Topics of today:

1. Canonical DCJ distance and sorting
2. Relational graph
3. Restricted canonical DCJ sorting

Canonical DCJ

Given two canonical genomes $\mathbb{A}$ and $\mathbb{B}$,...

Canonical DCJ Distance Problem:	Compute the minimum number of DCJ operations required to transform $\mathbb{A}$ into $\mathbb{B}$. Denote by $\mathrm{d}_{\mathrm{DCJ}}(\mathbb{A}, \mathbb{B})$ the DCJ distance of $\mathbb{A}$ and $\mathbb{B}$.
Canonical DCJ Sorting Problem:	Find a sequence of $\mathrm{d}_{\mathrm{DCJ}}(\mathbb{A}, \mathbb{B})$ DCJ operations that transform $\mathbb{A}$ into $\mathbb{B}$.

Let $\xi(\mathbb{G}) = \{g^t : g \in \mathcal{G}(\mathbb{G})\} \cup \{g^h : g \in \mathcal{G}(\mathbb{G})\}$ be the set of extremities of all genes in genome $\mathbb{G}$.

Ex: $\mathbb{G} = [2\,\bar{3}\,1]$, $\mathcal{G}(\mathbb{G}) = \{1, 2, 3\}$ and $\xi(\mathbb{G}) = \{1^t, 1^h, 2^t, 2^h, 3^t, 3^h\}$.

Note that, if genomes $\mathbb{A}$ and $\mathbb{B}$ are canonical, then $\xi(\mathbb{A}) = \xi(\mathbb{B})$.

Relational graph of canonical genomes

Given two canonical genomes $\mathbb{A}$ and $\mathbb{B}$, their **relational graph** $RG(\mathbb{A},\mathbb{B}) = (V, E)$ 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 $\mathbb{B}$

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

   For a given gene g, let $\begin{cases} \text{vertices } u \text{ and } v \text{ represent } g^t \text{ and } g^h \text{ in genome } \mathbb{A} \text{ and} \\ \text{vertices } u' \text{ and } v' \text{ represent } g^t \text{ and } g^h \text{ in genome } \mathbb{B} \end{cases}$

   Then: $\ell(u) = \ell(u') = g^t$ and $\ell(v) = \ell(v') = g^h$

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

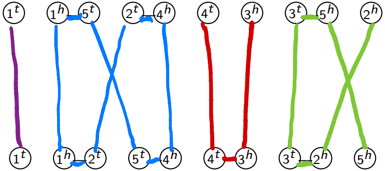
   - **Adjacency edges:** $\begin{cases} E_\alpha(\mathbb{A}) = \{uv : u, v \in V(\xi(\mathbb{A})) \text{ and } \ell(u)\ell(v) \in \alpha(\mathbb{A})\} \\ E_\alpha(\mathbb{B}) = \{uv : u, v \in V(\xi(\mathbb{B})) \text{ and } \ell(u)\ell(v) \in \alpha(\mathbb{B})\} \end{cases}$
   - **Extremity edges:**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

Note that:

- Let $n = |\mathcal{G}_\star|$. The number of edges in E_ξ is $2n$ (two edges per element of $\mathcal{G}_\star$).

Relational graph of canonical genomes

$\mathbb{A} =$ [1 5 3] [4 2]



$\mathbb{B} =$ [1 2 3 4 5]

$n = |\mathcal{G}_\star| = 5$, $\kappa(\mathbb{A}) = 2$ and $\kappa(\mathbb{B}) = 1$

Every vertex has degree one or two:
$RG(\mathbb{A},\mathbb{B})$ is a collection of paths and cycles
(alternating edes in E_ξ and in $E_\alpha(\mathbb{A}) \cup E_\alpha(\mathbb{B})$)

cycle with k edges in E_ξ: k-cycle or c_k
path with k edges n E_ξ: k-path or p_k

$$\begin{cases} \mathcal{C} = \{c_k\} \ : \ \text{set of cycles } (k \text{ is even}) \\ \mathcal{P}_{\mathbb{AA}} = \{p_k : \text{starts and ends in } \mathbb{A}\} \ : \\ \qquad \text{set of } \mathbb{AA}\text{-paths } (k \text{ is even}) \\ \mathcal{P}_{\mathbb{BB}} = \{p_k : \text{starts and ends in } \mathbb{B}\} \ : \\ \qquad \text{set of } \mathbb{BB}\text{-paths } (k \text{ is even}) \\ \mathcal{P}_{\mathbb{AB}} = \{p_k : \text{starts in } \mathbb{A} \text{ and ends in } \mathbb{B}\} \ : \\ \qquad \text{set of } \mathbb{AB}\text{-paths } (k \text{ is odd}) \end{cases}$$

