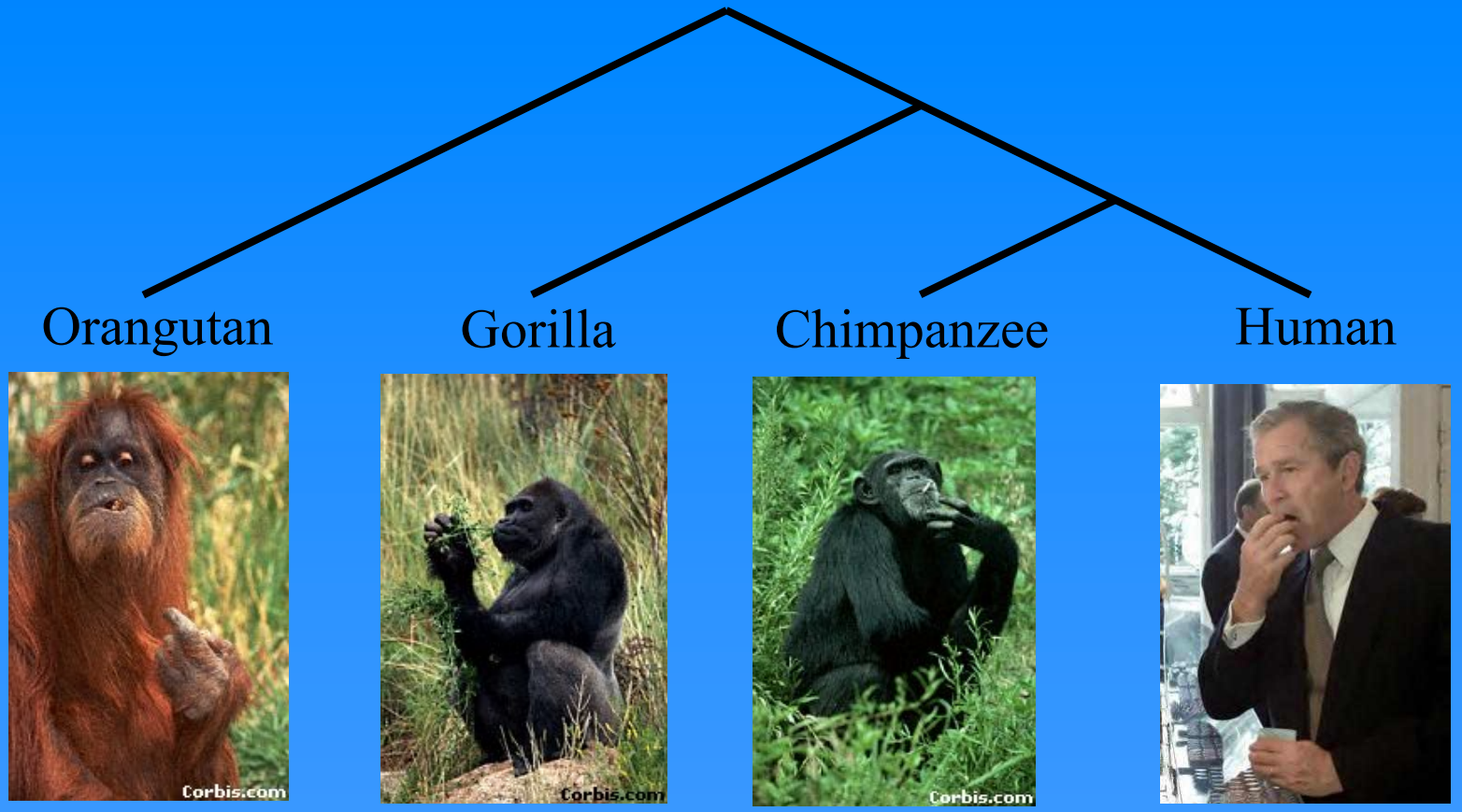
Introduction to Phylogenetics II



From the Tree of the Life Website, University of Arizona

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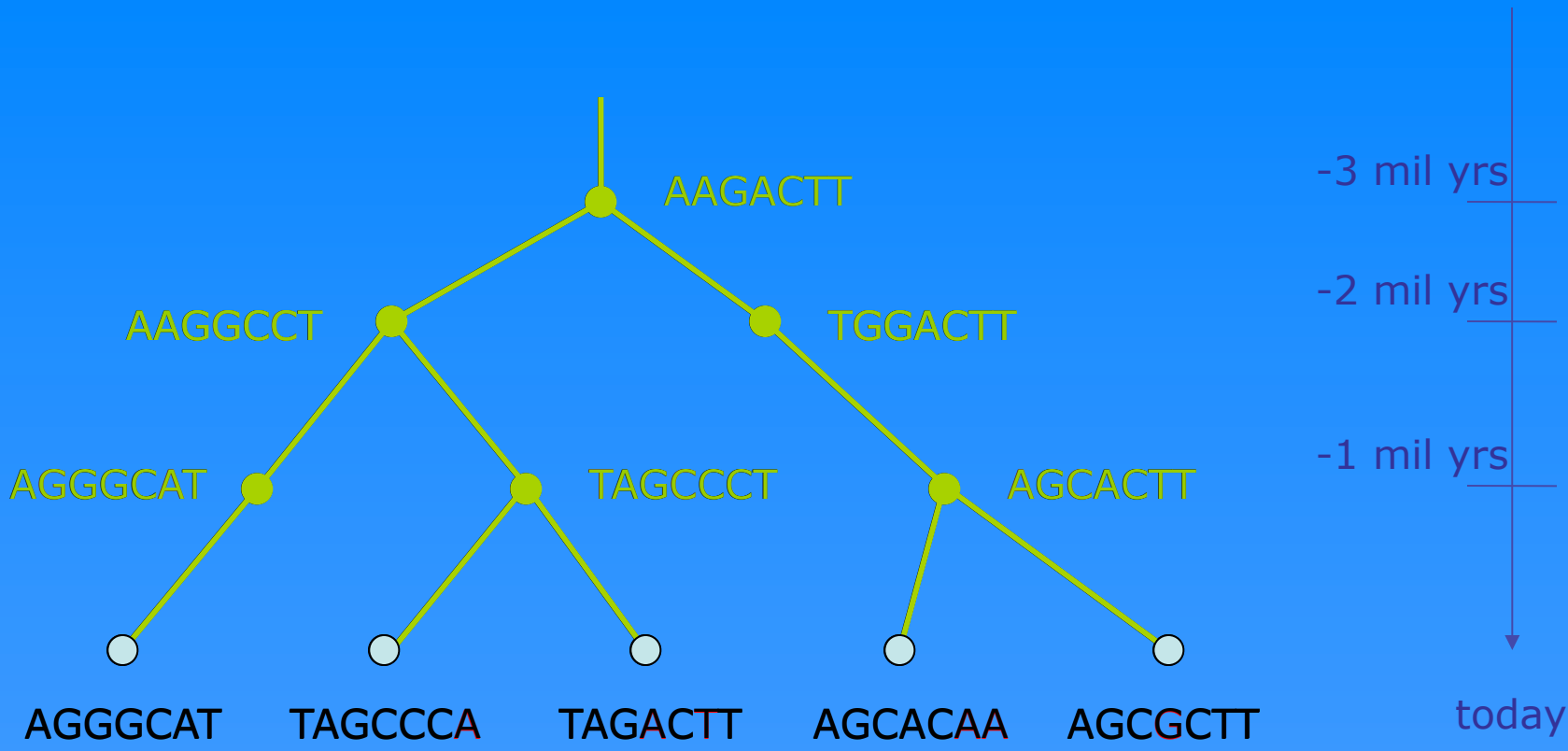
Introduction to Phylogenetics II

