The MAX-CMO problem

and its dual representation

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Outline

Contact map

A bit of molecular biology

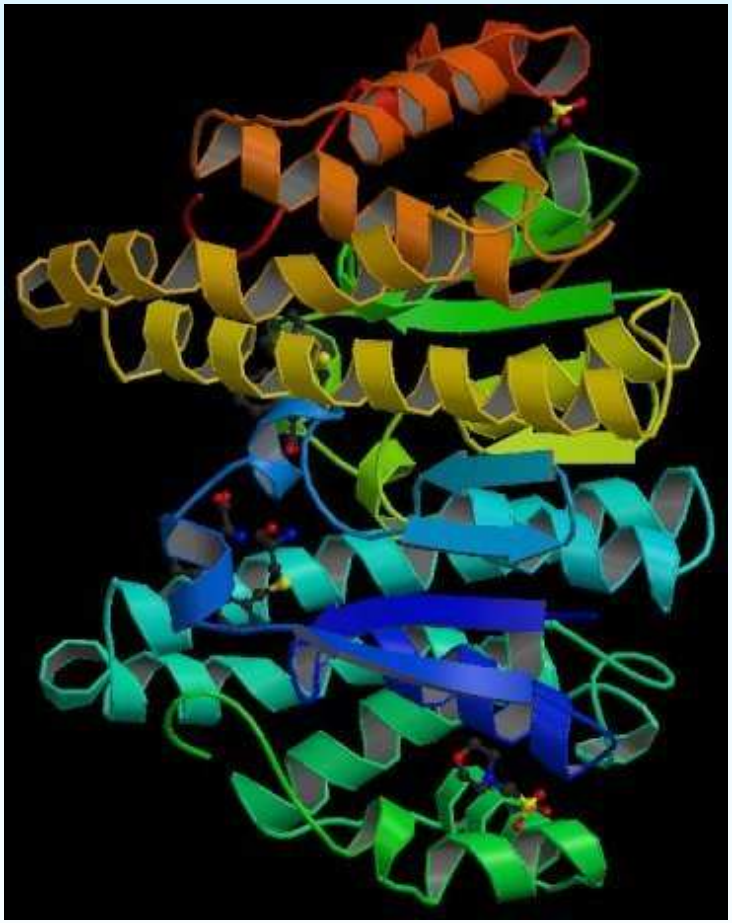

Figure: 10GS (GLUTATHIONE S-TRANSFERASE P1-1)

Protein

- linear arrangement of amino acids (polymer chain)
- amino acid residues linked with peptide bond

Contact map

Mathematical construct capturing the **proximity relation** between residues.

Contact map

A bit of molecular biology

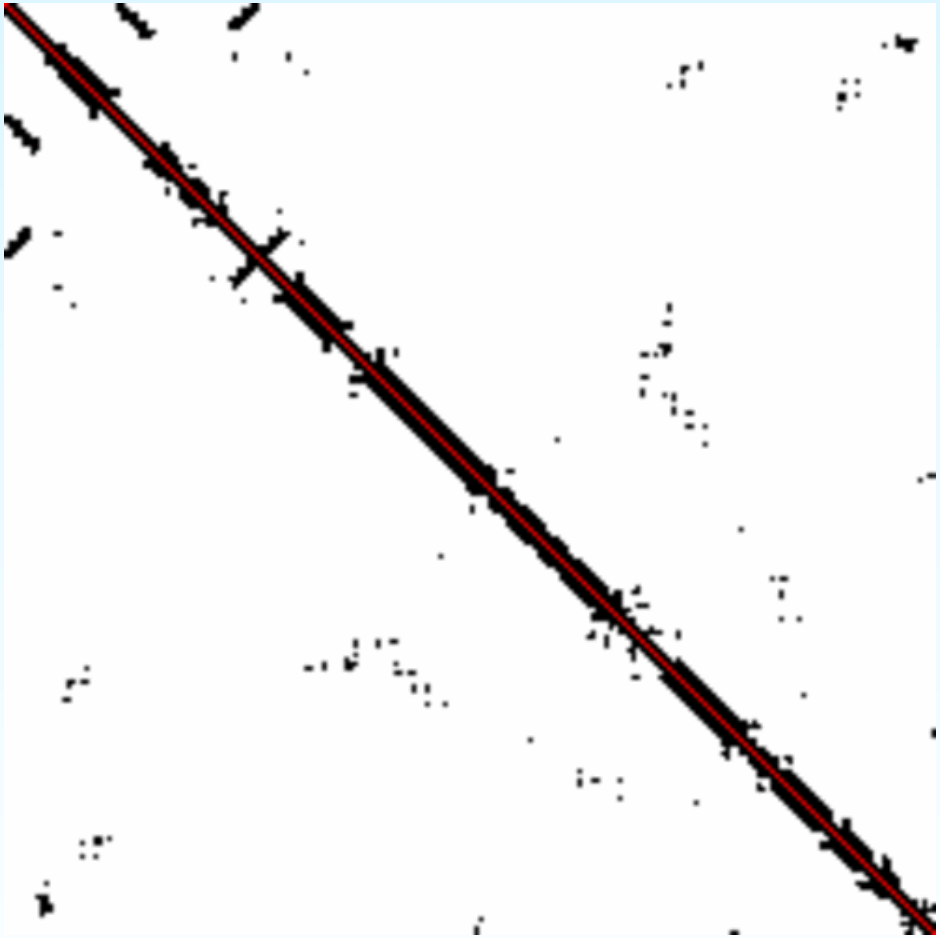

Figure: CM for 10GS:A (210), $\alpha = 0.5\mathring{A}$

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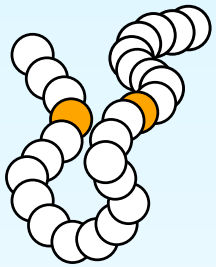
Proximity relation depicted as graph

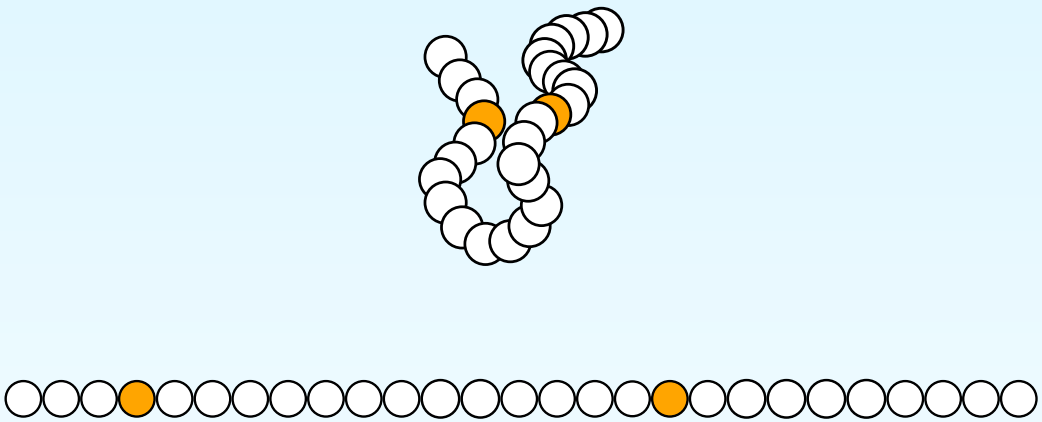


Contact map graph

- $r_i \mathbf{R} r_j \Leftrightarrow \delta(r_i, r_j) \leqslant \alpha$, $\alpha \in [2\text{Å}, 9\text{Å}]$
- node $\leftrightarrows$ residue
- edge $\leftrightarrows$ contact

