

Topics of today:

Canonical inversion distance and sorting:

1. Relational / Breakpoint diagram
2. Split / Neutral / Joining inversions
3. Good / bad components
4. Hurdles and fortress

Canonical inversion model - circular chromosomes

(Unichromosomal genomes \equiv chromosomes)

Given two canonical circular chromosomes \mathbb{A} and \mathbb{B} ,...

Canonical Inversion Distance Problem: Compute the minimum number of inversions required to transform \mathbb{A} into \mathbb{B} .

Denote by $d_{\text{INV}}(\mathbb{A}, \mathbb{B})$ the inversion distance of \mathbb{A} and \mathbb{B} .

Canonical Inversion Sorting Problem: Find a sequence of $d_{\text{INV}}(\mathbb{A}, \mathbb{B})$ inversions that transform \mathbb{A} into \mathbb{B} .

Relational diagram of canonical circular chromosomes

Given canonical circular chromosomes \mathbb{A} and \mathbb{B} , their **relational diagram** $RD(\mathbb{A}, \mathbb{B}) = (V, E)$ is described as follows:

1. $V = V(\xi(\mathbb{A})) \cup V(\xi(\mathbb{B}))$: there is a vertex for each extremity of each gene in \mathbb{A}
and a vertex for each extremity of each gene in \mathbb{B}

The vertices corresponding to $\xi(\mathbb{A})$ are drawn in an upper line,
while the vertices corresponding to $\xi(\mathbb{B})$ are drawn in a lower line.

In each line, the vertices must follow the same (circular) order of the corresponding extremities in the respective chromosome, according to one of the two reading directions.

Each vertex v has a label $\ell(v)$, that corresponds to the extremity it represents.

2. $E = E_\alpha(\mathbb{A}) \cup E_\alpha(\mathbb{B}) \cup E_\xi$, where:

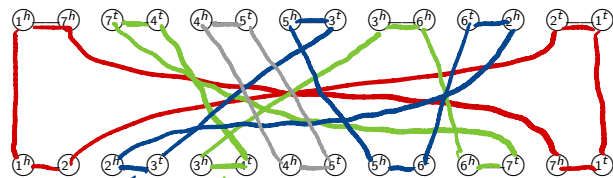
- **Adjacency edges:**
$$\begin{cases} E_\alpha(\mathbb{A}) = \{uv : u, v \in V(\xi(\mathbb{A})) \text{ and } \ell(u)\ell(v) \in \alpha(\mathbb{A})\} \\ E_\alpha(\mathbb{B}) = \{uv : u, v \in V(\xi(\mathbb{B})) \text{ and } \ell(u)\ell(v) \in \alpha(\mathbb{B})\} \end{cases}$$
- **Extremity edges:** $E_\xi = \{uv : u \in V(\xi(\mathbb{A})) \text{ and } v \in V(\xi(\mathbb{B})) \text{ and } \ell(u) = \ell(v)\}$

Note that:

- Let $n = |\mathcal{G}_\star|$. The number of edges in $E_\alpha(\mathbb{A}) \cup E_\alpha(\mathbb{B})$ is $2n$ (n adjacency edges per chromosome).

Relational diagram of canonical circular chromosomes

$$\mathbb{A} = (1 \bar{7} 4 5 3 \bar{6} \bar{2})$$



$$\mathbb{B} =$$

$$(1 2 3 4 5 6 7)$$

$$n = |\mathcal{G}_\star| = 7$$

Every vertex has degree two:

$RD(\mathbb{A}, \mathbb{B})$ is a collection of (even) cycles
(alternating edges in E_ξ and in $E_\alpha(\mathbb{A}) \cup E_\alpha(\mathbb{B})$)

cycle with k edges in $E_\alpha(\mathbb{A}) \cup E_\alpha(\mathbb{B})$: k -cycle

\mathcal{C} = set of cycles in $RD(\mathbb{A}, \mathbb{B})$

If $\mathbb{A} = \mathbb{B}$,
 $RG(\mathbb{A}, \mathbb{B})$ has only 2-cycles:

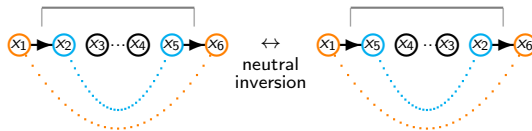
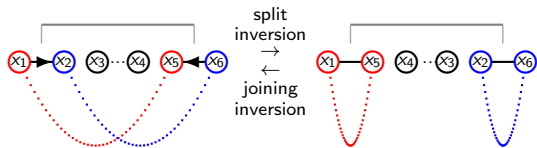
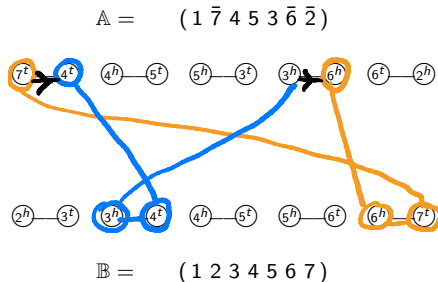
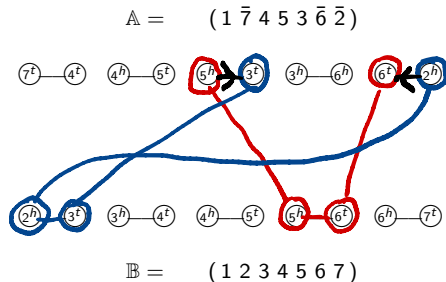
$$2n = 2|\mathcal{C}| \Rightarrow n = |\mathcal{C}|$$

Otherwise, if $\mathbb{A} \neq \mathbb{B}$:

$$n > |\mathcal{C}|$$

Types of inversion and lower bound for the inversion distance

Assign one (arbitrary) direction to each cycle of $RD(\mathbb{A}, \mathbb{B})$



Lower bound for the inversion distance: $d_{\text{INV}}(\mathbb{A}, \mathbb{B}) \geq n - |\mathcal{C}|$

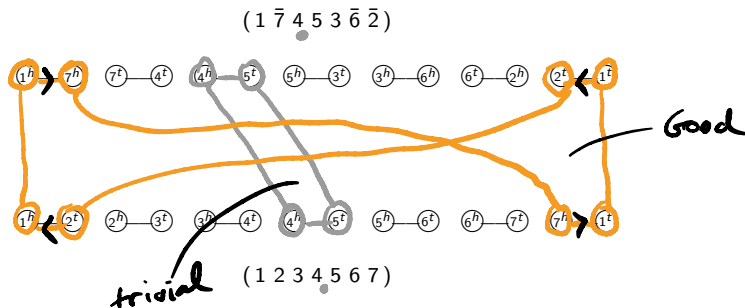
Types of cycles

Trivial cycle: one adjacency in each chromosome

2-cycle (sorted)

Good cycle: $\left\{ \begin{array}{l} \text{at least one pair of adjacencies with opposite directions in chromosome } \mathbb{A} \\ \text{at least one pair of adjacencies with opposite directions in chromosome } \mathbb{B} \end{array} \right.$

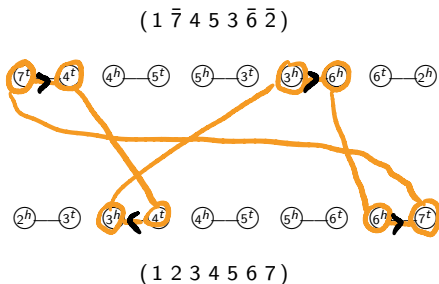
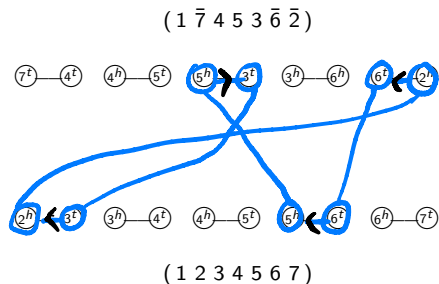
Can be split into two cycles by applying an inversion in \mathbb{A} or in \mathbb{B}



Types of cycles

Semi-good cycle: $\begin{cases} \text{at least one pair of adjacencies with opposite directions in one of the two chromosomes} \\ \text{all adjacencies have the same direction in the other chromosome} \end{cases}$

