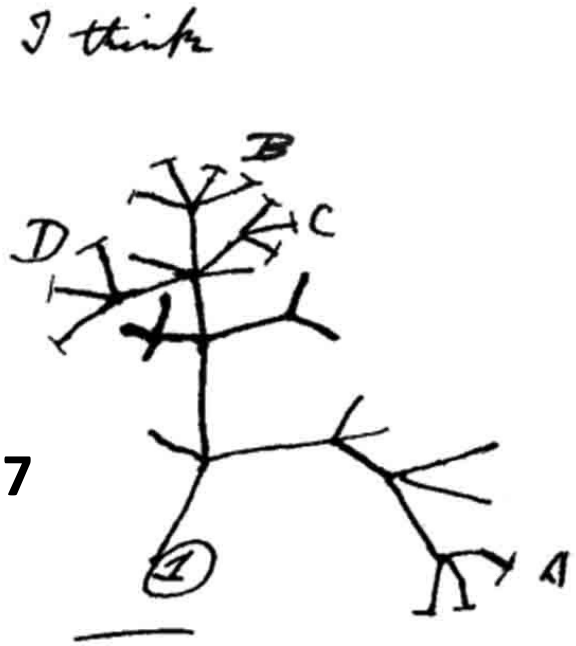
Lecture 1.1

Introduction to Molecular Phylogenetics

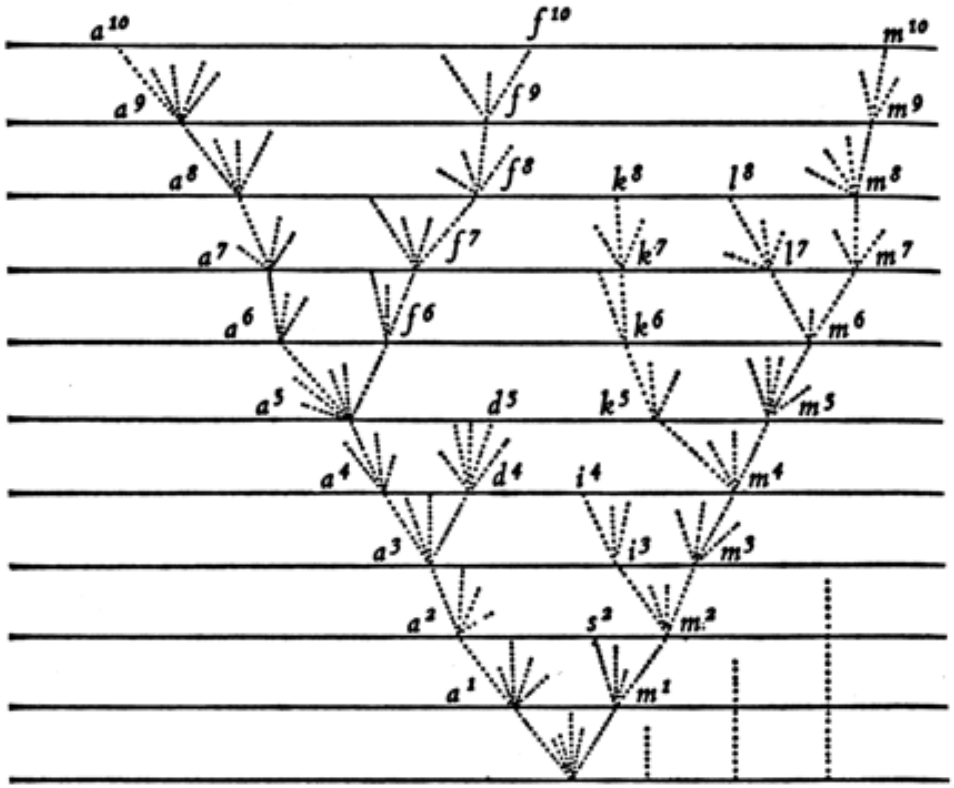
Phylogenetic Trees

What is a phylogenetic tree?

