Deciphering Reticulate Evolution Using Phylogenetic Reconciliation

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The Phylogenetic Networks Workshop
July 27, 2015

Supertrees or Supernetworks?

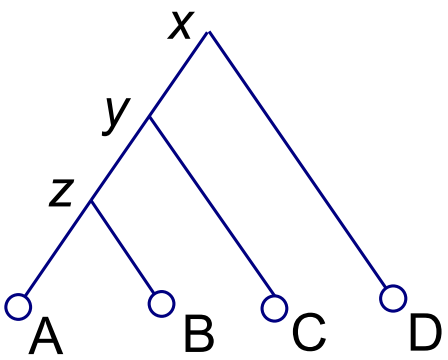
Gene Family Evolution

Problem

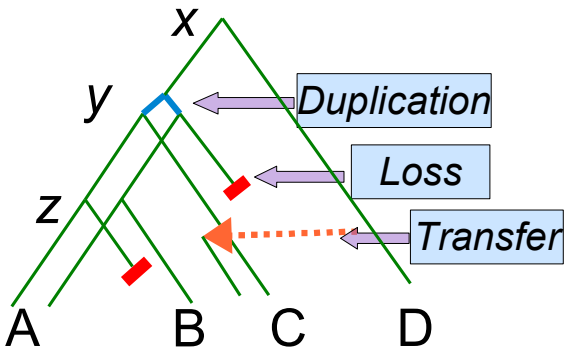
How did any given gene family evolve?

- Gene families evolve inside species trees.
- Affected by evolutionary events such as gene duplication, horizontal gene transfer, and gene loss.

