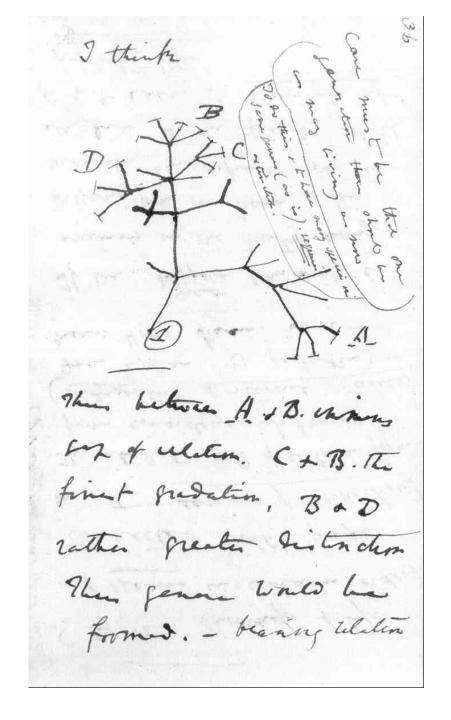
# Phylogenetics

December 2023



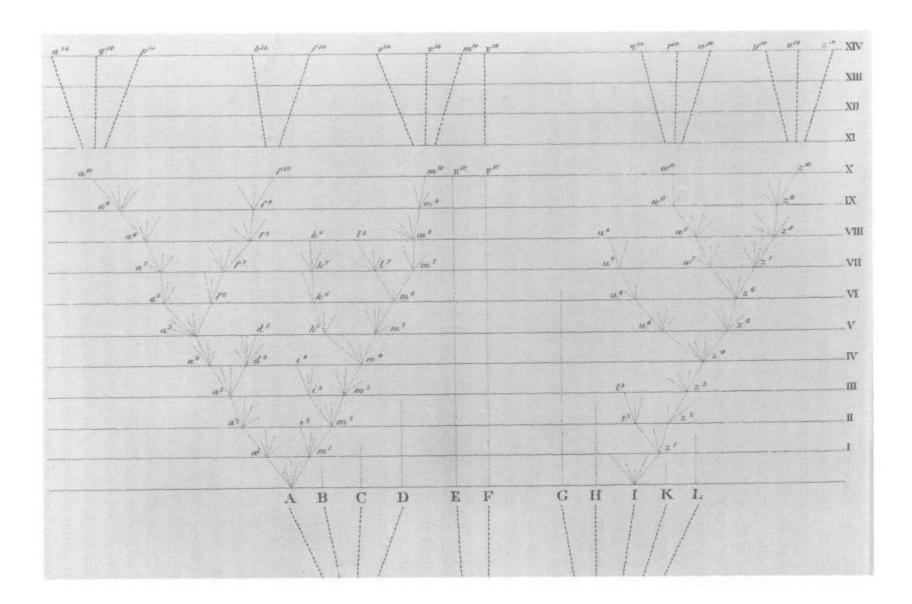
Gustav Klimt 1905 "Tree of Life"



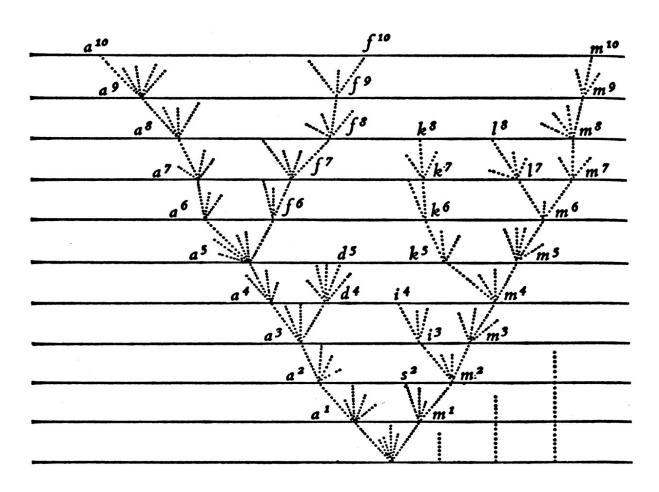


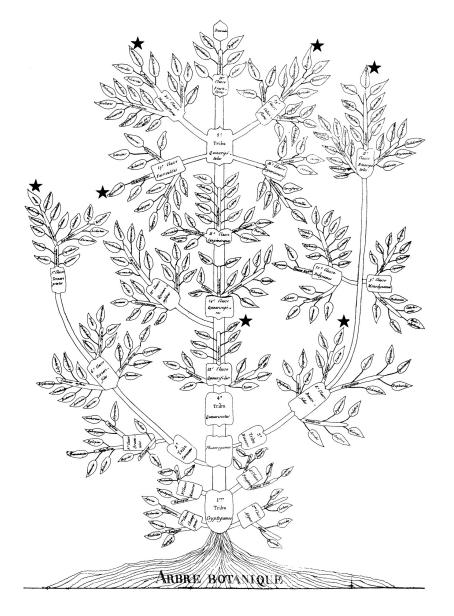
Notebook around July 1837





# Detail from only figure in origin of species





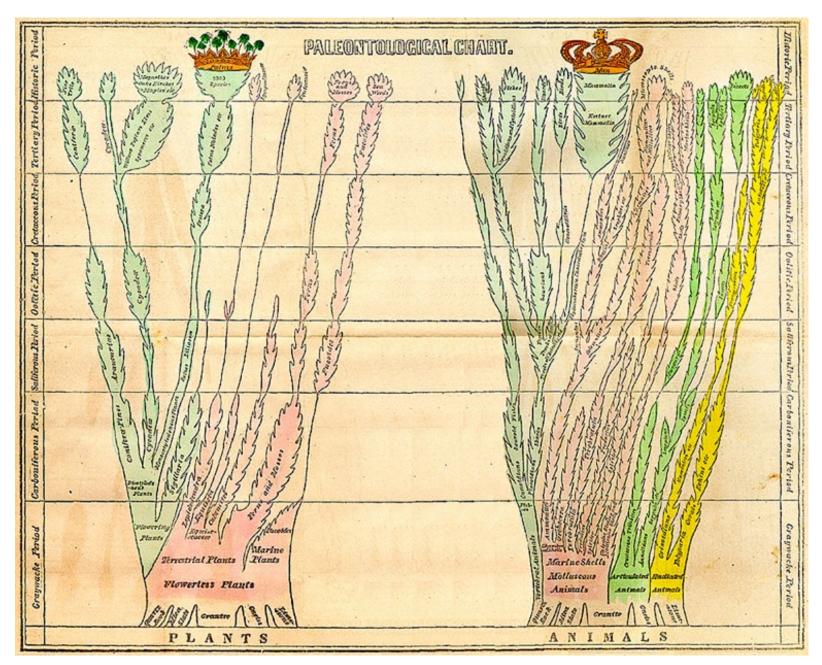
Augustin Augier 1801

#### TABLEAU

Servant à montrer l'origine des différens animaux.

