Algorithms for Exploring the Space of Gene Tree/Species Tree Reconciliations

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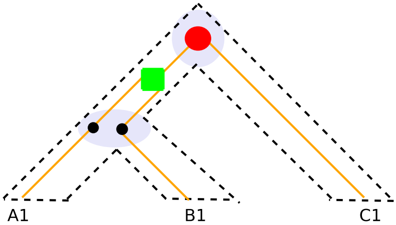
Gene Family Evolution

The evolution of a genome is determined by

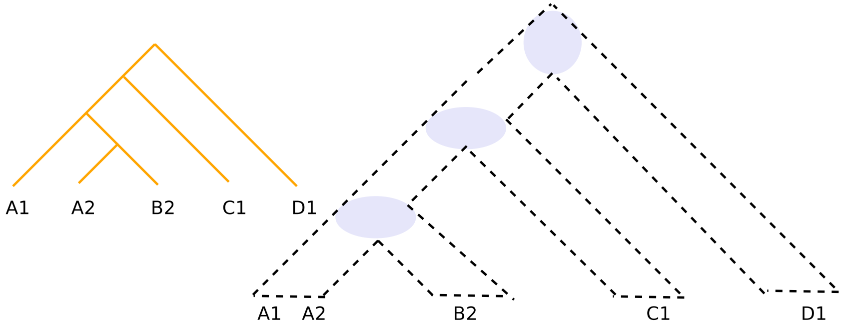
- speciation (●): new species are created;
- duplication (■): a gene is duplicated into two copies;
- loss (•): a gene has no function or is deleted from the genome.



Why it is important to study the evolution of homologous genes?

- Orthologous and paralogous genes
- Gene content of ancestral genomes
- Phylogenomic

The Problem



The Main Question

Define the evolution of the gene tree (G) according to species tree (S) in term of speciation, duplication, and loss events.

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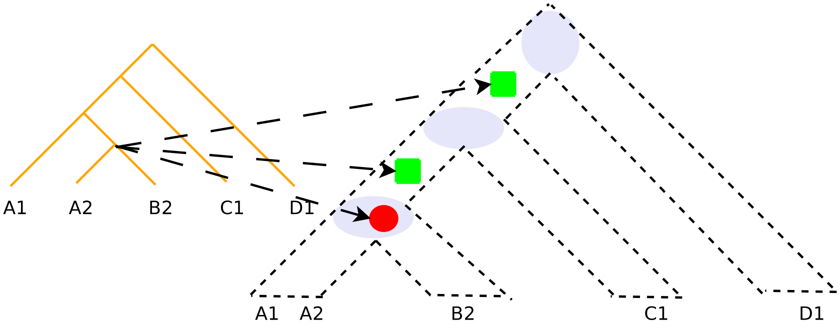

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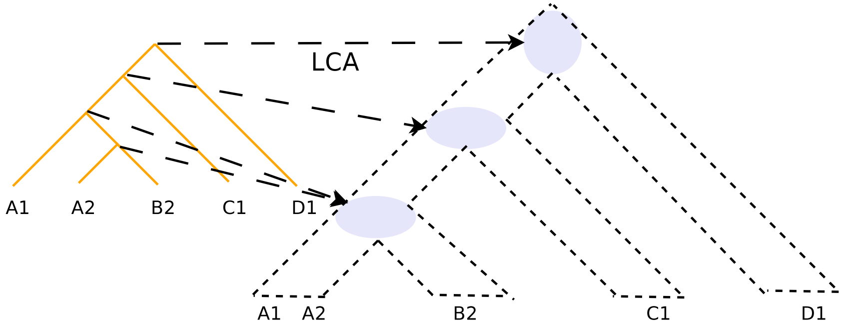
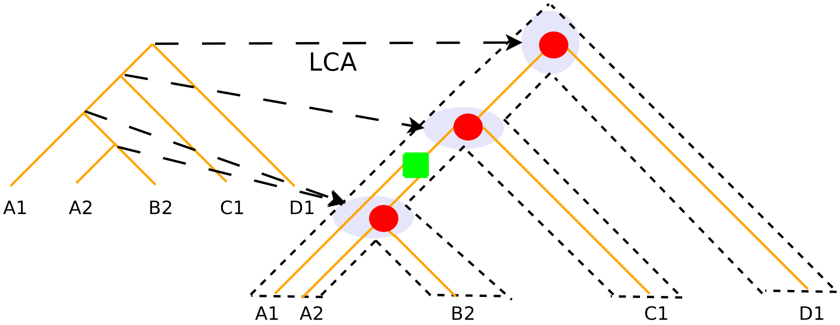


