CSEP 527
Spring 2016

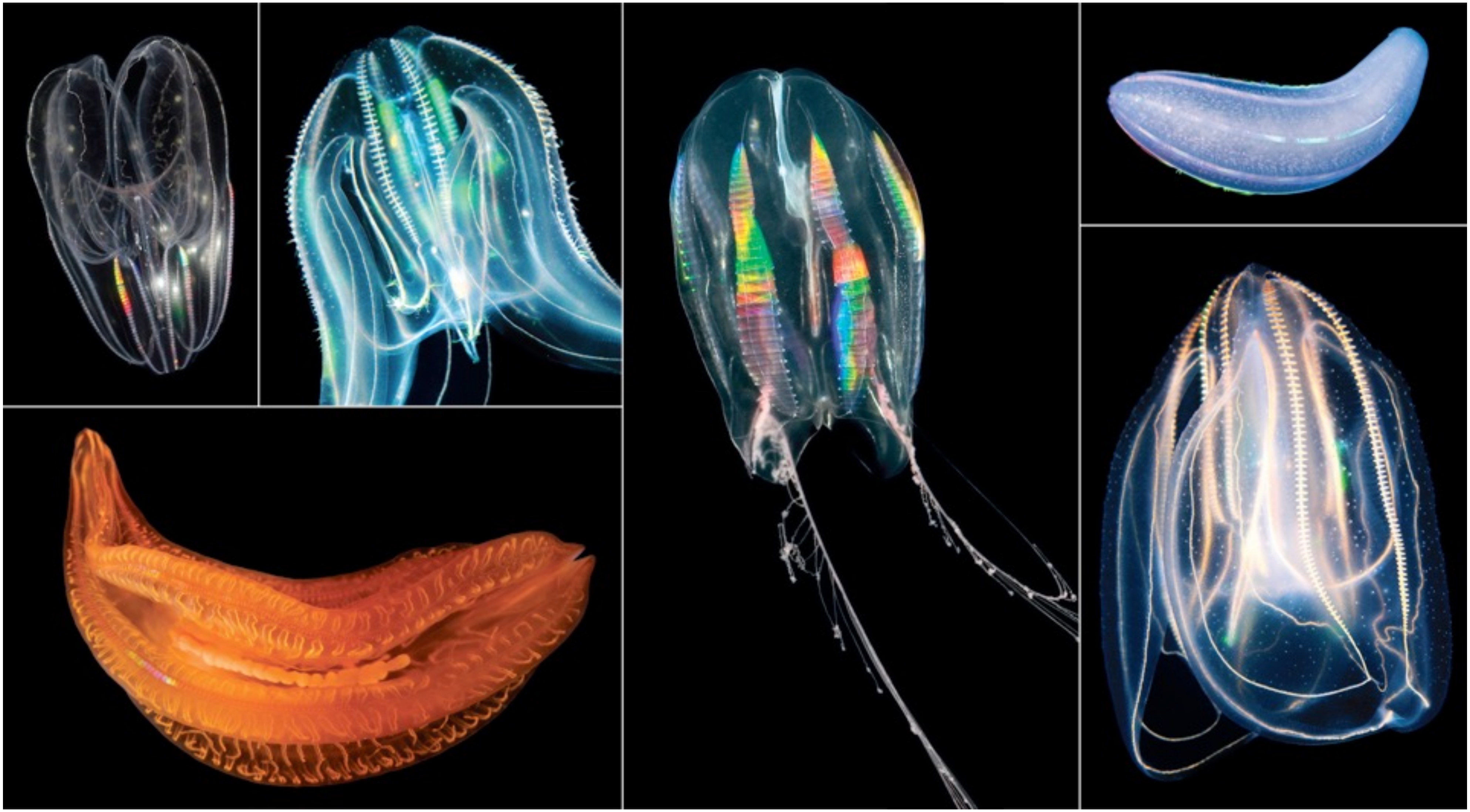
Phylogenies: Parsimony Plus a Tantalizing Taste of Likelihood

Phylogenies
(aka Evolutionary Trees)

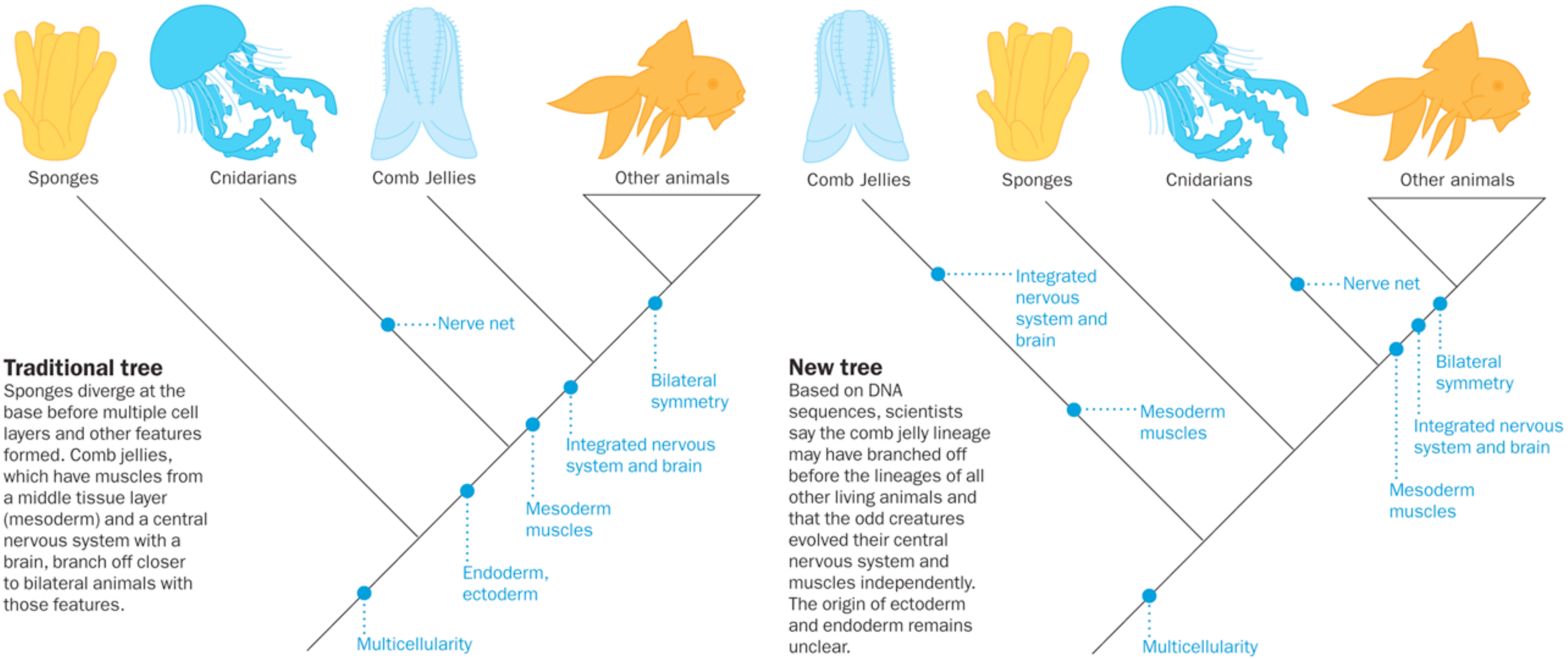
“Nothing in biology makes sense, except in the light of evolution”

-- Theodosius Dobzhansky, 1973

Comb Jellies: Evolutionary enigma



http://www.sciencenews.org/view/feature/id/350120/description/Evolutionary_enigmas



