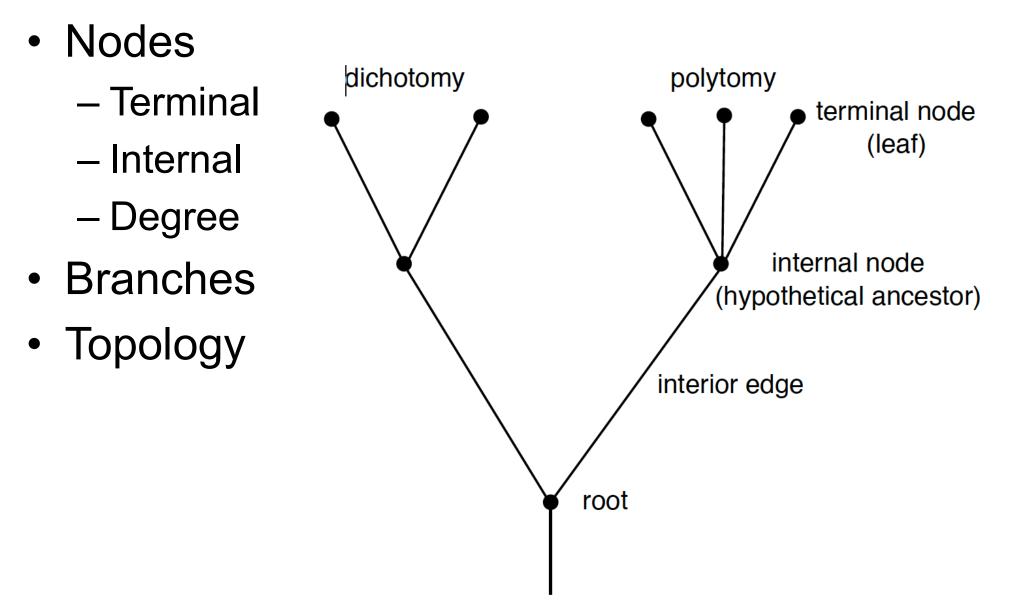
Phylogenetics

What is phylogenetics?

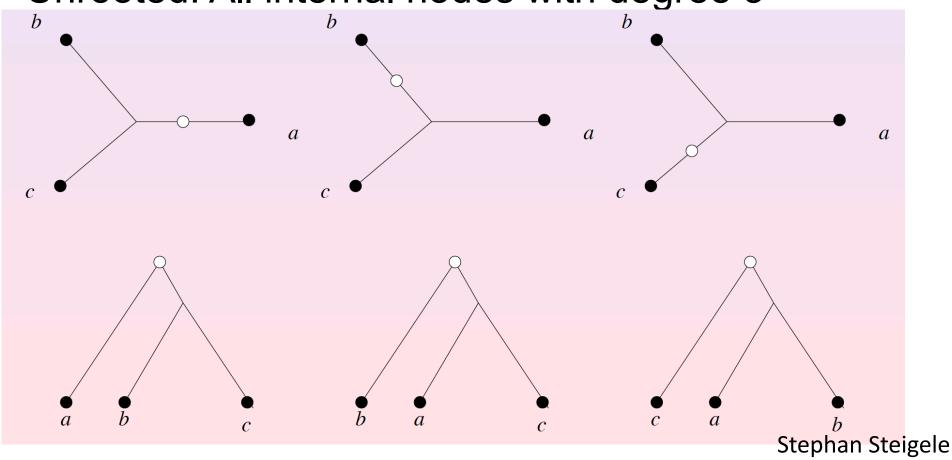
- Study of branching patterns of descent among lineages
- Lineages
 - Populations
 - Species
 - Molecules
- Shift between population genetics and phylogenetics is often the species boundary
 - Distantly related populations also show patterning
 - Patterning across geography

What is phylogenetics?

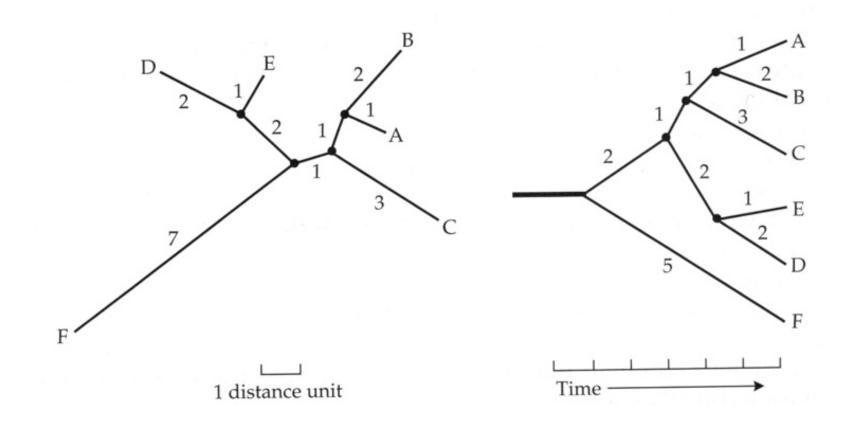
- Goal: Determine and describe the evolutionary relationships among lineages
 - Order of events
 - Timing of events
- Visualization: Phylogenetic trees
 - Graph
 - No cycles



- Rooted or unrooted
 - Rooted: Precisely 1 internal node of degree 2
 - Node that represents the common ancestor of all taxa
 - Unrooted: All internal nodes with degree 3+

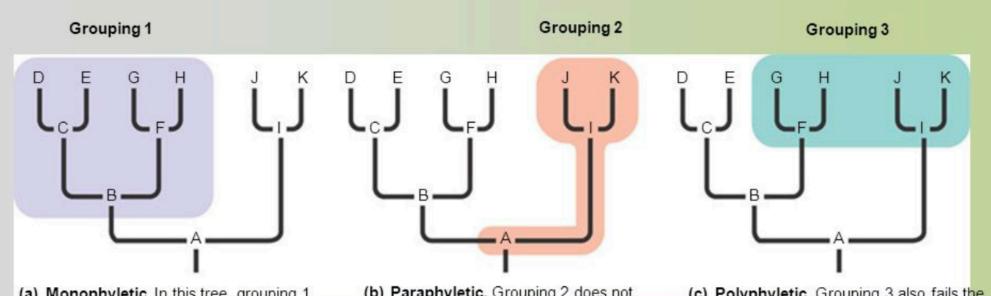


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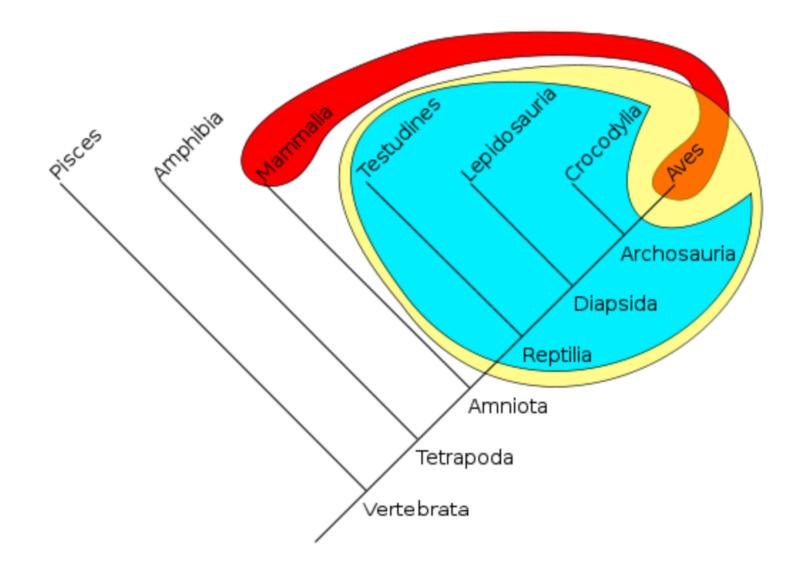
- Rooted or unrooted
 - Rooted: Precisely 1 internal node of degree 2
 - Node that represents the common ancestor of all taxa
 - Unrooted: All internal nodes with degree 3+
- Binary: all speciation events produce two lineages from one
- Cladogram: Topology only
- Phylogram: Topology with edge lengths representing time or distance
- Ultrametric: Rooted tree with time-based edge lengths (all leaves equidistant from root)