Phylogeny
evolutionary relationships among a set of organisms



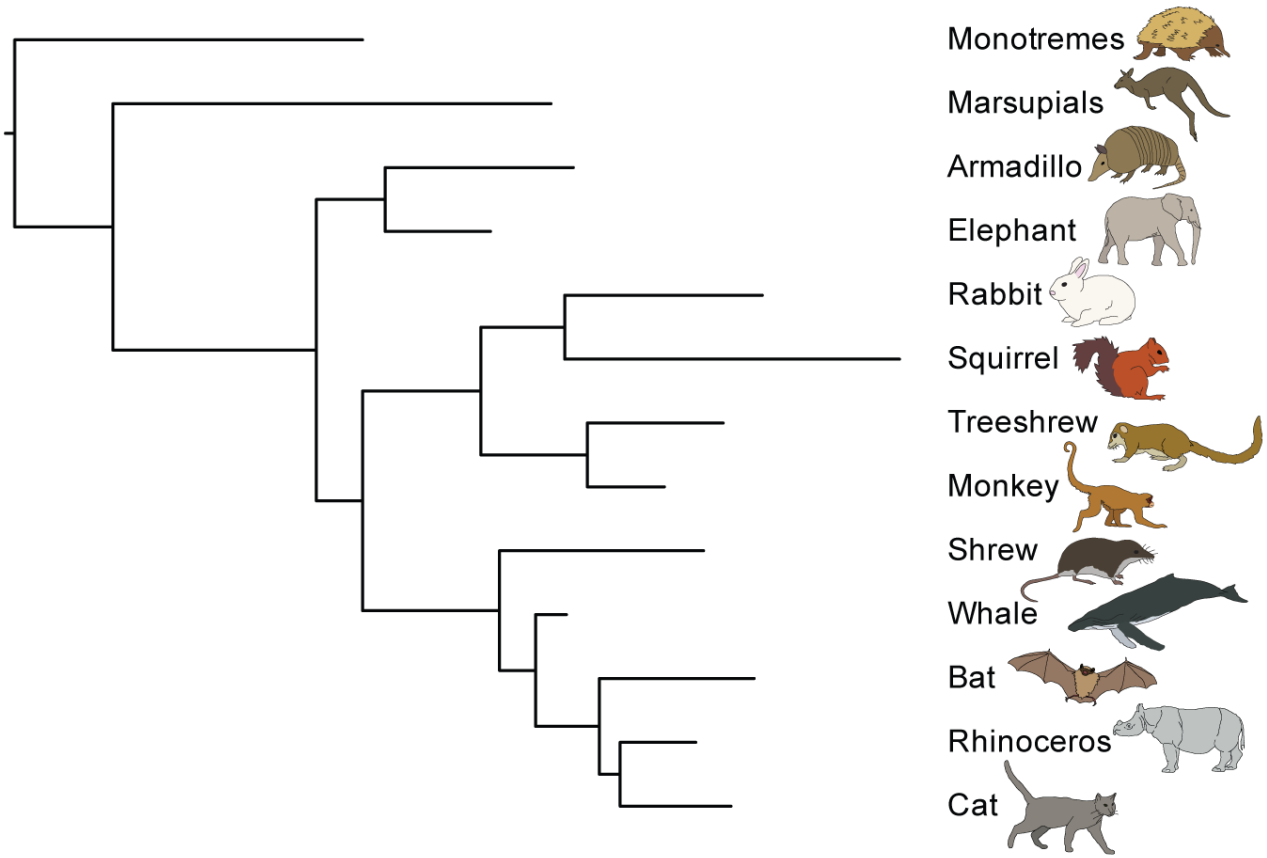
1837

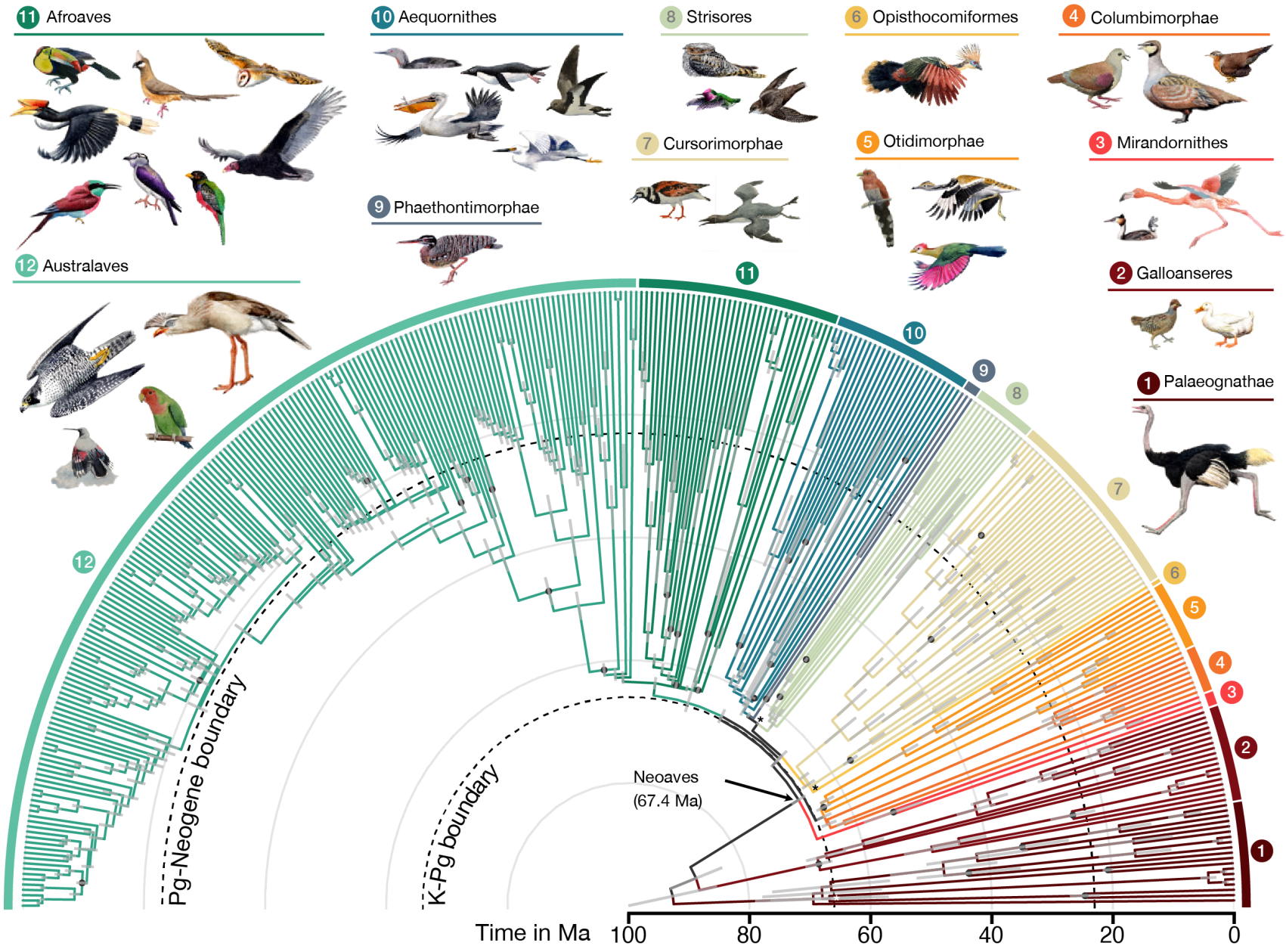


1859

Phylogenetic trees

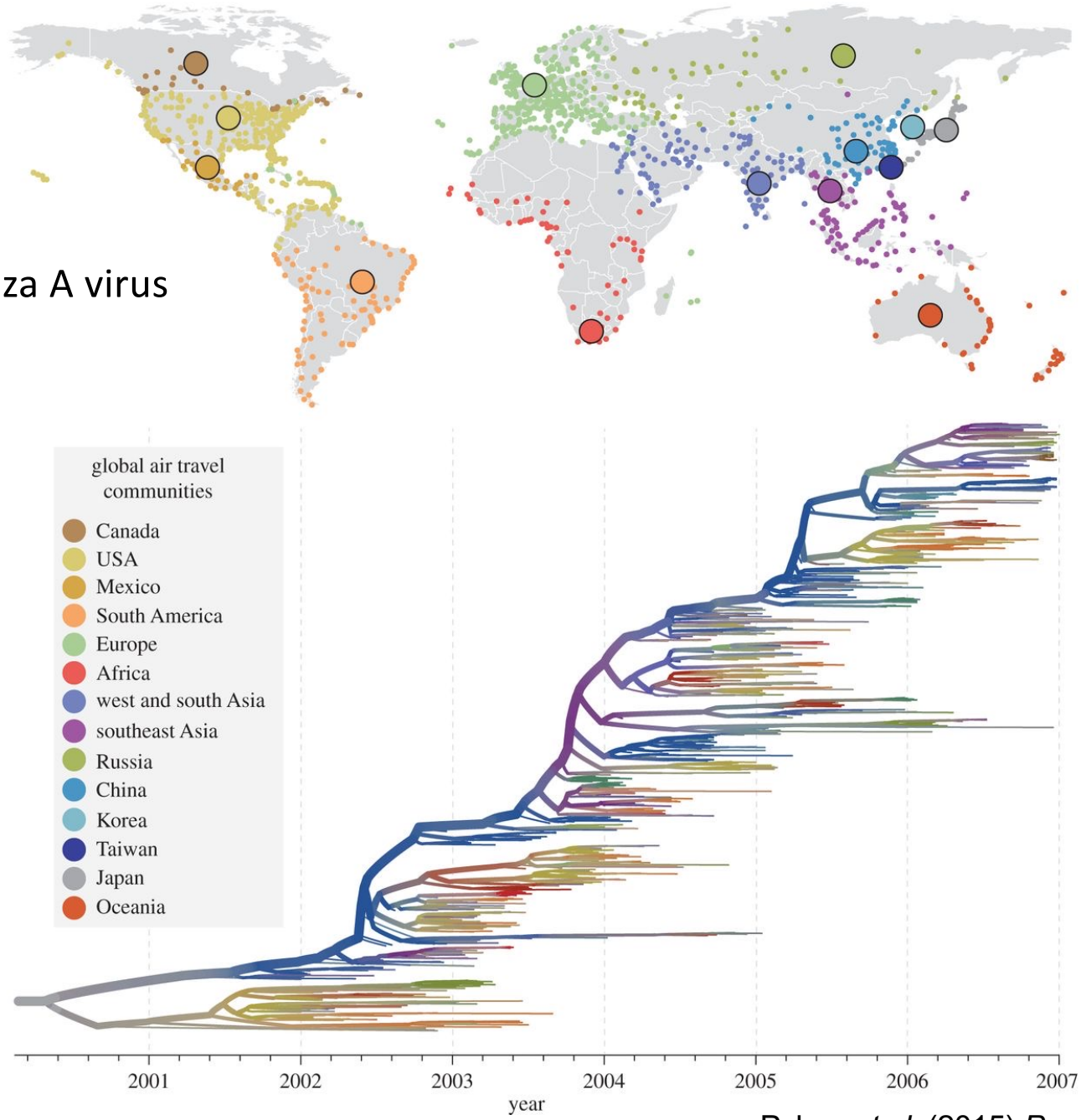
- Topology (relationships)
- Branch lengths (amount of evolutionary change or time)





Stiller *et al*. (2024) *Nature*

Human influenza A virus
Subtype H3N2

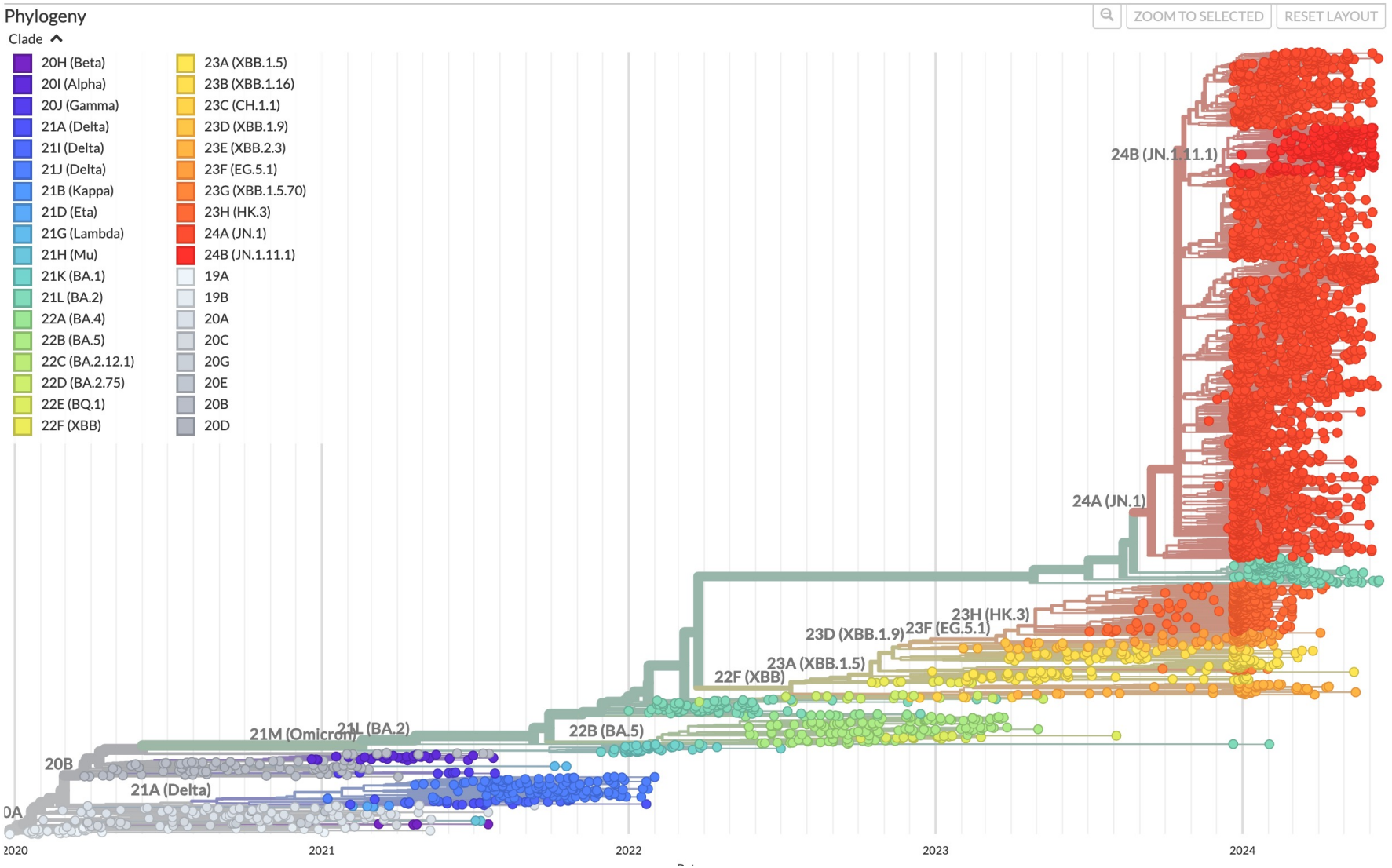


Pybus *et al*. (2015) *Proc Roy Soc B*

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

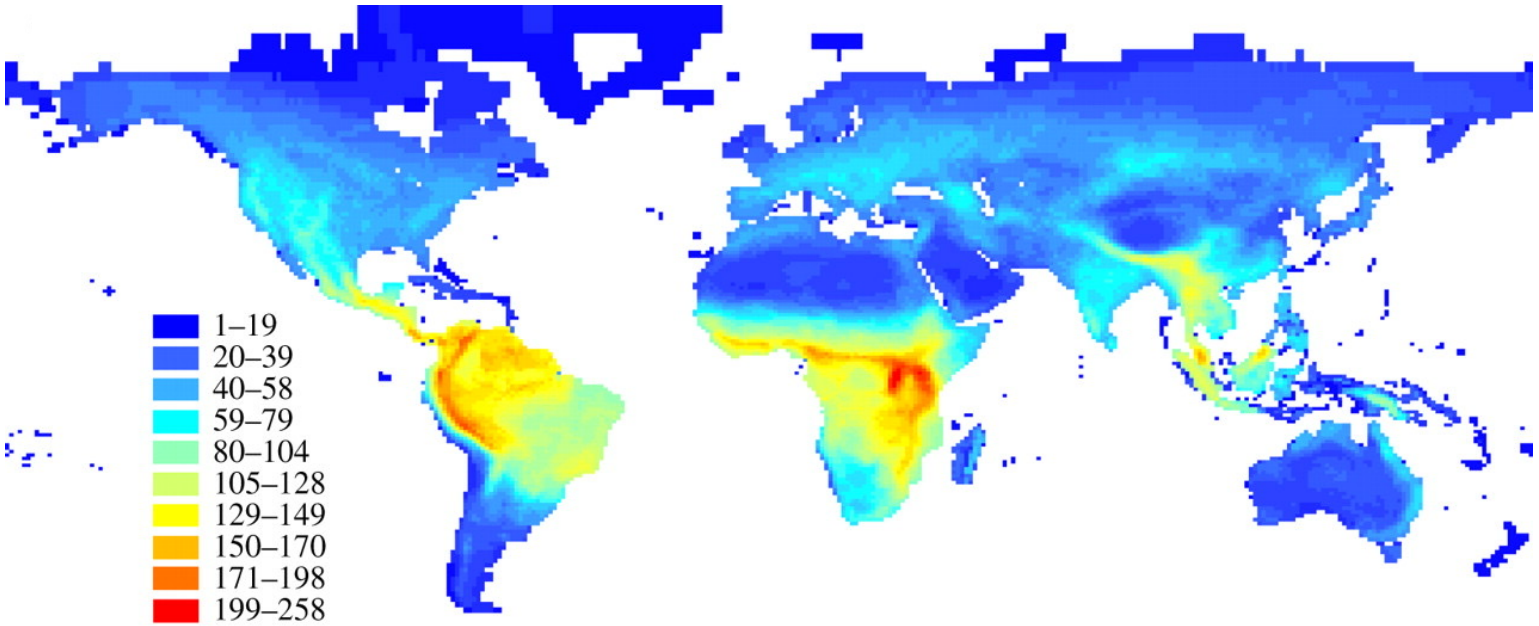
Built with nextstrain/ncov. Maintained by the Nextstrain team. Data updated 2024-06-21. Enabled by data from GISAID.

Showing 4002 of 4002 genomes sampled between Dec 2019 and Jun 2024.