$|\mathcal{P}_{\mathbb{AB}}|$ is even (E_ξ has $2n$ edges)
$|\mathcal{P}_{\mathbb{AA}}| + |\mathcal{P}_{\mathbb{BB}}| + |\mathcal{P}_{\mathbb{AB}}| = \kappa(\mathbb{A}) + \kappa(\mathbb{B})$

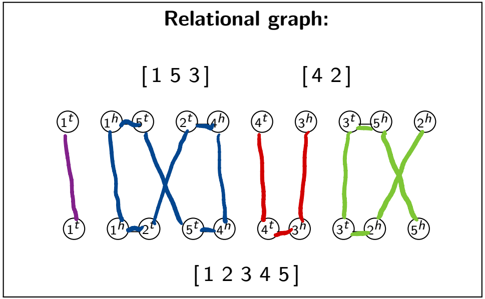
If $\mathbb{A} = \mathbb{B}$,
$RG(\mathbb{A},\mathbb{B})$ has only 2-cycles and 1-paths:

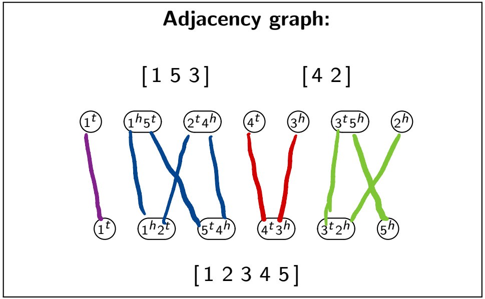
$$2n = 2|\mathcal{C}| + |\mathcal{P}_{\mathbb{AB}}| \quad \Rightarrow \quad n = |\mathcal{C}| + \frac{|\mathcal{P}_{\mathbb{AB}}|}{2}$$

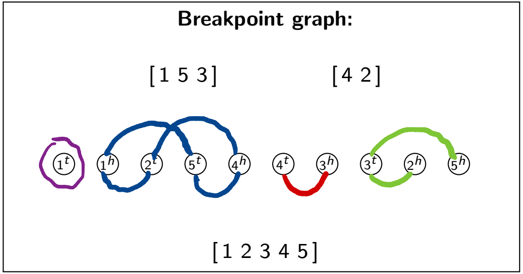
Otherwise, if $\mathbb{A} \neq \mathbb{B}$:

$$n > |\mathcal{C}| + \frac{|\mathcal{P}_{\mathbb{AB}}|}{2}$$

Relational graph ≅ Adjacency graph ≅ Breakpoint graph


Relational graph:
[1 5 3]
[4 2]
1^t 1^h 5^t 2^t 4^h 4^t 3^h 3^t 5^h 2^h
1^t 1^h 2^t 5^t 4^h 4^t 3^h 3^t 2^h 5^h
[1 2 3 4 5]


Adjacency graph:
[1 5 3]
[4 2]
1^t 1^h5^t 2^t4^h 4^t 3^h 3^t5^h 2^h
1^t 1^h2^t 5^t4^h 4^t3^h 3^t2^h 5^h
[1 2 3 4 5]

