Bridging Disparate Views on the DCJ-indel Model

WABI 2023

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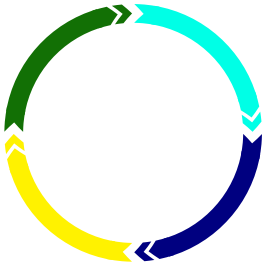
Bielefeld University

September 4, 2023

The Genomic Distance Problem



Genome $\mathbb{A}$

Genome $\mathbb{B}$

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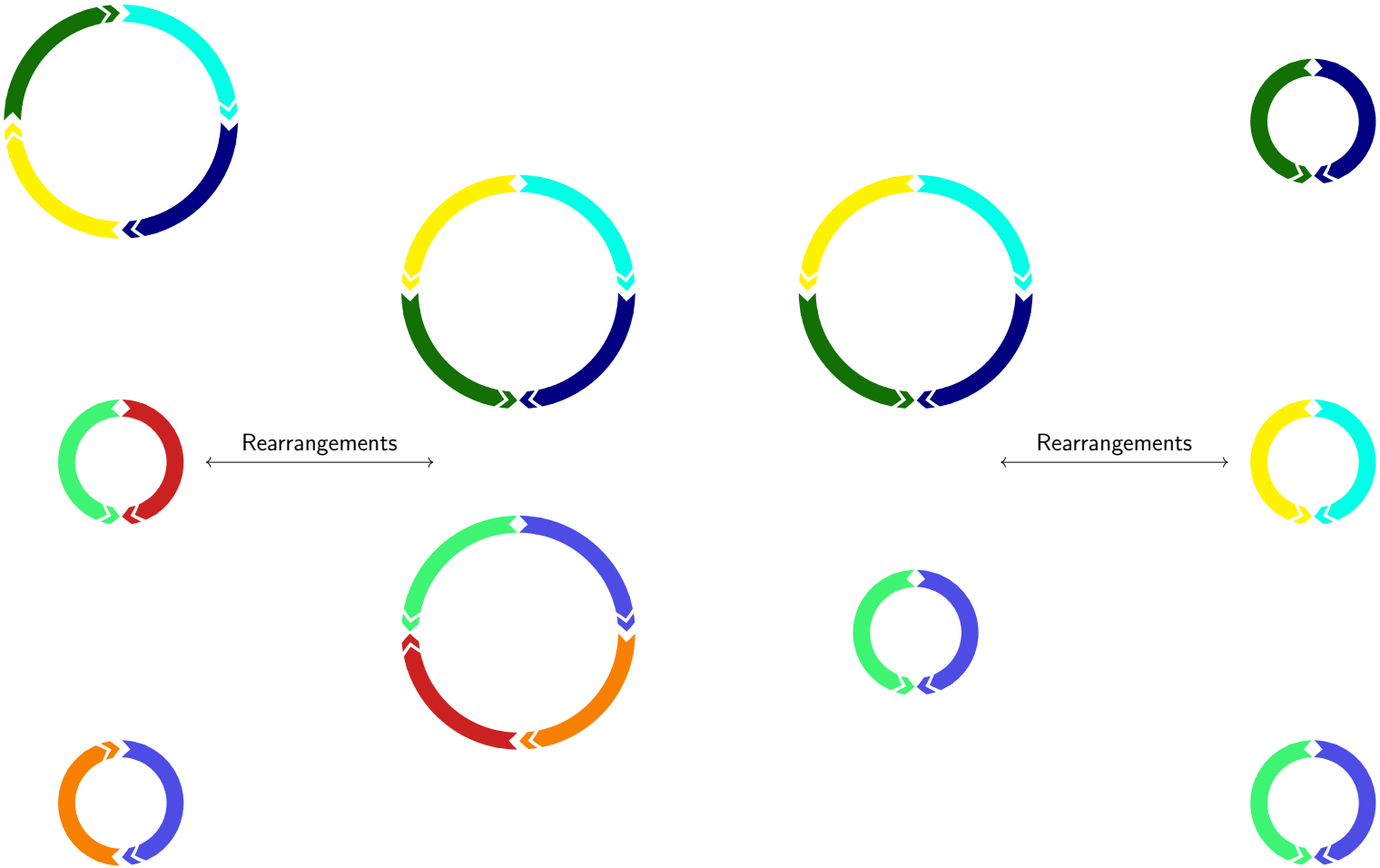

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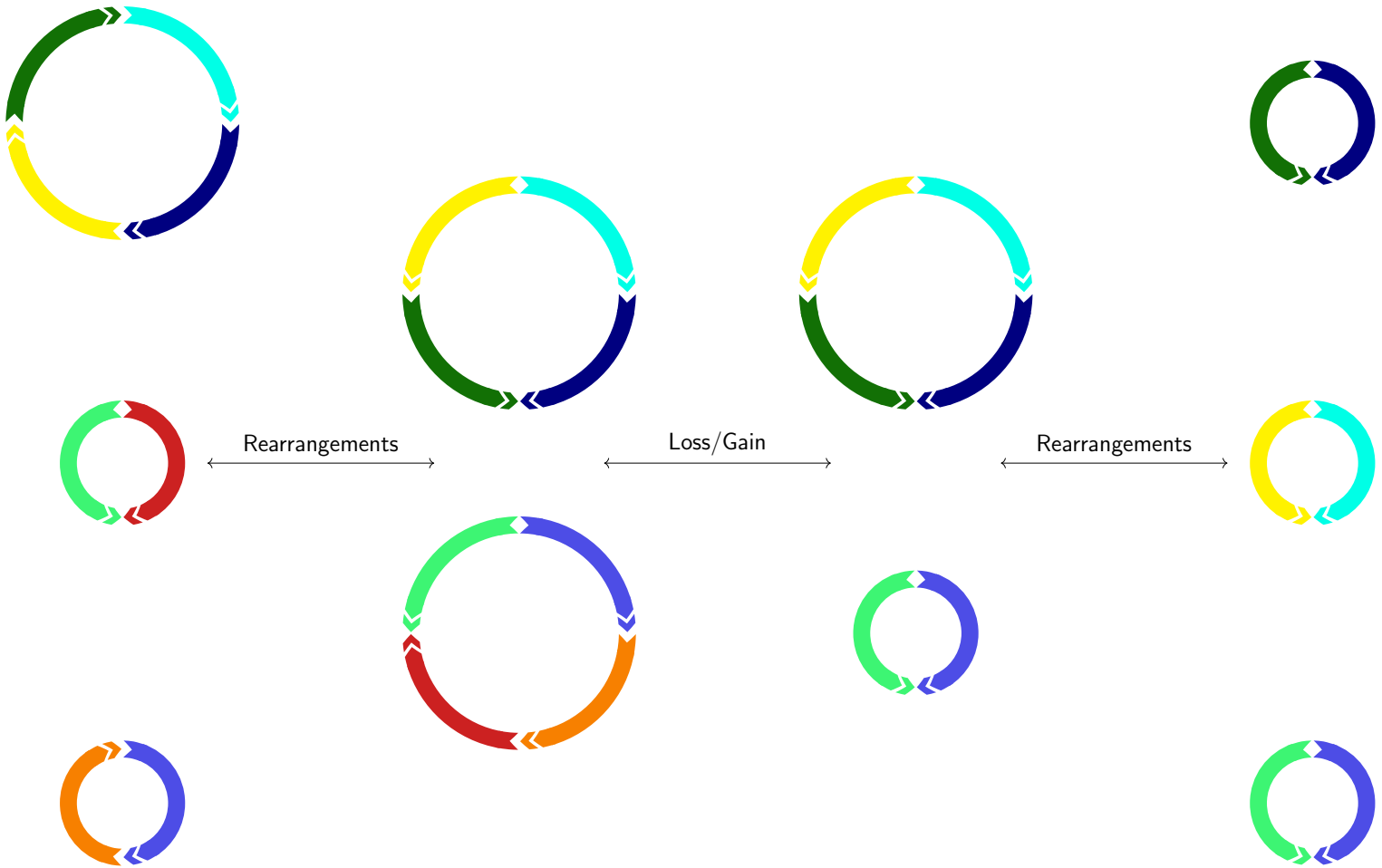

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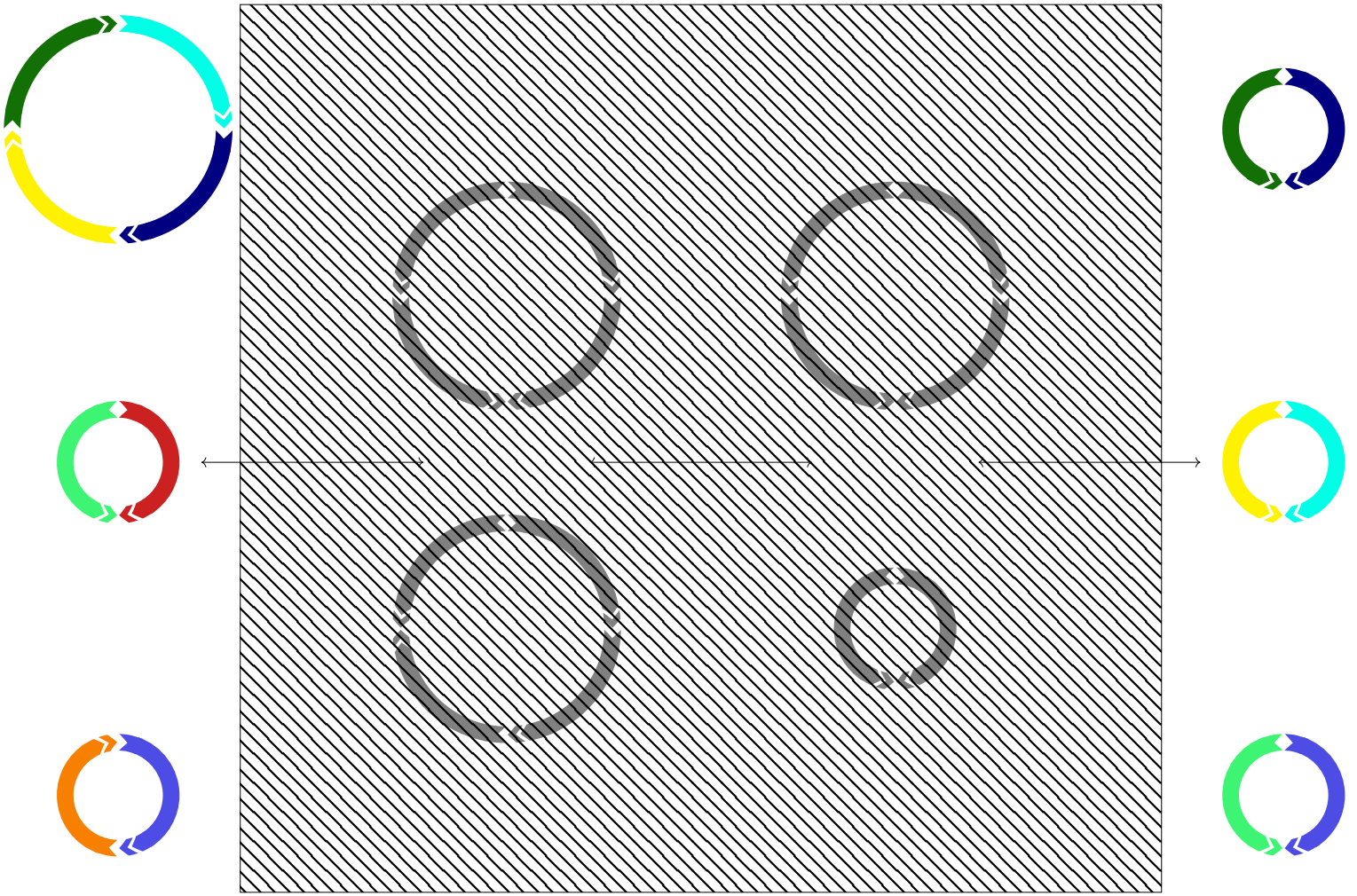

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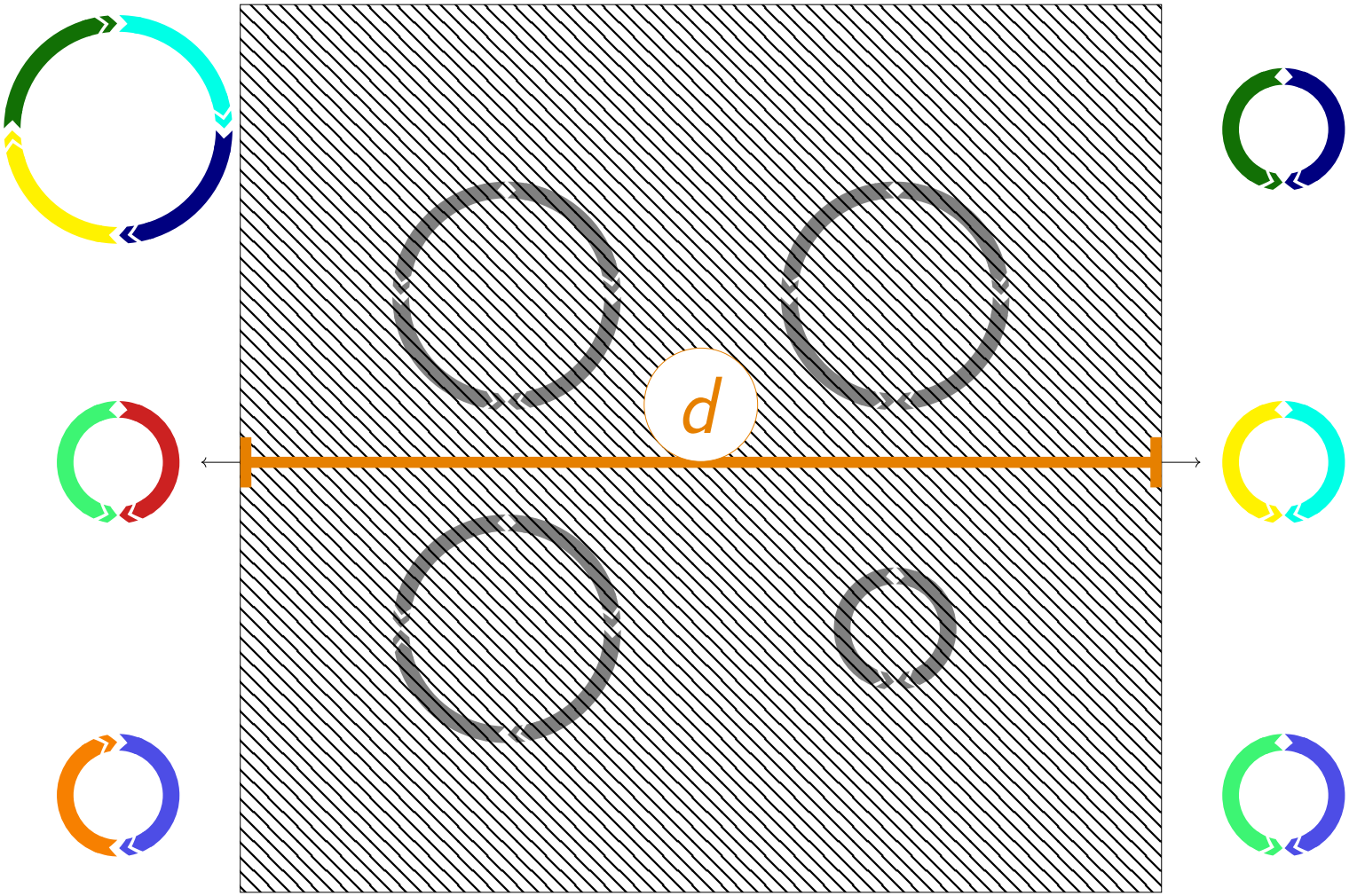
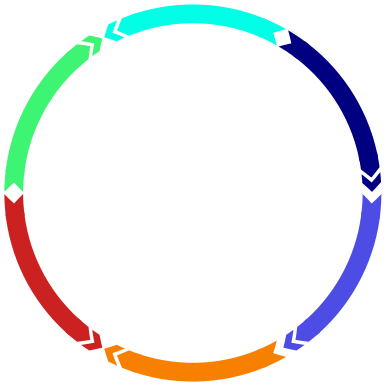


Operations: Double-Cut-and-Join (DCJ)



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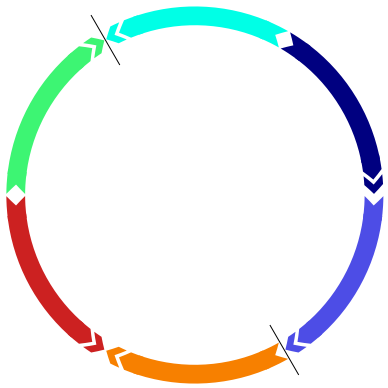

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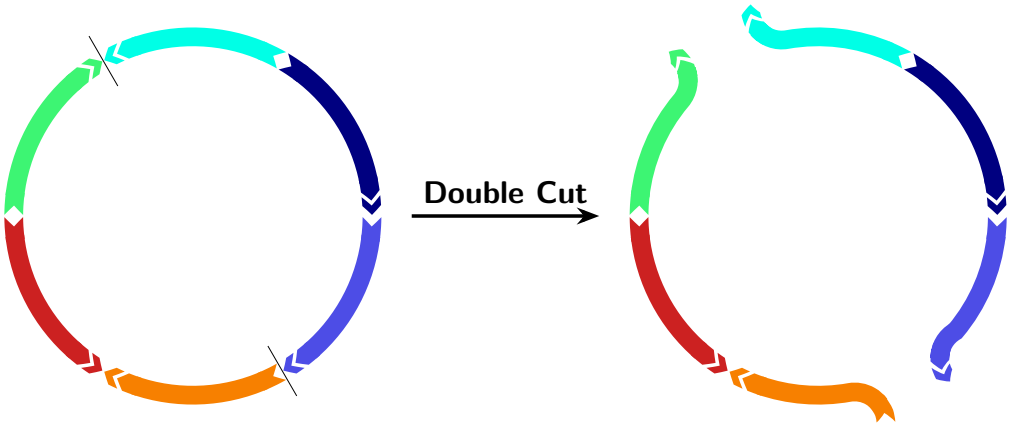

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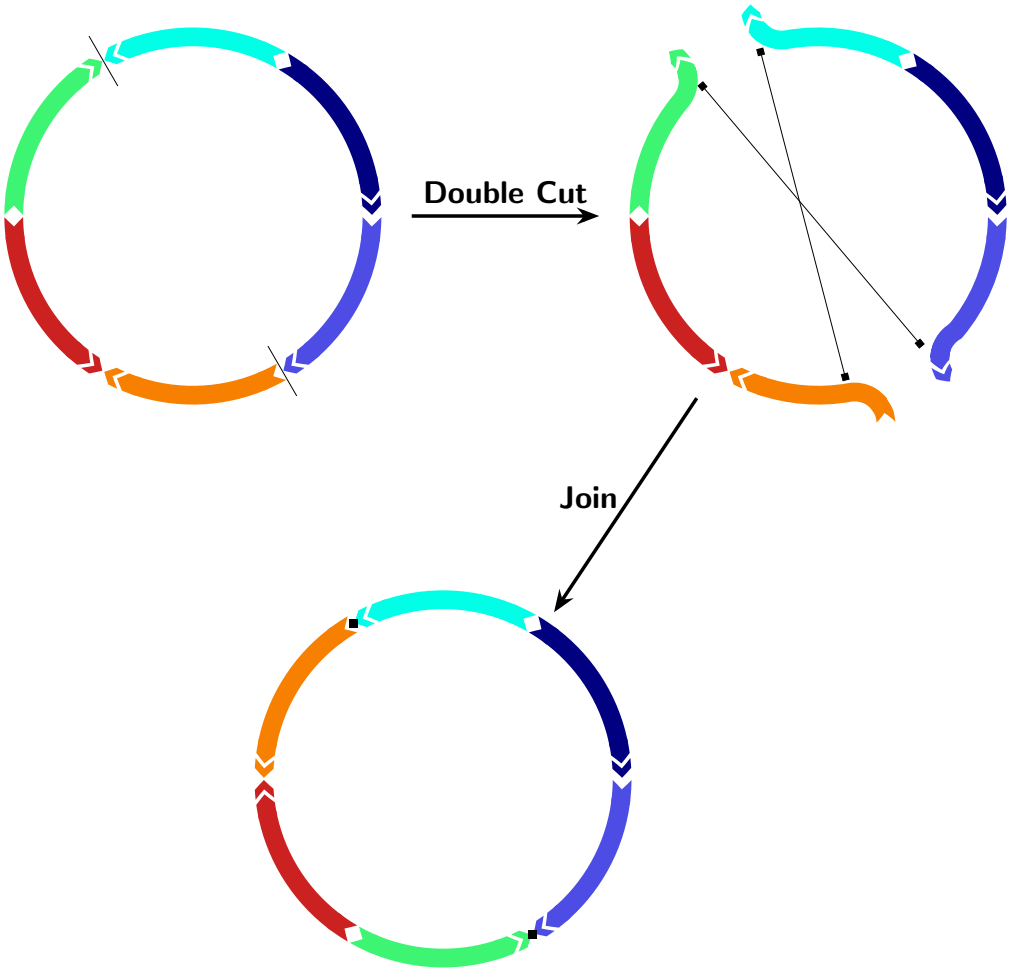