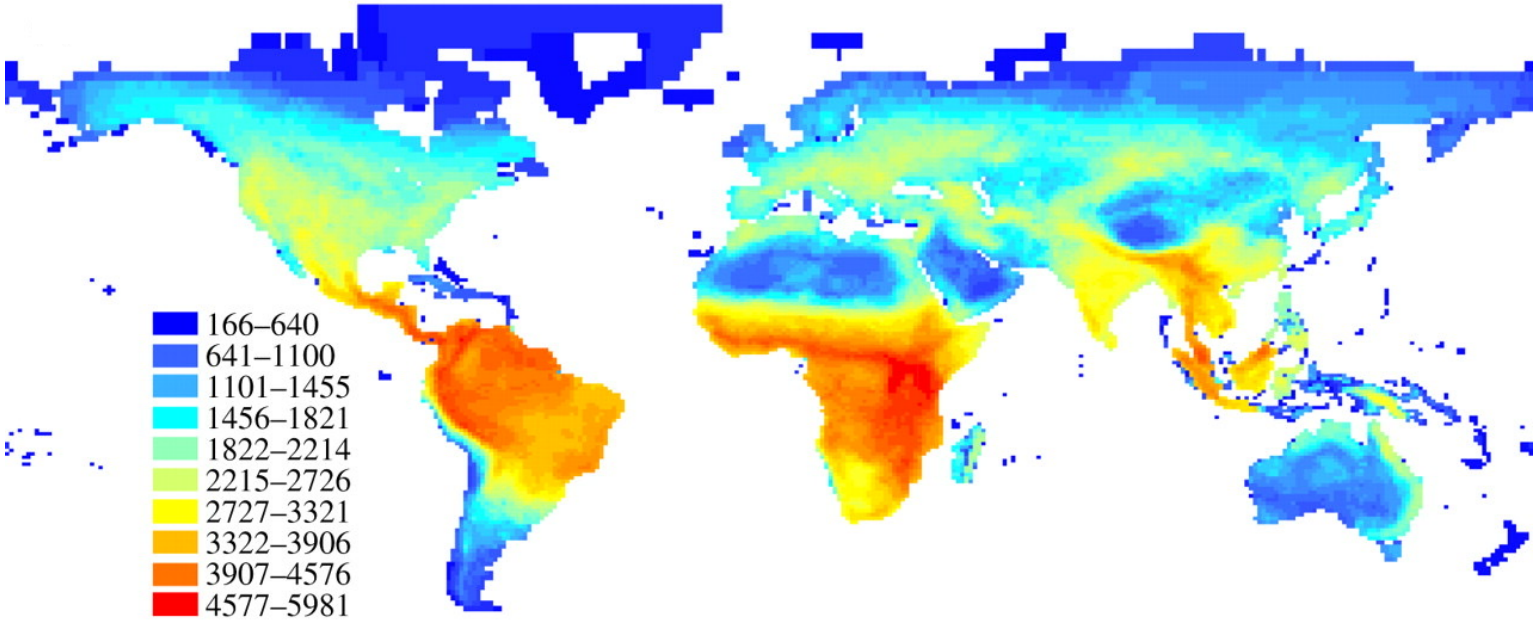


nextstrain.org, June 2024

Mammal species richness



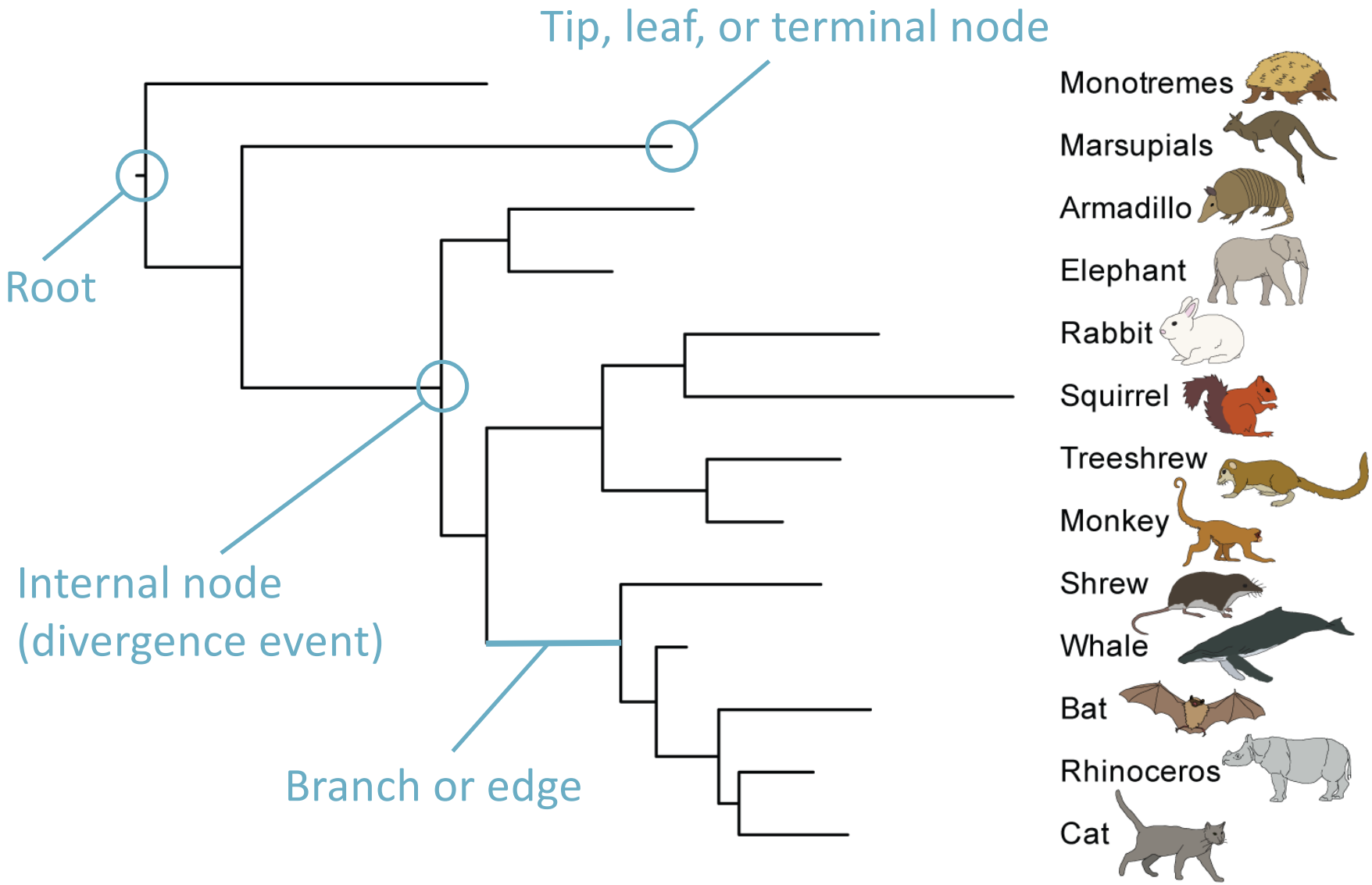
Mammal phylogenetic diversity



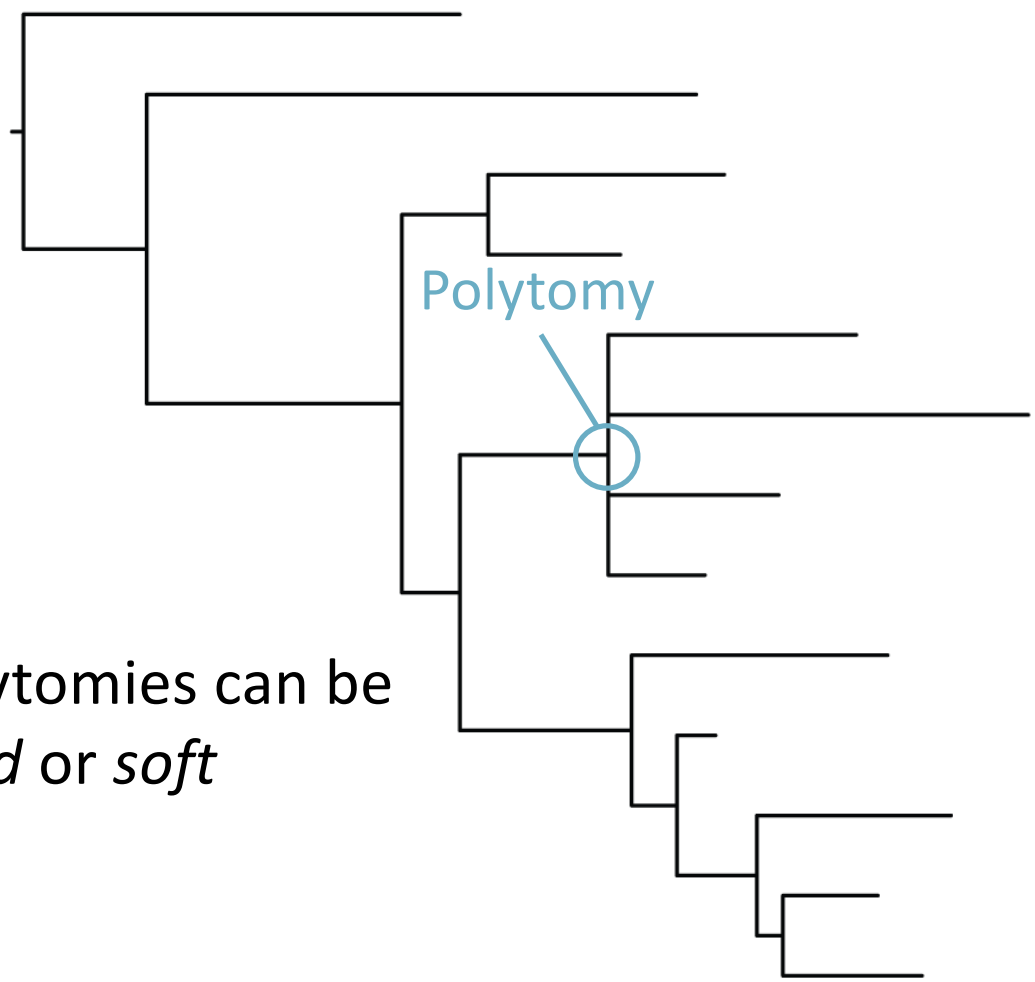
Davies & Buckley (2011) *Phil Trans Roy Soc B*

