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## Lecture 1.1

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# **Introduction to Molecular Phylogenetics**

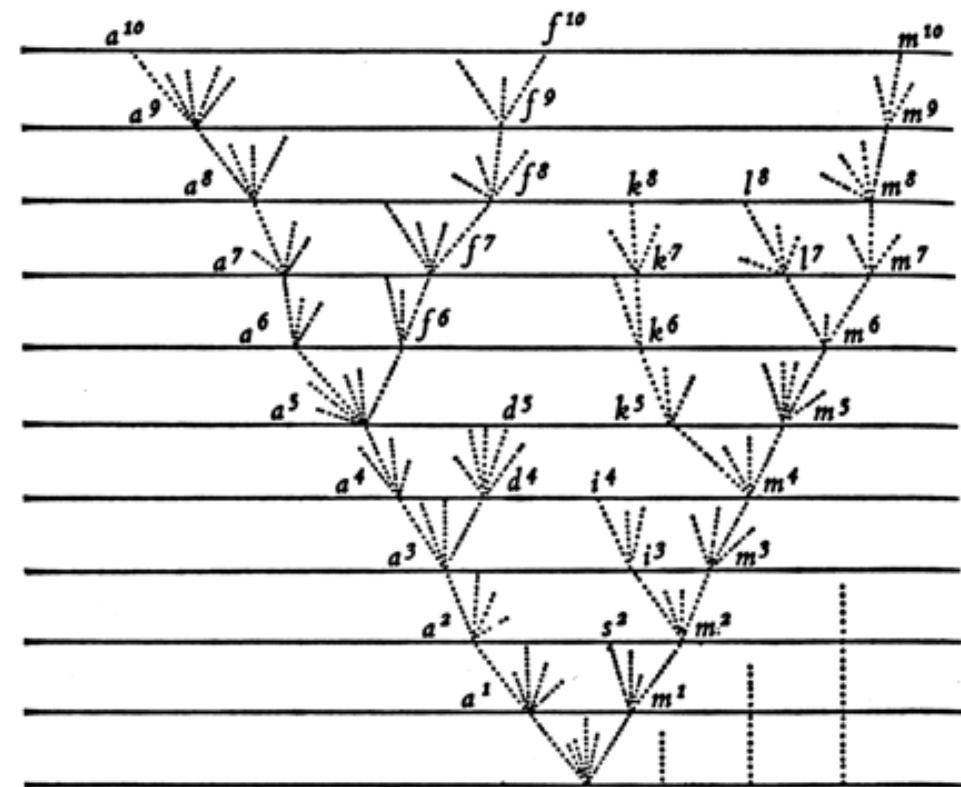
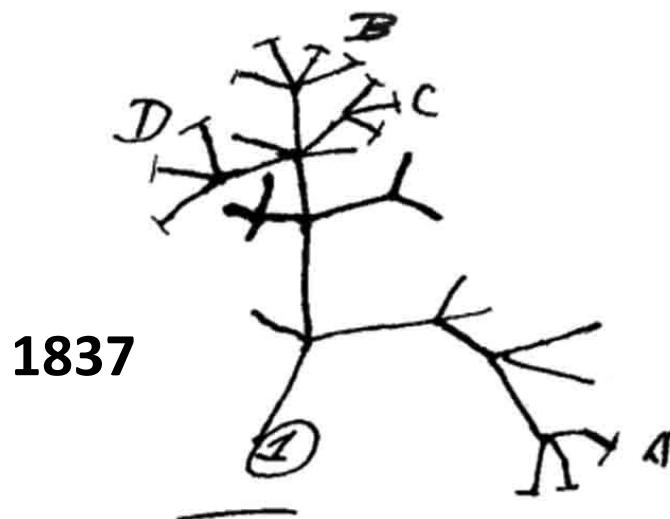
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# Phylogenetic Trees

