# Enhanced de Bruijn Graphs

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# Plan

# Next Generation Sequencing

- NGS technologies allow to produce millions of short sequences (100-300 bases), called reads
- These reads contain sequencing errors ($\sim 1\%$)
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- Two main technologies: Pacific Biosciences and Oxford Nanopore
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# Overlap graph

An overlap graph is a graph structure that allows to compute overlaps of variable length between the reads of a given set.

**Formal definition**

For a set of reads $R = \{r_1, r_2, ..., r_n\}$, $OG(R) = (V, E)$ such as:

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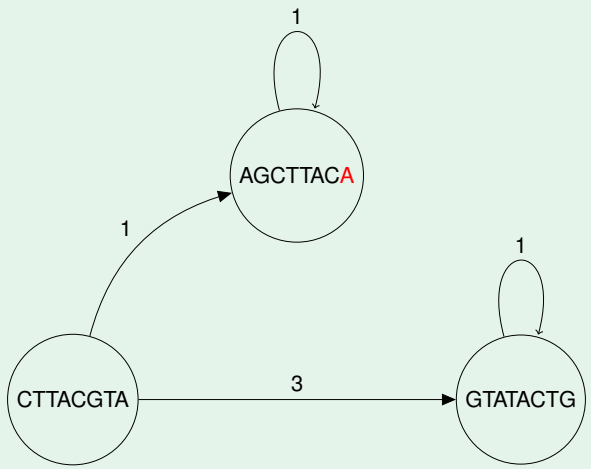


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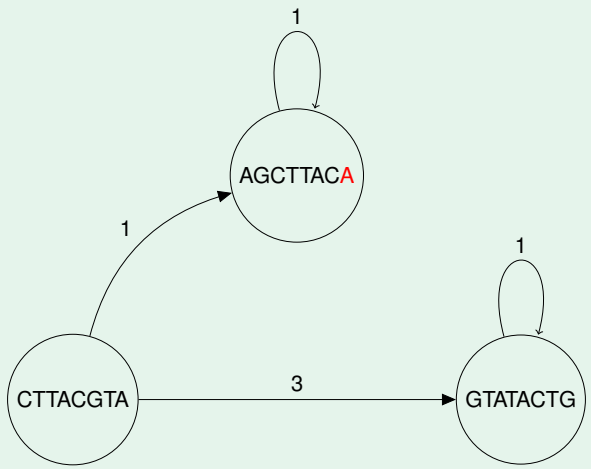


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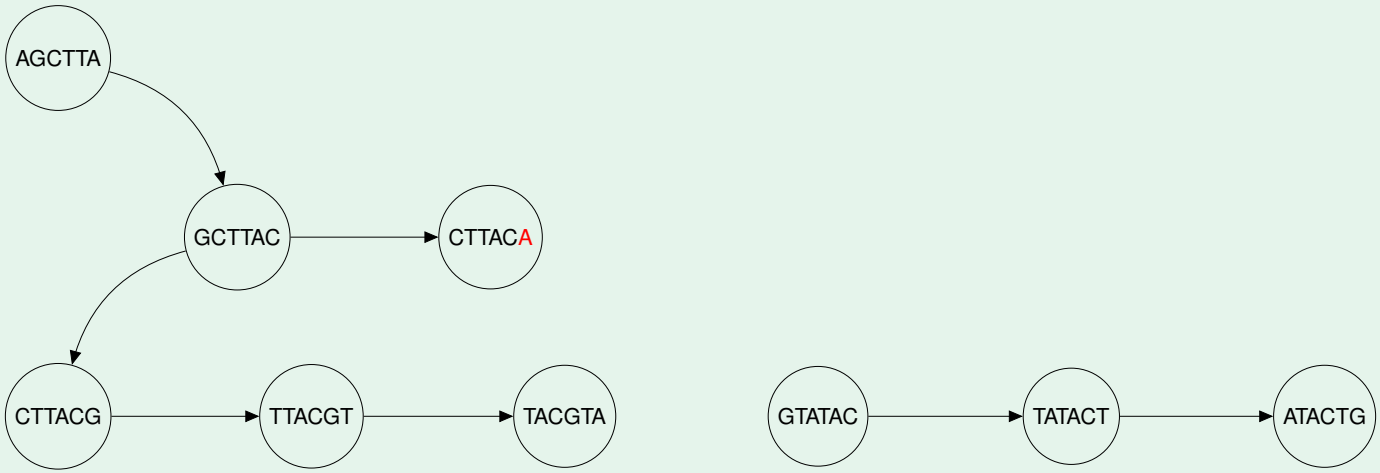


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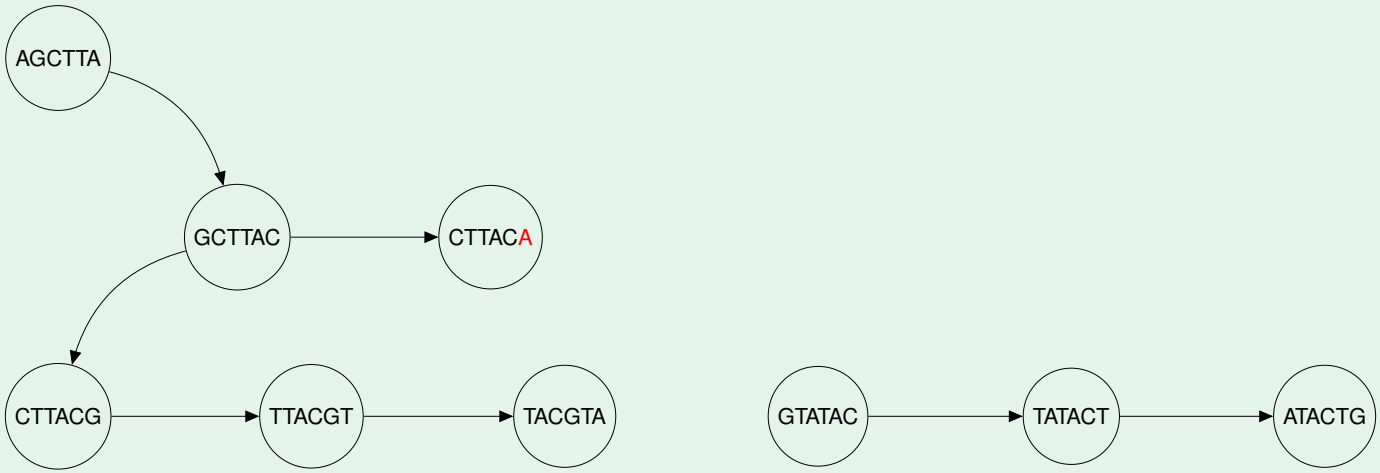


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## Idea

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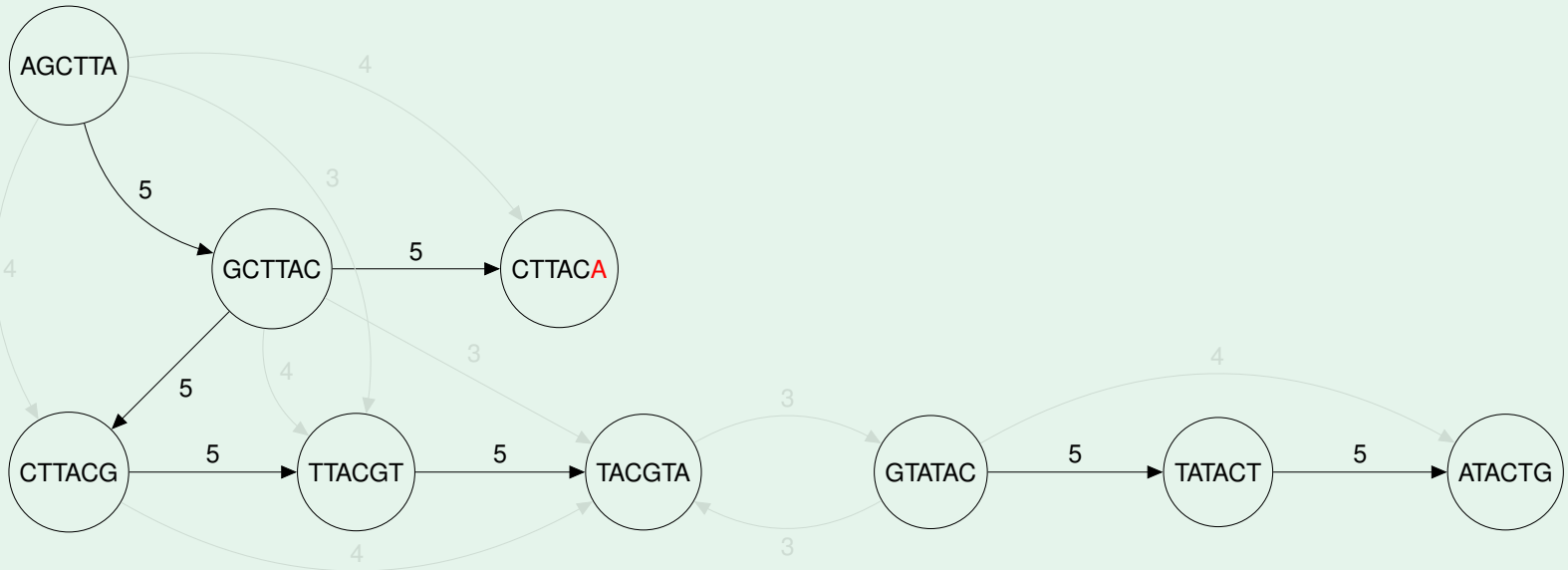

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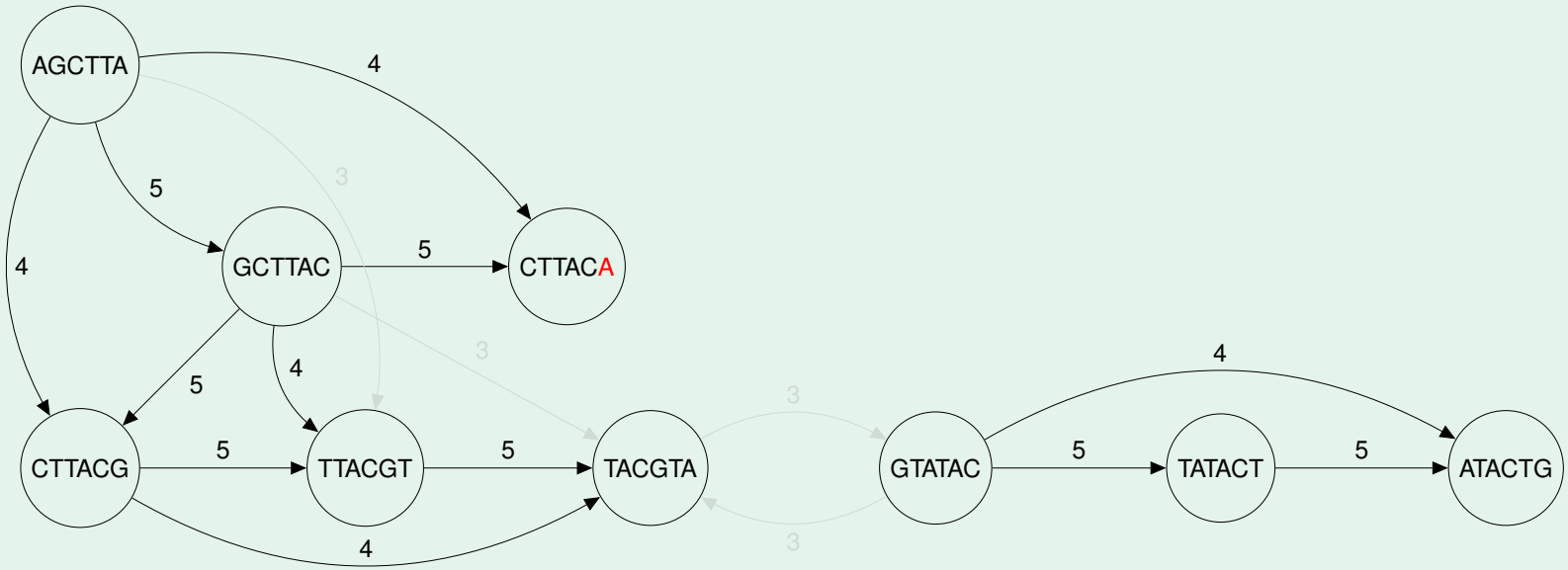

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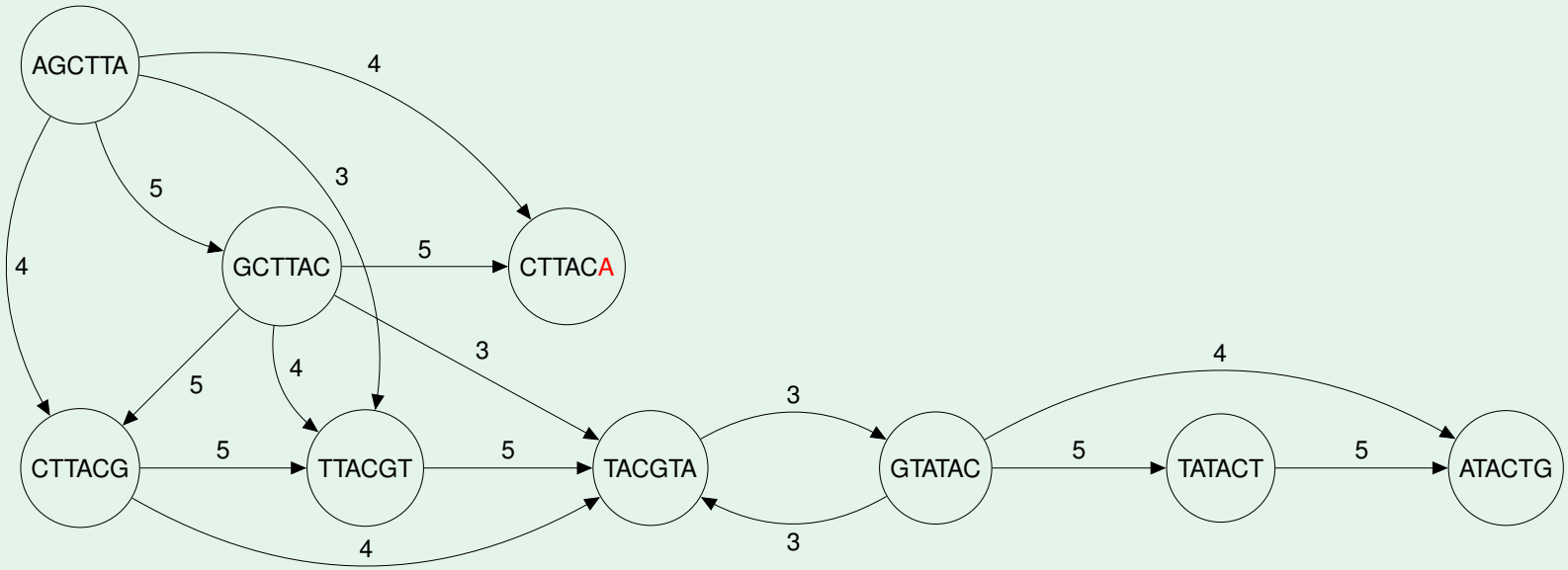