Tree Thinking

Phylogenetic trees

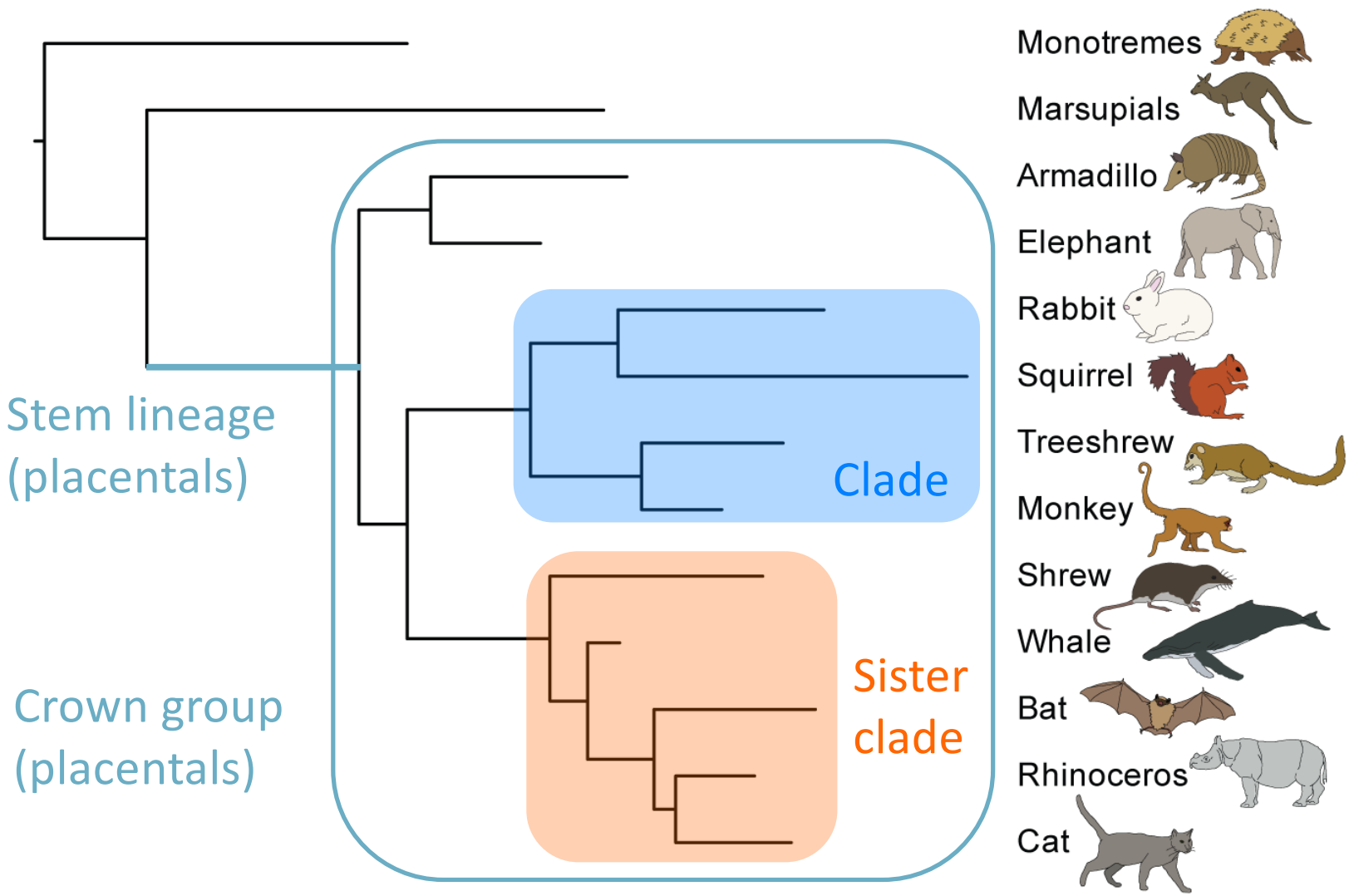


Phylogenetic trees

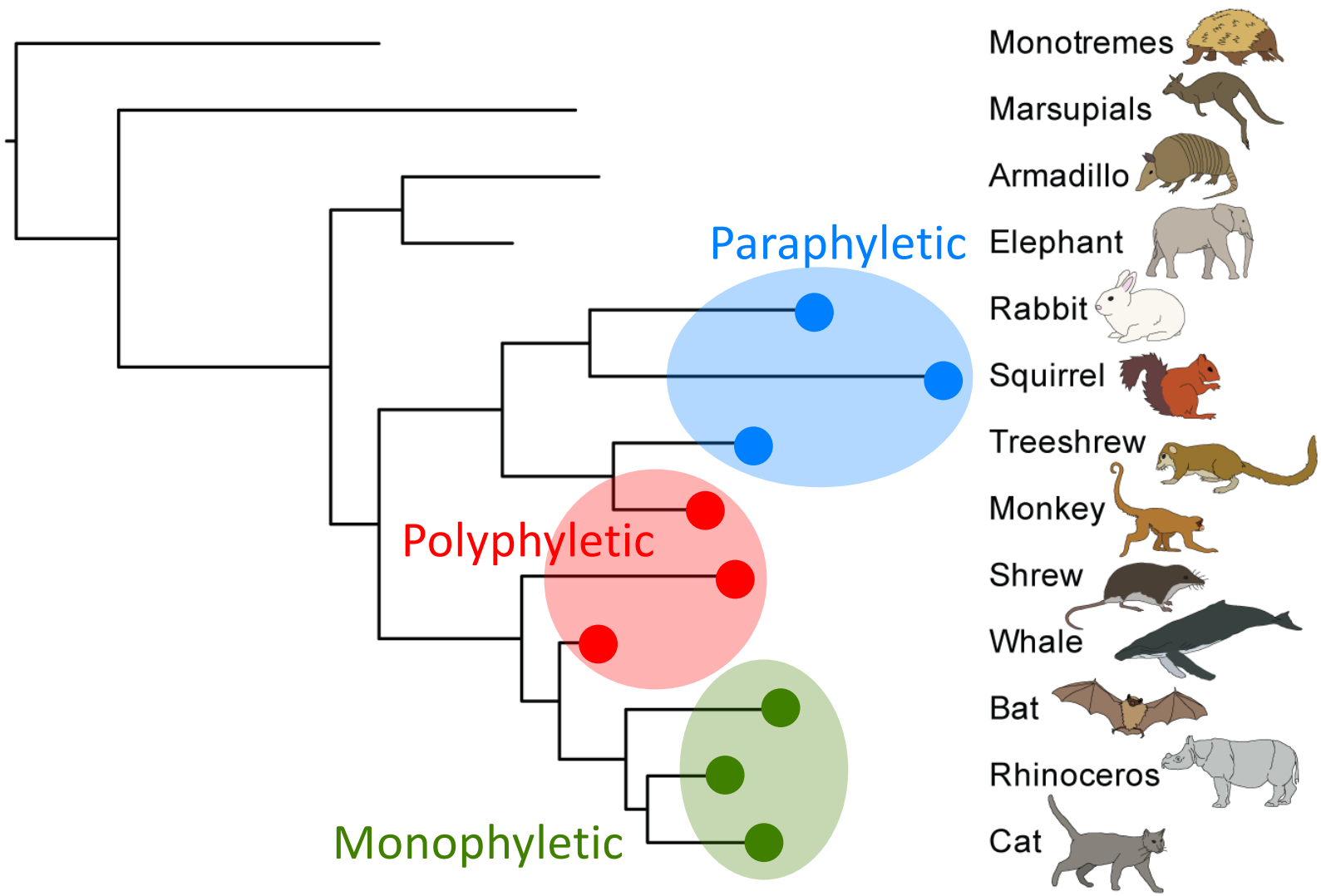


Polytomies can be *hard* or *soft*

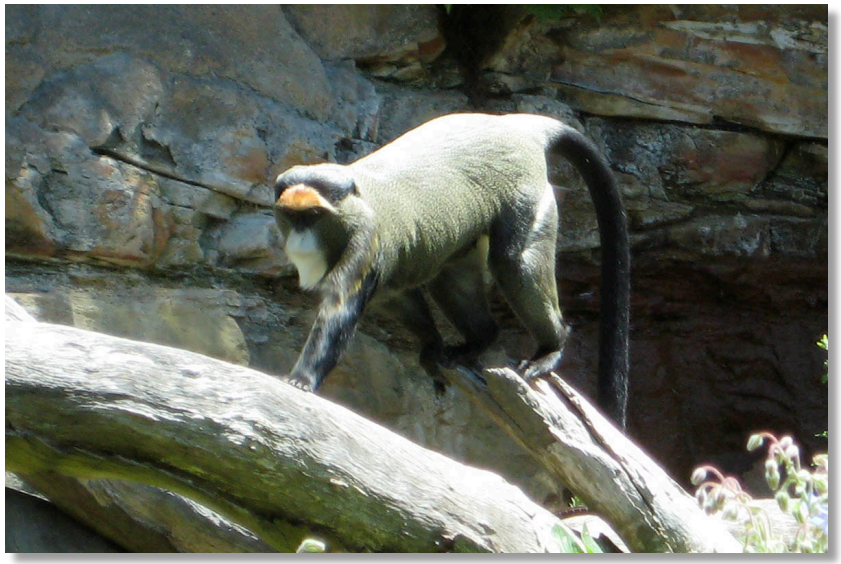
Phylogenetic trees



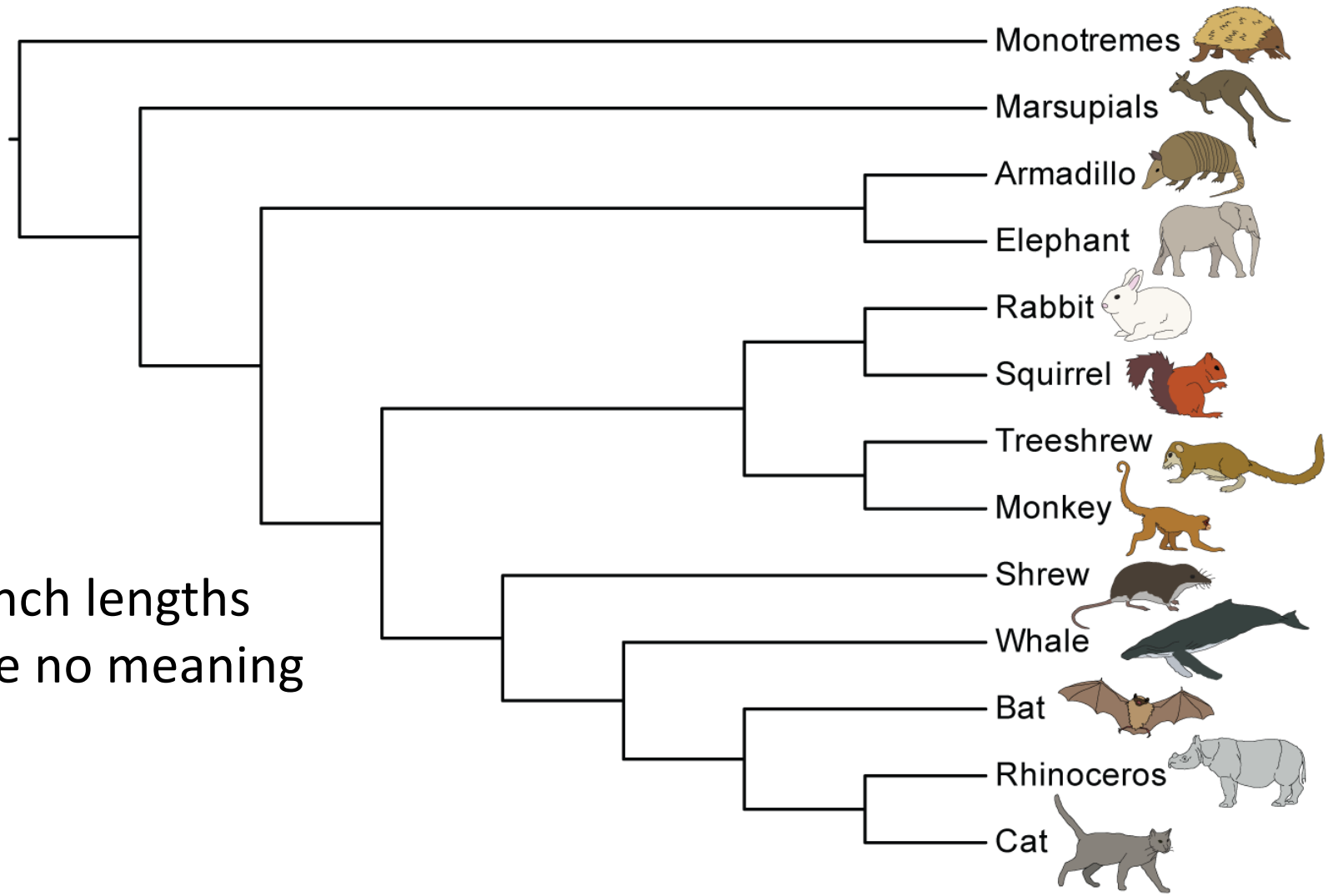
Cladistic terms



Paraphyletic groups

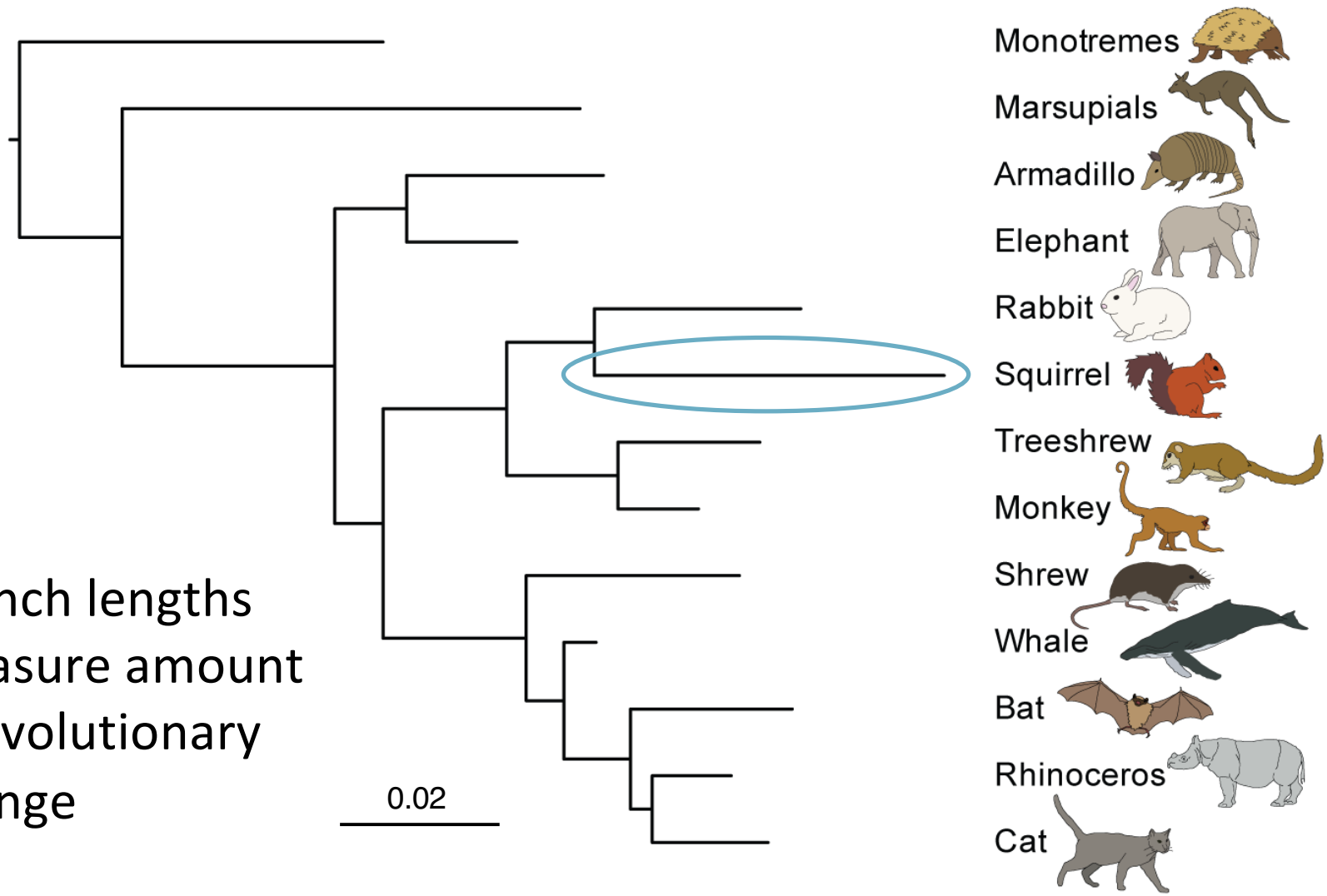