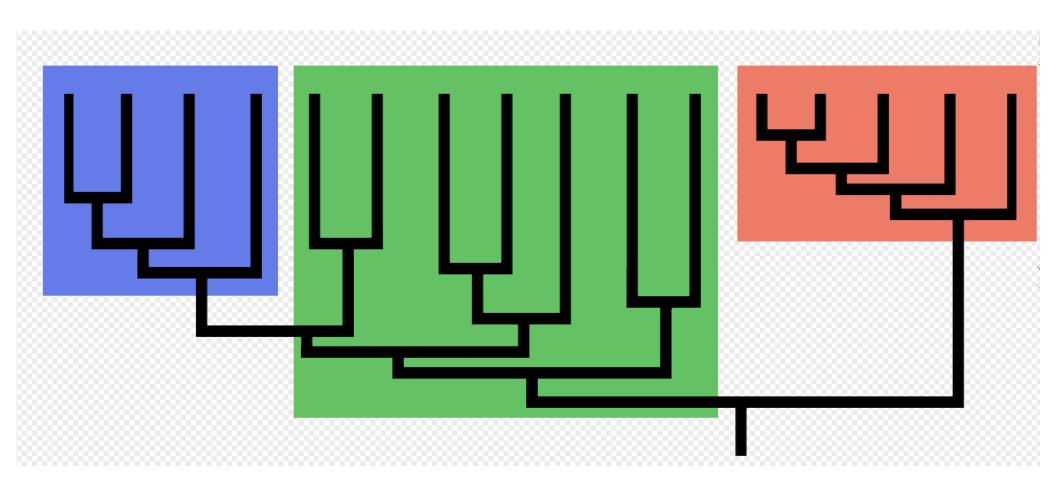
- Clade: Group of ancestral and descendant lineages
- Monophyly: All of the descendants of a unique common ancestor
- Polyphyly: Descendants include lineages from multiple ancestors
- Paraphyly: One or more monophyletic subgroups are left apart from all other descendants of a unique common ancestor

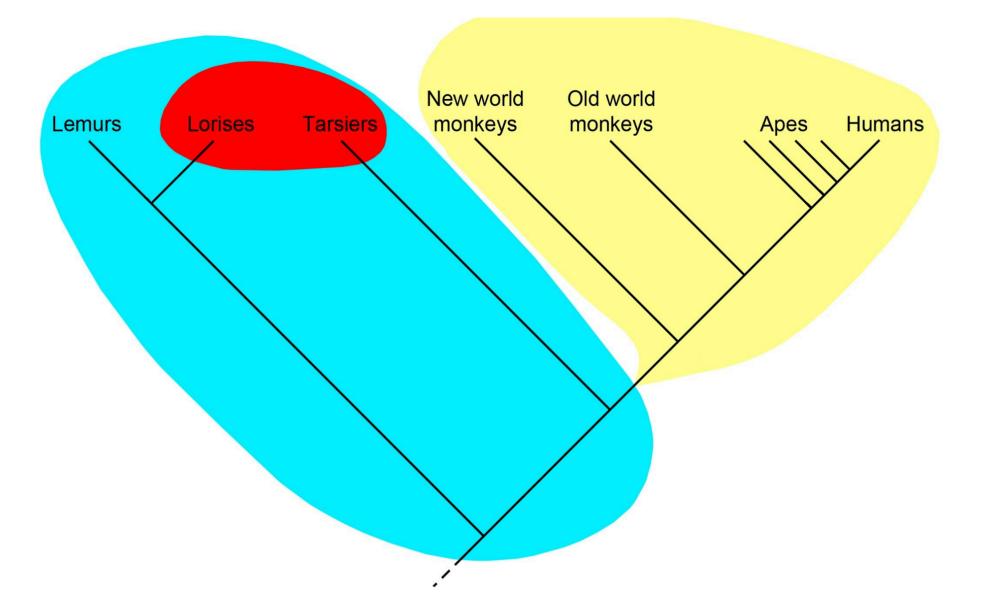


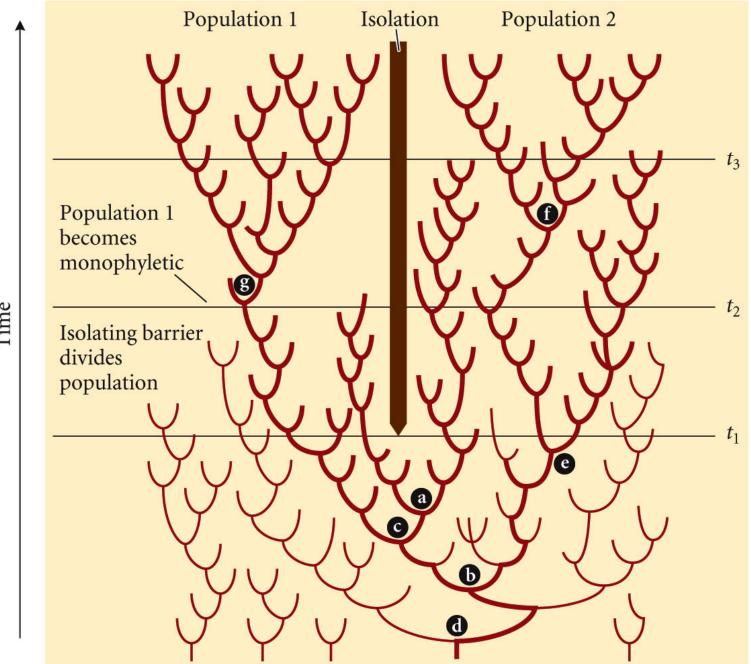
- (a) Monophyletic. In this tree, grouping 1, consisting of the seven species B– H, is a monophyletic group, or clade. A monophyletic group is made up of an ancestral species (species B in this case) and all of its descendant species. Only monophyletic groups qualify as legitimate taxa derived from cladistics.
- (b) Paraphyletic. Grouping 2 does not meet the cladistic criterion: It is paraphyletic, which means that it consists of an ancestor (A in this case) and some, but not all, of that ancestor's descendants. (Grouping 2 includes the descendants I, J, and K, but excludes B–H, which also descended from A.)
- (c) Polyphyletic. Grouping 3 also fails the cladistic test. It is polyphyletic, which means that it lacks the common ancestor of (A) the species in the group. Furthermore, a valid taxon that includes the extant species G, H, J, and K would necessarily also contain D and E, which are also descended from A.