Infusoires. Vers. Polypes. Radiaires. Insectes. Arachnides. Annelides. Crustacés. Cirrhipèdes. Mollusques. Poissons. Reptiles. Oiseaux. Monotrèmes. M. Amphibies. M. Cétacés. M. Ongulés. M. Onguiculés. Cette série d'animaux commençant par deux

Jean-Baptiste Lamark 1809

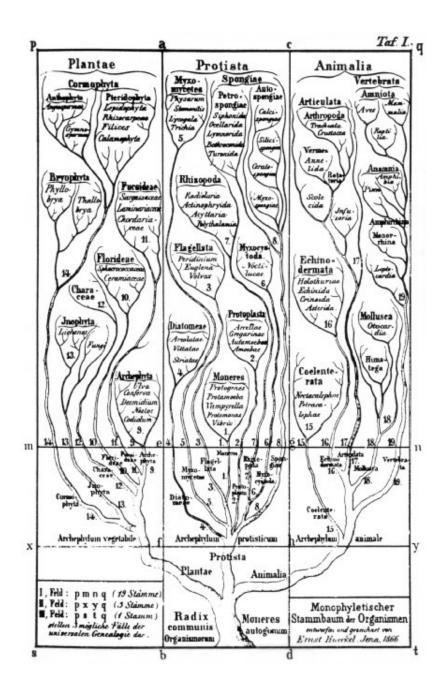


Elementary Geology Edward Hitchcock (1840)

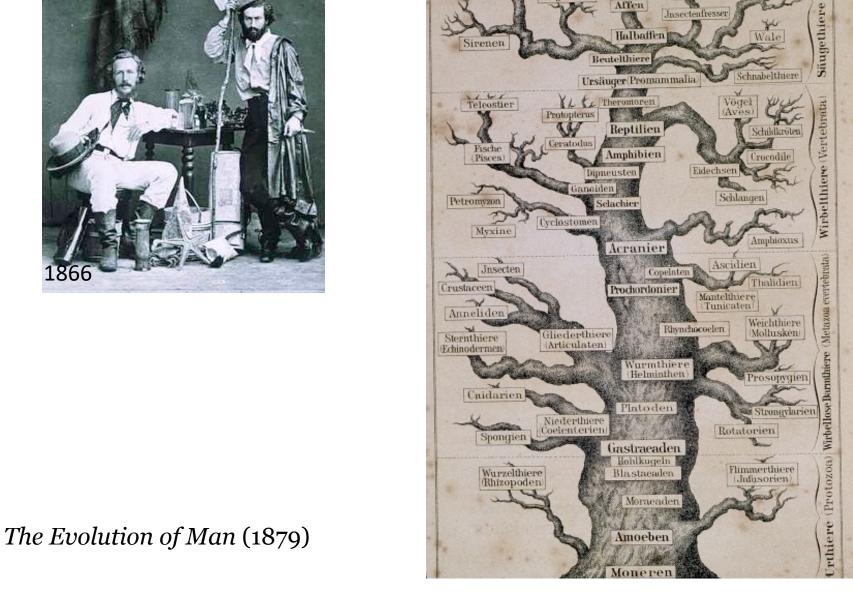


# Ernst Haeckel MD.PhD. (1834-1919)

- "ontogeny recapitulates phylogeny"
- -coined words "protista", "phylum", "ecology", "phylogeny"
- -TREE OF LIFE







