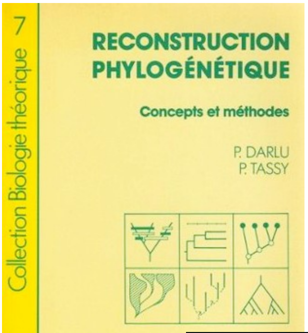
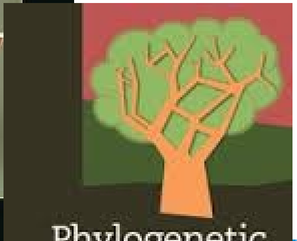
Master Parisien de Recherche en Informatique - c-1-32
Algorithmique pour la bioinformatique

Algorithmics & Phylogenetics

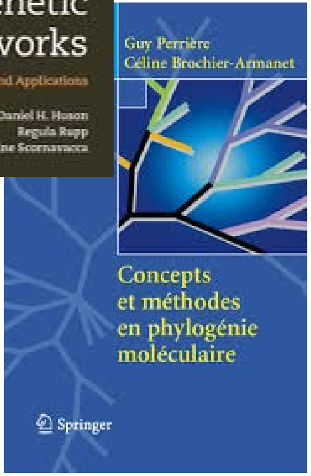


Darlu & Tassy, 1993 http://sfs.snv.jussieu.fr/?q=node/11

Felsenstein, 2002

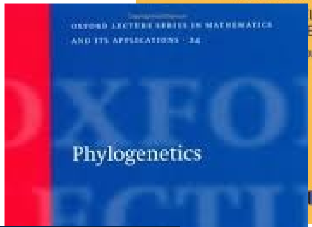


Huson, Rupp & Scornavacca, 2010

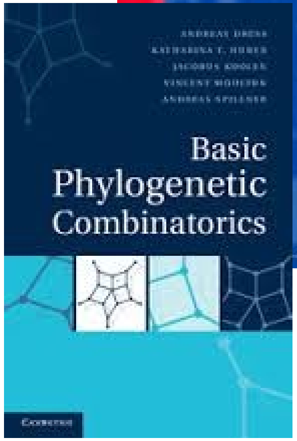


Perrière & Brochier-Armanet, 2010

Barthelémy & Guénoche, 1988


OXFORD LECTURE SERIES IN MATHEMATICS AND ITS APPLICATIONS · 24
Phylogenetics

Semple & Steel, 2003



Dress, Huber, Koolen, Moulton & Spillner, 2011

UNIVERSITÉ PARIS-EST MARNE-LA-VALLÉE

GASPARD - MONGE INSTITUT

Philippe Gambette

References

Finding **bibliographic references**:

- Google Scholar: large coverage, including noise (preprints, fake papers...)
- Bibliographic resources with university access:

http://www.u-pem.fr/bibliotheque/consulter-les-ressources-en-ligne/ressources-en-ligne-de-a-a-z/

→ Science Direct for Elsevier journals, Springer, JSTOR, etc.

- University library

Conferences with computer science papers applied to phylogenetics:

- International: ISMB, RECOMB, WABI, ECCB, ISBRA, etc.
+ algorithmics conferences: SODA, CPM, ISAAC, COCOON, etc.
- In France: JOBIM, Alphy

Scholarly organizations:

iSCB INTERNATIONAL SOCIETY FOR COMPUTATIONAL BIOLOGY

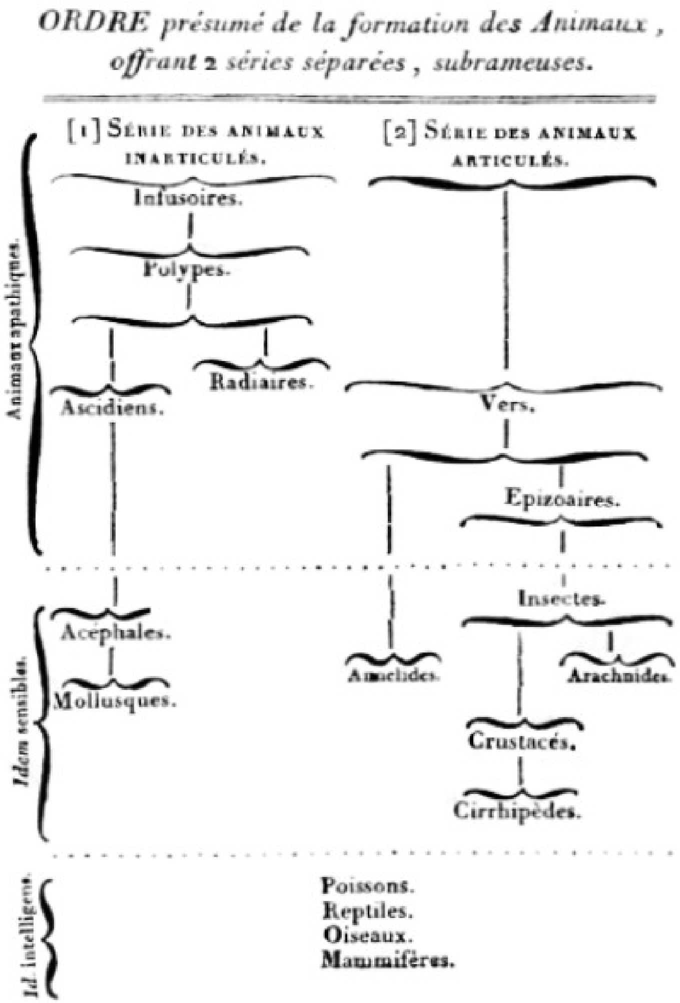
iSCB Student COUNCIL INTERNATIONAL SOCIETY FOR COMPUTATIONAL BIOLOGY

SFBi

Phylogenetic trees

Phylogenetic tree of a set of species:

- **organizing** them according to common characters **classification**
- describing their evolution



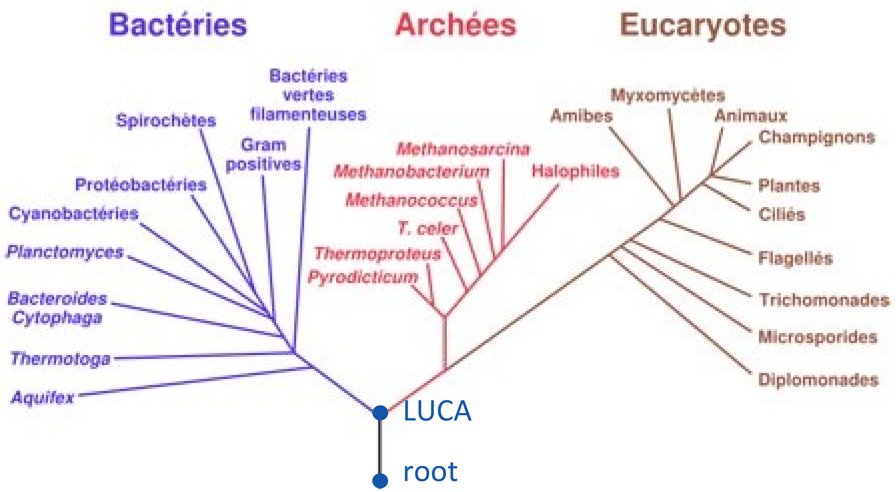
Lamarck : Histoire naturelle des animaux sans vertèbres (1815)

Phylogenetic trees

Phylogenetic tree of a set of species:

- organizing them according to common characters
- **describing** their evolution

modelization



Woese, Kandler, Wheelis : Towards a natural system of organisms: proposal for the domains Archaea, Bacteria, and Eucarya, Proceedings of the National Academy of Sciences, 87(12), 4576–4579 (1990)

