Gene Tree Parsimony for Incomplete Gene Trees

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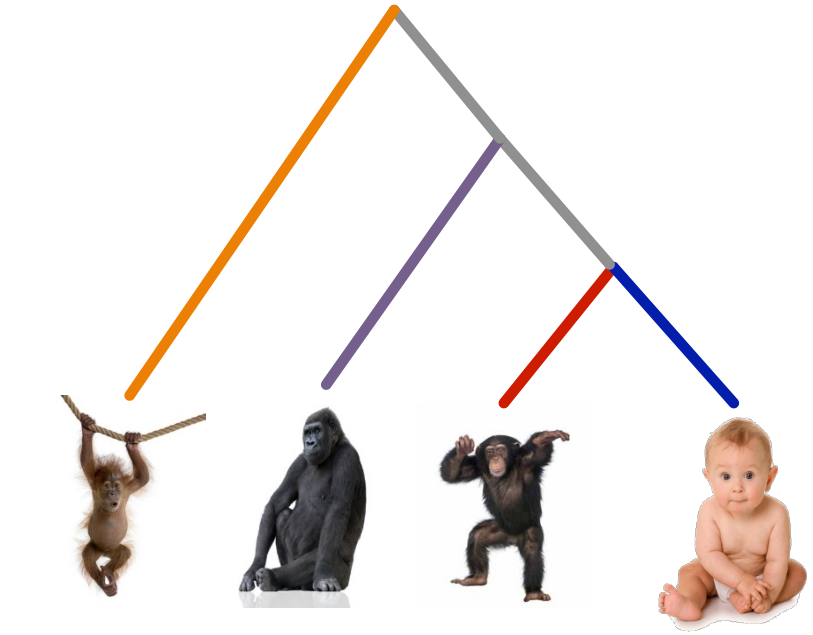
Outline

- Background
  - Gene trees and species trees
  - Species tree estimation techniques
- GTP for Incomplete gene trees
  - Summary of our contributions
  - Descriptions of our algorithms
- Conclusion

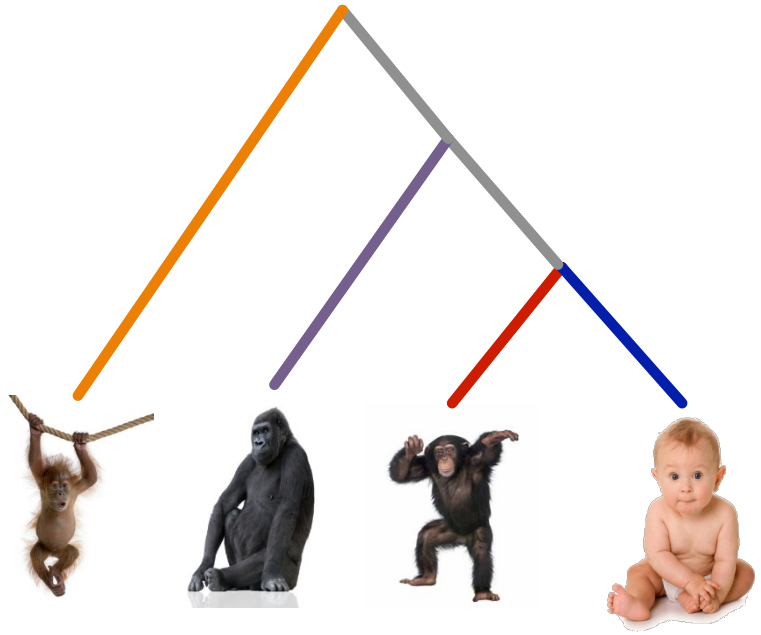
Species tree

- represents the evolutionary history of a group of organisms.

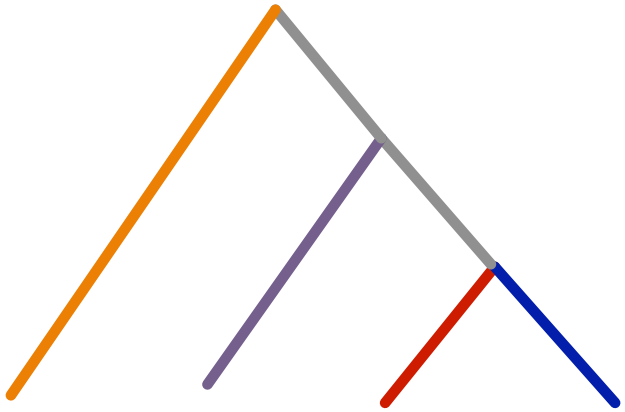


Gene trees and species tree

- Species tree – Pattern of branching of species lineages via speciation.
- Gene tree – A phylogenetic tree that depicts how a *single* gene has evolved in a group of related species.



Orangutan Gorilla Chimpanzee Human



Hemoglobin

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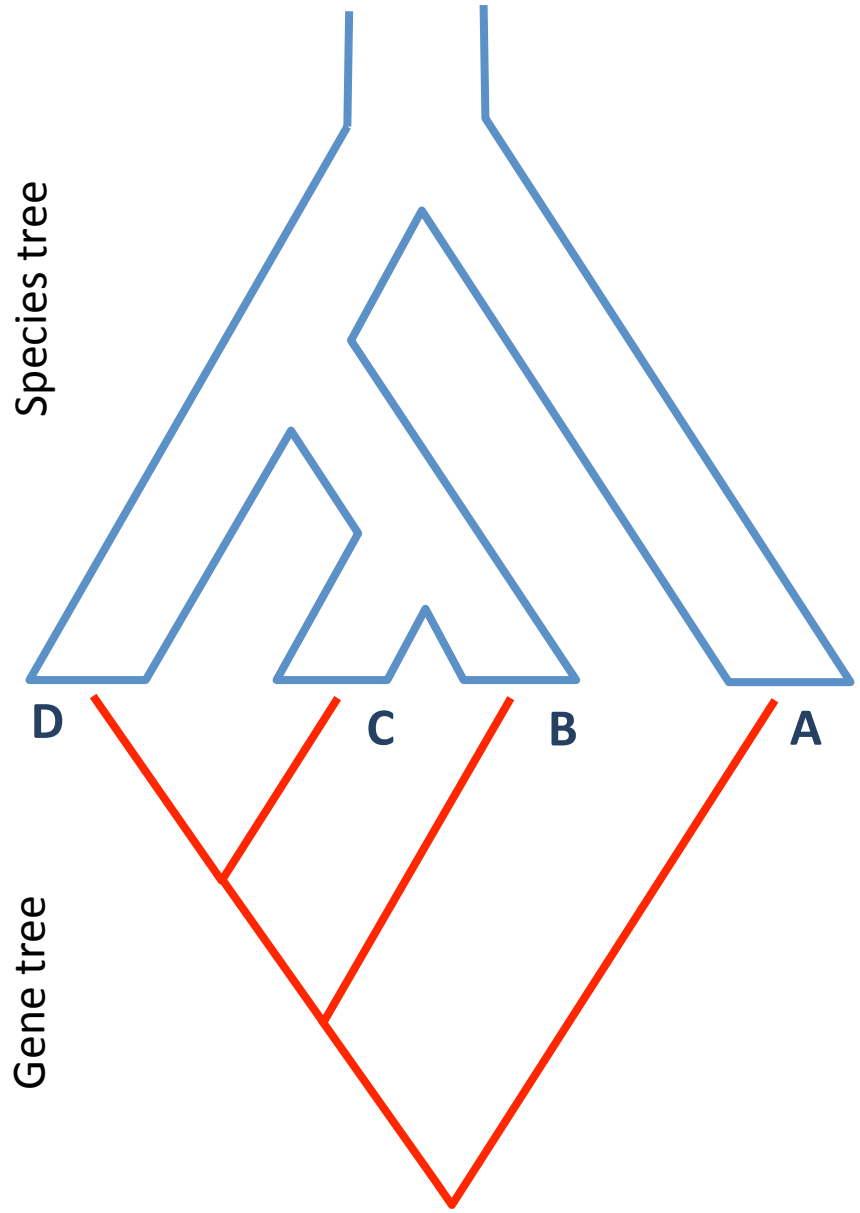
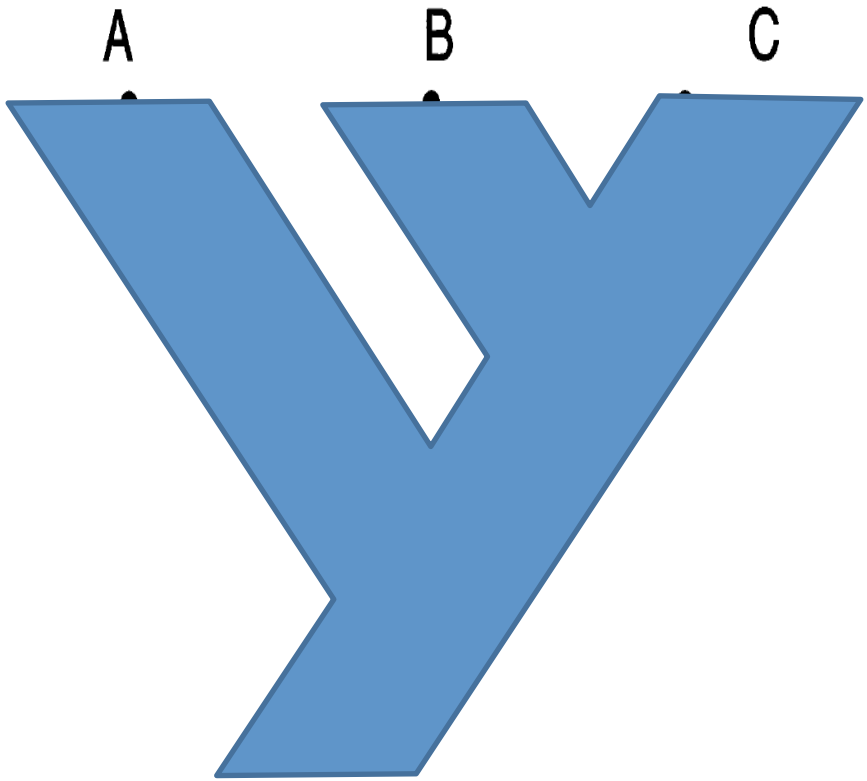
Orangutan Gorilla Chimpanzee Human

Discordance



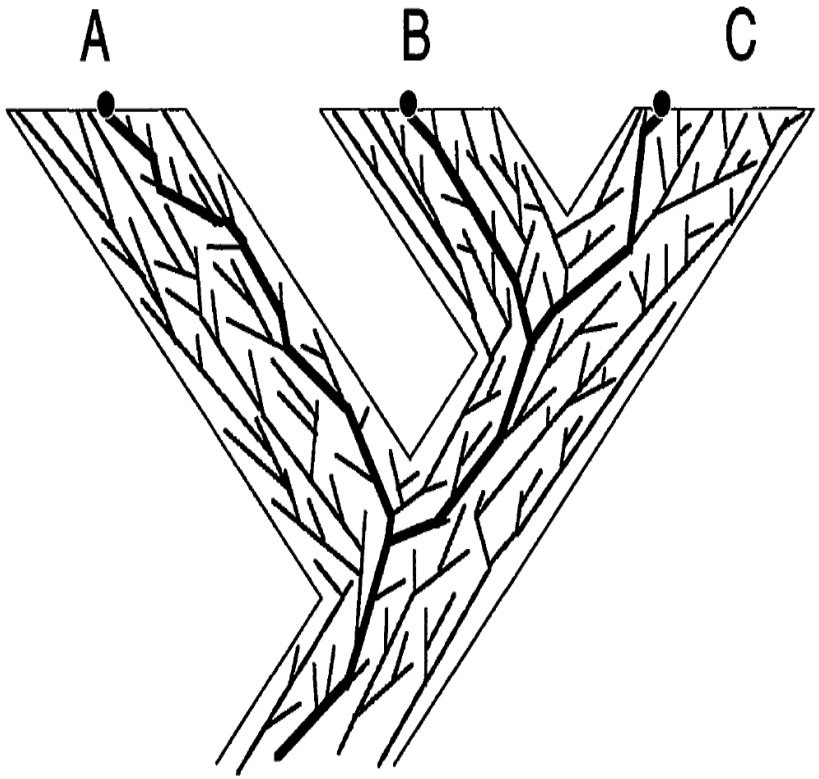
- Gene trees don't necessarily show the same branching pattern as their containing species tree