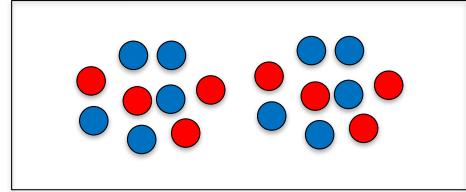


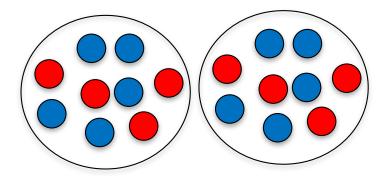


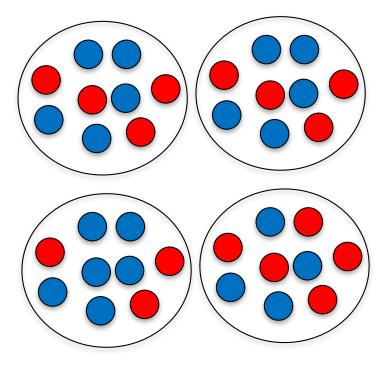


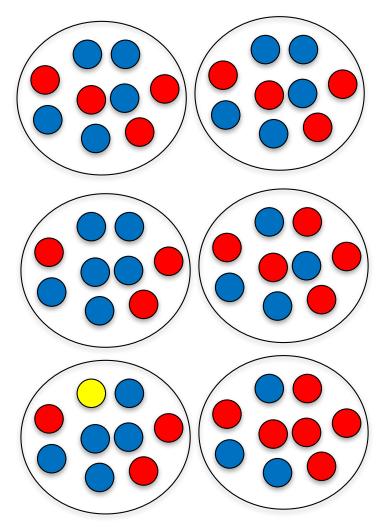


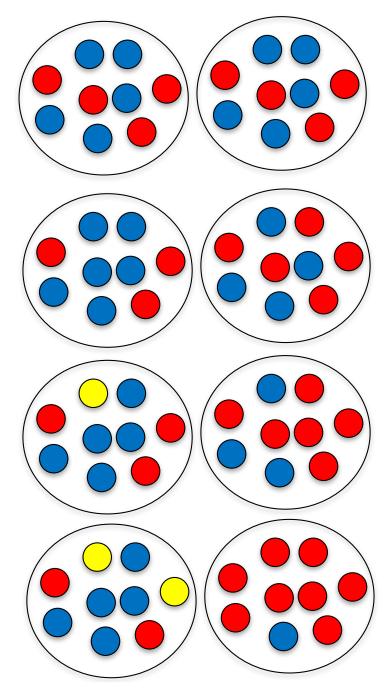
Time











- In each lineage, new mutations are fixed independently
- Each subsequent mutation is placed on a the previously fixed sequence
- Given enough time, each lineage goes through a unique sequence of (nested) fixation events
- Sequential fixation generates a readable history of sequence similarity and differences
- How to read this sequence?
 - Given extant taxa, how to reconstruct history?
 - Use nested shared similarity to infer history

Building phylogenetic trees

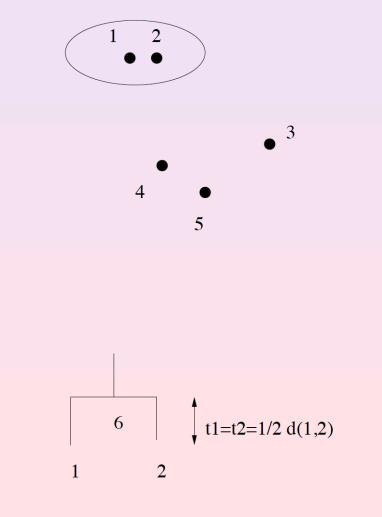
- Distance: Estimate distance matrix given data, generate tree that represents these distances
- Parsimony: Attempts to find a tree that minimizes the number of changes given data
- Maximum likelihood & Bayesian: Model-based approach to find the most-likely tree given the data

- Compute a distance matrix given a set of biological data
 - UPGMA
 - Neighbor joining
- Compute a tree that most resembles this distance matrix

- Unweighted pair group method using arithmetic averages (UPGMA)
- Given a set of taxa and a distance matrix, UPGMA produces a rooted tree with edge lengths
- Clusters taxa, then merging clusters
- Assembled outside in

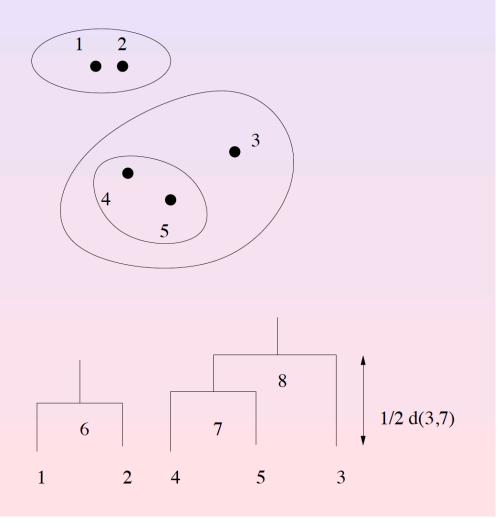
Example $X = \{1, 2, 3, 4, 5\}$, distances given by distance in the plane:

cluster 1 and 2:



Stephan Steigele

cluster 7 and 3:

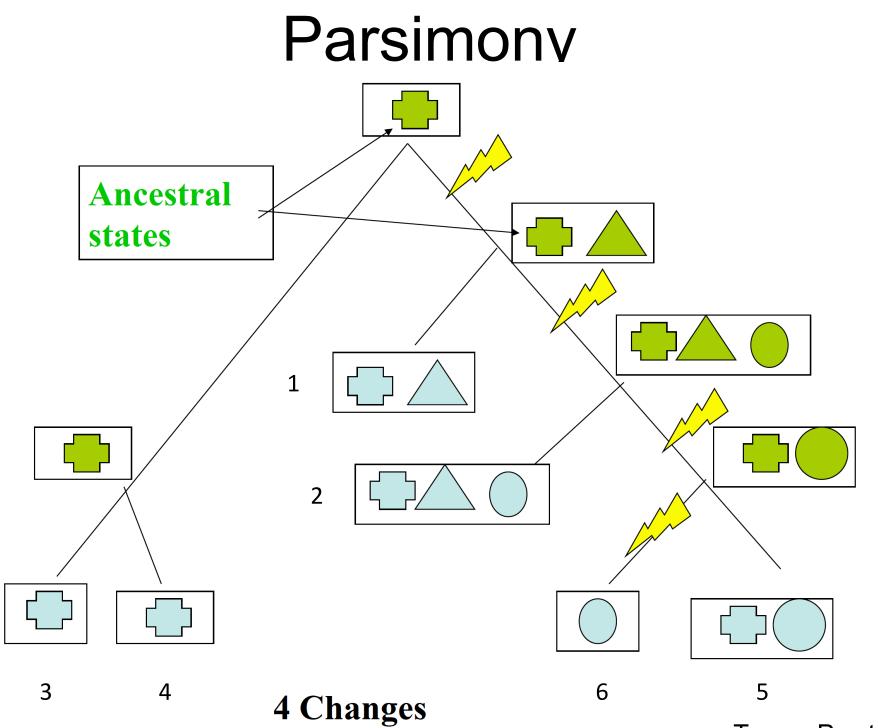


Stephan Steigele

- Neighbor-Joining (NJ)
- Saitou and Nei 1987
- Given distance matrix, produces an unrooted phylogenetic tree with edge lengths
- Repeatedly pairing neighboring taxa
- Determine which nodes are neighbors based only on distance matrix

