RECONSTRUCTING A **SUPERGENETREE** MINIMIZING RECONCILIATION

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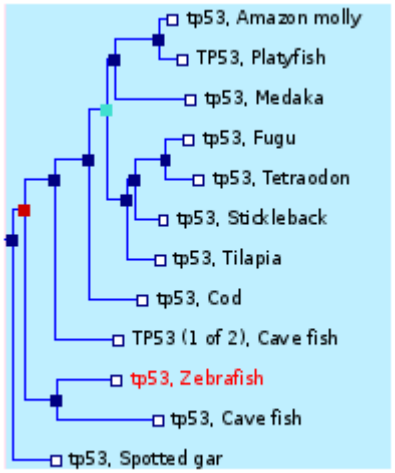
The plan

In this talk I…

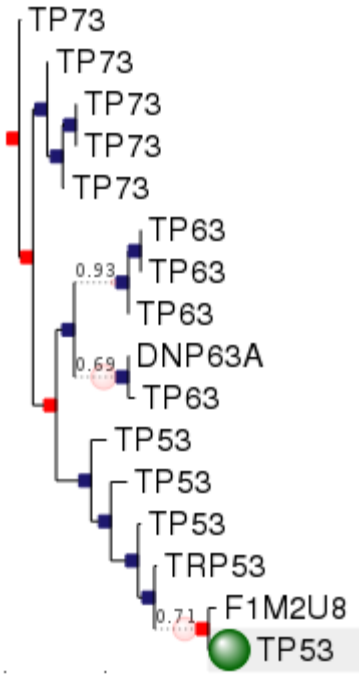
- …come up with supertree problems
  - Finding a supergenetree that minimizes duplications
- …convince you that they're hard
- …try to do something about it
  - Exact, brute-force algorithm
  - A greedy heuristic

TP53 gene tree(s)

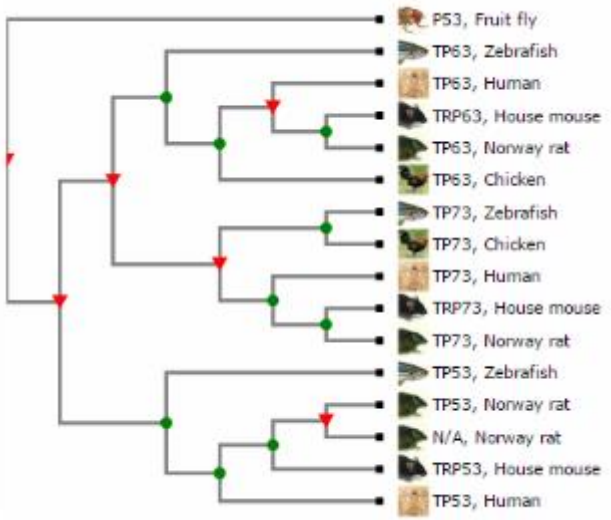
Ensembl

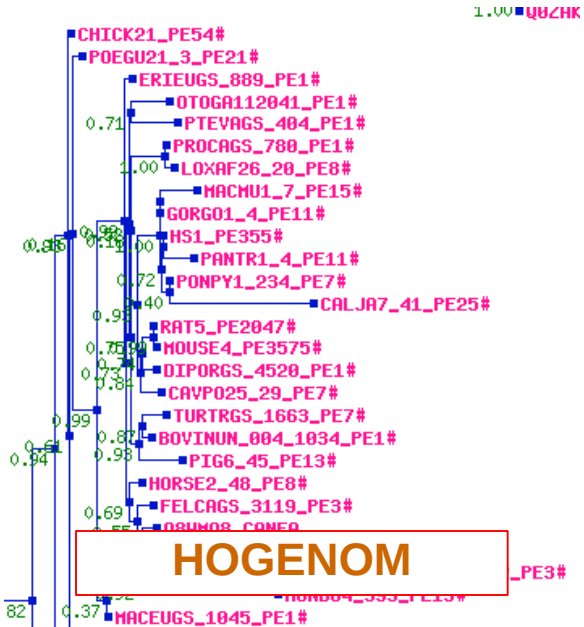


PhylomeDB



TreeFam





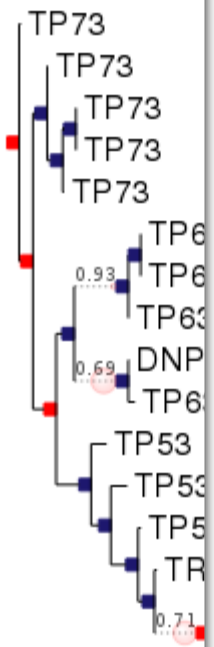
HOGENOM

TP53 gene tree(s)

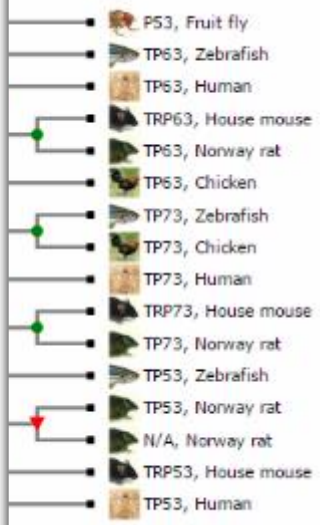
Ensembl

Phylome

Ensembl + PhylomeDB + TreeFam + HOGENOM + …



eeFam



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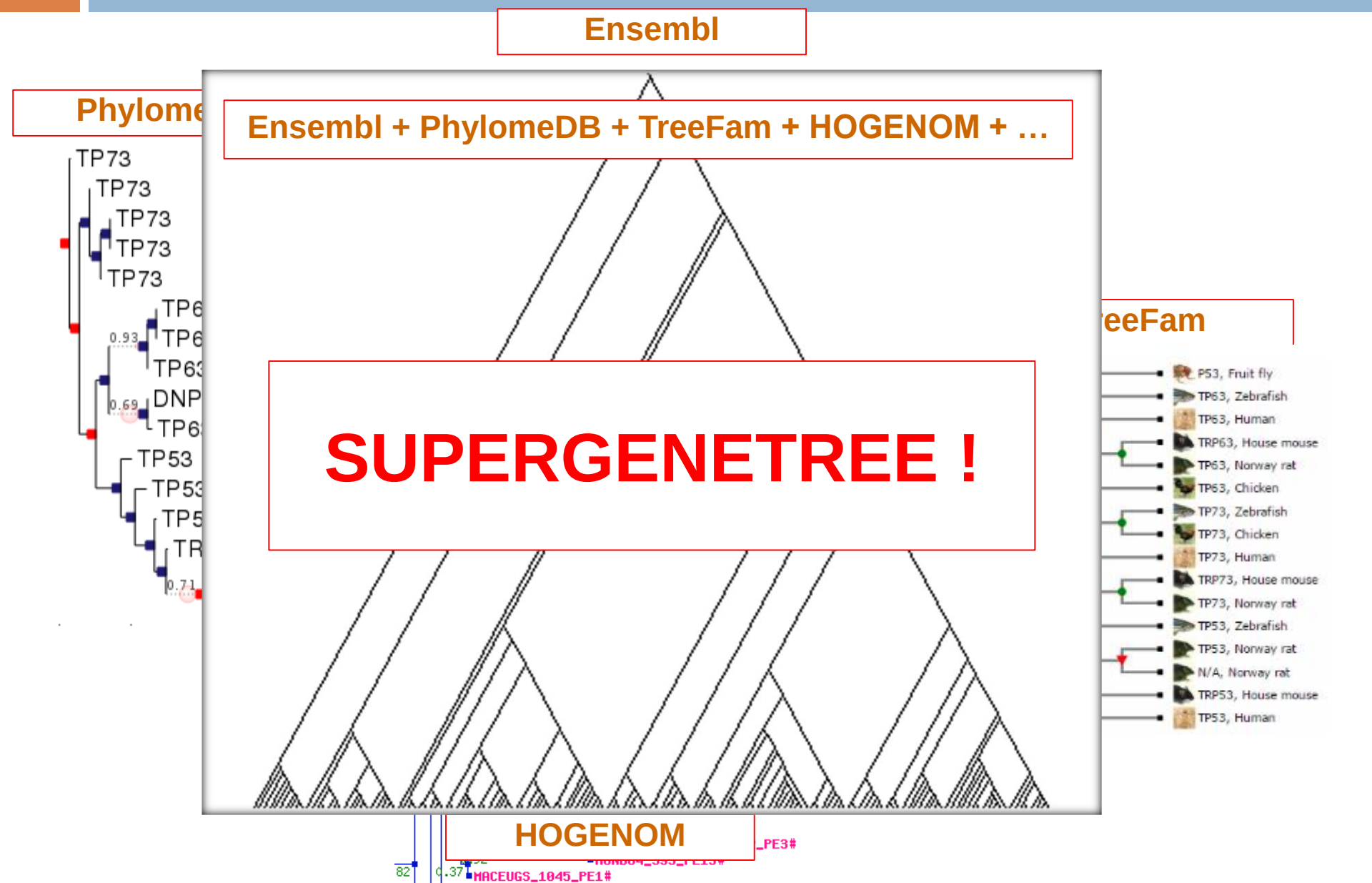
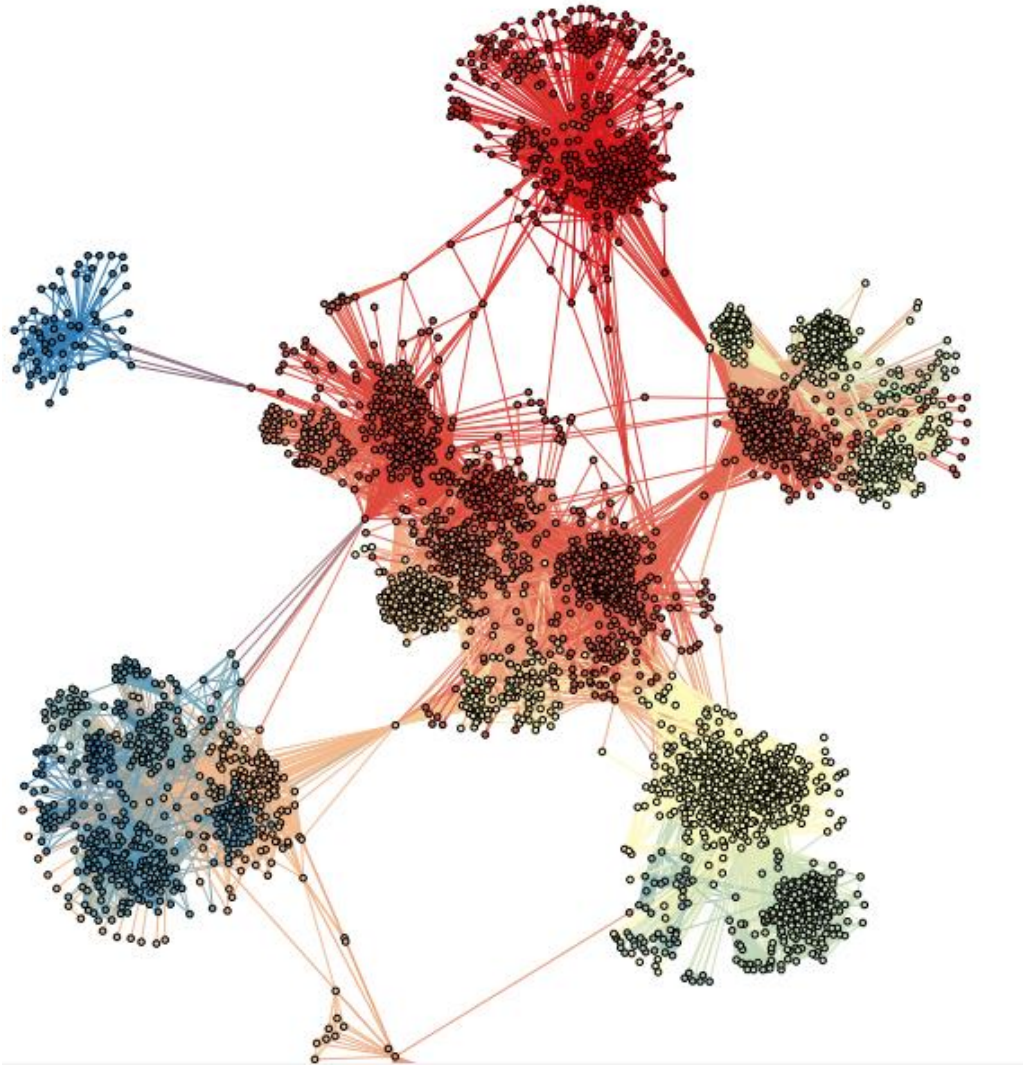


Clusters of orthologous groups



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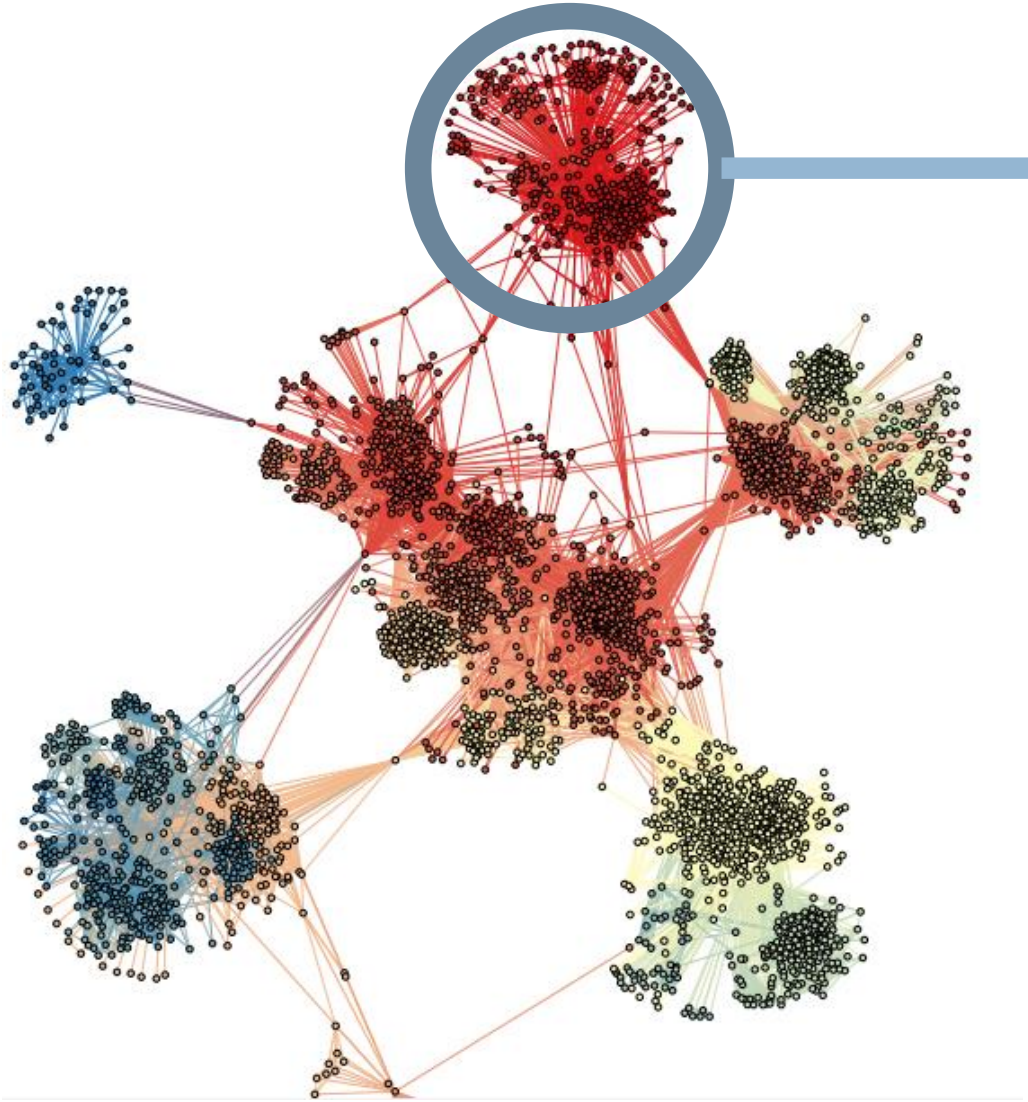

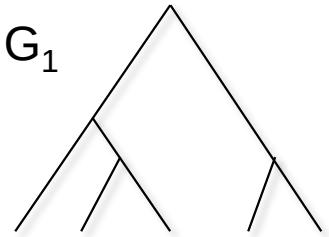

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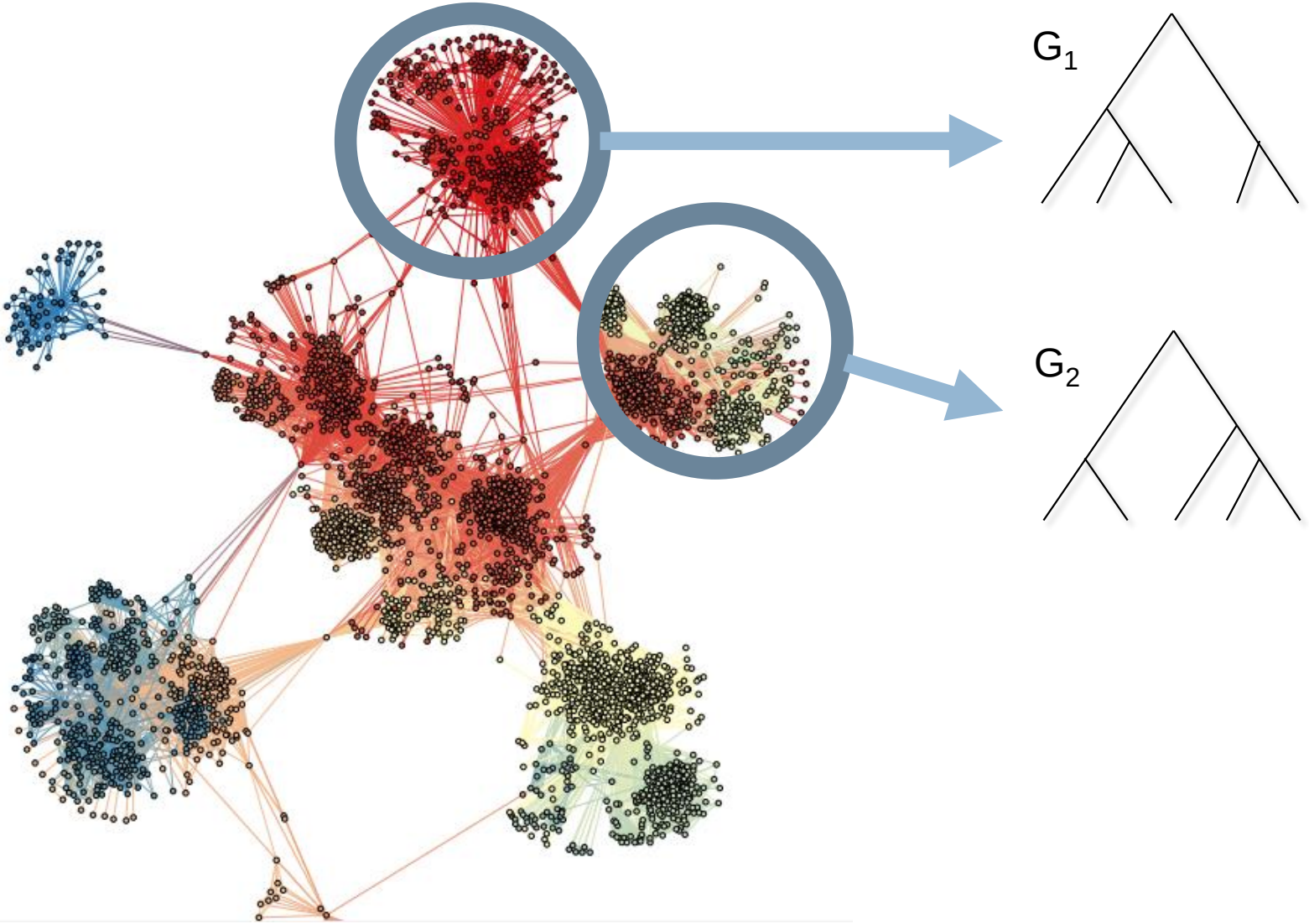