# What is a phylogenetic tree?

**Phylogeny**  
evolutionary relationships  
among a set of organisms

I think

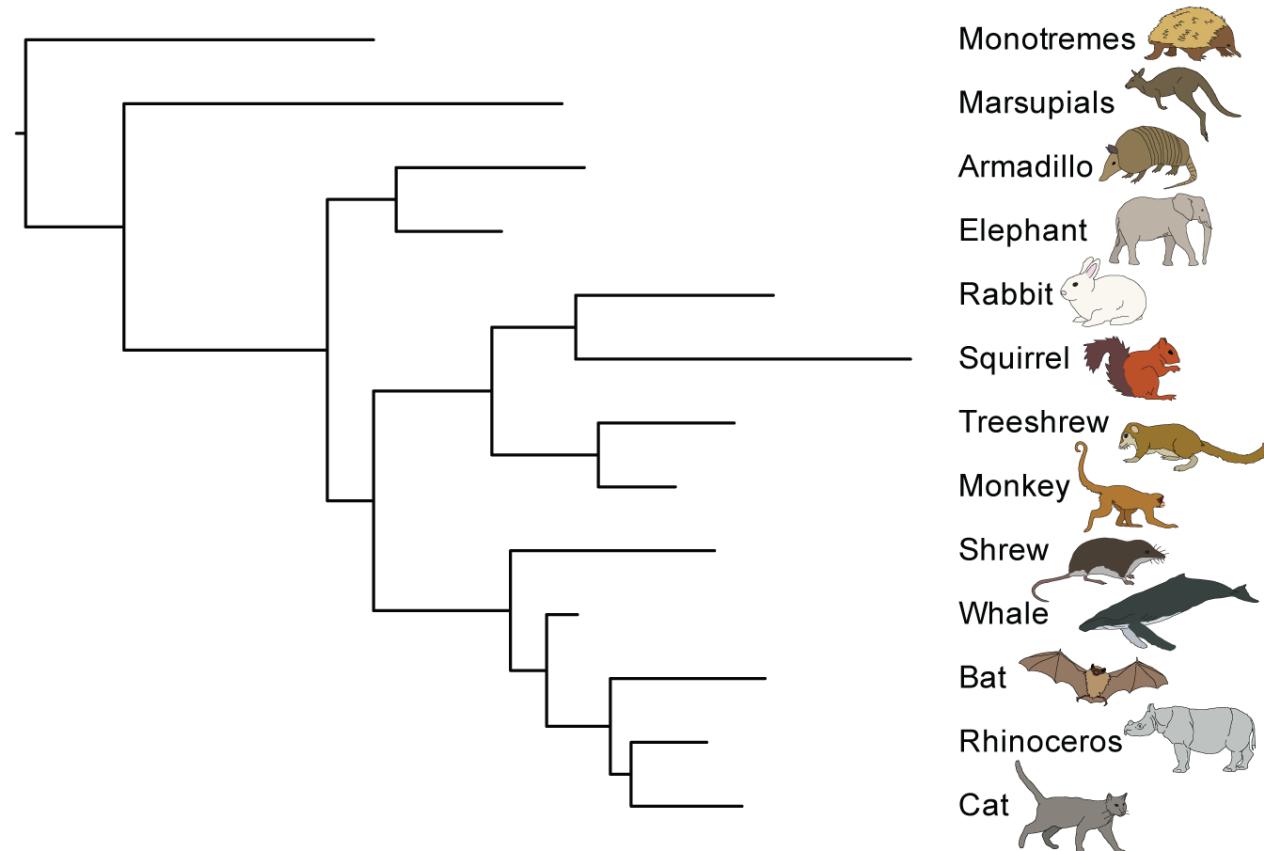


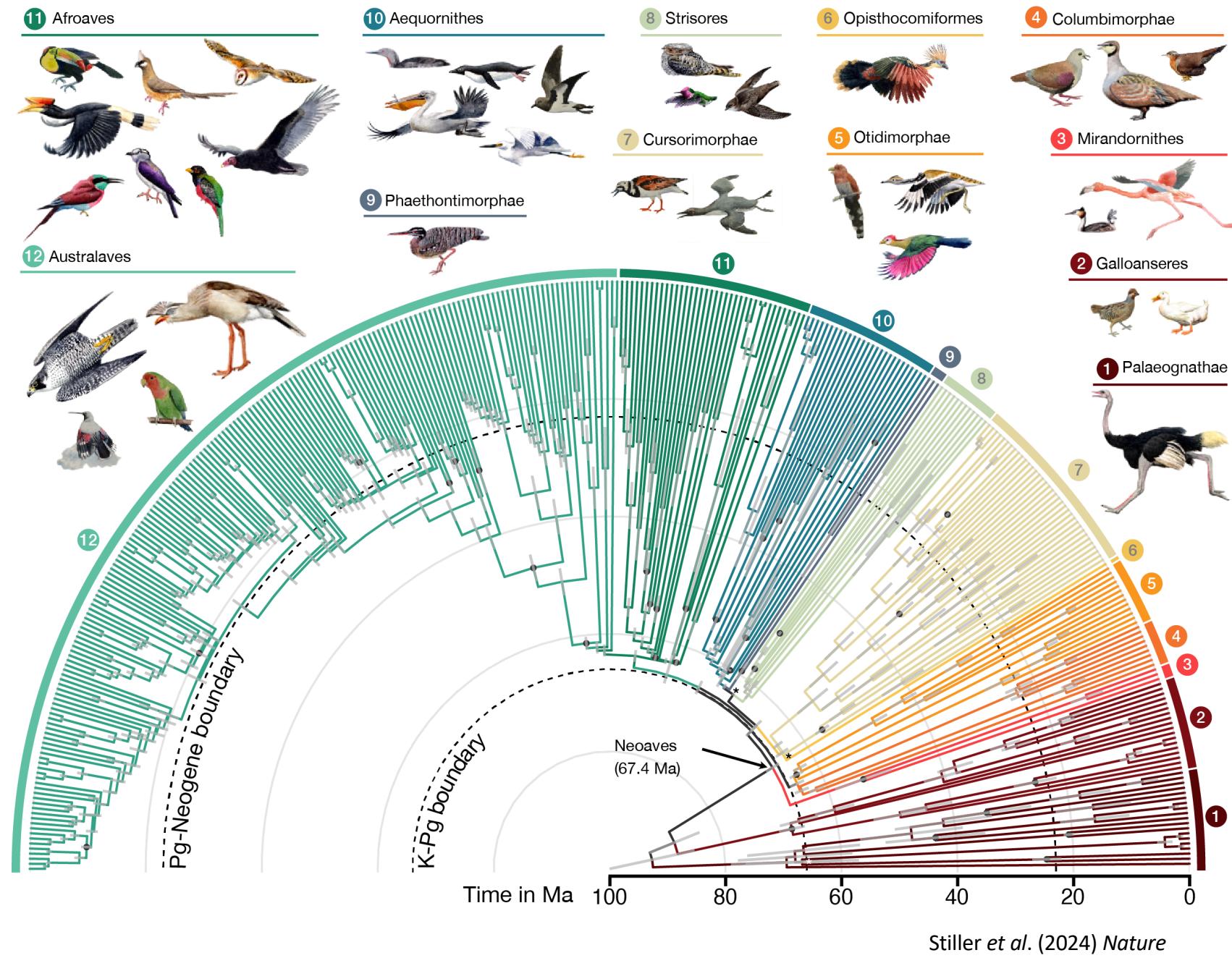
1859

# Phylogenetic trees

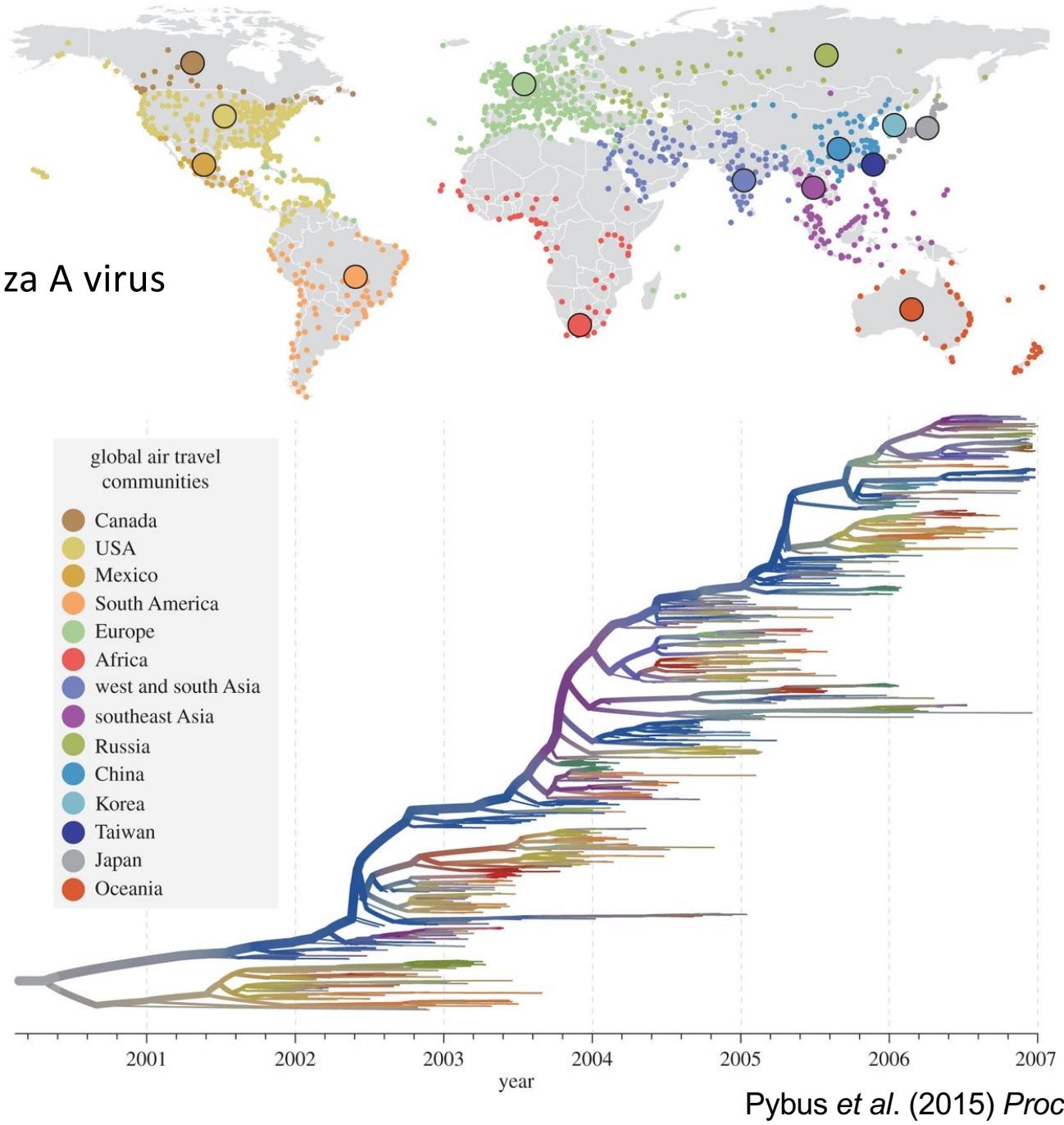
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- Topology (relationships)
- Branch lengths (amount of evolutionary change or time)





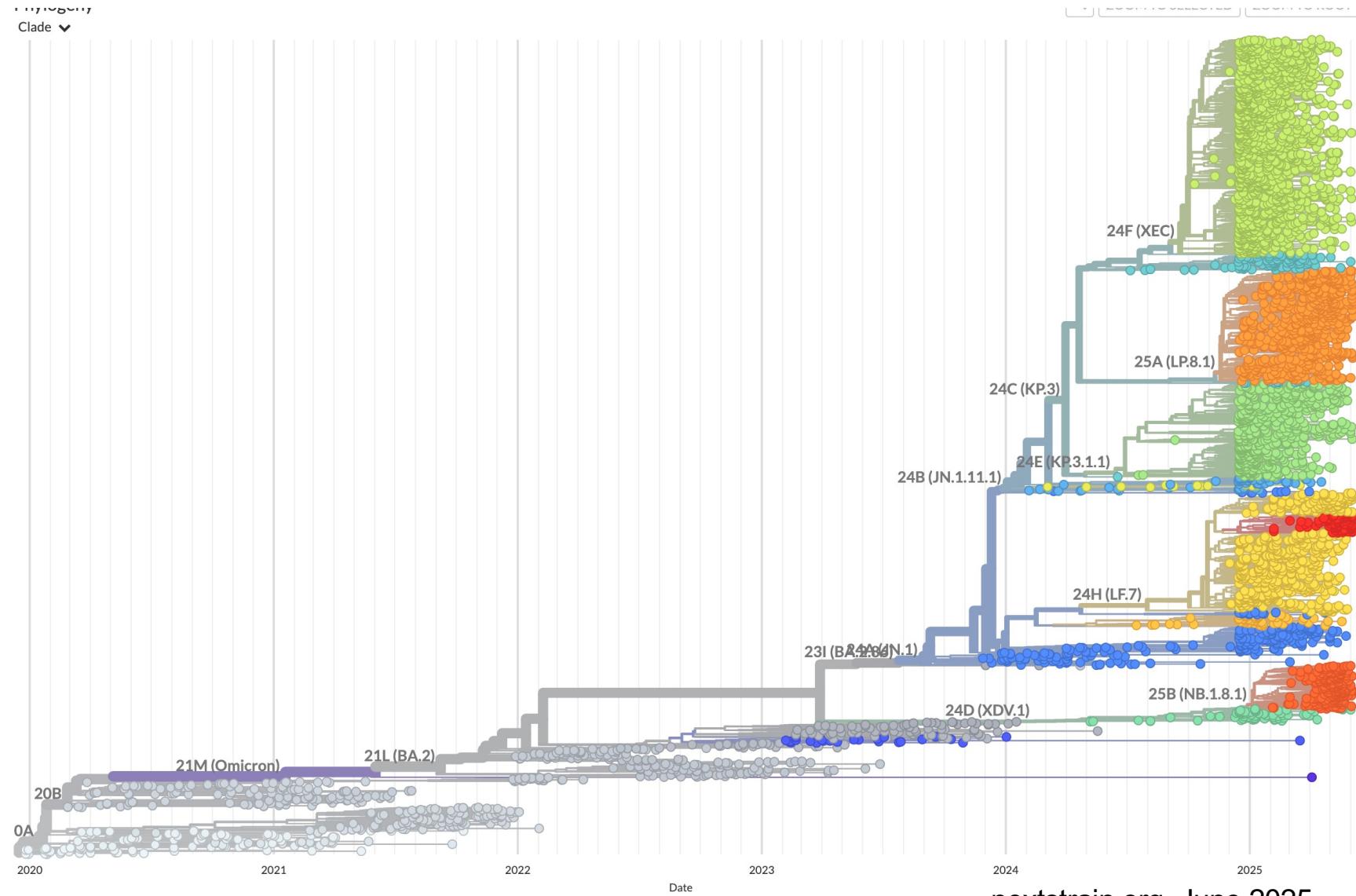
## Human influenza A virus Subtype H3N2



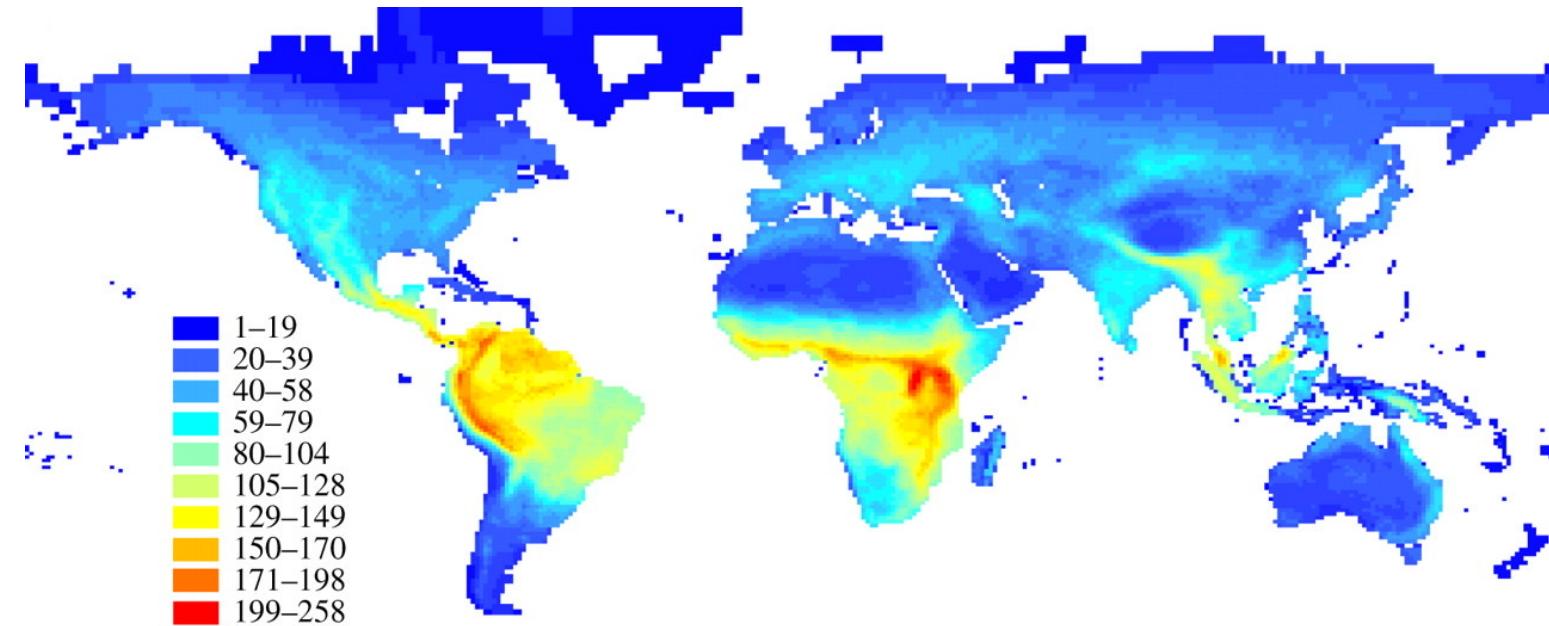
# Genomic epidemiology of SARS-CoV-2 with subsampling focused globally over the past 6 months



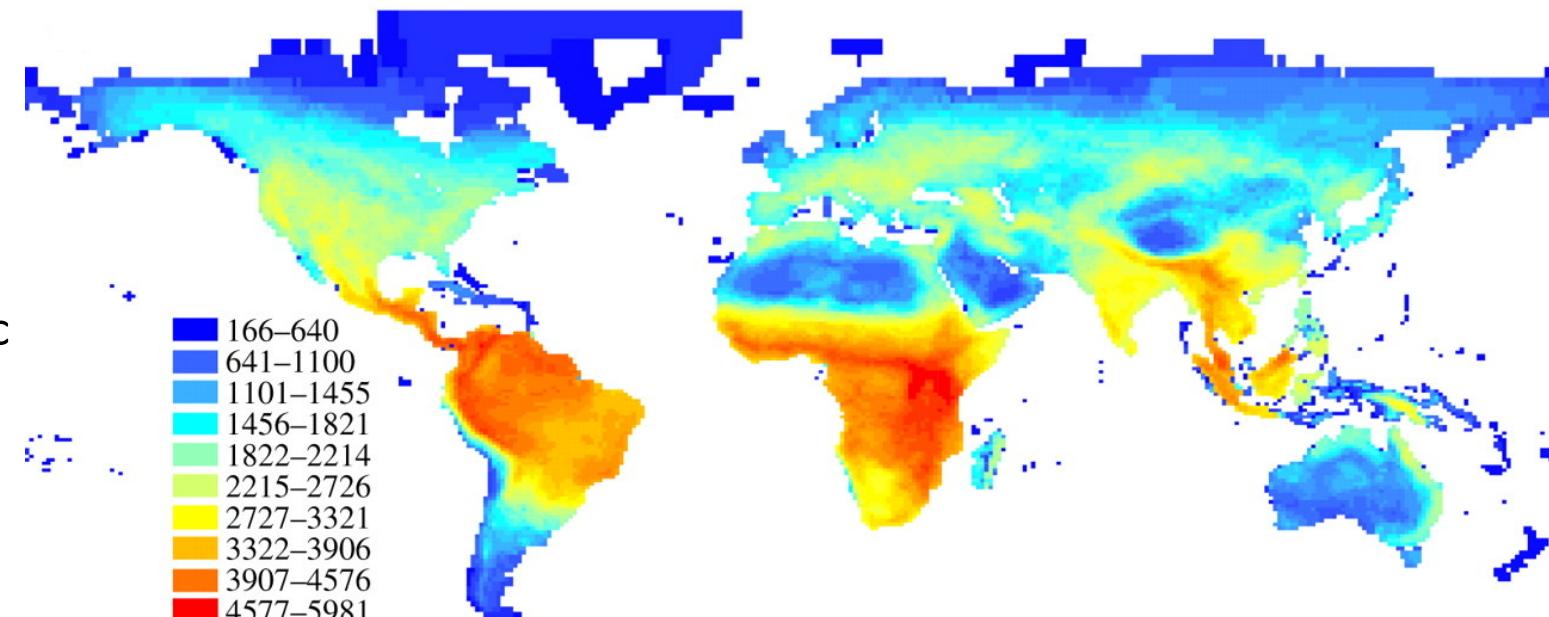
Built with [nextstrain/ncov](#). Maintained by [the Nextstrain team](#). Data updated 2025-06-15. Enabled by data from [GISAID](#).



