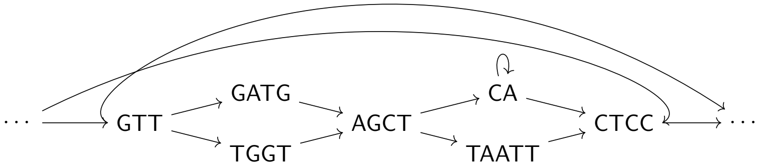
CARP - Quantifying Structural Complexity of Pangenomes

Leonard Bohnenkämper

March 5th, 2025

Pangenomes, Rearrangements and Recombinations

Abstracting from Local Variations



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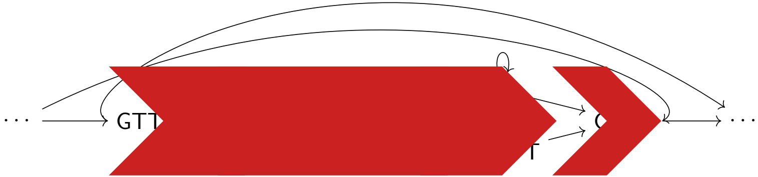

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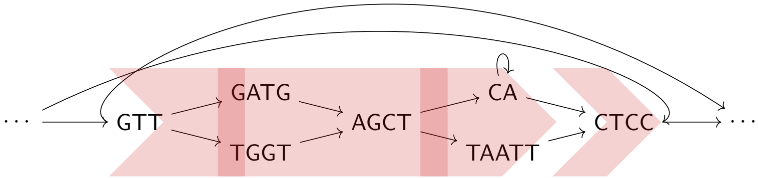

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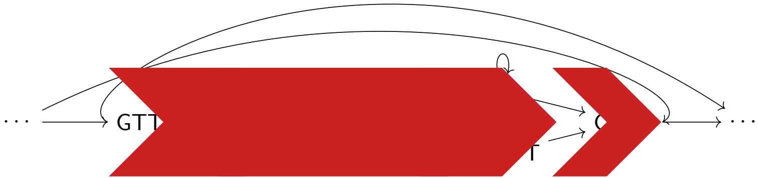
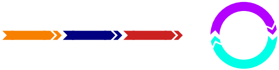


→ Collinear Block Detection.

Pangenome

Pangenome



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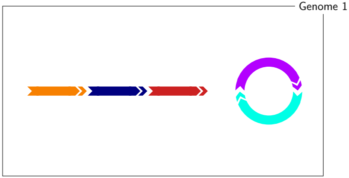

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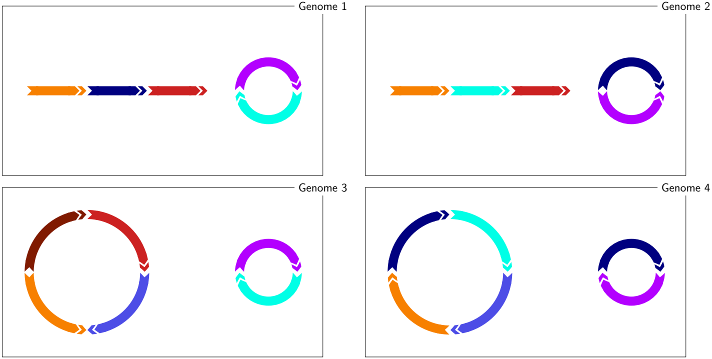

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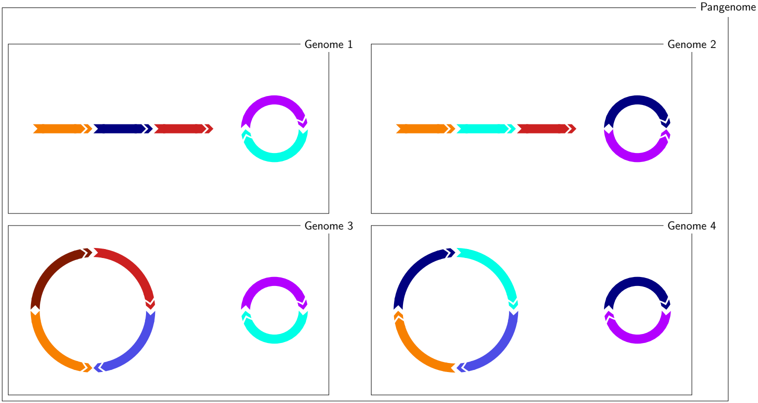
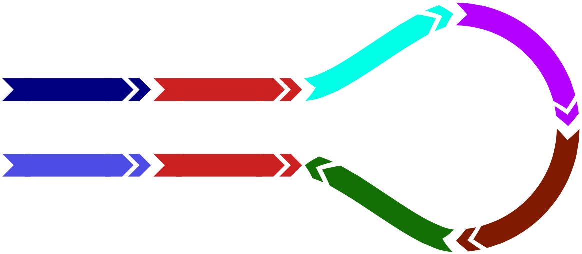