Encoding a tree

“Newick” format:

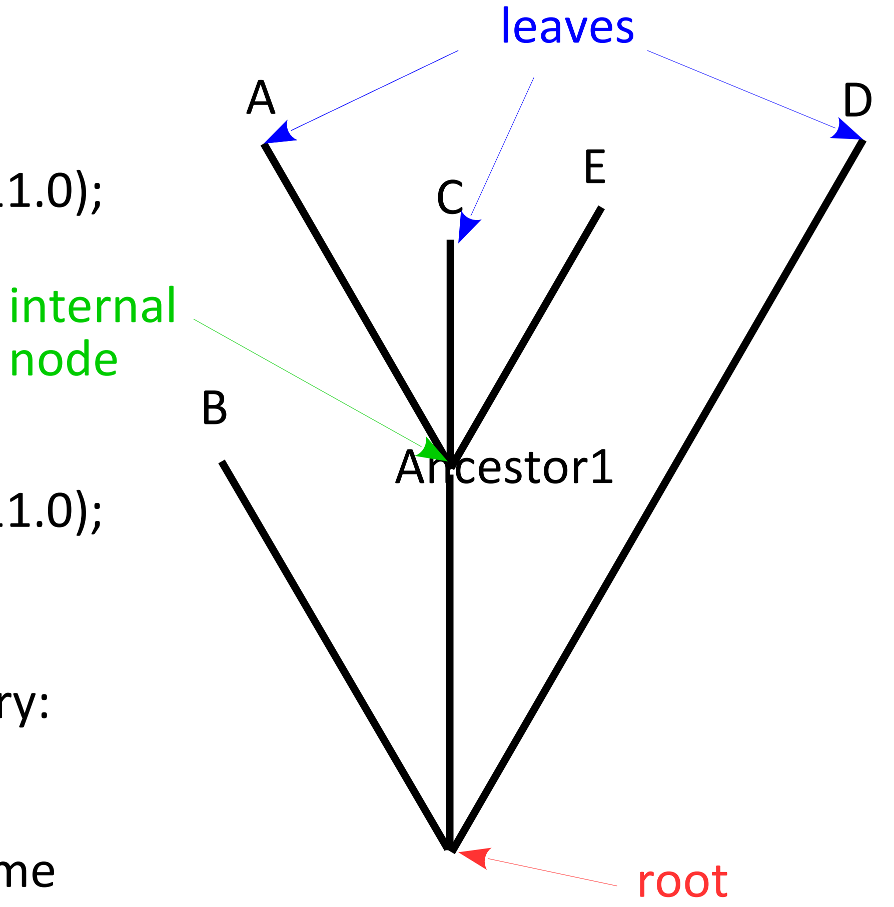
(B:6.0,(A:5.0,C:3.0,E:4.0)Ancestor1:5.0,D:11.0);

Not unique:

((A:5.0,C:3.0,E:4.0)Ancestor1:5.0,B:6.0,D:11.0);

Possible to have nodes which are not binary:

- uncertainty
- or speciation known to be at the same time



http://evolution.genetics.washington.edu/phylip/newicktree.html

Properties of phylogenetic trees

Characterizing a tree with:

- its “clusters”: one cluster of *T* = the set of leaves below one vertex of *T*
- its “triplets”: one triplet of *T* = a tree on 3 leaves contained in *T*
- distances between the leaves

Properties of rooted/unrooted phylogenetic trees

Characterizing a **rooted tree** with:

- its “clusters”: one cluster of *T* = the set of leaves below one vertex of *T*
- its “triplets”: one triplet of *T* = a tree on 3 leaves contained in *T*
- ~~distances between the leaves~~

Characterizing an **unrooted tree** with:

- its “splits”: one split of *T* = bipartition of the leaves induced by one edge of *T*
- its “quartets”: one quartet of *T* = an unrooted tree on 4 leaves contained in *T*
- distances between the leaves

Properties of rooted and unrooted trees

Clusters: “laminar family”, i.e. it contains no overlapping sets

→ reconstruction from clusters: Hasse Diagram of cluster inclusion

Triplets (binary trees): do not contain {ab|c, b|cd, a|bd} or {ab|c, b|cd, ad|b}

Guillemot & Mnich, Kernel and fast algorithm for Dense Triplet Inconsistency, 2013

Splits: “compatible split system”, i.e. for any pair of splits A1|B1, A2|B2, at least one of the sets $A1 \cap A2$, $A1 \cap B2$, $B1 \cap A2$, $B1 \cap B2$ is empty

Quartets (binary trees): for any leaf *e*, $ab|cd \in Q \Rightarrow ab|ce \in Q$ or $ae|cd \in Q$

Bandelt & Dress, Reconstructing the shape of a tree from observed dissimilarity data, 1986

Properties of rooted and unrooted trees

Tree distances:

Characterized by Buneman's **four-point condition**:

for all a, b, c, d, $d(a,b)+d(c,d) \leq \max\{d(a,c)+d(b,d), d(a,d)+d(b,c)\}$

⇔ for any four points, we can relabel them a, b, c, d such that $d(a,b)+d(c,d) \leq d(a,c)+d(b,d) = d(a,d)+d(b,c)$.

Given a tree distance, only one possible tree.

Buneman, A Note on the Metric Properties of Trees, 1974

Tree distances when the tree contains a center at equal distance from all leaves:

Characterized by the **ultrametric inequality**:

For all a, b, c, $d(a,b) \leq \max\{d(a,c), d(b,c)\}$

molecular clock hypothesis!

Reconstructing a tree from an ultrametric

UPGMA algorithm (Unweighted Pair Group Method with Arithmetic Mean):

- Initialize all clusters with leaf singletons
- While there are more than 2 clusters:

  - pick the nearest two clusters

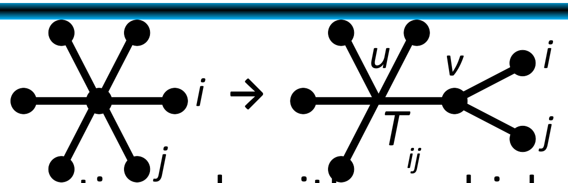
  - combine them and update the distance matrix with average values (average weighted by the size of each of the two clusters)

Sokal & Michener, A statistical method for evaluating systematic relationships, 1958

→ Correctly reconstructs ultrametric distances, but not all tree distances

→ Neighbor-Joining...

Reconstructing a tree from distances



Discovering the **Neighbor-Joining algorithm**:

The Neighbor-Noining algorithm (NJ) is a tree reconstruction algorithm which identifies at each step the **two neighbor leaves** which **minimizes the total expected length of the tree**, and **replaces them by their parent**.

Q1. Given a tree T_{ij} made of a central vertex *u* with *n*-2 leaf neighbors, as well as a neighbor *v* of *u* having two leaf neighbors *i* and *j*, and an additive metric *d* corresponding to T_{ij}, evaluate the total length L_{ij} of T_{ij} depending on:

- the sum S1 of all distances between leaf neighbors of *u* on the one side and *i* and *j* on the other side ;
- the sum S2 of all distances between leaf neighbors of *u* ;
- the distance d(*i*,*j*) between *i* and *j*.

Reconstructing a tree from distances

Discovering the **Neighbor-Joining algorithm**:

Saitou & Nei, 1987

Q2. Rewrite L_{ij} to express this total length depending on the sum of distances between all pairs of leaves of T_{ij}, as well as $d(i,j)$, r_i and r_j, where r_x is the sum of distances between leaf x and all other leaves of T_{ij}.

