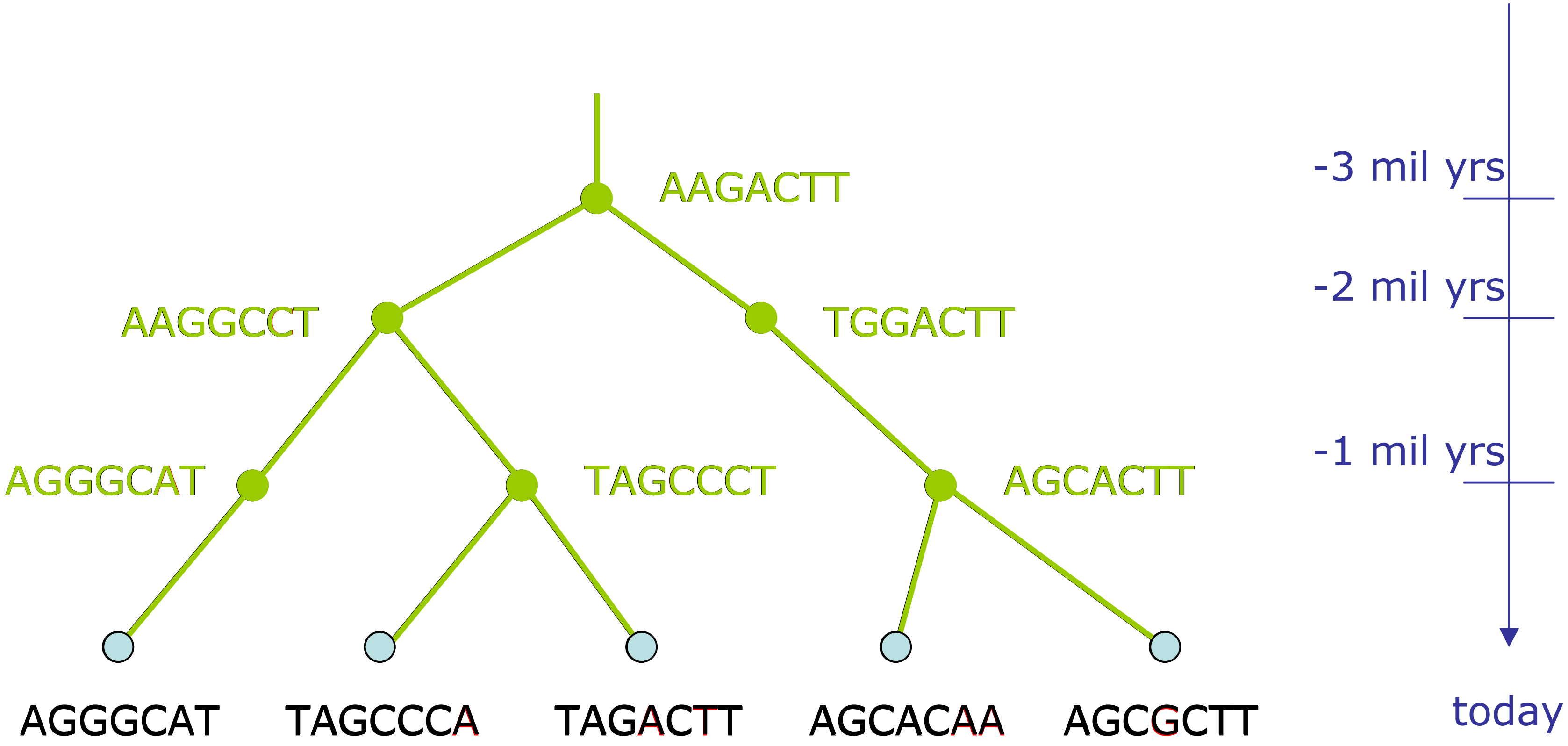
DNA Sequence Evolution



AAGACTT

AAGGCCT
TGGACTT

AGGGCAT
TAGCCCT
AGCACTT

AGGGCAT
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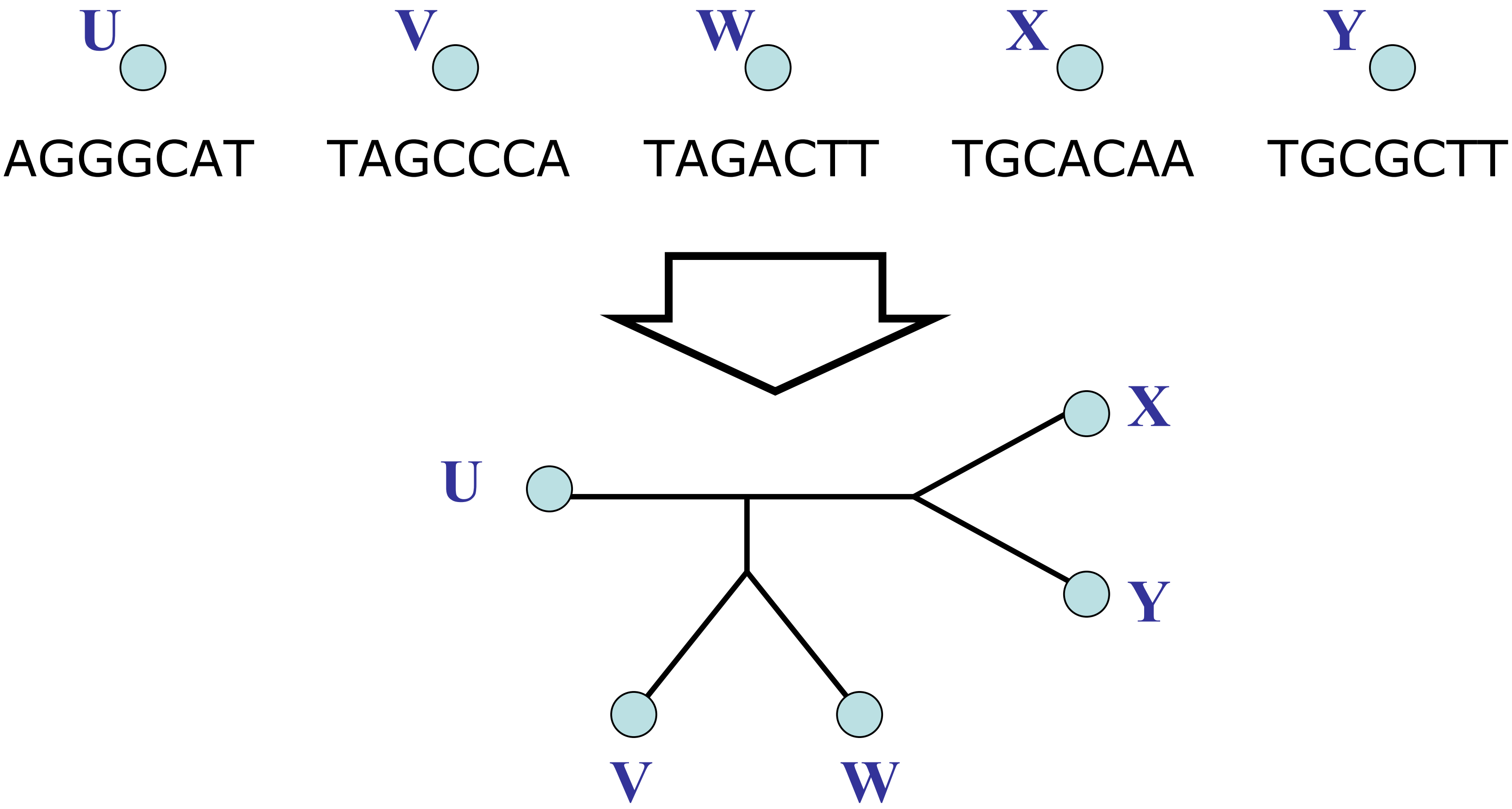