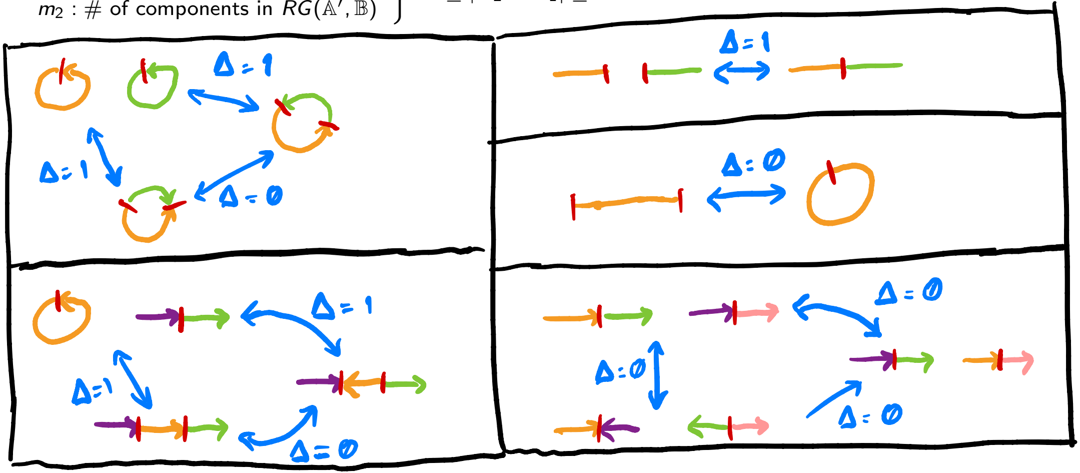


DCJ operations are applied only in A or only in B

Types of DCJ operation

Let a DCJ operation transform a genome $\mathbb{A}$ into another genome $\mathbb{A}'$:

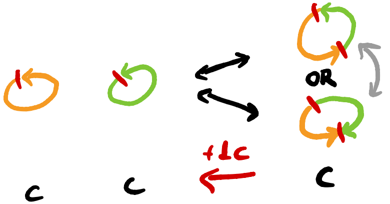
$$\left.\begin{array}{l} m_1 : \#\text{ of components in } RG(\mathbb{A},\mathbb{B}) \\ m_2 : \#\text{ of components in } RG(\mathbb{A}',\mathbb{B}) \end{array}\right\} \quad 0 \leq \overbrace{|m_2 - m_1|}^{\Delta} \leq 1$$



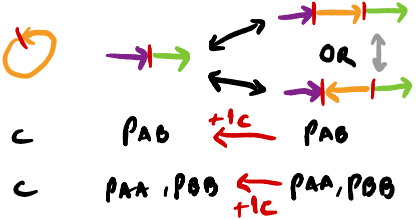
Goal: increase the number of cycles ($|\mathcal{C}|$) and/or the number of $\mathbb{AB}$-paths ($|\mathcal{P}_{\mathbb{AB}}|$) in RG

Types of DCJ operation

Goal: increase the number of cycles ($|\mathcal{C}|$) and/or the number of $\mathbb{AB}$-paths ($|\mathcal{P}_{\mathbb{AB}}|$) in *RG*



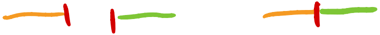
$\Delta c = 1$, $\Delta P_{AB} = 0$



$\}\ \Delta c = 1$, $\Delta P_{AB} = 0$

Types of DCJ operation

Goal: increase the number of cycles ($|\mathcal{C}|$) and/or the number of $\mathbb{AB}$-paths ($|\mathcal{P}_{\mathbb{AB}}|$) in *RG*



P_{AA}	P_{AA}	P_{AA}
P_{BB}	P_{BB}	P_{BB}
P_{AB}	P_{BB}	P_{AB}
P_{AA}	P_{AB}	P_{AB}

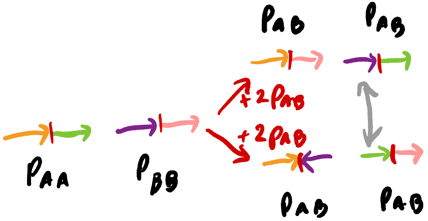
$\Delta c = 0, \Delta P_{AB} = 0$

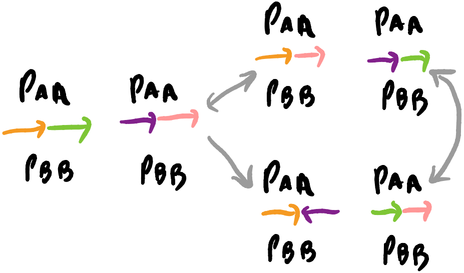
$$\begin{tikzcd}
P_{AB} & P_{BA} & P_{AA} \arrow[l, "+2P_{AB}"'] \\
P_{BA} & P_{AB} & P_{BB} \arrow[l, "+2P_{AB}"]
\end{tikzcd}$$