# Construction

- The enhanced de Bruijn graph does not need to be explicitly built
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PgSA [Kowalski et al., 2015] is a data structure that allows the indexing of a set of reads, in order to answer the following queries on the reads, for a given string $f$:

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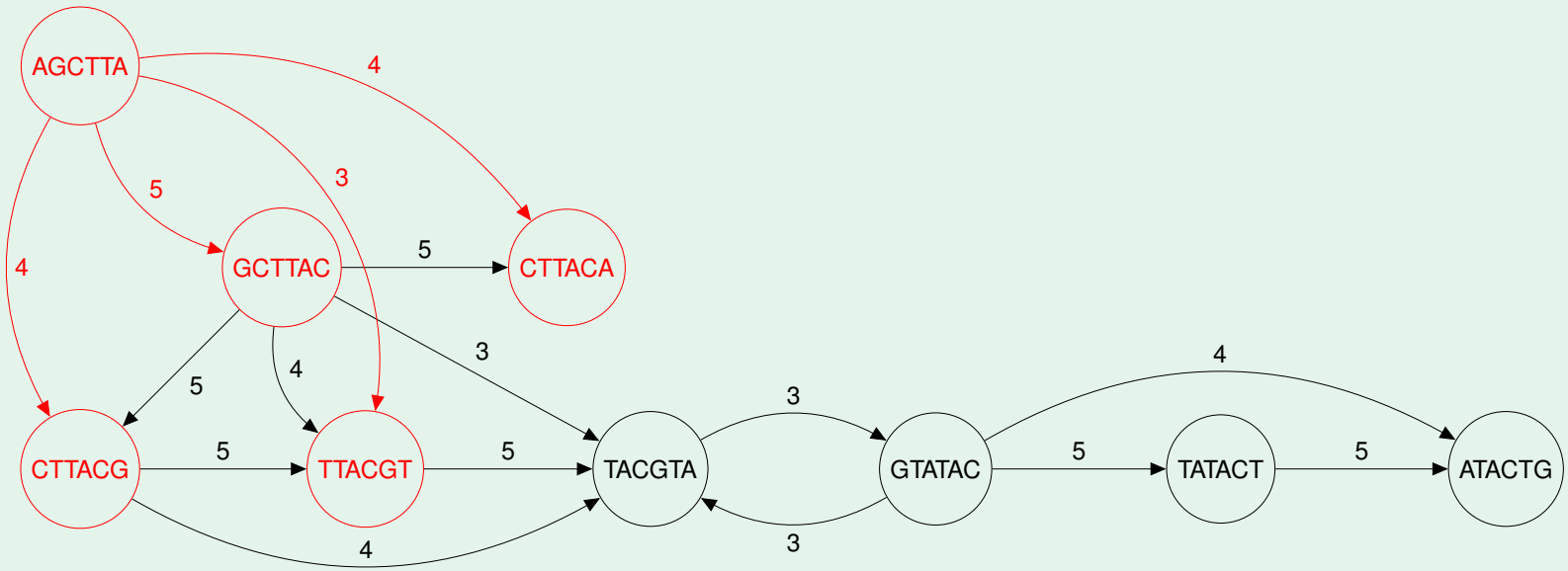
Traversing the previous enhanced de Bruijn graph:



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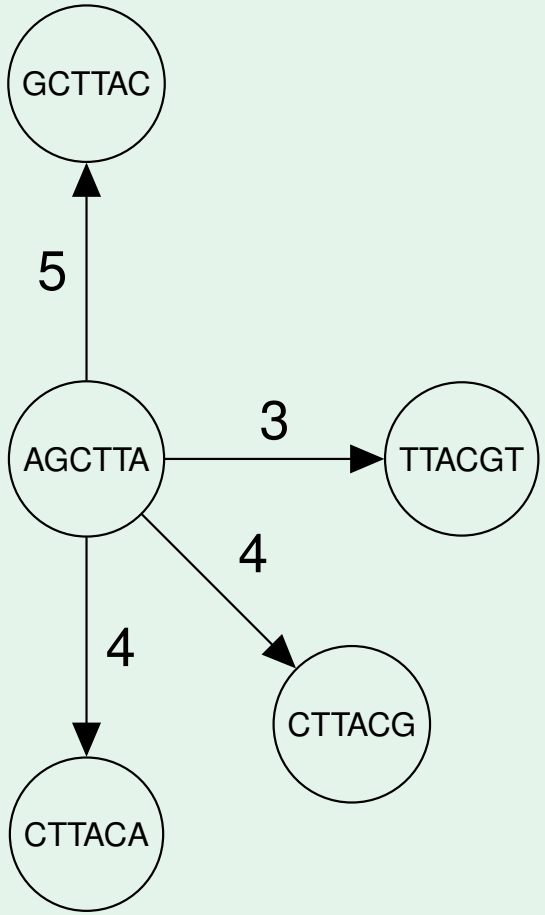
PgSA Index



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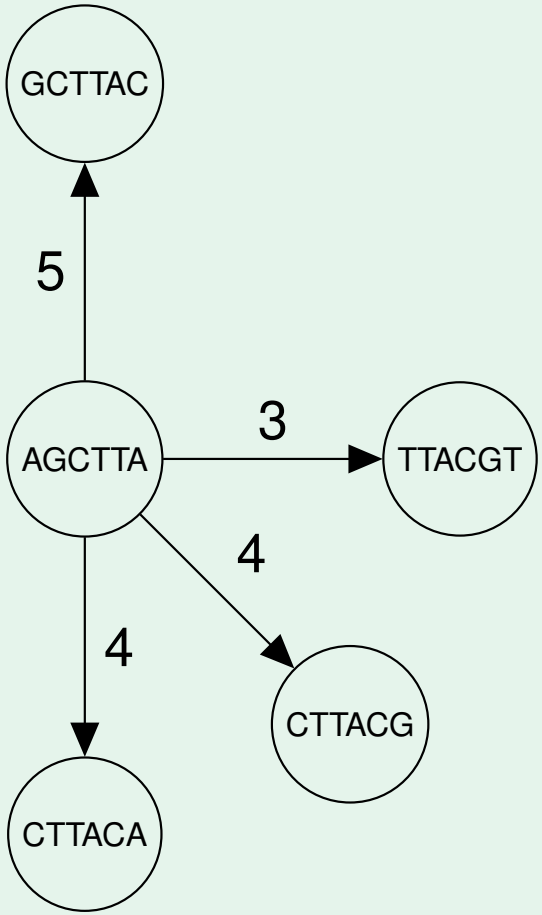

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Occurrences positions?

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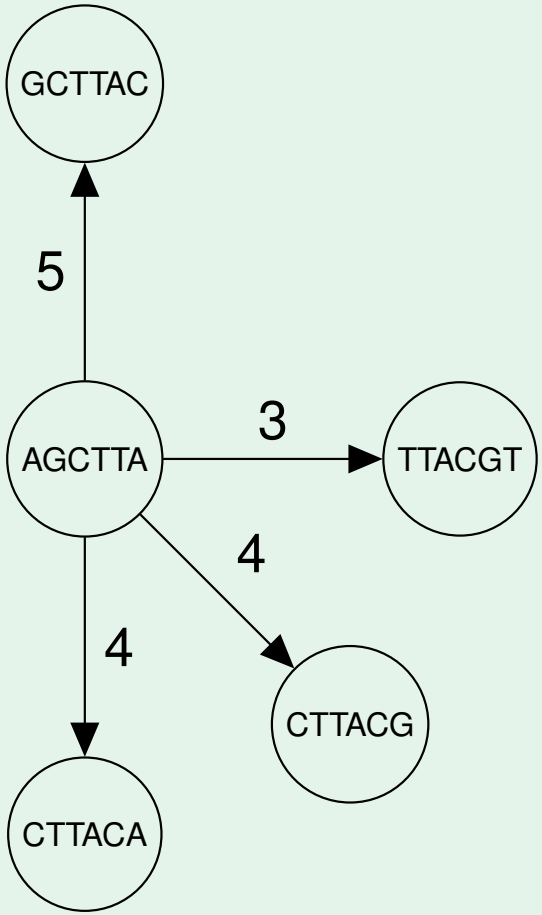

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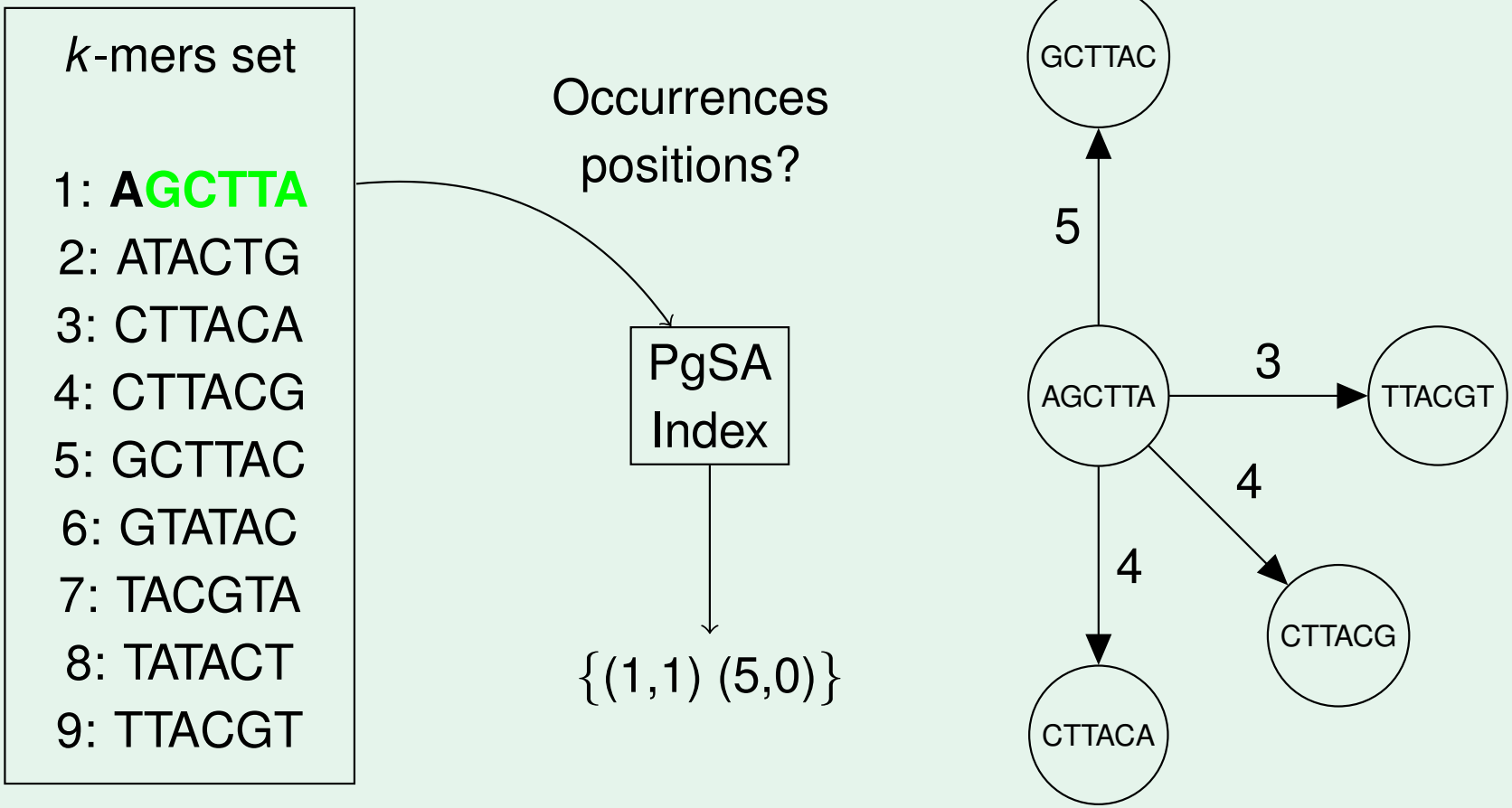

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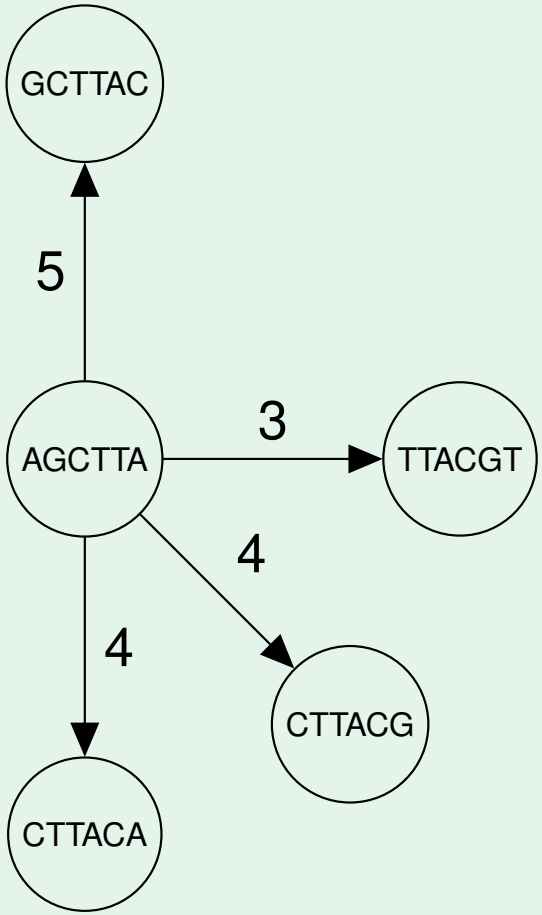

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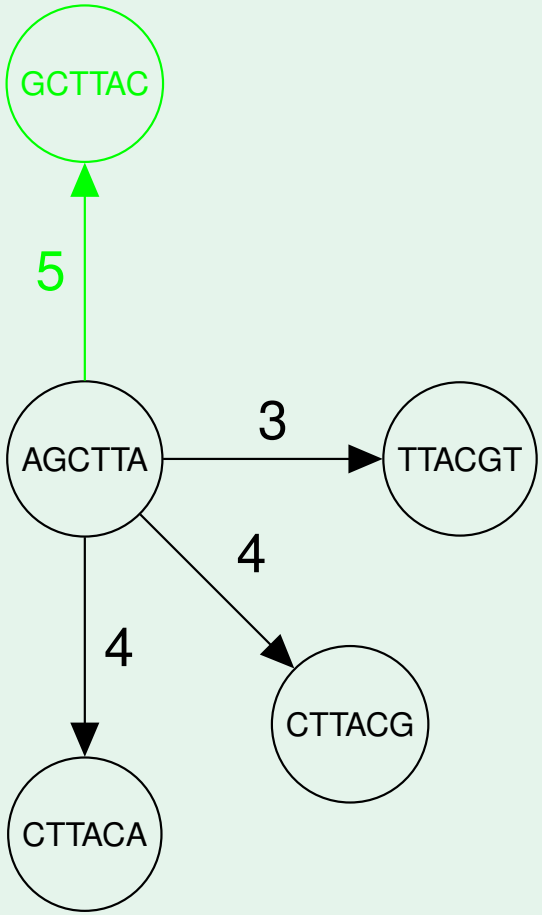