Q3. The NJ algorithm consists in repeating, starting from a star tree: choose two vertices i and j which minimize L_{ij} and replace them by node v in the distance matrix corresponding to d. Give an appropriate formula to compute $d(v,k)$ for each leaf k of T_{ij} depending on the distances between leaves of T_{ij} (including i and j: for them, use $d(i,j)$, r_i and r_j).

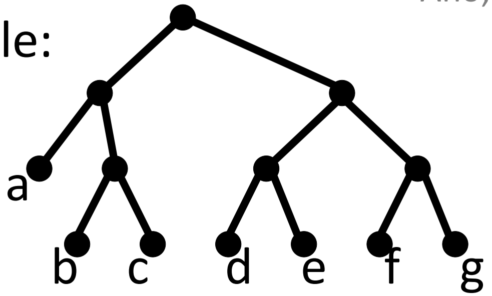
Reconstructing a tree from its triplets

BUILD algorithm:

- Build the following graph: leaves as vertices; for each triplet a|bc, add edge bc.
- While there is more than one connected component:
  - each connected component corresponds to one subtree
  - recursively apply the algorithm on the leaf set of each connected component

Aho, Sagiv, Szymanski & Ullman, Inferring a tree from lowest common ancestors with an application to the optimization of relational expressions, 1981.

Example:



{a|bc, a|de, a|df, b|dg, b|ef, c|df,
d|ac, d|fg, e|ab, f|de, g|ab, g|ac}

→ When missing triplets, efficient implementation in O(|*T*|+n^2 log *n*)

Henzinger, King & Warnow, Constructing a tree from homeomorphic subtrees, with applications to computational evolutionary biology, 1999.

Reconstructing a tree from its triplets

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→ When missing triplets, efficient implementation in O(|T|+n^2 log n)

Henzinger, King & Warnow, Constructing a tree from homeomorphic subtrees, with applications to computational evolutionary biology, 1999.

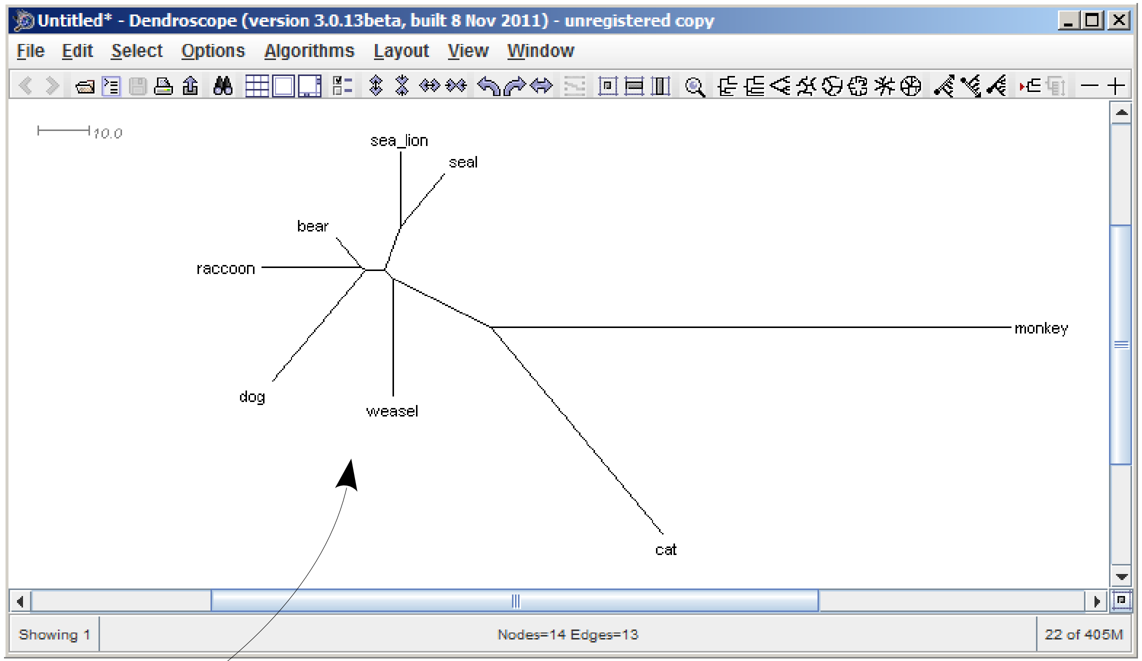
Visualizing phylogenetic trees

Visualize branch lengths or not

```
((raccoon:19.19959,bear:6.80041):0.84600,((sea_lion:11.99700,
seal:12.00300):7.52973,((monkey:100.85930,cat:47.14069):20.59201,
weasel:18.87953):2.09460):3.87382,dog:25.46154);
```

Several kinds of visualizations:

- rectangular phylogram
- rectangular cladogram
- slanted cladogram
- circular phyogram
- circular cladogram
- inner circular cladogram
- radial phylogram
- radial cladogram



Showing 1 | Nodes=14 Edges=13 | 22 of 405M

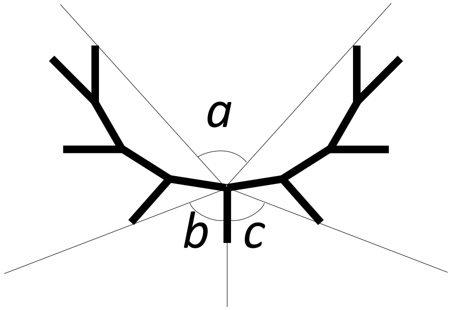
http://www.dendroscope.org

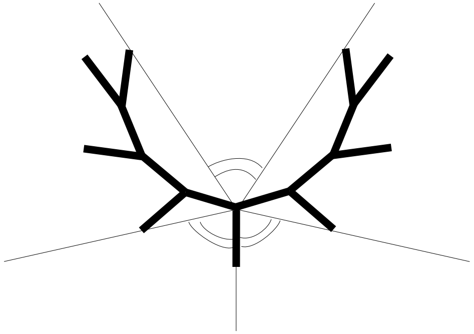
Visualizing phylogenetic trees: radial phylogram

“Equal angle” algorithm to draw a radial phylogram on *n* leaves:

- Compute the angles “bottom-up” starting with angle $2i\pi/n$ for leaf *i*
- Locate the nodes “top-down” using:
  - the angles
  - the edge lengths
- Add the labels (avoiding overlap)

“Equal daylight” algorithm to optimize used space:





Felsenstein, Inferring phylogenies, 2002, 579-583

Comparing trees

- **Maximum Agreement Subtree** (MAST): Finden & Gordon, Obtaining common pruned trees, 1985

  - Given T1 and T2 on the set X of leaves, an *agreement subtree* T of T1 and T2, on a subset X' of leaves, is such that T1 and T2 restricted to X' are equal to T.