$\Delta c = 0, \Delta P_{AB} = 2$

$$\begin{tikzcd}
P_{AA} \arrow[r, "+1c"] & C \\
P_{BB} \arrow[r, "+1c"] & C
\end{tikzcd}$$

$\Delta c = 1, \Delta P_{AB} = 0$





Canonical DCJ Distance & Sorting

Recall that, if $\mathbb{A} = \mathbb{B}$, we have $n = |\mathcal{C}| + \frac{|\mathcal{P}_{\mathbb{A}\mathbb{B}}|}{2}$, otherwise $n > |\mathcal{C}| + \frac{|\mathcal{P}_{\mathbb{A}\mathbb{B}}|}{2}$

A DCJ operation ρ is called **optimal** if $\begin{cases} \rho \text{ increases the number of cycles by one, or} \\ \rho \text{ increases the number of } \mathbb{A}\mathbb{B}\text{-paths by two.} \end{cases}$

Given two canonical genomes $\mathbb{A}$ and $\mathbb{B}$, it is possible to find an optimal DCJ operation at each sorting step. Therefore:

$$\mathrm{d}_{\mathrm{DCJ}}(\mathbb{A}, \mathbb{B}) = n - |\mathcal{C}| - \frac{|\mathcal{P}_{\mathbb{A}\mathbb{B}}|}{2}$$

Quiz 1

1 Which of the following statements about the Relational Graph are true?

odd : AB

even : AA or BB

[✓ A] Closing an even path into a cycle is always optimal.

B Breaking an odd path into two paths is always optimal.

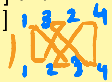
[✓ C] Breaking an even path into two odd paths is always optimal.

[✓ D] Breaking an even cycle into two cycles is always optimal.

[✓ E] Recombining two even paths into two odd paths is always optimal.

Compute the DCJ distance for the following pairs of genomes:

2 $\mathbb{A} = [1\ 3\ 2\ 4]$ and
$\mathbb{B} = [1\ 2\ 3\ 4]$



A 0

B 1

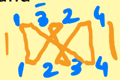
[✓ C 2]

D 2,5

E 3

$d = 4 - 1 - 1 = 2$

3 $\mathbb{A} = [1\ \bar{3}\ 2\ 4]$ and
$\mathbb{B} = [1\ 2\ 3\ 4]$



A 0

B 1

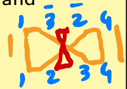
[✓ C 2]

D 2,5

E 3

$d = 4 - 1 - 1 = 2$

4 $\mathbb{A} = [1\ \bar{3}\ \bar{2}\ 4]$ and
$\mathbb{B} = [1\ 2\ 3\ 4]$



A 0

[✓ B 1]

C 1,5

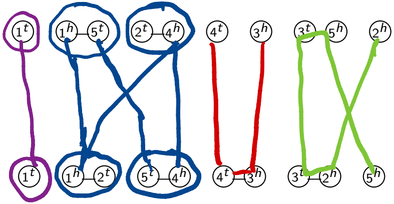
D 2

E 3

$d = 4 - 2 - 1 = 1$

Computing the canonical DCJ Distance in linear time

$\mathbb{A} =$ [1 5 3] [4 2]



$\mathbb{B} =$ [1 2 3 4 5]

