Greedy Algorithms And Genome Rearrangements

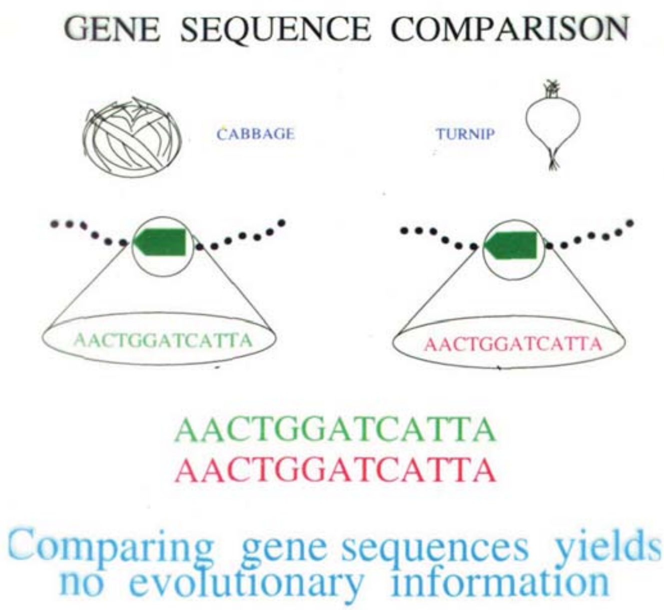
Outline

- Transforming Cabbage into Turnip
- Genome Rearrangements

Turnip vs Cabbage: Look and Taste Different

- Although cabbages and turnips share a recent common ancestor, they look and taste different

Turnip vs Cabbage: Comparing Gene Sequences Yields No Evolutionary Information

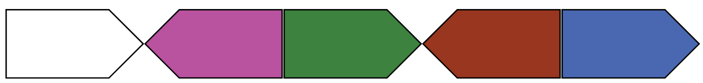


Turnip vs Cabbage: Almost Identical mtDNA gene sequences

- In 1980s Jeffrey Palmer studied evolution of plant organelles by comparing mitochondrial genomes of the cabbage and turnip
- 99% similarity between genes
- These surprisingly identical gene sequences differed in gene order
- This study helped pave the way to analyzing genome rearrangements in molecular evolution

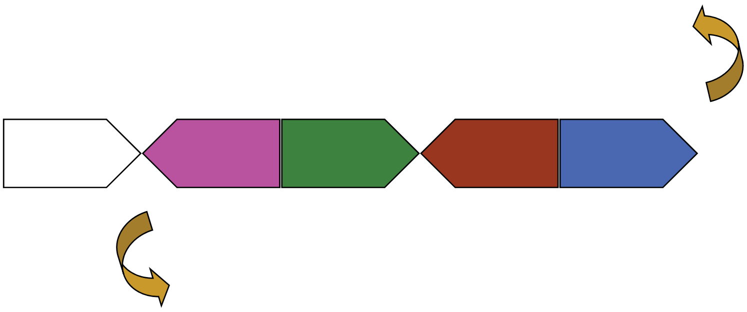
Turnip vs Cabbage: Different mtDNA Gene Order

- Gene order comparison:



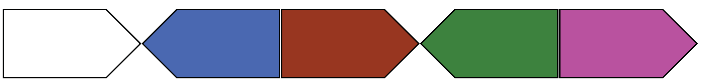
Turnip vs Cabbage: Different mtDNA Gene Order

- Gene order comparison:



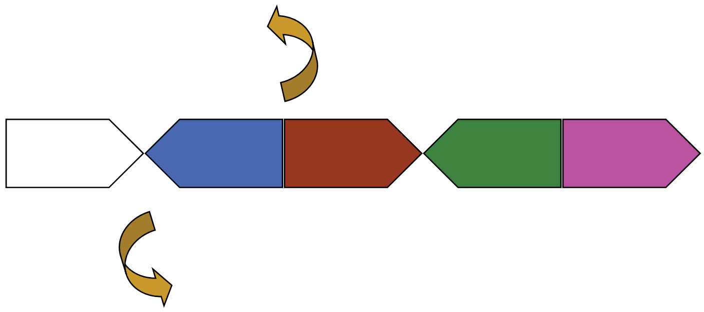
Turnip vs Cabbage: Different mtDNA Gene Order

