Julius-Maximilians-
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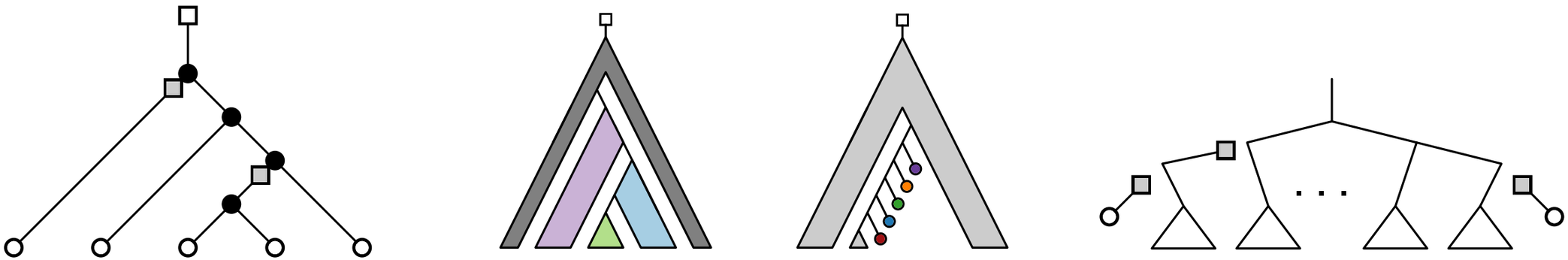
Advanced Algorithms

Rearrangement distance of phylogenetic trees

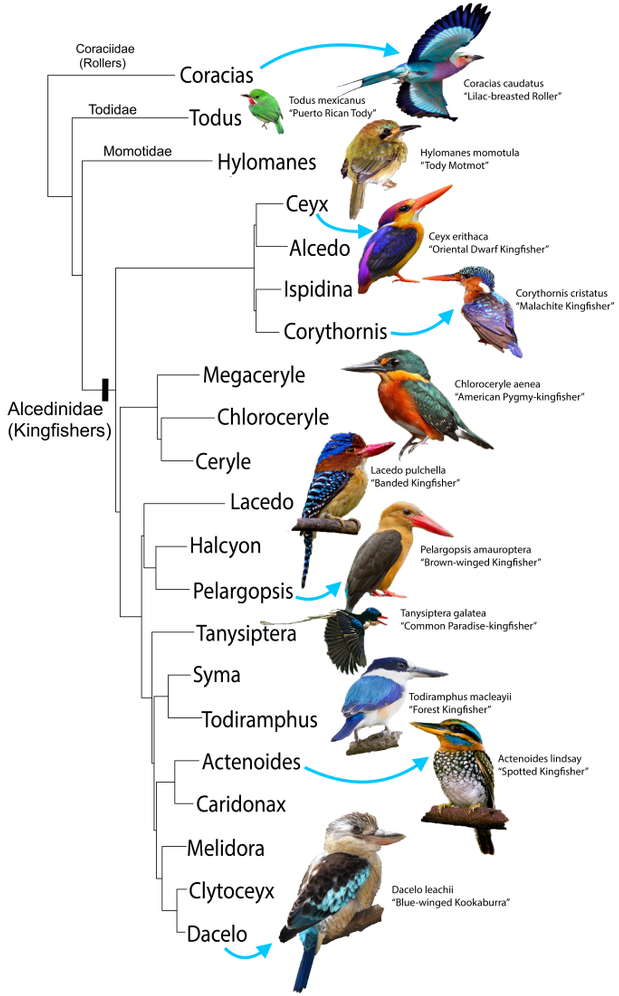
Kernelisation, fpt and approximation algorithm

Jonathan Klawitter · WS20



Phylogenetic trees

... represent the evolutionary history of a set of taxa.



by Jenna McCullough 2016

- Leaves are labelled with taxa.
- Each taxon represents a species, population, individual organism, gene, chromosome, ...
- Edge lenghts represents amount of time passed or genetic distance.

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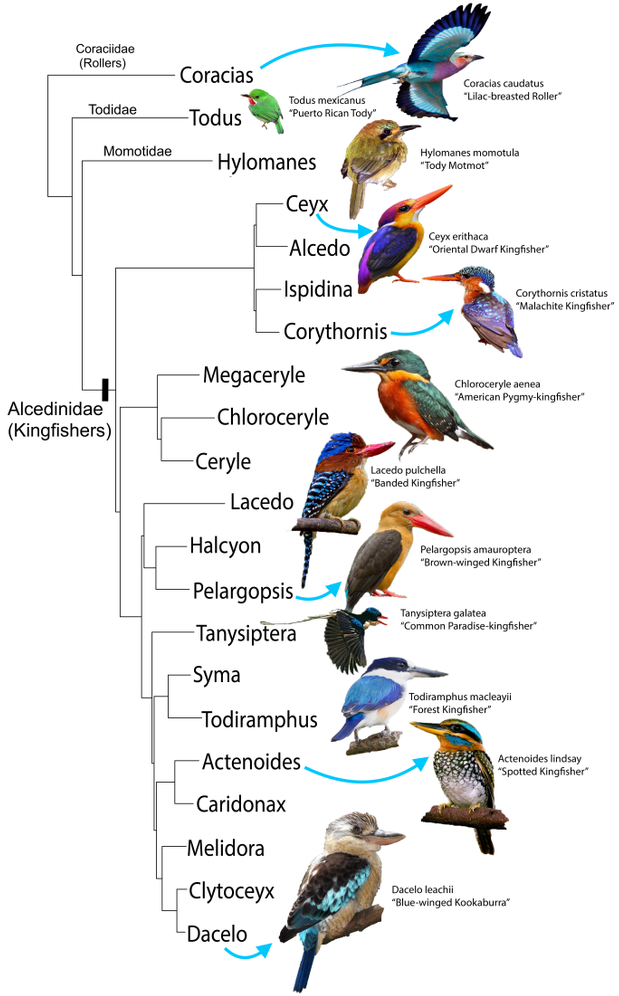

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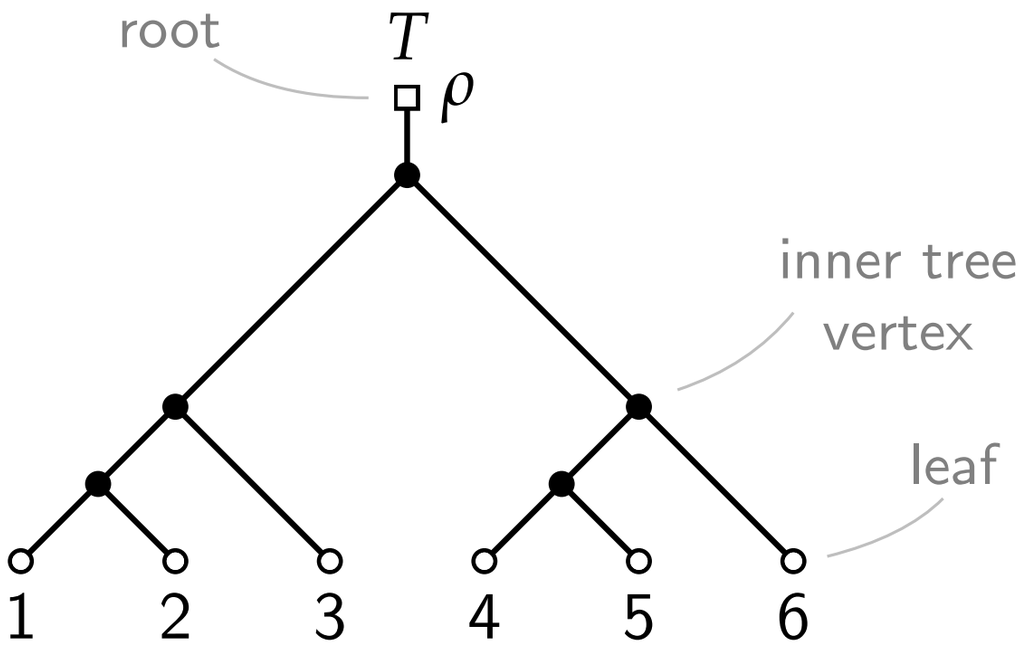
- Leaves are labelled with taxa.
- Each taxon represents a species, population, individual organism, gene, chromosome, ...
- Edge lenghts represents amount of time passed or genetic distance.
- Inference methods compute a phylogenetic tree based on some model and data.