Rearrangements and Homologous Recombinations



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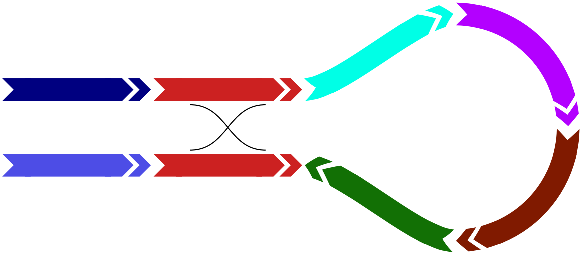

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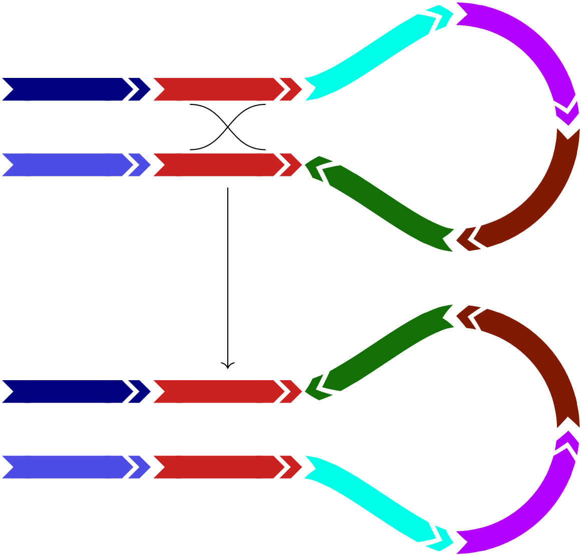

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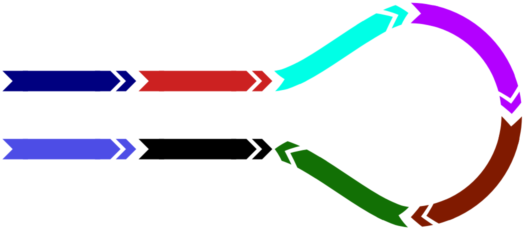

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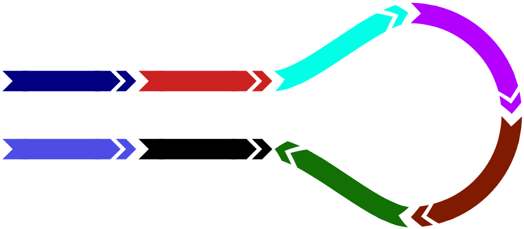
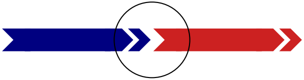
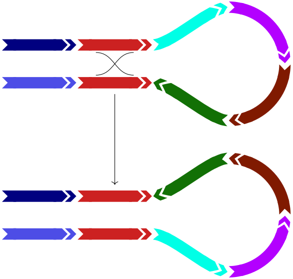


- No rearrangements via Homologous Recombination.

Flash Forward: Adjacencies



(Non)-Adjacency Modifying Operations



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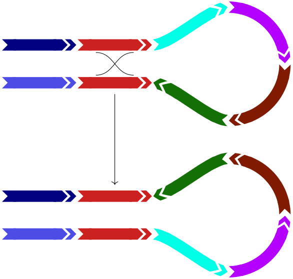

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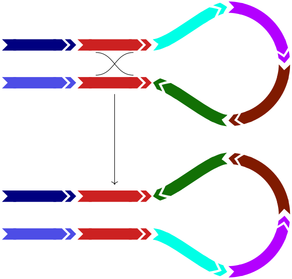
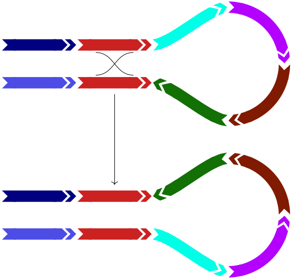


- No change in adjacencies!
  → Non-Adjacency Modifying Operations (Namos)

(Non)-Adjacency Modifying Operations



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  ↔ Adjacency Modifying Operations (Amos)

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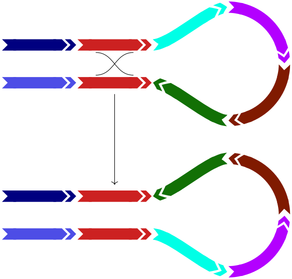

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Amos can introduce structural complexity!