  - a *maximum agreement subtree* is an agreement subtree of maximum size

→ Polynomial-time algorithm for 2 trees (rooted or not), with fixed degree (or not)

Steel & Warnow, Kaikoura tree theorems: Computing the maximum agreement subtree, 1993

→ O(n log n) algorithm for 2 rooted binary trees

Cole & Hariharan, An O(n log n) algorithm for the maximum agreement subtree problem for binary trees, 1996

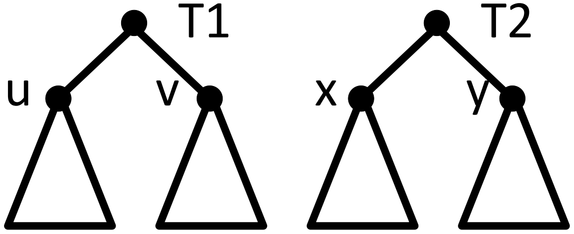
→ NP-hard for 3 (or more) trees of unbounded degree

Amir & Keselman, Maximum agreement subtree in a set of evolutionary trees, 1997

→ Polynomial-time algorithm if one of the trees has bounded maximum degree

Farach, Przytycka & Thorup, On the agreement of many trees, 1995

Dynamic programming for 2 rooted binary trees:



$$n_{MAST}(T1,T2)=\max\left\{\begin{array}{l} \\ \\ \\ \end{array}\right.$$

Comparing trees

- **Maximum Compatible Tree** (MCT):

  - if a tree is not binary, several binary trees *refine* it

  - a compatible tree on a subset X' of leaves is a binary tree which refines the trees T1 and T2 restricted to the leaves of X'.

→ Polynomial-time algorithm for 2 trees of bounded degree
→ NP-hard if one tree can have arbitrarily large degree

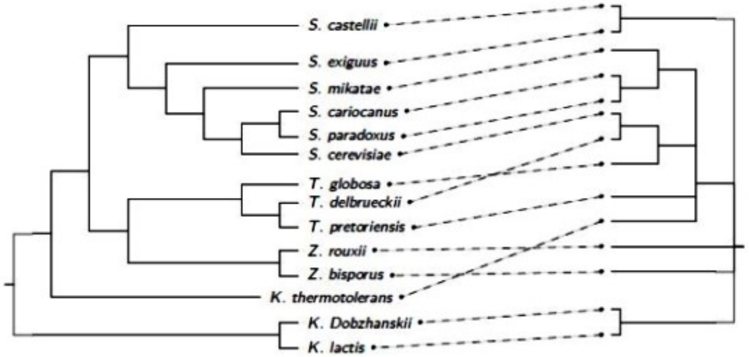
Hein, Jiang, Wang & Zhang, On the complexity of comparing evolutionary trees, 1996

→ $O(\min\{3^p kn, 2.27^p + kn^3\})$ for k trees, where p is the number of leaves to remove

Berry & Nicolas, Improved parametrized complexity of the maximum agreement subtree and maximum compatible tree problems, 2006

- **Tanglegrams**:

  - display both trees for visual comparison, linking their leaves with edges, minimizing edge crossings.
  → general problem NP-complete
  → planar embedding in linear time
  → if one tree is fixed, O(n log n)



Venkatachalam, Apple, St John, Gusfield, Untangling tanglegrams: comparing trees by their drawings, 2010

Comparing trees

Distances between trees:

- **Robinson Foulds distance** between T1 and T2:
  - Number of different splits ("symmetric difference metric")

  Robinson and Foulds, Comparison of phylogenetic trees, 1981

  - Minimum number of edge contractions/decontractions to go from T1 to T2

- **quartet distance** between T1 and T2:
  - Number of different quartets

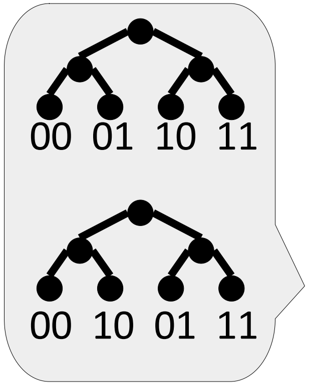
  → computed in O(*dn* log *n*) for trees of max degree *d*

  Brodal, Fagerberg, Pedersen, Mailund and Sand, SODA 2013

  Survey: Sand, Holt, Johansen, Fagerberg, Brodal, Pedersen and Mailund. *Biology*, 2014

  → diameter of the quartet distance?

  - Conjecture: at most (2/3+o(1)) BINOM(n,4) — Bandelt & Dress, *Advances in Applied Mathematics*, 1986
  - 2014: > 2/3 BINOM(*n*,4)
    at most (0.9+o(1)) BINOM(*n*,4) — Alon, Snir & Yuster, SODA 2014
  - 2016: at most (0.69+o(1)) BINOM(*n*,4) — Alon, Naves & Sudakov, SODA 2016
    at most (2/3+o(1)) BINOM(*n*,4) for caterpillars
  - 2019: strongly explicit example for > 2/3 BINOM(*n*,4) — Chor, Erdős & Komornik, Ann. Comb. 2019



Comparing trees

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  - Number of different splits ("symmetric difference metric")

    Robinson and Foulds, Comparison of phylogenetic trees, 1981
  - Minimum number of edge contractions/decontractions to go from T1 to T2

- **quartet distance** between T1 and T2:
  - Number of different quartets

  → computed in O(dn log n) for trees of max degree d

  Brodal, Fagerberg, Pedersen, Mailund and Sand, SODA 2013

  Survey: Sand, Holt, Johansen, Fagerberg, Brodal, Pedersen and Mailund. *Biology*, 2014

- **SPR distance** between T1 and T2:
  - Minimum number of SPR moves to go from T1 to T2

  → NP-hard

  Rooted trees: Bordewich and Semple, *Annals of Combinatorics* 2005

  Unrooted trees: Hickey, Dehne, Rau-Chaplin and Blouin, *Evolutionary Bioinformatics* 2008

  → computed in O($2.42^k\ k + n^3$) for 2 rooted binary trees with SPR distance k

  Whidden, Beiko, and Zeh, *SIAM Journal on Computing* 2013

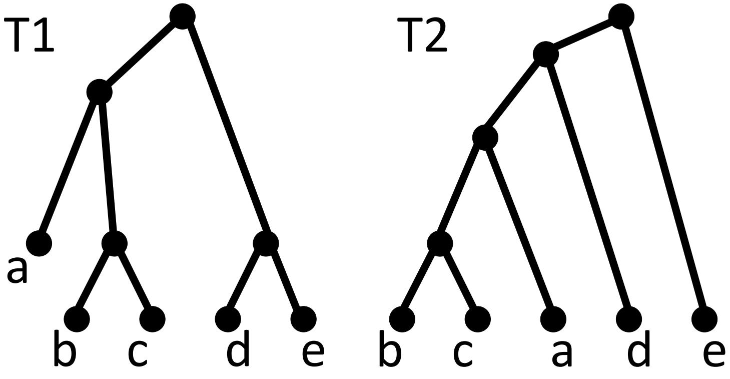
  Survey: Shi, Feng, Chen, Wang, Wang, *Tsinghua Science and Technology* 2013

Comparing trees

Day's algorithm Day, Optimal algorithms for comparing trees with labeled leaves, 1985

Linear-time computation of the Robinson Foulds distance between two rooted binary trees T1 and T2:

- relabel leaves of T1 (from left to right) from 1 to n, relabel T2's leaves accordingly
- represent the leaves below each internal node x of T1 as an interval $[i_x,j_x]$
- store these intervals in an array *t*: $[i_x,j_x]$ stored in $t[i_x]$ if x is the right child of its parent, in $t[j_x]$ otherwise
- visit the internal nodes of T2, finding the minimum *m*, the maximum *M*, and the number *l* of leaves below each of them: if $l=M-m+1$ and the corresponding interval exists in *t* (in the *m*'th or in the *M*'th cell), then the interval is present both in T1 and T2. Otherwise it corresponds to a cluster in T2 but not in T1.



Exploring the tree space

NNI: nearest neighbor interchange
Consider an edge *e* and exchange the adequate subtrees connected to *e.*

SPR: subtree pruning and regrafting
Disconnect a subtree and reattach it somewhere else.

TBR: tree bisection and reconnection
Delete an edge in the tree, reconnect the two parts with a new edge anywhere.