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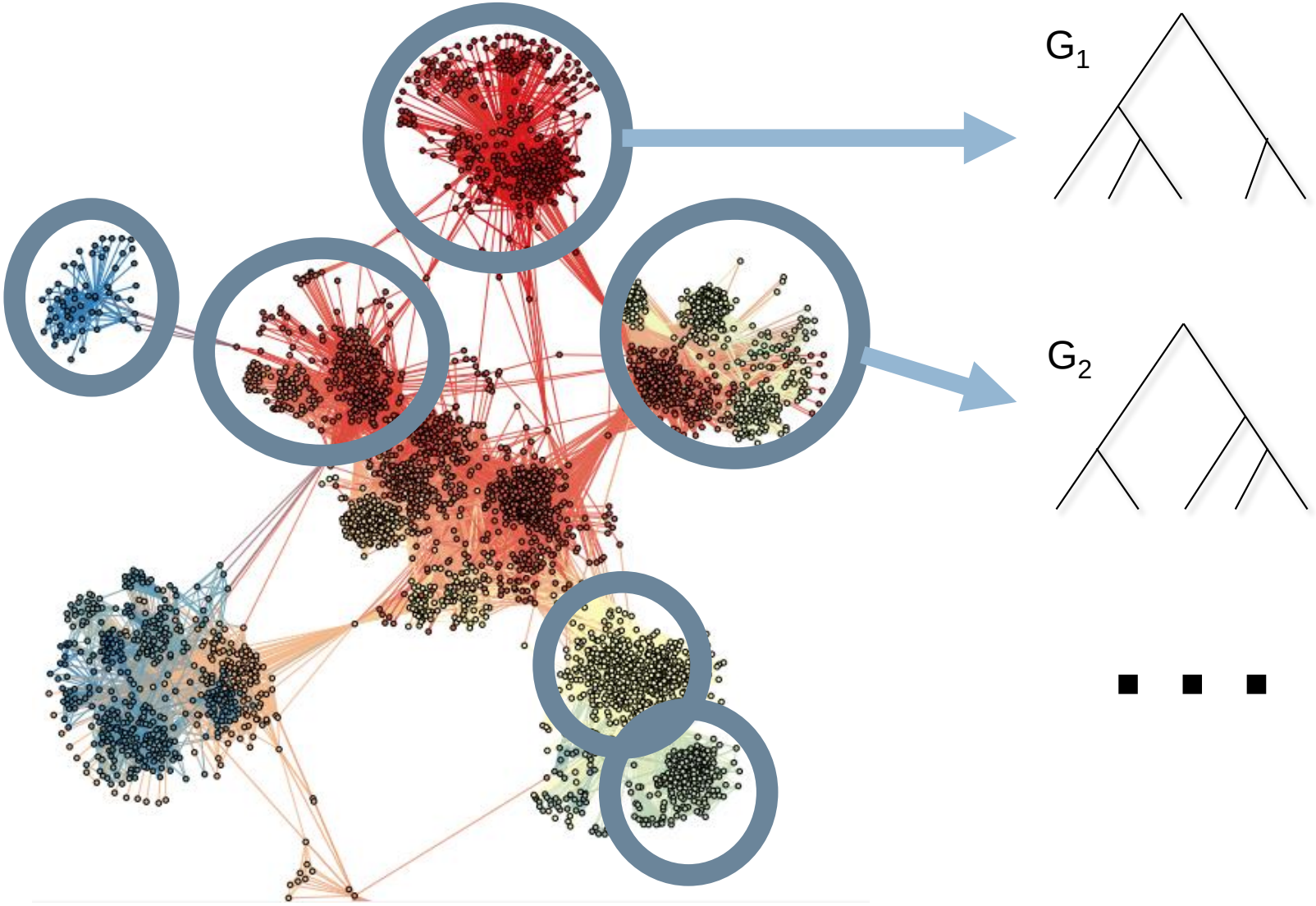
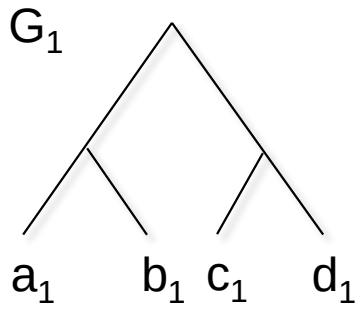
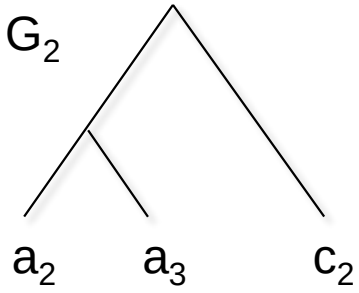


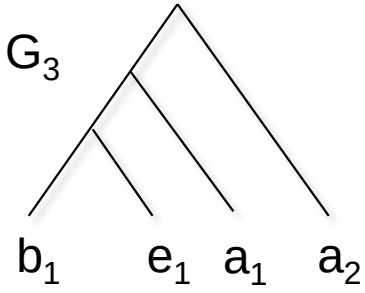
Clusters of orthologous groups

The Supergenetree problem

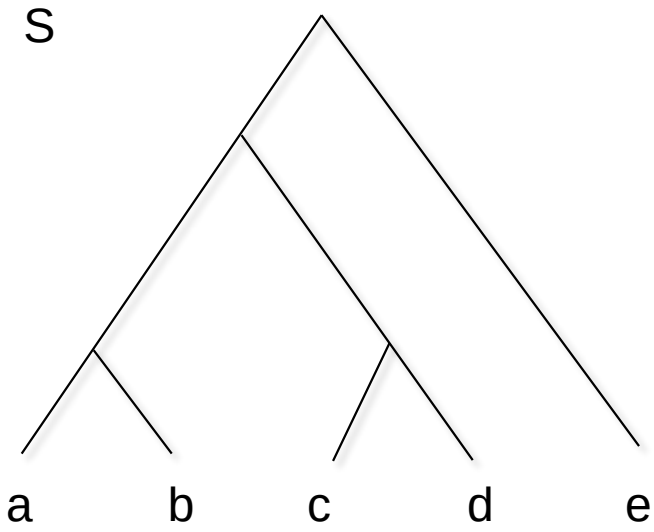
Multiple gene trees







Species tree



- **Gene tree label = species**
- **Multiple copies (paralogs)**
  - **e.g. a_1, a_2, a_3**
- **Gene trees may be partial + discordant with S (e.g. G_3)**

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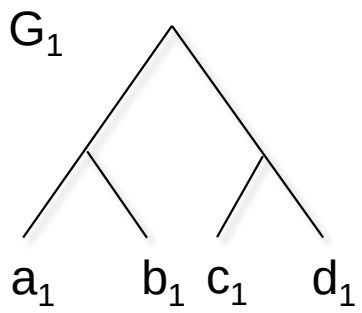
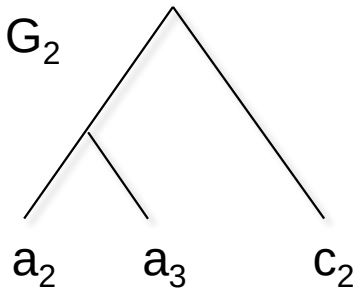
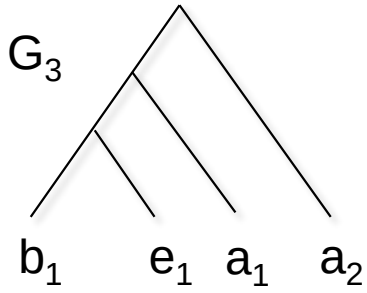
Multiple gene trees







- **Our goal : find a gene tree that displays them all**

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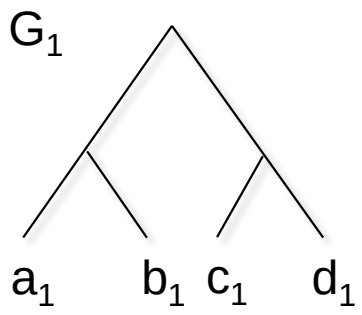

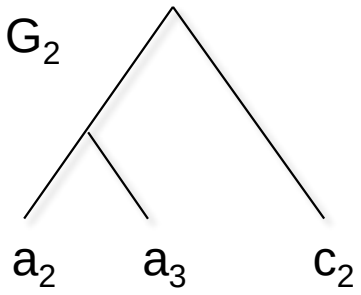

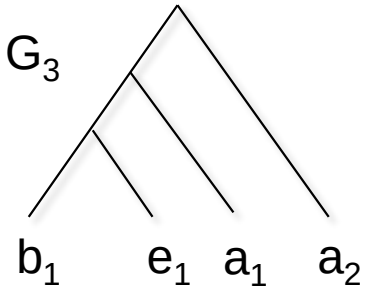

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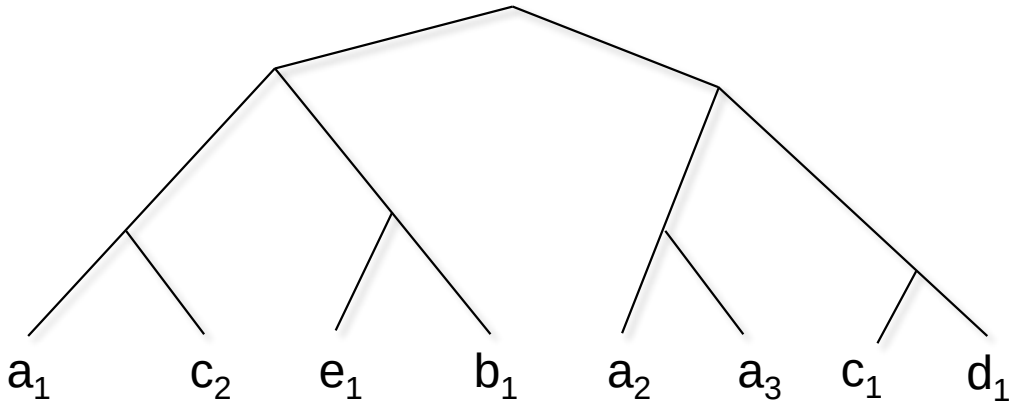

The Supergenetree problem

Multiple gene trees

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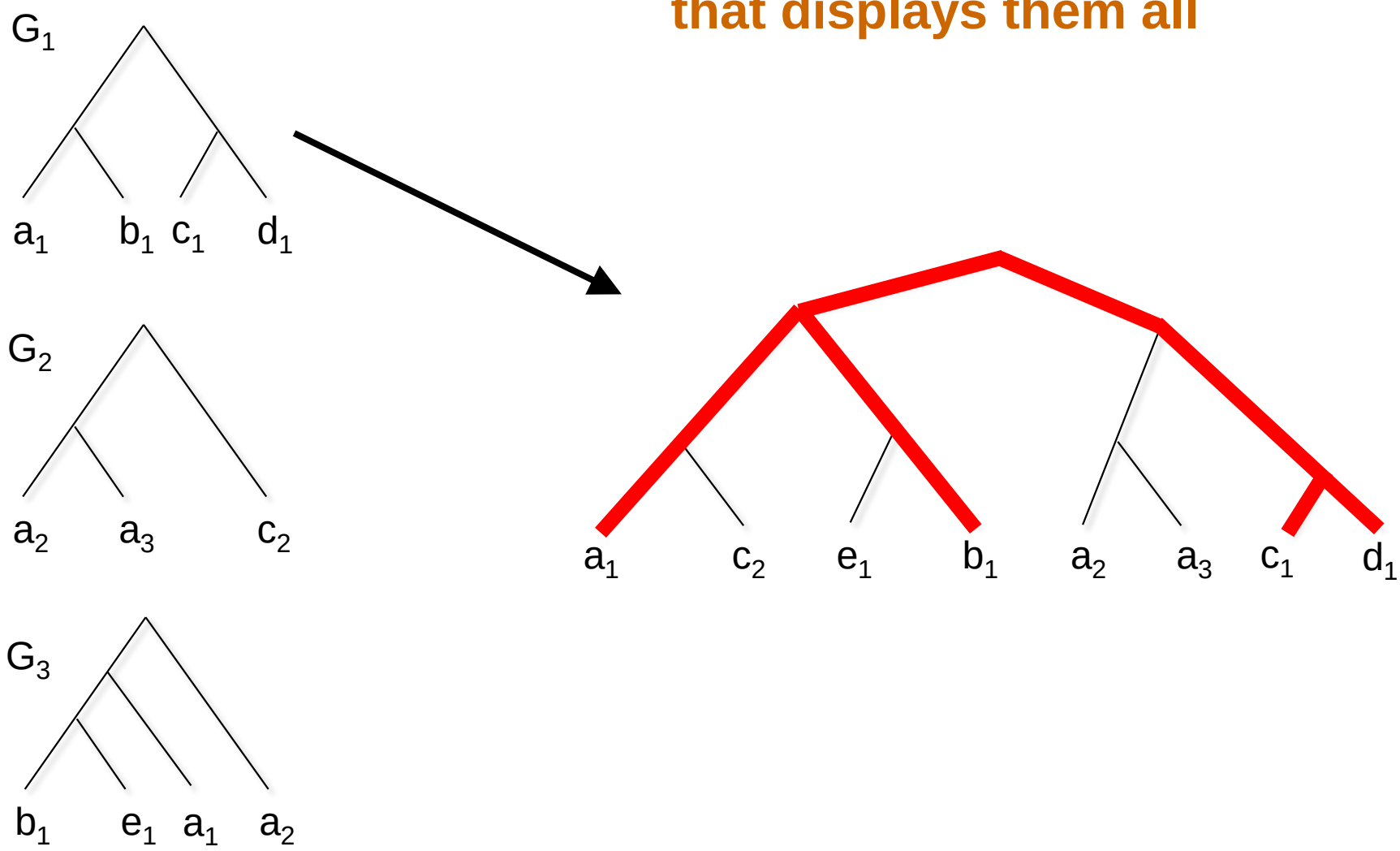

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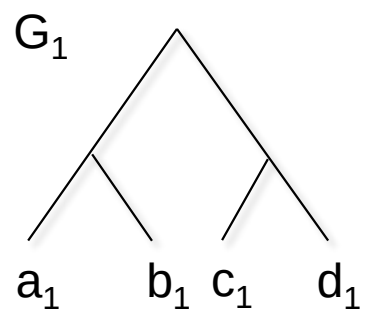

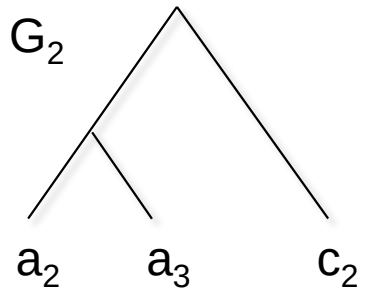

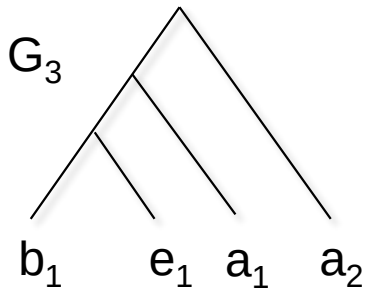

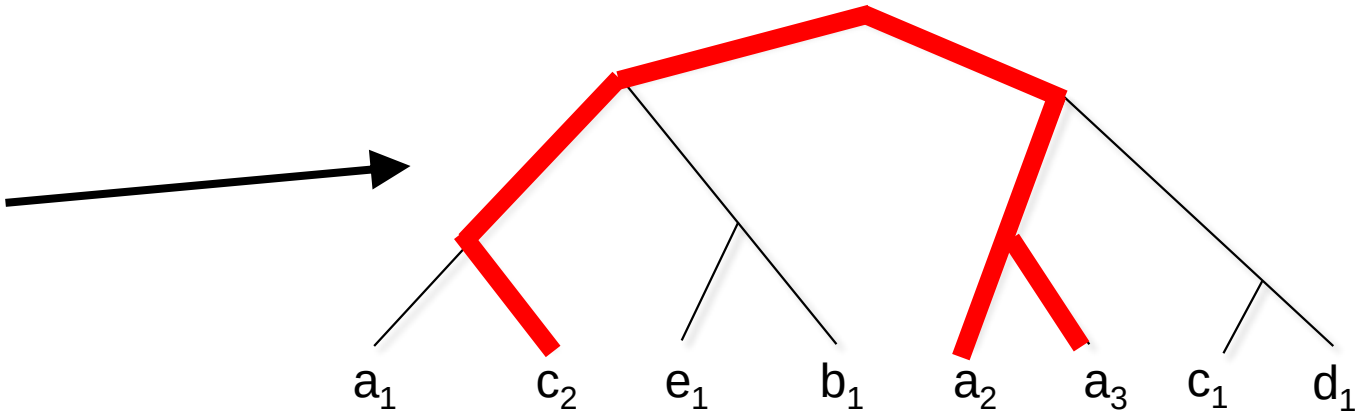

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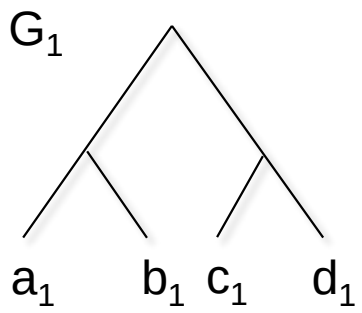

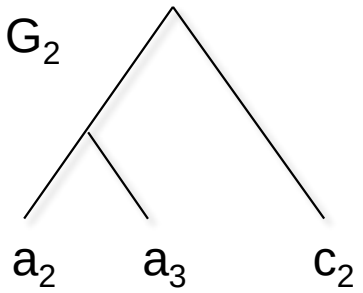

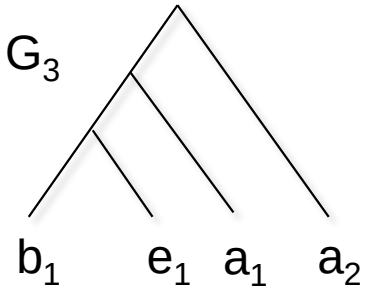

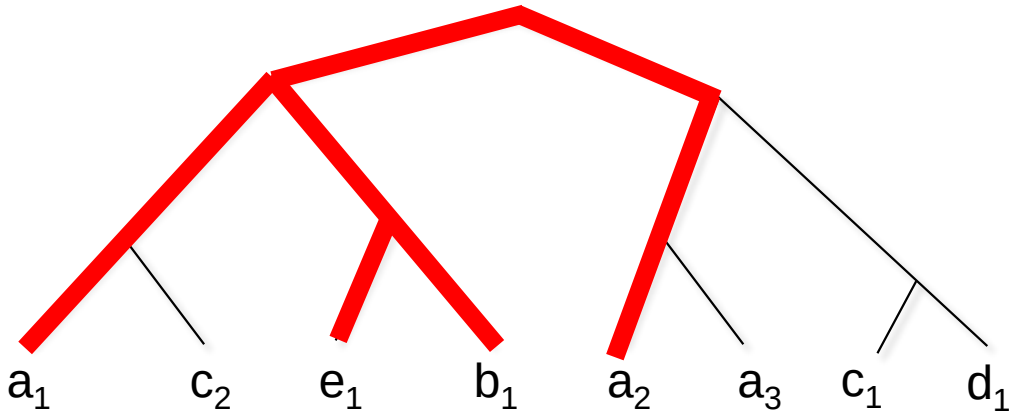

SuperGeneTree

- Our trees are said **compatible** if there is a supertree displaying them all
- Finding a supertree (or determining incompatibility) is an old problem
  - The BUILD algorithm does that *(Aho & al., 1981)*
- What's different about super**gene**trees ?

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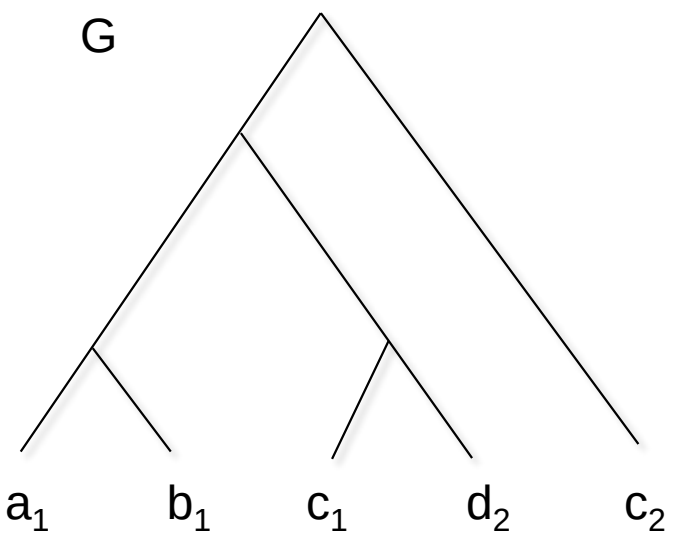
- Finding a supertree (or determining incompatibility) is an old problem
  - The BUILD algorithm does that *(Aho & al., 1981)*
- What's different about super**gene**trees ?
- We have the **species tree**

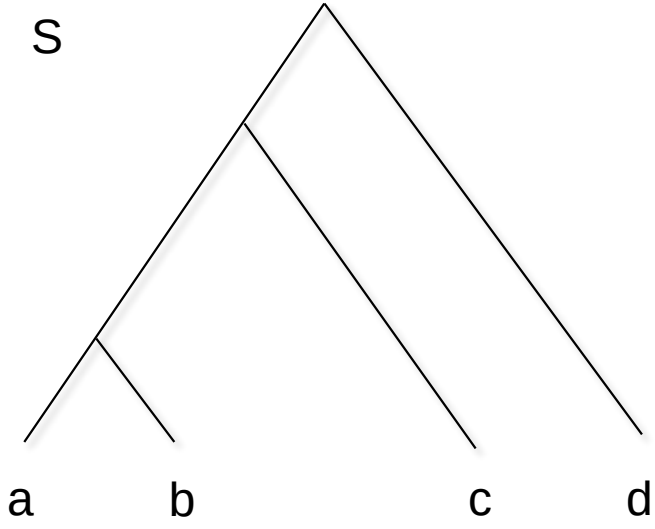
SuperGeneTree

- Often, many supergenetrees exist
- Which one is the best ?
- We **explore ways to choose** using information from the species tree S
- More specifically, we **explore ways to use reconciliation** with S to pick the best supergenetree

Reconciliation

Reconciliation identifies **duplication**, **speciation** and **loss** events in G.