Phylogenetic trees

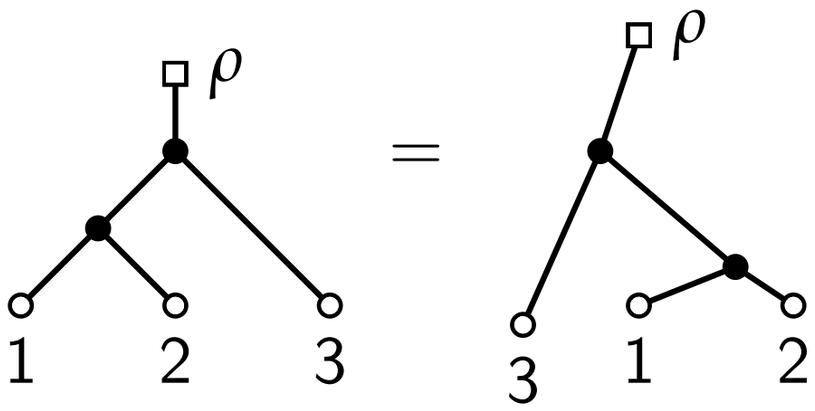
Let $X = \{1, 2, 3, \ldots n\}$.
A **(rooted, binary) phylogenetic tree** T is a rooted tree with the following properties:

- The unique **root** is labeled ρ and has outdegree 1.
- The leaves are bijectively labeled by X.
- All other vertices have indegree 1 and outdegree 2.



Remarks.
Here, in our definition

- vertices have **no heights** and
- the order of leaves does not matter.

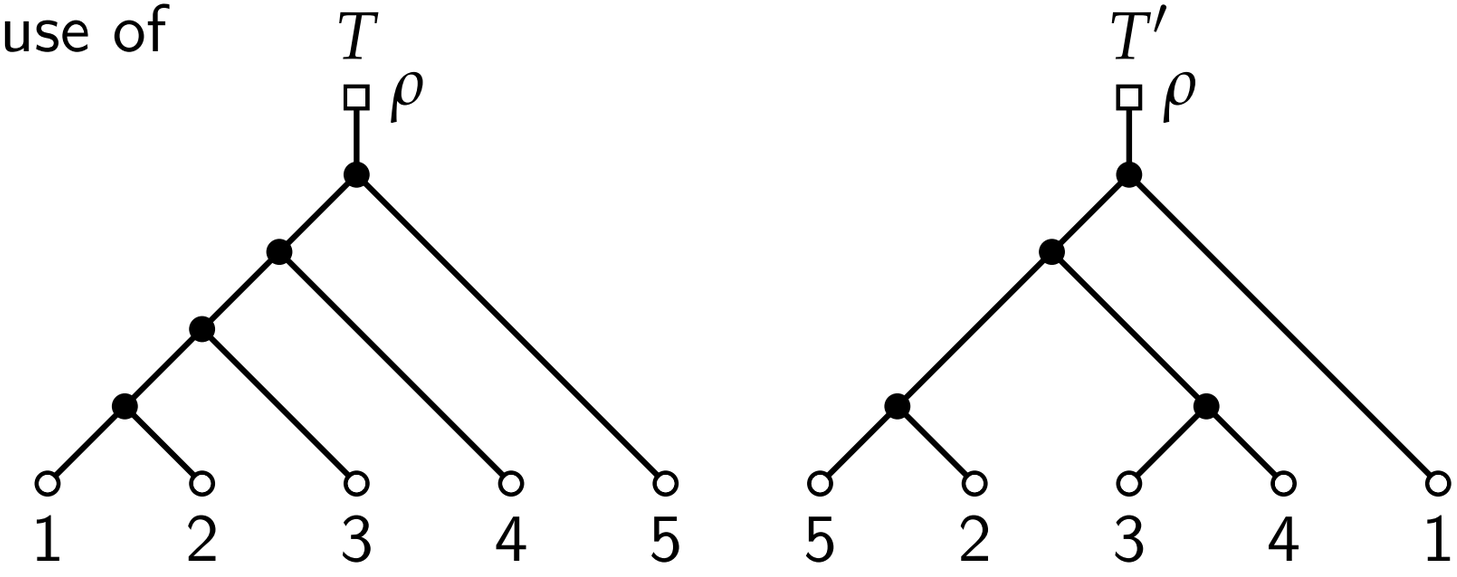


Problem

For the same taxa, we may infer **different** phylogenetic trees because of the use of

- different inference methods,
- different models, or
- different data.

We want to be able to **compare** different phylogenetic trees. How?

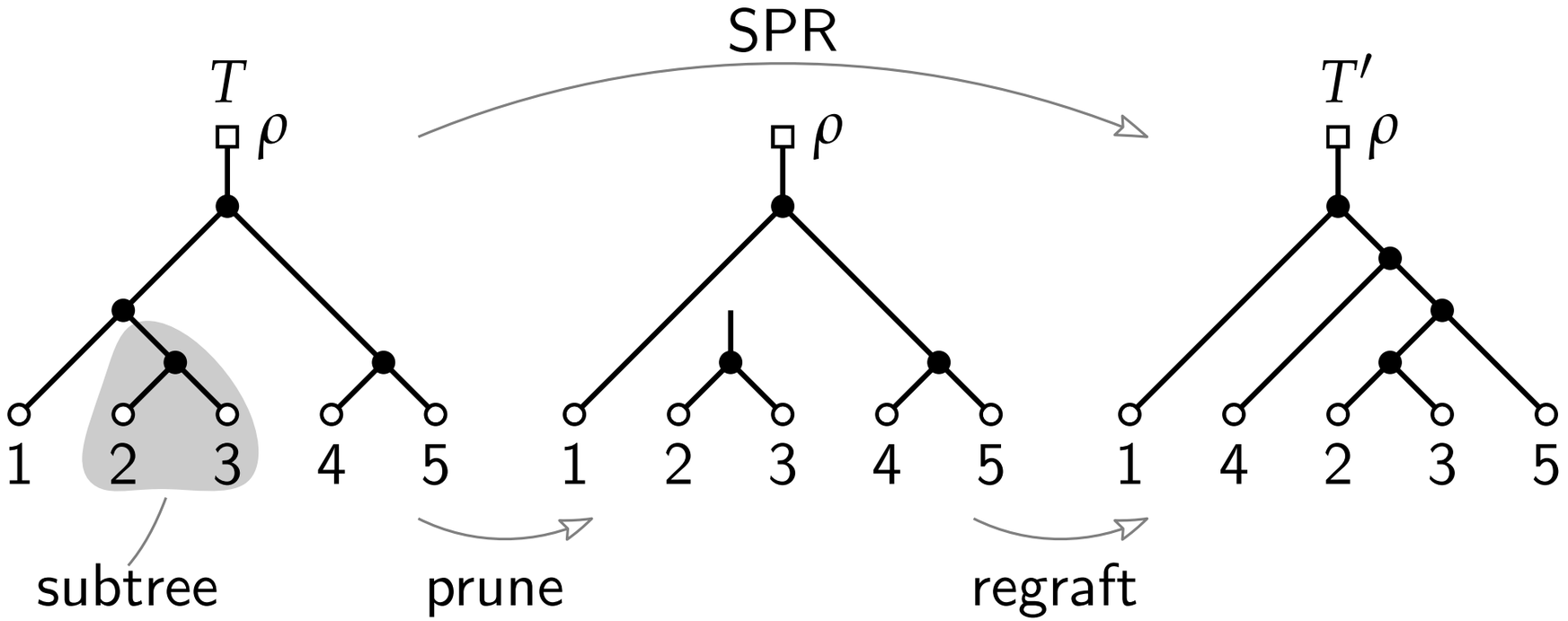


Goal.
Define a **metric** on phylogenetic trees on X and devise algorithms to compute it.

Idea.
Count the number of **rearrangement operations** that are necessary to transform T into T'.

Subtree Prune & Regraft (SPR)

An **SPR** operation transforms one phylogenetic tree into another one.

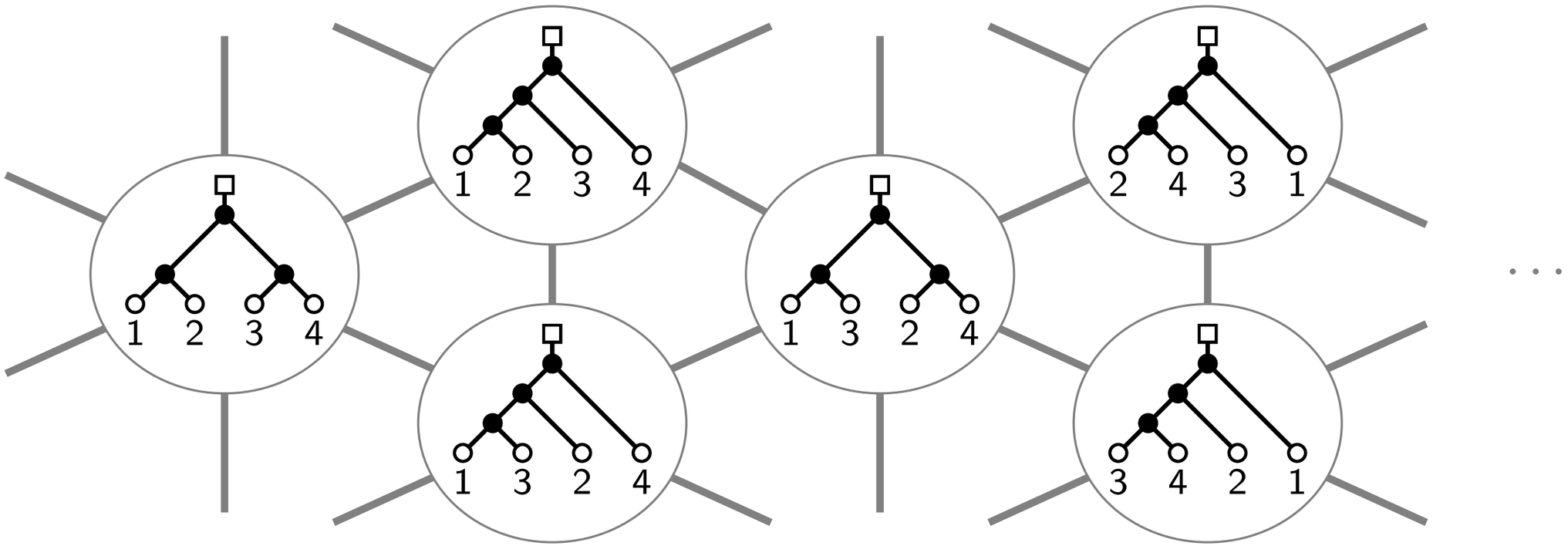


- Note that an SPR operation is reversible.