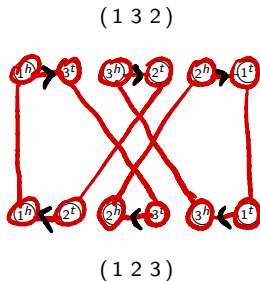
Can be split into two cycles by applying an inversion only in \mathbb{A} or only in \mathbb{B}



Types of cycles

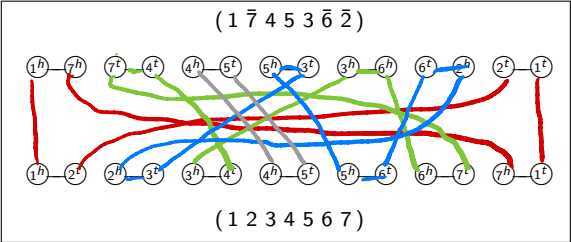
Bad cycle: $\begin{cases} \text{all adjacencies in chromosome } \mathbb{A} \text{ have the same direction} \\ \text{all adjacencies in chromosome } \mathbb{B} \text{ have the same direction} \end{cases}$

Cannot be split into two cycles



Relational diagram \cong Breakpoint diagram

Relational diagram:



Looking either at the top line or at the bottom line of the diagram:

Two interleaving cycles: $c \dots c' \dots c \dots c'$

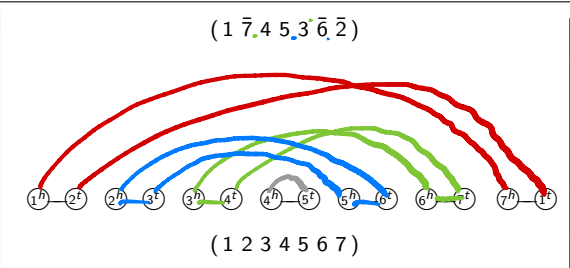
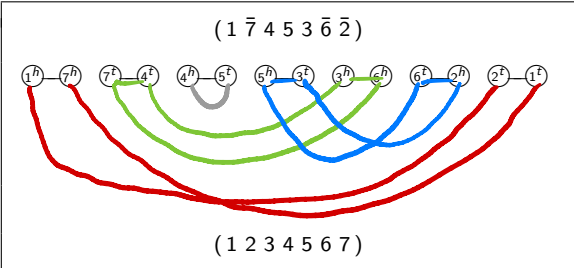
Interleaving sequence of cycles: c_1, c_2, \dots, c_k such that c_i and c_{i+1} are interleaving for all $1 \leq i \leq k - 1$

Interleaving component or simply component K :

- for each pair of cycles $c, c' \in K$ there is an interleaving sequence from c to c'
- K is maximal

$$c' \subset c' \subset c'' \subset c''$$

Breakpoint diagrams:

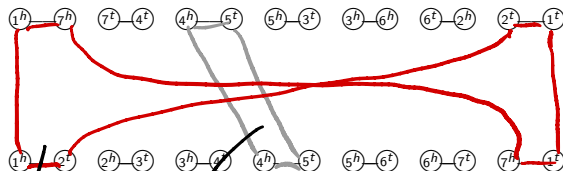


Types of (interleaving) components

Trivial component: only one trivial 2-cycle

Good component: at least one good or semi-good cycle

$(1 \bar{7} 4 5 3 \bar{6} \bar{2})$

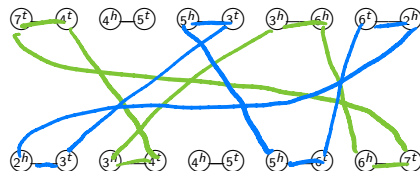


$(1 2 3 4 5 6 7)$

Good

Trivial

$(1 \bar{7} 4 5 3 \bar{6} \bar{2})$

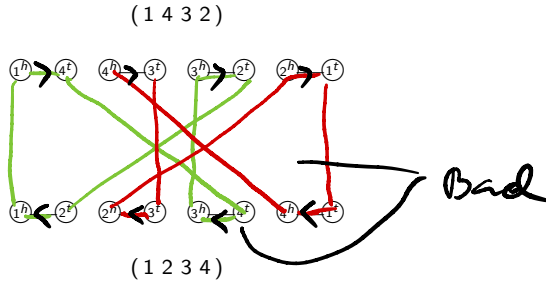


$(1 2 3 4 5 6 7)$

✓
Good

Types of (interleaving) components

Bad component: only bad cycles



Quiz 1

1 Which of the following statements about the relational diagram are true?

☒ A cycle can always be split into two cycles with an inversion.