The mapping $LCA : V(G) \to V(S)$

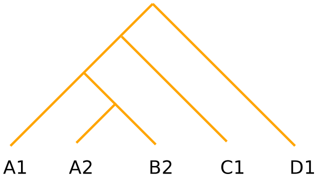
maps a gene u (of G) onto the **Last Common Ancestor** species (of S) of all species that contain a gene descendant of u.

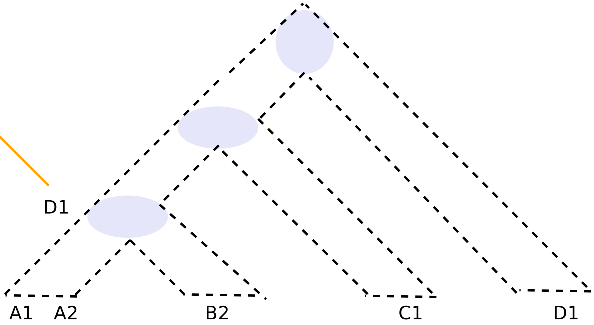
Definitions



- **LCA reconciliation**: the most parsimonious one (Chauve and El-Mabrouk (2009)).
- Arvestad et al. (2004), Bonizzoni et al. (2005), Górecki and Tiuryn (2006).

A more General Definition





A Reconciliation between *G* and *S*

- Each leaf of *G* is mapped on the corresponding leaf of *S*.
- Each internal node is mapped either on the LCA or on an edge above.
- The descendance relationship of two nodes of *G* has to be respected in their mappings in *S*.

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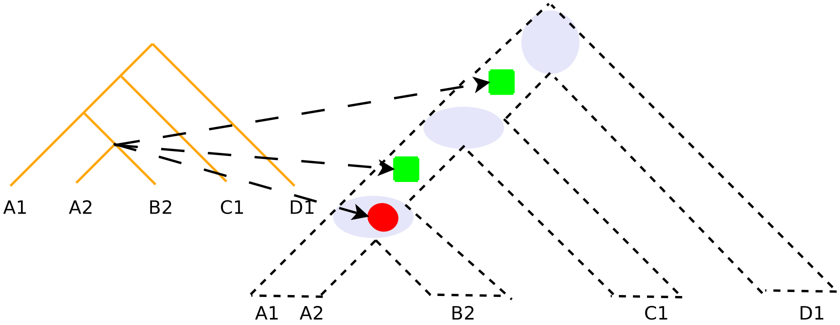

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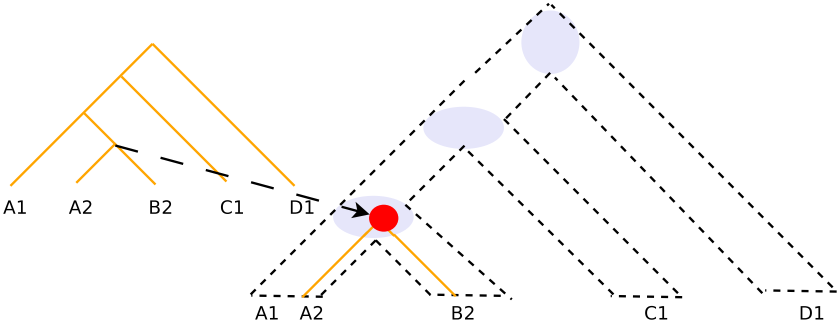