Gene trees in species tree



[Maddison, Syst.biol., 1997]

Gene trees in species tree



[Maddison, Syst.biol., 1997]

Causes of gene tree discordance

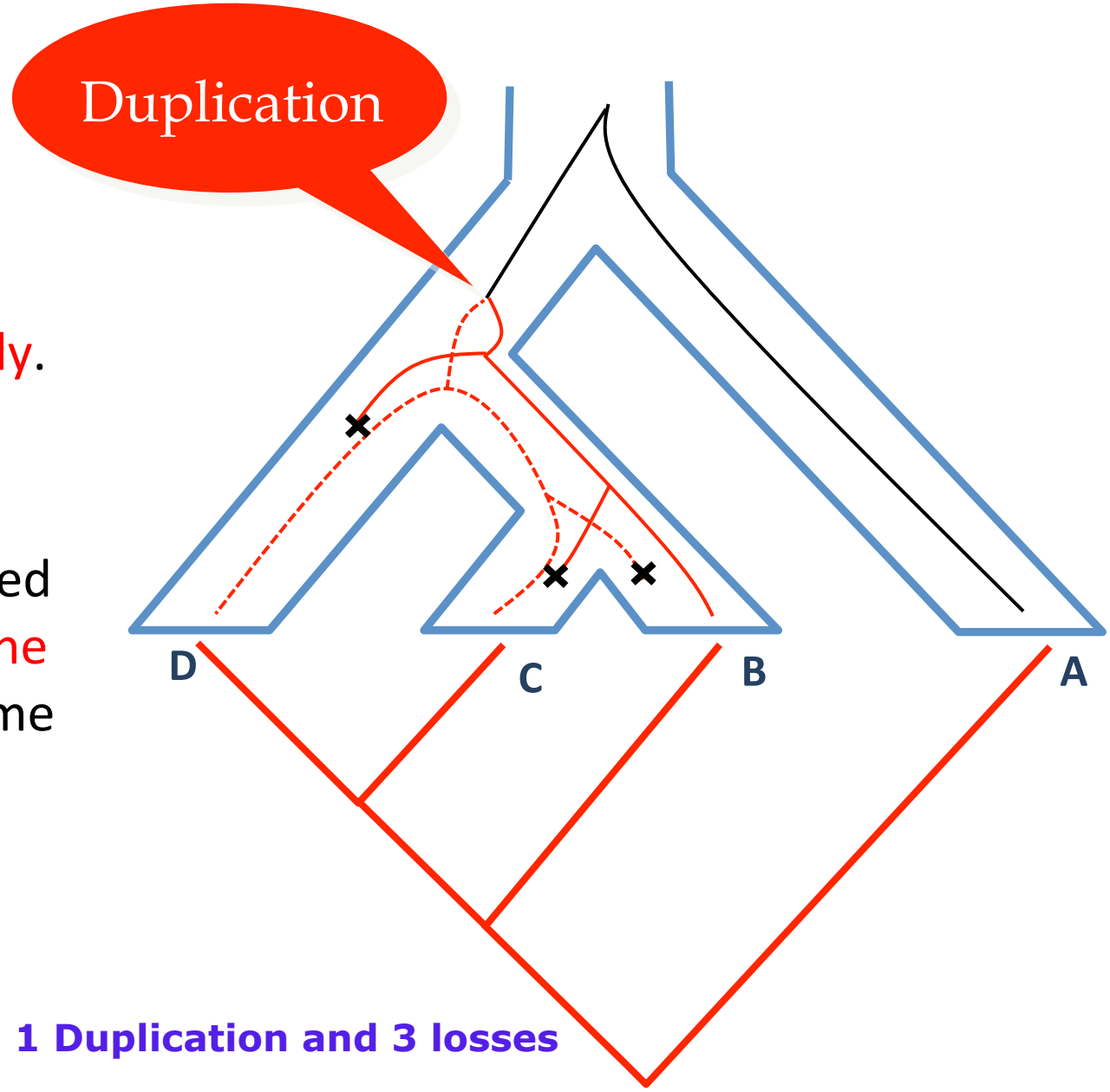
- Discord can arise from
  - Deep Coalescence (ILS = incomplete lineage sorting)
  - Gene Duplication/Loss (GDL)
  - Horizontal Gene Transfer (HGT) etc.

- Estimation error may also introduce discordance.

Gene Duplication/Loss

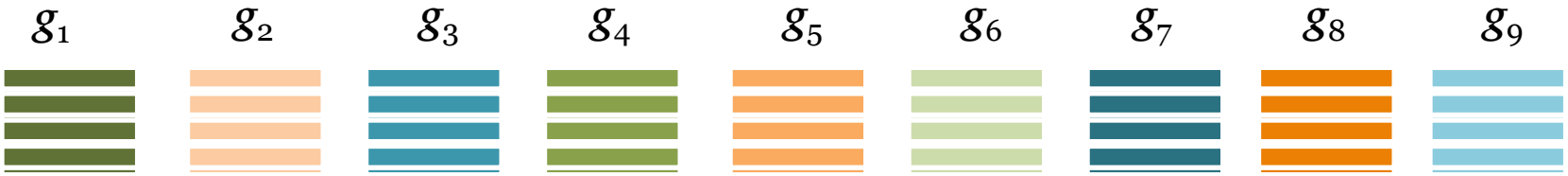
- A gene might get duplicated and both copies descend and evolve independently.

- Discordance can occur if some sampled copies come from one locus and others come from another locus



1 Duplication and 3 losses

Species tree estimation – concatenation?



Supergene alignment g^*

Sequence-based tree estimation method

Species Tree

Species Tree Estimation

Concatenation – standard approach, but: needs single copy of each species, and does not take gene tree heterogeneity into account

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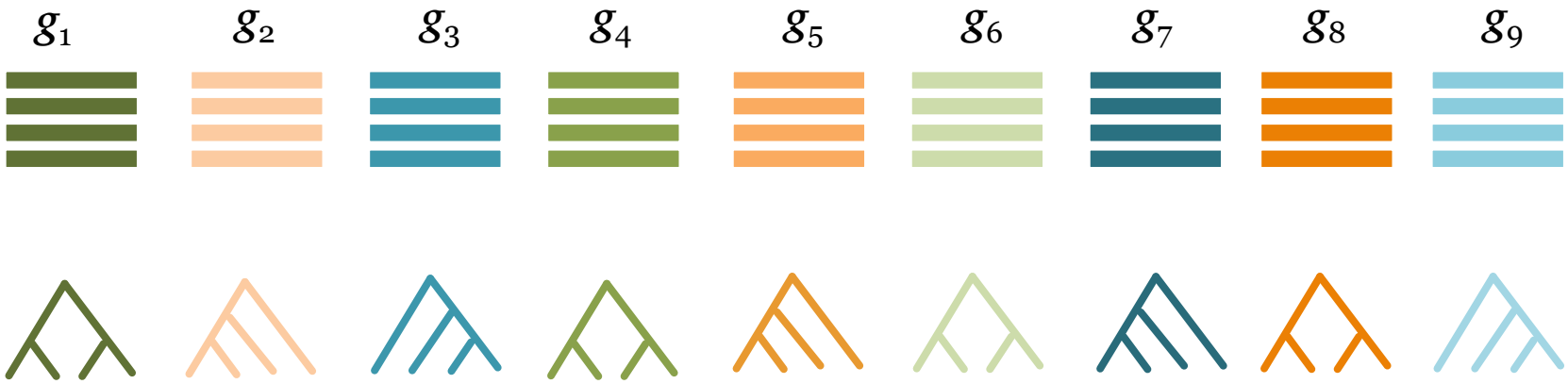
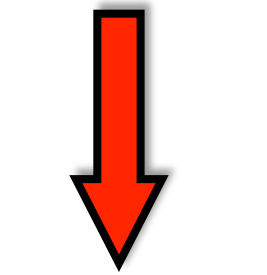
Summary methods (e.g., gene tree parsimony) – NP-hard optimization problems, but fast in practice

Species tree estimation: Summary methods



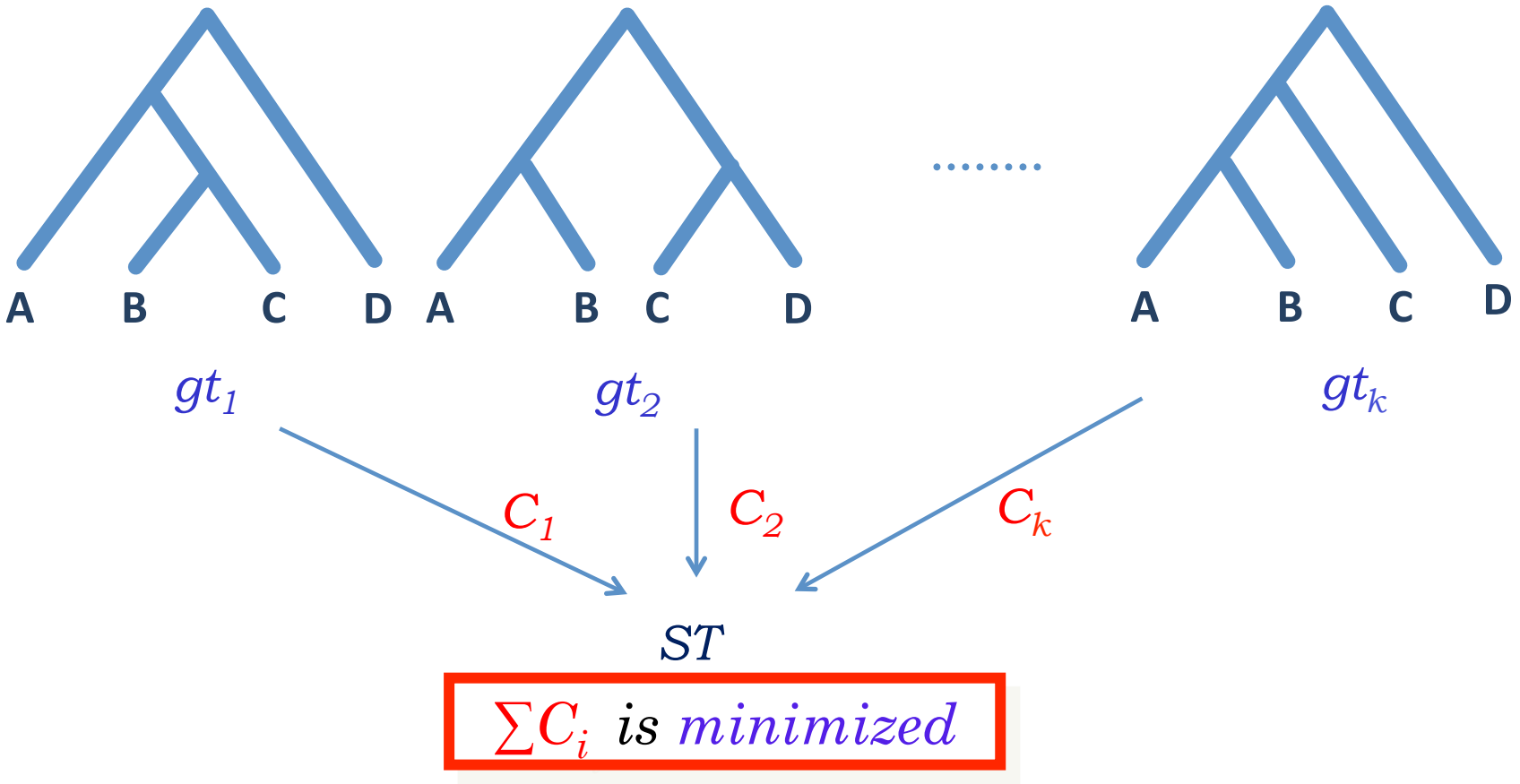


Species Tree

Gene Tree Parsimony (GTP, formulated by Guigo, first method by Rod Page), Supertree methods

GTP: Minimize Gene Duplication+Loss

- Input: A set of rooted binary gene trees (multi-copy)
- Output: A species tree *ST* that minimizes total number of duplications and losses



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Scoring a single species tree with respect to a set of gene trees is polynomial time

Finding a best species tree is NP-hard, but good heuristics exist:

iGTP (Chaudhary, Bansal, Wehe, Fernandez-Baca, and Eulenstein. BMC Bioinformatics 2010)

DupTree (Wehe, Bansal, Burleigh, and Eulenstein, Bioinformatics 2008)

Incomplete gene trees

- Incomplete gene tree: not all gene trees have individuals from all the species.