An NNI is a special kind of SPR, which is a special kind of TBR.

NNIs allow to explore the whole tree space. *Proof: induction on...*

Felsenstein, Inferring phylogenies, 2002, 39-44

Exploring the tree space... to find the optimal tree

Exploring the tree space is useful to find the optimal topology for:

Felsenstein, Inferring phylogenies, 2002, 39-44
http://evolution.genetics.washington.edu/phylip/software.html

- **Parsimony**

Given the tree topology, find the scenario which explains current genetic sequences with the minimum number of operations along the tree edges

- **Likelihood**

Given the tree topology and a statistical model of evolution, find the scenario which produces current genetic sequences with the highest probability

Models of evolution: Jukes Cantor’69, Kimura’80, Felsenstein’81

http://en.wikipedia.org/wiki/Models_of_DNA_evolution

- **Distance optimization**

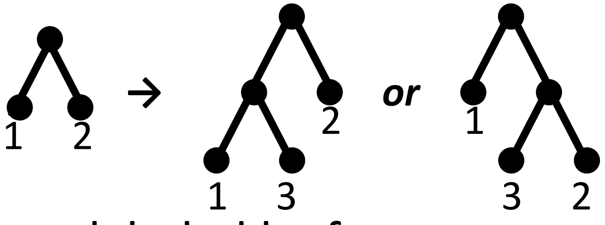
Given the tree topology, find edge lengths which best explain distance data between current genetic sequences

Tree quality: Is the obtained tree “robust”?
Bootstrap: apply the same algorithm on “resampled” data

Exploring the tree space... by randomly generating trees

Which model do you choose to randomly generate (rooted binary) trees?
→ *Random tree generation also used to simulate data to test algorithms!*

- Labeled tree **equiprobability**

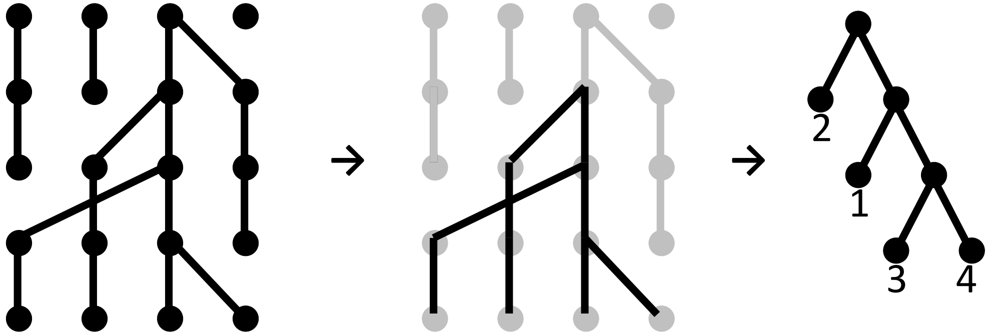


- **Yule-Harding model** :
  - start from a root with two labeled children
  - choose one leaf at random to split it, creating a new labeled leaf

Felsenstein, Inferring phylogenies, 2002, 559-562

- **Kingman's coalescent model** (population genetics) :
  - start from a population of *n* leaves (each leaf representing a gene copy)
  - the probability that two gene copies come from the same copy in the previous generation is 1/2*n*

equivalent to repeating, for *k* gene copies:
- go back ≈4*n*/(*k*(*k*-1)) generations in time
- combine 2 random lineages
- decrease *k* by 1



Felsenstein, Inferring phylogenies, 2002, 450-460

Random rooted phylogenetic tree generation

Exercise – Tree shapes and random generation models

Q1. Evaluate the probability of each rooted binary tree shape on 4 leaves, for each of the three random generation models.

Q2. Evaluate the probability of the rooted binary caterpillar tree (i.e. a tree where no node has two children having two children) on *n* leaves with the tree equiprobability model, the Yule-Harding model as well as with Kingman's coalescent model.

Dealing with real data to build the tree of life

The model of evolution seen so far is **too simple**, not only mutations but also:

- deletions
- insertions
- duplications (paralogs), tandem duplications
- inversions
- translocations
- gene transfer across species / hybridization

Differences (number of leaves, tree topology, etc.):

- between gene trees
- between gene tree and species tree

→ "Tree of 1 percent" (31-protein tree of life) Dagan & Martin, The tree of one percent, 2006
→ Consensus tree (same leaf set) / supertree (partial leaf sets)
→ Reconciliation between trees
→ Duplication/Loss/Transfer models

Consensus trees

How to combine information from several gene trees on the same set of taxa?

Semple & Steel, Phylogenetics, p. 54

- Strict consensus tree: keep only splits which appear in all unrooted trees
- Majority consensus tree: keep splits which appear in more than half the trees

→ The resulting splits are compatible

Consensus trees

How to combine information from several gene trees on the same set of taxa?

Semple & Steel, Phylogenetics, p. 54

- **Strict consensus** tree: keep only splits which appear in all unrooted trees

- **Majority consensus** tree: keep splits which appear in more than half the trees
  → The resulting splits are compatible
  (suppose they are not and consider two incompatible splits: as those two splits both appear in a majority of trees, they are the splits of one common tree at least, so they are compatible: contradiction)

- **Adams consensus** tree (for rooted trees):
  - for all trees, consider its maximal clusters for inclusion
  - considering all non-empty intersections between maximal clusters, one gets a partition of X
  - apply the same procedure recursively on each set of the partition

Margush & McMorris, Consensus n-trees, 1981

O(kn^2) algorithm for *k* trees improved to O($kn \log n$) in 2017

Adams, Consensus Techniques and the Comparison of Taxonomic Trees, 1972
Adams, N-Trees as Nestings: Complexity, Similarity and Consensus, 1986
Jansson, Li & Sung, On Finding the Adams Consensus Tree, 2017

Gusfield's algorithm for perfect phylogeny

Dan Gusfield (1991), Efficient algorithms for inferring evolutionary trees. Networks, vol. 21(1), pages 19-28.

The **perfect phylogeny** problem

Matrix M of binary sequences with n lines (species) and m columns (characters).
Given M, decide if there exists a tree and binary sequences labeling internal nodes such that:

- the root is labeled by a sequence of only zeros
- each character may change only once from a zero to a one, never from a one to a zero, from a parent to a child in the tree.

Gusfield's test for perfect phylogeny in $O(nm)$:

- sort the columns of M in decreasing order (radix sort), considering them as binary numbers
- remove duplicate columns to get matrix M'
- for each cell $M'_{i,j}=1$, define $S_{i,j}=\{k<j \mid M'_{i,k}=1\}$;
  $L_{i,j}=\max S_{i,j}$ if $S_{i,j}$ not empty, 0 otherwise ;
  for each column j, $L_j=\max\{L_{i,j} \mid \text{M}'_{i,k} = 1\}$
- check if $L_{i,j}=L_j$ for each $M'_{i,j}=1$

Lowest common ancestor in constant time

Linear time preprocessing to answer **lowest common ancestor queries** in constant time.