Contact map

Proximity relation depicted as graph



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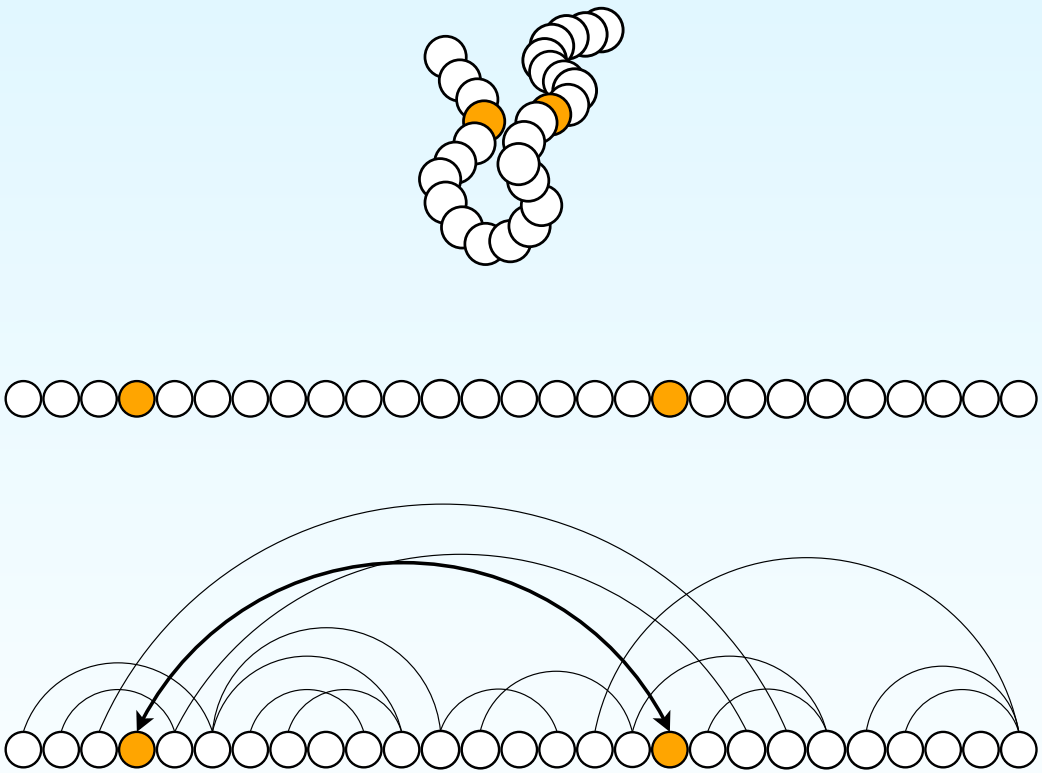

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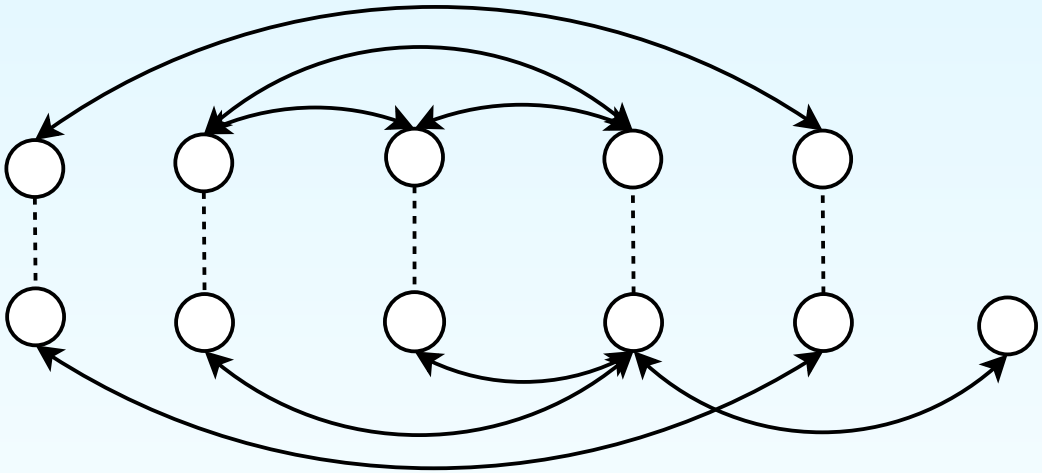
MAX-CMO problem

Definition and biological background



Definition

Maximum contact map overlap is an **alignment** of two proteins that **maximises** the structural **similarity**.

Biological application

- proteins structure comparison
- proteins classification

MAX-CMO problem

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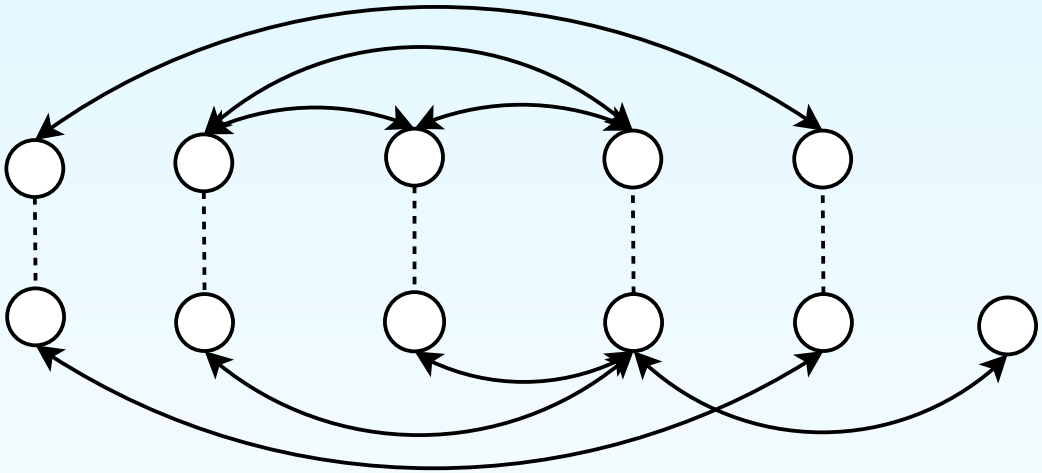

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Graph isomorphism

A bit of graph theory

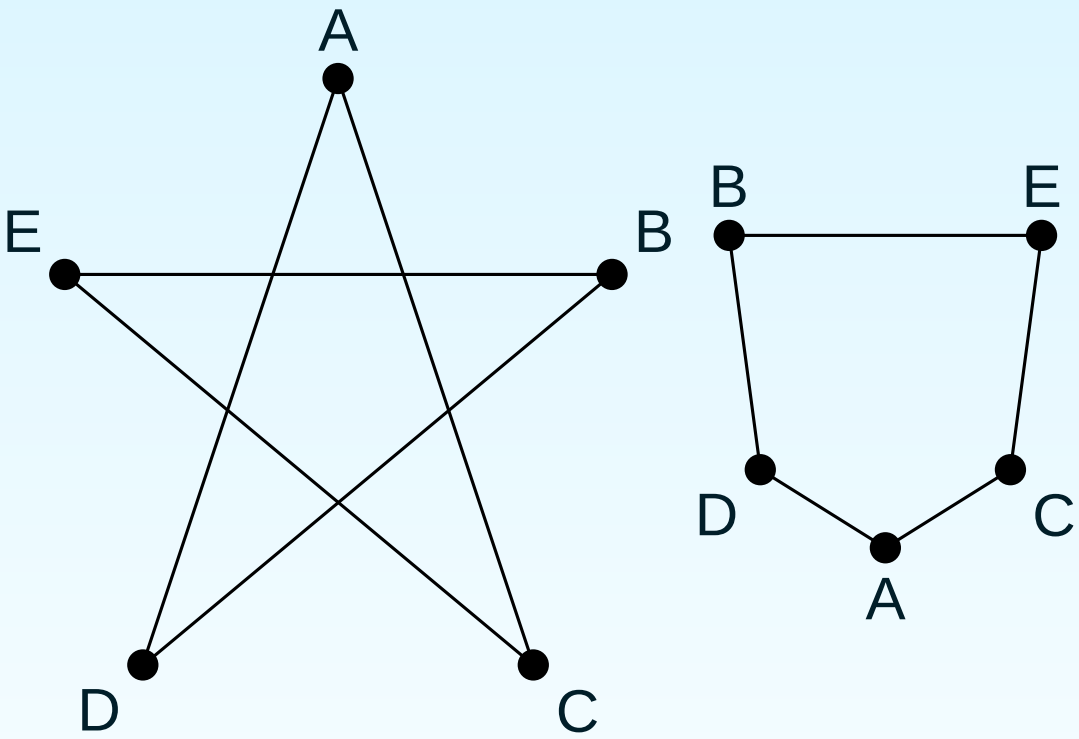

Figure: Isomorphic or not?