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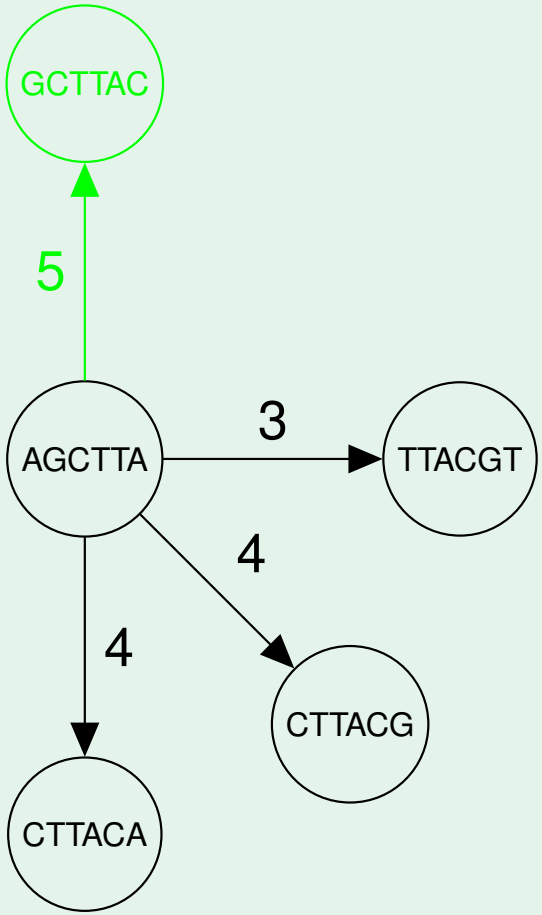
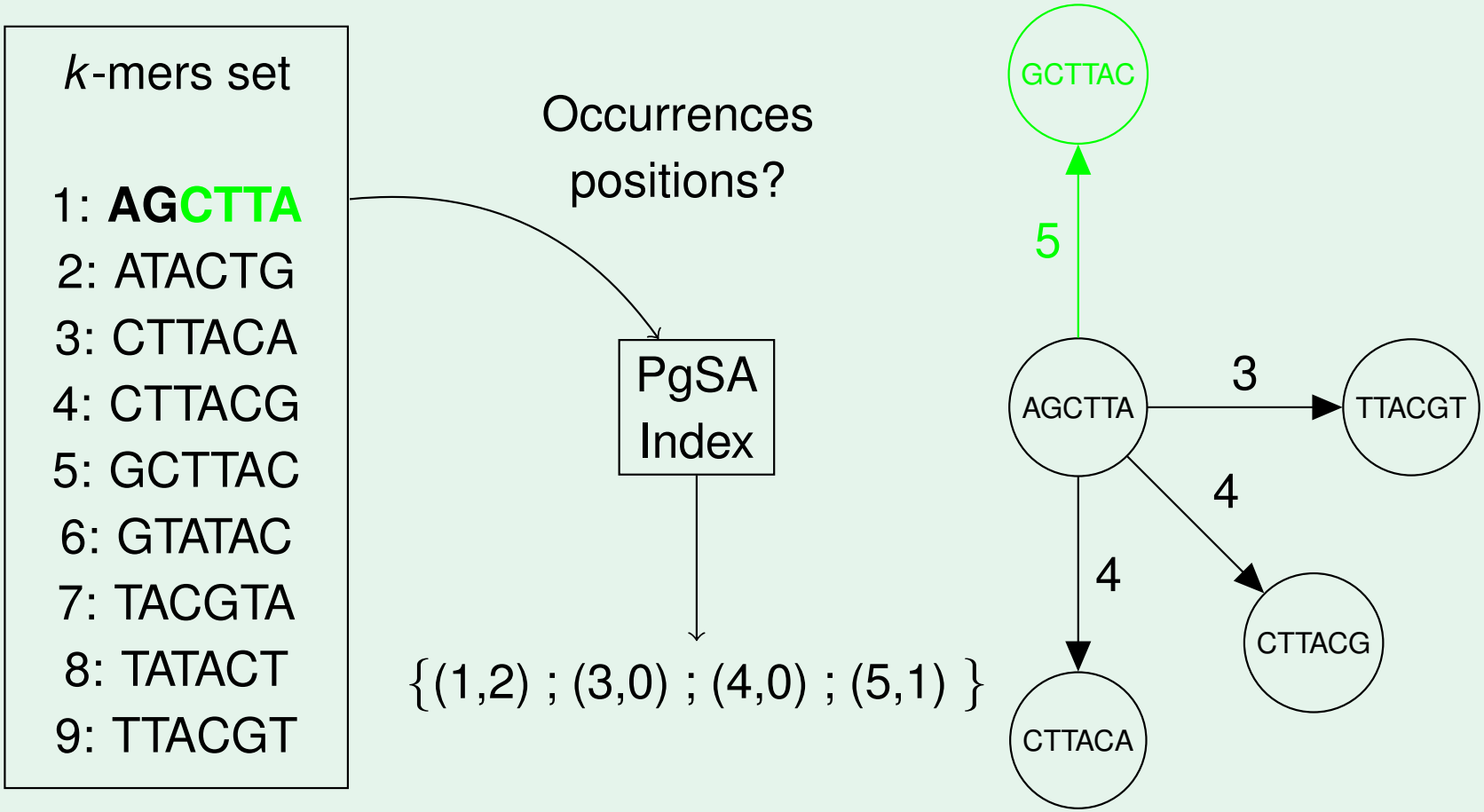
Occurrences positions?

PgSA Index



# Traversal of the enhanced de Bruijn graph

## Example



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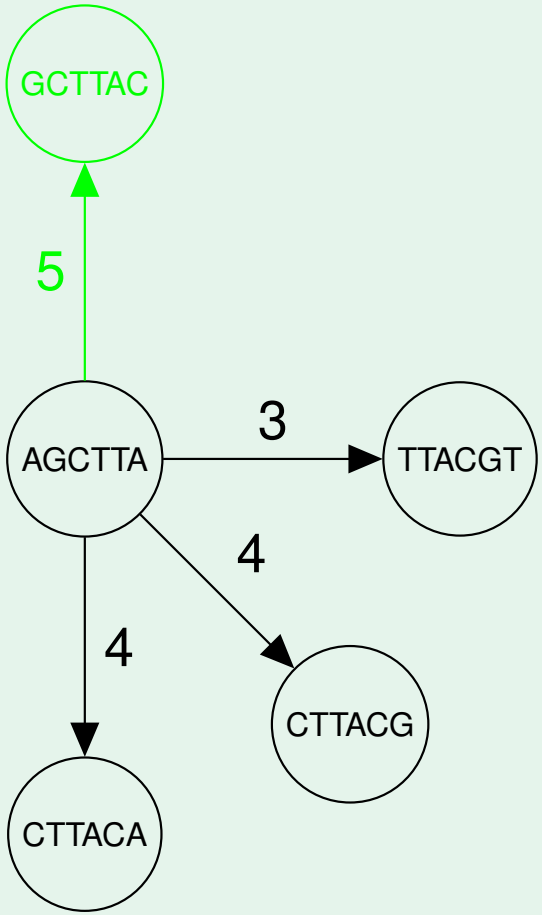

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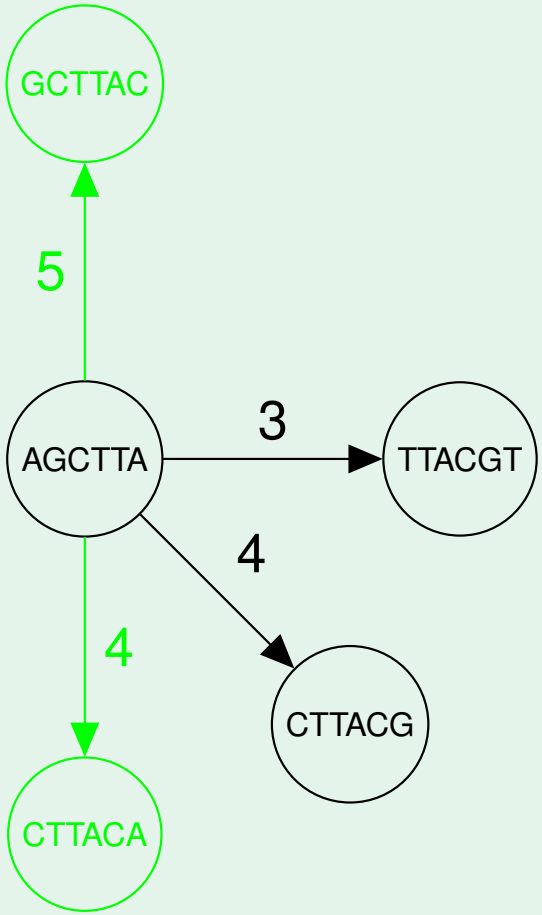

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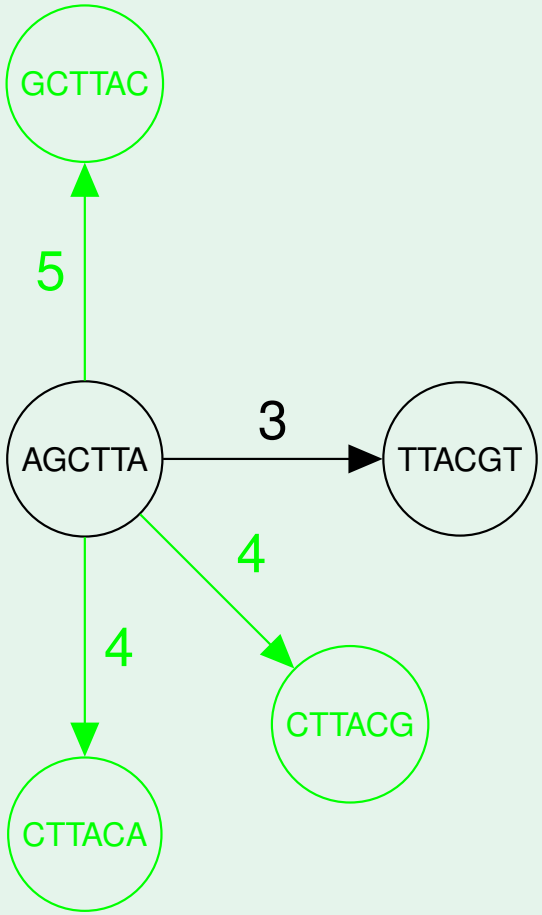

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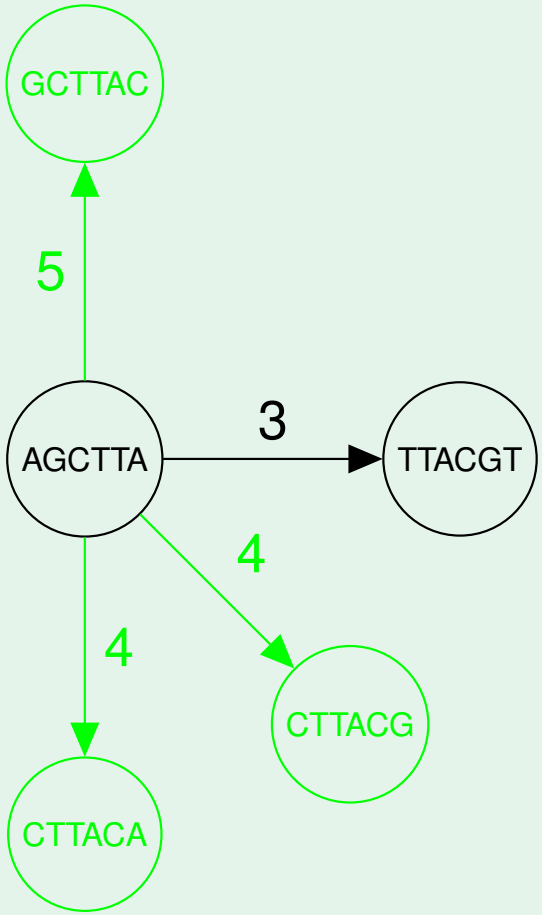

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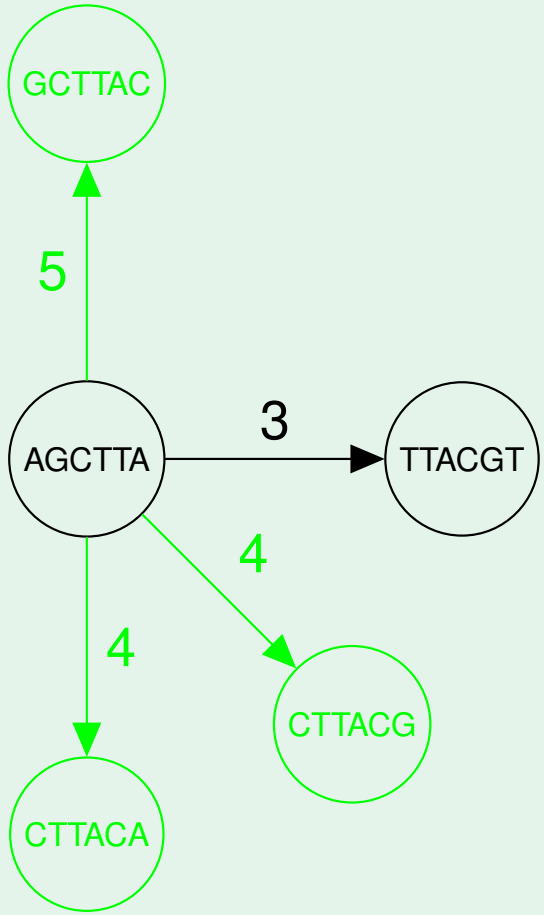

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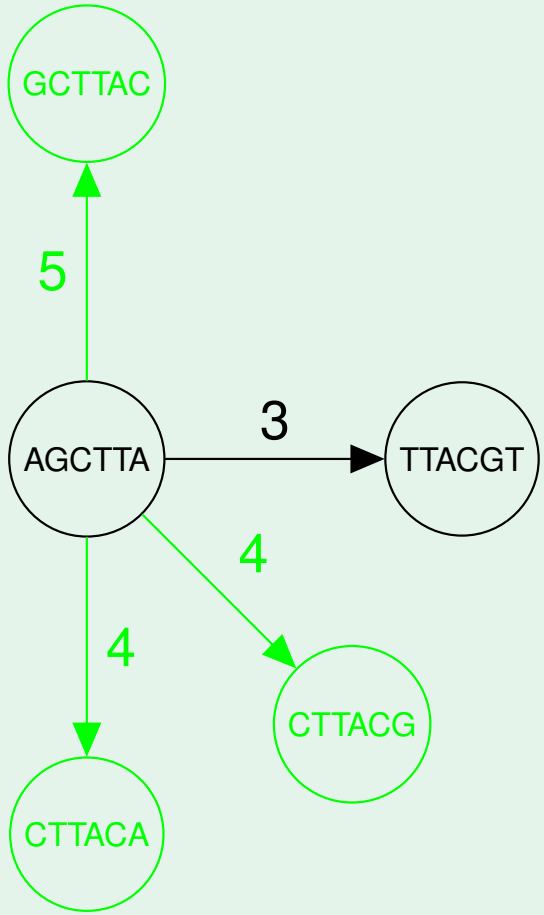