  - Sampling Error
    - The gene may be available in the species' genome, but it was not sampled when the gene tree was estimated
  - True biological gene loss
    - Gene birth/death

Summary of our contributions

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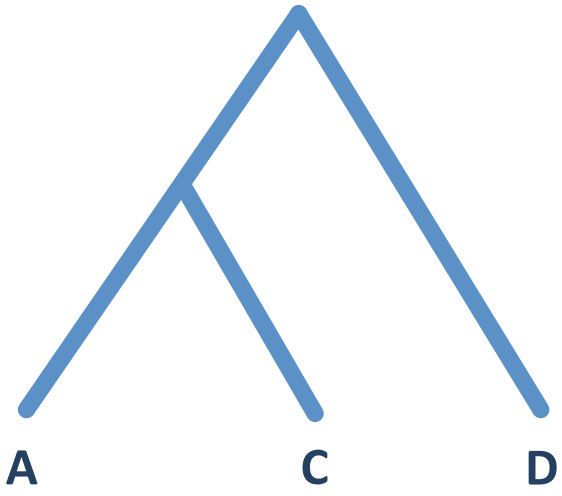
- We prove that the standard calculation correctly computes losses when incompleteness is due to sampling
- We show by example that the standard calculation for losses in GTP can be incorrect when incompleteness is due to true biological loss
- We show how to compute the number of losses implied by a gene tree and species tree, when incompleteness is due to true biological loss
- We formulate variants of the GTP problem (when gene tree incompleteness is due to true biological loss) as minimum weight maximum clique problems, and we show a dynamic programming algorithm to find the optimal species tree.

Reconciliation

- Given a gene tree *gt* and a species tree *ST*,
  - *the objective is to explain the differences in terms of gene duplication and loss*



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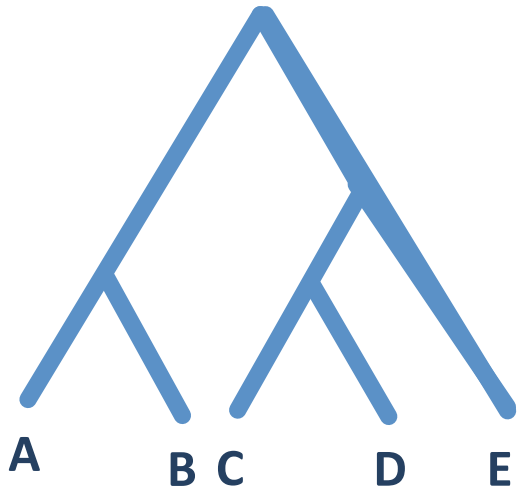
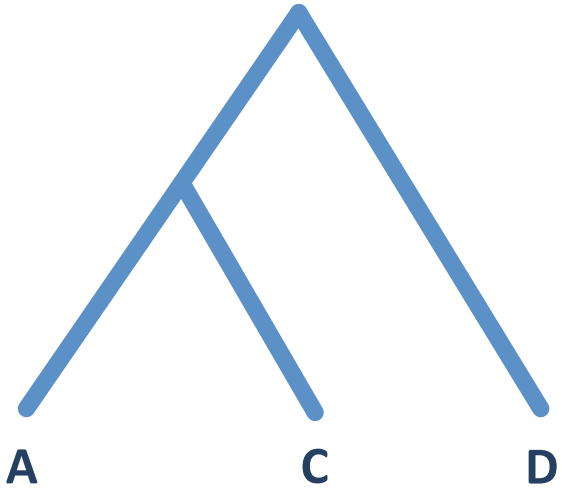


ST

Standard Reconciliation

- Step 1: Restrict the two trees to the same leafset
- Step 2: Map each internal node in the gene tree to MRCA in the species tree
- Step 3: Identify duplication nodes in gene tree
- Step 4: Calculate losses



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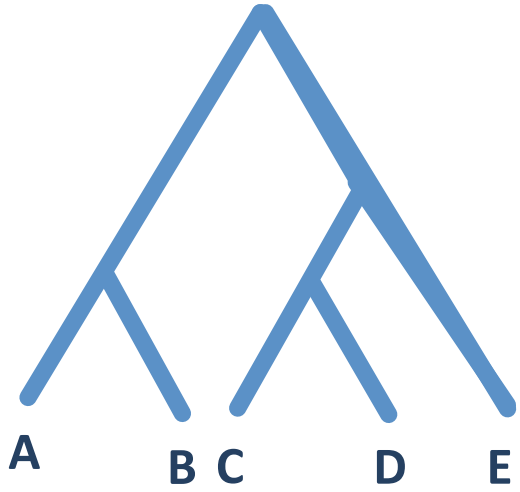

ST

Step 1: Restrict to the same leafset

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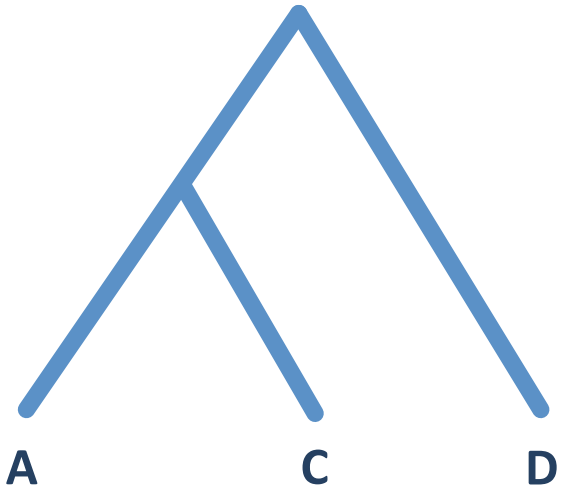
  - Given a gene tree *gt* and a species tree *ST*, *ST(gt)* is the *homeomorpic* subtree of *ST* induced by the leafset of *gt*.



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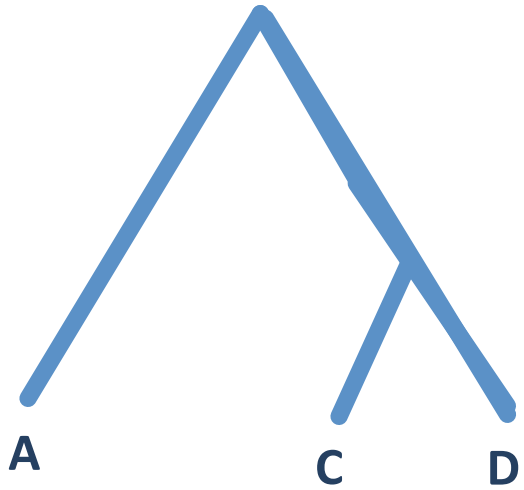
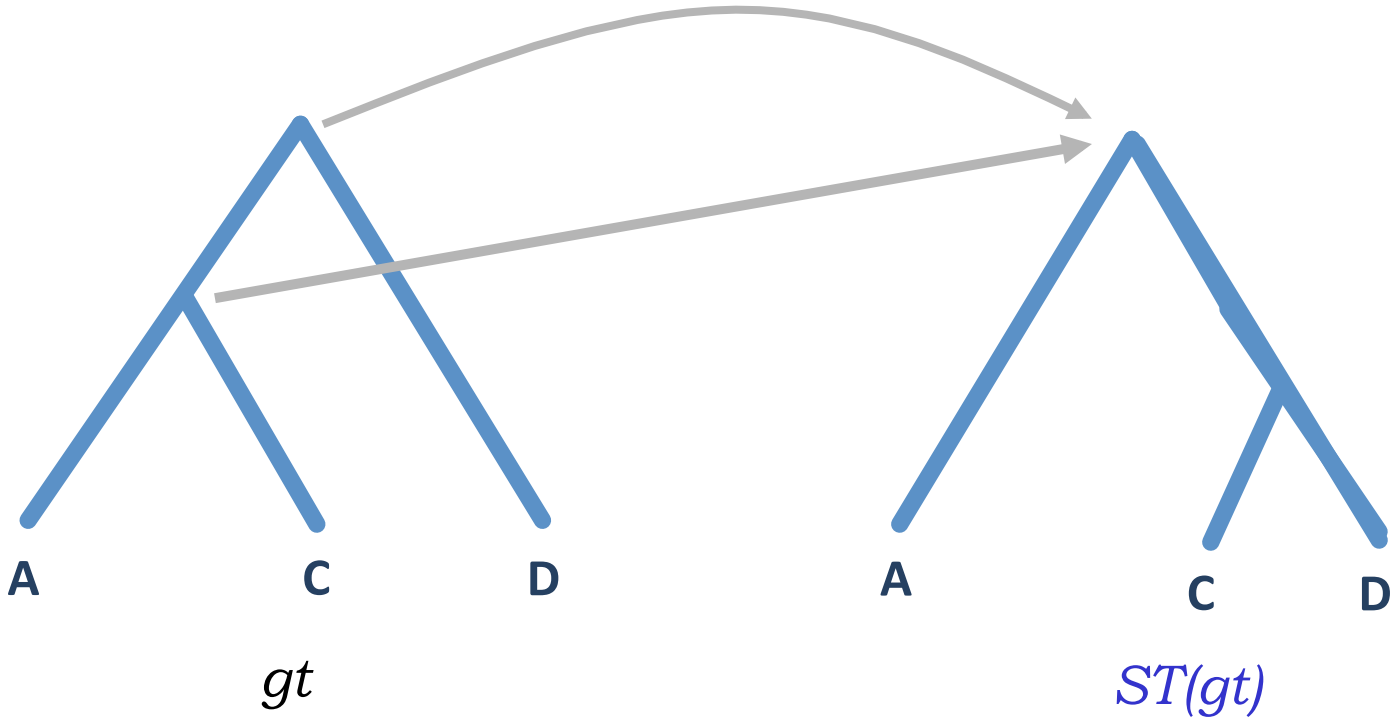


ST(gt)