Amos - Example: Segmental Duplication

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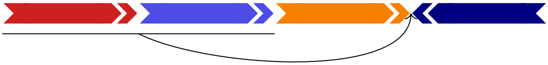

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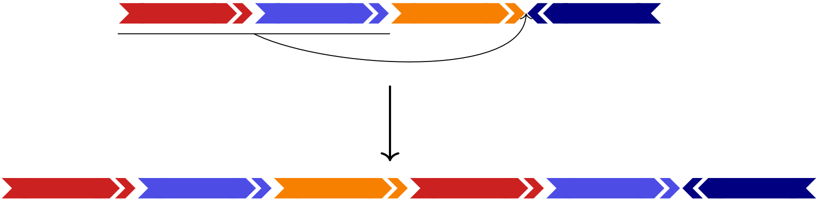
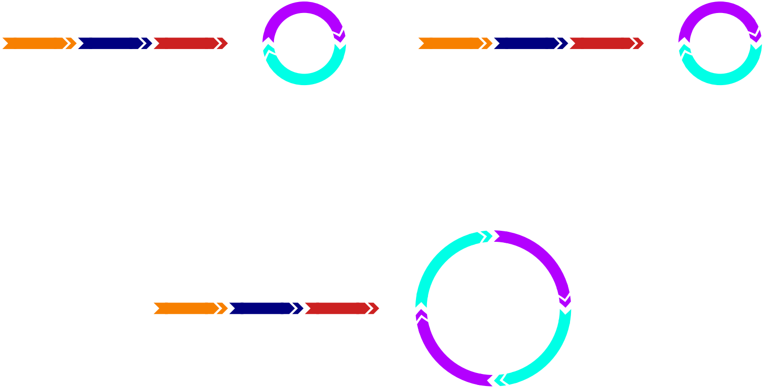


Pangenomes with Minimal Structural Complexity



~~Boring~~ **Simple Pangenome**

General Ancestral Reconstruction Problem (GARP)

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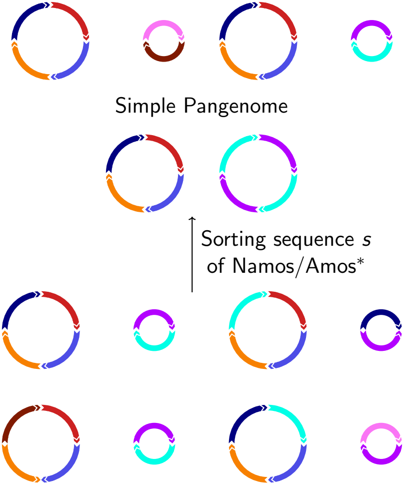

Simple Pangenome

Sorting sequence *s* of Namos/Amos*

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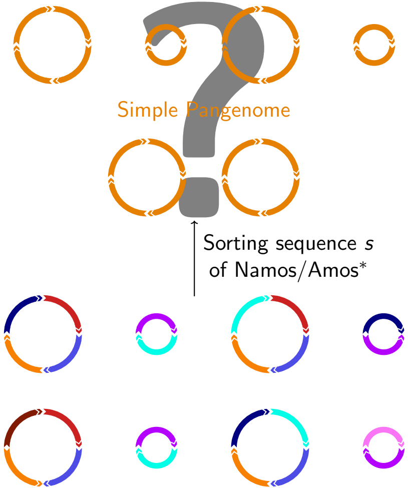

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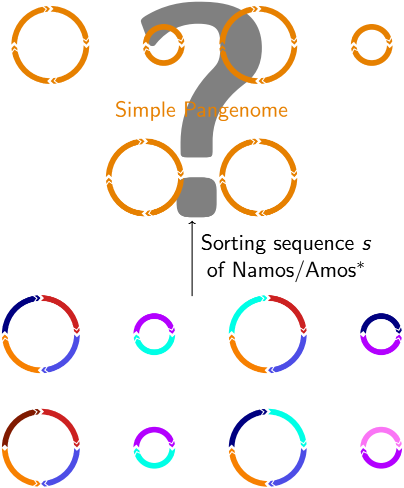

- #Amos in *s*: measure of the Structural Complexity.