☒ A joining inversion cannot be optimal.

☒ A split inversion is always optimal.

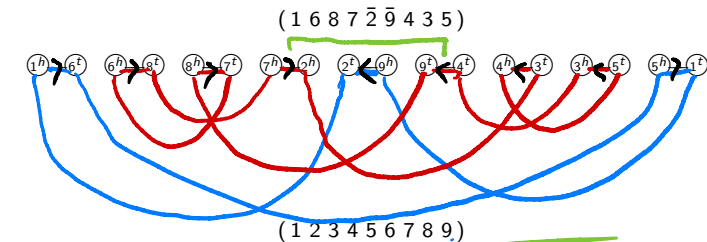
☒ D It is always possible to split a good or a semi-good cycle into two.

☒ E A bad cycle cannot be split by an inversion.

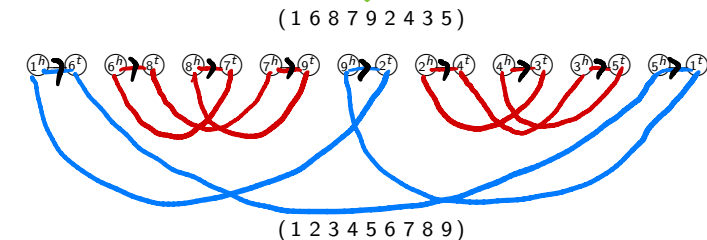
Unsafe inversions

good

A split inversion applied to a cycle of a good component can create bad components



- One good component



- 3 bad components

Sorting a good component - finding safe split inversions

Target adjacency: $\begin{cases} \text{good} \\ \text{bad} \end{cases}$

Overlapping target adjacencies

Overlap graph of a good component

(1 5 $\bar{4}$ 2 $\bar{6}$ $\bar{3}$)



(1 2 3 4 5 6)

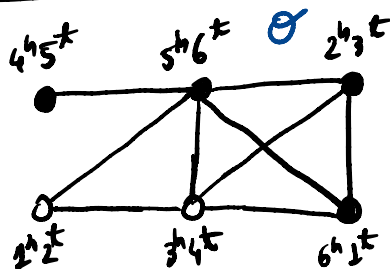
Good:

Bad:



Overlapping:

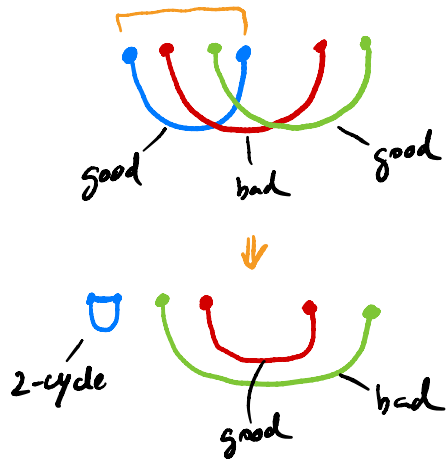
Non overlapping:



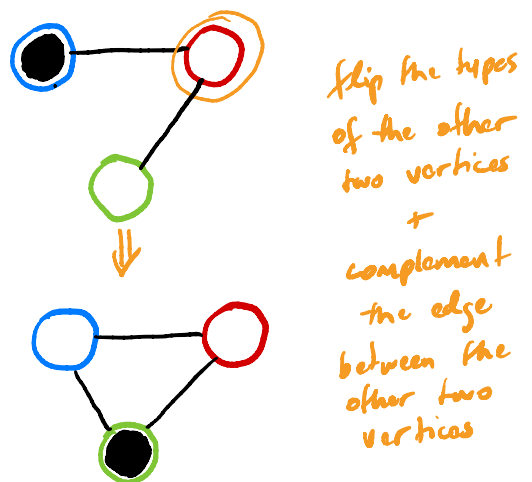
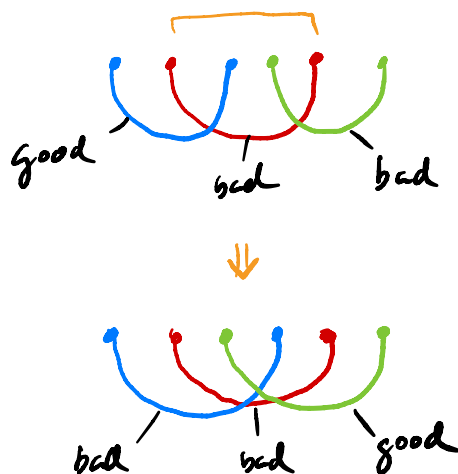
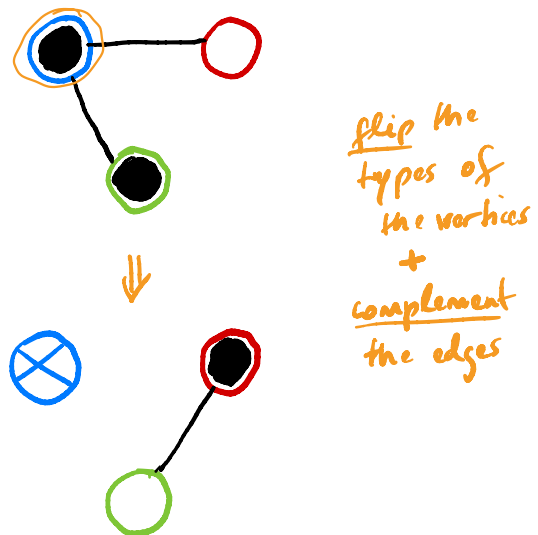
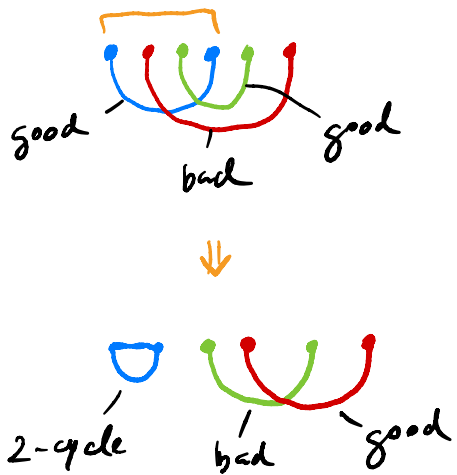
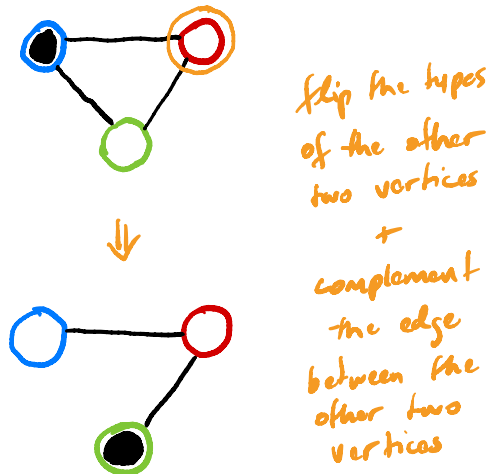
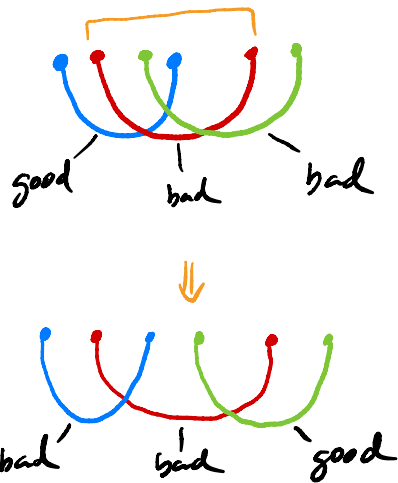
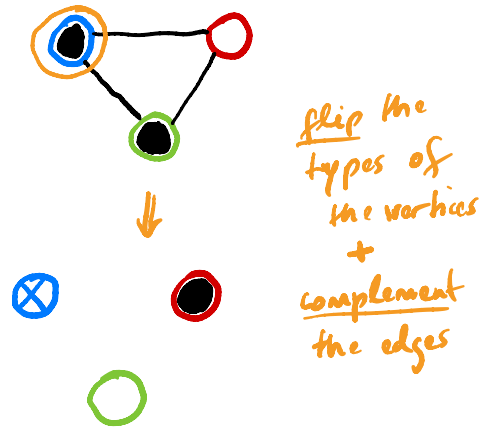
good
adjacency
↓
black vertex