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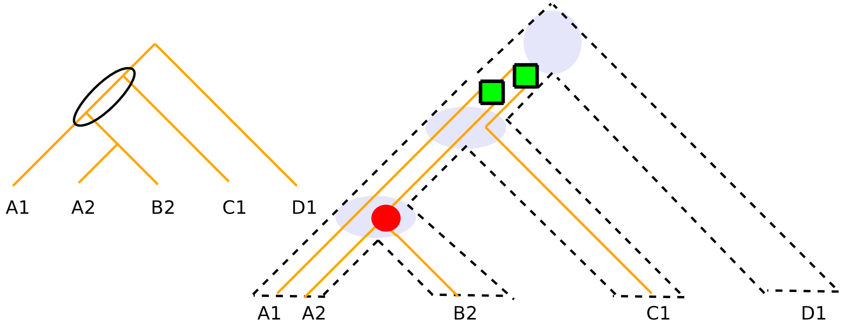

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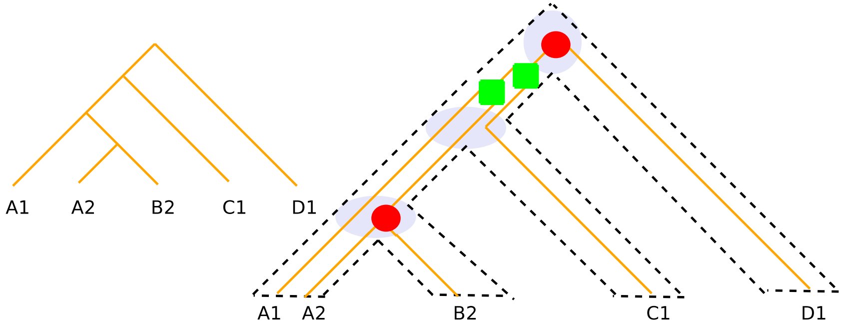

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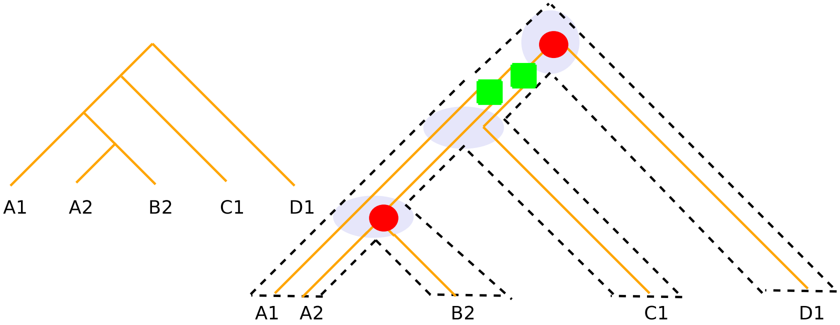


Properties

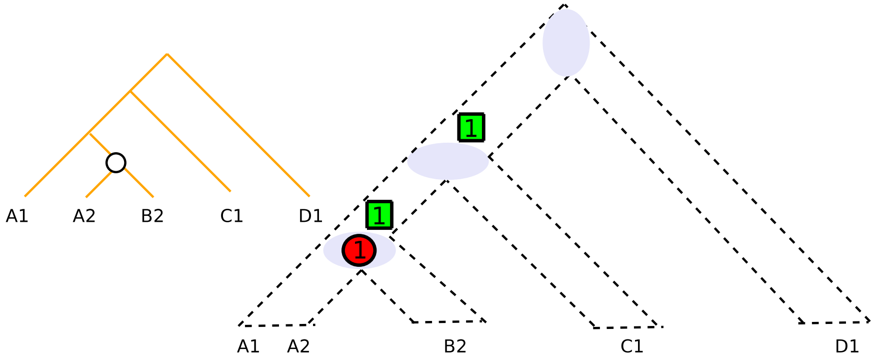
- Does not ONLY induce the LCA reconciliation.
- The number of reconciliations is finite, but can be exponential.

Reconciliation Space Exploration

This simple definition allows

- Count the number of reconciliations.
- Generate randomly and uniformly a reconciliation.
- Define operators used to explore the whole space.
- Exhaustively explore the space.