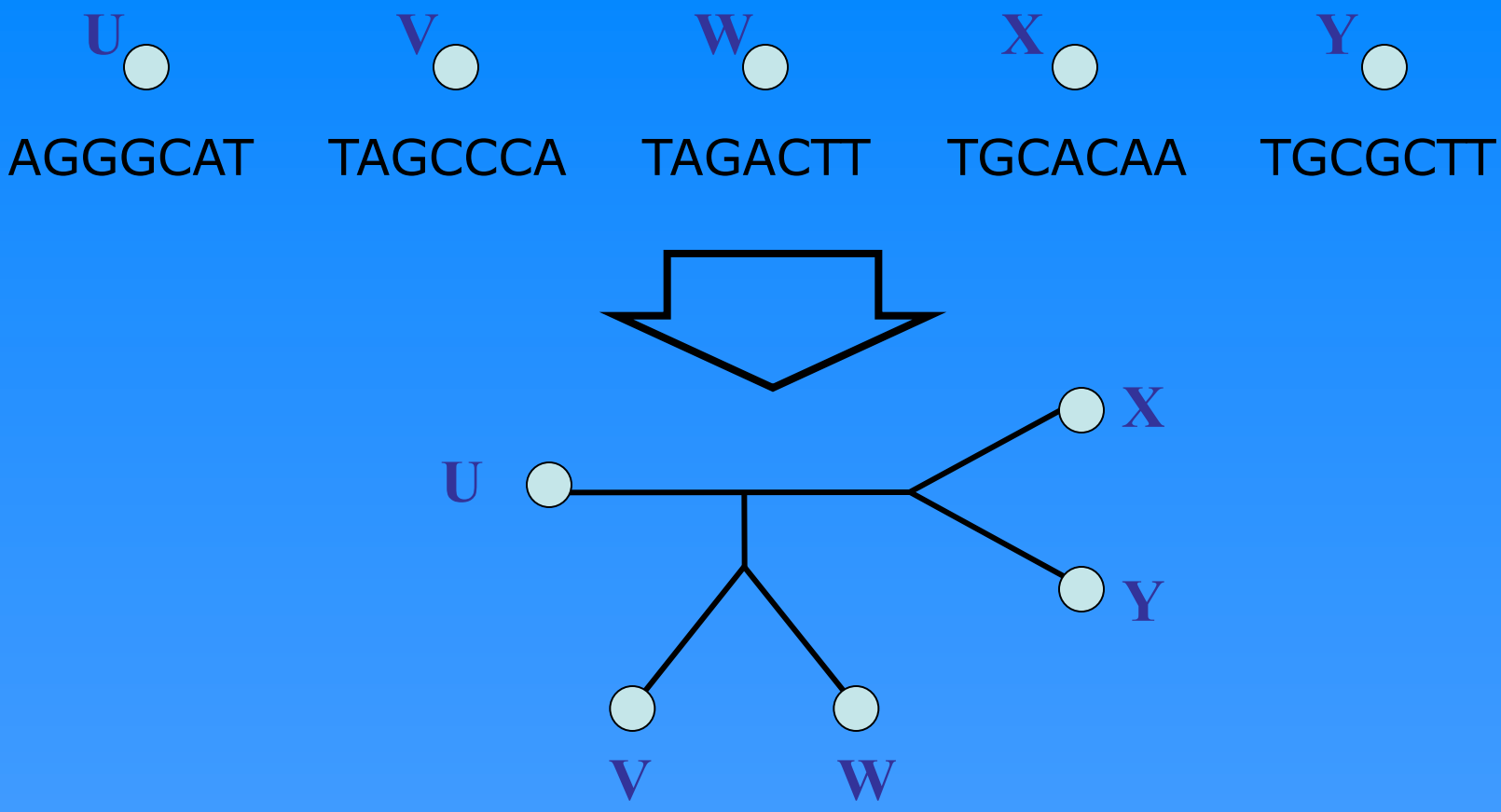
Character based methods – Maximum Parsimony

- Sequence based methods:
  - –Two main categories:
    - *Character based methods*: Trees are constructed by comparing the characters of the corresponding sequences. Characters are mainly molecular (nucleotides in homologous DNA).
    - *Distance based methods*: Input is a square symmetric distance matrix. Seeks trees (edge-weighted) best-describing these distances.
- Supertree methods:
  - –Construct small (reliable) trees form any data and combine it to a complete tree by combinatorial algorithms.
  - –Quartet based methods.

Sequence Evolution
(substantially simplified)



Reconstructing the Tree



Unrooted trees!

Character Based Methods

species	C_1	C_2	C_3	C_4	…												C_m
dog	A	A	C	A	G	G	T	C	T	T	C	G	A	G	G	C	C	C
horse	A	A	C	A	G	G	C	C	T	A	T	G	A	G	A	C	C	C
frog	A	A	C	A	G	G	T	C	T	T	T	G	A	G	T	C	C	C
human	A	A	C	A	G	G	T	C	T	T	T	G	A	T	G	A	C	C
pig	A	A	C	A	G	T	T	C	T	T	C	G	A	T	G	G	C	C
	*	*	*	*	*			*	*			*	*				*	*

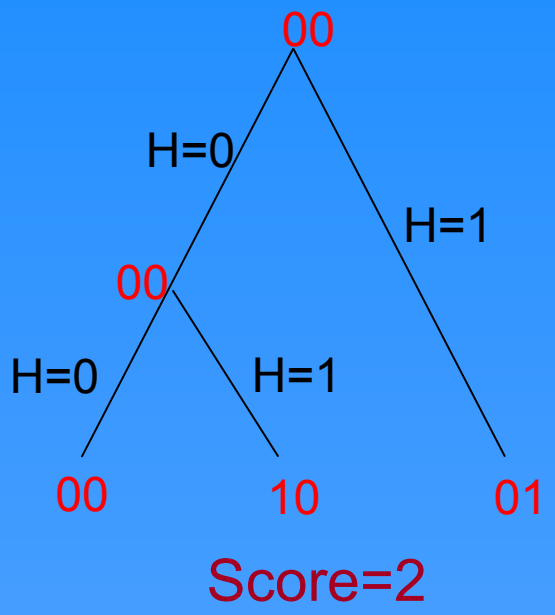
1. Input: A n*m matrix.
2. Each character (column) is processed independently.
3. Task: Find a tree that best explains simultaneously all characters.

Maximum Parsimony

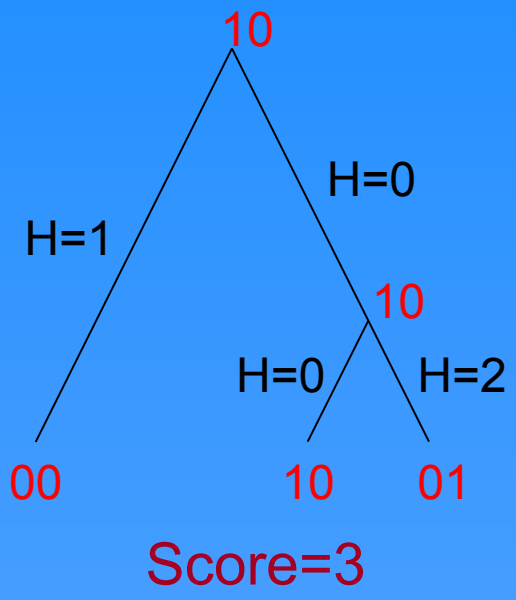
- Introduced at 1971 by Walter Fitch: *Fitch, Toward defining the course of evolution: minimum change for a specific tree topology,* 1971.
- based on the "*Occam's Razor*" principle that evolution is parsimonious.
- A combinatorial, non-parametric method.
- Seeks for the tree that minimizes the number of changes along the tree branches.
- A very widespread technique in biology.
- “If you know only one method for phylogenetics, MP should be the one”

The Parsimony Criterion on Trees

- Given a tree (topology) with *equal length* sequences labeling its nodes.
- The *parsimony score*: The number of changes along the edges of the tree.
- Can be thought of as the sum of *Hamming distances* along the edges.