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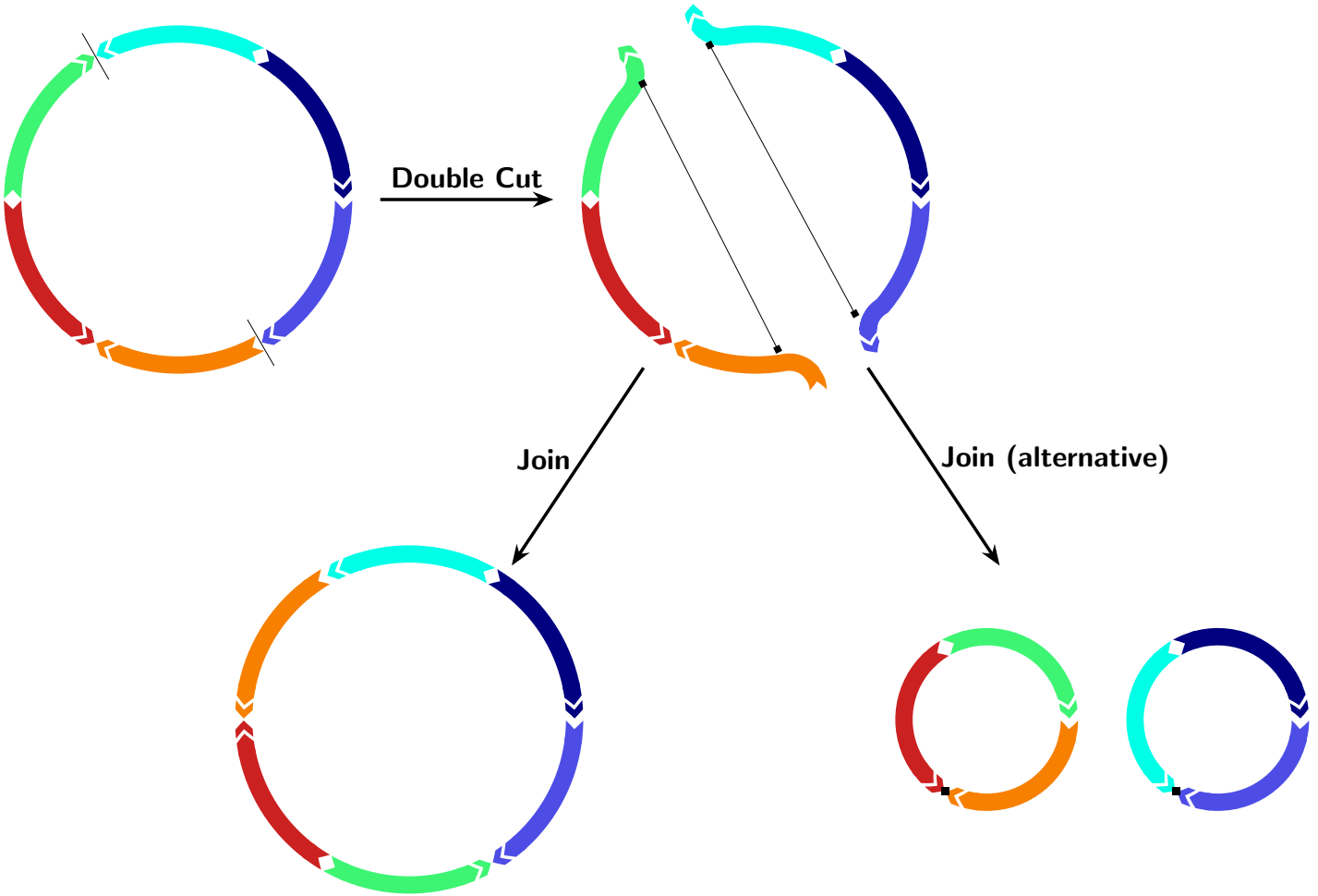
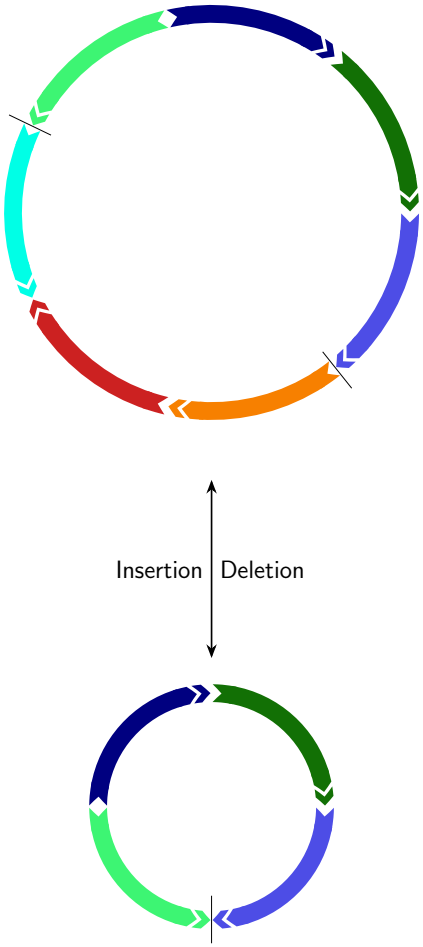
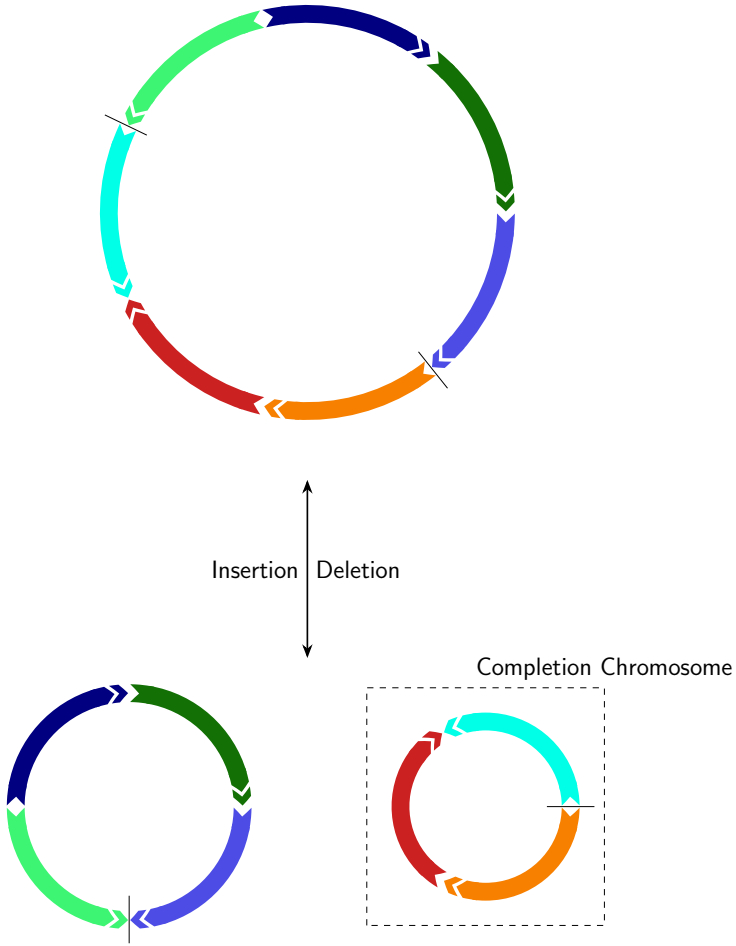


Operations: Indels

Explicitly (BWS, 2011)



Via Completion (Compeau, 2013)



Problems with the BWS- and Compeau-Conceptualizations

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	Sources	Reusable Resultants	Unsat. after safe internal ops.					Unsat. after all safe ops. in group					No partner due to
			$A \circ a$	$B \vert a$	$a \vert b$	$A \vert b$	$B \circ b$	$A \circ a$	$B \vert a$	$p_{a \vert b}$	$A \vert b$	$B \circ b$	
P													
1	$AA_{\mathcal{AB}} + BB_{\mathcal{AB}}$		1	1	2	1	1	0	0	0	0	0	
Q													
1	$2AA_{\mathcal{AB}} + BB_{\mathcal{A}} + BB_{\mathcal{B}}$		2	2	2	2	2	0	0	0	0	0	
2	$2BB_{\mathcal{AB}} + AA_{\mathcal{A}} + AA_{\mathcal{B}}$		2	2	2	2	2	0	0	0	0	0	
T													
1	$AA_{\mathcal{AB}} + BB_{\mathcal{A}} + AB_{\mathcal{AB}}$		2	2	2	1	1	0	0	0	0	0	
2	$AA_{\mathcal{AB}} + BB_{\mathcal{B}} + AB_{\mathcal{BA}}$		1	1	2	2	2	0	0	0	0	0	
3	$BB_{\mathcal{AB}} + AA_{\mathcal{A}} + AB_{\mathcal{BA}}$		2	2	2	1	1	0	0	0	0	0	
4	$BB_{\mathcal{AB}} + AA_{\mathcal{B}} + AB_{\mathcal{AB}}$		1	1	2	2	2	0	0	0	0	0	
5	$2AA_{\mathcal{AB}} + BB_{\mathcal{A}}$	$AA_{\mathcal{B}}$	2	2	2	2	0	0	0	0	2	0	$P_{A\vert b} \to T1, Q1, P1;$
6	$2AA_{\mathcal{AB}} + BB_{\mathcal{B}}$	$AA_{\mathcal{A}}$	2	0	2	2	2	2	0	0	0	0	$P_{A \circ a} \to T2, Q1, P1;$
7	$2BB_{\mathcal{AB}} + AA_{\mathcal{A}}$	$BB_{\mathcal{B}}$	2	2	2	0	2	0	0	0	0	2	$P_{B \circ b} \to Q2, P1, T3;$
8	$2BB_{\mathcal{AB}} + AA_{\mathcal{B}}$	$BB_{\mathcal{A}}$	0	2	2	2	2	0	2	0	0	0	$P_{B\vert a} \to Q2, P1, T4;$
S													
1	$AA_{\mathcal{A}} + BB_{\mathcal{A}}$		2	2	0	0	0	0	0	0	0	0	
2	$AA_{\mathcal{B}} + BB_{\mathcal{B}}$		0	0	0	2	2	0	0	0	0	0	
3	$AB_{\mathcal{AB}} + AB_{\mathcal{BA}}$		1	1	2	1	1	0	0	0	0	0	
4	$AA_{\mathcal{AB}} + BB_{\mathcal{A}}$	$AB_{\mathcal{BA}}$	1	2	1	1	0	0	1	1	1	0	$P_{B\vert a} \to S1, T5, T1;$ $\star P_{a\vert b} \to T5, T1, P1;$

Problems with the BWS- and Compeau-Conceptualizations

- Unwieldy formulas:
  - Compeau:

$$d_{DCJ}^{ind}(\Pi,\Gamma) = N - [(c + p^{\pi,\pi} + p^{\gamma,\gamma} + \lfloor\frac{p^{\pi,\gamma}}{2}\rfloor)$$
$$+ \frac{1}{2}(p_{even}^{0} + \min\{p_{odd}^{\pi}, p_{even}^{\pi}\} + \min\{p_{odd}^{\gamma}, p_{even}^{\gamma}\} + \delta)]$$

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$\delta = 1$ when $p^{\pi,\gamma}$ odd and either $p_{odd}^{\pi} > p_{even}^{\pi}, p_{odd}^{\gamma} > p_{even}^{\gamma}$ or $p_{odd}^{\pi} < p_{even}^{\pi}, p_{odd}^{\gamma} < p_{even}^{\gamma}$; otherwise $\delta = 0$.

Problems with the BWS- and Compeau-Conceptualizations

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- Models known to be equivalent, but unclear how formulas relate.

The Relational Diagram

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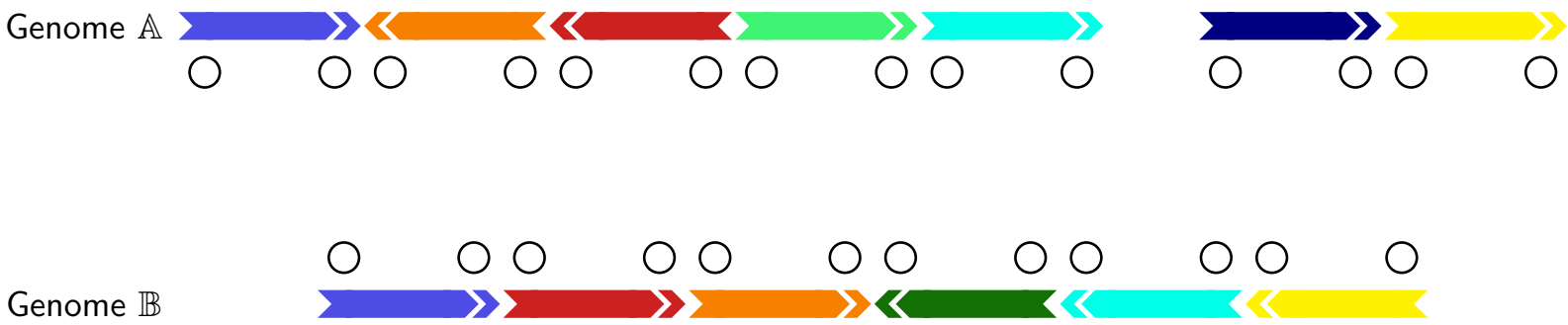

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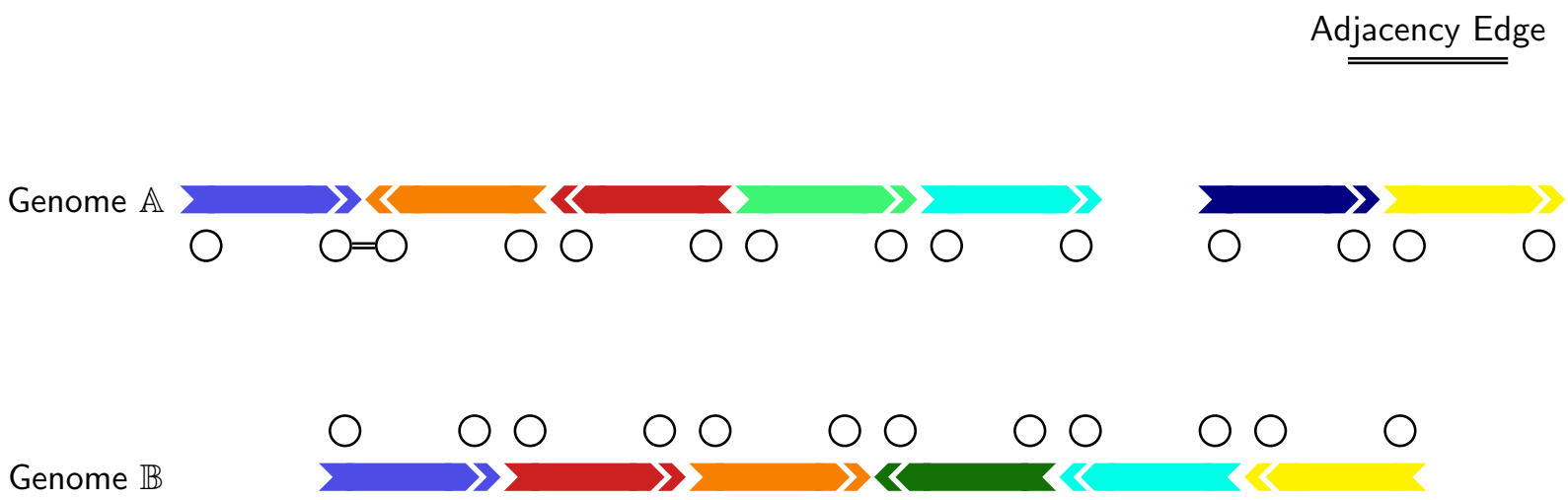

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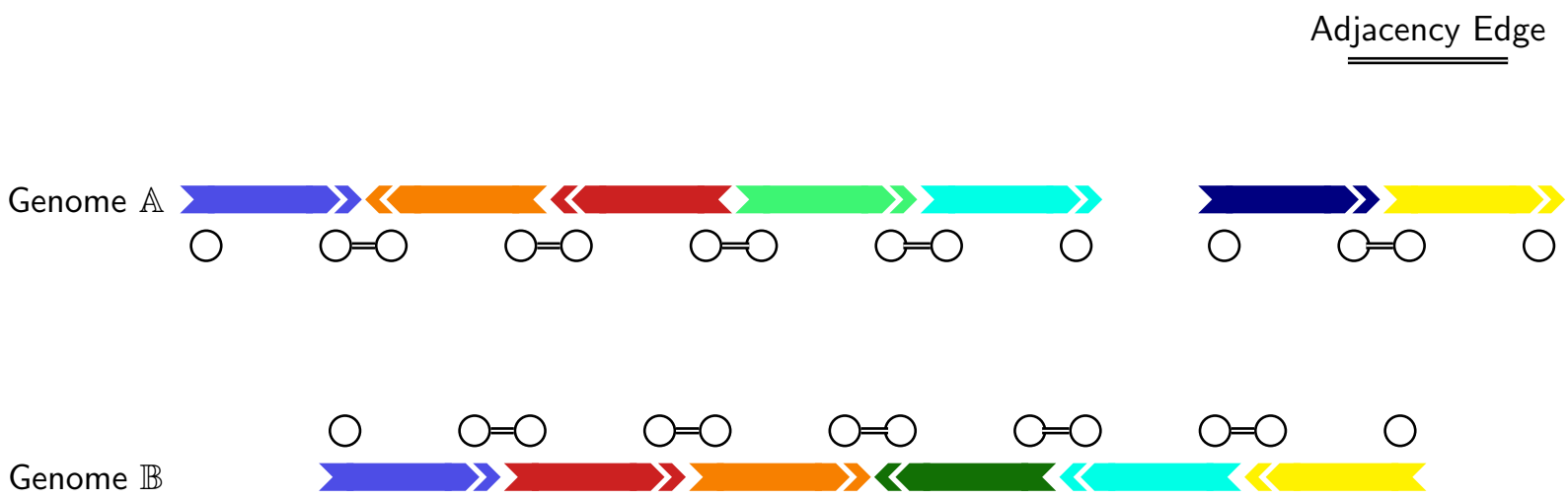

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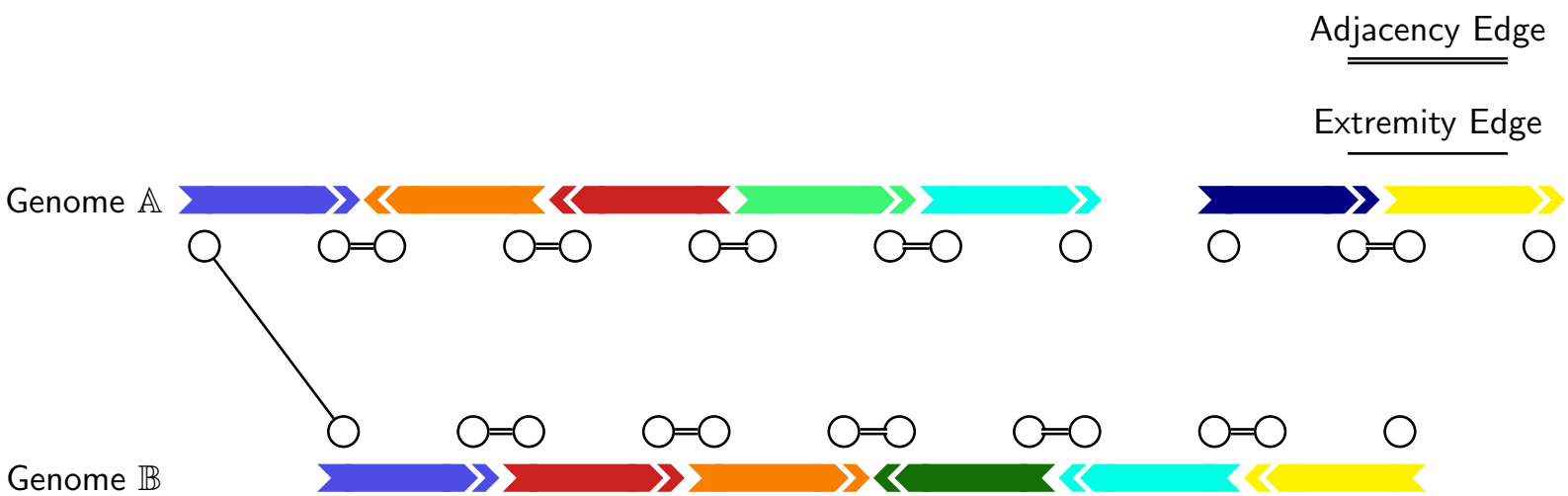

