Gene and genome duplication

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Plan

1. Genome rearrangement and multigene families
2. Genome duplication
3. Duplication of chromosomal segments
4. Conclusion

Genome rearrangement

Chromosomes evolved by insertion, deletion, movement of genes

Genomic approach: Compare gene orders

Hypothesis: Homologous genes are known

Chromosome ⟹ sequence of signed genes (or blocks)

$$b \quad -a \quad d \quad -e \quad -c \quad f$$

Multigene families

In the human genome ~15% protein genes duplicated

(*Li, Wang, Nekrutenko, 2001*)

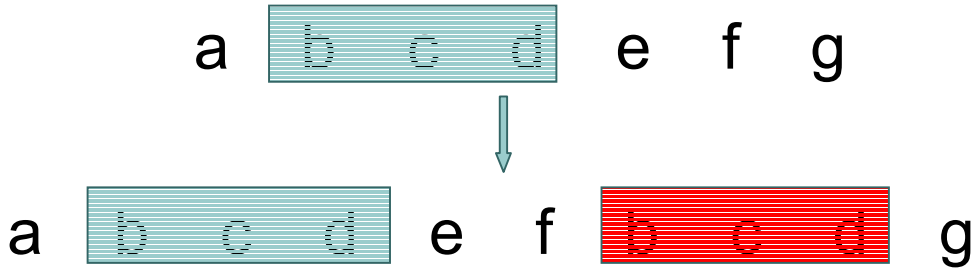
~16% yeast, ~25% Arabidopsis (*Wolfe, 2001*)

Compare sequences of signed genes allowing many copies of each gene

b –a d a –e –c e f d a

Multigene families due to:

- Single gene duplication;
- Segment duplication: Tandem duplication or duplication transposition



- Horizontal gene transfer;
- Genome-wide doubling event

Algorithms and models

- Genome rearrangement with multigene families
  - → Exemplar approach, *Sankoff 1999*
  - → Insertion, deletion, gene duplication,

    Marron,Swensen, Moret 2003
- Reconciliation analysis, projecting gene tree on phylogenetic tree

  Hallett, Lagergren 2000, Page, Cotton 2000;

  Chen, Durand, Farach 2000, Sankoff, El-Mabrouk 2000
- Probabilistic models for the generation of multigene families

Find the ancestor of a genome with multiple gene copies

- Genome duplication

  N. El-Mabrouk and D. Sankoff, SIAM, J. Comp., 2003

- Duplication of chromosomal segments

  N. El-Mabrouk, J. Comp. Sys. Sci., 2002

- Genome duplication for unordered chromosomes

  N. El-Mabrouk and D. Sankoff 1998

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Genome doubling

1: a b –d ; 2: h c f –g e

1: a b –d ; 2: h c f –g e

1': a b –d ; 2': h c f –g e

Tetraploid = 4n chromosomes

Evidence across the eukaryote spectrum; Two duplications in early vertebrate evolution (*McLysaght et al. 2002)*

Particularly prevalent in plants (rice, oats, corn, wheat, soybeans, Arabidopsis…)

Wolfe, Shields 1997: Traces of duplication in Saccharomyces cerevisiae. 55 duplicated regions representing 50% of the genome

From 8 to 16 chromosomes

I -- +2 -1
II -- +4 -3 -7 +8 -5 +6
III -- +9 -10 -11
IV -- +20 +12 +12 +54 +15 +21 -3 -13 -16 +17 -24 -22 -14 -23 -19 +18 -9
V -- +28 -25 -27 -4 -26 -13
VI -- +55 -36
VII -- +36 +25 +26 +32 +6 -33 +5 -30 -34 -31 -29
VIII -- +35 -14 -37 -20 -1
IX -- +38 +39 +27
X -- +10 +40 +41 -28 -42
XI -- +42 +40 +43 +35 -41 -52 -38
XII -- +53 -53 -31 -55 -16 -18 -17 -45 -30 -15 -44
XIII -- +46 +44 +10 -43 -54 -48 -47 -46
XIV -- +49 +20 +37 +50 +39 -11
XV -- +49 +21 -22 -52 -50 -23 -45 -51 -47 -2
XVI -- +48 +32 +33 +51 +8 +24 -7 -34