Mammal  
species  
richness

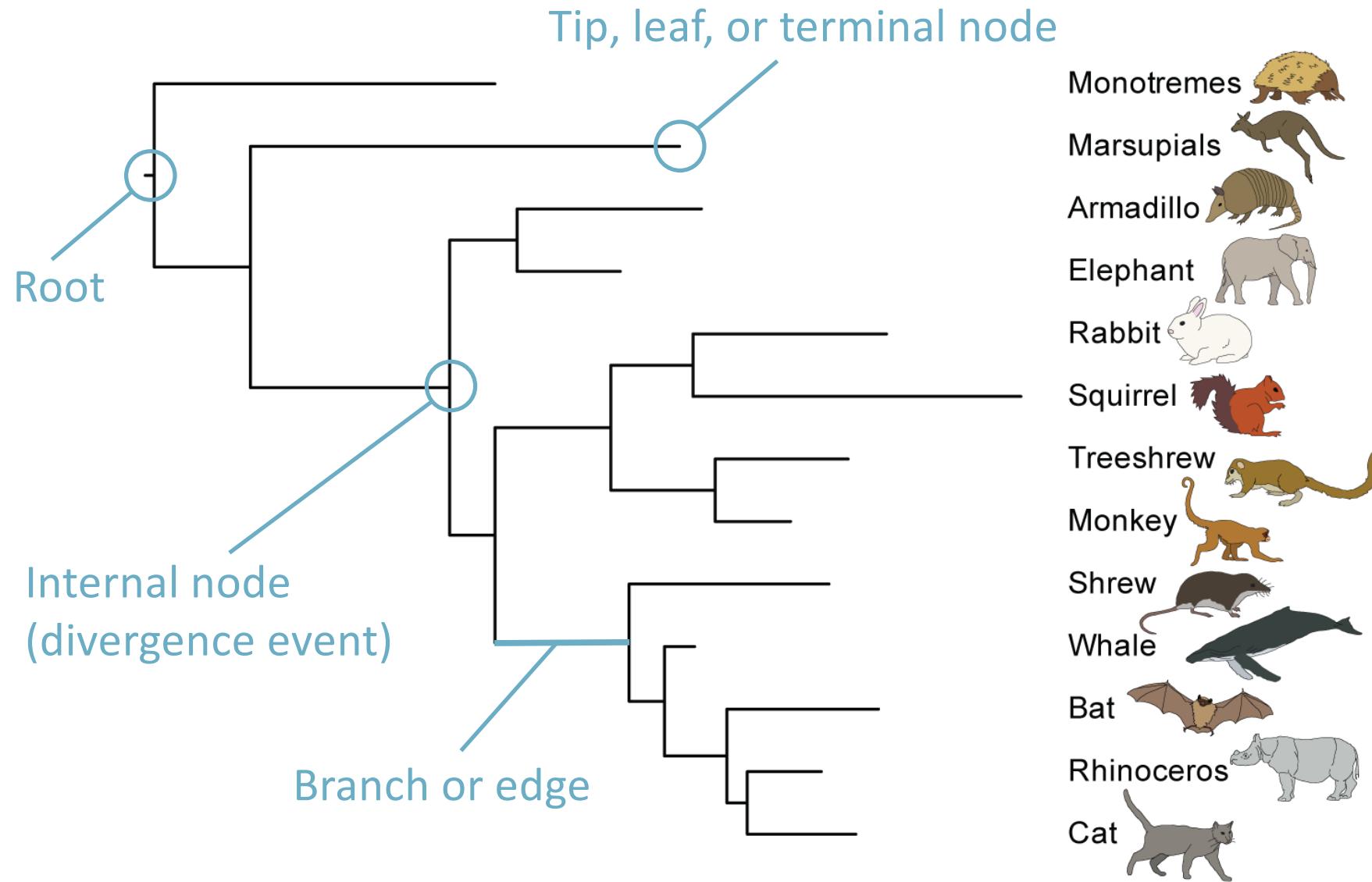


Mammal  
phylogenetic  
diversity

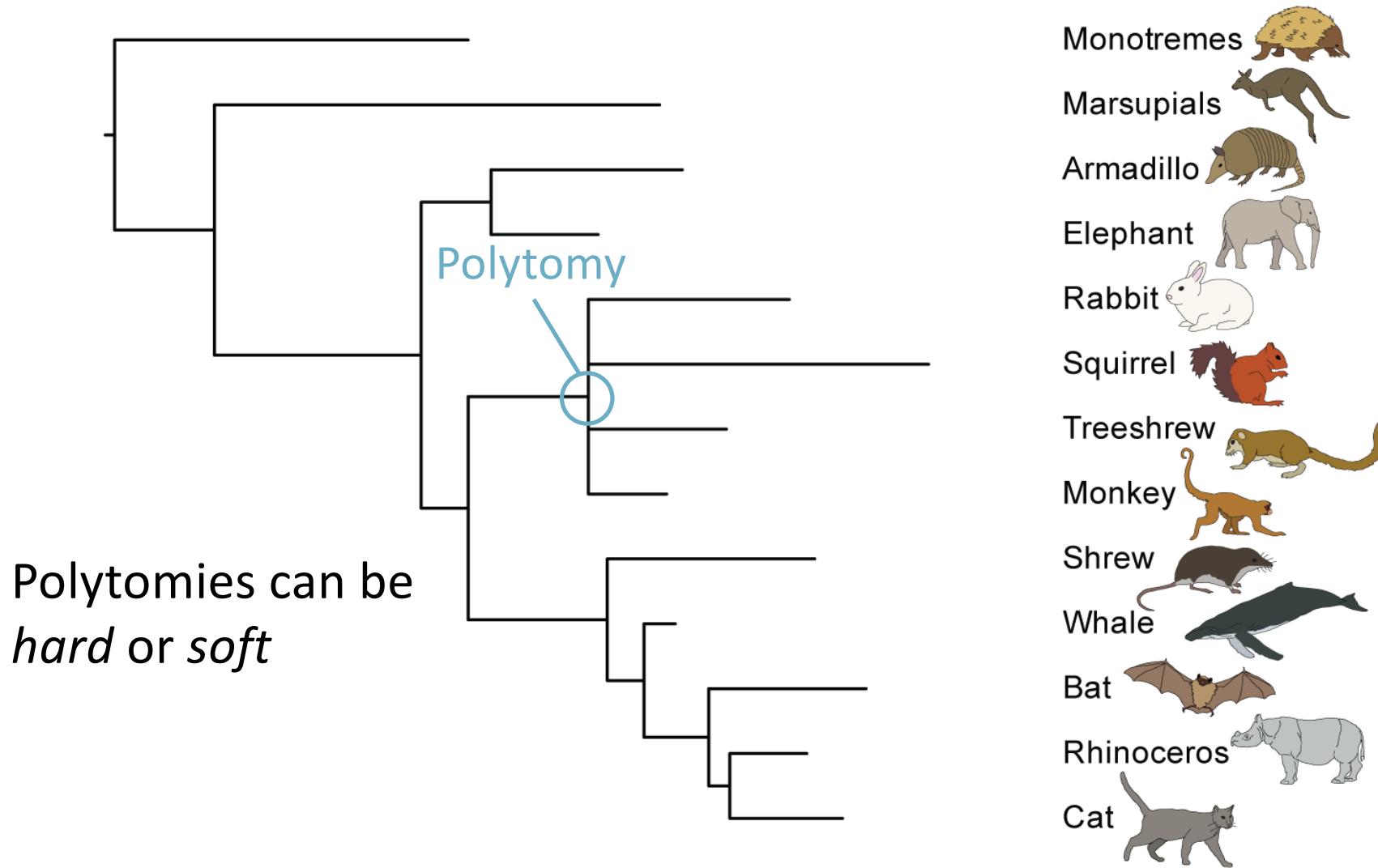


# Tree Thinking

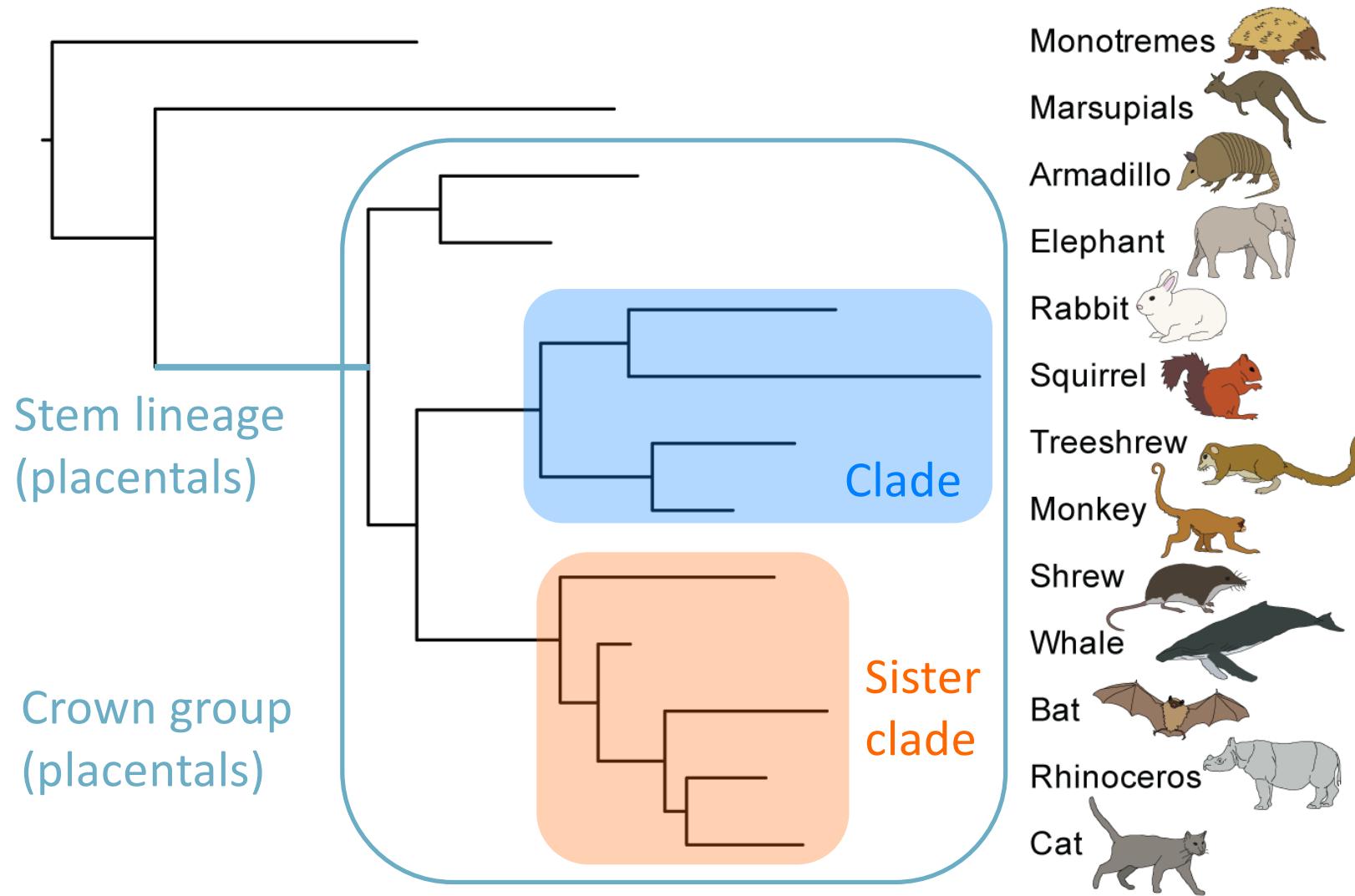
# Phylogenetic trees



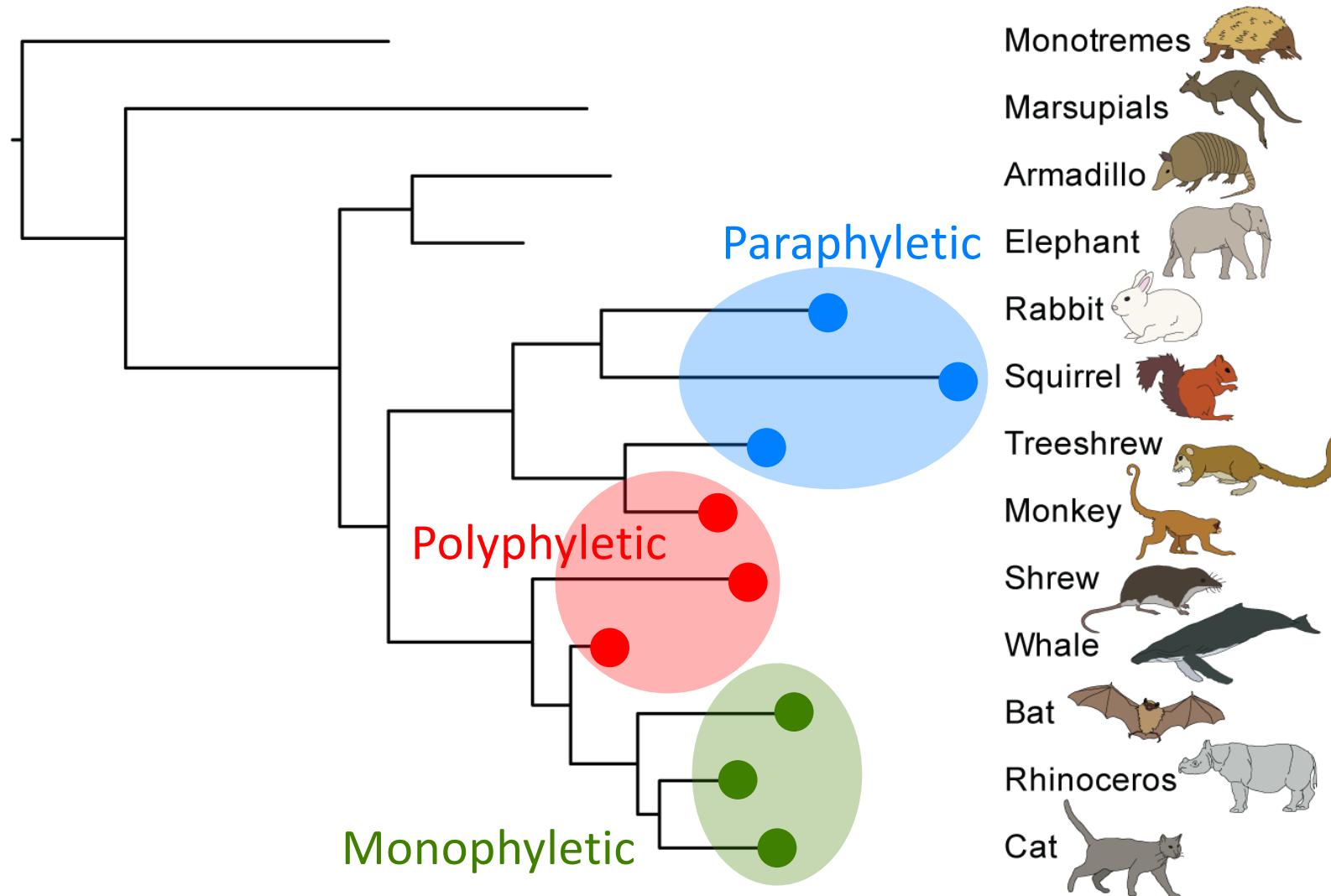