Graph isomorphism

Two graphs are isomorphic if there is a one-to-one correspondence between their vertices and there is an edge between two vertices of one graph if and only if there is an edge between the two corresponding vertices in the other graph.

Subgraph isomorphism

Is G1 isomorphic to a subgraph of G2?

Graph isomorphism

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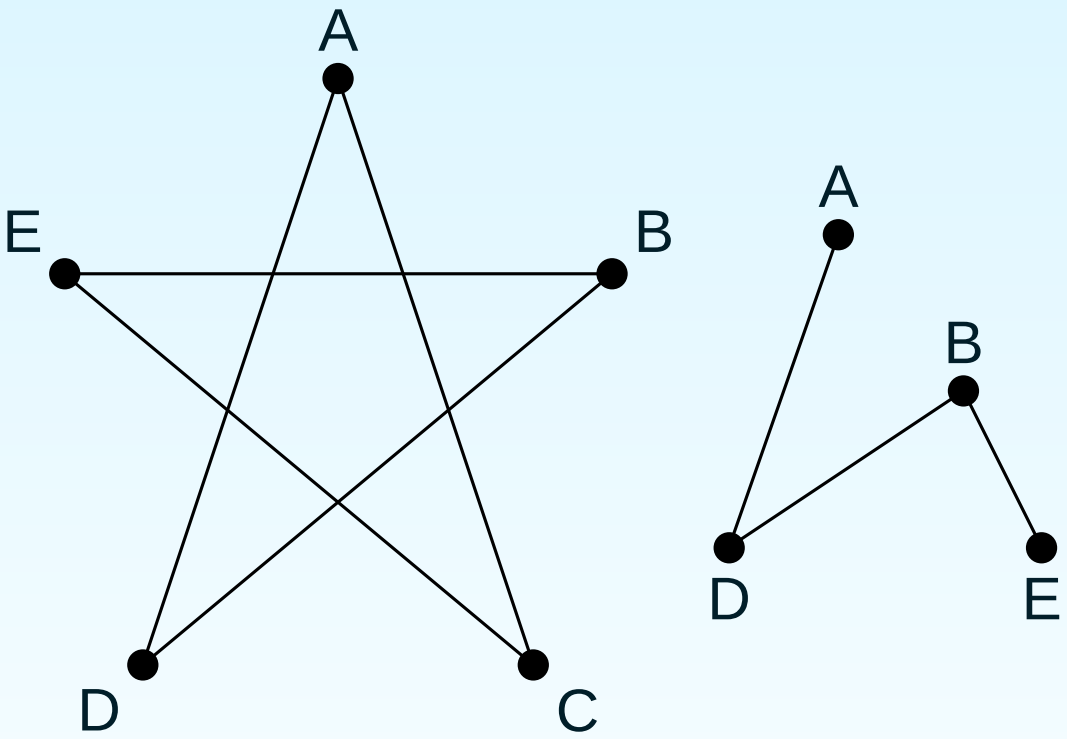

Figure: What about a subgraph?

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Subgraph isomorphism

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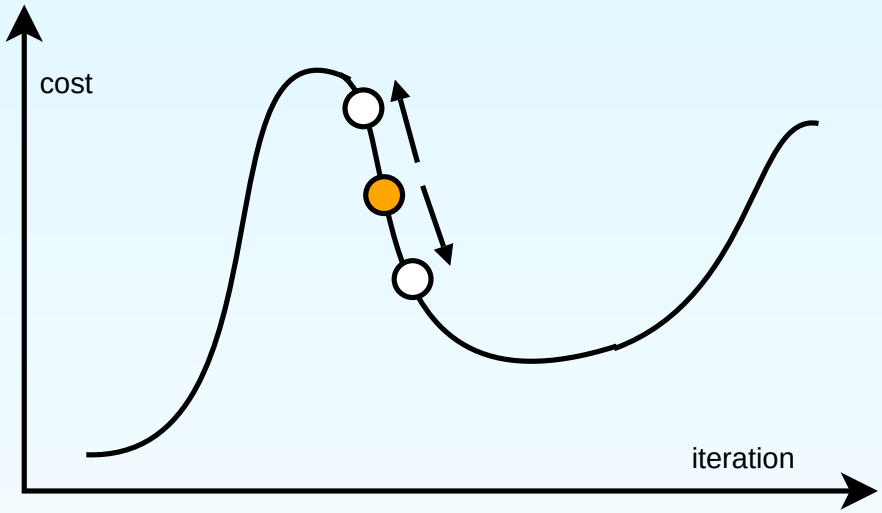
Search strategy

Beyond random walk



Metaheuristic framework

- iterative improvement
- uphill movements acceptance
- based on **neighbourhood** search
- solution **attributes** and **moves**
- global search guidance

Representation issues

Definition of a move

1 2 3 4 5 6 7

1 2 6 4 5 3 7

$\{ 1, 2, 3, 4, 5 \} \rightarrow \{ 1, 2, 3 \}$

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$\{ 1, 2, 3, 4, 5 \} \rightarrow \{ 1, 2, 4 \}$

Move as a transition

- permutation
- n-opt

Move as a building block

- construction vs. destruction
- oscillation strategy

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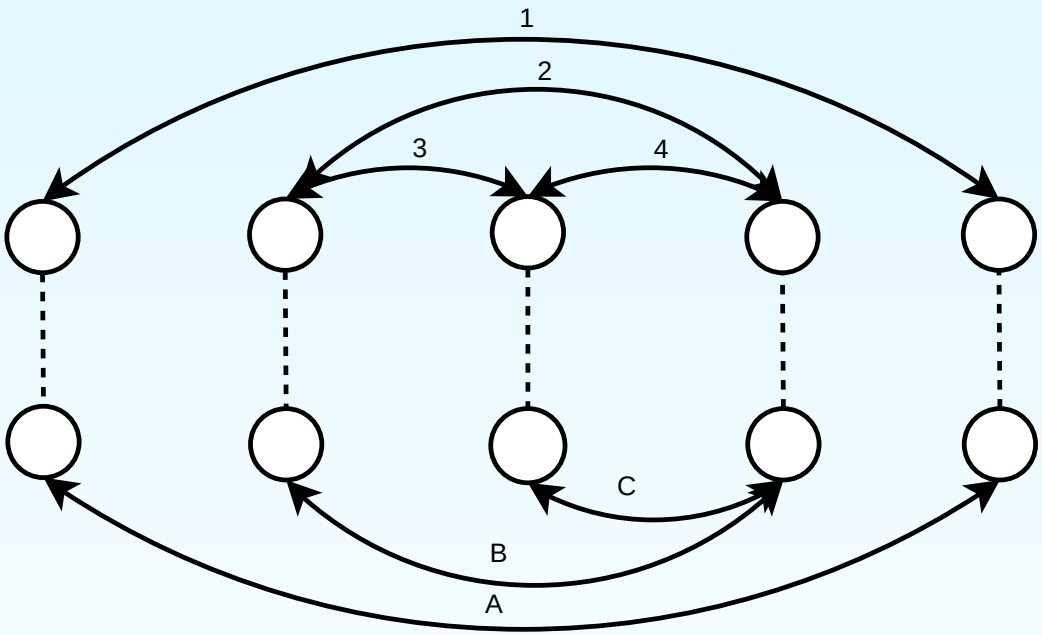
Classical approach