Originally, duplicated genome =
2 identical copies of each chromosome

After rearrangements, duplicated segments scattered among the genome

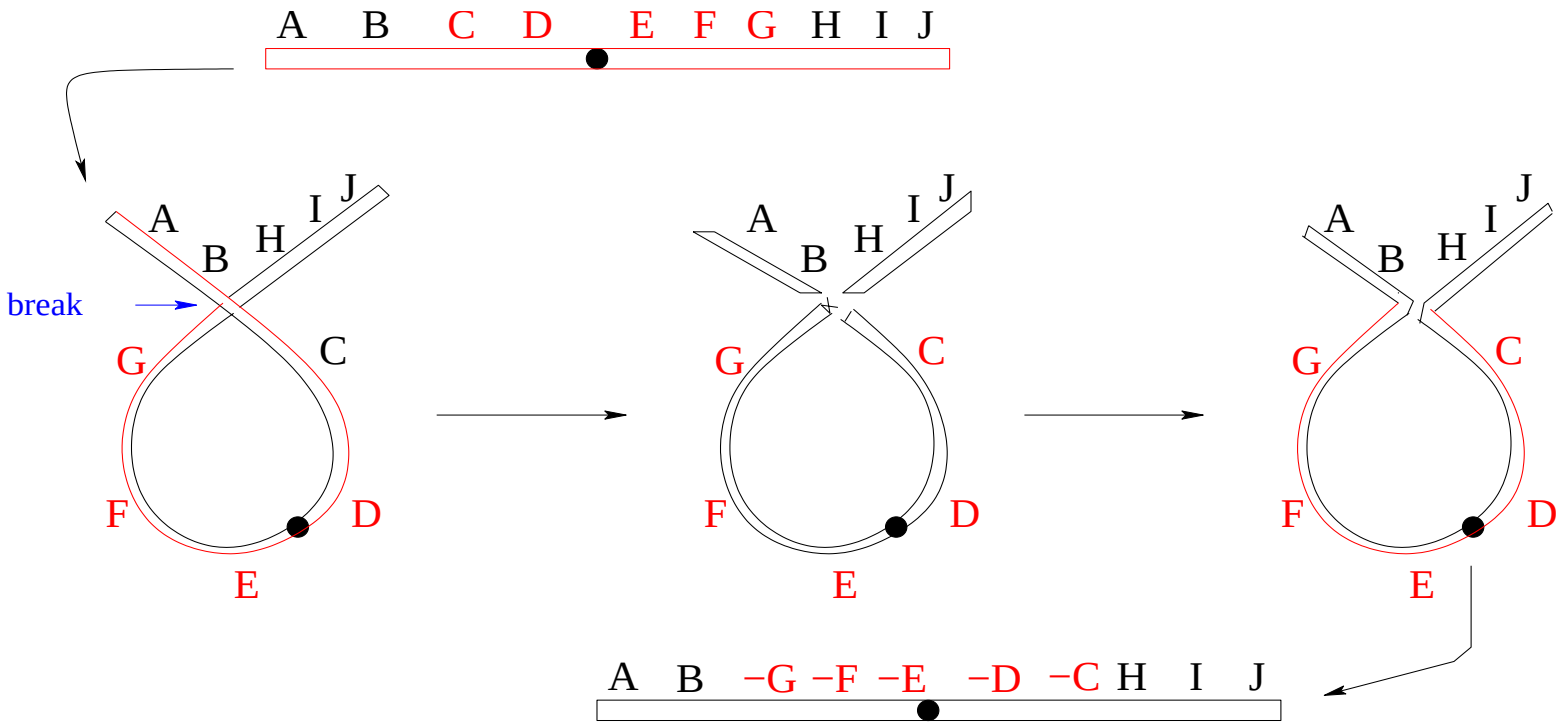
Present–day genome: Signed gene sequences, 2 copies of each gene

Reconstruct original gene order at time of duplication

Minimum number of reversal and/or translocation

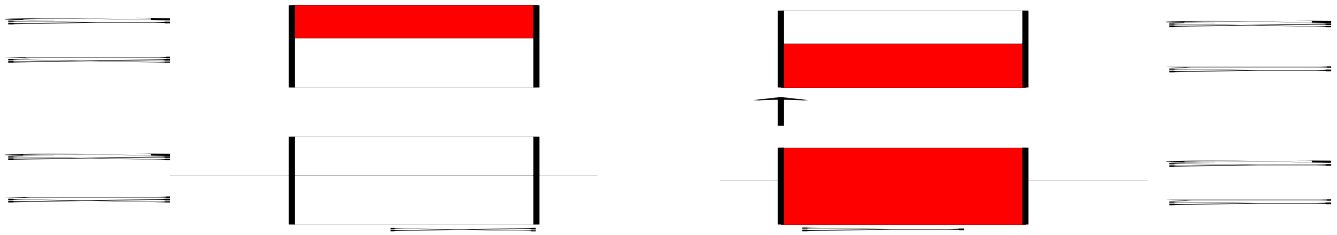

TCS
SSTT634

Inversion


A B C D E F G H I J
break
A B H I J
G C
F D
E
A B H I J
G C
F D
E
A B H I J
G C
F D
E
A B −G −F −E −D −C H I J

Translocation

Reciprocal translocation:



Fusion:

Fission:

Problem:

Rearranged duplicated genome G:

1: +a +b –c +b -d

2: -c -a +f

3: -e +g -f -d

4: +h +e -g +h

Unknown duplicated genome H:

1: +a +b -d

2: +a +b -d

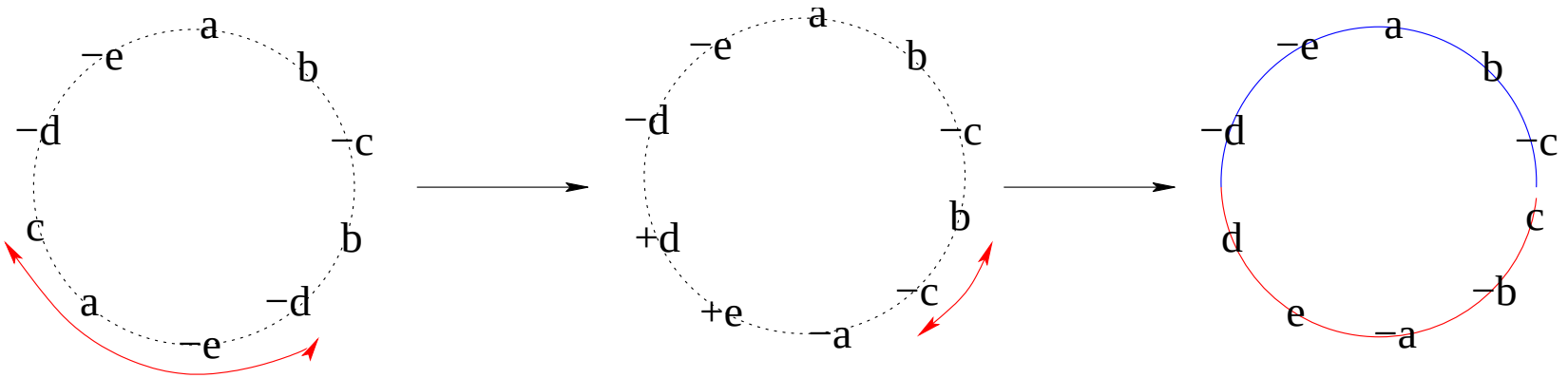
3: +h +c +f -g +e

4: +h +c +f -g +e

Min. num. of inversion and/or translocation transforming G into H

Multi-chromosomal case: H has an even number of chromosomes. Not necessarily the case for G