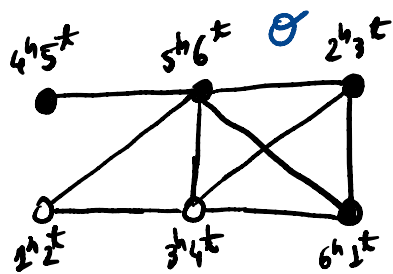
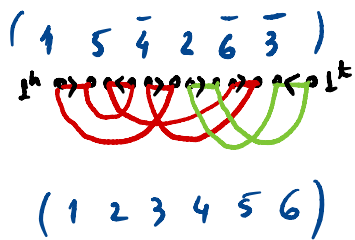
bad
adjacency
↓
white vertex

Three overlapping adjacencies:



overlap graph:



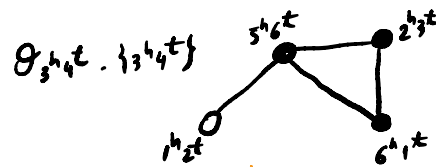
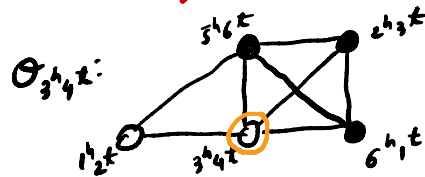


Θ_{xy} : subgraph of Θ composed of xy and its adjacent vertices
 Effect of an inversion on the overlap graph Θ :

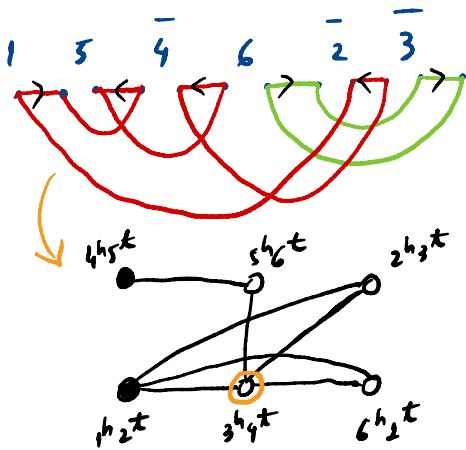
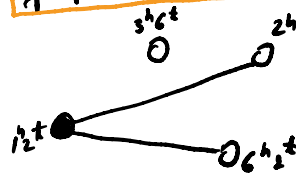
if xy is bad:

- 1) flip the types of the vertices of $\Theta_{xy} - \{xy\}$
- 2) complement the edges of $\Theta_{xy} - \{xy\}$

Ex: $xy = 3^h_4^t$

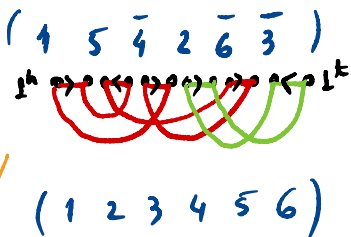


flip and complement

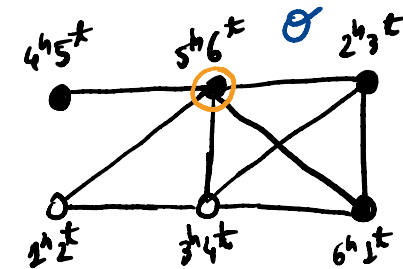


if xy is good:

- 1) flip the types of all vertices of Θ_{xy}
- 2) complement the edges of Θ_{xy}