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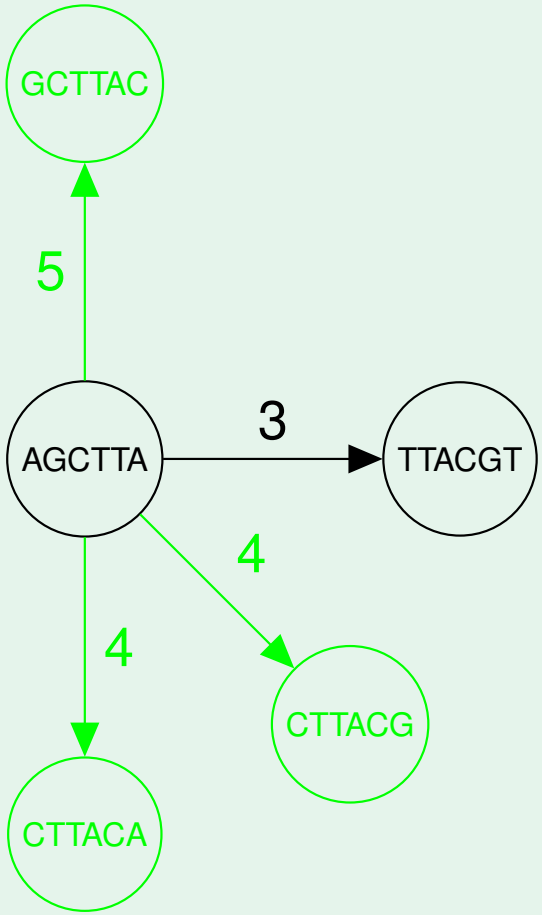

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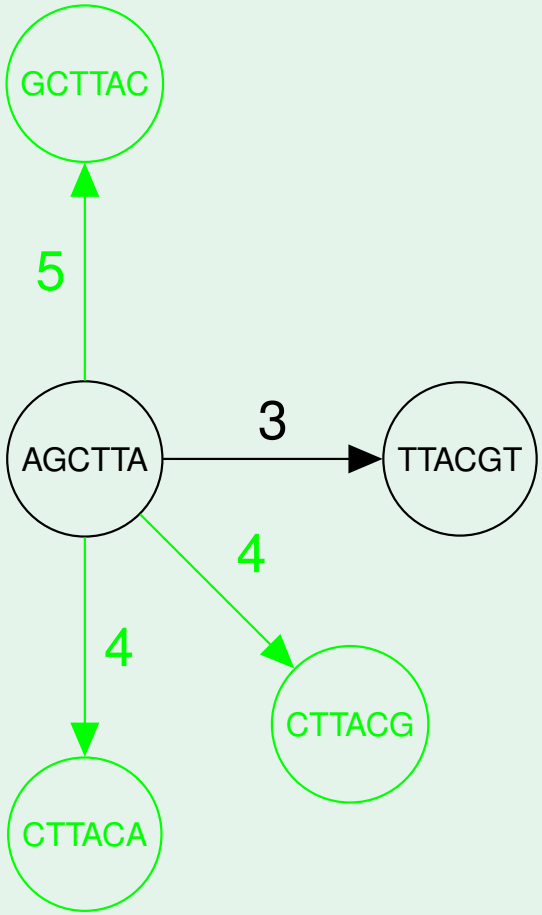

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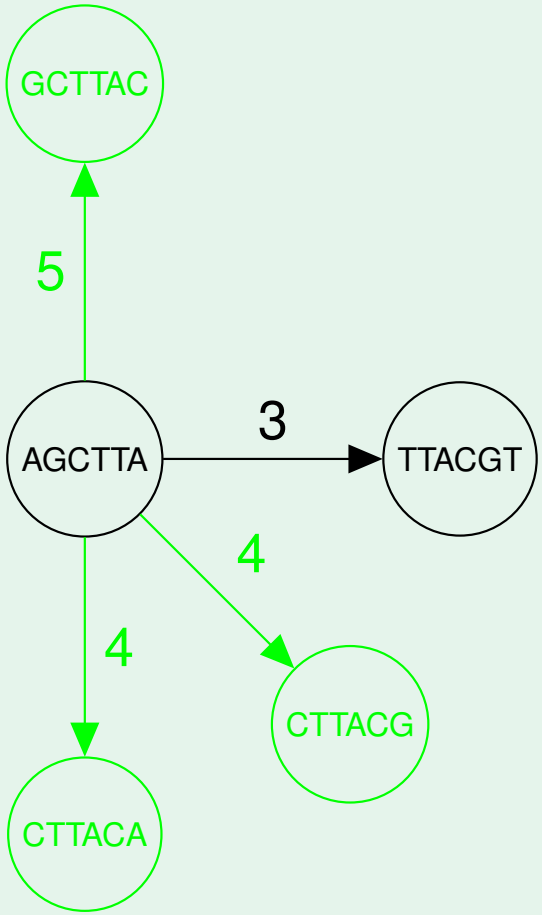

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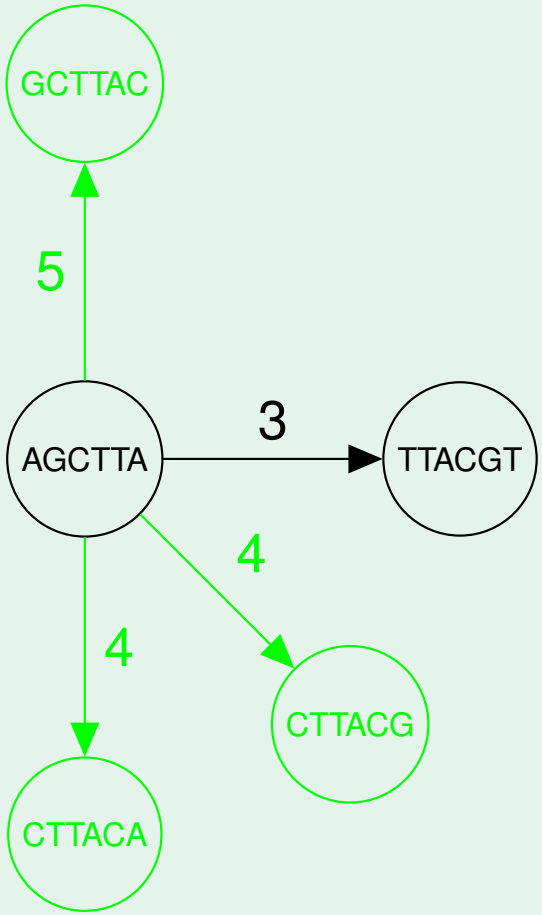

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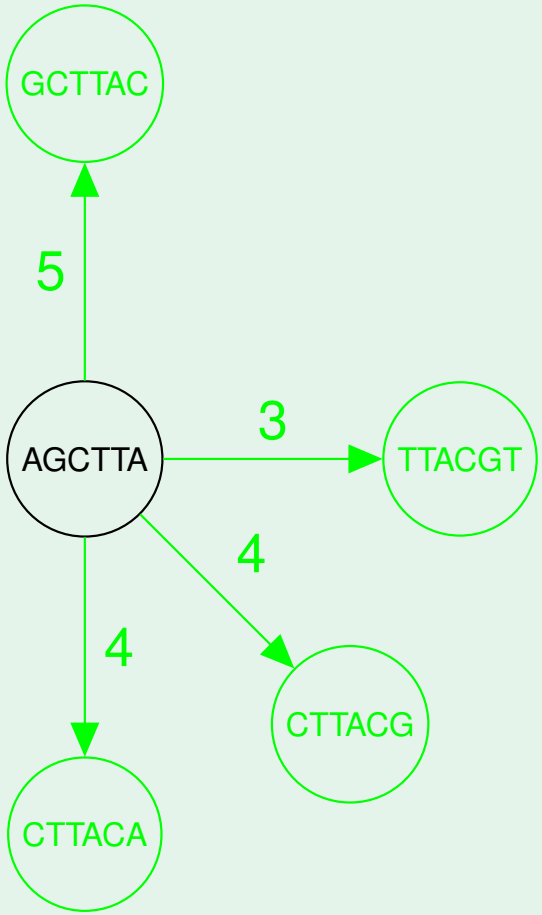

# Context

- Due to their high error rate, error correction of long reads is mandatory
- Various methods already exist for the correction of short reads, but are not applicable to long reads
- Forces the development of new error correction methods
- Two main categories: self-correction and hybrid correction

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# Workflow

5 steps:

1. Correct the short reads
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3. Merge the overlapping seeds
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- Seeds are used as anchor points on the enhanced de Bruijn graph
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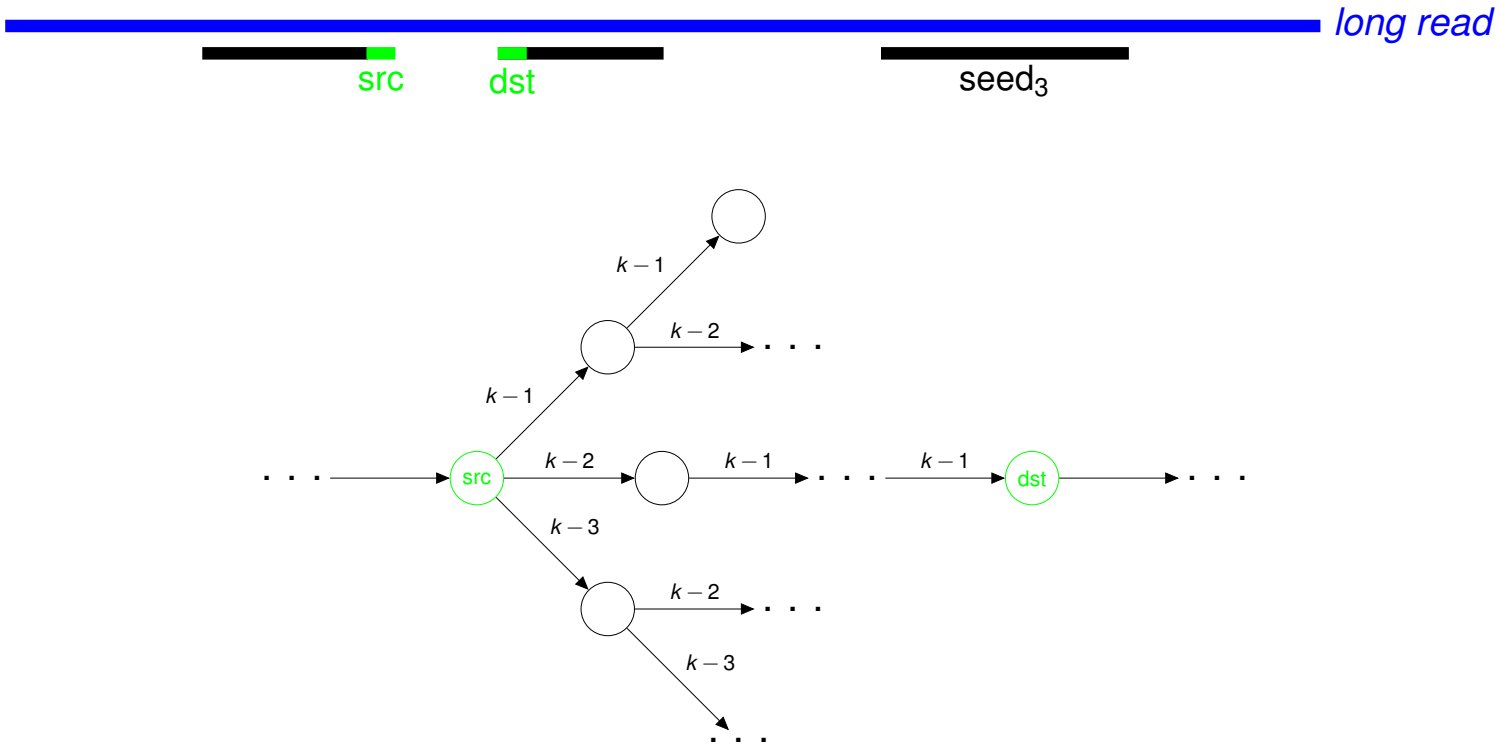

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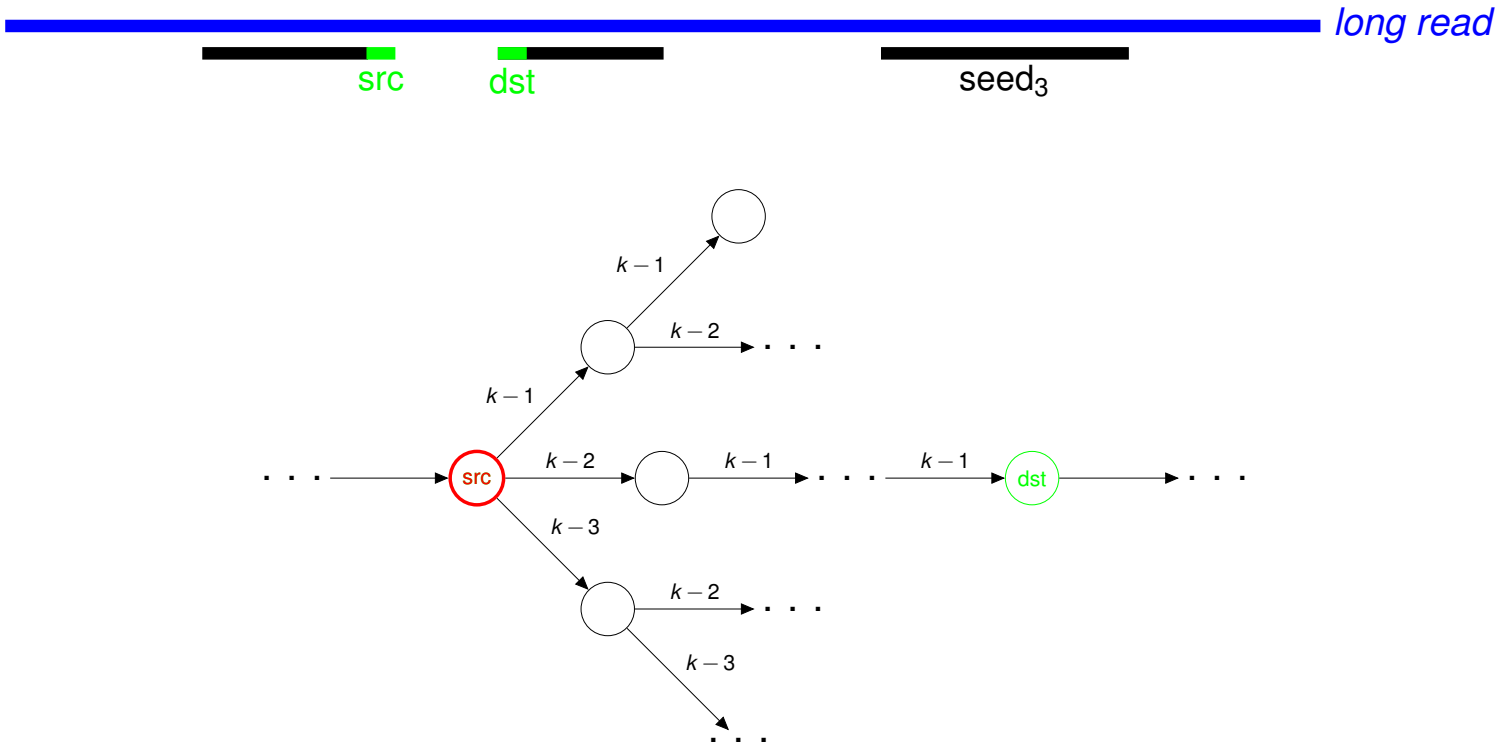