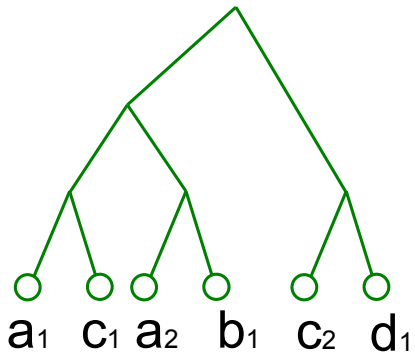
Species Tree *S*



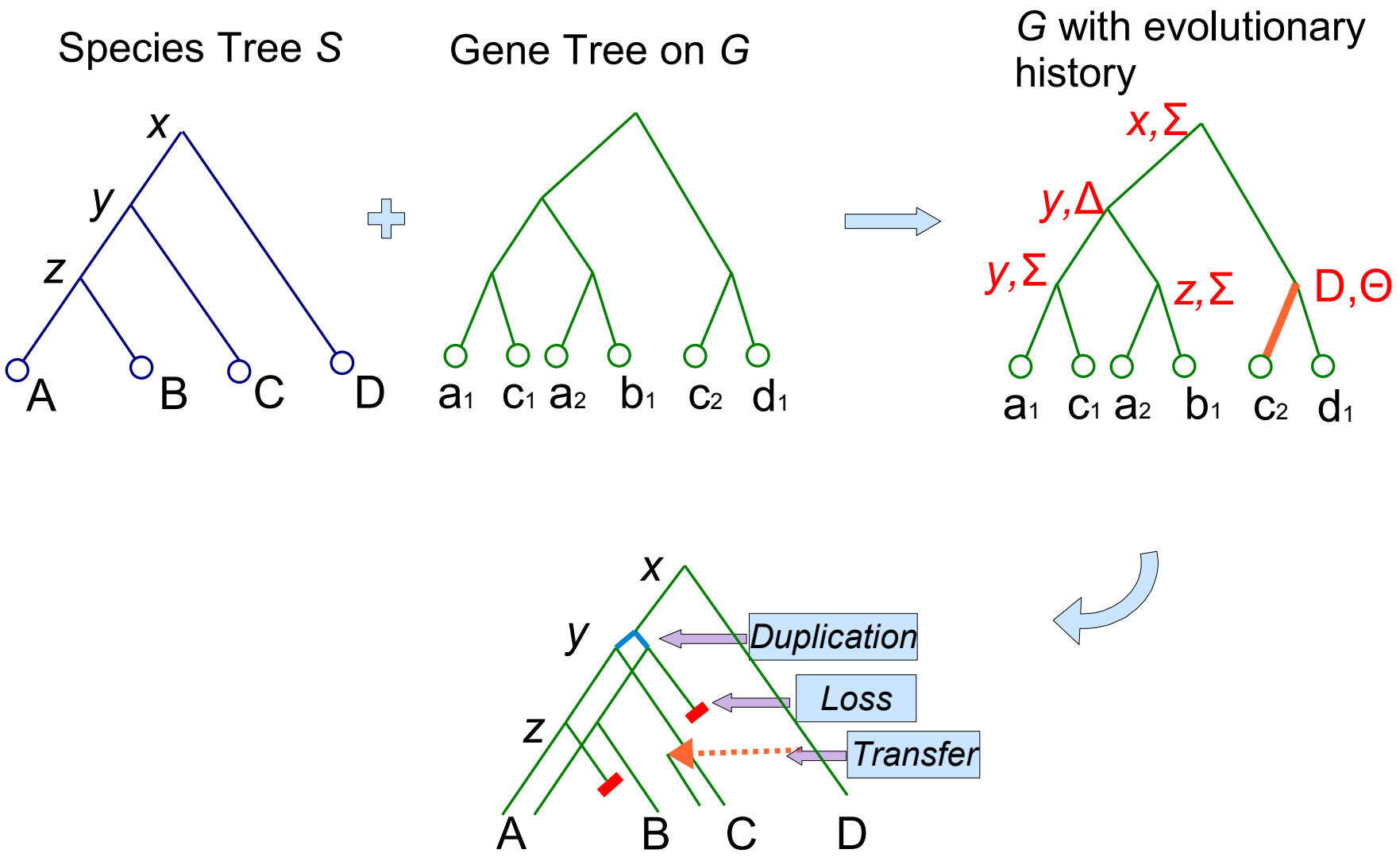
Evolution of Gene Family *G*



Gene Tree on *G*



Definition: DTL Reconciliation



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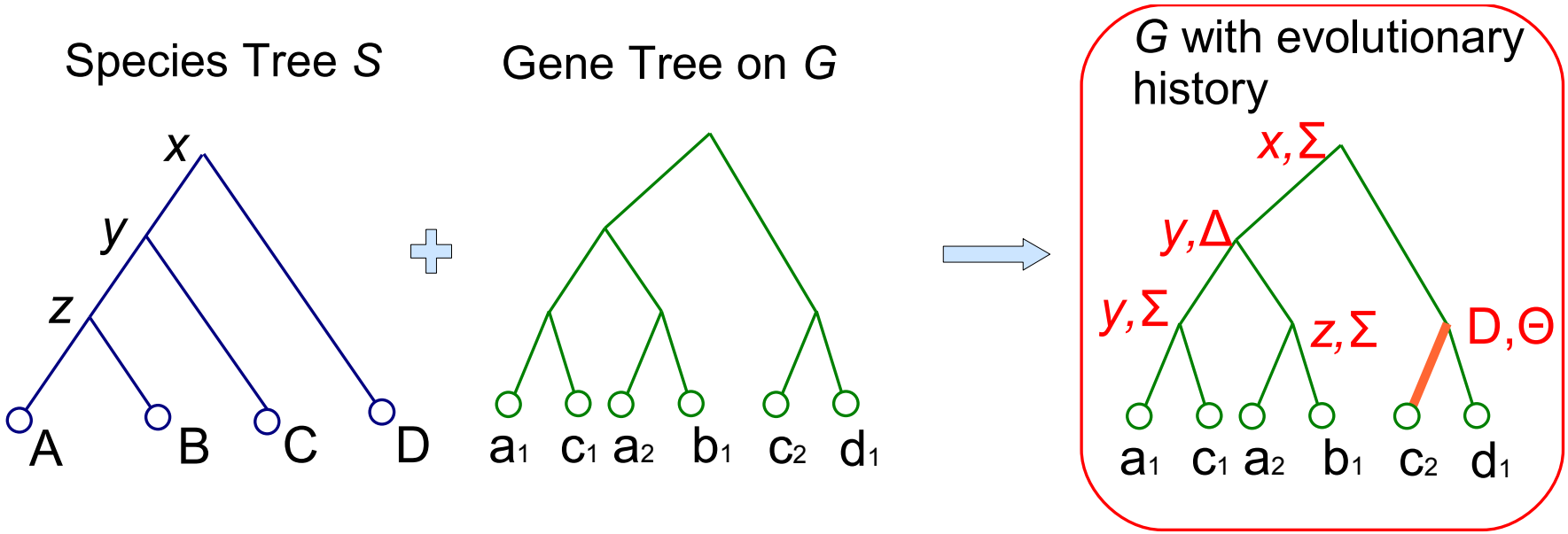


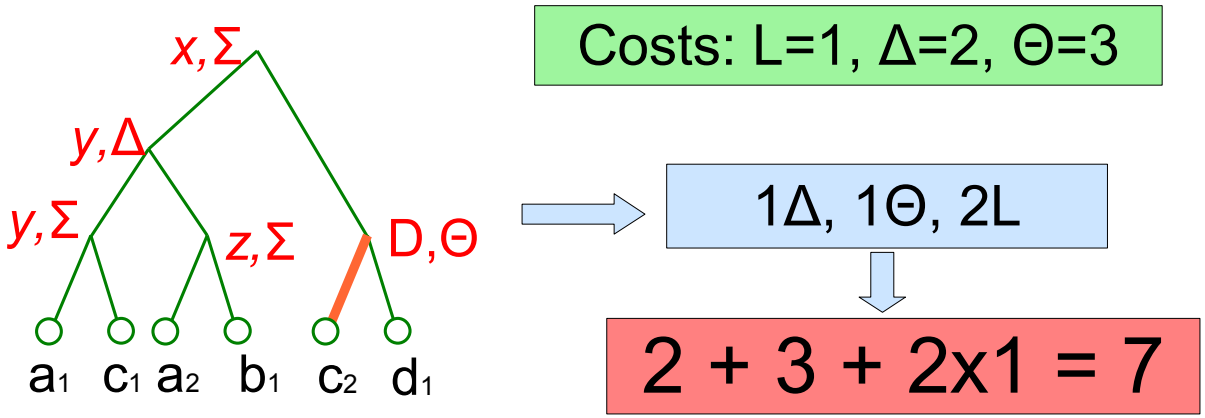
Input: A gene tree for that gene family, and a trusted rooted species tree.

Output: An evolutionary history of that gene family showing horizontal gene transfers, gene duplications, losses, and speciation events.