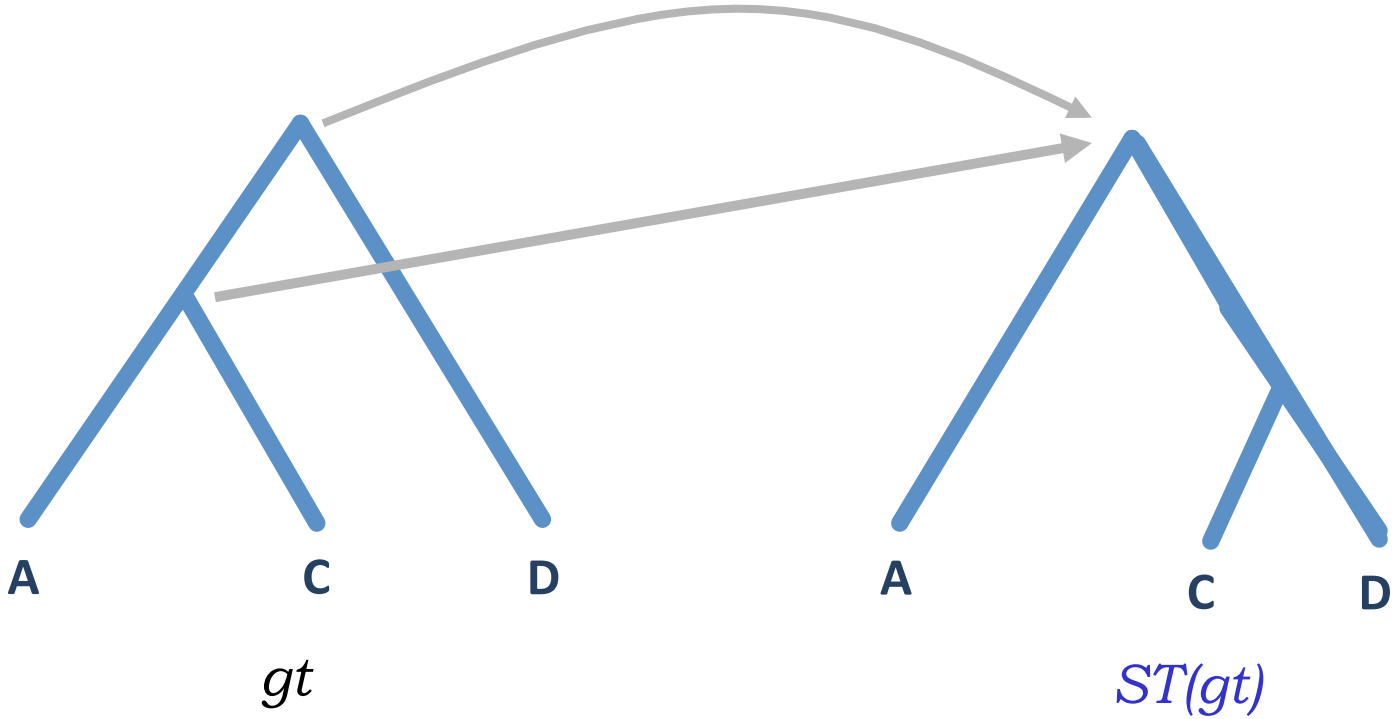
Step 2: Map nodes in gene tree to species tree

- The standard approach maps the internal nodes in gt to the nodes in ST(gt) using MRCA mapping, called “M”.



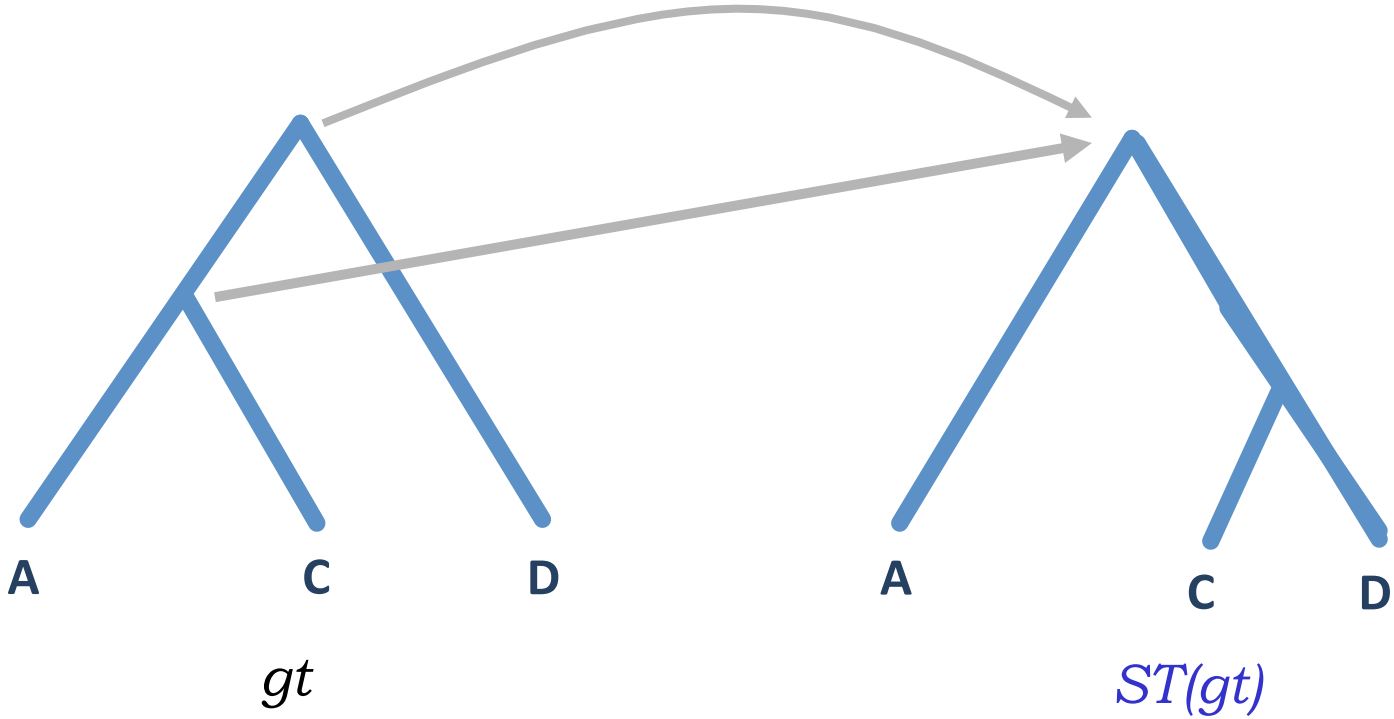
Step 3: Identify duplication nodes in gt

- Every node v in gt that has a child v' for which M(v)=M(v') is a duplication node (Guigo et al. 1996, Ma et al. 2000); all others are speciation nodes.



Step 4: Calculating losses

- Losses are associated to nodes in the gene tree.
- Each node u has two children l (left) and r (right)
- Calculation of losses depends on MRCA mapping of u, l, r



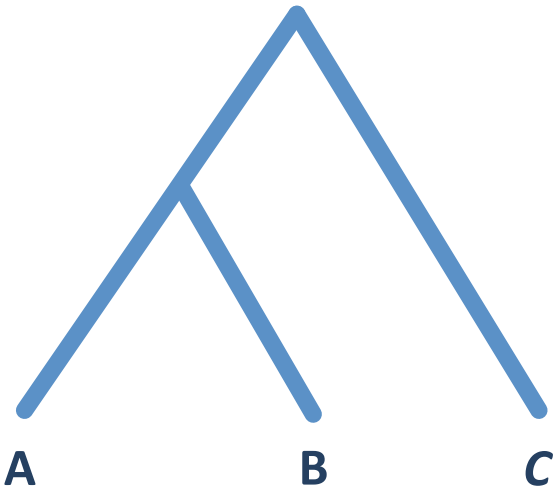
Step 4: Standard technique for calculating losses

- Let d(x,y) denote the number of vertices in the path between x and y. Then (by Ma et al. 2000, Gorecki 2004),

$$F(u,T) = \begin{cases} d(\mathcal{M}(r),\mathcal{M}(u)) + 1 & \text{if } \mathcal{M}(r) \neq \mathcal{M}(u) \ \& \ \mathcal{M}(l) = \mathcal{M}(u), \\ d(\mathcal{M}(l),\mathcal{M}(u)) + 1 & \text{if } \mathcal{M}(l) \neq \mathcal{M}(u) \ \& \ \mathcal{M}(r) = \mathcal{M}(u), \\ d(\mathcal{M}(r),\mathcal{M}(u)) & \\ +d(\mathcal{M}(l),\mathcal{M}(u)) & \text{if } \mathcal{M}(r) \neq \mathcal{M}(u) \ \& \ \mathcal{M}(l) \neq \mathcal{M}(u), \\ 0 & \text{if } \mathcal{M}(r) = \mathcal{M}(l) = \mathcal{M}(u). \end{cases}$$

$$L_{std}(gt, ST) = \sum_{u \in V_{int}(gt)} F(u, ST(gt))$$

What would the reconciliation cost be?



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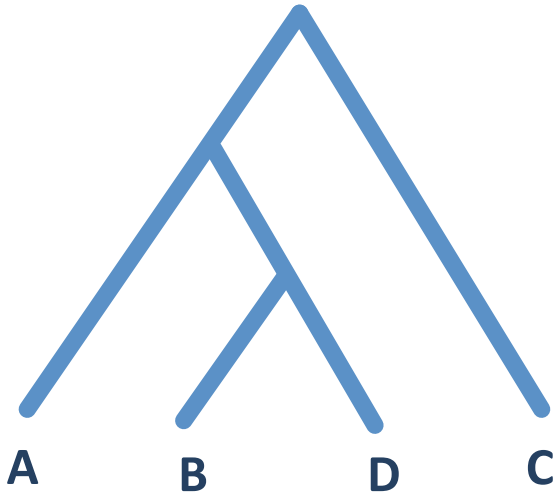
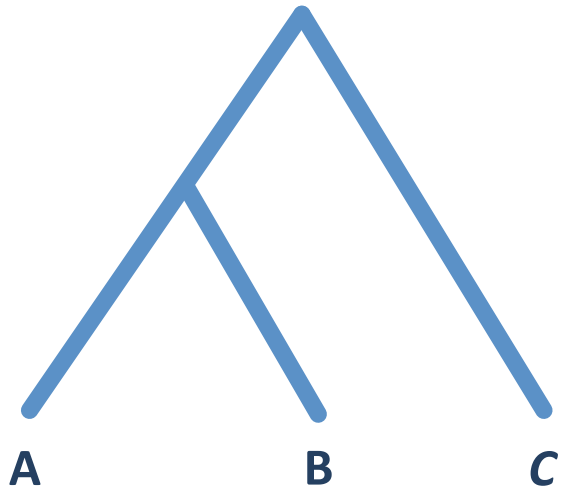


ST

Answer using standard formula: 0 losses!

- Standard formula by calculating the homeomorphic tree ST(gt) implies zero loss!