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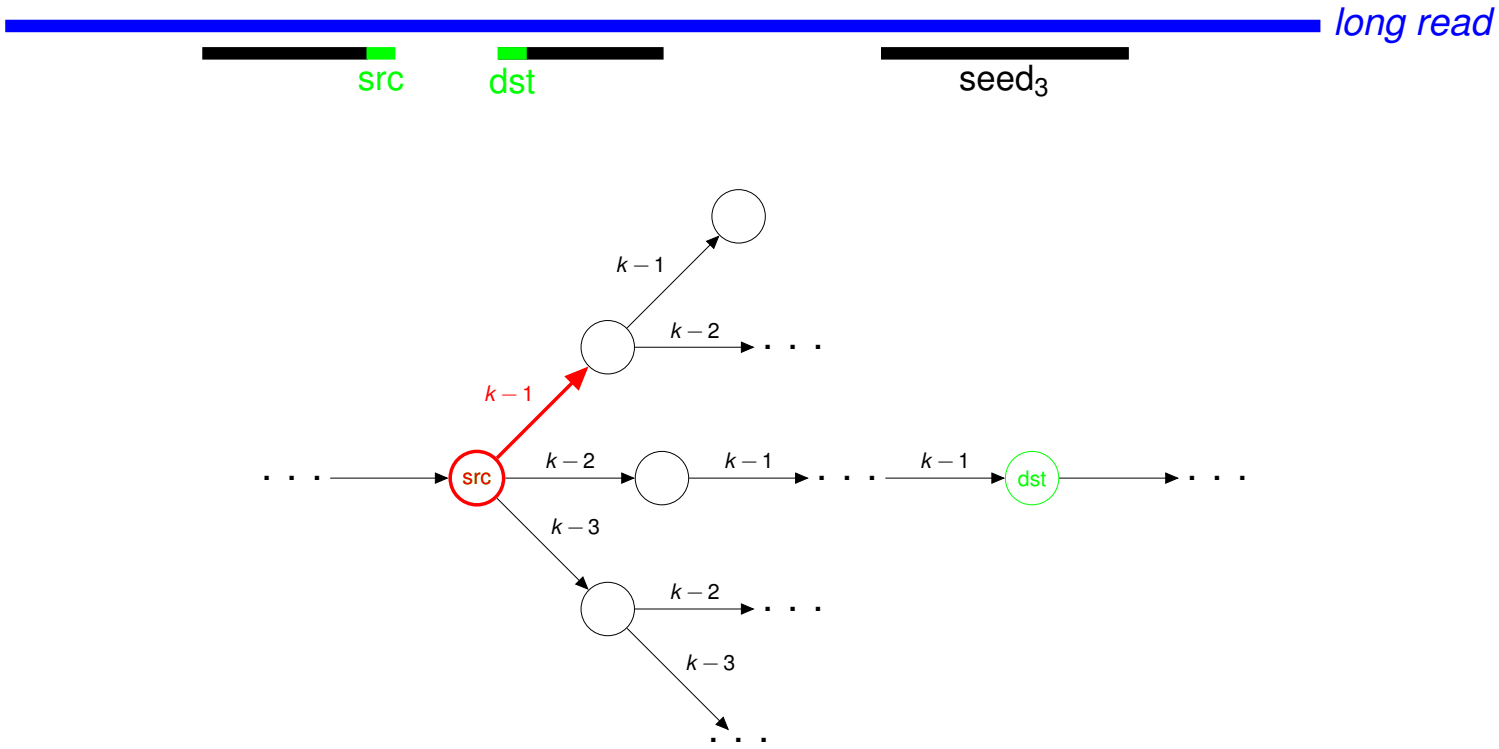

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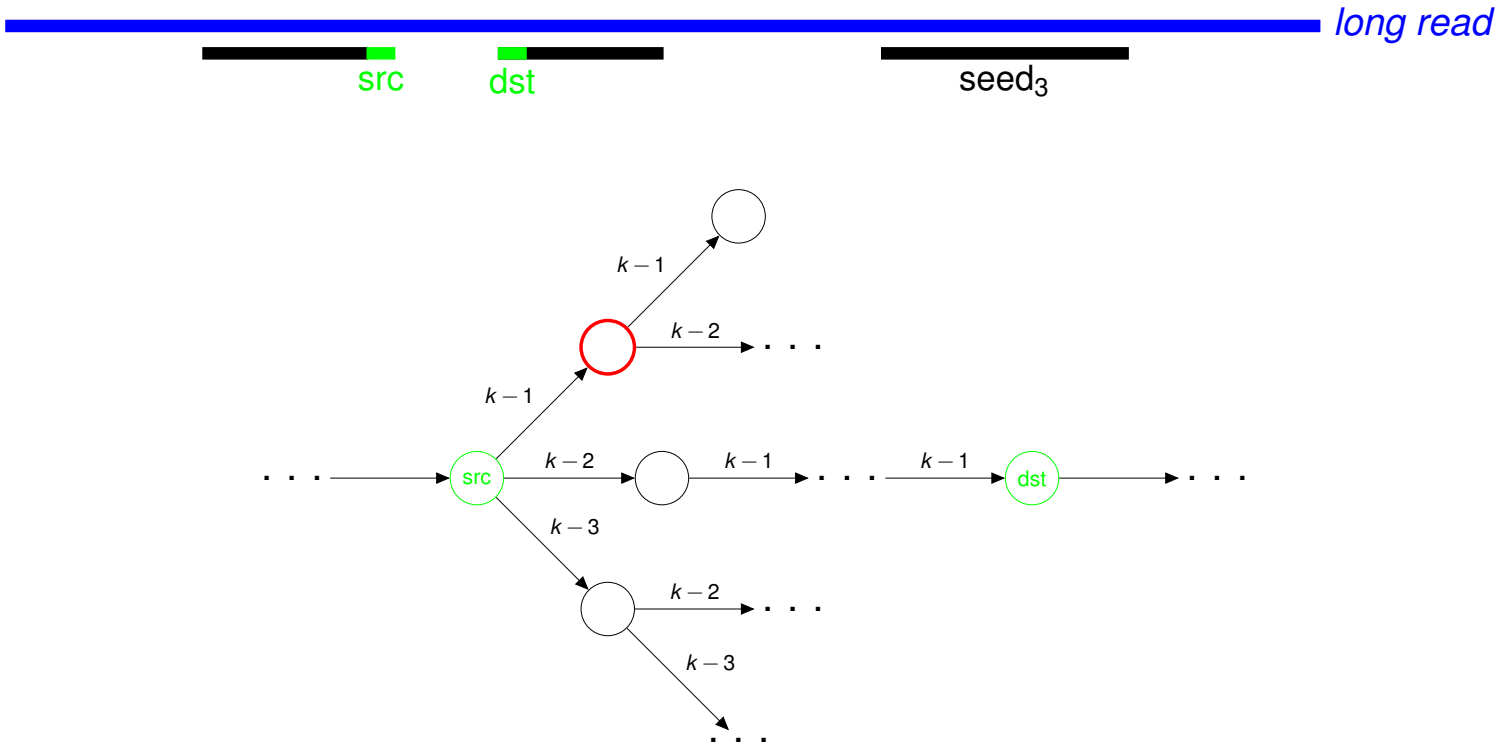

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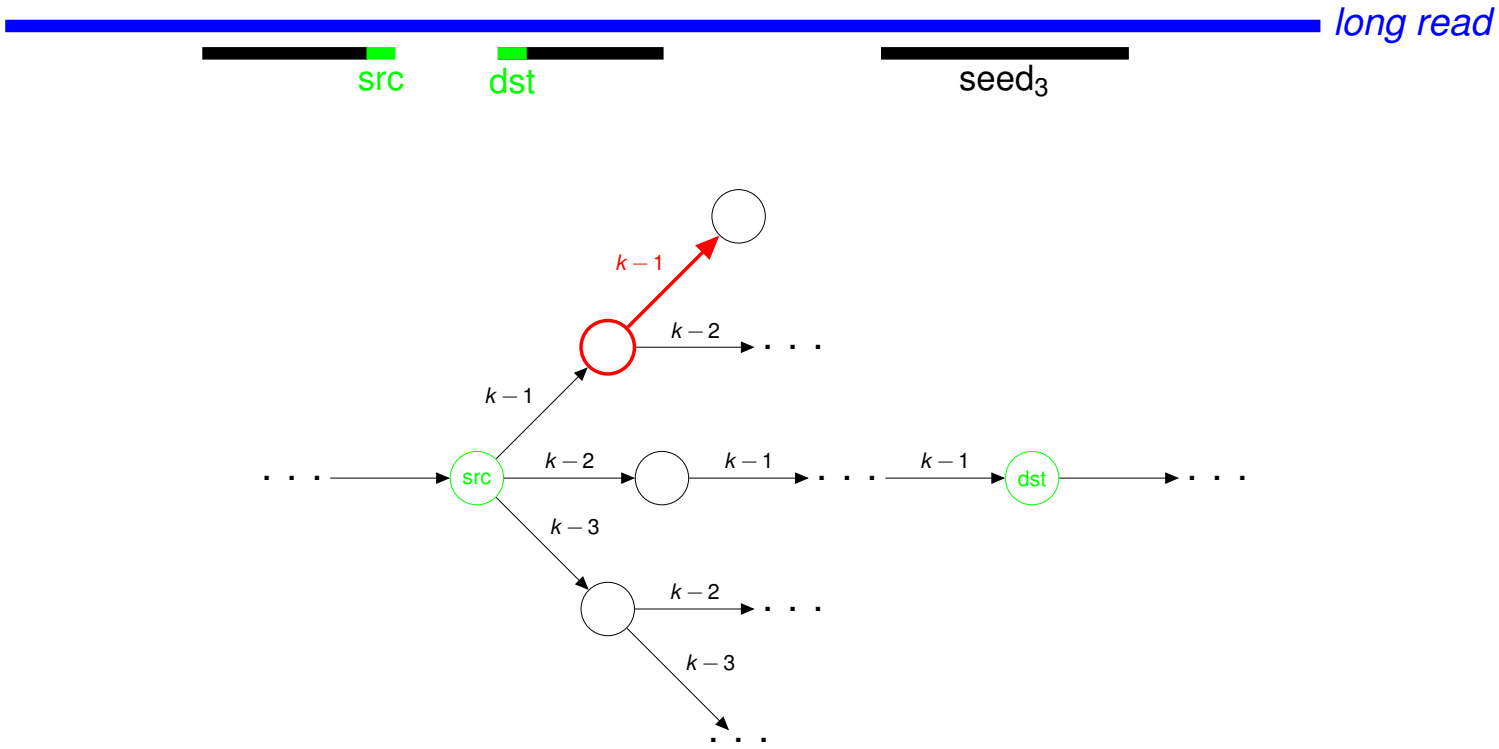

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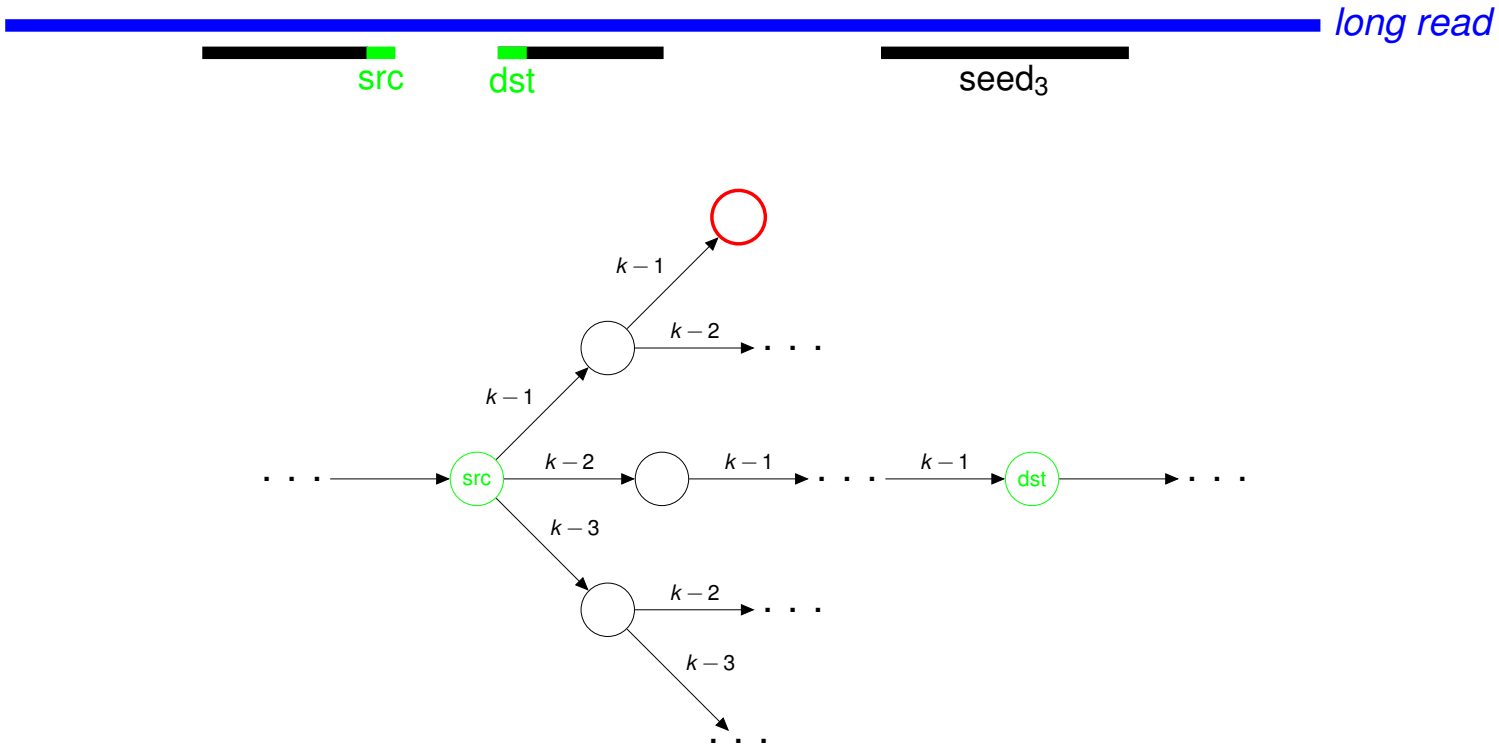