DTL Reconciliation Problem Formulation

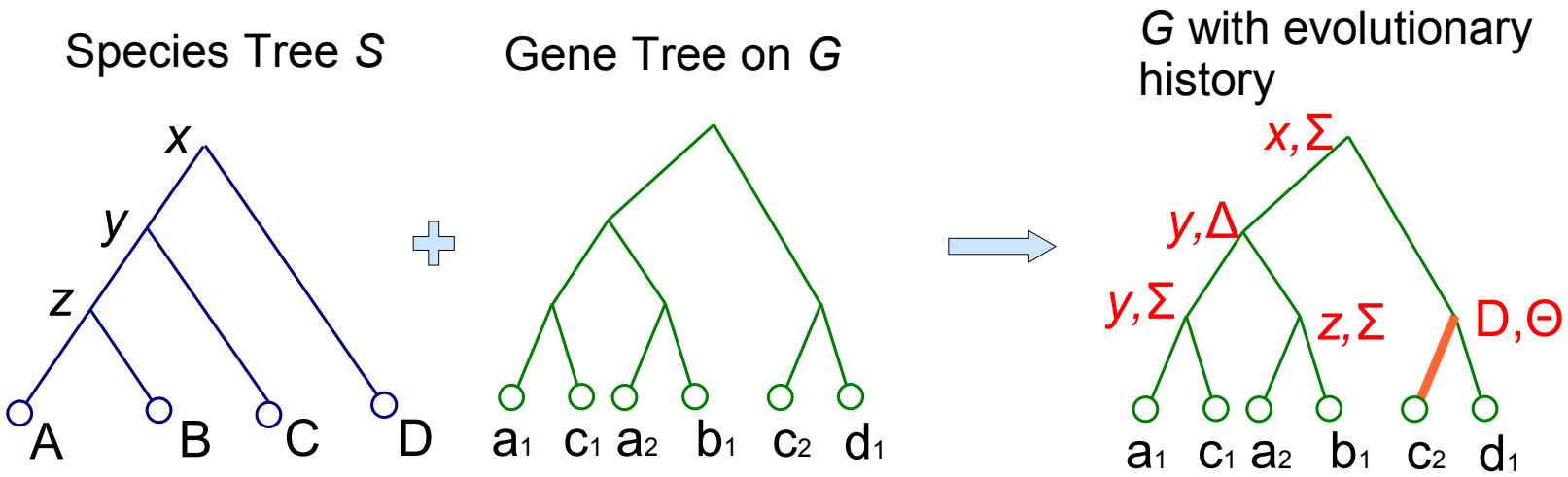
Parsimony formulation:

- Costs are assigned to duplications, transfers, and losses.
- Goal: Find the reconciliation that minimizes the total cost.
- Easy to compute cost for a given reconciliation.



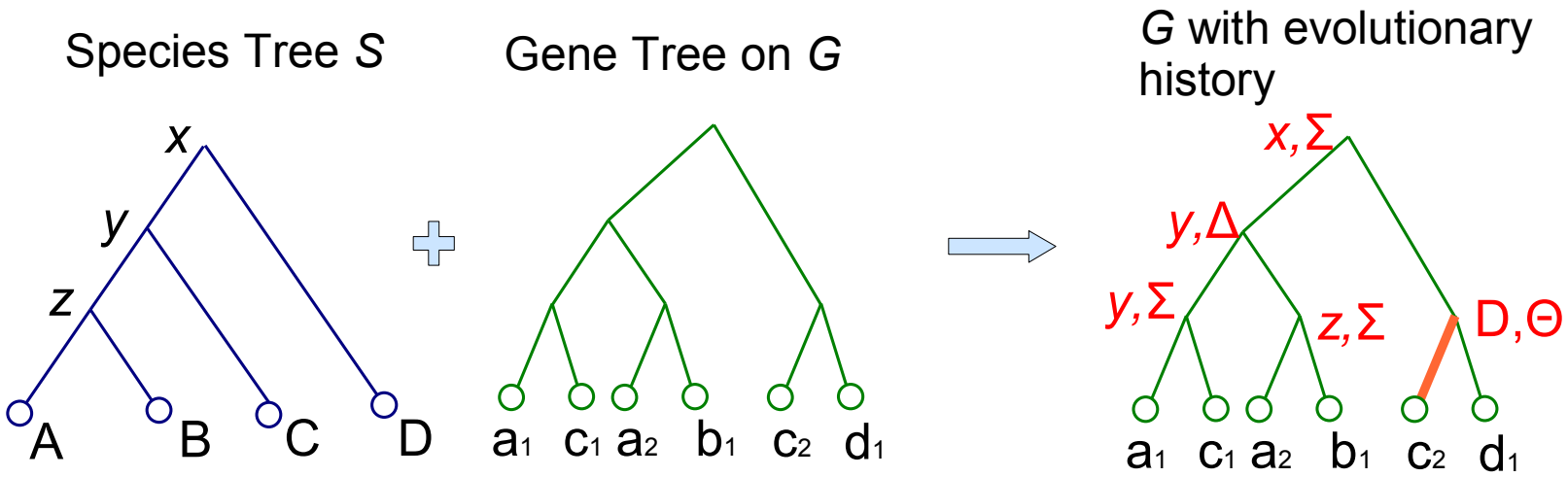
Different reconciliation could have different cost.

Applications of DTL Reconciliation



- Understanding how gene families evolve.
- Dating gene birth.
- Inferring orthologs/paralogs/xenologs.
- Gene tree error-correction.
- Whole genome species tree construction.
- Constructing species phylogenetic networks.

Applications of DTL Reconciliation



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Background: Computing Optimal DTL Reconciliations

For undated species tree:

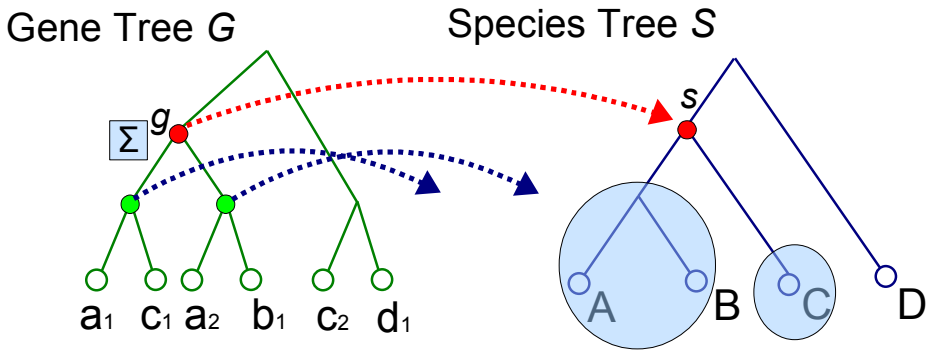
- Best time-consistent reconciliation: NP-hard (Tofigh et al., 2011; Ovadia et al., 2011)
- If time-consistency not enforced: $O(mn)$-time algorithm (Bansal et al., 2012)

For dated species trees:

- Best time-consistent reconciliation: $O(mn^2)$-time algorithm (Doyon et al., 2010)