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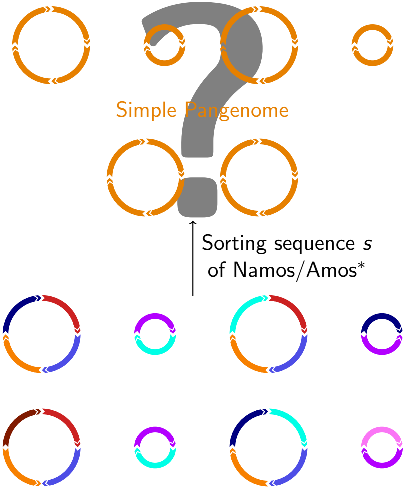

- #Amos in *s*: measure of the Structural Complexity.
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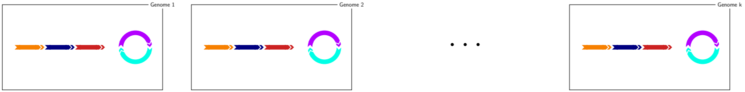
k-Coalescence – an important Namo



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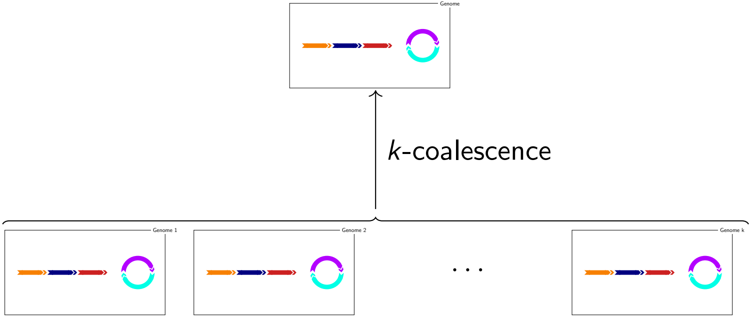
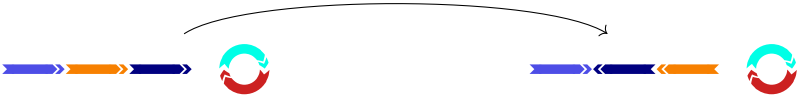


k-coalescence

Classical Problems and GARP

Distance Problem and GARP



Distance Problem and GARP

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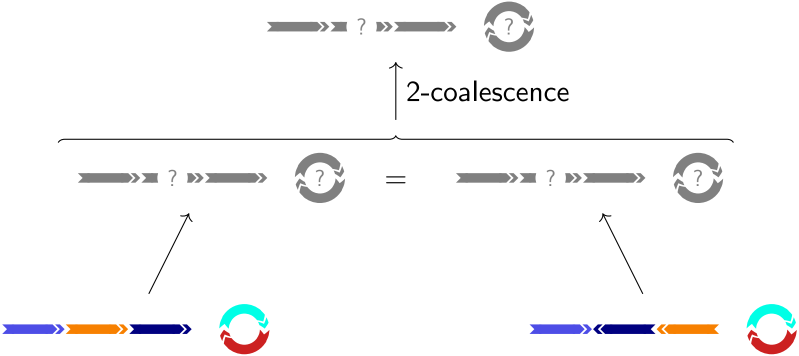
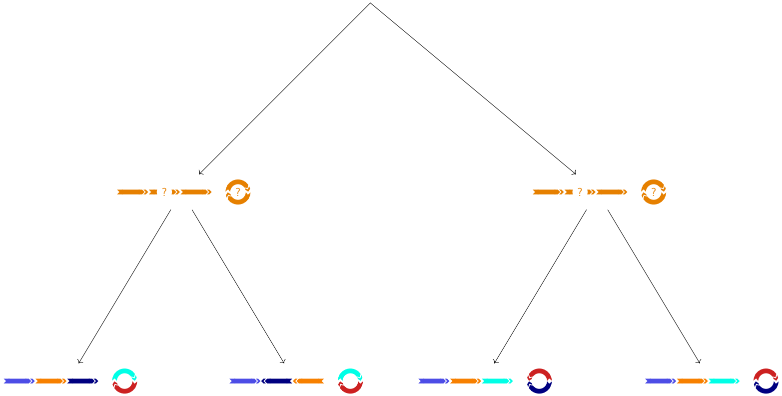


Large Parsimony Problem and GARP



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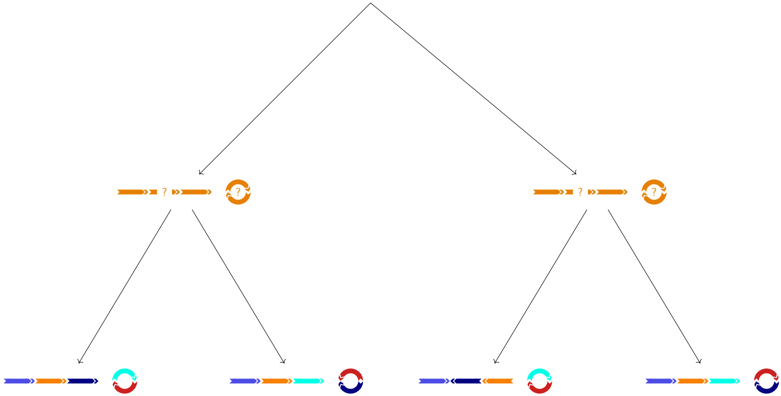