Score=2



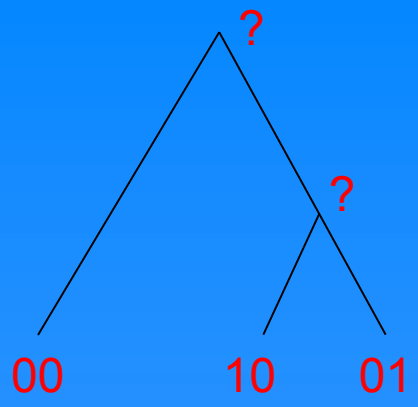
Score=3

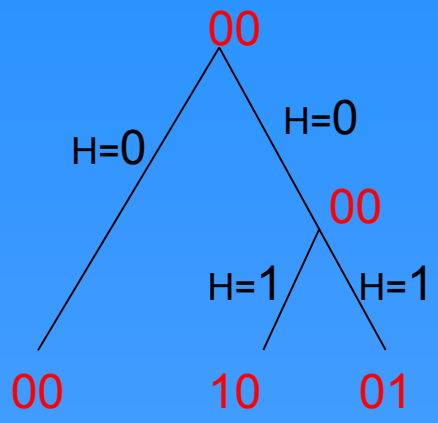
The *Maximum Parsimony* Problem

- Input: A set of sequences (representing some *gene* at a group of species).
- Task: Find a topology leaf labeled by the input sequences, and labeling to internal nodes *minimizing the parsimony score*.
- Decomposes into two problems:
  - A *Small Problem*: Given a topology leaf labeled by a set of sequences, find *internal nodes labeling* minimizing the parsimony score.
  - A *Big Problem*: Find a topology under which the small problem is minimized.

The *Small* MP problem on Trees

Task: finding internal labeling.





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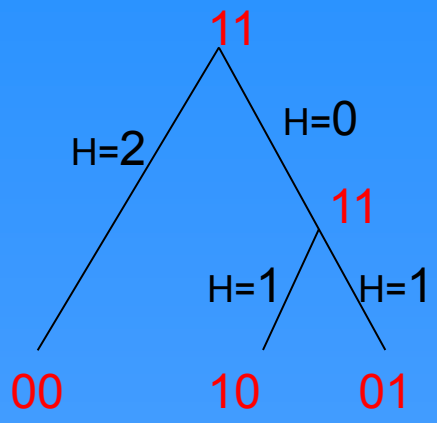
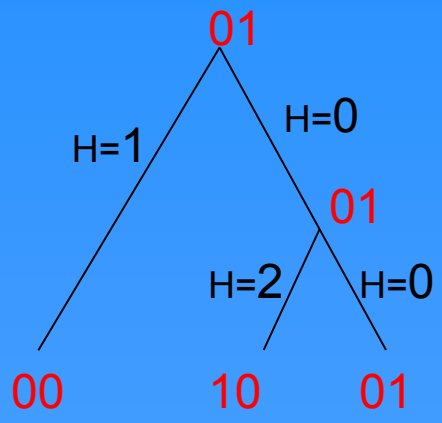


Score=4



Score=3

Fitch Algorithm for Small MP on Trees

- A classical DP style algorithm.
- Works separately on each column.

First Phase: bottom up (v_1 and v_2 are children of v):

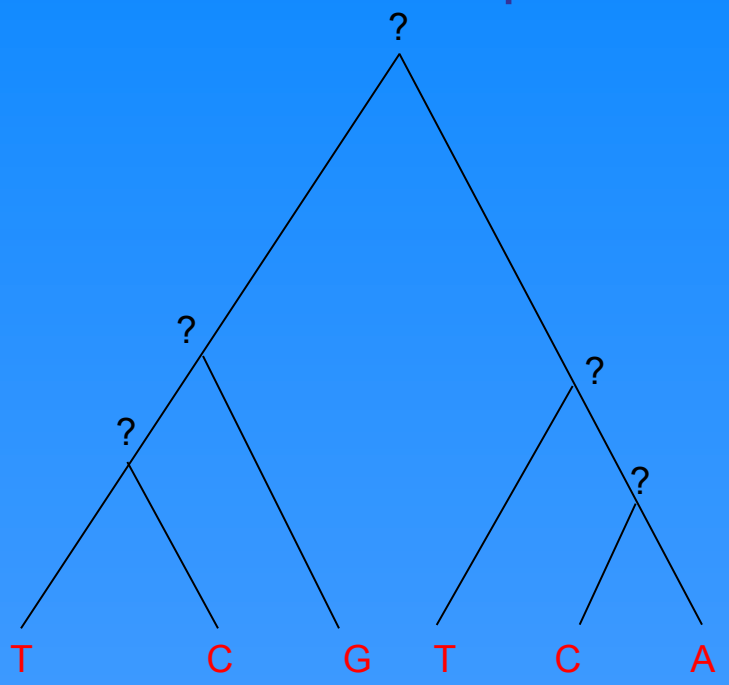
$$A(v) = \begin{cases} A(v_1) \cap A(v_2) & \text{if } A(v_1) \cap A(v_2) \neq \phi \\ A(v_1) \cup A(v_2) & \text{otherwise} \end{cases}$$

Second Phase: top down ($f(v)$ is a parent of v):

$$B(v) = \begin{cases} \sigma \in A(v) \cap A(f(v)) & \text{if } A(v) \cap A(f(v)) \neq \phi \\ \sigma \in A(v) & \text{otherwise} \end{cases}$$

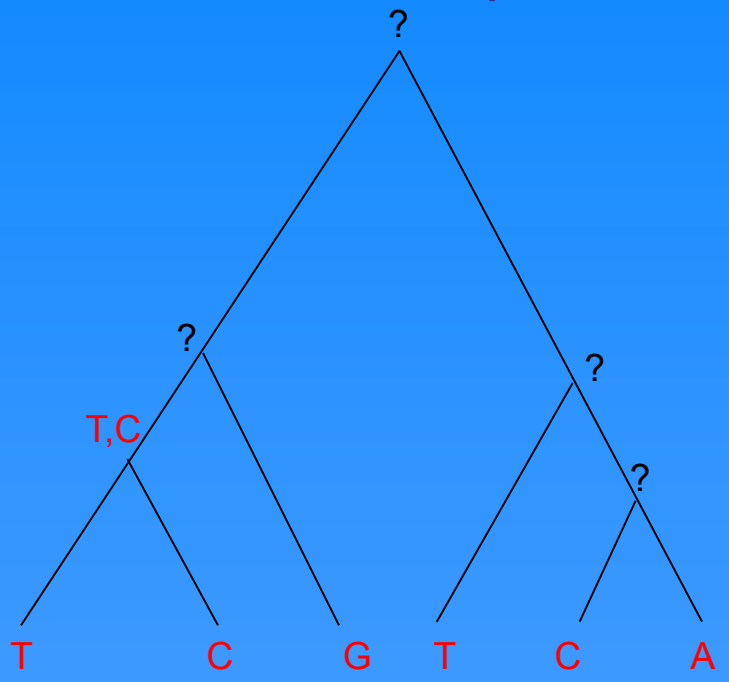
Fitch Algorithm (example)

Input:

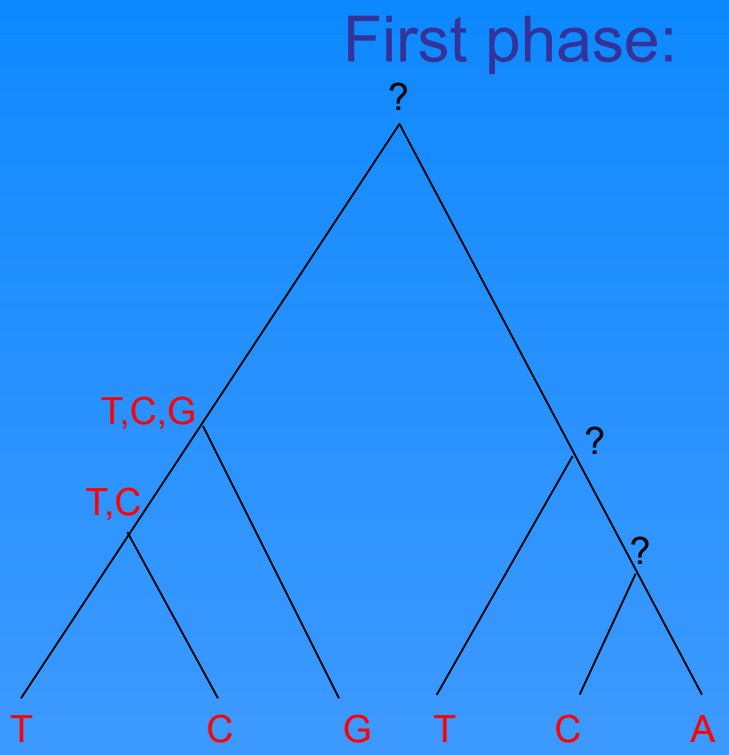


Fitch Algorithm (example)