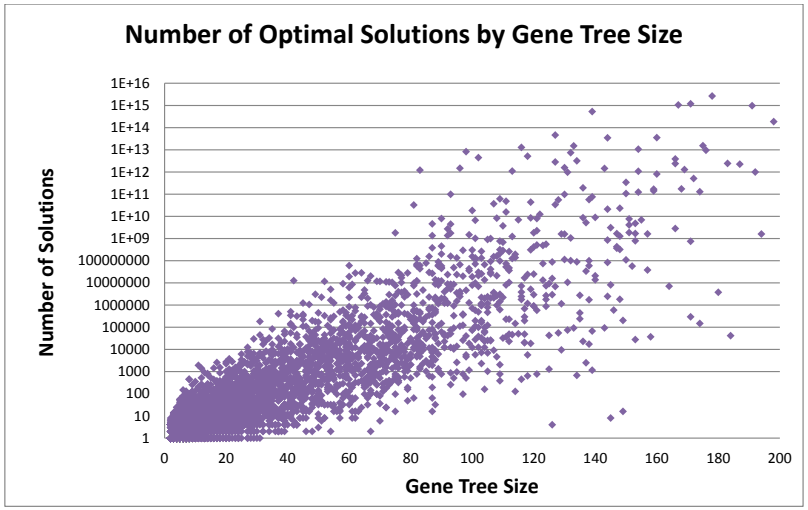
DTLI model:

- Considers ILS at unresolved species tree nodes (Stolzer et al., 2012)



Background: Handling Multiple Optima

- There can be many optimal DTL reconciliations.

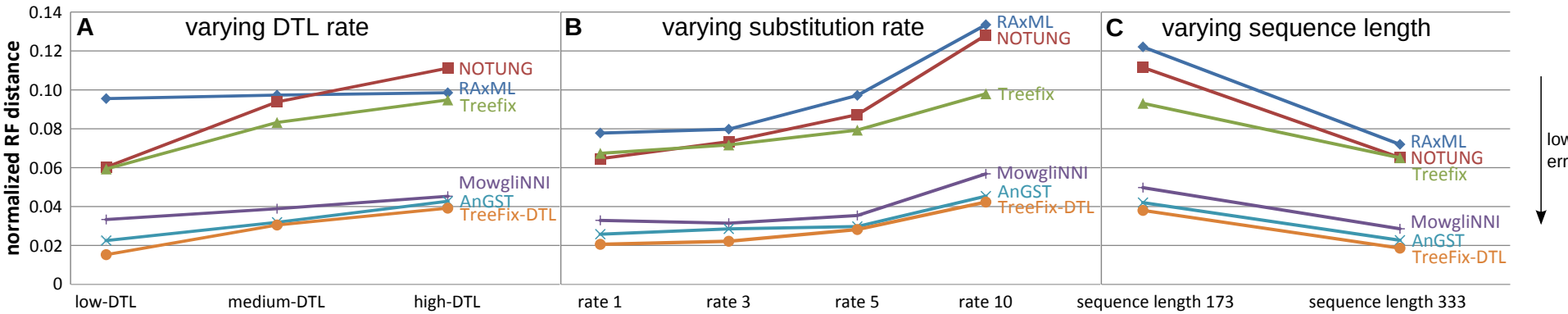


- Enumeration: Exponential in input size (Tofigh. et al., 2011; Chen et al., 2012)
- Uniform random sampling and aggregation: $O(mn^2)$-time (Bansal et al., 2013)
- Compact representation in reconciliation graph: $O(mn^3)$-time (Scornavacca et al., 2013)
- Median reconciliation (Nguyen et al., 2013)

Background: Gene Tree Error-Correction

Gene tree construction is highly error-prone. Garbage in, garbage out.

- First-attempts: Mowgli-NNI (Nguyen et al., 2012), AnGST (David and Alm, 2011)
- New methods: TreeFix-DTL (Bansal et al., 2015), ALE (szollosi et al. 2013)), TERA (Scornavacca et al., 2015))

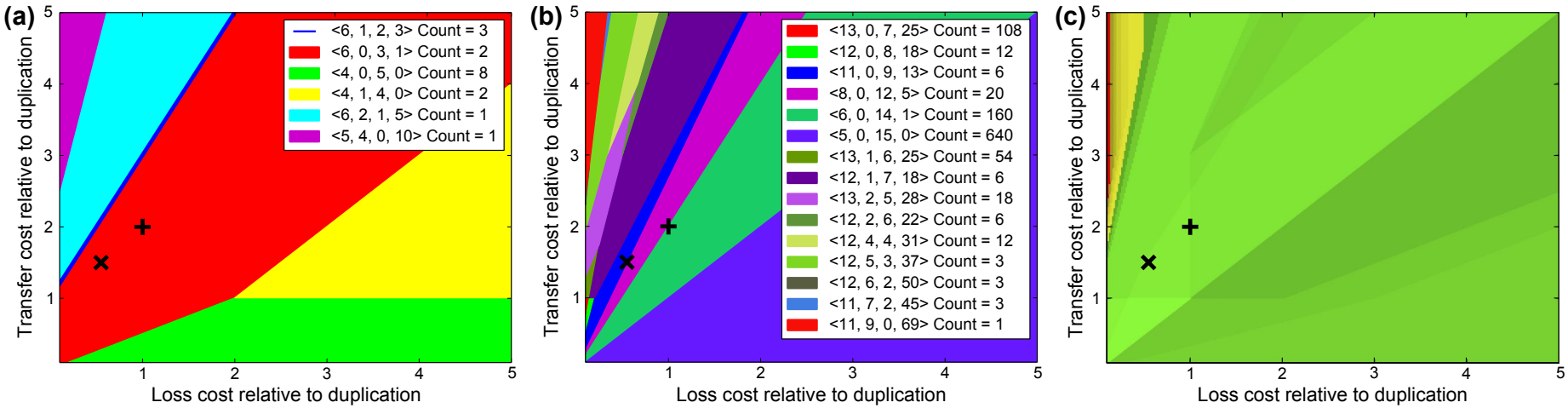


Background: Event Cost Assignment

Fundamental questions:

- What are the "best" event costs to use?
- How do reconciliations vary as we change event costs?