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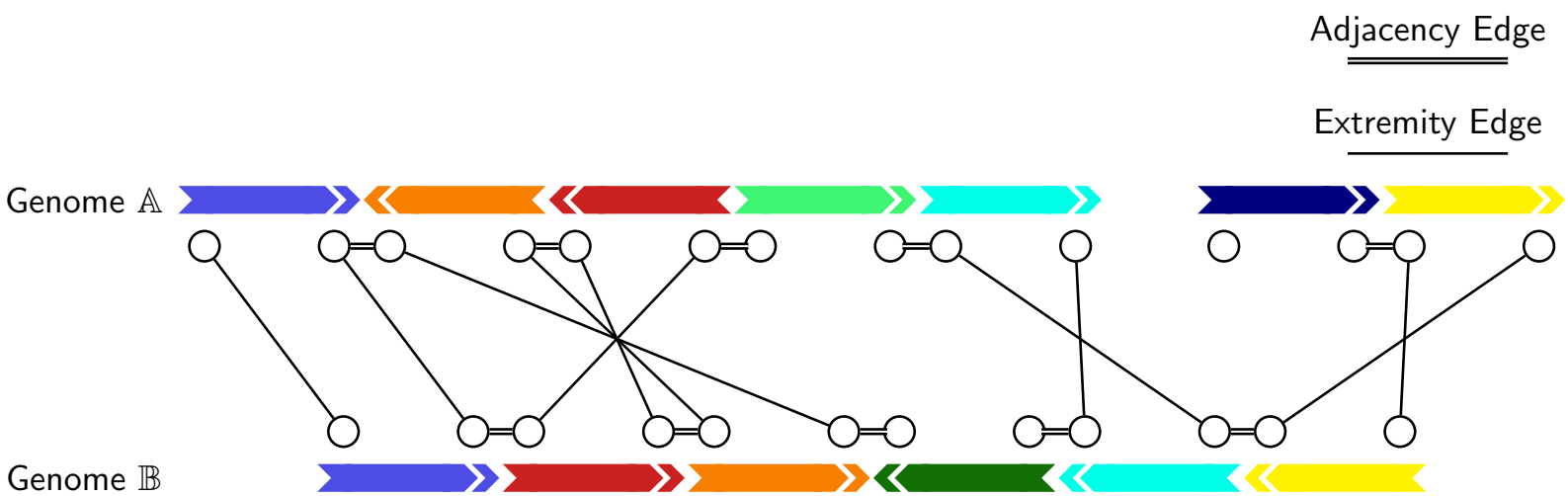

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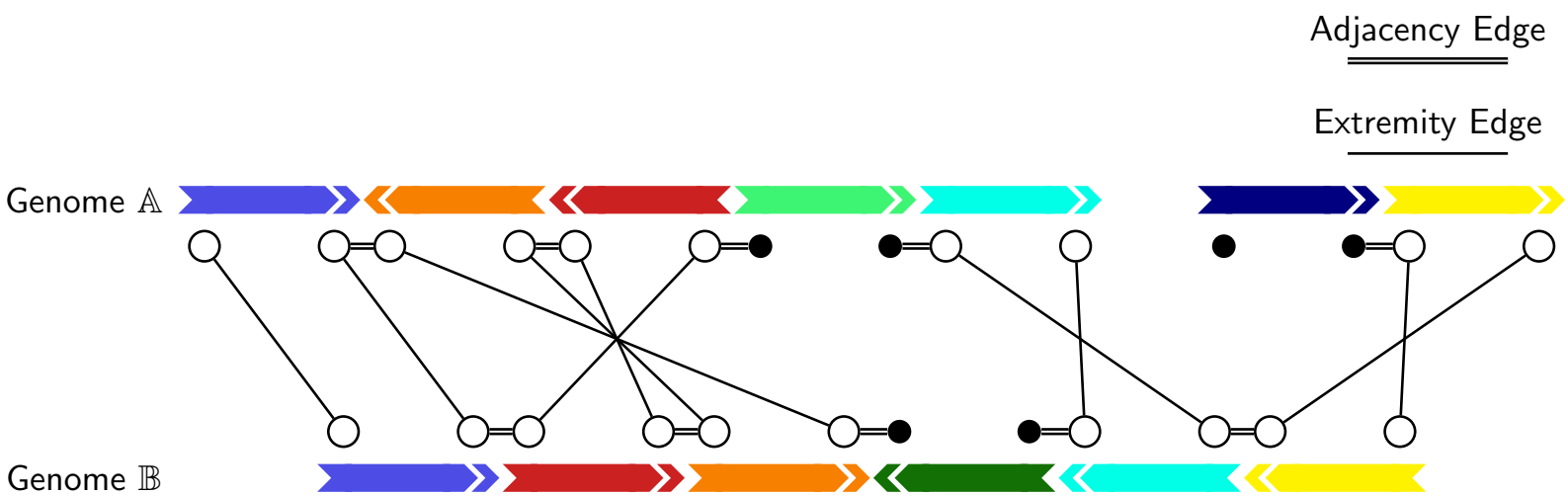

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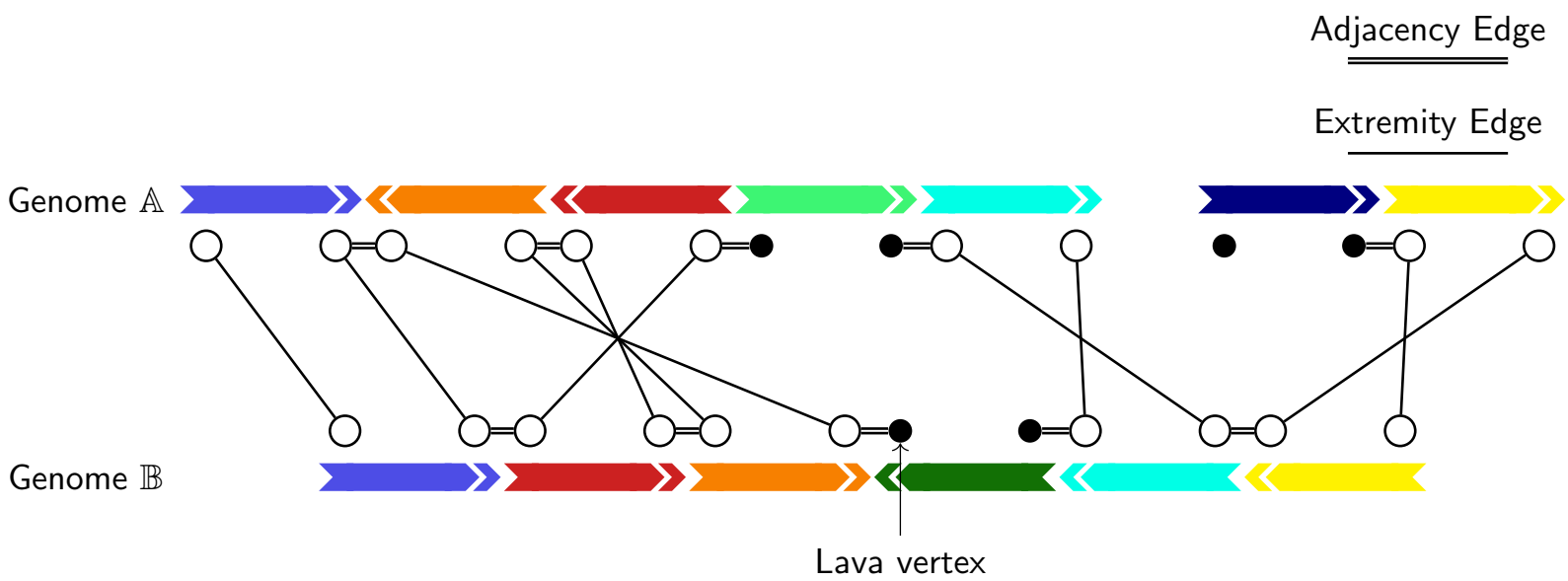

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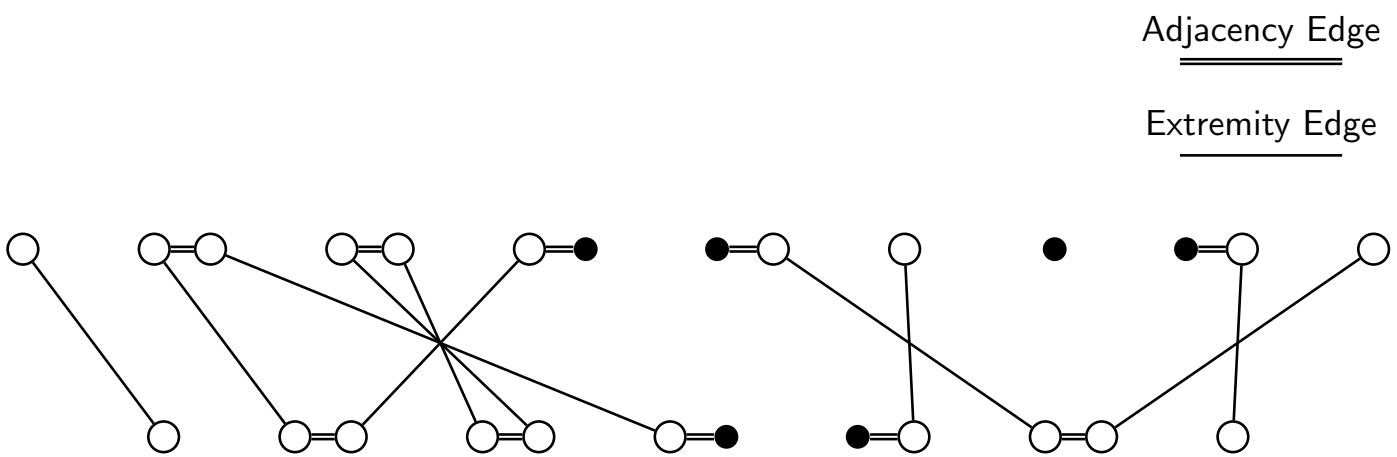
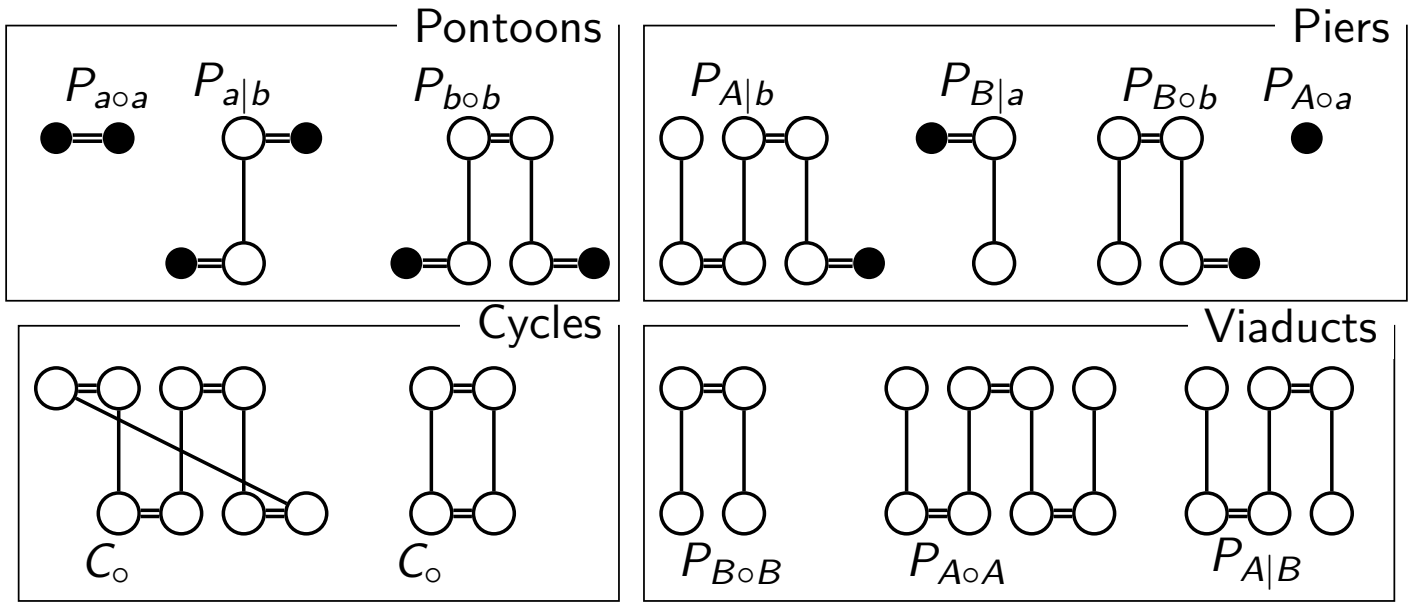
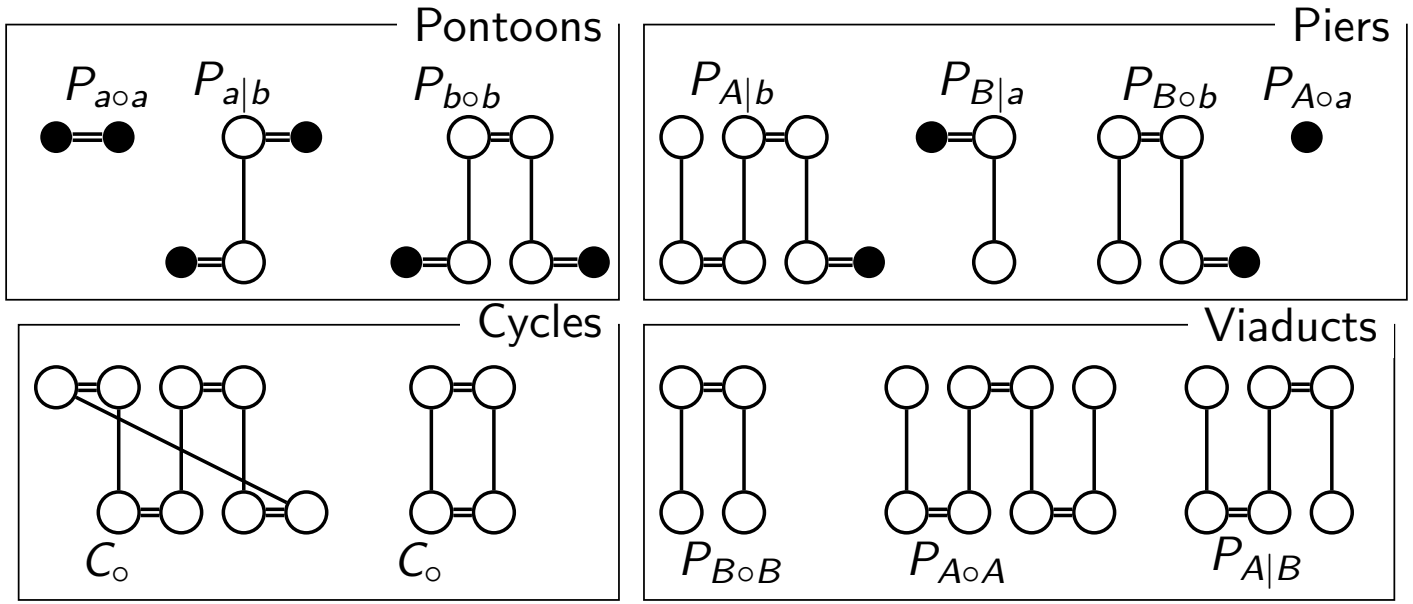


Types of Components



Earlier work, Recomb-CG 2023.

A New Formula



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$$d_{DCJ}^{id}(\mathbb{A},\mathbb{B}) = n - c_\circ + \left\lceil \frac{p_{a|b} + \max(p_{A\circ a}, p_{B|a}) + \max(p_{A|b}, p_{B\circ b}) - p_{A|B}}{2} \right\rceil$$

Safe Operations

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Safe operations reduce the formula by 1, no matter the rest of the graph.

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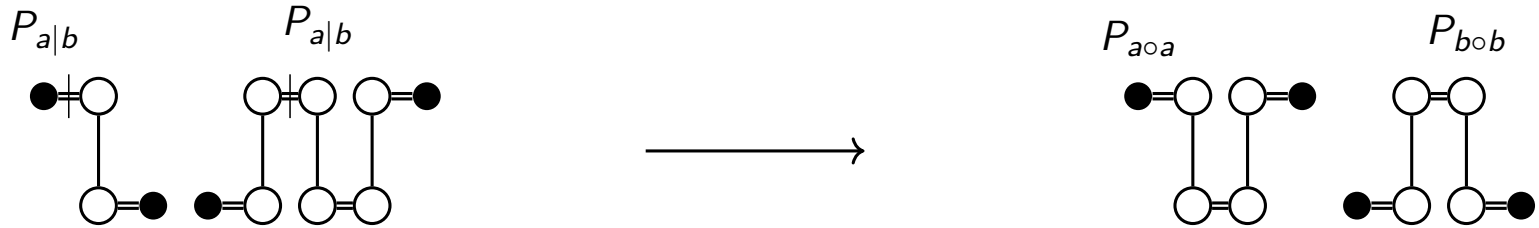

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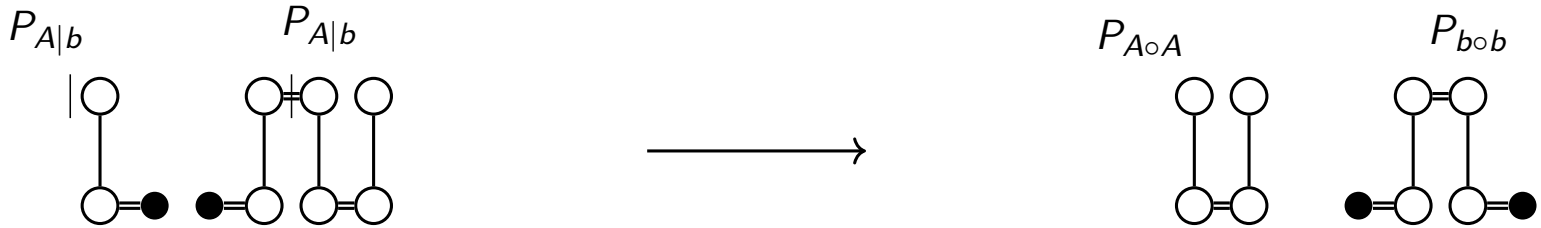
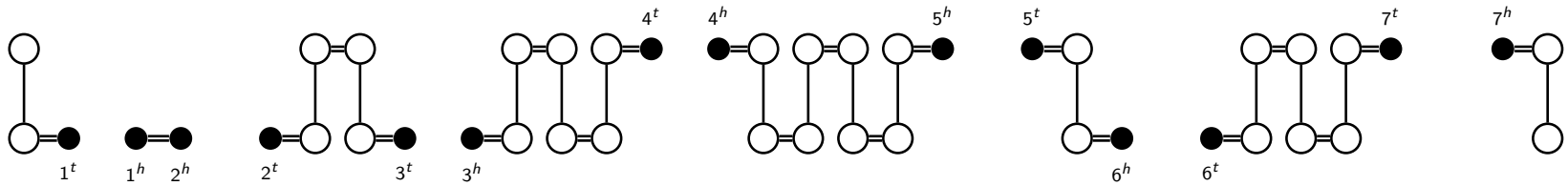


Unsafe operation

BWS-Conceptualization: Basics



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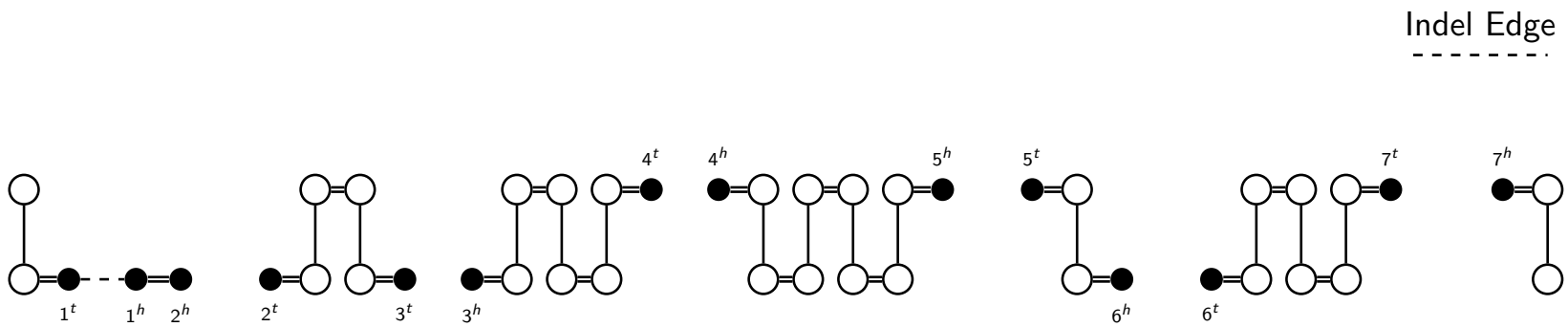