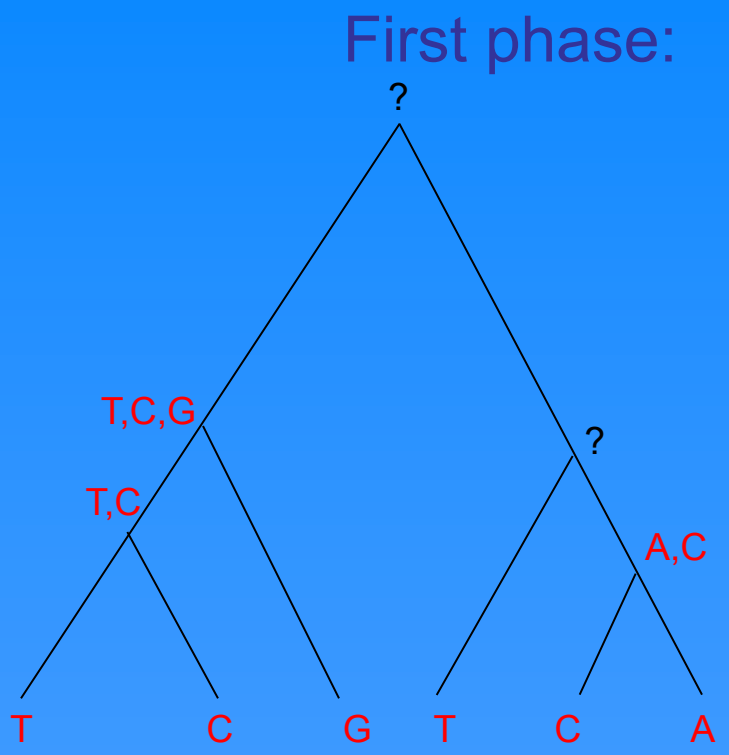
First phase:



Fitch Algorithm (example)



Fitch Algorithm (example)



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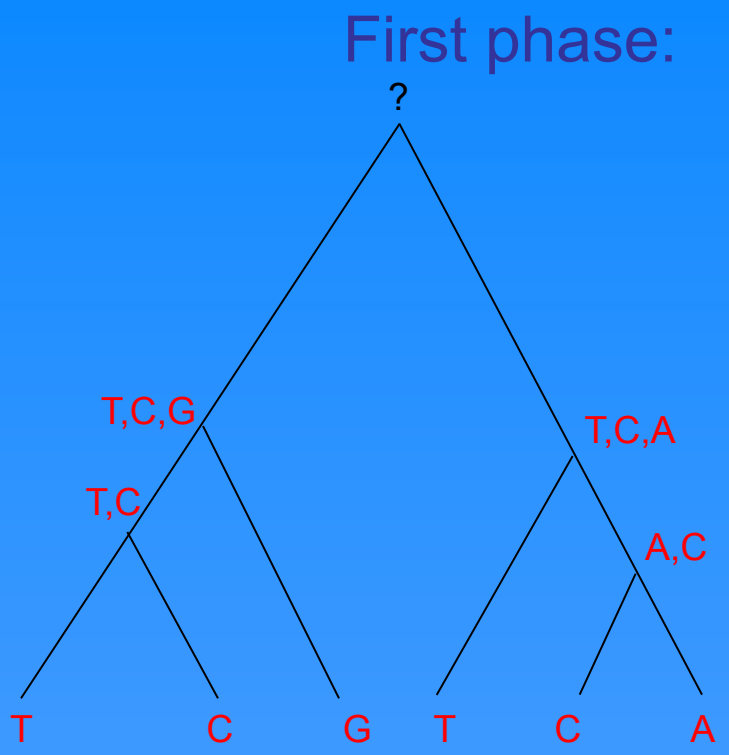

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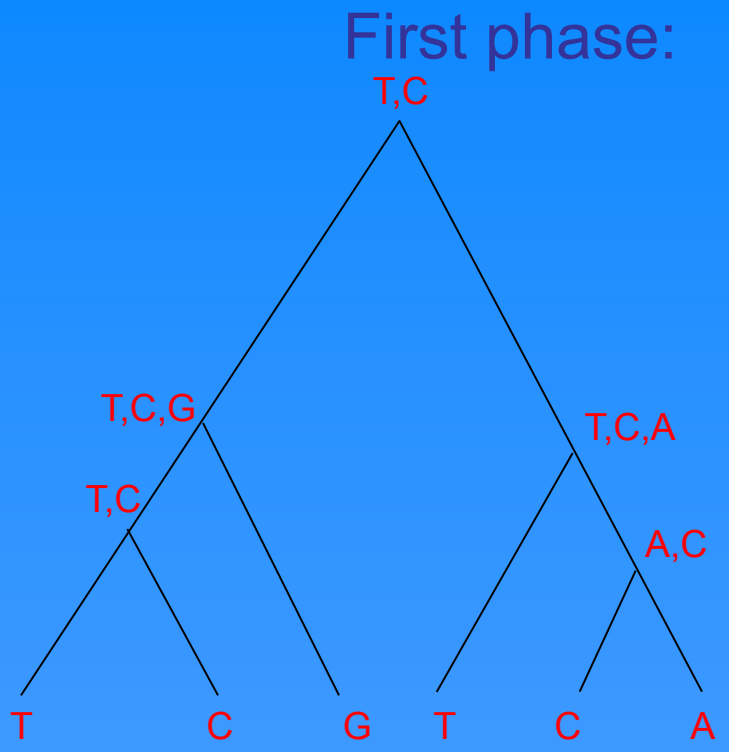
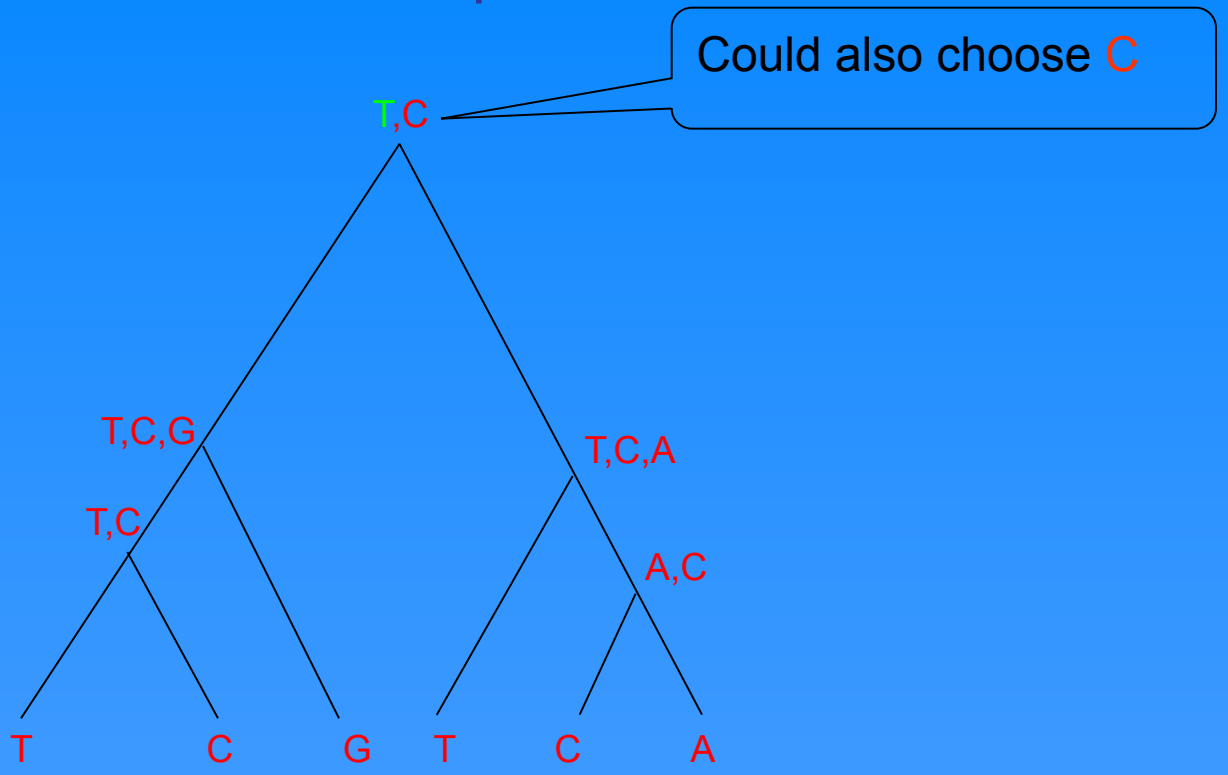