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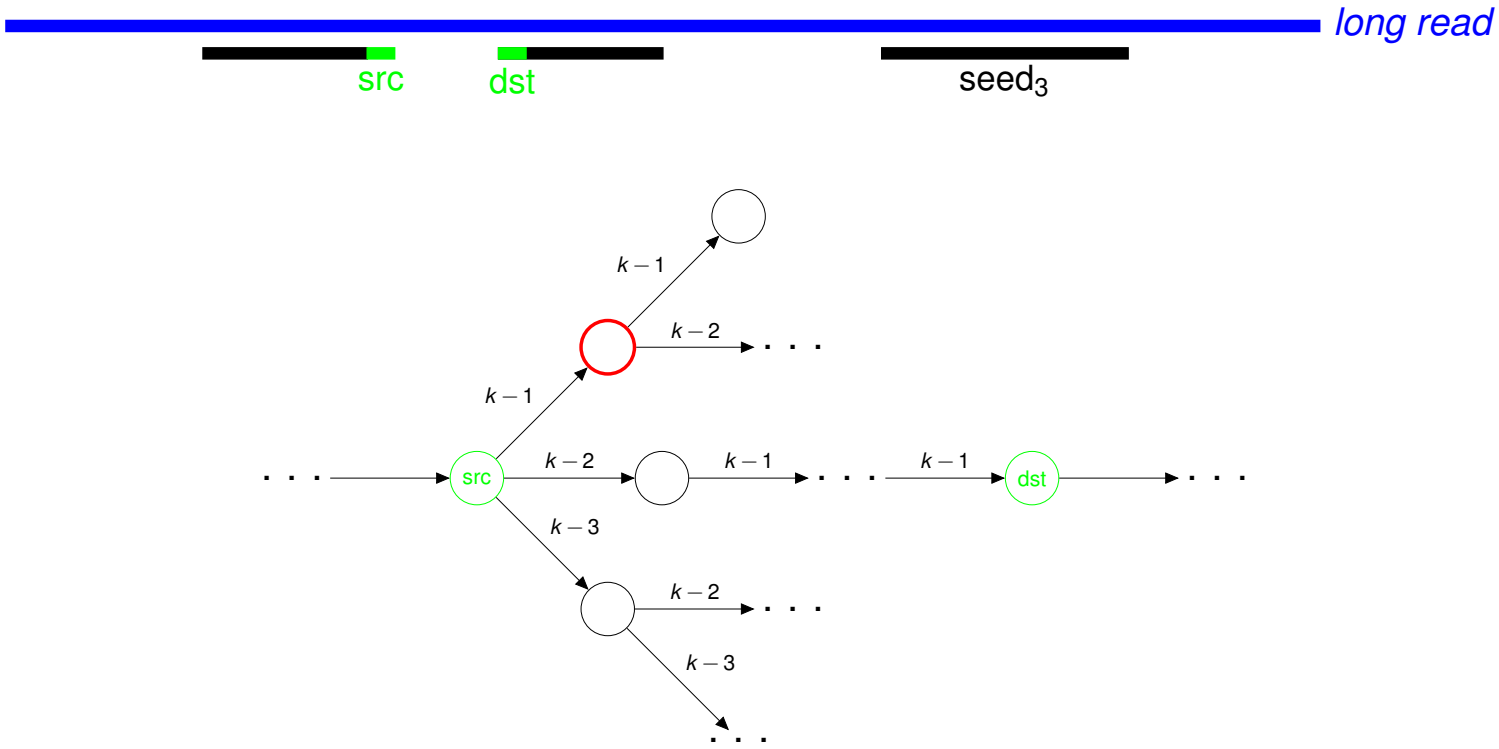

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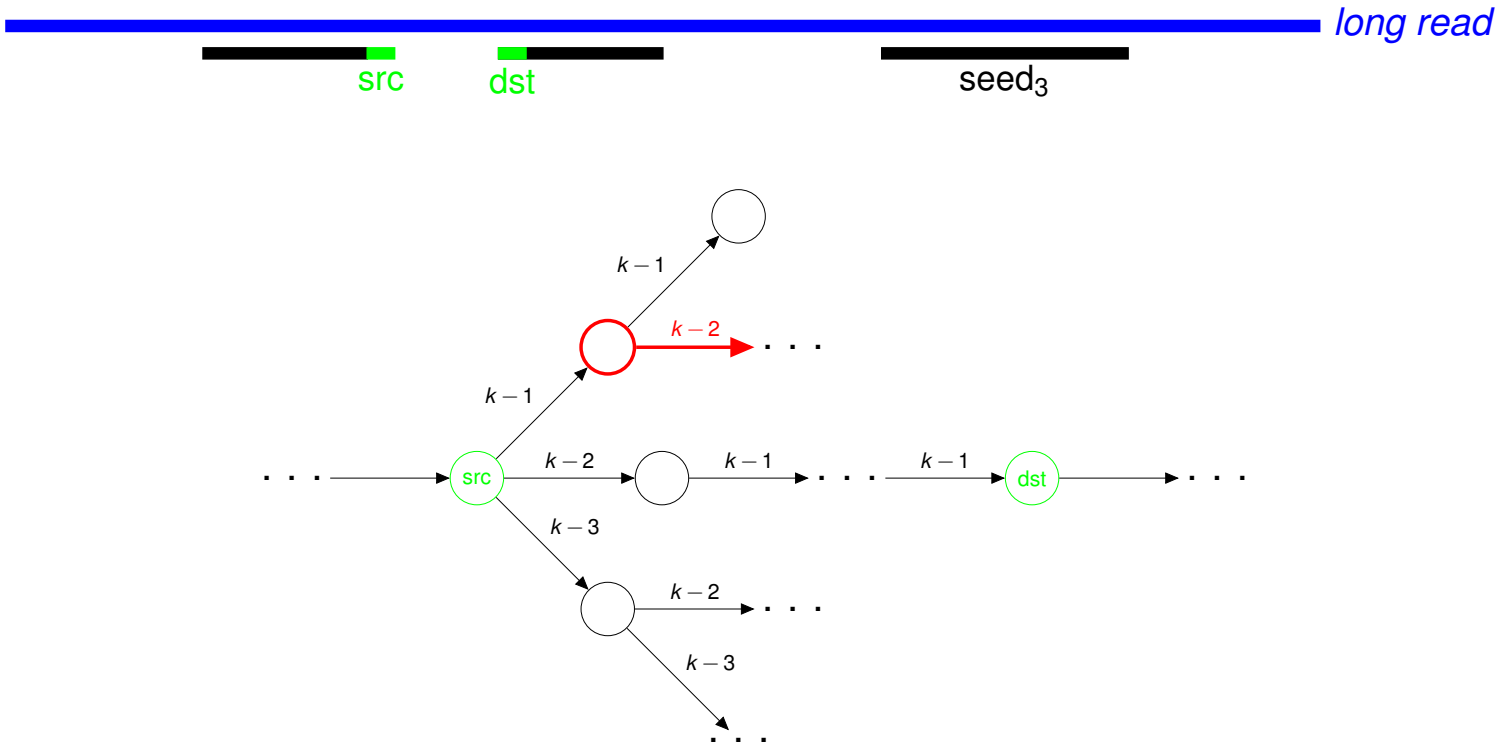

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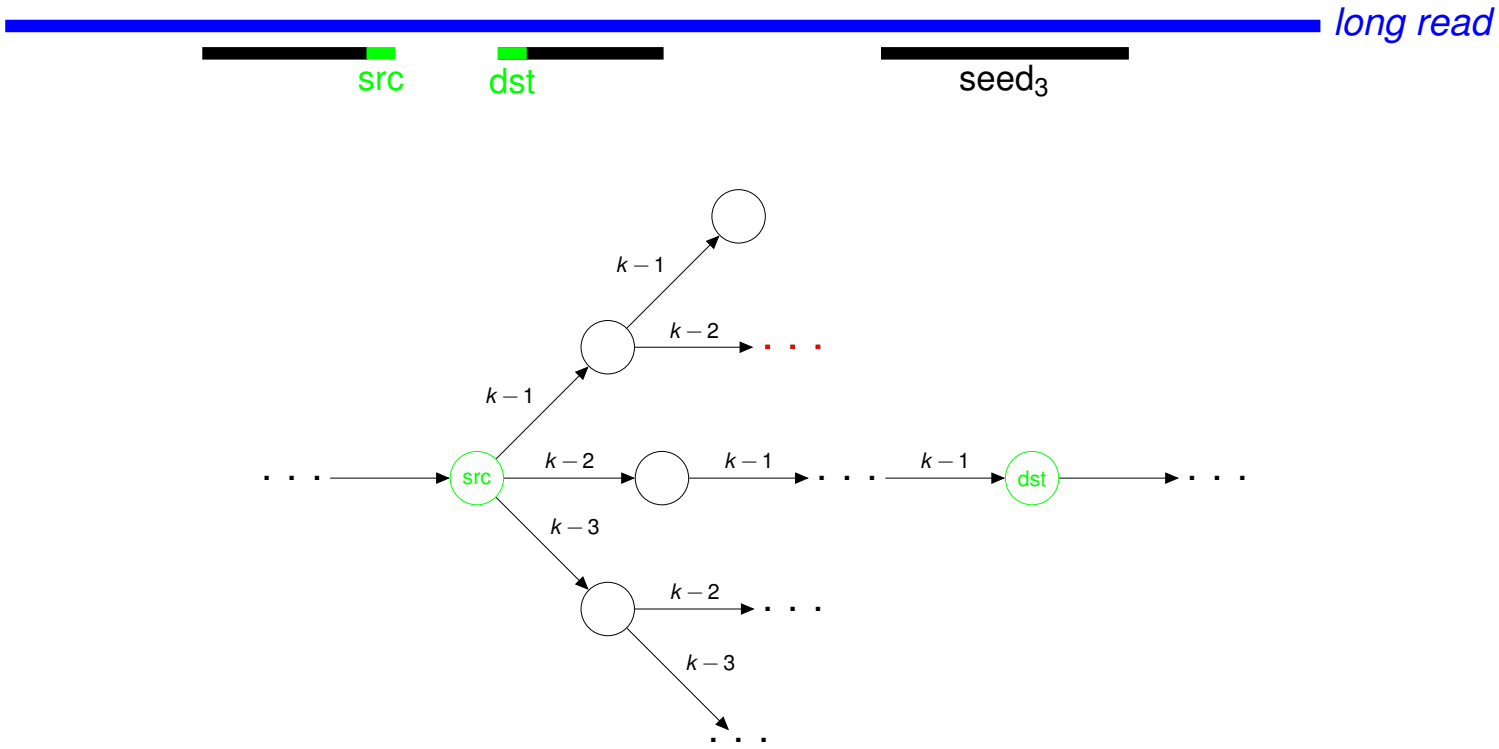

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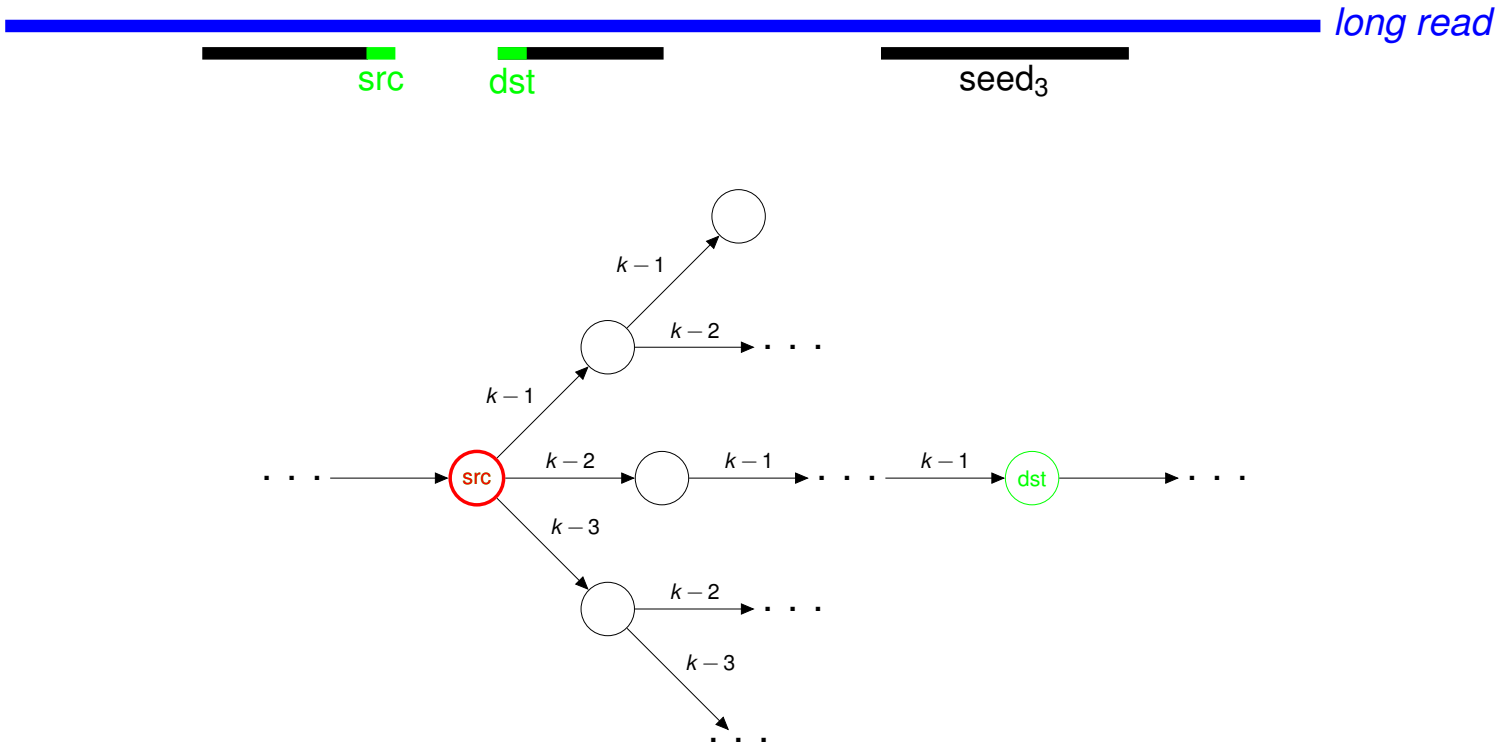

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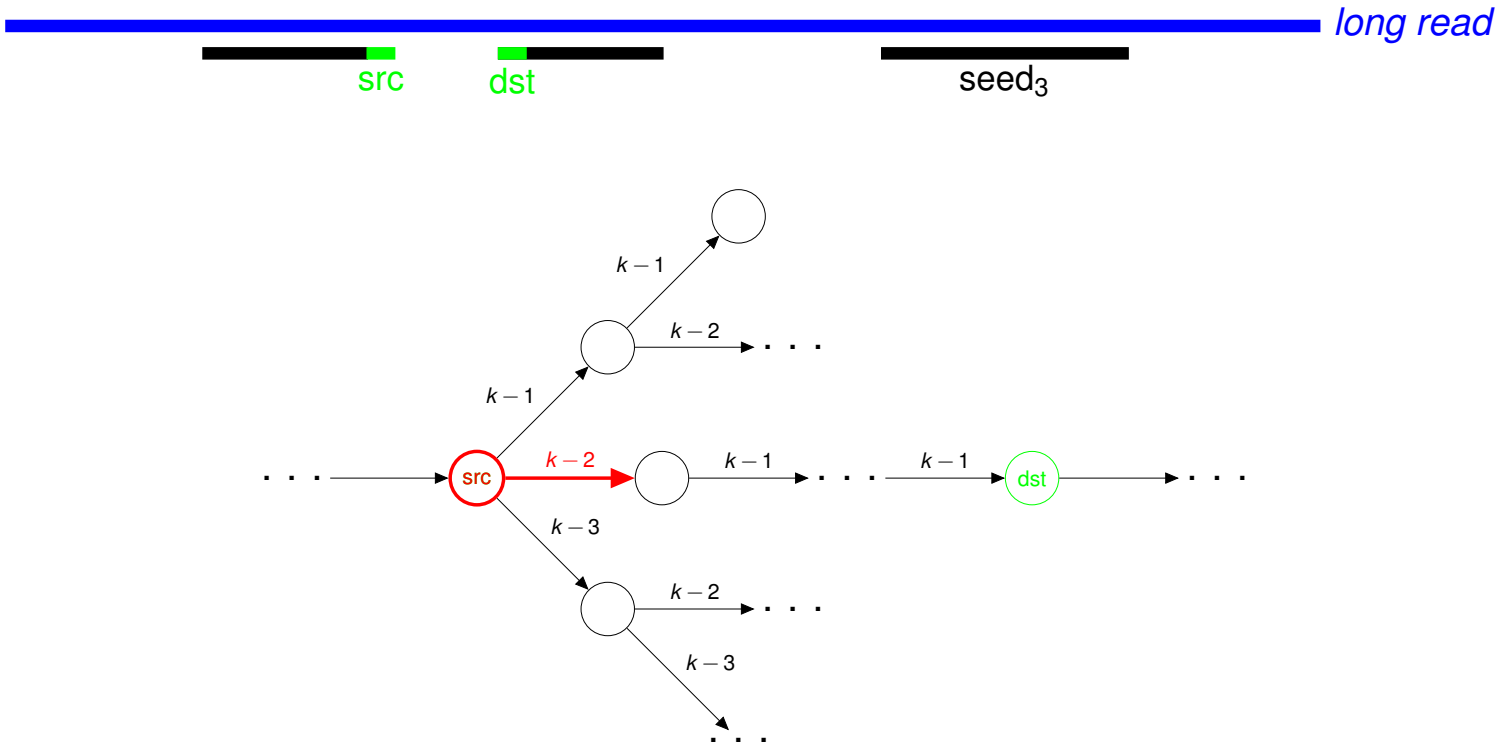