AGCGCTT

-3 mil yrs
-2 mil yrs
-1 mil yrs
today

Phylogeny Problem



U	V	W	X	Y
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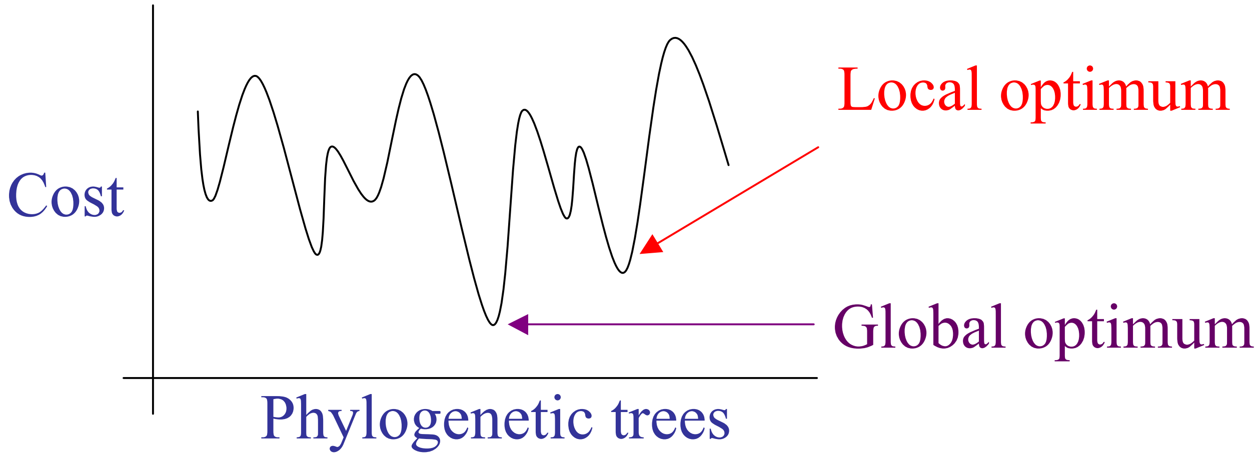
Phylogenetic reconstruction methods