Anthropogeme, IV. Auri

Sirenen

Menschen

Gorilla

Anthropoiden Affen

Halbaffen

Nagethiere

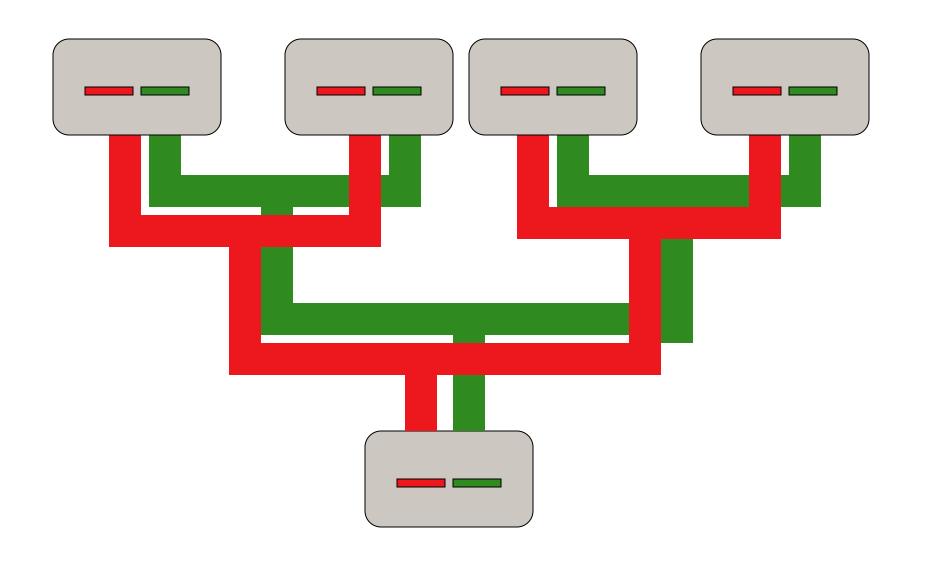
Gibbon

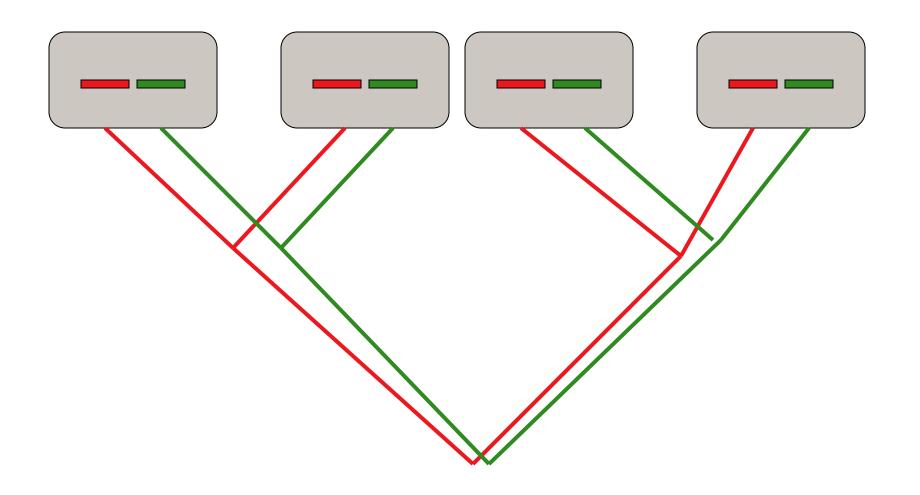
Fledermäuse

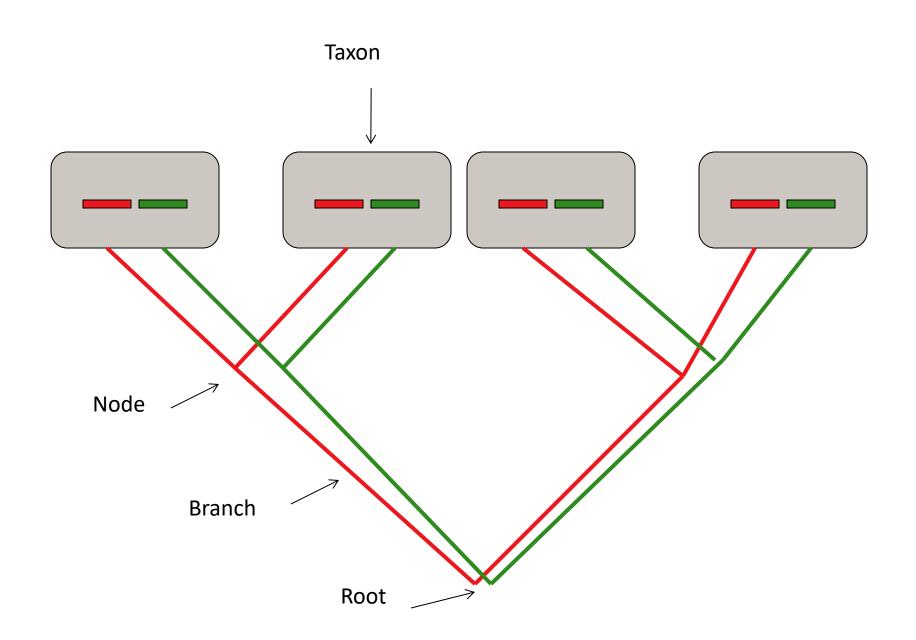
Jasectenfresser

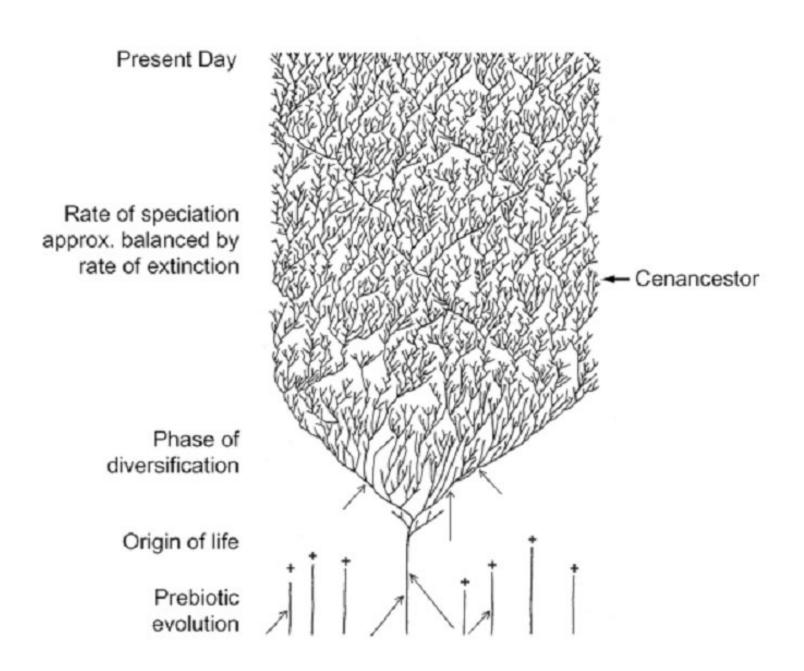
(Mammal

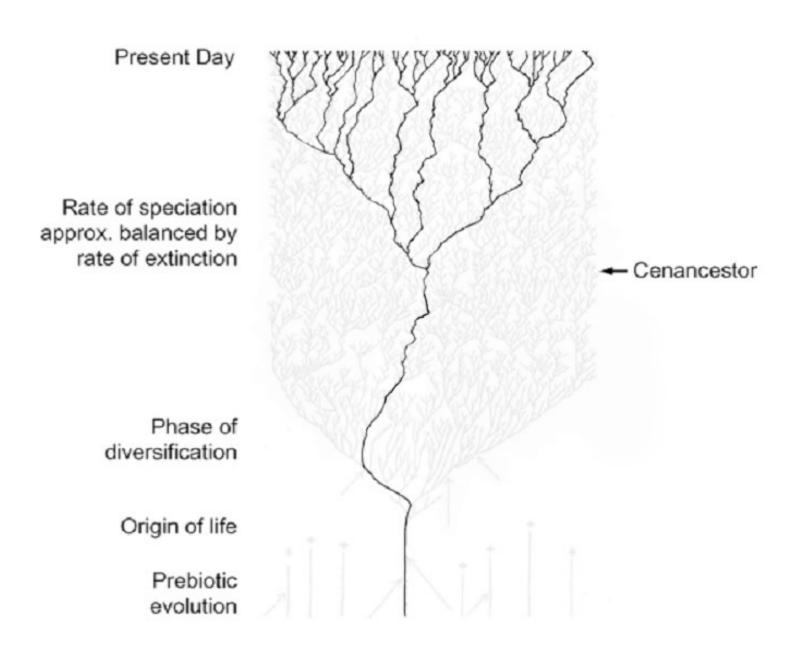
Raubthiere



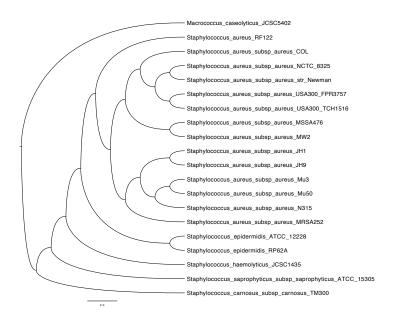




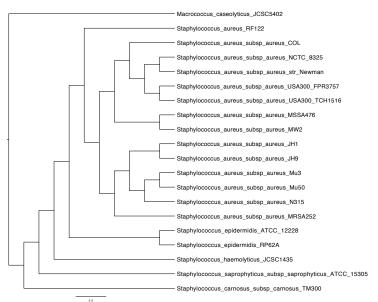




#### Look Different but Same Topologies



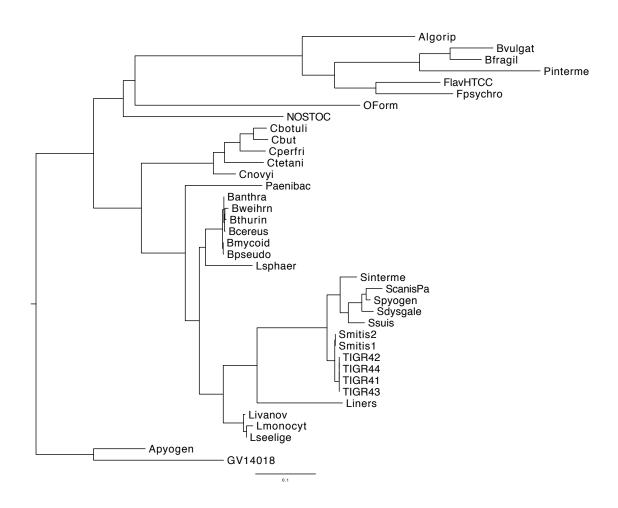


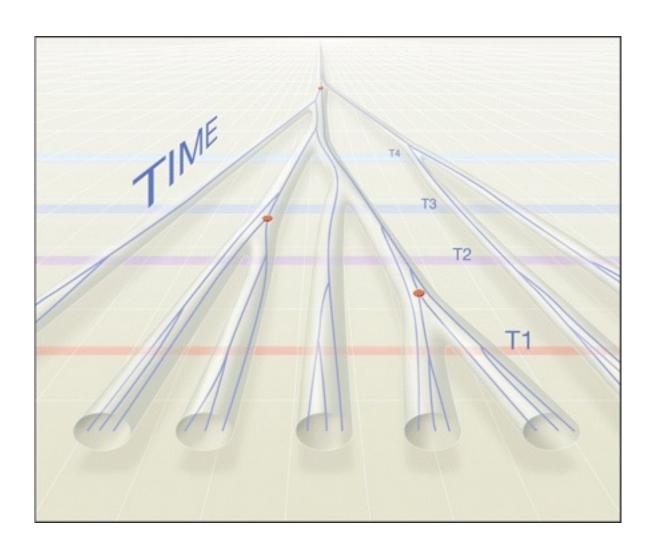


Time

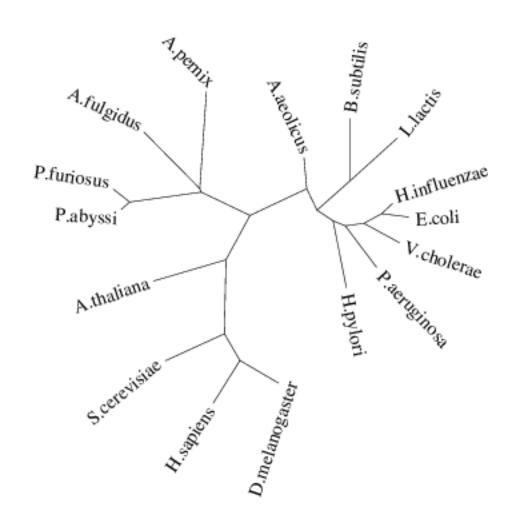
#### What about branch length:

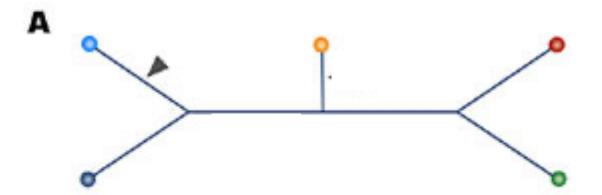
- 1. Branch length can signify many different things (time, difference, inferred changes)
- 2. General rule: longer branch length indicates more evolutionary change