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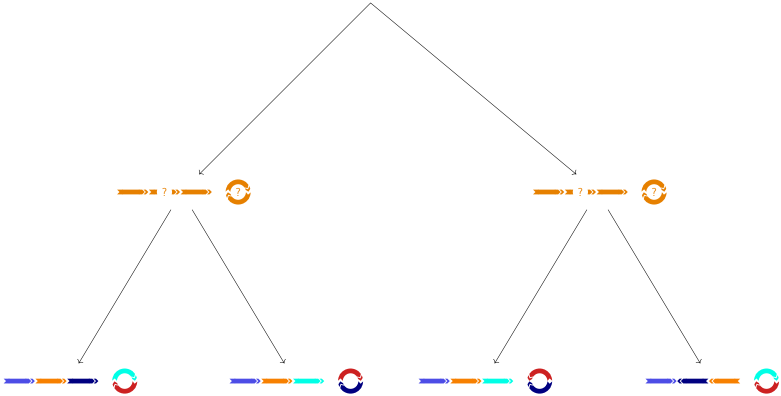

Large Parsimony Problem and GARP

2-coalescence

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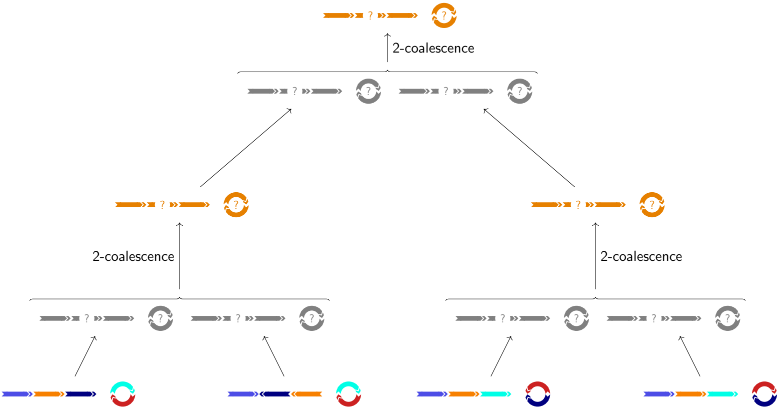

Complete Ancestral Reconstruction for Pangenomes (CARP)

GARP and Classical Problem Formulations

- Very limited interaction between genomes (only Coalescence)

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→ Classical Problem Formulations would overestimate structural complexity for pangenomes (missing Namos substituted with Amos)

→ For a lower bound, we need a "maximally powerful" set of Namos

Multi-Breakpoint Graph (MBPG)

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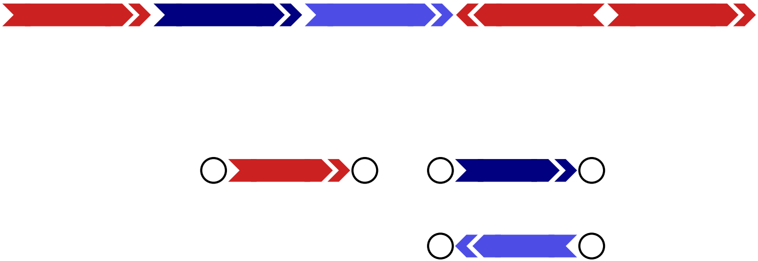

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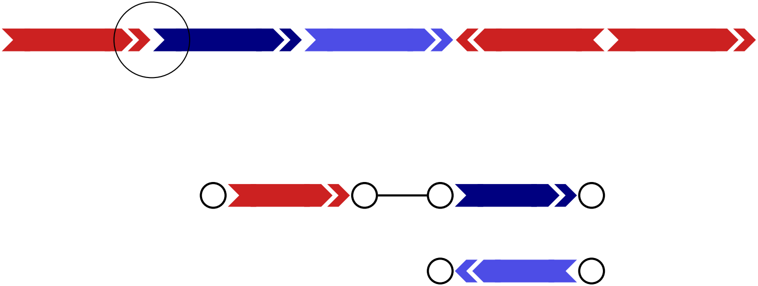