Trees: Cladogram



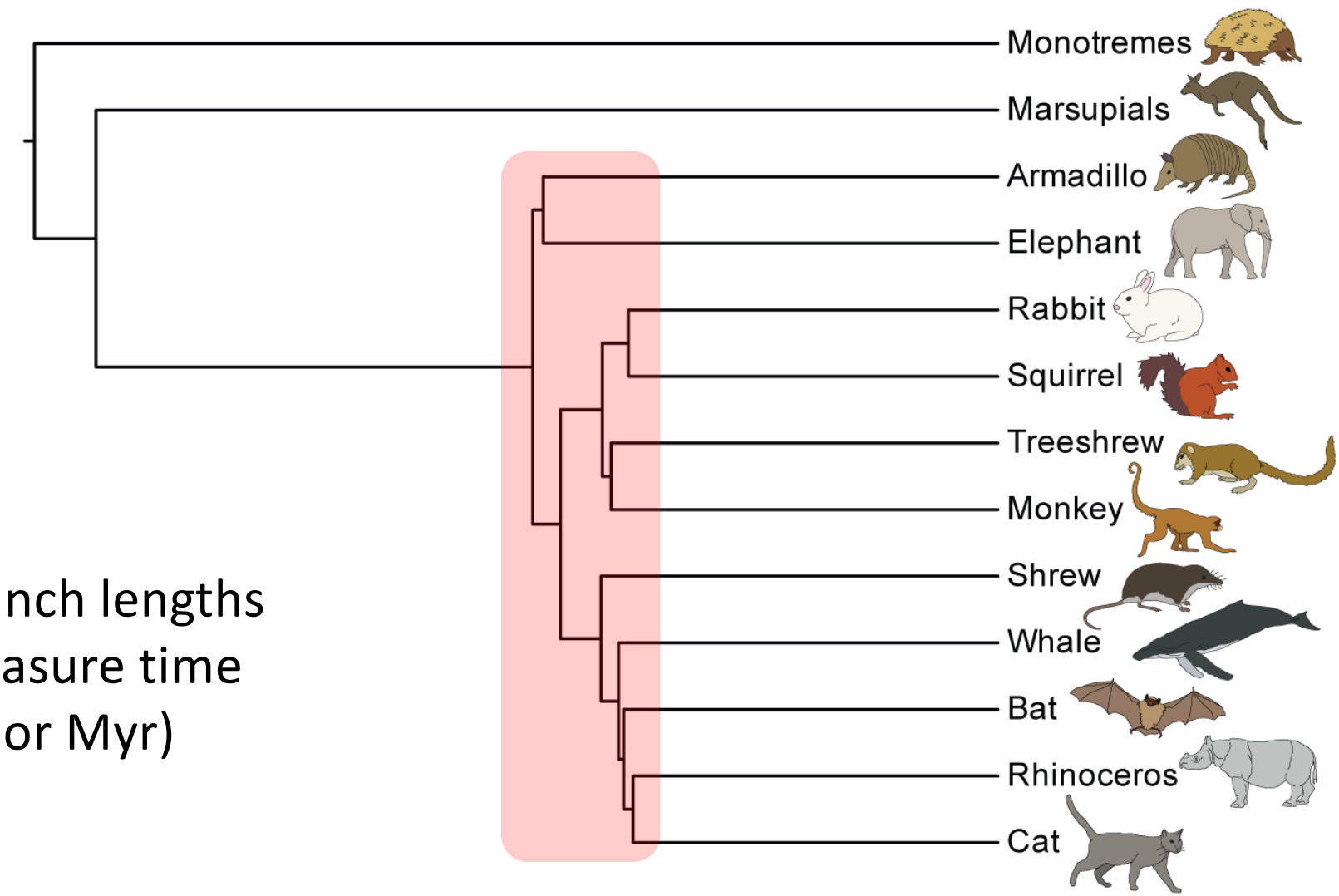
Branch lengths have no meaning

Trees: Phylogram



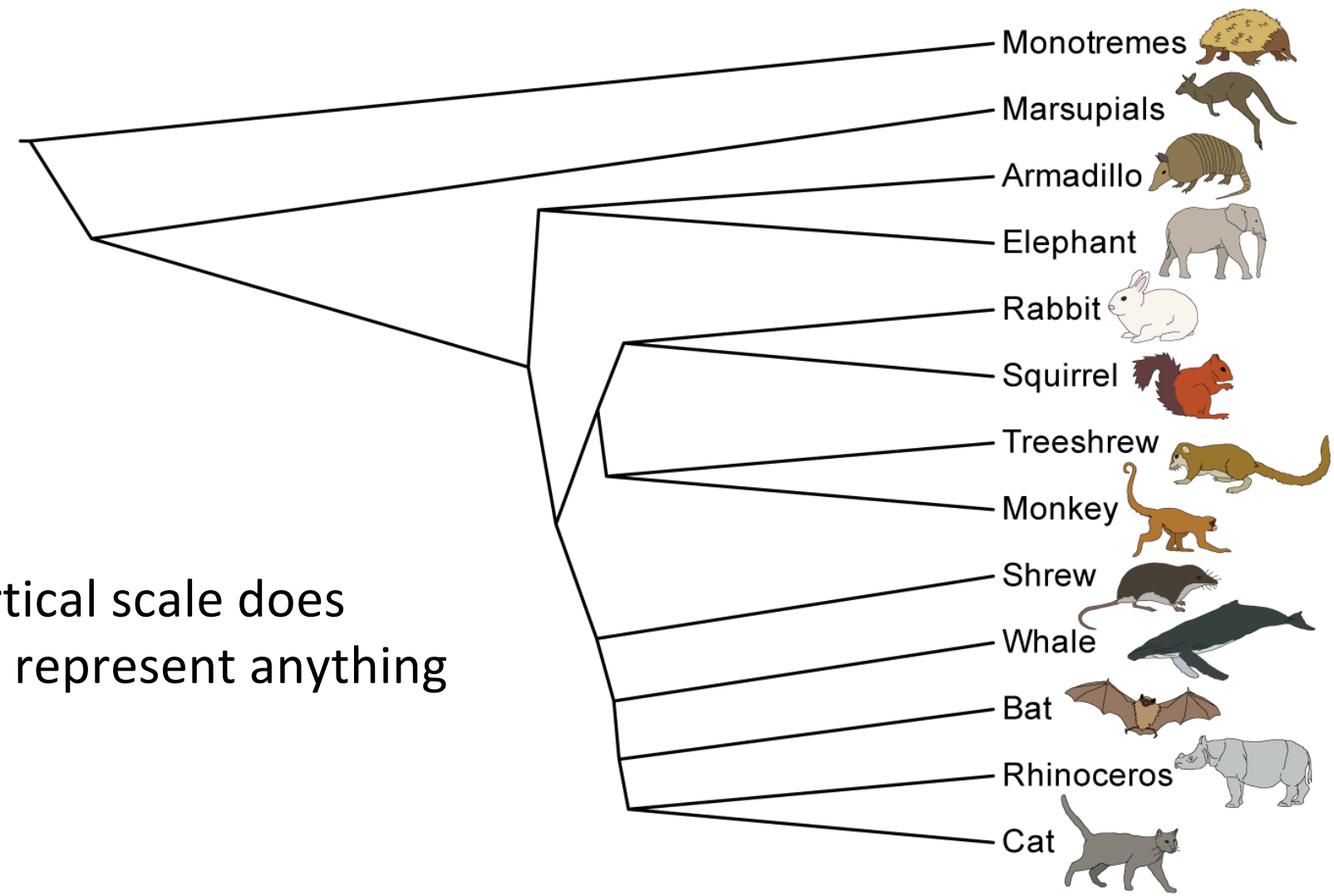
Branch lengths measure amount of evolutionary change

Trees: Chronogram or time-tree



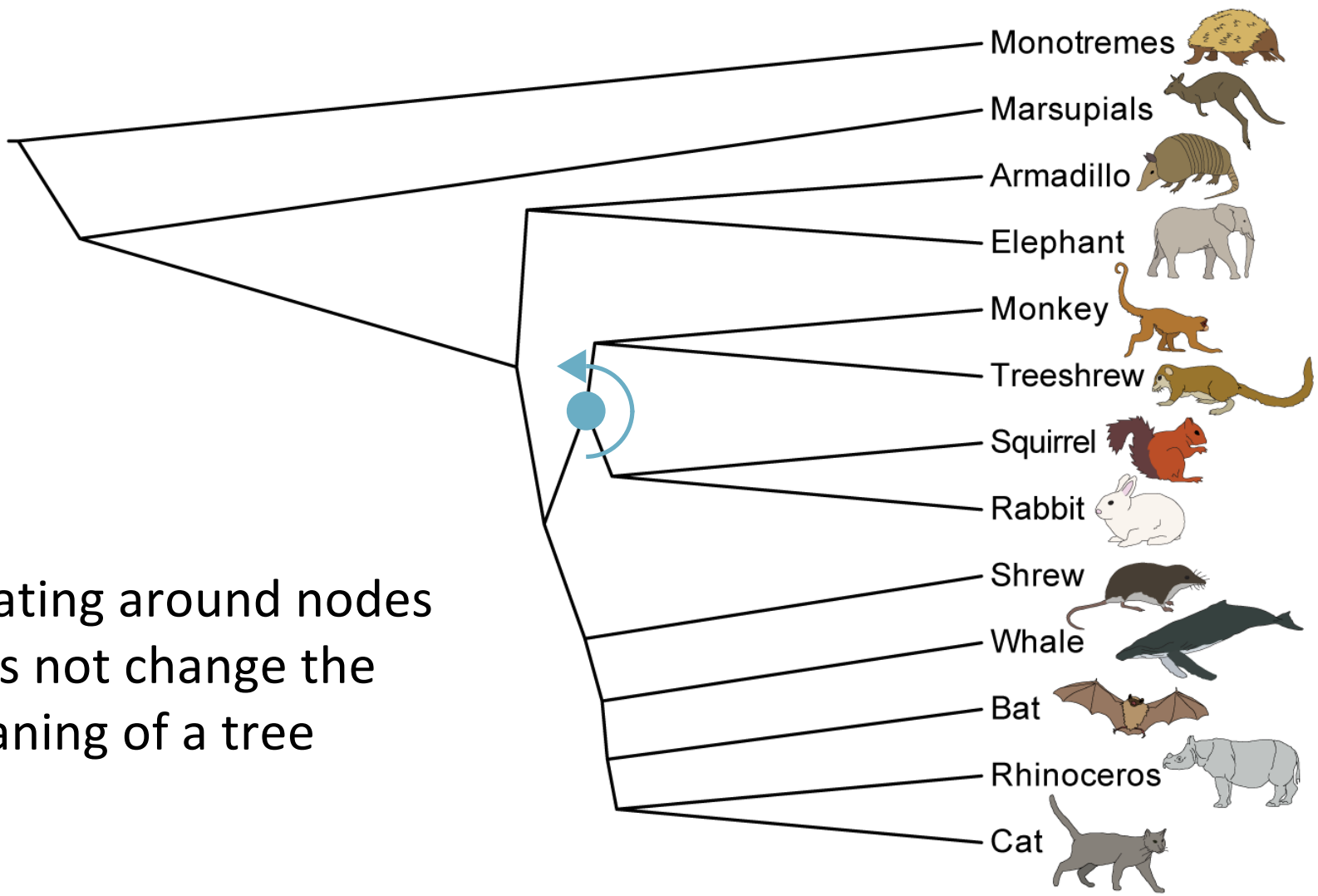
Branch lengths measure time (yr or Myr)