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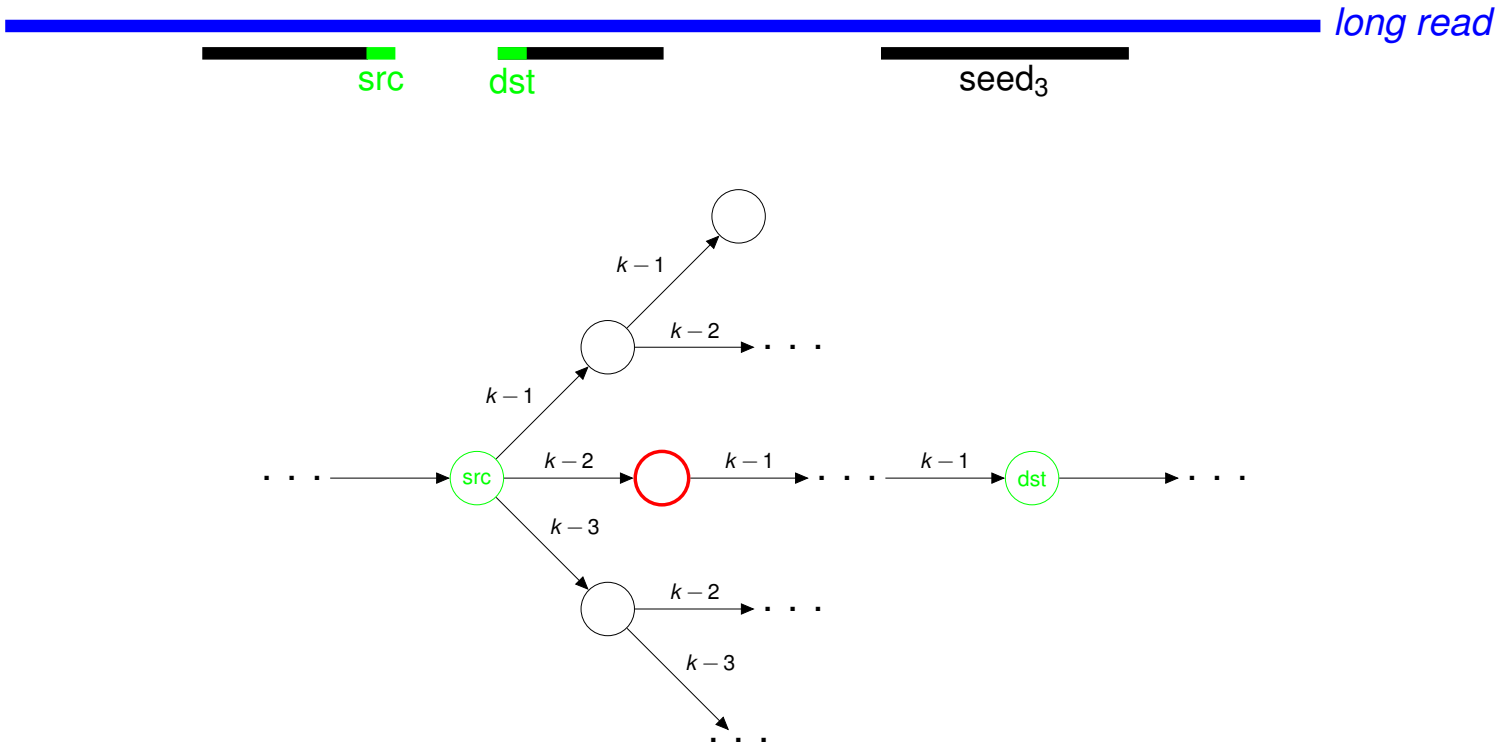

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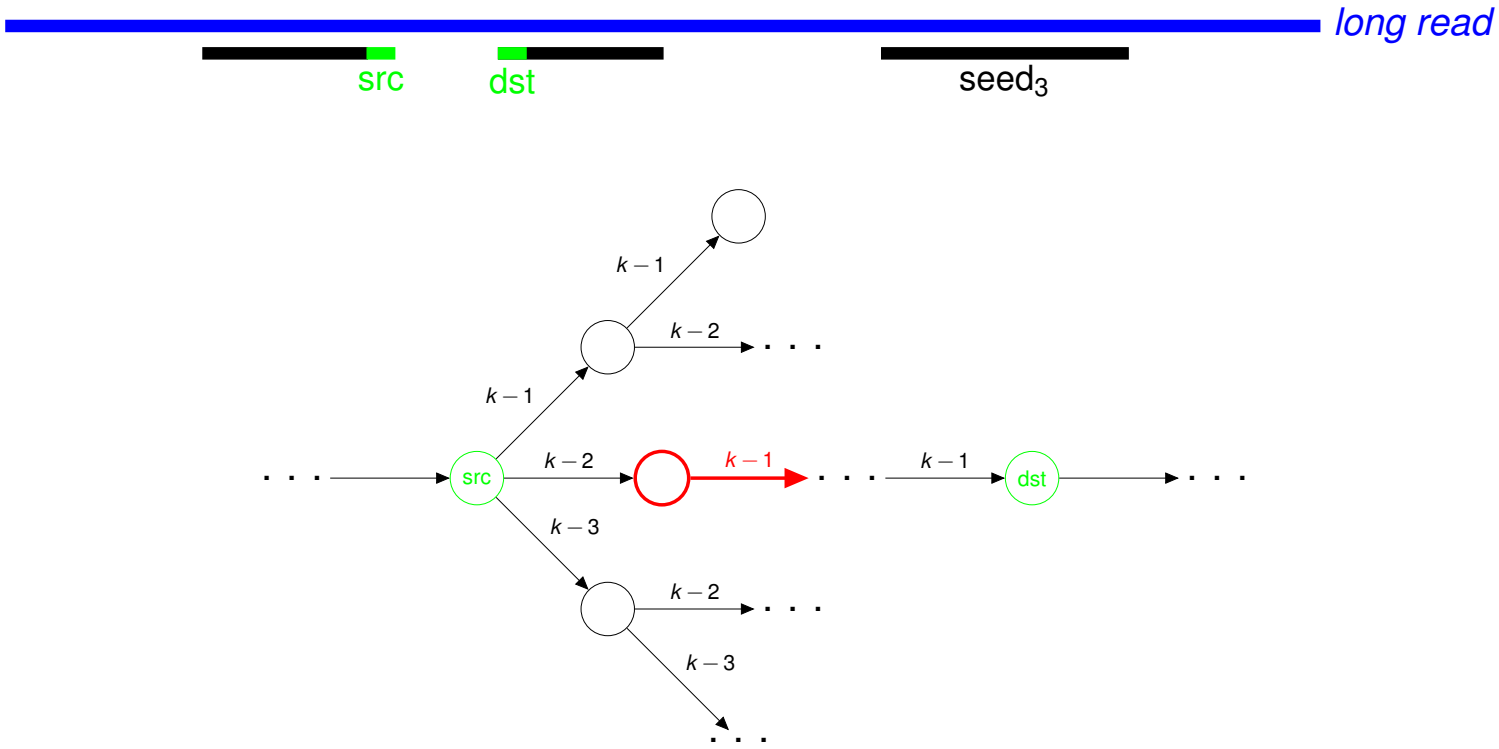

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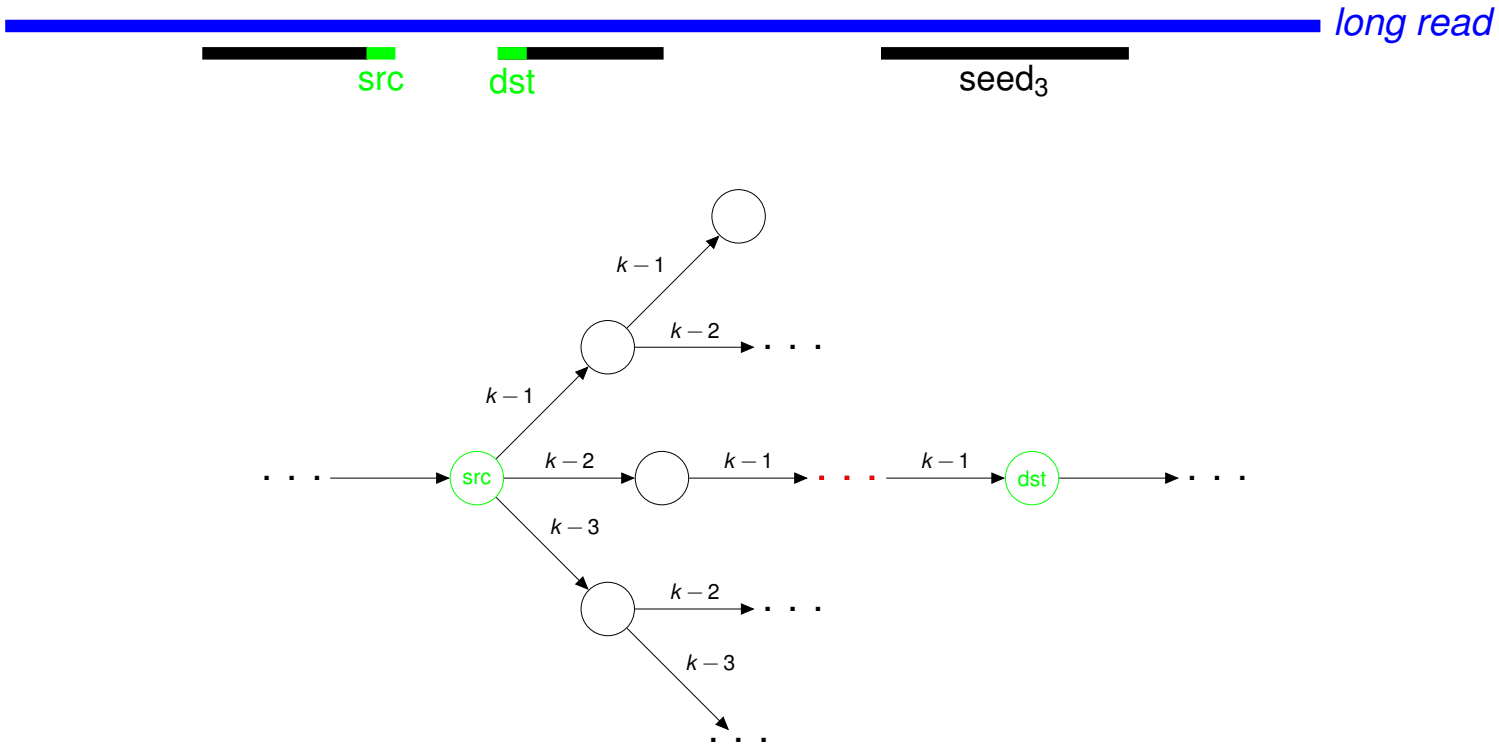

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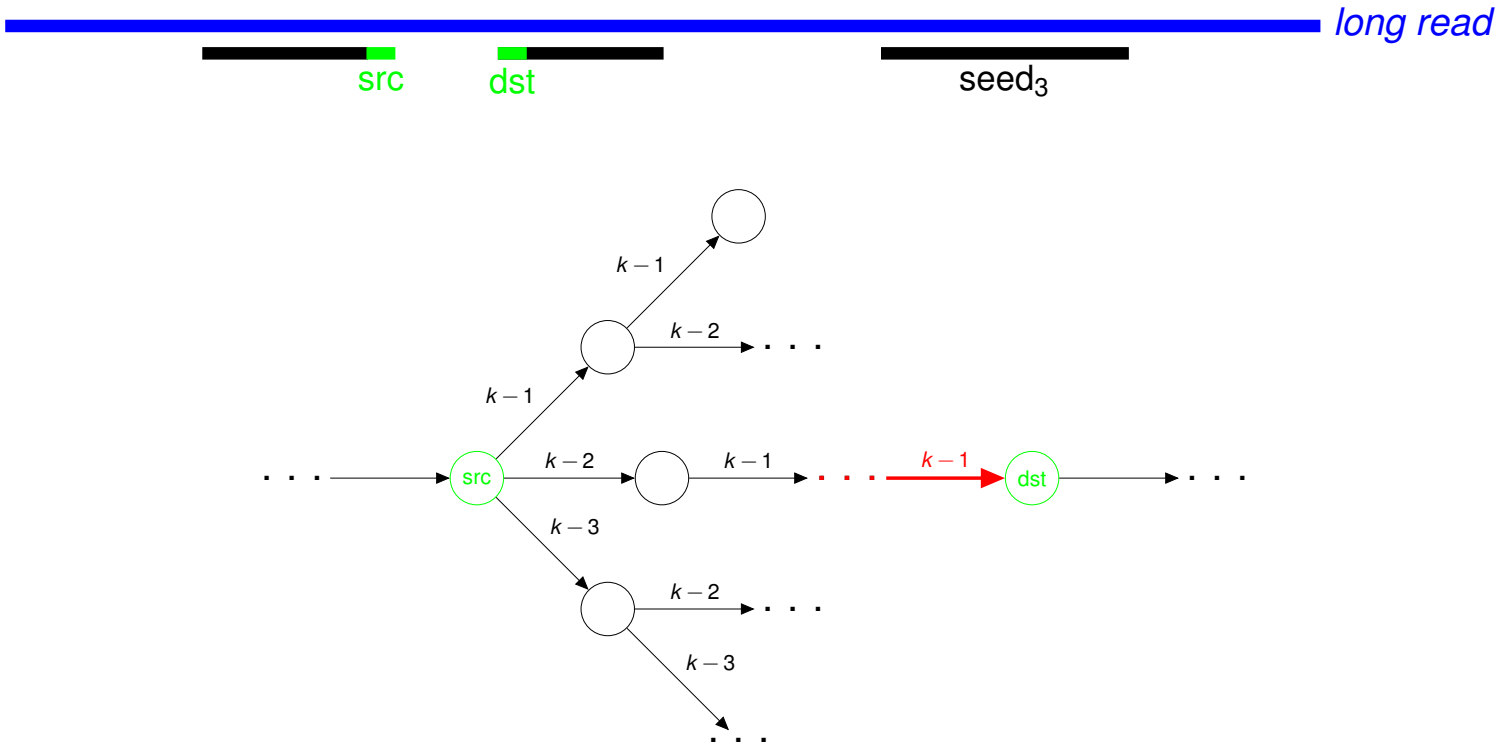