The circular case



Rearranged genome

Ancestral duplicated genome

Method

Genome rearrangement: Minimum number of rearrangements to transform one genome into another

First polynomial algorithm by ***Hannenhalli and Pevzner*** for

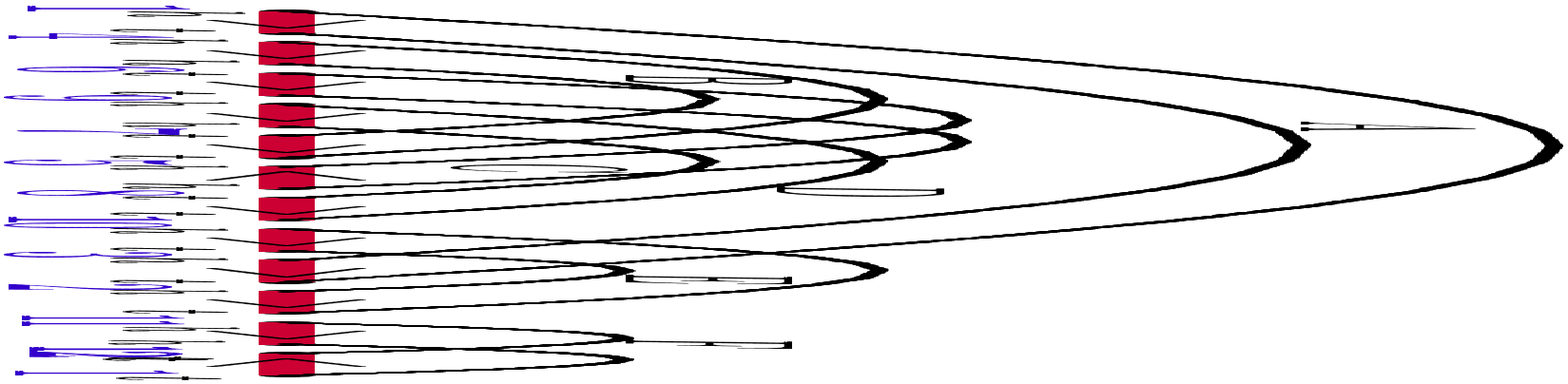
- Reversals only
- Translocations only
- Reversals and translocations

Ancestral duplicated genome of G minimizing the HP formula

The breakpoint graph

G_1 = +1 +4 -6 +9 -7 +5 -8 +10 +3 +2 +11 +12

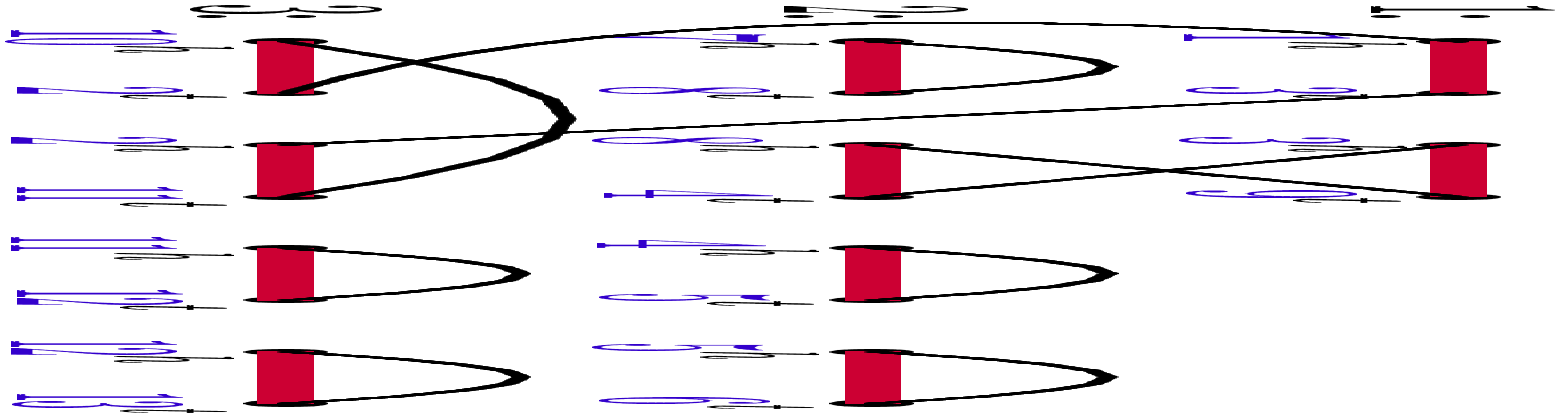
G_2 = +1 +2 +3 +4 +5 +6 +7 +8 +9 +10 +11 +12