- The preferred evolutionary tree is the one that requires "the minimum net amount of evolution" (Edwards and Cavalli-Sforza, 1963)
- Each taxon described by a set of characters
- Each character can be in one of a finite number of states
- Steps = changes in character states
- Goal: Find the tree that explains the distribution of character sets across taxa with the fewest number of steps

Taxon1	Yes	Yes	No
Taxon 2	YES	Yes	Yes
Taxon 3	Yes	No	No
Taxon 4	Yes	No	No
Taxon 5	Yes	No	Yes
Taxon 6	No	No	Yes



Teresa Przytycka

- Binary characters
- Multistate characters
- Ordered changes
- Reversible changes

- Fitch
- Wagner
- Dollo
- Carmin-Sokal
- prefect

Maximum likelihood

- Given a set of biological data, and a probabilistic model of evolution, find the tree that has the highest probability of generating the data
 - Multiple sequence alignment
 - Nucleotide substitution model

Tree Search methods

- Exhaustive search (exact)
- Branch and bound (exact)
- Heuristic (approximate)

Exhaustive

• Evaluate lengths of every possible tree

Number of Taxa	Number of trees
3	1
5	15
10	2,027,025
20	10 ²⁰
50	10 ⁷⁴

Branch and Bound

- Hendy and Penny 1982
- Much faster, still guaranteed to find the best tree
- Determine upper bound of length of shortest tree

Follow predictable search path through tree possible tree topology

 Abandon any fork of search tree where the upper bound is exceeded before the last taxon is added

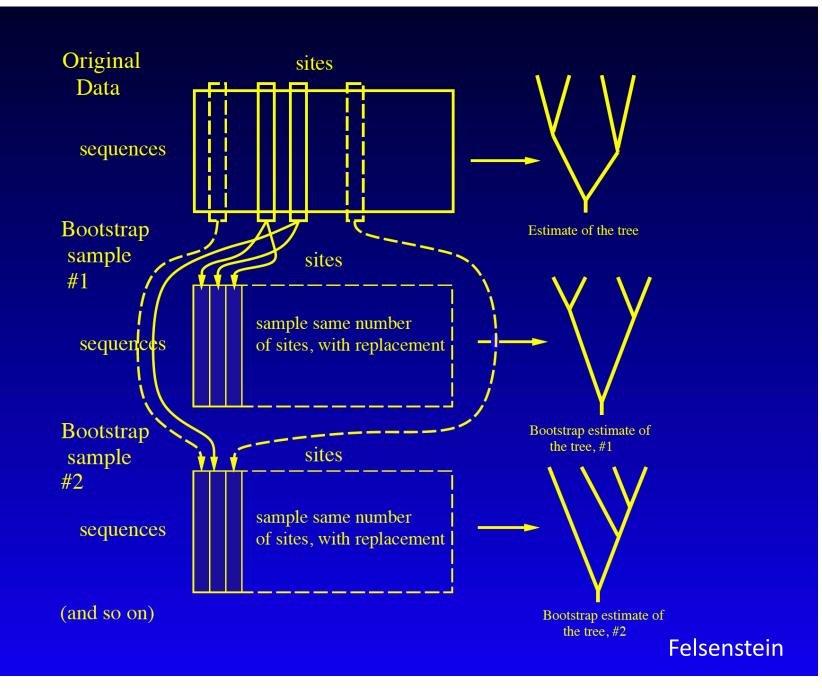
Heuristic

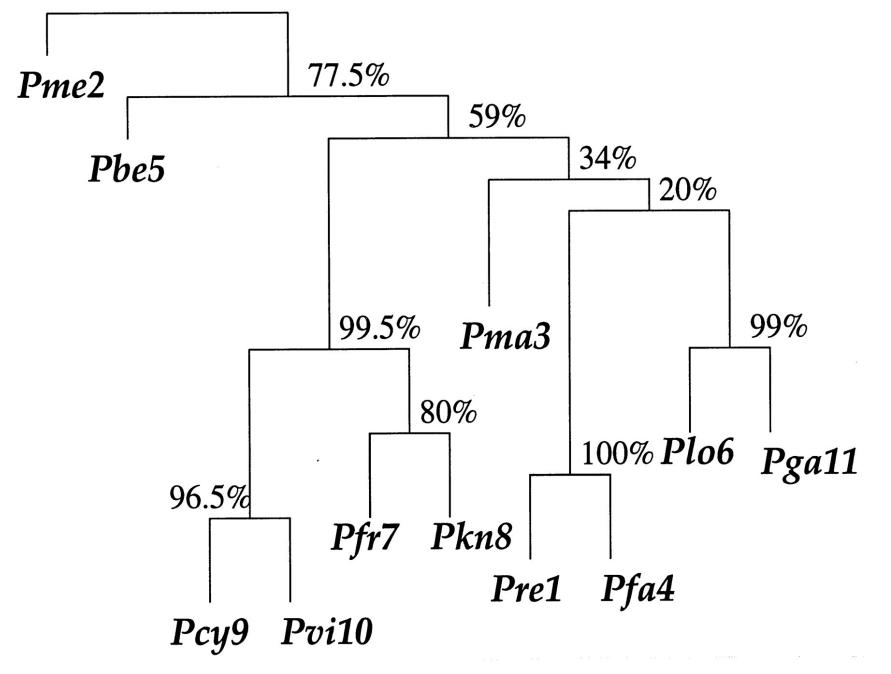
- Search trees by swapping
- Very fast
- Find a starting tree
 - Stepwise addition
 - Star decomposition
- Rearrange tree to find better trees
 - Nearest neighbor Interchange (NNI)
 - Subtree pruning and regrafting (SPR)
 - Tree bisection and Reconnection (TBR)

Heuristic

- Bootstrap
 - Randomly resample the data with replacement
 - Rebuild tree
 - What fraction of the bootstrap samples show support for a particular node?