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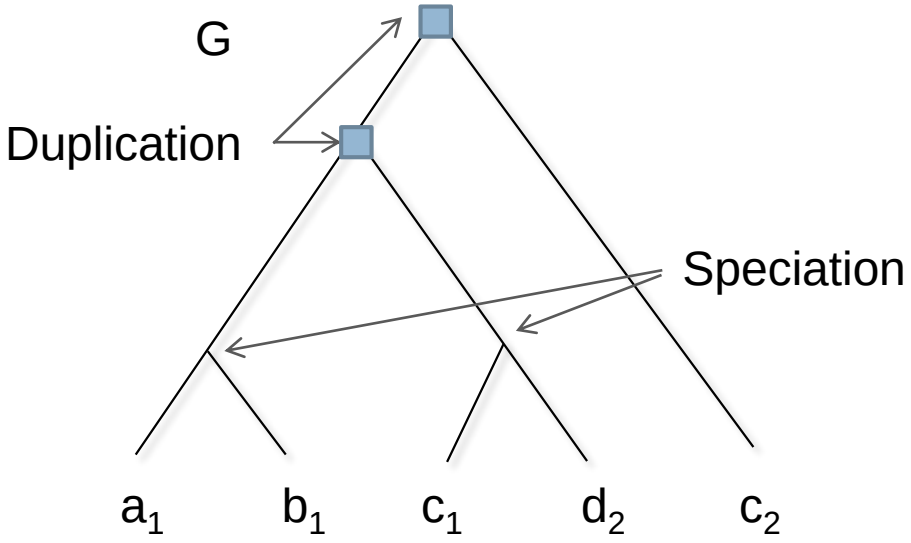

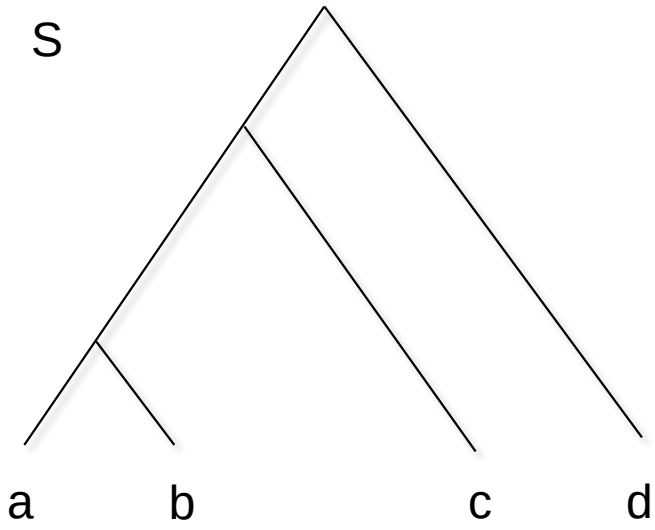

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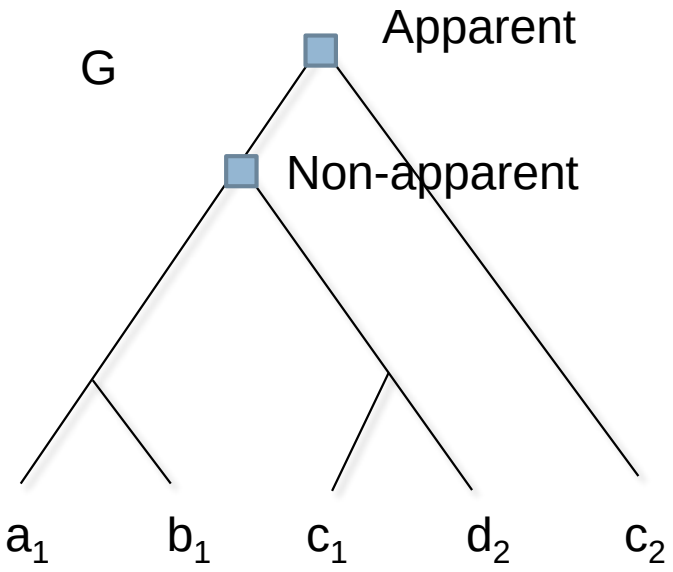

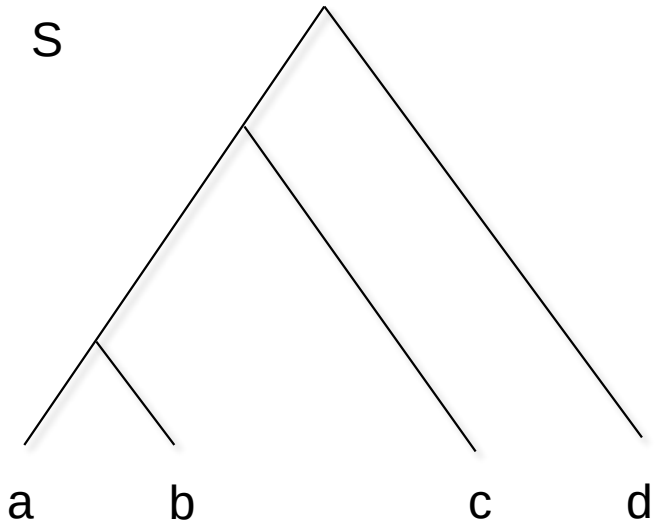

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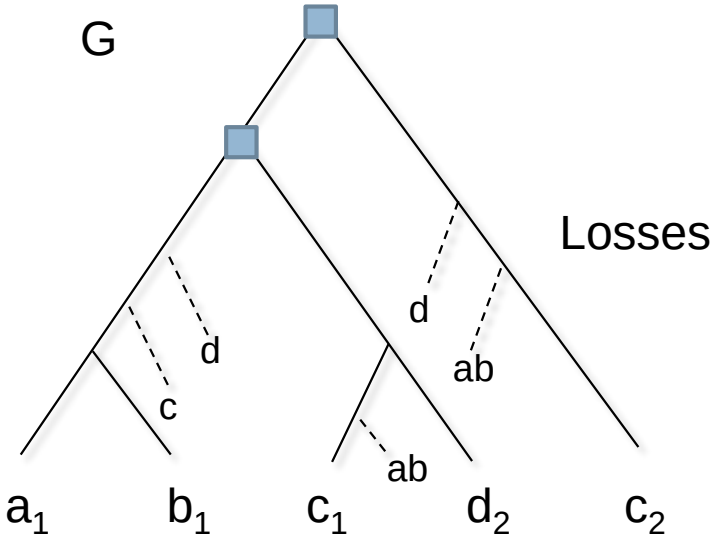

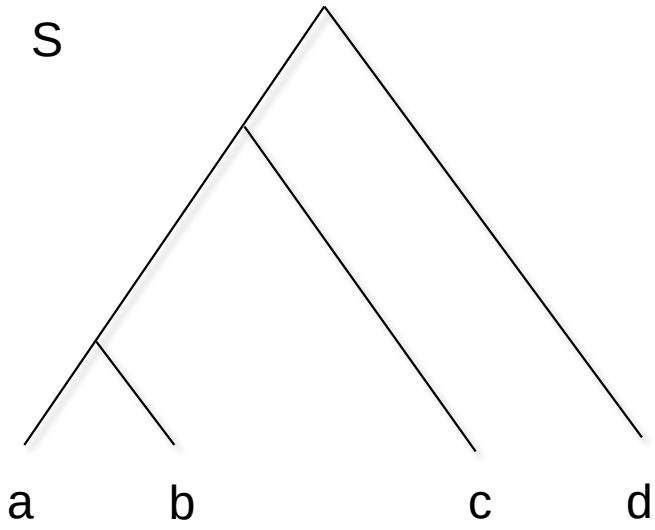

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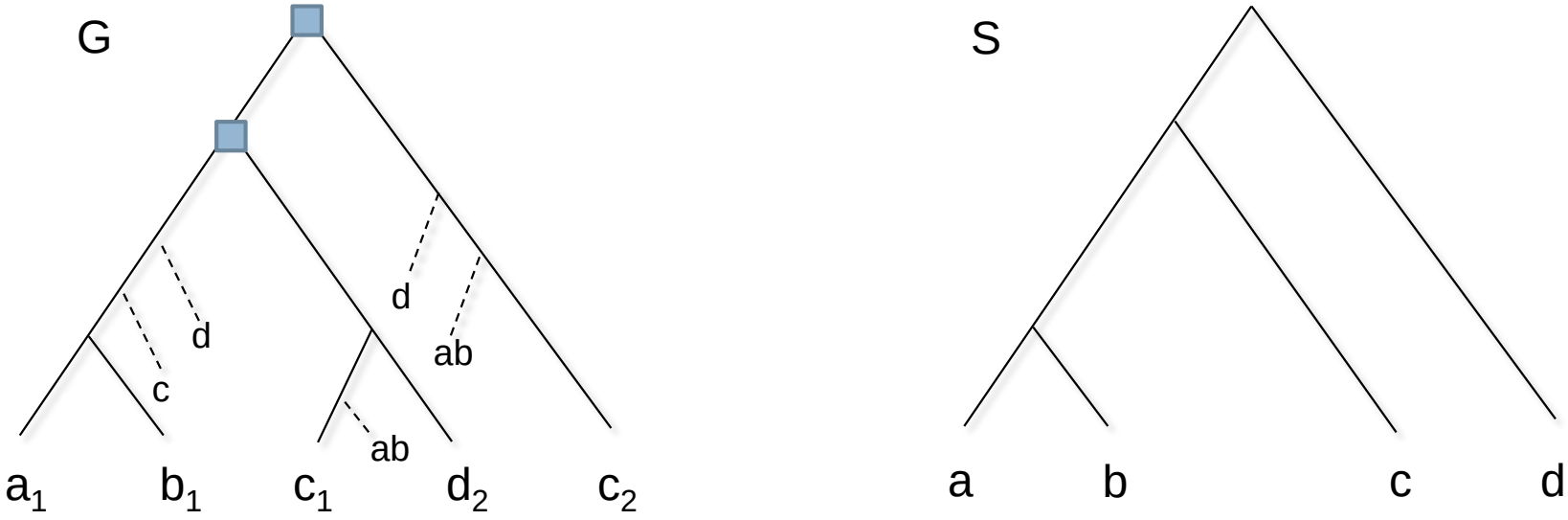

Possible reconciliation costs : #dups, #dups + #losses

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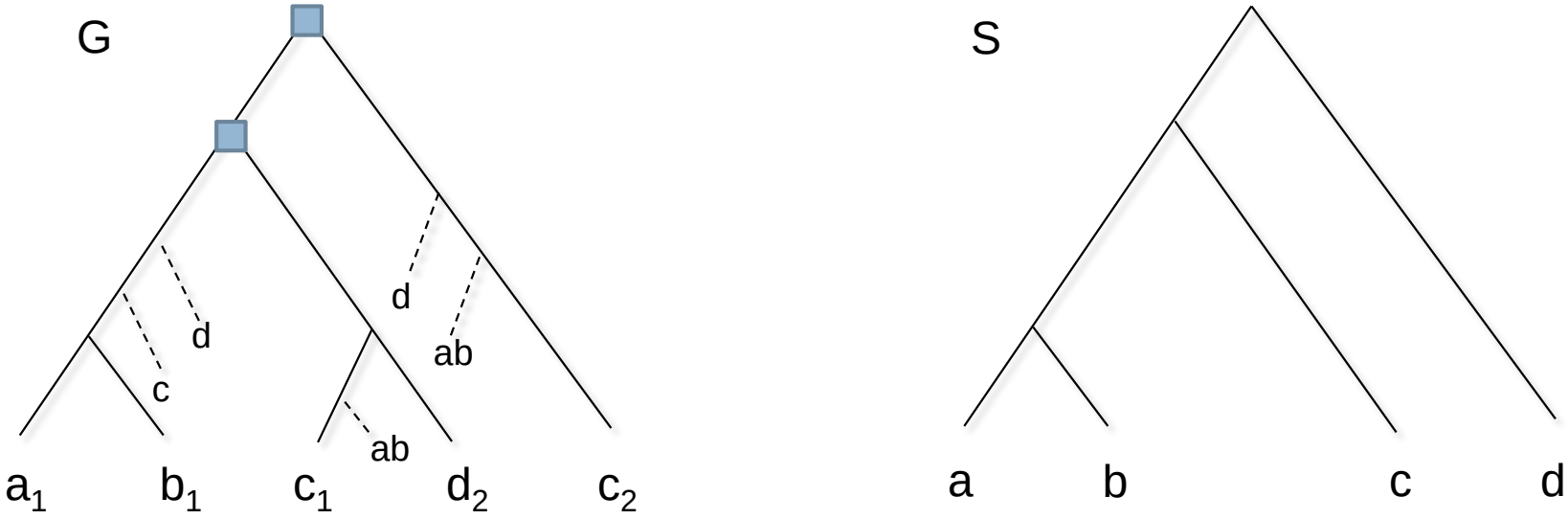

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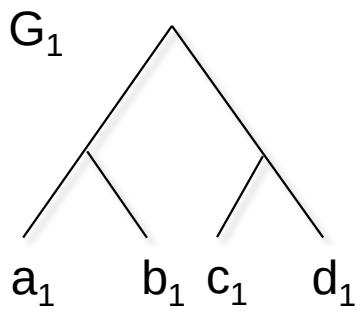
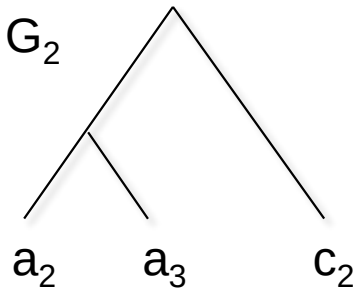
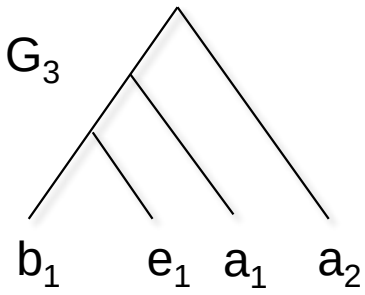
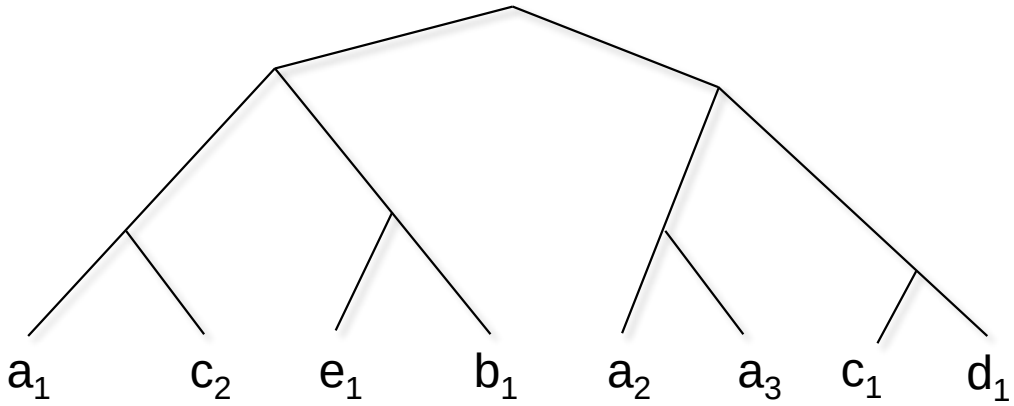
The Supergenetree problem









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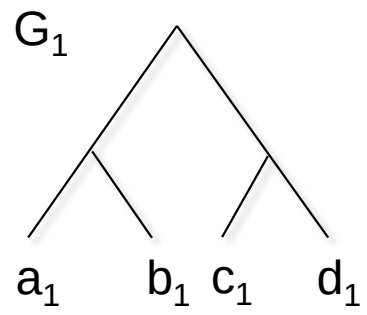

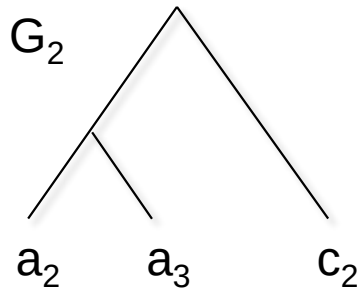

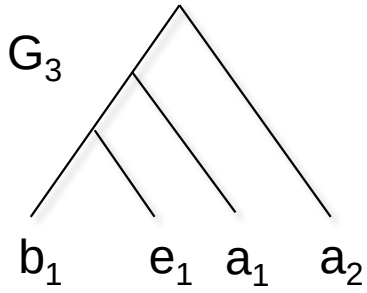

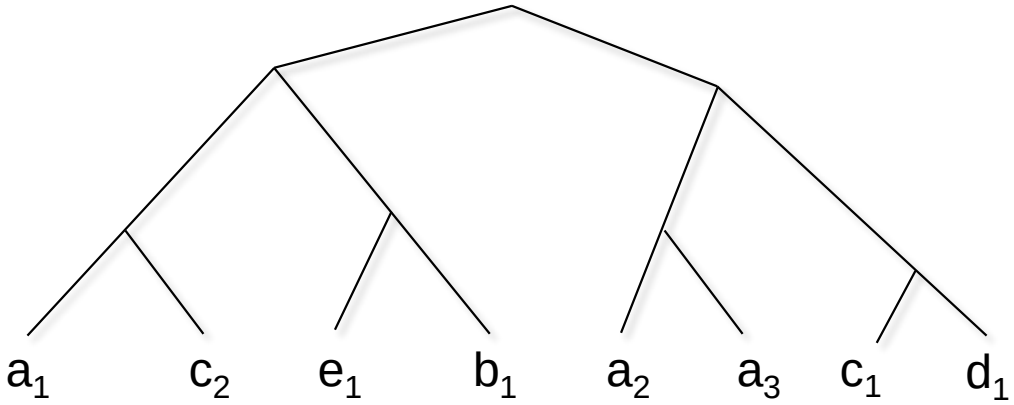

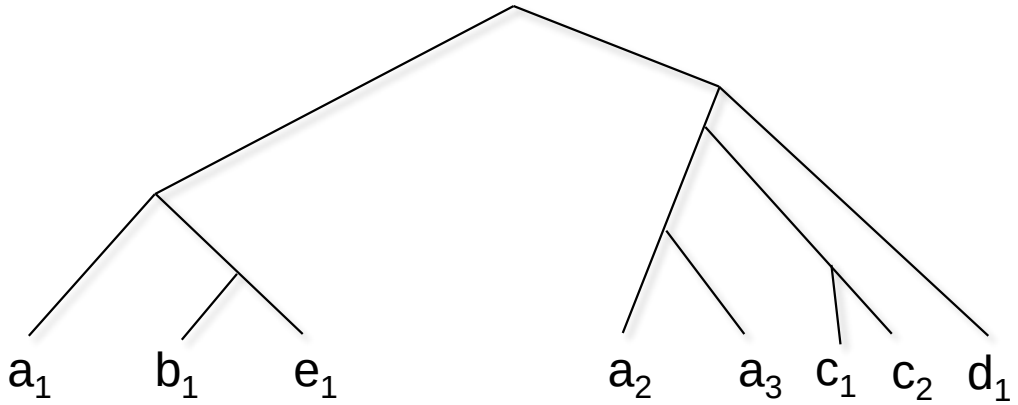

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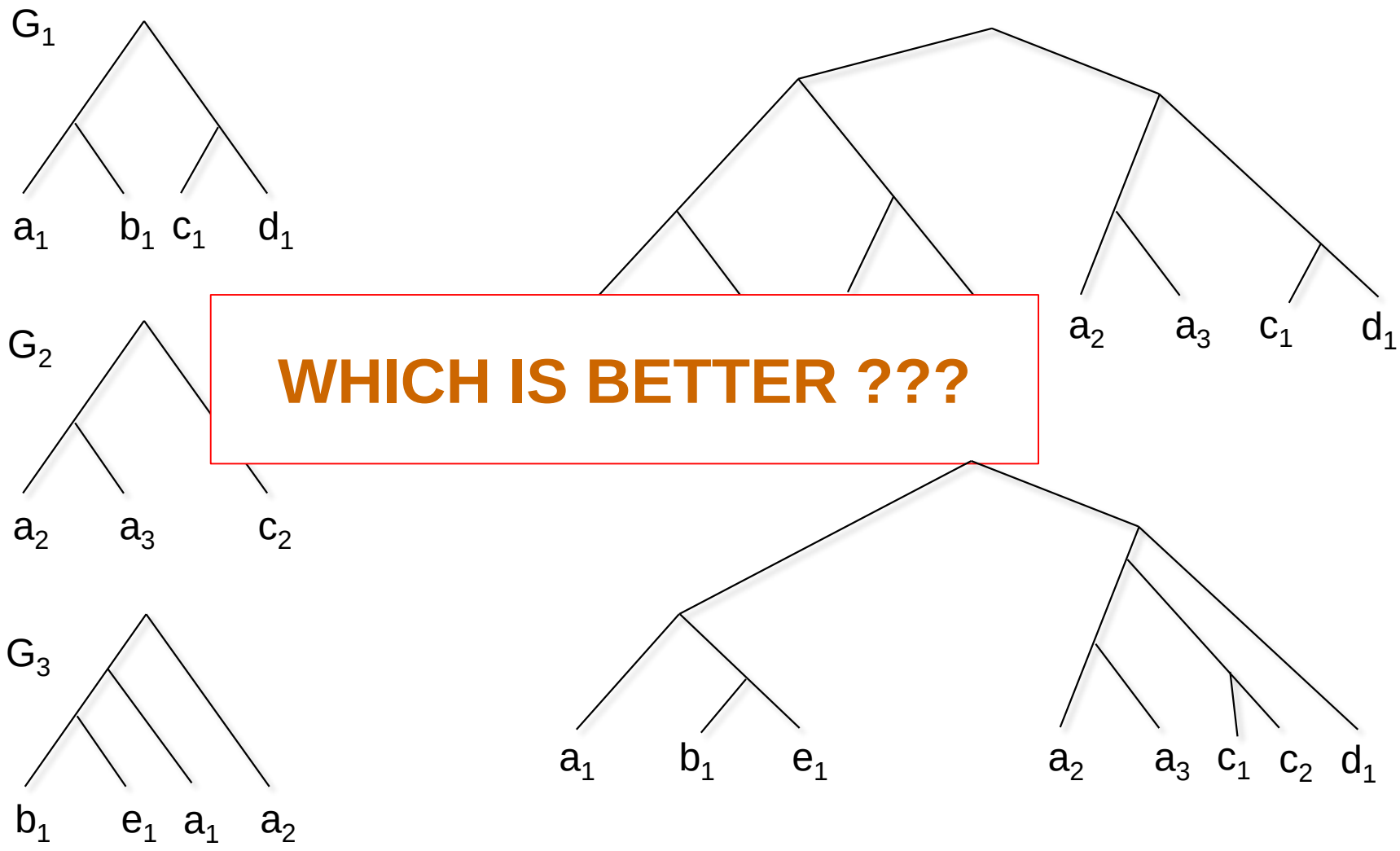