Harel & Tarjan, Fast Algorithms for Finding Nearest Common Ancestors, 1984
Bender & Farach-Colton, The LCA Problem Revisited, 2000
Erik Demaine: Advanced Data Structures course at MIT, 2012
https://courses.csail.mit.edu/6.851/spring12/lectures/

Linear-time reduction to Minimum Range Queries with a -/+ 1 difference
(find the minimum in table *T* between indices *i* and *j*) :
→ Eulerian tour of the tree storing node depth
→ Minimum Range Queries with a -/+ 1 difference

Solve Minimum Range Queries in **constant time** with **O(*n* log *n*)** preprocessing
→ Compute & store minimums for all intervals of range a power of 2: O(*n* log *n*)
→ Answer queries in constant time combining 2 intervals (starts in *i* + ends in *j*)

Strategy to obtain **linear** space and preprocessing time:
→ Group table cells into groups of size ½ log *n*
→ Compute the min for each group: table of size O(*n* / log *n*) → O(*n*) time
→ For each group, subtract the first element:
    → each group starts with 0: limited number of group types
    → store the location of the min for each group type in a lookup table

Maximizing triplet consistency

We have seen the BUILD algorithm to reconstruct a tree from its triplets.

Can we reconstruct the tree if there are errors in the triplets?

Triplet edition problem:
Input: set X of leaves, set R of triplets, positive integer $k \leq n^3$.
Output: yes if there exists a tree containing k triplets of R, no otherwise.

Triplet edition is NP-complete:
- In NP: check in polynomial time that a solution is correct → BUILD algorithm!
- NP-hard: reduction from Cyclic ordering

Jansson, On the Complexity of inferring rooted evolutionary trees, 2001

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Cyclic ordering problem:
Input: set A of elements, set C of ordered triples (a,b,c) of distinct elements of A
Output: yes if there exists a bijection f: $A \rightarrow [1..|A|]$ such that for each (a,b,c) in C, either $f(a)<f(b)<f(c)$ or $f(b)<f(c)<f(a)$ or $f(c)<f(a)<f(b)$

Reduction:
Given an instance of the Cyclic ordering problem, build an instance of the Triplet edition problem:

- $X=A \cup \{x_0,x_1,x_2,\ldots,x_{|C|}\}$, $k=|A|(|A|-1)/2+2|C|$;
- for all $a \neq b$ in X, add $b|ax_0$ and $a|bx_0$ to R;
- for each i in $[1..|C|]$, add $b|ax_i$, $c|bx_i$ and $a|cx_i$ to R.

Jansson, On the Complexity of inferring rooted evolutionary trees, 2001

Maximizing triplet consistency

Removing *k* triplets to obtain a triplet set consistent with a tree?

NP-complete

Bryant, Building trees, hunting for trees, and comparing trees : theory and methods in phylogenetic analysis, 1997
Jansson, On the Complexity of inferring rooted evolutionary trees, 2001
Wu, Constructing the maximum consensus tree from rooted triples, 2004

But fixed-parameter tractable using the “obstructions” (or “conflicts”) on *dense* instances (one triplet for each set of 3 leaves):
“do not contain {$ab|c$, $b|cd$, $a|bd$} or {$ab|c$, $b|cd$, $ad|b$}”

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"Bounded search tree" algorithm:
while there is a conflict, solve it in all possible ways

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“Bounded search tree” algorithm:
while there is a conflict, solve it in all possible ways

⇒ $O(6^k \text{poly}(n))$ time algorithm

Optimized algorithm in $O(n^4)+2^{O(k^{1/3}\log k)}$

Guillemot & Mnich, Kernel and fast algorithm for dense triplet inconsistency, 2010

Taking into account horizontal transfer or hybridization

Fit gene trees into a *phylogenetic network* of the species:

- rooted direct acyclic graph with labeled leaves
- contains some vertices with indegree >1: *hybrid vertices*

Hybridization number

A tree *T* is *contained* in *N* if *T* can be obtain from *N* by arc contractions & deletions.

Given an integer *k*, and 2 trees *T*1 and *T*2, does there exist a *hybridization network N*, i.e. a phylogenetic network which contains the two trees, with at most *k* hybrid vertices?

Hybridization number: minimum *k* for a hybridization network of *T*1 and *T*2.

Computing the hybridization number is NP-complete
but fixed-parameter tractable.

Bordewich & Semple, Computing the minimum number of hybridization events for a consistent evolutionary history, 2007
Bordewich & Semple, Computing the hybridization number of two phylogenetic trees is fixed-parameter tractable, 2007

Property: HybridizationNumber($T1$,$T2$) ≥ $d_{SPR}(T1,T2)$

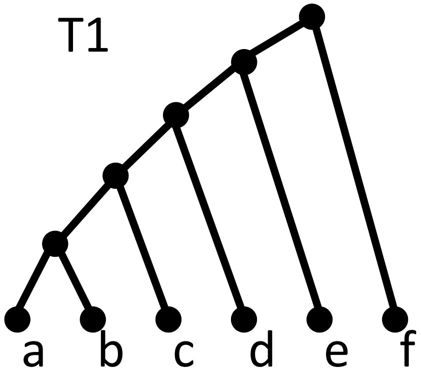
SPR distance and hybridization number

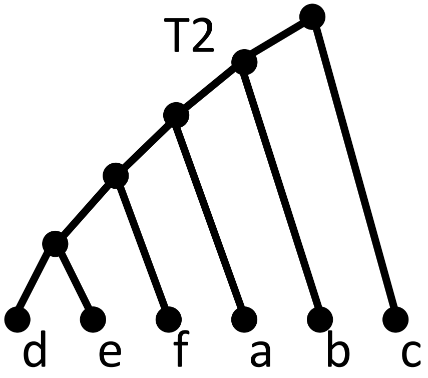
Property: HybridizationNumber(T1,T2) ≥ SPR(T1,T2)

→ deduce the SPR scenario from the hybridization network

The converse is false: problems with cycles!

Example:





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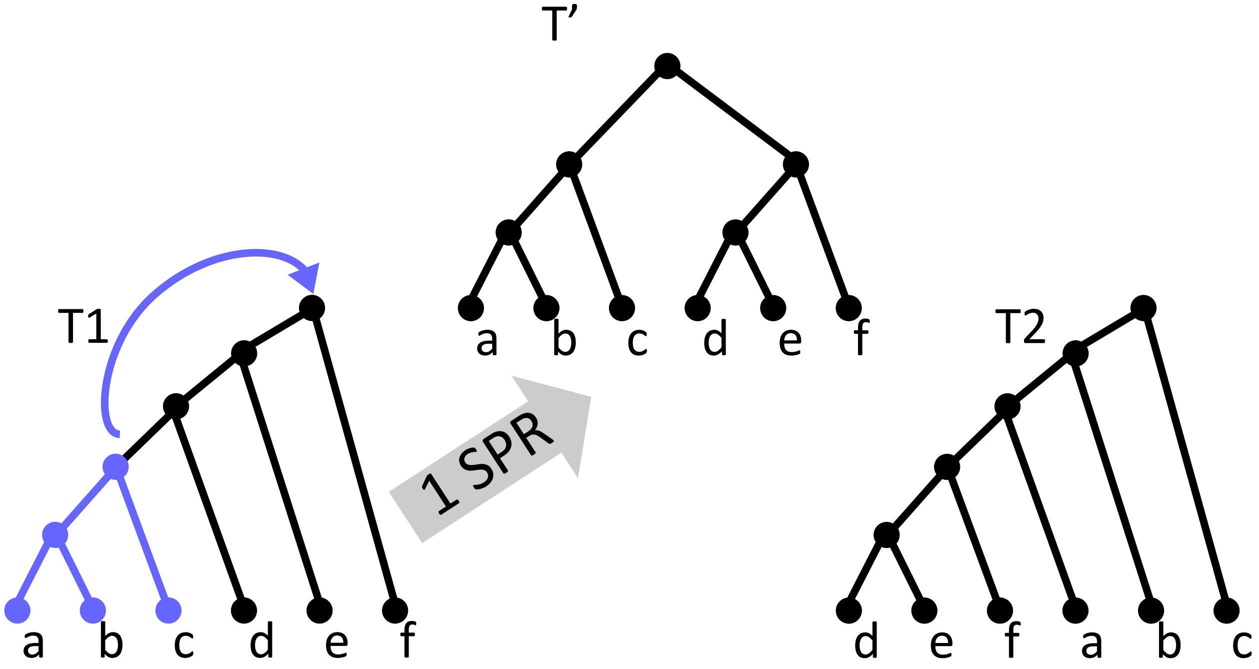