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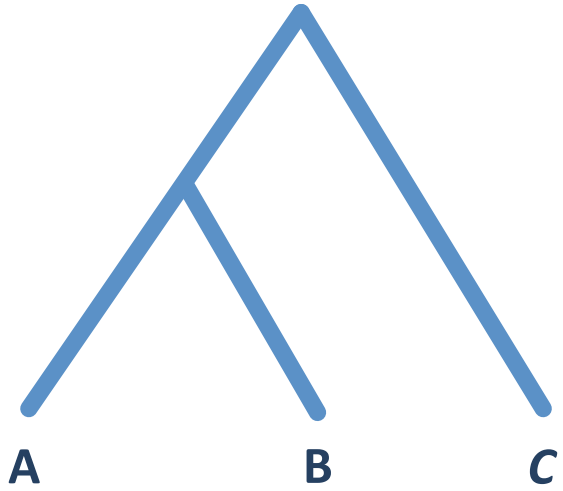
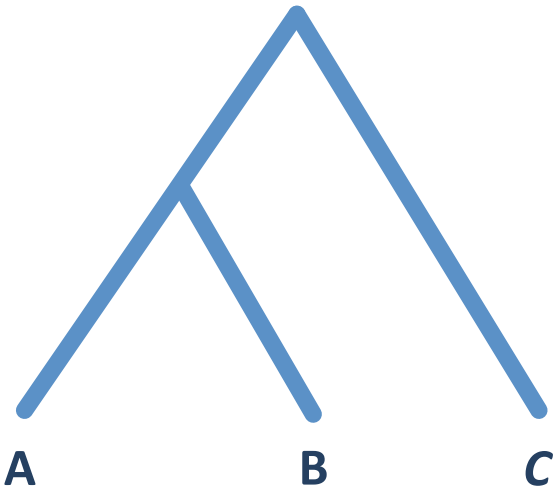


ST(gt)

Incompleteness due to sampling



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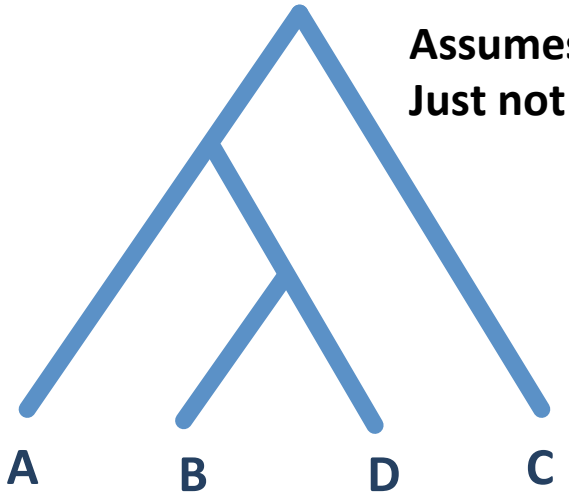


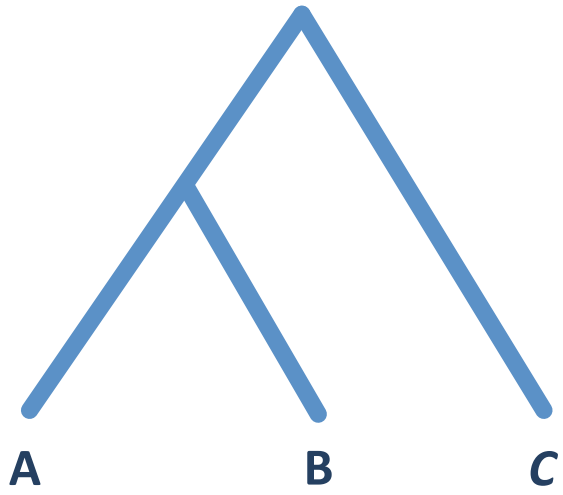
Assumes D was
Just not sampled.

ST

$L_{std}(gt, ST) = L_{samp}(gt, ST)$

▶ **Theorem 1.** *Given a binary rooted gene tree gt and a binary rooted species tree ST such that* $L(gt) \subseteq L(ST)$*, the MRCA mapping defines a reconciliation that minimizes the number of duplications, the number of losses, and hence also the total number of duplications and losses, where we treat losses as due to sampling. Furthermore,* $L_{std}(gt, ST) = L_{samp}(gt, ST)$*, which means the standard formula correctly computes the number of losses when we treat incompleteness as due to sampling.*

Incompleteness due to gene birth/death



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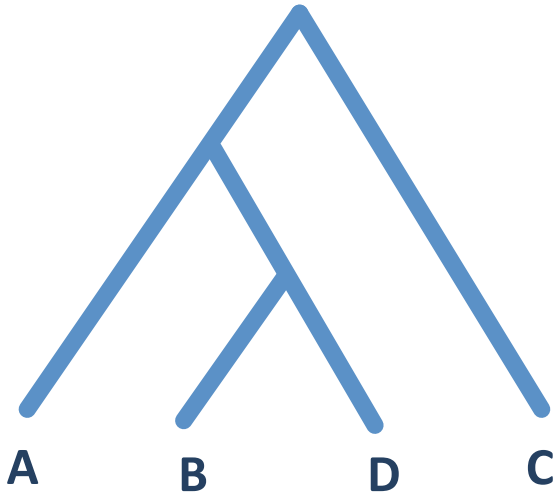
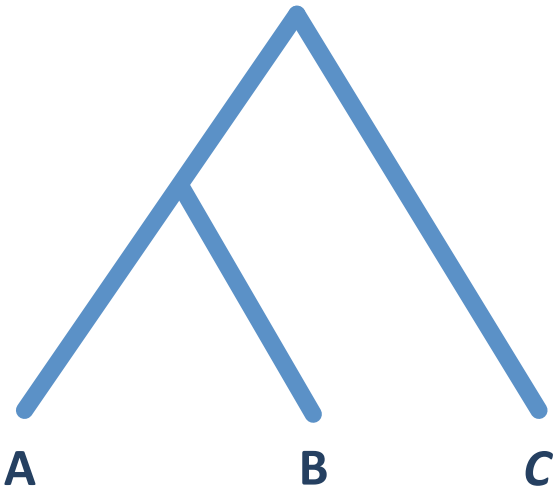


ST

What should the reconciliation cost be?



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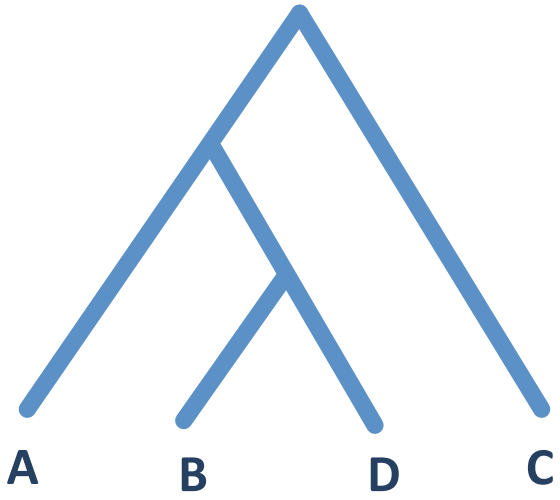

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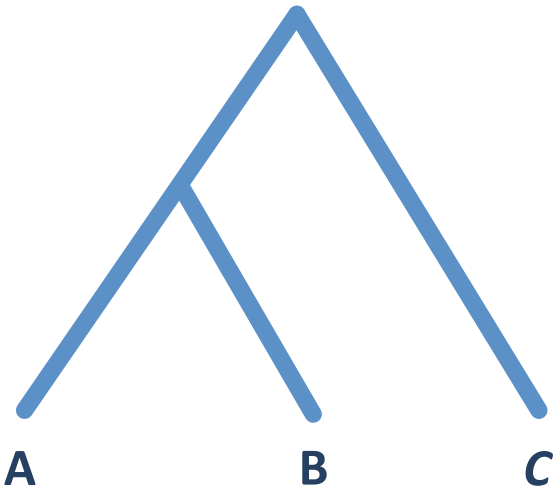

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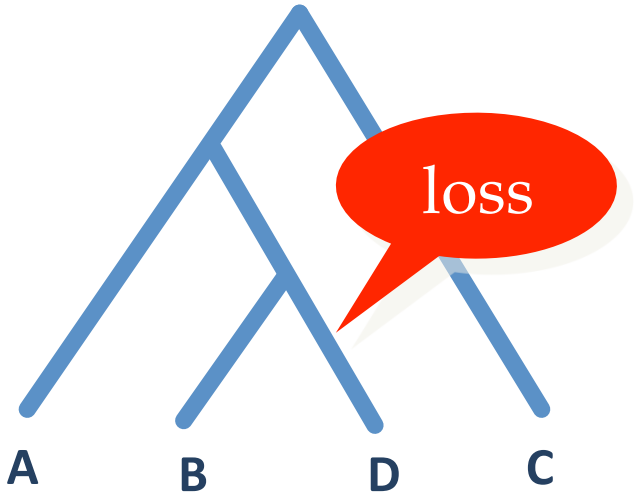
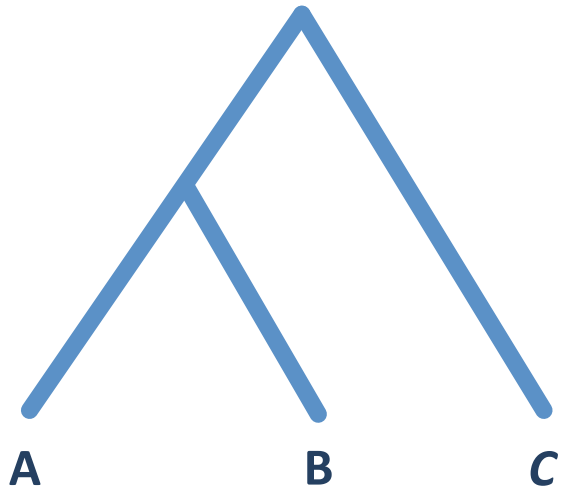


ST

What should the reconciliation cost be?

- Standard formula by calculating the homeomorphic tree ST(gt) implies zero loss!



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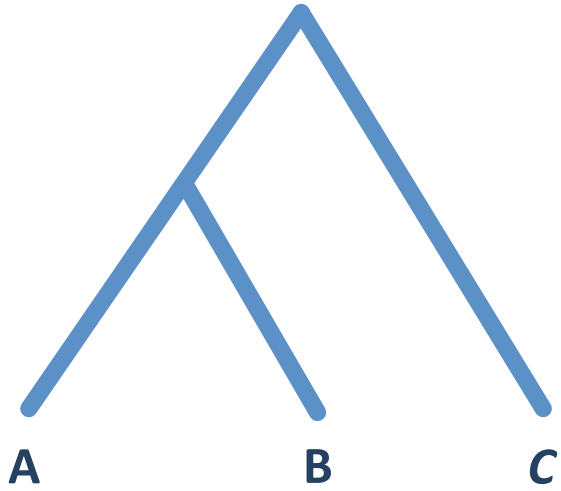

ST(gt)

Standard Formula doesn't work here

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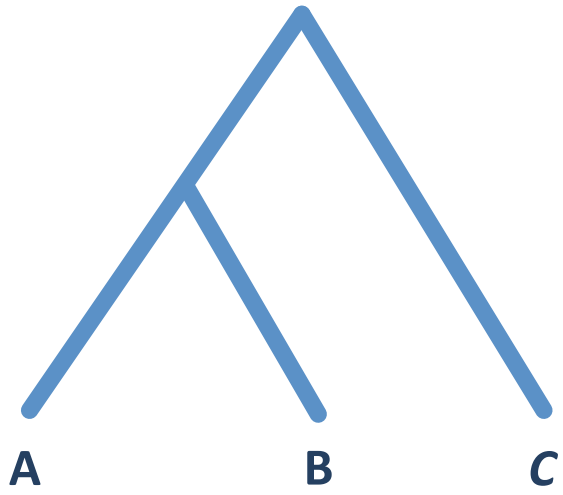