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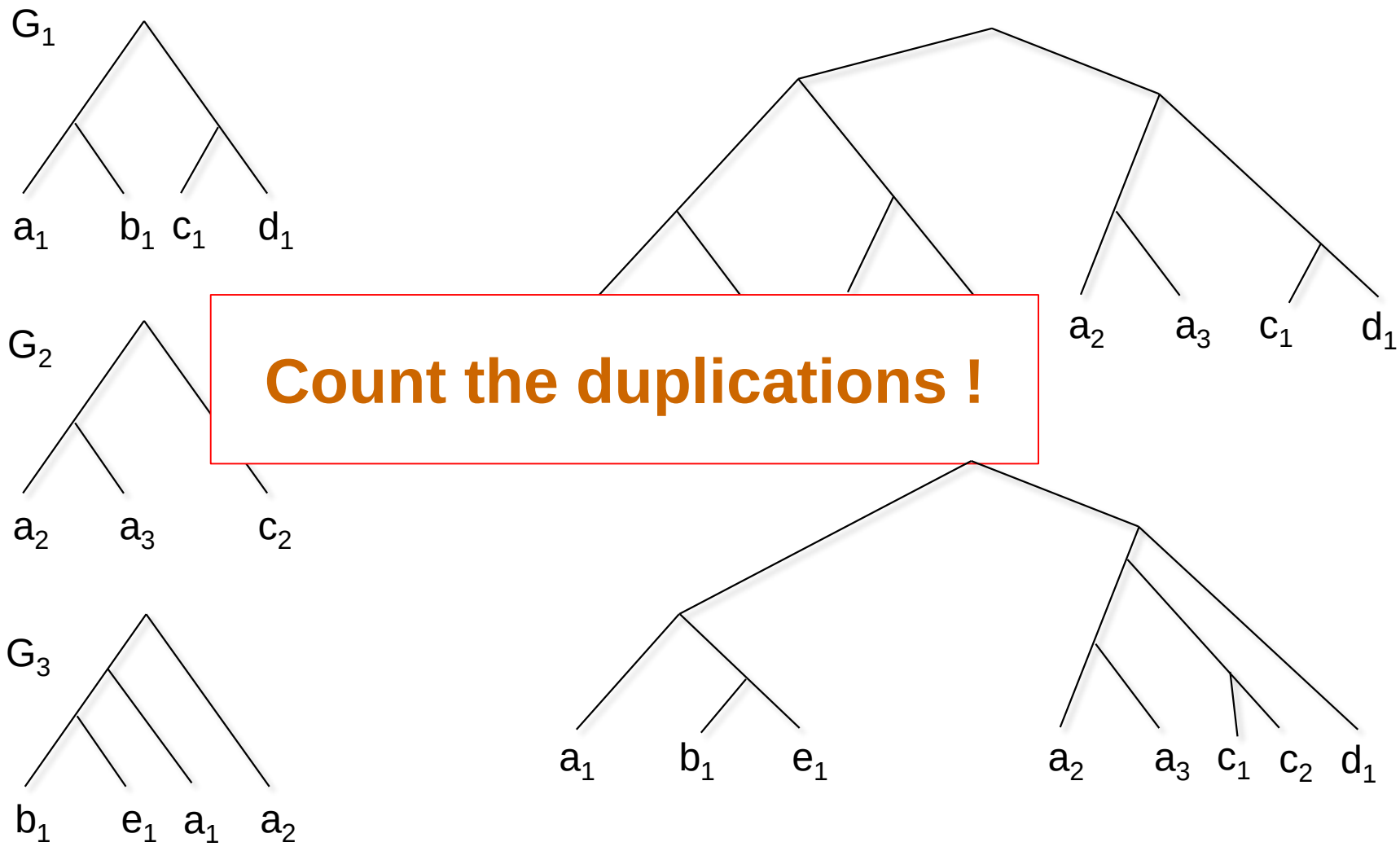

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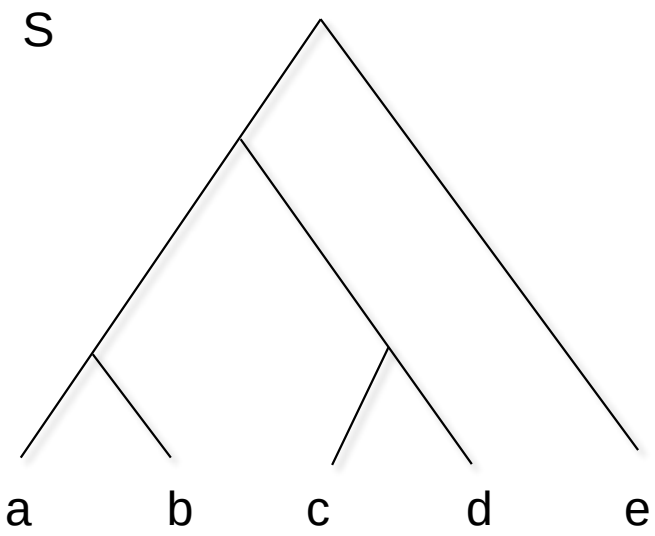
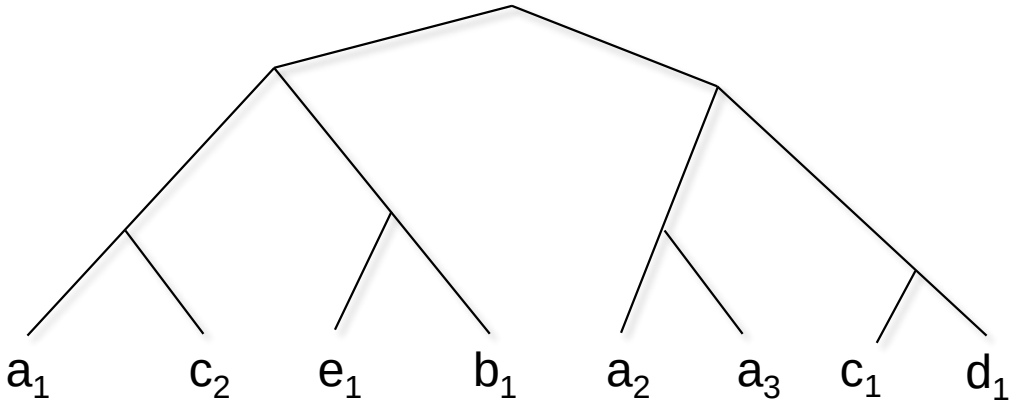
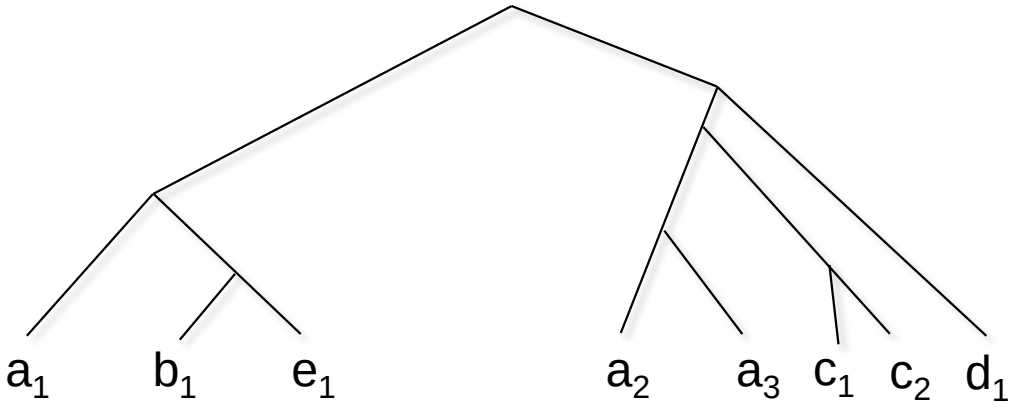
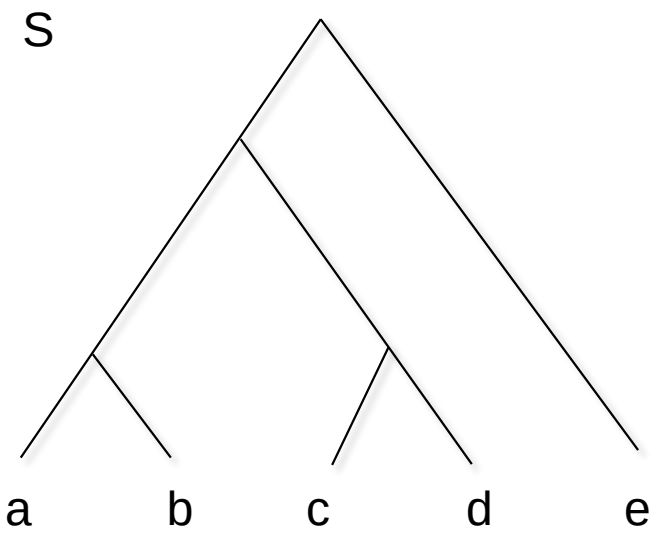
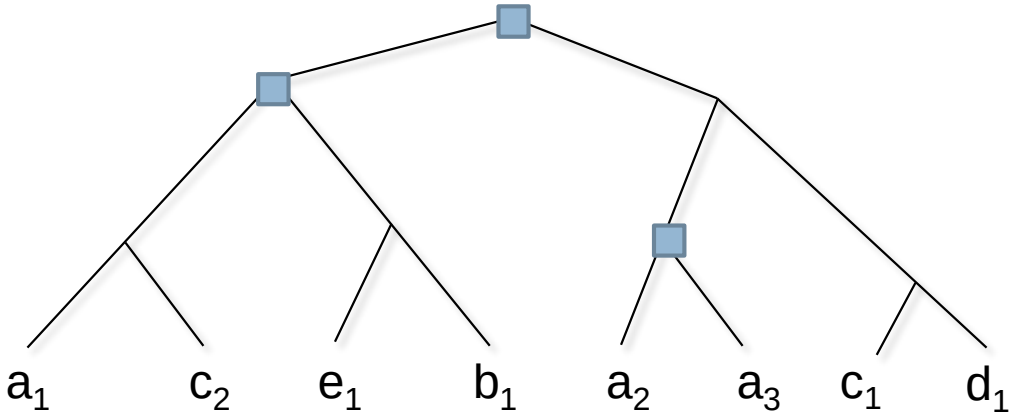


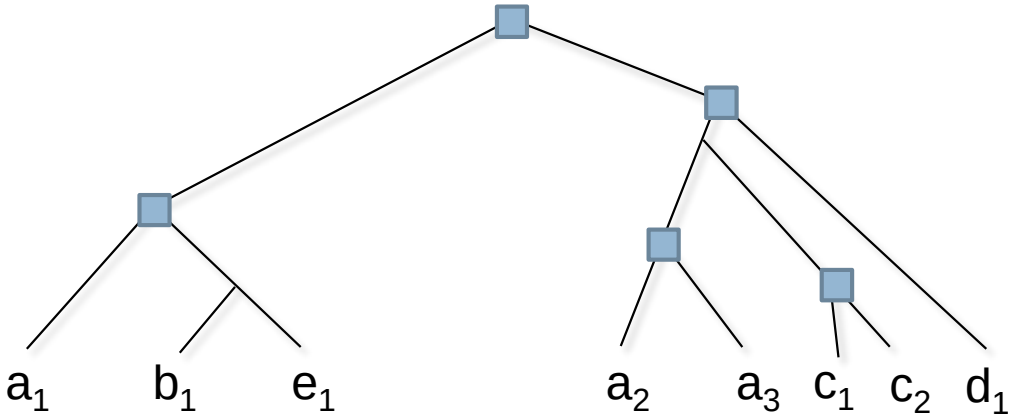




The Supergenetree problem







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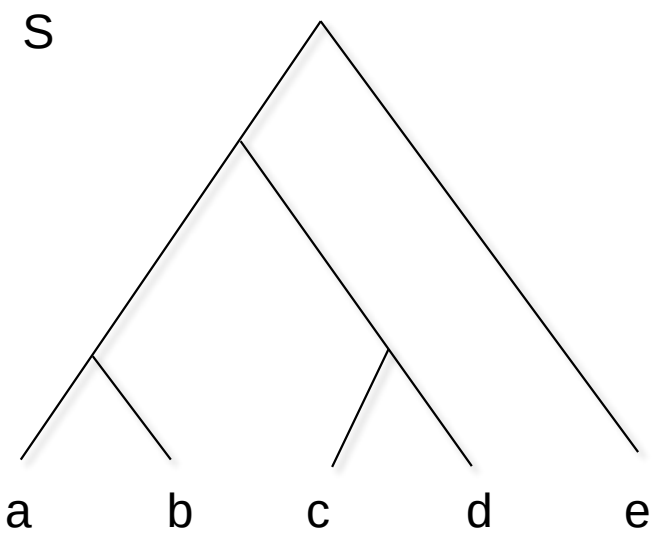

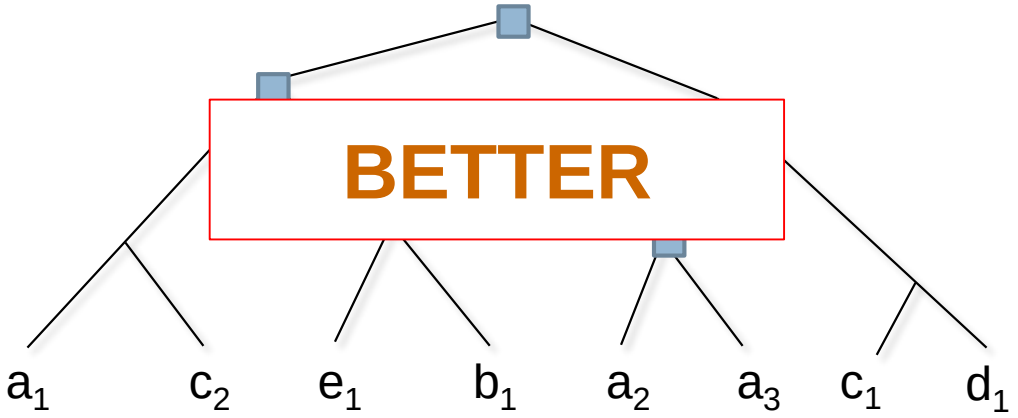

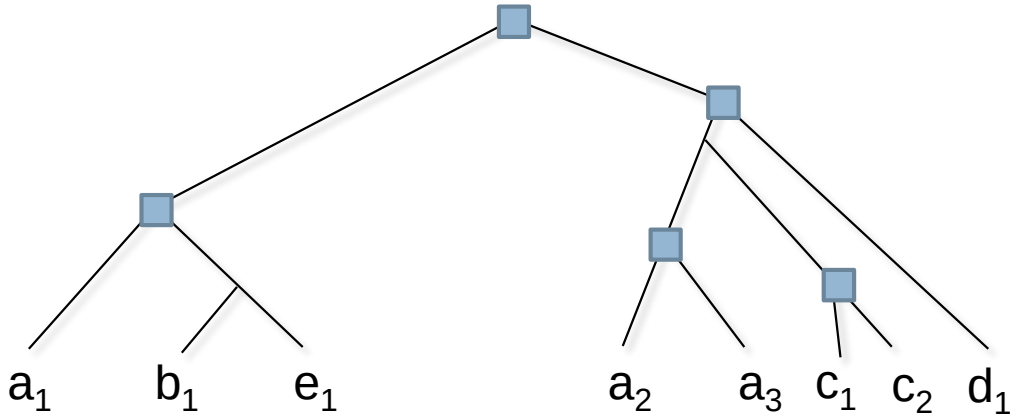

The plan

In this talk I…

- …come up with supertree problems
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- …convince you that they're hard
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SuperGeneTree Problem 1

- **Given:** a set of compatible gene trees $G = \{G_1, \ldots, G_k\}$ and a species tree S
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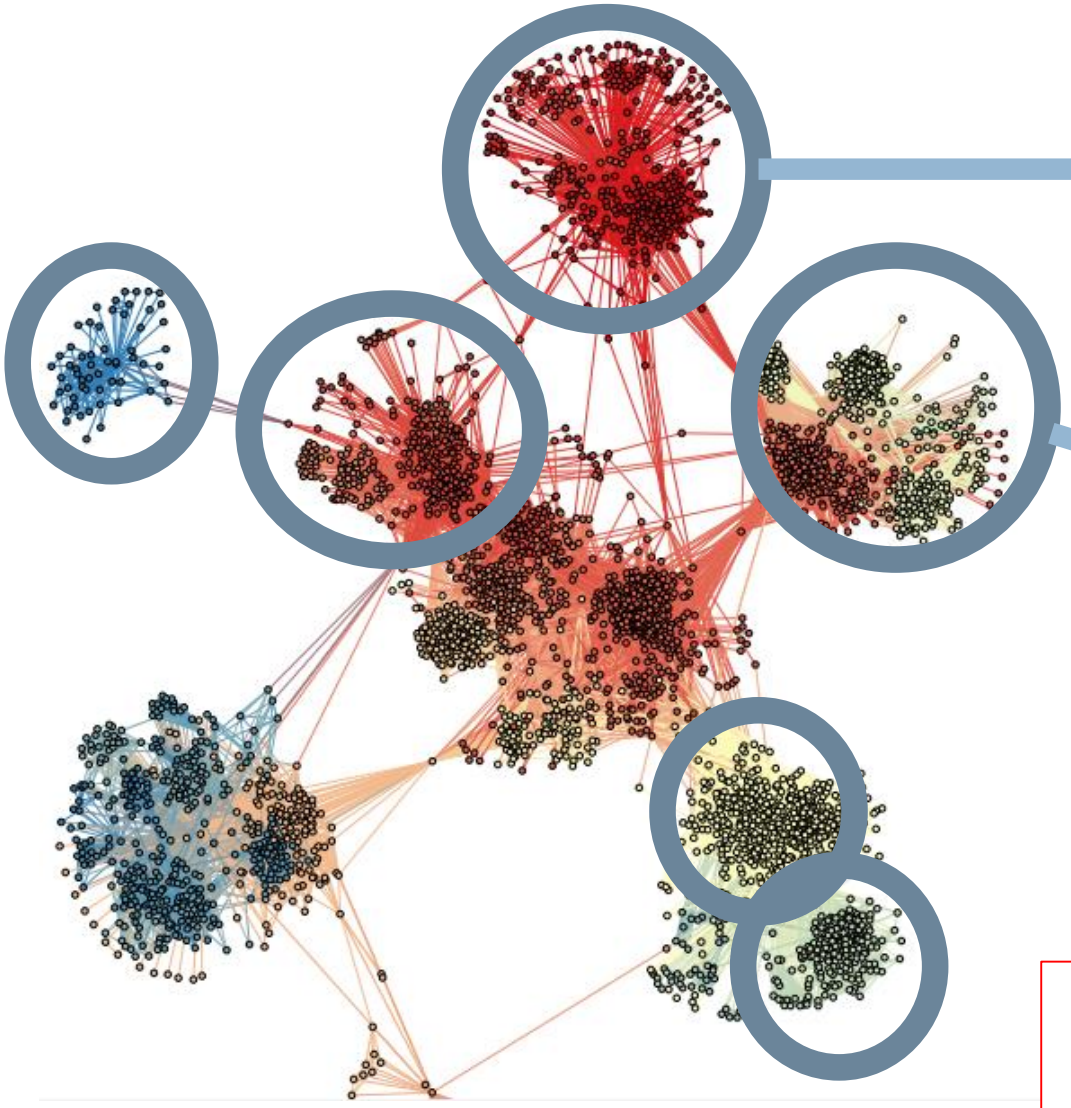
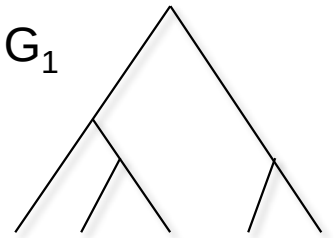
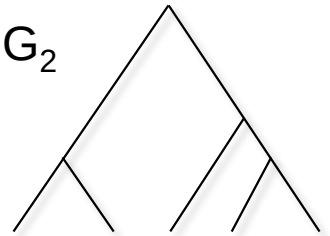
- NP-Hard to approximate within a $n^{1-\varepsilon}$ factor