Counting the Number of Reconciliations



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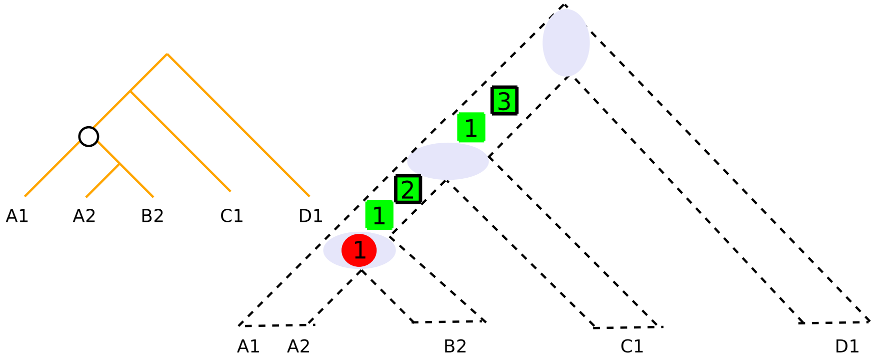

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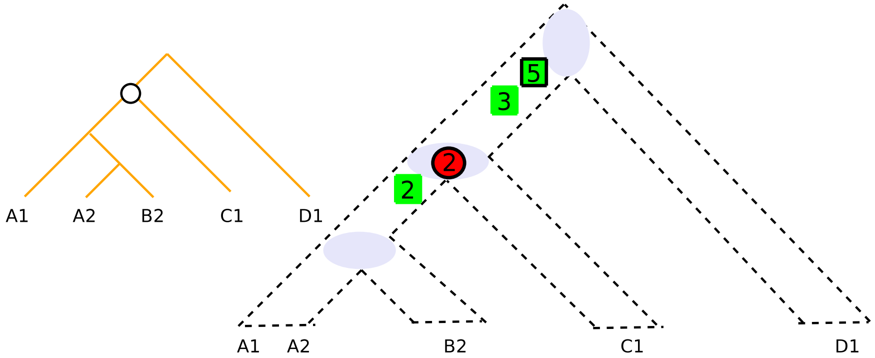

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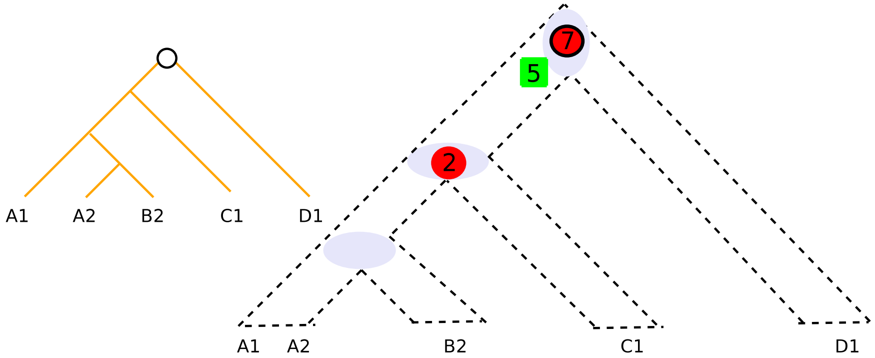

Propositions

- Dynamic programming algorithm in $O(|G||S|)$ time and space.
- Similar algorithm for the # of reconciliations that minimizes the duplication cost.

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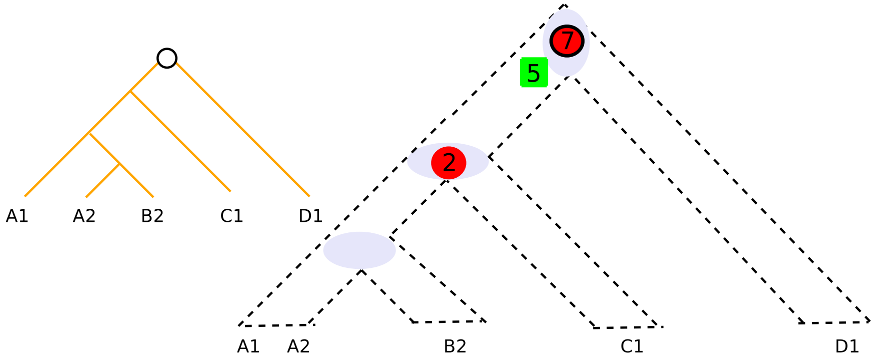