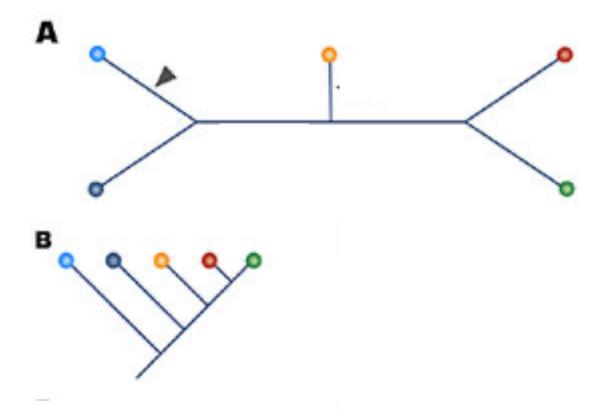


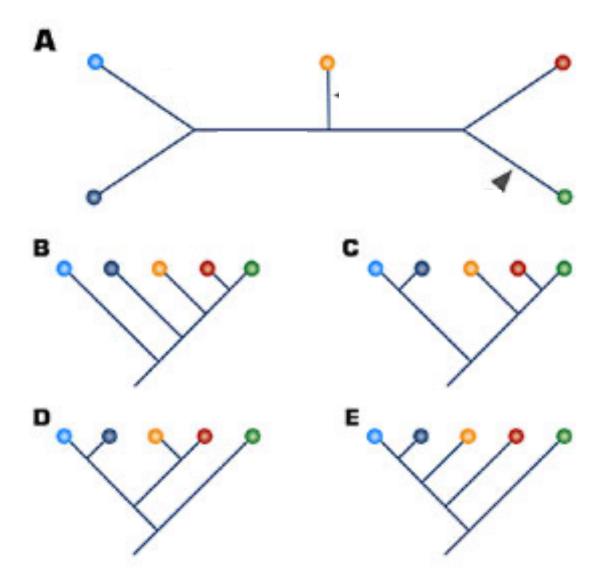


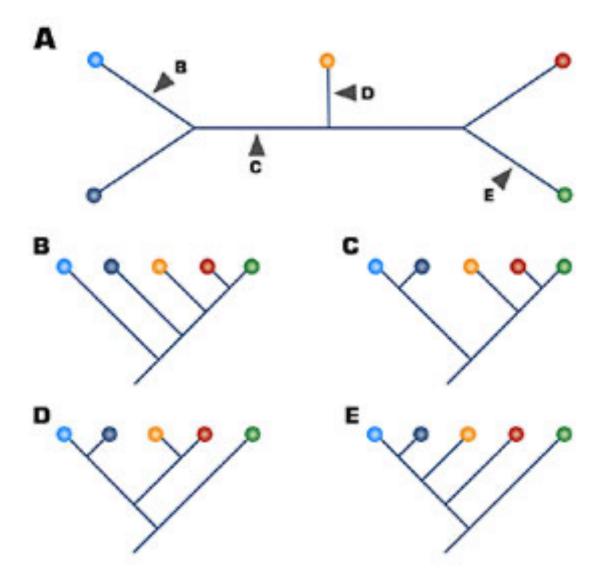
## **UNROOTED TREES**











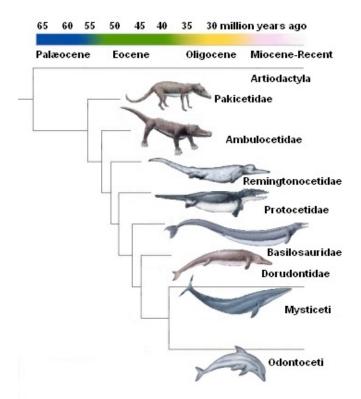
How do you decide how to root a phylogeny?

#### 1. Use an outgroup:

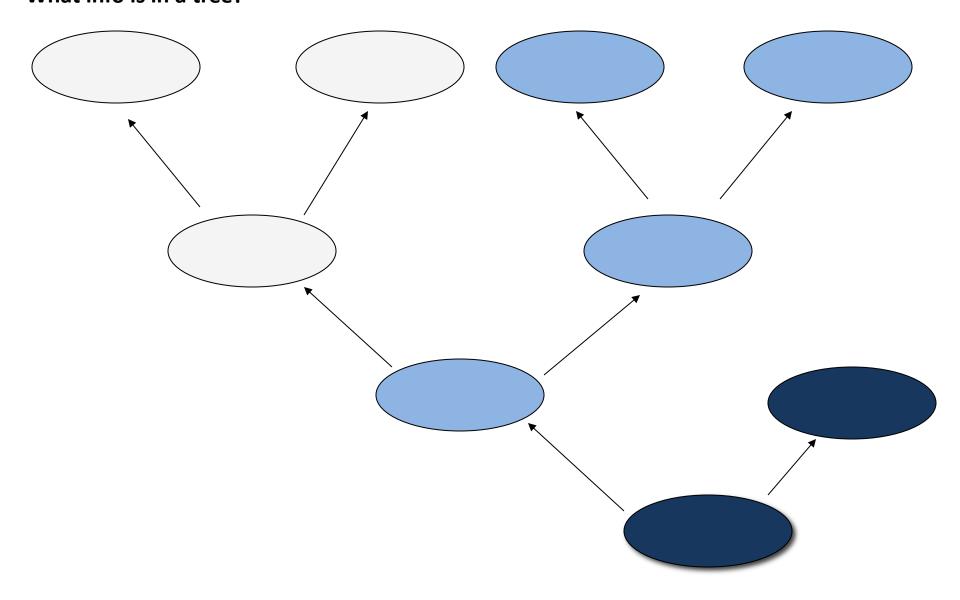
- a. The best outgroup is a taxon that is a close relative that you are pretty sure is not in the ingroup.
- b. The more outgroups the better.
- c. The branch of the outgroup becomes the root.

#### 2. Character polarity

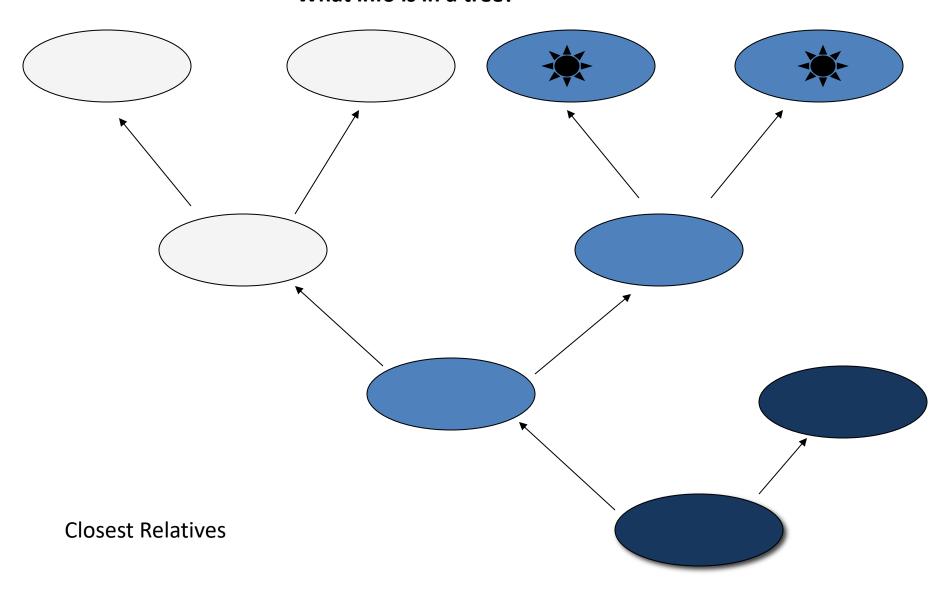
- a. Polarity is the direction of evolutionary change (ie., forelimb evolves into wing)
- b. Make sure that the topology has all of the assumed polarities going in the right direction.