Traditional tree

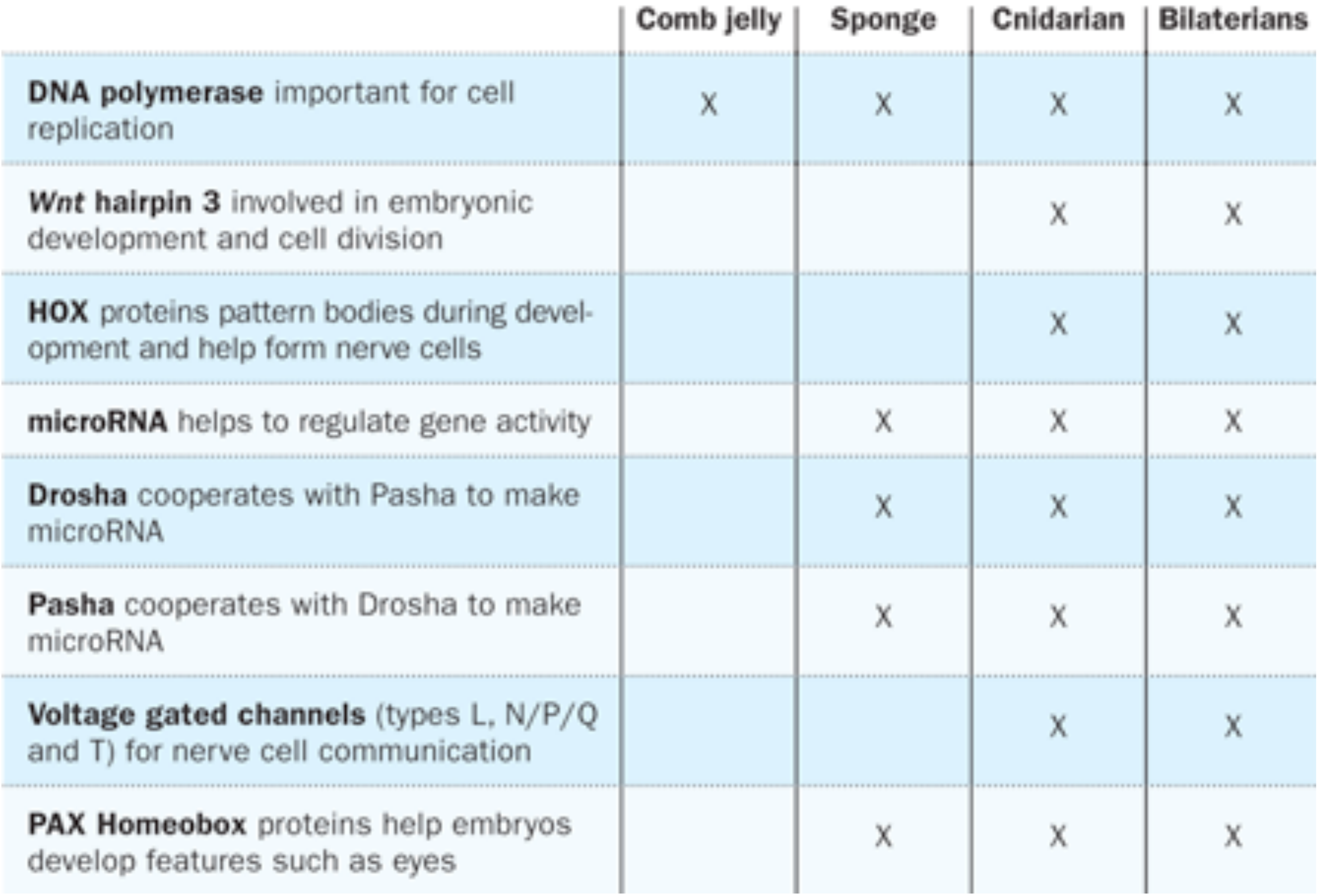
Sponges diverge at the base before multiple cell layers and other features formed. Comb jellies, which have muscles from a middle tissue layer (mesoderm) and a central nervous system with a brain, branch off closer to bilateral animals with those features.

New tree

Based on DNA sequences, scientists say the comb jelly lineage may have branched off before the lineages of all other living animals and that the odd creatures evolved their central nervous system and muscles independently. The origin of ectoderm and endoderm remains unclear.

TREE OF LIFE

Diagrams depict the history of animal lineages as they evolved over time. Each branch represents a lineage that shares an ancestor with all of the animals that branch after the point where it splits from the tree. Biologists traditionally build trees by comparing species' anatomies; now they also compare DNA sequences.



	Comb jelly	Sponge	Cnidarian	Bilaterians
DNA polymerase important for cell replication	X	X	X	X
***Wnt* hairpin 3** involved in embryonic development and cell division			X	X
HOX proteins pattern bodies during development and help form nerve cells			X	X
microRNA helps to regulate gene activity		X	X	X
Drosha cooperates with Pasha to make microRNA		X	X	X
Pasha cooperates with Drosha to make microRNA		X	X	X
Voltage gated channels (types L, N/P/Q and T) for nerve cell communication			X	X
PAX Homeobox proteins help embryos develop features such as eyes		X	X	X

A Complex Question:

Given data (sequences, anatomy, ...) infer the phylogeny

A Simpler Question:

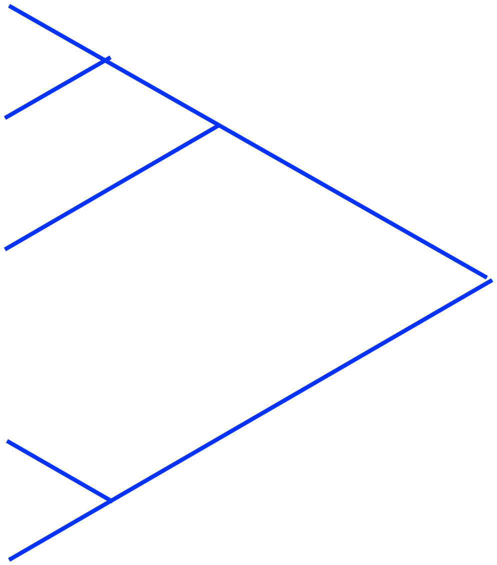
Given data *and a phylogeny*, evaluate “how much change” is needed to fit data to tree

(The former question is usually tackled by sampling tree topologies & comparing them by the later metric…)

Parsimony

General idea ~ Occam's Razor:
Given data where change is rare, prefer an explanation that requires few events

Human	A	T	G	A	T	...
Chimp	A	T	G	A	T	...
Gorilla	A	T	G	A	G	...
Rat	A	T	G	C	G	...
Mouse	A	T	G	C	T	...



