A short (?) introduction to phylogenetic networks

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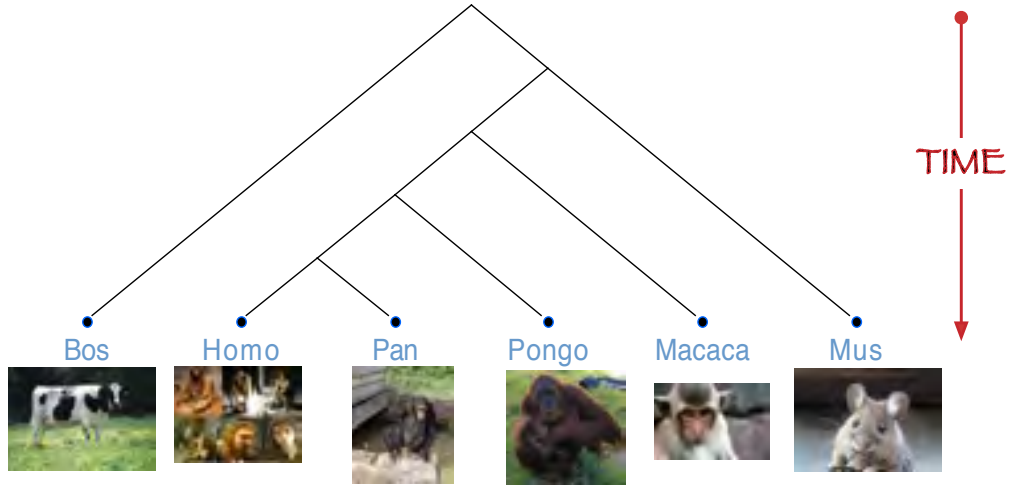
Rooted species trees ...

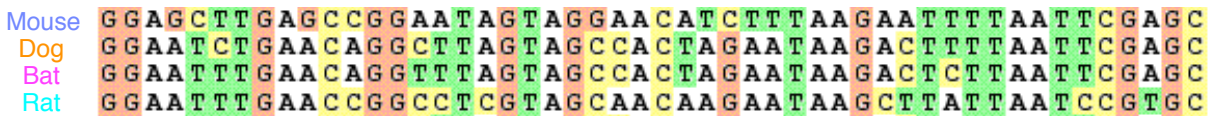
... are oriented connected and acyclic graphs, where terminal nodes are associated to a set of species:

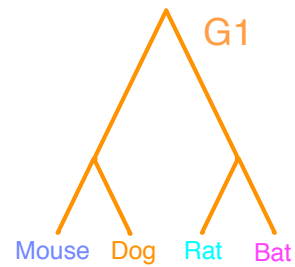
- the leaves or taxa represent extant organisms
- internal nodes represent hypothetical ancestors
- each internal node represents the lowest common ancestor of all taxa below it (clade)
- the only node without ancestor is called root



Gene trees

- Gene trees are built by analyzing a gene family, i.e., homologous molecular sequences appearing in the genome of different organisms.





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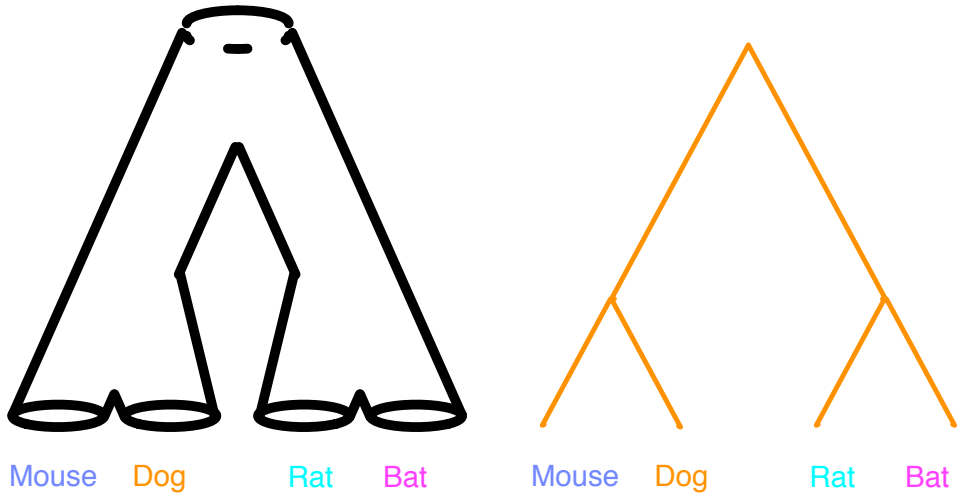

- Used, among other things, to estimate species trees.

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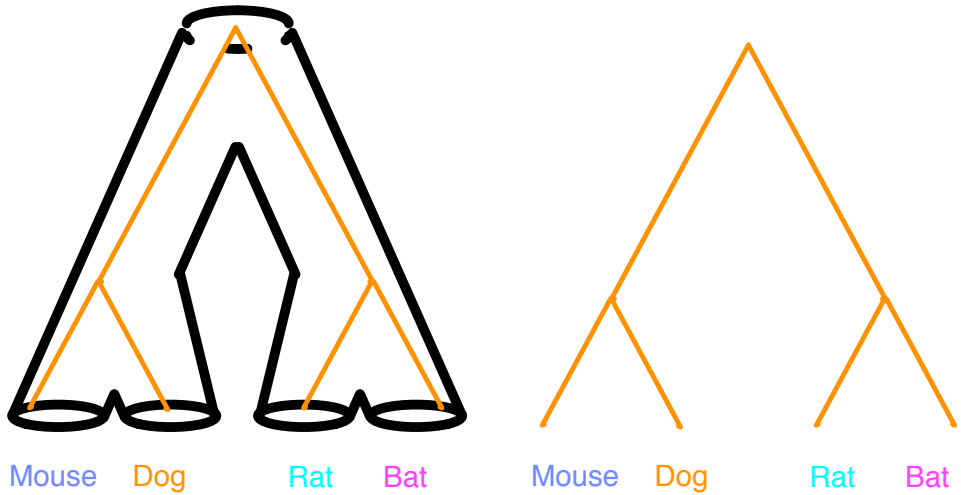

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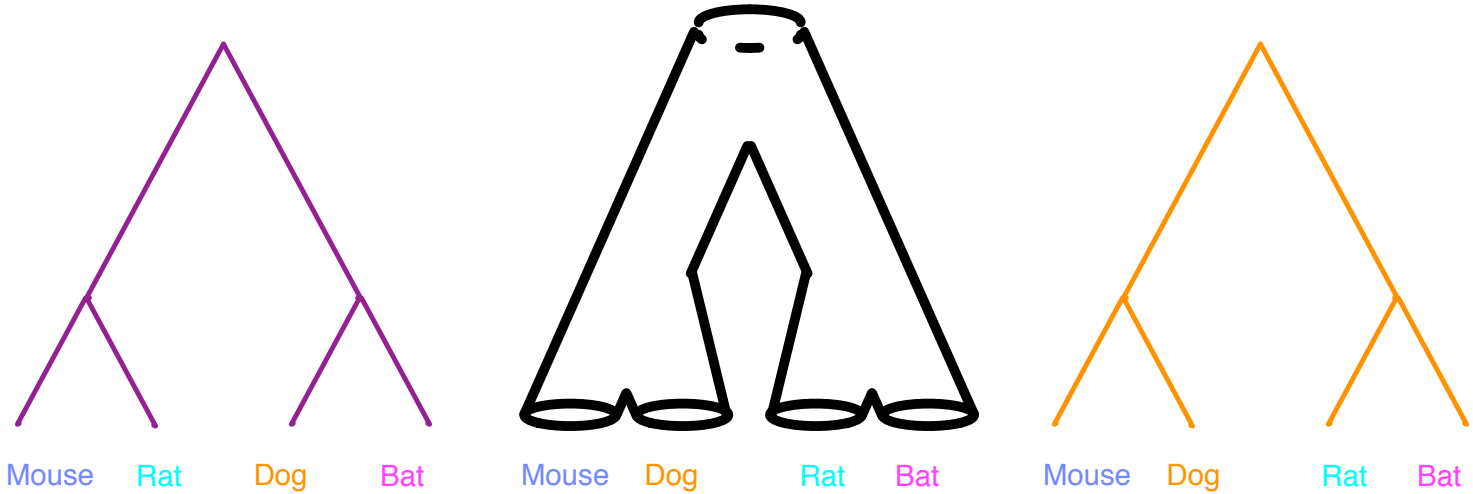

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Gene trees can significantly differ from the species tree for:

- methodological reasons
- biological reasons

Gene trees

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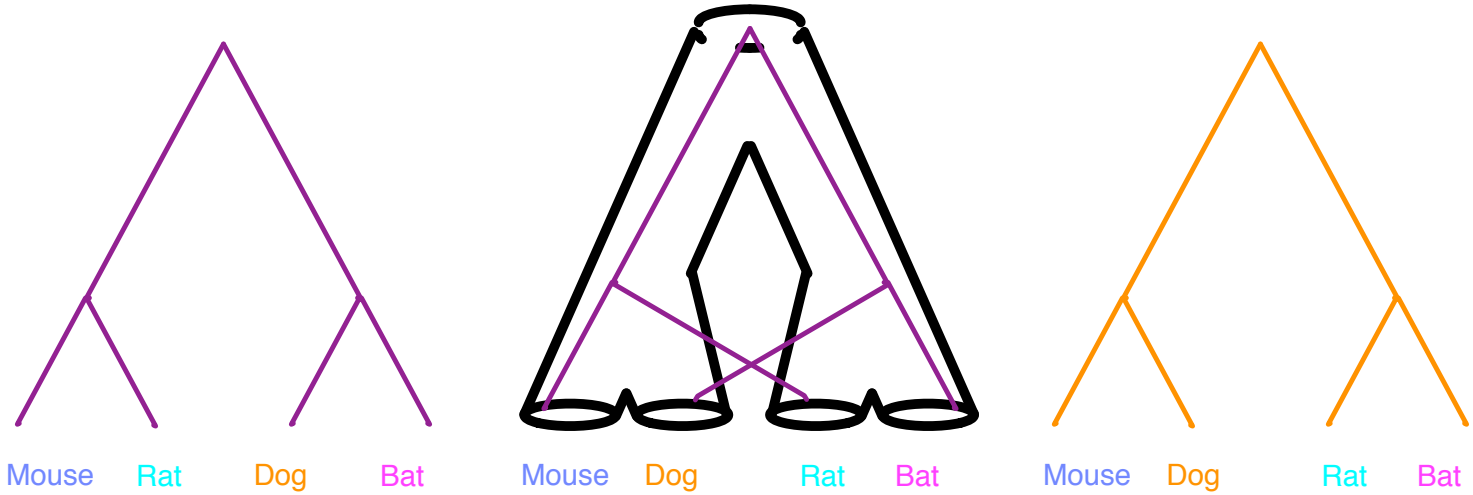

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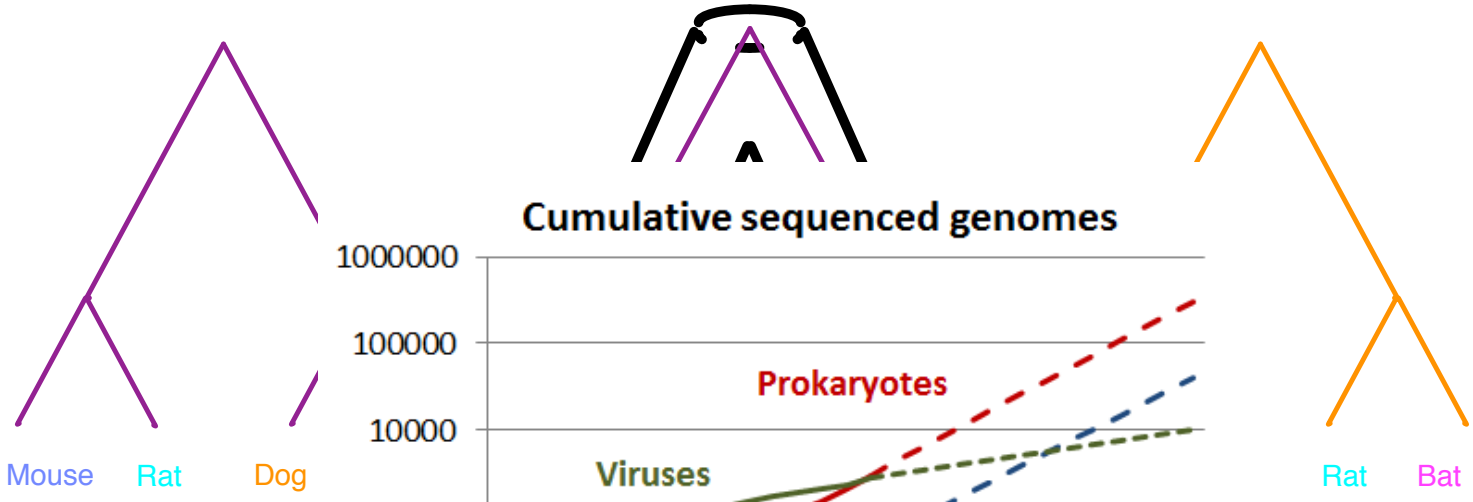

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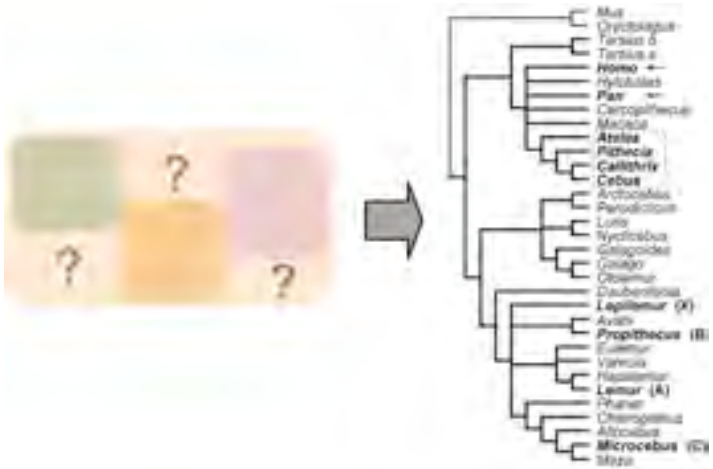
http://sulab.org/2013/06/sequenced-genomes-per-year/

Reconstruction of phylogenies for multiple datasets

The two main *classic* approaches:

- Supermatrix approach: assembling primary data



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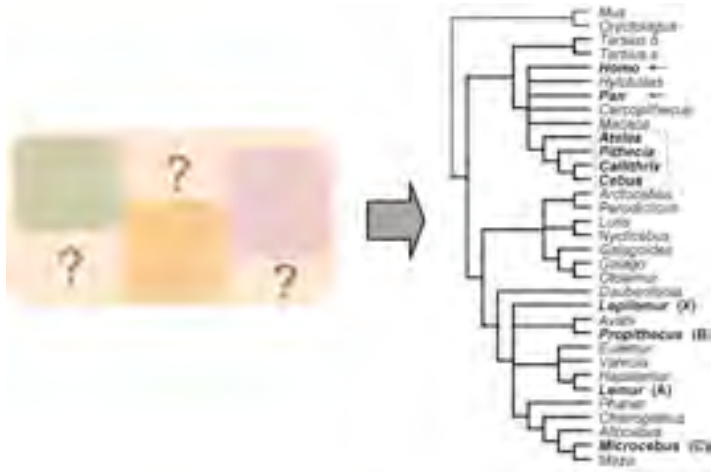
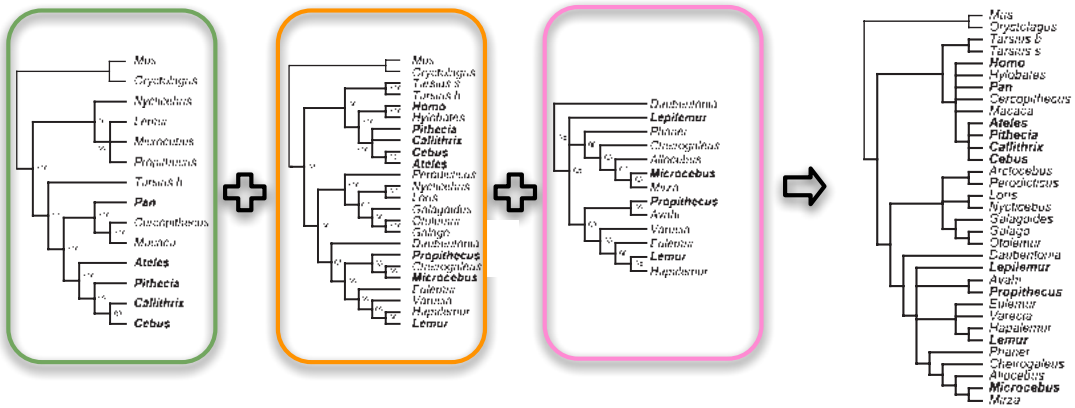
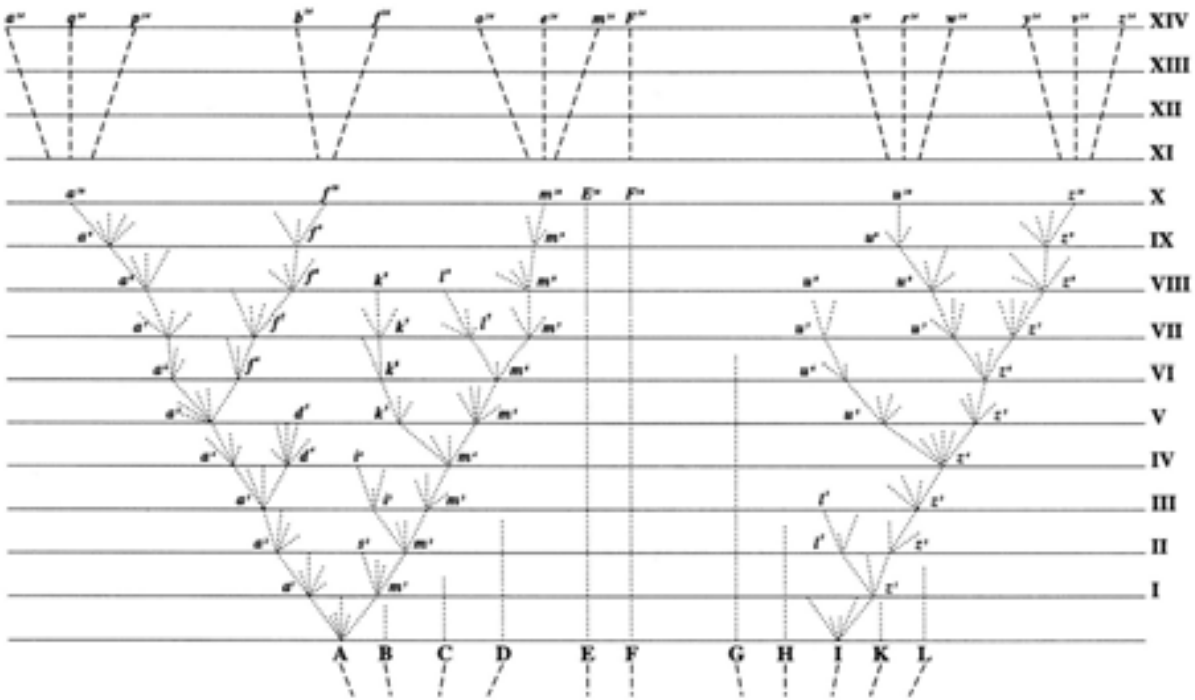


- Supertree approach: assembling trees



An implicit assumption

The implicit assumption of using trees is that, at a macroevolutionary scale, each (current or extinct) species or gene only descends from one ancestor. Darwin described evolution as "descent with modification", a phrase that does not necessarily imply a tree representation...



A *new* approach: building phylogenic networks

Why do we need them? Due to reticulate evolutionary phenomena (hybridization, recombination, horizontal gene transfer) the evolution of a set of species sometimes cannot be described using phylogenetic trees.

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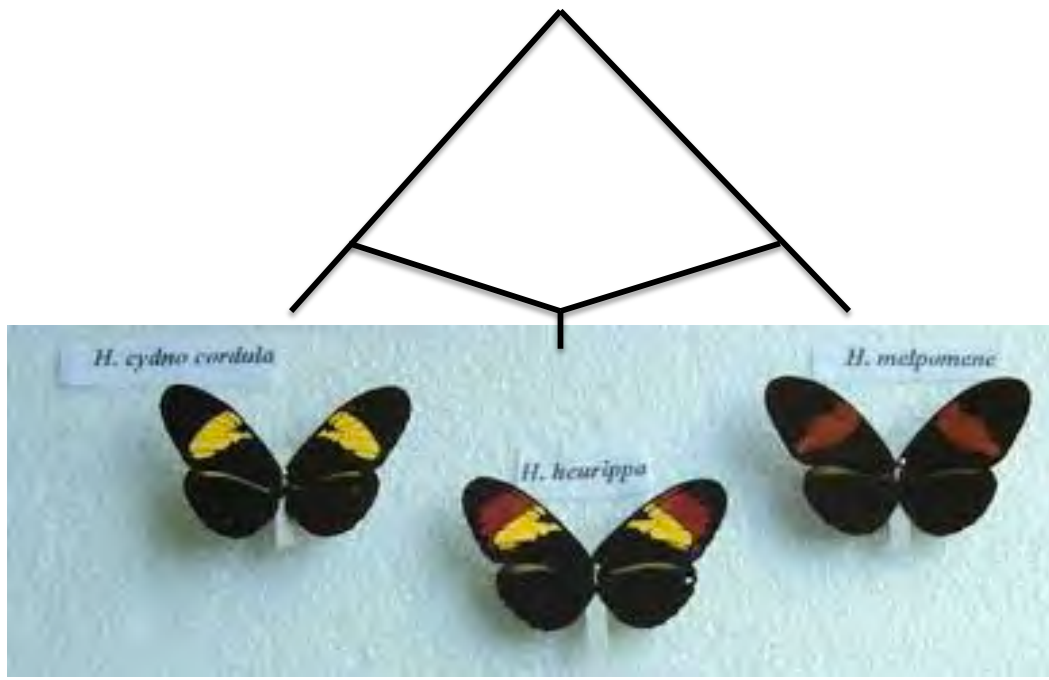

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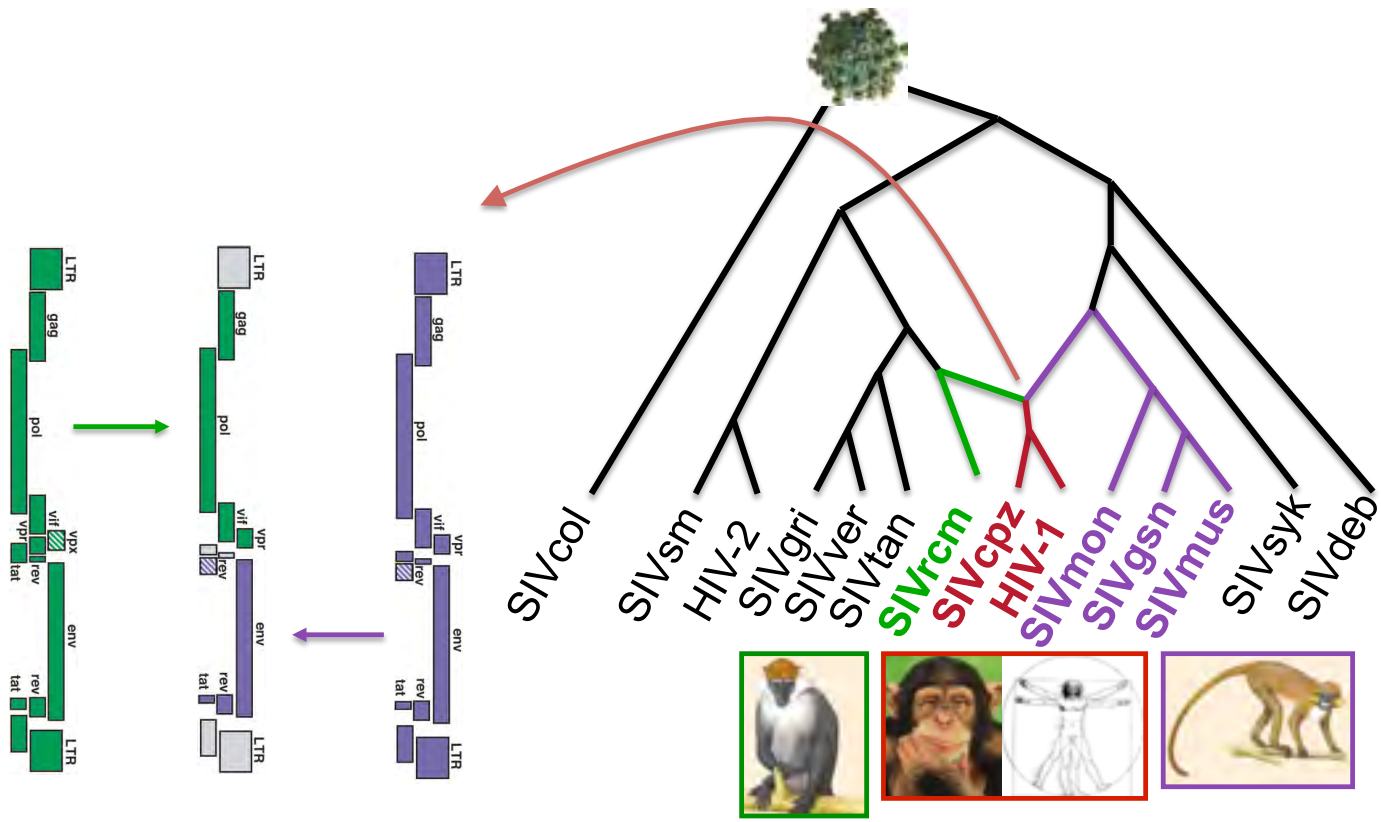

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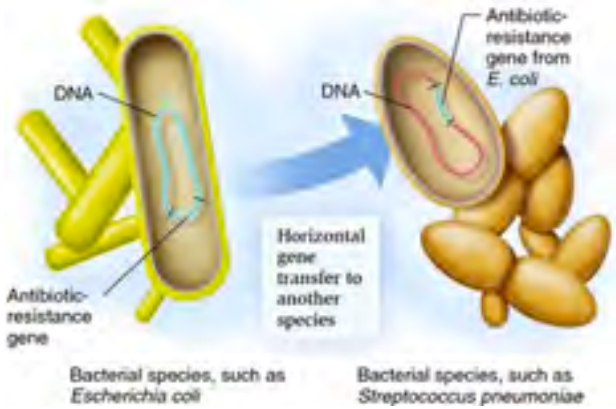
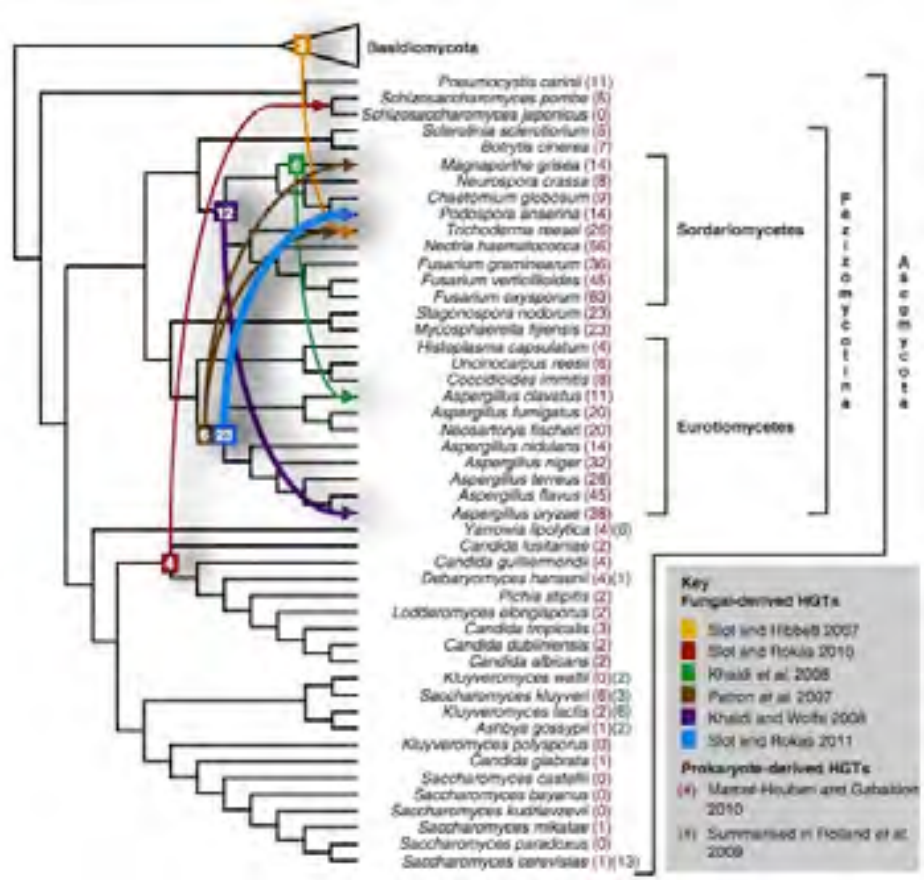
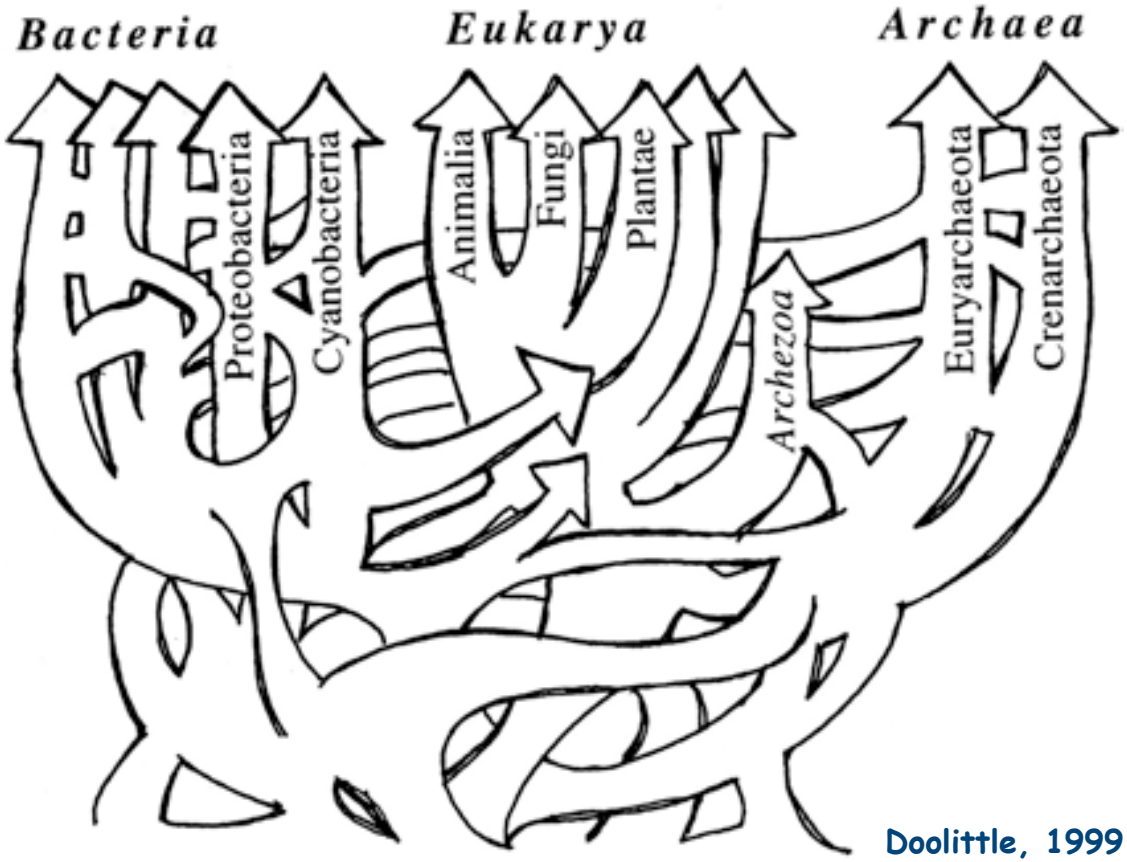