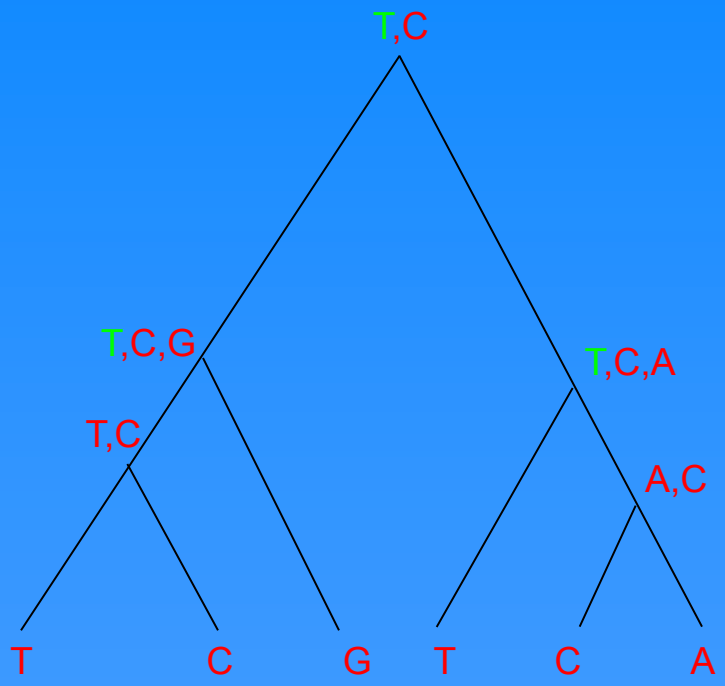
Fitch Algorithm (example)

Second phase:



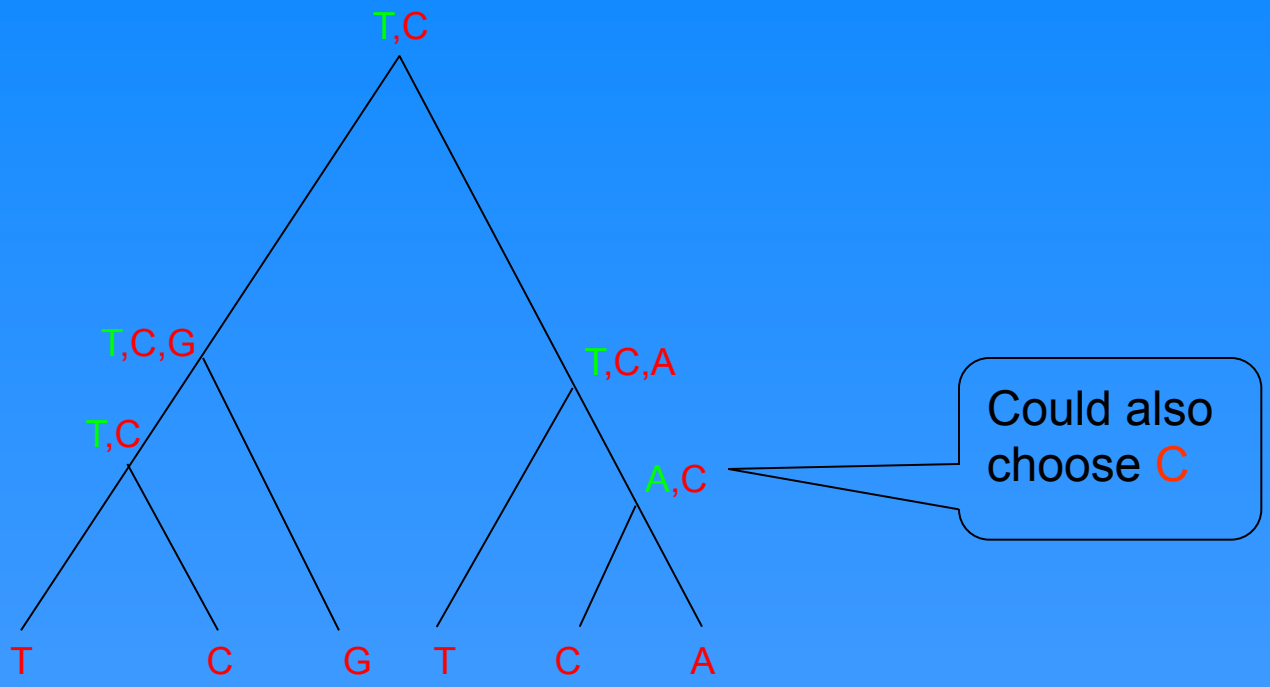
Fitch Algorithm (example)

Second phase:



Fitch Algorithm (example)

Second phase:



Fitch Algorithm

Claim: Fitch algorithm solves small MP

- Optimality for single character (simple induction).
- Global optimum (change summation order).

The *Big* MP problem on Trees

- Input: A set of sequences.
- Task: Find a topology over the sequences under which the *small problem minimizes*.

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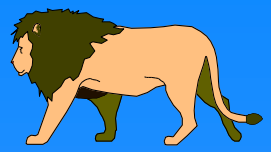

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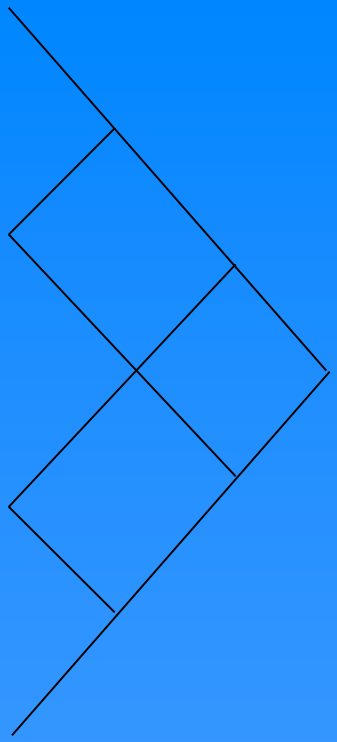
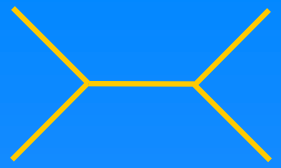
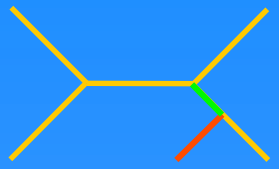
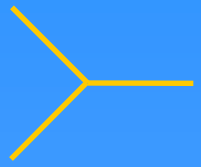


Number of trees

- Binary unrooted trees
- First cuont number of edges
- Divide into
  - External edges (always *n*).
  - Internal edges.
- New taxons are always added in a middle of an existing edge.
- Observation: adding a taxon splits an existing edge, creating a new internal edge.
- Summarizing: adding a new taxon adds 2 edges – the new internal edge and the external edge leading to that taxon.
- As for n=3 we have no internal edges, we obtain $|E_n| = 2n-3$

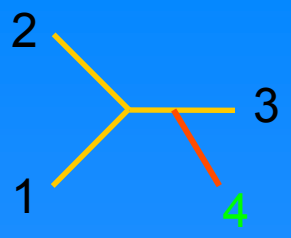






Number of trees

- Back to number of trees, N_u.
- For n=3 we have $N_u(3) = 1$
- We can insert the new taxon 4 on any existing edge



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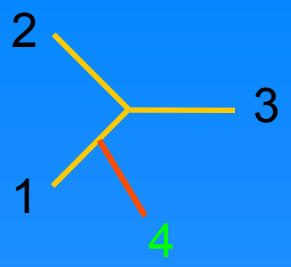

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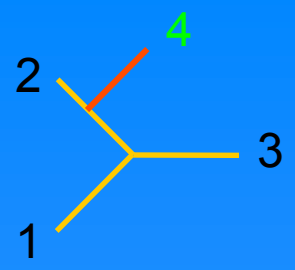
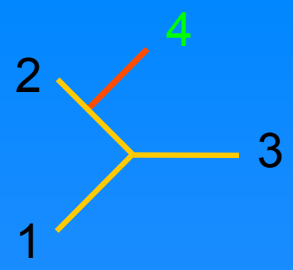