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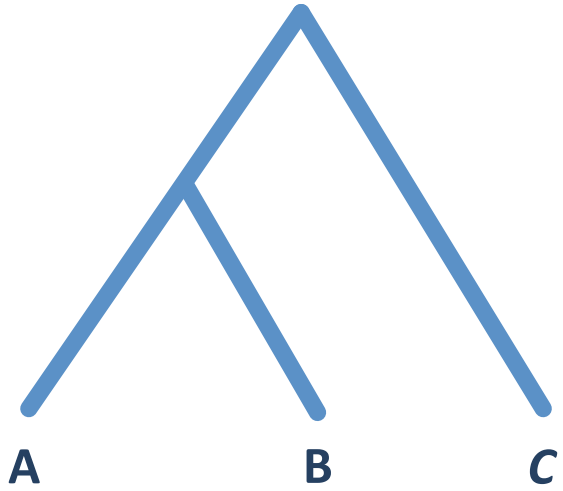
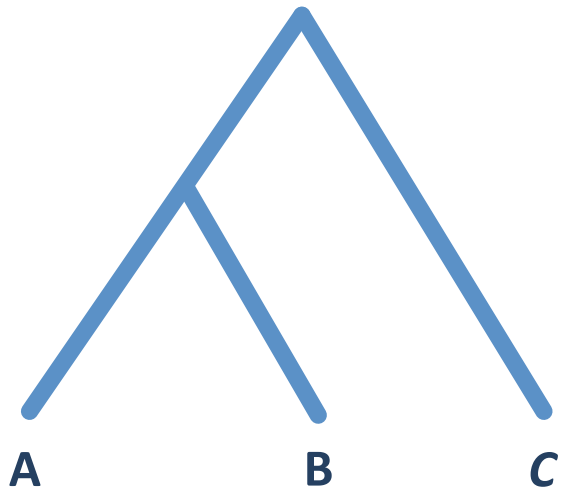


ST(gt)

Solution: Use ST instead of ST(gt)



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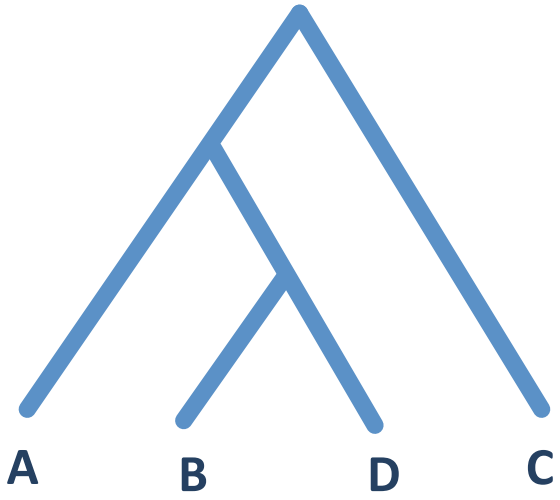
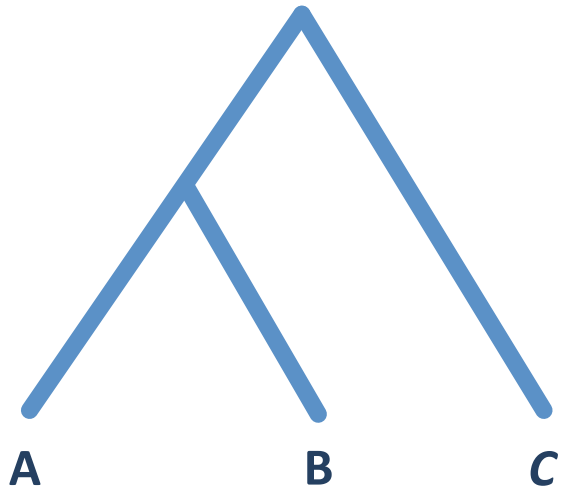


ST

Use ST instead of ST(gt) for reconciliation

No problem with calculating duplications



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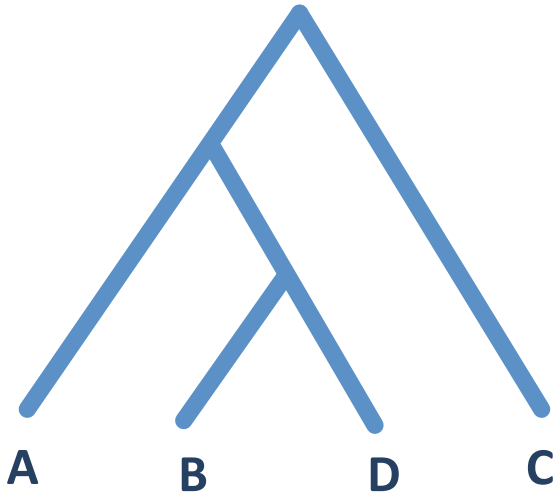
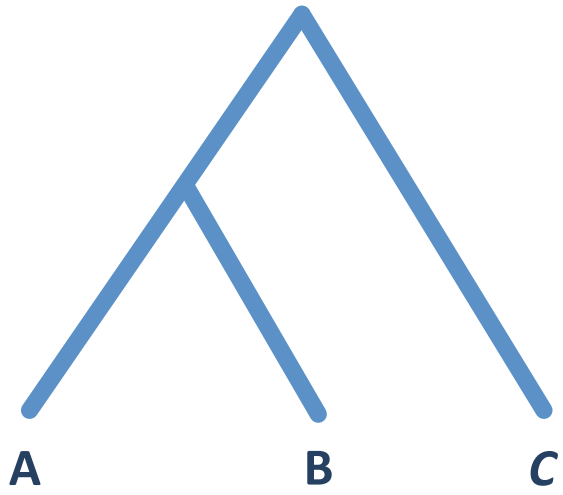


ST

Use ST instead of ST(gt) for reconciliation

No problem with calculating duplications

Standard formula for losses with ST in place of ST(gt) works



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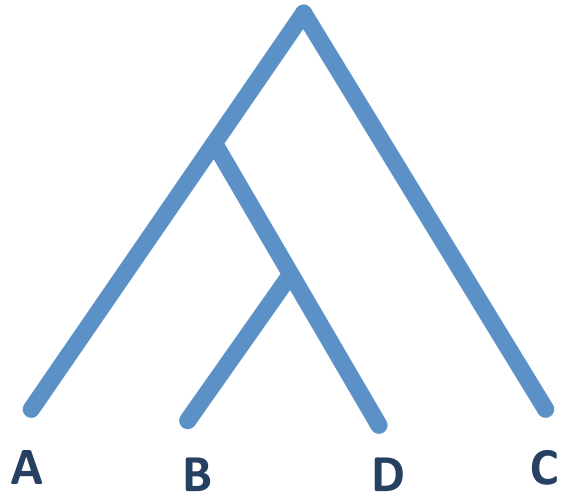
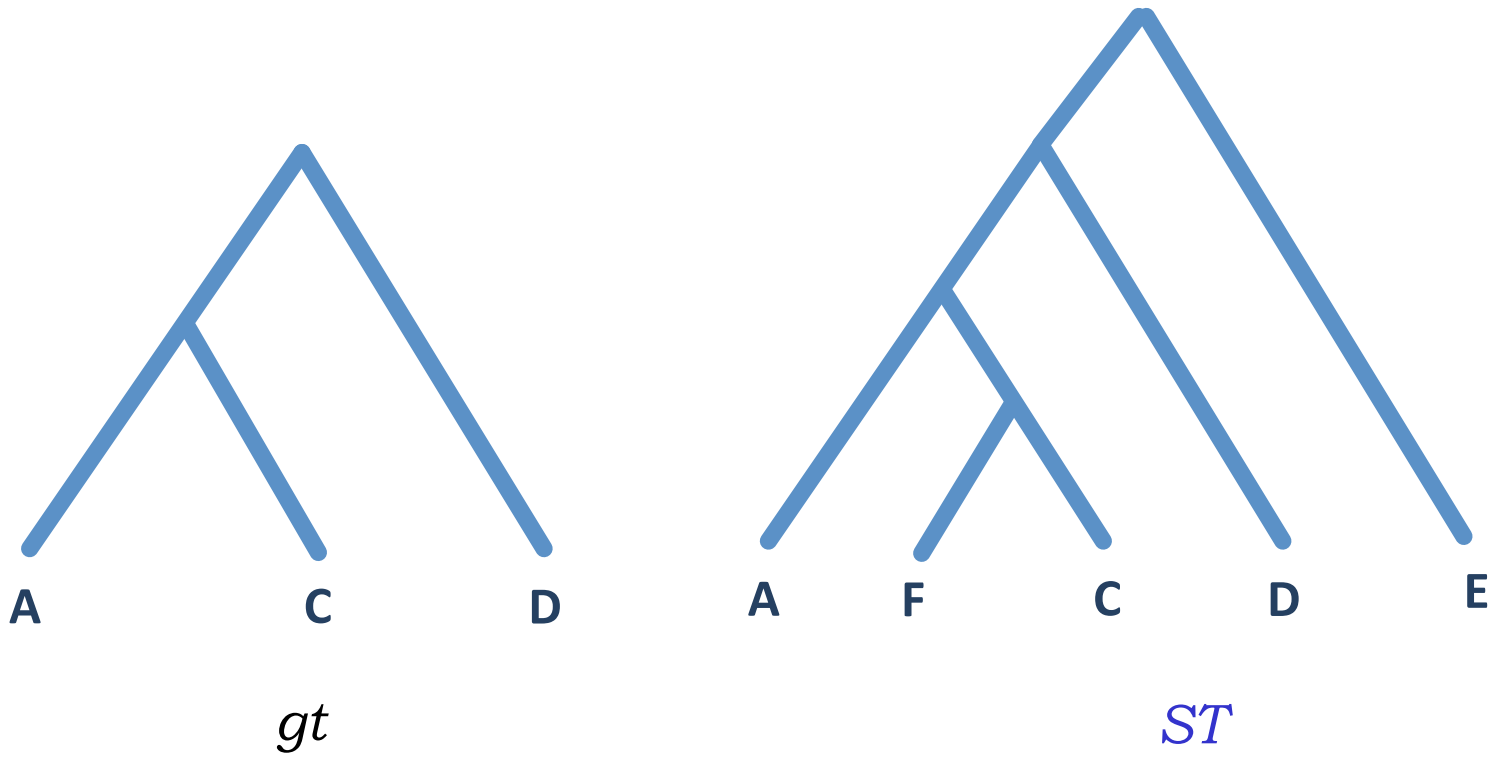


