Group theoretic formalization of double-cut-and-join model of chromosomal rearrangement

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Rare is better – large scale mutations

- *Large scale genome rearrangements* such as insertion or deletion of genes, gene duplications, inversions of genes make good phlyogenetic markers, precisely because they are rare.
- Our focus - Determining a measure of difference between various species bssed on such large scale genome rearrangements.
- Our tool - algebra/group theory.

An example – Double cut and join

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- Genome representation – graph.

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- Rearrangement events
  - Inversion of a section
  - Translocation of a section
  - Fission/Fusion of strands

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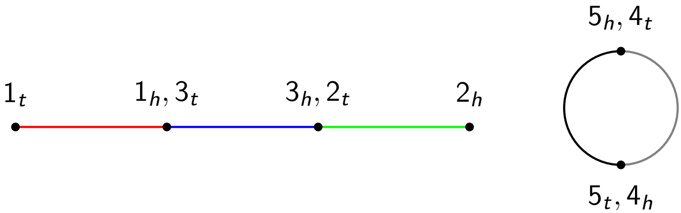
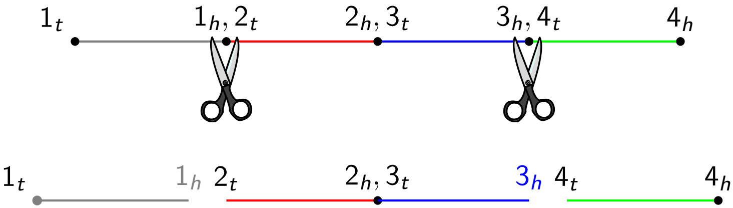
- Example

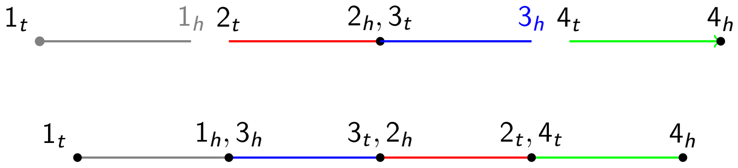


$$\{1_t, \{1_h, 3_t\}, \{3_h, 2_t\}, 2_h, \{5_h, 4_t\}, \{5_t, 4_h\}\}$$

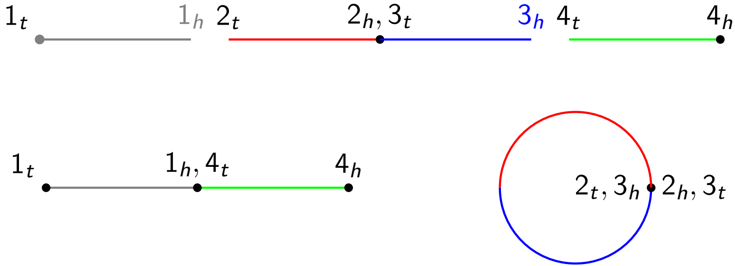
Double cut and join – the cut



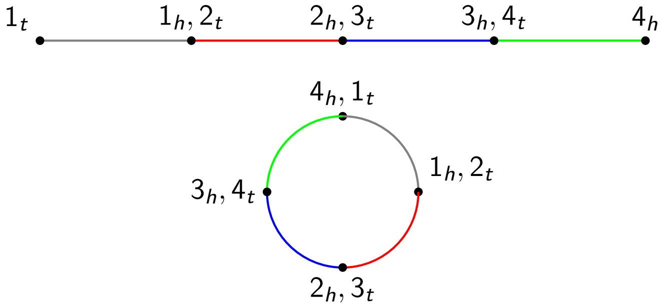
Double cut and join operation — inversion



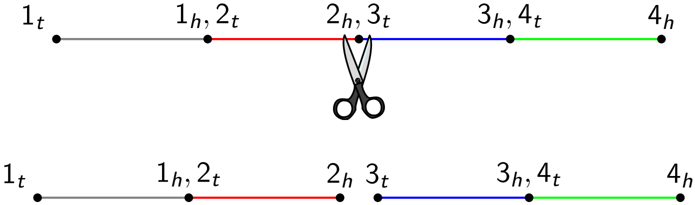
Double cut and join operation — excision