- Gene order comparison:



Turnip vs Cabbage: Different mtDNA Gene Order

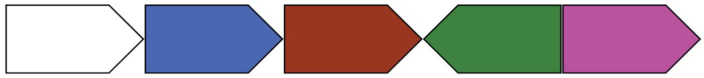
- Gene order comparison:



An Introduction to Bioinformatics Algorithms www.bioalgorithms.info

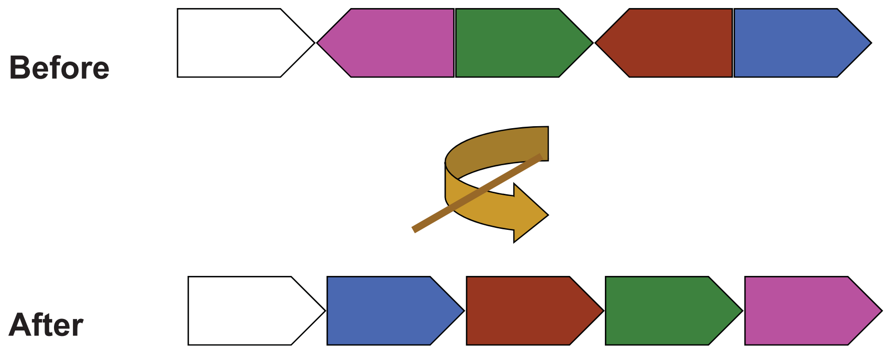
Turnip vs Cabbage: Different mtDNA Gene Order

- Gene order comparison:



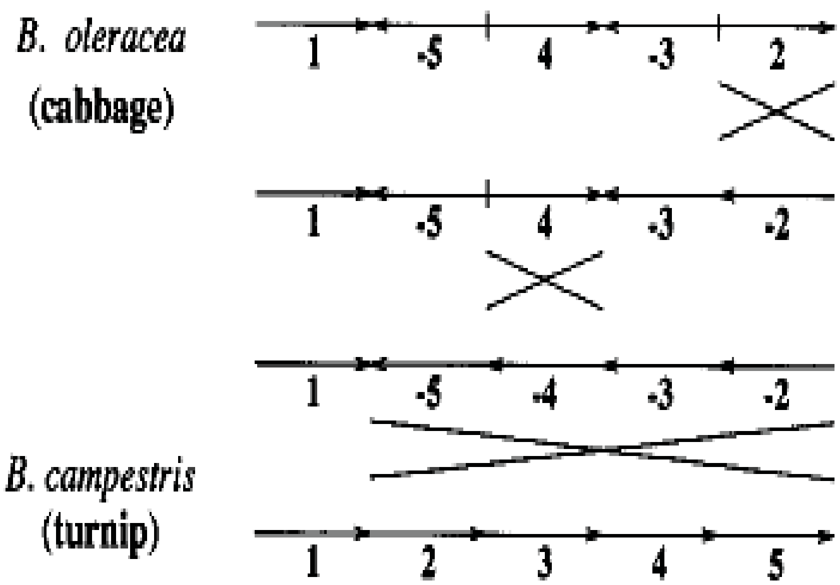
Turnip vs Cabbage: Different mtDNA Gene Order

- Gene order comparison:

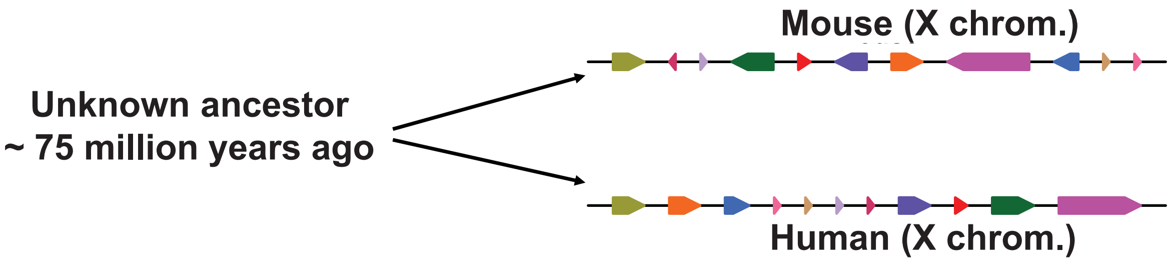


Evolution is manifested as the divergence in gene order

Transforming Cabbage into Turnip

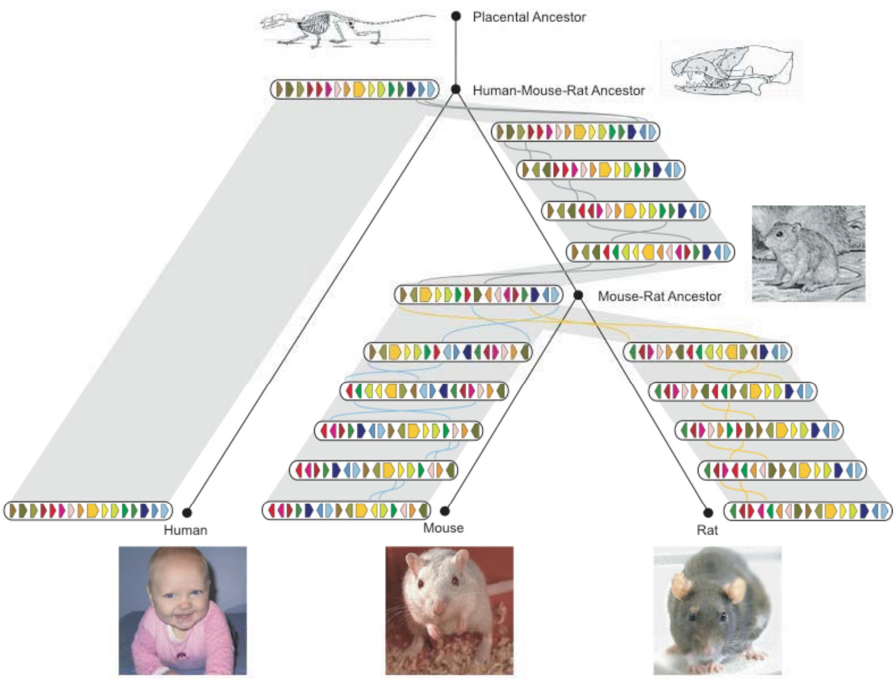


Genome rearrangements



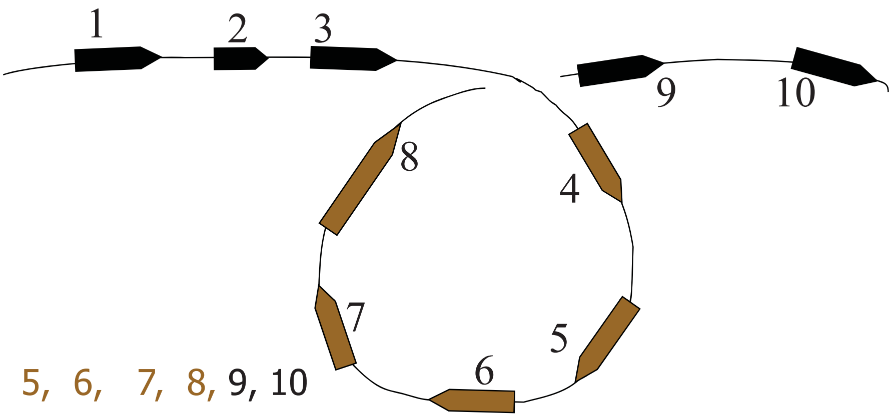
- What are the similarity blocks and how to find them?
- What is the architecture of the ancestral genome?
- What is the evolutionary scenario for transforming one genome into the other?