# Phylogenetic trees



# Phylogenetic trees

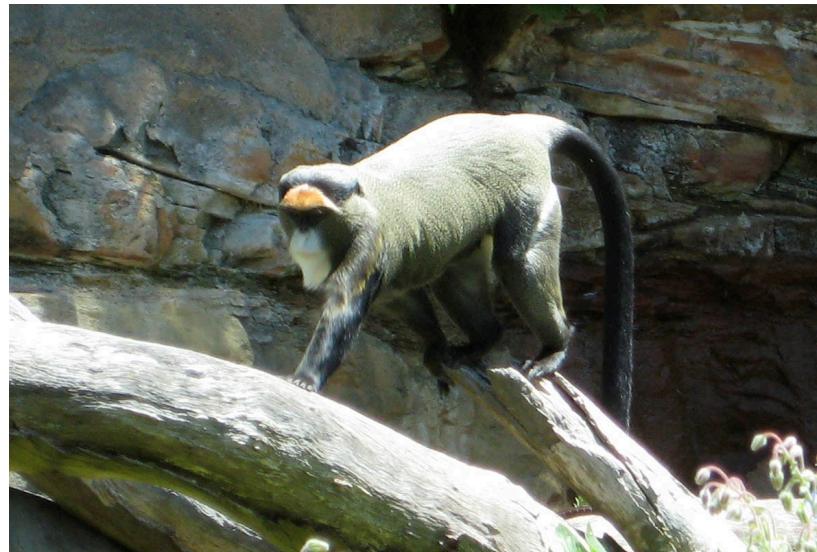


# Cladistic terms



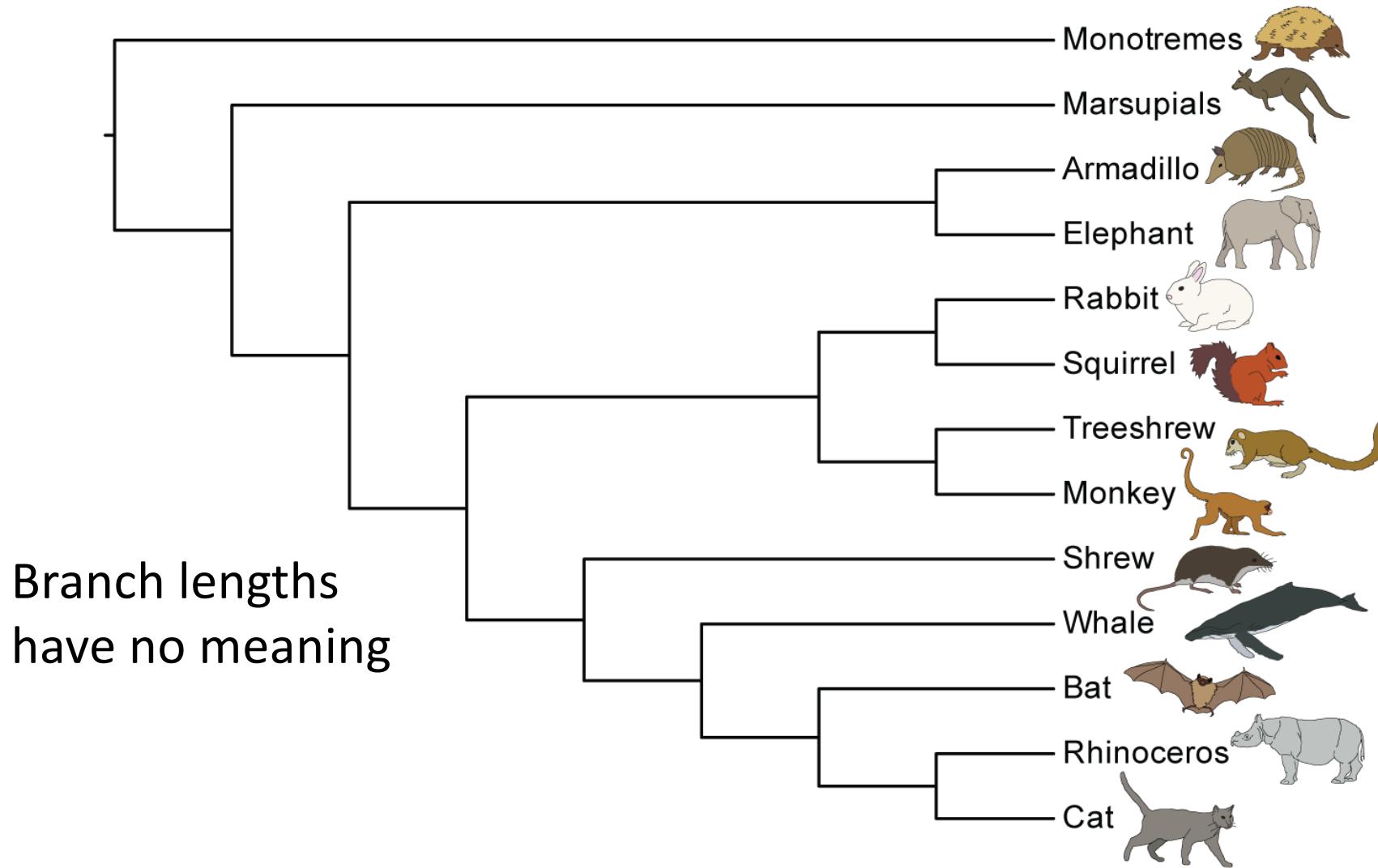
# Paraphyletic groups

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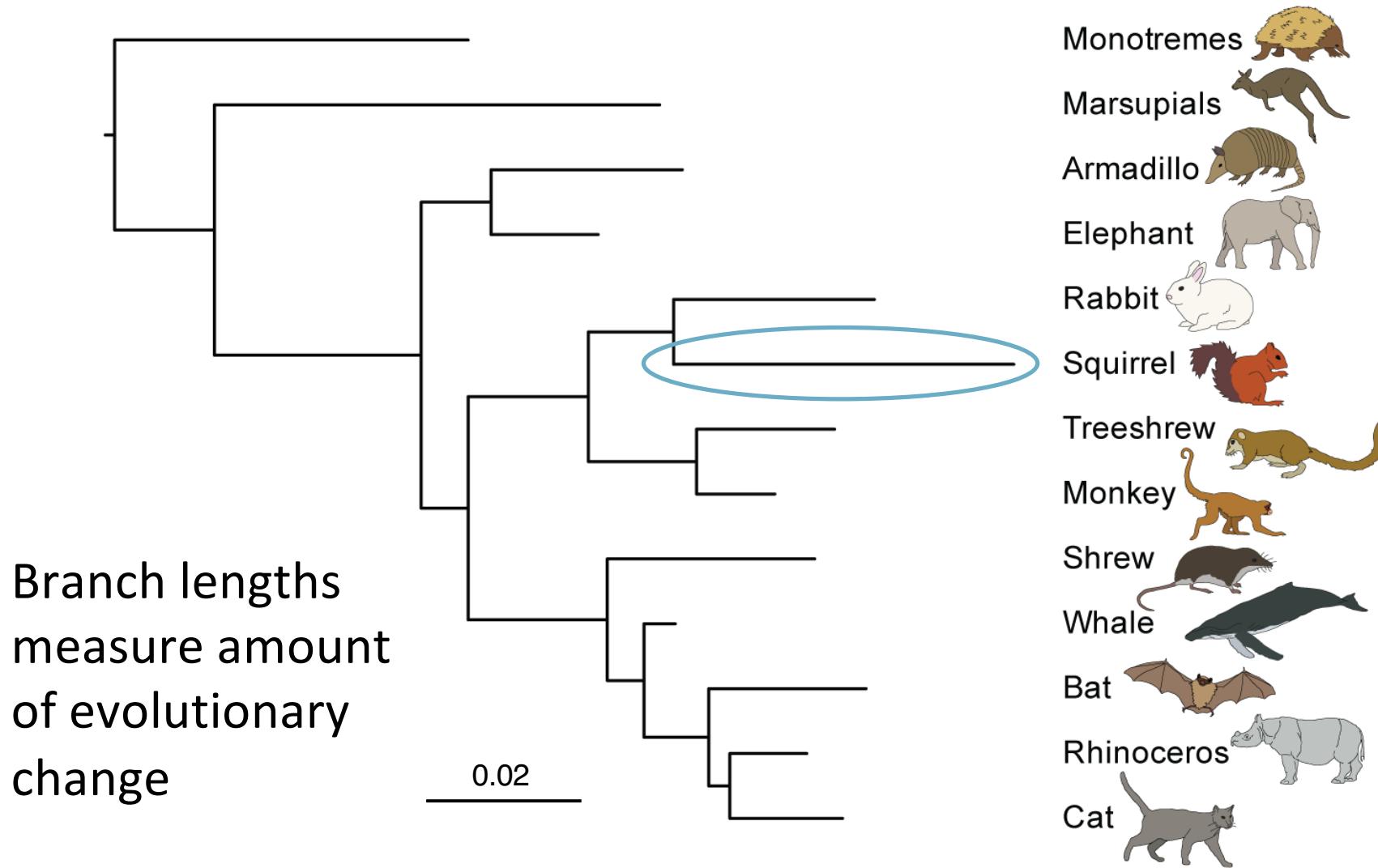