# What info is in a tree?

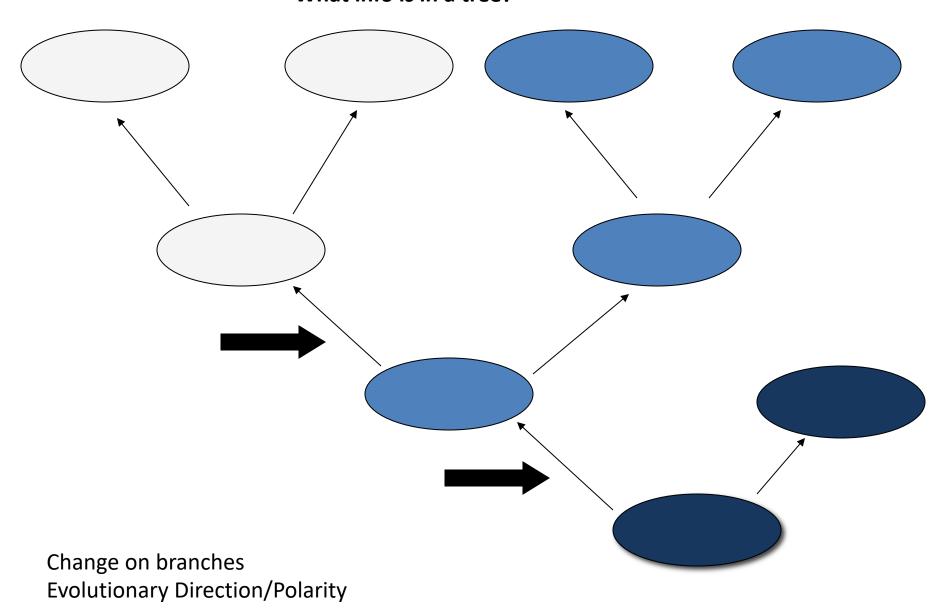


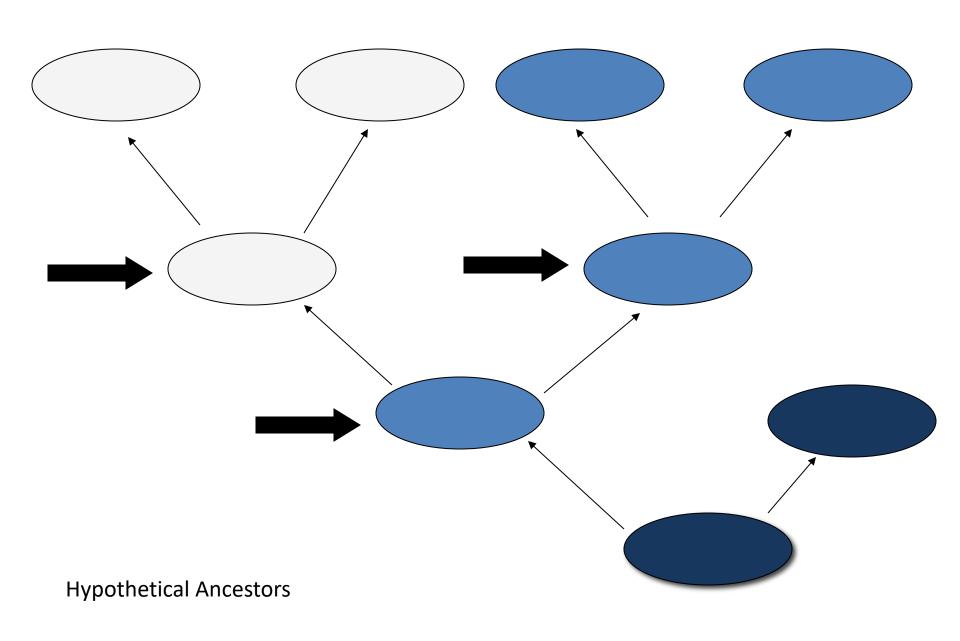
## What info is in a tree?



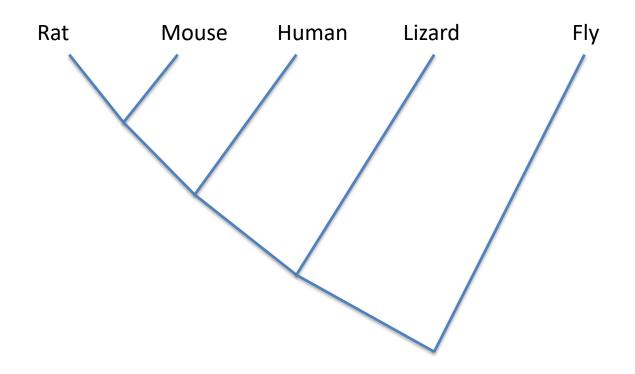
# What info is in a tree? Closest Relatives/Biogeography

### What info is in a tree?

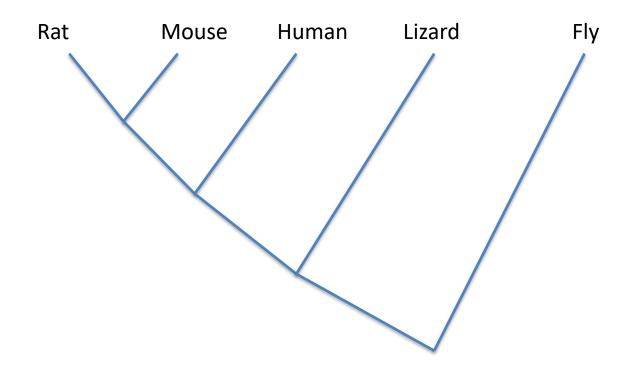




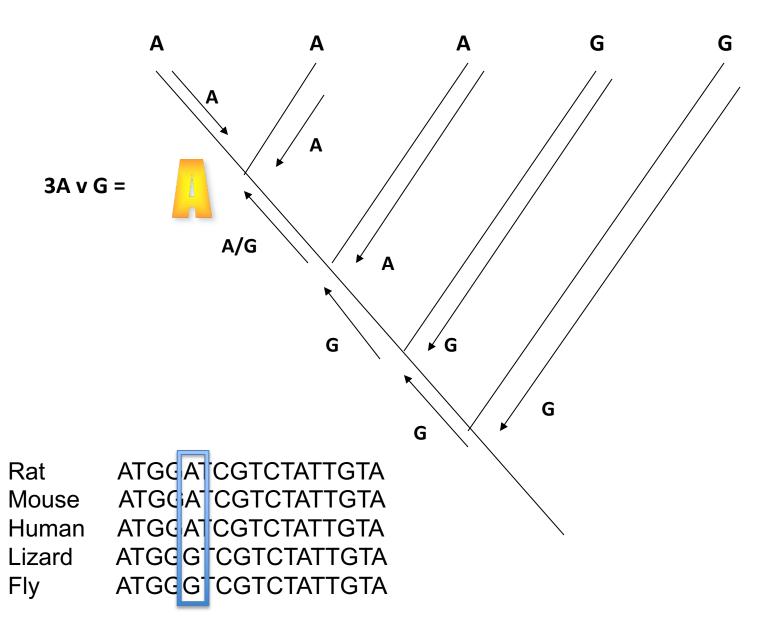
Rat ATGGATCGTCTATTGTA
Mouse ATGGATCGTCTATTGTA
Human ATGGATCGTCTATTGTA
Lizard ATGGGTCGTCTATTGTA
Fly ATGGGTCGTCTATTGTA



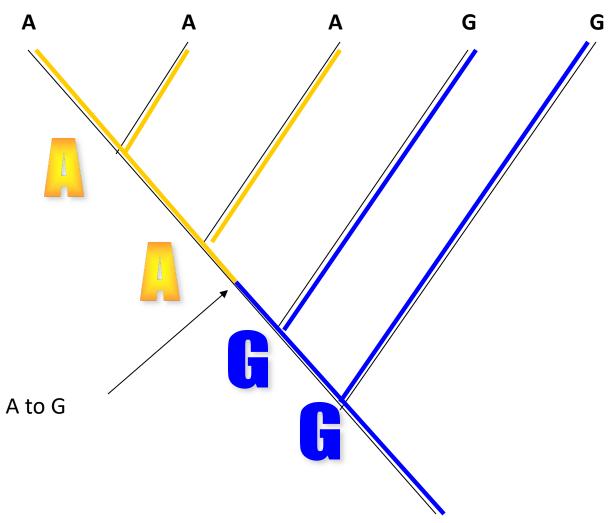
Rat ATGC AT CGTCTATTGTA
Mouse ATGC AT CGTCTATTGTA
Human ATGC AT CGTCTATTGTA
Lizard ATGC GTCTATTGTA
Fly ATGC GTCTATTGTA



#### **FITCH OPTIMIZATION**



#### **FITCH OPTIMIZATION**



Disclaimer: There are other more complicated statistical methods for this using maximum likelihood and Bayesian analysis but I did not think it was necessary to make you integrate!