$P_{AB} = 11$

$c = 1$

$d = 5 - 1 - 1 = 3$

A. Telomeres and adjacencies of genome $\mathbb{A}$

Pos	1	2	3	4	5	6	7
1st	1^t	1^h	5^h	3^h	4^t	h^h	2^h
2nd	-	5^t	3^t	-	-	2^t	-

Positions of gene extremities in Tab. **A**

gene	1	2	3	4	5
head	2	7	4	6	3
tail	1	6	3	5	2

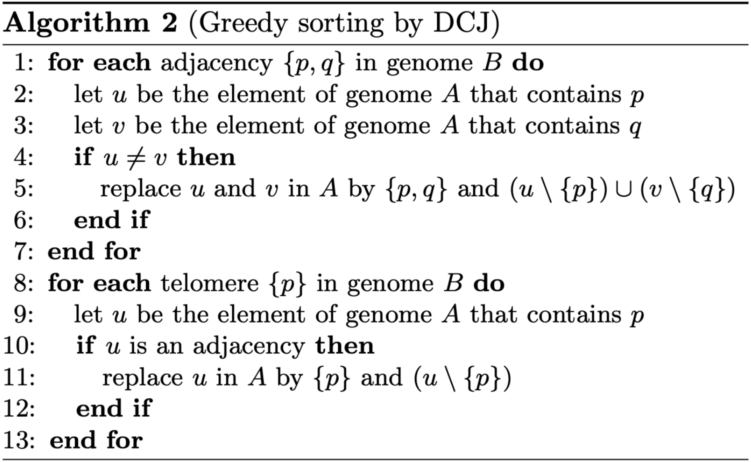
B. Telomeres and adjacencies of genome $\mathbb{B}$

Pos	1	2	3	4	5	6
1st	1^t	1^h	2^h	3^h	4^h	5^h
2nd	-	2^t	3^t	4^t	5^t	-

Positions of gene extremities in Tab. **B**

gene	1	2	3	4	5
head	2	3	4	5	6
tail	1	2	3	4	5

Canonical DCJ Sorting



Algorithm 2 (Greedy sorting by DCJ)

```
for each adjacency $\{p, q\}$ in genome $B$ do
    let $u$ be the element of genome $A$ that contains $p$
    let $v$ be the element of genome $A$ that contains $q$
    if $u \neq v$ then
        replace $u$ and $v$ in $A$ by $\{p, q\}$ and $(u \setminus \{p\}) \cup (v \setminus \{q\})$
    end if
end for
for each telomere $\{p\}$ in genome $B$ do
    let $u$ be the element of genome $A$ that contains $p$
    if $u$ is an adjacency then
        replace $u$ in $A$ by $\{p\}$ and $(u \setminus \{p\})$
    end if
end for
```

Canonical DCJ Sorting

$\mathbb{A} =$ [1 5 3] [4 2]

[1 2] [4 5 3]

[1 2 3] [4 5]

[1 2 3 4 5]

$\mathbb{B} =$ [1 2 3 4 5]

A. Telomeres and adjacencies of genome $\mathbb{A}$

Pos	1	2	3	4	5	6	7
1st	1^t	1^h	5^h	3^h	4^t	4^h	2^h
2nd	-	5^t	3^t	-	-	2^t	-

Positions of gene extremities in Tab. **A**

gene	1	2	3	4	5
head	2	7	4	6	3
tail	1	6	3	5	2

B. Telomeres and adjacencies of genome $\mathbb{B}$

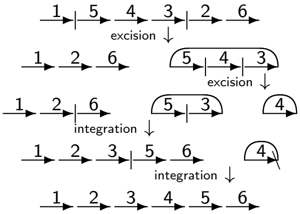
Pos	1	2	3	4	5	6
1st	1^t	1^h	2^h	3^h	4^h	5^h
2nd	-	2^t	3^t	4^t	5^t	-

Positions of gene extremities in Tab. **B**

gene	1	2	3	4	5
head	2	3	4	5	6
tail	1	2	3	4	5

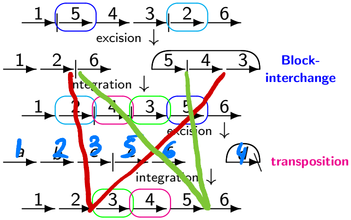
DCJ model - circular excision/integration

Canonical DCJ model



Many circular chromosomes can coexist in the intermediate genomes.