# Trees: Cladogram

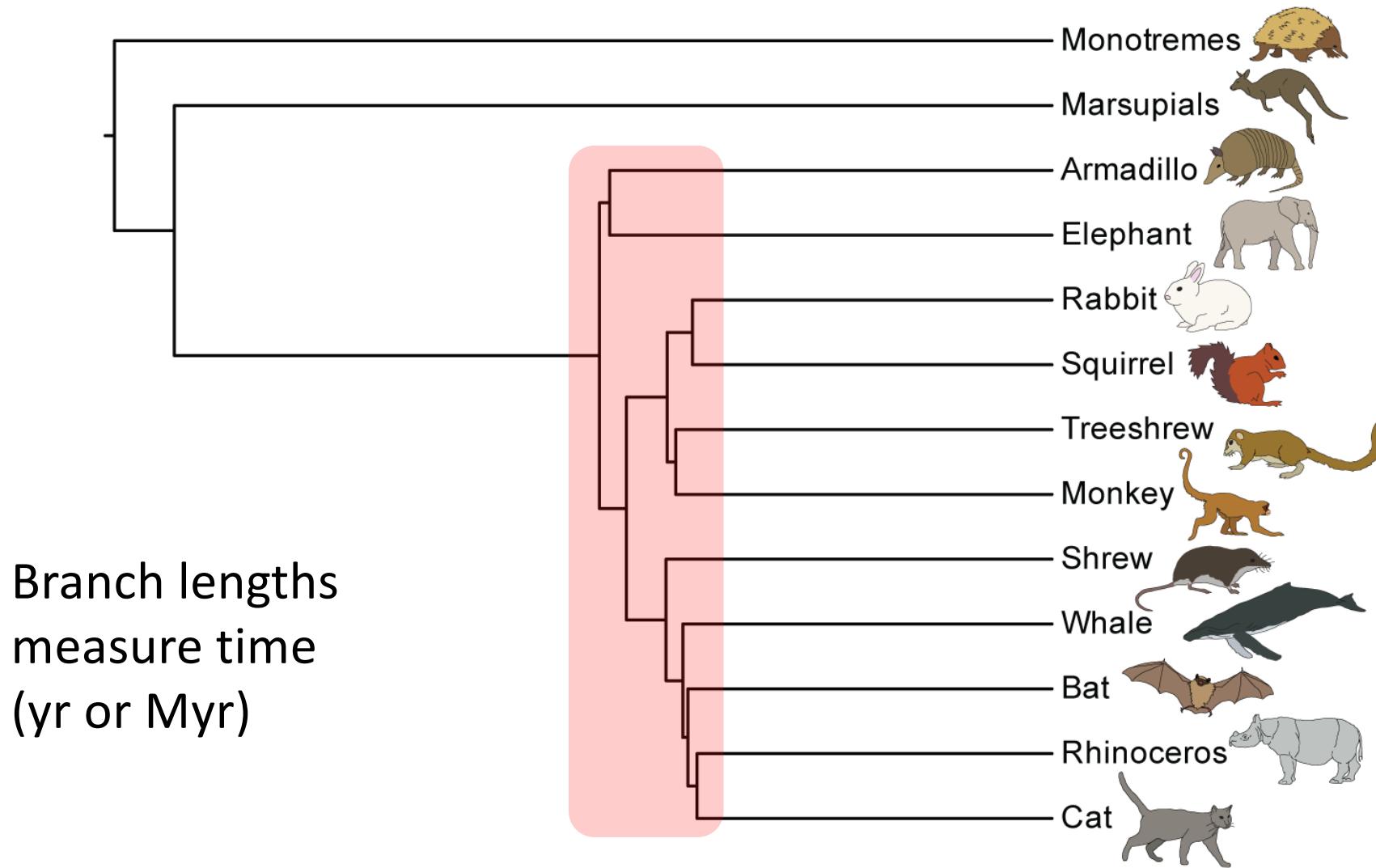
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# Trees: Phylogram