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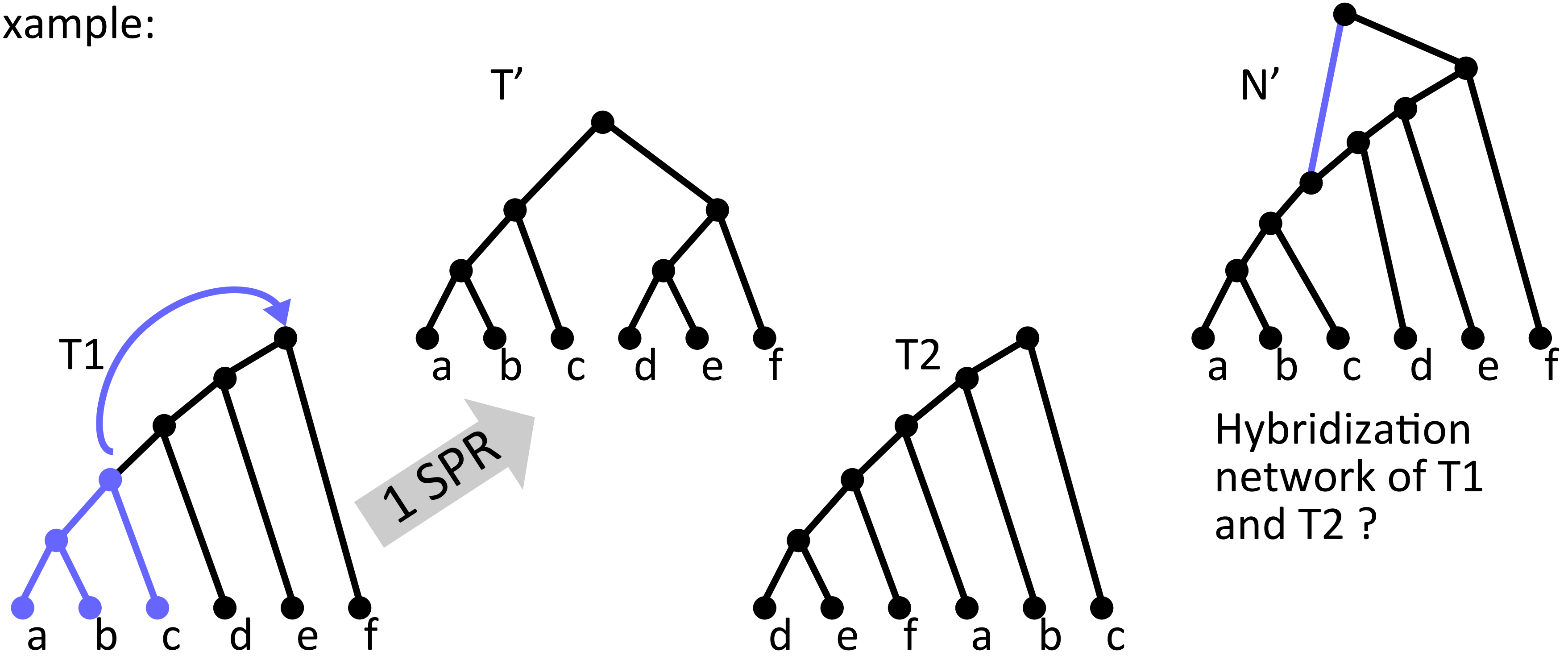

Hybridization network of T1 and T2 ?

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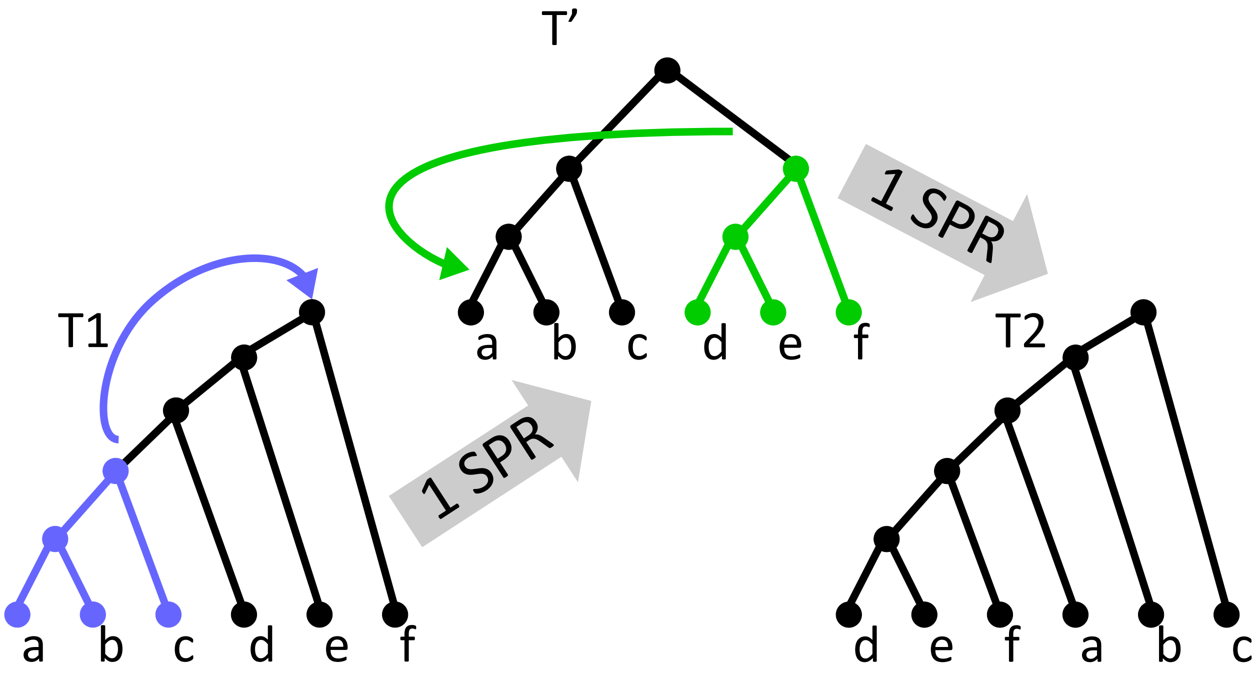