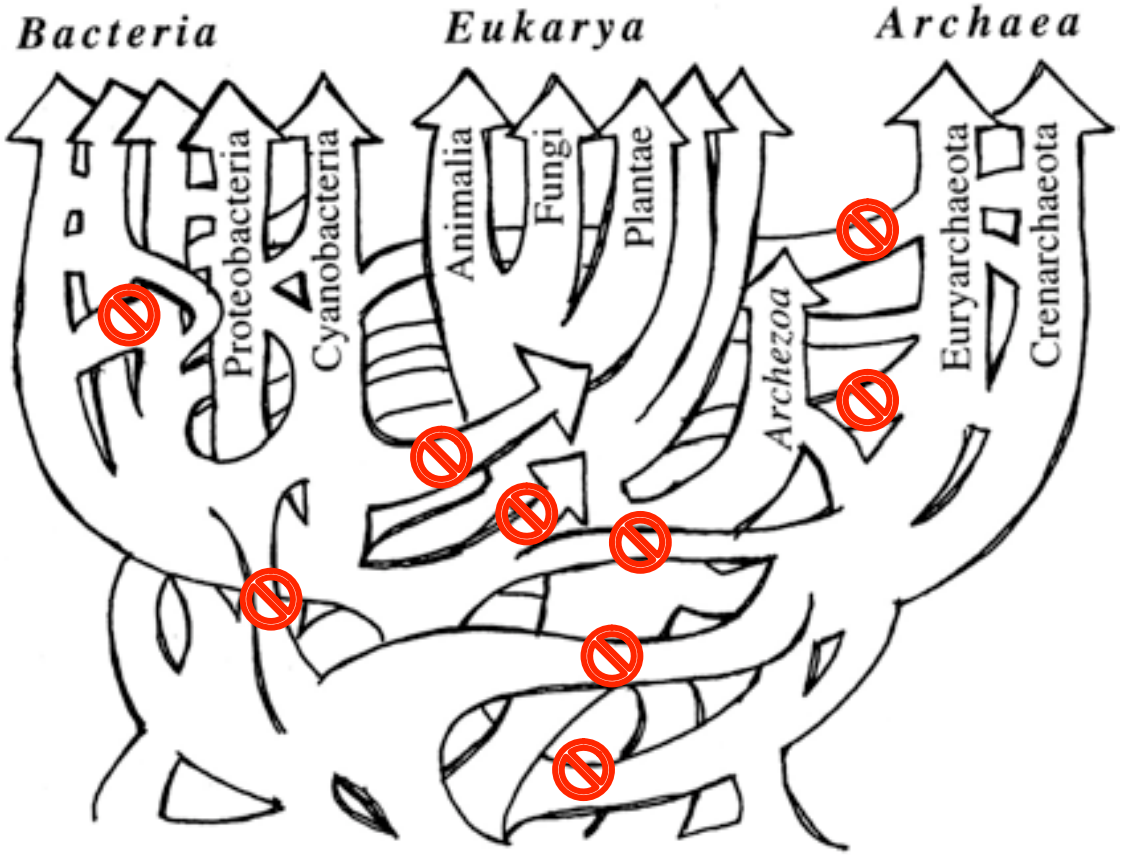
The network of life



Doolittle, 1999

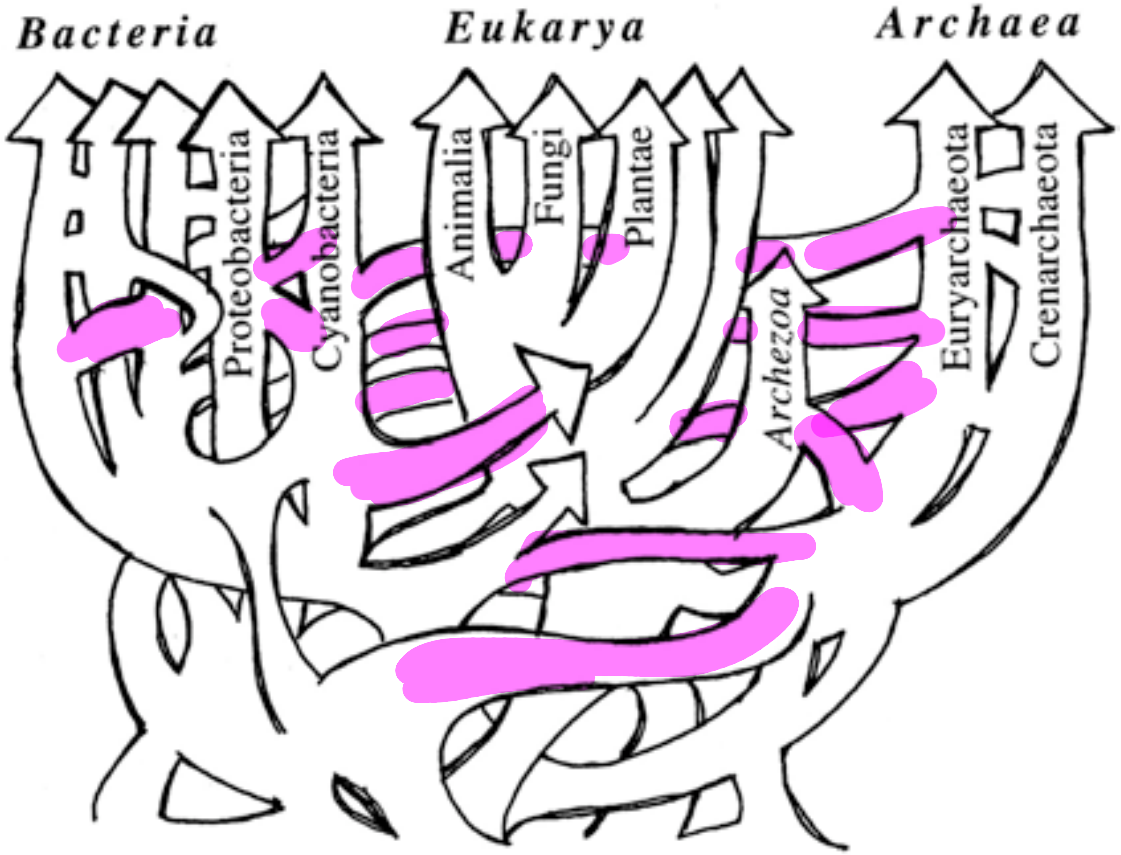
Three different paradigms

We (want to) see only the tree



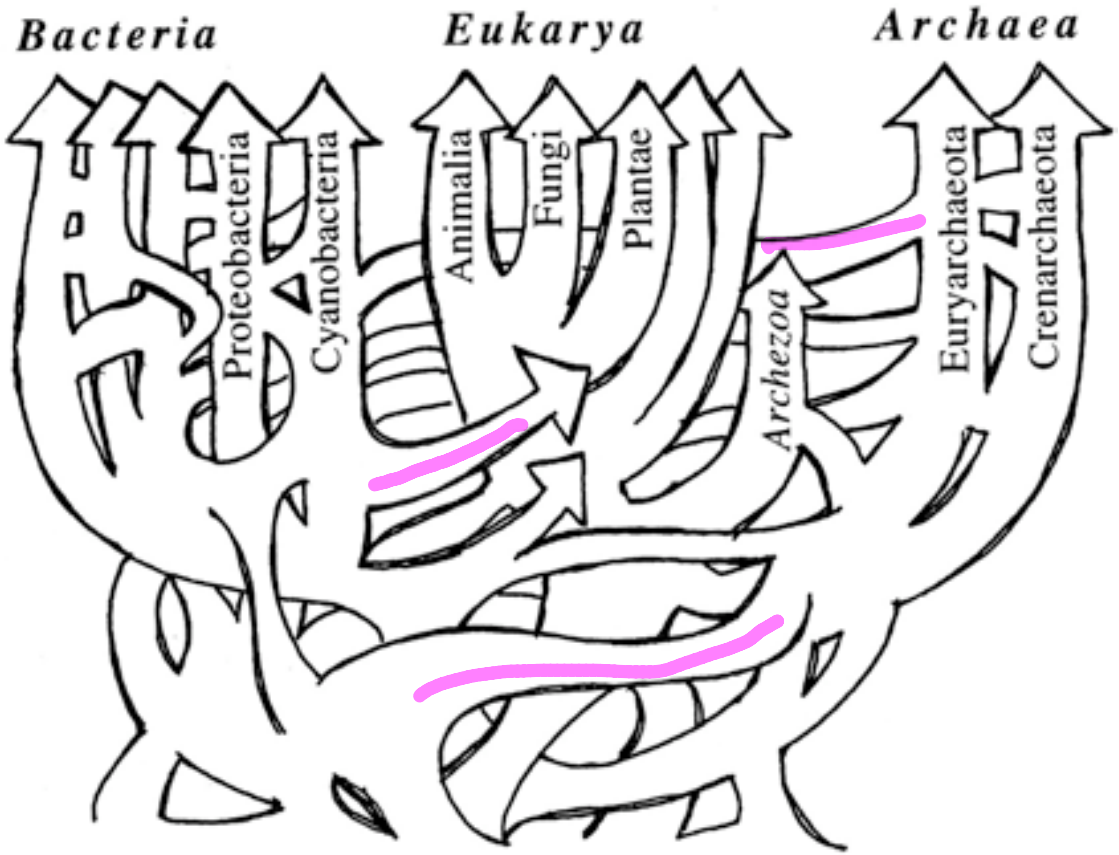
Three different paradigms

It is a big mess, no chance to retrieve the past

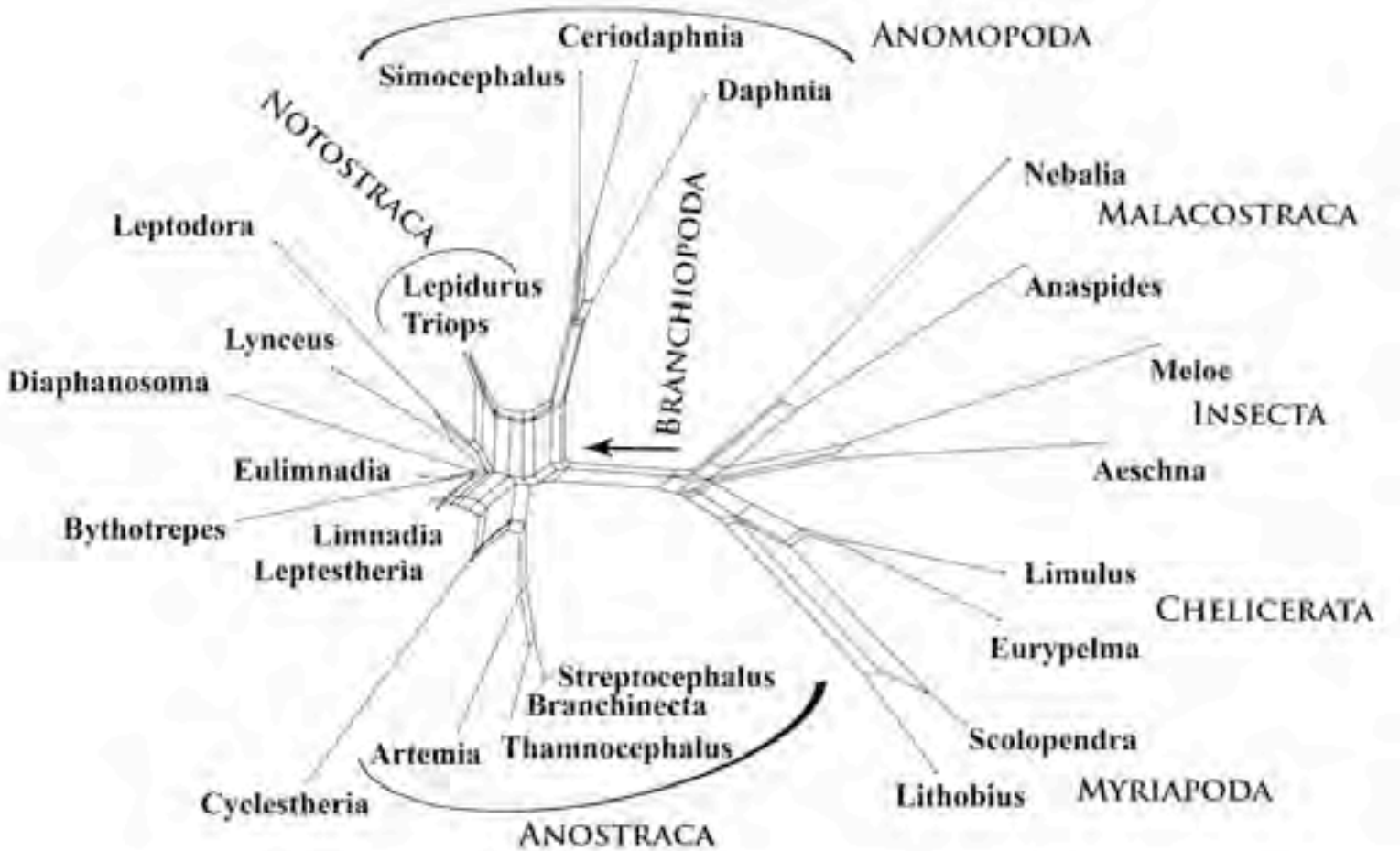


Three different paradigms

There is an underlying tree structure, with some reticulate events

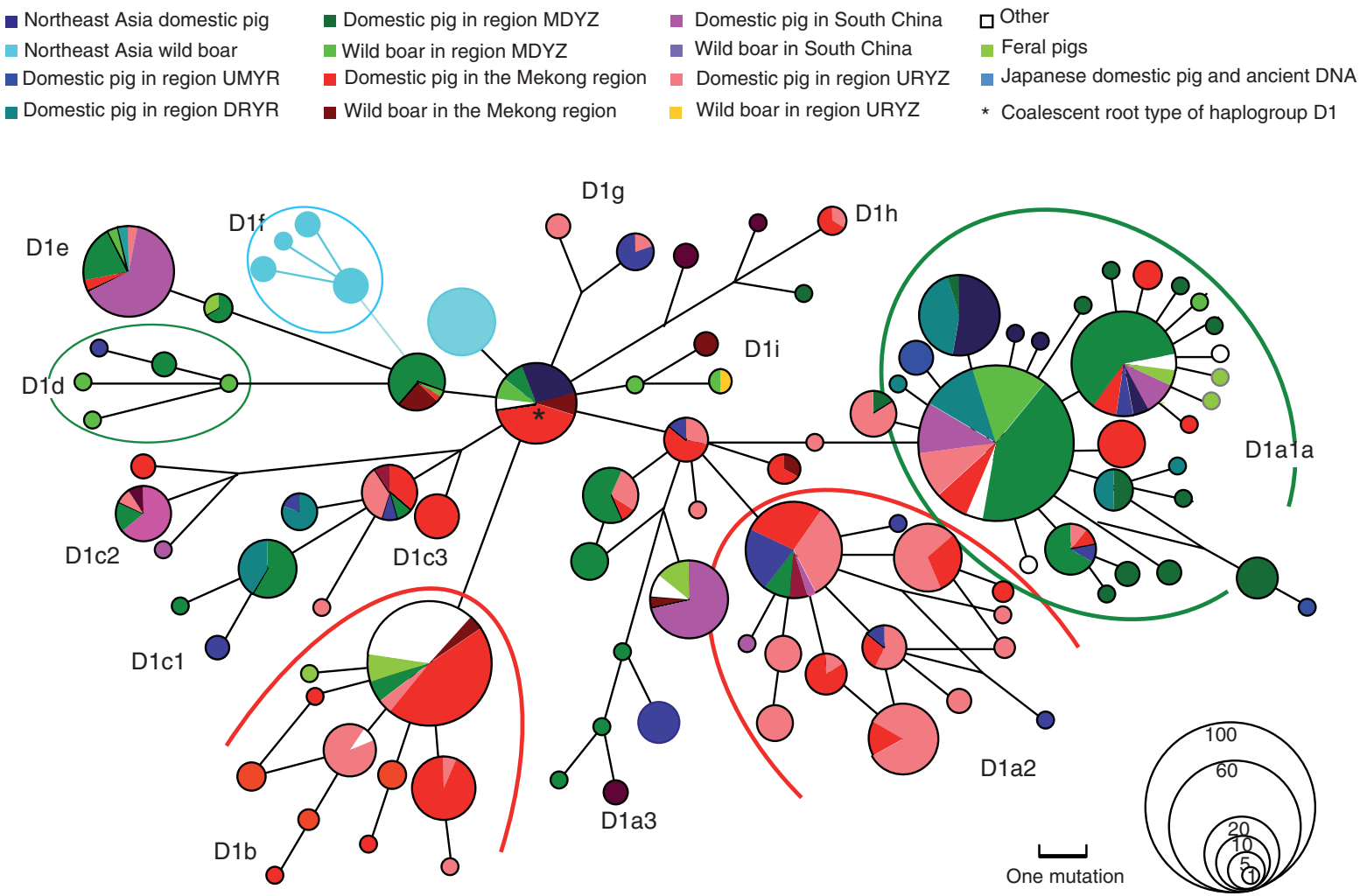


An example - a split network



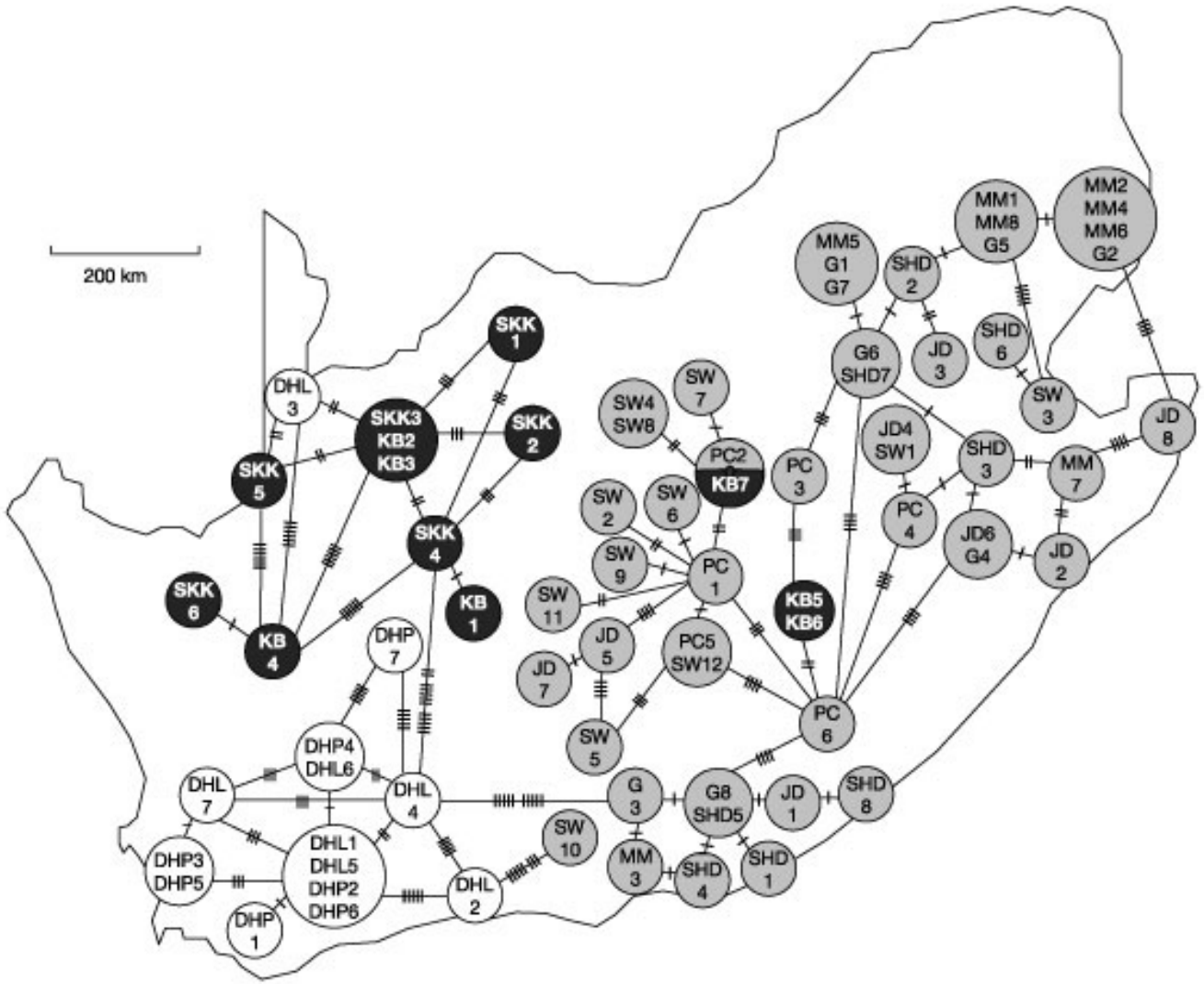
J. Wagele and C. Mayer. Visualizing differences in phylogenetic information content of alignments and distinction of three classes of long-branch effects. BMC Evolutionary Biology, 7(1):147, 2007

An example - a reduced median network



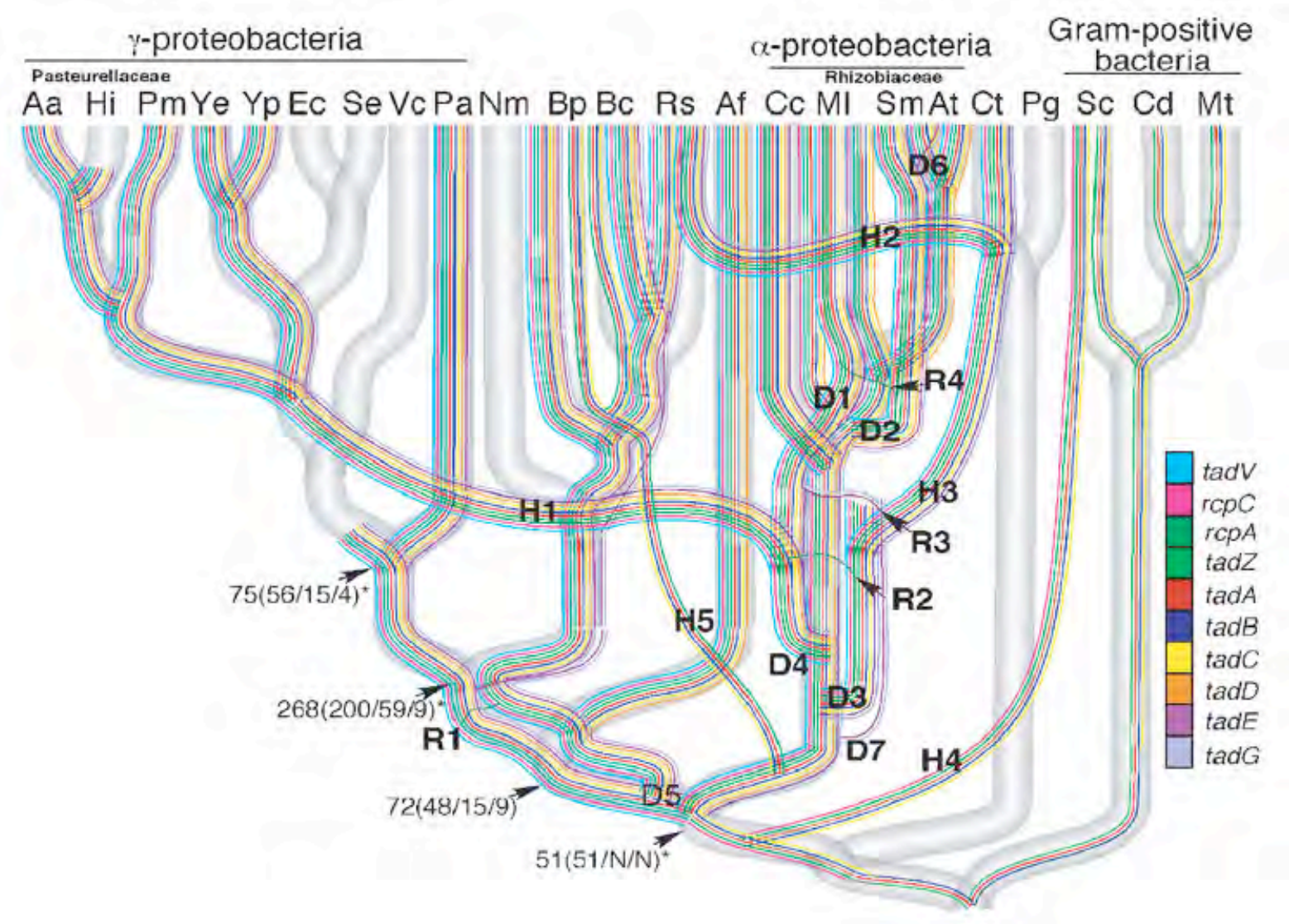
G.-S. Wu, Y.-G. Yao, K.-X. Qu, Z.-L. Ding, H. Li, M. Palanichamy, Z.-Y. Duan, N. Li, Y.-S. Chen, and Y.-P. Zhang. Population phylogenomic analysis of mitochondrial DNA in wild boars and domestic pigs revealed multiple domestication events in East Asia. Genome Biology, 8(11):R245, 2007

An example - a minimum spanning network



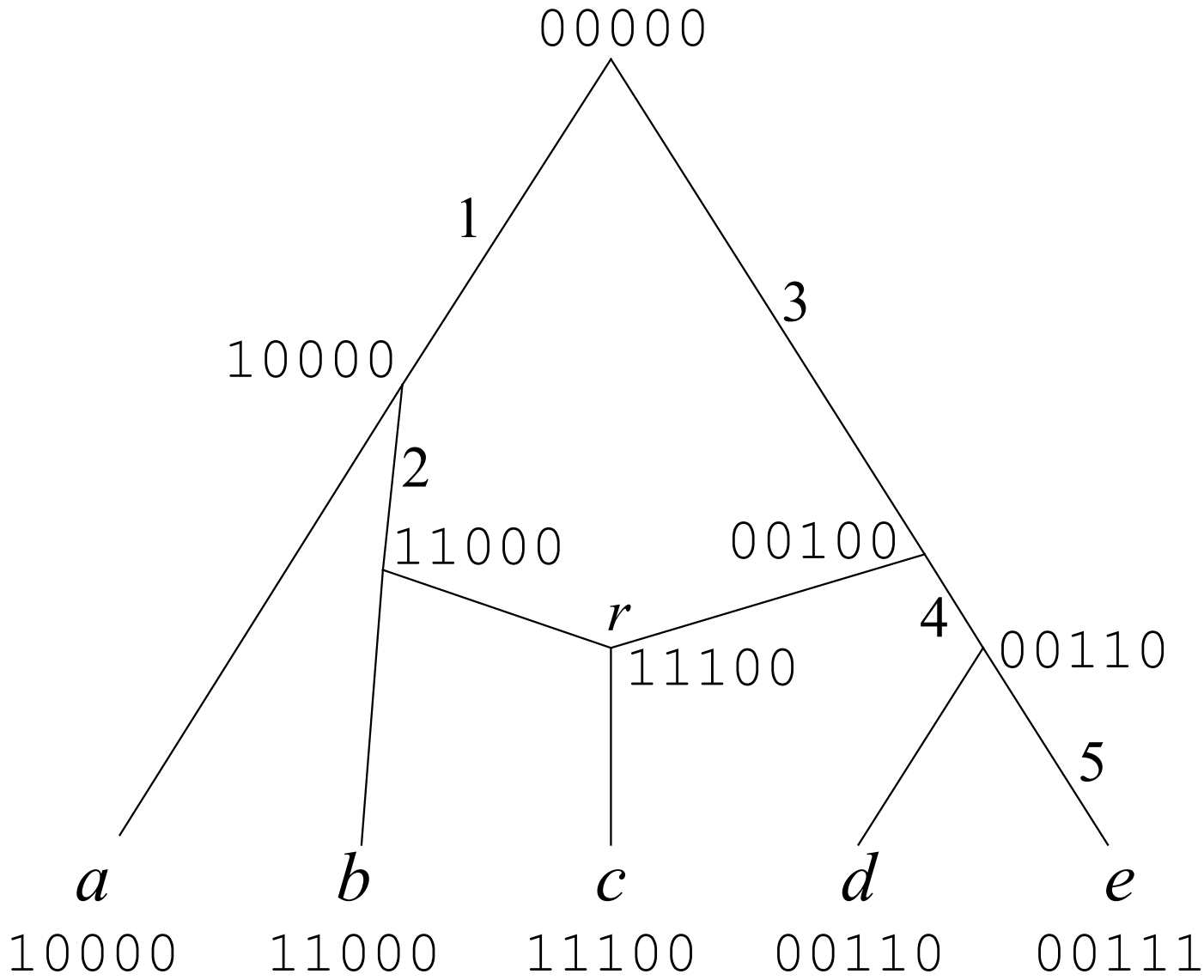
C. M. Miller-Butterworth, D. S. Jacobs, and E. H. Harley. Strong population sub- structure is correlated with morphology and ecology in a migratory bat. Nature, 424(6945):187-191, 2003

An example - a DTLR network



P.J. Planet, S.C. Kachlany, D.H. Fine, R. DeSalle, and D.H. Figurski. The wide spread colonization island of actinobacillus actinomycetemcomitans. Nature Genetics, 34:193–198, 2003.