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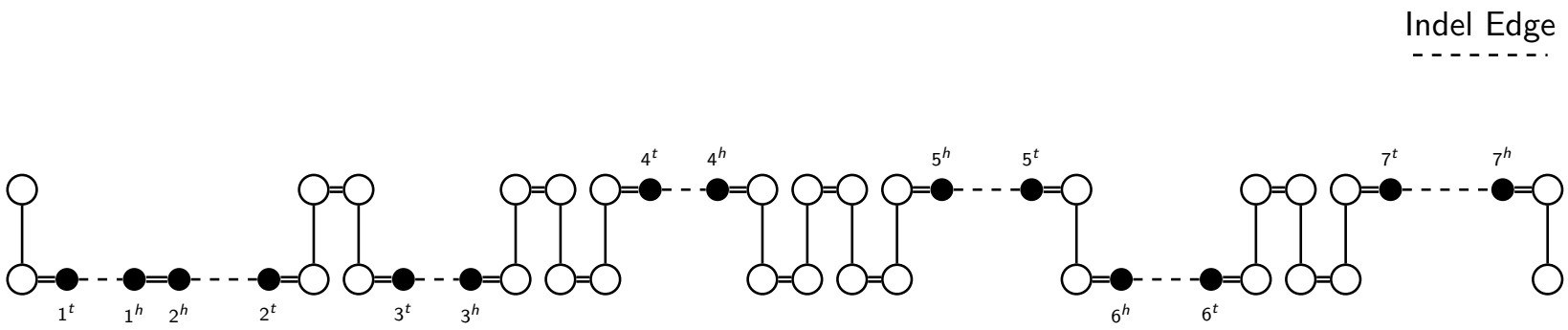

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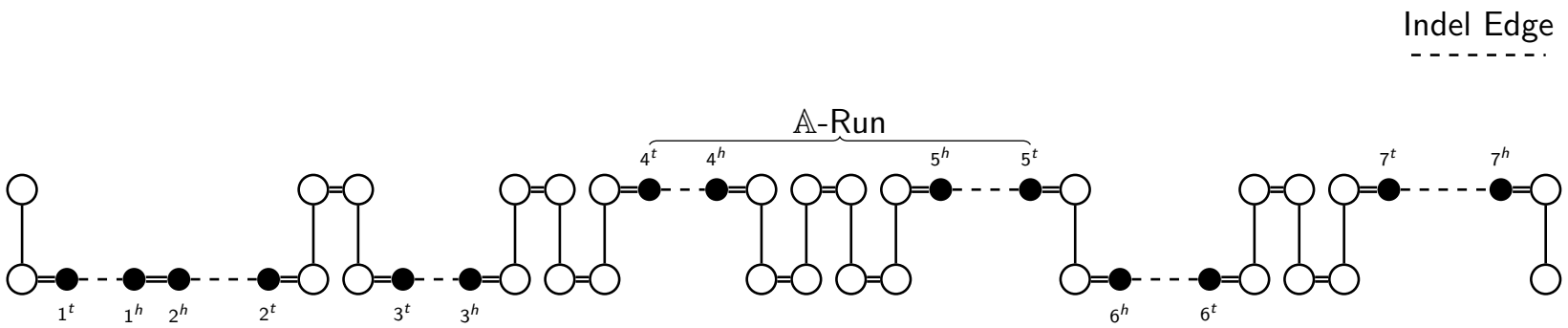

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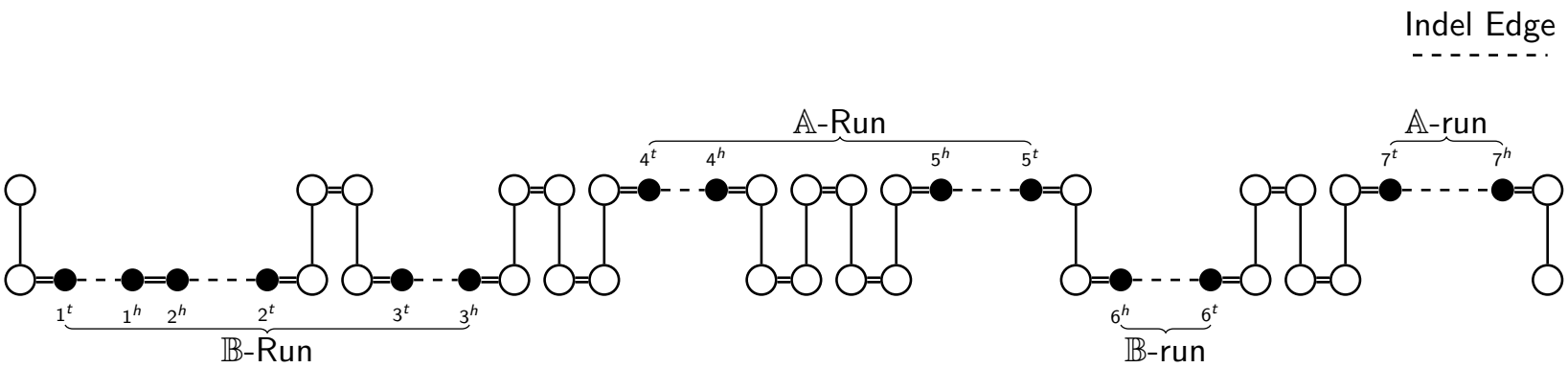
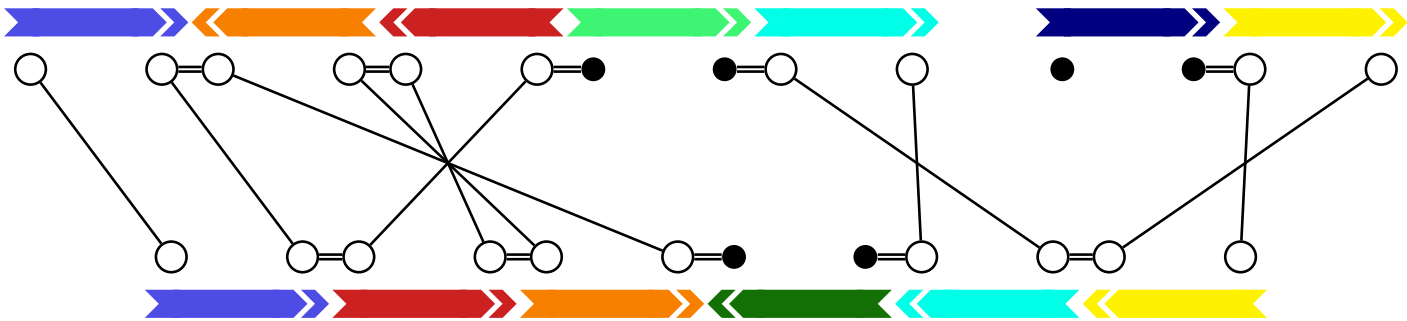


Compeau-Conceptualization: Basics



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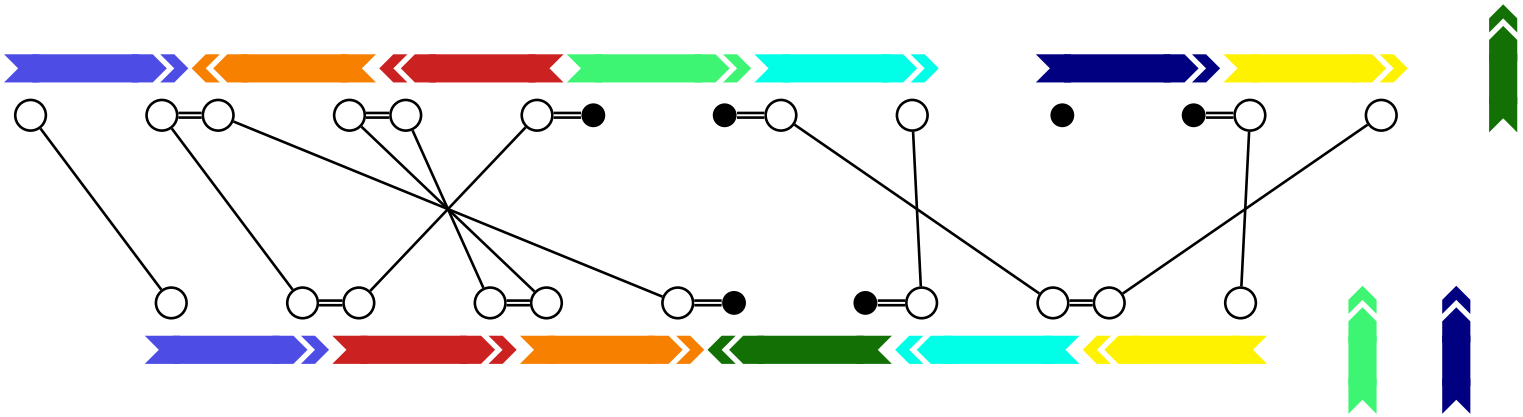

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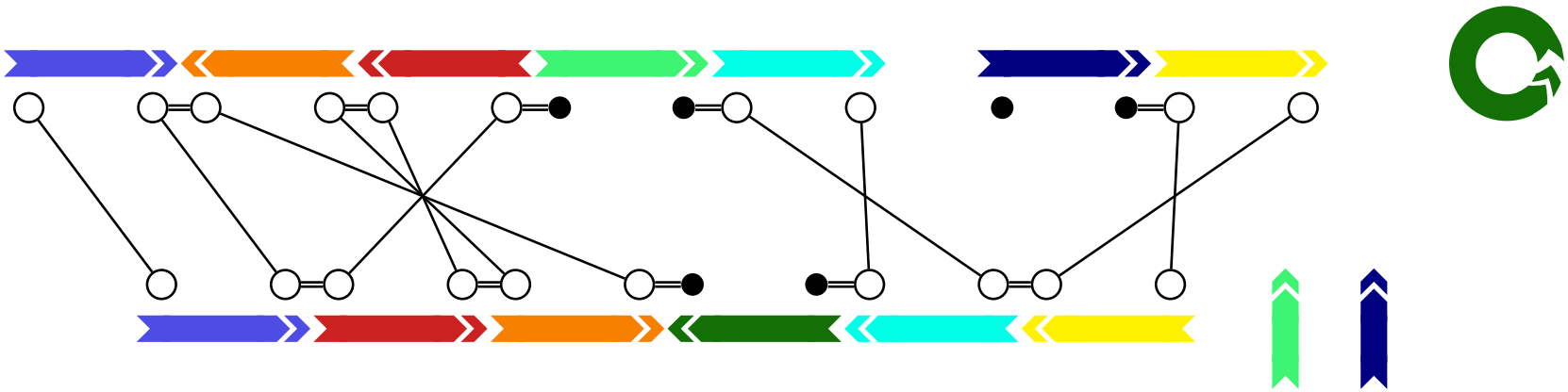

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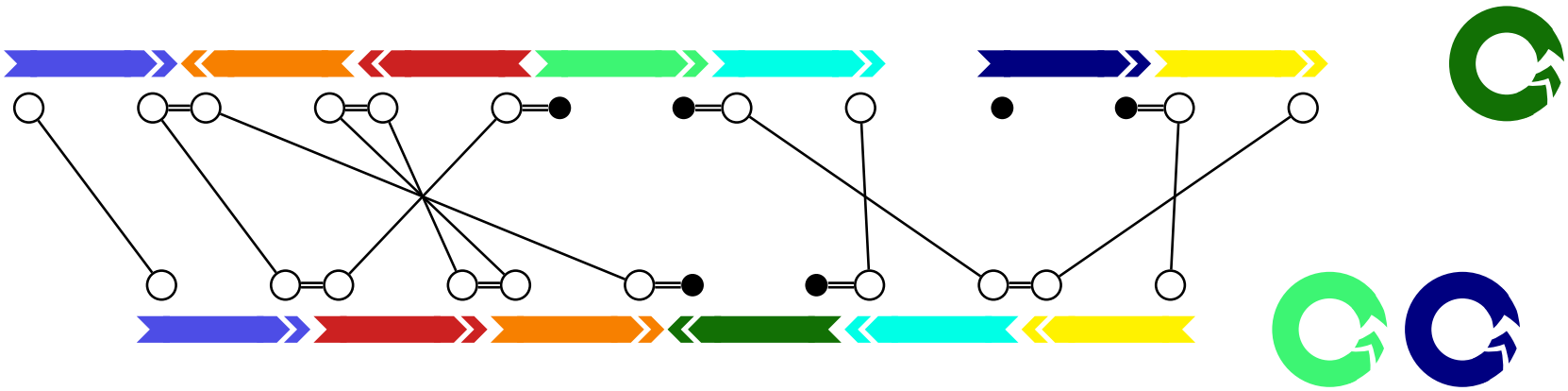

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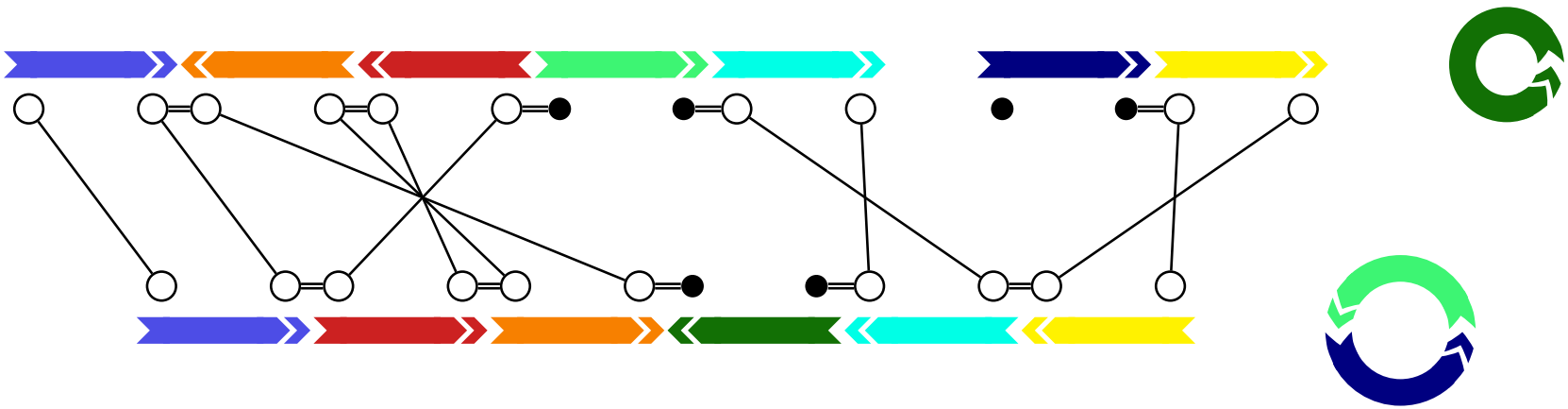

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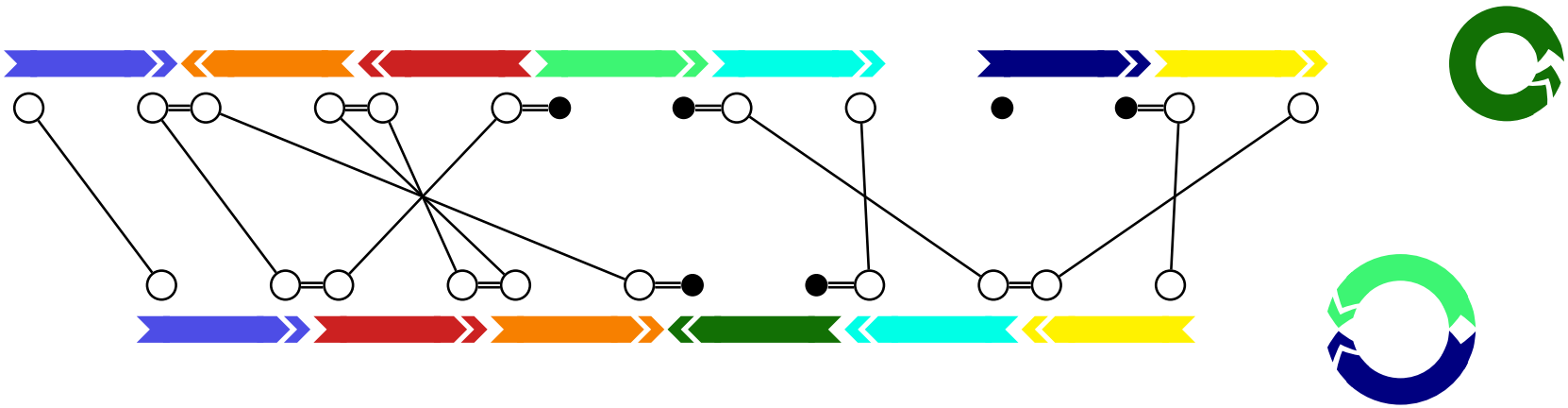

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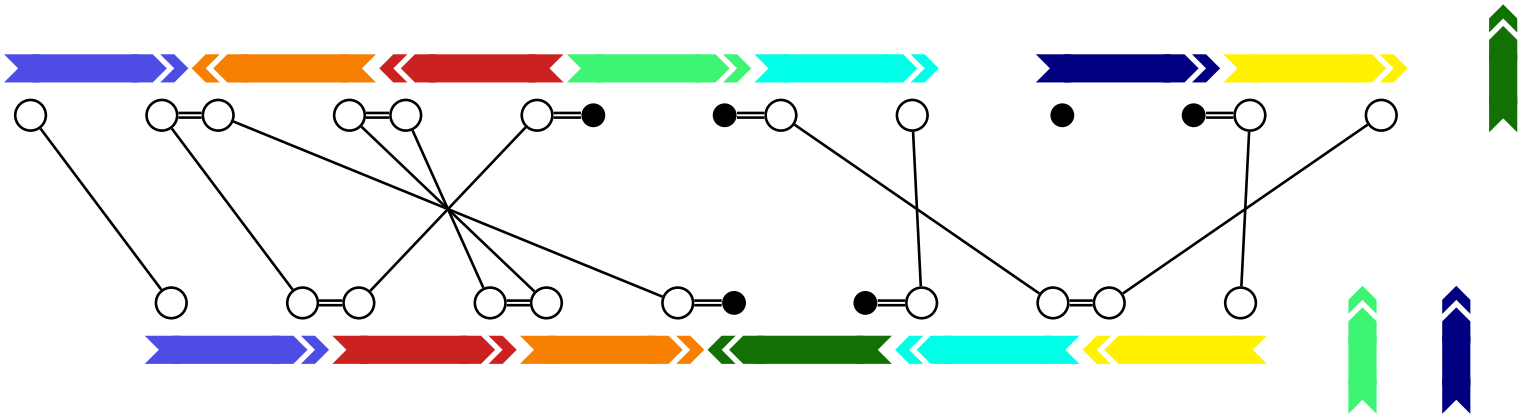
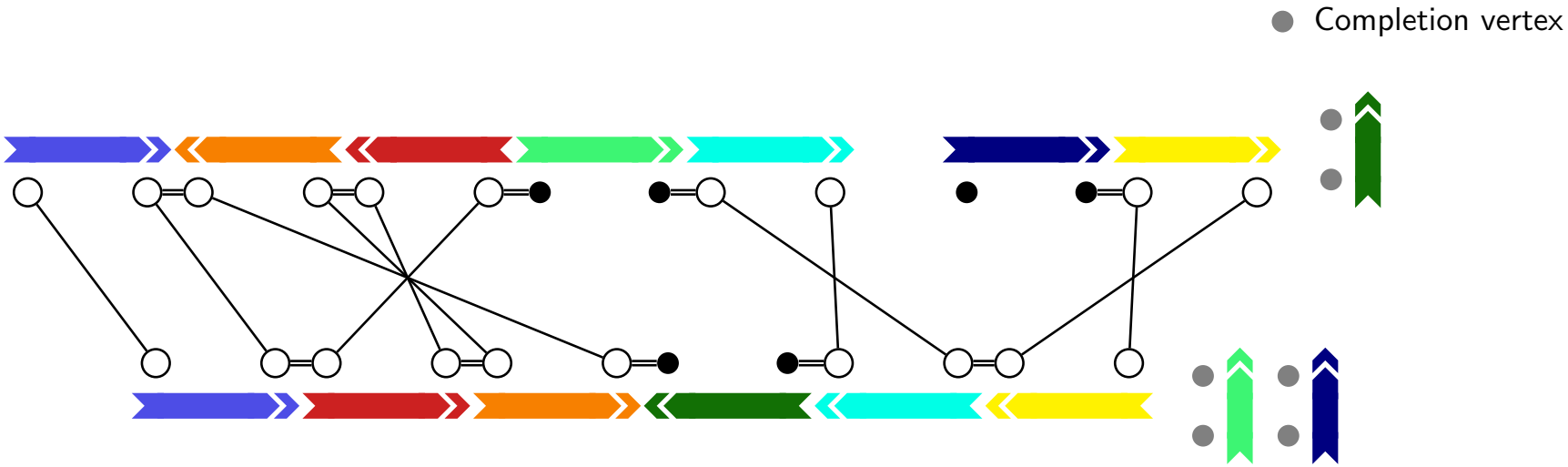
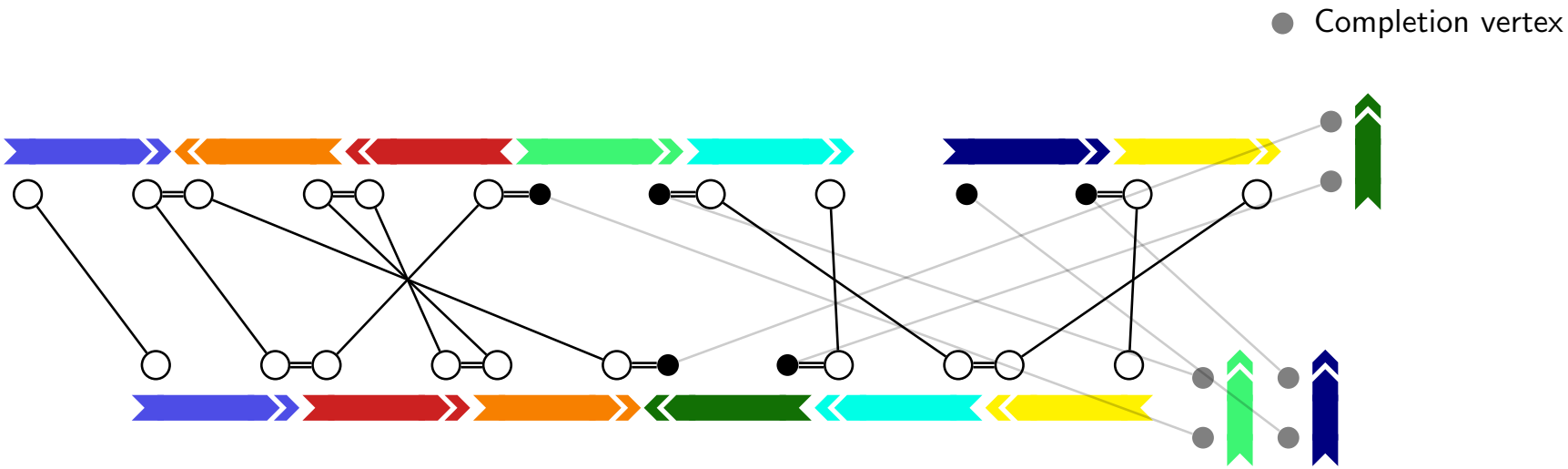