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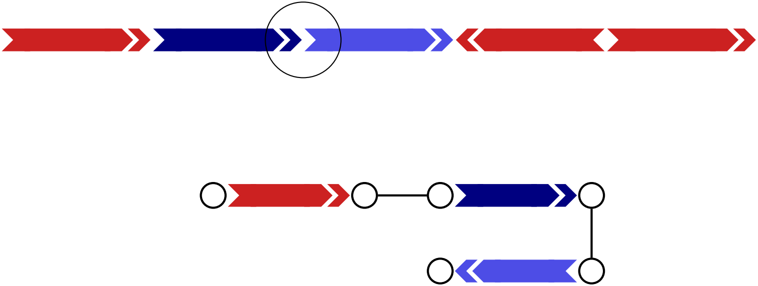

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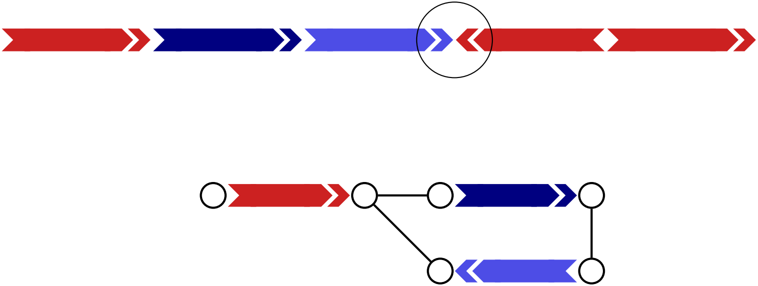

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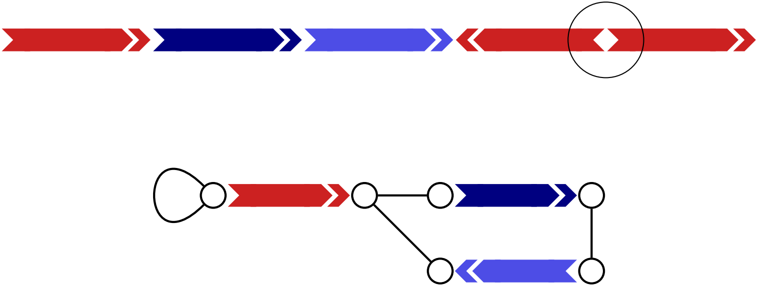

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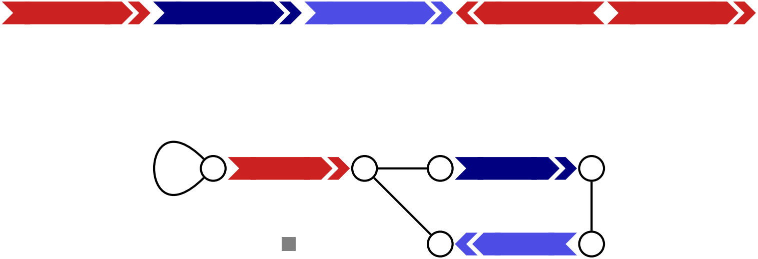

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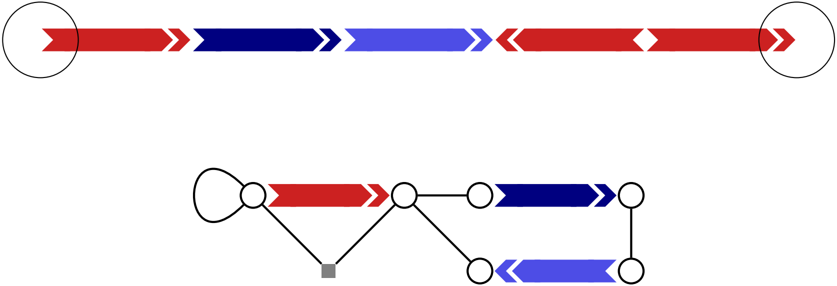
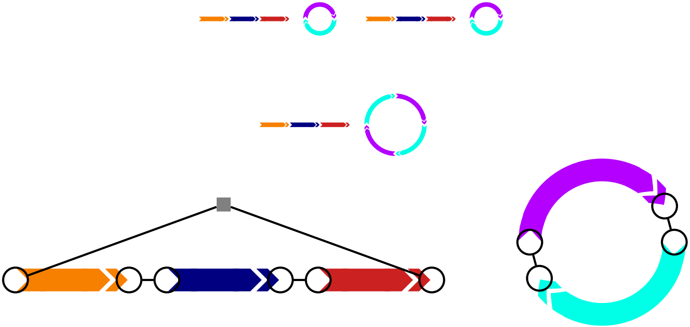
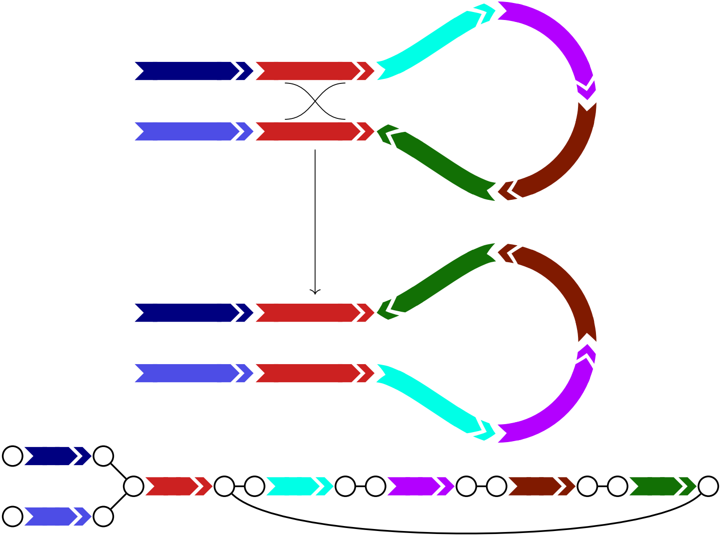