1. Heuristics for NP-hard optimization criteria (Maximum Parsimony and Maximum Likelihood)



2. Polynomial time distance-based methods: Neighbor Joining, FastME, etc.
3. Bayesian MCMC methods.

Course outline

- Basics: phylogenies, data, stochastic models of evolution, and representations of trees
- Phylogeny reconstruction methods: distance-based and character-based (MP, ML, and Bayesian), and their performance issues
- Multiple sequence alignment, and the connections (both ways) between MSA and phylogenetics
- Special topics: reticulate evolution, whole genome evolution, metagenomics, etc. (Student interest will impact this.)

Today

- Newick Representations of trees
- Characterizations of trees using distances, clades, splits (bipartitions), and quartets
- Computing trees from dissimilarity matrices: the “naïve” quartet method
- (Hints) Connections to estimation of phylogenies from empirical data

Newick representations

- For a rooted tree, we represent a graph with a string with the taxa, commas, and nested parentheses.
- For example, what tree is represented by (a,(b,(c,((d,e),(f,g))))))?
- How do we represent an unrooted tree? (Easy - root it somewhere, and write down the Newick representation of the rooted version.

Rooted vs. unrooted

- Task: be able to move between rooted and unrooted representations of trees
- Task: be able to compare two trees and see if they are different or the same

Clades

- Definition: Let T be a *rooted* tree leaf-labelled by S, let v an internal node in T, and let $\mathbf{X_v}$ be the set of leaves in T below v. Let

  Clades(T) = {$\mathbf{X_v}$: v in V(T)}.

  Note: X_v is also called the "cluster" at node v, so this is sometimes called Clusters(T).

- Question: Given Clades(T), can we compute T?

Bipartitions

- Given an edge e in a leaf-labelled unrooted tree T, the removal of the edge e (but not its endpoints) defines a bipartition on the leaves of the tree T. We denote by **c_e** the bipartition defined by the edge e. We let

  $C(T)=\{c_e: e \text{ in } E(T)\}$.

- Questions: Given C(T), can we compute T?

Quartet subtrees

- Given tree T leaf-labelled by S, and quartet a,b,c,d of leaves, we let T|{a,b,c,d} denote the minimal homeomorphic subtree of T restricted to {a,b,c,d}. We let **Q(T)** denote {T|X: X is a four taxon subset of S}.

- Question: Given Q(T), can we compute T?

Computing trees

- Given Q(T) (the quartet subtrees of T), can we determine T?
- Given C(T) (the bipartitions of S defined by the edges of T), can we determine T?
- Given Clades(T) (the sets of leaves defined by internal nodes in the rooted tree T), can we determine T?

Quartet-based reconstruction

- Definition: Let T be a tree leaf-labelled by a set S, and let Q(T) be the set of quartet subtrees of T (derived from each of the four-taxon subsets of S).

Question: can we reconstruct T from Q(T)?

Computing T from Q(T): Naïve Quartet Method

- Given Q(T):
  - Find a sibling pair A, B (a pair of leaves which are always together in every quartet in which they both appear)
  - Compute the tree T’ for S-{A} by recursing on the subset of Q(T) that doesn’t include taxon A
  - Insert A into T’ by making A sibling to B, and return the tree obtained

Analysis of the algorithm

Questions:

- Accuracy?
- Running time?
- But: *how are we to compute quartet subtrees?*

Clade compatibility

- Definition: Let T be a rooted tree leaf-labelled by S, v an internal node in T, and X_v the leaves in T below v. Let Clades(T)={X_v: v in V(T)}.
- Theorem: Let X be a set of subsets of S. Then there exists a tree T leaf-labelled by S such that X = Clades(T) if and only if for all A, B in X, either A and B are disjoint, or one contains the other.