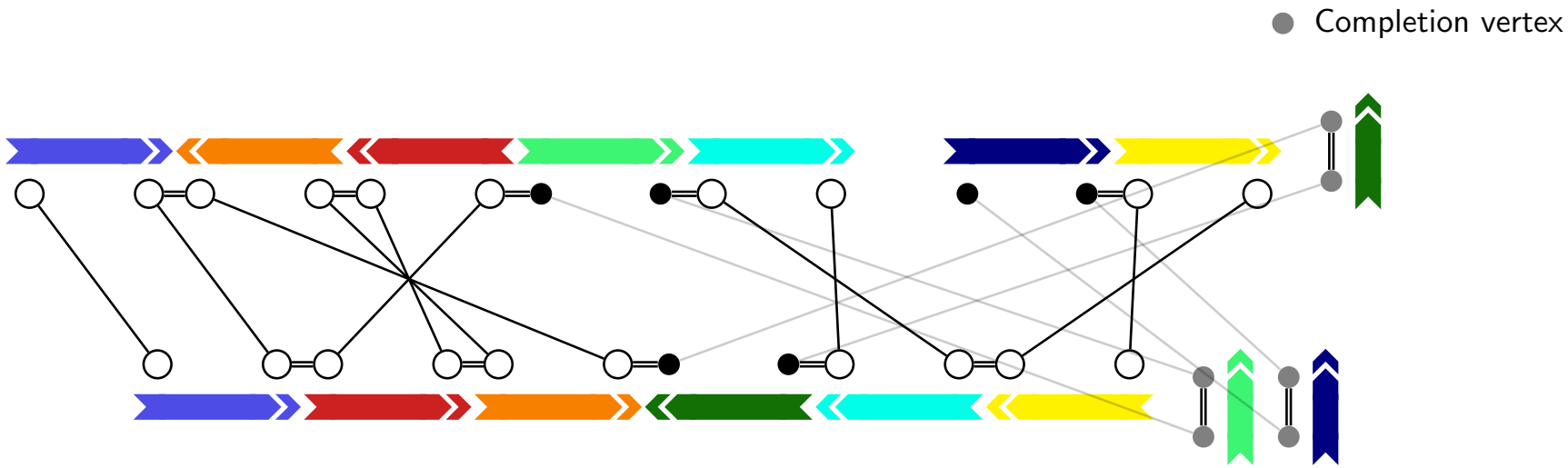
Compeau-Conceptualization: Basics



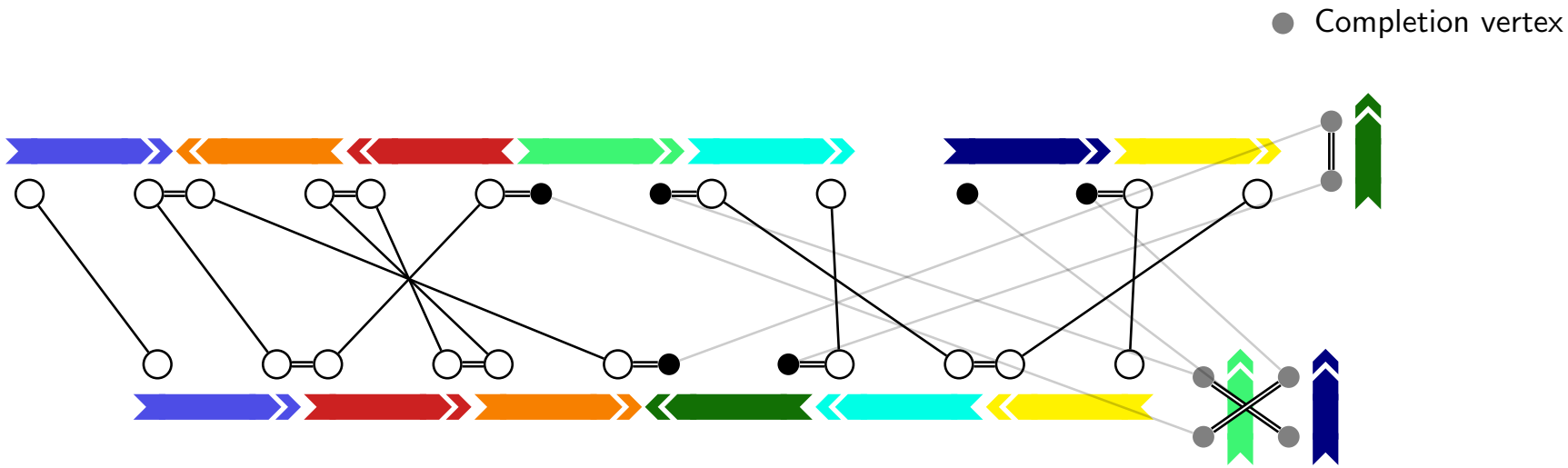
Compeau-Conceptualization: Basics



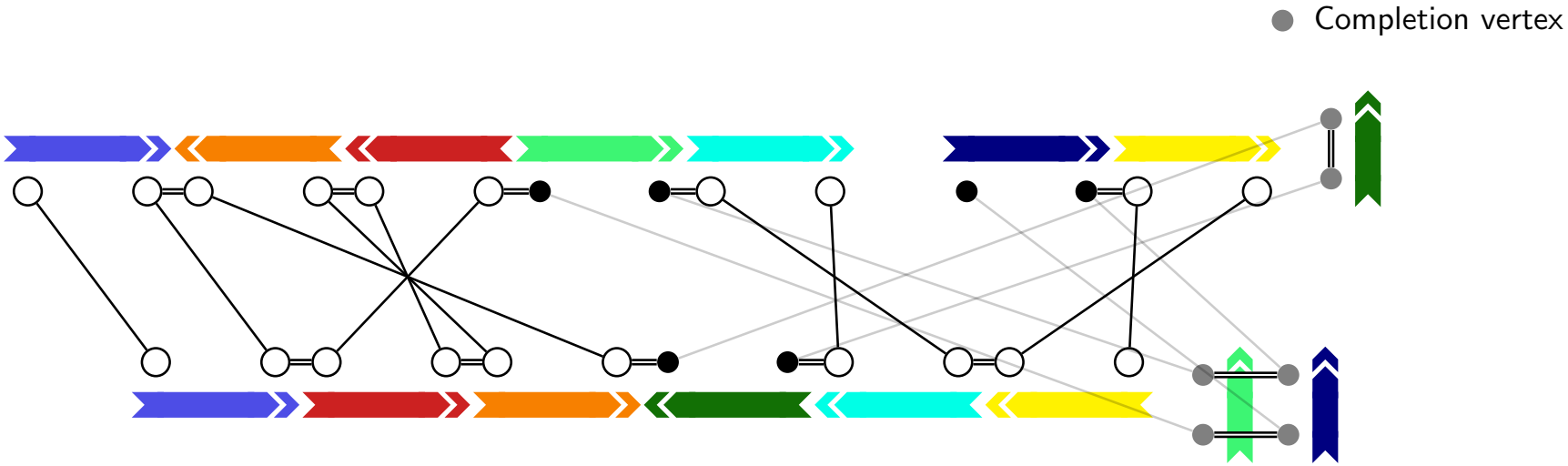
Compeau-Conceptualization: Basics



Compeau-Conceptualization: Basics

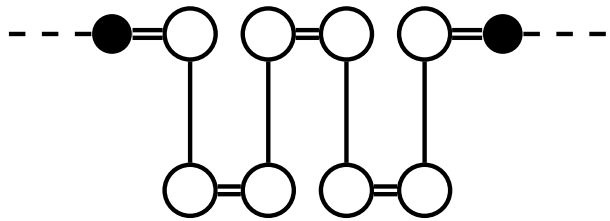


Compeau-Conceptualization: Basics



Bridging BWS- and Compeau-Conceptualizations

BWS: Runs can be accumulated.



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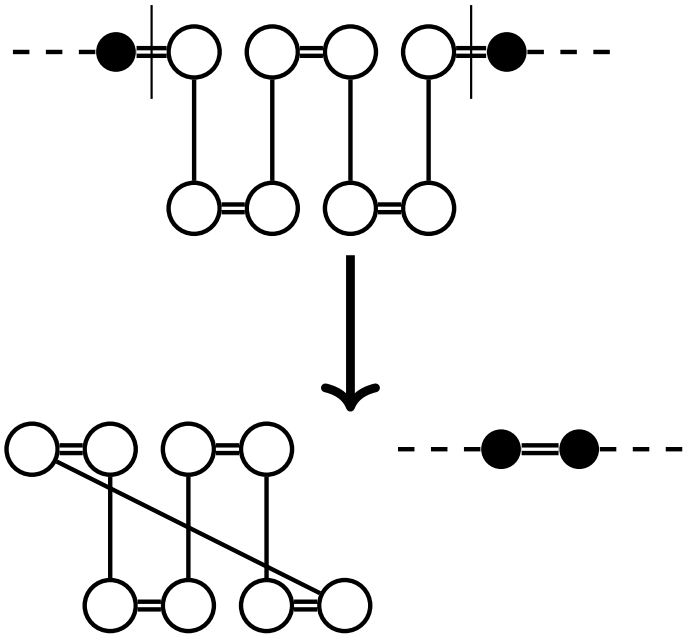

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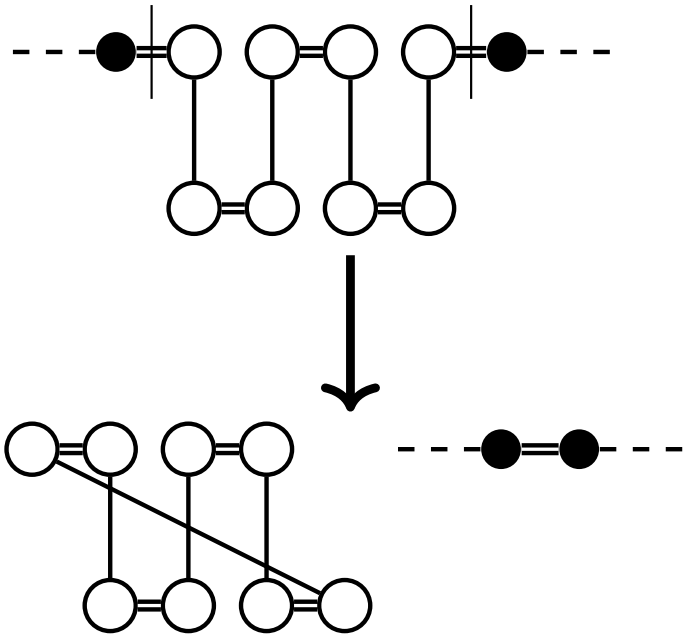
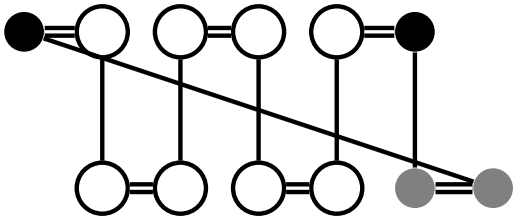


Compeau: Optimal 1-bracelet



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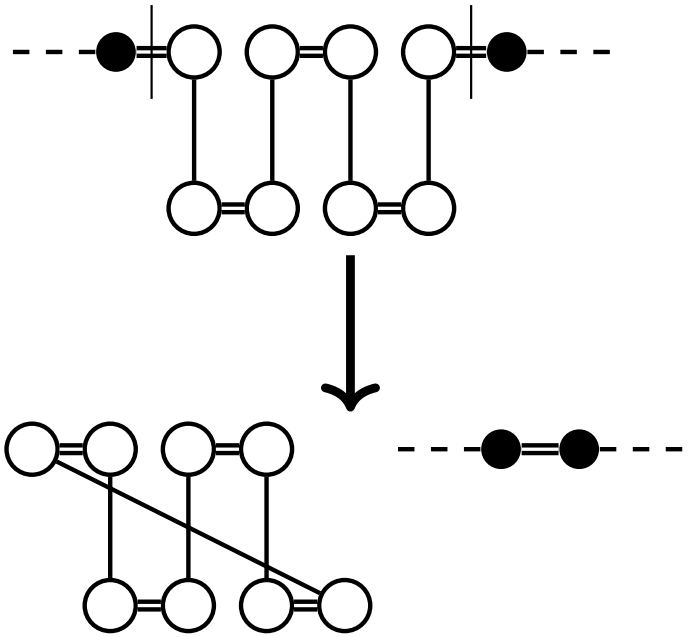
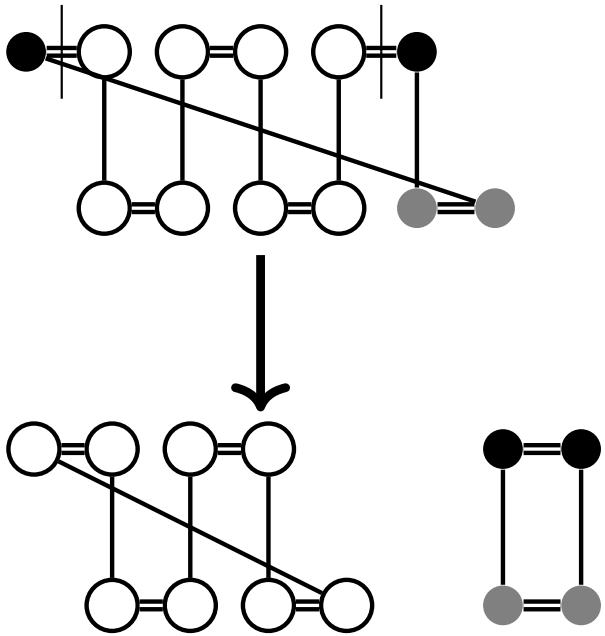


Compeau: Optimal 1-bracelet



Bridging BWS- and Compeau-Conceptualizations

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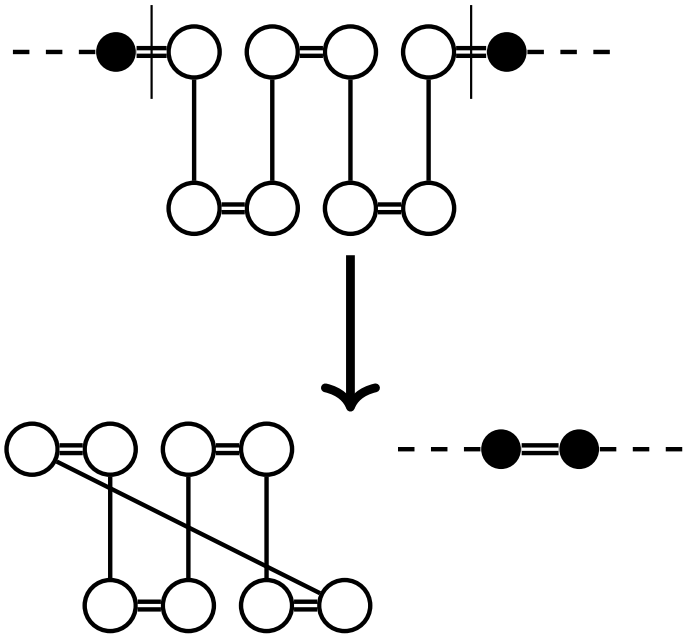

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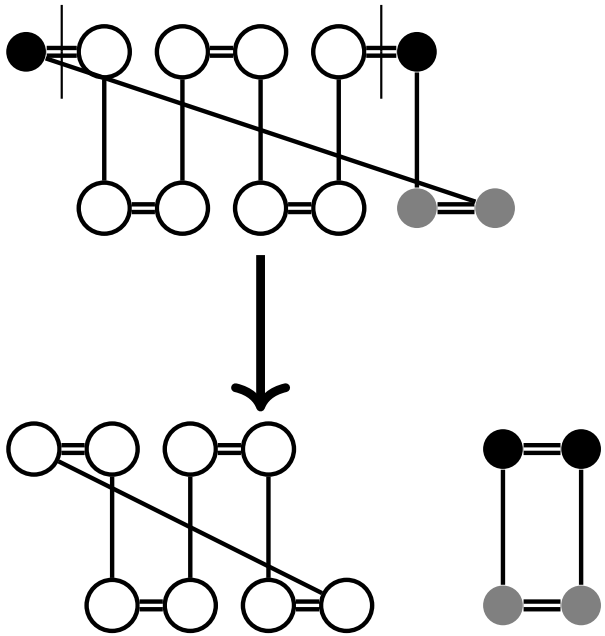


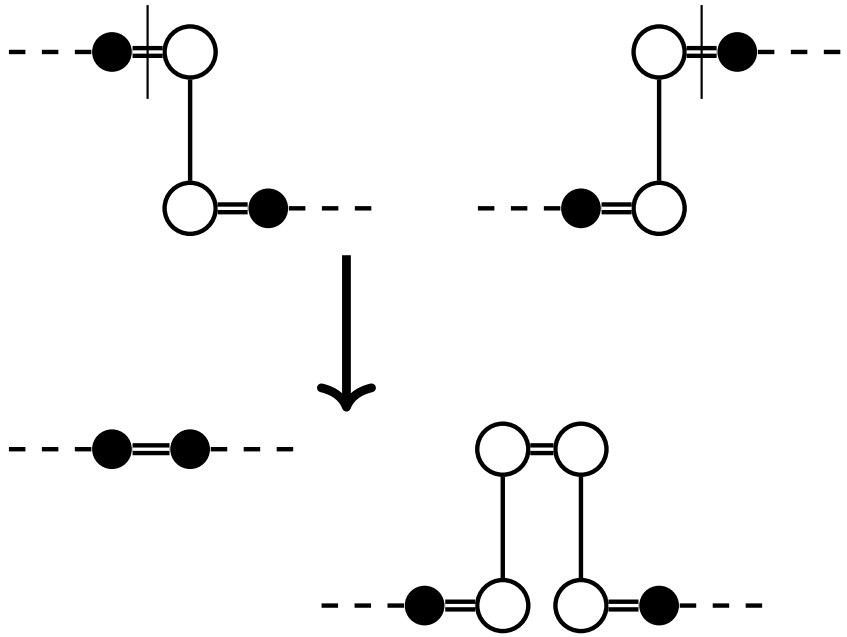
Common Ground: Safe operation!

Bridging BWS- and Compeau-Conceptualizations

BWS: Runs can be recombined.

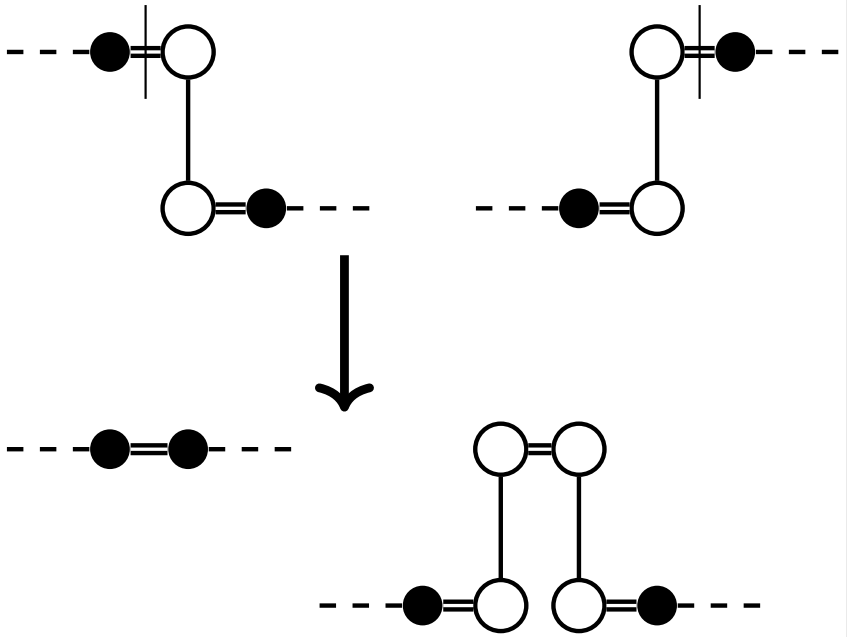
Bridging BWS- and Compeau-Conceptualizations

BWS: Runs can be recombined.