SPR-graph

SPR induces the **SPR-graph** $G = (V, E)$:

- $V = \{T \mid T$ is a phylogenetic tree on X$\}$
- $\{T, T'\} \in E$ if T can be transformed into T' with a single SPR operation



SPR-distance

The **SPR-distance** $\mathrm{d}_{\mathrm{SPR}}(T, T')$ of T and T' is defined as the distance of T and T' in the SPR-graph G.

Lemma 1.
The SPR-graph G is connected.

Proof as exercise or in discussion.

Lemma 2.
The SPR-distance is a metric.

Proof. G is connected and undirected.

Goal.
Compute the SPR-distance $\mathrm{d}_{\mathrm{SPR}}(T, T')$.

...but G is huge!

$$|V(G)| = (2n-3)!! = (2n-3) \cdot (2n-5) \cdot \ldots \cdot 5 \cdot 3$$

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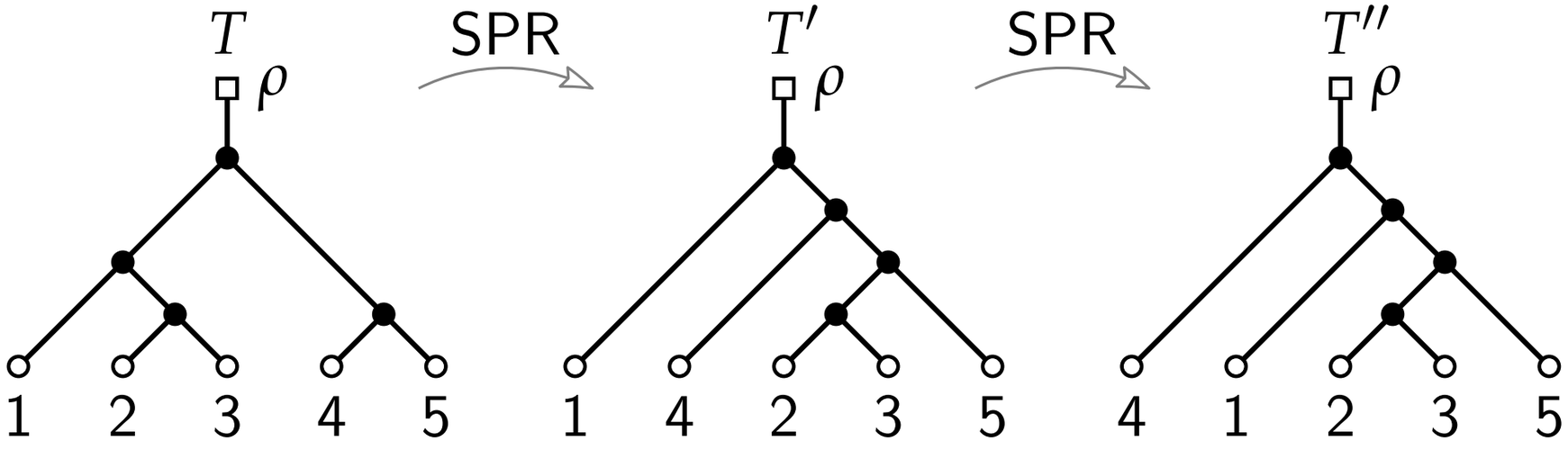
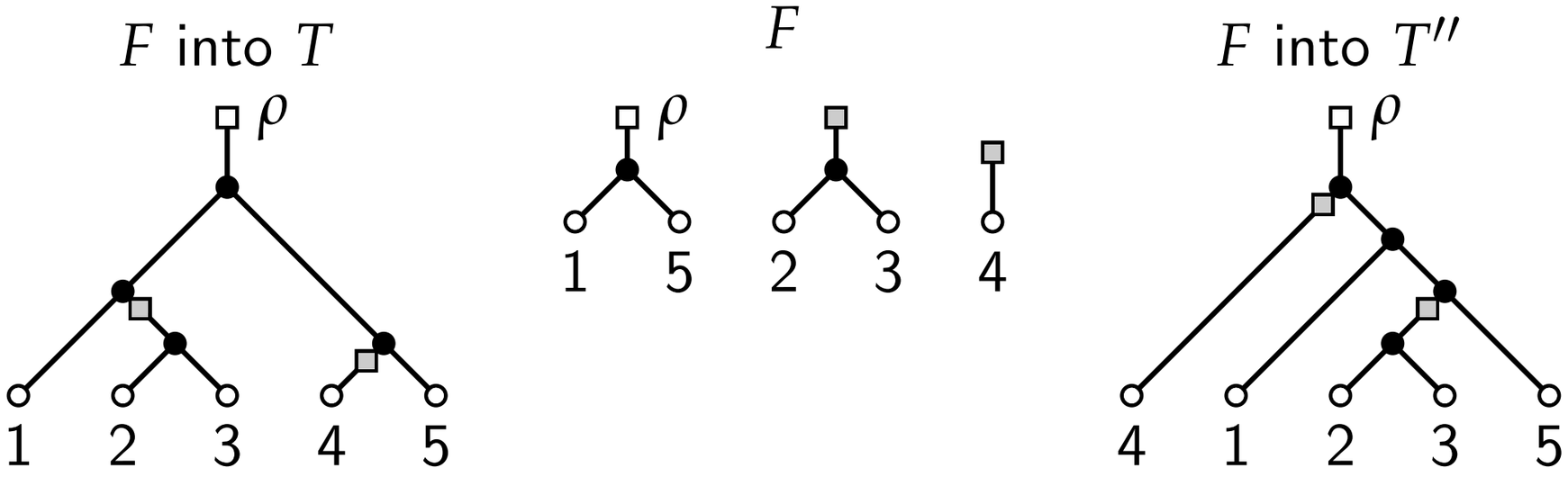
- Can we rephrase the problem?

Maximum agreement forests





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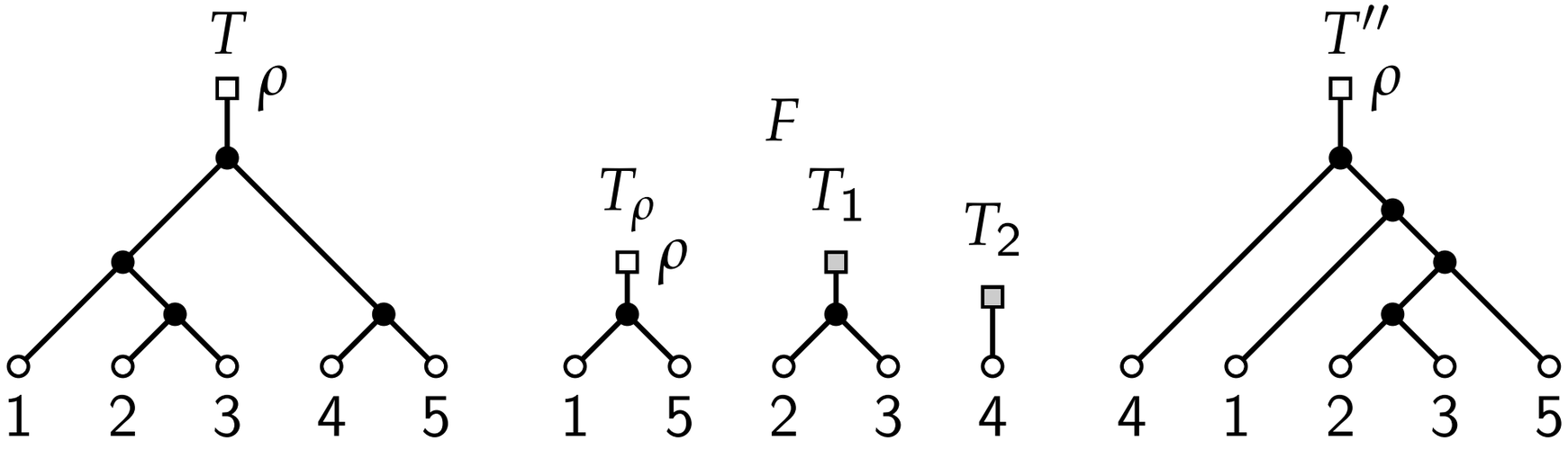


An **agreement forest** F of T and T'' is a forest $\{T_\rho, T_1, T_2, \ldots, T_k\}$ such that

- the label sets of the T_i partition $X \cup \{\rho\}$,
- ρ is in the label set of T_ρ, and
- there exist edge-disjoint embeddings of subdivisions of the T_i's into T and T'' that cover all edges.