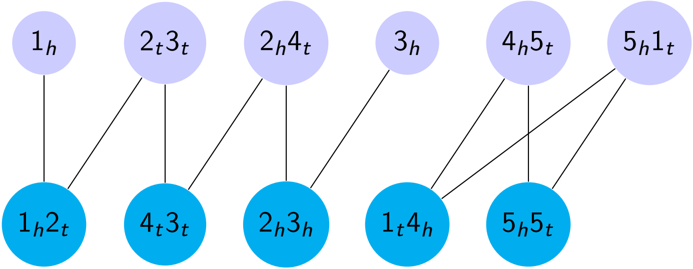
Circularization/Linearization



Fusion/Fission



Distance under the DCJ model – Adjacency graph



DCJ operator — Our re-formulation

- We assign a numeric label to each gene extremity. Let i be a gene. Then

$$i_t \to 2i - 1$$

$$i_h \to 2i$$

- Thus if there are n genes, we get $2n$ labels. Let us call this set X.

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- Thus if there are n genes, we get $2n$ labels. Let us call this set X.
- A genome on n genes is a permutation π on the set X such that

$$\pi(i) = j \iff \pi(j) = i$$

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- For example for the genome $\{1_t, (1_h, 2_h), 2_t\}$, the labels are

$$1_t \rightarrow 1, 1_h \rightarrow 2$$

$$2_t \rightarrow 3, 2_h \rightarrow 4$$

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$$1_t \to 1, 1_h \to 2$$

$$2_t \to 3, 2_h \to 4$$

and it is encoded as

$$\begin{pmatrix} 1 & 2 & 3 & 4 \\ 1 & 4 & 3 & 2 \end{pmatrix}$$

DCJ operator — Our re-formulation

For $i, j \in X$

$$D_{ij}(\pi) = \begin{cases} (i\ j)\pi(i\ j) & \textit{if } \pi = \ldots(k\ i)(l\ j) \textit{ and } k \neq i \textit{ or } j \neq l \\ (i\ j)\pi & \textit{if } i \textit{ and } j \textit{ are fixed in } \pi \textit{ or } \pi = \ldots(i\ j) \end{cases}$$

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- Clearly, $D_{ij} = D_{ji}$.
- Also, D_{ij}^2 is identity.

KEY RESULTS

Key result # 1 – Structure of the group of D_{ij}s

- Let Γ_n be the set of genomic permutations on n regions. D_{ij} is a bijection on Γ_n.
- Let D be the subgroup of S_{Γ_n} generated by the D_{ij} operators.

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- Conjecture: $\gamma/2$ is even $\forall n > 2$.

Key result # 2 – Characterization of cycles and paths of $AG(A, B)$

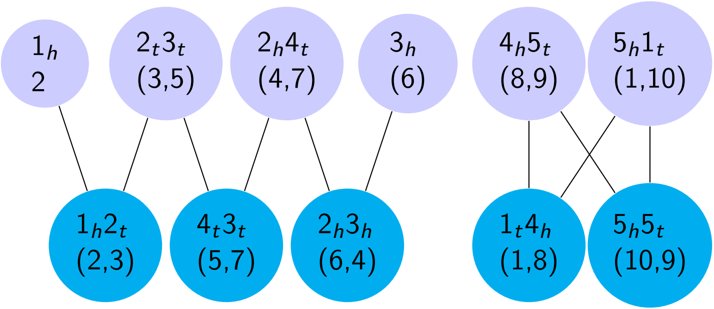
Theorem

Let A and B be genomes and let α be a k-cycle in the product $\pi_A\pi_B$. If α contains a point that is fixed in π_A or π_B, then the extremities in α form a path of length k in $AG(A, B)$.

If α does not contain any point of that is fixed in π_A or π_B then let β be the cycle in $\pi_A\pi_B$ that contains $\pi_B(i)$ for any $i \in \alpha$. Then $\alpha\beta$ is a cycle in $AG(A, B)$.