Domain of a problem

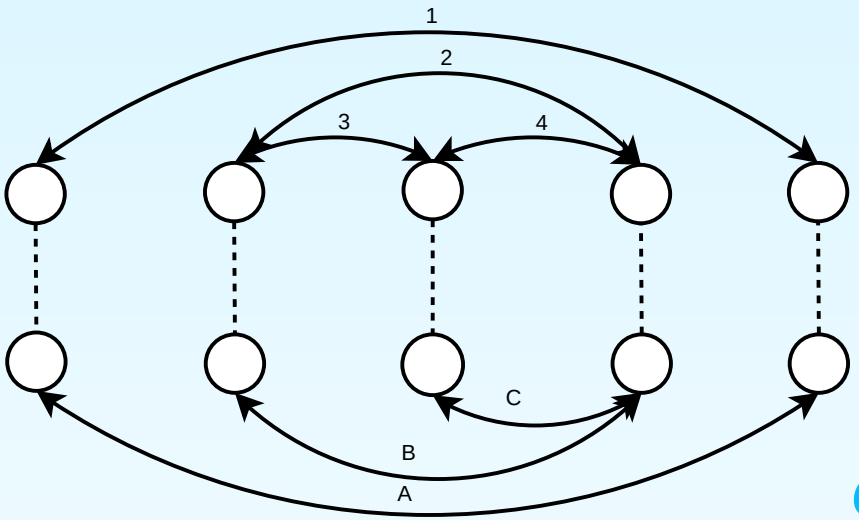


Representation

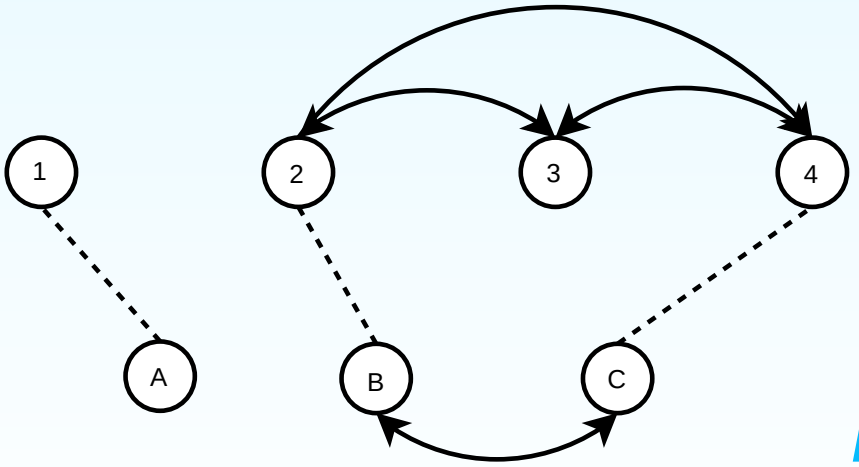
- protein alignment
- nodes matching

Line graph approach

Domain of a solution



G



$L(G)$

Line graph

- a node of L(G) represents an edge of G
- two nodes of L(G) are adjacent if edges in G share common node

Representation

- graph isomorphism
- edges matching

Line graph approach

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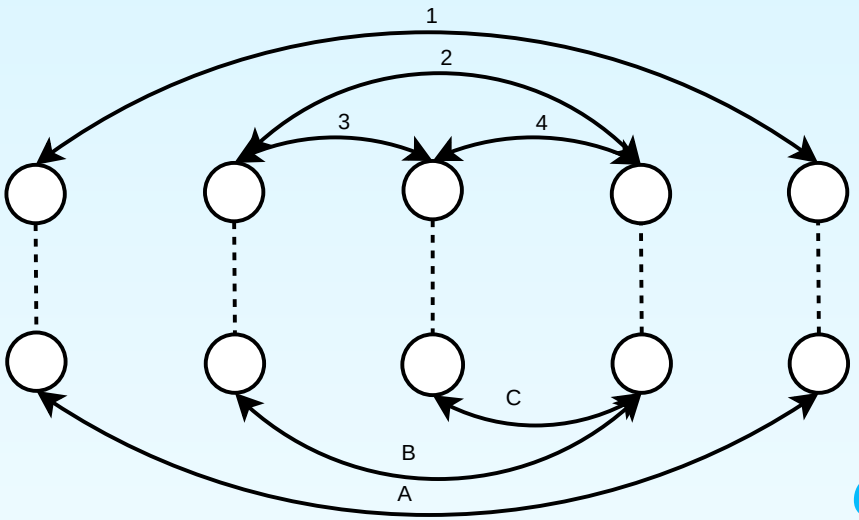

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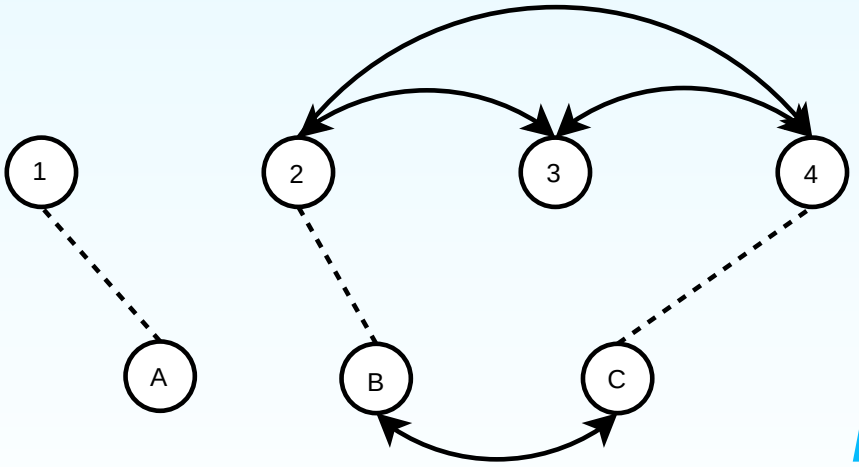