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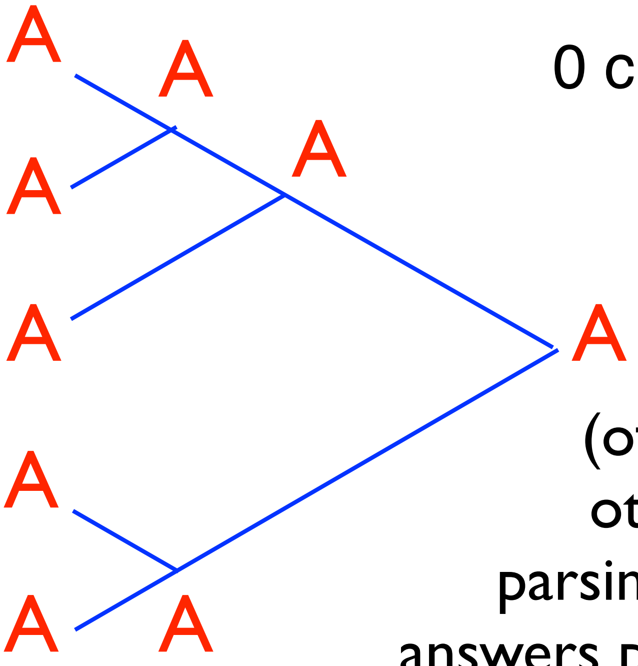

0 changes

(of course other, less parsimonious, answers possible)

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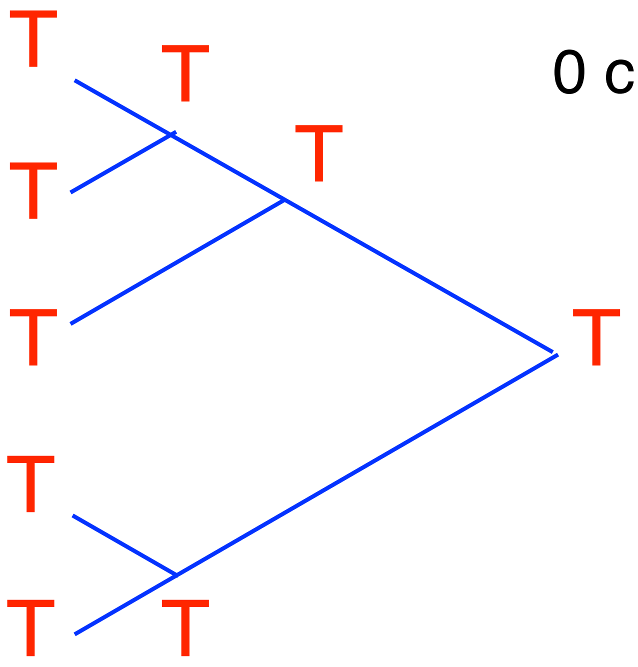

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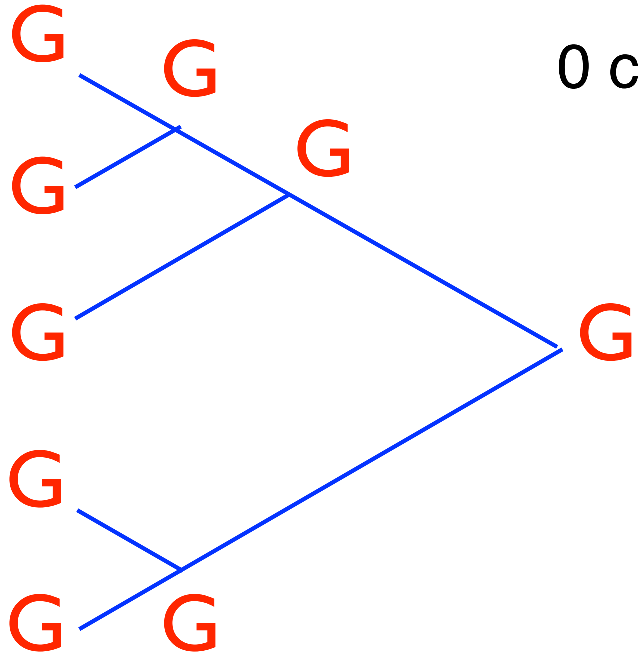

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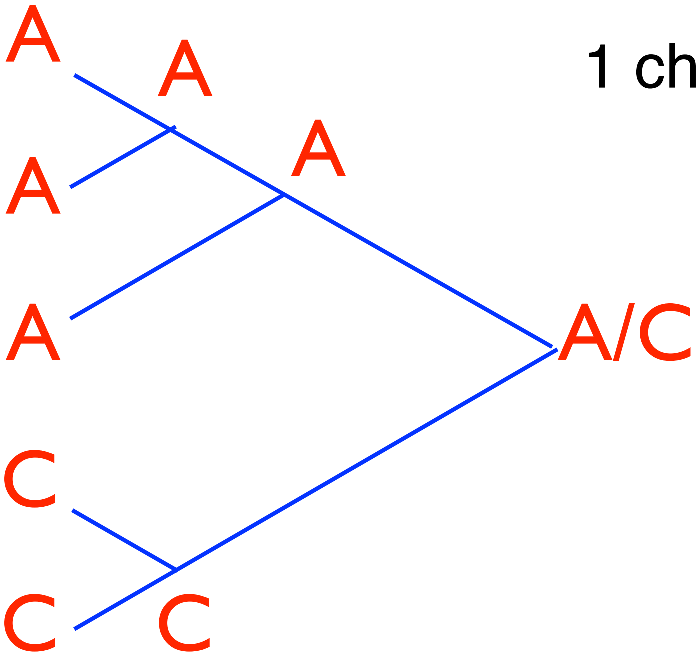

1 change

Parsimony

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Gorilla	A	T	G	A	G	...
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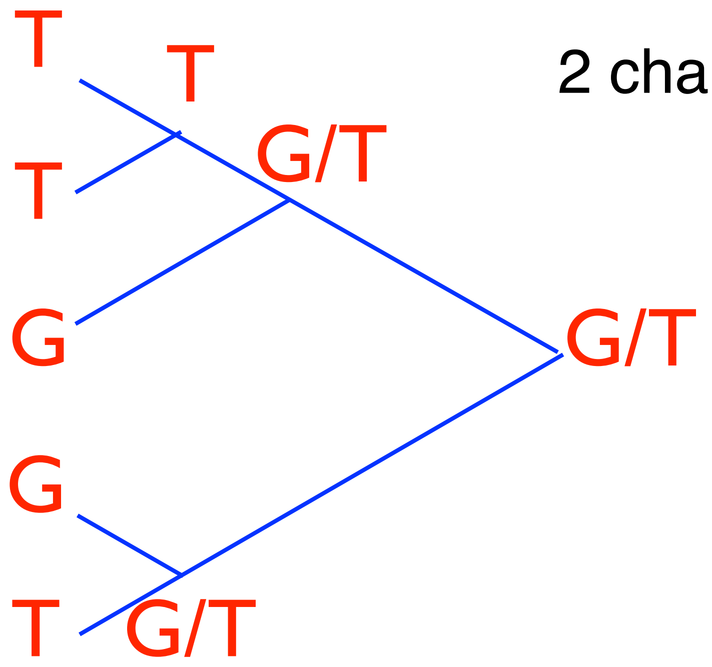
Mouse	A	T	G	C	T	...