Algorithm to partition event cost space into equivalence regions based on pareto-optimality of event counts: $O(m^5 n \log m)$-time (Libeskind-Hadas et al., 2014)



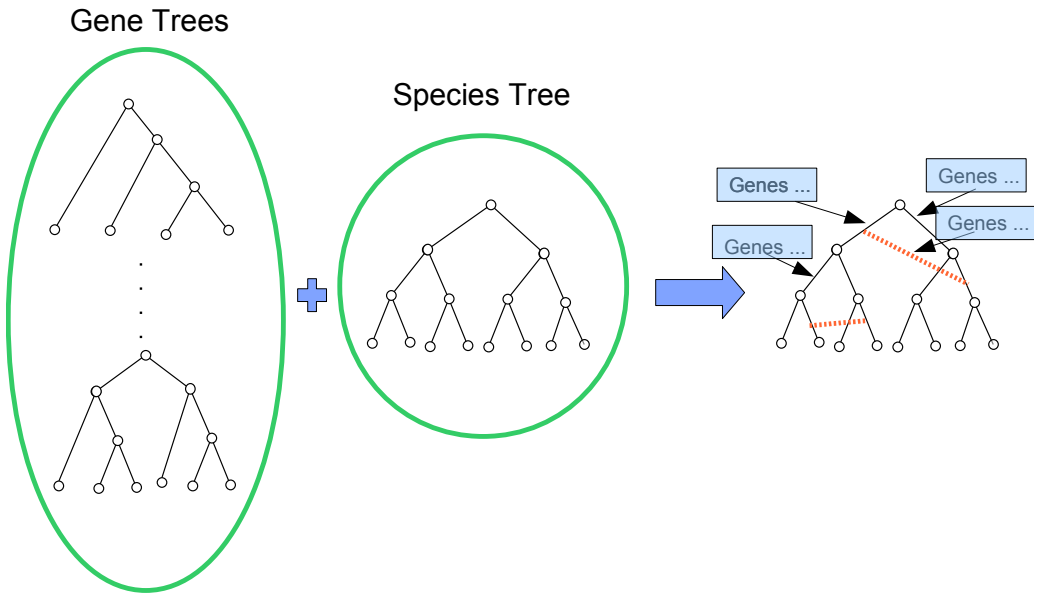
Constructing Phylogenetic Networks

- Microbial phylogenetic networks are distinct from hybridization networks.

Problem formulation

Input: A collection of gene families (sequence alignments) and a reference species tree.

Output: Species tree augmented with horizontal edges (representing transfer events), and labels for each vertical and horizontal edge specifying the genes that traveled through it.



Constructing Phylogenetic Networks

Advantages of using a reference species tree:

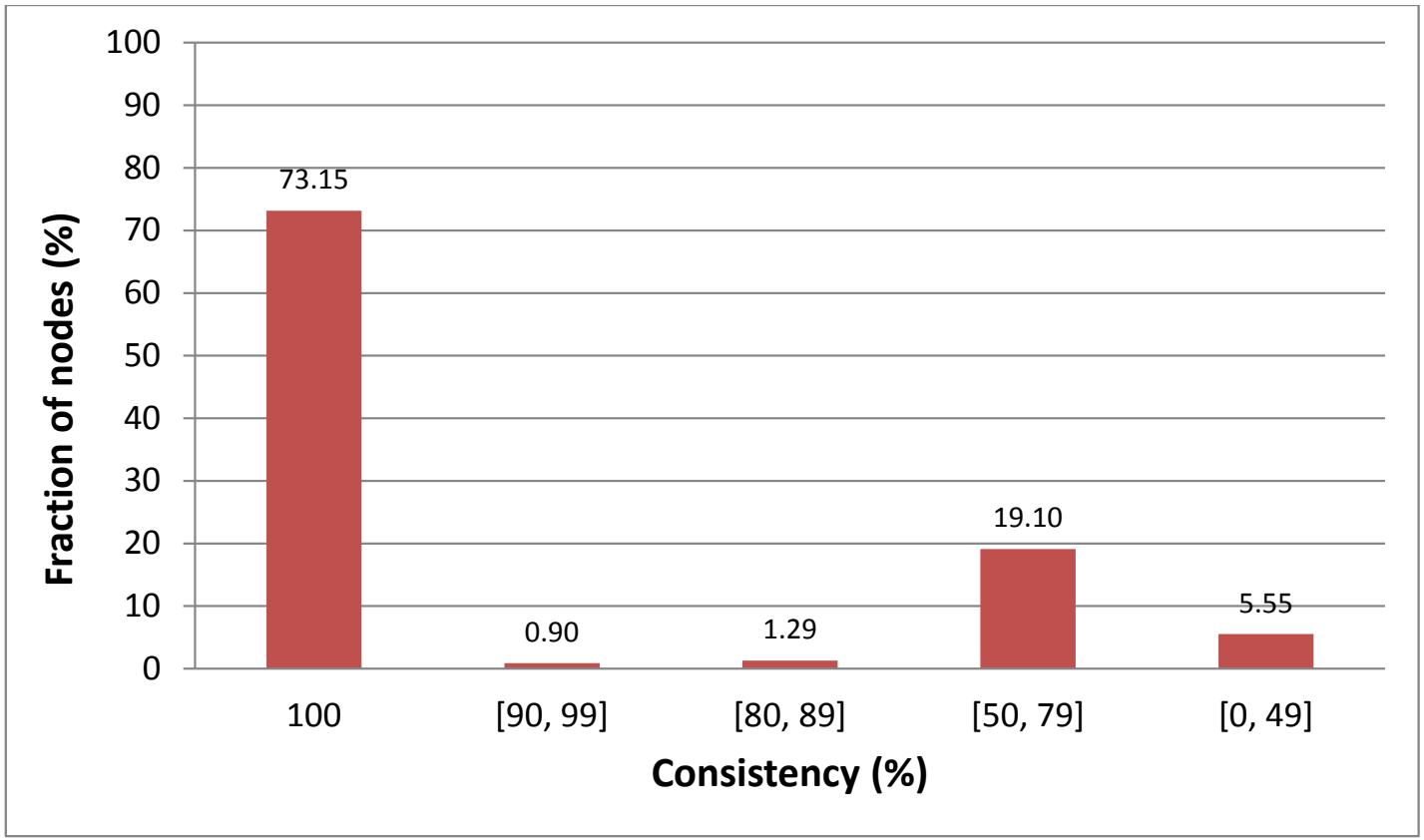
- Improved complexity and scalability.
- Inferred network does not depend on reference tree.
- Customizable and easily interpretable network view.