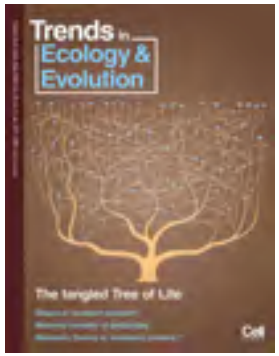
An example - a recombination network

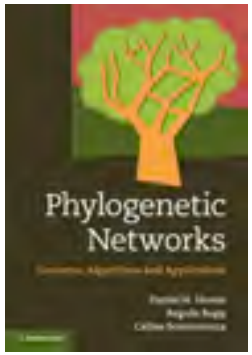


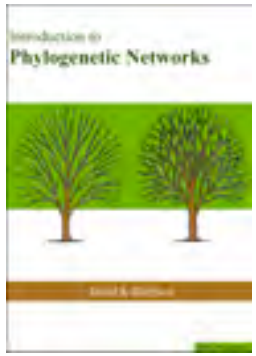
Daniel H. Huson, Regula Rupp, Celine Scornavacca. Phylogenetic Networks. Cambridge University Press. 2011

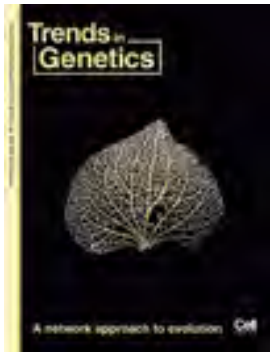
Phylogenetic networks

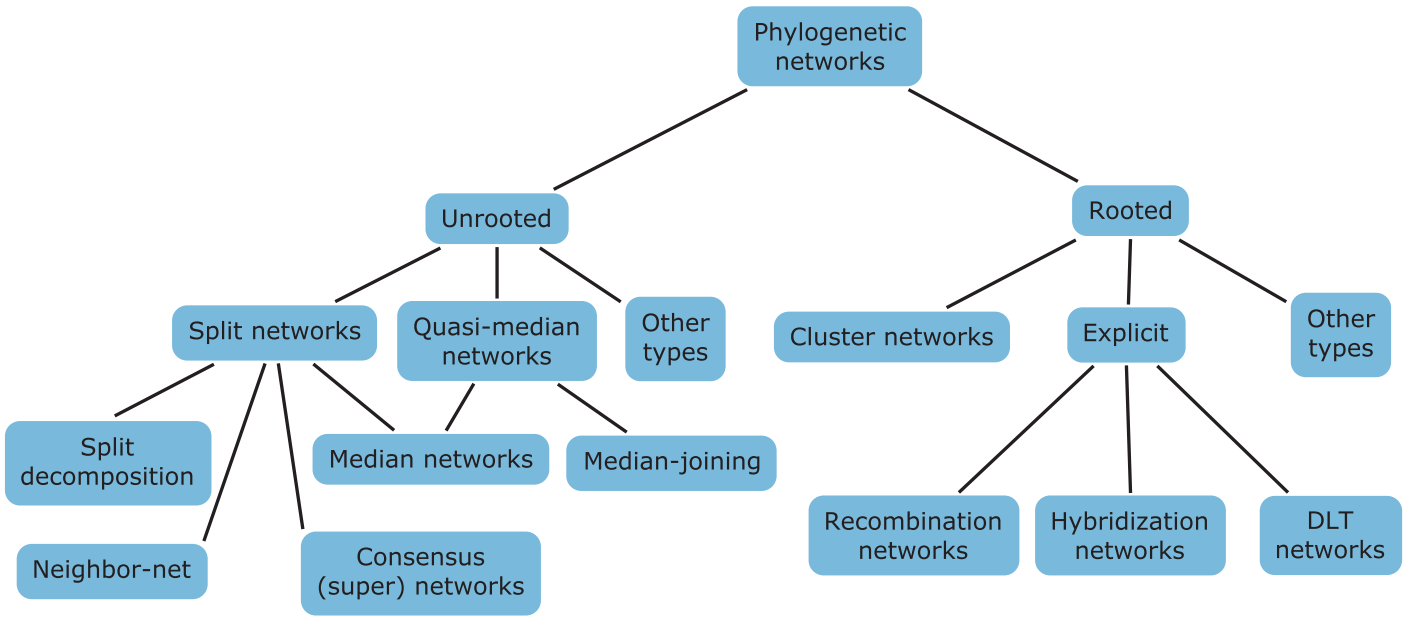
2008 2010 2011 2013 2014











Phylogenetic networks

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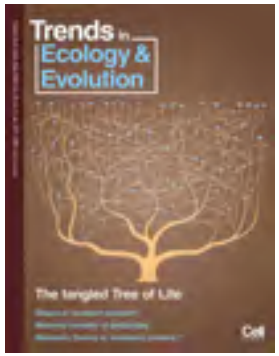
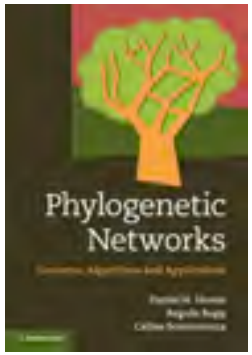
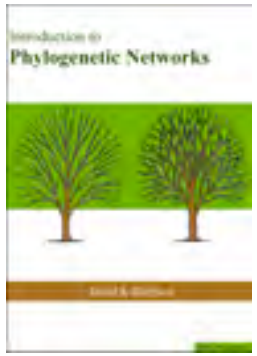
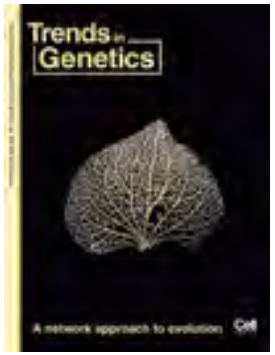
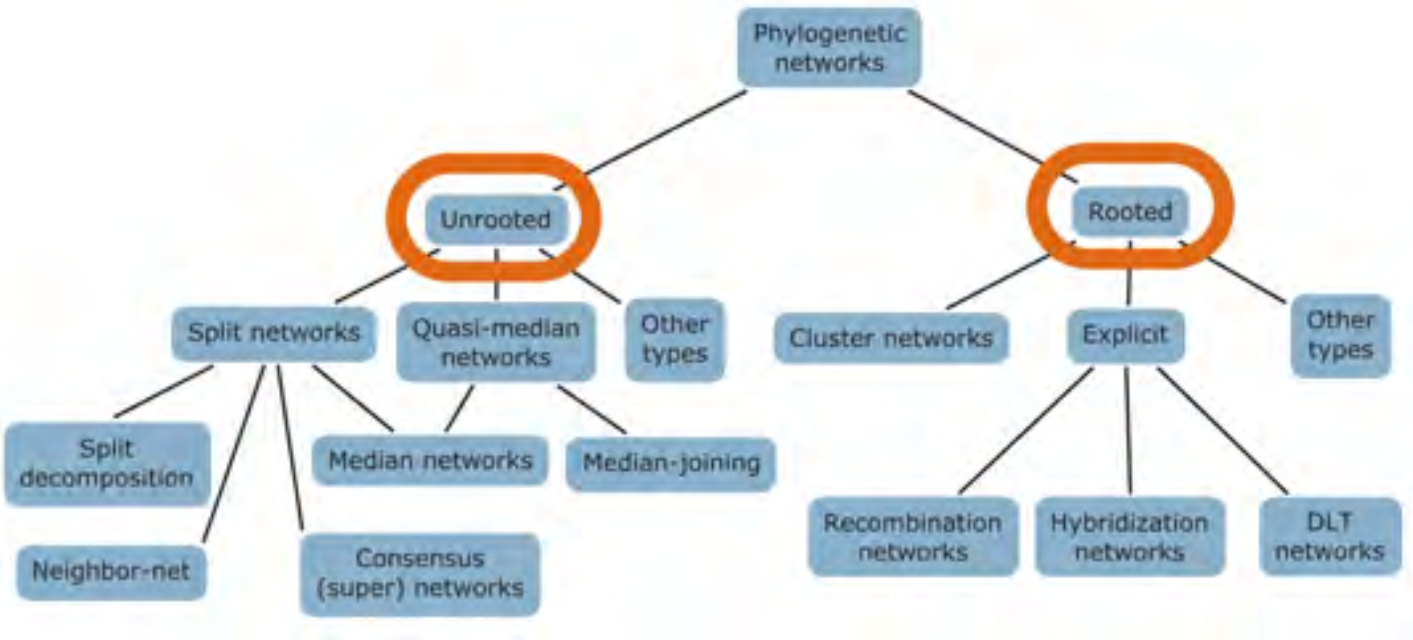




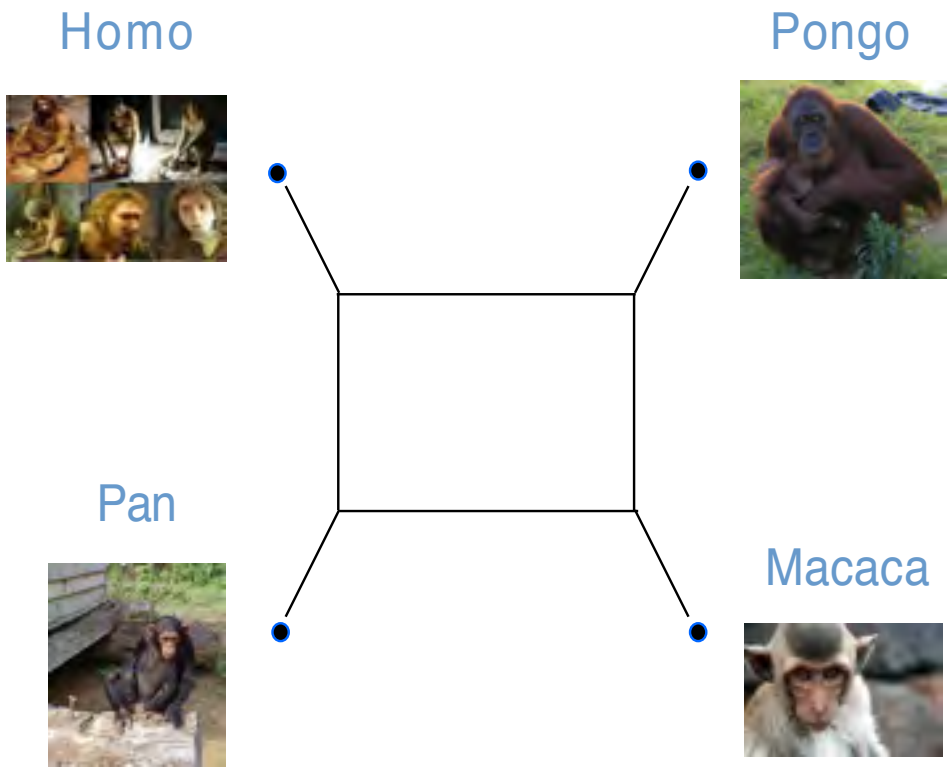






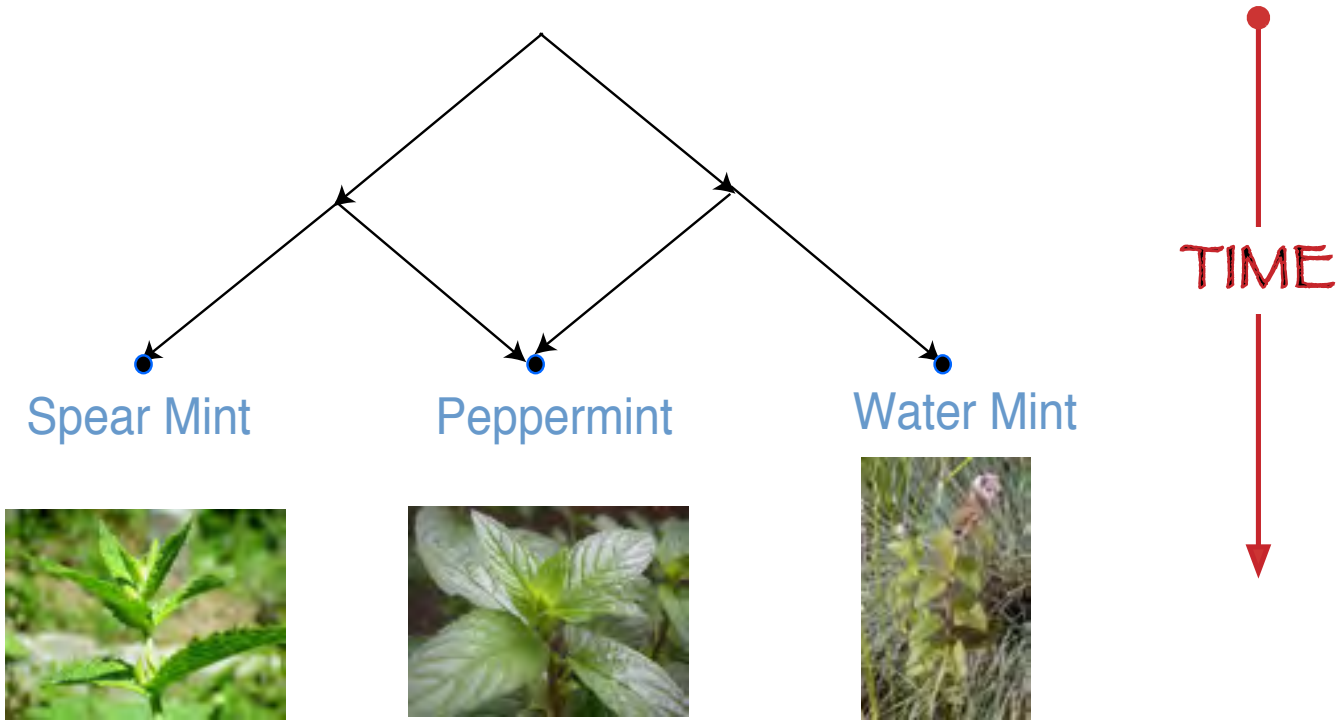
A phylogenetic network ...

... is any connected graph, where terminal nodes are associated to a set of species.



A rooted phylogenetic network ...

... is any single-rooted directed acyclic graph, where terminal nodes are associated to a set of species.



Phylogenetic networks

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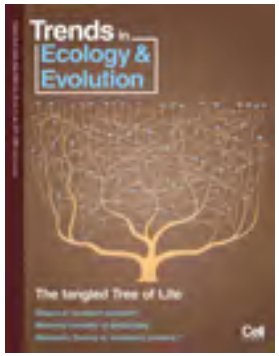
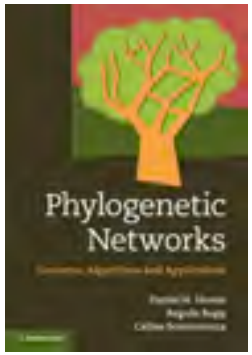
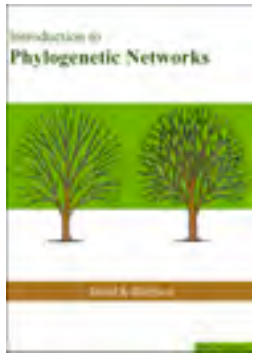
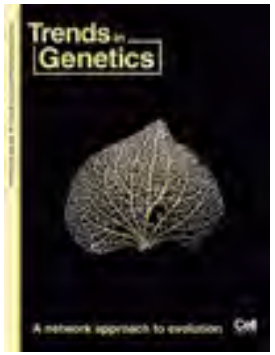
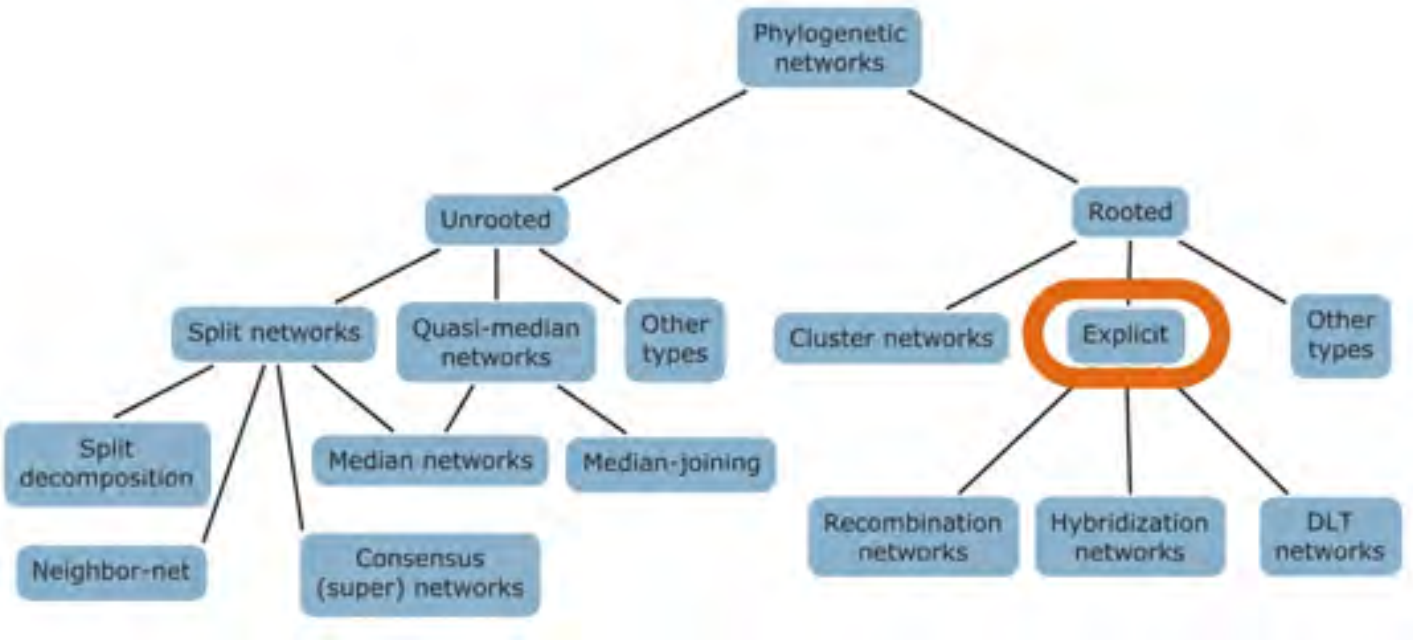




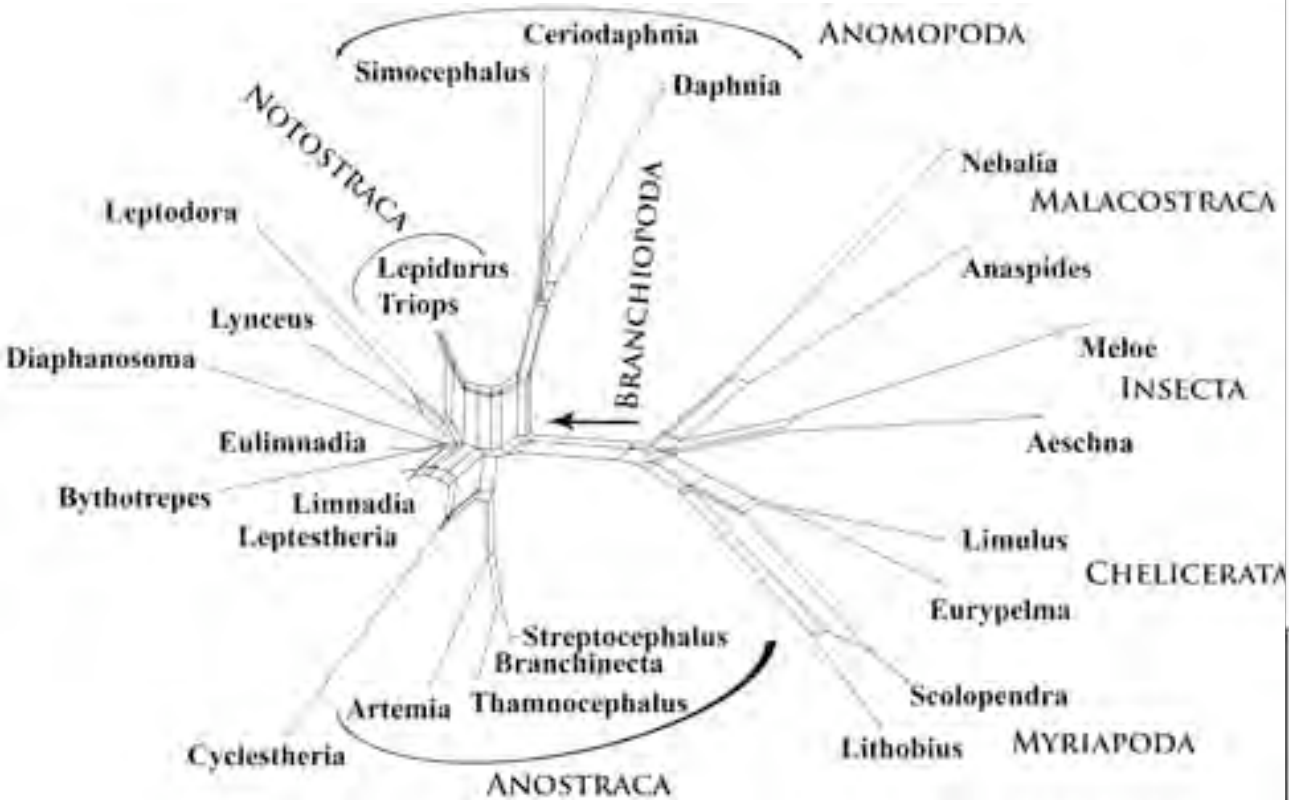






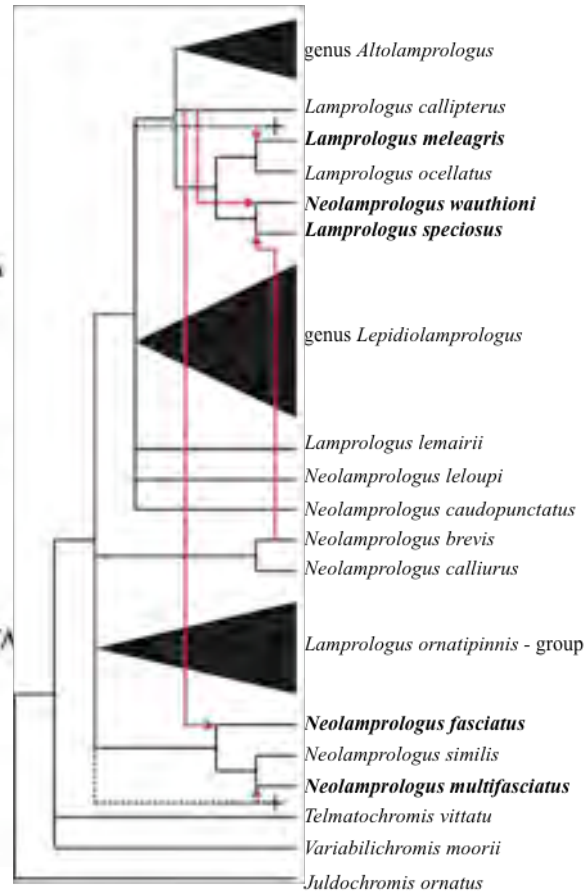
Abstract VS explicit phylogenetic networks

Split network:



Shows conflicting placement of taxa

Hybridization network:



Shows putative hybridization history

The plan of the survey

1. combinatorial and distance methods not accounting for ILS
   - unrooted networks
   - rooted networks (explicit or not)
2. methods accounting for ILS (always explicit)

Unrooted phylogenetic networks

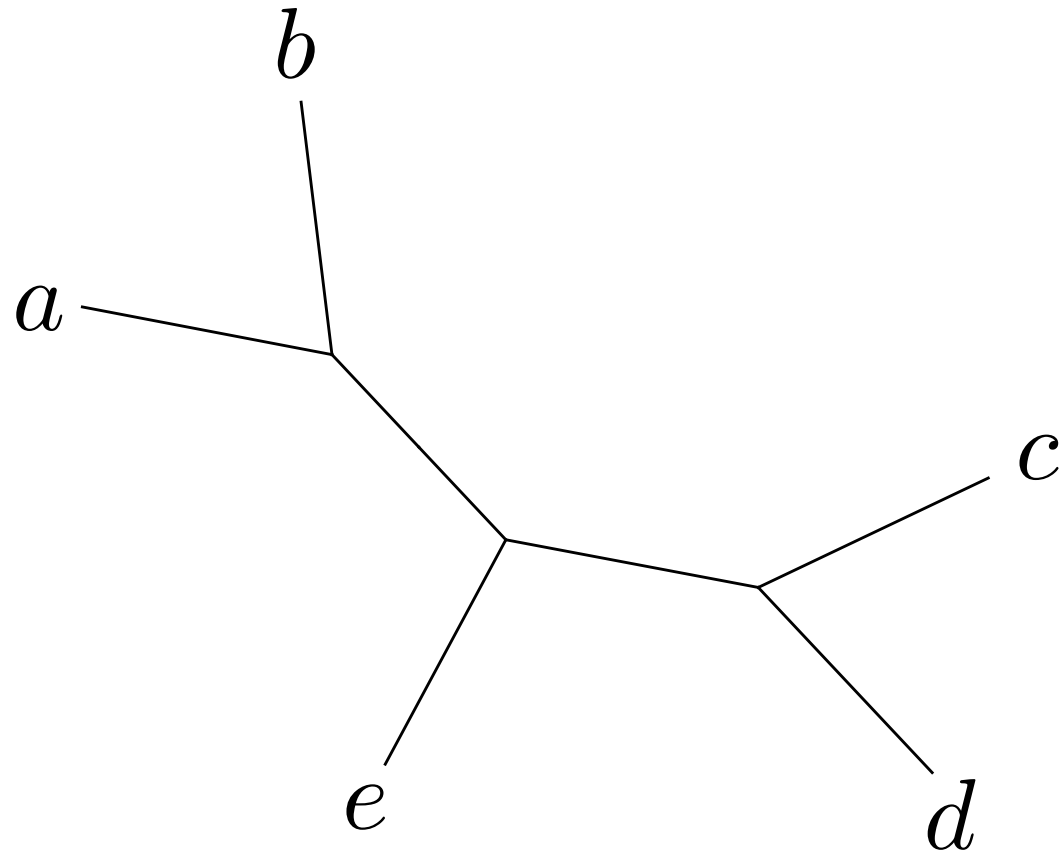

SplitsTree4
by Daniel Huson and David Bryant
with contributions from Markus Franz, Migüel Jette',
Tobias Kloepper and Michael Schröder
www.splitstree.org

Reconstruction of unrooted phylogenetic networks

- from splits
- from distances (via splits or not)
- from trees (via splits)
- from sequences (via splits or not)

Splits

A *split* $A \mid B$ on $\mathcal{X}$ is a partition of a taxon set $\mathcal{X}$ into two non-empty sets.



Compatible splits

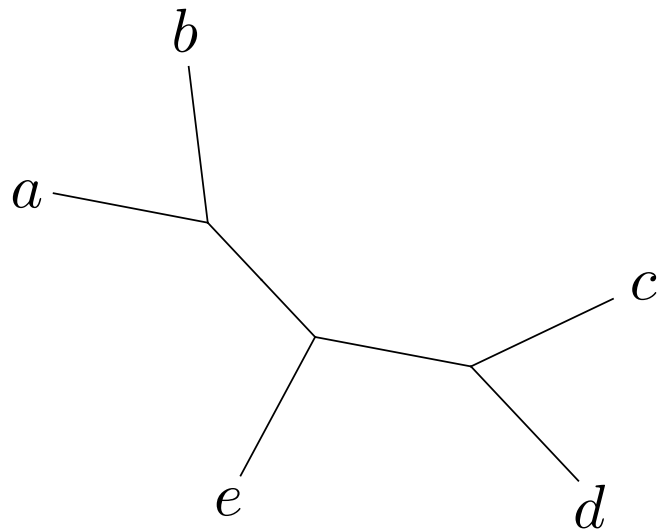
Two splits are $S_1 = A_1|B_1$ and $S_2 = A_2|B_2$ are compatible, if one of the $A_1 \cap A_2$, $A_1 \cap B_2$, $B_1 \cap A_2$ or $B_1 \cap B_2$ is empty. A set of splits $\mathcal{S}$ is called compatible if all pairs of splits in $\mathcal{S}$ are compatible.

Example

$$\mathcal{S}_1 = \begin{array}{l} \{a\}|\{b,c,d,e\} \\ \{b\}|\{a,c,d,e\} \\ \{c\}|\{a,b,d,e\} \\ \{d\}|\{a,b,c,e\} \\ \{e\}|\{a,b,c,d\} \\ \{a,b\}|\{c,d,e\} \\ \{a,b,e\}|\{c,d\} \end{array} \qquad \mathcal{S}_2 = \begin{array}{l} \{a,b,d,e,h\} \mid \{c,f,g\} \\ \{a,c,d,e,g,h\} \mid \{b,f\} \\ \{a,c,e,g\} \mid \{b,d,f,h\} \\ \{a,c,g\} \mid \{b,d,e,f,h\} \\ \{a,c,e,f,g\} \mid \{b,d,h\} \\ \{a,e,h\} \mid \{b,c,d,f,g\} \end{array}$$

Compatible splits

A set of compatible splits corresponds univocally to a unrooted phylogenetic tree.



(a) Unrooted tree T

$\{a\}|\{b,c,d,e\}$
$\{b\}|\{a,c,d,e\}$
$\{c\}|\{a,b,d,e\}$
$\{d\}|\{a,b,c,e\}$
$\{e\}|\{a,b,c,d\}$
$\{a,b\}|\{c,d,e\}$
$\{a,b,e\}|\{c,d\}$

(b) Split encoding of T

Circular splits

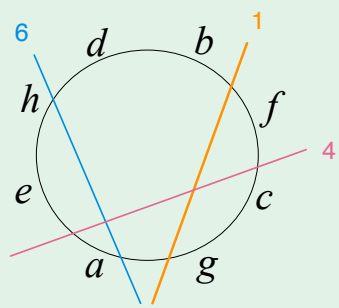
A set of splits $\mathcal{S}$ on $\mathcal{X}$ is called *circular*, if there exists a linear ordering $\pi = (x_1, \ldots, x_n)$ of the elements of $\mathcal{X}$ *for* $\mathcal{S}$ such that each split $S \in \mathcal{S}$ is *interval-realizable*, that is, has the form

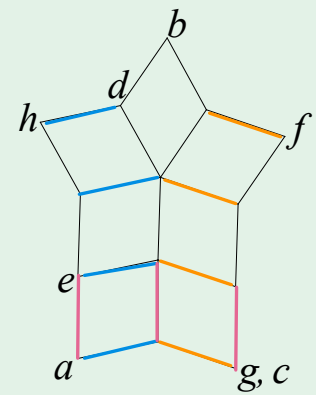
$$S = \{x_p, x_{p+1}, \ldots, x_q\} \mid (\mathcal{X} \setminus \{x_p, x_{p+1}, \ldots, x_q\}),$$

for appropriately chosen $1 < p \leq q \leq n$.

Example

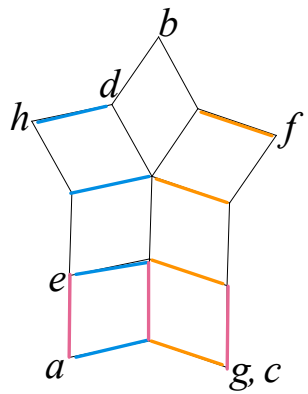
$\{a, b, d, e, h\} \mid \{c, f, g\}$
$\{a, c, d, e, g, h\} \mid \{b, f\}$
$\{a, c, e, g\} \mid \{b, d, f, h\}$
$\{a, c, g\} \mid \{b, d, e, f, h\}$
$\{a, c, e, f, g\} \mid \{b, d, h\}$
$\{a, e, h\} \mid \{b, c, d, f, g\}$





Circular splits

A set of circular splits corresponds to a unrooted network that is outer-labeled planar.



(a) Planar network

$\{a, b, d, e, h\} \mid \{c, f, g\}$
$\{a, c, d, e, g, h\} \mid \{b, f\}$
$\{a, c, e, g\} \mid \{b, d, f, h\}$
$\{a, c, g\} \mid \{b, d, e, f, h\}$
$\{a, c, e, f, g\} \mid \{b, d, h\}$
$\{a, e, h\} \mid \{b, c, d, f, g\}$

(b) Circular splits

Weakly compatible splits

Three splits $S_1 = \frac{A_1}{B_1}$, $S_2 = \frac{A_2}{B_2}$, and $S_3 = \frac{A_3}{B_3}$ *weakly compatible*, if

1. at least one of the following four intersections is empty:
   $A_1 \cap A_2 \cap A_3$, $A_1 \cap B_2 \cap B_3$, $B_1 \cap A_2 \cap B_3$ and $B_1 \cap B_2 \cap A_3$,
2. at least one of the following four intersections is empty:
   $B_1 \cap B_2 \cap B_3$, $B_1 \cap A_2 \cap A_3$, $A_1 \cap B_2 \cap A_3$ and $A_1 \cap A_2 \cap B_3$.

A set of splits $\mathcal{S}$ on $\mathcal{X}$ is called weakly compatible, if any *three* distinct splits in $\mathcal{S}$ are weakly compatible.