Proof of the theorem

- One direction is easy
- The other direction is a proof by construction!

Computing rooted trees from clades

- Partially order the set of clades by containment, add in the full set S, and compute the Hasse Diagram of the resultant poset

Tree construction from clades

Questions:

- Accuracy?
- Running time?
- But, *how are we to compute clades?*

Bipartition compatibility

- Definition: Let X be a set of bipartitions on a set S. Then X is said to be **compatible** if there exists a tree T leaf-labelled by S such that X = C(T), where C(T) = $\{c_e$: e in E(T)$\}$.

Question: Can we construct the tree T from C(T)?

Computing trees from bipartitions

Given the set of bipartitions on the leaf-set induced by the edges of a tree T, how can we compute the tree T?

Hint: “root” the tree T by picking it up at a leaf, and then consider the set of bipartitions as a set of “clades”, and apply the previous algorithm. (Note: the choice of leaf does not matter!)

Computing trees from bipartitions

- Questions:

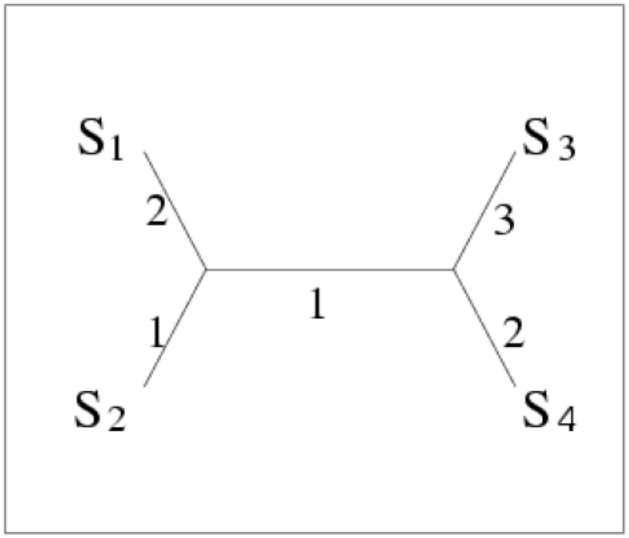
  How are we to obtain bipartitions?

Additive Distance Matrices

	S_1	S_2	S_3	S_4
S_1	0	3	6	5
S_2		0	5	4
S_3			0	5
S_4				0

POLYTIME
INVERTIBLE

↔



Four-point condition

Theorem (Buneman and others): A matrix D is additive if and only if for every four indices i,j,k,l, the maximum and median of the three pairwise sums are identical

$$D_{ij}+D_{kl} < D_{ik}+D_{jl} = D_{il}+D_{jk}$$

Proof: one direction is easy. The other direction requires some work!

Four-point method

- The Four-Point Method computes trees on quartets using the ideas in the Four-point condition
- Given a "dissimilarity" matrix D (may not satisfy the triangle inequality, but will be symmetric and zero on the diagonal), we compute a tree on four leaves s_i, s_j, s_k, s_l as follows:
- If

$D_{ij}+D_{kl}$ is less than both $D_{ik}+D_{jl}$, and $D_{il}+D_{jk}$

then set the tree to be $((s_i,s_j),(s_k,s_l))$.

So?

- We can compute a tree from its set of clades, bipartitions, or quartets. But how do we get these sets?
  - Primary data are generally characters (columns within alignments of biomolecular sequences, morphological features, or other such features). These don't directly produce clades, bipartitions, or quartets.
- We can compute a tree from an additive distance matrix. But how do we get these distances?
  - Evolutionary biologists have techniques for estimating "evolutionary distances" between taxa. How do they do this?

Comparing two trees using bipartition sets

- To see if two trees T and T’ are the same, write down C(T) and C(T’) and see if they are the same set.

- When computing the error in an estimated tree T with respect to a true tree T*, we set
  - C(T)-C(T*) = false positives, and
  - C(T*)-C(T) = false negatives (missing branches)

Homework assignments

- Monday Jan 30: Read chapters 1-5. Do problems 2.3(2), 2.5(1), 2.5(2), 2.5(3), and 2.5(5).
- Monday Feb 6: Do problems 5.2(3), 5.2(4), and 5.2(5). Extra credit: 5.2(6) and 5.2(7).

Undergrads or biology students: you have the option of replacing any problems above with other problems (see webpage).