2 changes

Counting Events Parsimoniously

Lesson of example – no unique reconstruction

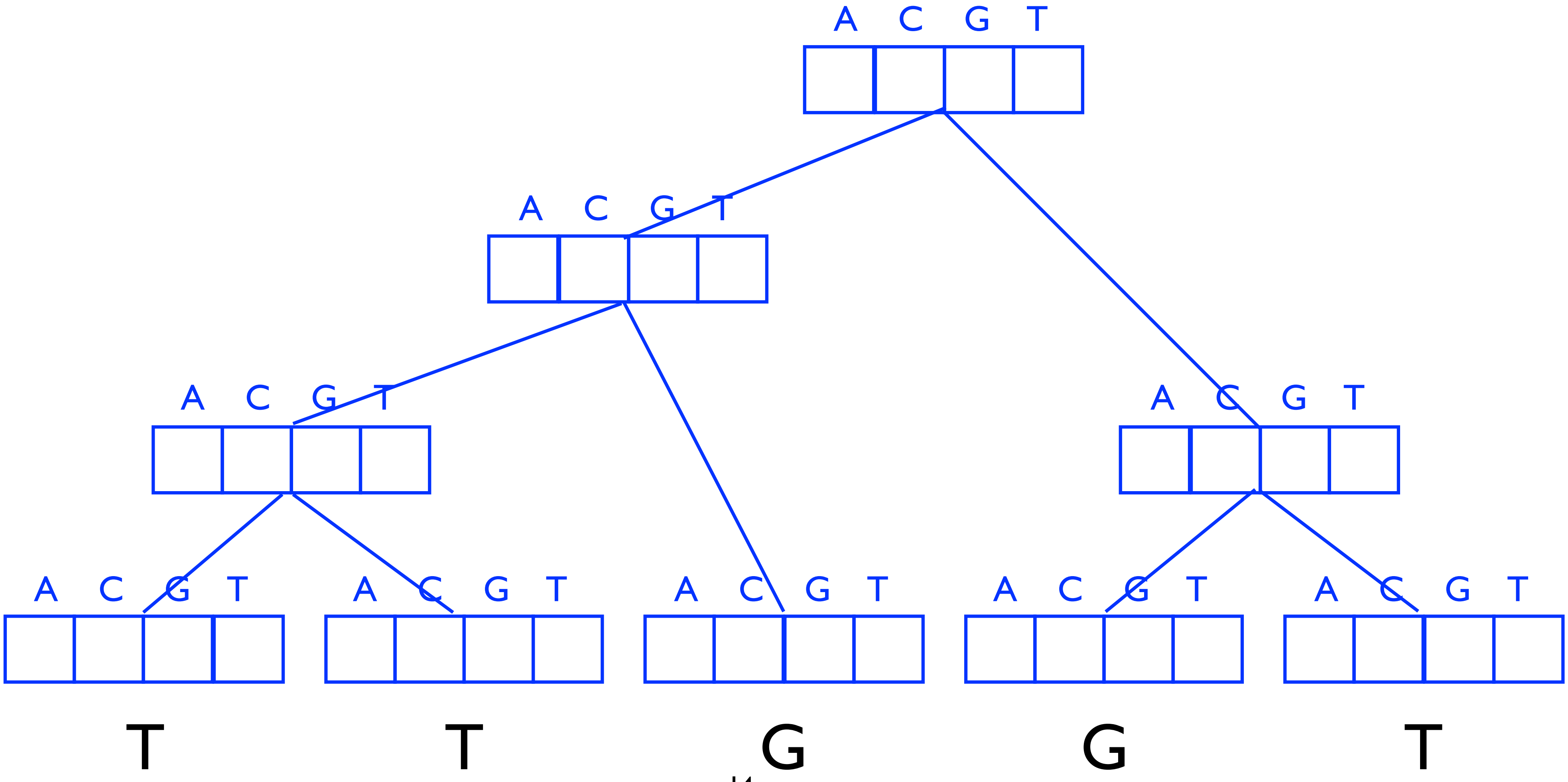
But there is a unique minimum number, of course

How to find it?

Early solutions 1965-75

Sankoff & Rousseau, '75

$P_u(s)$ = best parsimony score of subtree rooted at node *u*, assuming *u* is labeled by character *s*



Sankoff-Rousseau Recurrence

$P_u(s)$ = best parsimony score of subtree rooted at node *u*, assuming *u* is labeled by character *s*

For Leaf *u*:

$$P_u(s) = \begin{cases} 0 & \text{if } u \text{ is a leaf labeled } s \\ \infty & \text{if } u \text{ is a leaf not labeled } s \end{cases}$$

For Internal node *u*:

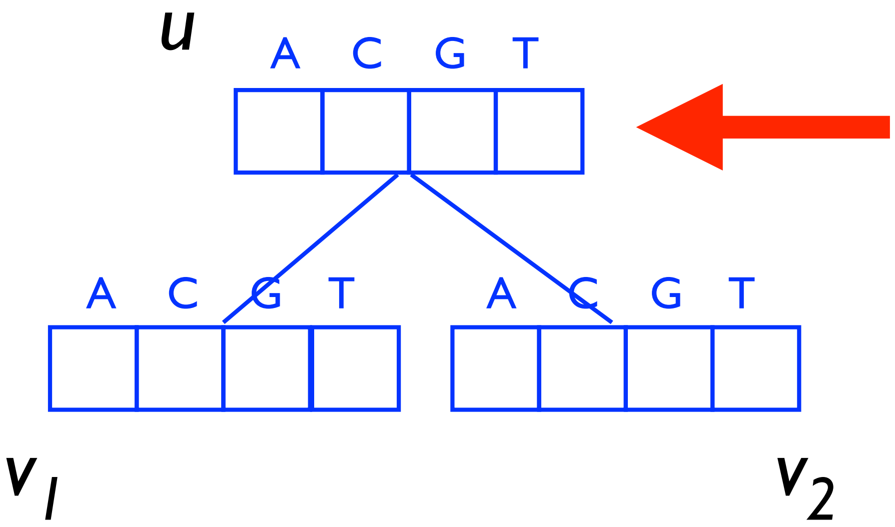
$$P_u(s) = \sum_{v \in \text{child}(u)} \min_{t \in \{A,C,G,T\}} \text{cost}(s,t) + P_v(t)$$

Time: O(alphabet^2 x tree size)

Sankoff & Rousseau, '75

$P_u(s)$ = best parsimony score of subtree rooted at node *u*, assuming *u* is labeled by character *s*

$$P_u(s) = \sum_{v\in\text{child}(u)} \min_{t\in\{A,C,G,T\}} \text{cost}(s,t) + P_v(t)$$

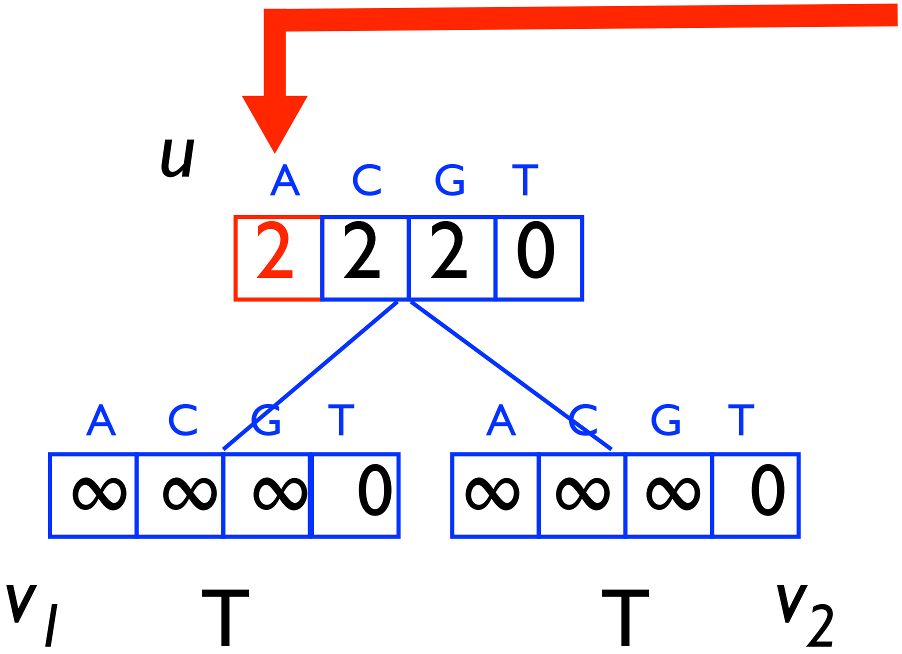


s	*v*	*t*	cost(*s*,*t*)+P_v(t)	min
	v_1	A		
		C		
		G		
		T		
	v_2	A		
		C		
		G		
		T		
sum: P_u(s) =				

Sankoff & Rousseau, '75

$P_u(s)$ = best parsimony score of subtree rooted at node *u*, assuming *u* is labeled by character *s*

$$P_u(s) = \sum_{v \in \text{child}(u)} \min_{t \in \{A,C,G,T\}} \text{cost}(s,t) + P_v(t)$$