Characterization of cycles and paths of $AG(A, B)$ *– example*

$$\pi_A = (1,10)(2)(3,5)(4,7)(6)(8,9)$$
$$\pi_B = (1,8)(2,3)(4,6)(5,7)(9,10)$$



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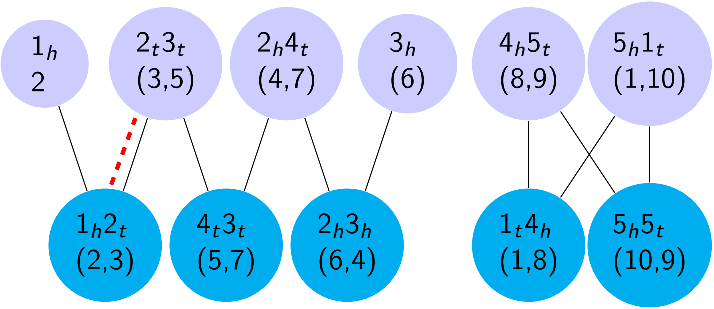

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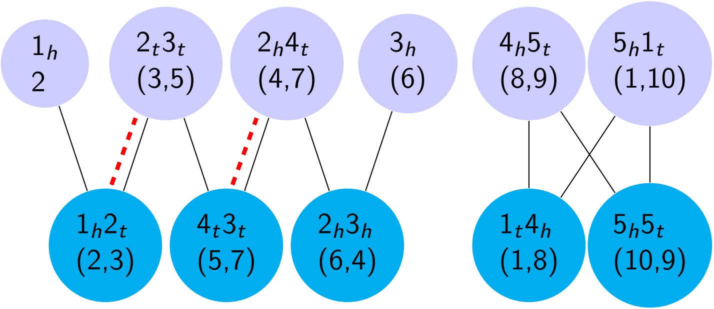

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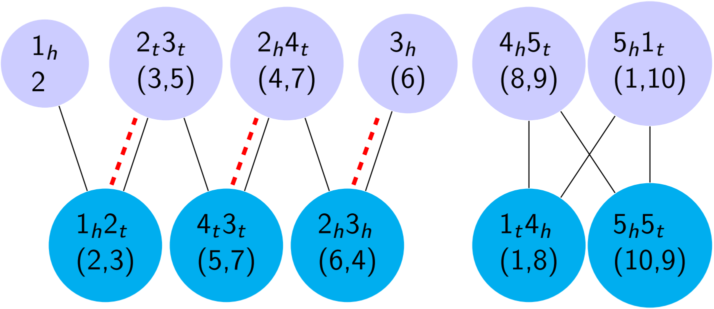

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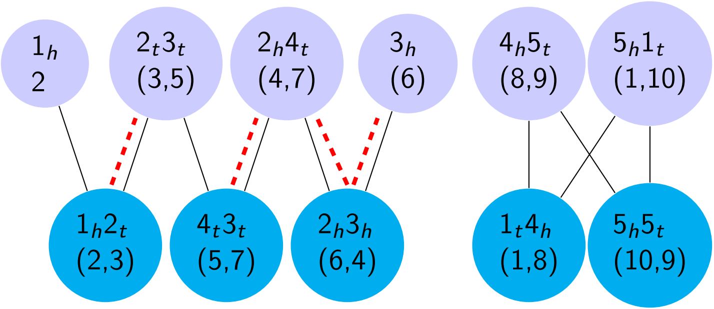

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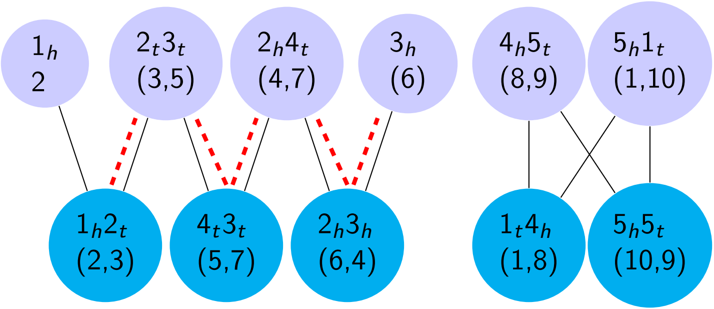