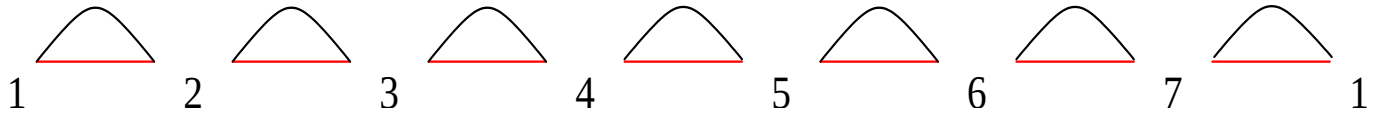
Multichromosomal case

G_1: I: 1 3 9 II: 7 8 4 5 6 III: 10 2 11 12 13

G_2: I: 1 2 3 4 5 6 II: 7 8 9 III: 10 11 12 13



When G_1=G_2 , maximum number of cycles



Perform reversals increasing nb of cycles

Good component: Can be solved by good reversals

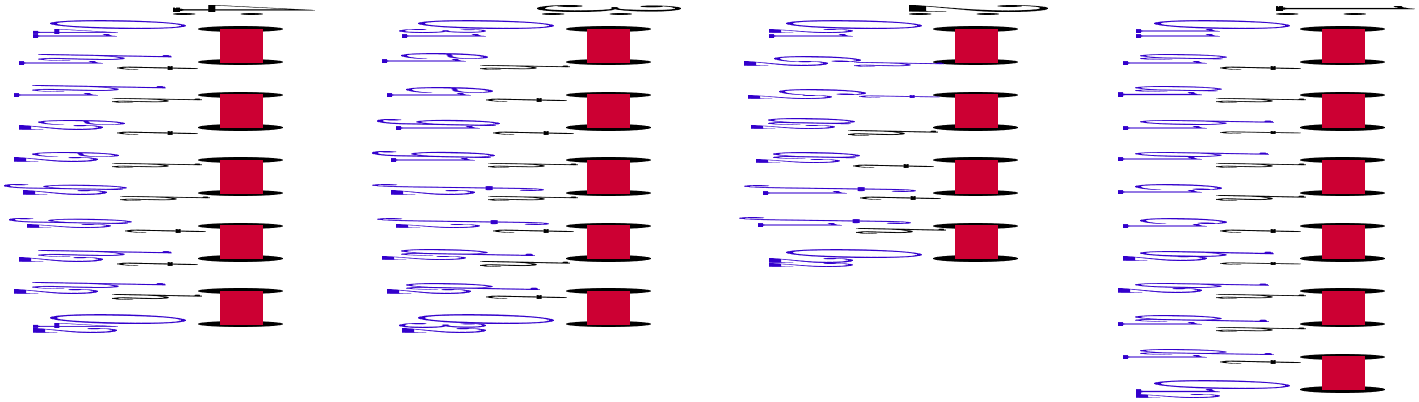
Bad component: Requires bad reversals

HP: $RD(G_1, G_2) = b - c + m + f$

b : red edges; c : cycles; m : bad components; f : Correction of 0, 1 or 2

Genome halving

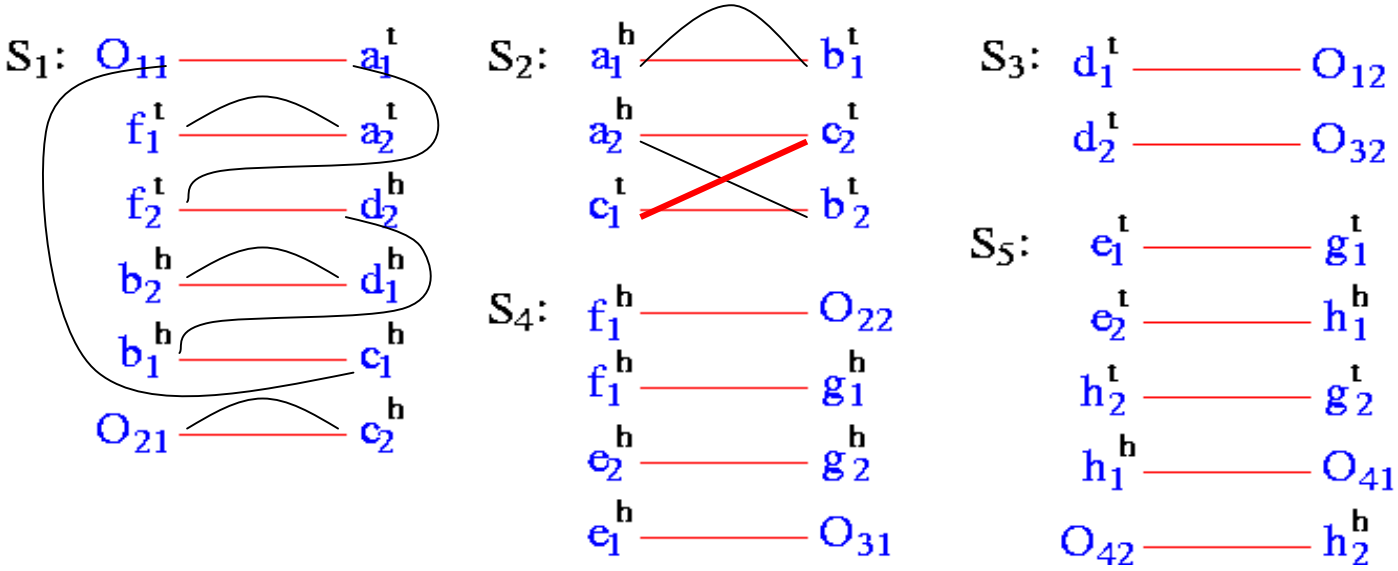
Partial graph for *G:*



Set of valid black edges representing a duplicated genome

Find a set of valid black edges minimizing HP

Decomposition into natural subgraphs



Natural subgraphs of even size are completable

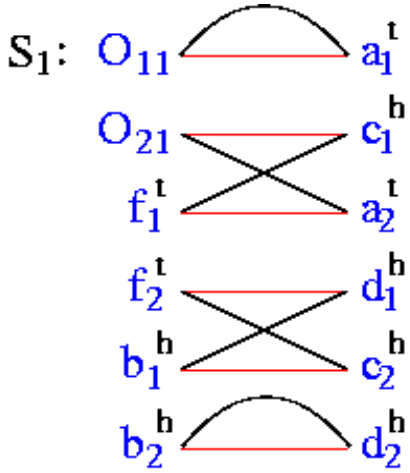
Amalgamate natural graphs into completable supernatural graphs