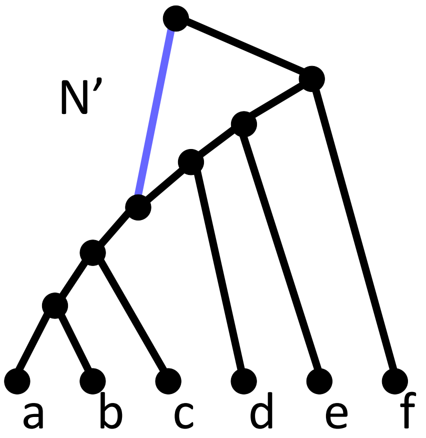

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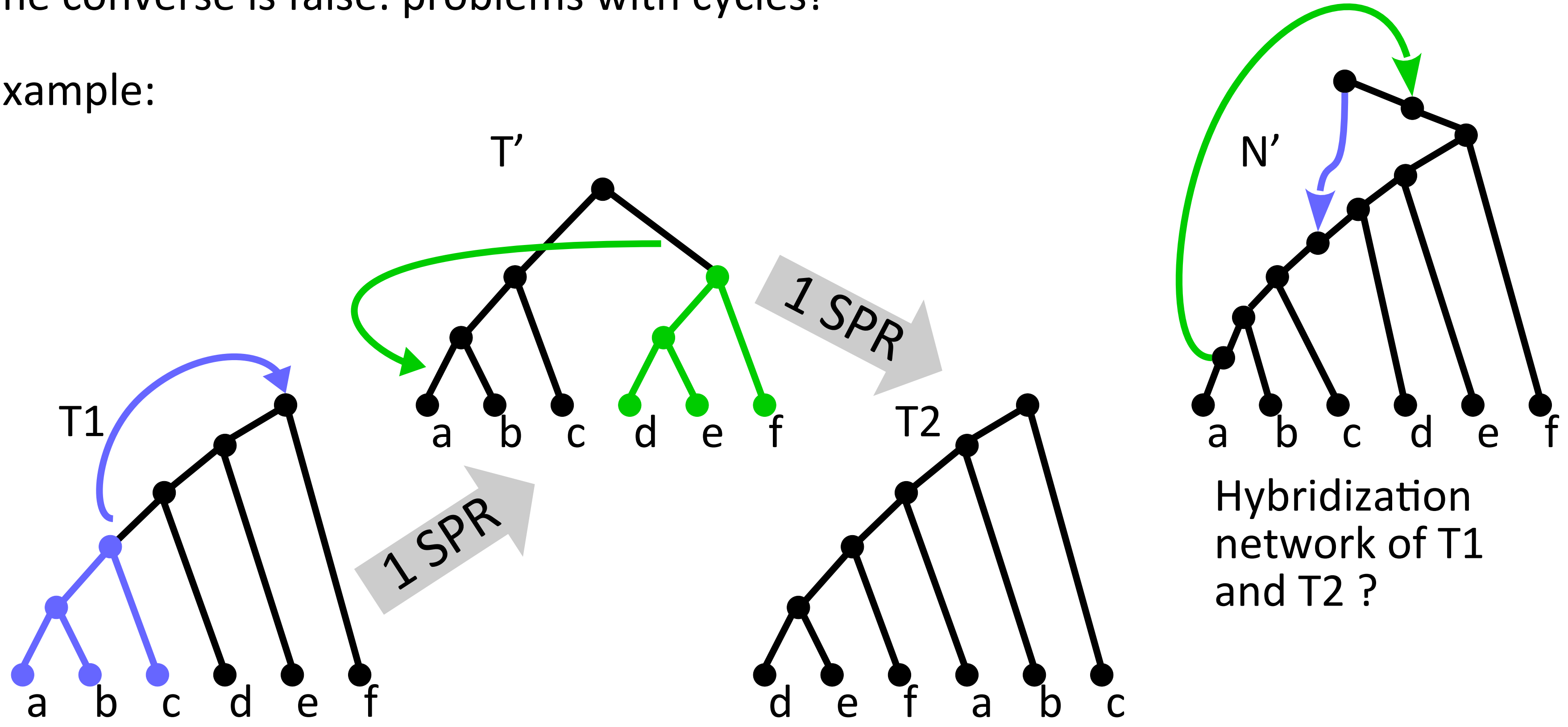

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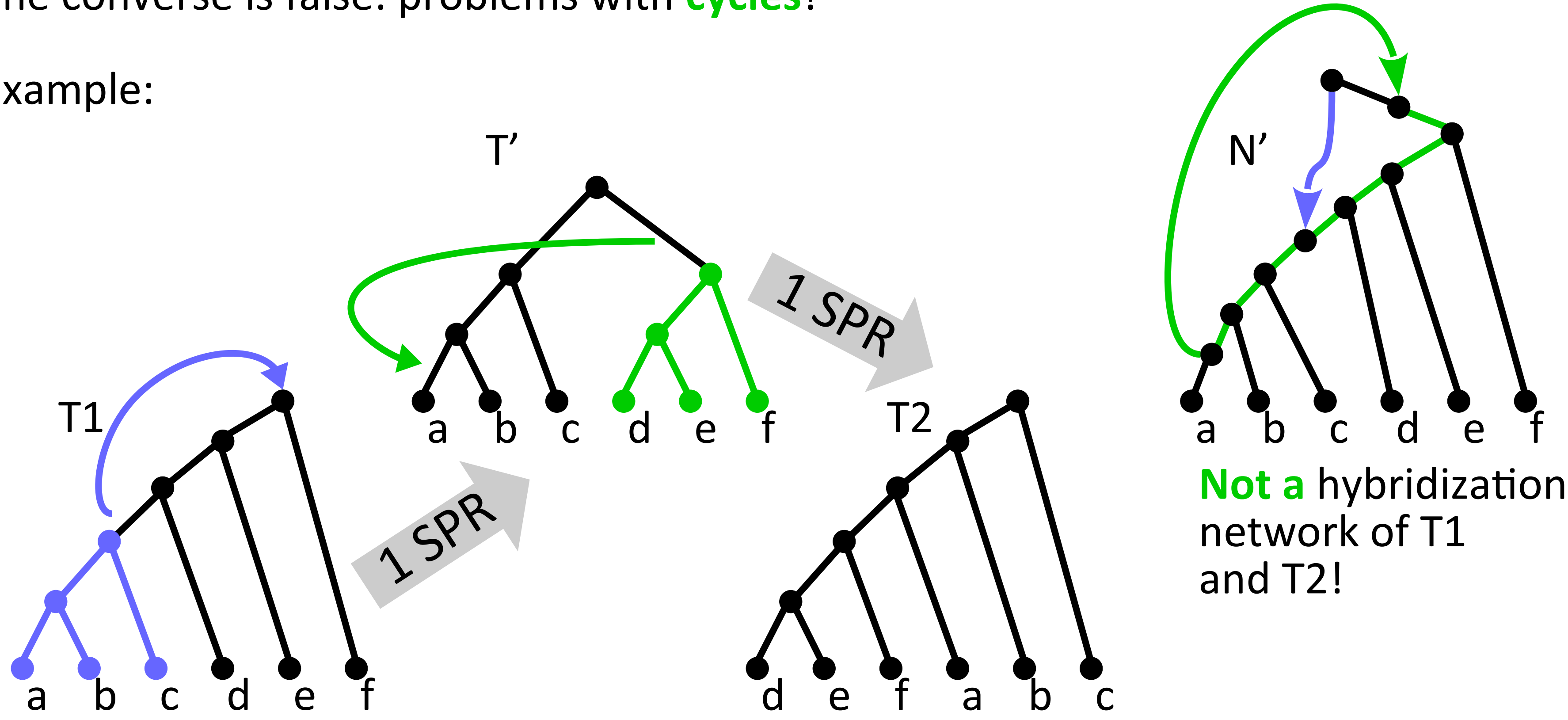

Not a hybridization network of T1 and T2!

Properties of trees not valid on phylogenetic networks

- Possible to have several lowest common ancestors

- Possible to have a triplet present «twice» in the network

- Several paths between two leaves
→ how to define the distance between them?

→ a lot of problems are **NP-complete** on **phylogenetic networks**

→ a lot of challenges to get **efficient algorithms in practice**
(FPT algorithms, approximation algorithms, linear programming, heuristics, etc.)

A fundamental problem on phylogenetic networks with recent progress:
TreeContainment

→ Presentation on *Finding a gene tree in a phylogenetic network*