Maximum Likelihood Analysis of Phylogenetic Trees

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- Many concrete questions are still unresolved (*e.g.* mammalian evolutionary tree).
- Most realistic formulations of the problem, which take errors into account, give rise to hard computational problems.

Popular Reconstruction Methods

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- Ancestral maximum likelihood (AML) and its computational complexity.

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- Likelihood is a common optimization criteria in numerous settings, including phylogenetic (Felsenstein 1981).

Neyman 2–State Substitution Model

species	observed data
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- Just two characters states, X and Y.

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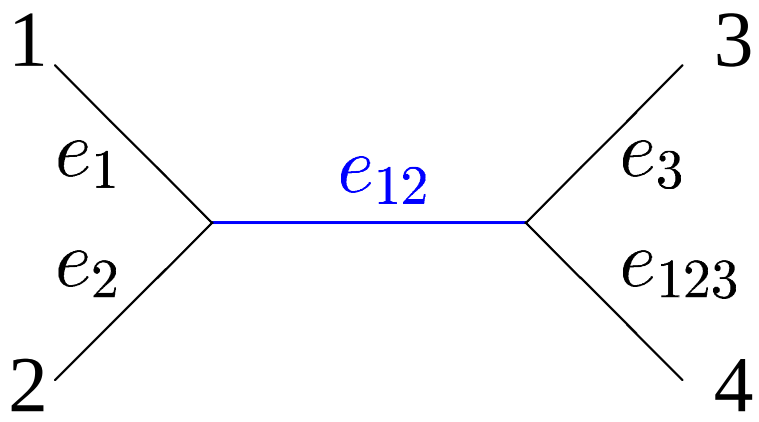
- Every column induces a pattern.
- Remark: A simple model, yet very powerful.

Neyman 2–State Substitution Model



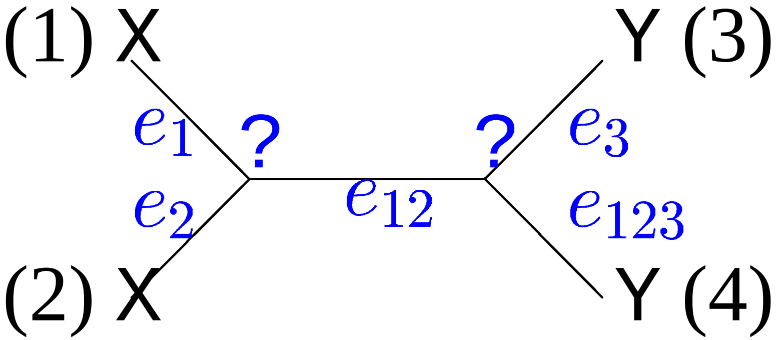
For each edge e of a tree T, the edge weight p_e represents the probability of having different states at the two ends of e.

A **Very** Simple Example

Four species ($n = 4$), just one site ($c = 1$)

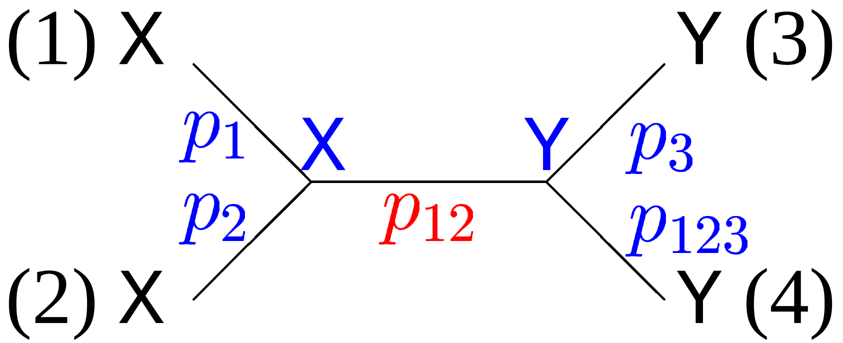
species	observed data
1	X
2	X
3	Y
4	Y

Analyze the *natural* tree $(12)(34)$



Computing the Likelihood

Each unknown state (?) can assume one of two possibilities, X or Y. For example, the assignment



contributes $(1-p_1)\cdot(1-p_2)\cdot p_{12}\cdot(1-p_3)\cdot(1-p_{123})$.

The likelihood is the sum of this

$+$ three similar expressions. . .

