Evolution and Phylogeny
Charles Darwin’s 1859 book (*On the Origin of Species By Means of Natural Selection, or the Preservation of Favoured Races in the Struggle for Life*) introduced the **Theory of Evolution**.

Struggle for existence induces a natural selection. Offspring are dissimilar from their parents (that is, variability exists), and individuals that are more fit for a given environment are selected for. In this way, over long periods of time, species evolve. Groups of organisms change over time so that descendants differ structurally and functionally from their ancestors.
All existing organisms are derived from a common ancestor and that new species arise by splitting of a population into subpopulations that do not cross-breed.

Organization: Directed Rooted Tree; Existing species: Leaves; Common ancestor species (divergence event): Internal node; Length of an edge: Time.
Five kingdom system (Haeckel, 1879)

- plants
- animals
- fungi
- protists
- monera

- mammals
- vertebrates
- invertebrates
- protozoa
At the molecular level, evolution is a process of mutation with selection.

Molecular evolution is the study of changes in genes and proteins throughout different branches of the tree of life.

Phylogeny is the inference of evolutionary relationships. Traditionally, phylogeny relied on the comparison of morphological features between organisms. Today, molecular sequence data are also used for phylogenetic analyses.
Questions for Phylogenetic Analysis

- How many genes are related to my favorite gene?
- How related are whales, dolphins & porpoises to cows?
- Where and when did HIV or other viruses originate?
- What is the history of life on earth?
- Was the extinct quagga more like a zebra or a horse?
Molecular phylogeny uses trees to depict evolutionary relationships among organisms. These trees are based upon DNA and protein sequence data.
Tree Nomenclature

Slide by Pevsner

Fig. 7.8
Tree nomenclature

operational taxonomic unit (OTU)
such as a protein sequence

taxon

---

Fig. 7.8  Page 232
Tree nomenclature

Node (intersection or terminating point of two or more branches)

branch (edge)

Fig. 7.8
Page 232
Tree nomenclature

Branches are unscaled...

Branches are scaled...

...OTUs are neatly aligned, and nodes reflect time

...branch lengths are proportional to number of amino acid changes

Fig. 7.8
Page 232
Tree nomenclature

bifurcating internal node

multifurcating internal node

Fig. 7.9
Examples of multifurcation: failure to resolve the branching order of some metazoans and protostomes

Rokas A. et al., Animal Evolution and the Molecular Signature of Radiations Compressed in Time, *Science* 310:1933 (2005), Fig. 1.
Tree nomenclature: clades

Clade ABF (monophyletic group)
Tree nomenclature

Fig. 7.8

Slide by Pevsner

Clade CDH
Tree nomenclature

Clade ABF/CDH/G

Slide by Pevsner
Examples of clades

Lindblad-Toh et al., *Nature* 438: 803 (2005), fig. 10
Tree nomenclature: roots

Rooted tree
(specifies evolutionary path)

Unrooted tree

Slide by Pevsner

Fig. 7.10
Page 234
Tree nomenclature: outgroup rooting

Rooted tree

Outgroup (used to place the root)
2 broad categories:

- **Distance-based methods**
  - Ultrametric
  - Additive:
    - UPGMA
    - Transformed Distance
    - Neighbor-Joining

- **Character-based**
  - Maximum Parsimony
  - Maximum Likelihood
  - Bayesian Methods
An ultrametric tree:
- decreasing internal node labels
- distance between two nodes is label of least common ancestor.

An ultrametric distance matrix:
- Symmetric matrix such that for every i, j, k, there is tie for maximum of $D(i,j)$, $D(j,k)$, $D(i,k)$
**Molecular Clock Hypothesis**, Zuckerkandl & Pauling, 1962: **Accepted** point mutations in amino acid sequence of a protein occurs at a **constant** rate.

- Varies from protein to protein
- Varies from one part of a protein to another
Lab-based methods: hybridization
- Take denatured DNA of the 2 taxa and let them hybridize. Then measure energy to separate.

Sequence-based methods: distance
### Ultrametric: Example

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- **A** is connected to **C, G**
- **B, D, F, H** form a cluster.
- **E** is connected to **B, D, F, H**
- **5** is the maximum distance from **A** to **E**
Ultrametric: Example

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A tree diagram showing distances between nodes A, C, G, B, F, and E, with distances labeled as 5, 4, 3, 2, 1, and 0.
### Ultrametric: Distances Computed

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The distances are represented in a tree structure as follows:

- **A** is the root, with distances to **C, G, B, F**.
- **C, G** are connected with a distance of 2.
- **B** is connected with a distance of 4 to **C, G**.
- **E** is connected with a distance of 3 to **B**.
- **H** is connected with a distance of 5 to **B**.