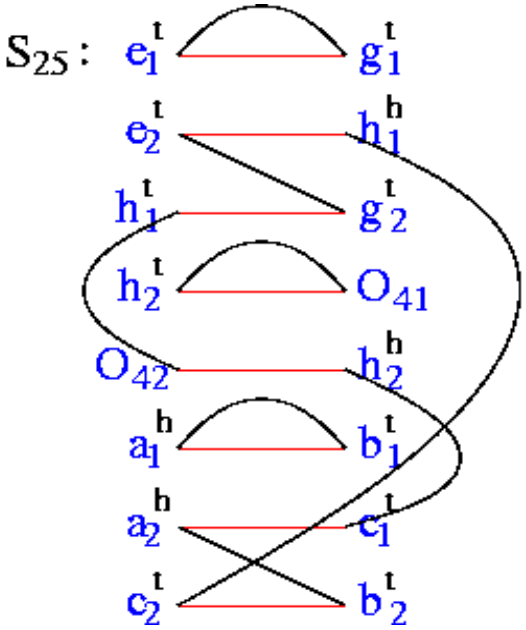
Example: Amalgamate S_2 and S_5 ⟹ S_1, S_{25}, S_3, S_4

Upper bound on the number of cycles

S_e a supernatural graph of n edges, $S_e(\Gamma_e)$ a completed graph with c_e cycles

- If S_e not amalgamated, $c_e \leq n/2 + 1$
- Otherwise, $c_e \leq n/2$

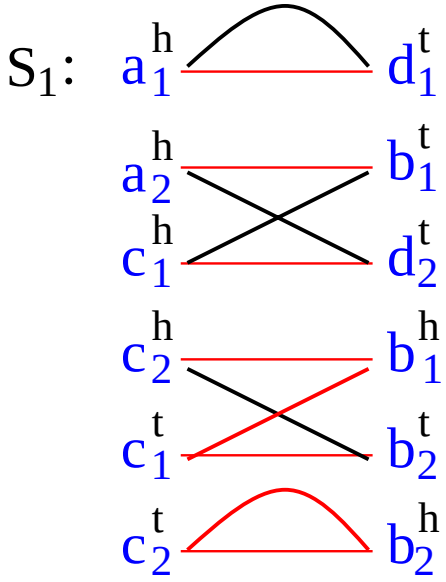


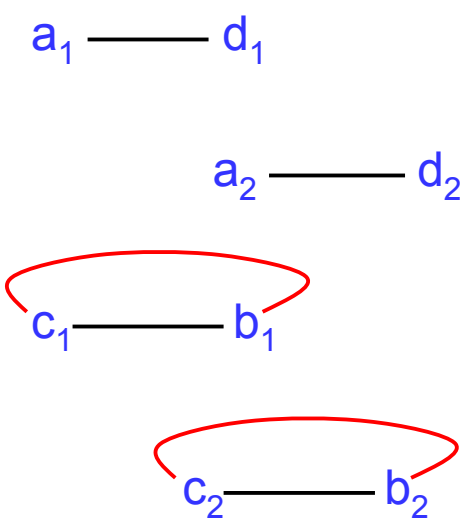


Maximizing cycles – Multichromosomal case

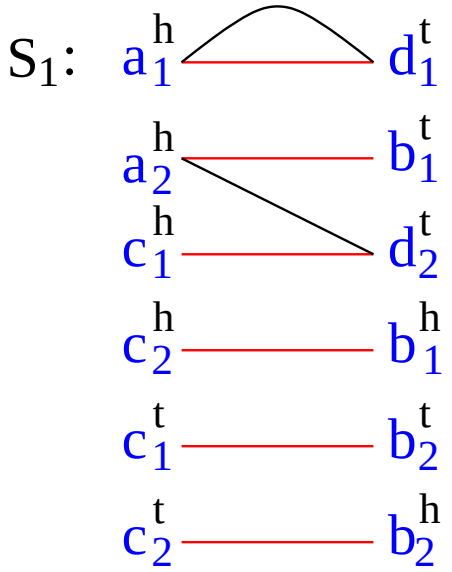
Complete each subgraph separately

Avoid to create circular fragments



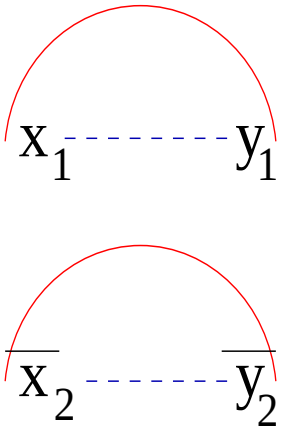


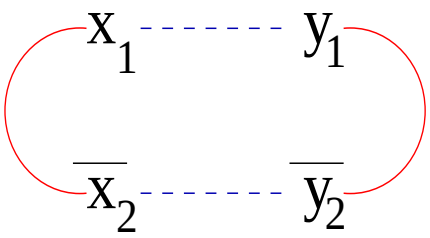
Bad graph:



Maximizing cycles 2

Avoid black edges creating circular fragments:

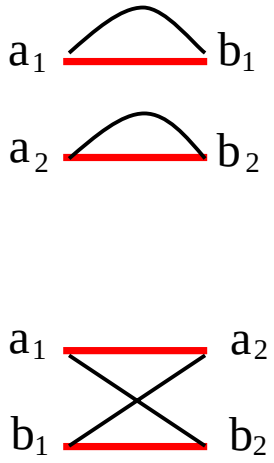




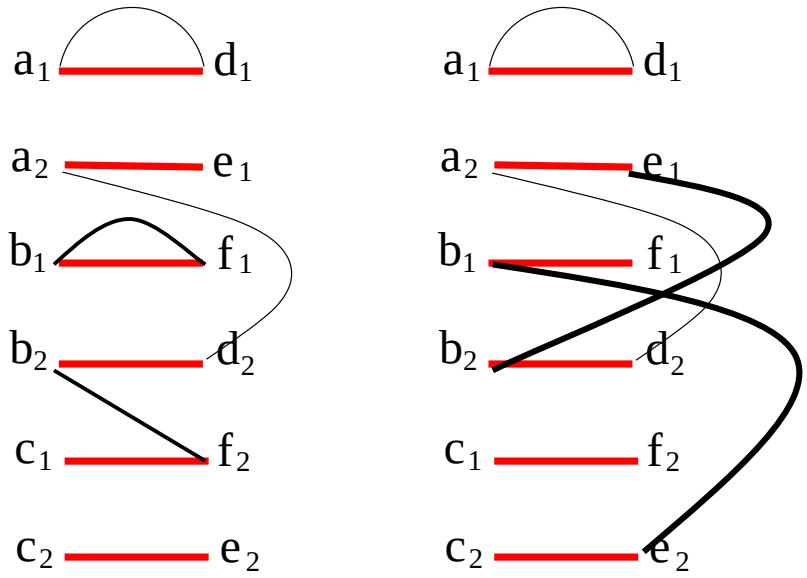
A pair of edges that does not create a circular fragment nor a bad graph is called possible