Heuristic

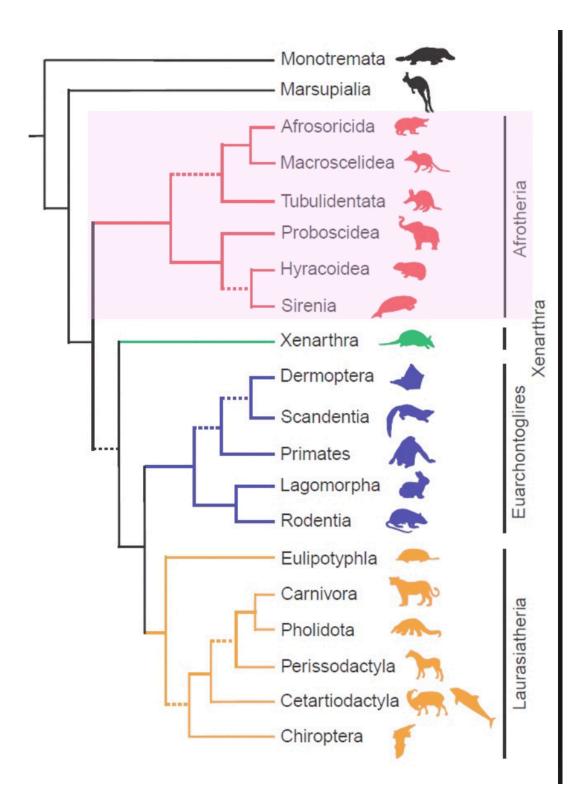


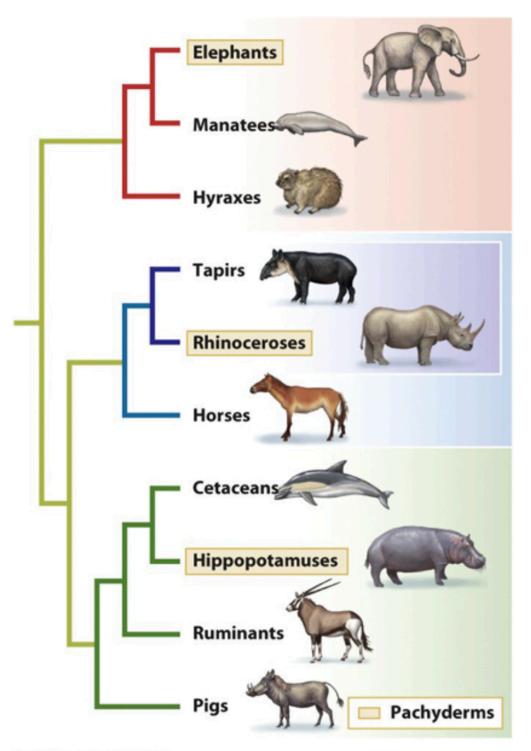


Efron et al. 1996

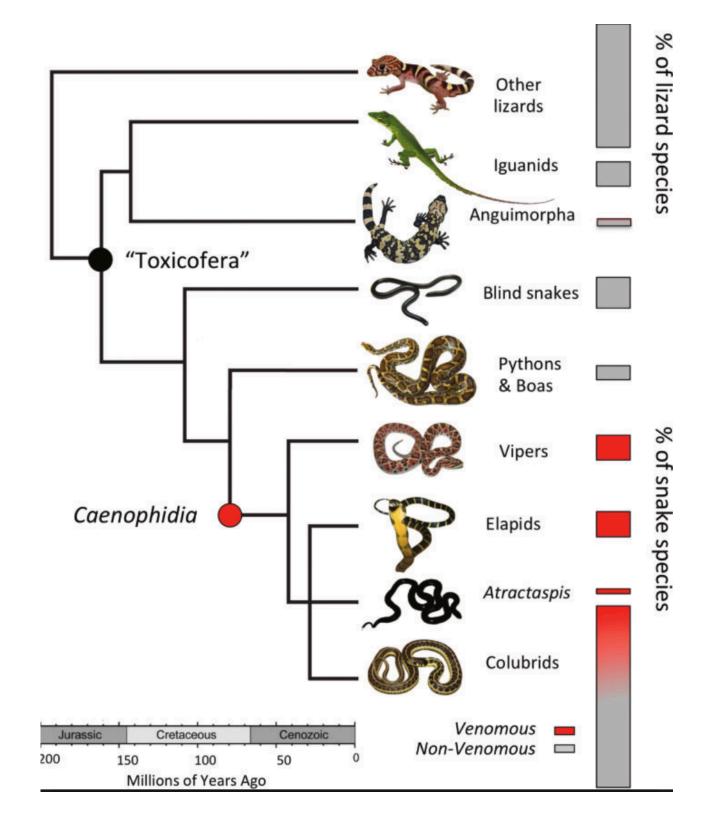
Heuristic

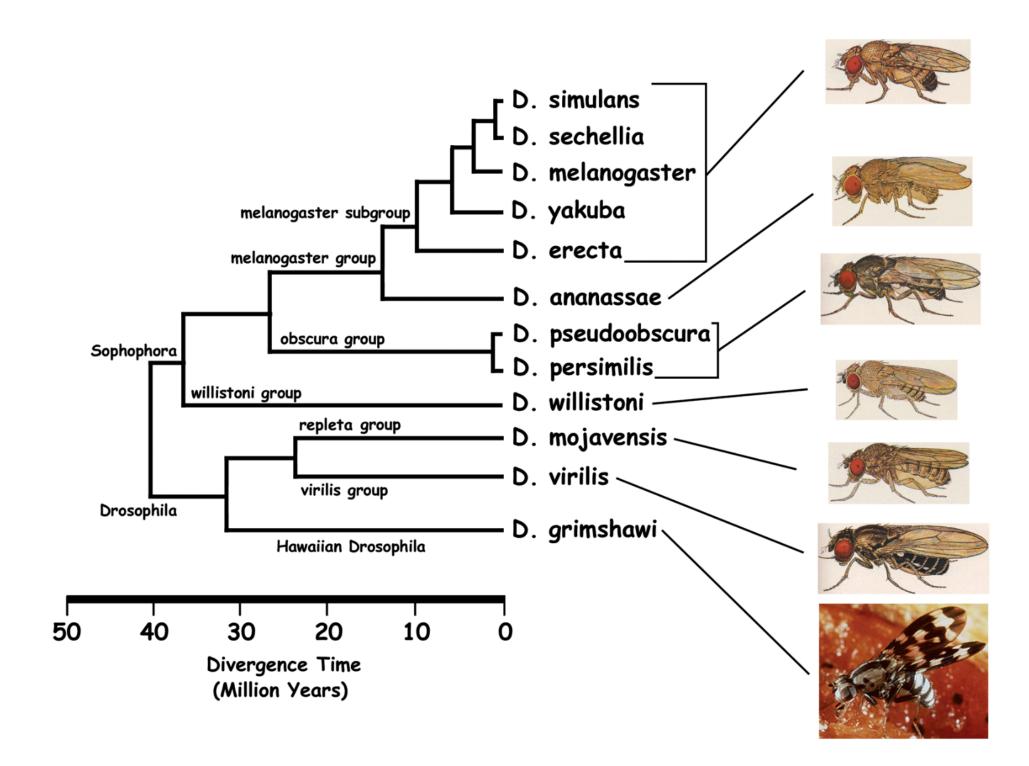
- Bootstrap
 - Randomly resample the data with replacement
 - Rebuild tree
 - What fraction of the bootstrap samples show support for a particular node?
- Jackknife
 - Randomly subset data
 - Rebuild tree
 - What fraction of jackknife samples show support for particular node
 - Whether excluding certain characters has major effect on tree