4/5/15
Molecular Clock Hypothesis, Zuckerkandl & Pauling, 1962: Accepted point mutations in amino acid sequence of a protein occurs at a constant rate.

- Varies from protein to protein
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Lab-based methods: **hybridization**
- Take denatured DNA of the 2 taxa and let them hybridize. Then measure energy to separate.

Sequence-based methods: **distance**
Additive-Distance Trees

Additive distance trees are edge-weighted trees, with distance between leaf nodes are exactly equal to length of path between nodes.
Unrooted Trees on 4 Taxa

A

B

C

D

A

B

C

D

4/5/15

CAP5510 / CGS5166
If the true tree is as shown below, then

1. $d_{AB} + d_{CD} < d_{AC} + d_{BD}$, and
2. $d_{AB} + d_{CD} < d_{AD} + d_{BC}$
Unweighted pair-group method with arithmetic means (UPGMA)

\[ d_{(AB)C} = \frac{d_{AC} + d_{BC}}{2} \]
Transformed Distance Method

- UPGMA makes errors when rate constancy among lineages does not hold.
- Remedy: introduce an outgroup & make corrections

\[ D_{ij}' = \frac{D_{ij} - D_{iO} - D_{jO}}{2} + \left(\sum_{k=1}^{n} \frac{D_{kO}}{n}\right) \]

- Now apply UPGMA
Start with a star topology.

Find the pair to separate such that the total length of the tree is minimized. The pair is then replaced by its arithmetic mean, and the process is repeated.

\[ S_{12} = \frac{D_{12}}{2} + \frac{1}{2(n-2)} \sum_{k=3}^{n} (D_{1k} + D_{2k}) + \frac{1}{(n-2)} \sum_{3 \leq i \leq j \leq n} D_{ij} \]
Neighbor-Joining

\[ S_{12} = \frac{D_{12}}{2} + \frac{1}{2(n-2)} \sum_{k=3}^{n} (D_{1k} + D_{2k}) + \frac{1}{(n-2)} \sum_{3 \leq i \leq j \leq n} D_{ij} \]
2 broad categories:

- **Distance-based methods**
  - Ultrametric
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    - Transformed Distance
    - Neighbor-Joining

- **Character-based**
  - Maximum Parsimony
  - Maximum Likelihood
  - Bayesian Methods
Character-based Methods

- Input: characters, morphological features, sequences, etc.
- Output: phylogenetic tree that provides the history of what features changed. [Perfect Phylogeny Problem]
- one leaf/object, 1 edge per character, path ⇔ changed traits

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A

4/5/15
CAP5510 / CGS5166 38
Perfect phylogeny does not always exist.

Example

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Maximum Parsimony

- Minimize the total number of mutations implied by the evolutionary history
## Examples of Character Data

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### Maximum Parsimony Method: Example

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Unrooted Trees on 4 Taxa

A
  / 
 B  C
  / 
 D

A
  / 
 B  D
  / 
 C

A
  / 
 B  D
  / 
 C

4/5/15
CAP5510 / CGS5166
Figure 5.14 Three possible unrooted trees (I, II, and III) for four DNA sequences (1, 2, 3, and 4) that have been used to choose the most parsimonious tree. The possible phylogenetic relationships among the four sequences are shown in Newick format. The terminal nodes are marked by the sequence number and the nucleotide type at homologous positions in the extant species. Each dot on a branch means a substitution is inferred on that branch. Note that the nucleotides at the two internal nodes of each tree represent one possible reconstruction from among several alternatives. For example, the nucleotides at both the internal nodes of tree III(d) (bottom right) can be A instead of T. In this case, the two substitutions will be positioned on the branches leading to species 2 and 4. Alternatively, other combinations of nucleotides can be placed at the internal nodes. However, these alternatives will require three substitutions or more. The minimum number of substitutions required for site 9 is two.
Inferring nucleotides on internal nodes

Figure 5.15  Nucleotides in six extant species (1–6) and inferred possible nucleotides in five ancestral species (7–11) according to the method of Fitch (1971). Unions are indicated by parentheses. Two different trees (a and b) are depicted. Note that the inference of an ancestral nucleotide at an internal node is dependent on the tree. Modified from Fitch (1971).
Searching for the Maximum Parsimony Tree: Exhaustive Search