Basic implementation:

1. Infer gene trees.
2. Use DTL reconciliation to reconcile individual gene trees with reference tree.
3. Aggregate transfers inferred for gene trees onto species tree; e.g., NOTUNG.

Challenges due to reconciliation uncertainty

- Multiple optima, gene tree error, and event cost assignment confound reconciliation accuracy.



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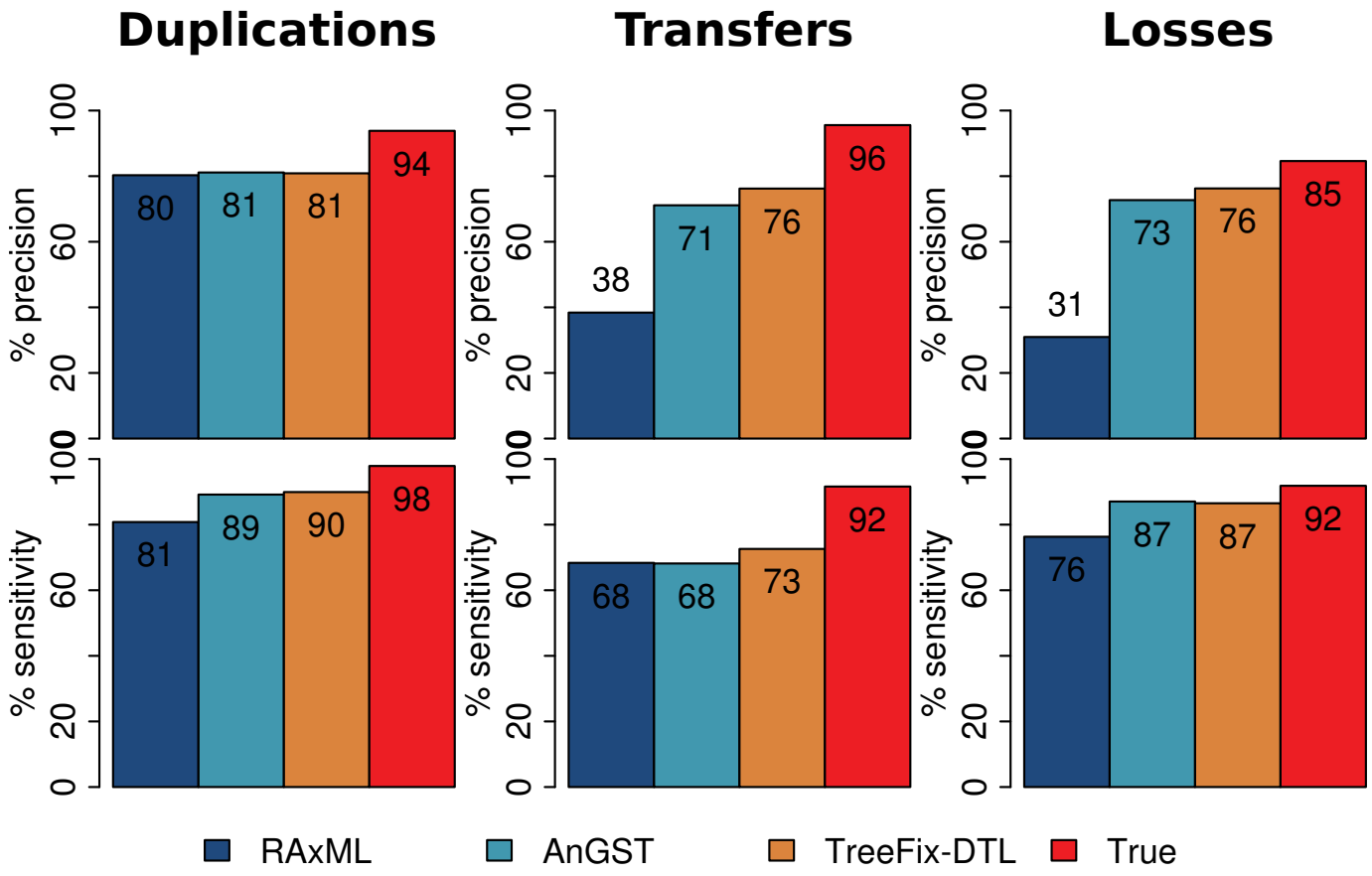


Possible Solution

Proposal: Distinguish between highly-supported and weakly-supported events across multiple optima, multiple event costs, and gene tree topologies.

- Easy to do for multiple optima and event costs based on developed algorithms.
- No such algorithms for gene tree error.