Example

$$\mathcal{S}_1 = \begin{array}{c} \{a,b,d,e,h\} \mid \{c,f,g\} \\ \{a,c,d,e,g,h\} \mid \{b,f\} \\ \{a,c,e,g\} \mid \{b,d,f,h\} \\ \{a,c,g\} \mid \{b,d,e,f,h\} \\ \{a,c,e,f,g\} \mid \{b,d,h\} \\ \{a,e,h\} \mid \{b,c,d,f,g\} \end{array} \qquad \mathcal{S}_2 = \begin{array}{c} \{a,b,d,e,h\} \mid \{c,f,g\} \\ \{a,c,d,e,g,h\} \mid \{b,f\} \\ \{a,c,e,g\} \mid \{b,d,f,h\} \\ \{a,c,d,e\} \mid \{b,f,g\} \\ \{a,b\} \mid \{c,d,e,f,g\} \\ \{a,e,f\} \mid \{b,c,d,g\} \end{array}$$

Weakly compatible splits

Phylogenetic networks reconstructed from weakly compatible are easier than the ones reconstructed from generic splits

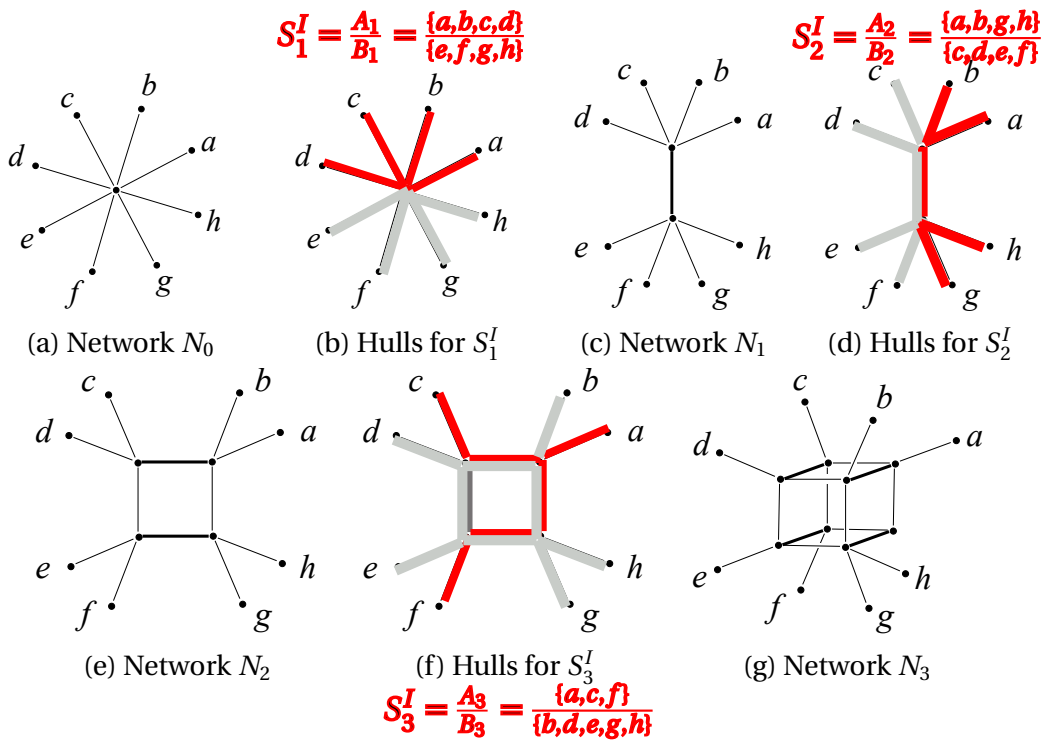
UPN from splits

or “what to do with the splits?”

PN from splits: the Convex hull algorithm

We start with the start tree and we add a split $S = \frac{A}{B}$ as follows:

1. Compute the two convex hulls $H(A)$ and $H(B)$ in N and let M be the graph induced by the nodes in $H(A) \cap H(B)$.
2. Create a copy M' of M and denote v' and e' the copies of a node v and an edge e in M.
3. Substitute any edge $f = (u, v)$ where u in $H(B) \setminus H(A) \neq \emptyset$ and v in M with edge $f = (u, v')$.
4. Connect each pair of nodes v in M and v' in M' by a new edge.



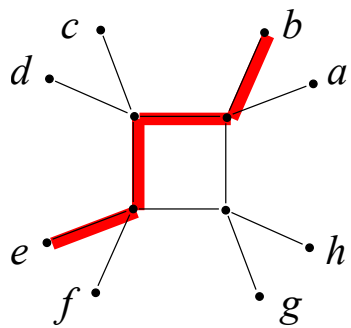
(a) Network N_0 (b) Hulls for S_1^I (c) Network N_1 (d) Hulls for S_2^I

(e) Network N_2 (f) Hulls for S_3^I (g) Network N_3

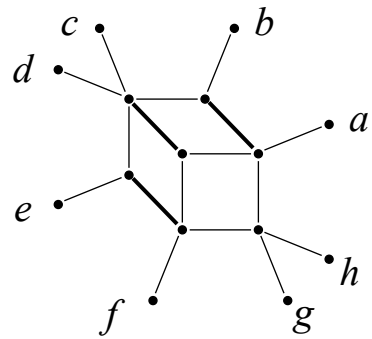
PN from splits: the circular network algorithm

We start with the start tree and we add a split $S = \frac{\{x_p,\ldots,x_q\}}{\mathcal{X}\setminus\{x_p,\ldots,x_q\}}$ as follows:
(splits have to be considered in a certain order)

1. Determine the path $M(x_p, x_q)$ and let $\dot{M}$ denote the path obtained by removing the first and last (leaf) edges from $M(x_p, x_q)$.
2. Create a copy $\dot{M}'$ of $\dot{M}$ and denote v' and e' the copies of a node v and an edge e in $\dot{M}$.
3. Substitute any edge $f = (u, v)$ where $u = \lambda(x_i)$ and v in $\dot{M}$ with edge $f = (u, v')$, for all $i = p, \ldots, q$.
4. Connect each pair of nodes v in $\dot{M}$ and v' in $\dot{M}'$ by a new edge.



(a) Network N_2

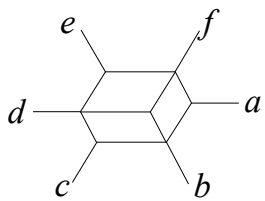


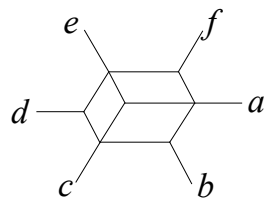
(b) Network N_3

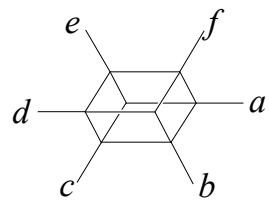
$\frac{A}{B} = \frac{\{a,f,g,h\}}{\{b,c,d,e\}}$

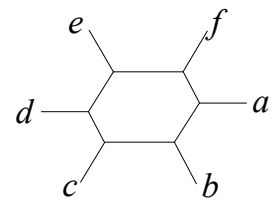
PN from splits: attention!!!

All four different split networks shown below represent the same set of splits.







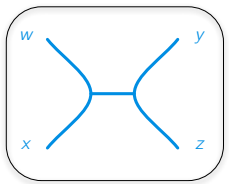


UPN from distances

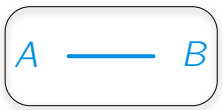
or “how to get the splits from distances”

PN from distances: the split decomposition

Given a distance matrix D on $\mathcal{X} = \{x_1, \ldots, x_n\}$ the split decomposition algorithm [Bandelt and Dress, 1992] starts by computing the isolation index for quartets and splits:



- for any four taxa w, x, y and z with $\{w, x\} \cap \{y, z\} = \emptyset$, : $\hat{\alpha}_D(\frac{\{w,x\}}{\{y,z\}}) = \frac{1}{2}(\max\{d(w,x) + d(y,z), d(w,y) + d(x,z), d(w,z) + d(x,y)\} - d(w,x) - d(y,z))$.
- for any (partial) split S: $\alpha_D(S) = \min\{\hat{\alpha}_D(\frac{\{w,x\}}{\{y,z\}}) \mid w, x \in A,\ y, z \in B\} \geq 0$.



Then, we set $X_0 = \emptyset$ and $\mathcal{S}_0 = \emptyset$. Given the set of splits $\mathcal{S}_i$ on the first i taxa, we obtain $\mathcal{S}_{i+1}$ by, for each split $\frac{A}{B} \in \mathcal{S}_i$ doing:

1. Consider $S = \frac{A \cup \{x_{i+1}\}}{B}$. If $\alpha_D(S) > 0$, set $\omega(S) = \alpha_D(S)$ and add S to $\mathcal{S}_{i+1}$.
2. Do the same with $S = \frac{A}{B \cup \{x_{i+1}\}}$ and $S = \frac{\mathcal{X}_i}{\{x_{i+1}\}}$

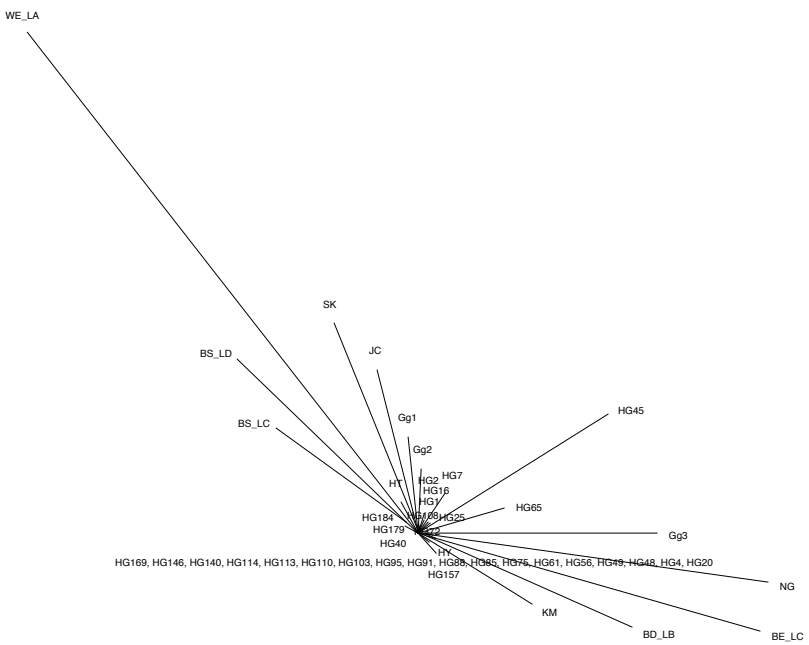
The result is given by $\mathcal{S}_n$.

PN from distances: the split decomposition

- A split S whose isolation index $\alpha_D(S)$ is greater than 0 is called a D-split. D-splits are always weakly compatible.
- It follows from this that the split decomposition always computes a set of weakly compatible splits

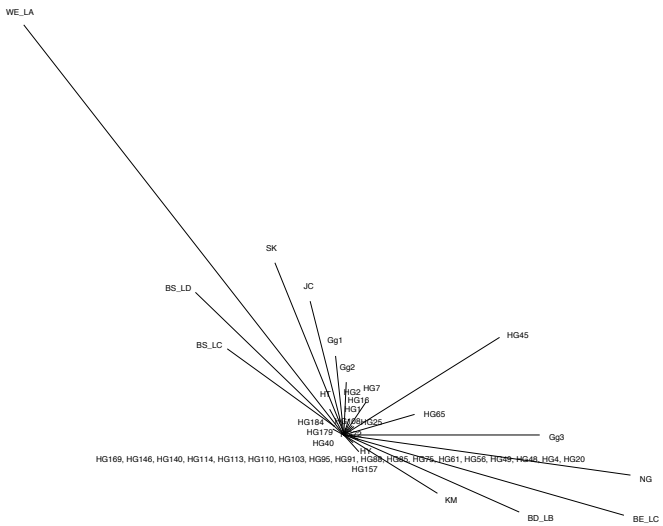
PN from distances: the split decomposition

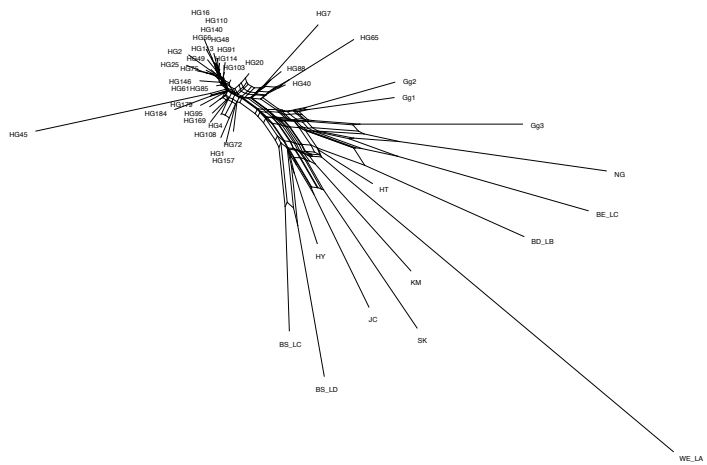
- A split S whose isolation index $\alpha_D(S)$ is greater than 0 is called a D-split. D-splits are always weakly compatible.
- It follows from this that the split decomposition always computes a set of weakly compatible splits
- The SD is a conservative method
- It can be used for small number of taxa or low divergence



PN from distances: Neighbor-Net

- Given a distance matrix D on $\mathcal{X}$, the Neighbor-Net algorithm [Bryant and Moulton, 2004] computes a circular ordering π of $\mathcal{X}$ from D and then a set of weighted splits $\mathcal{S}$ that are interval-realizable with respect to π:
  - produces circular splits
  - uses together with circular network algorithm to get planar networks
  - can be used for large number of taxa and high divergence





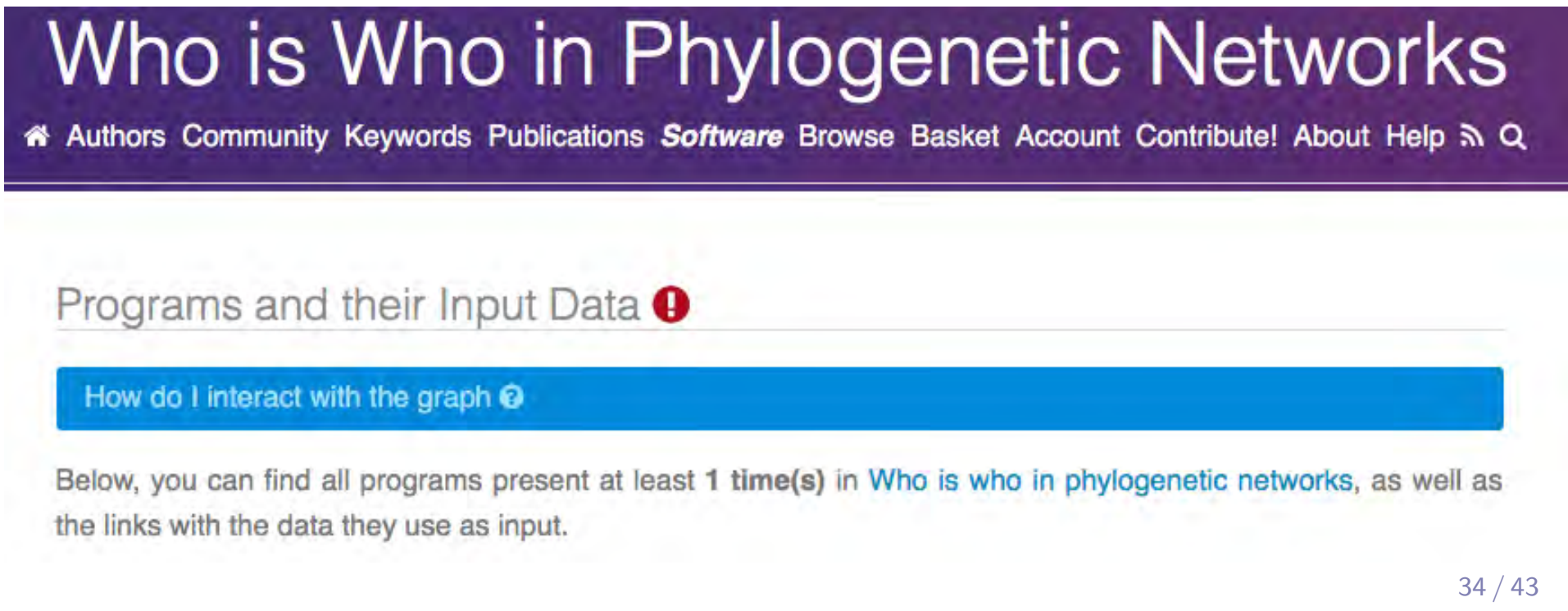
PN from distances

Other algorithms from distances:

- Minimum spanning network
- T-Rex
- ...

A great source of information:

http://phylnet.univ-mlv.fr/



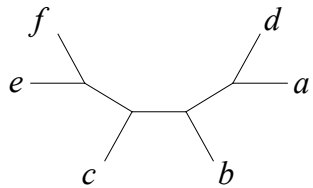
UPN from trees

or “how to get splits from a bunch of trees”

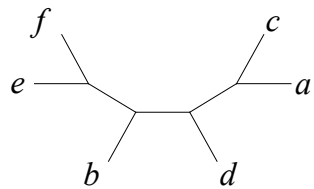
PN from trees: Consensus split networks

Consensus splits [Holland et al, 2004]

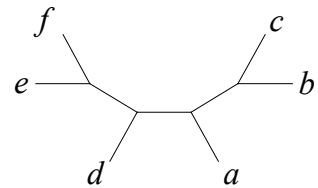
- Input: Trees on identical taxon sets
- Determine splits in more than X% of trees
- For >50%, the result is compatible



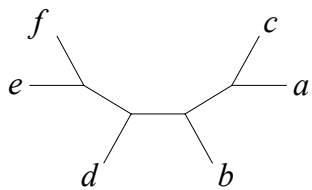
(a) Tree T_1



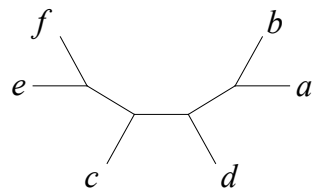
(b) Tree T_2



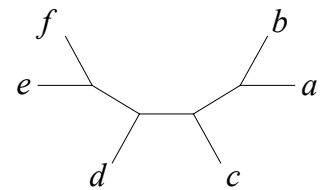
(c) Tree T_3



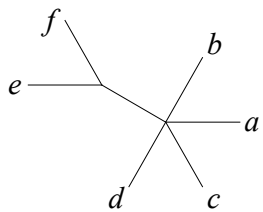
(d) Tree T_4



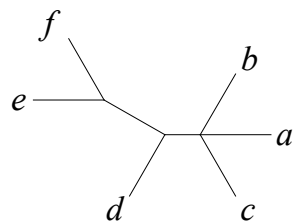
(e) Tree T_5



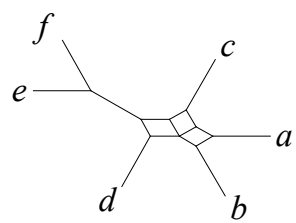
(f) Tree T_6



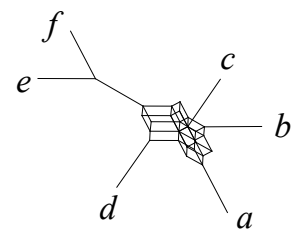
(g) Majority



(h) $d = 2$



(i) $d = 5$



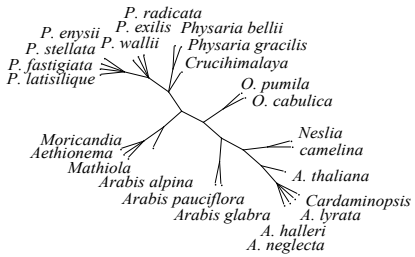
(j) All splits

PN from trees: Consensus super splits networks

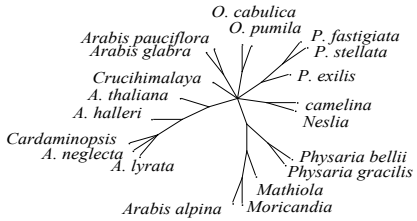
Consensus super splits [Huson et al, 2004, Whitfield et al 2008].

Input: Trees on overlapping taxon sets

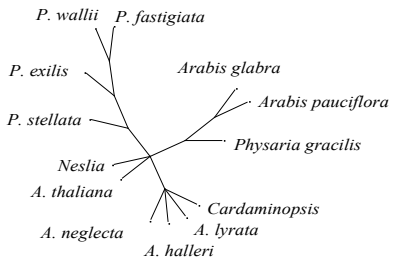
- Use the Z–closure to complete partial splits
- Use the "distortion" values to filter splits



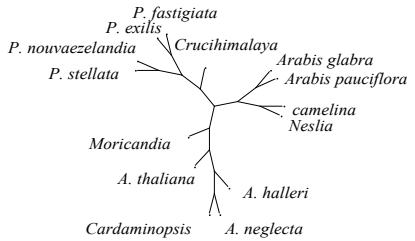
(a) Tree T_1



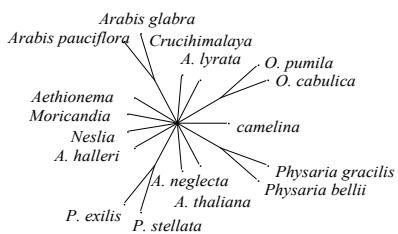
(b) Tree T_2



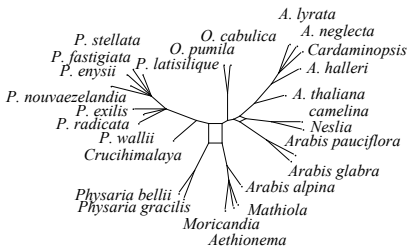
(c) Tree T_3



(d) Tree T_4



(e) Tree T_5



(f) Super network N

The Z-closure

- Two partial splits $S_1 = \frac{A_1}{B_1} \in \mathcal{S}$ and $S_2 = \frac{A_2}{B_2} \in \mathcal{S}$ are said to be in *Z-relation* to each other, if exactly one of the four intersections $A_1 \cap A_2$, $A_1 \cap B_2$, $B_1 \cap A_2$ or $B_1 \cap B_2$ is empty. Then we can create of two new splits (the *Z-operation*)

$$S_1' = \frac{A_1}{B_1 \cup B_2} \text{ and } S_2' = \frac{A_1 \cup A_2}{B_2}.$$

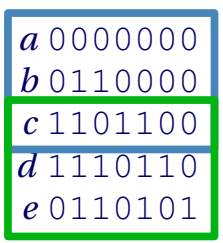
- If at least one of the two new splits contains more taxa than its predecessor, the pair of splits is called *productive*.

From a set partial splits $\mathcal{S}$ on $\mathcal{X}$, *Z-closure* method infers a set of complete splits on $\mathcal{X}$ as follows: While $\mathcal{S}$ contains a productive pair of splits $\{S_i, S_j\}$, apply the Z-operation to obtain two new splits $\{S_i', S_j'\}$ and then replace the former pair by the latter pair in $\mathcal{S}$. Finally, add all trivial splits on $\mathcal{X}$.

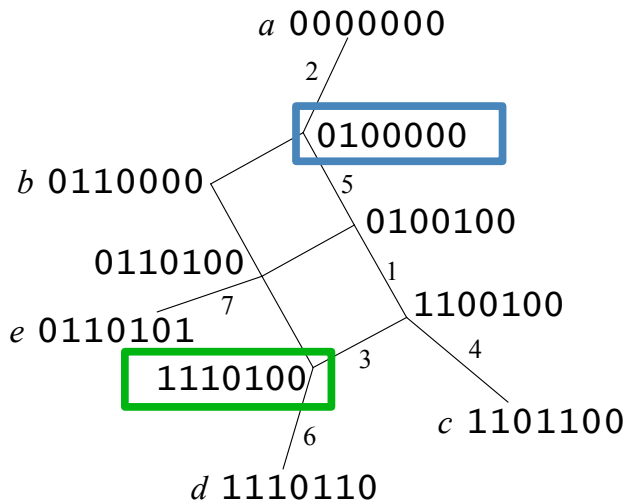
UPN from sequences

Median networks

For a multiple alignment M of binary sequences on $\mathcal{X}$, its median network is a phylogenetic network $N = (V, E, \sigma, \lambda)$ whose node set is given by the median closure $V = \bar{M}$ and in which any two nodes a and b are connected by an edge e of color $\sigma(e) = i \in E$, if any only if they differ in exactly in their i-th position (as haplotypes). An associated taxon labeling $\lambda : X \to V$ maps each taxon x onto the node $\lambda(x)$ that represents the corresponding sequence.



(a) Alignment M



(b) Median network N

Quasi median networks

a	A A A A A
b	B B A A A
c	A B A B B
d	A A B B C
e	A A C B C

(a) Input M

a	0	0	0	0	0	0	0	0	0
b	1	1	0	0	0	0	0	0	0
c	0	1	0	0	0	1	1	1	0
d	0	0	1	1	0	1	1	0	1
e	0	0	1	0	1	1	1	0	1

(b) Binary expansion M_1

a	0	0	0	0	0	0	0
b	1	1	0	0	0	0	0
c	0	1	0	0	0	1	1
d	0	0	1	1	0	1	0
e	0	0	1	0	1	1	0

(c) Condensed M_1

0	0	0	0	0	0	0	0
1	1	0	0	0	0	0	0
0	1	0	0	0	1	1	1
0	0	1	1	0	1	0	1
0	0	1	0	1	1	0	1
0	0	1	0	0	1	0	1
0	0	0	0	0	1	0	0
0	1	0	0	0	0	0	0
0	1	0	0	0	1	0	0

(d) Median closure M_2

0	0	0	0	0	0	0	0	0	0
1	1	0	0	0	0	0	0	0	0
0	1	0	0	0	1	1	1	1	0
0	0	1	1	0	1	1	1	0	1
0	0	1	0	1	1	1	1	0	1
0	0	1	0	0	1	1	1	0	1
0	0	0	0	0	1	1	0	0	0
0	1	0	0	0	0	0	0	0	0
0	1	0	0	0	1	1	0	0	0

(e) Expanded M_2

A	A	A	A	A
B	B	A	A	A
A	B	A	B	B
A	A	C	B	C
A	A	B	B	C
A	A	$\star$	B	C
A	A	A	B	$\star$
A	B	A	A	A
A	B	A	B	$\star$

(f) Multi-states M_3

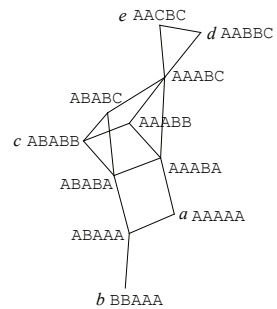
A	0	0	0
B	1	1	0
C	1	0	1

$$
\begin{aligned}
\texttt{AA}\star\texttt{BC} &= \left\{ \begin{array}{ccccc} \texttt{A} & \texttt{A} & \texttt{A} & \texttt{B} & \texttt{C} \\ \texttt{A} & \texttt{A} & \texttt{B} & \texttt{B} & \texttt{C} \\ \texttt{A} & \texttt{A} & \texttt{C} & \texttt{B} & \texttt{C} \end{array} \right. \\
\texttt{AAAB}\star &= \left\{ \begin{array}{ccccc} \texttt{A} & \texttt{A} & \texttt{A} & \texttt{B} & \texttt{A} \\ \texttt{A} & \texttt{A} & \texttt{A} & \texttt{B} & \texttt{B} \\ \texttt{A} & \texttt{A} & \texttt{A} & \texttt{B} & \texttt{C} \end{array} \right. \\
\texttt{ABAB}\star &= \left\{ \begin{array}{ccccc} \texttt{A} & \texttt{B} & \texttt{A} & \texttt{B} & \texttt{A} \\ \texttt{A} & \texttt{B} & \texttt{A} & \texttt{B} & \texttt{B} \\ \texttt{A} & \texttt{B} & \texttt{A} & \texttt{B} & \texttt{C} \end{array} \right.
\end{aligned}
$$

(g) Expansion of virtual medians

A	A	A	A	A
B	B	A	A	A
A	B	A	B	B
A	A	C	B	C
A	A	B	B	C
A	A	A	B	C
A	A	A	B	A
A	A	A	B	B
A	B	A	A	A
A	B	A	B	A
A	B	A	B	C

(h) Final matrix M_4



(i) Quasi-median network N

How to keep the complexity of the network down...

The number of nodes of the quasi-median network can be very large, even for a small number of short sequences. Thus, the quasi-median network is rarely useful in practice. There exist two alternative methods:

- median-joining algorithm, which aims at computing an UPN that is as informative as a quasi-median network, but usually much smaller. The algorithm has a parameter Δ that is used to control how complex the resulting phylogenetic network will be.
- geodesically-pruned quasi-median networks: a method that aims at computing a pruned version of the full quasi-median network by considering only those sequences that lie on a geodesic between two of the original input sequences.

How to keep the complexity of the network down...

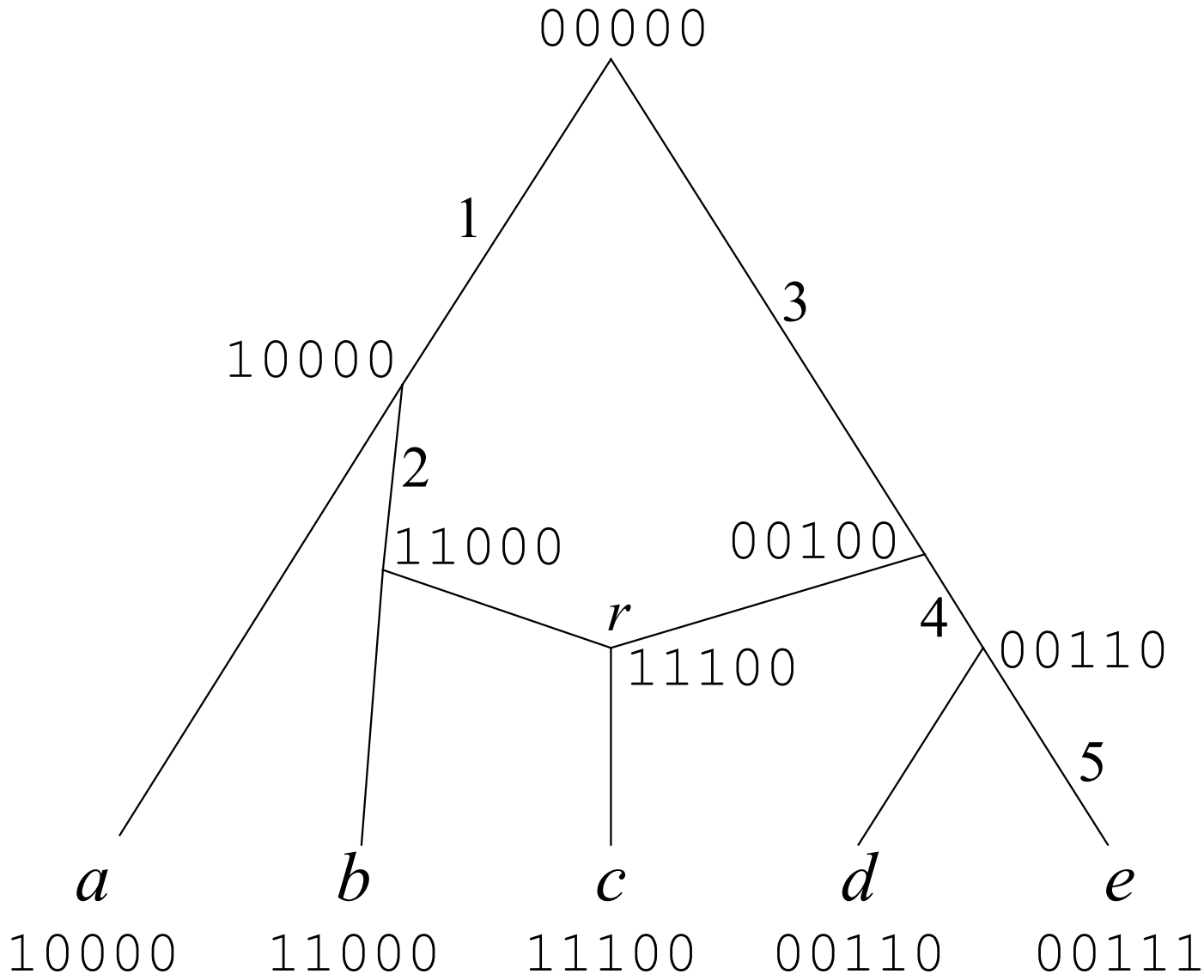
UPN from ...

quartets ... QNet

`http://www2.cmp.uea.ac.uk/~vlm/qnet/`

`http://phylnet.univ-mlv.fr/`

Recombination networks



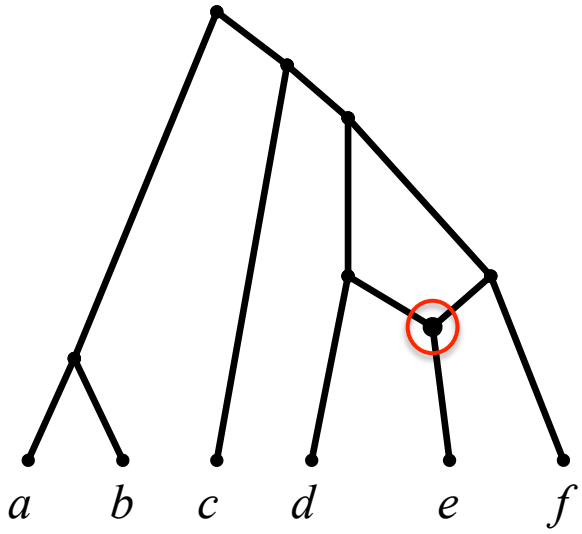
Daniel H. Huson, Regula Rupp, Celine Scornavacca. Phylogenetic Networks. Cambridge University Press. 2011

Methods for reconstructing rooted phylogenetic networks not accounting for ILS

some slides have been kindly provided by Fabio Pardi

Trees displayed by a network

In a phylogenetic network, a reticulate event is represented as a reticulation, where branches converge to give rise to a new lineage:



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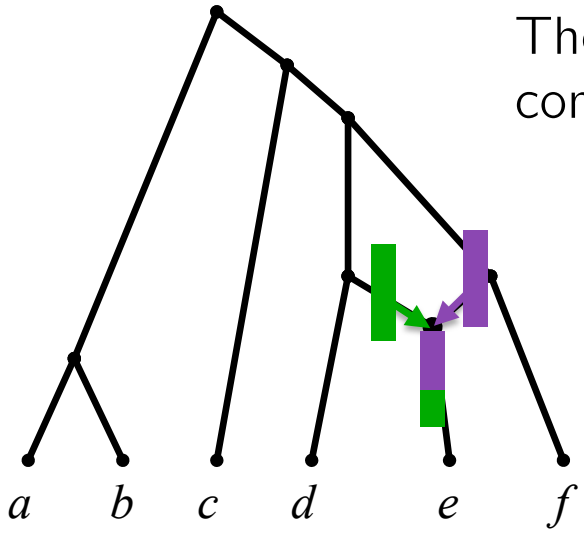
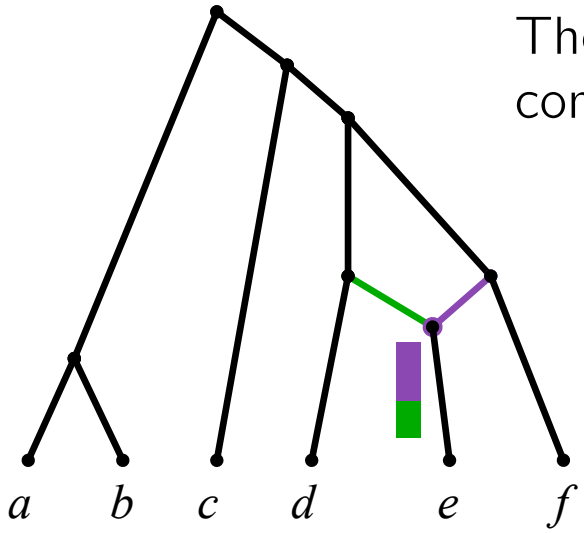


The genome at the start of the new lineage is a composition of those of the parent lineages.