Figure 5.16  Exhaustive stepwise construction of all 15 possible trees for five OTUs. In step 1, we form the only possible unrooted tree for the first three OTUs (A, B, and C). In step 2, we add OTU D to each of the three branches of the tree in step 1, thereby generating three unrooted trees for four OTUs. In step 3, we add OTU E to each of the five branches of the three trees in step 2, thereby generating 15 unrooted trees. Additions of OTUs are shown as heavier lines. Modified from Swofford et al. (1996).
Searching for the Maximum Parsimony Tree: Branch-&&-Bound
Assuming a model of substitution,

\[ \Pr\{S_i(t+\Delta) = Y | S_i(t) = X\} \]

Using this formula it is possible to compute the likelihood that data D is generated by a given phylogenetic tree T under a model of substitution. Now find the tree with the maximum likelihood.

- Time elapsed? \( \Delta \)
- Prob of change along edge? \( \Pr\{S_i(t+\Delta) = Y | S_i(t) = X\} \)
- Prob of data? Product of prob for all edges
Computing Maximum Likelihood Tree

Figure 5.19  Schematic representation of the calculation of the likelihood of a tree. (a) Data in the form of sequence alignment of length n. (b) One of three possible trees for the four taxa whose sequences are shown in (a). (c) The likelihood of a particular site, in this case site 5, equals the sum of the 16 probabilities of every possible reconstruction of ancestral states at nodes 5 and 6 in (b). (d) The likelihood of the tree in (b) is the product of the individual likelihoods for all n sites. (e) The likelihood is usually evaluated by summing the logarithms of the likelihoods at each site, and reported as the log likelihood of the tree. Modified from Swofford et al. (1996).

\[ \begin{align*}
L(5) &= \text{Prob} \left( \begin{array}{c}
\text{C} \\
\text{A} \\
\text{A} \\
\text{G} \\
\text{G}
\end{array} \right) + \text{Prob} \left( \begin{array}{c}
\text{C} \\
\text{A} \\
\text{C} \\
\text{A} \\
\text{G} \\
\text{G}
\end{array} \right) + \text{Prob} \left( \begin{array}{c}
\text{C} \\
\text{A} \\
\text{T} \\
\text{A} \\
\text{G} \\
\text{G}
\end{array} \right) + \text{Prob} \left( \begin{array}{c}
\text{C} \\
\text{A} \\
\text{G} \\
\text{G}
\end{array} \right) \\
+ \text{Prob} \left( \begin{array}{c}
\text{C} \\
\text{C} \\
\text{A} \\
\text{A}
\end{array} \right) + \text{Prob} \left( \begin{array}{c}
\text{C} \\
\text{C} \\
\text{C} \\
\text{A} \\
\text{G} \\
\text{G}
\end{array} \right) + \text{Prob} \left( \begin{array}{c}
\text{C} \\
\text{C} \\
\text{T} \\
\text{A} \\
\text{G} \\
\text{G}
\end{array} \right) + \text{Prob} \left( \begin{array}{c}
\text{C} \\
\text{C} \\
\text{G} \\
\text{A}
\end{array} \right) \\
+ \text{Prob} \left( \begin{array}{c}
\text{C} \\
\text{T} \\
\text{A} \\
\text{A}
\end{array} \right) + \text{Prob} \left( \begin{array}{c}
\text{T} \\
\text{C} \\
\text{A} \\
\text{A}
\end{array} \right) + \text{Prob} \left( \begin{array}{c}
\text{T} \\
\text{T} \\
\text{T} \\
\text{A}
\end{array} \right) + \text{Prob} \left( \begin{array}{c}
\text{T} \\
\text{T} \\
\text{T} \\
\text{G} \\
\text{A}
\end{array} \right) \\
+ \text{Prob} \left( \begin{array}{c}
\text{G} \\
\text{G} \\
\text{A} \\
\text{A}
\end{array} \right) + \text{Prob} \left( \begin{array}{c}
\text{G} \\
\text{G} \\
\text{C} \\
\text{A}
\end{array} \right) + \text{Prob} \left( \begin{array}{c}
\text{G} \\
\text{G} \\
\text{T} \\
\text{A}
\end{array} \right) + \text{Prob} \left( \begin{array}{c}
\text{G} \\
\text{G} \\
\text{G} \\
\text{A}
\end{array} \right)
\end{align*} \]

\[ L = L(1) \times L(2) \times L(3) \times \ldots \times L(n) = \prod_{i=1}^{n} L(i) \]

\[ \ln L = \ln L(1) + \ln L(2) + \ln L(3) + \ldots + \ln L(n) = \sum_{i=1}^{n} \ln L(i) \]