Independent speciation trees







■ ■ ■

No two trees share a common gene + all trees of orthologous groups

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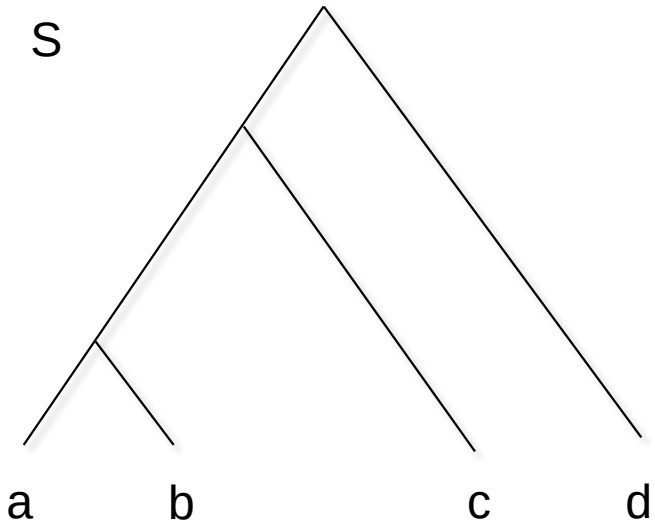

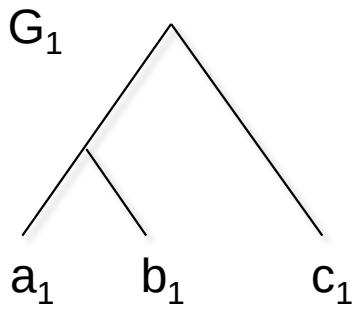

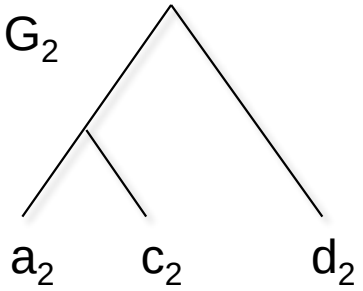

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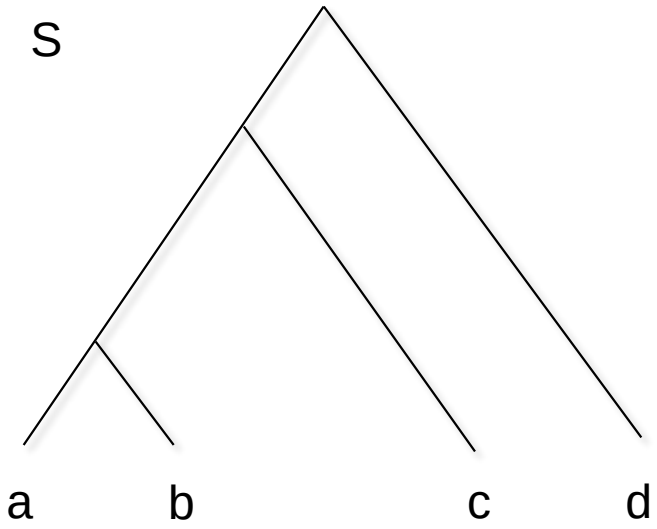
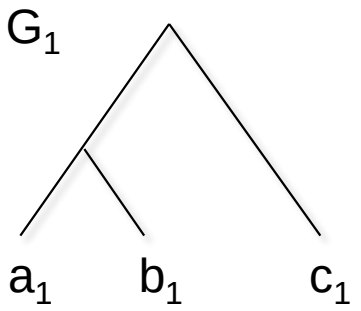
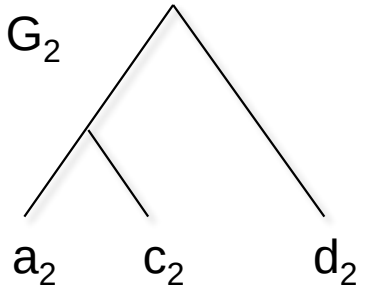
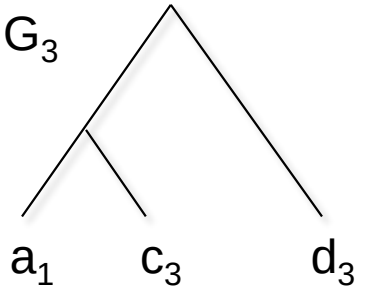
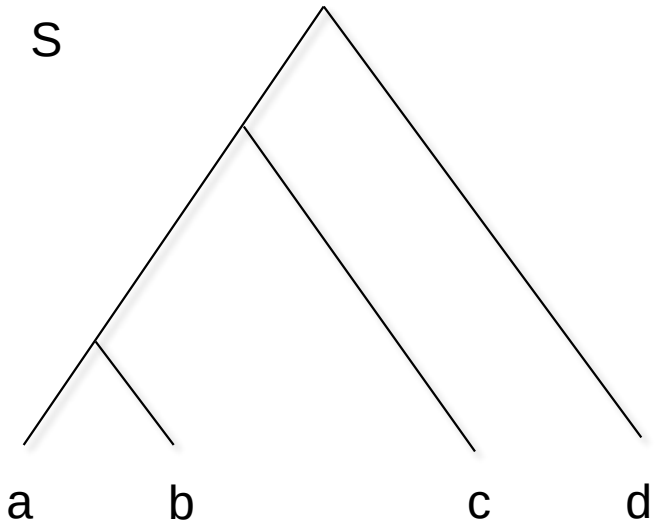


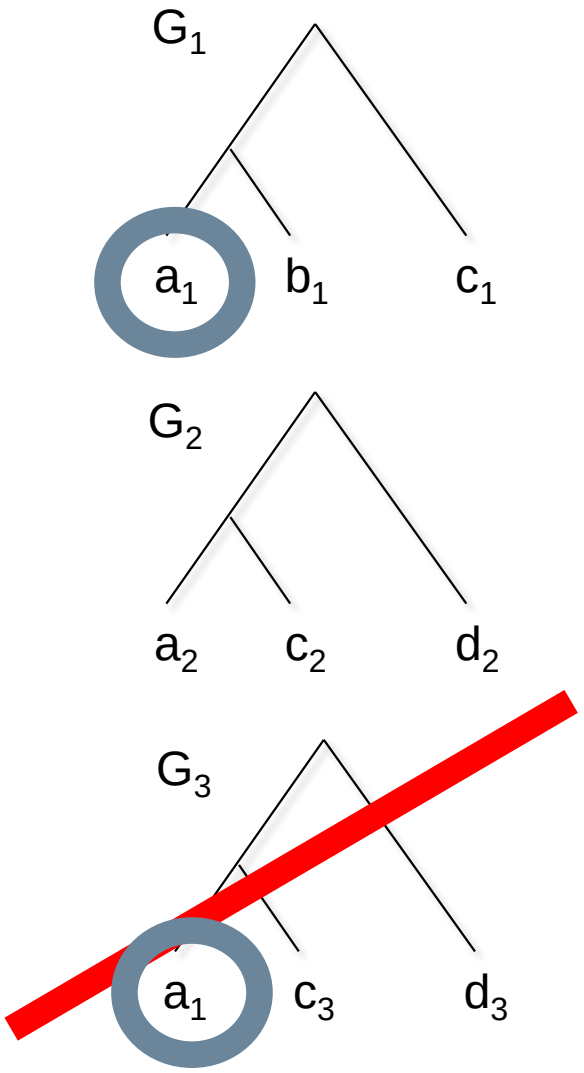






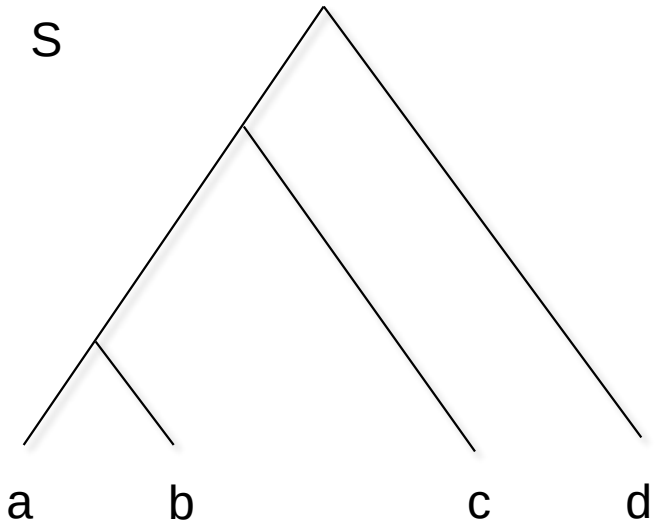
Independent speciation trees

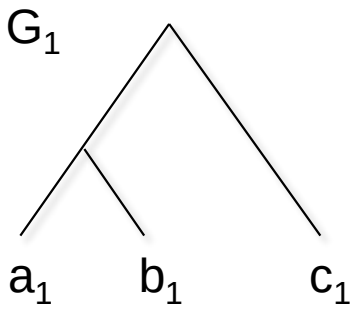


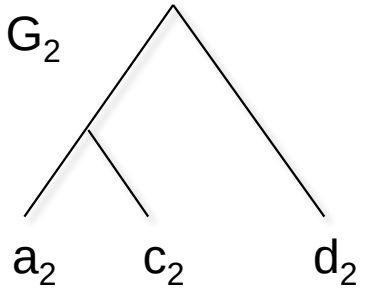


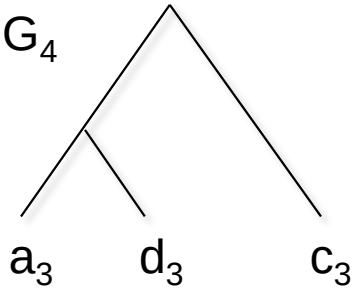
Independent = each gene appears only once

Independent speciation trees









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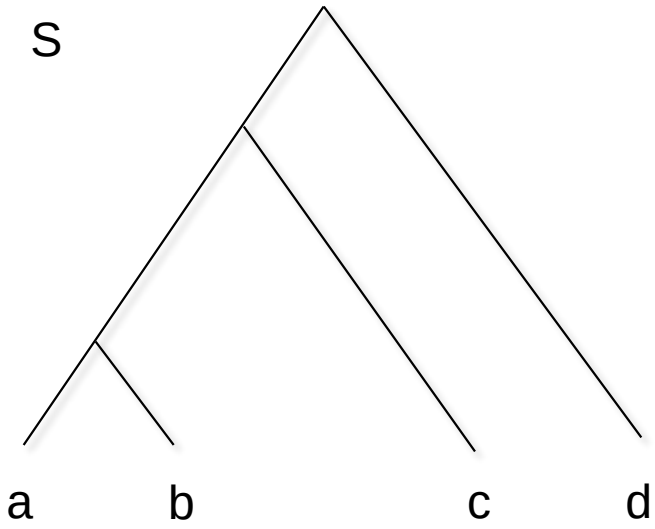

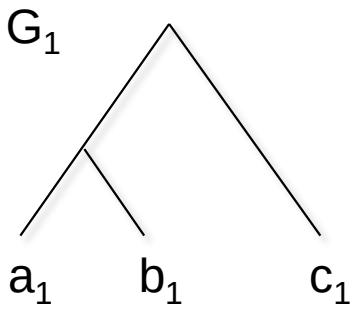

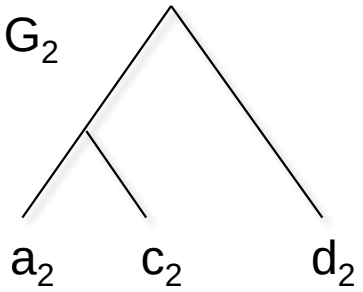

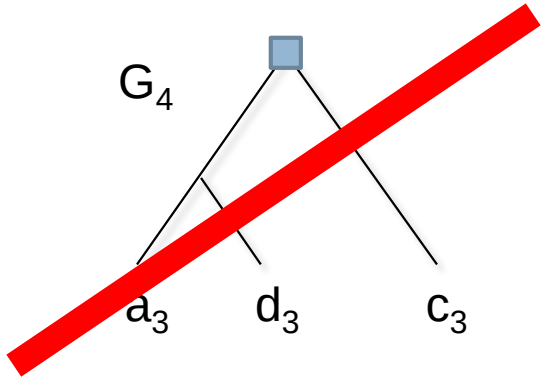

Speciation trees = all speciation (all agree with S)

SuperGeneTree Problem 2

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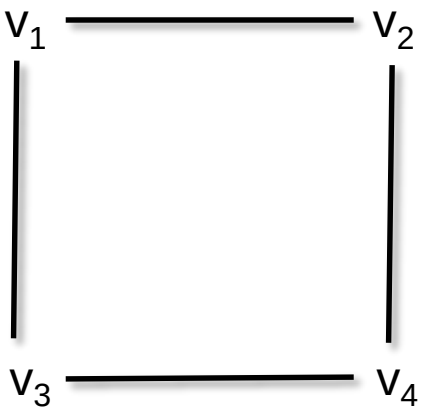

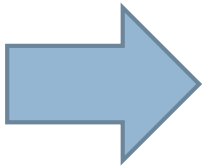

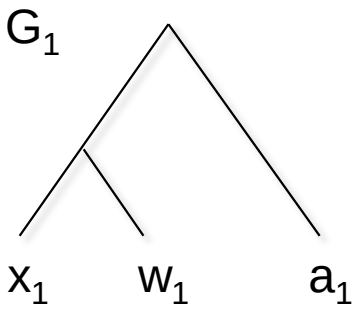

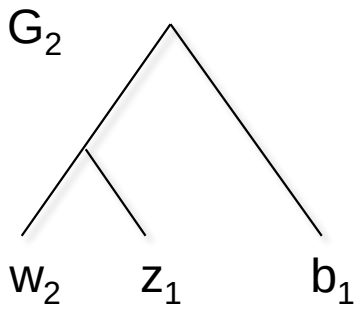

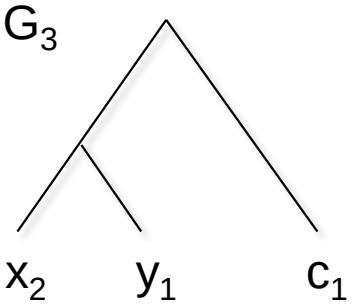

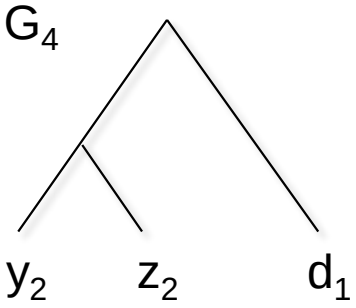

We will find a vertex-coloring of our graph

(a partition into independent sets)

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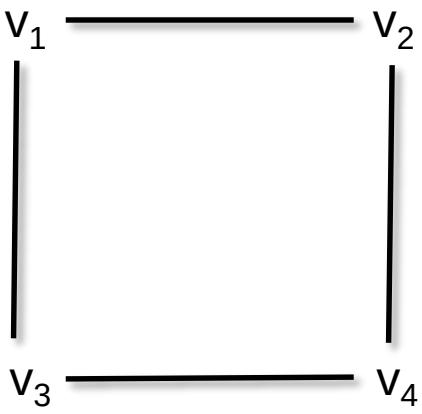

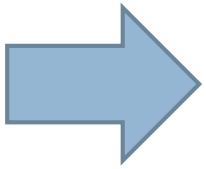

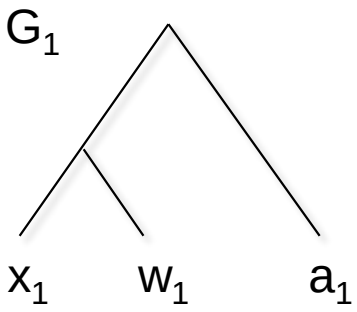

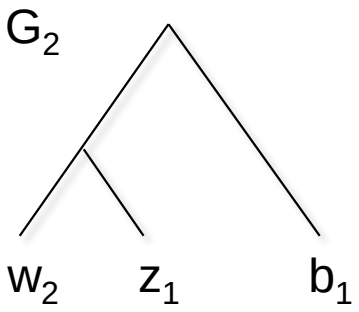

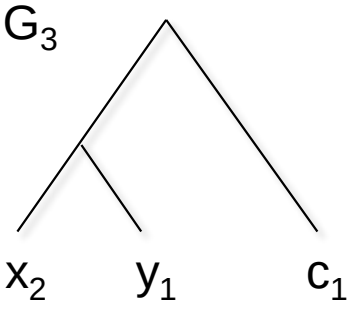

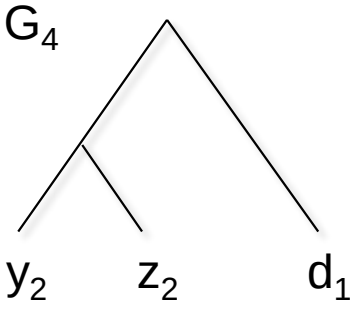

G_i, G_j **share a gene from the same species (i.e. a label)** iff v_i, v_j **share an edge**

⇔

G_i, G_j can be merged into a supertree **without duplications** iff v_i, v_j **share no edge**

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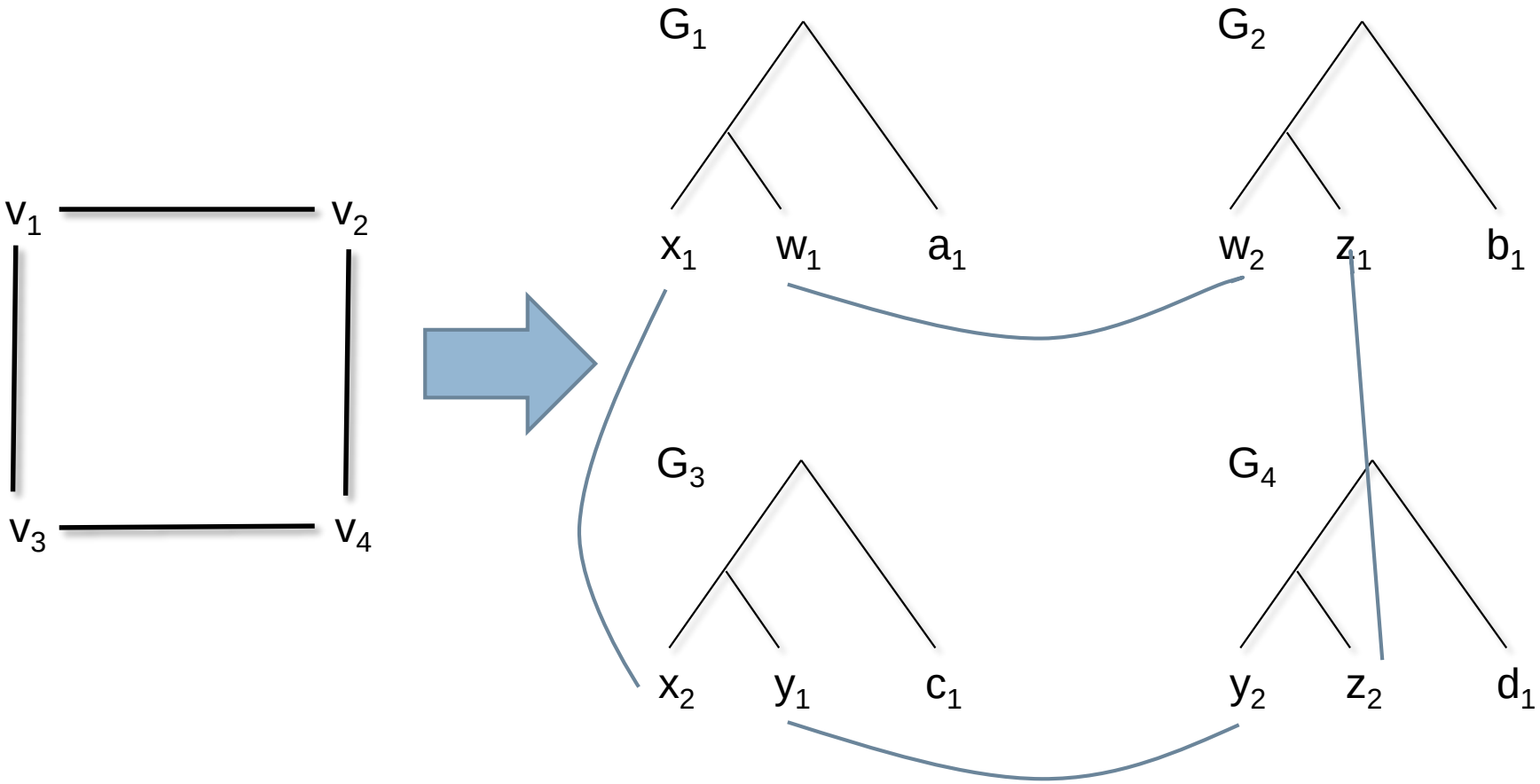