If k is minimal, F is a **maximum agreement forest (MAF)**.

Characterisation

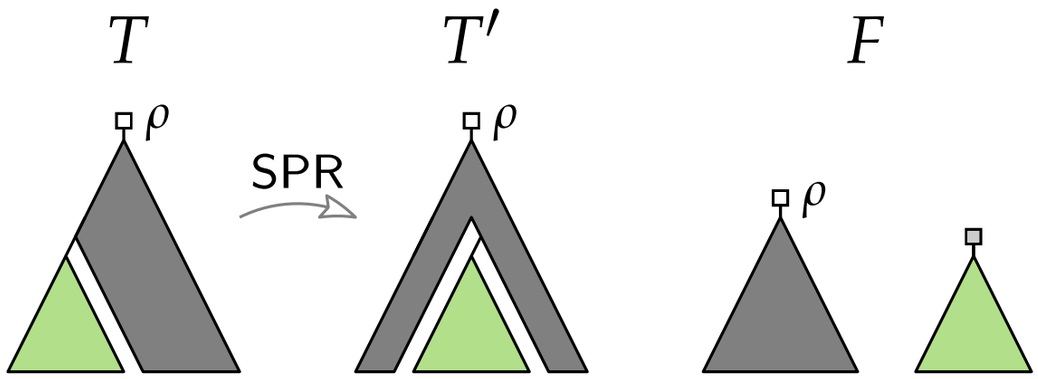
Let T and T' be two phylogenetic trees on X.
Let $F = \{T_\rho, T_1, T_2, \ldots, T_k\}$ be a MAF of T and T'.
Define

$$\mathsf{m}(T, T') = k = |F| - 1.$$

Theorem 3. $\mathsf{m}(T, T') = \mathsf{d}_{\mathsf{SPR}}(T, T')$

Proof of "$\leq$" by induction on $d = \mathsf{d}_{\mathsf{SPR}}(T, T')$.

- Case $d = 1$ is easy. ✓



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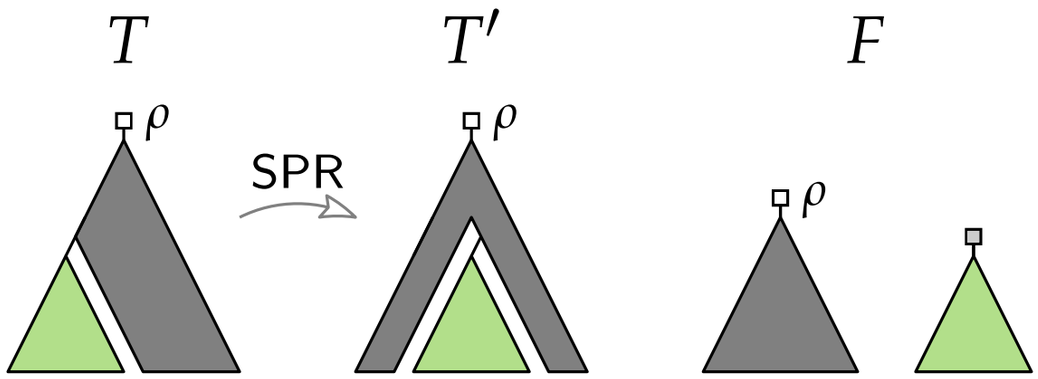

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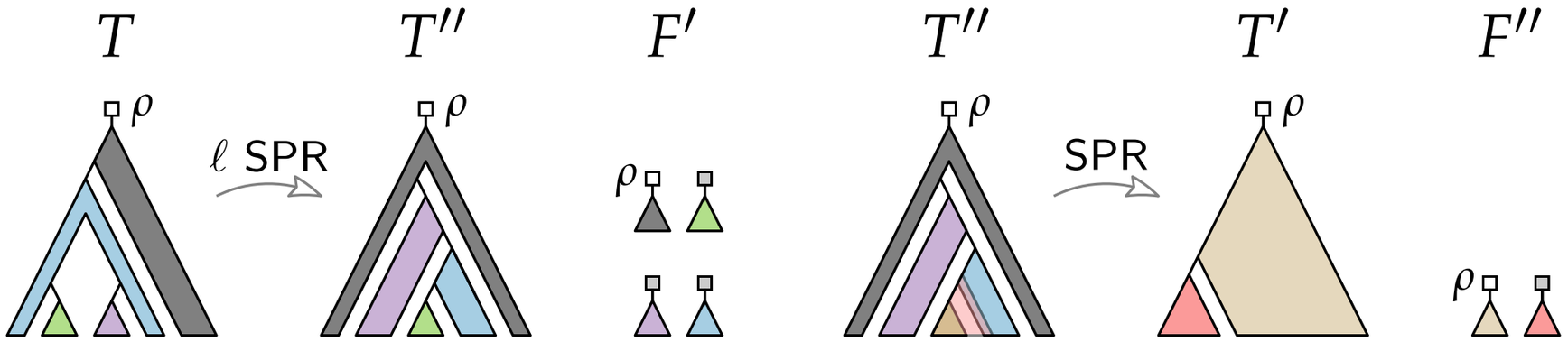
Proof of "$\leq$" by induction on $d = \mathsf{d}_{\mathsf{SPR}}(T, T')$.

- If $d = \ell + 1$, then there exists T'' with $\mathsf{d}_{\mathsf{SPR}}(T, T'') = \ell$ and $\mathsf{d}_{\mathsf{SPR}}(T'', T') = 1$.
- There exists MAF F' for T and T'' and MAF F'' for T'' and T'.



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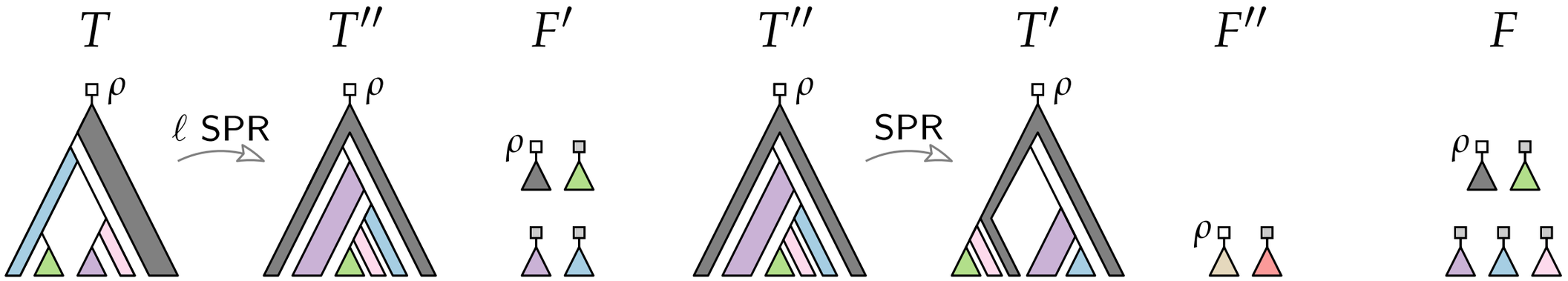

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Proof of "$\geq$" by induction on $d = \mathsf{m}(T, T')$.

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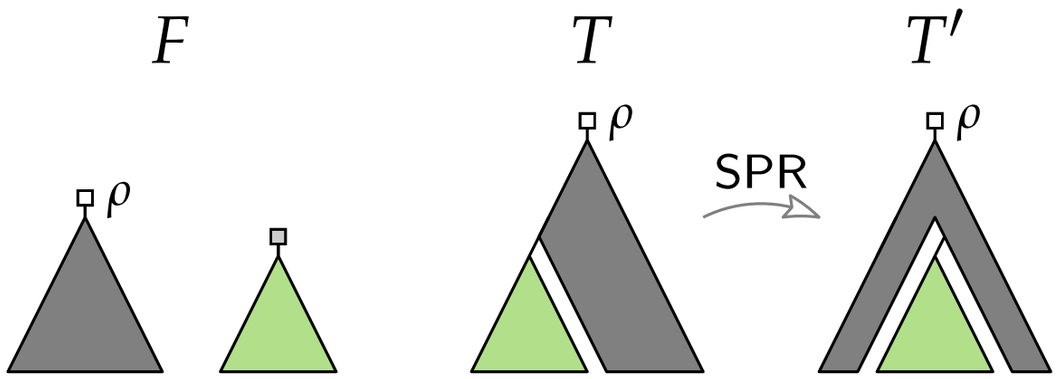