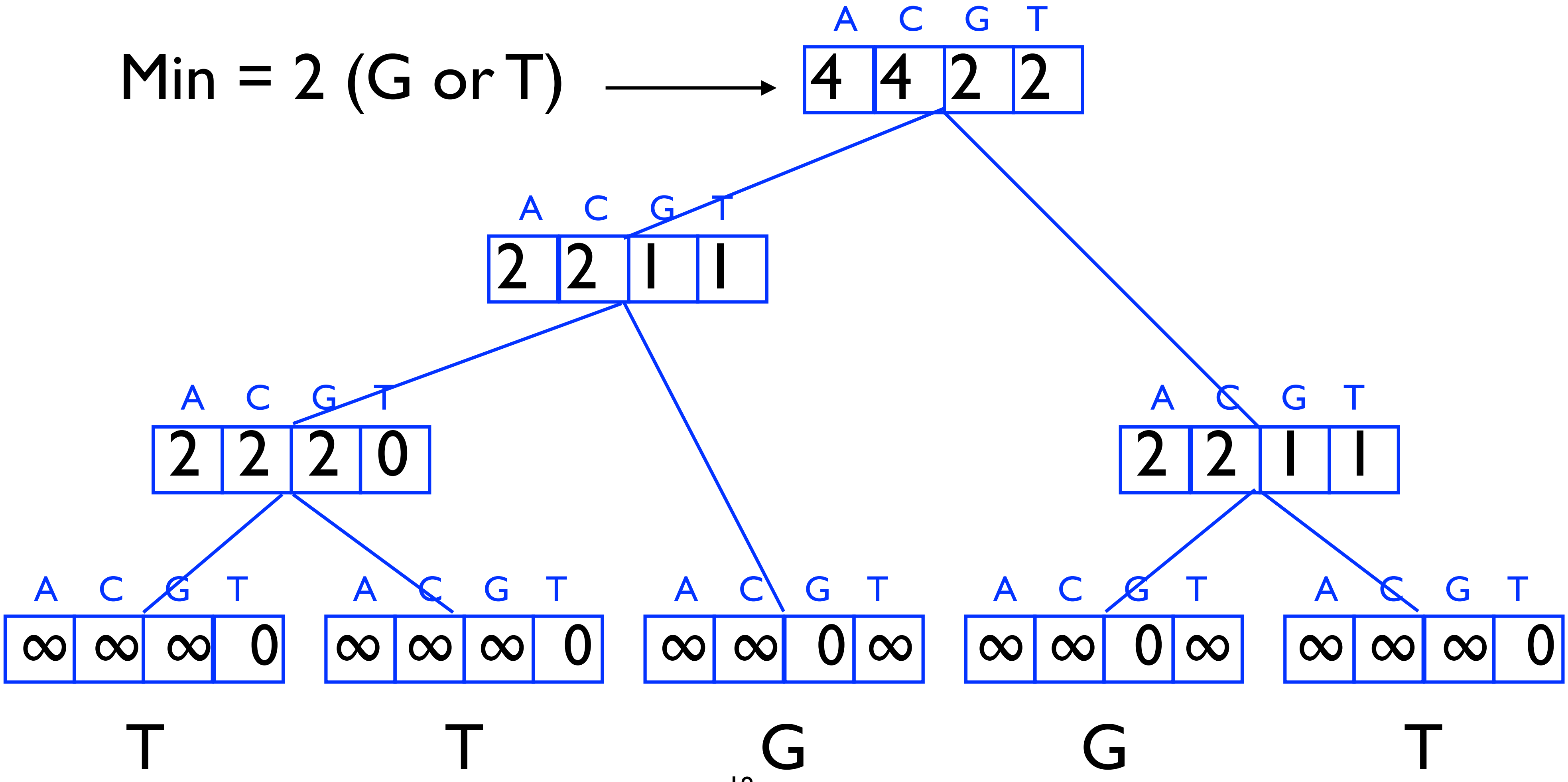


s	*v*	*t*	cost(*s*,*t*)+P_v(t)	min
A	v_1	A	0 + ∞	1
		C	1 + ∞	
		G	1 + ∞	
		T	1 + 0	
	v_2	A	0 + ∞	1
		C	1 + ∞	
		G	1 + ∞	
		T	1 + 0	
			sum: P_u(s) =	2

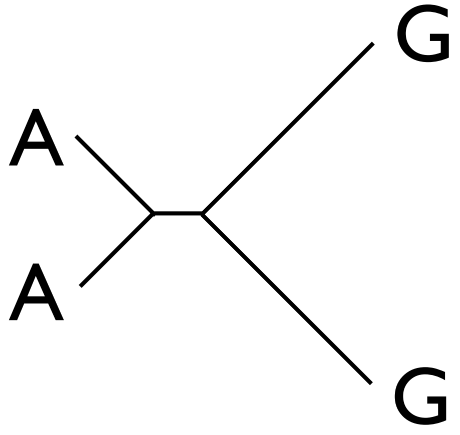
Sankoff & Rousseau, ‘75

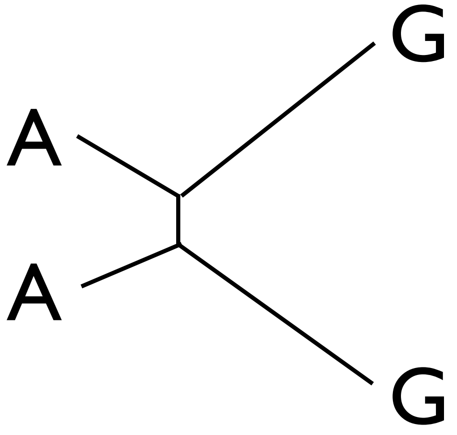
$P_u(s)$ = best parsimony score of subtree rooted at node *u*, assuming *u* is labeled by character *s*

Min = 2 (G or T) →



Which tree is better?





Which has smaller parsimony score?

Which is more likely, assuming edge length proportional to evolutionary rate?

Parsimony – Generalities

Parsimony is *not* the best way to evaluate a phylogeny (maximum likelihood generally preferred - as previous slide suggests)

But it is a natural approach, works well in many cases, and is fast.

Finding the best tree: a much harder problem

Much is known about these problems; ***Inferring Phylogenies*** by Joe Felsenstein is a great resource.

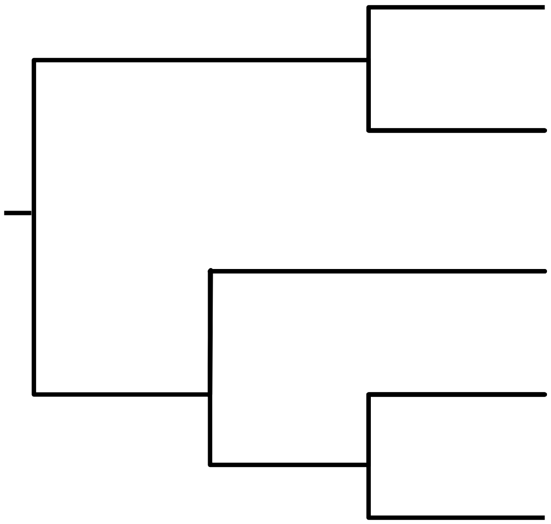
Phylogenetic Footprinting

A lovely extension of the above ideas. E.g., suppose promoters of orthologous genes in multiple species all contain (variants of) a common k-base transcription factor binding site. Roughly as above, but 4^k table entries per node…

1. M Blanchette, B Schwikowski, M Tompa, Algorithms for Phylogenetic Footprinting. *J Comp Biol*, vol. 9, no. 2, 2002, 211-223