History of Chromosome X



Rat Consortium, *Nature*, 2004

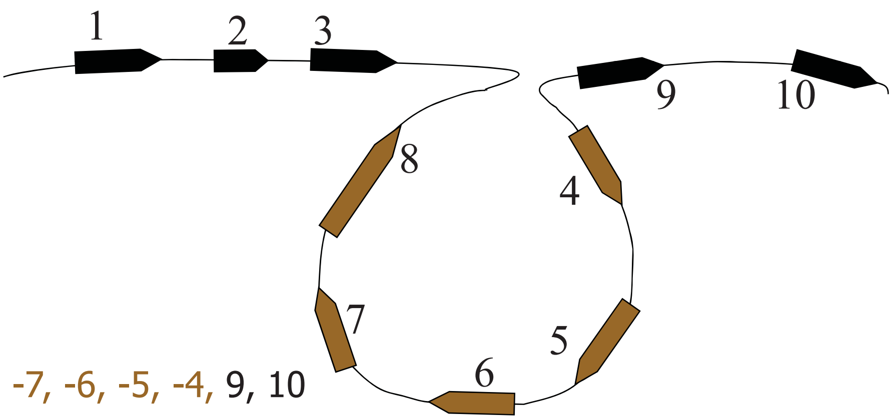
Reversals



1, 2, 3, 4, 5, 6, 7, 8, 9, 10

- Blocks represent conserved genes.

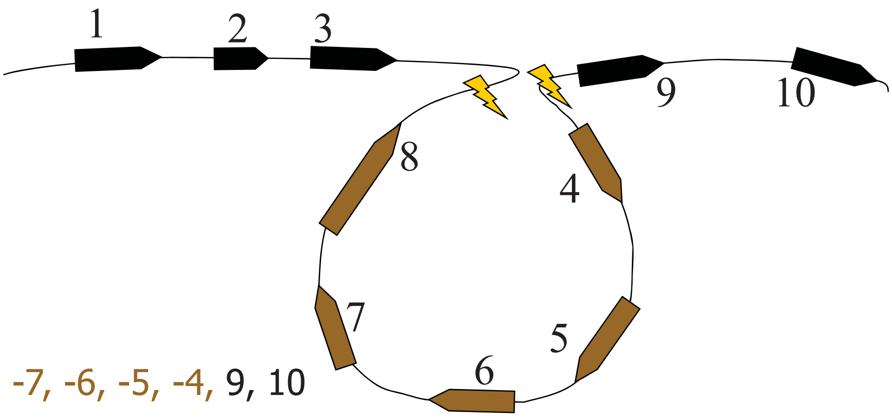
Reversals



1, 2, 3, -8, -7, -6, -5, -4, 9, 10

- Blocks represent conserved genes.
- In the course of evolution or in a clinical context, blocks 1,…,10 could be misread as 1, 2, 3, -8, -7, -6, -5, -4, 9, 10.