Restricted canonical DCJ model



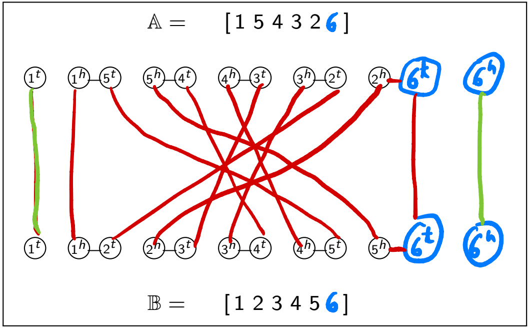
A circular chromosome is immediately reintegrated after its excision.

The DCJ distance is the same for both the general and the restricted DCJ models

Restricted canonical DCJ sorting

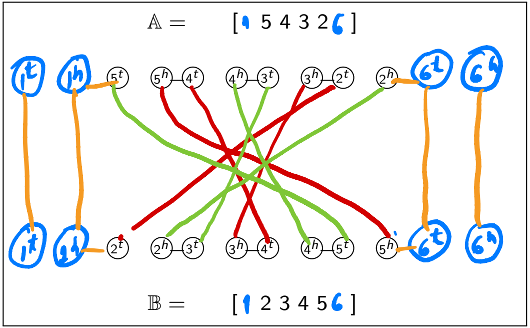
Canonical genomes $\mathbb{A}$ and $\mathbb{B}$ are linear.

Transform $\mathbb{A}$ and $\mathbb{B}$ into **co-tailed** genomes $\mathbb{A}'$ and $\mathbb{B}'$:



$\mathbb{A} =$ [1 5 4 3 2 6]

$\mathbb{B} =$ [1 2 3 4 5 6]



$\mathbb{A} =$ [1 5 4 3 2 6]

$\mathbb{B} =$ [1 2 3 4 5 6]

$n: 5 \to 6\ (+1)$

$P_{AB}: 2 \to 2$

$c: 0 \to 1\ (-1)$

Assume that the genes in chromosomes of $\mathbb{B}'$ are consecutive numbers
(otherwise renumber the genes of $\mathbb{A}'$ and of $\mathbb{B}'$)

$n: 4 \to 6\ (+2)$

$P_{AB}: 0 \to 2\ (-1)$

$c: 0 \to 1\ (-1)$

Restricted canonical DCJ sorting

Canonical genomes $\mathbb{A}'$ and $\mathbb{B}'$ are linear and co-tailed.

$\mathbb{A} = [\,1\ 5\ 4\ 3\ 2\ 6\,]$

↓ 2 DCJs

$A = [\,1\ 2\ 4\ 3\ 5\ 6\,]$

↓ 2 DCJs

$A = [\,1\ 2\ 3\ 4\ 5\ 6\,]$

$\mathbb{B} = [\,1\ 2\ 3\ 4\ 5\ 6\,]$

Sort $\mathbb{A}'$ into $\mathbb{B}'$ from left to right:

Once we have transformed the beginning of a chromosome in $\mathbb{A}'$ to $k\ k{+}i\ \ldots \ell$, we extend it by moving $\ell{+}1$ next to ℓ. Cases:

1. $\ell{+}1$ is on a different chromosome: translocation

Otherwise the situation is $\ell \ldots \ell{+}1 \ldots$

2. ℓ and $\ell{+}1$ have distinct orientations: inversion

Otherwise, find the highest gene m between ℓ and $\ell{+}1$ and find $m{+}1$

3. $m{+}1$ is on a different chromosome: translocation to move it next to m; this operation also moves $\ell{+}1$ to another chromosome, with another translocation we put it next to ℓ

Otherwise the situation is $\ell \ldots m \ldots \ell{+}1 \ldots m{+}1$

4. m and $m{+}1$ have distinct orientations: inversion to move $m{+}1$ next to m; this also changes the orientation of $\ell{+}1$, with another inversion we put it next to ℓ
5. m and $m{+}1$ have the same orientation: interchange blocks

   $\ell\ \langle \ldots m\rangle \ldots \langle \ell{+}1 \ldots\rangle\ m{+}1 \rightsquigarrow \ell\ \ell{+}1 \ldots m\ m{+}1$