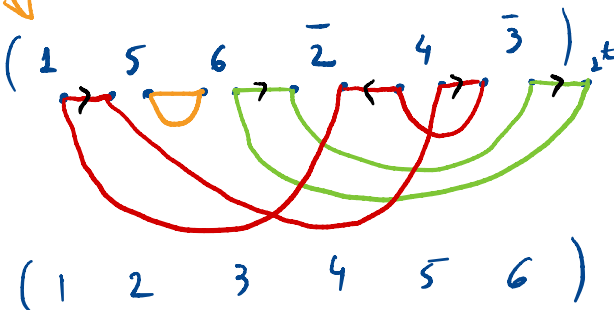
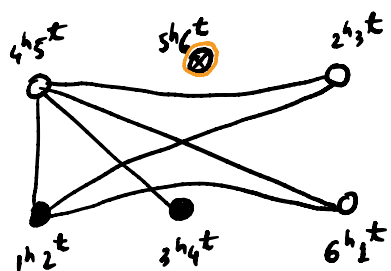


Ex: $xy = 5^h_6^t$



$\Theta_{5^h_6^t} = \Theta$

flip and complement



Sorting a good component - finding safe split inversions

G : # of good adjacencies in $RD(A, B)$

$g(xy)$: # of good adjacencies overlapping xy in $RD(A, B)$

$b(xy)$: # of bad adjacencies overlapping xy in $RD(A, B)$

$score(xy)$: # good adjacencies in the diagram after fixing xy

$$score(xy) = G + b(xy) - g(xy) - 1$$

An inversion that fixes a good target adjacency with maximal score is SAFE. (does not create new bad components)

Sorting a good component - finding safe split inversions

Let \mathcal{O} be the overlap graph of component K

Suppose $\{xy$ is a good adjacency with maximal score in \mathcal{O}
inversion fixing xy creates a bad component K_B

At least one (bad) adjacency $zw \in K_B$ was
adjacent to xy in $\mathcal{O} \Rightarrow zw$ was good in \mathcal{O}

$$\text{scores in } \mathcal{O} \quad \begin{cases} \text{score}(xy) = G + b(xy) - g(xy) - 1 \\ \text{score}(zw) = G + b(zw) - g(zw) - 1 \end{cases}$$

Sorting a good component - finding safe split inversions

→ set of back target adjacencies connected to xy in \mathcal{O}

$$\text{But: } B(xy) \subseteq B(zw) \Rightarrow b(xy) \leq b(zw)$$

$$G(zw) \subseteq G(xy) \Rightarrow g(zw) \leq g(xy)$$

⇓

we cannot have $\left\{ \begin{array}{l} b(xy) = b(zw) \text{ and} \\ g(xy) = g(zw) \end{array} \right.$

⇓

$$\text{score}(zw) > \text{score}(xy)$$

Sorting a bad component with a neutral inversion

Overlap graph of a bad component

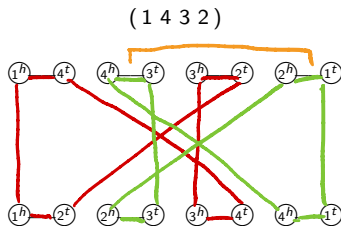
neutral inversion

$$hcs \Delta_{inv} = +1$$

(Cutting handle)

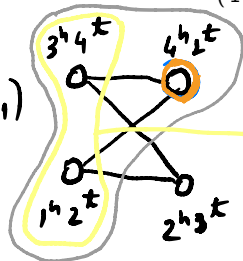
Any neutral inversion applied to a bad adjacency of a bad component k turns k into a good component

\mathcal{D}_1



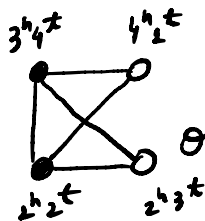
(1 2 3 4)

$\Theta(\mathcal{D}_1)$

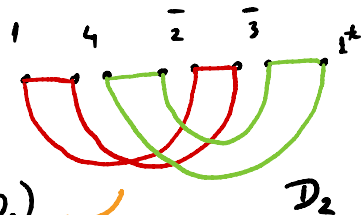


$\Theta_{4^h 1^t}$

flip and complement



$\Theta(\mathcal{D}_2)$



\mathcal{D}_2

Sorting bad components - hurdles

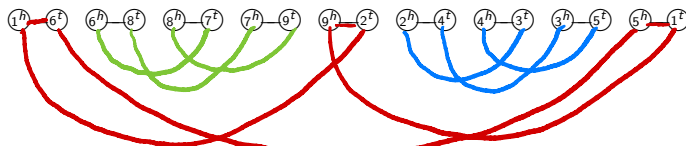
merging two cycles: $\Delta_{mv} = +2$

K_1, K_2 and K_3 are three distinct components in $RD(\mathbb{A}, \mathbb{B})$ so that $K_3 \dots K_1 \dots K_1 \dots K_3 \dots K_2 \dots K_2$