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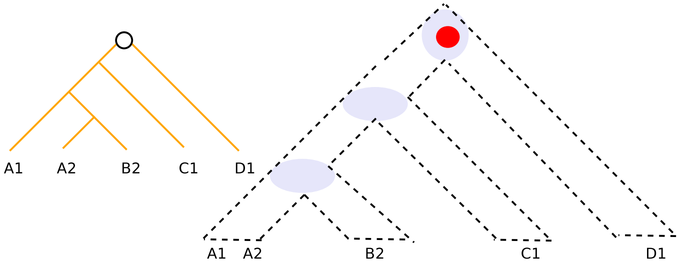
Uniform Random Generation

Algorithm

- Prefix traversal of G (u is the current node);
- Randomly select a node/edge c of S according to $Nb(u, c)$.



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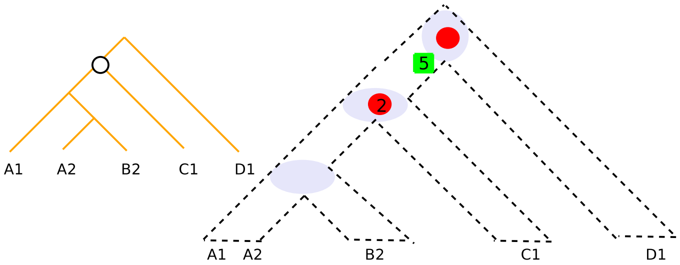

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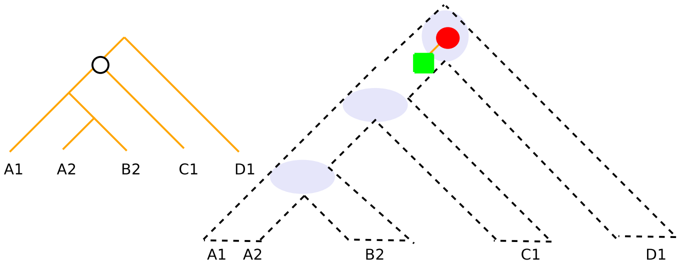

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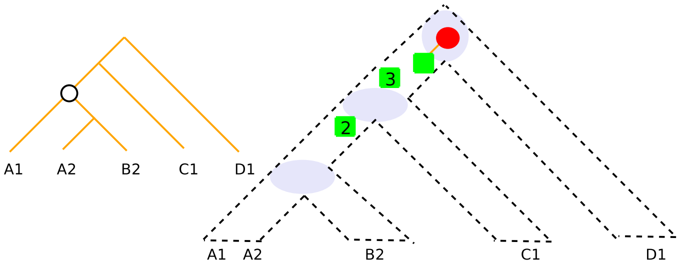

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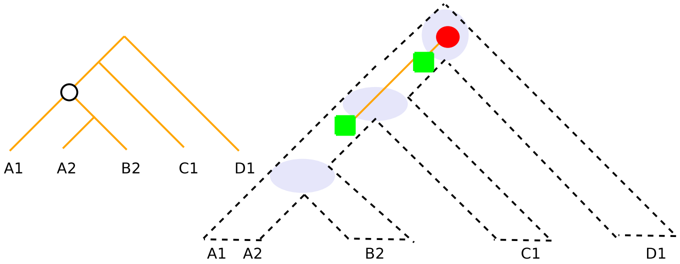

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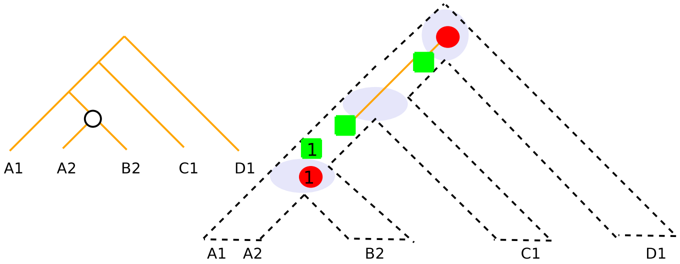