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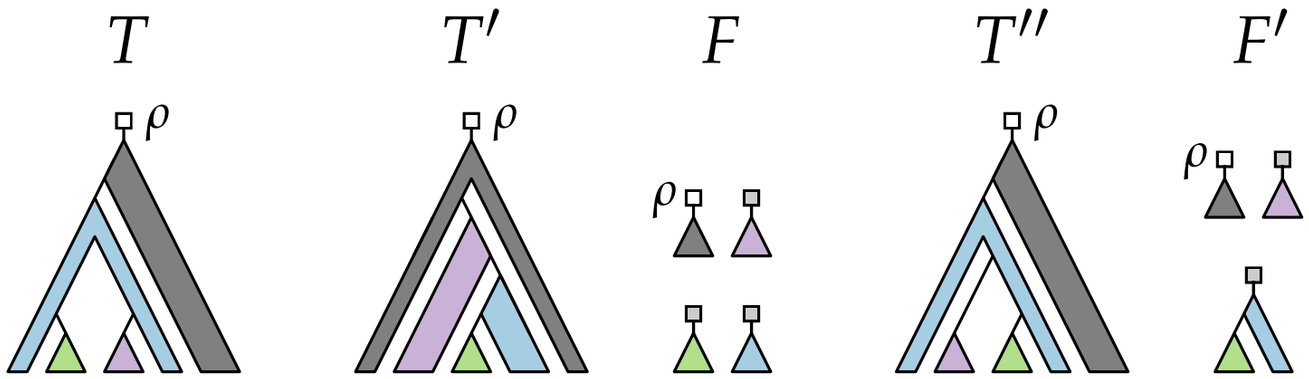
Proof of "$\geq$" by induction on $d = \mathsf{m}(T, T')$.

- Let F be a MAF of T and T' of size $\ell + 2$.
- There exists a T_i that can be pruned in T.



- Regraft T_i according to the embedding of F into $T' \Rightarrow T''$ & F'
- F' is an AF for T' and T''
- $\Rightarrow \mathsf{d}_{\mathsf{SPR}}(T'', T') \leq \ell$
- $\mathsf{d}_{\mathsf{SPR}}(T, T'') = 1$
- $\mathsf{d}_{\mathsf{SPR}}(T, T') \leq \ell + 1 = \mathsf{m}(T, T')$

Problem & Plan

Theorem 4. [HJWZ '96, BS '05]
Computing $\mathrm{d}_{\mathrm{SPR}}(T, T')$ is NP-hard.

Proof is by reduction from Exact Cover by 3-Sets.

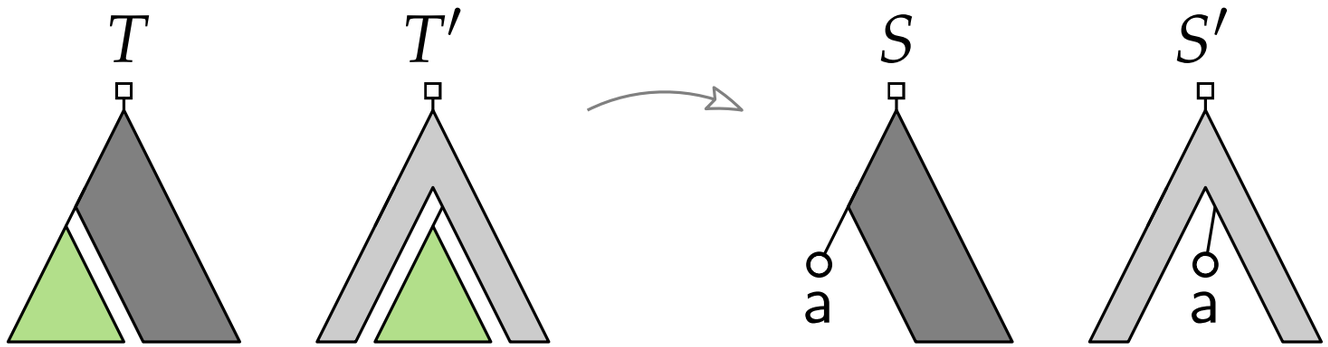
Plan.

- Construct **kernel** of the problem.
  - Replace T and T' with smaller S and S'.
  - We should be able to get $\mathrm{d}_{\mathrm{SPR}}(T, T')$ from $\mathrm{d}_{\mathrm{SPR}}(S, S')$.
- Show that size of the kernel depends on $\mathrm{d}_{\mathrm{SPR}}(T, T')$.
- Devise an fpt algorithm by computing $\mathrm{d}_{\mathrm{SPR}}$ for kernel.
- Devise an approximation algorithm.

Kernelisation – Subtrees

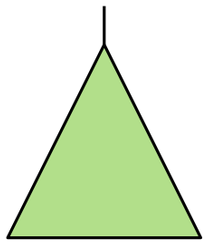
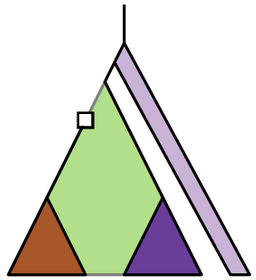
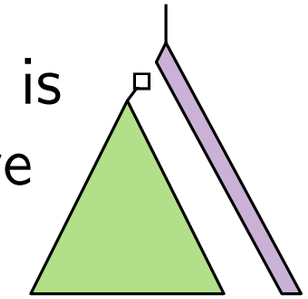
Common subtree reduction.

- Replace any pendant subtree that occurs identically in both trees by a single leaf with a new label.



Lemma 5. Applying the common subtree reduction is safe; i.e. $\mathrm{d}_{\mathrm{SPR}}(T, T') = \mathrm{d}_{\mathrm{SPR}}(S, S')$.

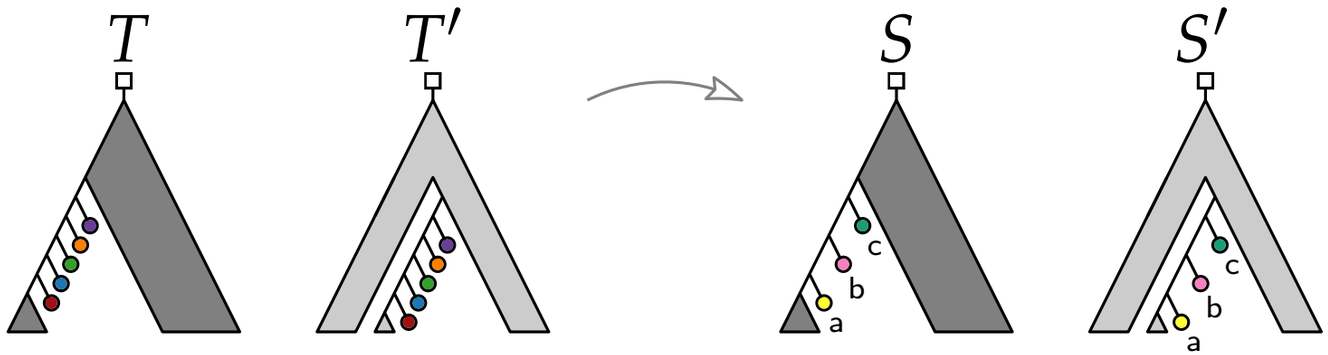
Proof.

Suppose  is covered by two trees of MAF  then there is alternative MAF 

Kernelisation – Chains

Chain reduction.

- Replace any chain of leaves that occurs identically in both trees by three new leaves.



Lemma 6. Applying chain reduction is safe; i.e. $\mathrm{d_{SPR}}(T, T') = \mathrm{d_{SPR}}(S, S')$.

Proof.

- Show there is a tree with abc-chain in a MAF of S and S'.
- Swap abc-chain with original chain for MAF of T and T'.

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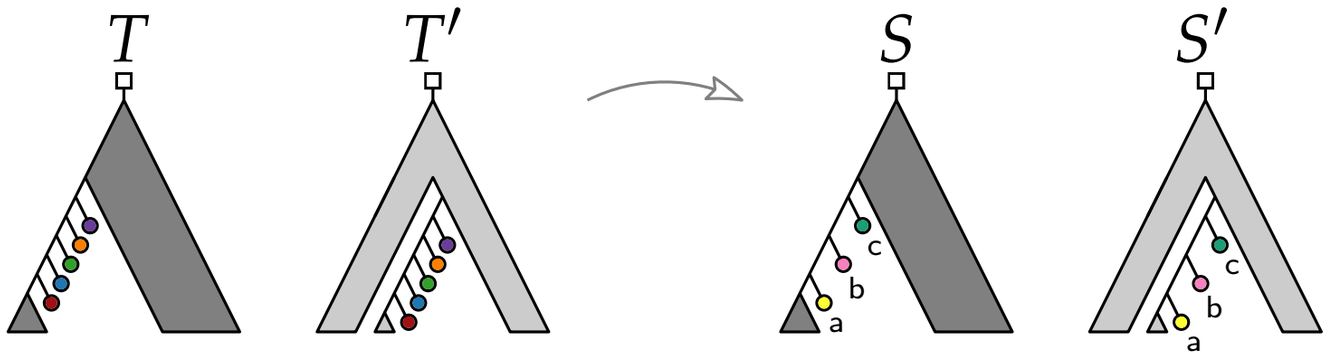

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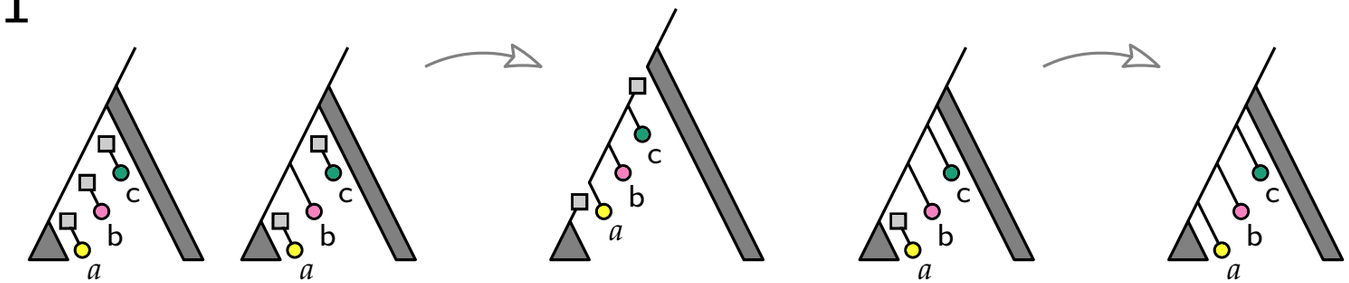
Proof.