MBPG of a Simple Pangenome



- Simple pangenome $\iff$ adjacencies are a perfect matching

MBPG and Namos



- Namos don't change the graph!

Conclusions from the MBPG

Observation

Given a Namo o and pangenomes $\mathbb{P}, \mathbb{P}'$, *where* $\mathbb{P} \xrightarrow{o} \mathbb{P}'$, *the MBPGs of* $\mathbb{P}$ *and* $\mathbb{P}'$ *are identical.*

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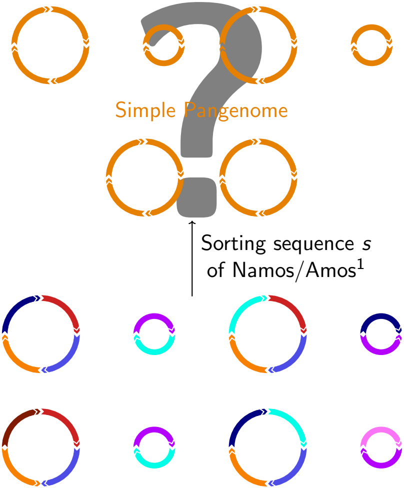
Definition

A set of Namos N is called MBPG-complete, if for all pairs of pangenomes $\mathbb{P}, \mathbb{P}'$ with the same MBPG there is a sequence of Namos $o_1 o_2 \dots o_k \in N^*$, such that $\mathbb{P} \xrightarrow{o_1}\xrightarrow{o_2} \cdots \xrightarrow{o_k} \mathbb{P}'$.

Complete Ancestral Reconstruction for Pangenomes (CARP)



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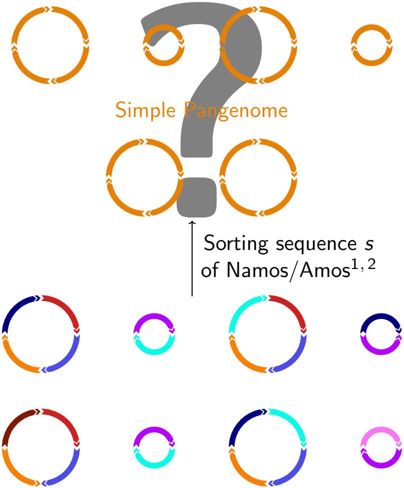

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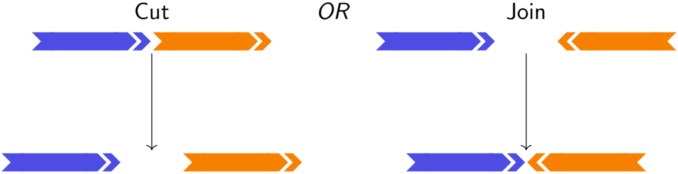
- [2] MBPG-complete set of Namos

SCJ-CARP

Amos: SCJ-operations



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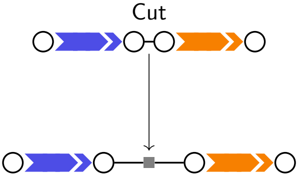
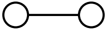


Modifying the MBPG with SCJs



Nothing to be done for adjacencies at non-branching nodes.