Algorithm dedouble

2-edges graph:



n-edges graph:



Algorithm dedouble 2

Linear time algorithm constructing a maximal completed graph with c cycles:

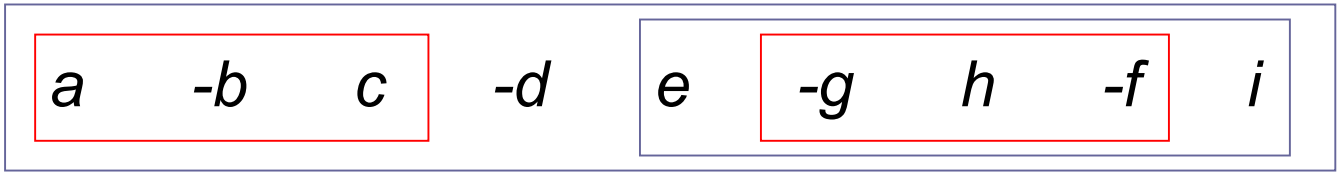
$$c = n/2 + \gamma$$

- n : number of red edges
- γ : number of natural graphs (not amalgamated)

Bad components

Related to subpermutations or conserved intervals

minSP: SP not contained in any SP



- Rearrangement by translocations:

  Bad components = minSPs

- Rearrangement by invertions and/or translocations:

  Bad components subset of minSPs

Bad components 2

Local SPs of *G* :

$$a_1 \quad b_1 \quad c_1 \quad d_1 \quad e_1 \quad -d_2 \quad b_2 \quad c_2 \quad -a_2 \quad e_2$$

Lemma: In a max completed graph, if there is minSP not a local SP, then correction to eliminate the minSP

Corollary: If *G* does not contain local SPs, then duplicated genome H produced by the algorithm is such that:

RO(G,H) minimal

Bad components 3

General case:

$$RO(G) = n/2 - \gamma(G) + m(G) + \phi(G)$$

n : nb of red edges; $\gamma(G)$: nb of natural graphs; $m(G)$: nb of bad local SPs; $\phi(G)$: correction depending on local SPs

Multichromosomal case: Exact algorithm

Circular case: Uncertainty of up to 2 reversals

Application: Yeast genome

Degenerate tetraploid, duplication 10^8 years ago (*Wolfe and Shield, 1997*). 55 duplicated regions

Sorting by translocations: 45 translocations

Sorting by inversions and/or translocations: No local SPs, thus no reversal. Still 45 translocations

A circular genome

Mitochondrial genome of Marchantia polymorpha: many genes in 2 or 3 copies (*Oda et al. 1992*)

Unlikely to be a tetraploid

A map with 25 pairs of genes was extracted from the Genbank entry

Sorting by reversals: minimum of 25 reversals

Similar to a random distribution ⟹ No trace of duplication

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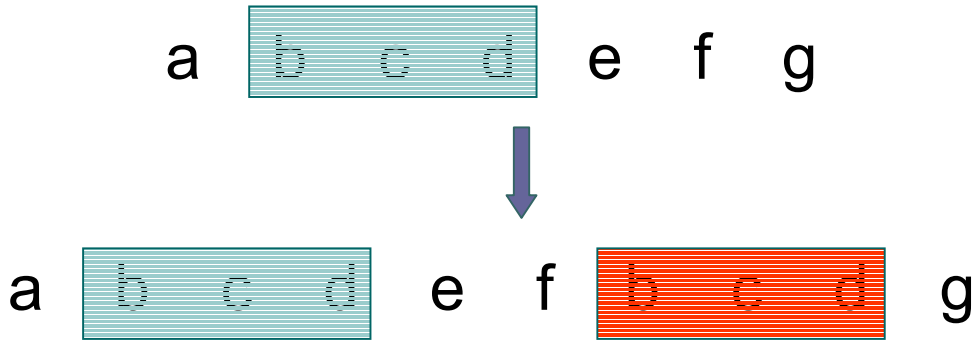
Duplication of chromosomal segments

Duplication of entire regions from one location to another in the genome

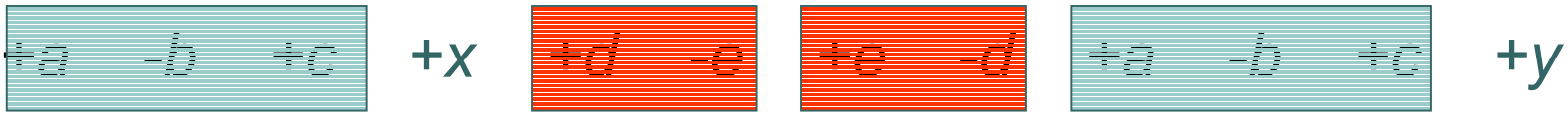


Very recent segment duplication in the human genome (*Eichler et al., 1999*)