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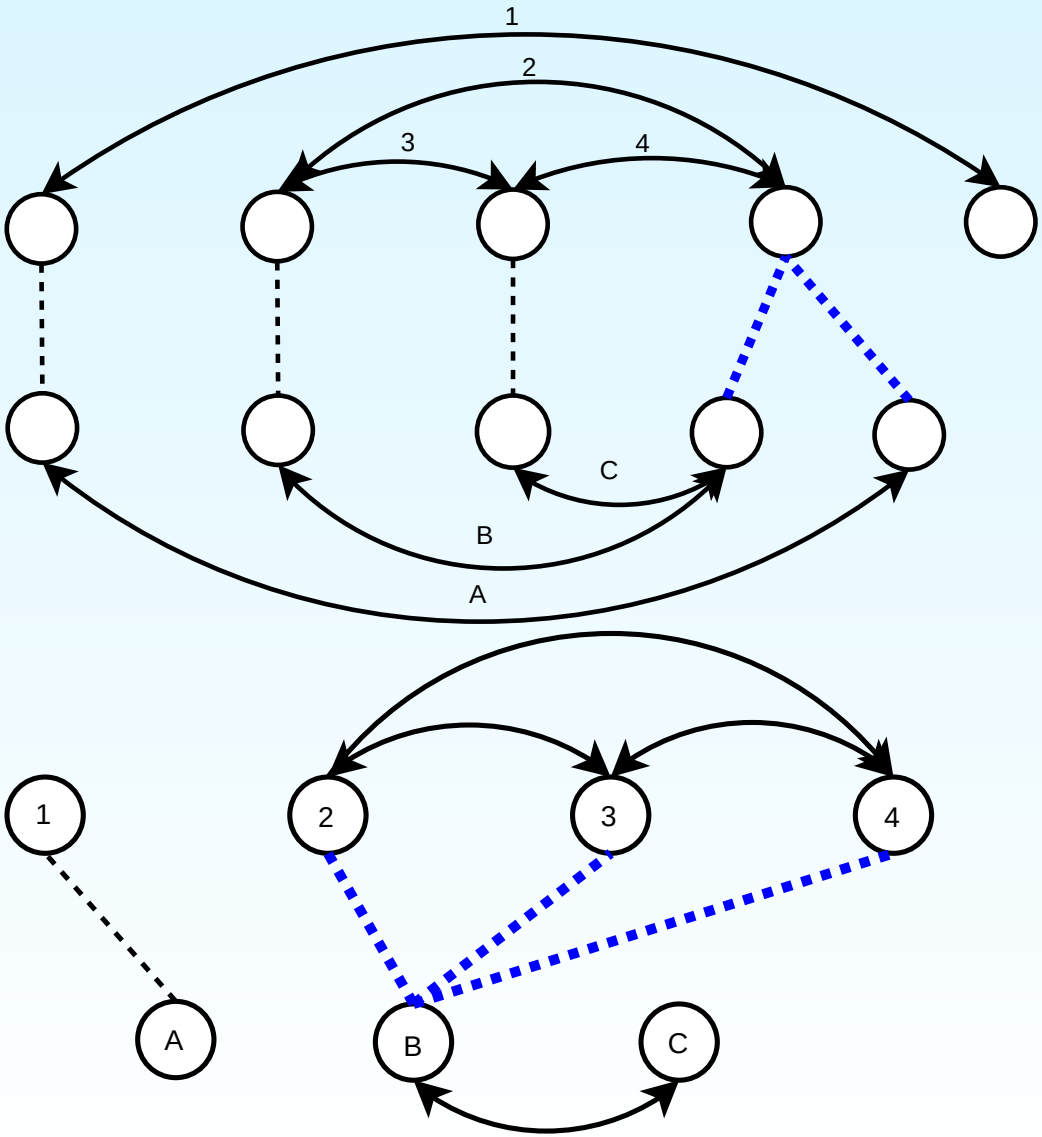
Representation comparison

Construction of a neighbourhood

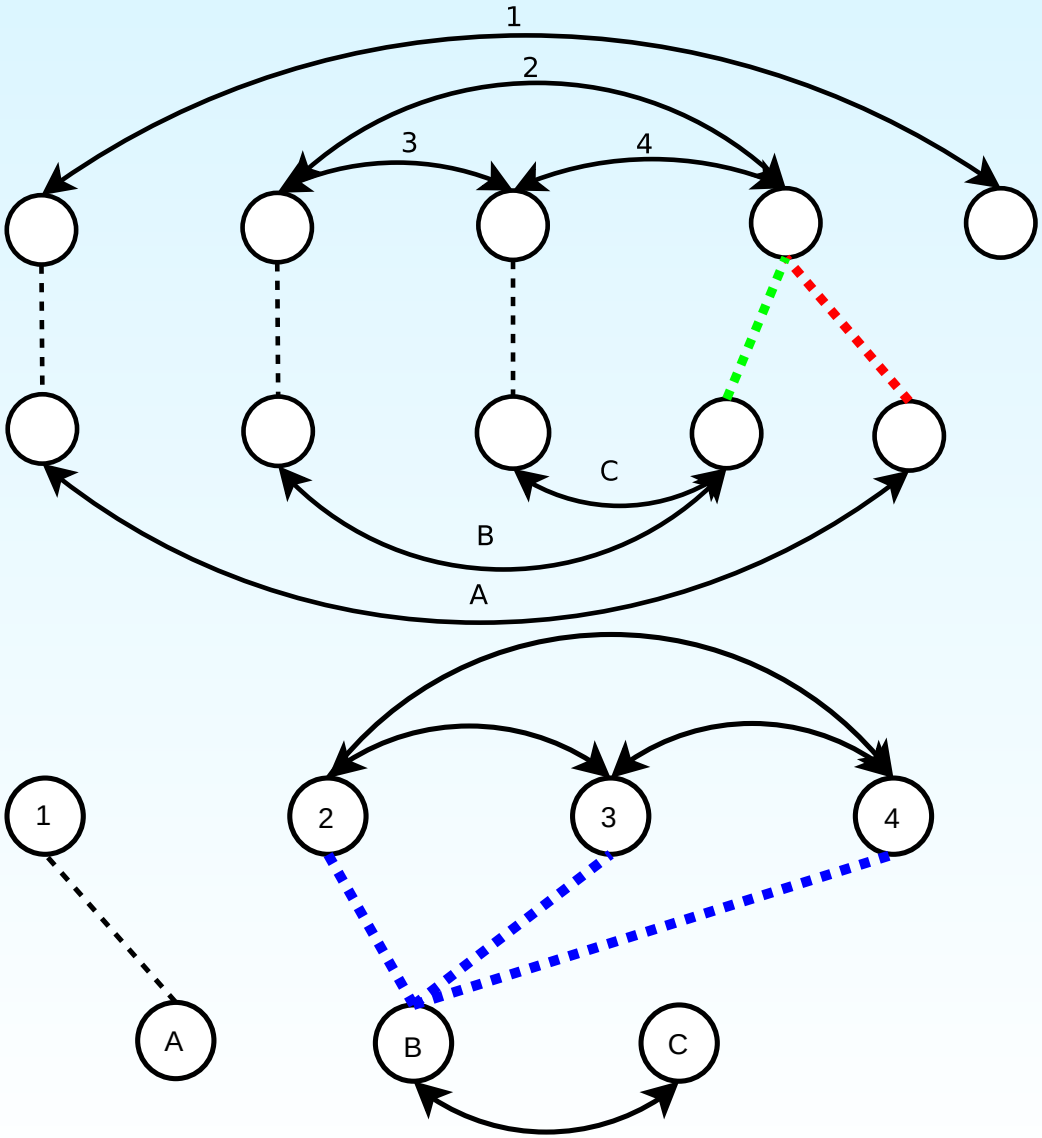


Complexity

- single - $O(1)$
- whole set - $O(n^2)$

Representation comparison

Solution evaluation

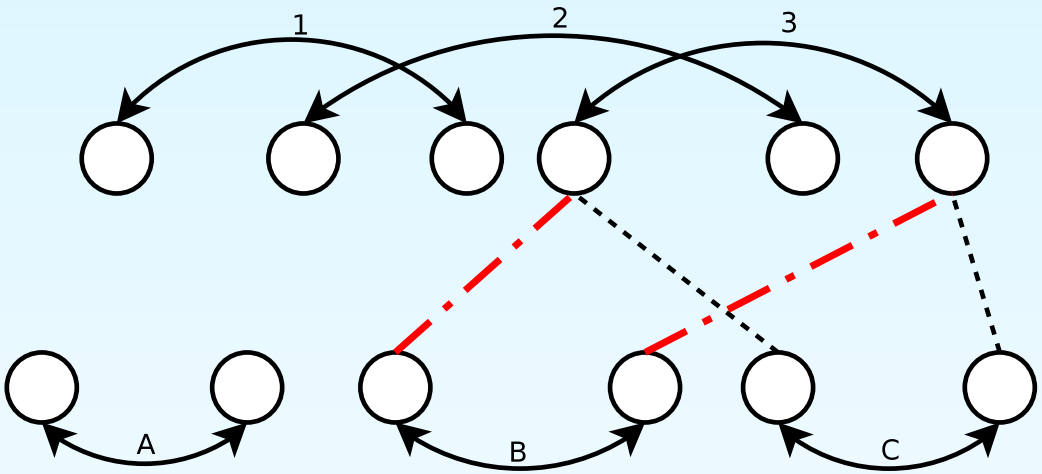


Complexity

- classic
  - $O(n * d(V))$ – full
  - $O(d(V))$ – only new
- dual
  - $O(n)$ – full
  - $O(1)$ – only new

Representation comparison

Solution feasibility



Complexity

- classic - $O(n)$
- dual - ?