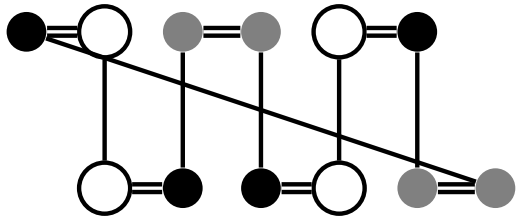


Bridging BWS- and Compeau-Conceptualizations

BWS: Runs can be recombined.

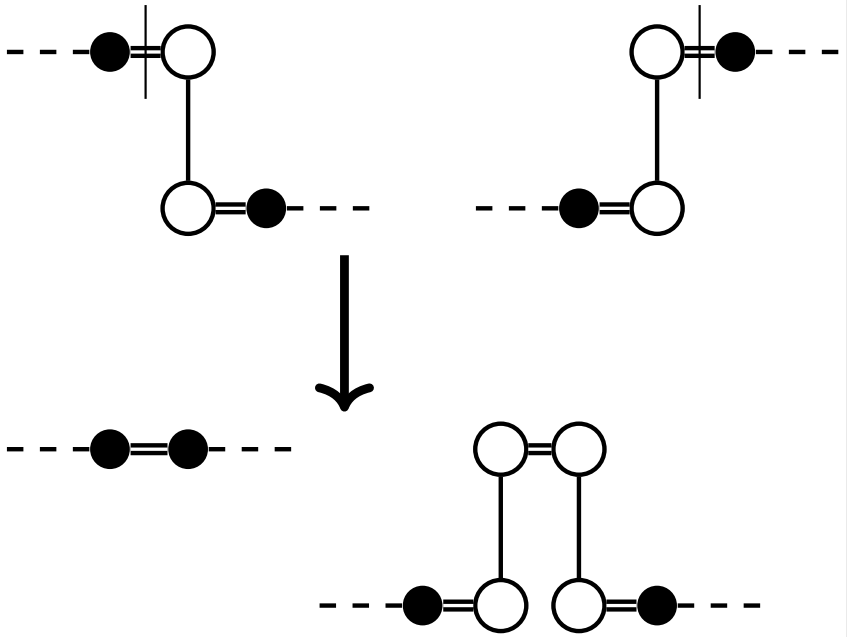


Compeau: Optimal 2-bracelet.

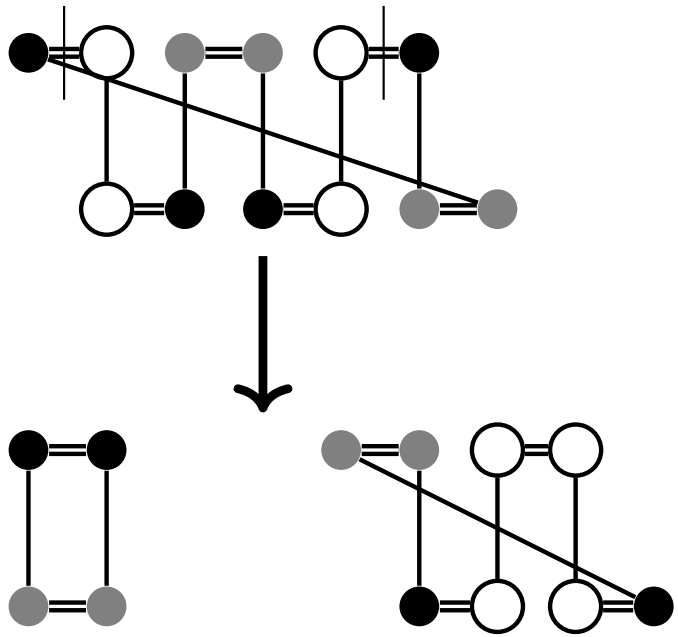


Bridging BWS- and Compeau-Conceptualizations

BWS: Runs can be recombined.



Compeau: Optimal 2-bracelet.



Bridging BWS- and Compeau-Conceptualizations

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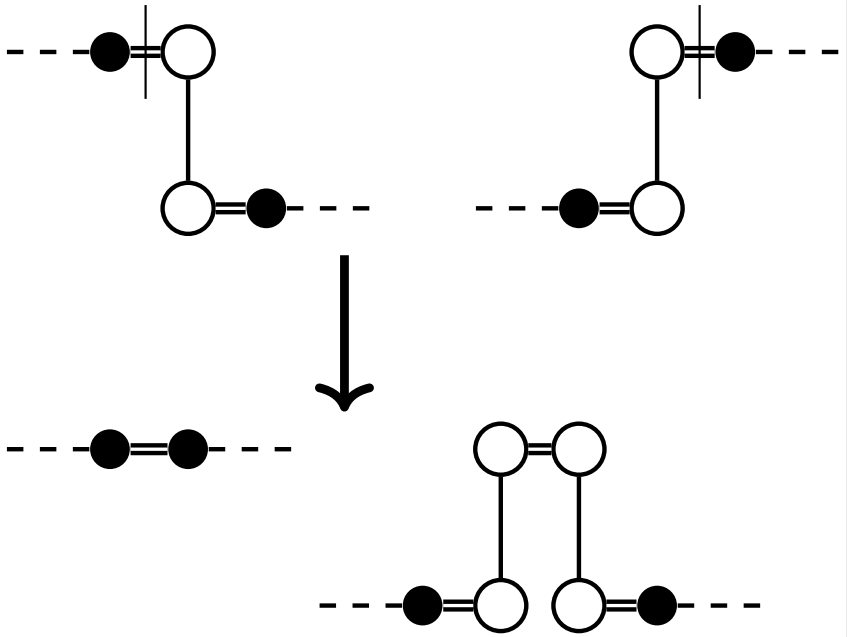
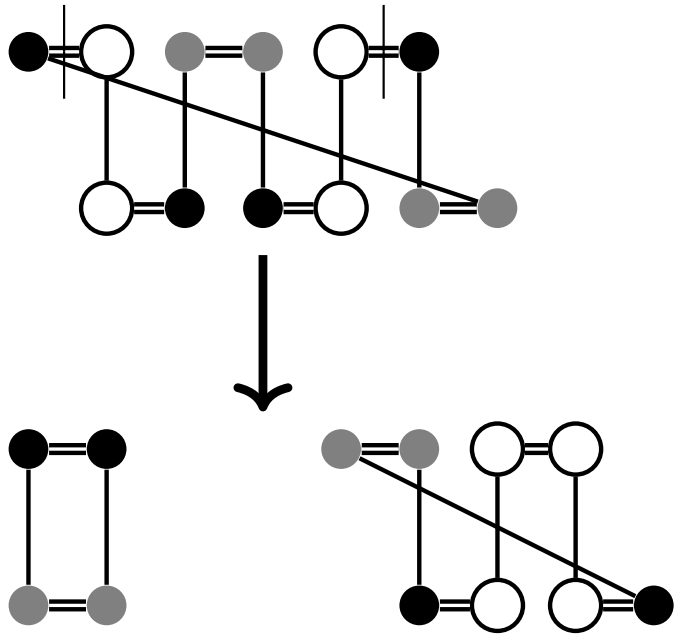


Compeau: Optimal 2-bracelet.

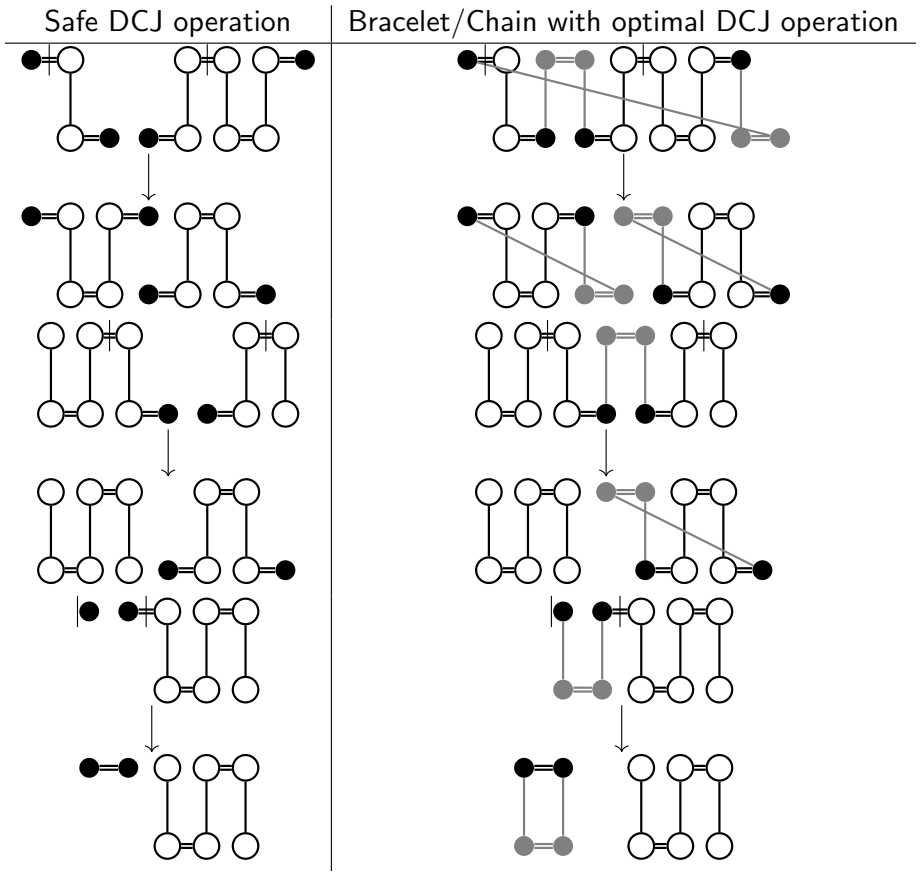


Common Ground: Safe operation!

Safe Operations and the BWS-Conceptualization

	Sources	Reusable Resultants	Unsat. after safe internal ops.					Unsat. after all safe ops. in group					No partner due to
			$A \circ a$	$B \mid a$	$a \mid b$	$A \mid b$	$B \circ b$	$A \circ a$	$B \mid a$	$p_{a \mid b}$	$A \mid b$	$B \circ b$	
P													
1	$AA_{\mathcal{AB}} + BB_{\mathcal{AB}}$		1	1	2	1	1	0	0	0	0	0	
Q													
1	$2AA_{\mathcal{AB}} + BB_{\mathcal{A}} + BB_{\mathcal{B}}$		2	2	2	2	2	0	0	0	0	0	
2	$2BB_{\mathcal{AB}} + AA_{\mathcal{A}} + AA_{\mathcal{B}}$		2	2	2	2	2	0	0	0	0	0	
T													
1	$AA_{\mathcal{AB}} + BB_{\mathcal{A}} + AB_{\mathcal{AB}}$		2	2	2	1	1	0	0	0	0	0	
2	$AA_{\mathcal{AB}} + BB_{\mathcal{B}} + AB_{\mathcal{BA}}$		1	1	2	2	2	0	0	0	0	0	
3	$BB_{\mathcal{AB}} + AA_{\mathcal{A}} + AB_{\mathcal{BA}}$		2	2	2	1	1	0	0	0	0	0	
4	$BB_{\mathcal{AB}} + AA_{\mathcal{B}} + AB_{\mathcal{AB}}$		1	1	2	2	2	0	0	0	0	0	
5	$2AA_{\mathcal{AB}} + BB_{\mathcal{A}}$	$AA_{\mathcal{B}}$	2	2	2	2	0	0	0	0	2	0	$P_{A \mid b} \to T1, Q1, P1;$
6	$2AA_{\mathcal{AB}} + BB_{\mathcal{B}}$	$AA_{\mathcal{A}}$	2	0	2	2	2	2	0	0	0	0	$P_{A \circ a} \to T2, Q1, P1;$
7	$2BB_{\mathcal{AB}} + AA_{\mathcal{A}}$	$BB_{\mathcal{B}}$	2	2	2	0	2	0	0	0	0	2	$P_{B \circ b} \to Q2, P1, T3;$
8	$2BB_{\mathcal{AB}} + AA_{\mathcal{B}}$	$BB_{\mathcal{A}}$	0	2	2	2	2	0	2	0	0	0	$P_{B \mid a} \to Q2, P1, T4;$
S													
1	$AA_{\mathcal{A}} + BB_{\mathcal{A}}$		2	2	0	0	0	0	0	0	0	0	
2	$AA_{\mathcal{B}} + BB_{\mathcal{B}}$		0	0	0	2	2	0	0	0	0	0	
3	$AB_{\mathcal{AB}} + AB_{\mathcal{BA}}$		1	1	2	1	1	0	0	0	0	0	
4	$AA_{\mathcal{AB}} + BB_{\mathcal{A}}$	$AB_{\mathcal{BA}}$	1	2	1	1	0	0	1	1	1	0	$P_{B \mid a} \to S1, T5, T1;$ $\star P_{a \mid b} \to T5, T1, P1;$

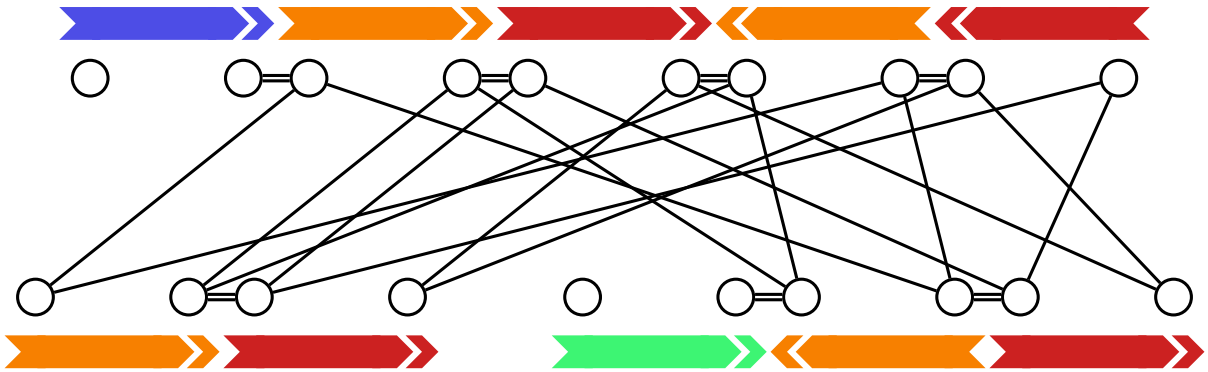
Safe Operations and the Compeau-Conceptualization



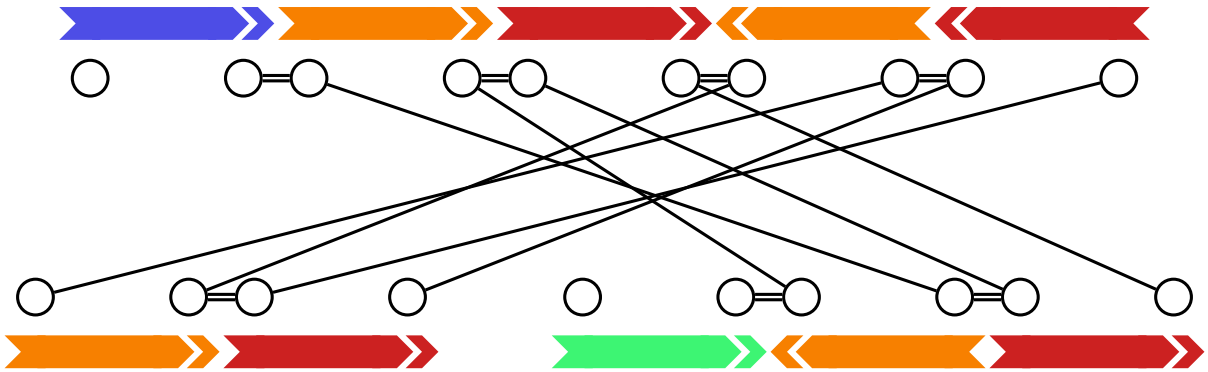
What's the use?

(Besides didactics)

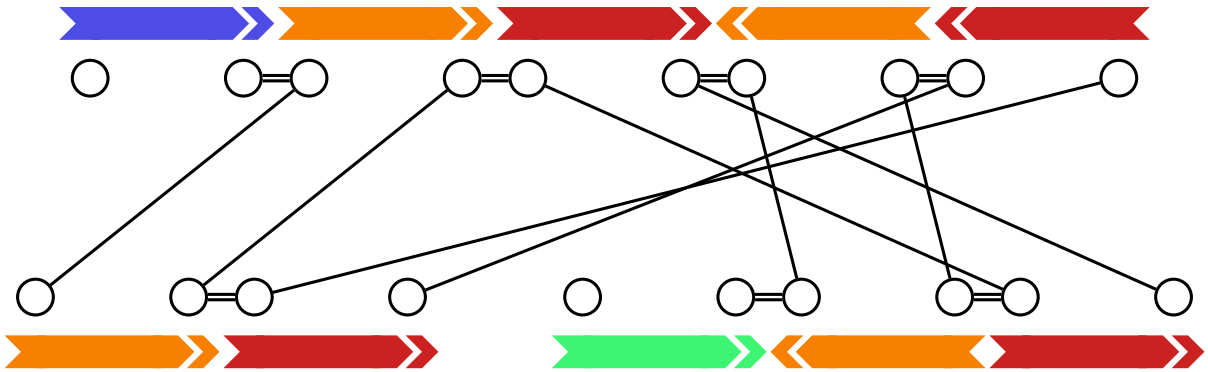
Duplicate Markers make the Problem NP-hard



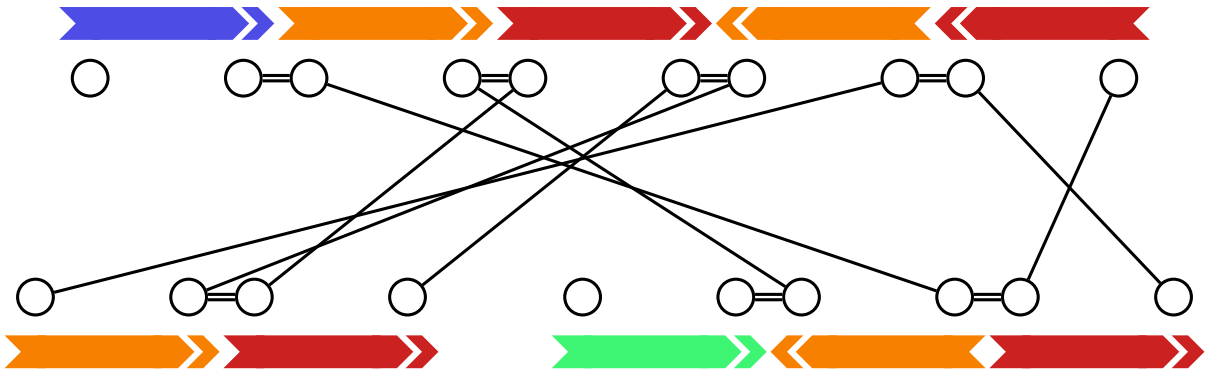
Duplicate Markers make the Problem NP-hard



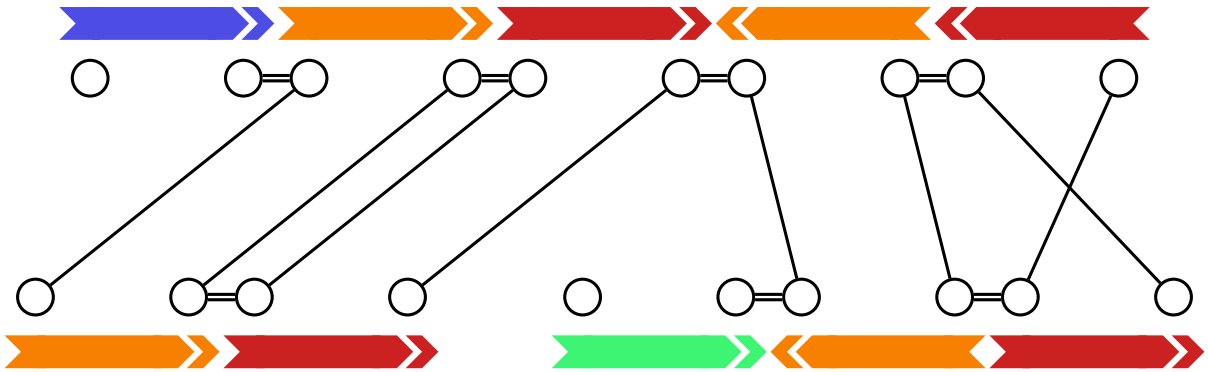
Duplicate Markers make the Problem NP-hard