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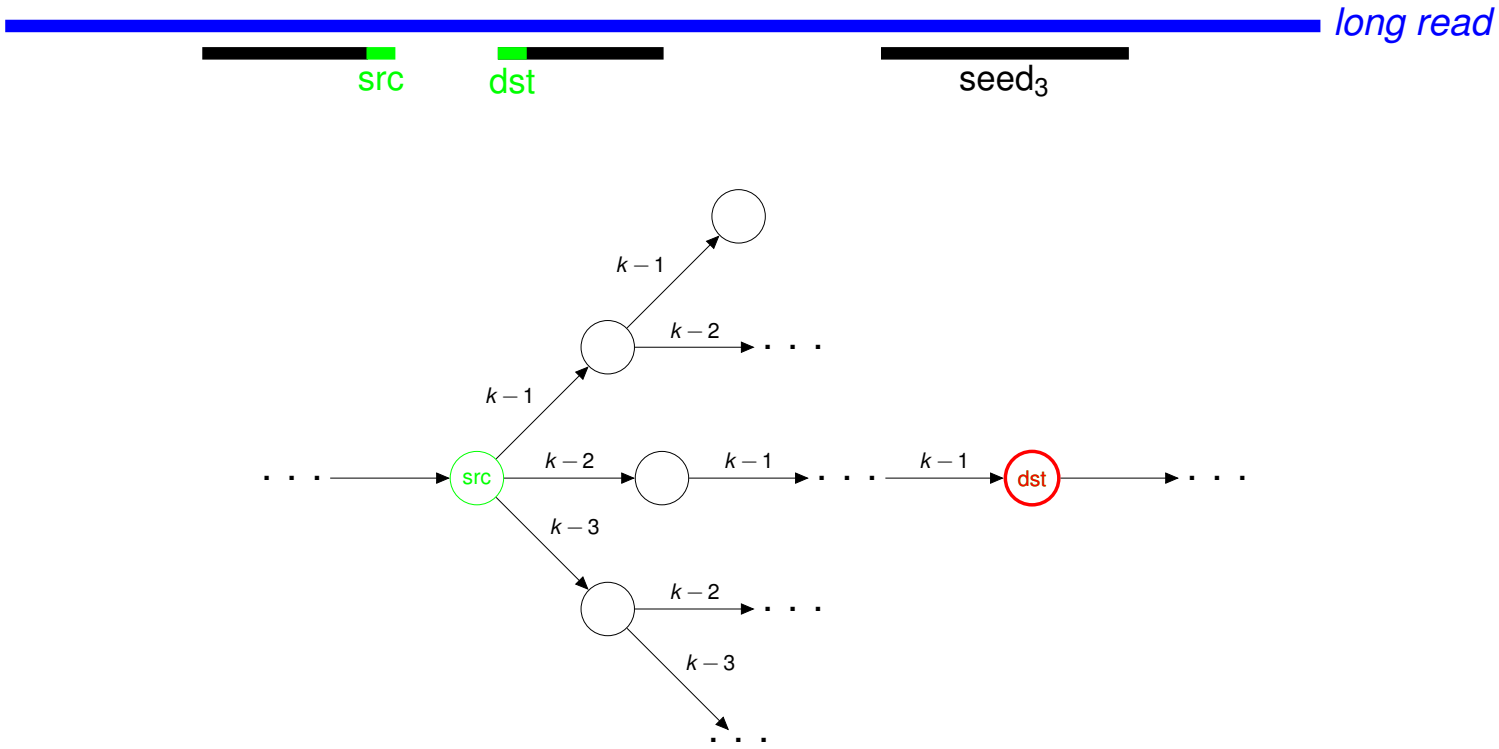

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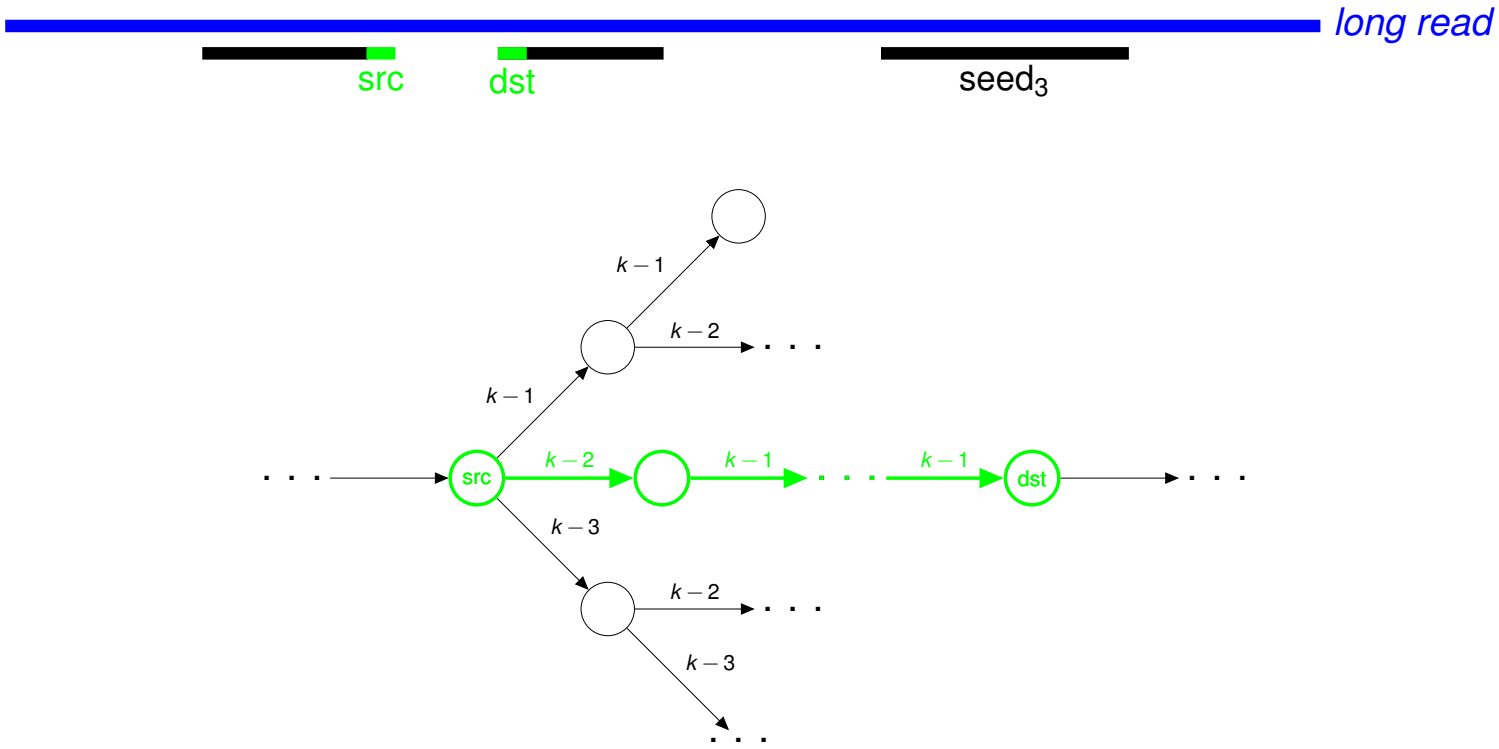

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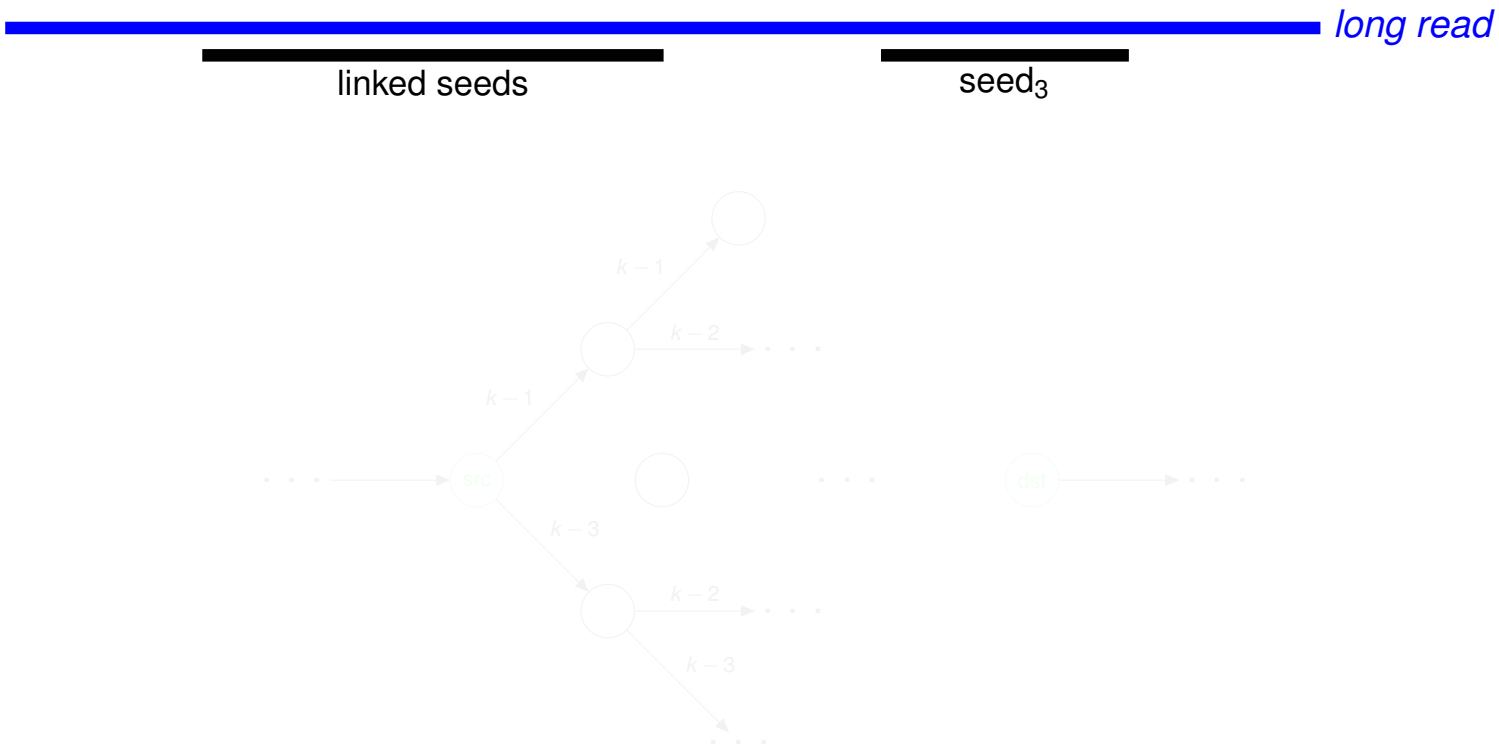

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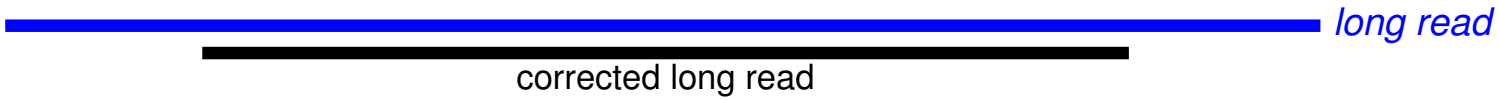

# Step 5: Tips extension

- Seeds don't always map right at the beginning or until the end of the long read
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# Remark

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# Datasets

We replaced the enhanced de Bruijn graph in the HG-CoLoR implementation with an overlap graph and with a classical de Bruijn graph, in order to compare the obtained results.

Experiments were run on the following datasets

| Dataset | Reference genome | | Oxford Nanopore data | | | Illumina data | | |
|---|---|---|---|---|---|---|---|---|
| | Name | Genome size | # Reads | Average length | Coverage | # Reads | Read length | Coverage |
| *E. coli* | *E. coli* | 4.6 Mbp | 22,270 | 5,999 | 28x | 465,000 | 300 | 30x |
| Yeast | *S. cerevisae* | 12.4 Mbp | 118,763 | 5,512 | 34x | 2,500,000 | 250 | 50x |

# Alignment-based comparison

| Dataset | Graph | # Reads | # Fragmented reads | Average length | Average identity | Runtime |
|---|---|---|---|---|---|---|
| *E. coli* | Raw reads | 22,270 | N/A | 5,999 | 79.46% | N/A |
| | Overlap graph | 19,592 | 1,319 | 5,979 | 99.91% | 40min |
| | de Bruijn graph ($k = 100$) | 21,782 | 132 | 6,144 | 99.75% | 1h53 |
| | Enhanced de Bruijn graph ($k = 100, m = 50$) | 21,786 | 40 | 6,174 | 99.72% | 1h46 |
| *Yeast* | Raw reads | 118,763 | N/A | 5,512 | 68.63% | N/A |
| | Overlap graph | 60,649 | 14,095 | 4,694 | 99.42% | 6h10 |
| | de Bruijn graph ($k = 100$) | 69,610 | 11,763 | 6,060 | 98.61% | 18h20 |
| | Enhanced de Bruijn graph ($k = 100, m = 50$) | 69,784 | 11,567 | 6,078 | 99.03% | 17h58 |

# Assembly-based comparison

| Dataset | Graph | # Expected contigs | # Obtained contigs |
|---|---|---|---|
| *E. coli* | Overlap graph | 1 | 20 |
| | de Bruijn graph ($k = 100$) | 1 | 4 |
| | Enhanced de Bruijn graph ($k = 100, m = 50$) | 1 | 1 |
| Yeast | Overlap graph | 16 | 197 |
| | de Bruijn graph ($k = 100$) | 16 | 124 |
| | Enhanced de Bruijn graph ($k = 100, m = 50$) | 16 | 103 |

# Conclusion

- We showed that multiple de Bruijn graphs of different orders can be combined into a single enhanced de Bruijn graph
- We showed how to traverse an enhanced de Bruijn graph without explicitly building it
- We introduced a new long read hybrid error correction method relying on an enhanced de Bruijn graph
- We proved the usefulness of enhanced de Bruijn graphs by comparing them with overlap graphs and classical de Bruijn graphs on the HG-CoLoR implementation
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- We introduced a new long read hybrid error correction method relying on an enhanced de Bruijn graph
- We proved the usefulness of enhanced de Bruijn graphs by comparing them with overlap graphs and classical de Bruijn graphs on the HG-CoLoR implementation
- HG-CoLoR is available from: `https://github.com/pierre-morisse/HG-CoLoR`

# Future work

- Use a greedy selection at branching paths
- Run HG-CoLoR on larger genomes
- Build a proper assembly tool relying on enhanced de Bruijn graphs
- Compare it with already existing assemblers using multiple de Bruijn graphs of different orders

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# References I


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