- Consider embedding of a MAF F into S.

Case 1



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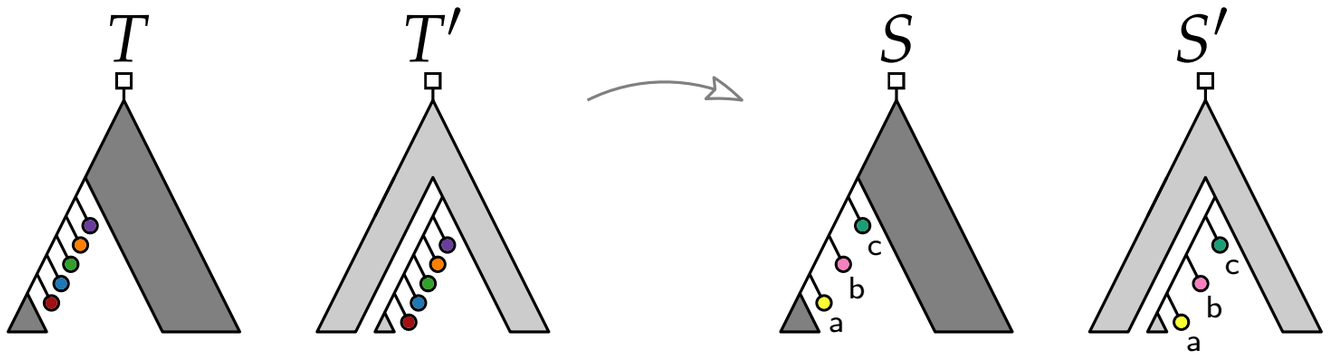

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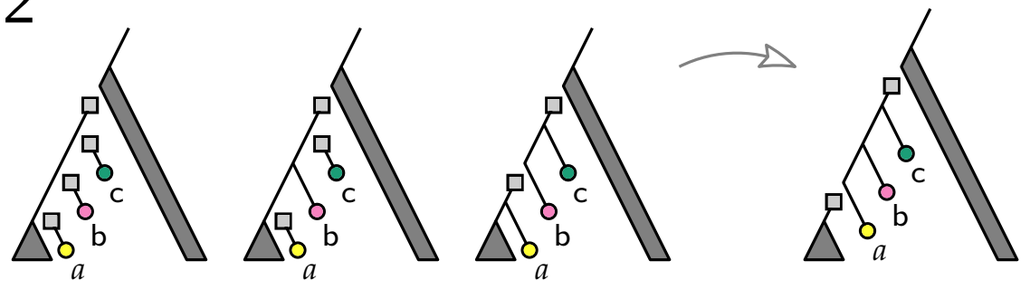
Case 2



Kernel size

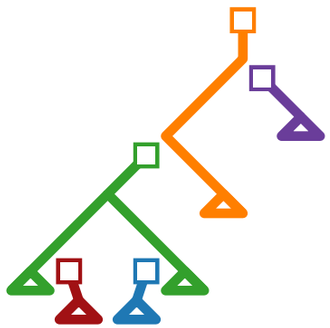
Theorem 7.
Reduce T and T' to S and S' by exhaustively applying the reduction rules. Let S and S' be on X'. Then

$$|X'| \leq 28\, \mathrm{d}_{\mathsf{SPR}}(T, T').$$

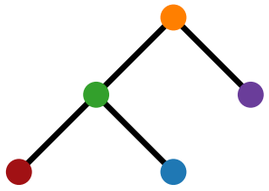
Proof. Let $F = \{T_\rho, T_1, \ldots, T_k\}$ be MAF for S and S'.

Let $n(T_i)$ be # of T_j that T_i overlaps with in embedding of F into S.

Claim 1. $\sum_{i=\rho}^{k}(n(T_i) + n'(T_i)) \leq 4k = 4\, \mathrm{d}_{\mathsf{SPR}}(T, T')$.



H



$$|V(H)| = k + 1 = |E(H)| + 1$$

$$\sum n(T_i) = 2|E(H)| \leq 2k$$

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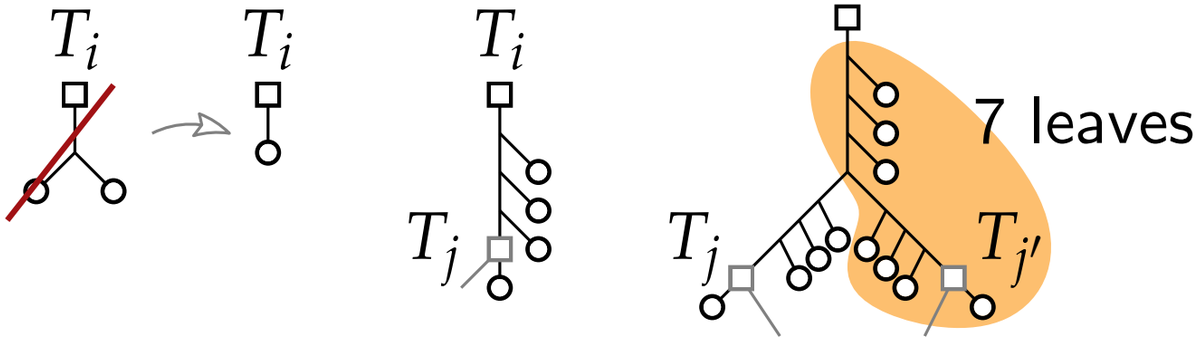
Claim 2. # leaves of $T_i \leq 7(n(T_i) + n'(T_i))$.



$\sum_{i=\rho}^{k}$ # leaves of T_i
$\leq \sum_{i=\rho}^{k} 7(n(T_i) + n'(T_i))$
$\leq 28k$

FPT algorithm

Theorem 8.
Computing $\mathrm{d_{SPR}}(T, T')$ is fixed-parameter tractable when parameterized by $\mathrm{d_{SPR}}(T, T')$.

Proof.

- Reduce T and T' to S and S' by exhaustively applying the reduction rules.
- Let S and S' be on X' and let $k = \mathrm{d_{SPR}}(S, S')$.
- S has at most $4|X'|^2$ neighbours.
  - S has less than $2|X'|$ edges to cut and to attach to.
- Length-k BFS from S visits at most $O\left(\left(4|X'|^2\right)^k\right) = O\left((56k)^{2k}\right)$ trees. by Theorem 7
- Since $k = \mathrm{d_{SPR}}(S, S') = \mathrm{d_{SPR}}(T, T')$, this yields an fpt algorithm.

Approximation algorithm

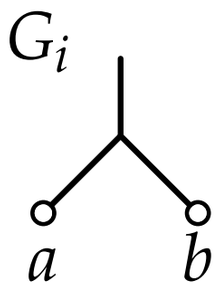
Idea.

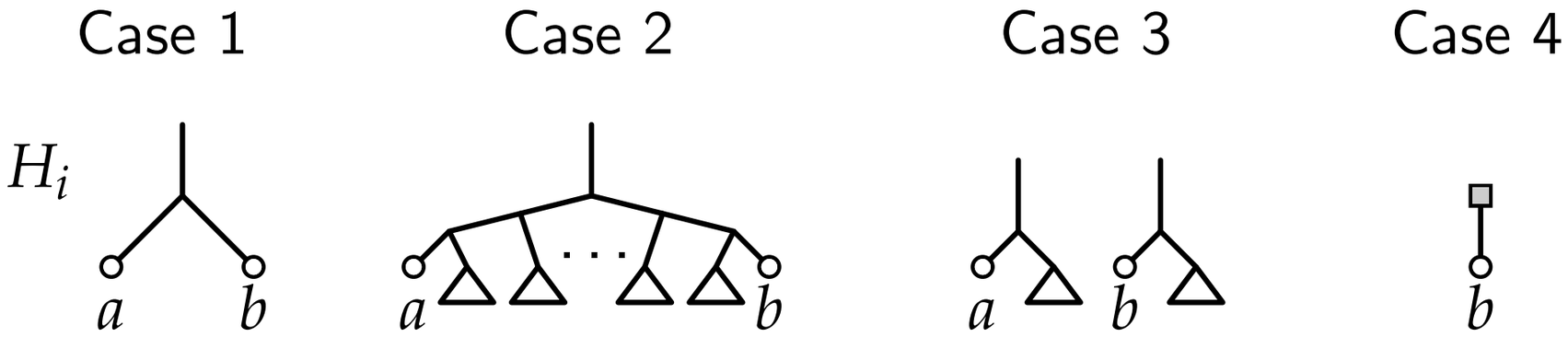
- Given reduced trees T and T' we compute an agreement forest F by
- successively making "cuts" and "eliminations".
- This shrink T and T' further and further.
- Show that $|F|$ is at most $3|F'|$, where F' is a MAF of T and T'.