Duplicate Markers make the Problem NP-hard



Duplicate Markers make the Problem NP-hard



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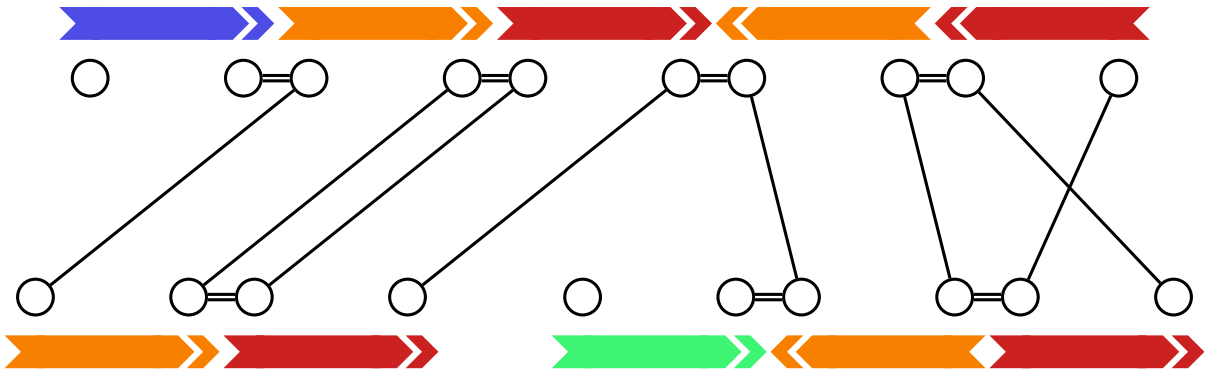
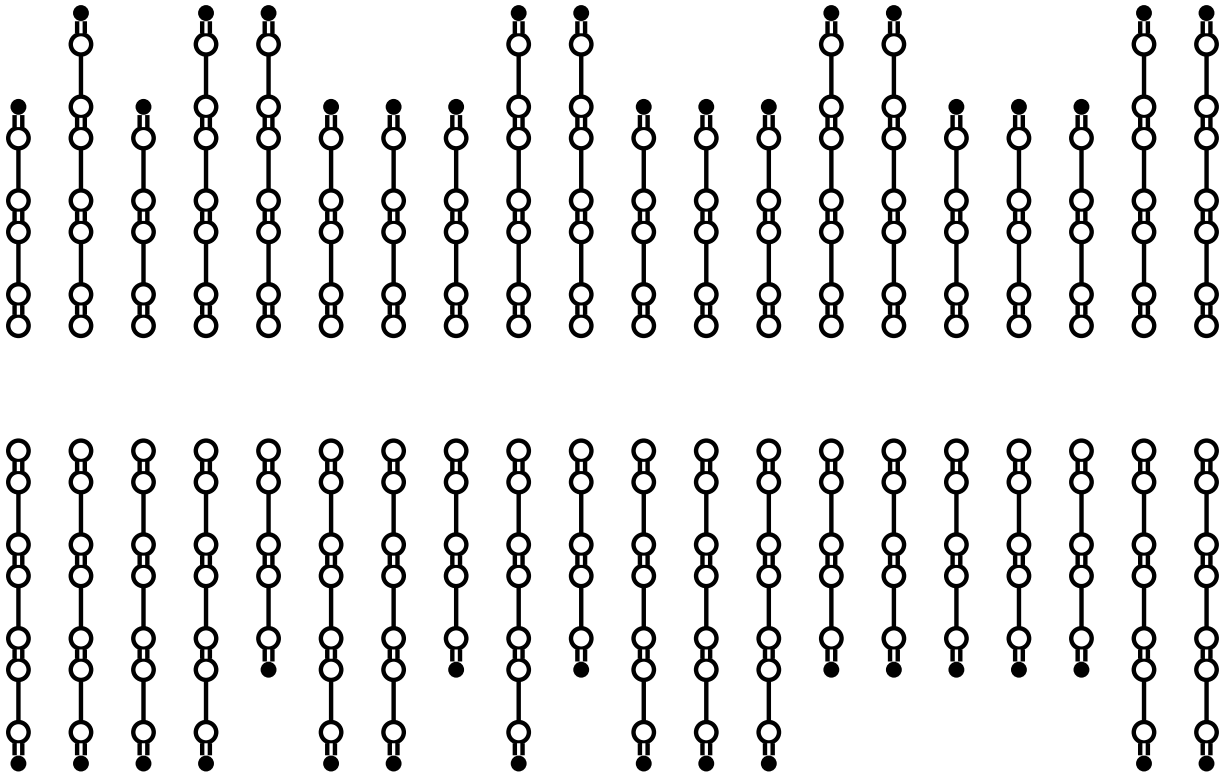


→ Solved by `ding`, ILP based on BWS-model (BBDS,2023).

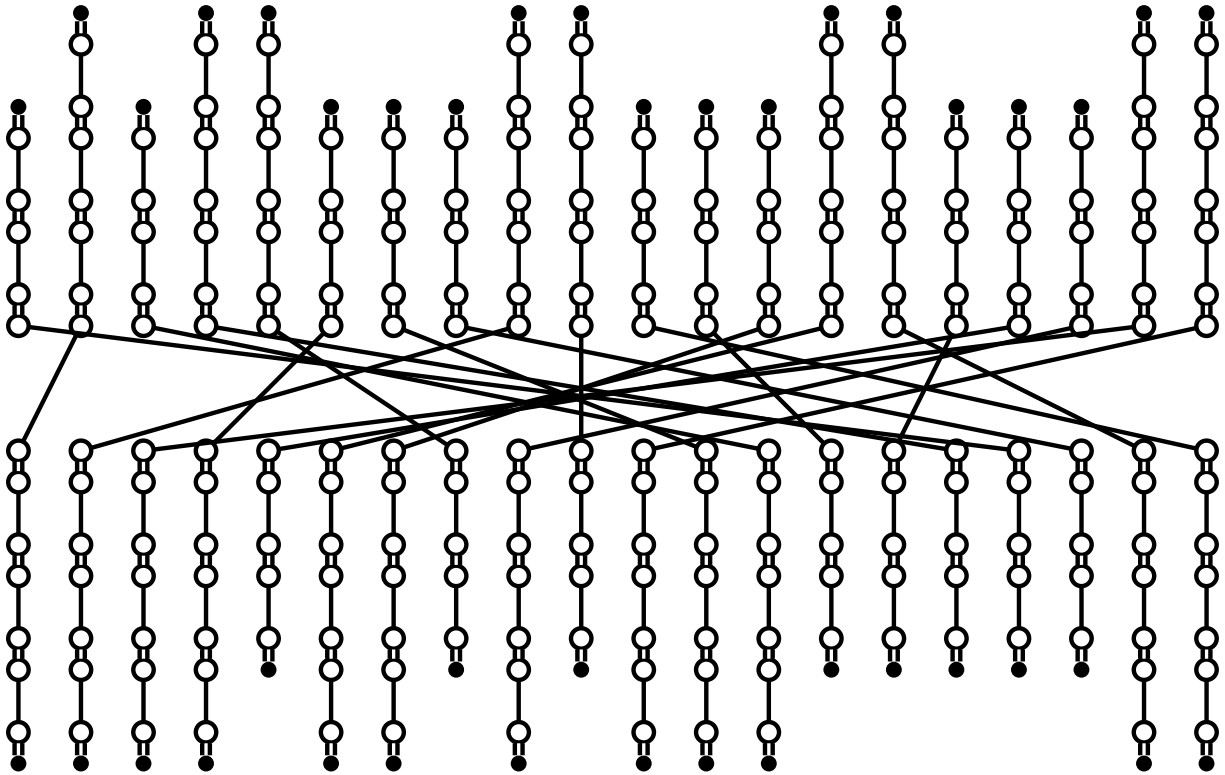
Path-Recombinations in BWS-model are too Complicated for an ILP.

	Sources	Reusable Resultants	Unsat. after safe internal ops.					Unsat. after all safe ops. in group					No partner due to
			$A \circ a$	$B \vert a$	$a \vert b$	$A \vert b$	$B \circ b$	$A \circ a$	$B \vert a$	$p_{a \vert b}$	$A \vert b$	$B \circ b$	
P													
1	$AA_{\mathcal{AB}} + BB_{\mathcal{AB}}$		1	1	2	1	1	0	0	0	0	0	
Q													
1	$2AA_{\mathcal{AB}} + BB_{\mathcal{A}} + BB_{\mathcal{B}}$		2	2	2	2	2	0	0	0	0	0	
2	$2BB_{\mathcal{AB}} + AA_{\mathcal{A}} + AA_{\mathcal{B}}$		2	2	2	2	2	0	0	0	0	0	
T													
1	$AA_{\mathcal{AB}} + BB_{\mathcal{A}} + AB_{\mathcal{AB}}$		2	2	2	1	1	0	0	0	0	0	
2	$AA_{\mathcal{AB}} + BB_{\mathcal{B}} + AB_{\mathcal{BA}}$		1	1	2	2	2	0	0	0	0	0	
3	$BB_{\mathcal{AB}} + AA_{\mathcal{A}} + AB_{\mathcal{BA}}$		2	2	2	1	1	0	0	0	0	0	
4	$BB_{\mathcal{AB}} + AA_{\mathcal{B}} + AB_{\mathcal{AB}}$		1	1	2	2	2	0	0	0	0	0	
5	$2AA_{\mathcal{AB}} + BB_{\mathcal{A}}$	$AA_{\mathcal{B}}$	2	2	2	2	0	0	0	0	2	0	$P_{A\vert b} \to T1, Q1, P1;$
6	$2AA_{\mathcal{AB}} + BB_{\mathcal{B}}$	$AA_{\mathcal{A}}$	2	0	2	2	2	2	0	0	0	0	$P_{A\circ a} \to T2, Q1, P1;$
7	$2BB_{\mathcal{AB}} + AA_{\mathcal{A}}$	$BB_{\mathcal{B}}$	2	2	2	0	2	0	0	0	0	2	$P_{B\circ b} \to Q2, P1, T3;$
8	$2BB_{\mathcal{AB}} + AA_{\mathcal{B}}$	$BB_{\mathcal{A}}$	0	2	2	2	2	0	2	0	0	0	$P_{B\vert a} \to Q2, P1, T4;$
S													
1	$AA_{\mathcal{A}} + BB_{\mathcal{A}}$		2	2	0	0	0	0	0	0	0	0	
2	$AA_{\mathcal{B}} + BB_{\mathcal{B}}$		0	0	0	2	2	0	0	0	0	0	
3	$AB_{\mathcal{AB}} + AB_{\mathcal{BA}}$		1	1	2	1	1	0	0	0	0	0	
4	$AA_{\mathcal{AB}} + BB_{\mathcal{A}}$	$AB_{\mathcal{BA}}$	1	2	1	1	0	0	1	1	1	0	$P_{B\vert a} \to S1, T5, T1;$ $\star P_{a\vert b} \to T5, T1, P1;$

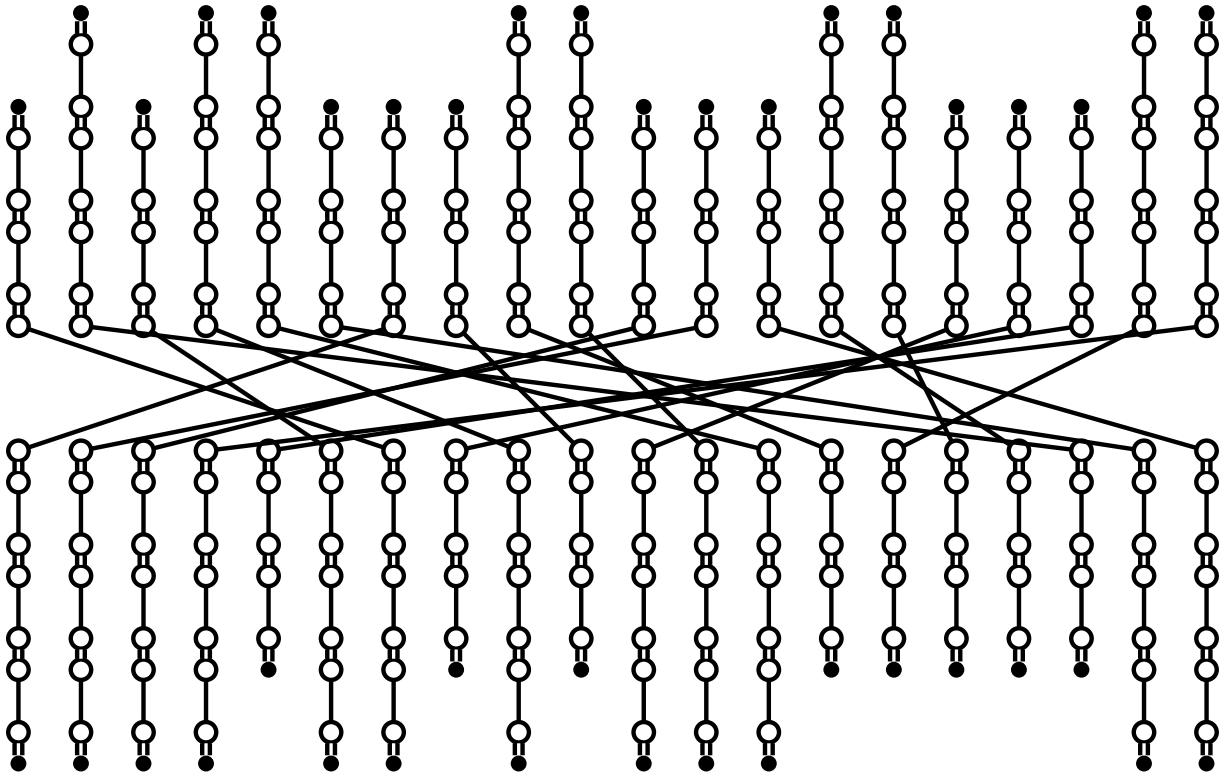
Transforming Paths into Cycles - Capping



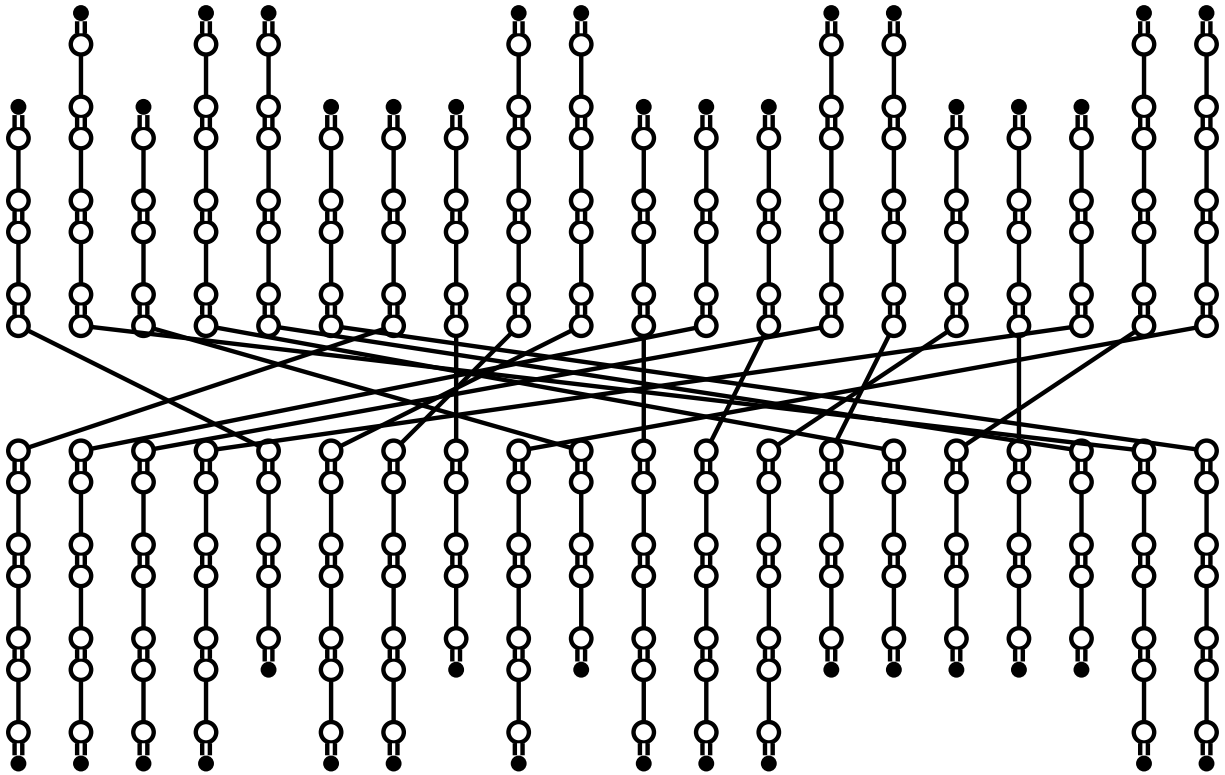
Transforming Paths into Cycles - Capping



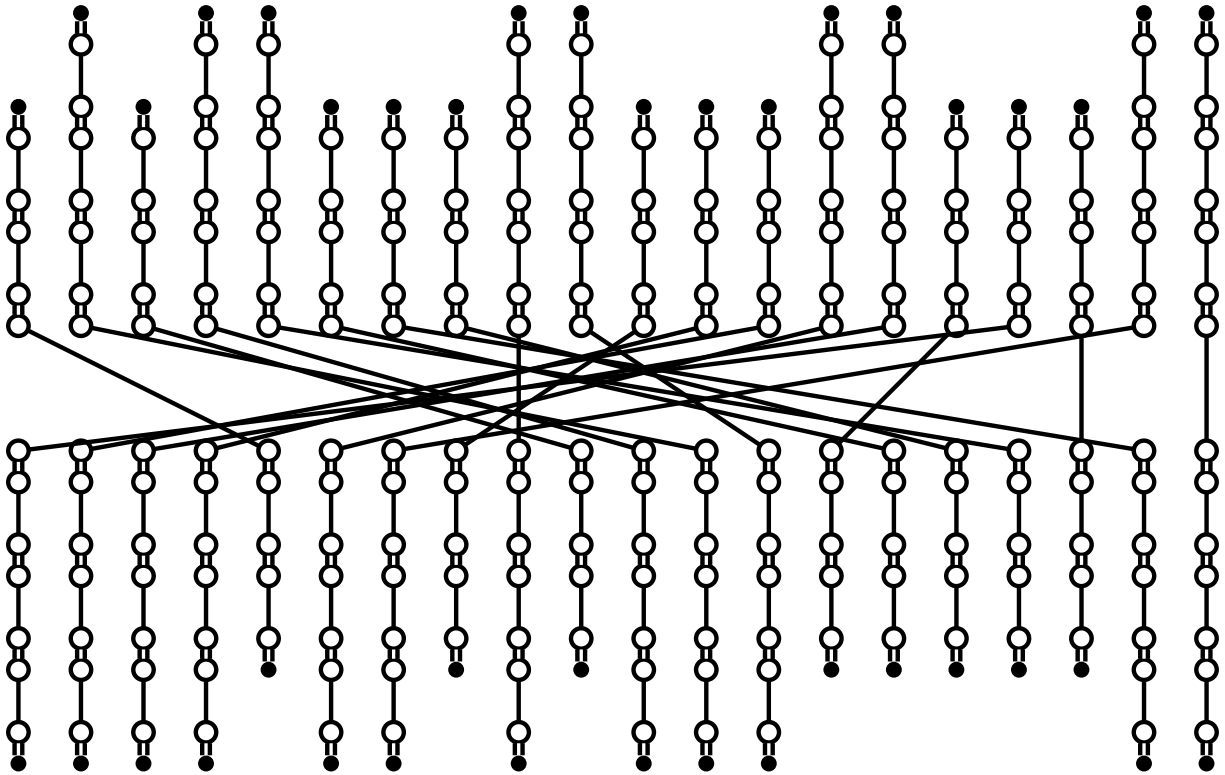
Transforming Paths into Cycles - Capping