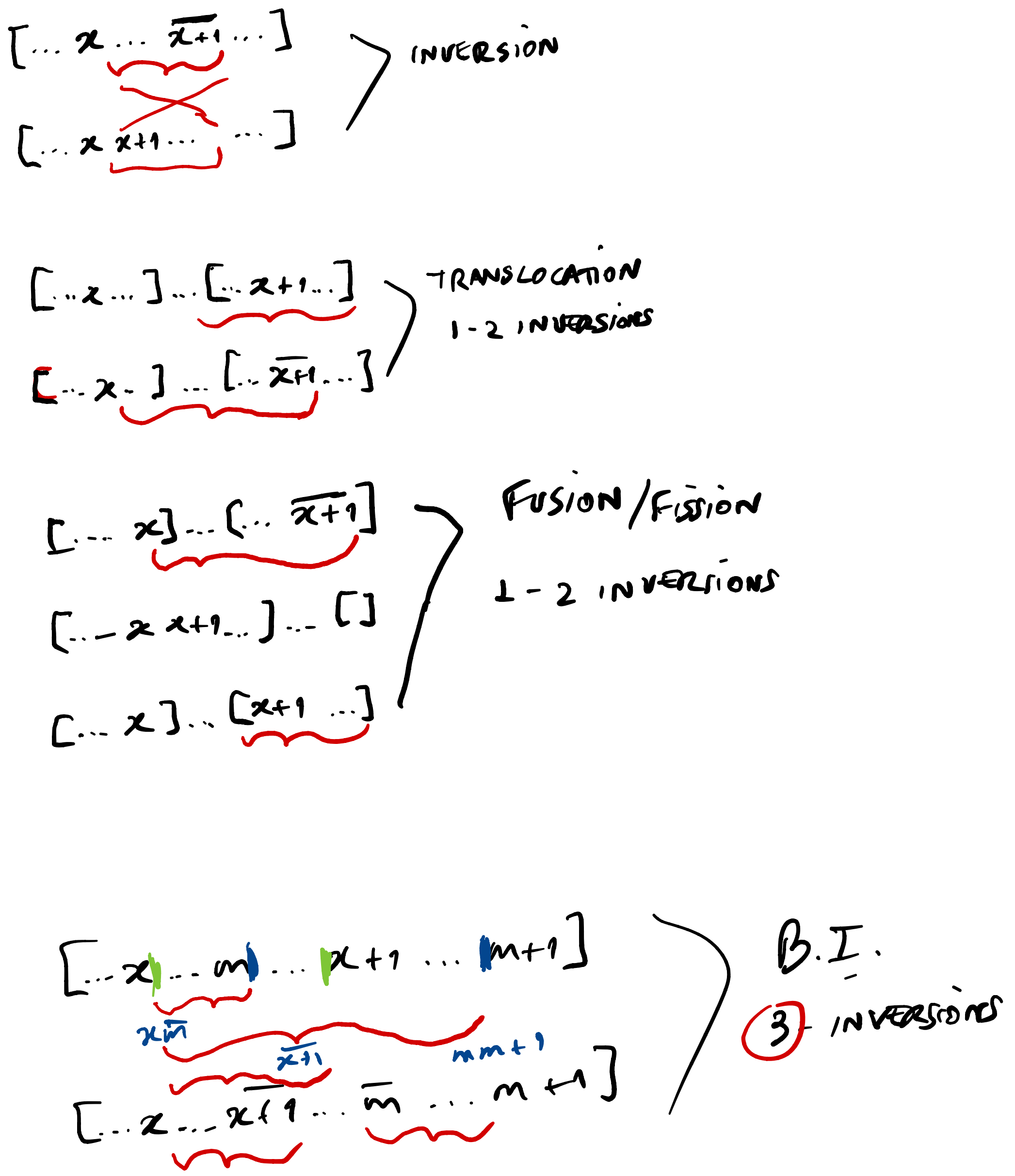
   (if both m and $m{+}1$ have positive orientation)