How to make a tree from scratch starting with this sequence:

Human ACTCCAATGATAAATTTATAGTGGTGGAGCGCAATAAGAAATCACTGACAACTTCAC

# **Find Homologs and Align**

Human	ACTCCAATGATAAATTTATAGTGGTGGAGCGCAATAAGAAATCACTGACAACTTCAC
Chimp	ATTCAAATGGTAAATTTGTAGTAGTGGAACGCGAGAAAAAATCACTTACAACGTCAC
Chimp2	AAATCATTTCTGAGACATTATGGGATAATGGGTTTGGTAAAACAATTCATGCACAGG
Gorilla	ATTCAAATGGTAAATTTGTAGTAGTGGAACGCGAGAAAAAATCACTTACAACTTCAC
Gorilla2	AAATCATTTCTGAGACATTATGGGATAATGGGTTTGGTAAAACAATTCATGCACAGG
Gibbon	AAACTCCAAATAAATATGTTGTAGTAAAACGAGAAAAGAAAAGTGTTTCAGATTCTA
	ATATTGAGGATAAATTCATTGTTGTAGAACGTACAAAAAAAA
Human2	AAAATCCAGATAAATATATAGTAATAAAGCGTGAAAAGAAAAGCATATCAGATTCAA
Lucy	AGACTGGTAATAAATTTATAGTTGTAGAACGTCAAAAAAGATCCCTTACAACATCAC
Macaca	AAAATCCAGATAAGTTCATTGTGGTAAAACGTGAGAAGAAGAGTATTTCAGATTCCA

# **Find Homologs and Align**

Human	ACTCCAATGATAAATTTATAGTGGTGGAGCGCAATAAGAAATCACTGACAACTTCAC
Chimp	ATTCAAATGGTAAATTTGTAGTAGTGGAACGCGAGAAAAAATCACTTACAACGTCAC
Chimp2	AAATCATTTCTGAGACATTATGGGATAATGGGTTTGGTAAAACAATTCATGCACAGG
Gorilla	ATTCAAATGGTAAATTTGTAGTAGTGGAACGCGAGAAAAAATCACTTACAACTTCAC
Gorilla2	AAATCATTTCTGAGACATTATGGGATAATGGGTTTGGTAAAACAATTCATGCACAGG
Gibbon	AAACTCCAAATAAATATGTTGTAGTAAAACGAGAAAAGAAAAGTGTTTCAGATTCTA
Siamang	ATATTGAGGATAAATTCATTGTTGTAGAACGTACAAAAAAAA
Human2	AAAATCCAGATAAATATATAGTAATAAAGCGTGAAAAGAAAAGCATATCAGATTCAA
Lucy	AGACTGGTAATAAATTTATAGTTGTAGAACGTCAAAAAAGATCCCTTACAACATCAC
Macaca	AAAATCCAGATAAGTTCATTGTGGTAAAACGTGAGAAGAAGAGTATTTCAGATTCCA

#### **Align Homologs**



Find the best tree: that optimizes "some function"



Find the best tree: that optimizes "some function"

How many trees do I need to look through?

FOR UNROOTED TREES: (2n-5)!/[2n-3(n-3)!]

FOR UNROOTED TREES: (2n-3)!/[2n-2(n-2)!]

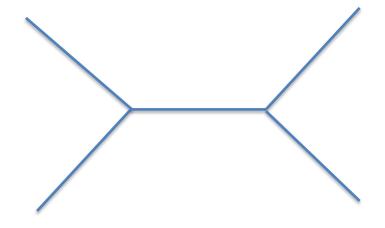
# How tree building actually works.

A AAAAT

B AATTA

C TTTTA

D AATAT



#### Number of Taxa Number of Rooted Trees

- 3 3
- 4 15
- 5 105
- 6 945
- 7 10395
- 8 135135
- 9 2027025
- 10 34459425
- 11 654729075
- 12 13749310575
- 13 316234143225
- 14 7905853580625
- 15 213458046676875
- 16 6190283353629375
- 17 191898783962510625
- 18 6332659870762850625
- 19 221643095476699771875
- 20 8200794532637891559375
- 21 319830986772877770815625
- 22 13113070457687988603440625
- 23 563862029680583509947946875
- 24 25373791335626257947657609375
- 25 1192568192774434123539907640625

Human
Chimp
ACTCCAATGATAAATTTATAGTGGTGGAGCGCAATAAGAAATCACTGACAACTTCAC
Chimp
Gorilla
Orang
AATCAATTGTAAATTTGTAGTAGTGGAACGCGAGAAAAAATCACTTACAACGTCAC
ATTCAAATGGTAAATTTGTAGTAGTGGAACGCGAGAAAAAATCACTTACAACTTCAC
AAATCATTTCTGAGACATTATGGGATAATGGGTTTGGTAAAACAATTCATGCACAGG

# **4 taxa = 15 trees** These trees have a simple "bifurcating" topology. These trees have a "double-branching" topology.

# Deciding which tree to pick: Optimality Criteria

- Maximum Parsimony (what is the simplest explanation that accounts for all the data)
- Maximum Likelihood (what is the highest likelihood of observing the data given a tree)
- Bayesian (what is the highest probability that the tree is correct given the data)
- Distance/Similarity (minimize the distance or group the most similar things together)

# **Tree-Building Methods**



No explicit model of sequence evolution



Application of the parsimony principle



Explicit model of sequence evolution

pairwise comparison of sequences

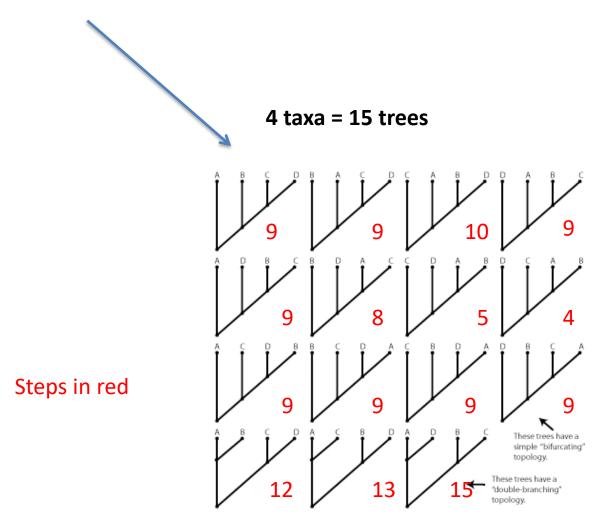
Statistical approach



maximum likelihood and bayesian

A. Human
B. Chimp
C. Gorilla
ACTCCAATGATAAATTTATAGTGGTGGAGCGCAATAAGAAATCACTGACAACTTCAC
ATTCAAATGGTAAATTTGTAGTAGTGGAACGCGAGAAAAAATCACTTACAACGTCAC
ATTCAAATGGTAAATTTGTAGTAGTGGAACGCGAGAAAAAATCACTTACAACTTCAC

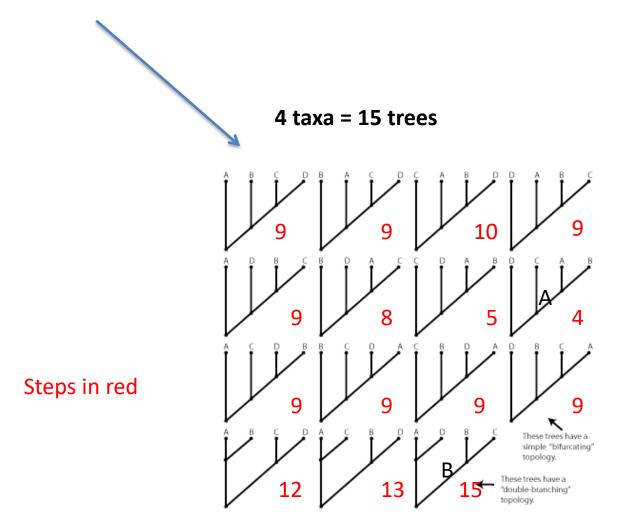
D. Orang AAATCATTTCTGAGACATTATGGGATAATGGGTTTGGTAAAACAATTCATGCACAGG