Number of trees

- Back to nomber of trees, N_u.
- For n=3 we have $N_u(3) = 1$
- We can insert the new taxon 4 on any existing edge
- Therefore we get
  - $N_u(n+1) = N_u(n)\ |E_n| = N_u(n)\ (2n-3)$
  - Or $N_u(n+1)/N_u(n) = 2n-3$
  - Or $N_u(n)/N_u(n-1) = 2n-5$



$$\frac{(2n-5)!}{2*4*6*8*10} = \frac{(2n-5)!}{\prod_{n-3} 2i} = \frac{(2n-5)!}{2^{n-3}(n-3)!}$$

3	1
4	1*3
5	1*3*5
6	1*3*5*7
7	1*3*5*7*9
8	1*3*5*7*9*11

2n - 5

2n - 5

2n - 5

2n - 5

2n - 5

Solving NP-hard problems exactly is … unlikely

- Number of (unrooted) binary trees on *n* leaves is (2n-5)!! = (2n-5)!/[2^{n-3}(n-3)!]
- If each tree on **1000** taxa could be analyzed in **0.001** seconds, we would find the best tree in **2890 millennia**
- NP-hard in general.
- Heuristics use **branch and bound** techniques.

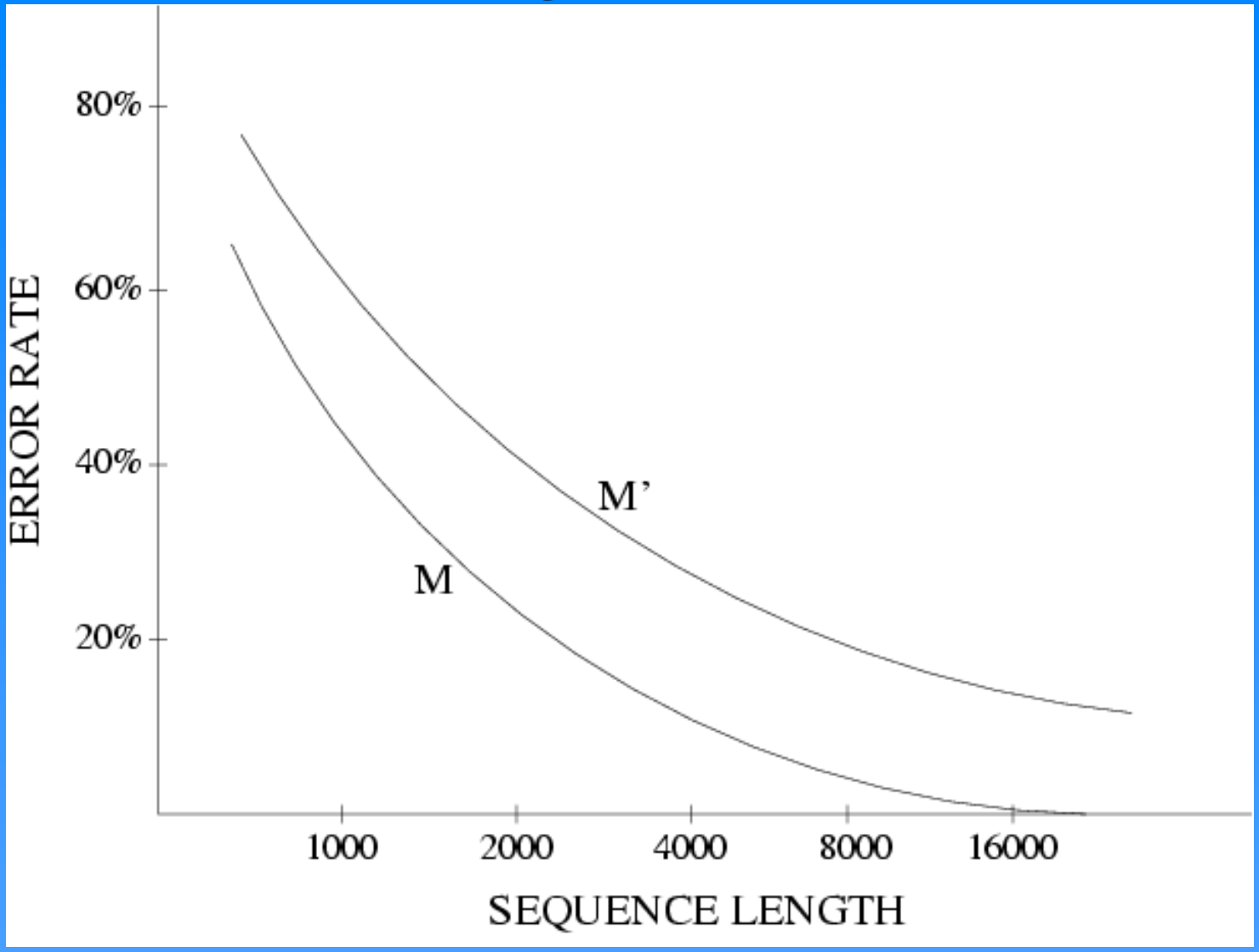
#leaves	#trees
4	3
5	15
6	105
7	945
8	10395
9	135135
10	2027025
20	2.2×10^{20}
100	4.5×10^{190}
1000	2.7×10^{2900}

Statistical performance issues

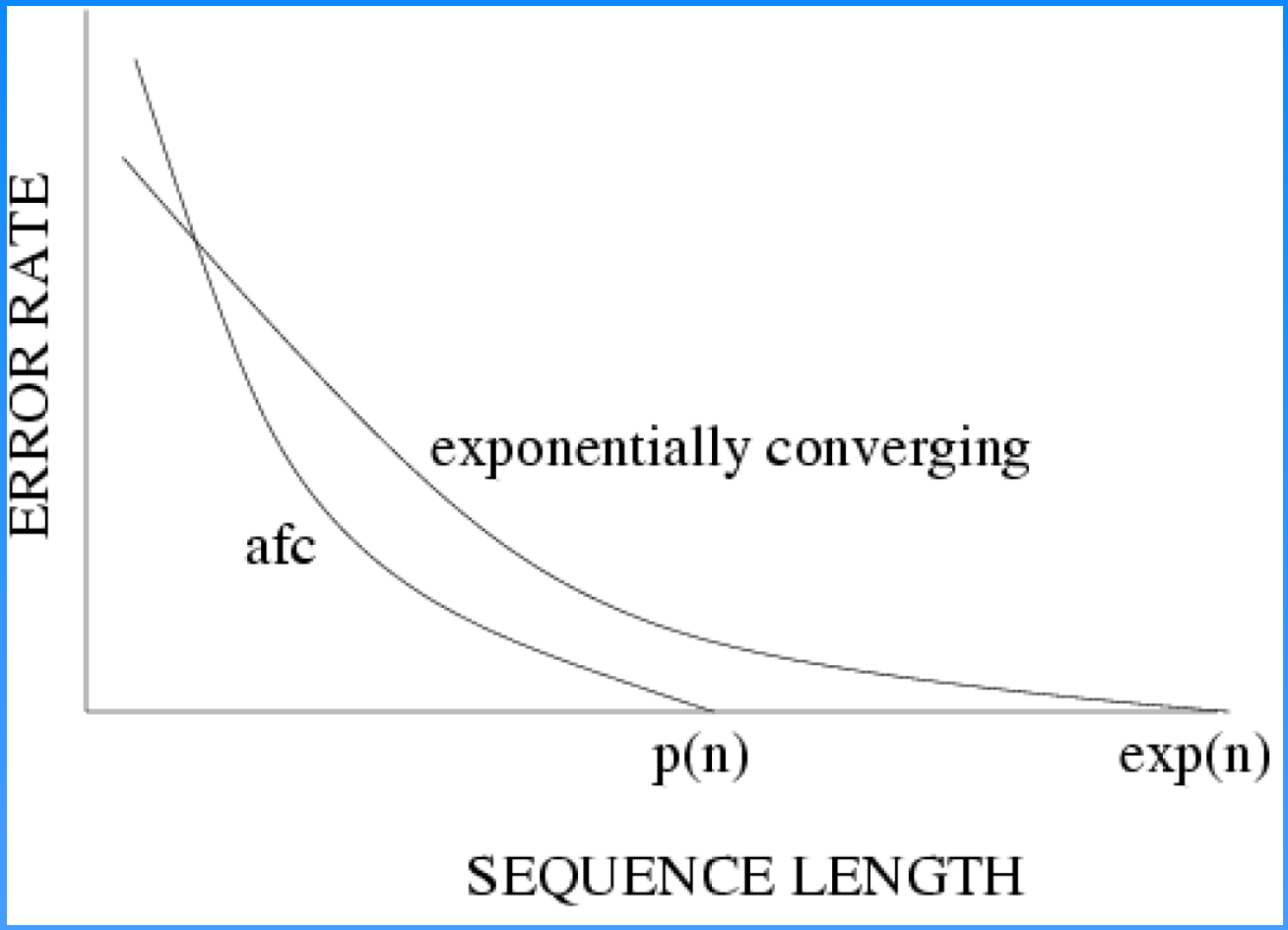
- An estimation method is *statistically consistent* under a model if the probability that the method returns the true tree goes to 1 as the sequence length goes to infinity.