Phylogenetic trees



Vertical scale does not represent anything

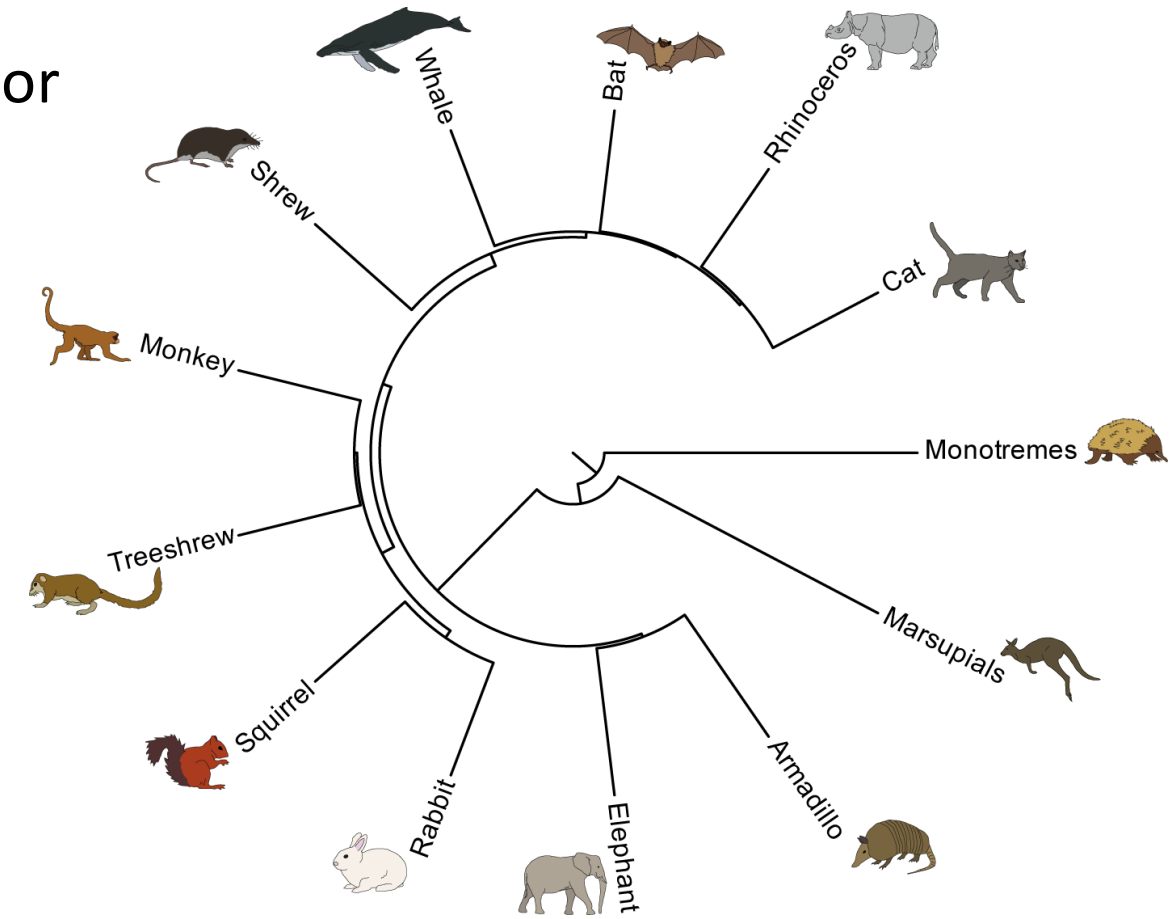
Phylogenetic trees



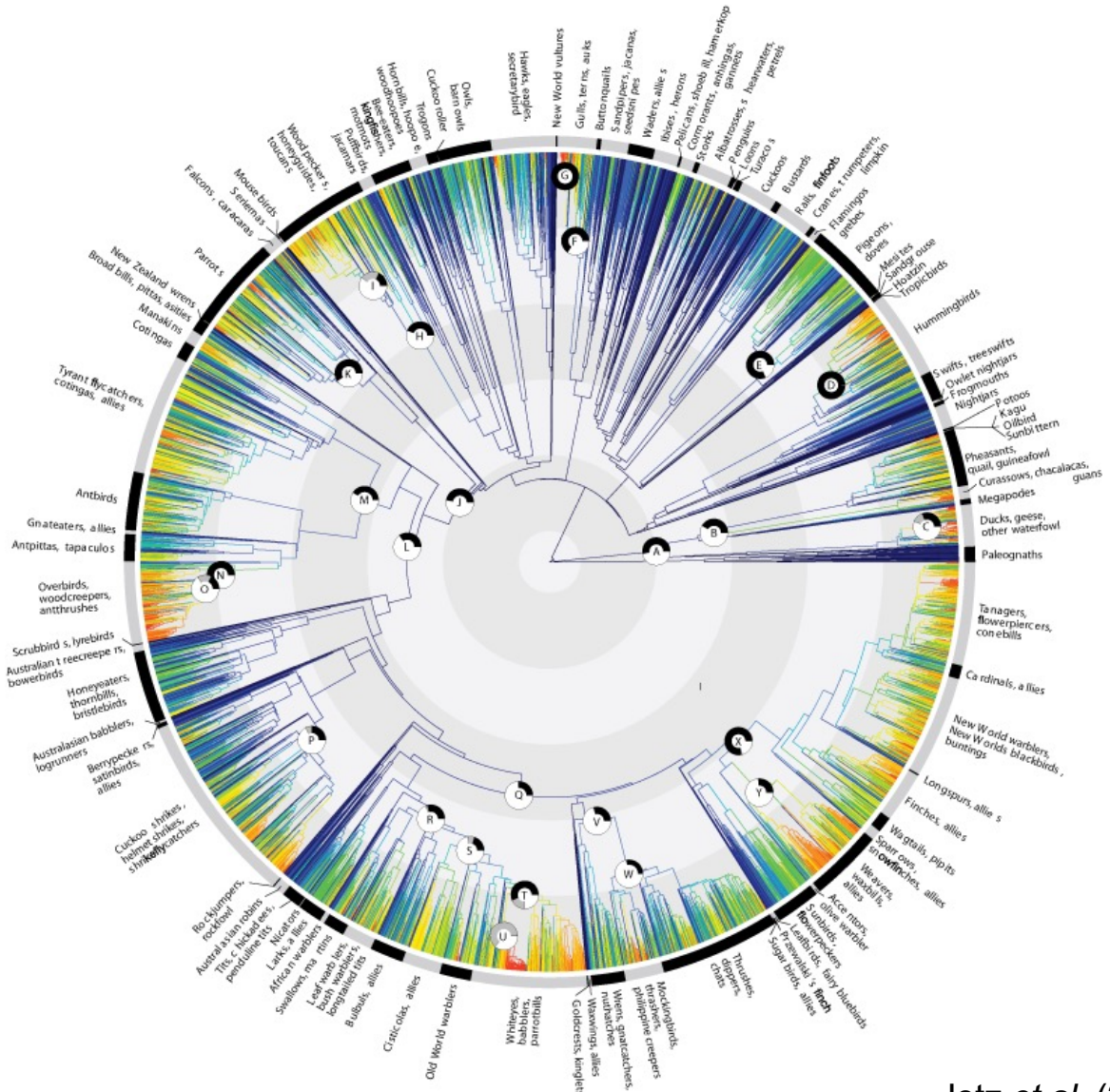
Rotating around nodes does not change the meaning of a tree

Phylogenetic trees: Circular

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

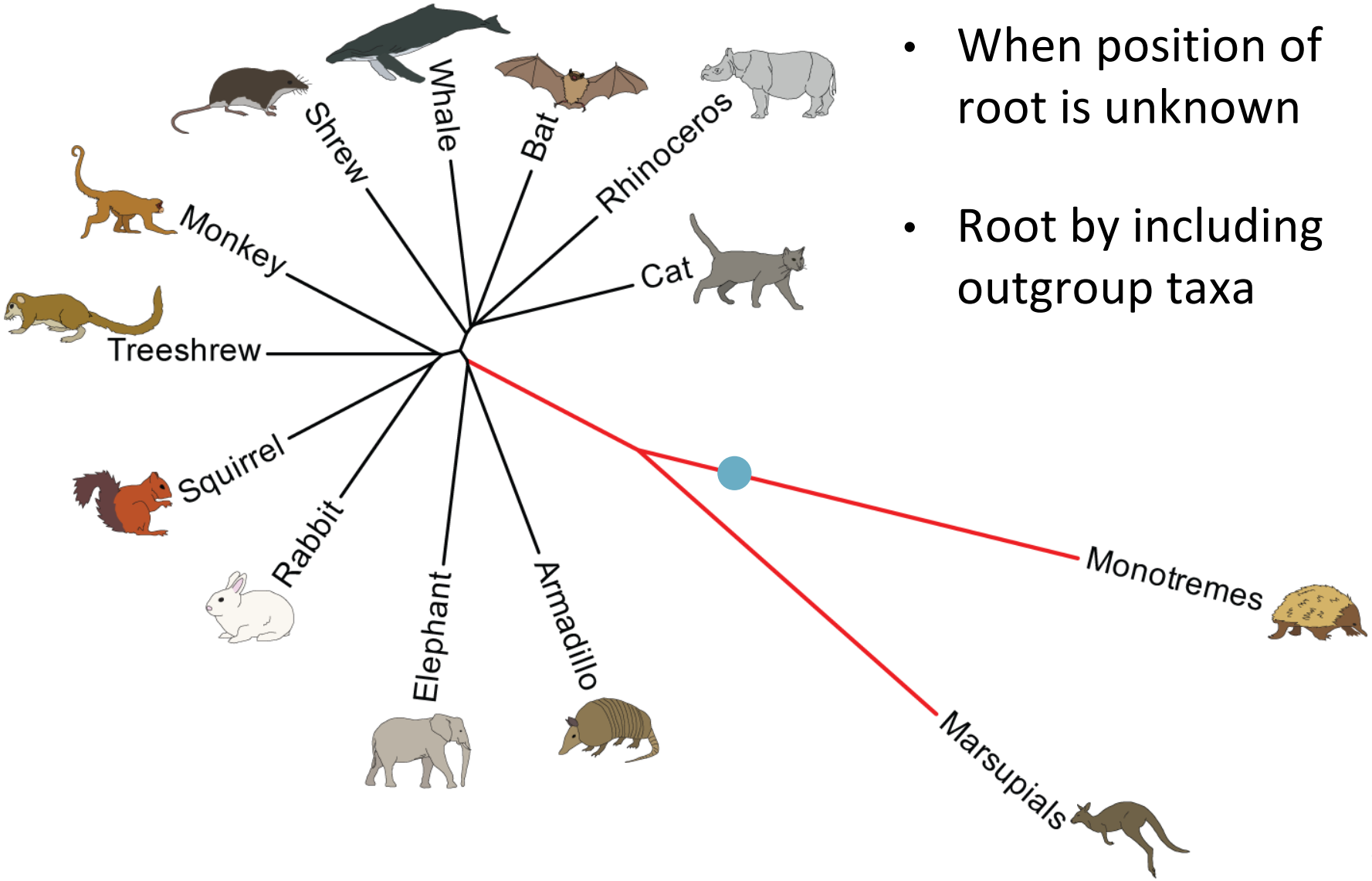


Phylogenetic trees: Circular



Jetz *et al*. (2012) *Nature*

Phylogenetic trees: Unrooted



- When position of root is unknown
- Root by including outgroup taxa

Rooting

- **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

- 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):1.0);

Molecular Phylogenetics

Phylogenetic analysis

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

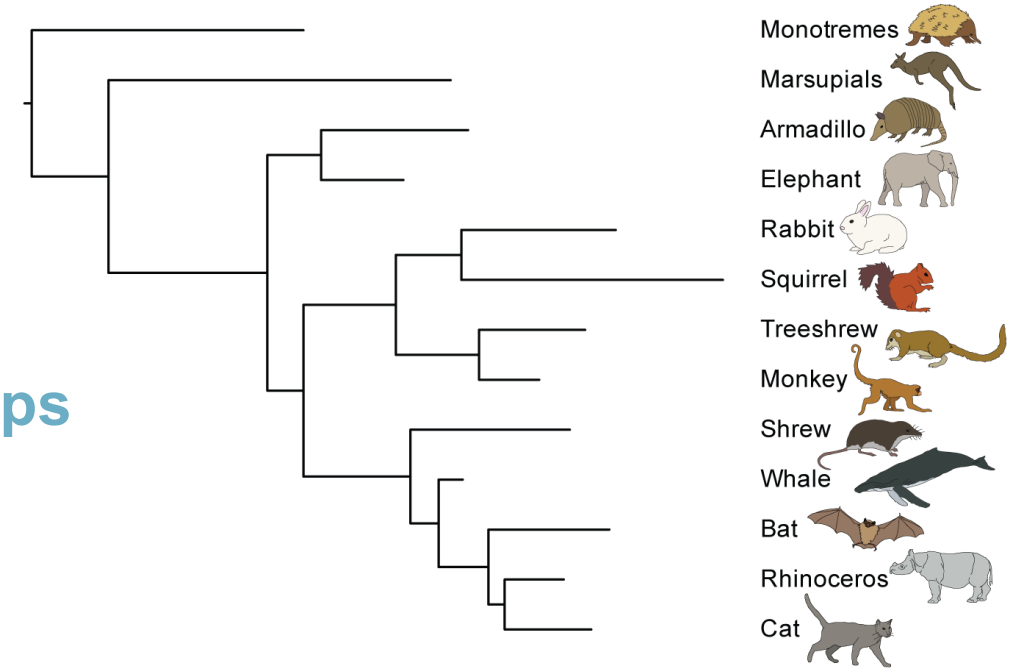
We possess no pedigrees or armorial bearings; and we have to discover and trace the many diverging lines of descent in our natural genealogies, by characters of any kind which have long been inherited