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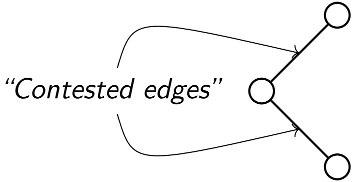

“Contested edges”

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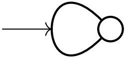

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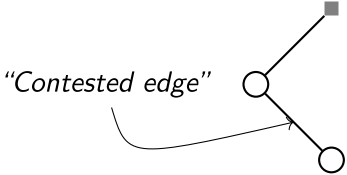


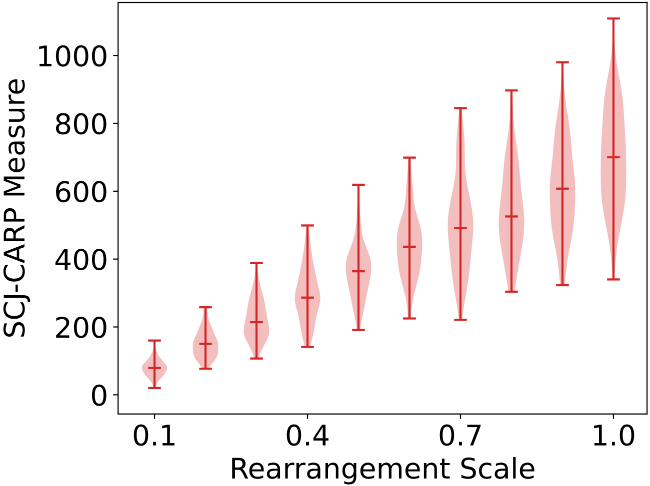
“Contested edge”

Modifying the MBPG with SCJs

Lemma

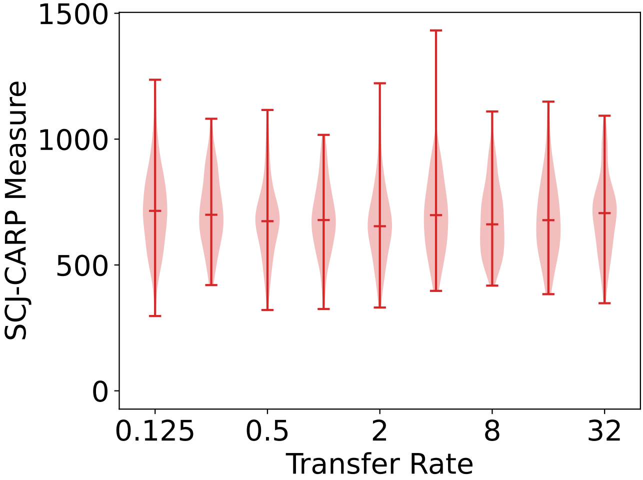
Need exactly $|E_C|$ SCJs to transform the MBPG into a simple MBPG where E_C is the set of contested adjacencies. We call $|E_C|$ the SCJ-CARP measure.

SCJ-CARP Tracks Structural Complexity



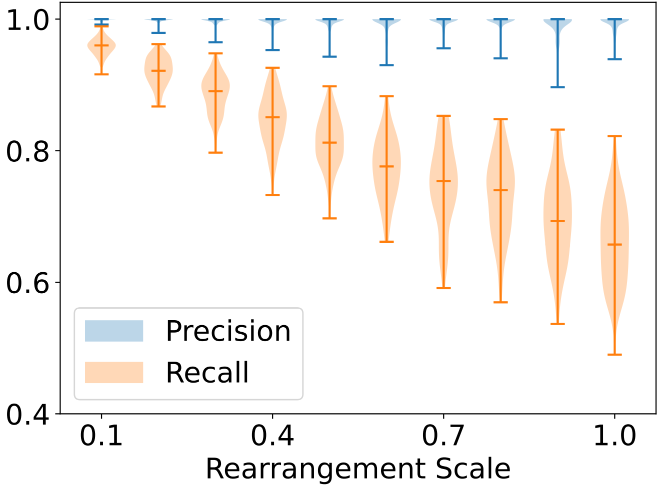
Pearson Coefficient: 0.88

SCJ-CARP Does Not Track Horizontal Effects



Pearson Coefficient: -0.01

SCJ-CARP Reconstructs Ancestral Adjacencies (to a Limited Extent)



Conclusion

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  - Advanced:
    - Among all possible CARP ancestors A_a, A_b
    - $d(\mathbb{P}_a, \mathbb{P}_b) = \min_{\mathbb{A}_a \in A_a, \mathbb{A}_b \in A_b} d(\mathbb{A}_a, \mathbb{A}_b)$

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  - Simple:
    - Calculate CARP ancestors $\mathbb{A}_a, \mathbb{A}_b$
    - $d(\mathbb{P}_a, \mathbb{P}_b) = d(\mathbb{A}_a, \mathbb{A}_b)$
  - Advanced:
    - Among all possible CARP ancestors A_a, A_b
    - $d(\mathbb{P}_a, \mathbb{P}_b) = \min_{\mathbb{A}_a \in A_a, \mathbb{A}_b \in A_b} d(\mathbb{A}_a, \mathbb{A}_b)$
- (Formal definition for) Marker segmentation on pangenomes

Thank you!

slides

github