Approximation algorithm

$\textsc{approx}\mathrm{DSPR}(T, T')$

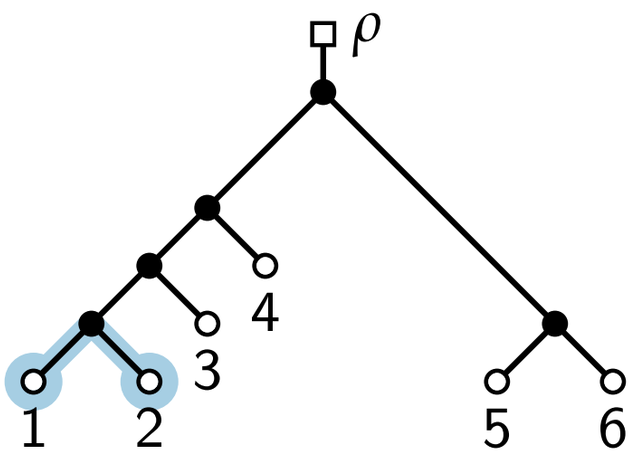
$i \leftarrow 1$
$G_i \leftarrow T$
$H_i \leftarrow T'$
while $\exists$ pair of sibling leaves a and b in G_i **do**
  find the case that applies to a and b in H_i
  apply the corresponding transaction
  to obtain G_{i+1} from G_i and H_{i+1} from H_i
  $i++$
return $|H_i| - 1$



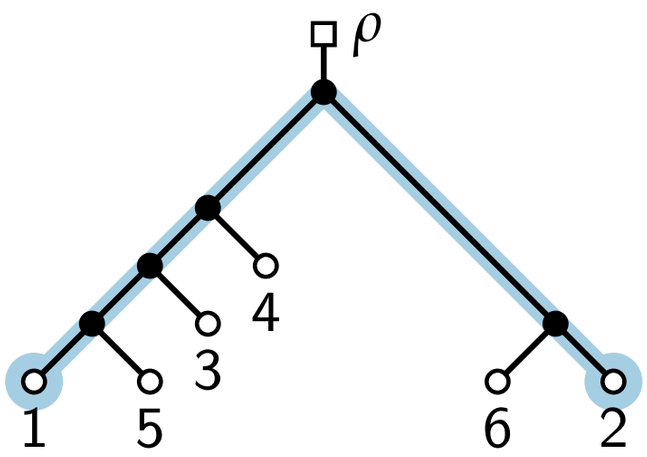


Approximation algorithm – example

$T = G_1$



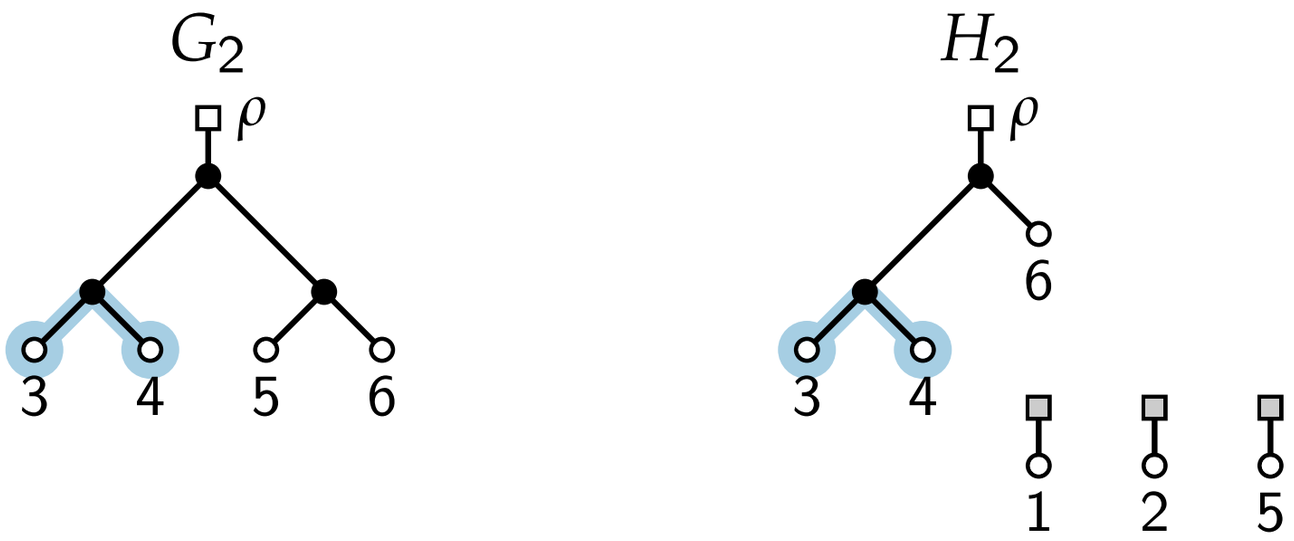
$T' = H_1$



Case 2

- Should we cut of the leaves 1 or 2 or all in between them in H_1?
- Do parts of each!

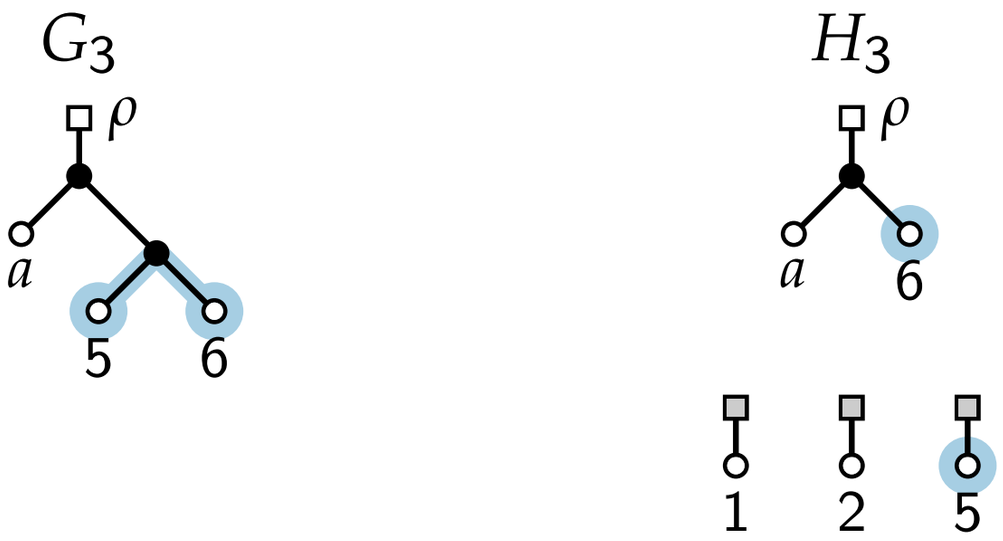
Approximation algorithm – example



Case 1

- If the same cherry occurs in H_i, we can simply reduce it.