Charles Darwin, 1859

Fundamental assumptions

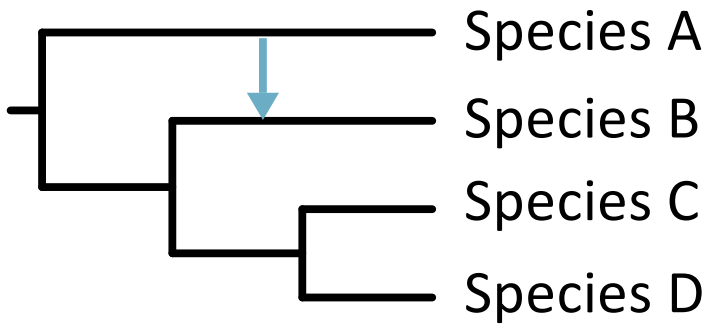
- Phylogenetic methods make several fundamental assumptions:
  - Relationships among taxa can be represented by a tree
  - Homologous characters are being compared
  - Characters are mutually independent

When might relationships not be treelike?

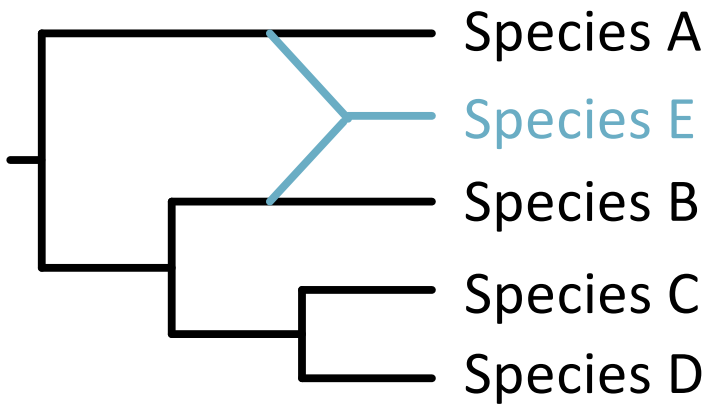


Non-treelike evolution

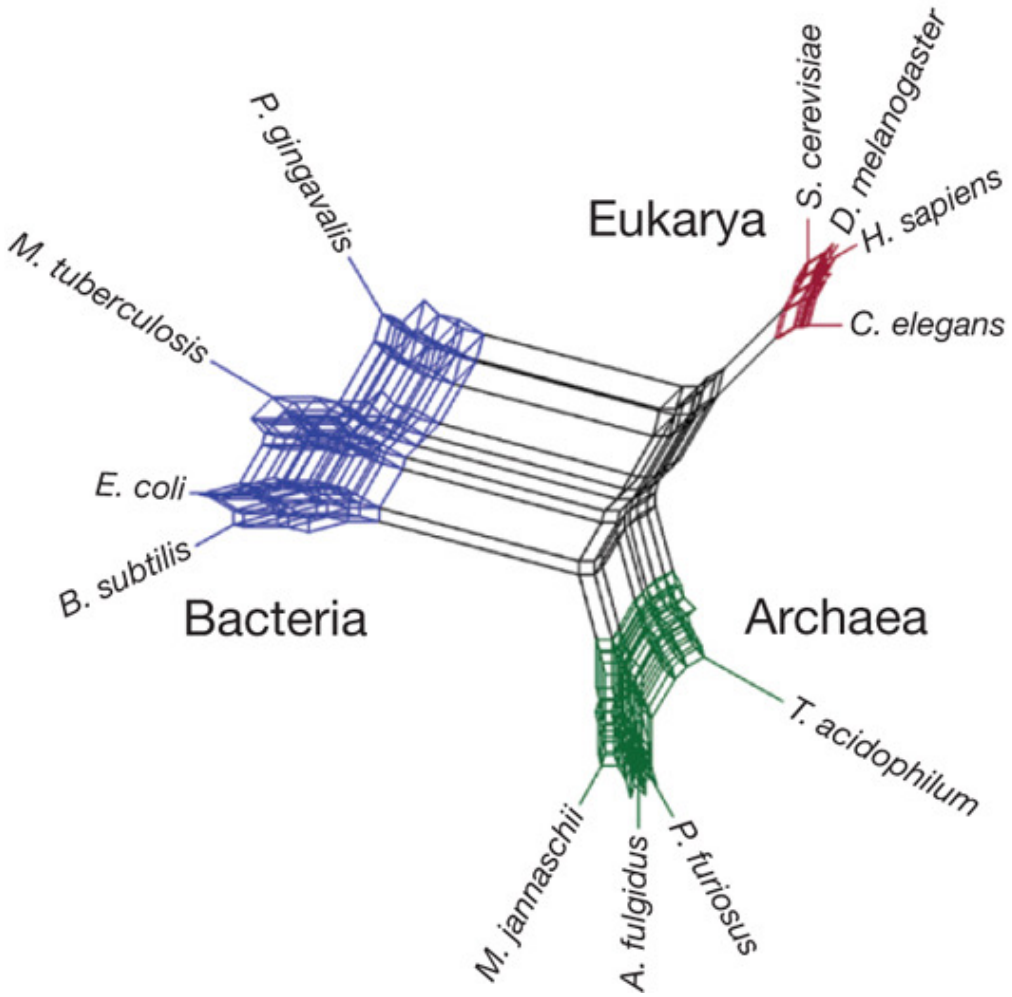
Horizontal gene transfer



Hybrid speciation



Phylogenetic networks



Theobald (2010) *Nature*

Fundamental assumptions

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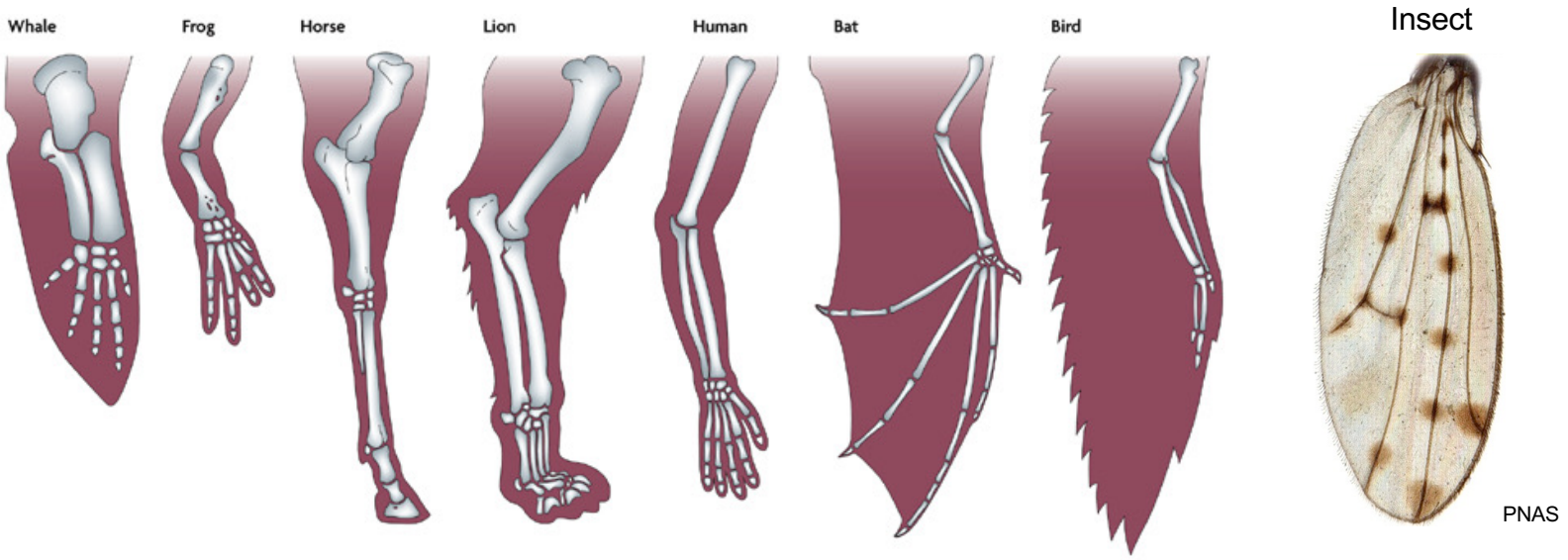