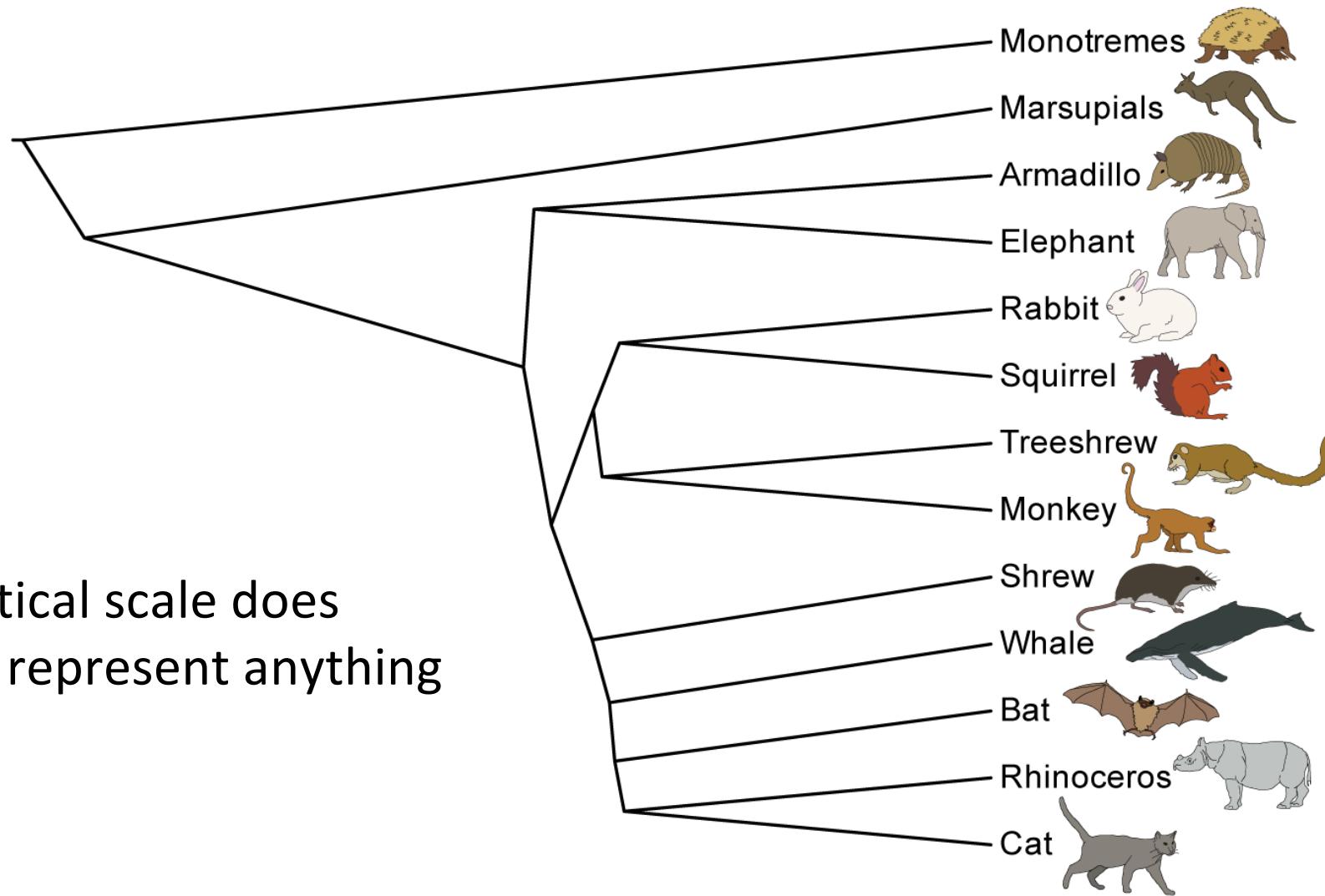


# Trees: Chronogram or time-tree



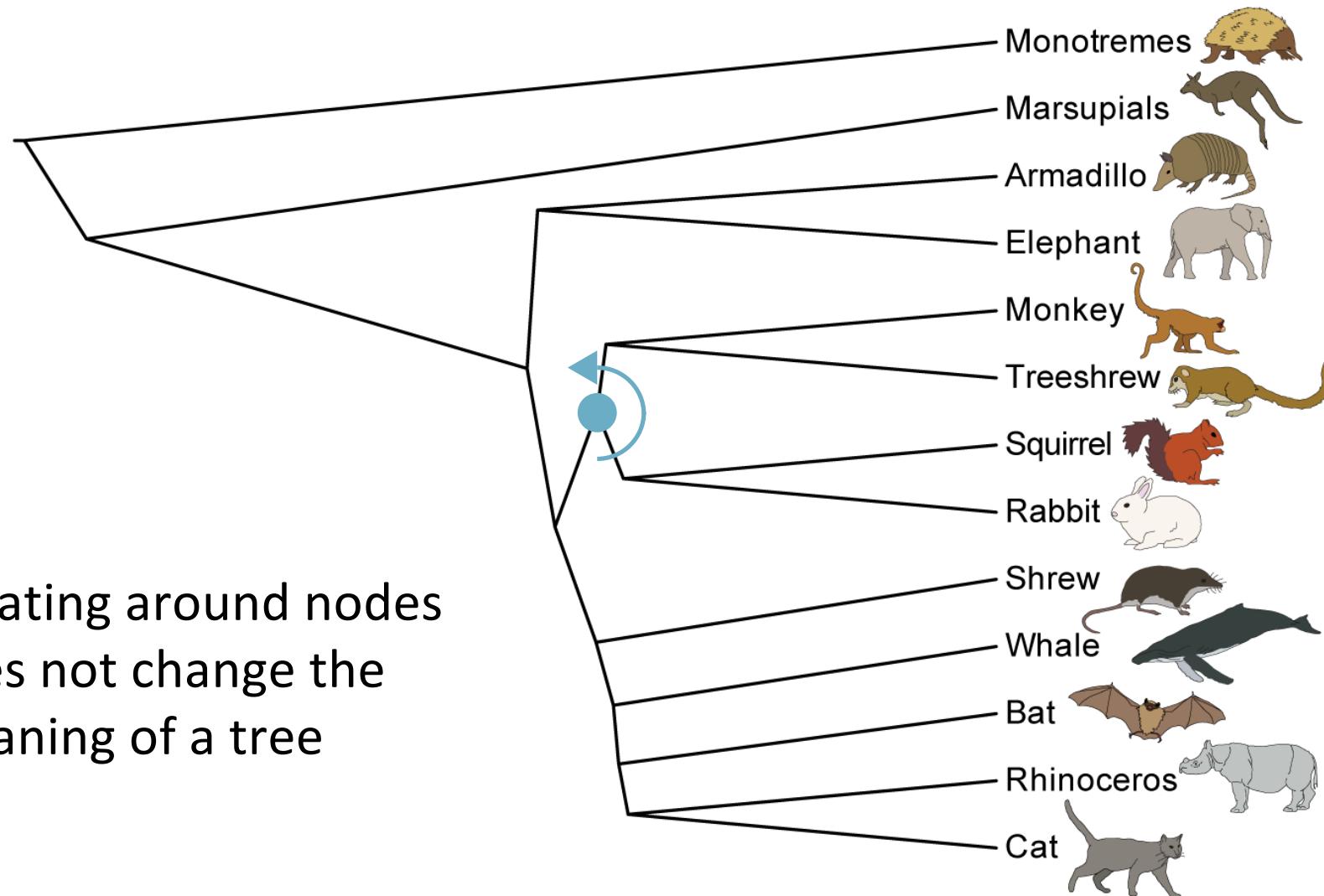
# Phylogenetic trees

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# Phylogenetic trees

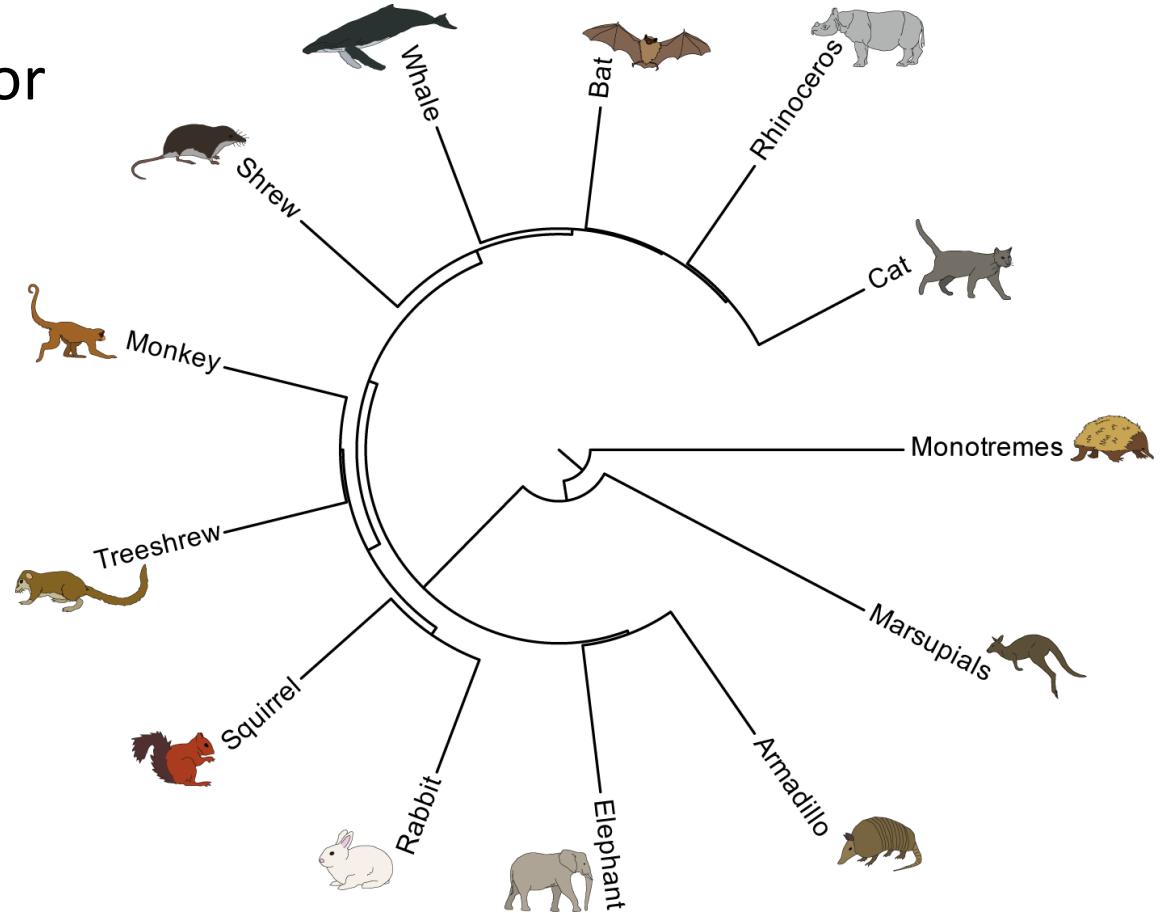
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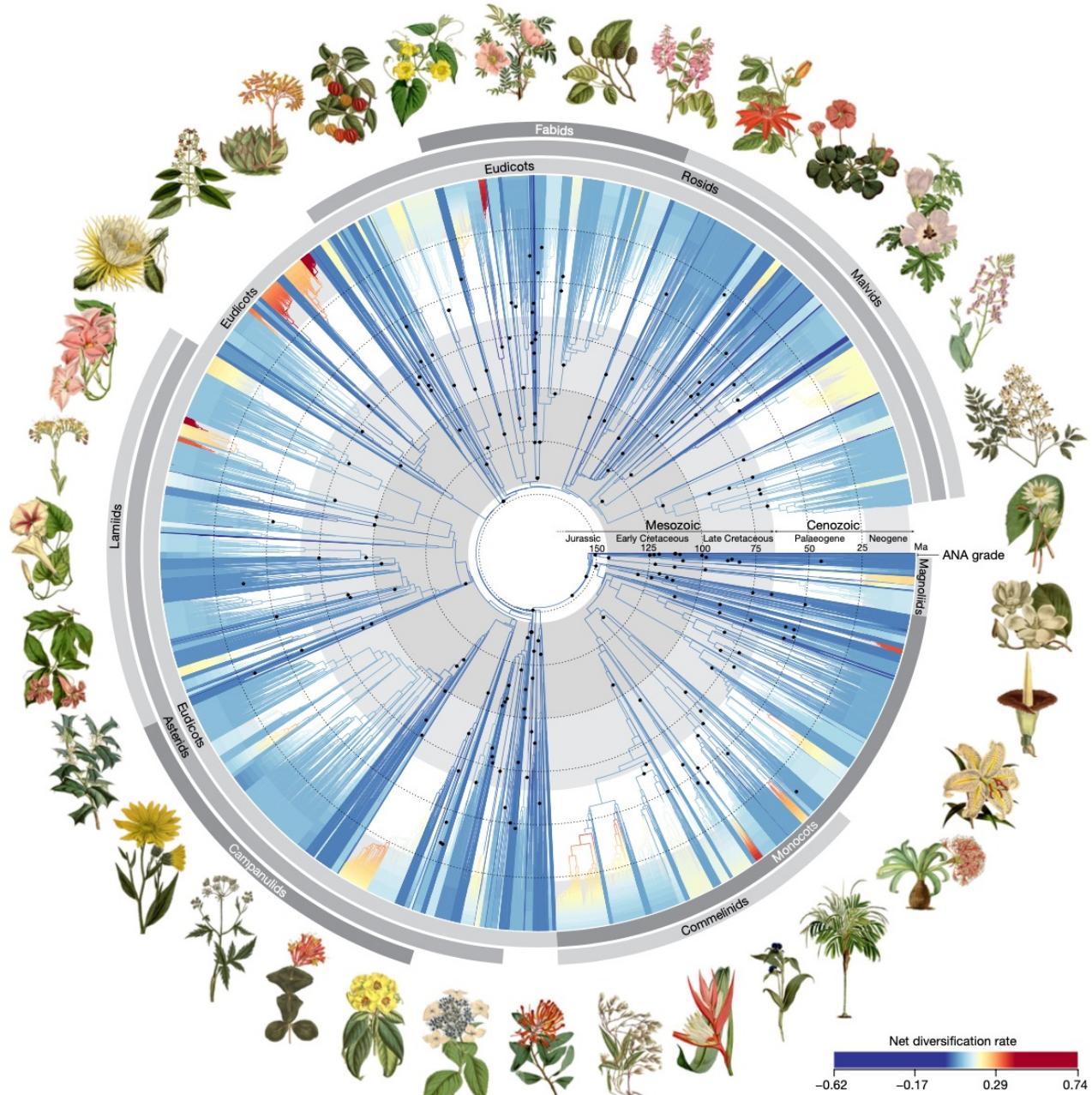


Rotating around nodes  
does not change the  
meaning of a tree

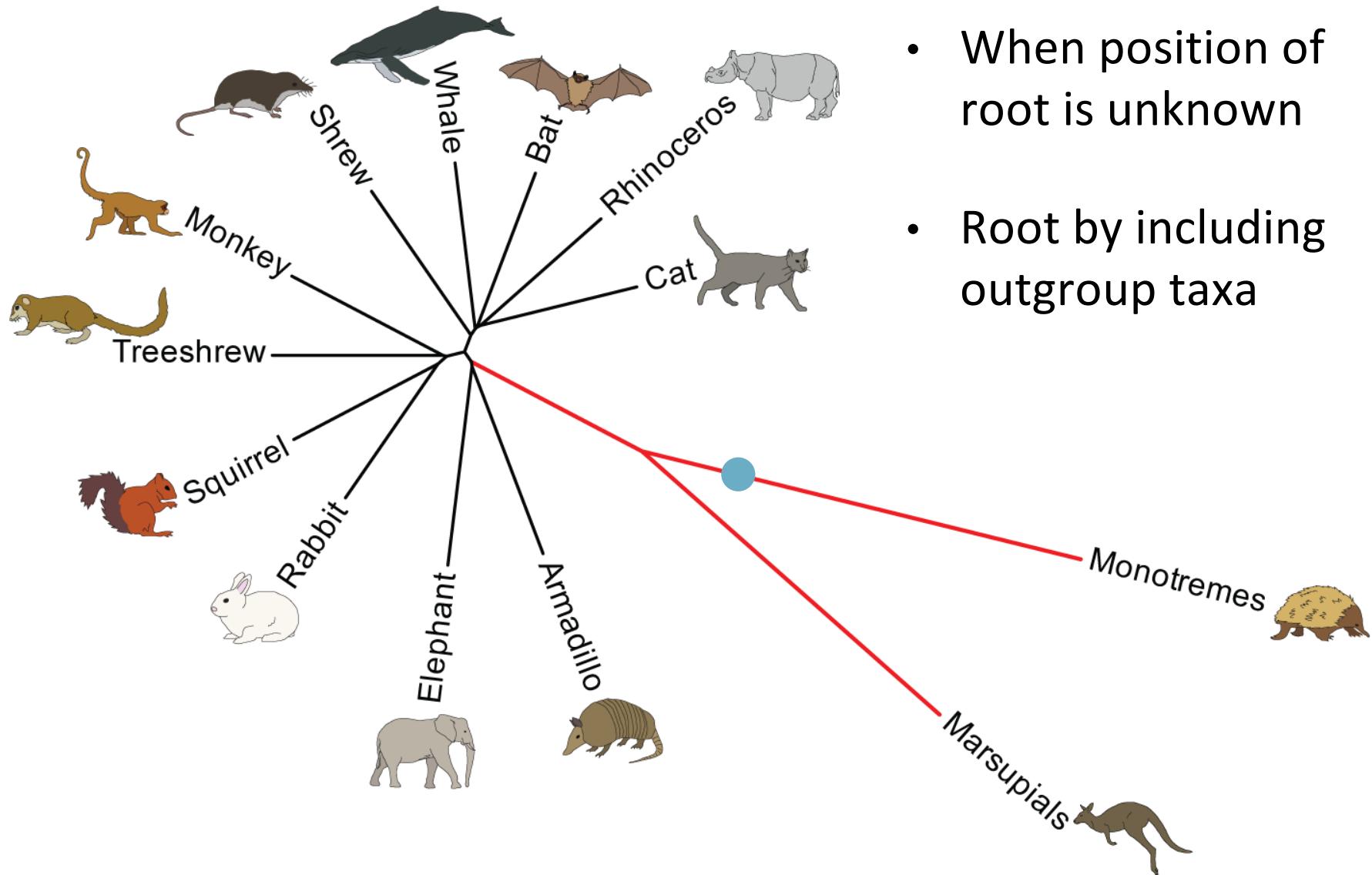
# Phylogenetic trees: Circular

- Root is placed in centre
- Cladogram, phylogram, or chronogram
- Often used to display large trees
- Difficult to interpret





# Phylogenetic trees: Unrooted



# Rooting

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- **Include outgroup taxa**
  - Taxon is not part of ingroup
  - Taxon closely related to ingroup
- **Root at midpoint**
  - Highly unreliable if internal branches are short
- **Use a molecular clock**
  - Phylogenetic analysis infers a rooted tree

# Phylogenetic trees: Newick format

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- Without branch lengths (cladogram):
  - (Monotremes,(Marsupials,((Elephant,Armadillo),(((Squirrel,Rabbit),(Monkey,Treeshrew)),(Shrew,(Whale,(Bat,(Cat,Rhinoceros)))))));
- With branch lengths (phylogram/chronogram):
  - (Monotremes:12.0,(Marsupials:11.0,((Elephant:1.0,Armadillo:1.0):9.0,(((Squirrel:1.0,Rabbit:1.0):2.0,(Monkey:1.0,Treeshrew:1.0):2.0):5.0,(Shrew:4.0,(Whale:3.0,(Bat:2.0,(Cat:1.0,Rhinoceros:1.0):1.0):1.0):1.0):4.0):2.0):1.0);

# Molecular Phylogenetics

# Phylogenetic analysis

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- We rarely know the actual evolutionary history of a set of individuals or species
  - Viral transmission histories
  - Pedigrees (humans, domesticated animals, lab organisms, etc.)