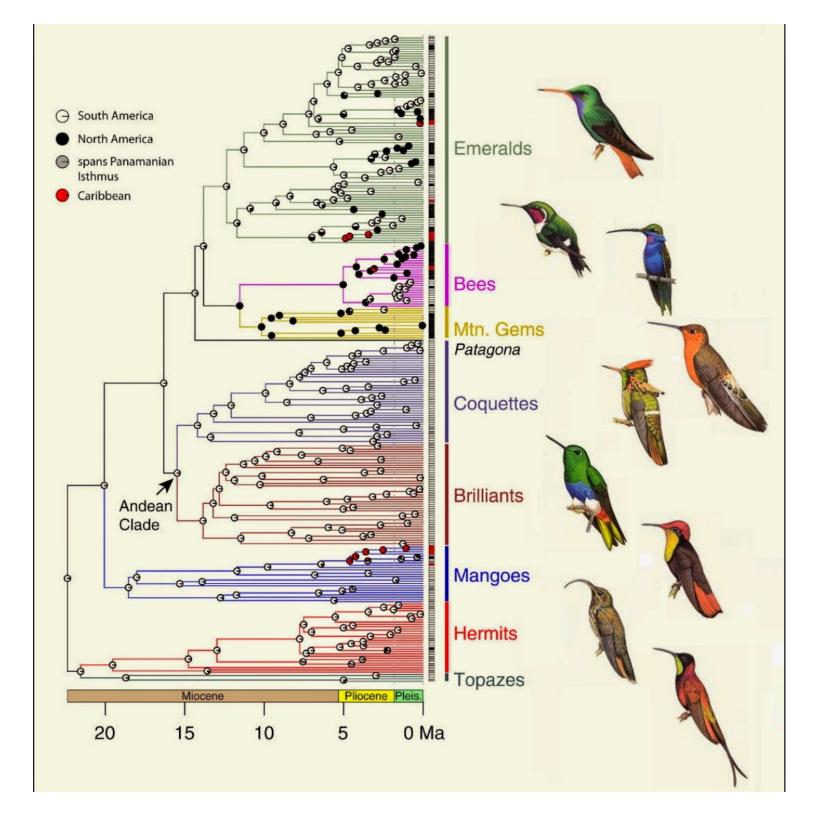


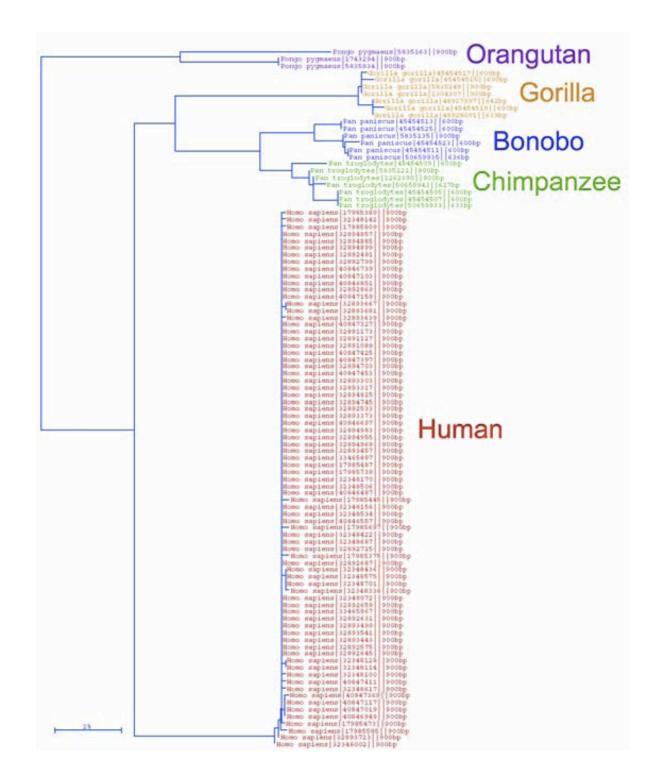


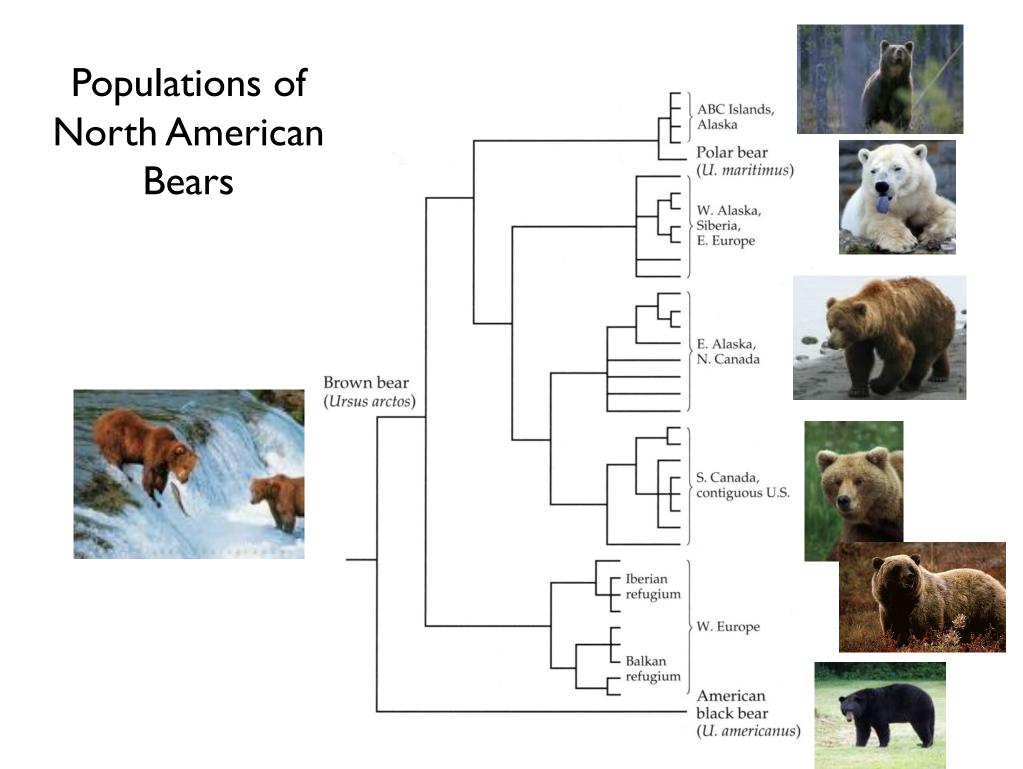
Evolution, 1/e Figure 4.11 © 2012 W. W. Norton & Company, Inc.











Software: PHYLIP

- Joe Felsenstein (1980)
- Over 29,000 registered users
- Parsimony, distance matrix, ML
- DNA, RNA, protein, restriction sites, discrete characters, continuous characters, allele frequencies, distance matrices
- Freely available
- <u>http://evolution.gs.washington.edu/phylip.html</u>
- Webservers available as well

Software: MEGA

- Molecular Evolutionary Genetic Analysis
- Sudhir Kumar
- Parsimony, distance matrix, ML
 - NJ
 - UPGMA
 - Minimum evolution
- Molecular data (nucleic acid, protein sequences)
- Bootstrapping, consensus trees
- Data editing
- Sequence alignment (with ClustalW)
- http://www.megasoftware.net

Software: EMBOSS

- European Molecular Biology Open Software Suite
- Peter Rice, Alan Bleasby, Jon Ison
- General sequence analysis
- Phylogeny (PHYLIP)
- Alignment (CLUSTAL)
- All sequence formats
- Many alignment formats
- http://emboss.sourceforge.net/what/

Software: Mesquite

- Wayne and David Maddison, Peter Midford, Danny Mandel, Jeff Oliver
- Set of Java modules for comparative biology
 - Over 500 functions available for data editing, management, and processing
 - Sequence alignment, visualization
 - Coalescent simulations
 - Inferences of fit of gene tree to species tree
 - Reconstruction of ancestral state (ML, parsimony)
 - Tree visualization, manipulation
- http://mesquiteproject.org



- 392 phylogeny packages
- 54 free webservers
- Most comprehensive list

Table of contents by methods available

- General-purpose packages
- <u>Parsimony programs</u>
- Distance matrix methods
- Computation of distances
- <u>Maximum likelihood methods</u>
- <u>Bayesian inference methods</u>
- Quartets methods
- <u>Artificial-intelligence and genetic algorithms methods</u>
- Invariants (or Evolutionary Parsimony) methods
- Interactive tree manipulation
- Looking for hybridization or recombination events
- Bootstrapping and other measures of support
- Compatibility analysis
- Consensus trees, subtrees, supertrees, distances between trees

- Tree-based alignment
- <u>Gene duplication and genomic analysis</u>
- Biogeographic analysis and host-parasite comparison
- <u>Comparative method analysis</u>
- Simulation of trees or data
- Examination of shapes of trees
- Clocks, dating and stratigraphy
- Model Selection
- Description or prediction of data from trees
- Tree plotting/drawing
- Sequence management/job submission
- Teaching about phylogenies
- <u>Web or e-mail servers that can analyze data for you</u>