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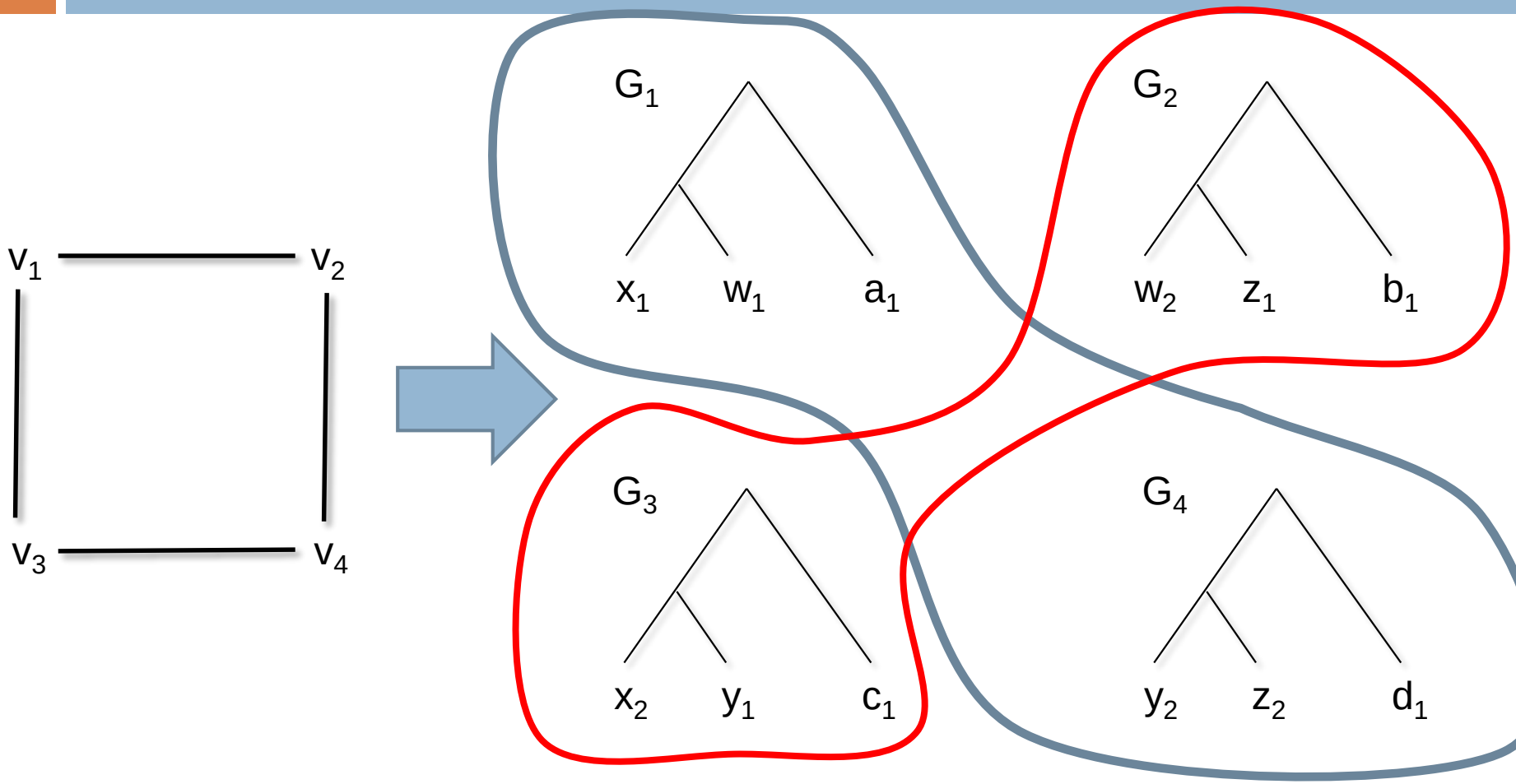

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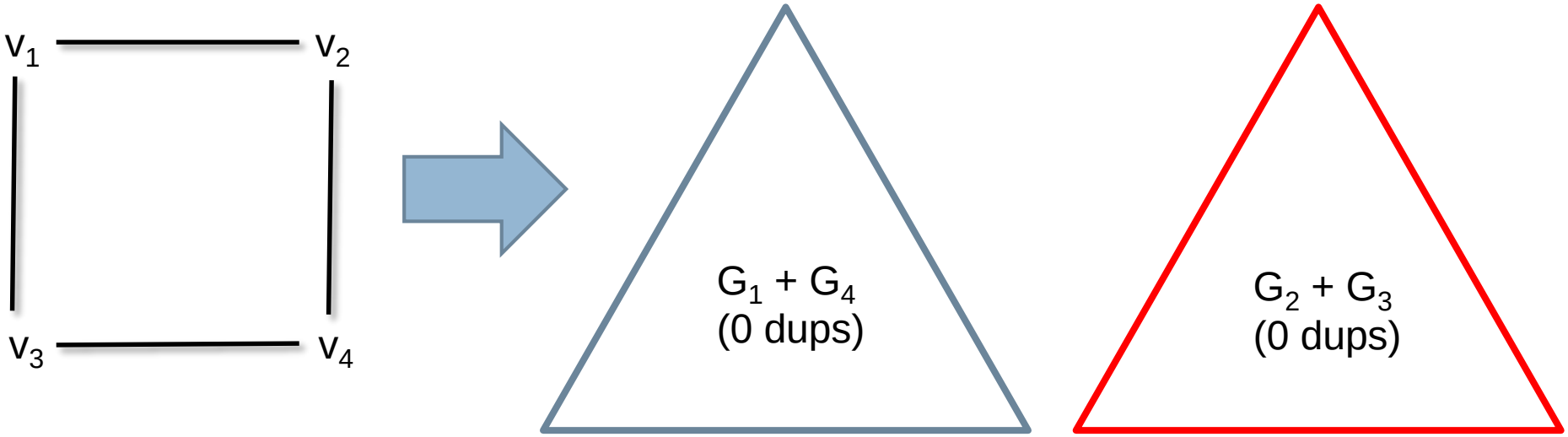

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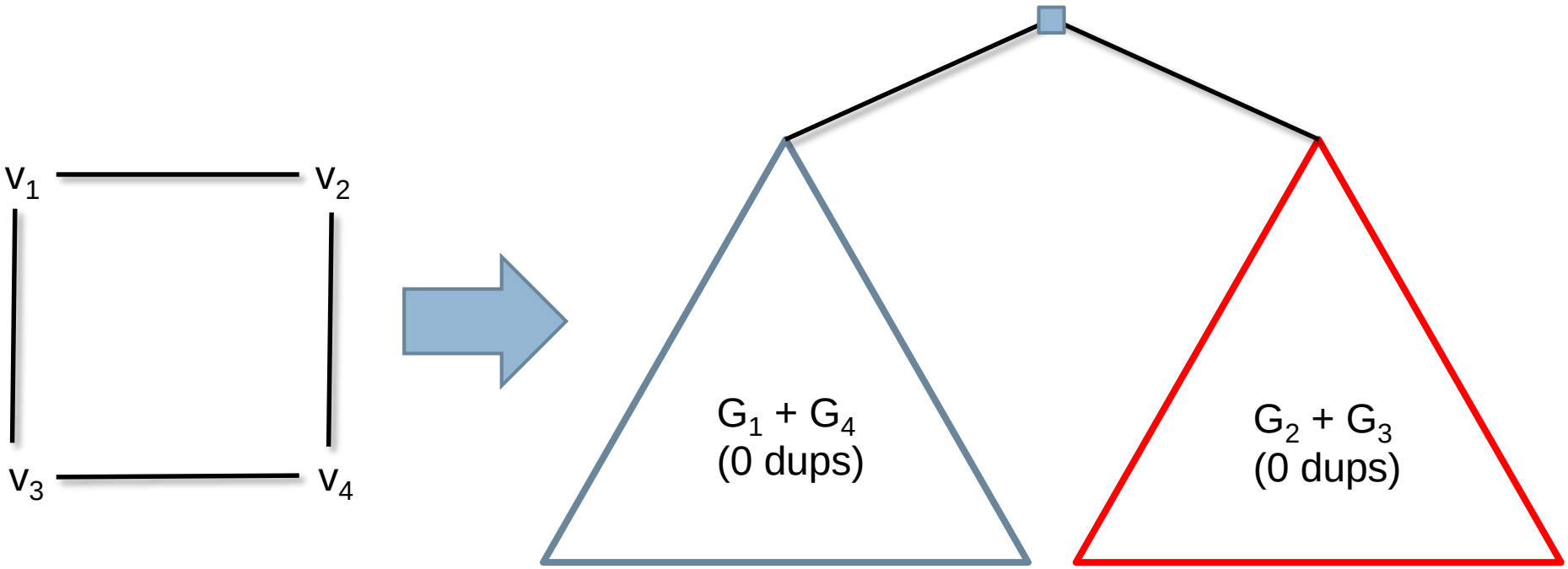

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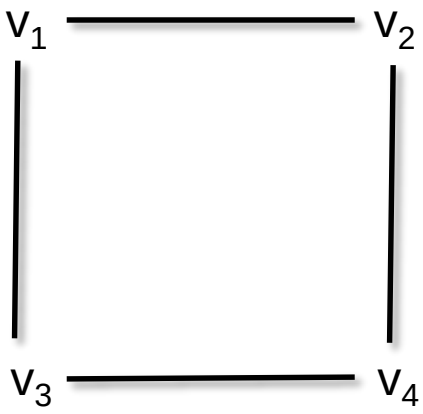

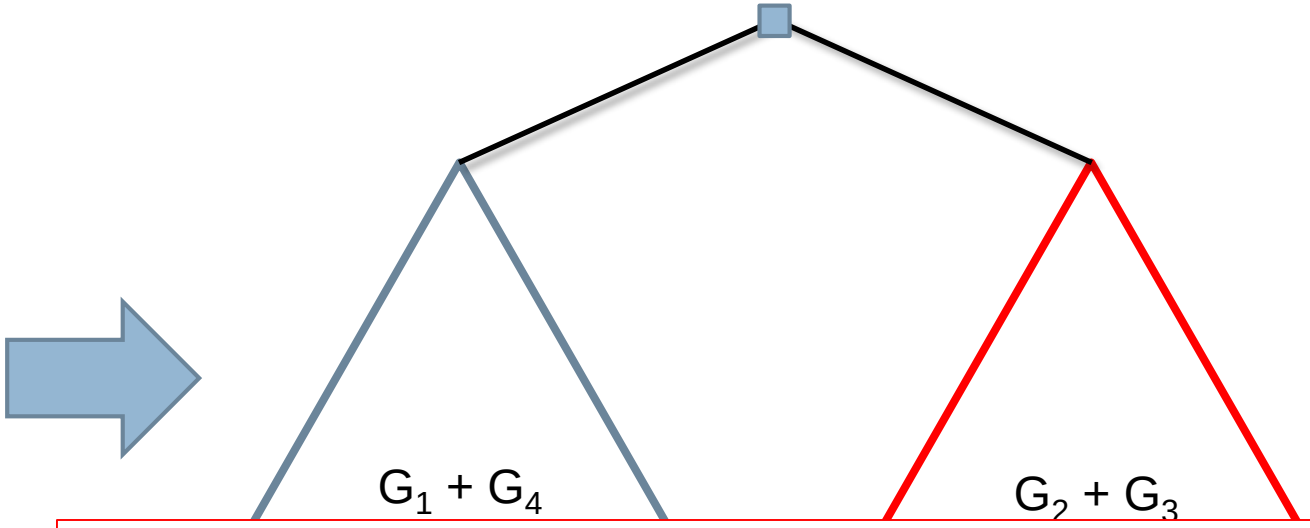

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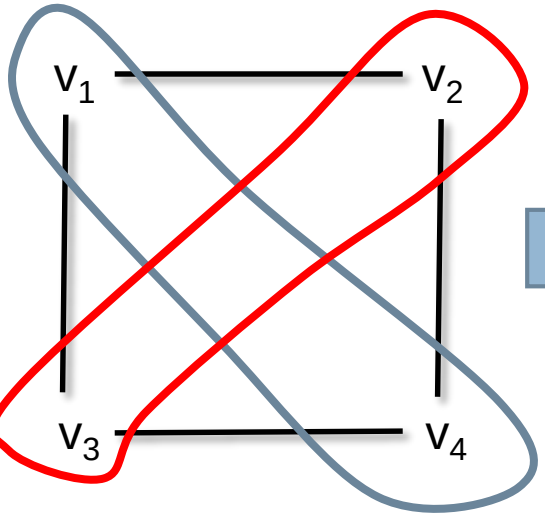

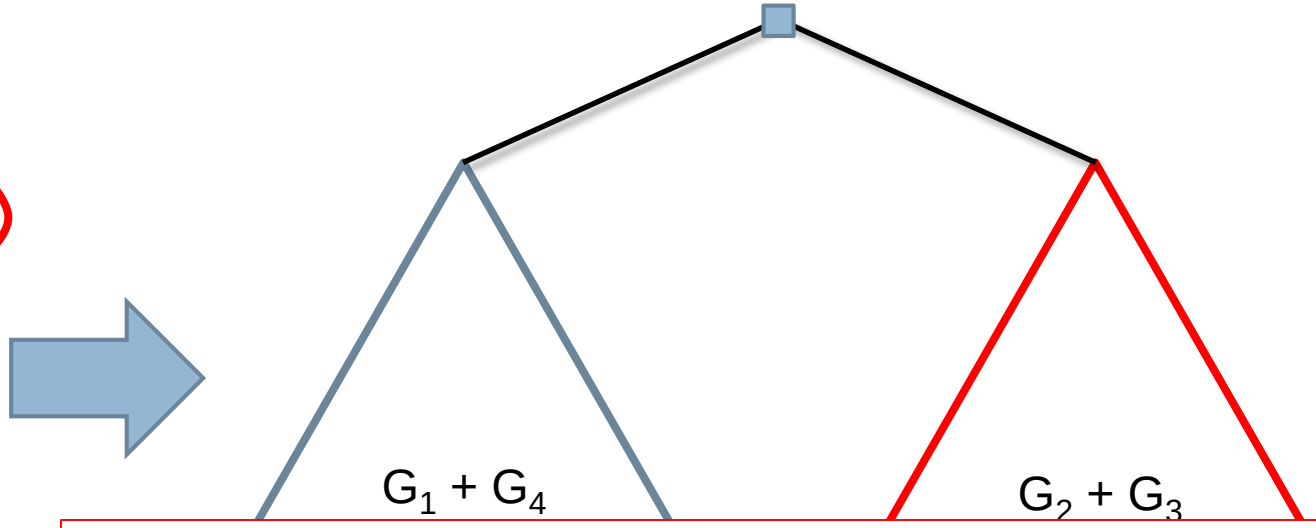

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  - Finding a supergenetree that minimizes duplications
- …convince you that they're hard
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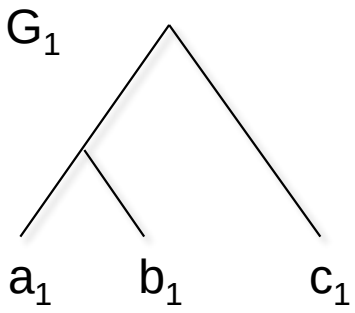
  - Exact, brute-force algorithm
  - A greedy heuristic

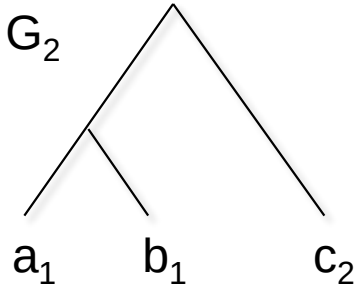
Extending the BUILD algorithm

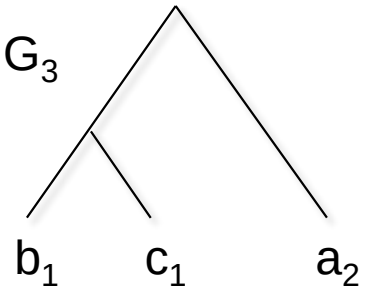
- Given a set of trees G, the BUILD algorithm outputs, if it exists, a supertree T displaying every tree of G
  - T might be partially resolved (non-binary)
  - Every binary resolution of T displays G

- BUILD can be extended to output **every** supertree displaying G + every minimally resolved *(Constantinescu & Sankoff, 1995, Ng & Wormald, 1996, Semple, 2003)*

Extending the BUILD algorithm



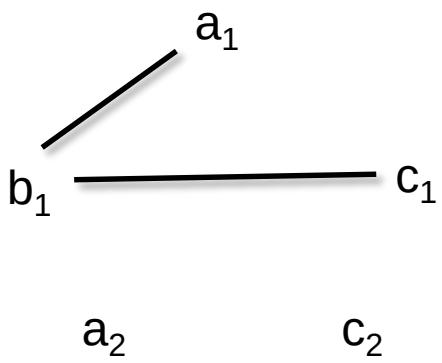




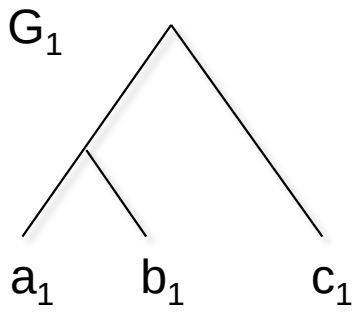
BUILD graph

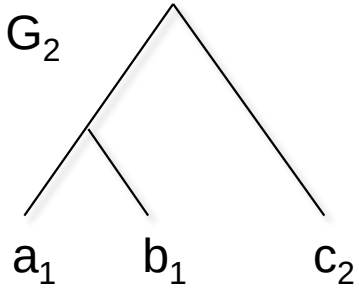
vertices = genes

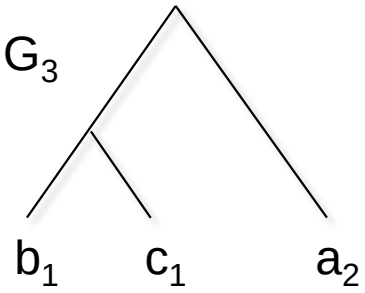
edges = genes together in some triplet



Extending the BUILD algorithm







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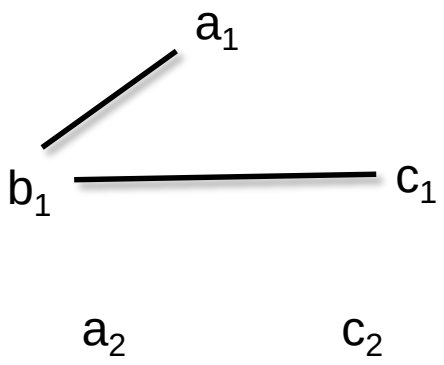
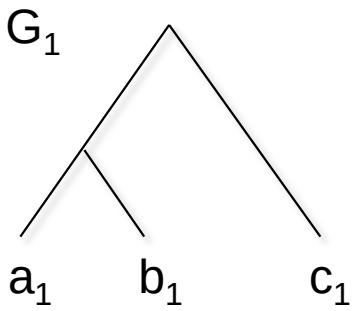
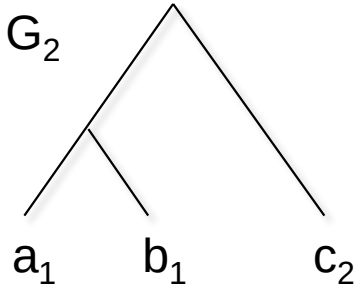
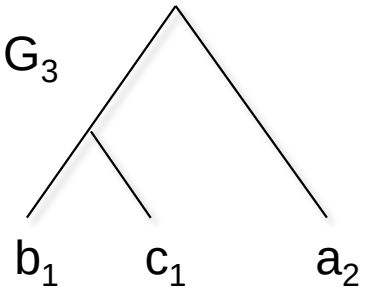


Partition of connected components = possible splits at the root

Extending the BUILD algorithm







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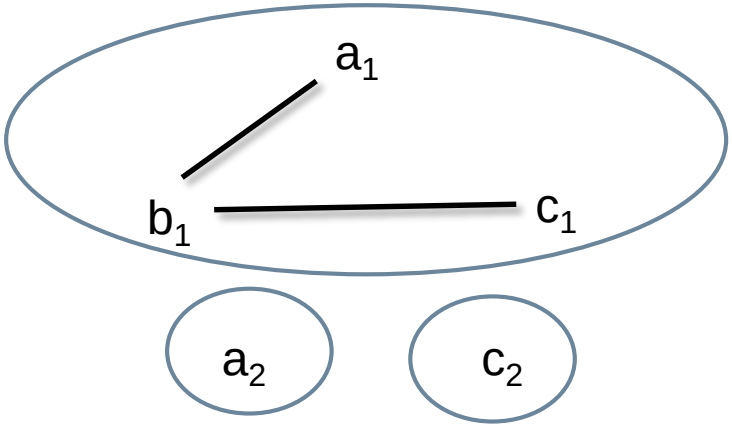

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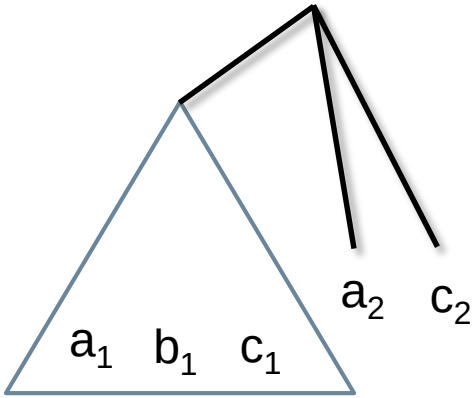

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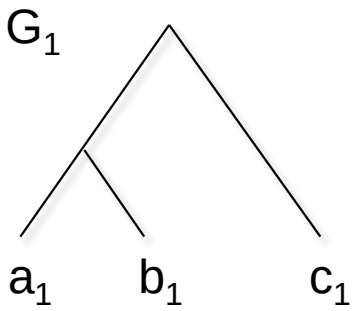