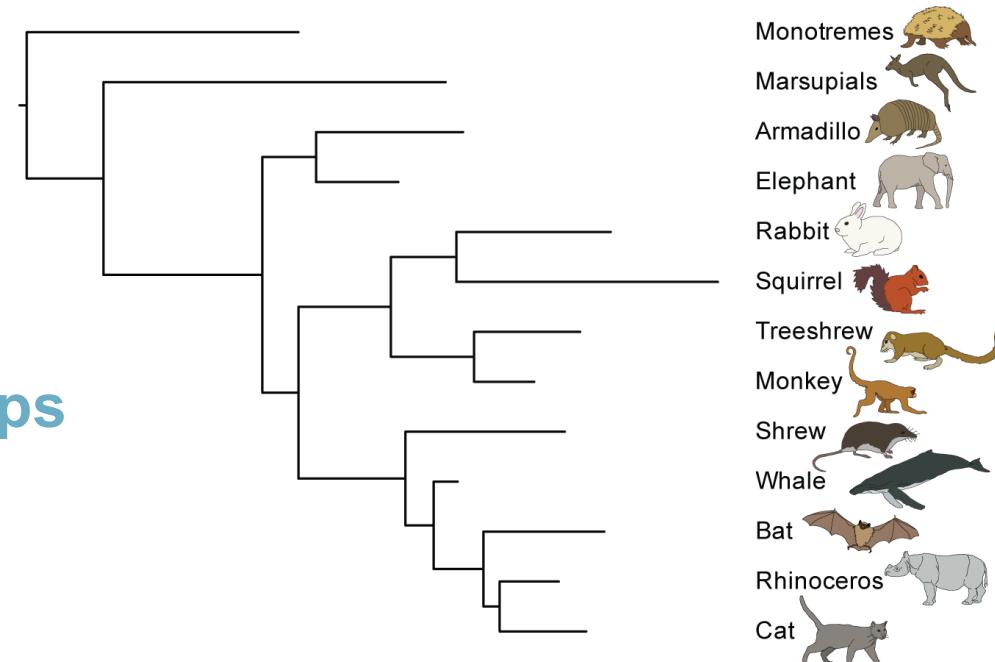
*We possess no pedigrees or armorial bearings; and we have to discover and trace the many diverging lines of descent in our natural genealogies, by characters of any kind which have long been inherited*

Charles Darwin, 1859

# Fundamental assumptions

- Phylogenetic methods make several fundamental assumptions:
  - Relationships among taxa can be represented by a tree
  - Homologous characters are being compared
  - Characters are mutually independent

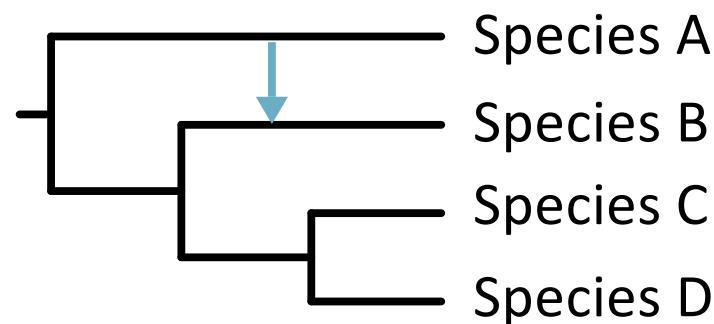
When might relationships  
not be treelike?



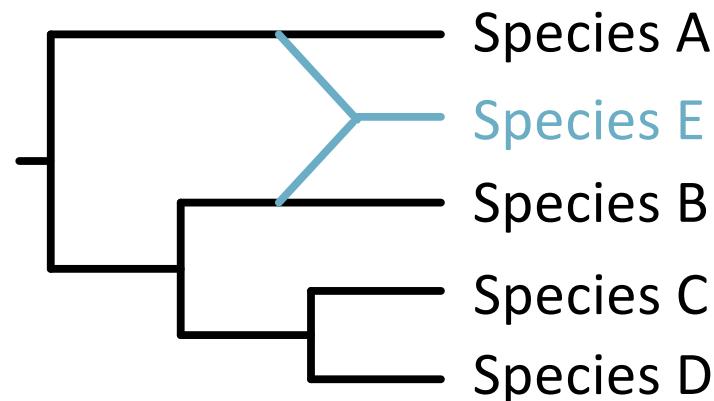
# Non-treelike evolution

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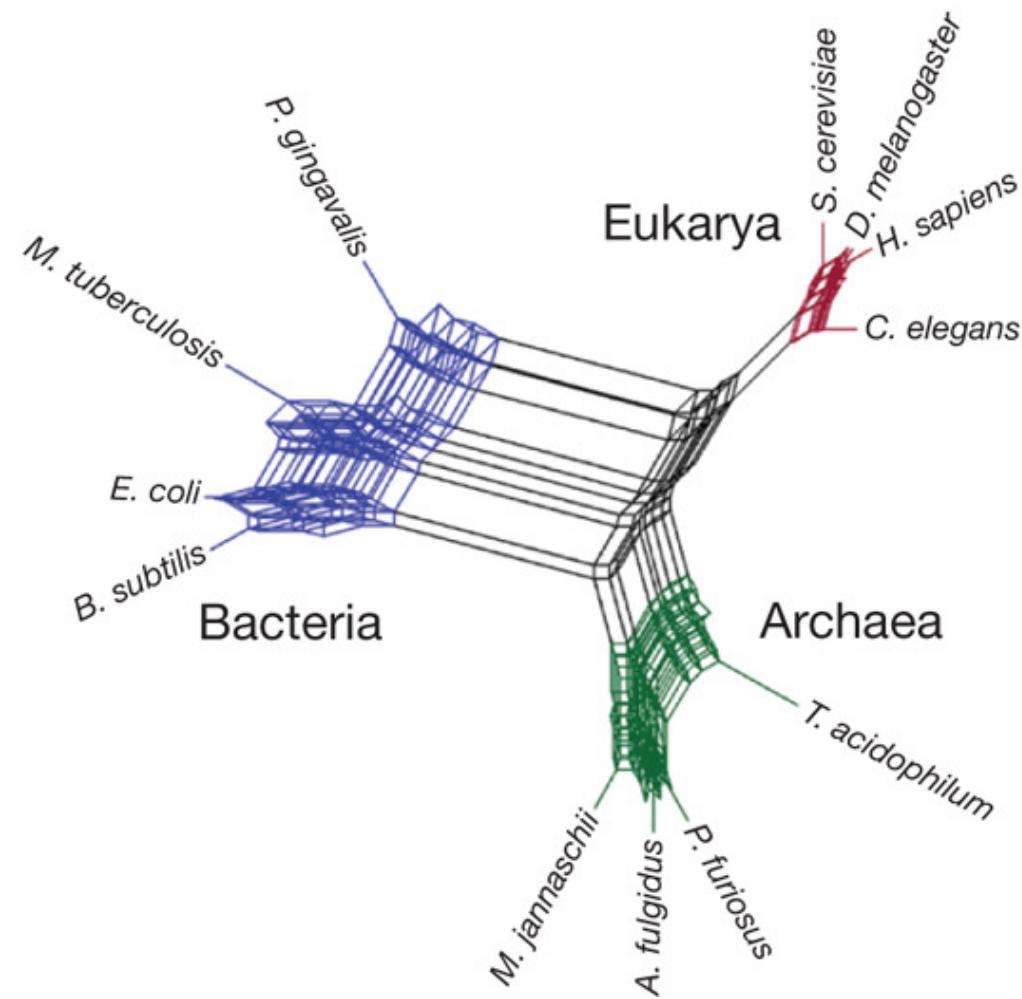
Horizontal gene transfer



Hybrid speciation

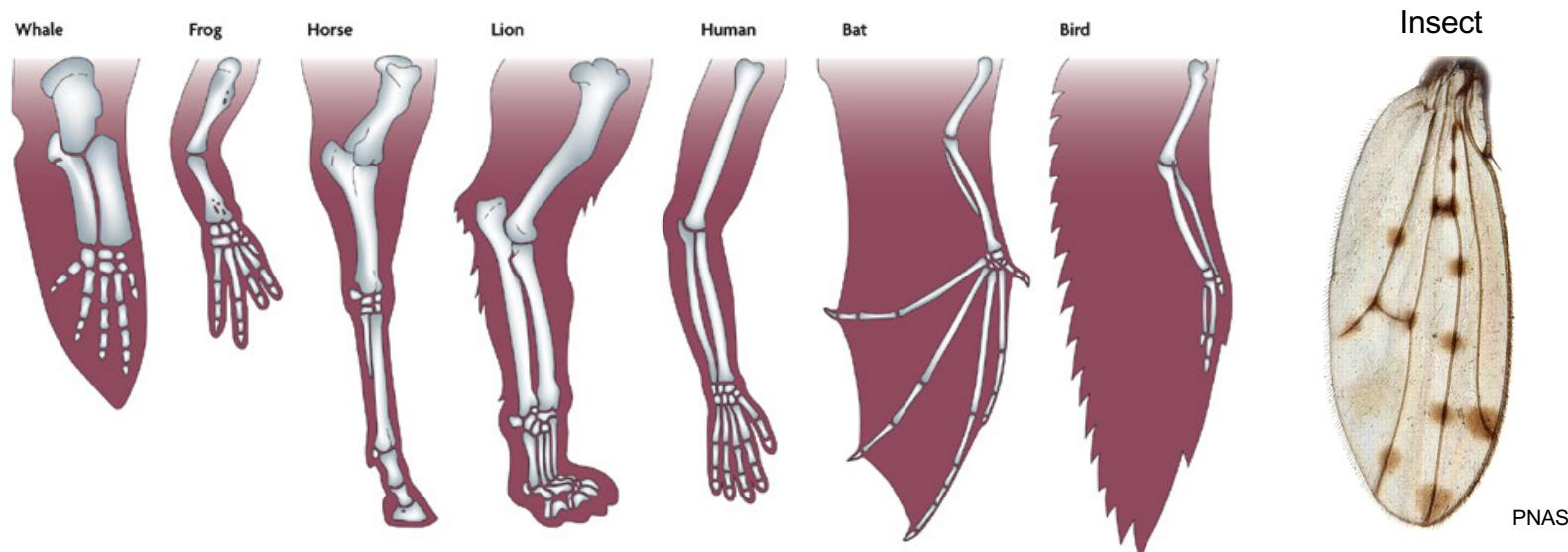


# Phylogenetic networks



# Fundamental assumptions

- Phylogenetic methods make several fundamental assumptions:
  - Relationships among taxa can be represented by a tree
  - Homologous characters are being compared
  - Characters are mutually independent