2. M Blanchette and M Tompa, FootPrinter: a Program Designed for Phylogenetic Footprinting. *Nucleic Acids Research*, vol. 31, no. 13, July 2003, 3840-3842

Small Example



AGTCGTACGTGAC... (Human)

AGTAGACGTGCCG... (Chimp)

ACGTGAGATACGT... (Rabbit)

GAACGGAGTACGT... (Mouse)

TCGTGACGGTGAT... (Rat)

Size of motif sought: $k = 4$

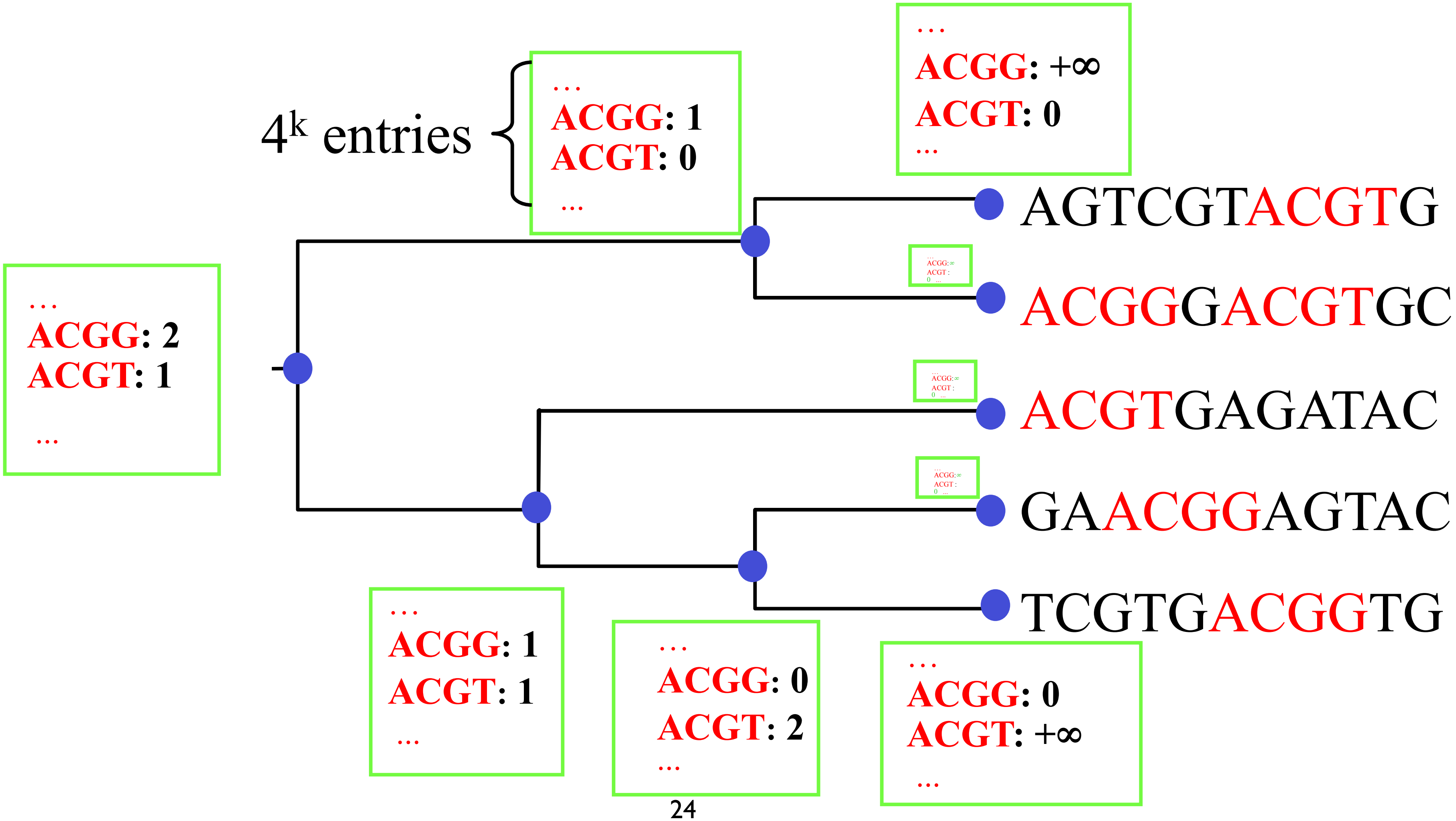
CLUSTALW multiple sequence alignment (rbcS gene)

```
Cotton      ACGGTT-TCCATTGGATGA---AATGAGATAAGAT---CACTGTGC---TTCTTCCACGTG--GCAGGTTGCCAAAGATA-------AGGCTTTACCATT
Pea         GTTTTT-TCAGTTAGCTTA---GTGGGCATCTTA----CACGTGGC---ATTATTATCCTA--TT-GGTGGCTAATGATA-------AGG--TTAGCACA
Tobacco     TAGGAT-GAGATAAGATTA---CTGAGGTGCTTTA---CACGTGGC---ACCTCCATTGTG--GT-GACTTAAATGAAGA-------ATGGCTTAGCACC
Ice-plant   TCCCAT-ACATTGACATAT---ATGGCCCGCCTGCGGCAACAAAAA---AACTAAAGGATA--GCTAGTTGCTACTACAATTC--CCATAACTCACCACC
Turnip      ATTCAT-ATAAATAGAAGG---TCCGCGAACATTG--AAATGTAGATCATGCGTCAGAATT--GTCCTCTCTTAATAGGA-------A-------GGAGC
Wheat       TATGAT-AAAATGAAATAT---TTTGCCCAGCCA-----ACTCAGTCGCATCCTCGGACAA--TTTGTTATCAAGGAACTCAC--CCAAAAACAAGCAAA
Duckweed    TCGGAT-GGGGGGGCATGAACACTTGCAATCATT-----TCATGACTCATTTCTGAACATGT-GCCCTTGGCAACGTGTAGACTGCCAACATTAATTAAA
Larch       TAACAT-ATGATATAACAC---CGGGCACACATTCCTAAACAAAGAGTGATTTCAAATATATCGTTAATTACGACTAACAAAA--TGAAGTACAAGACC

Cotton      CAAGAAAAGTTTCCACCCTC------TTTGTGGTCATAATG-GTT-GTAATGTC-ATCTGATTT----AGGATCCAACGTCACCCTTTCTCCCA-----A
Pea         C---AAAACTTTTCAATCT-------TGTGTGGTTAATATG-ACT-GCAAAGTTTATCATTTTC----ACAATCCAACAA-ACTGGTTCT---------A
Tobacco     AAAAATAATTTTCCAACCTTT---CATGTGTGGATATTAAG-ATTTGTATAATGTATCAAGAACC-ACATAATCCAATGGTTAGCTTTATTCCAAGATGA
Ice-plant   ATCACACATTCTTCCATTTCATCCCCTTTTTCTTGGATGAG-ATAAGATATGGGTTCCTGCCAC----GTGGCACCATACCATGGTTTGTTA-ACGATAA
Turnip      CAAAAGCATTGGCTCAAGTTG-----AGACGAGTAACCATACACATTCATACGTTTTCTTACAAG-ATAAGATAAGATAATGTTATTTCT---------A
Wheat       GCTAGAAAAAGGTTGTGTGGCAGCCACCTAATGACATGAAGGACT-GAAATTTCCAGCACACACA-A-TGTATCCGACGGCAATGCTTCTTC--------
Duckweed    ATATAATATTAGAAAAAAATC-----TCCCATAGTATTTAGTATTTACCAAAAGTCACACGACCA-CTAGACTCCAATTTACCCAAATCACTAACCAATT
Larch       TTCTCGTATAAGGCCACCA-------TTGGTAGACACGTAGTATGCTAAATATGCACCACACACA-CTATCAGATATGGTAGTGGGATCTG--ACGGTCA

Cotton      ACCAATCTCT---AAATGTT----GTGAGCT---TAG-GCCAAATTT-TATGACTATA--TAT----AGGGGATTGCACC----AAGGCAGTG-ACACTA
Pea         GGCAGTGGCC---AACTAC--------------------CACAATTT-TAAGACCATAA-TAT----TGGAAATAGAA------AAATCAAT--ACATTA
Tobacco     GGGGGTTGTT---GATTTTT----GTCCGTTAGATAT-GCGAAATATGTAAAACCTTAT-CAT----TATATATAGAG------TGGTGGGCA-ACGATG
Ice-plant   GGCTCTTAATCAAAAGTTTTAGGTGTGAATTTAGTTT-GATGAGTTTTAAGGTCCTTAT-TATA---TATAGGAAGGGGG----TGCTATGGA-GCAAGG
Turnip      CACCTTTCTTTAATCCTGTGGCAGTTAACGACGATATCATGAAATCTTGATCCTTCGAT-CATTAGGGCTTCATACCTCT----TGCGCTTCTCACTATA
Wheat       CACTGATCCGGAGAAGATAAGGAAACGAGGCAACCAGCGAACGTGAGCCATCCCAACCA-CATCTGTACCAAAGAAACGG----GGCTATATATACCGTG
Duckweed    TTAGGTTGAATGGAAAATAG---AACGCAATAATGTCCGACATATTTCCTATATTTCCG-TTTTTCGAGAGAAGGCCTGTGTACCGATAAGGATGTAATC
Larch       CGCTTCTCCTCTGGAGTTATCCGATTGTAATCCTTGCAGTCCAATTTCTCTGGTCTGGC-CCA----ACCTTAGAGATTG----GGGCTTATA-TCTATA

Cotton      T-TAAGGGATCAGTGAGAC-TCTTTTGTATAACTGTAGCAT--ATAGTAC
Pea         TATAAAGCAAGTTTTAGTA-CAAGCTTTGCAATTCAACCAC--A-AGAAC
Tobacco     CATAGACCATCTTGGAAGT-TTAAAGGGAAAAAAGGAAAAG--GGAGAAA
Ice-plant   TCCTCATCAAAAGGGAAGTGTTTTTTCTCTAACTATATTACTAAGAGTAC
Larch       TCTTCTTCACAC---AATCCATTTGTGTAGAGCCGCTGGAAGGTAAATCA
Turnip      TATAGATAACCA---AAGCAATAGACAGACAAGTAAGTTAAG-AGAAAAG
Wheat       GTGACCCGGCAATGGGGTCCTCAACTGTAGCCGGCATCCTCCTCTCCTCC
Duckweed    CATGGGGCGACG---CAGTGTGTGGAGGAGCAGGCTCAGTCTCCTTCTCG
```