Representation comparison

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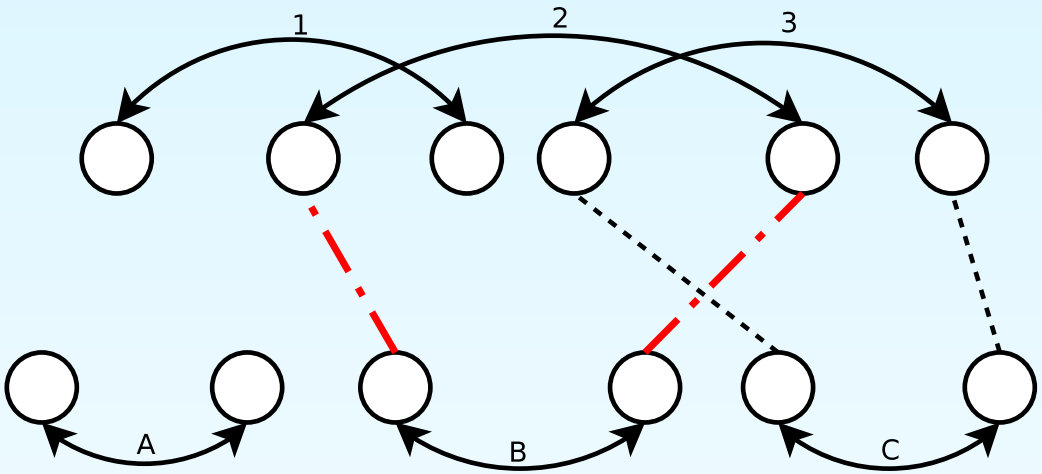

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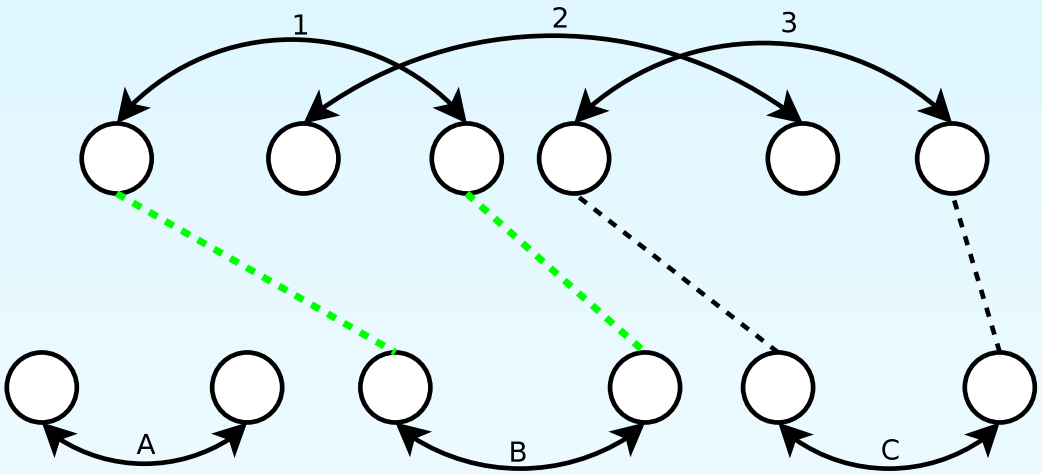

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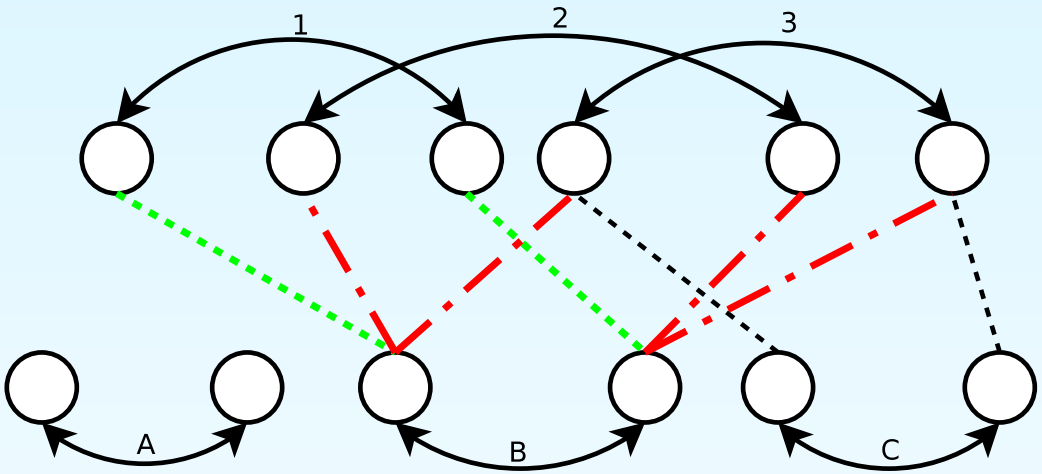

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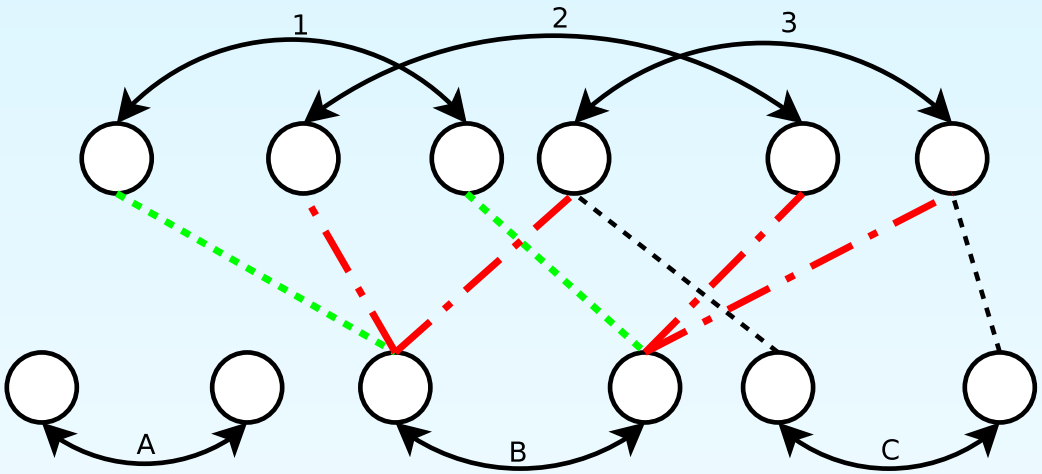