ST

Losses due to gene birth/death

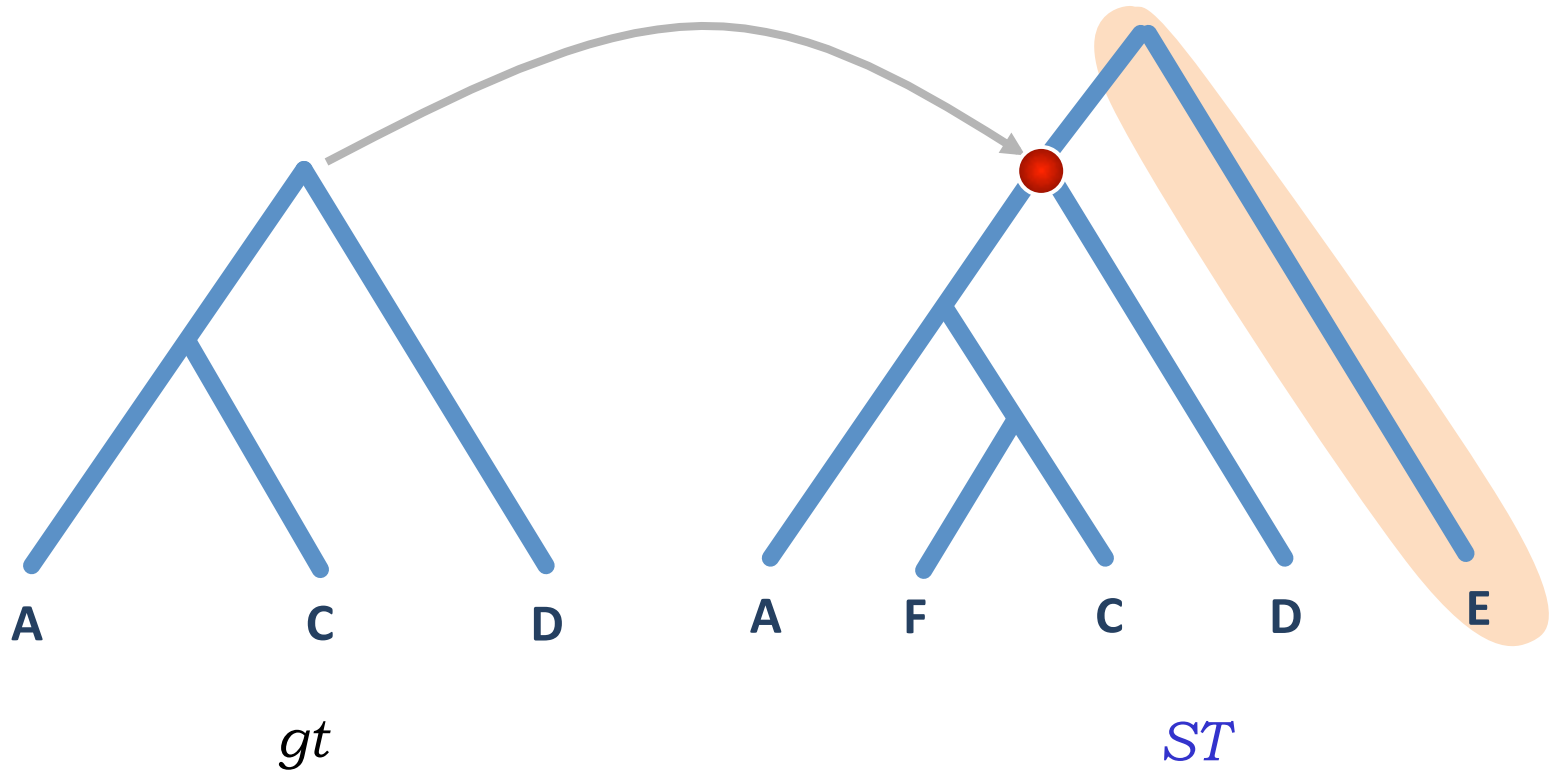
- Original species tree ST instead of the restriction ST(gt)



gt *ST*

Losses due to gene birth/death

- Original species tree ST instead of the restriction ST(gt)
  - Not enough!



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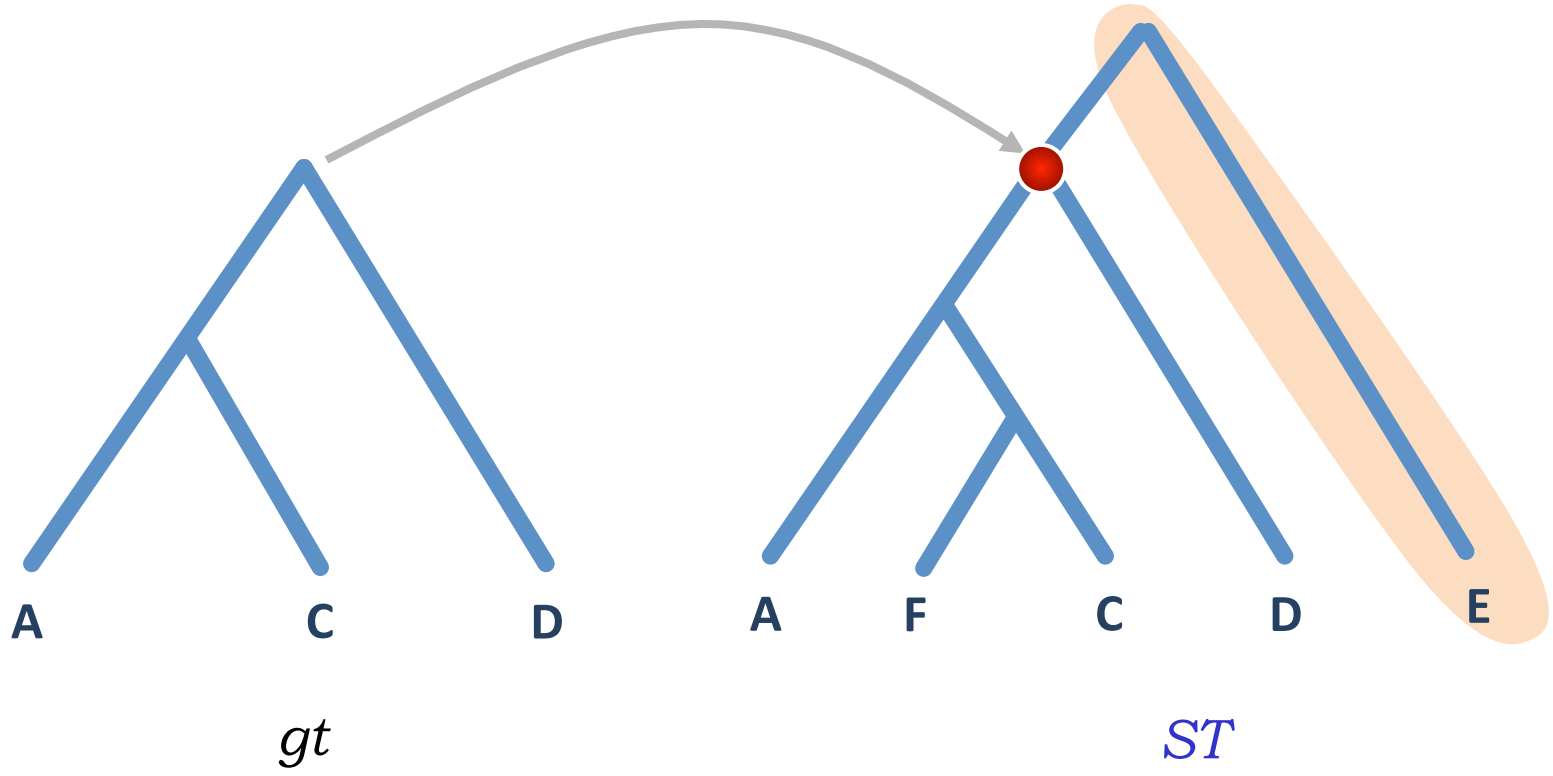
- Depends upon whether one assumes, *a priori*, that the gene is present in the root of the ST.



Losses due to gene birth/death

- Depends upon whether one assumes, *a priori*, that the gene is present in the root of the ST.
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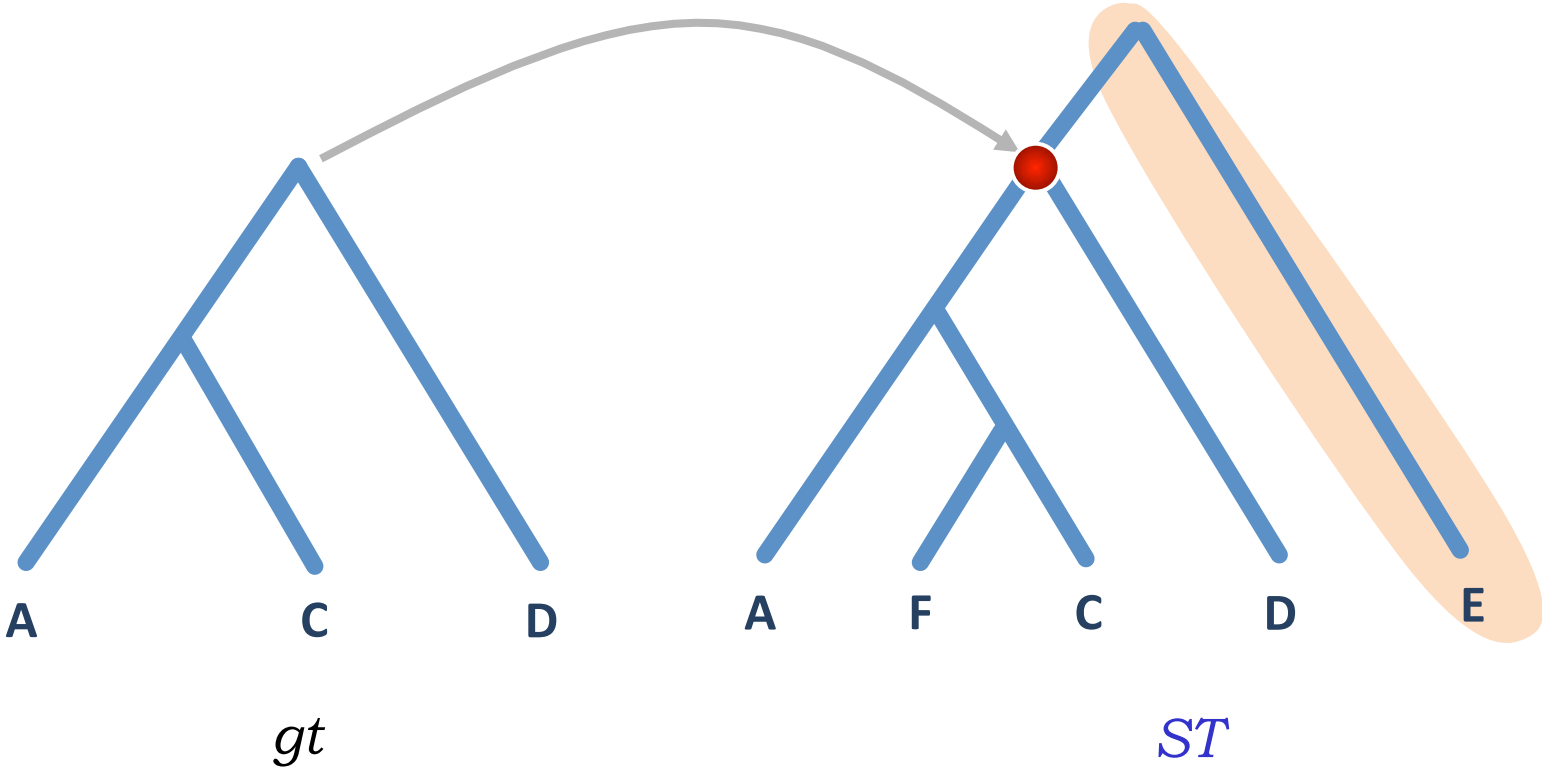
    - Need to consider the maximal clades above M(r(gt))