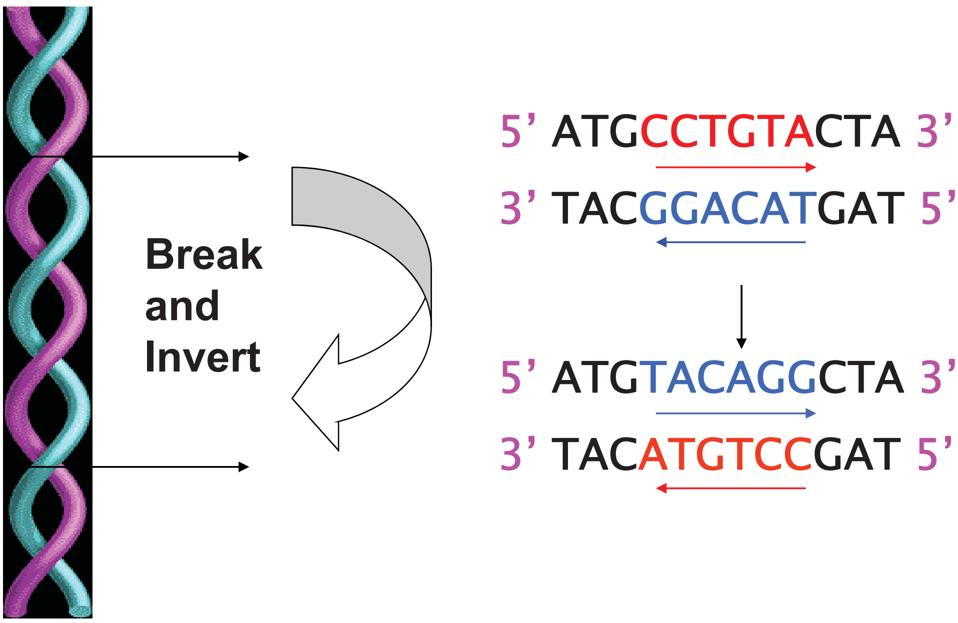
Reversals and Breakpoints



1, 2, 3, -8, -7, -6, -5, -4, 9, 10

The reversion introduced two *breakpoints* (disruptions in order).

Reversals: Example



Types of Rearrangements

Reversal

1 2 3 4 5 6 → 1 2 -5 -4 -3 6

Translocation

1 2 3 → 1 2 6
4 5 6 → 4 5 3

Fusion

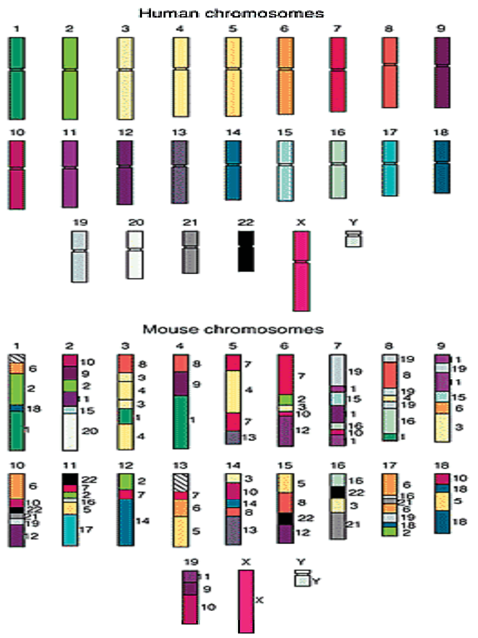
1 2 3 4
5 6 → 1 2 3 4 5 6

1 2 3 4 5 6 → 1 2 3 4
5 6

Fission

Comparative Genomic Architectures: Mouse vs Human Genome

- Humans and mice have similar genomes, but their genes are ordered differently
- ~245 rearrangements
  - Reversals
  - Fusions
  - Fissions
  - Translocation



Waardenburg's Syndrome: Mouse Provides Insight into Human Genetic Disorder

- Waardenburg's syndrome is characterized by pigmentary dysphasia
- Gene implicated in the disease was linked to human chromosome 2 but it was not clear where exactly it is located on chromosome 2

Waardenburg's syndrome and splotch mice

- A breed of mice (with splotch gene) had similar symptoms caused by the same type of gene as in humans
- Scientists succeeded in identifying location of gene responsible for disorder in mice
- Finding the gene in mice gives clues to where the same gene is located in humans by analyzing the relative architecture of human and mouse genomes

Reversals: Example

π = 1 2 <u>3 4 5</u> 6 7 8

$\rho(3,5)$ ↓

1 2 5 4 3 6 7 8

An Introduction to Bioinformatics Algorithms www.bioalgorithms.info

Reversals: Example

π = 1 2 <u>3 4 5</u> 6 7 8

$\rho(3,5)$ ↓

1 2 5 4 <u>3 6</u> 7 8

$\rho(5,6)$ ↓

1 2 5 4 6 3 7 8

Reversals and Gene Orders

- Gene order is represented by a permutation π:

$$\pi = \pi_1 \text{------} \pi_{i-1} \underline{\pi_i \pi_{i+1} \text{------} \pi_{j-1} \pi_j} \pi_{j+1} \text{-----} \pi_n$$

$$\downarrow \rho(i,j)$$

$$\pi_1 \text{------} \pi_{i-1} \pi_j \pi_{j-1} \text{------} \pi_{i+1} \pi_i \pi_{j+1} \text{-----} \pi_n$$

- Reversal ρ (*i, j*) reverses (flips) the elements from *i* to *j* in π