Joe Felsenstein

http://evolution.gs.washington.edu

General-purpose packages

- <u>PHYLIP</u>
- <u>PAUP*</u>
- <u>MEGA</u>
- Phylo win
- <u>ARB</u>
- DAMBE
- <u>PAL</u>
- **Bionumerics**
- <u>Mesquite</u>
- <u>PaupUp</u>
- <u>BIRCH</u>
- <u>Bosque</u>
- EMBOSS
- phangorn
- <u>Bio++</u>
- <u>ETE</u>
- <u>DendroPy</u>
- <u>SeaView</u>
- <u>Crux</u>

Parsimony programs

- <u>PHYLIP</u>
- <u>PAUP*</u>
- <u>Hennig86</u>
- <u>MEGA</u>
- <u>RA</u>
- <u>NONA</u>
- <u>CAFCA</u>
- <u>PHYLIP</u>
- <u>Phylo win</u>
- <u>sog</u>
- <u>gmaes</u>
- <u>LVB</u>
- <u>GeneTree</u>
- <u>ARB</u>
- DAMBE
- <u>MALIGN</u>
- <u>POY</u>
- <u>Gambit</u>
- <u>TNT</u>
- <u>GelCompar II</u>
- <u>Bionumerics</u>
- <u>Network</u>
- <u>TCS</u>
- <u>GAPars</u>
- <u>CRANN</u>

- <u>Mesquite</u>
- <u>PAST</u>
- FootPrinter
- **BPAnalysis**
- <u>Simplot</u>
- <u>Parsimov</u>
- <u>NimbleTree</u>
- <u>PaupUp</u>
- <u>Notung</u>
- <u>BIRCH</u>
- <u>IDEA</u>
- <u>PSODA</u>
- <u>PRAP</u>
- <u>SeqState</u>
- Bosque
- <u>PhyloNet</u>
- EMBOSS
- phangorn
- <u>Murka</u>
- Freqpars
- <u>SeaView</u>
- <u>PAUPRat</u>

Joe Felsenstein

http://evolution.gs.washington.edu

Distance matrix methods

- PHYLIP
- <u>PAUP*</u>
- <u>MEGA</u>
- <u>MacT</u>
- <u>ODEN</u>
- TREECON
- <u>DISPAN</u>
- <u>RESTSITE</u>
- NTSYSpc
- <u>METREE</u>
- <u>GDA</u>
- <u>SeqPup</u>
- PHYLTEST
- Lintre
- Phylo win
- POPTREE2
- Gambit
- gmaes
- DENDRON
- <u>BIONJ</u>
- TFPGA
- <u>MVSP</u>
- <u>ARB</u>
- Darwin

- <u>T-REX</u>
- <u>sendbs</u>
- <u>nneighbor</u>DAMBE
- <u>DANDE</u>
- <u>weighbor</u>
- DNASIS
- <u>MINSPNET</u>
- <u>PAL</u>
- <u>Arlequin</u>
- <u>PEBBLE</u>
- <u>HY-PHY</u>
- <u>Vanilla</u>
- <u>GelCompar II</u>
- Bionumerics
- <u>qclust</u>
- <u>TCS</u>
- Populations
- <u>Winboot</u>
- <u>SYN-TAX</u>
- **PTP**
- SplitsTree
- FastME
- APE
- <u>MacVector</u>
- <u>QuickTree</u>

- <u>Simplot</u>
- <u>ProfDist</u>
- <u>START2</u> • STC
- NimbleTree
- <u>CBCAnalyzer</u>
- PaupUp
- Geneious
- <u>BIRCH</u>
- <u>SEMPHY</u>
- FASTML
- <u>Rate4Site</u>
- <u>SWORDS</u>
- <u>IDEA</u>
- <u>FAMD</u>
- <u>Bosque</u>
- <u>GAME</u>
- **Bioinformatics Toolbox**
- <u>TreeFit</u>
- EMBOSS
- phangorn
- <u>PC-ORD</u>
- <u>Bio++</u>
- <u>UGENE</u>
- <u>NINJA</u>

Joe Felsenstein

http://evolution.gs.washington.edu

- <u>SeaView</u>
- <u>Statio</u>
- <u>TIMER</u>
- <u>Crux</u>
- Ancestor
- ANC-GENE
- <u>Bn-Bs</u>

Computation of distances

- <u>PHYLIP</u>
- <u>PAUP*</u>
- <u>RAPDistance</u>
- <u>MULTICOMP</u>
- <u>Microsat</u>
- <u>DIPLOMO</u>
- <u>OSA</u>
- <u>DISPAN</u>
- <u>RESTSITE</u>
- <u>NTSYSpc</u>
- <u>TREE-PUZZLE</u>
- <u>GCUA</u>
- DERANGE2
- <u>POPGENE</u>
- <u>TFPGA</u>
- <u>REAP</u>
- <u>MVSP</u>
- <u>RSTCALC</u>
- <u>Genetix</u>
- <u>DISTANCE</u>
- <u>Darwin</u>
- <u>sendbs</u>
- <u>Arlequin</u>
- <u>DAMBE</u>
- DnaSP

- <u>PAML</u>
- <u>puzzleboot</u>
- <u>PAL</u>
- <u>Vanilla</u>
- <u>GelCompar II</u>
- **Bionumerics**
- <u>qclust</u>
- <u>Populations</u>
- <u>Winboot</u>
- FSTAT
- <u>SYN-TAX</u>
- Phylo win
- <u>Phyltools</u>
- <u>MSA</u>
- <u>APE</u>
- <u>YCDMA</u>
- <u>NSA</u>
- <u>T-REX</u>
- <u>LDDist</u>
- <u>DIVAGE</u>
- <u>Genepop</u>
- <u>START2</u>
- <u>Swaap</u>
- <u>Swaap PH</u>
- <u>SPAGeDi</u>

- <u>CBCAnalyzer</u>
- <u>PaupUp</u>
- <u>SEMPHY</u>
- SWORDS
- rRNA phylogeny
- FAMD
- <u>GAME</u>
- **Bioinformatics Toolbox**
- <u>GenoDive</u>
- <u>analysis</u>
- <u>TreeFit</u>
- EMBOSS
- <u>Murka</u>
- <u>Bio++</u>
- <u>UGENE</u>
- POPTREE2
- DISTREE
- <u>SeaView</u>
- <u>Crux</u>
- <u>Bn-Bs</u>
- HON-new

Maximum likelihood methods

- PHYLIP
- PAUP*
- fastDNAml
- MOLPHY
- PAML
- Spectrum
- SplitsTree
- TREE-PUZZLE
- <u>SeqPup</u>
- <u>Phylo win</u>
- PASSML
- ARB
- Darwin
- Modeltest
- DAMBE
- PAL
- dnarates
- HY-PHY
- Vanilla
- DT-ModSel
- Bionumerics
- fastDNAmlRev
- RevDNArates
- rate-evolution
- CONSEL

- EDIBLE
- PLATO
- Mesquite
- PTP
- Treefinder
- MetaPIGA
- RAxML
- PHYML
- <u>r8s-bootstrap</u>
- MrMTgui
- MrModeltest
- BootPHYML • PARBOOT
- p4
- Porn*
- SIMMAP
- Spectronet
- Rhino
- TipDate
- ProtTest
- ModelGenerator
- Simplot
- MrAIC
- Modelfit
- IQPNNI