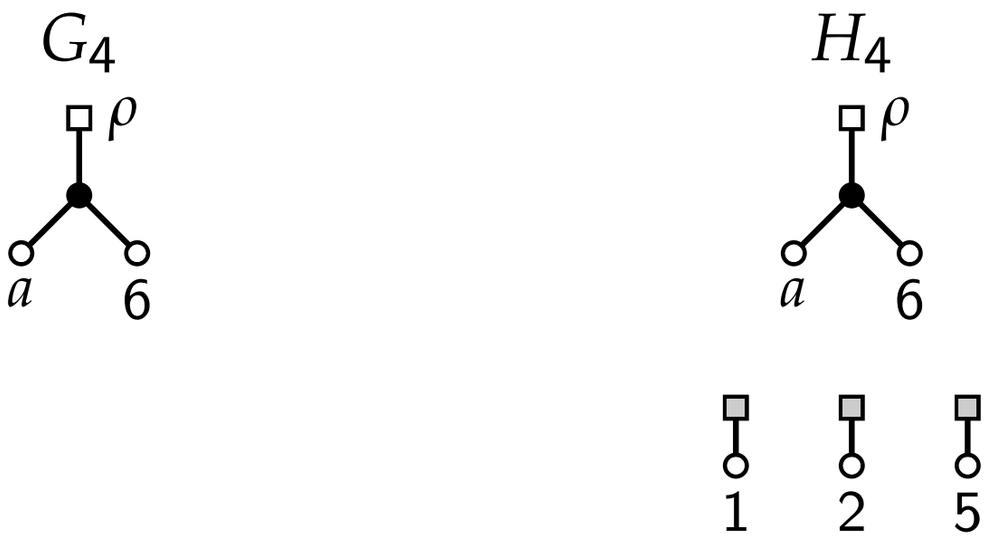
Approximation algorithm – example



Case 4

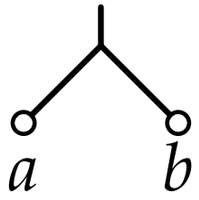
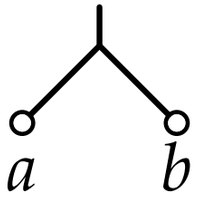
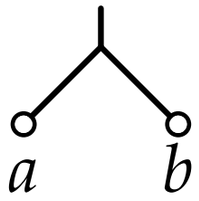
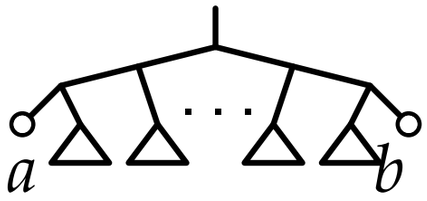
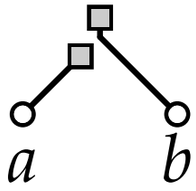
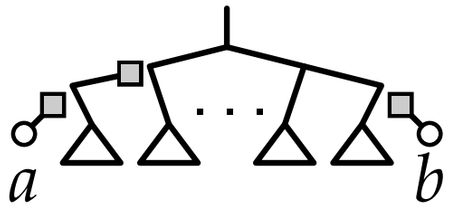
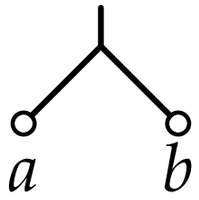
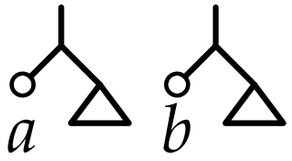
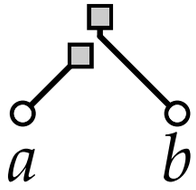
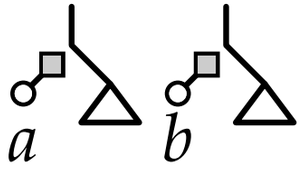
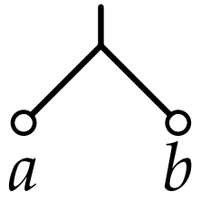
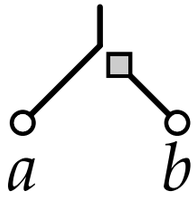
- Leaf b is the only leaf of a tree in H_i.
- Cut off b in G_i.

Approximation algorithm – example

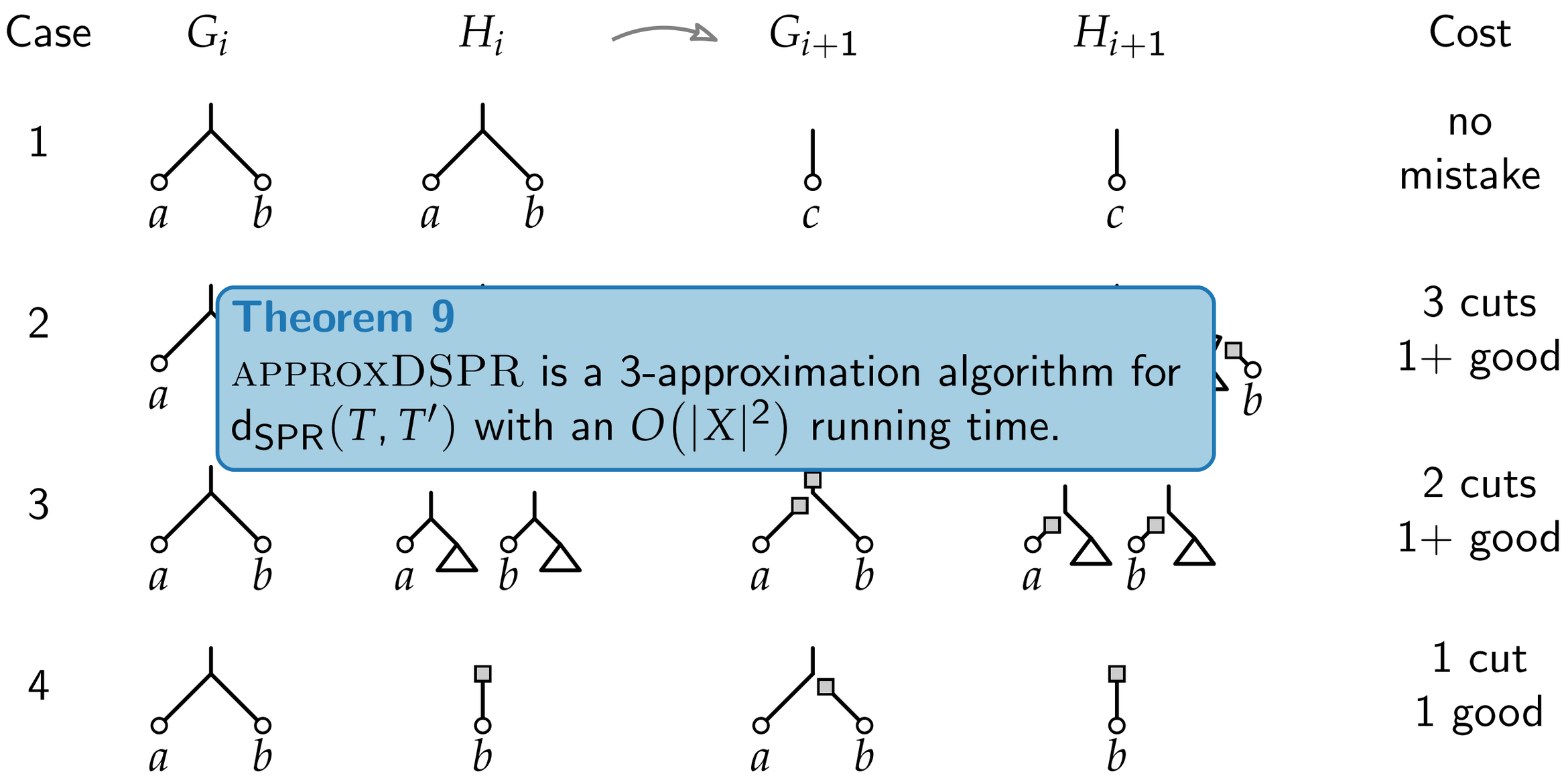


- Return 3.

Approximation algorithm – analysis

Case	G_i	H_i	$\rightarrow$	G_{i+1}	H_{i+1}	Cost
1						no mistake
2						3 cuts 1+ good
3						2 cuts 1+ good
4						1 cut 1 good

Approximation algorithm – analysis



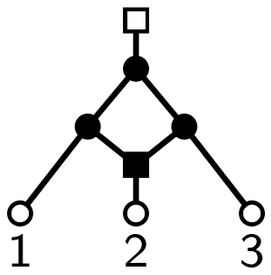
Theorem 9

APPROXDSPR is a 3-approximation algorithm for $\mathrm{d}_{\mathrm{SPR}}(T, T')$ with an $O(|X|^2)$ running time.

Discussion

Phylogenetic trees.

- There are other classes of phylogenetic trees: unrooted, non-binary, ranked, ...
- Trees can be generalized to **phylogenetic networks**, which can also have indegree 2 outdegree 1 vertices.



Maximum Agreement Forests.

- Reframing (characterising) a problem in a different way, can sometimes make your life a lot easier.
- MAF can be generalized to Maximum Agreement Graphs, but these don't characterize the SPR-distance of networks anymore.

Discussion

Kernelization.

- Kernelization is an important technique to construct fpt algorithms.
- Result important since SPR-distance small in practice.
- Reduction rules actually give a kernel of size at most $15k - 9$.
- With further reduction rules can get size below $11k - 9$. [KL '18]
- Divide & conquer algorithm can (in practice) reduce further reduce problem sizes. [LS '11]

Approximation algorithm.

- There exist 2-approximation algorithms for the SPR-distance with a running time in $\mathcal{O}(n^3)$. [CHW '17]

Literature

Original papers:

- [BS '05] "On the computational complexity of the rooted subtree prune and regraft distance" for SPR, MAF, characterisation, fpt, divide & conquer
- [RSW '06] "The maximum agreement forest problem: Approximation algorithms and computational experiments"

Referenced papers:

- [HJWZ '96] "On the complexity of comparing evolutionary trees" for NP-hardness proof
- [KL '19] "New reduction rules for the tree bisection and reconnection distance"
- [CHW '17] "A New 2-Approximation Algorithm for rSPR Distance"
- [LS11] "A cluster reduction for computing the subtree distance between phylogenies"