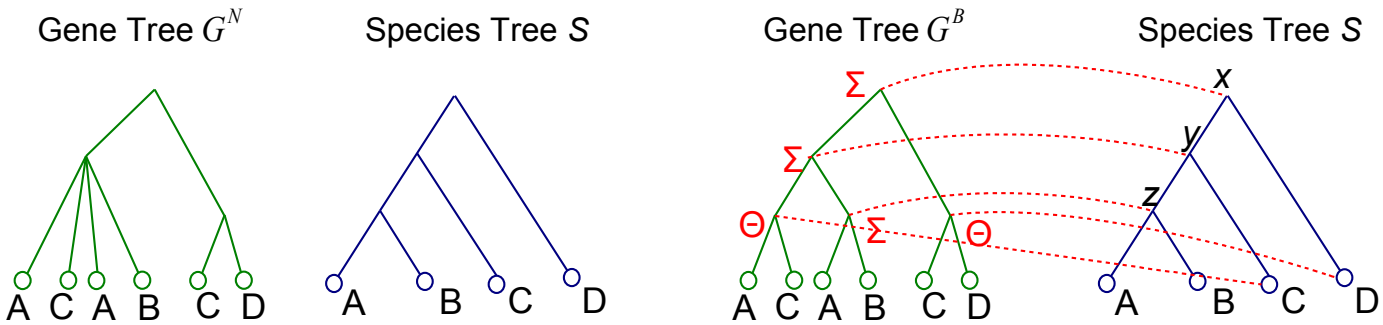
Goal: Develop algorithms to generate alternative gene tree topologies and study variability of reconciliation across them.

Optimal Gene Tree Resolution (OGTR)

Input: A non-binary gene tree G^N, a species tree S, and event costs.

Output: Find a binary resolution G^B of G^N such that, the most parsimonious DTL reconciliation of G^B and S has smallest reconciliation cost.

- Provides rigorous framework for uniformly sampling from *all* candidate gene trees.
- Non-binary gene tree obtained by collapsing weak edges.
- Fundamental question for DTL reconciliation.



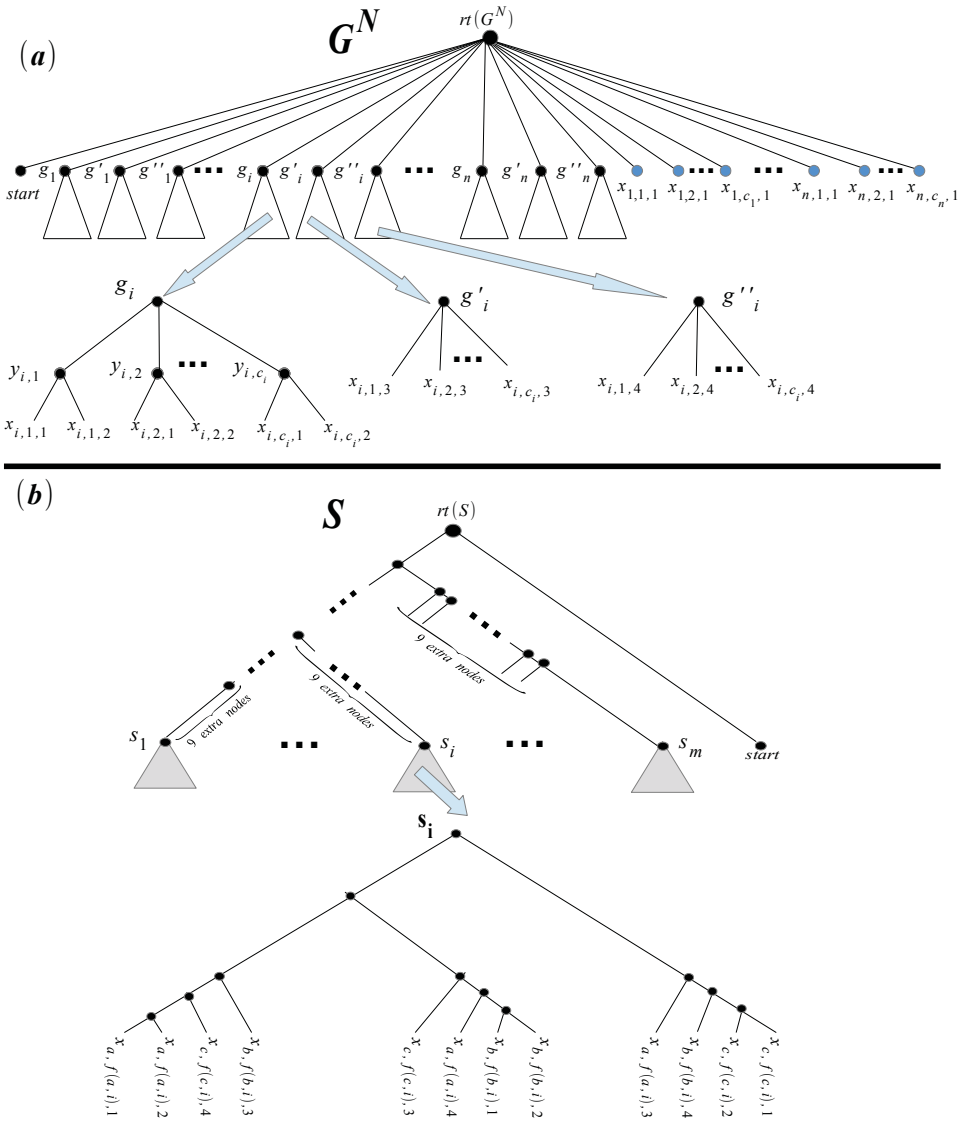
OGTR is NP-hard

- OGTR is NP-hard for both undated and dated species trees (Kordi and Bansal, 2015).
- Surprising since problem is linear-time solvable under duplication-loss model (Zheng and Zhang, 2014).

Key Ideas:

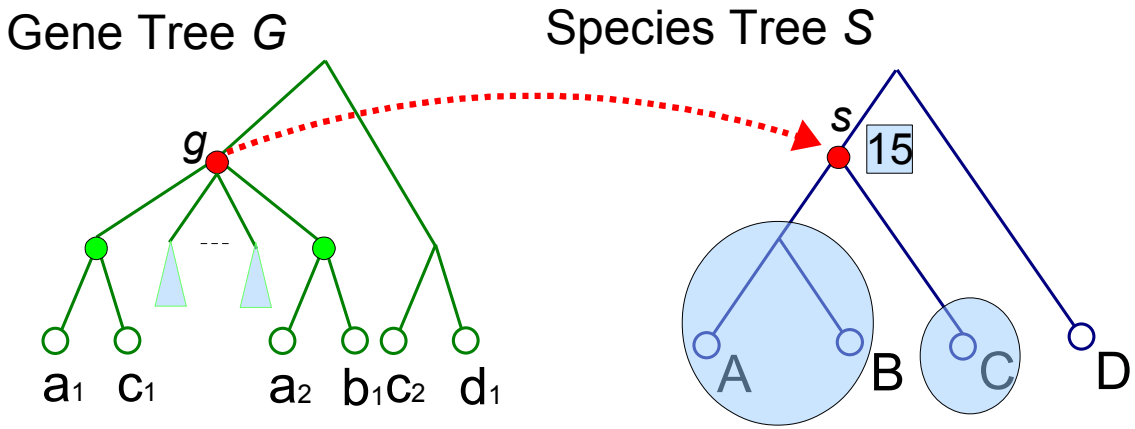
- Reduction from minimum 3 set cover problem.
- Subtrees in species tree correspond to sets
- Subtrees in unresolved gene tree correspond to elements of the universe.
- Structure of gadget forces root of each subtree (element) to map to a "set" in which that element occurs.
- Using more sets for the mapping results in higher reconciliation cost.

OGTR is NP-Hard



A Fixed-Parameter Algorithm for OGTR

- DP algorithms for binary gene trees can be extended to work with non-binary gene trees.
- Consider all possible resolutions at each non-binary gene tree node and fill DP-table for subproblem with best score over all resolutions.
- Gives $O(2^k \cdot k! \cdot ln + mn)$ and $O(2^k \cdot k! \cdot ln + mn^2)$-time algorithms for dated and undated species trees, respectively



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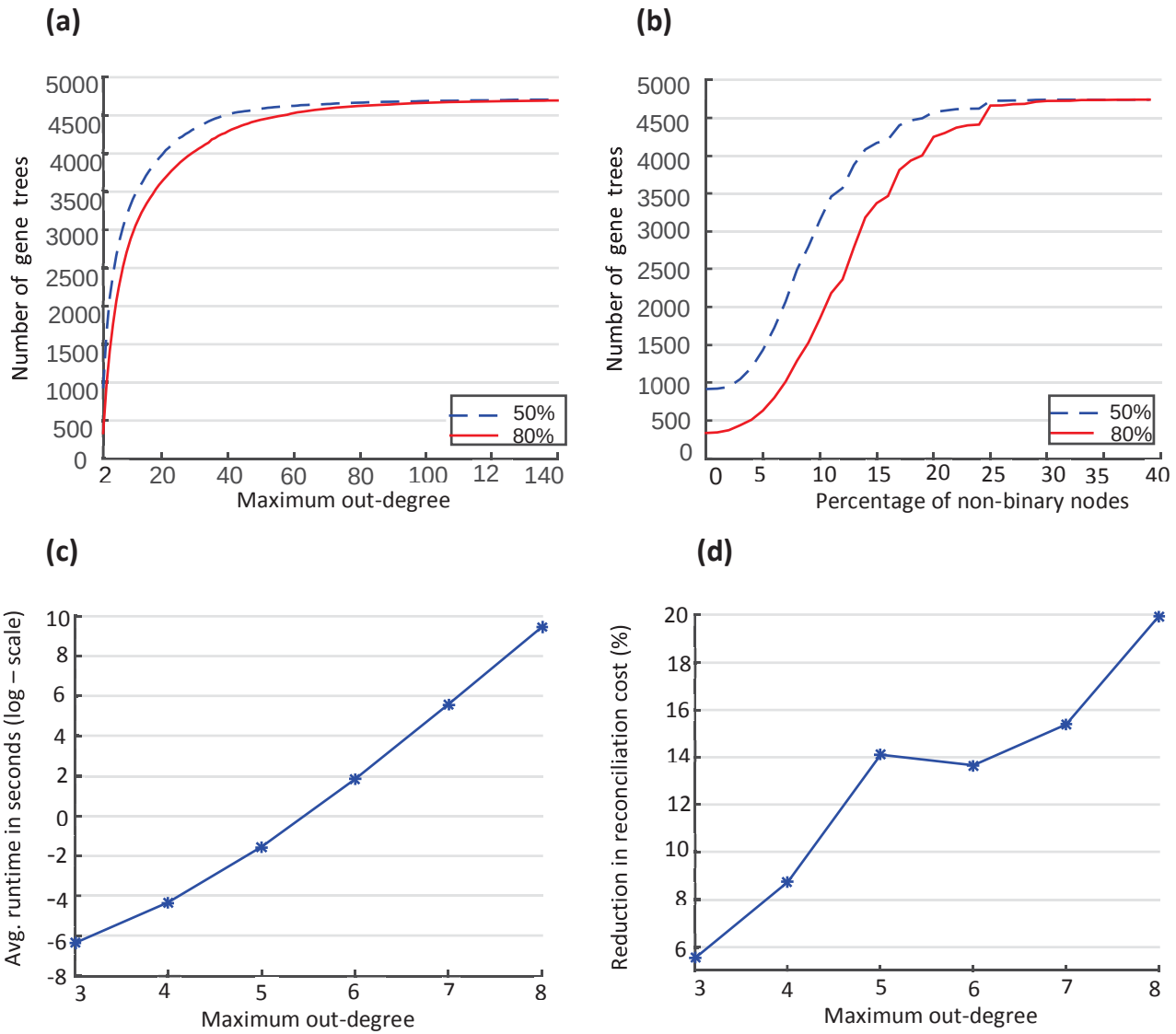

Uniform Sampling of Optimal Resolutions

- DP framework allows for sampling optimal resolutions uniformly at random.
- Samples can be combined with event cost and multiple optima analyses to assess robustness of individual events and mappings.
- Enables identification of highly- and weakly-supported events and mappings for network construction.

Future Directions: Assigning Weakly-Supported Events

1. Leverage high-support events to improve assignment of all other events:
   - Use highly-supported events to infer highways of transfers.
   - Improve assignment of other events based on inferred highways.
2. Use gene tree and species tree branch lengths to choose between alternative scenarios for low-support events.

Thank You!

Questions!