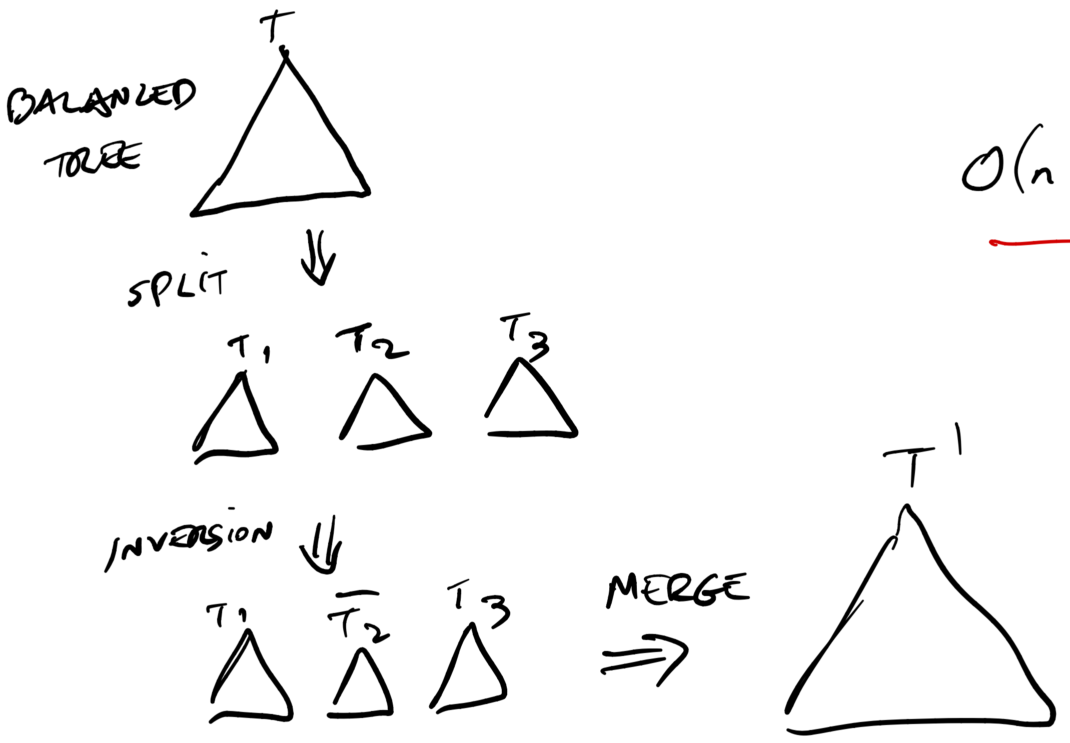
   or

   $\ell\ \langle \ldots\rangle\ \overline{m} \ldots \langle \ell{+}1 \ldots \overline{m{+}1}\rangle \rightsquigarrow \ell\ \ell{+}1 \ldots \overline{m{+}1}\ \overline{m}$

   (if m and $m{+}1$ have both reverse orientation)

With two operations we put $\ell{+}1$ next to ℓ and m next to $m{+}1$.


[... x ... x+1 ...]
[... x x+1 ... ...]
INVERSION
[... x ...] ... [... x+1 ...]
[... x ..] ... [... x+1 ...]
TRANSLOCATION
1-2 INVERSIONS
[... x] ... [... x+1]
[... x x+1 ...] ... []
[... x] ... [x+1 ...]
FUSION/FISSION
1-2 INVERSIONS
[... x ... m ... x+1 ... m+1]
x m
x+1
m m+1
[... x ... x+1 ... m ... m+1]
B.I.
3 INVERSIONS


T
BALANCED TREE
SPLIT
T1
T2
T3
INVERSION
T1
T2
T3
MERGE
T'

$O(n \log n)$

Quiz 2

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

[✓ A] Computing the canonical DCJ distance can be done in linear time.

[✓ B] Sorting a canonical genome $\mathbb{A}$ into another canonical genome $\mathbb{B}$ has the same complexity as computing the DCJ distance of $\mathbb{A}$ and $\mathbb{B}$. GREEDY SORTING

C DCJ distance and sorting are asymmetric.

D The canonical DCJ distance and the restricted canonical DCJ distance are distinct.

[✓ E] The canonical DCJ sorting can be done in linear time.

F The restricted canonical DCJ sorting can be done in linear time.

References

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(Jakub Kováč, Robert Warren, Marília D. V. Braga, and Jens Stoye)

JCB Volume 18, Number 9, 2011