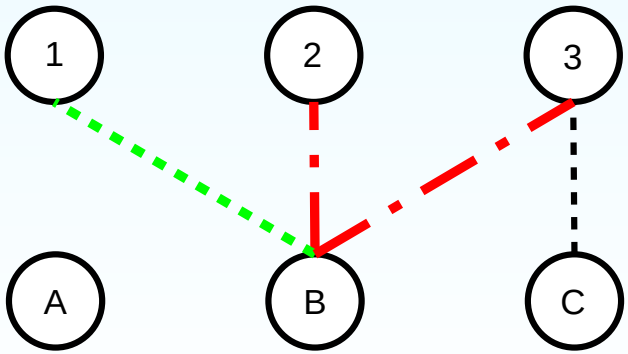

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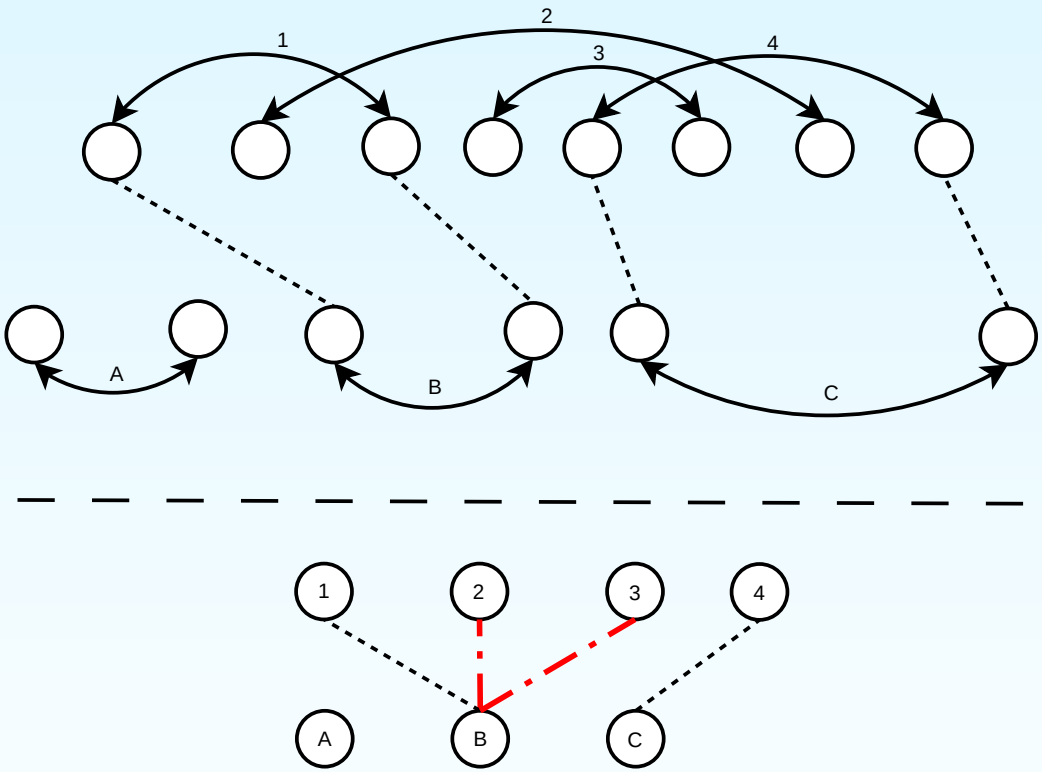
Feasibility issues

Interesting features of a line graph



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- crossmatching
- superedge boundary
- match consistency

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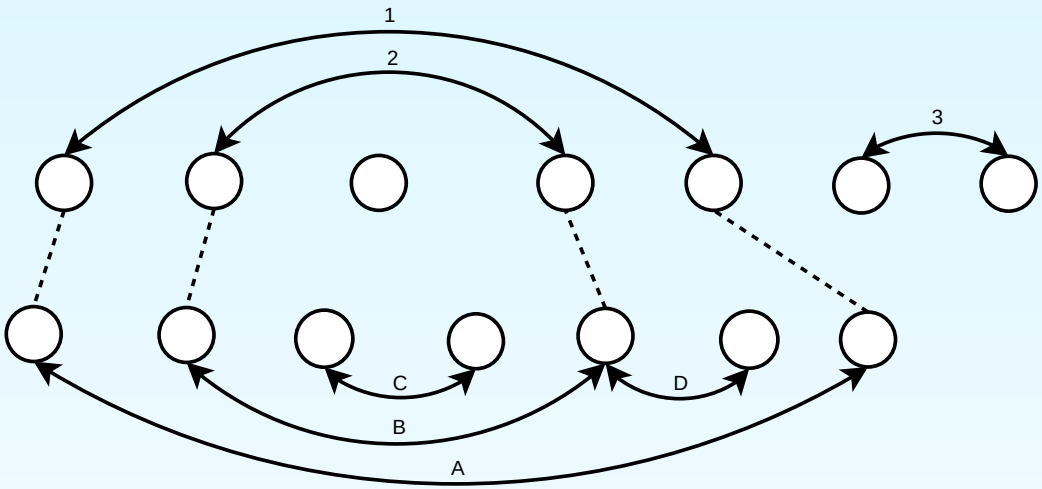

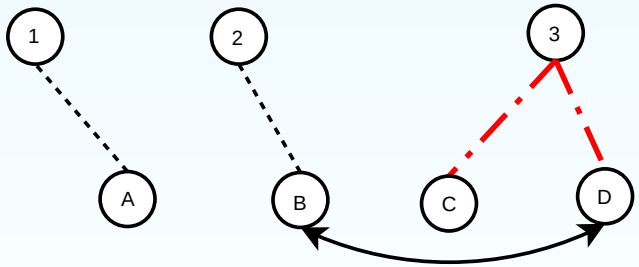

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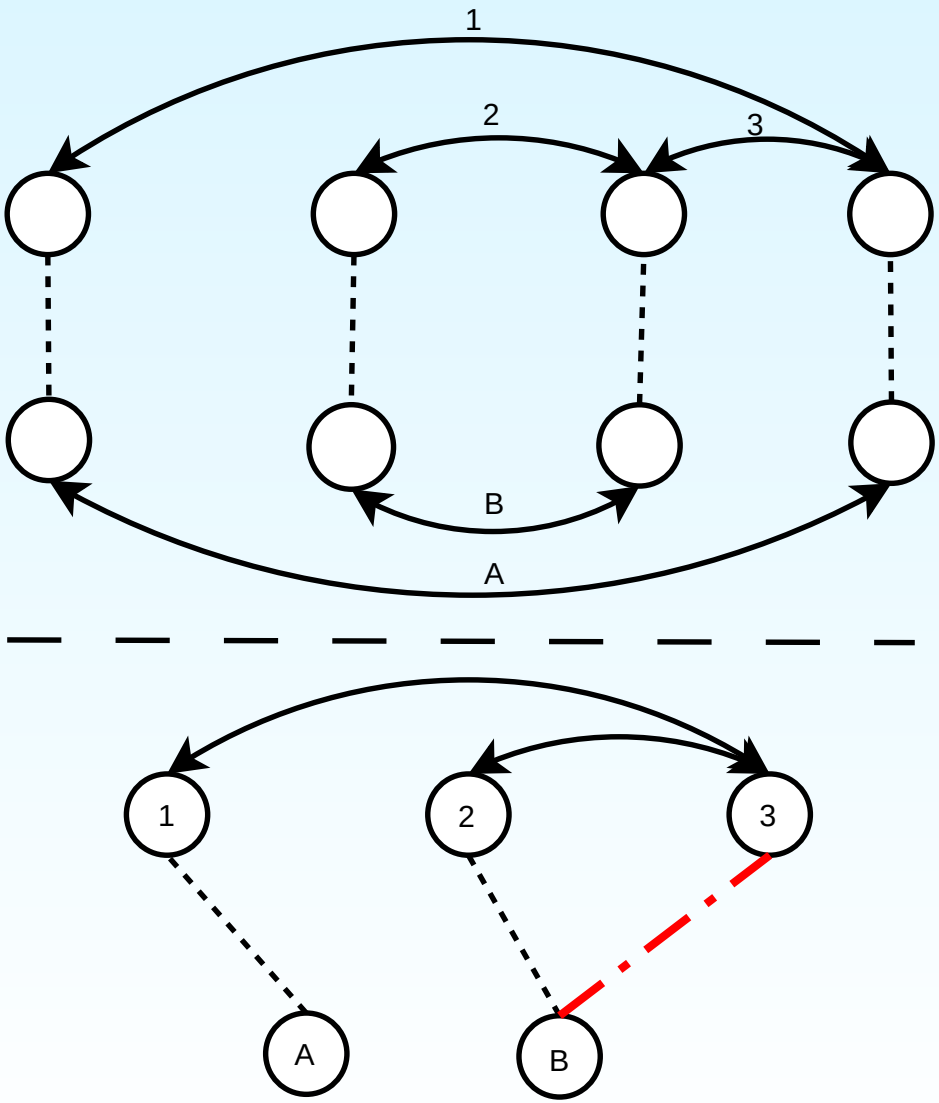