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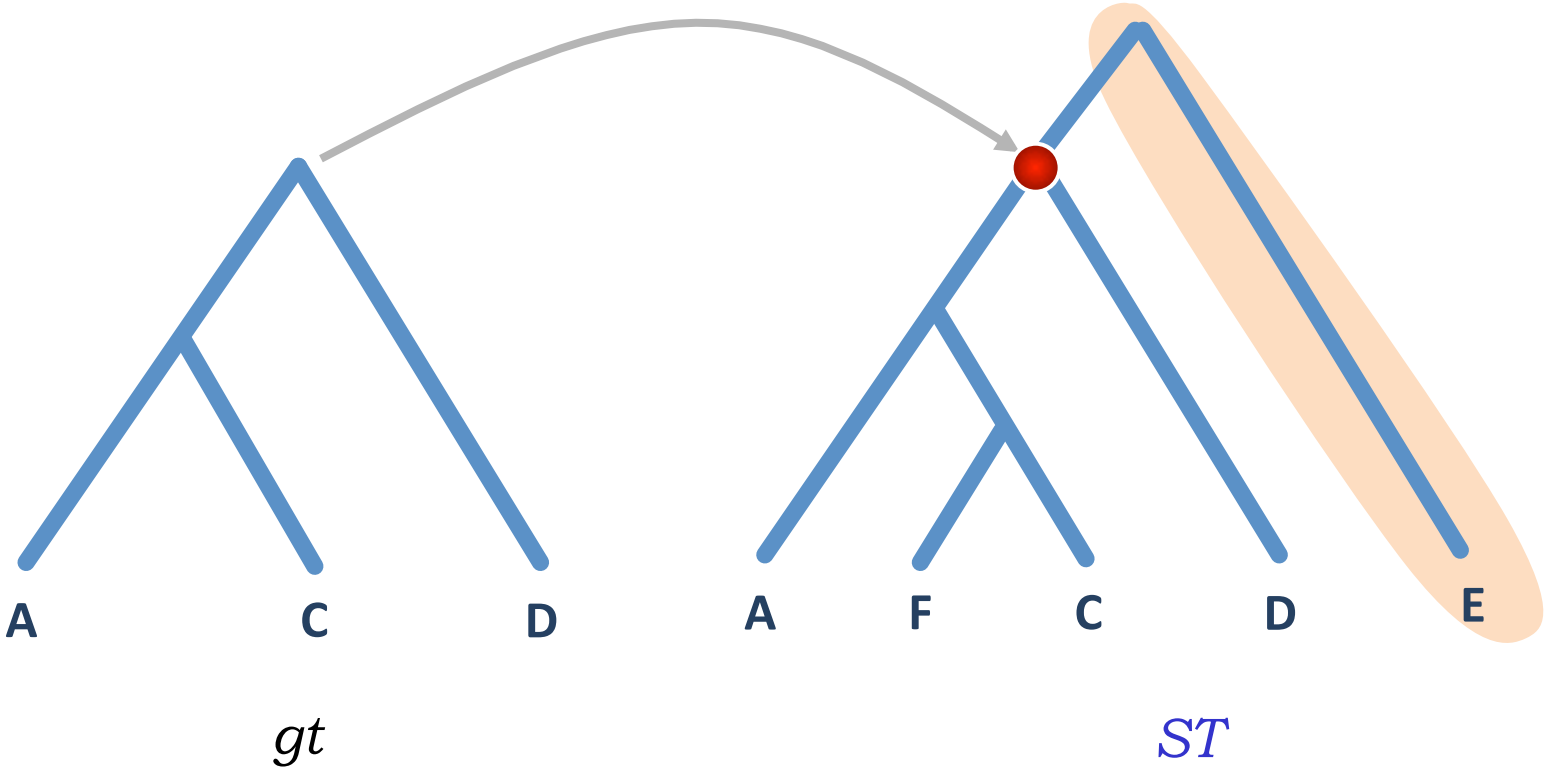

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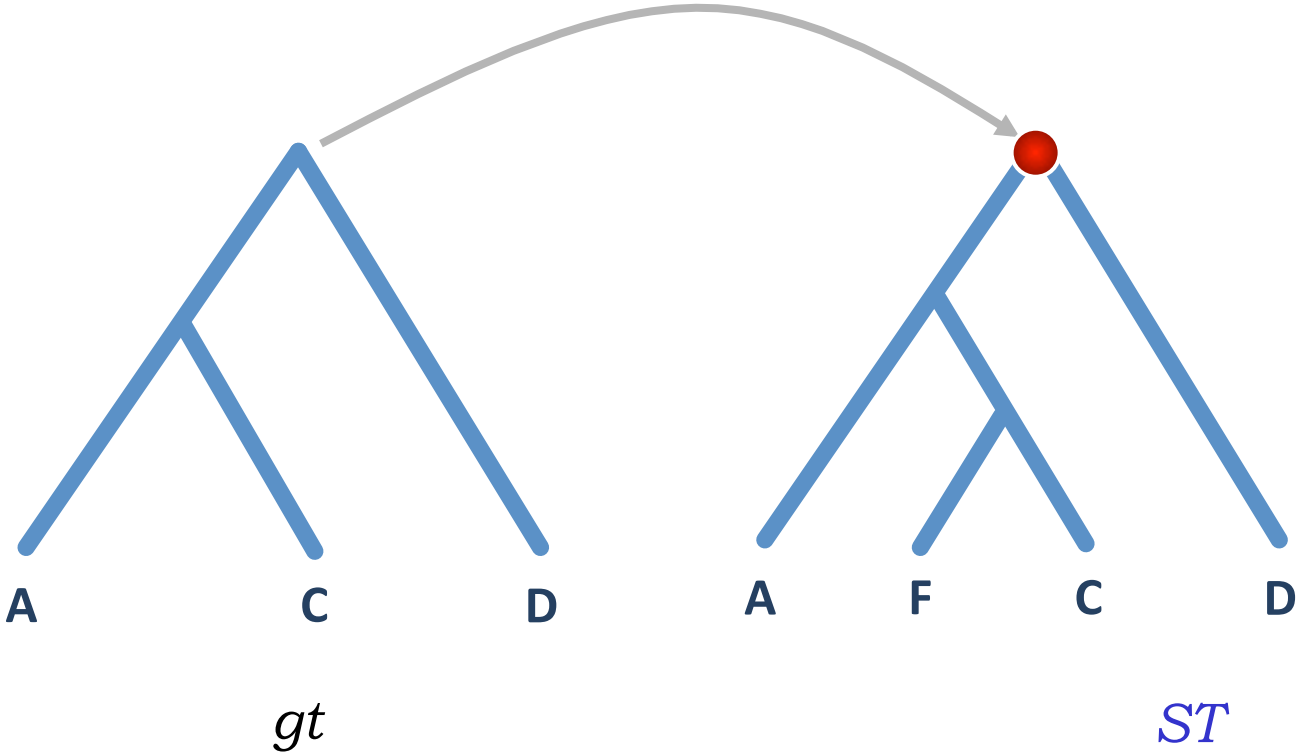

Losses due to gene birth/death

- See Theorem 2 in the paper for mathematical proofs!

Species tree estimation

Input: Set of rooted binary gene trees, and costs for duplication and losses

Output: Rooted binary species tree ST, minimizing the total (weighted) duplication-loss cost (treating incompleteness as true biological loss)

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NP-hard! (also NP-hard if you treat incompleteness as due to sampling)

Species tree estimation

- **Our approach:** We extend the technique from Bayzid, Mirarab, and Warnow PSB 2011, which found optimal species trees for weighted duploss problem, treating incompleteness as sampling error.

Species tree estimation

Input: Set of rooted binary gene trees, and costs for duplication and losses

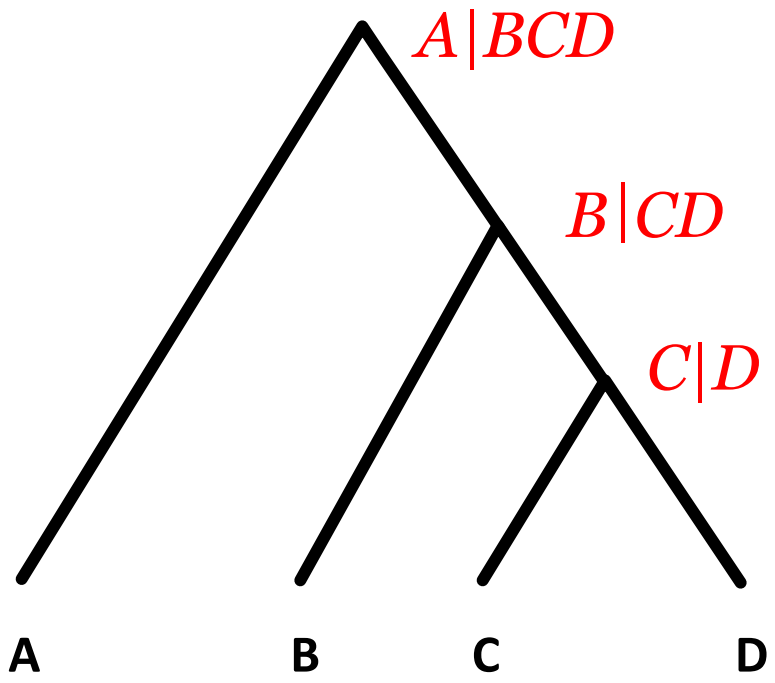
Output: Rooted binary species tree ST, minimizing the total (weighted) duplication-loss cost (treating incompleteness as true biological loss)

Constrained version:
Consider set *S* of "allowed subtree-bipartitions", and find species tree ST that draws its subtree-bipartitions from *S* and optimizes this weighted duploss score.

Terminology: Subtree-bipartition

- Subtree-bipartition
  - For an internal node u in a *binary-rooted* tree T,

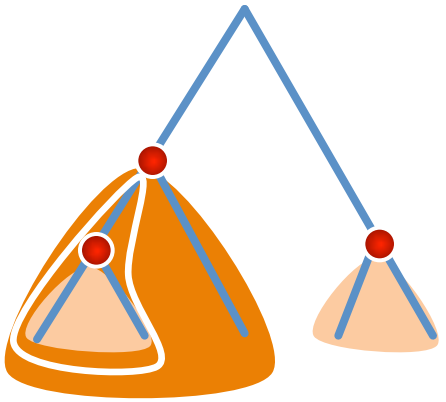
$$SBP(u) = cluster(T_L) \mid cluster(T_R)$$



Terminologies: Compatibility

- *Compatibility*
  - X|Y and P|Q are *compatible* if they can "co-exist" in a binary rooted tree.

Containment



Disjoint

Theorem: Two subtree-bipartitions are *compatible* if one *contains* the other, or they are *disjoint*

Species tree estimation

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Summary

» Investigated how different reasons for gene tree incompleteness affect the mathematical formulation of gene loss

- Sampling
- True Biological loss

» Presented mathematical formulation to model missing taxa due to true biological loss

» Proposed exact and heuristic algorithms to infer species trees from a set of incomplete gene trees by minimizing gene duplications and losses when the incompleteness is due to true biological loss

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PhD received 2016
Now at BUET (Bangladesh University of Engineering and Technology)

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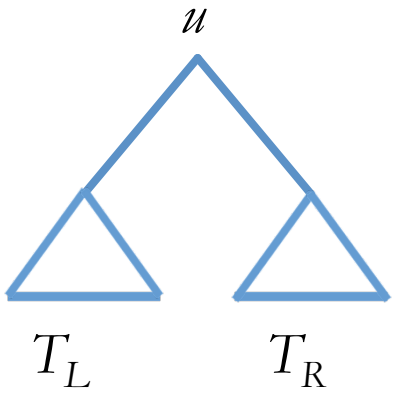
Research supported by NSF 1062335 and Fulbright Fellowship

Dynamic Programming approach

- Minimum Weight Clique problem is NP-hard!
- DP-based approach would be more efficient.



$$weight(T) = weight(T_L) + weight(T_R) + weight(u)$$

- The DP algorithm will compute a rooted, binary tree T_A for every cluster A such that T_A maximizes the sum, over all gene trees t, of the number of subtree-bipartitions in t that are dominated by some subtree-bipartition in T_A. We will denote this total number by value(A).

Dynamic Programming Contd.

weight(X|Y) = #sbp in gene trees dominated by X|Y

value(A) = weight ($a_1|a_2$); if A =$\{a_1,a_2\}$
value(A) = 0; if A =$\{a_1\}$ (base case)

value(A) = min$\{$value(A_1) + value(A-A_1) + weight($A_1|A-A_1$)$\}$;

if |A| > 2 (recursive step)

($A_1|A-A_1$)

Global Optimal Solution - if we allow any subtree-bipartition on A

Constrained version - if ($A_1|A-A_1$) has to come from set *S*

Running Time

- Depends on the number of subtree-bipartitions and number n of species.
- Let S be the set of subtree-bipartitions.
  - $O(n|S|^2)$ for finding the domination relationships (for every pair).
  - value(A) can be computed in $O(|S|)$ time, since at worst we need to look at every subtree-bipartition in S.
  - Running time is $O(n|S|^2)$.