Computing the Likelihood

- Last expression has the form $\sum_{\text{internal assignments}} \prod_{\text{edges}} m_{\text{e,a,t}}$ where each $m_{\text{e,a,t}}$ is either p_{e} or $1 - p_{\text{e}}$, depending on the assignment a, and input pattern t at two ends of the edge.

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- When the data has more then one column, we multiply the expressions to get the likelihood of the data, given the model parameters, $L(\text{data}|\text{tree \& edge weights})$:

$$\prod_{\text{columns}} \sum_{\text{internal assignments}} \prod_{\text{edges}} m_{\text{e,a,t}} \, .$$

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- Tiny likelihood can be efficiently computed using dynamic programming (Felsenstein, 1981).

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- Typical approach to small likelihood, used in practice:
- Start at some initial point with edge weights $\mathbf{p}$.
- Apply hill climbing on the likelihood function to reach a maximum.

The Likelihood Surface

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- Fukami and Tateno (89), Tillier (94): For any tree, the ML point will be unique.
- Steel (94): Proofs are erroneous - A simple but pathological counter example (multiple maxima on the wrong tree).
- (94–present): Hill climbing techniques still used. Steel's counter example is considered too "biologically unrealistic" to warrant concern.

The Likelihood Surface (cont.)

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  - Multiple optima are rare...
  - ...especially on the *correct* tree.
- Goal here: Investigate the problem analytically (joint work with Hendy, Holland, Penny).

Maximizing Likelihood on Trees

Tools used

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- Employing computer algebra and algebraic geometry tools.

Example: Conservative Data, Two Very Different ML Trees

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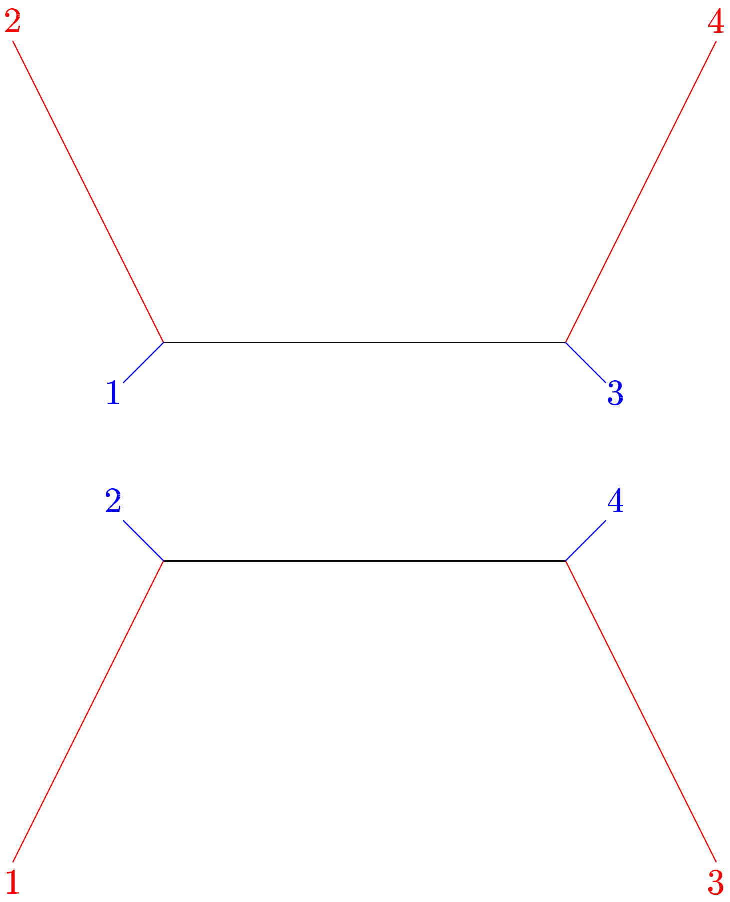

Molecular Clock Model

- Phylogenetic trees under a molecular clock (MC):