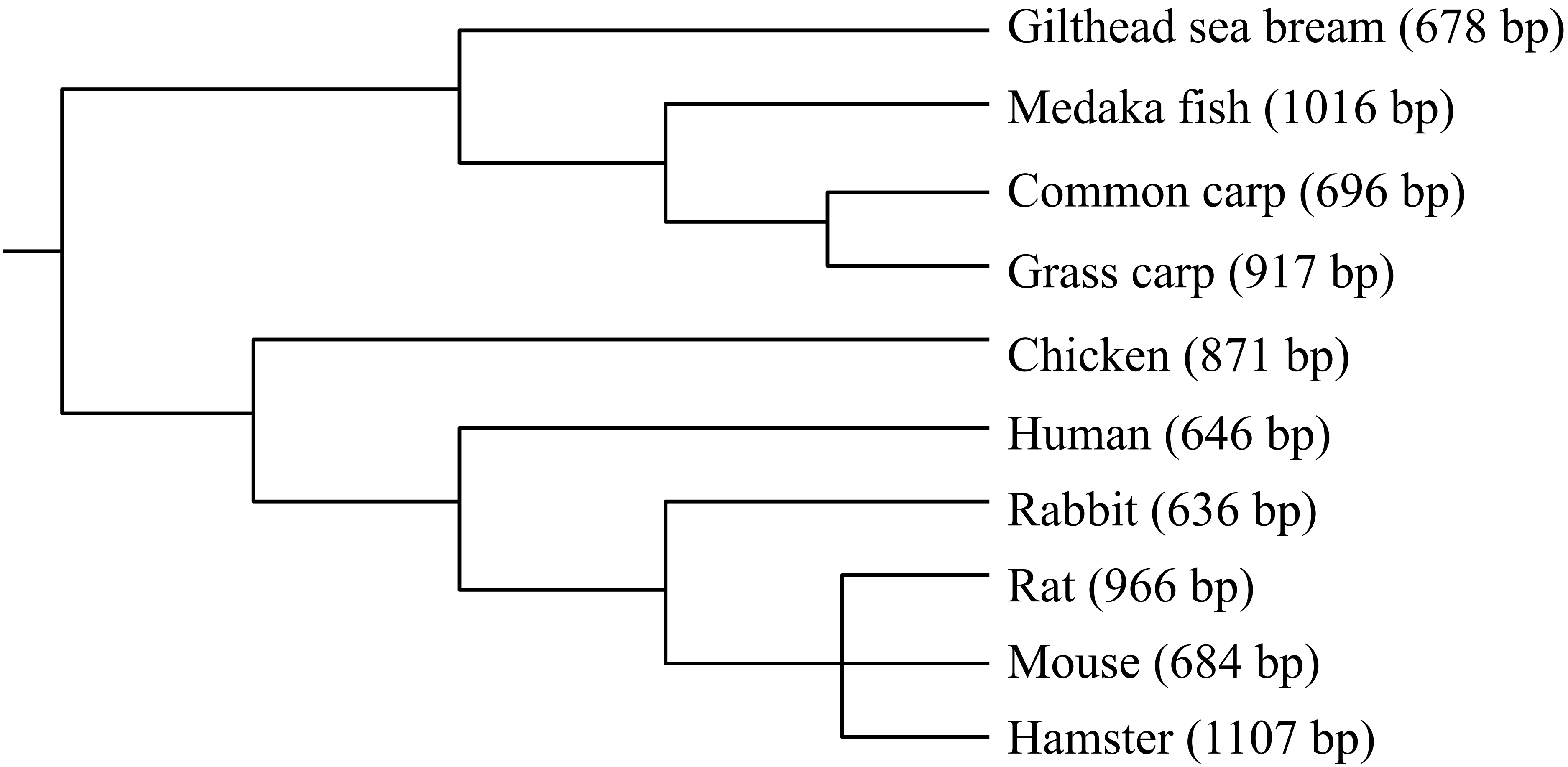
An Exact Algorithm

(generalizing Sankoff and Rousseau 1975)

$W_u[s]$ = best parsimony score for subtree rooted at node u, if u is labeled with string s.