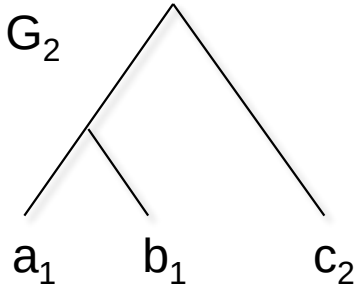

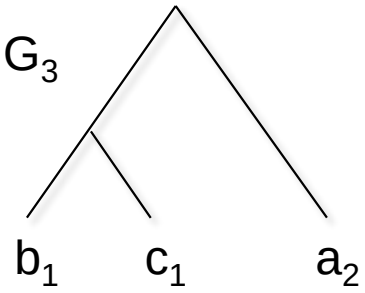

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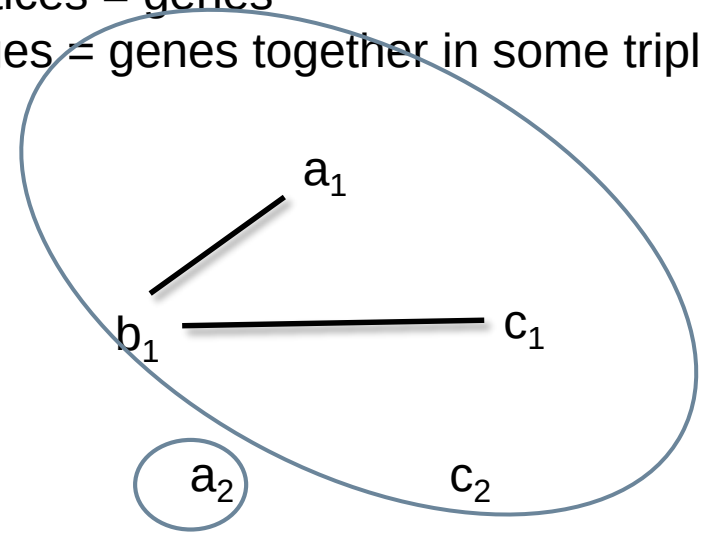

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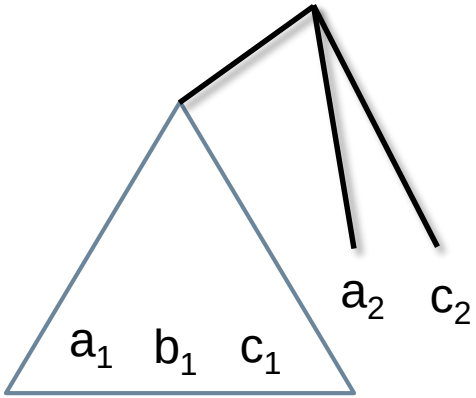

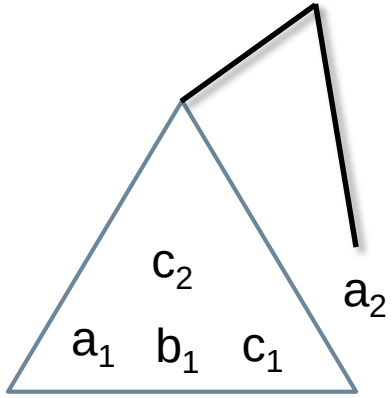

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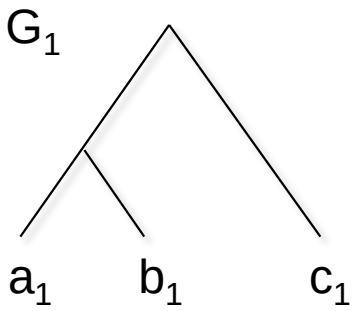

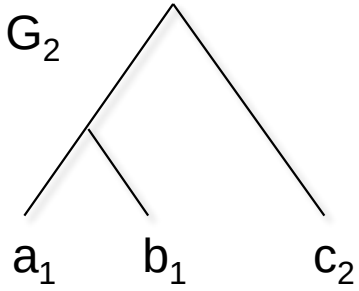

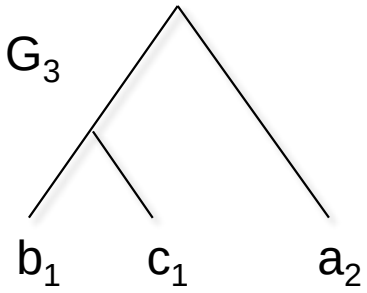

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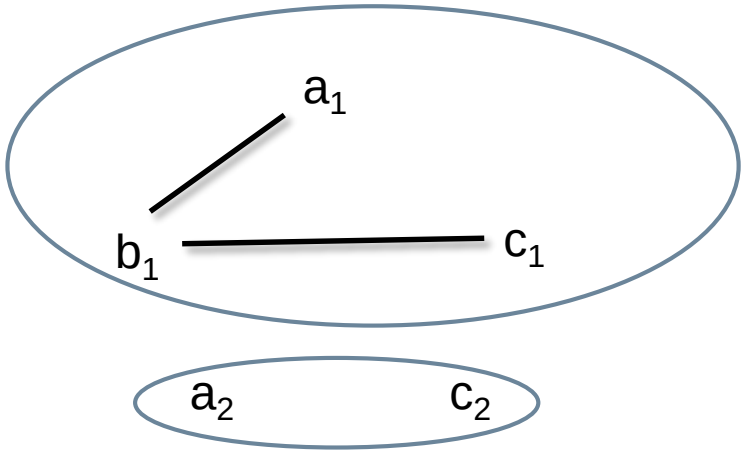

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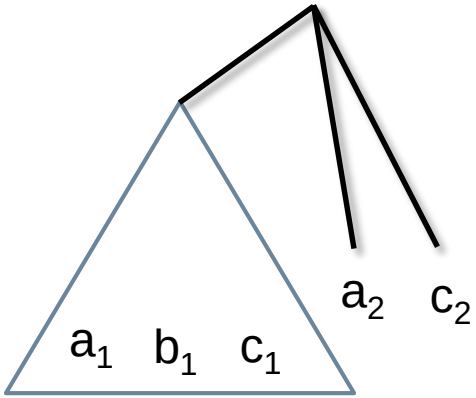
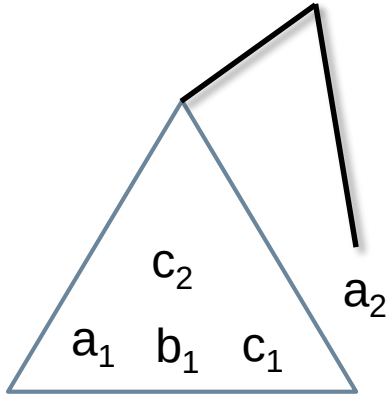




...

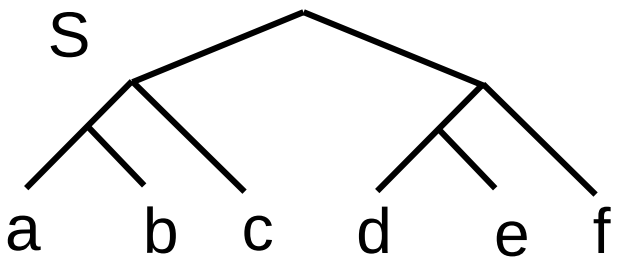
Extending the BUILD algorithm

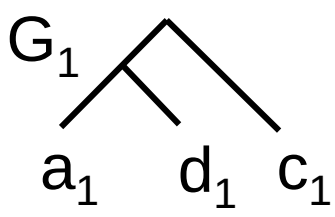
- For every partially unresolved tree T obtained in this fashion :
  - Find a resolution that minimizes the number of duplications *(linear time, Lafond & al. 2012)*
- In the worst case, there are $\Omega(n^{n/2})$ trees to resolve *(Jansson, Lemence, Lingas, 2012)*.
  - Total time : $\Omega(n * n^{n/2})$
- Worst case in practice : ?

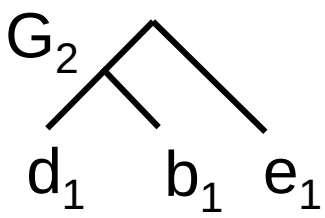
Extending the BUILD algorithm

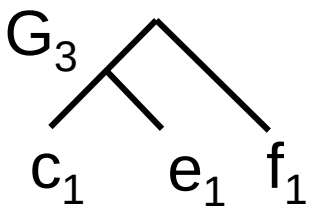
- Trying every partition of the components can take some time.
- Instead, let’s find a way to choose a partition that "looks good".

A greedy approach









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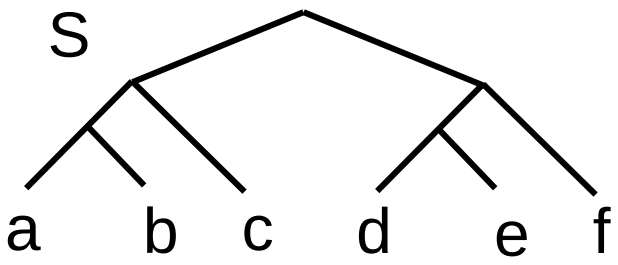
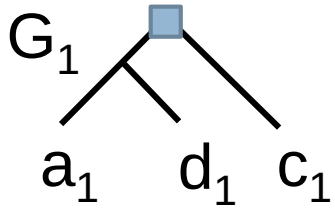
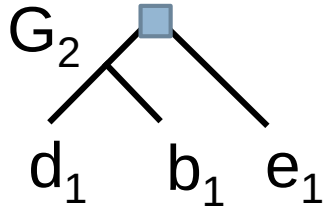
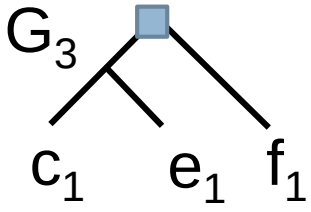


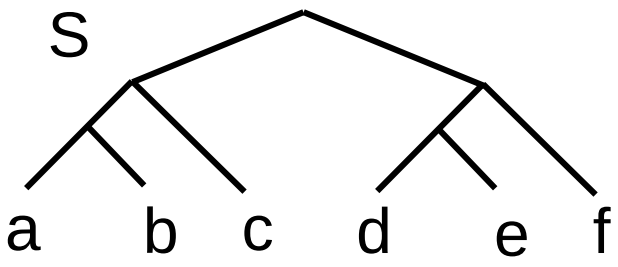


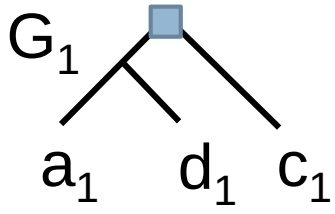


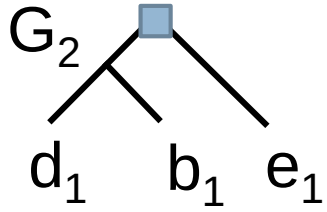


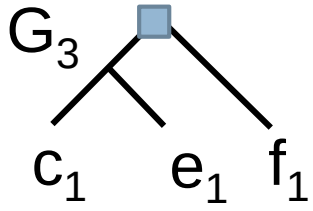
We already know that some duplications will be required.

A greedy approach









We already know that some duplications will be required.
Focus on the "highest" ones, i.e. those that occur before the first speciation in S.

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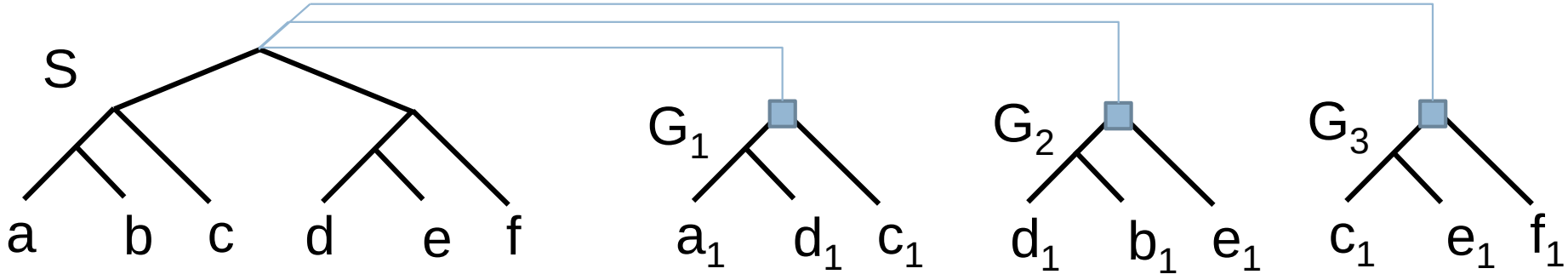

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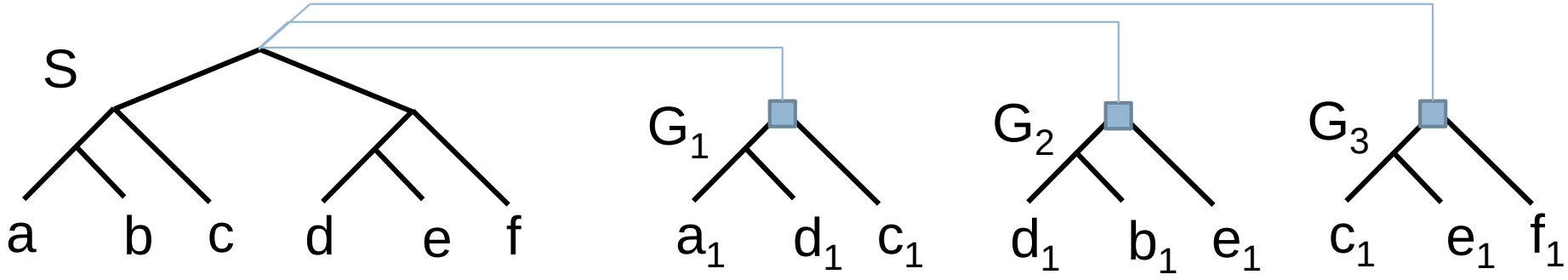

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We call those duplication Pre Speciation Duplications (PreSpecDups).

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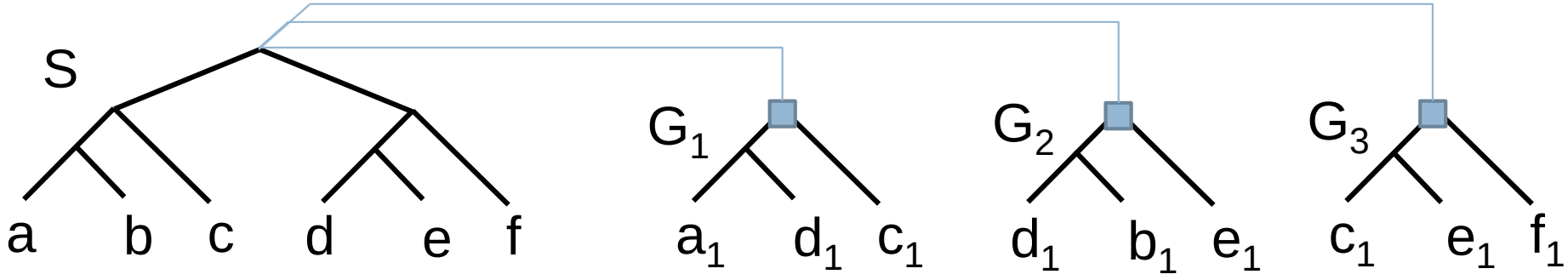

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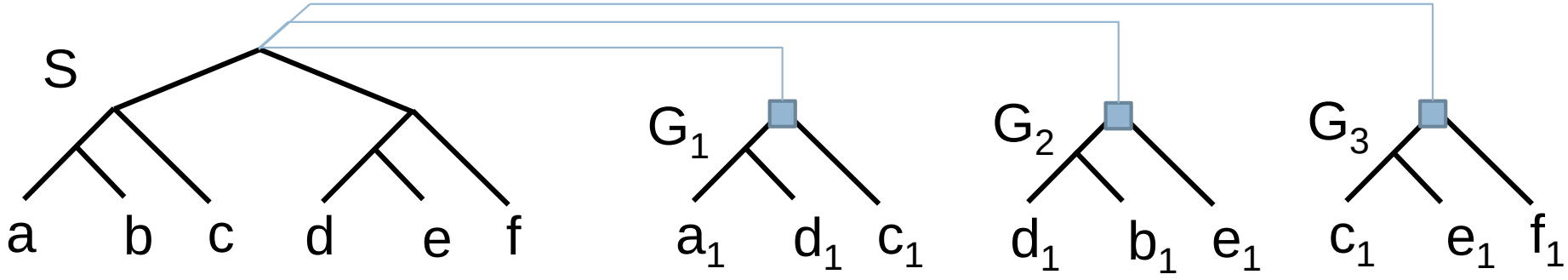
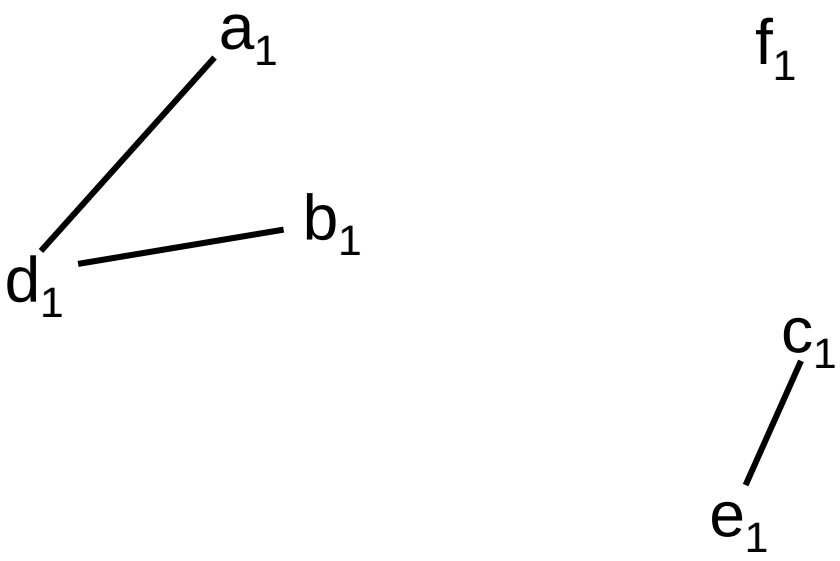
New subproblem : minimize only these PreSpecDups

A greedy approach



- Make the BUILD graph and identify the components.