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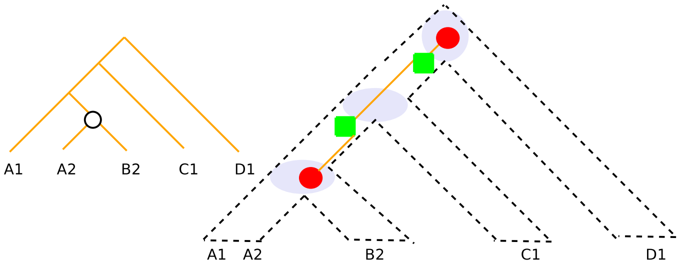

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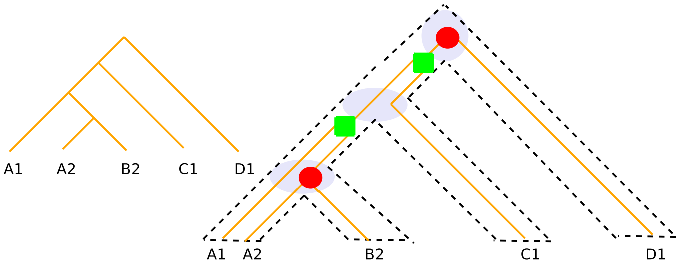

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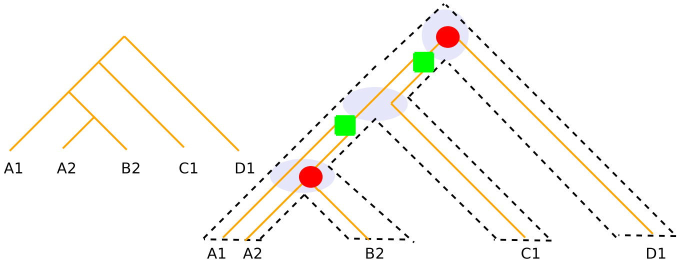


Theorem

- Uniform distribution over all reconciliations.
- Preprocessing of $O(|G||S|)$ for the counting.
- Worst case in $\Theta(|G||S|)$ and best case in $\Theta(|G|)$.
- Space in $O(|G||S|)$.

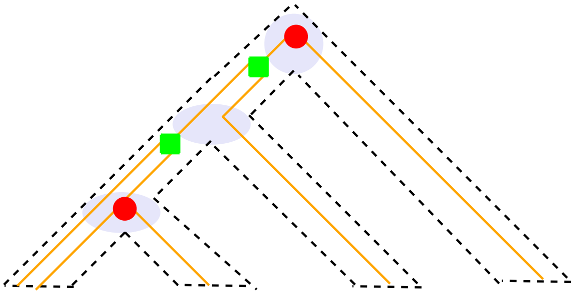
Nearest Mapping Change

Upward NMC

- Changes a speciation into a duplication.
- Moves a duplication upward.

Downward NMC

- Changes a duplication into a speciation.
- Moves a duplication downward.



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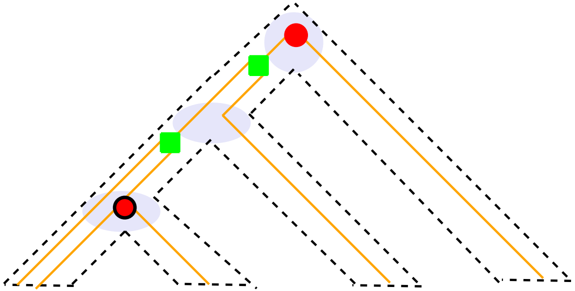

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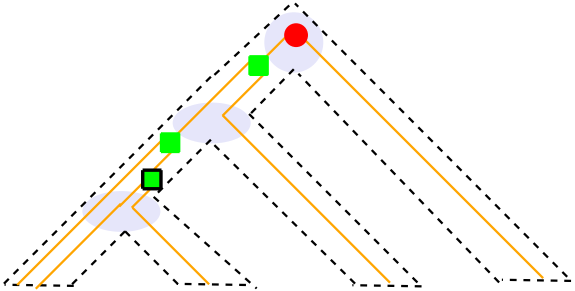