A. Human ACTCCAATGATAAATTTATAGTGGTGGAGCGCAATAAGAAATCACTGACAACTTCAC B. Chimp ATTCAAATGGTAAATTTGTAGTAGTGGAACGCGAGAAAAAATCACTTACAACGTCAC

C. Gorilla ATTCAAATGGTAAATTTGTAGTAGTGGAACGCGAGAAAAAATCACTTACAACTTCAC

D. Orang AAATCATTTCTGAGACATTATGGGATAATGGGTTTGGTAAAACAATTCATGCACAGG

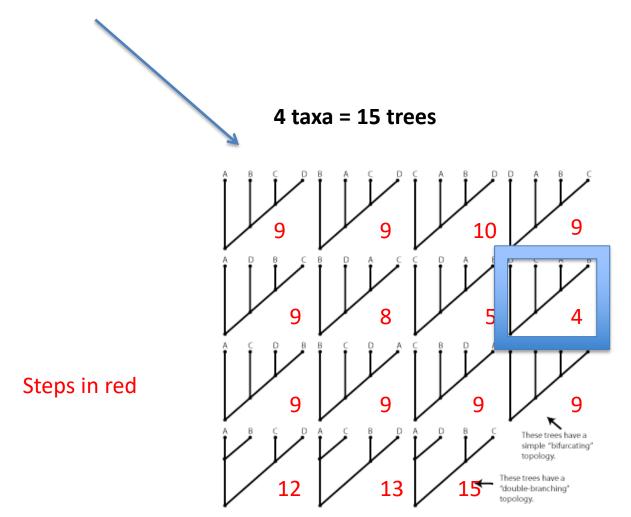


ACTCCAATGATAAATTTATAGTGGTGGAGCGCAATAAGAAATCACTGACAACTTCAC A. Human

ATTCAAATGGTAAATTTGTAGTAGTGGAACGCGAGAAAAAATCACTTACAACGTCAC B. Chimp

ATTCAAATGGTAAATTTGTAGTAGTGGAACGCGAGAAAAAATCACTTACAACTTCAC C. Gorilla

AAATCATTTCTGAGACATTATGGGATAATGGGTTTGGTAAAACAATTCATGCACAGG D. Orang

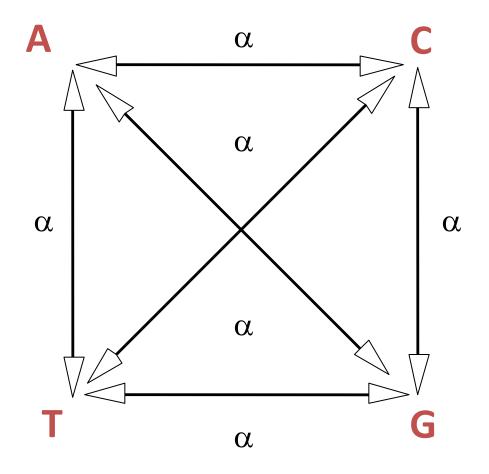


# **Estimating Genetic Distance**

SIVcpz	ATGGGTGCGA	GAGCGTCAGT	TCTAACAGGG	GGAAAATTAG	ATCGCTGGGA
HIV-1	ATGGGTGCGA	GAGCGTCAGT	ATTAAGCGGG	GGAGAATTAG	ATCGATGGGA
SIVcpz	AAAAGTTCGG	CTTAGGCCCG	GGGGAAGAAA	AAGATATATG	ATGAAACATT
HIV-1	AAAAATTCGG	TTAAGGCCAG	GGGGAAAGAA	AAAATATAAA	TTAAAACATA
SIVcpz	TAGTATGGGC	AAGCAGGGAG	CTGGAAAGAT	TCGCATGTGA	CCCCGGGCTA
HIV-1	TAGTATGGGC	AAGCAGGGAG	CTAGAACGAT	TCGCAGTTAA	TCCTGGCCTG
SIVcpz	ATGGAAAGTA	AGGAAGGATG	TACTAAATTG	TTACAACAAT	TAGAGCCAGC
HIV-1	TTAGAAACAT	CAGAAGGCTG	TAGACAAATA	CTGGGACAGC	TACAACCATC
SIVcpz	TCTCAAAACA	GGCTCAGAAG	GACTGCGGTC	CTTGTTTAAC	ACTCTGGCAG
HIV-1	CCTTCAGACA	GGATCAGAAG	AACTTAGATC	ATTATATAAT	ACAGTAGCAA
SIVcpz			GACATCACTG		
HIV-1	CCCTCTATTG	TGTGCATCAA	AGGATAGAGA	TAAAAGACAC	CAAGGAAGCT
SIVcpz	CTAGAACAGC	TAAAGCGGCA	TCATGGAGAA	CAACAGAGCA	AAACTGAAAG
HIV-1	TTAGACAAGA	TAGAGGAA	GAGCA	AAACAAAAGT	AAGAAAA
SIVcpz	TAACTCAGGA	AGCCGTGAAG	GGGGAGCCAG	TCAAGGCGCT	AGTGCCTCTG
HIV-1	AAGCACAGCA	AGCAG	CAGCTGACA-	-CAGGACAC-	AGCAGC
SIVcpz	CTGGCATTAG	TGGAAATTAC			
HIV-1	CAGGTCAG	CCAAAATTAC			

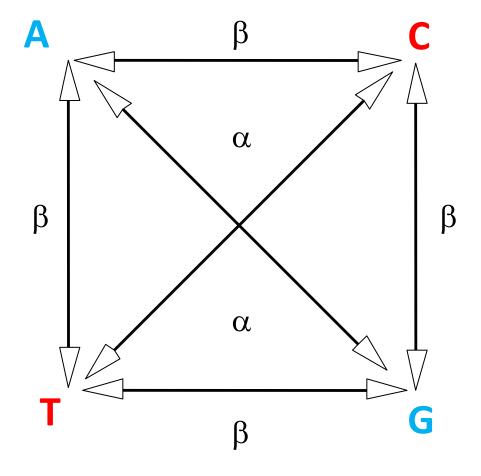
# **Models of DNA Substitution**

- Models of DNA sequence evolution are required to recover the missing information through correcting for multiple substitutions.
- i. The probability of substitution between bases (e.g. A to C, C to T...)
- ii. The probability of substitution along a sequence (different sites/regions evolve at different rates)



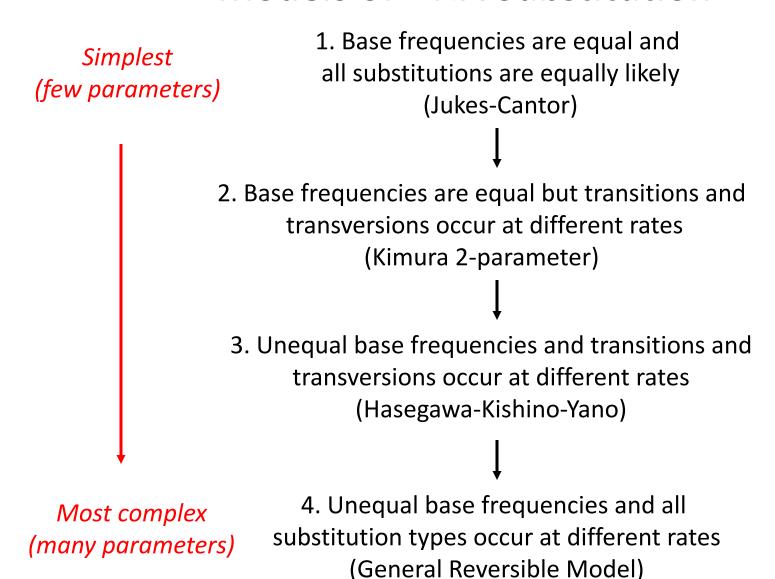
All substitutions occur at the same rate ( $\alpha$ )

Is this model too simple for real data?