$\Rightarrow K_3$ separates K_1 and K_2

(merging hurdles)

(1 6 8 7 9 2 4 3 5)



3 bad components

(1 2 3 4 5 6 7 8 9)

the red component separates the green and the blue components



only green and blue are hurdles

By joining with an inversion two cycles c_1 and c_2 , that belong to two distinct components K_1 and K_2 respectively, we merge not only the components K_1 and K_2 , but also all components that separate K_1 and K_2 , into a single **good** component K .

Another example:

bad component, non hurdle

hurdle

bad component, non hurdle

hurdle

bad component, non hurdle



Sorting bad components - simple hurdles and super hurdles

h : number of hurdles in $RD(A, B)$

hurdle : bad component that does
not separate 2 bad components

super hurdle K : fixing K by a neutral
inversion creates a new
hurdle

On the previous page, both green and blue are super hurdles:
fixing only the green or only the blue component with a
neutral inversion would turn the red component into a
hurdle

Sorting bad components - simple hurdles and super hurdles

simple hurdle: a hurdle that is not a super hurdle

* each simple hurdle can be fixed with a neutral inversion

(cutting a hurdle) $\Delta_{INV} = +1$

* each pair of super hurdles can be fixed with a

joining inversion

(merging hurdles) $\Delta_{INV} = +2$

Sorting bad components - fortress

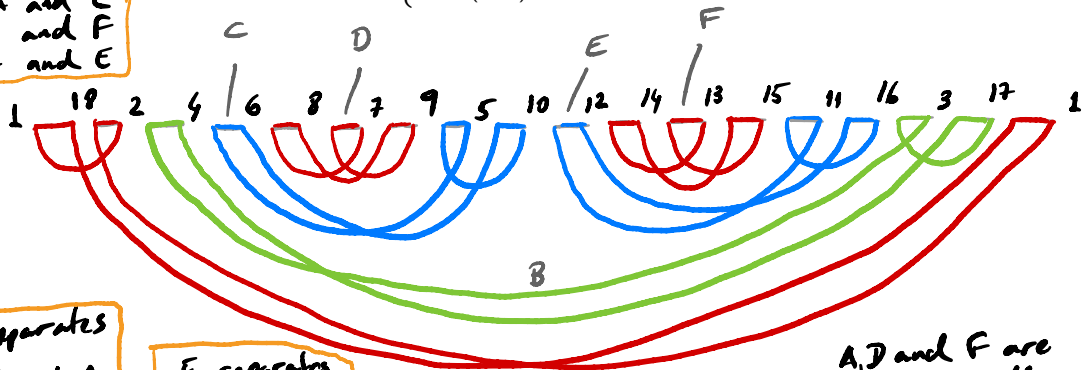
A, B, C, D, E, F are bad components

B separates

- A and D
- A and C
- A and F
- A and E

$$f: \begin{cases} 0 & RD(A, B) \text{ is not a fortress} \\ 1 & RD(A, B) \text{ is a fortress} \end{cases}$$

fortress { * there is an odd number of hurdles
* all hurdles are super hurdles



C separates

- D and A
- D and B
- D and E
- D and F


E separates

- F and A
- F and B
- F and C
- F and D

⇒ only A, D and F are hurdles

A, D and F are super-hurdles, but joining any pair among A, D, F creates a new hurdle

Canonical inversion distance of circular chromosomes

$$d_{\text{INV}}(\mathbb{A}, \mathbb{B}) = n - |\mathcal{C}| + h + f$$


Quiz 2

1 Which of the following statements about the inversion model are true?

- A The inversion distance depends only on the number of cycles in the relational diagram.
- B Every bad component in the diagram is a hurdle.
- C A good component can always be sorted with (safe) split inversions.
- D A super hurdle can be optimally sorted with a neutral inversion.
- E A diagram with an even number of bad components can be a fortress.

References

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In: Mathematics of Evolution and Phylogeny. Gascuel O (Ed); (2005)