Wagner (2007) *Nat Rev Genet*

# Character homology

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- Comparing strings of nucleotides (or amino acids)
- Each nucleotide site is a character
- But DNA sequences can vary in length

bat

CGTTAGTACACT

whale

CGATAGTTCACT

rabbit

CGTTAGTTTACC

elephant

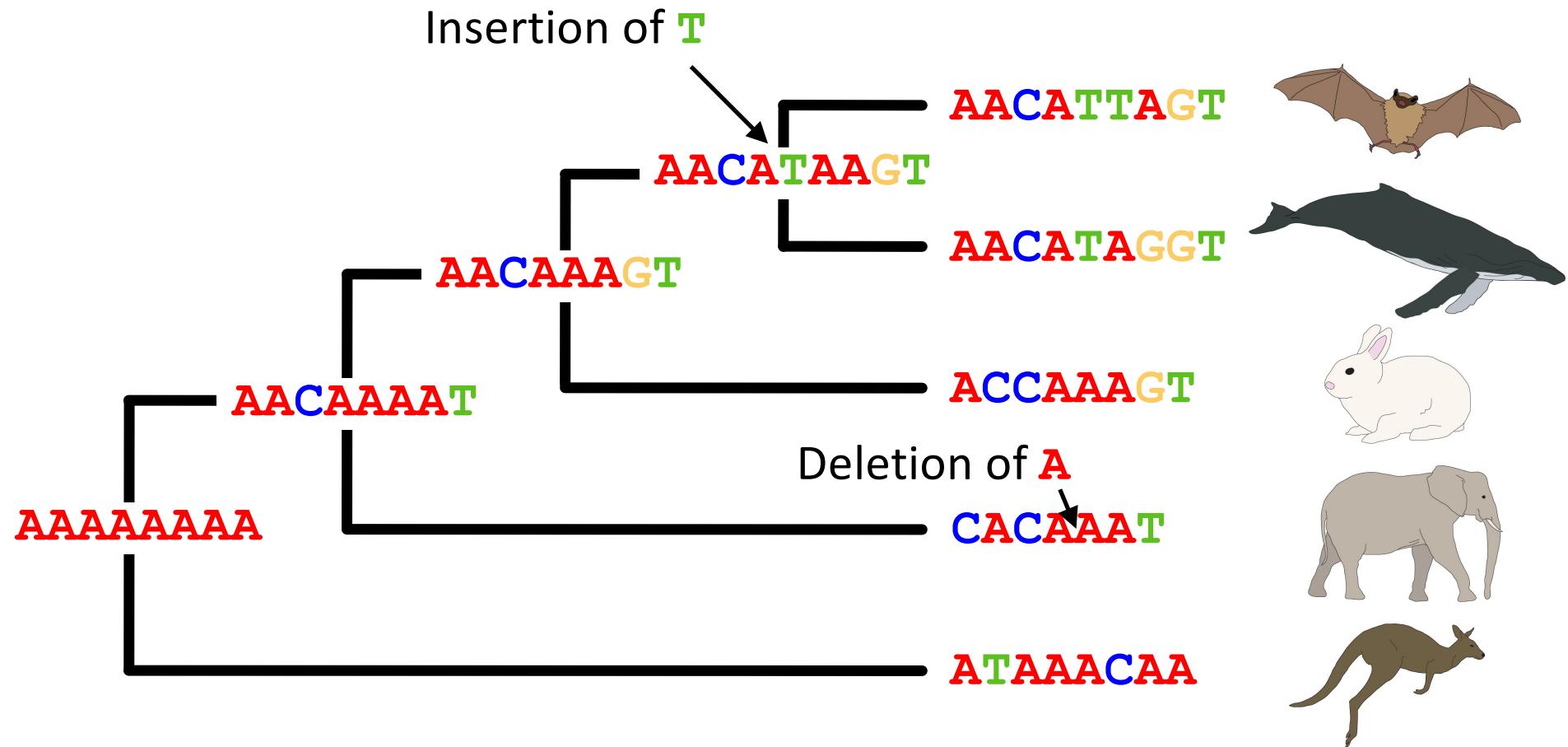
CATTGGATTACT

kangaroo

CATTGGTTTACT



# DNA sequence evolution

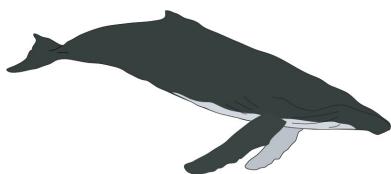


# DNA sequence alignment

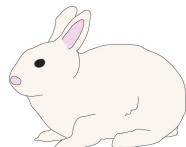
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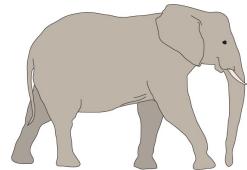
**AACATTAGT**



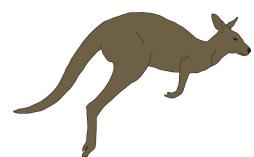
**AACATAGGT**



**ACCAAAAGT**



**CACAAAT**



**ATAAACAA**



**AACATTAGT**

**AACATAGGT**

**ACCA-AAGT**

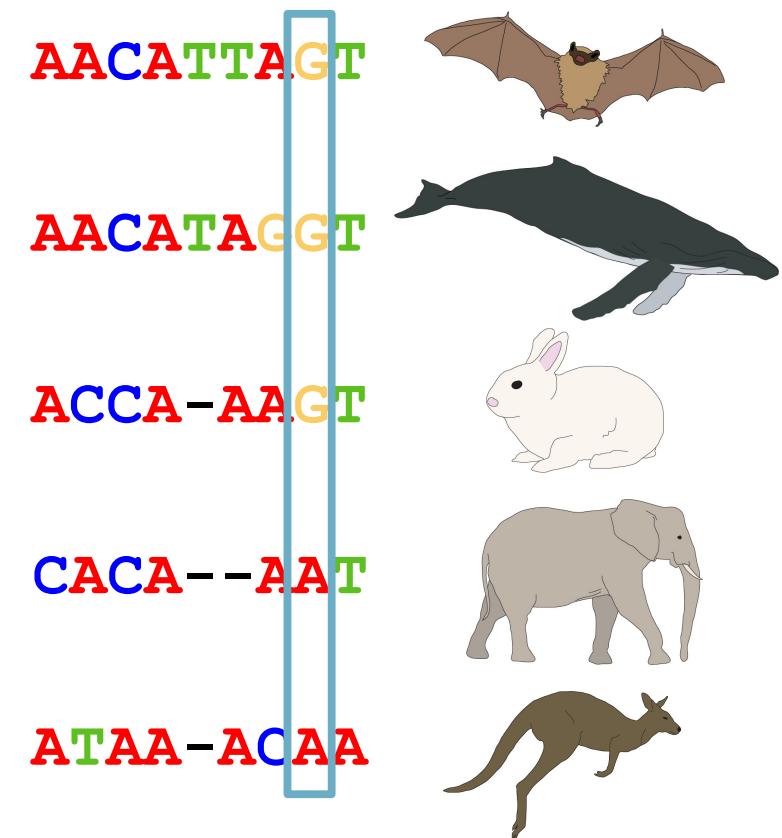
**CACA--AAT**

**ATAA-ACAA**

# DNA sequence alignment

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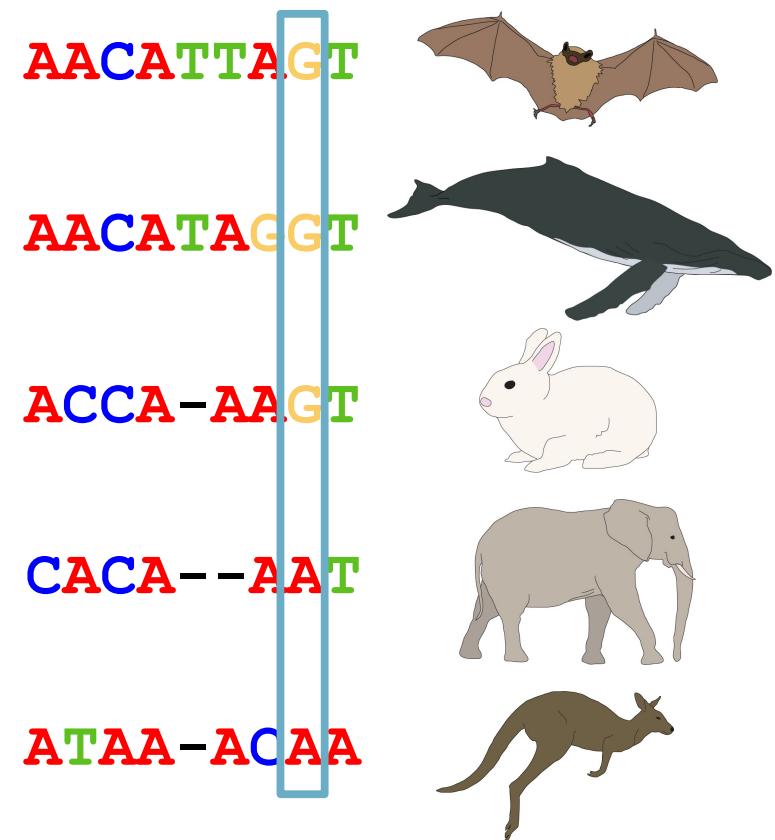
- Homologous site
- Inherited from the common ancestor of all sequences in the alignment
- The aim of sequence alignment is to ensure that we are comparing homologous characters throughout the data set



# DNA sequence alignment

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- Groups together the first 3 sequences
- Groups together the last 2 sequences
- Informative for all phylogenetic methods



# DNA sequence alignment

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- Does not group any sequences
  - Not useful for maximum parsimony
- But informative for estimating amount of evolutionary change
  - Useful for other methods

AACATTAGT

AACATAGGT

ACCA-AAGT

CACA--AAT

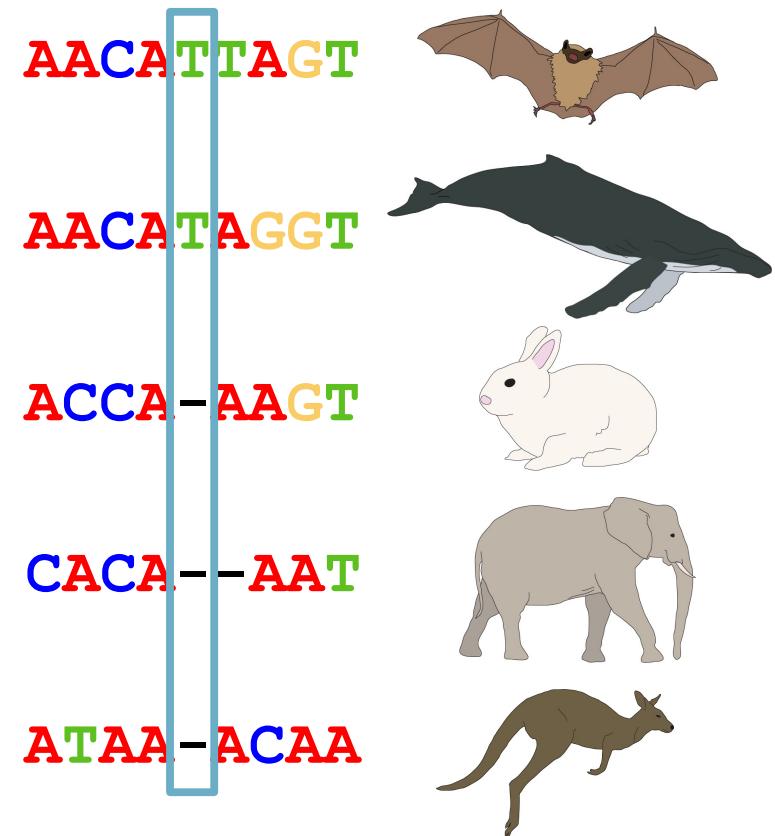
ATAA-ACAA



# DNA sequence alignment

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- Indel – insertion or deletion
- Potentially informative
- Most phylogenetic methods do not use indel data



# A practical approach

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Align sequences using automated methods

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**CLUSTAL W: improving the sensitivity of progressive multiple sequence alignment through sequence weighting, position-specific gap penalties and weight matrix choice**

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Julie D.Thompson, Desmond G.Higgins\* and Toby J.Gibson\*

Software

**MUSCLE: a multiple sequence alignment method with reduced time and space complexity**

Robert C Edgar\*

**MAFFT: a novel method for rapid multiple sequence alignment based on fast Fourier transform**

Kazutaka Katoh, Kazuharu Misawa<sup>1</sup>, Kei-ichi Kuma and Takashi Miyata\*

# A practical approach

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Align sequences using automated methods



Adjust alignments by eye

CTATGTGGCACCCAGCCCCATGCA--AGC

ATATGTGGCA-----CCCAGGCA--AG-

ATATGTGGCACCCAGCCCCATGCATT--

# A practical approach

Align sequences using automated methods



Adjust alignments by eye



Delete sites with uncertain homology

CTATGTGGCACCCAGCCCCATGCA -- AGC

ATATGTGGCA ----- CCCAGGGCA -- AG -

ATATGTGGCACCCAGCCCCATGCA TTT --

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# Useful references

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