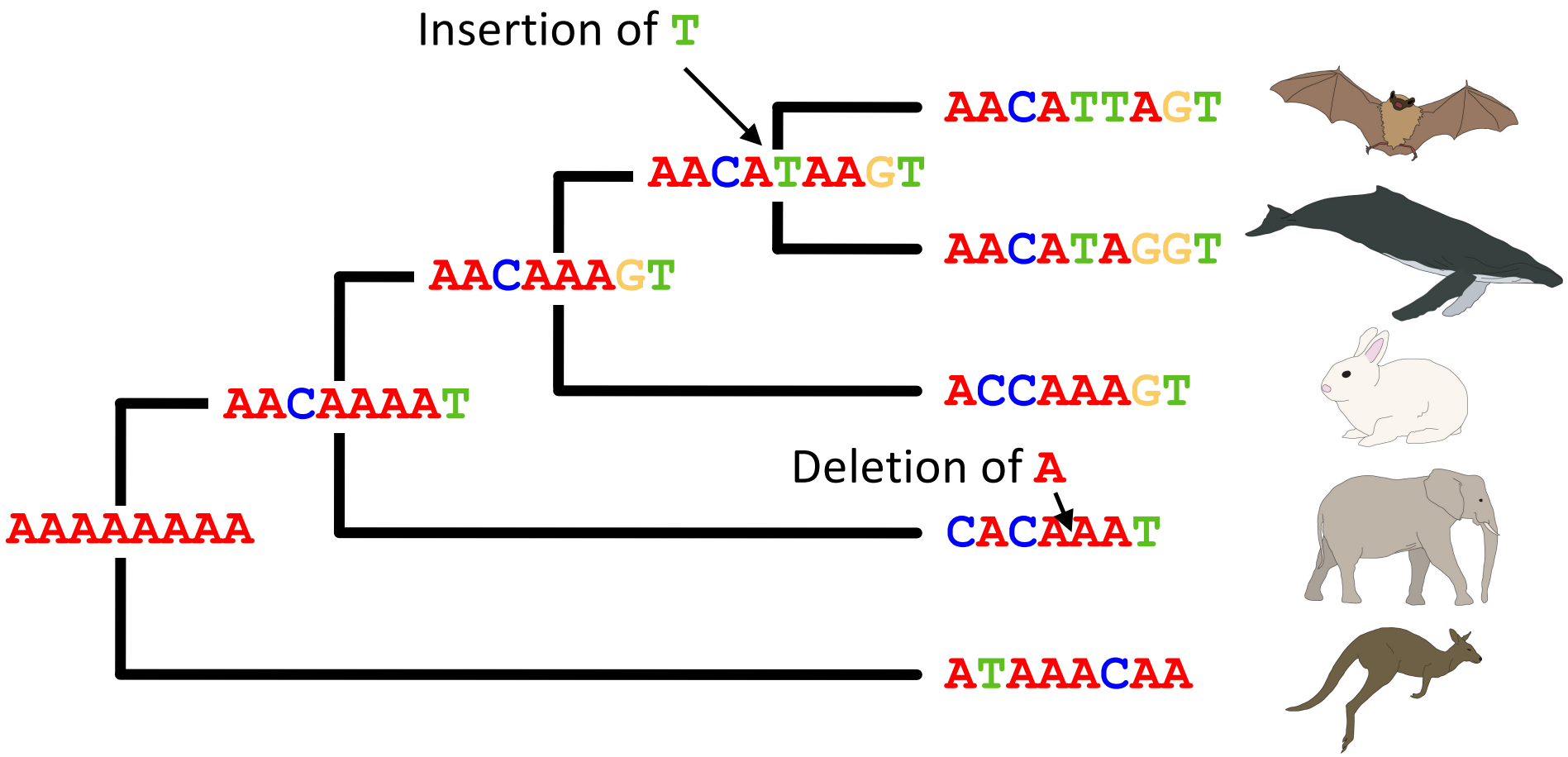
Wagner (2007) *Nat Rev Genet*

Character homology

- 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

AACATTAGT

AACATAGGT

ACCAAAGT

CACAAAT

ATAAACAA

AACATTAGT

AACATAGGT

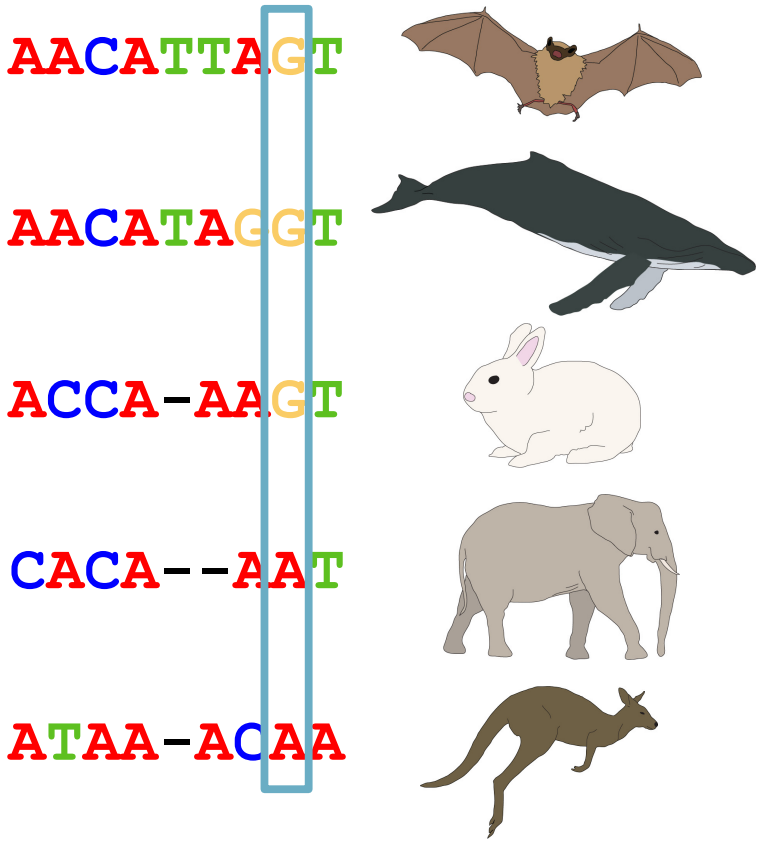
ACCA-AAGT

CACA--AAT

ATAA-ACAA

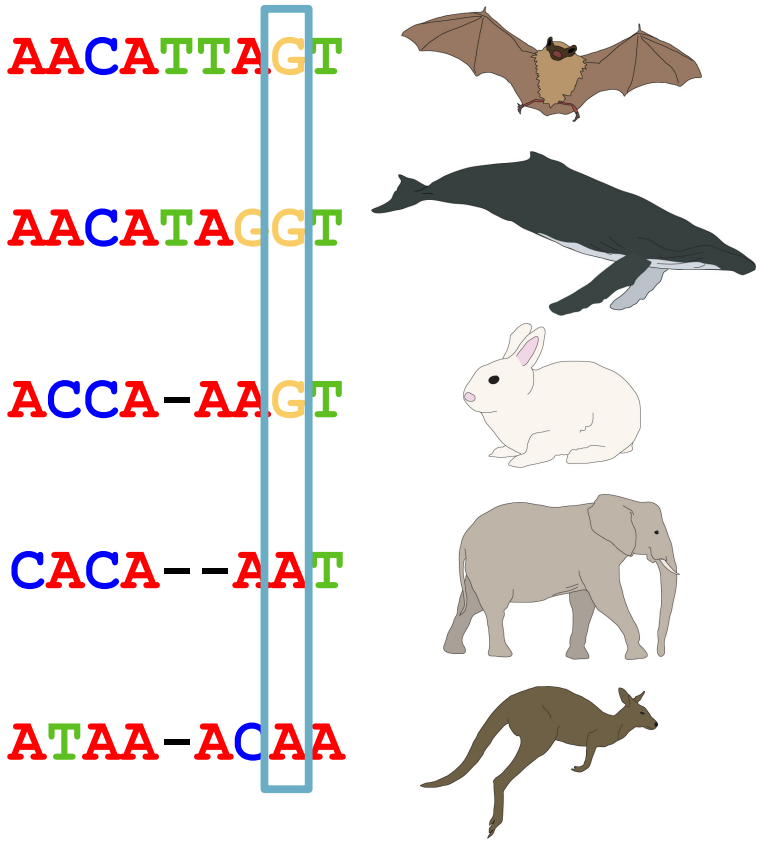
DNA sequence alignment

- Homologous site
- Inherited from the common ancestor of all sequences in the alignment
- The aim of sequence alignment is to maximise the number of sites for which you can infer homology



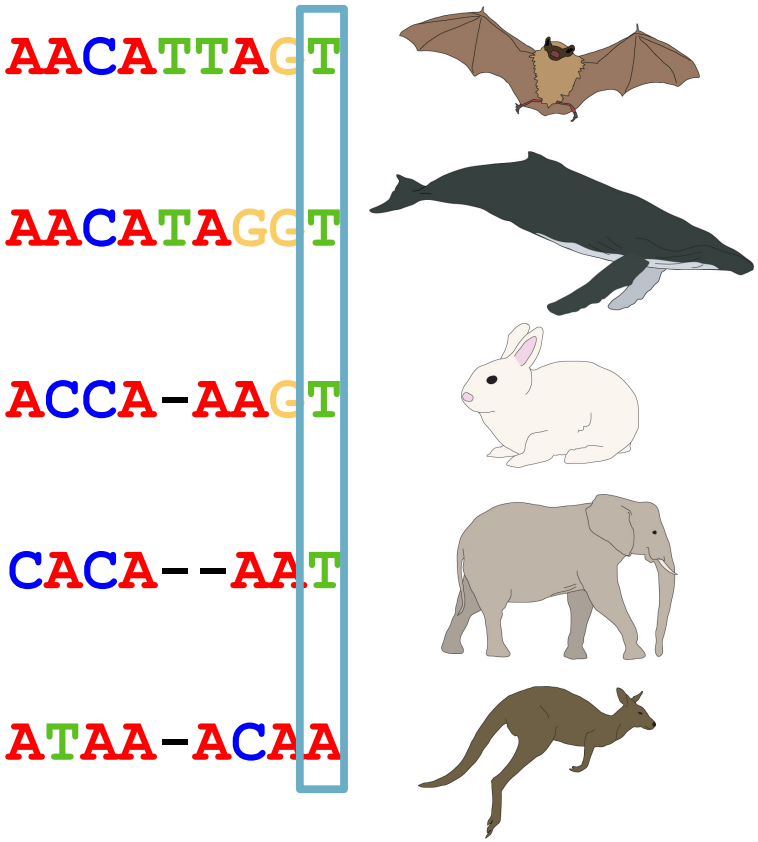
DNA sequence alignment

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



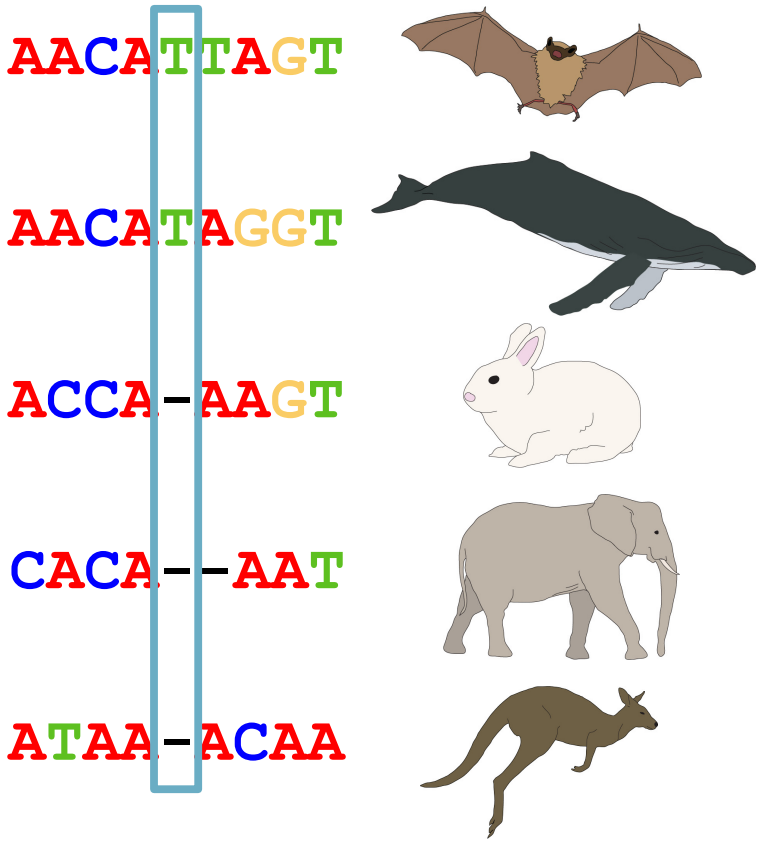
DNA sequence alignment

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



DNA sequence alignment

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



A practical approach

Align sequences using automated methods

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

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[1], Kei-ichi Kuma and Takashi Miyata*

A practical approach

Align sequences using automated methods

↓

Adjust alignments by eye

```
CTATGTGGCACCCAGCCCATGCA--AGC
ATATGTGGCA------CCCAGGCA--AG-
ATATGTGGCACCCAGCCCATGCATTT--
```

A practical approach

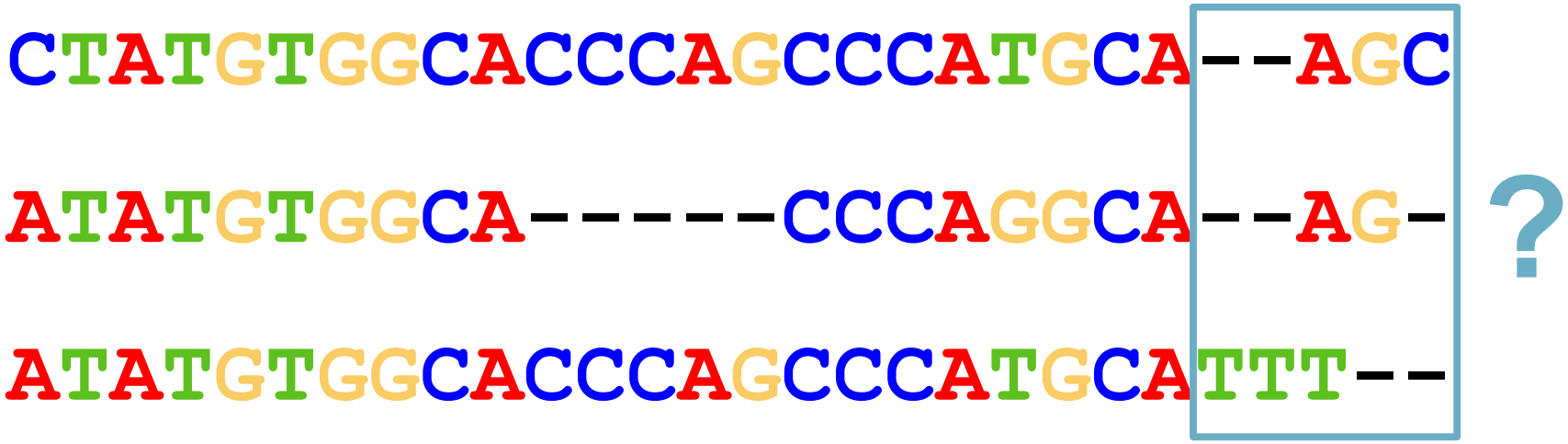
Align sequences using automated methods

↓

Adjust alignments by eye

↓

Delete sites with uncertain homology



Useful references