- Convergence rate: the amount of data that a method needs to return the true tree *with high probability*, as a function of the model tree.

Statistical consistency and convergence rates

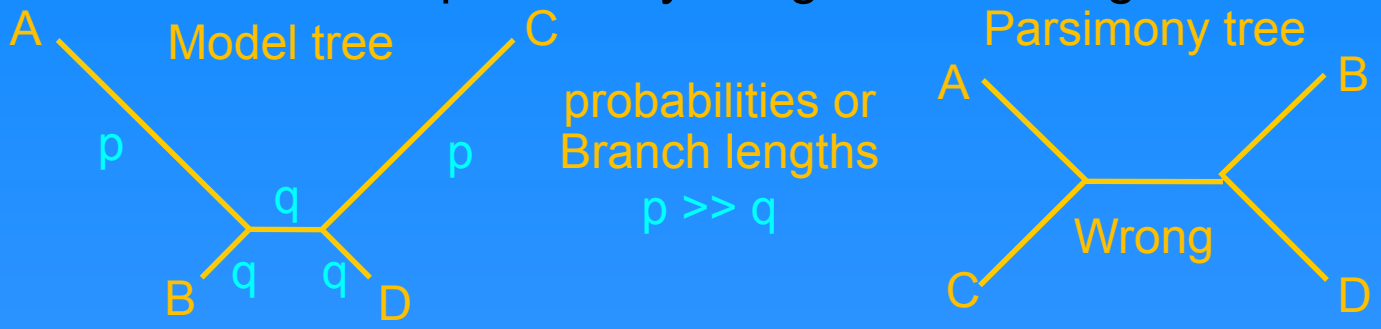


Absolute fast convergence vs. exponential convergence



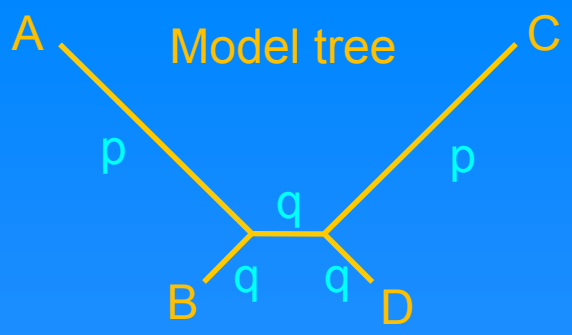
Parsimony can be inconsistent

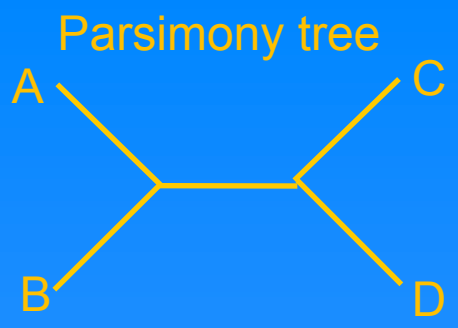
- Felsenstein (1978) developed a simple phylogeny model including four taxa and a mixture of short and long branches, *p* and *q*, indicating low and high substitution probabilities resp.
- Under this model parsimony will give the wrong tree.



- **The assumption is that *p,q* < ½ as these actually derived from *rate of substitutions* and by definition cannot exceed ½.**
- **With more data the certainty that parsimony will give the wrong tree increases - so that parsimony is statistically inconsistent.**

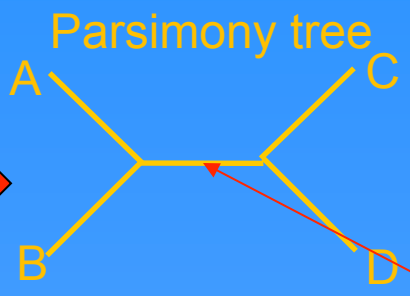
Parsimony can be inconsistent



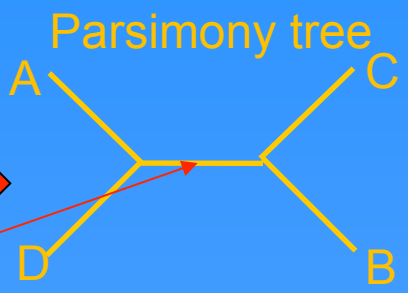


- Parsimony does not care of branch lengths (non parametric).
- Aims to minimize mutations (changes) over branches.
- That means putting together (nearby) taxa with same state.

A	1
B	1
C	0
D	0



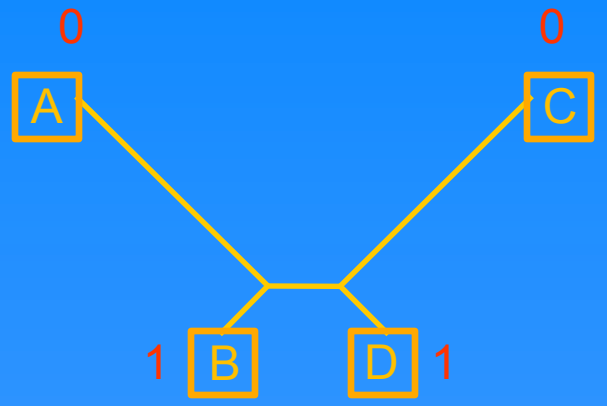
A	1
B	0
C	0
D	1

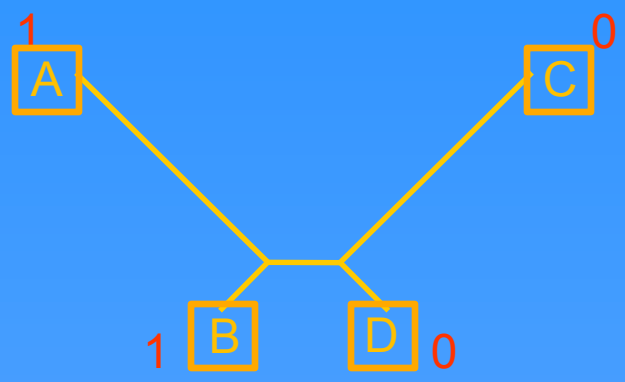


A change from 1 to 0

Parsimony inconsistency

- Our alphaet is {0,1} (can indicate purines/pyrimidines)
- Let C_{xyxy} be the case when leaves A,C get different values than B,D.
- Note that in this case, parsimony will return AC|BD.
- That is, parsimony *errs!*
- Equivalently, define C_{xxyy} to be the case when leaves A,B get different values than C,D.