Trees displayed by a network

In a phylogenetic network, a reticulate event is represented as a reticulation, where branches converge to give rise to a new lineage:



The genome at the start of the new lineage is a composition of those of the parent lineages.

The evolution of each part independently inherited is described by a *"gene" tree*

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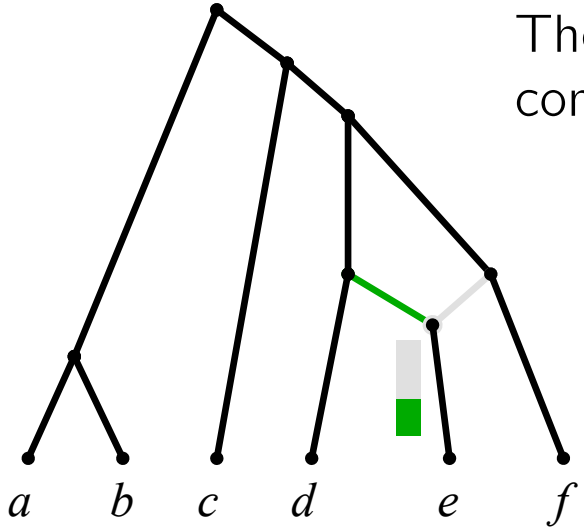

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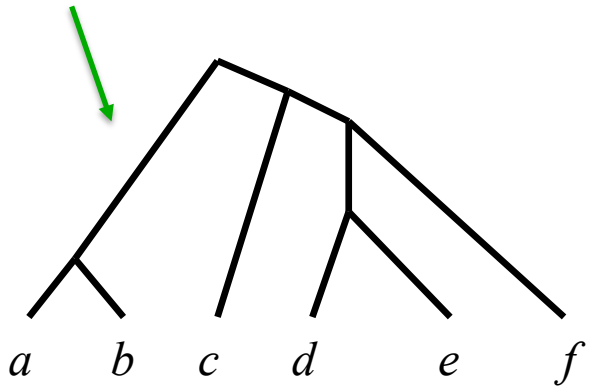

Trees displayed by a network

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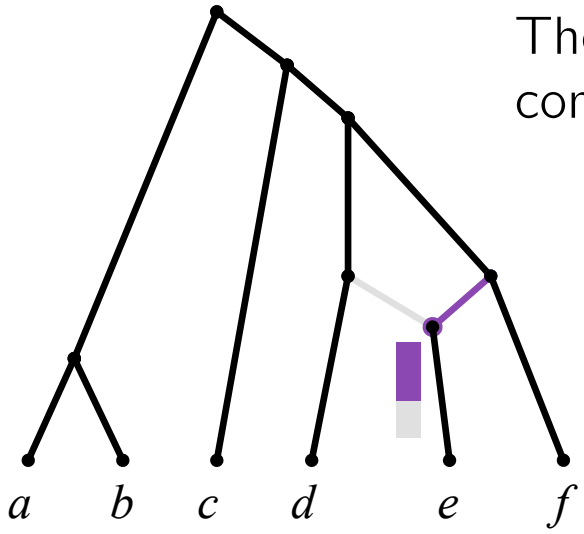

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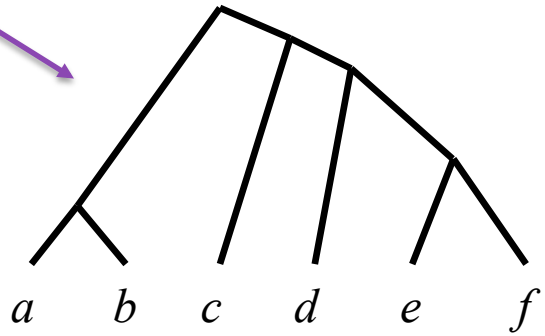

Trees displayed by a network

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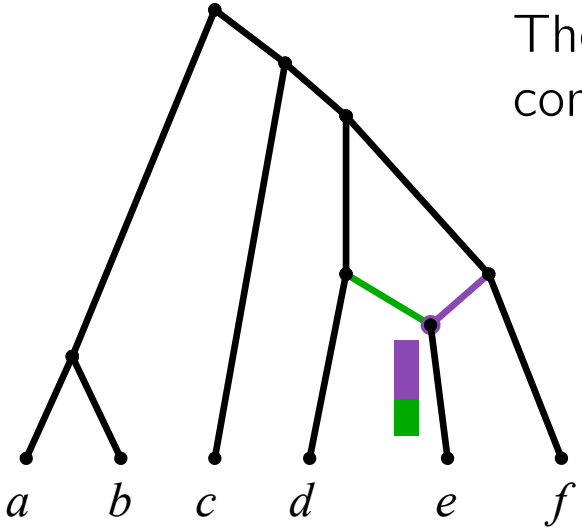
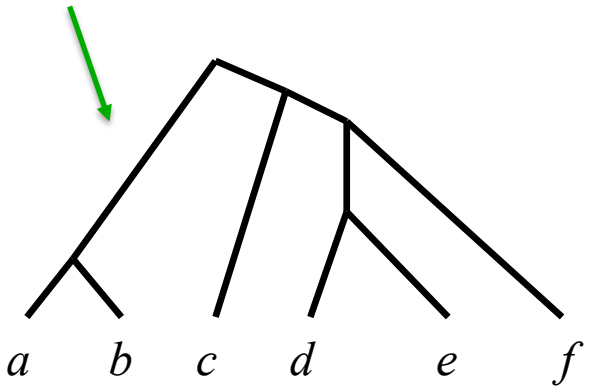
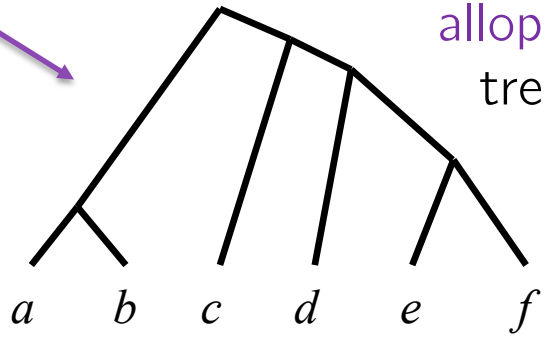


The genome at the start of the new lineage is a composition of those of the parent lineages.

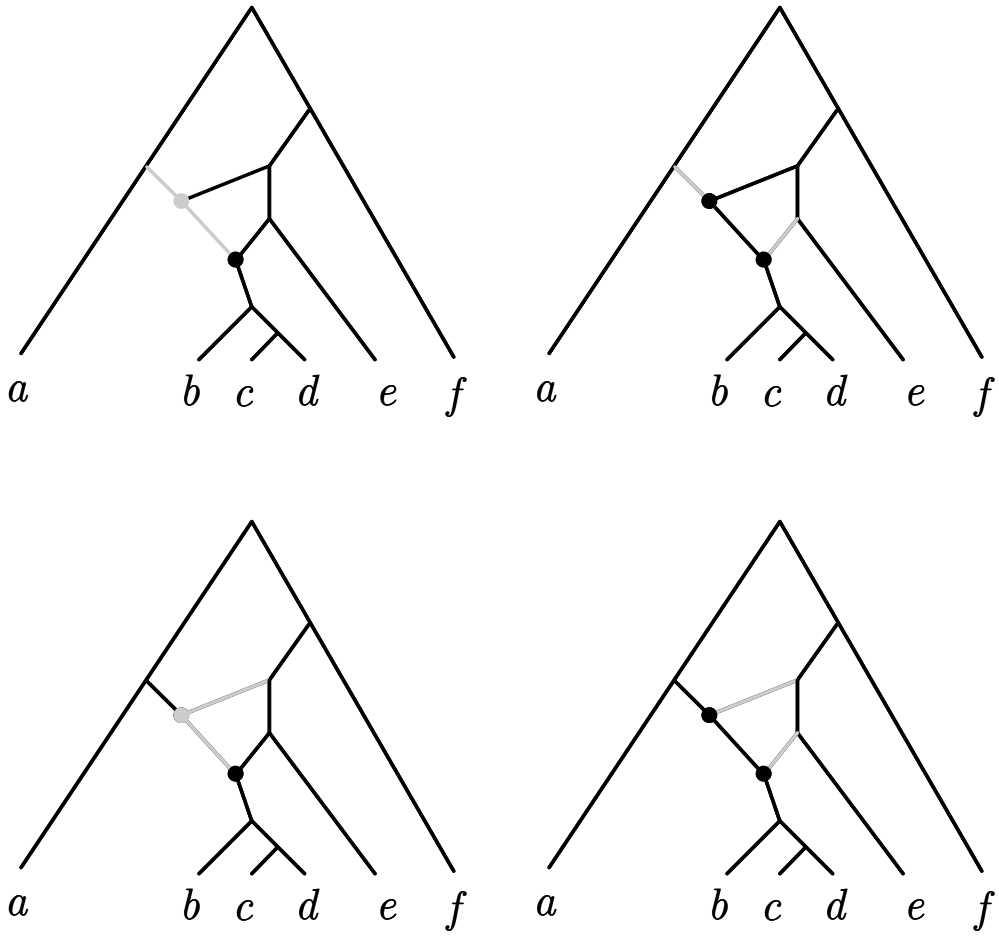
The evolution of each part independently inherited is described by a *"gene" tree*





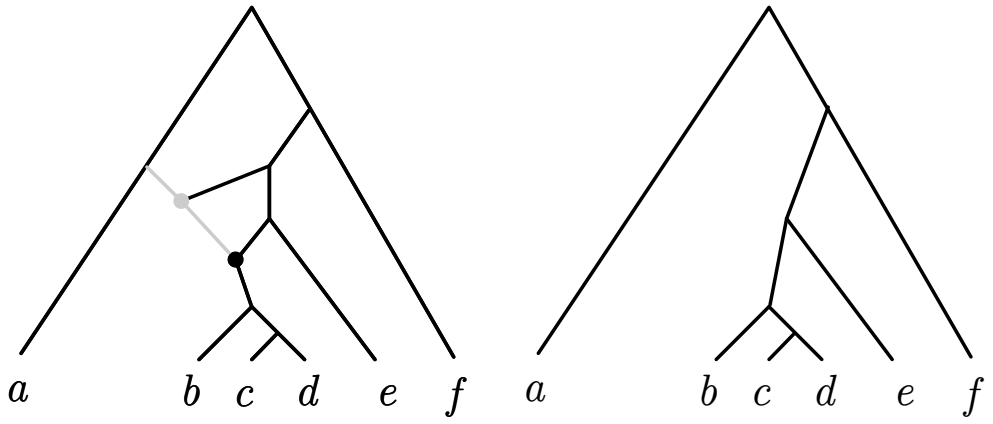
In the absence of deep coalescence and allopolyploidy, the gene trees are *displayed* by the network

Trees displayed by a network



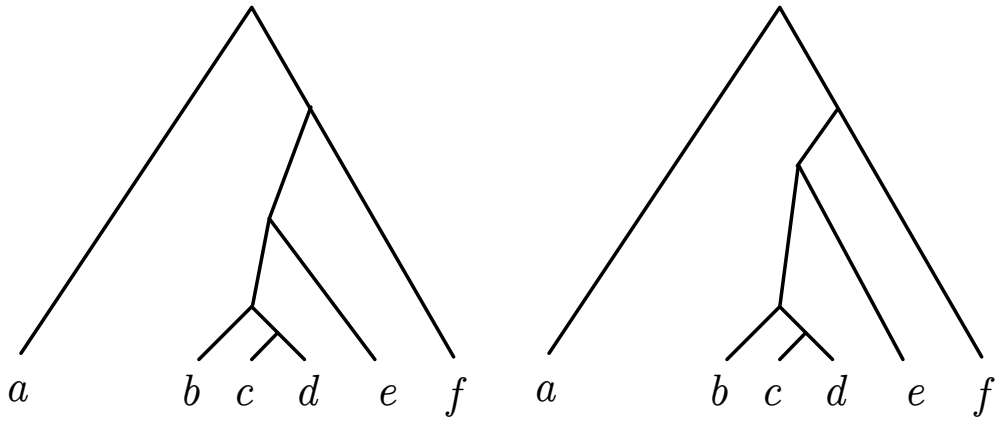
Switch on and off reticulated edged

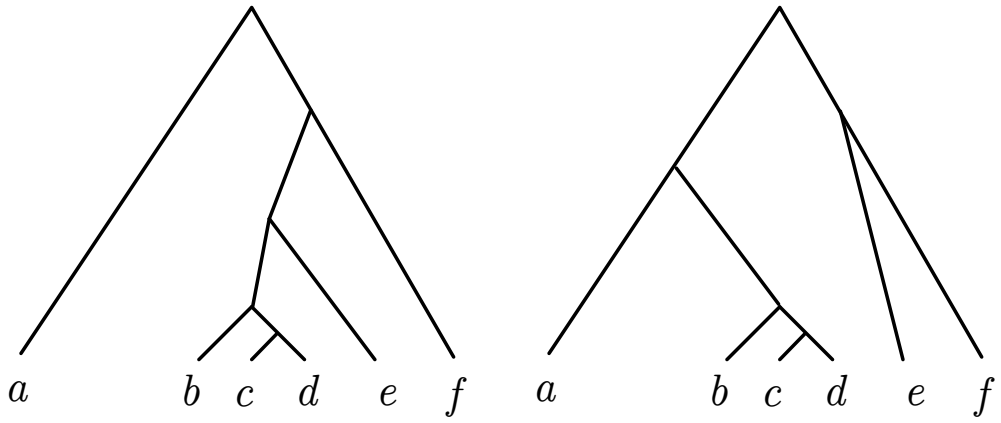
Trees displayed by a network



Delete switched off edges and unlabelled leaves and suppress outdgree-1 indegree-1 nodes

Trees displayed by a network

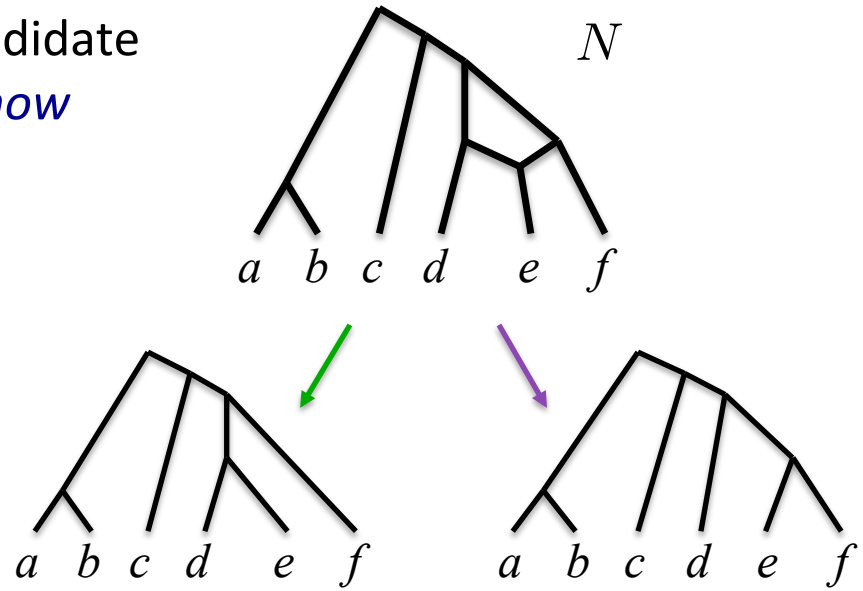




2^r possible trees!!!

Phylogenetic network inference

An optimization problem where a candidate network is evaluated *on the basis of how well the trees it displays fit the data:*



Many possible formulations:

Data:

Trees with 3 taxa:
(inferred from other data)

Goal:

Find the network N with the lower hybridization number such that the triplets are `consistent' with one of the trees displayed by N

subject to constraints on the complexity of N

Triplets - Software

- **LEV1ATHAN**: A practical algorithm for reconstructing level-1 phylogenetic networks. Combines any set of phylogenetic trees into a level-1 phylogenetic network that is consistent with a large number of the triplets of the input trees.

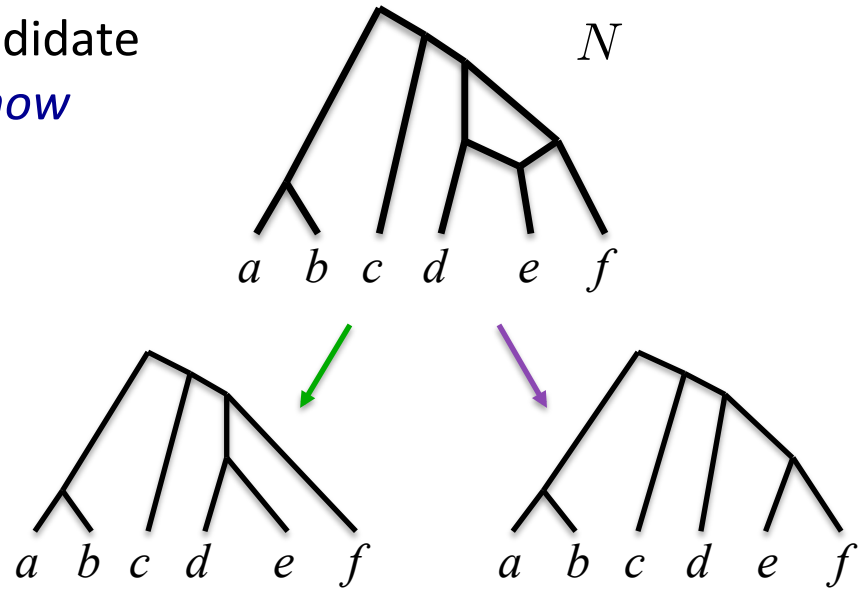
- **SIMPLISTIC**: Returns a phylogenetic network with minimum level consistent with all input triplets

- **MARLON**: Constructs a level-1 phylogenetic networks with a minimum number of reticulations consistent with a dense set of triplets, if such a network exists

- **LEVEL2**: Constructs a level-2 phylogenetic network consistent with a dense set of triplets, if such a network exists

Phylogenetic network inference

An optimization problem where a candidate network is evaluated *on the basis of how well the trees it displays fit the data:*



Many possible formulations:

Data:

Clusters of taxa: $\{a,b\}, \{d,e\}, \{d,e,f\}, \{a,b,c,d,e,f\}, \{e,f\}, \{c,d,e,f\}, \ldots$

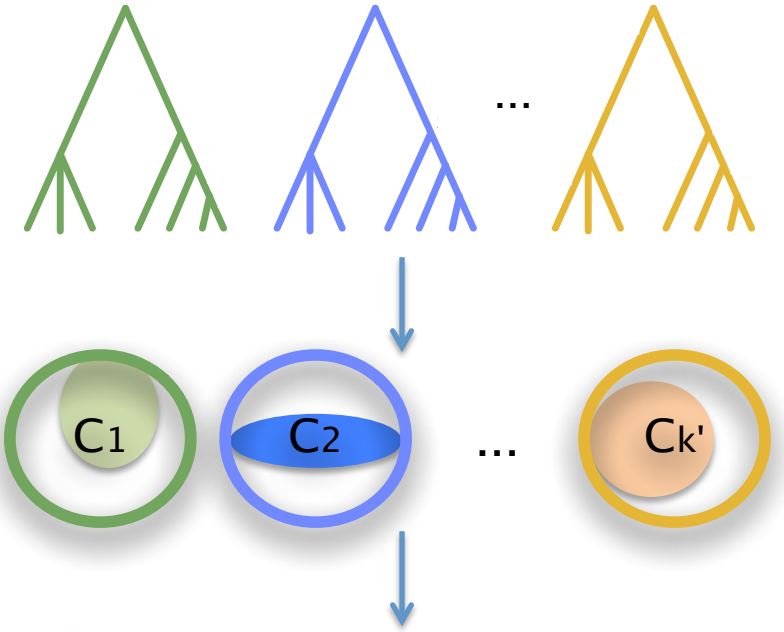
Goal:

Find the network N with the lower hybridization number such that the input clusters are `explained' by one of the trees displayed by N

subject to constraints on the complexity of N

Clusters

CASS algorithm : search for the level-k network containing a set of clusters

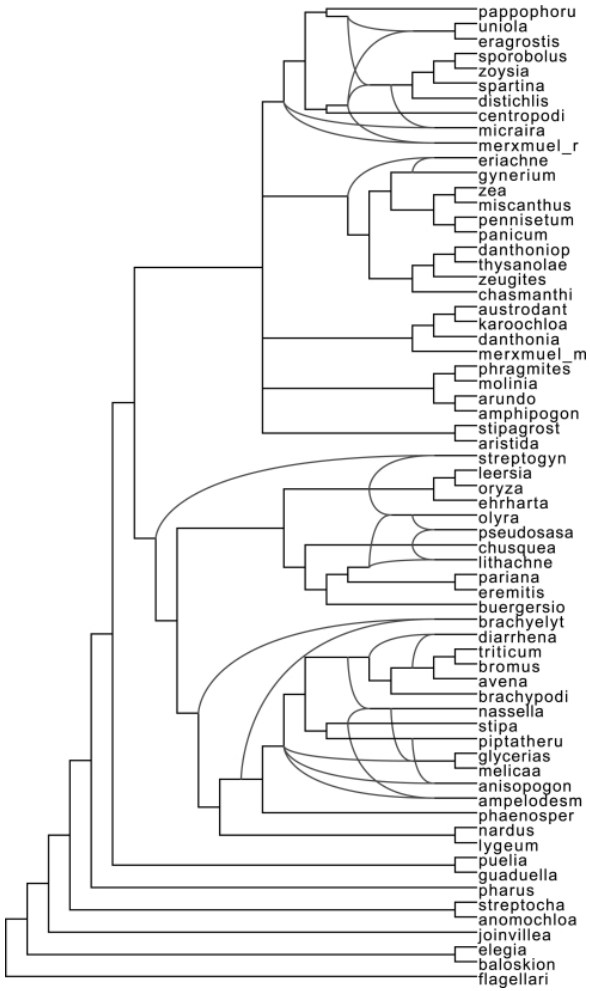


Dendroscope 3

by Daniel H. Huson

with contributions from Benjamin Albrecht. Philippe Gambette, Leo van Iersel, Celine Scornavacca and others.

www-ab.informatik.uni-tuebingen.de/software/dendroscope



Phylogenetic network inference

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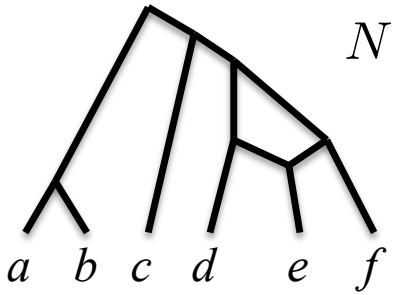

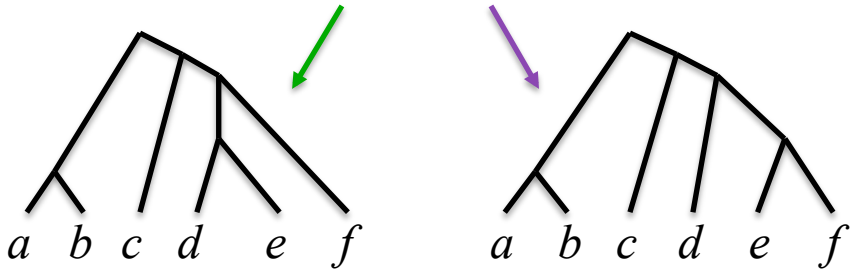

Many possible formulations:

Data:

Any trees on the same taxa:
(inferred from other data)

Goal:

Find the network N with the lower hybridization number such that the input trees are `consistent' with one of the trees displayed by N

subject to constraints on the complexity of N

Software

Hybroscale 1.5

Hybroscale

by
Benjamin Albrecht

www.bio.ifi.lmu.de/softwa

Dendroscope 3

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with contributions from Benjamin Albrecht.
Philippe Gambette, Leo van Iersel,
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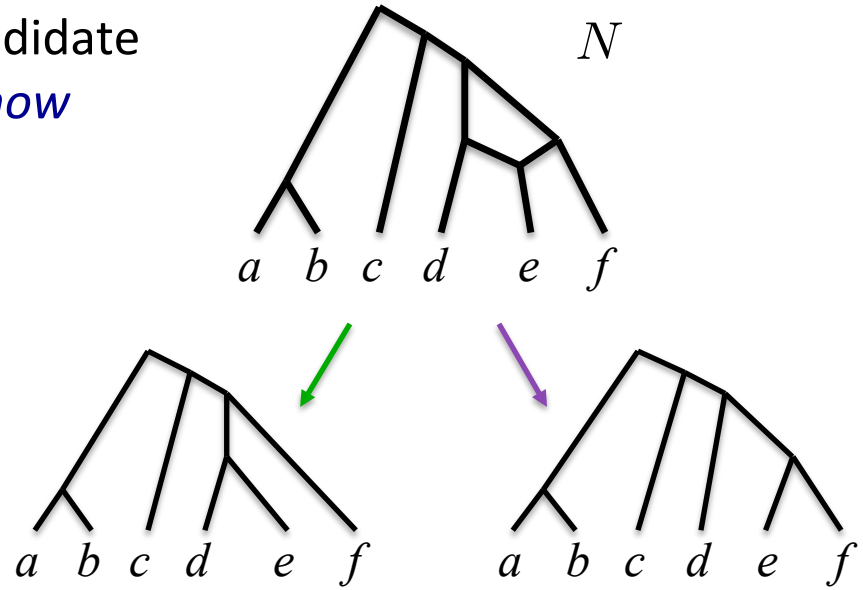
ultraNet

An UltraFast Tool for Minimum Reticulate Networks

Phylogenetic network inference

An optimization problem where a candidate network is evaluated *on the basis of how well the trees it displays fit the data:*



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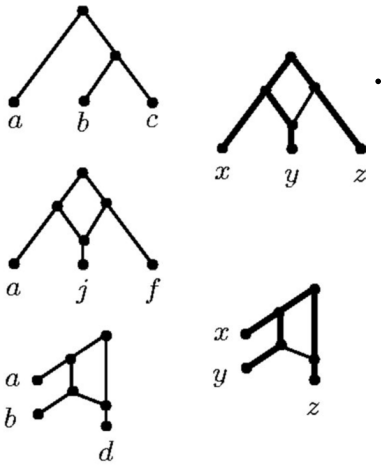
(inferred from other data)

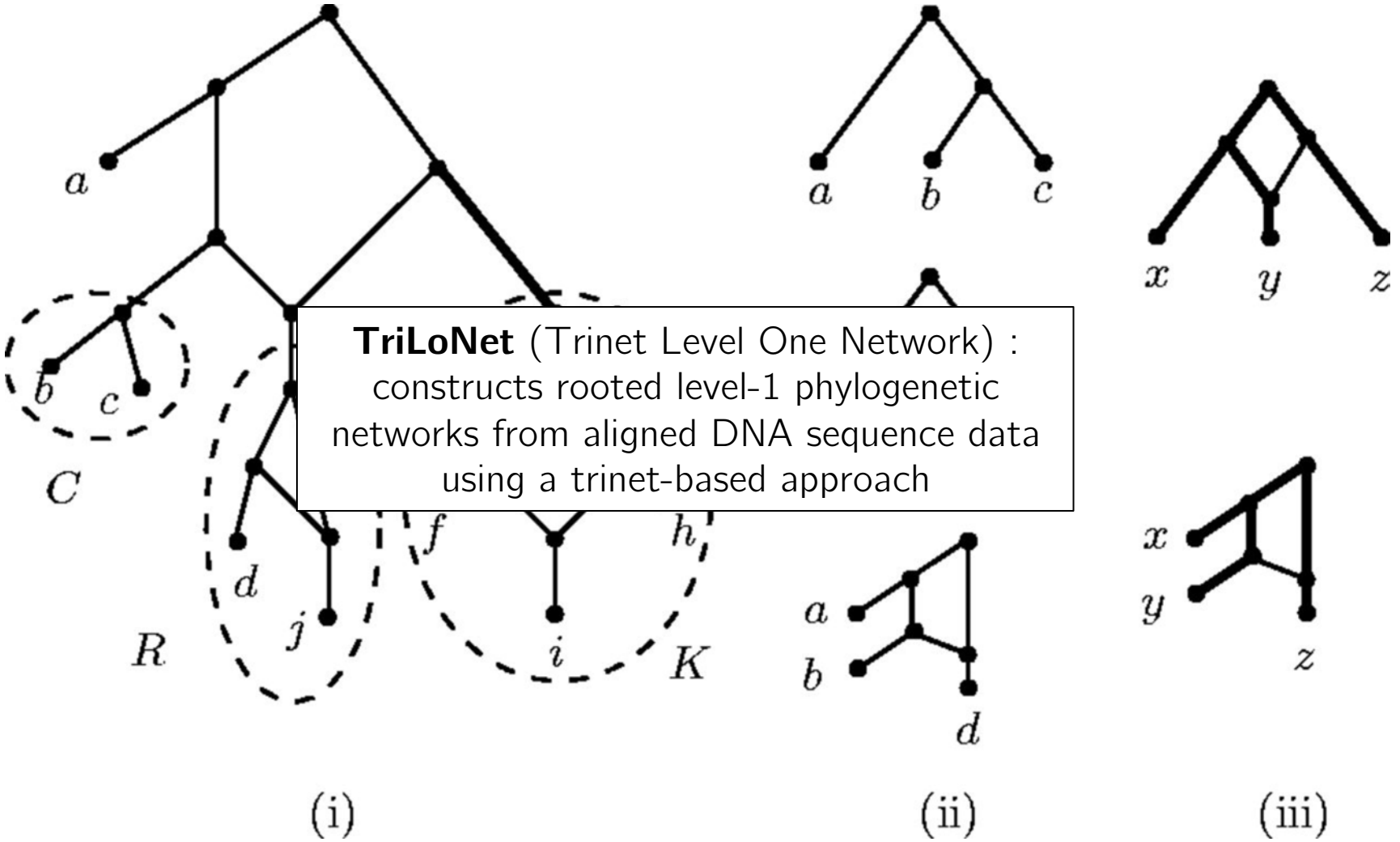


Goal:

Find the network N with the lower hybridization number such that the input trees are `consistent' with the N

subject to constraints on the complexity of N

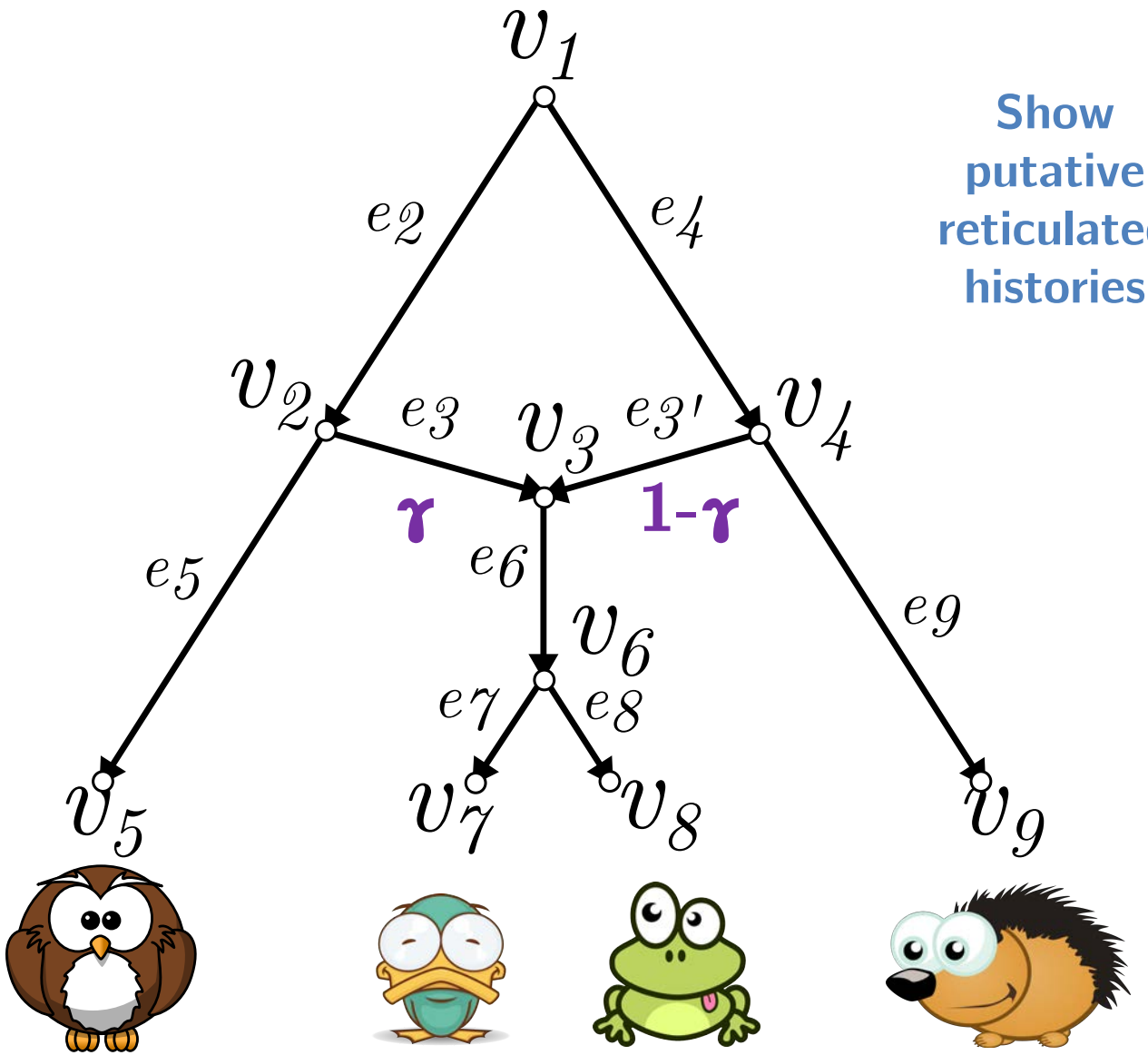
Trinets



TriLoNet (Trinet Level One Network) : constructs rooted level-1 phylogenetic networks from aligned DNA sequence data using a trinet-based approach

Oldman et al. TriLoNet: Piecing Together Small Networks to Reconstruct Reticulate Evolutionary Histories. 2016

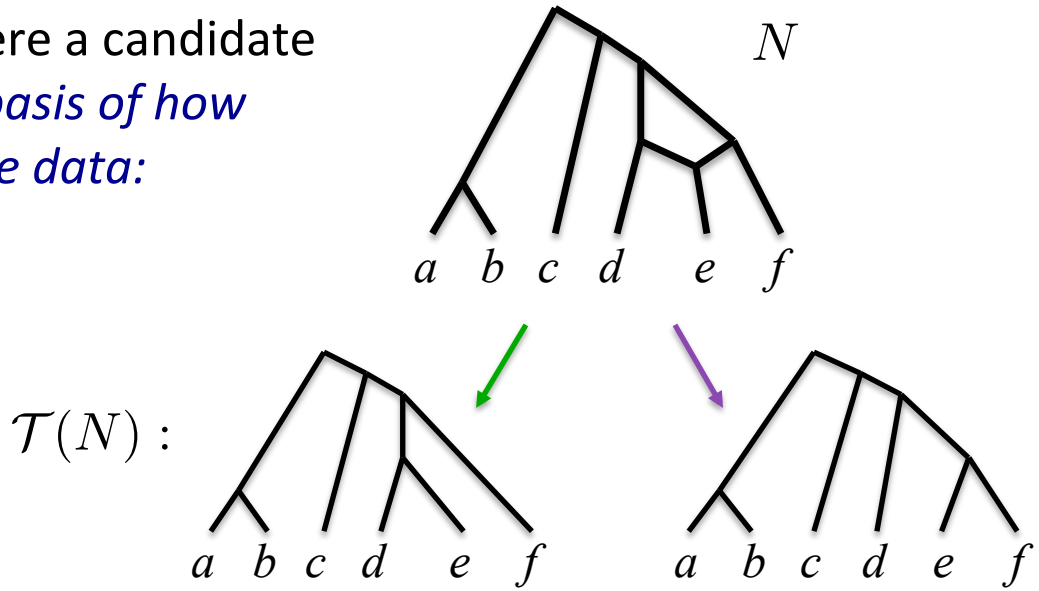
Explicit phylogenetic networks (rDAG)



Show putative reticulated histories

Phylogenetic network inference

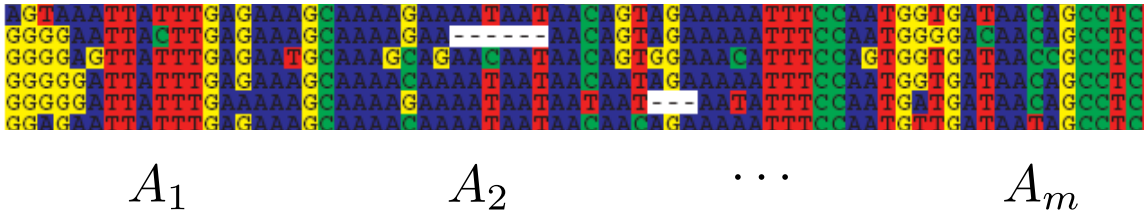
An optimization problem where a candidate network is evaluated *on the basis of how well the trees it displays fit the data:*



Many possible formulations:

Data:

Sequence alignments:
(typically given in blocks)



Goal:

Find N that minimizes $\boldsymbol{F}(N|A_1, A_2, \ldots, A_m) = \sum_{i=1}^{m} \min_{T \in \mathcal{T}(N)} F(T|A_i)$

subject to constraints on the complexity of N. $\boldsymbol{F}()$ is the parsimony score.

Jin et al. Parsimony Score of Phylogenetic Networks: Hardness Results and a Linear-Time Heuristic. TCCB. 2009.

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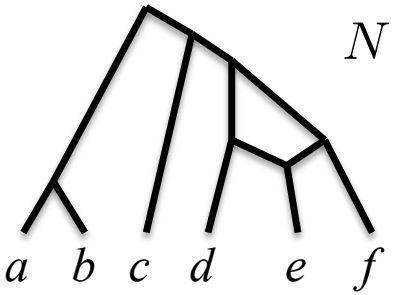
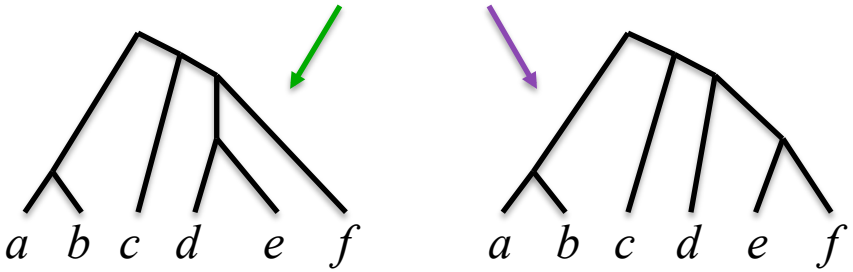


NEPAL
Phylogenetic Networks Parsimony and Likelihood Toolkit

$\mathcal{T}(N)$:



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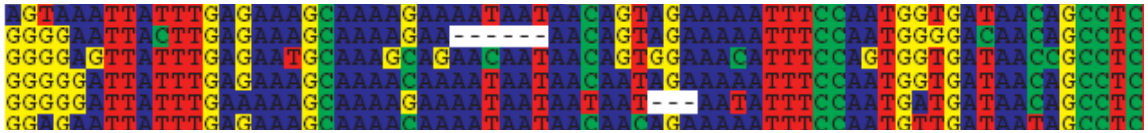

$A_1 \qquad A_2 \qquad \cdots \qquad A_m$

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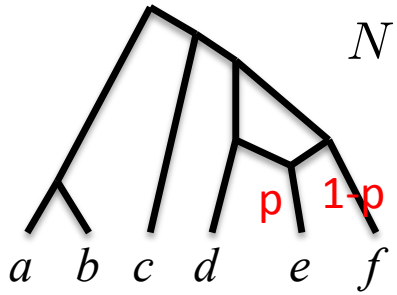

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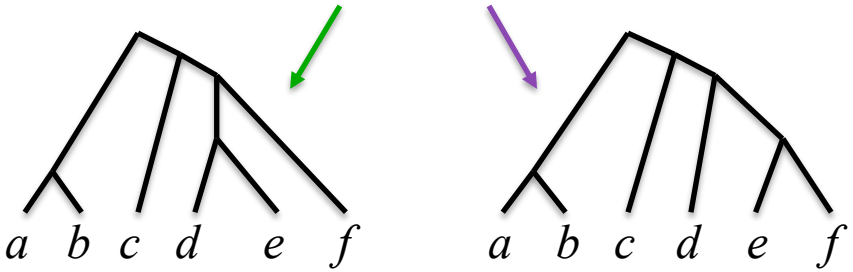

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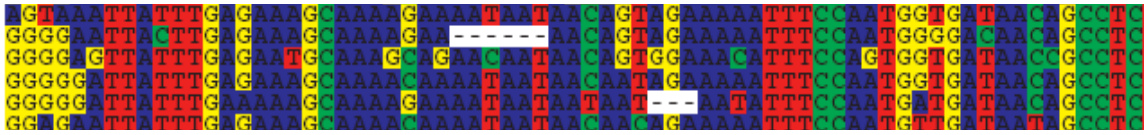


A_1 A_2 $\cdots$ A_m

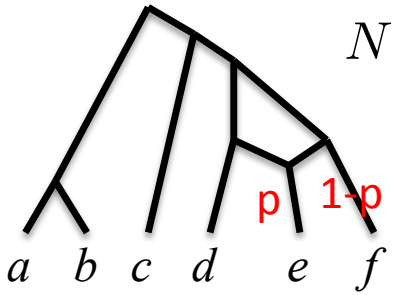
Goal:

Find N that maximises $\mathbf{Pr}(A_1, A_2, \ldots, A_m|N) = \prod_{i=1}^{m} \mathbf{Pr}(A_i|N) = \prod_{i=1}^{m} \left(\sum_{T \in \mathcal{T}(N)} \mathbf{Pr}(A_i|T)\mathbf{Pr}(T|N) \right)$

Jin et al.Maximum likelihood of phylogenetic networks. Bioinformatics 2006.

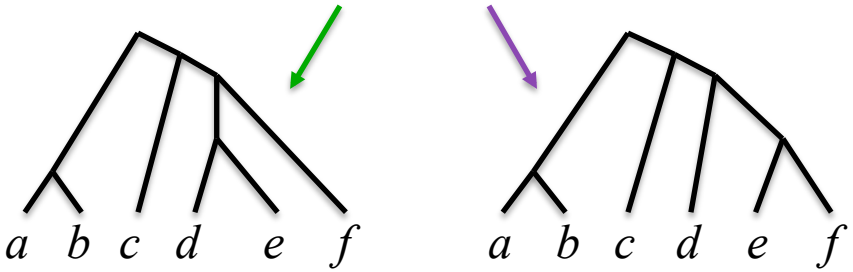
Phylogenetic network inference

An optimization problem where a candidate network is evaluated *on the basis of how well the trees it displays fit the data:*



NEPAL
Phylogenetic Networks Parsimony and Likelihood Toolkit

$\mathcal{T}(N)$:



Many possible formulations:

Data:

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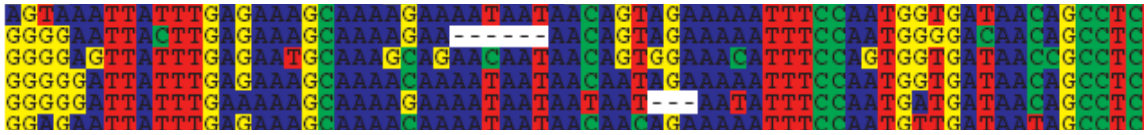


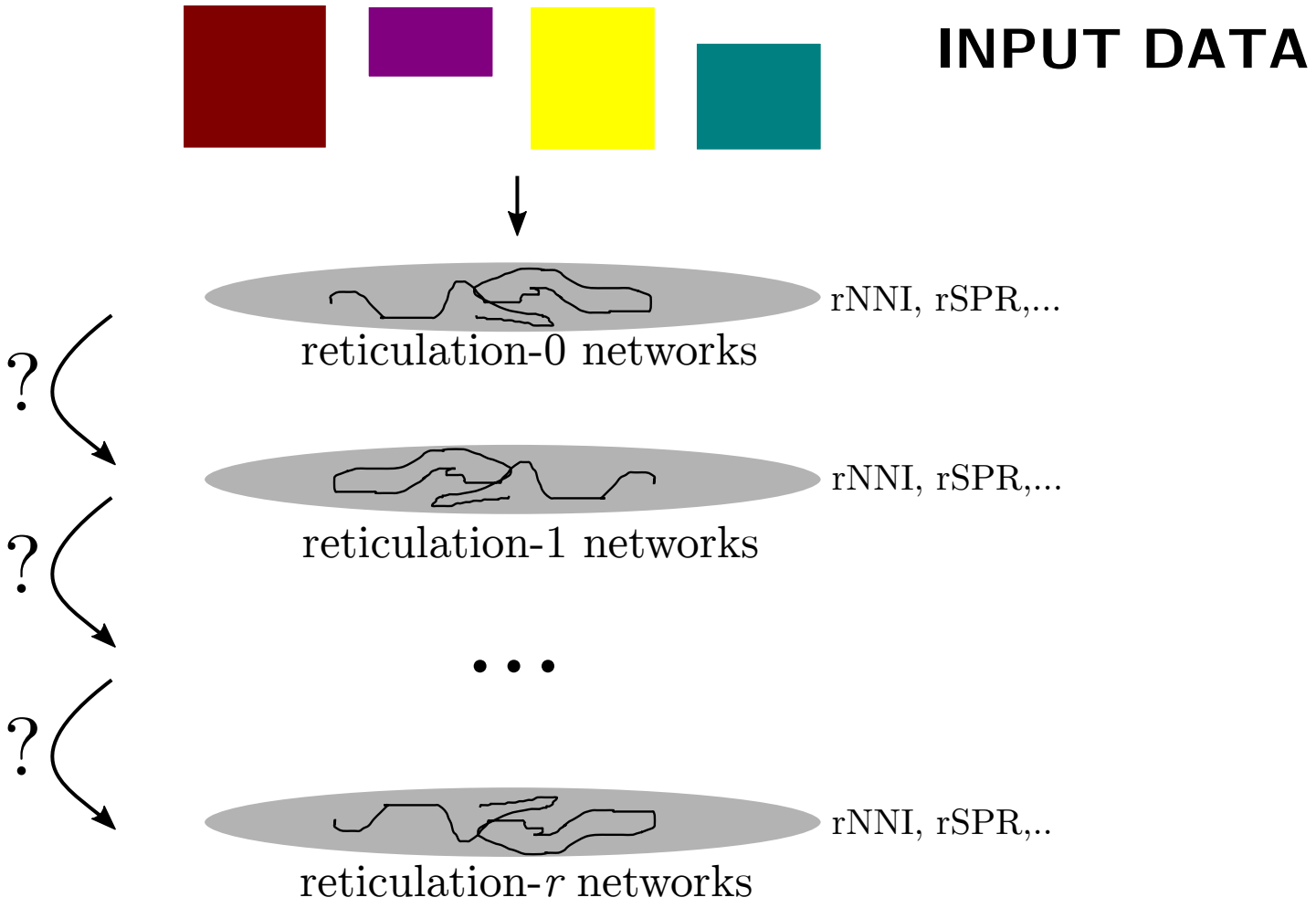
$A_1 \qquad A_2 \qquad \cdots \qquad A_m$

Goal:

Find N that maximises $\mathbf{Pr}(A_1, A_2, \ldots, A_m|N) = \prod_{i=1}^{m} \mathbf{Pr}(A_i|N) = \prod_{i=1}^{m} \left(\sum_{T \in \mathcal{T}(N)} \mathbf{Pr}(A_i|T)\mathbf{Pr}(T|N) \right)$

Jin et al.Maximum likelihood of phylogenetic networks. Bioinformatics 2006.

The strategy



Some issues

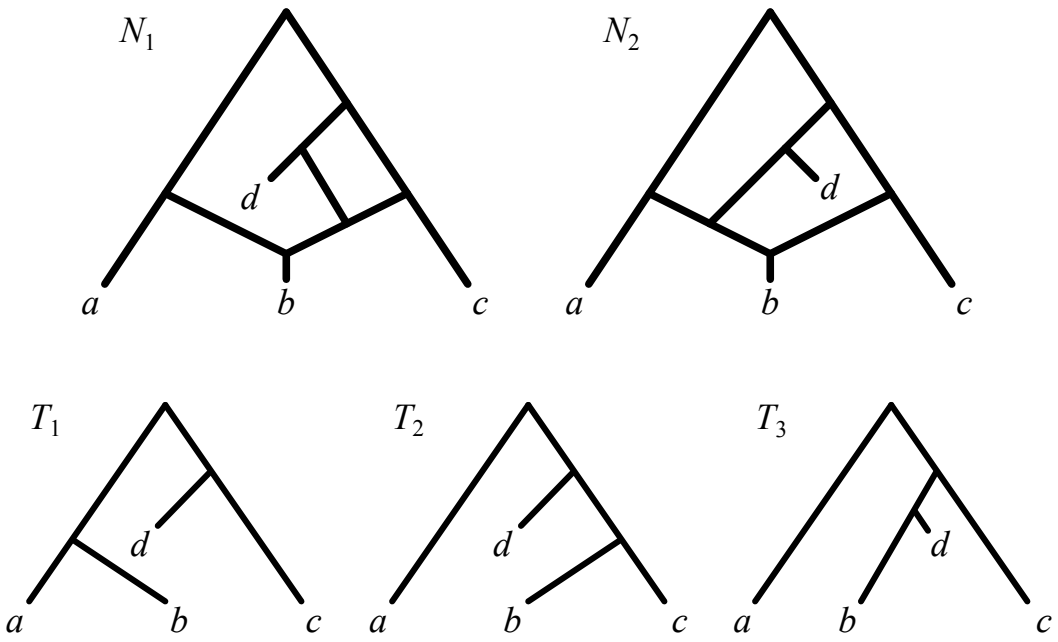
- Searching the space of phylogenetic networks
  The space of networks with k reticulations is infinite.
- Controlling for Model Complexity
  Because any network with k reticulations provides a more complex model than any network with (k-1) reticulations, we must handle the model selection problem (AIC, BIC, K-fold cross-validation, …).
- Identifiability issues

$$\mathbf{Pr}(A_1, A_2, \ldots, A_m|N) = \prod_{i=1}^{m} \mathbf{Pr}(A_i|N) = \prod_{i=1}^{m} \left(\sum_{T \in \mathcal{T}(N)} \mathbf{Pr}(A_i|T)\mathbf{Pr}(T|N) \right)$$

- Not accounting for ILS and allopolyploidy

Different networks can display the same trees

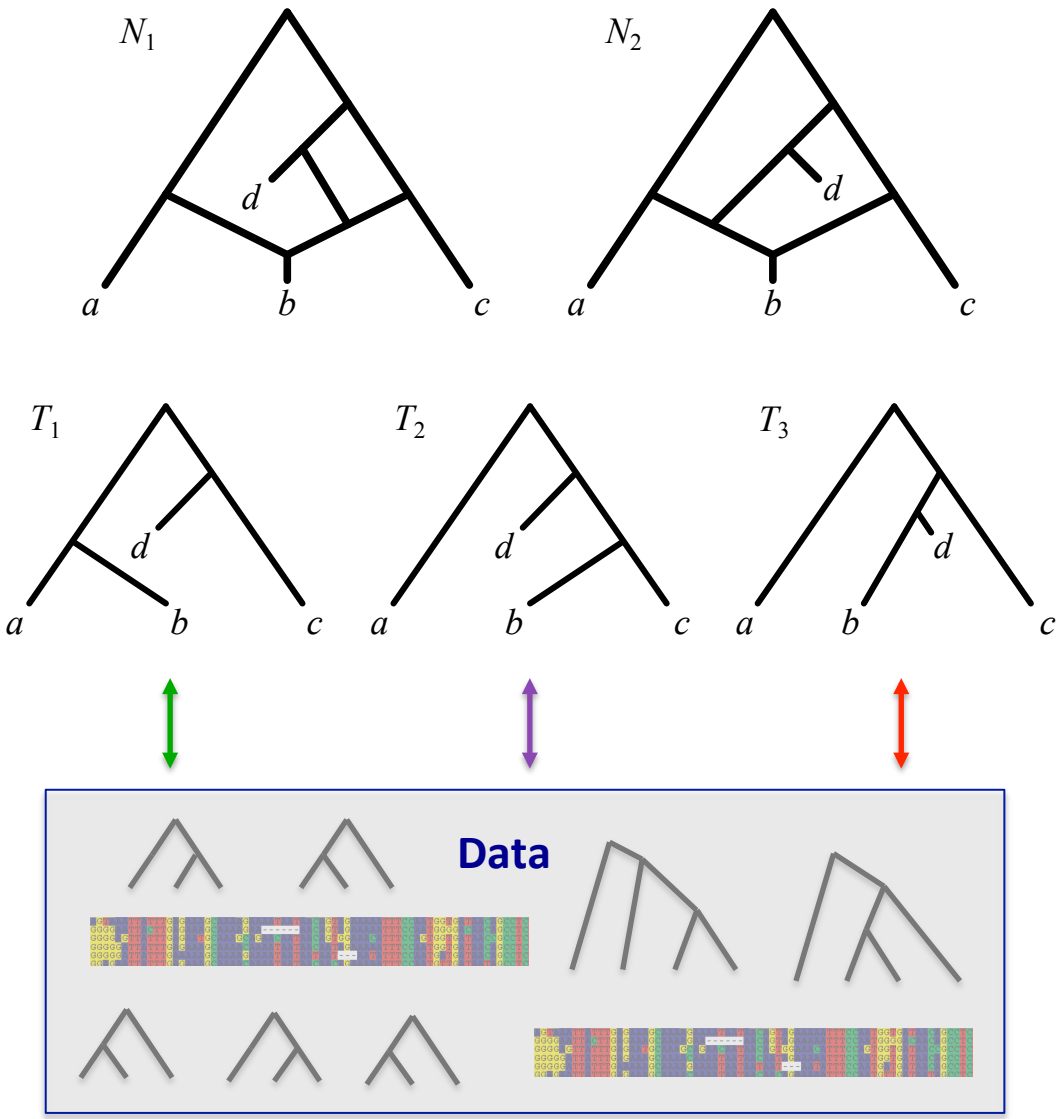
Some networks display exactly the same trees:



Different networks can display the same trees

Some networks display exactly the same trees:

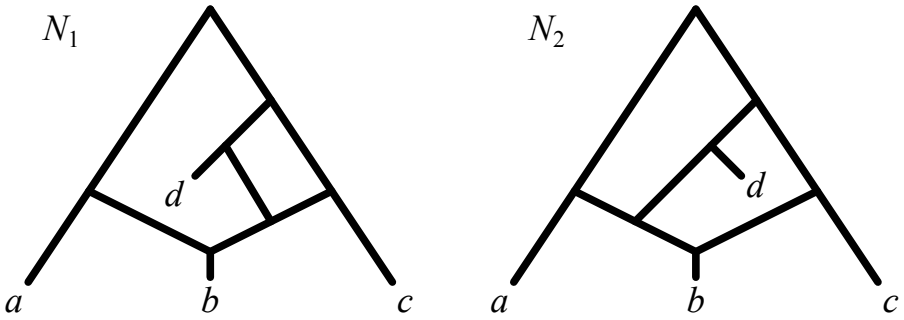
Because N_1 and N_2 display the same trees, they are equally good to any of the inference methods we saw – *no matter the input data*



(Recall that a network is evaluated *on the basis of how well the trees it displays fit the data*)

Different networks can display the same trees

Some networks display exactly the same trees:



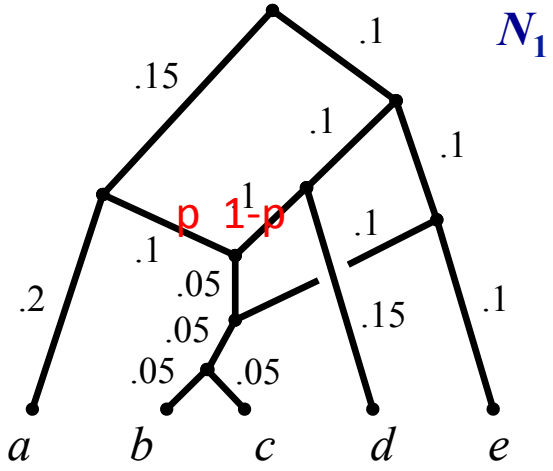
Because N_1 and N_2 display the same trees, they are equally good to any of the inference methods we saw – *no matter the input data*

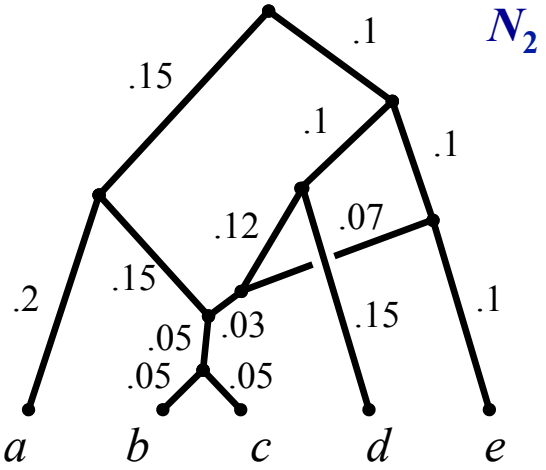
UNIDENTIFIABILITY

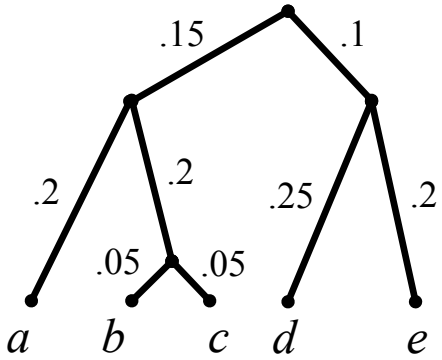
Indistinguishable networks

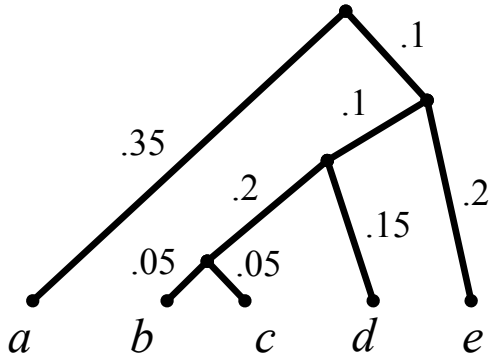
Branch lengths do not eliminate non-identifiability…

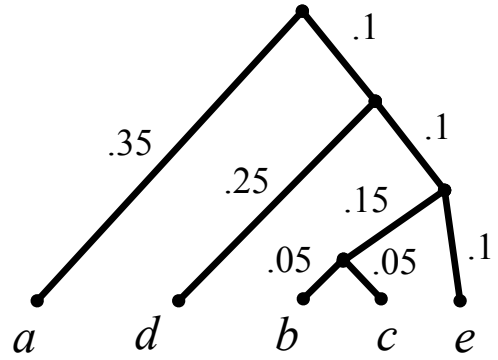
The same hold for inheritance probabilities







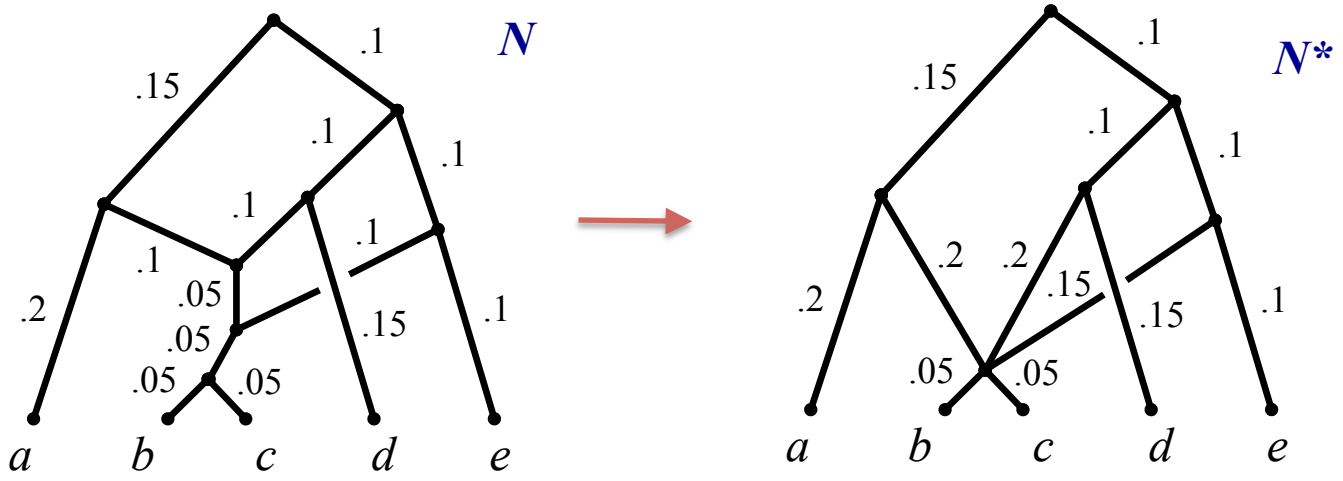




N_1 and N_2 display the same trees (i.e. including branch lengths) and are thus *indistinguishable* even to methods accounting for lengths