Transitions ( $\alpha$ ) and transversions ( $\beta$ ) occur at a different rate

# **Models of DNA Substitution**

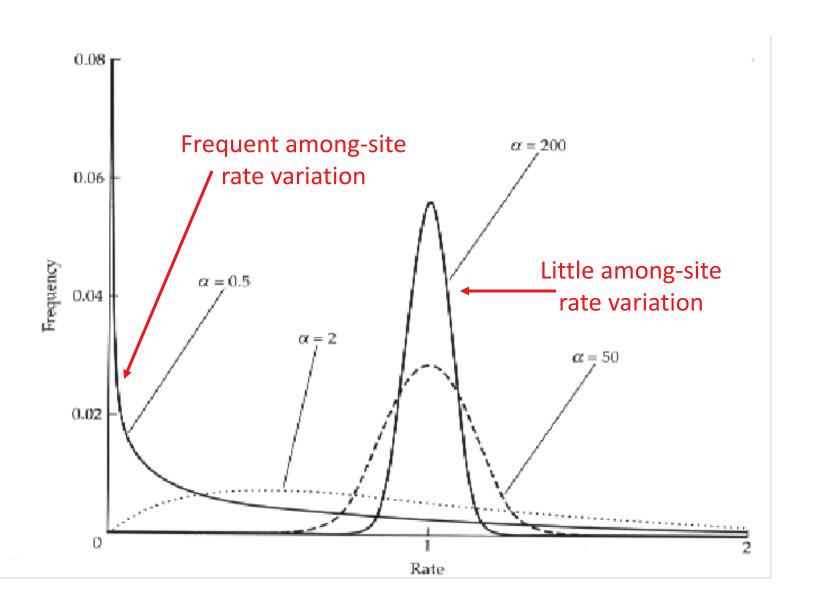


All these models can be tested using the program jMODELTEST (darwin.uvigo.es/software/jmodeltest.html)

# **Models of DNA Substitution**

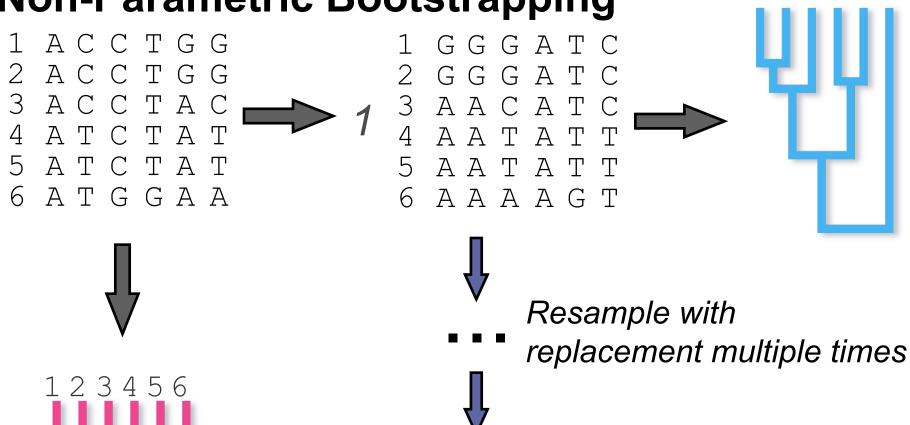
- i. The probability of substitution between bases (e.g. A to C, C to T...)
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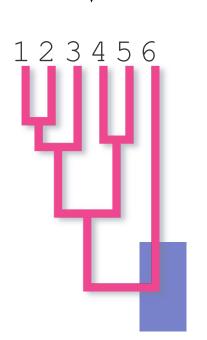
# A Gamma Distribution Can be Used to Model Among-Site Rate Heterogeneity



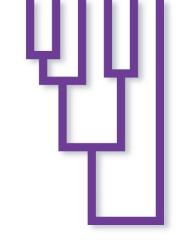
# Non-Parametric Bootstrapping

1000





1 T G C C A G
2 T G C C A G
3 T C C C A A
4 T T C C A A
5 T T C C A A
6 G A G G A A

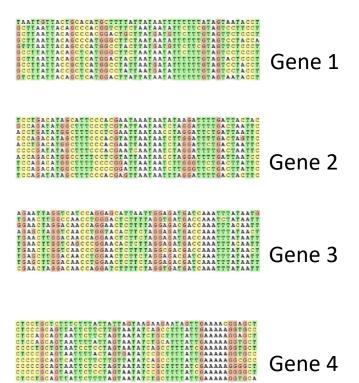


# LARGE-SCALE PHYLOGENETIC ANALYSIS

- 1. Genome Concatenation or Whole Genome alignments
- 2. SNP calling with reference to a matrix

## LARGE-SCALE STANDARD PHYLOGENETIC ANALYSIS

#### Concatenation



# LARGE-SCALE PHYLOGENETIC ANALYSIS

#### A CONCATENATED MATRIX

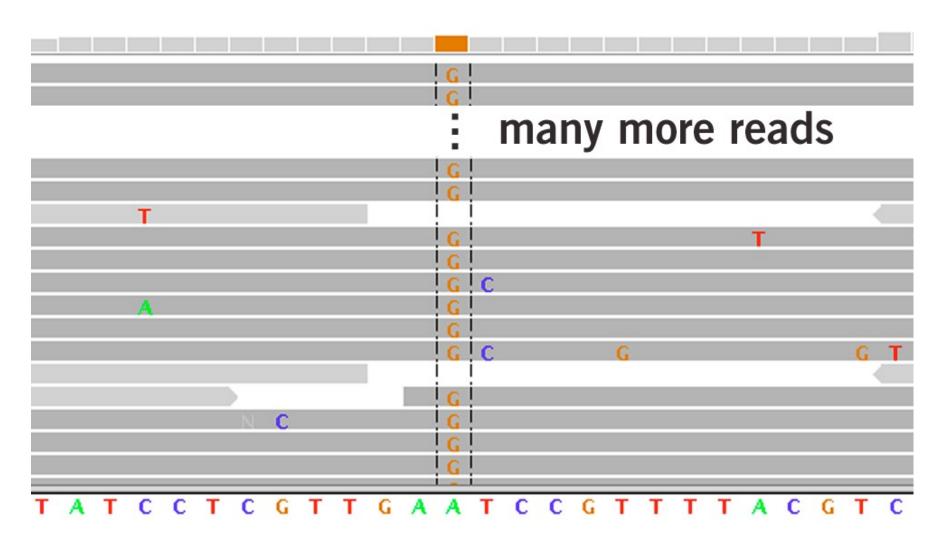
Final matrix has both variant and invariant positions.

Gene 1 Gene 2 Gene 3 ... Gene n

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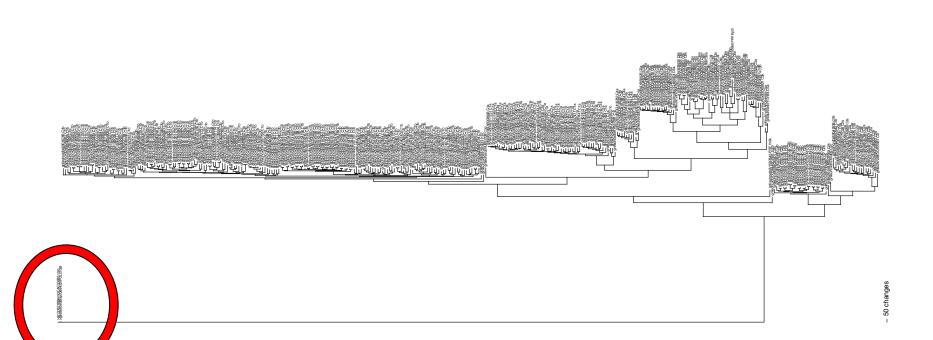
# LARGE-SCALE PHYLOGENETIC ANALYSIS (Reference Based)

SNP Calling (final matrix has only invariant positions=danger ascertainment bias)



# Things to think about when you look at a tree

- 1. How is it rooted?
- 2. What do the branch lengths mean?
- 3. Do the branch lengths make sense?



Tree scale: 0.0001 ⊢------