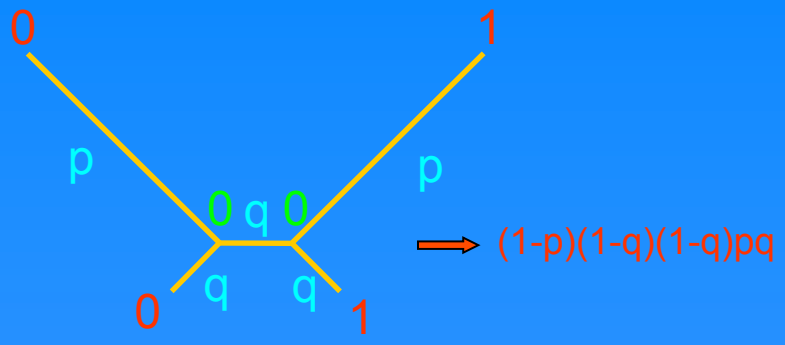




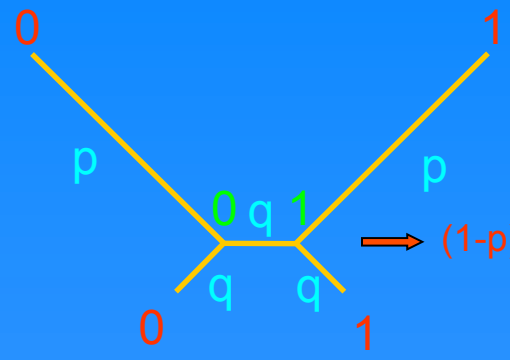
Parsimony inconsistency

- Let us calculate $P(C_{xxyy})$: the probability seeing C_{xxyy} seeing

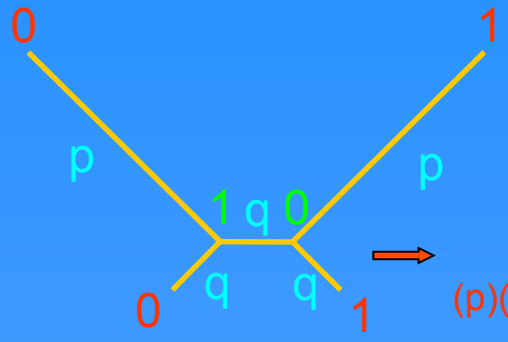
(note, species names were removed, but topology is A,B|C,D)



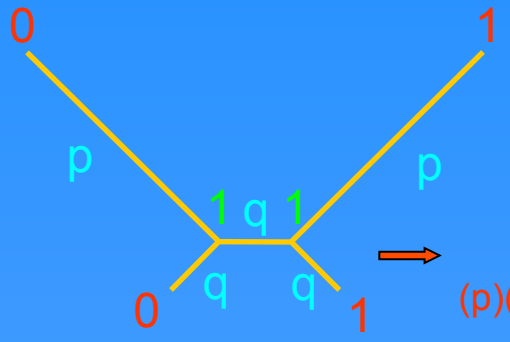
$\rightarrow (1-p)(1-q)(1-q)pq$



$\rightarrow (1-p)(1-q)(q)(1-p)(1-q)$



$\rightarrow (p)(q)(q)(p)(q)$

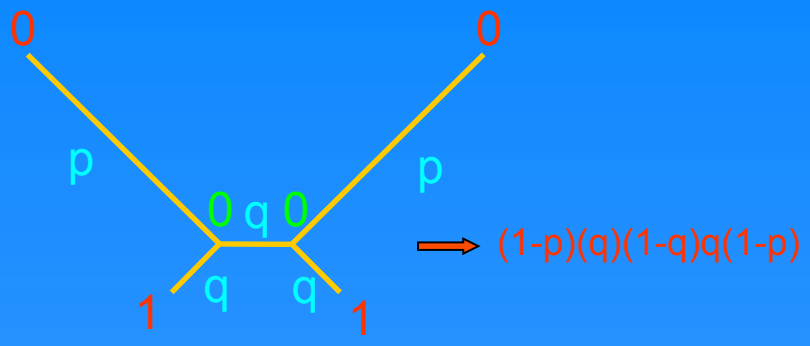


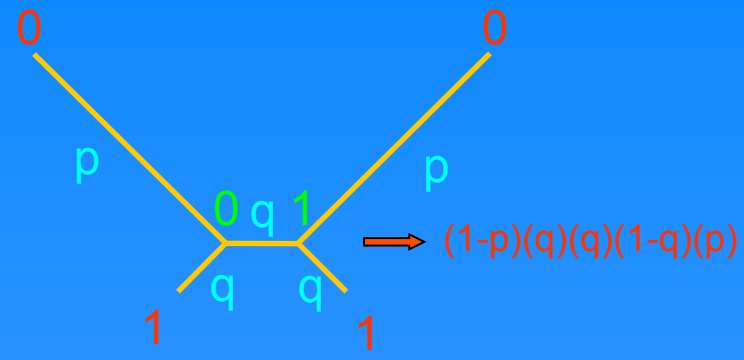
$\rightarrow (p)(q)(1-q)(1-p)(1-q)$

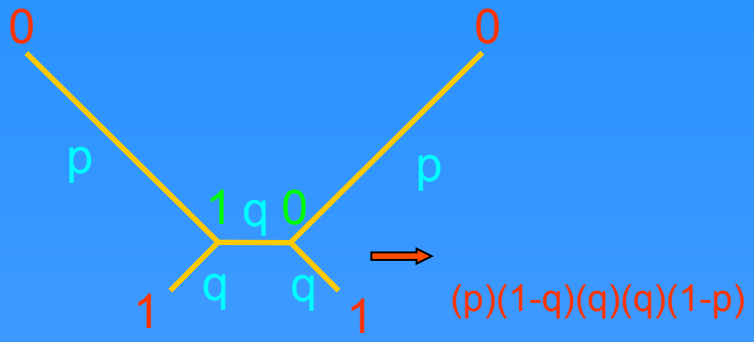
- We get $P(C_{xxyy}) = (1-p)(1-q)^2pq+(1-p)^2(1-q)2q+p^2q^3+(1-p)(1-q)^2pq$

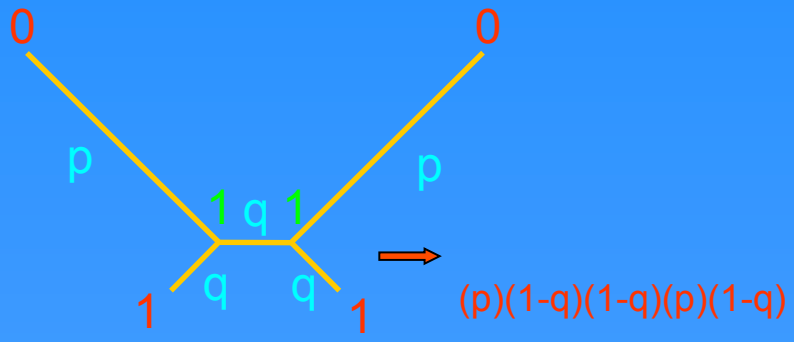
Parsimony inconsistency

- Let us calculate $P(C_{xyxy})$: the probability seeing C_{xyxy}









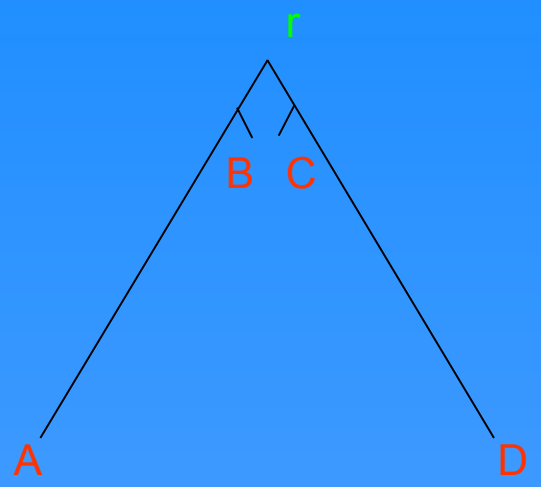
- We get $P(C_{xyxy}) = (1-q)(1-p)^2pq+(1-p)(1-q)pq^2+ (1-q)(1-p)pq^2 +(1-q)^3p^2$

Parsimony inconsistency

1. $P(Cxyxy) - P(Cxxyy) = (1-2q)[q^2(1-p)^2+(1-q)^2p^2]$

2. This is always positive as $q<1/2$.

- More intuitively:
  - B and C will mostly have *r*'s state (no mutation).
  - Whatever states A and D take is either uninformative for mp or misleading.



Long-branch Attraction

- Is all this realistic? *Very much!!!*
- Advocates of parsimony initially responded by claiming that Felsenstein's result showed only that his model was unrealistic.
- It is now recognised that the ***long-branch attraction*** (in the **Felsenstein Zone**) is one of the most serious problems in phylogenetic inference.