What it means for the evolutionary biologist

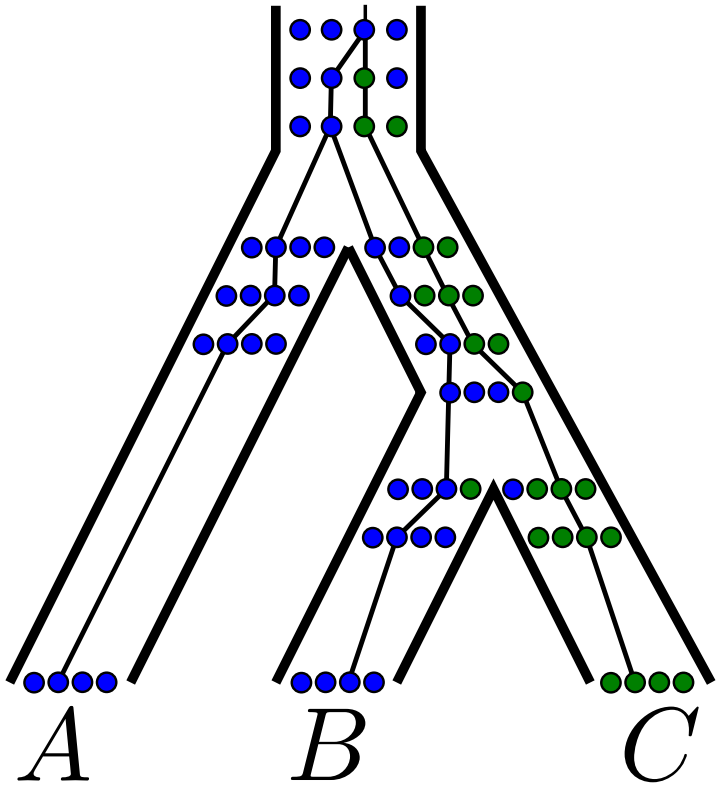
If N is reconstructed by a "classic" inference method, then even assuming perfect and unlimited data, the best you can hope is that the true phylogenetic network is just one of the many that are indistinguishable from N …



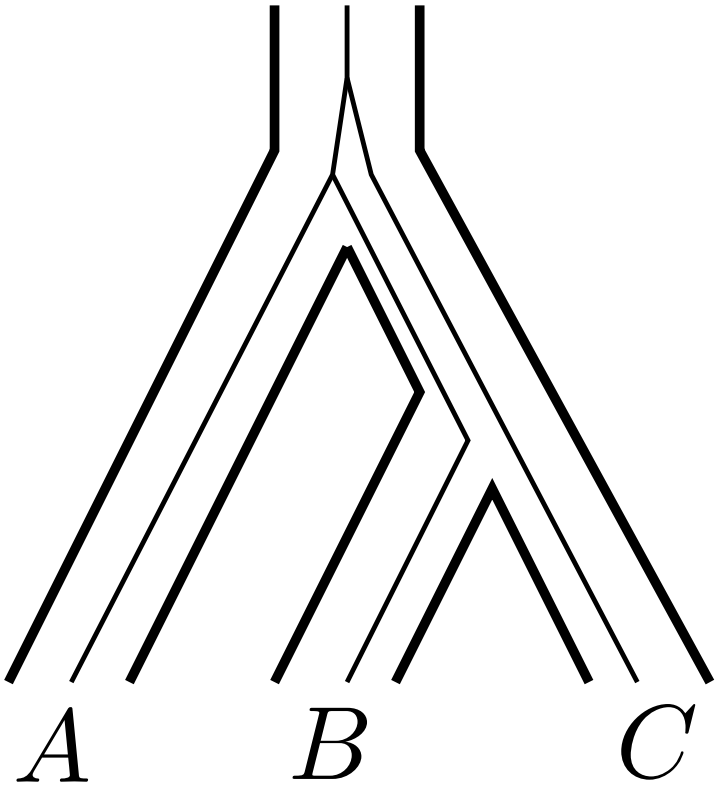
The canonical form of N is a unique representative of the networks indistinguishable from N, that excludes their unrecoverable aspects…

Methods for reconstructing rooted phylogenetic networks not accounting for ILS

Deep coalescence (ILS)

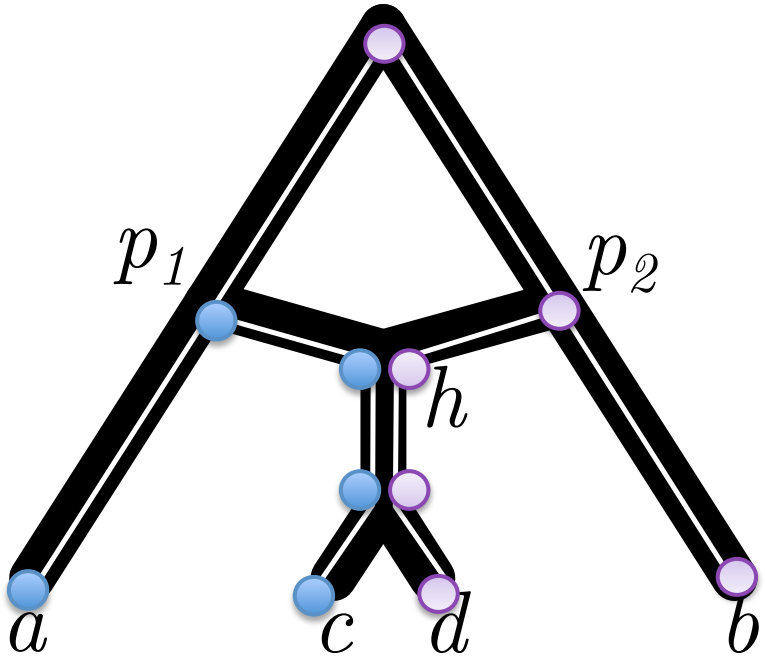


(a) Population view



(b) Reconciliation representation

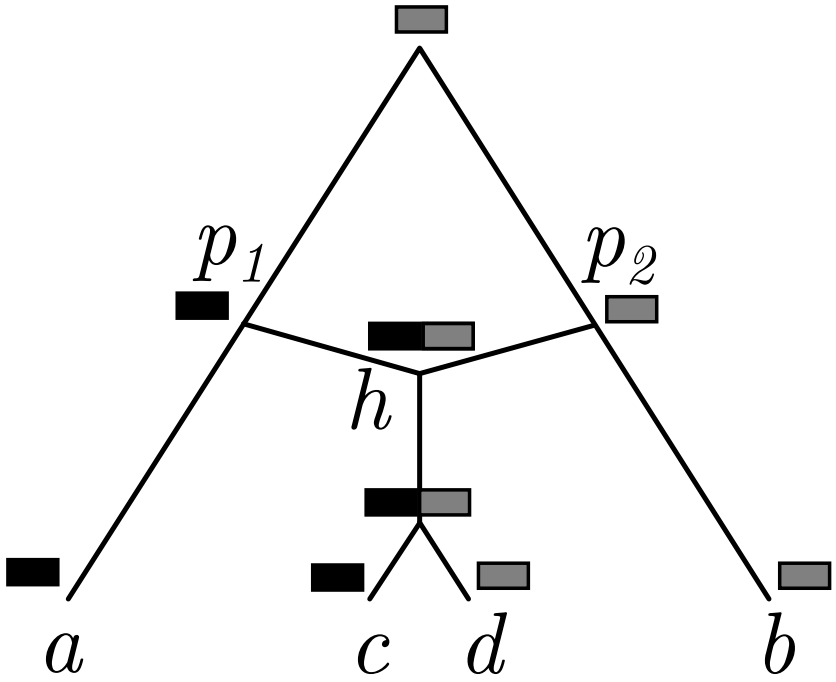
ILS in phylogentic networks



The true gene tree is **not displayed** by the network because it needs to *use* both edges entering the hybrid node

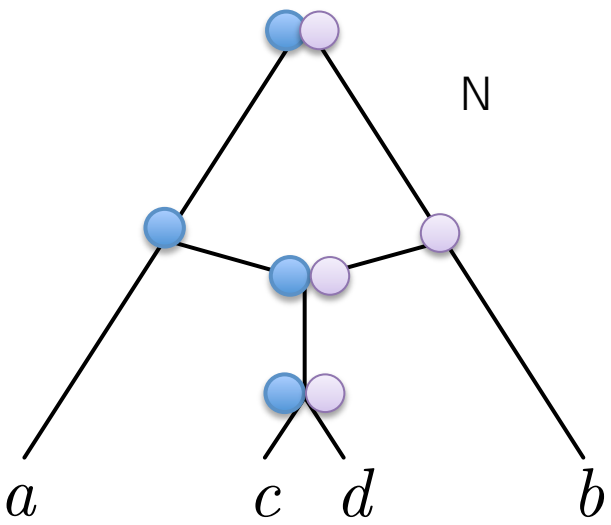
Yu et al. Maximum likelihood inference of reticulate evolutionary histories, 2014

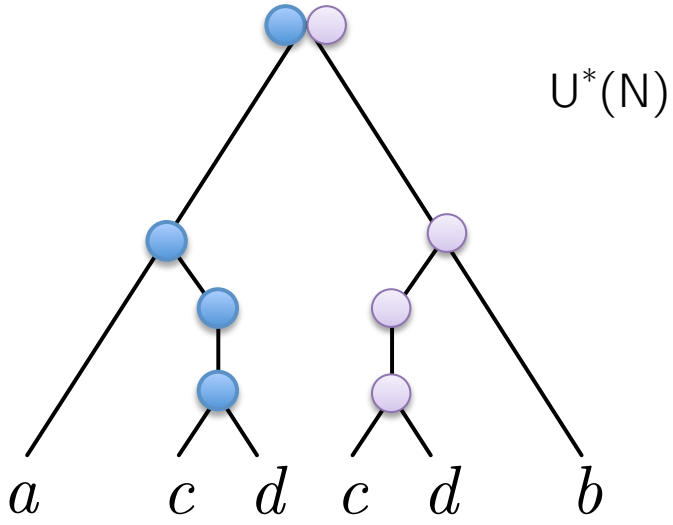
Allopolyploidy



The true gene tree is **not displayed** by the network because it needs to *use* both edges entering the hybrid node

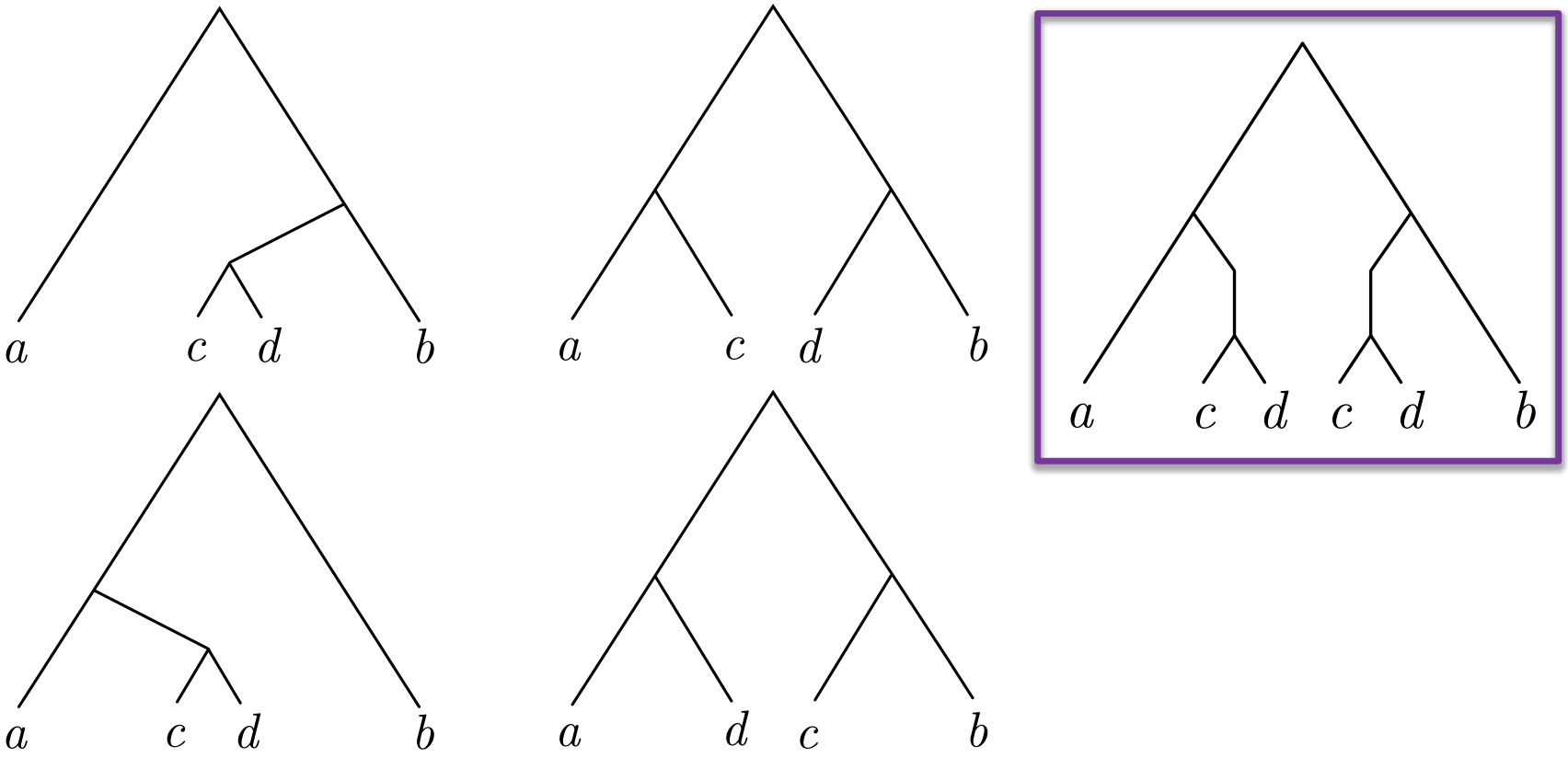
The multi-labelled tree U*(N)





- nodes are the directed paths in N starting at $r(N)$
- for each pair of paths p,p' in N, there is an edge in $U^*(N)$ from p to p' if and only if $p{=}p'e$ for some edge e in N
- each node in $U^*(N)$ corresponding to a path in N that starts at $r(N)$ and ends at x in X is labelled by x

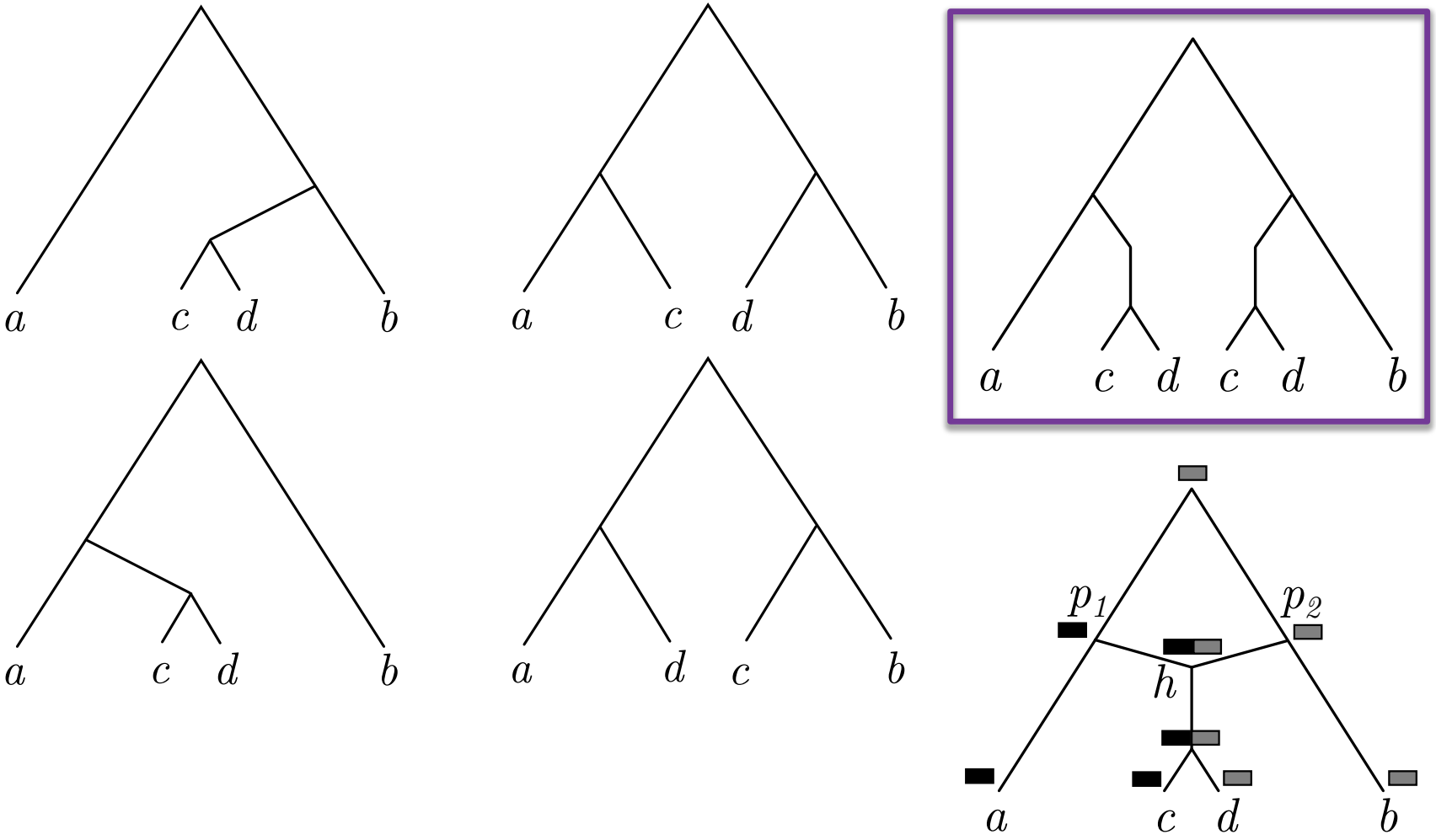
Parental trees



A phylogenetic tree T on X is a parental tree of N if it is displayed by $U^*(N)$

Huber et al. Folding and unfolding phylogenetic trees and networks, 2016 [**weakly displayed**]
Zhu al. In the light of deep coalescence: revisiting trees within networks, 2016
Zhu and Degnan. Displayed trees do not determine distinguishability under the network multispecies coalescent, 2016

Parental trees



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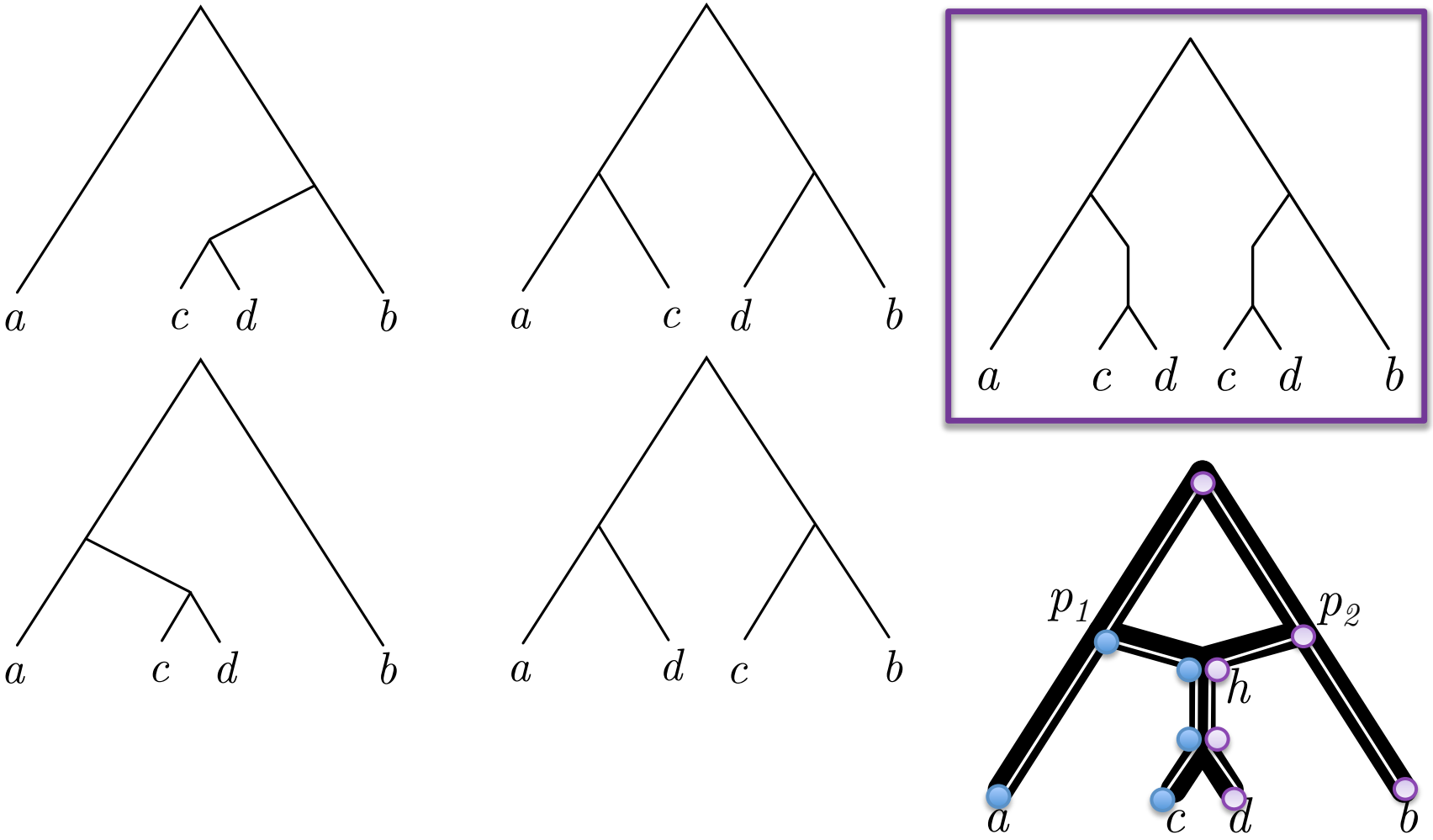
Parental trees



Huber et al. Folding and unfolding phylogenetic trees and networks, 2016 [**weakly displayed**]
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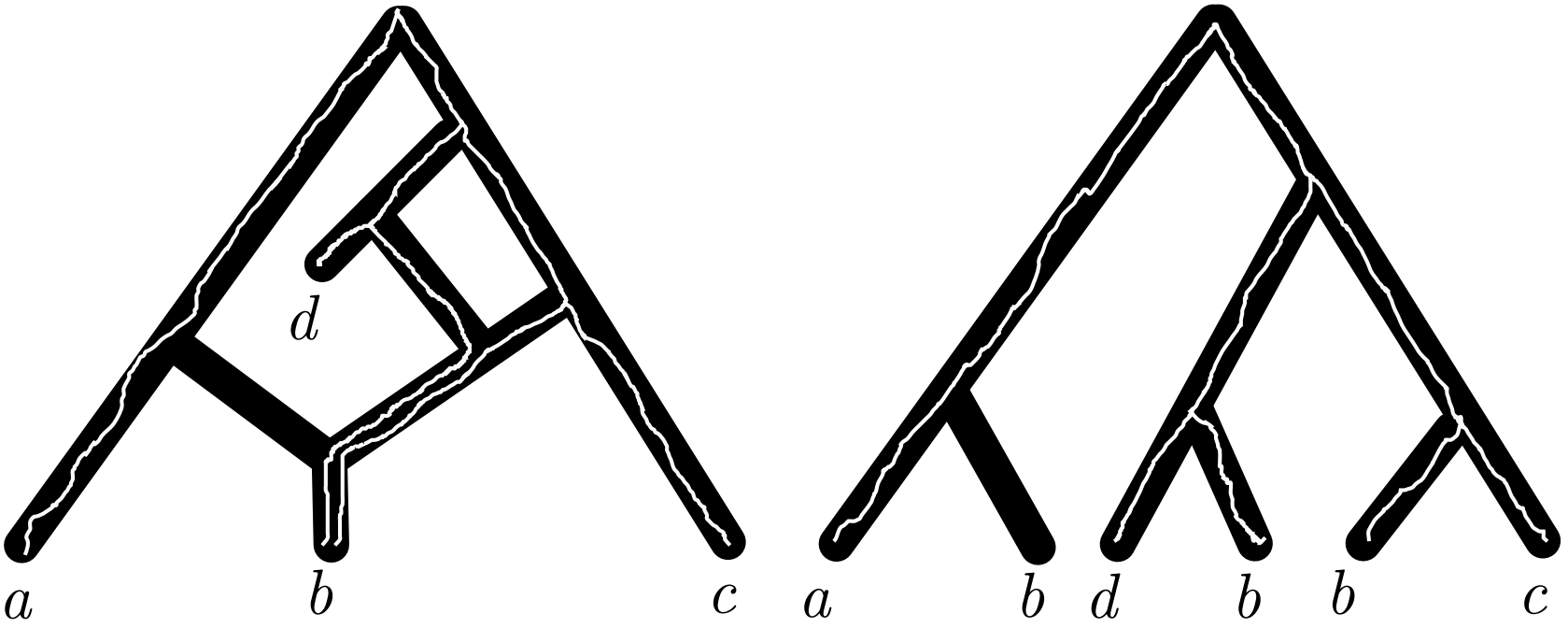
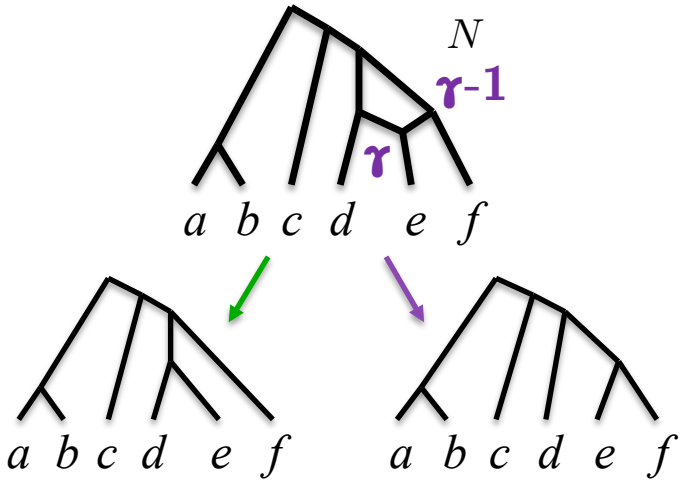
Zhu and Degnan. Displayed trees do not determine distinguishability under the network multispecies coalescent, 2016

Parental trees can be multi-labelled



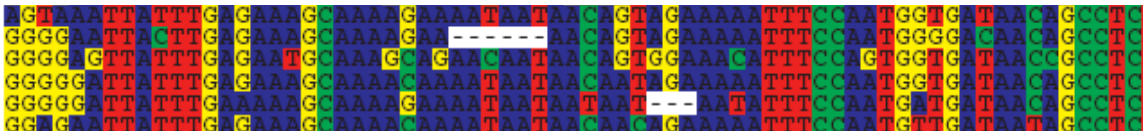
multiple individuals per species are allowed

Scoring schemes based on **parental** trees (NMSC)



Data:

Sequence alignments:
(typically given in blocks)



Goal:

Find N that maximises $\mathbf{Pr}(A_1, A_2, \ldots, A_m|N) = \prod_{i=1}^{m} \mathbf{Pr}(A_i|N) = \prod_{i=1}^{m} \left(\sum_{T \in \mathcal{T}(N)} \mathbf{Pr}(A_i|T)\mathbf{Pr}(T|N) \right)$

(A_1, A_2, A_m)

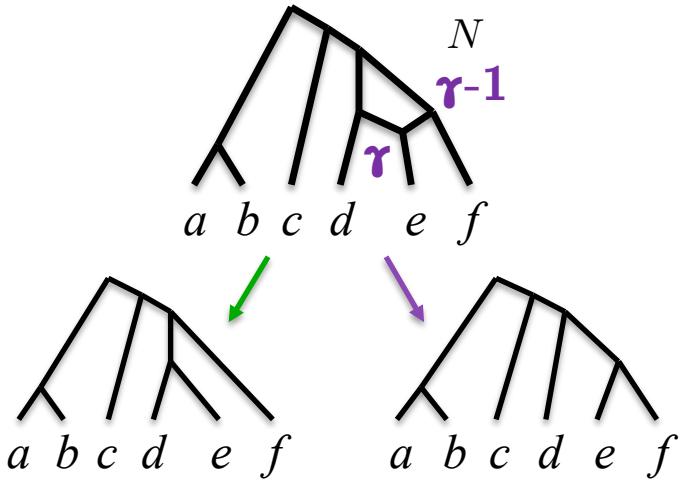
Yu et al. The Probability of a Gene Tree Topology within a Phylogenetic Network with Applications to Hybridization Detection, 2012

Yu et al. Maximum likelihood inference of reticulate evolutionary histories, 2014

Wen el al. PLOS Genetics 2016 (Bayesian method)

Scoring schemes based on **parental** trees (NMSC)

PhyloNet



Data:

Sequence alignments:
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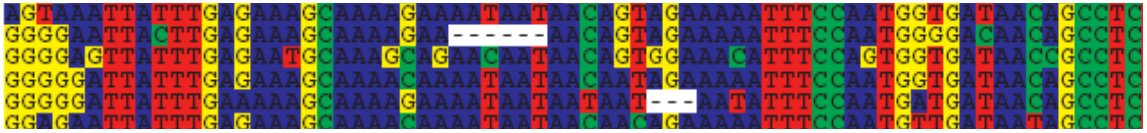


Goal:

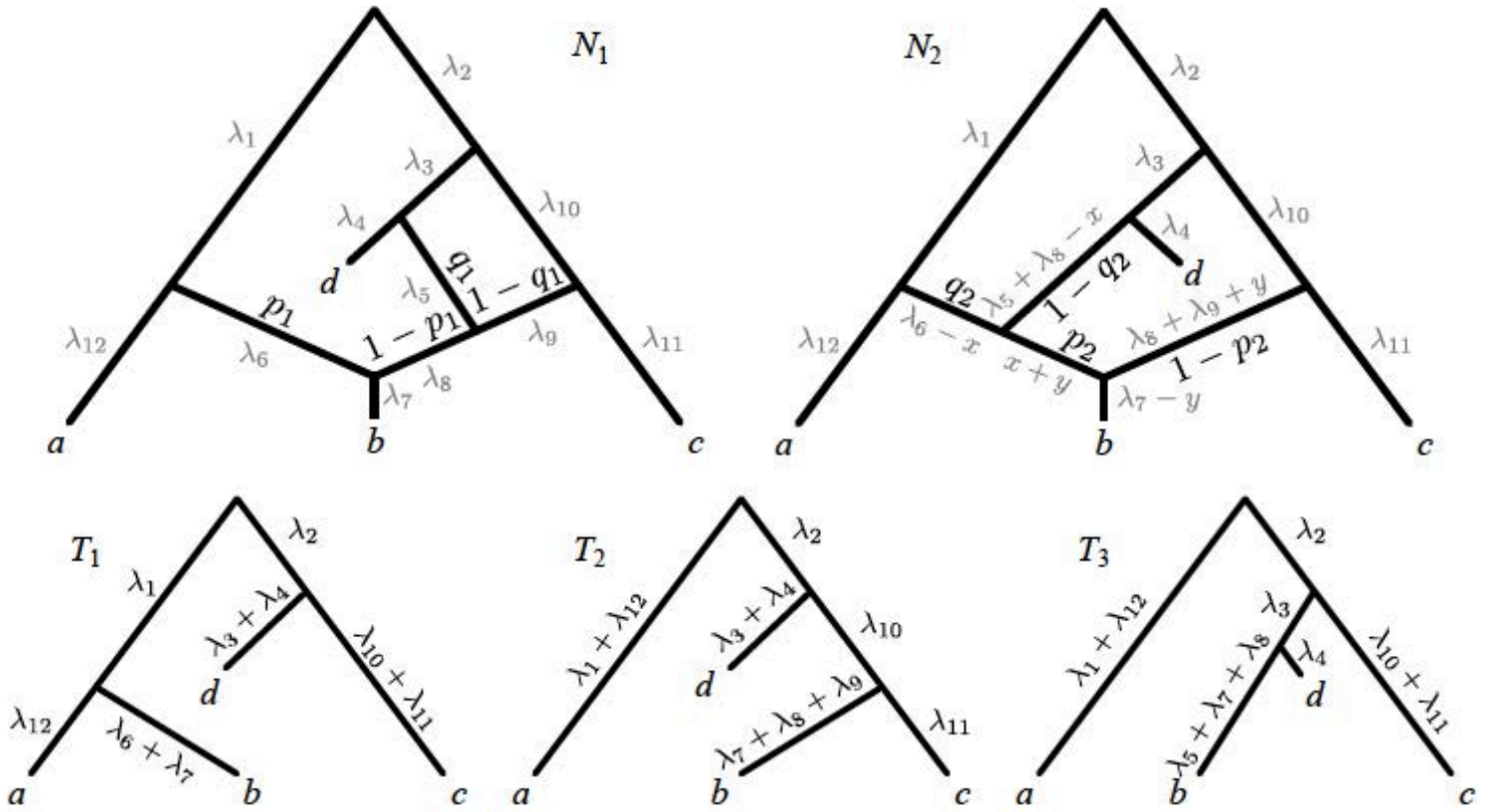
Find N that maximises

$$A_1 \qquad A_2 \qquad\qquad A_m$$

$$\mathbf{Pr}(A_1, A_2, \ldots, A_m | N) = \prod_{i=1}^{m} p(G_i|N).$$

Zhu and Degnan. Displayed trees do not determine distinguishability under the network multispecies coalescent, 2016

Scoring schemes based on **parental** trees (NMSC)

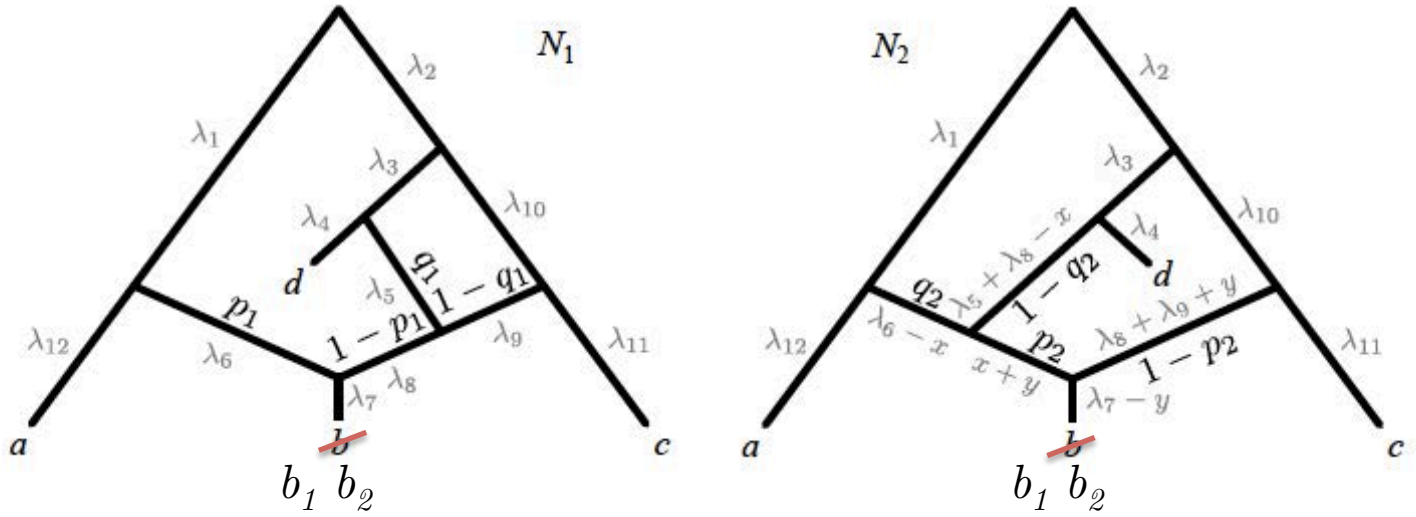


$$\mathbf{Pr}(T_1|N_1) = p_1 \qquad \mathbf{Pr}(T_2|N_1) = (1-p_1)(1-q_1) \qquad \mathbf{Pr}(T_3|N_1) = (1-p_1)q_1$$

$$\mathbf{Pr}(T_1|N_2) = p_2q_2 \qquad \mathbf{Pr}(T_2|N_2) = 1-p_2 \qquad \mathbf{Pr}(T_3|N_2) = p_2(1-q_2)$$

$p_1 = 1/3$ $p_2 = 2/3$ $q_1 = 7/9$ and $q_2 = 3/7$
$x = y = 1/2$ and $\lambda_i = 1$, for all i

Scoring schemes based on **parental** trees (NMSC)



$p_1 = 1/3$ $p_2 = 2/3$ $q_1=7/9$ and $q_2 = 3/7$
$x=y=1/2$ and $\lambda_i=1$, for all i

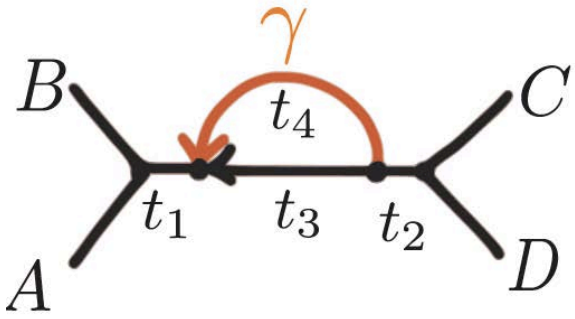
$g=((((a,d),c),b1),b2)$

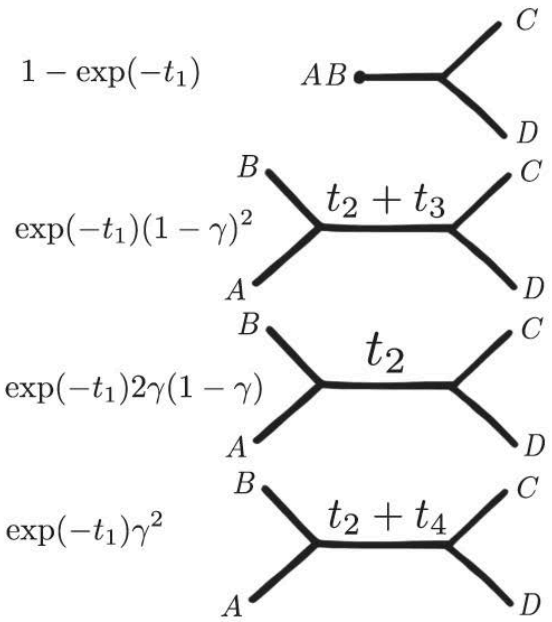
$P(g|N_1)\approx 7.7 \times 10^{-6}$, $P(g|N_1)\approx 7.6 \times 10^{-6}$

This may solve the **identifiability issues** for several practical cases but we need more samples per species "**well positioned**" in the phylogeny

SNaQ(Species Networks applying Quartets) – pseudo-likelihood

Input: **quartet CFs**
Output: **level-1 semidirected networks**

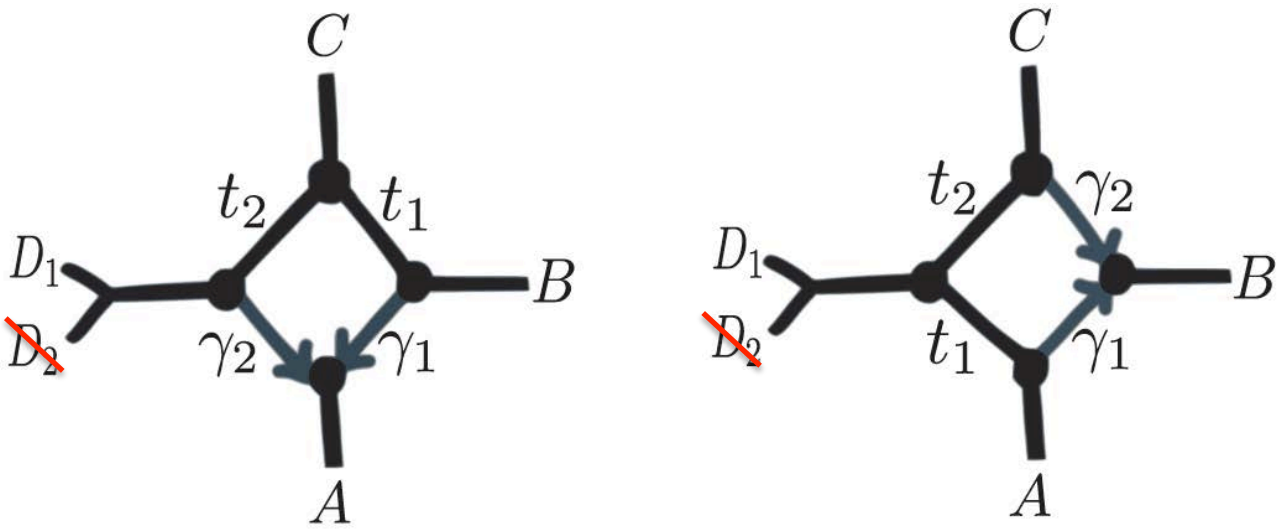




- quartet CFs do not depend on the root placement → semidirected networks
- if n=4, k=2,3 reticulations cannot be detected because equivalent to a tree

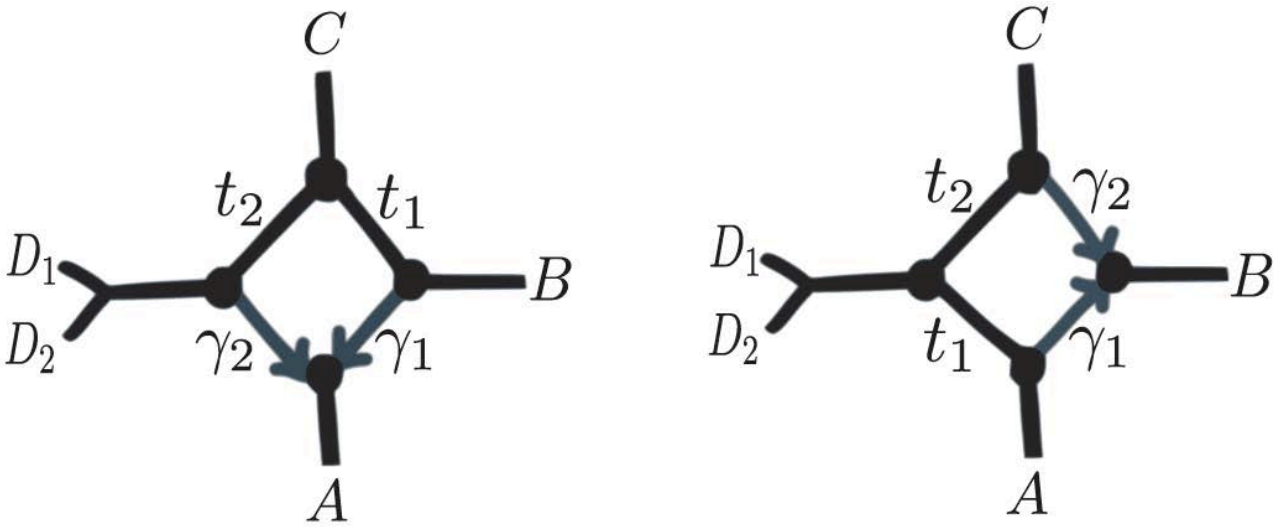
Solís-Lemus and Ané. Inferring Phylogenetic Networks with Maximum Pseudolikelihood under Incomplete Lineage Sorting, 2016.

SNaQ (Species Networks applying Quartets) – an example of how to cope with indistinguishability



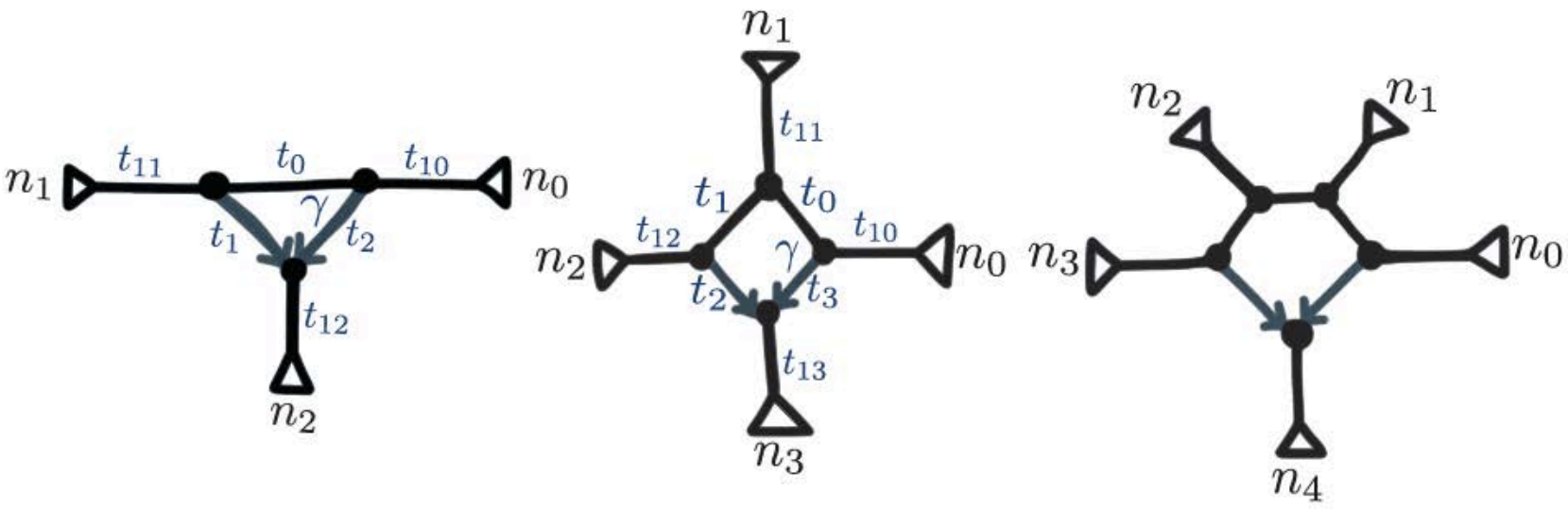
- quartet CFs do not depend on the root placement → semidirected networks
- if n=4, k=2,3 reticulations cannot be detected because equivalent to a tree
- if n=4, k=4, reticulations can be detected but not the "placement"

SNaQ (Species Networks applying Quartets) – an example of how to cope with indistinguishability



- quartet CFs do not depend on the root placement → semidirected networks
- if n=4, k=2,3 reticulations cannot be detected because equivalent to a tree
- if n=4, k=4, reticulations can be detected but not the "placement"
- for n≥4, k=2 reticulations are not detectable, k=3 sometimes and k=4 yes in general if n≥5, along with the placement

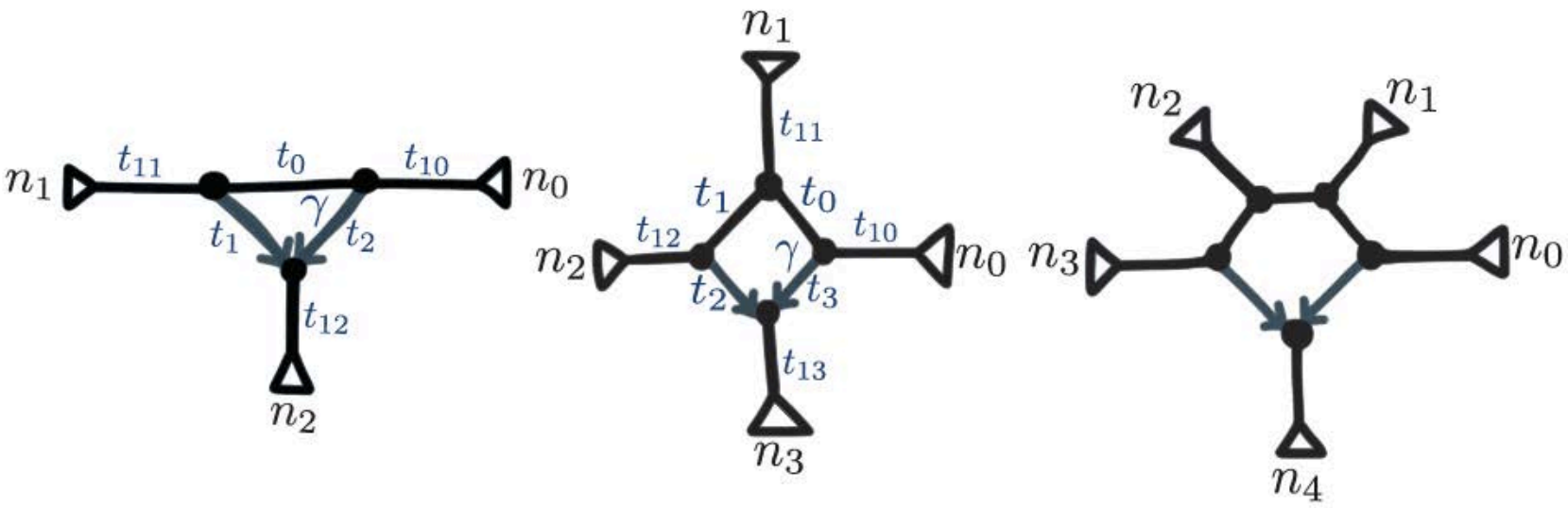
SNaQ (Species Networks applying Quartets) – an example of how to cope with indistinguishability



With only 4 taxa, there are more parameters than equations (3 quartet CFs), so focus on the case n ≥ 5.

- If k=3, parameters are identifiable if $n_1, n_2, n_3 \geq 2$, and setting $t_{12} = 0$.
- If $k = 4$, parameters are identifiable if either $n_0 \geq 2$ (or n_2 , symmetrically), or if both n_1 and $n_3 \geq 2$. Parameters are not all identifiable in the remaining 2 cases (bad diamonds I & II)
- If k=5, all the parameters are identifiable.

SNaQ (Species Networks applying Quartets) – an example of how to cope with indistinguishability

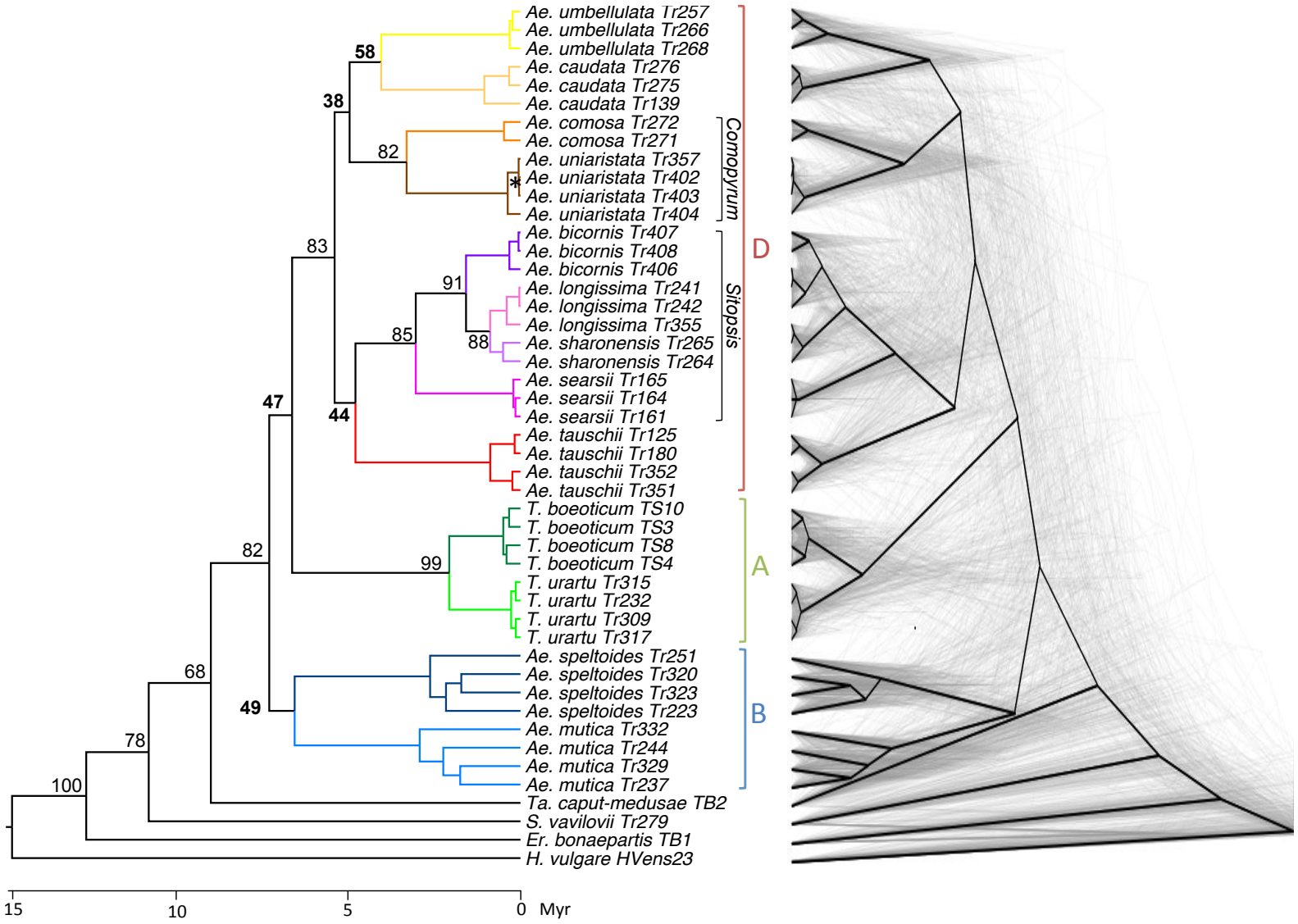


They search only in the space of identifiable networks:

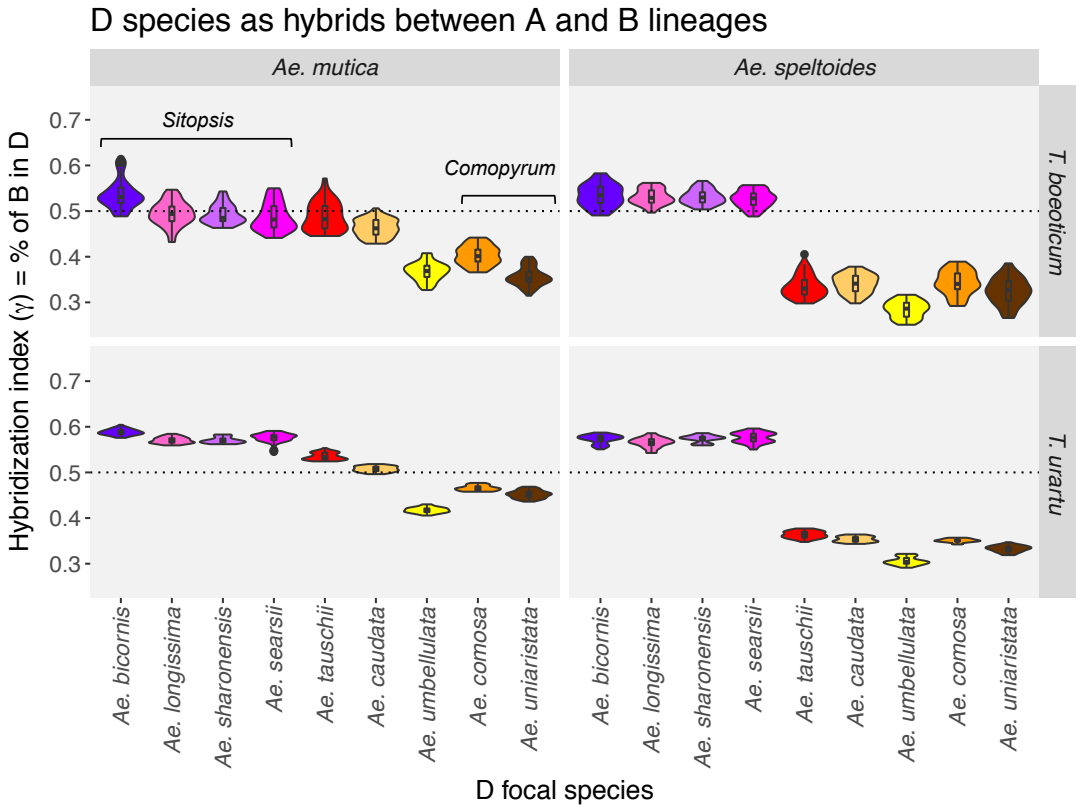
- k = 2 not considered
- k = 3, only $n_1, n_2, n_3 \geq 2$, and setting $t_{12} = 0$
- For bad diamonds I, they reparametrized the 3 nonidentifable values (γ, t_1, t_0) into 2 identifiable ones $\gamma(1-e^{-t0})$ and $(1-\gamma)(1-e^{-t1})$. For bad diamonds II, they set $t_{13} = 0$ and kept the other 5 parameters (γ, t_0, t_1, t_2, t_3).

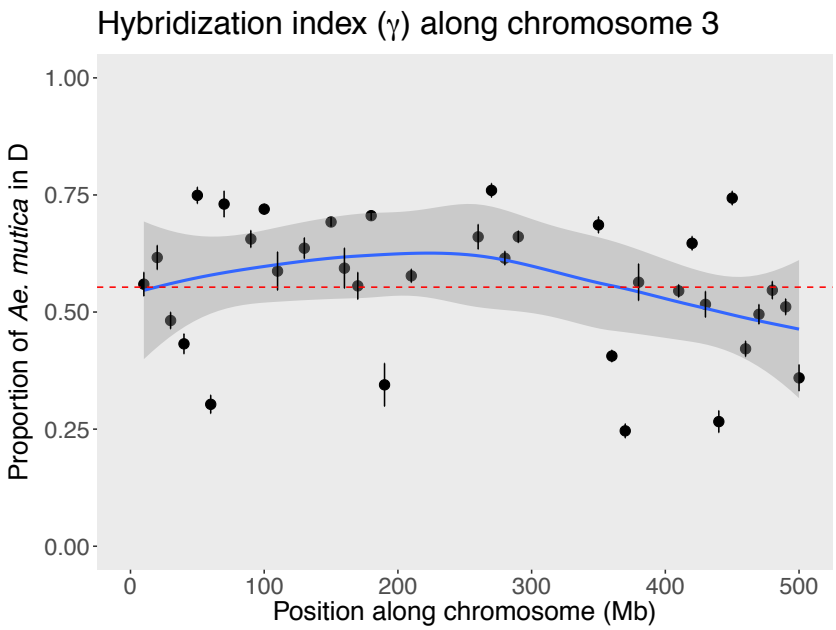
Thank you for your attention

Another (home made) approach



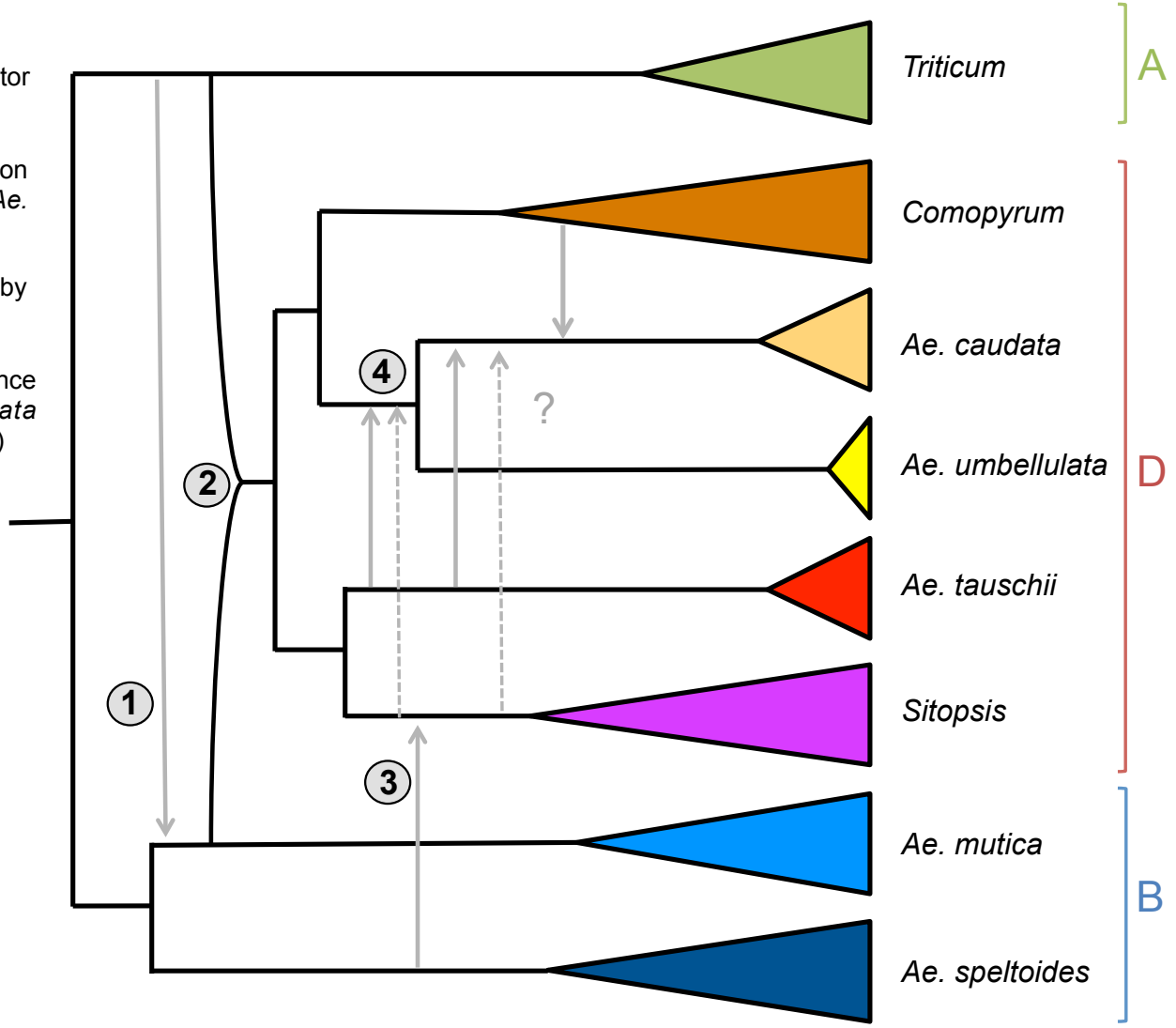
Another (home made) approach





Another (home made) approach

1. Introgression from the *Triticum* ancestor into the *Ae. mutica* ancestor
2. Origin of the D clade by hybridization between the A clade ancestor and the *Ae. mutica* ancestor
3. Introgression of the *Sitopsis* ancestor by the *Ae. speltoides* ancestor
4. Complex gene flows during the divergence of *Ae. caudata* and *Ae. umbellulata* probably involving three events (or more)



Another (home made) approach