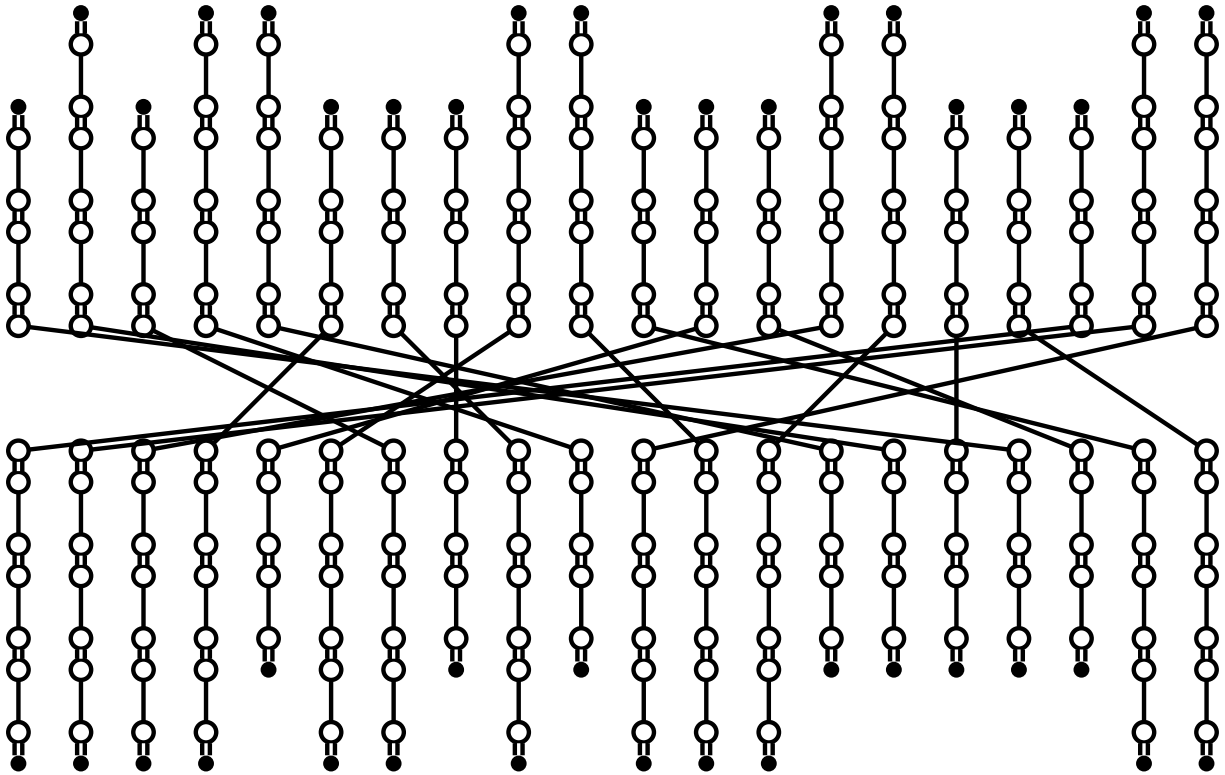
Transforming Paths into Cycles - Capping



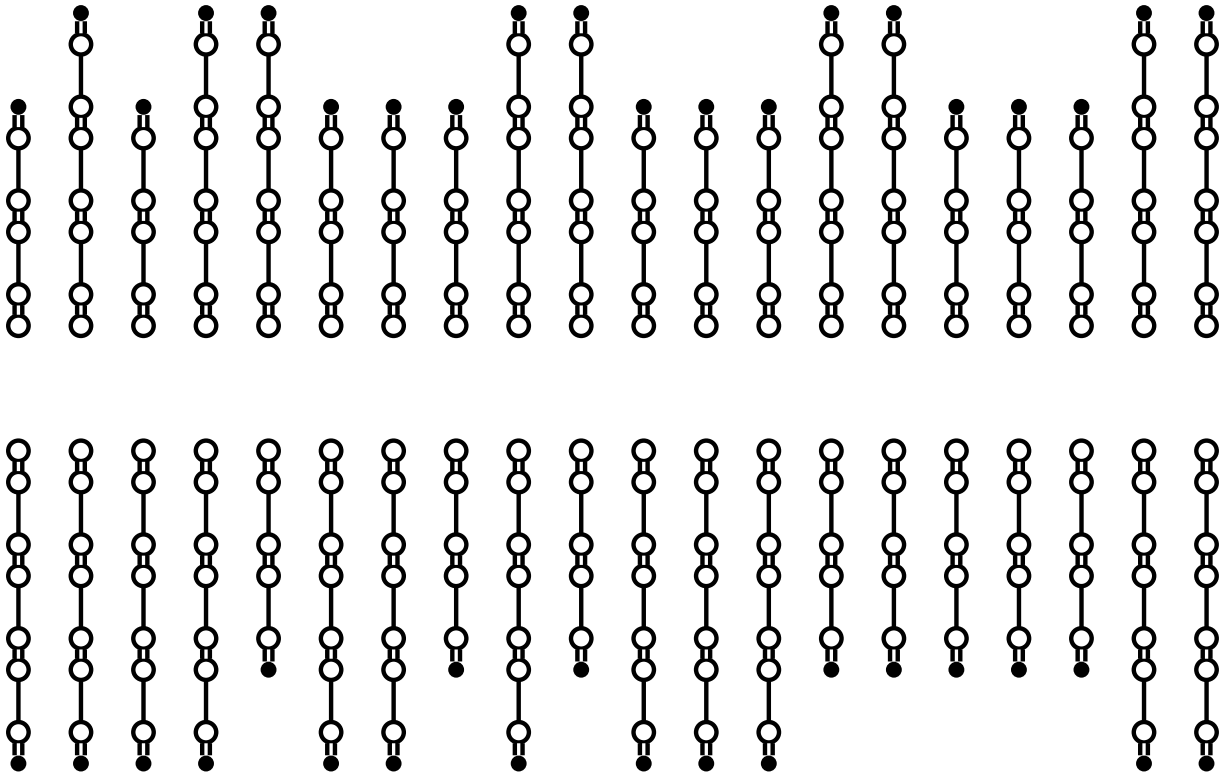
Transforming Paths into Cycles - Capping



Transforming Paths into Cycles - Capping



Transforming Paths into Cycles - Capping

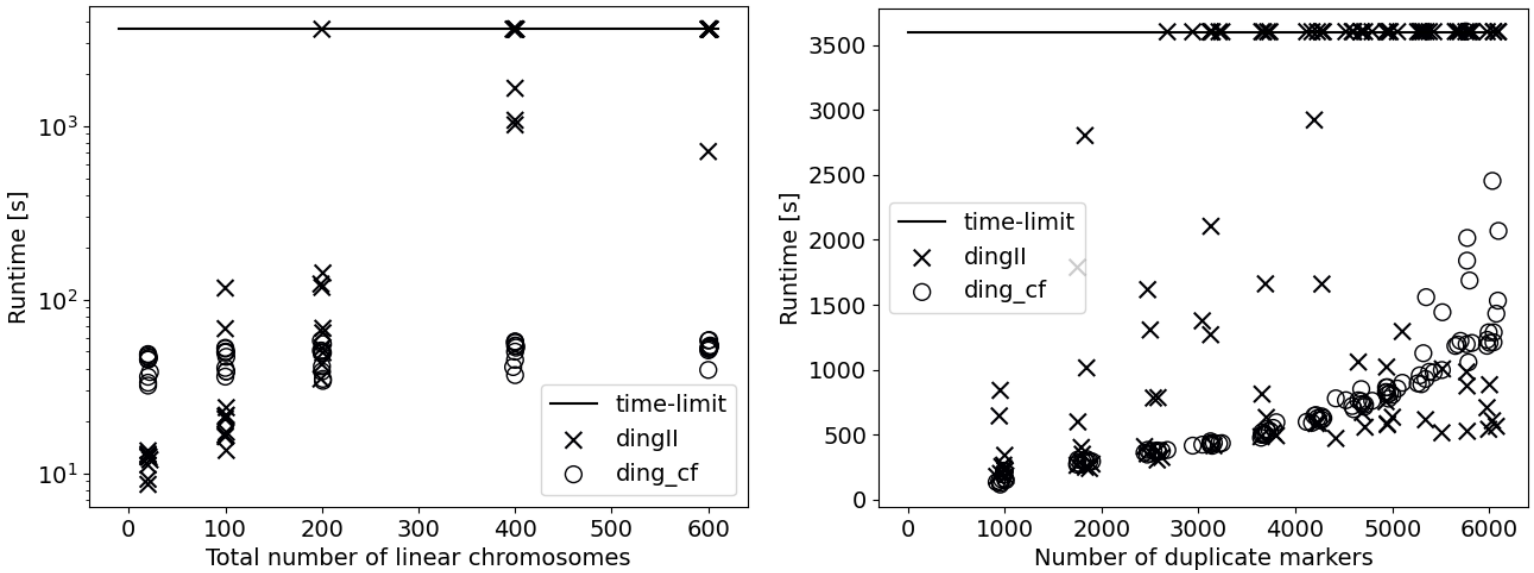


- Superexponential increase of Solution Space. (Rubert & Braga, 2022)

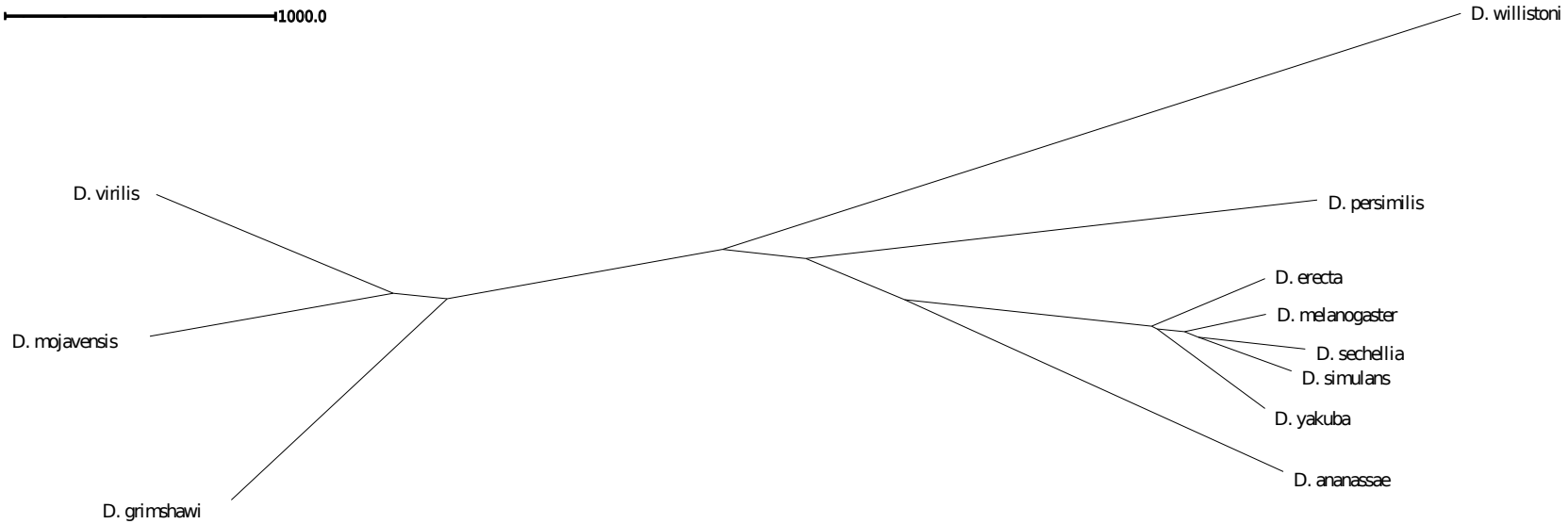
ILP Based on New Formula Avoids Capping!

$$d_{DCJ}^{id}(\mathbb{A},\mathbb{B}) = n - c_\circ + \left\lceil \frac{p_{a|b} + \max(p_{A\circ a}, p_{B|a}) + \max(p_{A|b}, p_{B\circ b}) - p_{A|B}}{2} \right\rceil$$

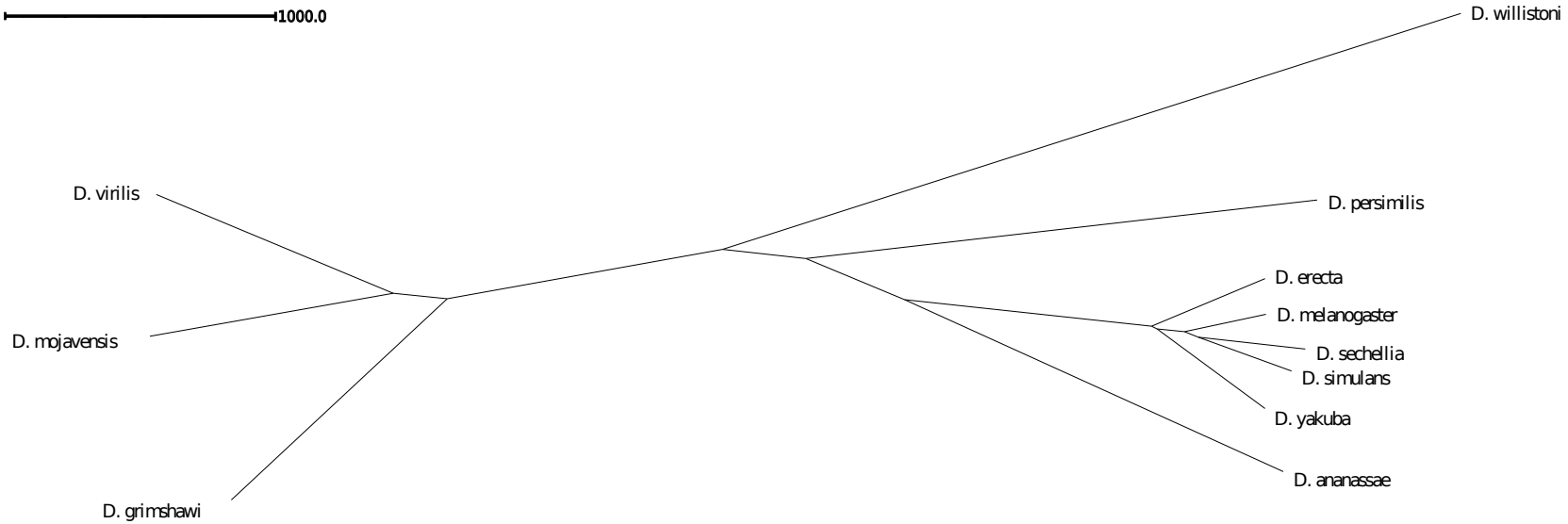
Considerable Performance Advantage when the Number of Linear Chromosomes is High



Computing Rearrangement Phylogenies on Contig-level resolved Genomes

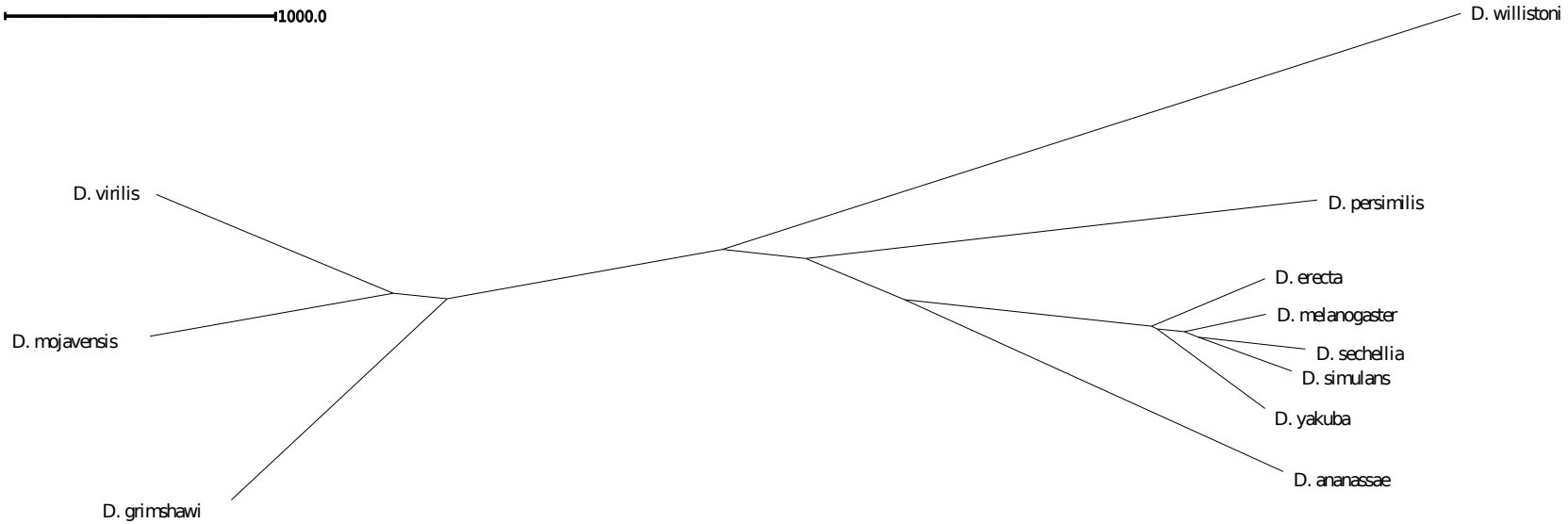


Computing Rearrangement Phylogenies on Contig-level resolved Genomes



- High quality

Computing Rearrangement Phylogenies on Contig-level resolved Genomes



- High quality
- Robust: On average only 0.53% deviation from computed pairwise distances.

Summarized Results

- More compact and simple DCJ-indel formula

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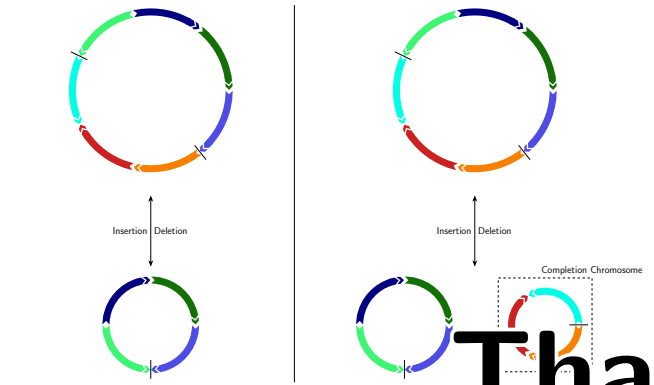
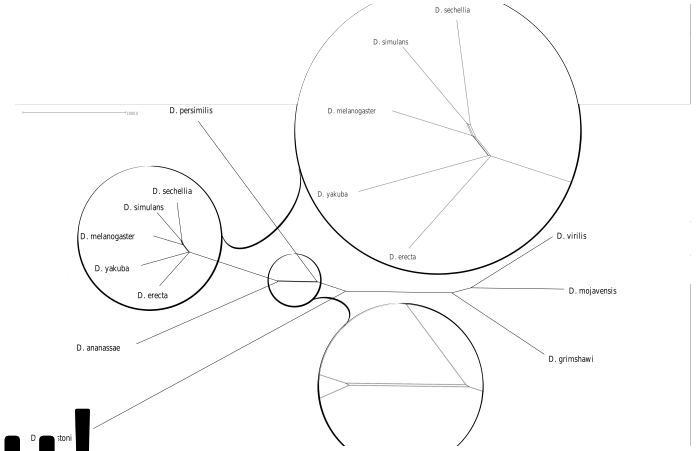
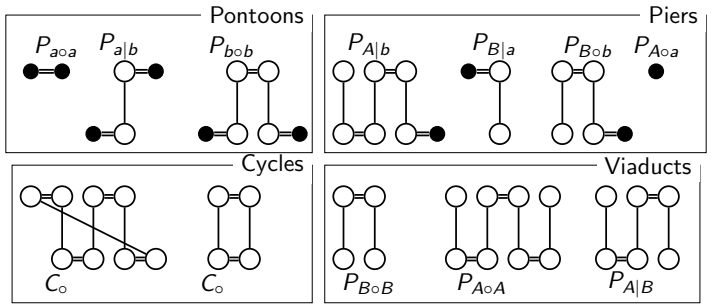
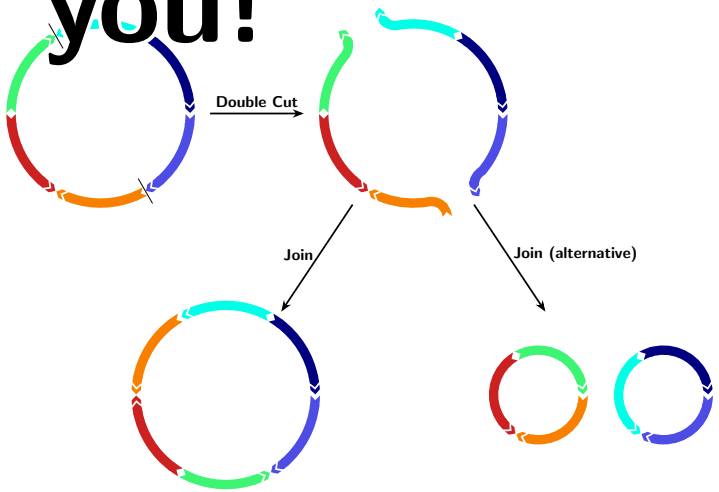
- More compact and simple DCJ-indel formula
  - Link between BWS and Compeau-conceptualizations
- Significant performance improvement of `ding` for high numbers of linear chromosomes/contigs


Insertion
Deletion
Insertion
Deletion
Completion
Chromosome


D. sechellia
D. simulans
D. persimilis
D. melanogaster
D. yakuba
D. virilis
D. erecta
D. mojavensis
D. ananassae
D. grimshawi

Thank you!


Pontoons
$P_{a\circ a}$
$P_{a|b}$
$P_{b\circ b}$
Piers
$P_{A|b}$
$P_{B|a}$
$P_{B\circ b}$
$P_{A\circ a}$
Cycles
$C_\circ$
$C_\circ$
Viaducts
$P_{B\circ B}$
$P_{A\circ A}$
$P_{A|B}$


Double Cut
Join
Join (alternative)