Γ



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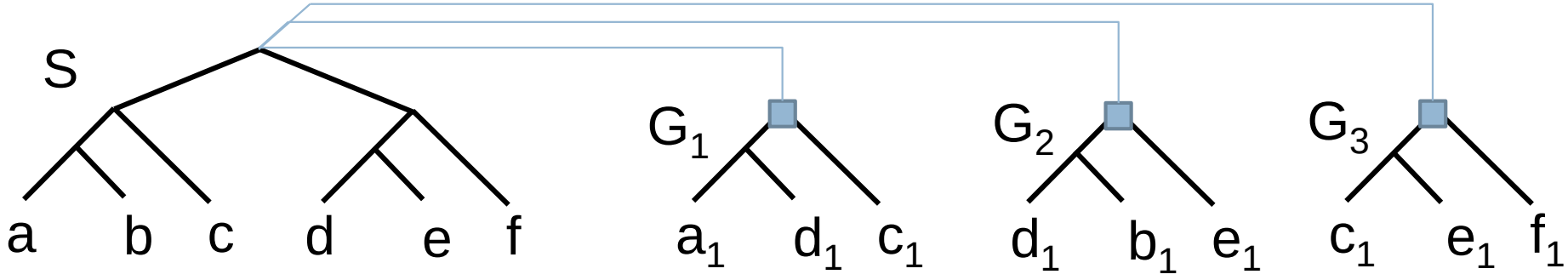
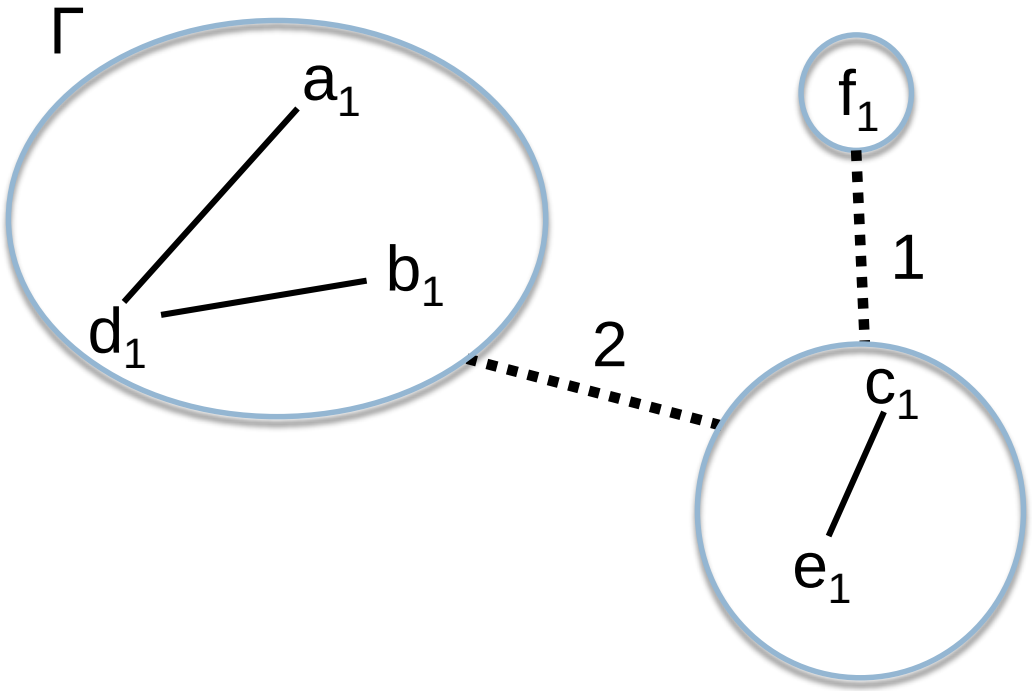
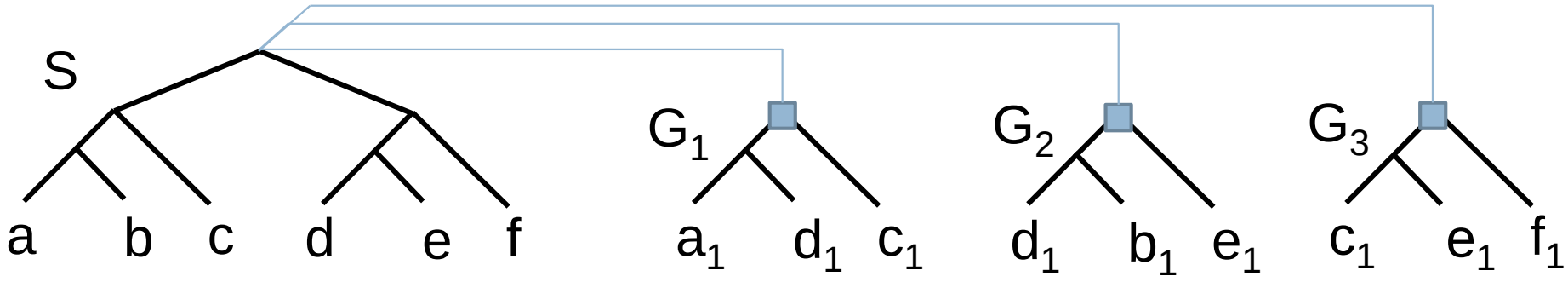
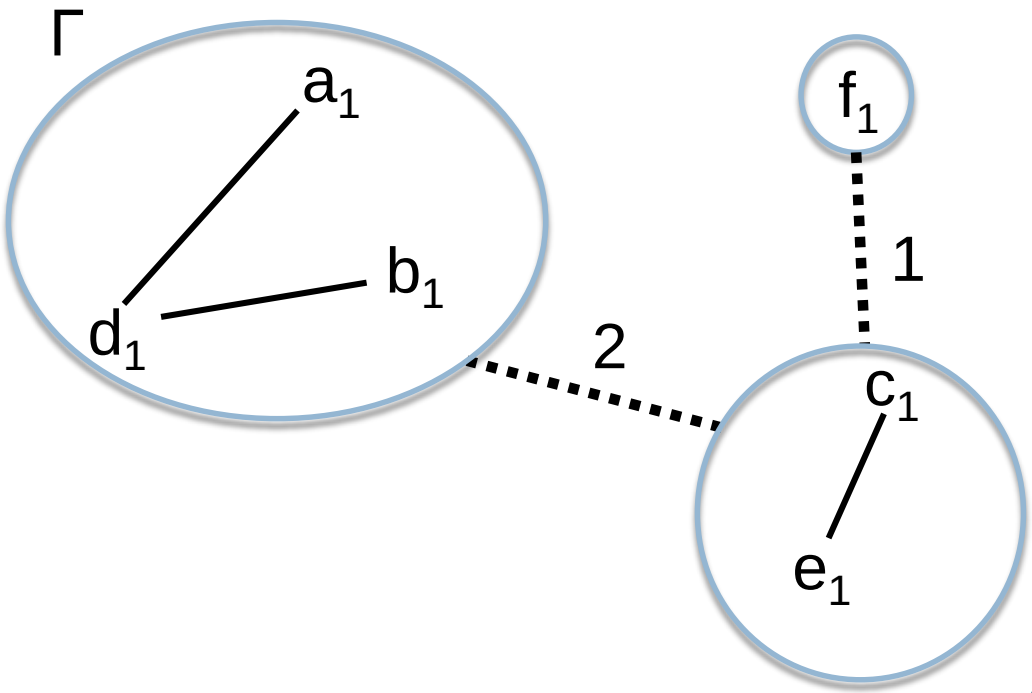




- Make the BUILD graph and identify the components.
- Add a special edge between components that requires a PreSpecDup when split.

A greedy approach





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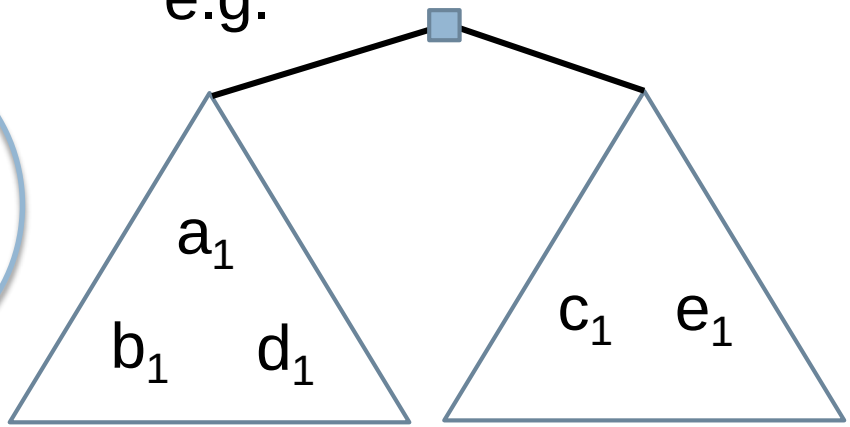
e.g.



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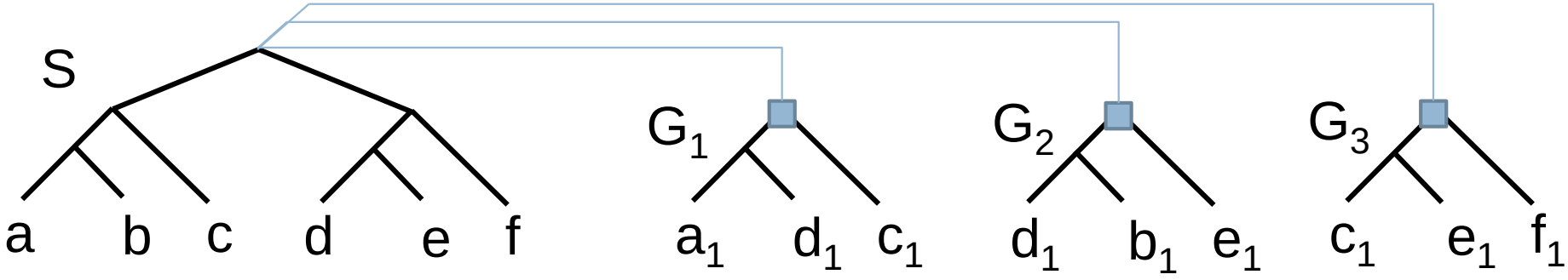

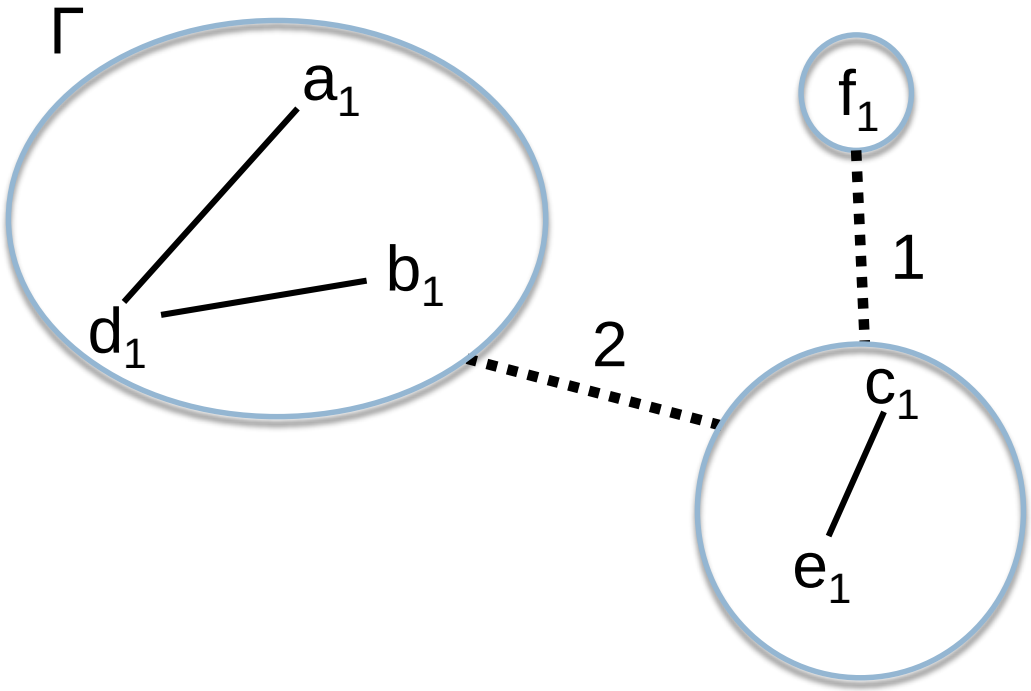

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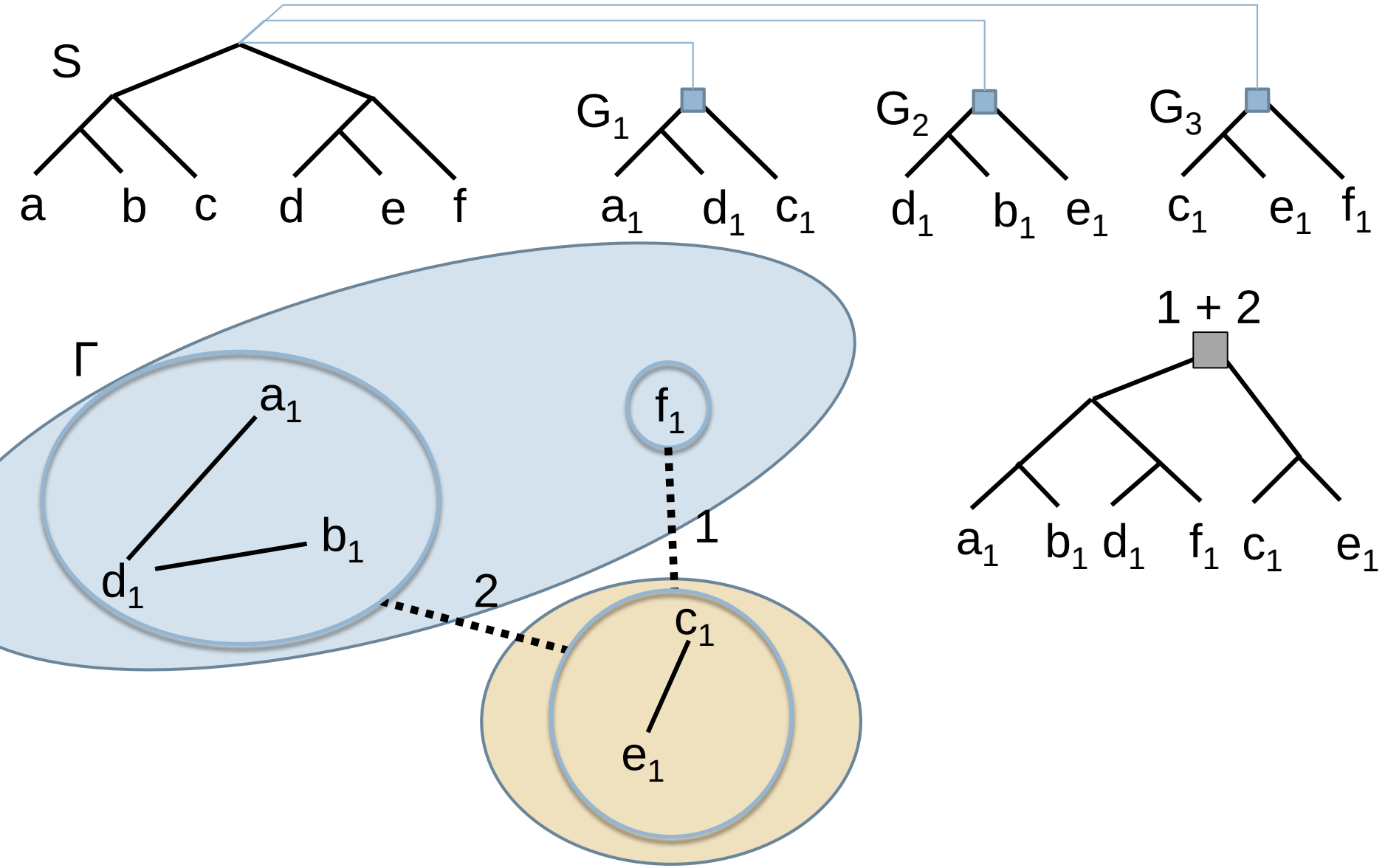
- Find the partition that merges a maximum of duplications.

A greedy approach



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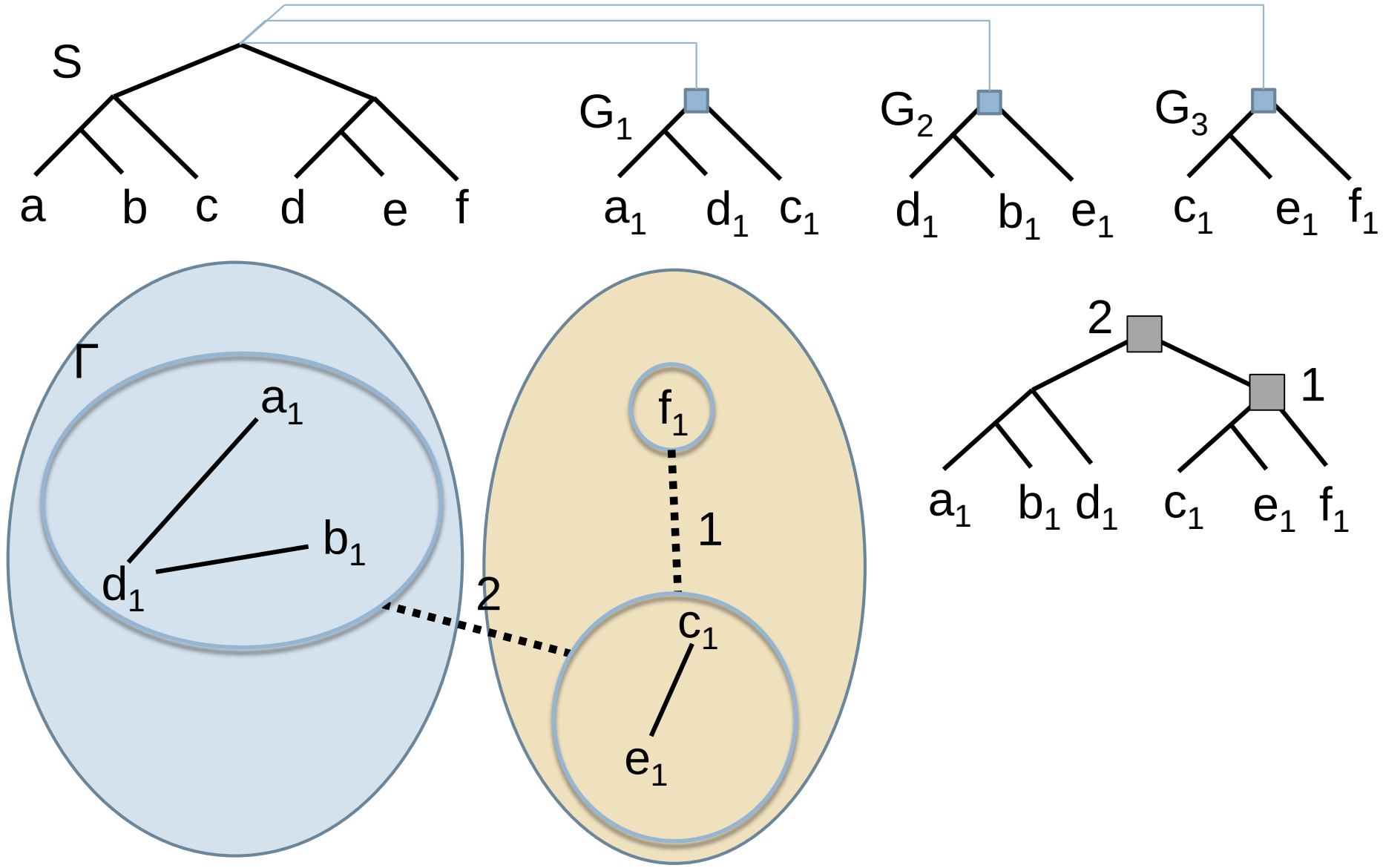

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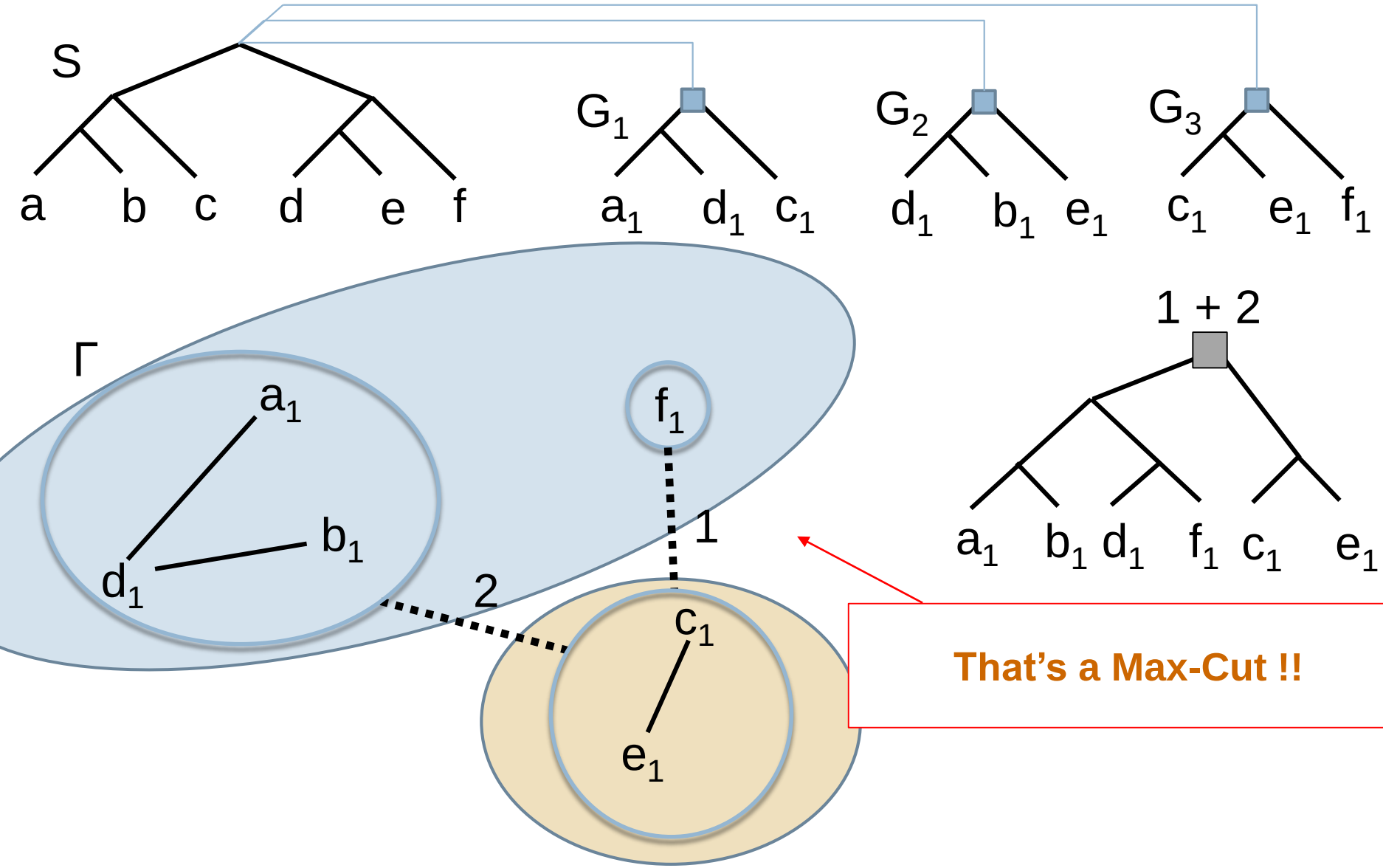

Extending the BUILD algorithm

To minimize the number of PreSpecDups :

- Make the BUILD graph
- Add the PreSpecDup edges
- Find a Max-Cut partition of the components
- Repeat recursively on the parts

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The result : even this problem is hard to approximate !

Conclusion

- Fixed Parameter Tractability ?
- Criteria other than duplications ?
  - e.g. gene losses
- What to do if the input gene trees are incompatible ?

Acknowledgements

Aïda Ouangraoua

Nadia El-Mabrouk

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CRSNG

Fonds de recherche
Nature et
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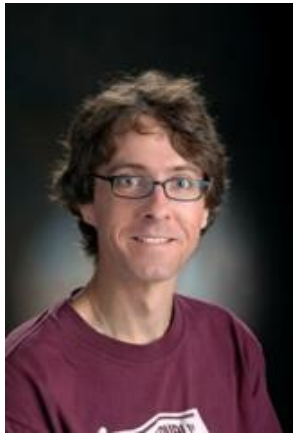
DIRO

The 14th RECOMB-CG

October 2016 in MONTRÉAL ☺

Probably from Monday 10 to Wednesday 12



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