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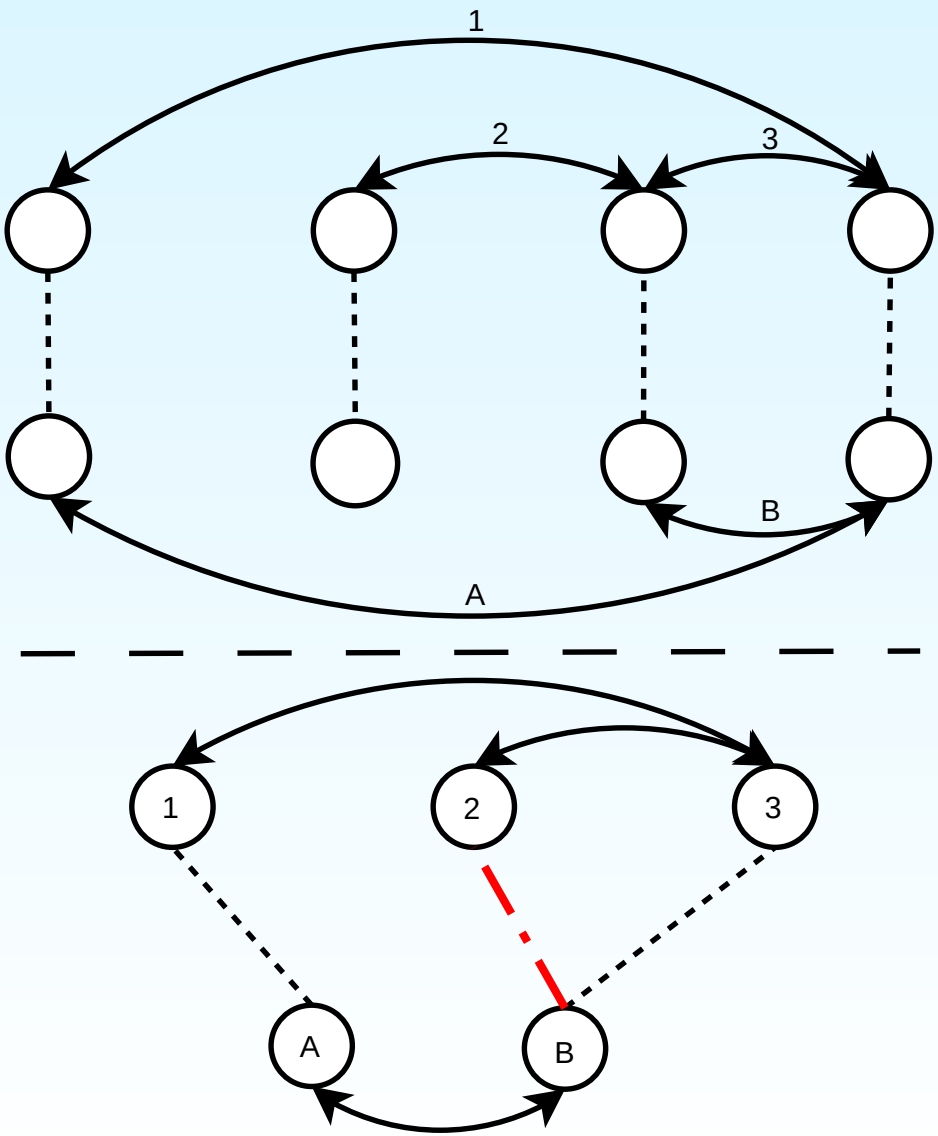

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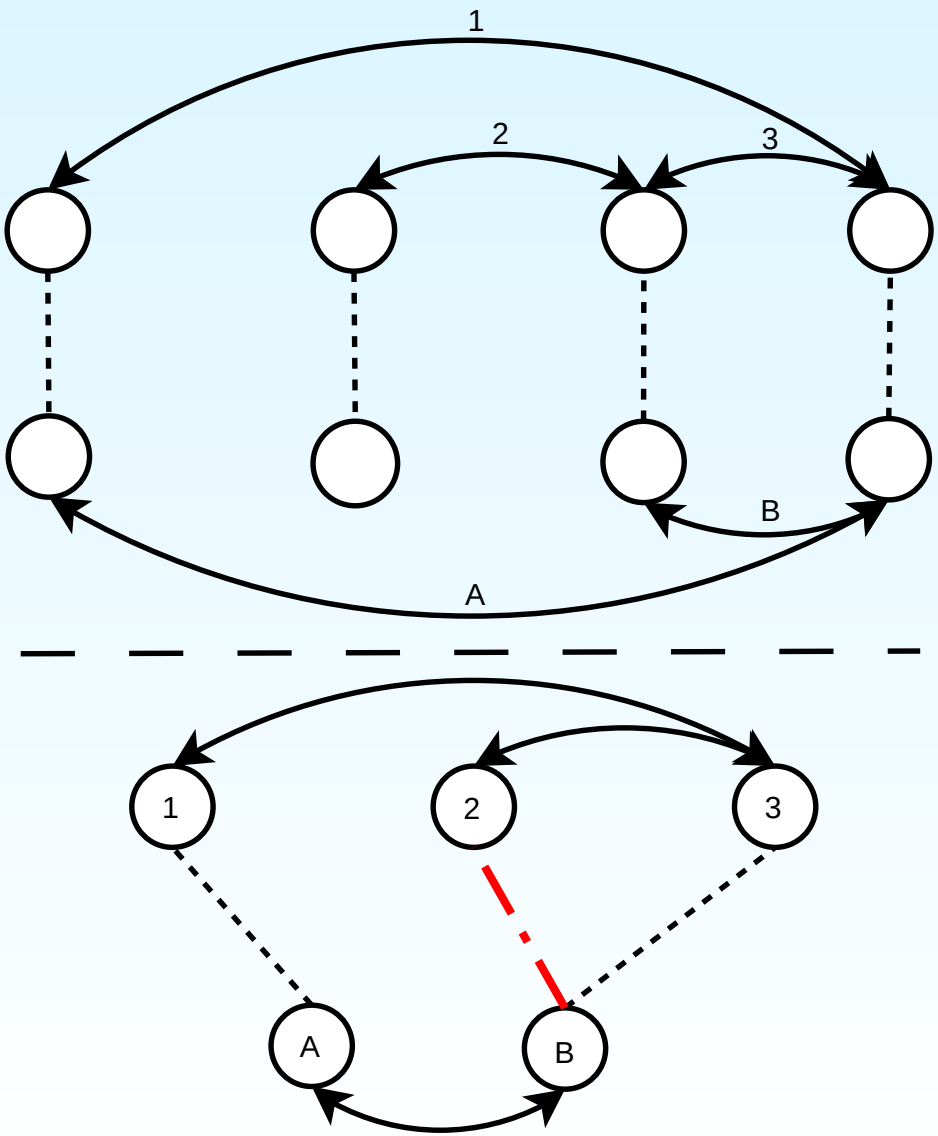

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Further work

Work in progress

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- frequency based intensification/diversification with Elite List
- empirical proof of correctness

Ideas to consider

- dynamic length of tabu list (reactive search)
- intensification with path relinking

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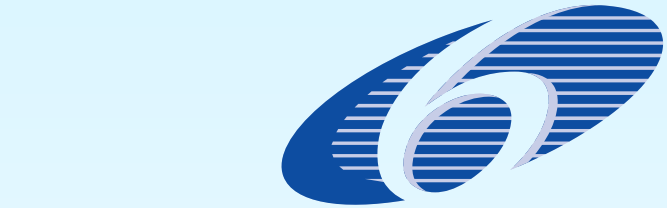

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