- PARAT
- ALIFRITZ
- PhyNav
- DPRML
- MultiPhyl
- NimbleTree
- PaupUp
- SSA
- CoMET
- BIRCH
- Mac5
- Kakusan4
- GARLI
- PHYSIG
- SEMPHY
- FASTML
- Rate4Site
- aLRT
- <u>McRate</u>
- EREM
- PROCOV
- DART
- PhyloCoCo
- PRAP Joe Felsenstein http://evolution.gs.washington.edu

- SeqState
- Leaphy
- NHML
- SLR
- rRNA phylogeny
- Bosque
- Concaterpillar
- PHYLLAB
- NEPAL
- EMBOSS
- CodeAxe
- phangorn
- Bio++
- FastTree
- nhPhyML
- PhyML-Multi
- Segminator
- raxmlGUI
- MixtureTree
- SeaView
- GZ-Gamma
- PAUPRat
- Crux

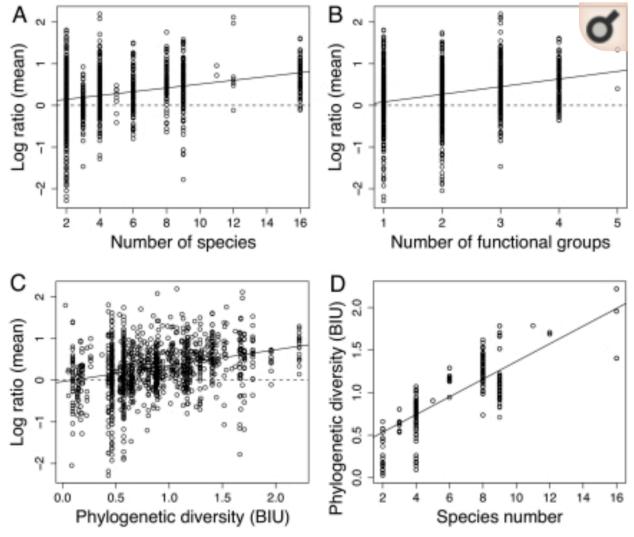
Bayesian inference methods

- <u>PAML</u>
- <u>BAMBE</u>
- <u>PAL</u>
- <u>Vanilla</u>
- <u>MrBayes</u>
- <u>Mesquite</u>
- PHASE
- <u>BEAST</u>
- MrBayes tree scanners
- <u>p4</u>
- <u>SIMMAP</u>
- <u>IMa2</u>
- BAli-Phy
- BayesPhylogenies
- MrBayesPlugin
- PhyloBayes
- <u>PHASE</u>
- <u>Cadence</u>
- <u>Multidivtime</u>
- <u>BEST</u>
- AMBIORE
- <u>PHYLLAB</u>
- <u>bms runner</u>
- <u>tracer</u>
- <u>burntrees</u>

- <u>Bio++</u>
- <u>Crux</u>
- ANC-GENE

Phylogenetics in conservation

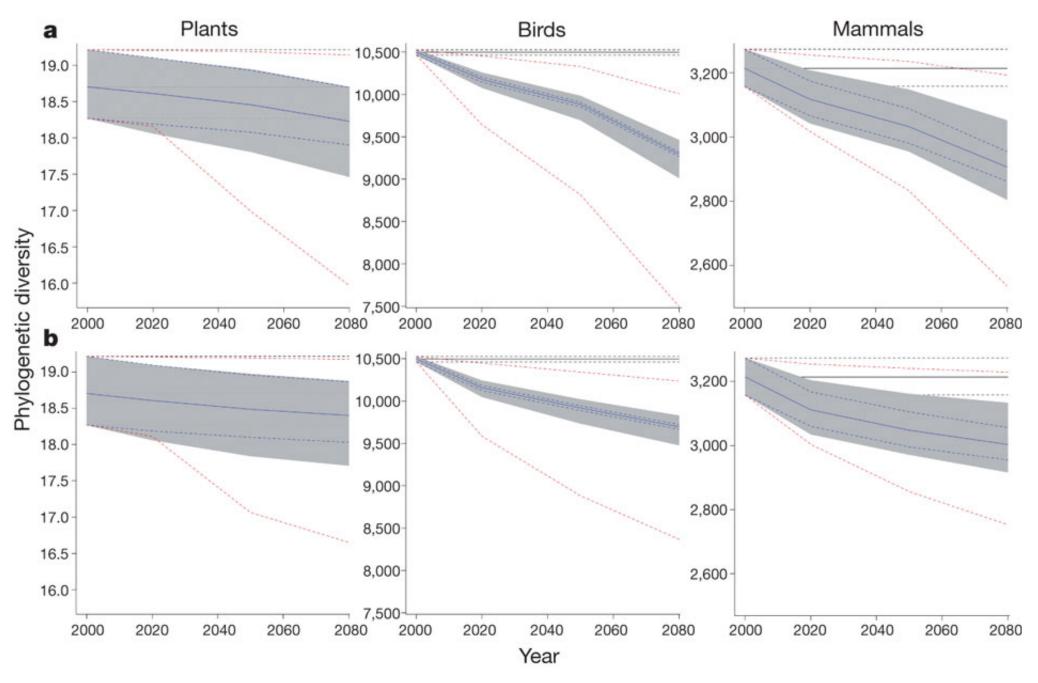
Phylogenetic diversity and ecosystem function



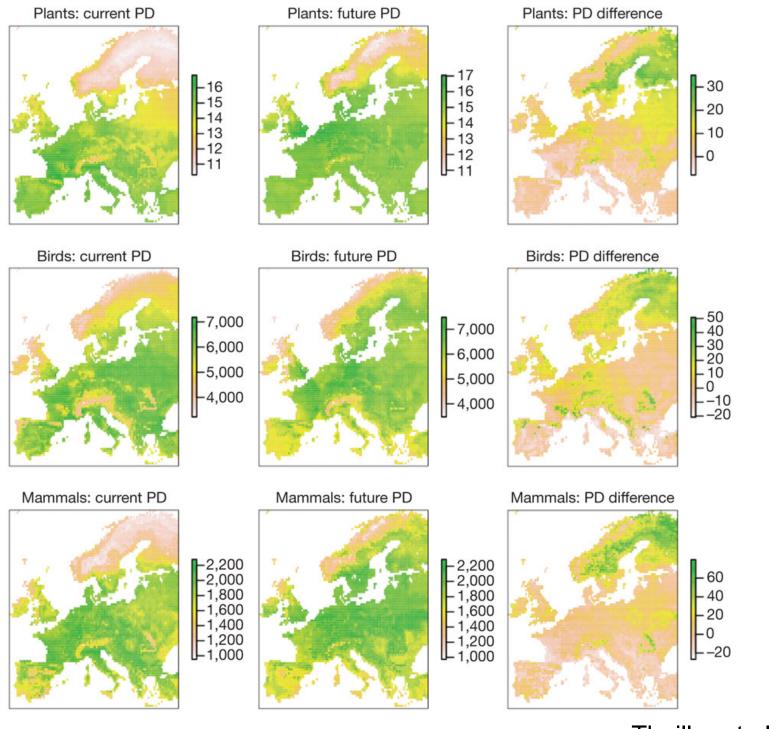
Cadotte et al. 2008

Phylogenetics in conservation

- Phylogenetic diversity and ecosystem function
- Global change and extinction



Thuiller et al. 2011.



Thuiller et al. 2011.

Phylogenetics in conservation

- Phylogenetic diversity and ecosystem function
- Global change and extinction
- Conservation planning