Application to *β-actin* Gene



Gilthead sea bream (678 bp)

Medaka fish (1016 bp)

Common carp (696 bp)

Grass carp (917 bp)

Chicken (871 bp)

Human (646 bp)

Rabbit (636 bp)

Rat (966 bp)

Mouse (684 bp)

Hamster (1107 bp)

Common carp

ACGGACTGTTACCACTTCACGCCGACTCAACTGCGCAGAGAAAAACTTCAAACGACAACATTGGCATGGCTTTTGTTATTTTTGGCGCTTGACTCAGG
ATCTAAAAACTGGAACGGCGAAGGTGACGGCAATGTTTTGGCAAATAAGCATCCCCGAAGTTCTACAATGCATCTGAGGACTCAATGTTTTTTTTTTTTTTTTT
CTTTAGTCATTCCAAATGTTTGTTAAATGCATTGTTCCGAAACTTATTTGCCTCTATGAAGGCTGCCCAGTAATTGGGAGCATACTTAACATTGTAGTATTGTATGTAAAT
TATGTAACAAAACAATGACTGGGTTTTTGTACTTTCAGCCTTAATCTTGGGTTTTTTTTTTTTTTTGGTTCCAAAAAACTAAGCTTTACCATTCAAGATGTAAAGGTTTCATTCC
CCCTGGCATATTGAAAAAGCTGTGTGGAACGTGGCGGTGCAGACATTTGGTGGGGCCAACCTGTACACTGACTAATTCAAATAAAAGTGCACATGTAAGAC
ATCCTACTCTGTGTGATTTTTCTGTTTGTGCTGAGTGAACTTGCTATGAAGTCTTTTAGTGCACTCTTTAATAAAAGTAGTCTTCCCTTAAAGTGTCCCTTCCCTTATGGCCTTC
ACATTTCTCAACTAGCGCTTCAACTAGAAAGCACTTTAGGACTGGGATGC

Chicken

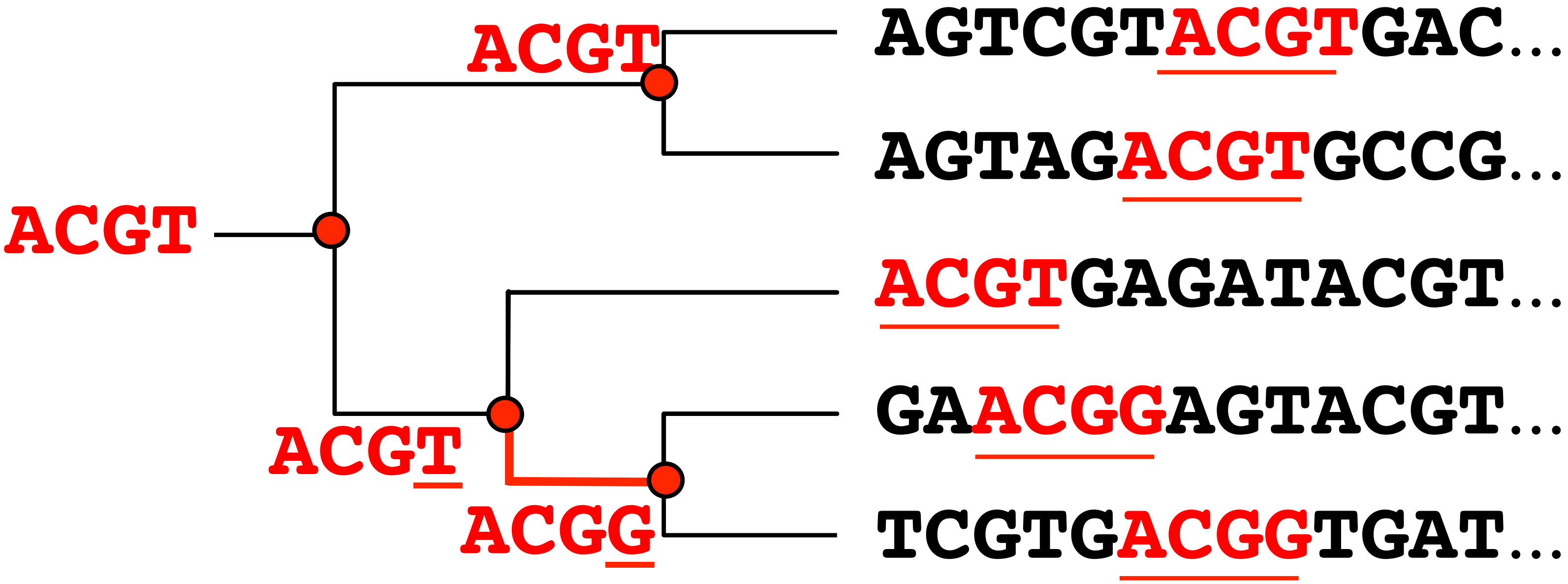
ACCGGACTGTTACCAACACCCACACCCCTGTGATGAAACAAAACCCATAAATGCGCATAAAACAAGACGAGATTGGCATGGCTTTATTTGTTTTTTCTTTTGGCGC
TTGACTCAGGATTAAAAAACTGGAATGGTGAAGGTGTCAGCAGCAGTCTTAAAATGAAACATGTTGGAGCGAACGCCCCCAAAGTTCTACAATGCAT
CTGAGGACTTTGATTGTACATTTGTTTCTTTTTTAATAGTCATTCCAAATATTGTTATAATGCATTGTTACAGGAAGTTACTCGCCTCTGTGAAGGCAACAGCCCAGCTGGG
AGGAGCCGGTACCAATTACTGGTGTTAGATGATAATTGCTTGTCTGTAAATTATGTAACCCAACAAGTGTCTTTTTGTATCTTCCGCCTTAAAAACAAAACACACTTGATCC
TTTTTGGTTTGTCAAGCAAGCGGGCTGTGTTCCCCAGTGATAGATGTGAATGAAGGCTTTACAGTCCCCCACAGTCTAGGAGTAAAGTGCCAGTATGTGGGGGAGGGAGGG
GCTACCTGTACACTGACTTAAGACCAGTTCAAATAAAAGTGCACACAATAGAGGCTTGACTGGTGTTGGTTTTTATTTCTGTGCTGCGCTGCTTGGCCGTTG
GTAGCTGTTCTCATCTAGCCTTGCCAGCCTGTGTGGGTCAGCTATCTGCATGGGCTGCGTGCTGGTGCTGTCTGGTGCAGAGGTTGGATAAACCGTGATGATATTTCAGCAA
GTGGGAGTTGGCTCTGATTCCATCCTGAGCTGCCATCAGTGTGTTCTGAAGGAAGCTGTTGGATGAGGGTGGGCTGAGTGCTGGGGGACAGCTGGGCTCAGTGGGACTG
CAGCTGTGCT

Human

GCGGACTATGACTTAGTTGCGTTACACCCTTTCTTGACAAAACCTAACTTGCGCAGAAAACAAGATGAGATTGGCATGGCTTTATTTGTTTTTTTTGTTTTGTTTTG
GTTTTTTTTTTTTTTTTGGCTTGACTCAGGATTTAAAAACTGGAACGGTGAAGGTGACAGCAGTCGGTTGGAGCGAGCATCCCCCAAAGTTCACAATG
TGGCCGAGGACTTTGATTGCATTGTTGTTTTTTTAATAGTCATTCCAAATATGAGATGCATTGTTACAGGAAGTCCCTTGCCATCCTAAAAGCCACCCCACTTCTCTCTAAG
GAGAATGGCCCAGTCCTCTCCCAAGTCCACACAGGGGAGGTGATAGCATTGCTTTCGTGTAAATTATGTAATGCAAAATTTTTTTAATCTTCGCCTTAATACTTTTTTATTTT
GTTTTATTTTGAATGATGAGCCTTCGTGCCCCCCCTTCCCCCTTTTTGTCCCCCAACTTGAGATGTATGAAGGCTTTTGGTCTCCCTGGGAGTGGGTGGAGGCAGCCAGGGC
TTACCTGTACACTGACTTGAGACCAGTTGAATAAAAGTGCACACCTTAAAAATGAGGCCAAGTGTGACTTTGTGGTGTGGCTGGGTTGGGGGCAGCAGAG
GGTG

Parsimony score over 10 vertebrates: 0 1 2

Solution



Parsimony score: 1 mutation