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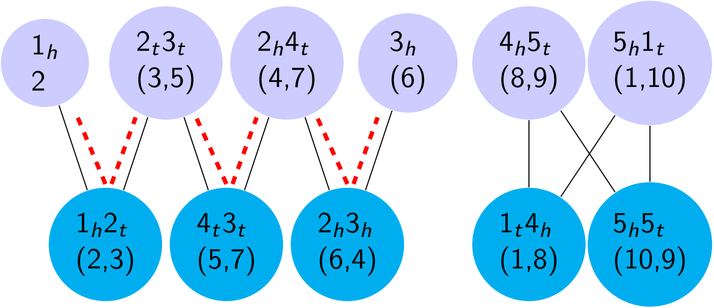

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Key result # 3 – DCJ Distance

$$d_{DCJ}(\pi_A, \pi_B) = \frac{l(\pi_A\,\pi_B)}{2} + \frac{E}{2}$$

where $l(\pi_A\pi_B)$ is the length $\pi_A\,\pi_B$ and E is the number of cycles in $\pi_A\,\pi_B$ that move two fixed points of π_A or of π_B.

Key result # 4 – Number of sorting scenarios

Let π_A and π_B be genomic permutations on n regions such that $\pi_B\pi_A$ encodes a cycle in the adjacency graph $AG(A, B)$. Then the number of optimal sorting scenarios between π_A and π_B is n^{n-2}.

An example

Let $\pi_a = (1,8)(2,3)(4,5)(6,7)$, $\pi_b = (1,2)(3,4)(5,6)(7,8)$

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$d_{28}(\pi_a) = (1,2)(8,3)(4,5)(6,7)$

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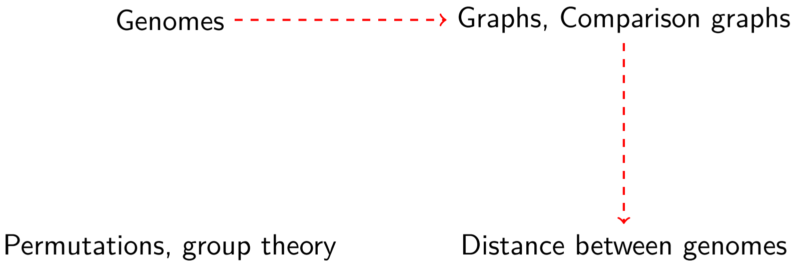
To summarize



Genomes

Graphs, Comparison graphs

Permutations, group theory

Distance between genomes

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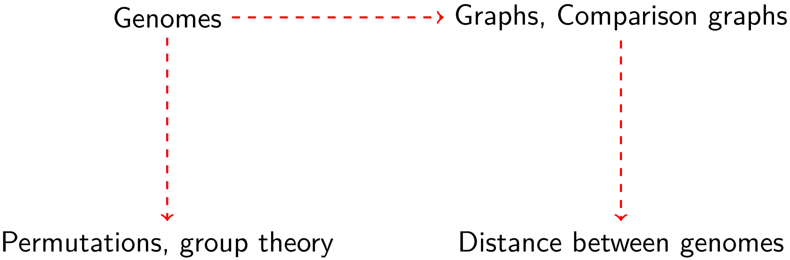

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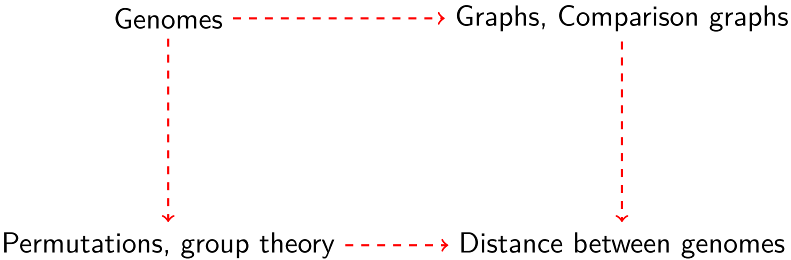

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Future work

- Of particular interest: evolution of mitochondrial DNA which is circular.
- Model important rearrangement events in circular chromosomes.
- Translocation event i.e. movement of a section of the genome to a different location on the genome can be modeled as a combination of two double cut and join events.
- Determine DCJ distance when the different events carry weights/probabilities.

Thank you!