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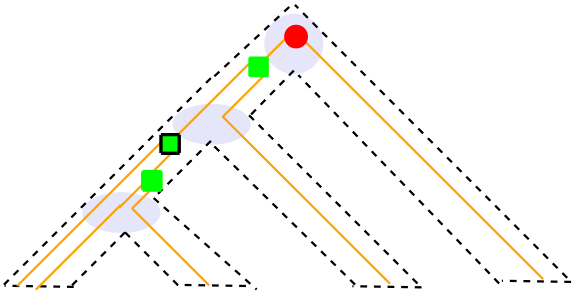

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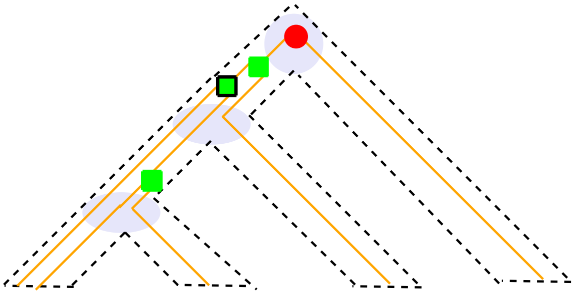

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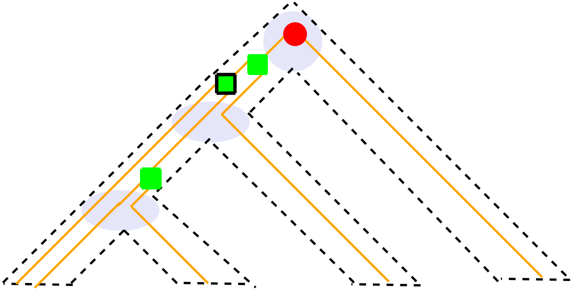
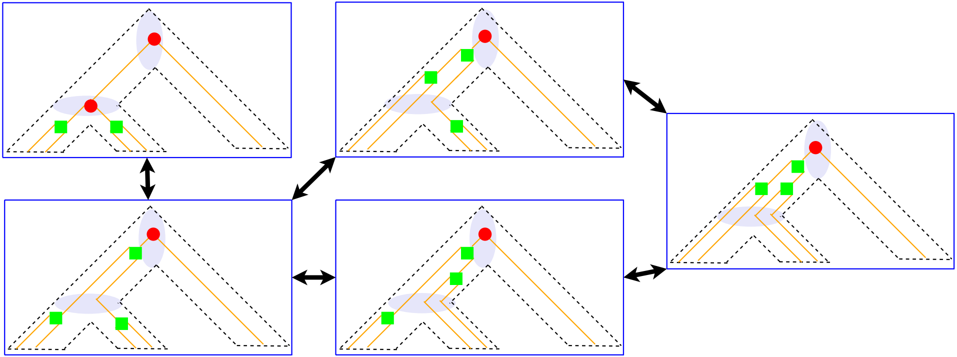


Properties

- Sufficient to explore the whole space of reconciliations.
- The number of duplications and losses can be updated in constant time.

Exhaustive Exploration



Graph over the space

- $V(G) = \{\text{reconciliations}\}$
- $E(G) = \{\text{NMC operators}\}$

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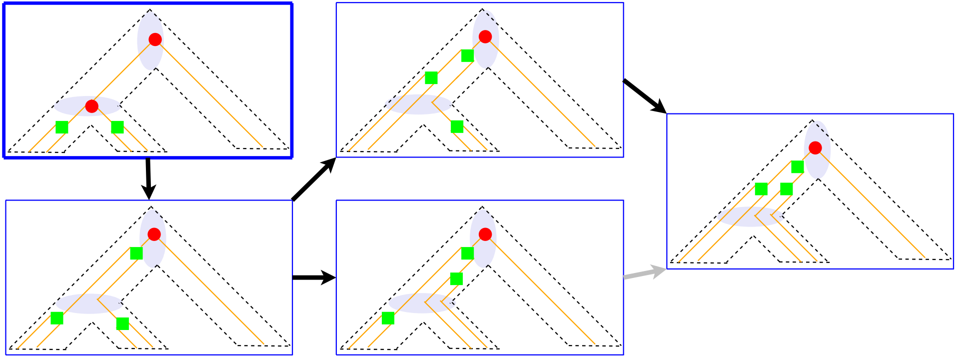

Tree over the graph

- The root is the LCA reconciliation
- Upward NMCs only
- Lexicographic order constraint on the NMCs.