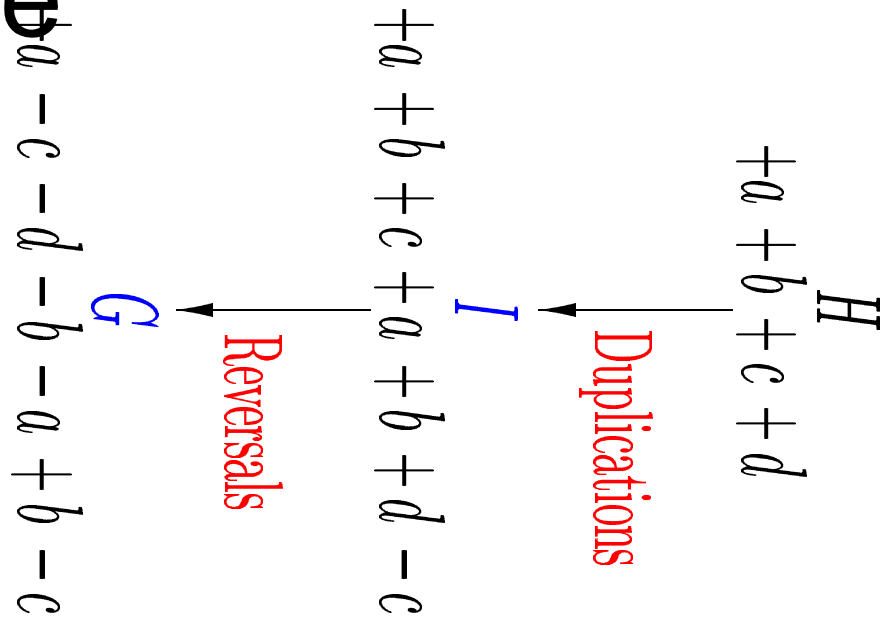
Data: A genome containing many copies of each gene

Problem: An ancestral genome containing one copy of each gene, minimizing reversals + segment duplication

D(G) : Number of repeats of G



At most two copies of each gene



A reversal can decrease by at most two number of repeats of G

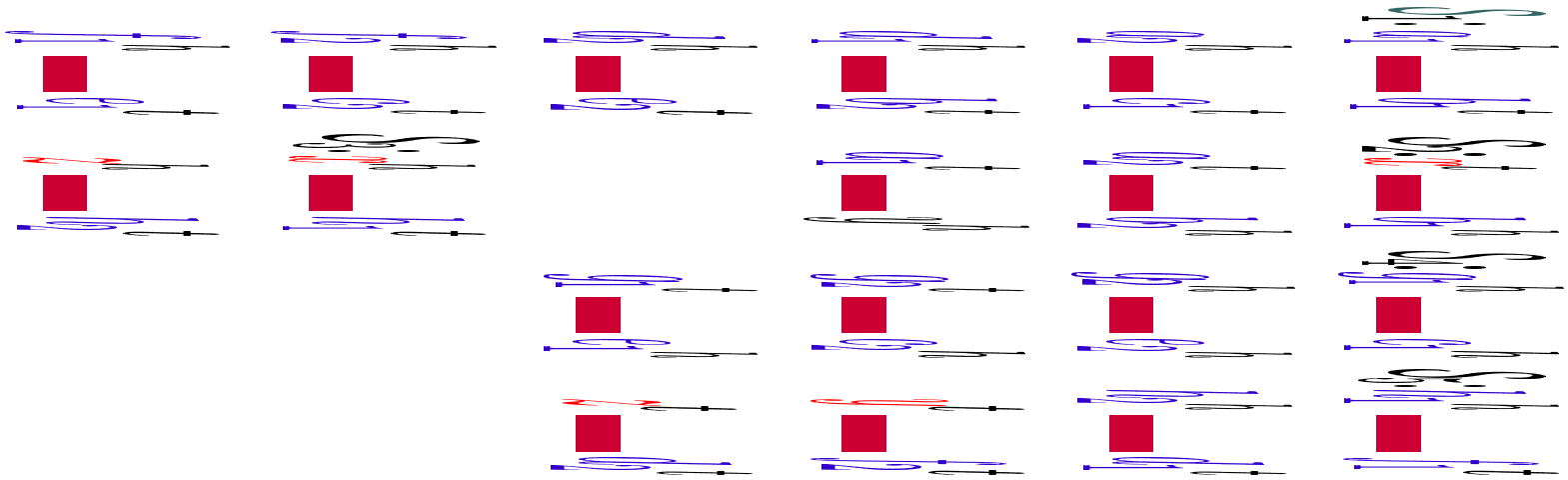
Find I minimizing $RD(G,I) = D(I) + R(G,I)$

Ignoring bad components ⟶ minimize $\Delta(G) = D(I) + n(G) - c(G,I)$

Genome:

$a_1\ b_1\ x\ h_1\ f_1\ e_1\ g_1\ -c_1\ -a_2\ -b_2\ -z\ d_2\ e_2\ -g_2\ -c_2\ -f_2\ y$

Natural graphs:

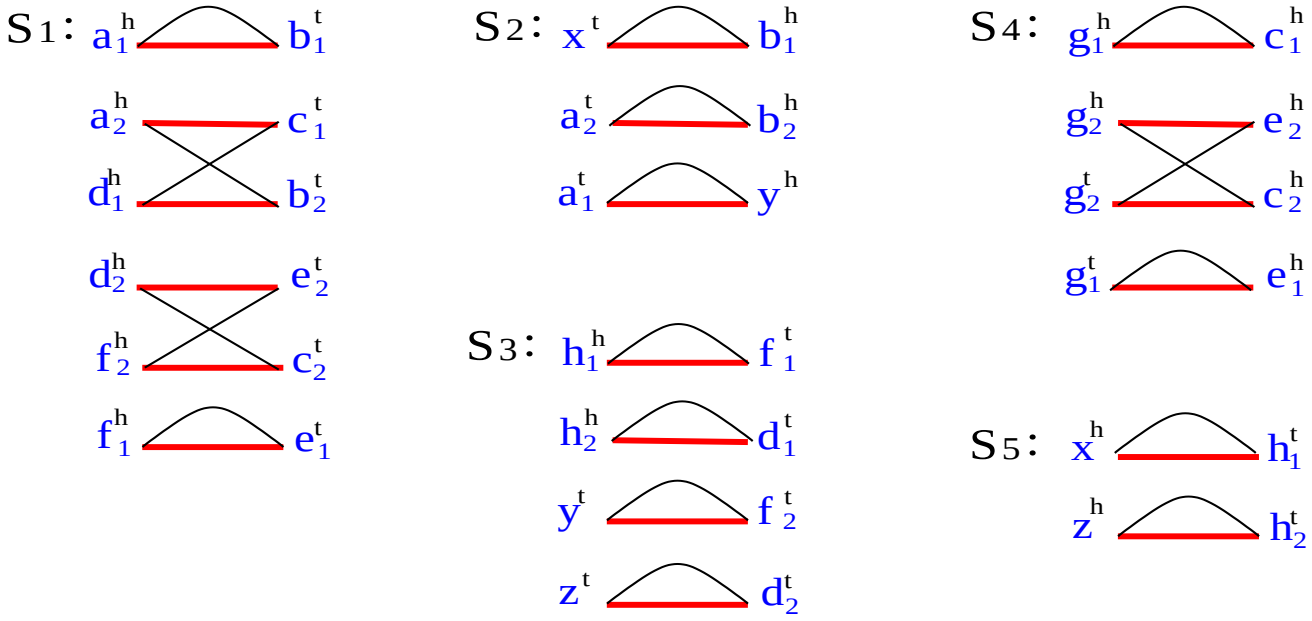


E: Graphs of even size with only duplicated genes

$$\Delta(G) \geq D(G) - |E|$$

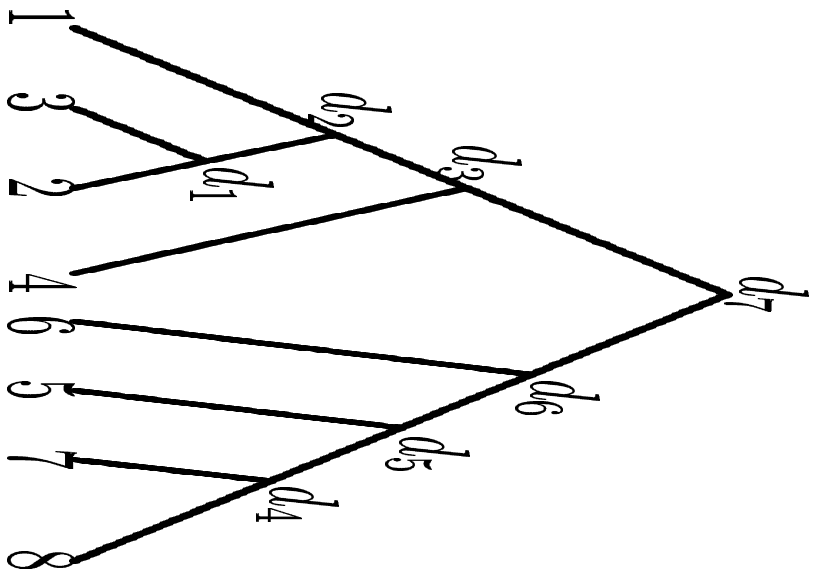
Algorithm

- For graphs not in E, red edges = black edges;
- For graphs in E, similar to genome duplication



BUT: Possibly more than one circular fragment. A correction is required

Approximation algorithm with tight bounds in $O(|E|\, n)$



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

Paralog pairings

1, {2, 3}, 4, 5, 6, {7, 8}

Remove one copy of each duplicate

1, 2, 4, 5, 6, 7

Paralog pairings

{1, 2}, 4, 6, {5, 7}

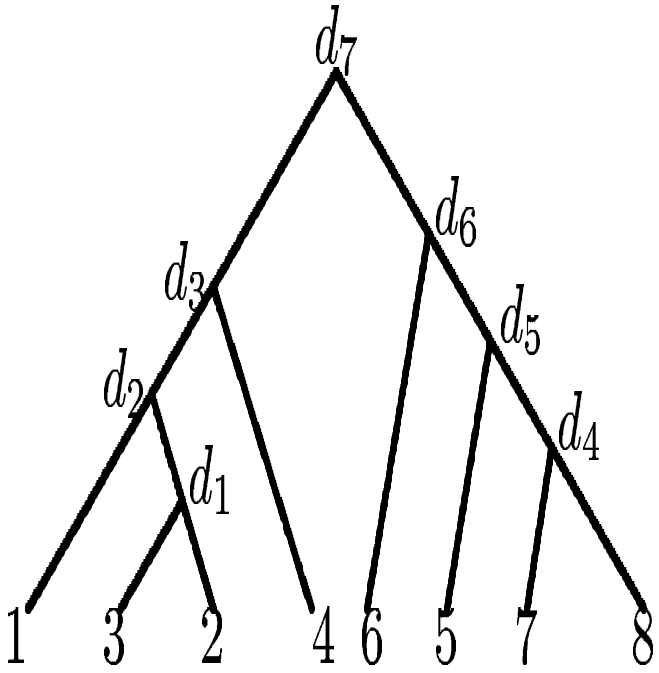
Remove one copy of each duplicate

1, 4, 6, 5

{1, 4}, {6, 5}

1, 6

1



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

paralogs pairings

1,{2,3},4,5,6,{7,8}

remove one copy of each d

1,2,4,5,6,7

paralogs pairings

{1,2},4,6,{5,7}

remove one copy of each d

1,4,6,5

{1,4},{6,5}

1,5

1

Conclusion

- First bioinformatics tools to reconstruct the evolutionary history of a single genome
- Genome duplication: A linear-time exact algorithm for reversals and/or translocations
- Segment duplication: A polynomial approximation algorithm with bounds for reversals
- Extension: Consider the centromere. Some translocations not allowed