3 taxa

one rooted topology

MC-triplet

4 taxa

two rooted topologies

MC-fork

MC-comb

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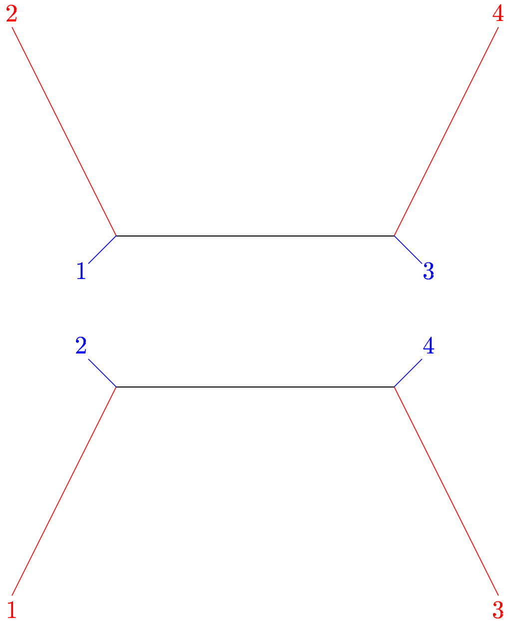

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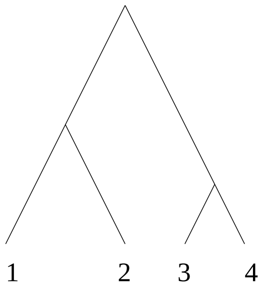

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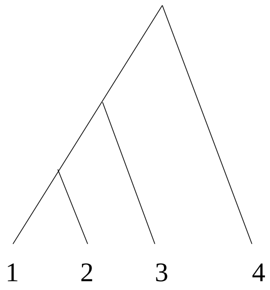

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- Fork: Closed form ML solution.

Joint work with Snir and Khetan.

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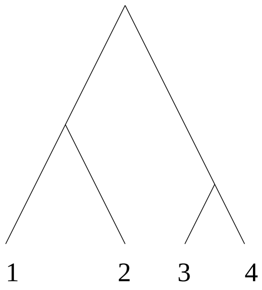

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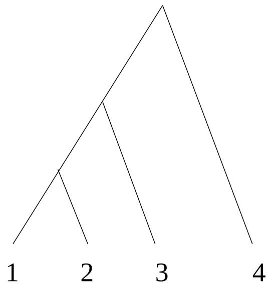

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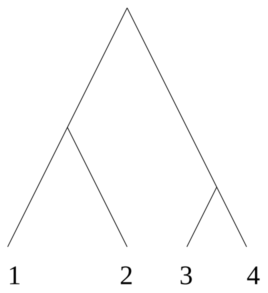

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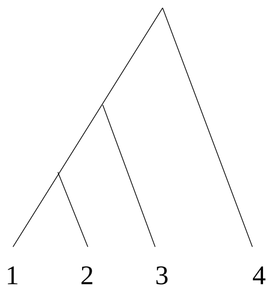

MC-comb

- Fork: Closed form ML solution.
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- In both cases, ML solution is unique.
- Attaining solutions requires fairly heavy math and computer algebra tools.

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- Multiple ML points for general case imply small likelihood cannot be solved by hill climbing.
- Not clear if small likelihood has efficient (worst case) solutions.

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- Small Parsimony: Given the sequence data and a tree, find internal assignment(s) that minimizes total number of changes.
- MP considered by practitioners easier than ML. Indeed small parsimony has efficient algorithms (Fitch 1971, Sankoff and Cedergren 1983).

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- Big likelihood – unknown. Given the importance of ML, it would be nice to know more about its complexity than just “seems harder than MP”.

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- AML computes the likelihood contribution resulting from best assignment to internal nodes, while “regular ML” sums up over all assignments.

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- ACHLPW 2003: Big AML is NP-hard.

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- The edge weights that maximize the likelihood of the data equal d_e/k.
- Where d_e equals the number of changes accross edge e, and k is the common sequence length.

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  2. the sum of all “edge entropies” $\sum_{e \in E(T)} H\left(d_e/k\right)$ is minimized.

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Optimization criteria

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- MP: Minimize the sum of all “edge differences” $\sum_{e \in E(T)} d_e/k$.
- Can think of the two problems as attempting to minimize different edge weights (functions of d_e).

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- Analogy of AML and MP optimization criteria suggests using similar approach.
- Reduction from VC indeed identical.
- Proof substantially more involved as entropy $H\left(d_e/k\right)$ is not as “well behaved” as plain edge differences d_e/k.

Conclusion and Open Problems

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- Hardness proof for big AML as a stepping stone for big ML?

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