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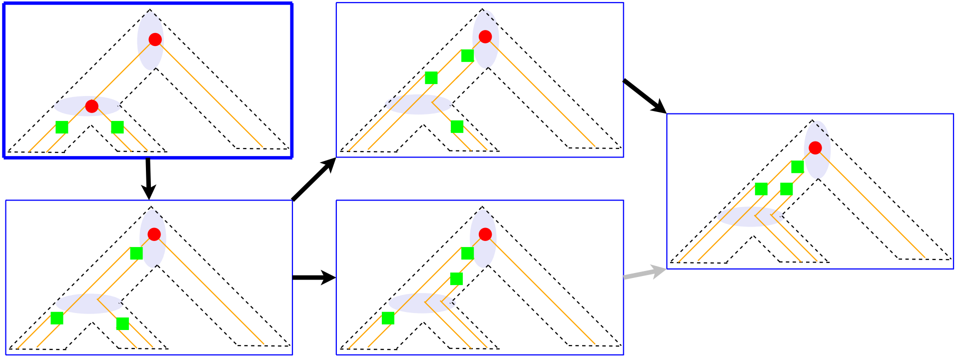
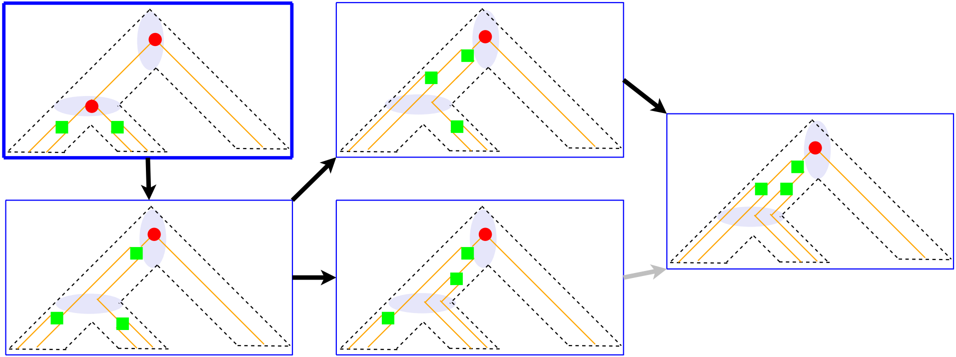


Proposition

The tree is a spanning tree of the graph

Exhaustive Exploration



Theorem

The algorithm is in Constant Amortized Time $\Theta(\#rec)$ and space $O(|G||S|)$.

Experimental Results

Generation of synthetic gene trees

- Phylogenetic tree of 12 *Drosophila* with valued branches (Hahn, 2007).
- 1000 gene trees were generated using the birth-and-death process.
- 249 gene trees were unique (6 to 22 leaves).

Distribution of the duplication cost

- 237 gene trees have 1 optimal reconciliation.
- 12 gene trees have 2 optimal rec., always seperated by 1 NMC.
- The LCA reconciliation is equal or at 1 NMC to the true one.
- $\#dup(\alpha) - \#dup(\alpha^*)$ is proportional both to ($\alpha^* =$ optimal rec.)
  - the NMC distance between α and α^*;
  - how much α differs from the true reconciliation.

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Conclusion

Theorical Contributions

- MCMC can use the random algorithm, and the NMCs.
- Exploration algorithm is optimal in time.

Experimental Contributions

- Large number of reconciliatons (1 000 000), even with low rates.
- Few (near) optimal reconciliations, always close to the LCA one.
- Parsimony can be a good criteria to find the true reconciliation.

Future Work

- Higher duplication and loss rates.
- Local neighbourhood exploration.
- Maximum likelihood cost.
- Non binary trees and multiple gene duplications.