EVALUATION AND BENCHMARKING OF A NEW SCAFFOLDING METHODOLOGY

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Overview

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- Some definitions
- Order and orient
- Challenging problem

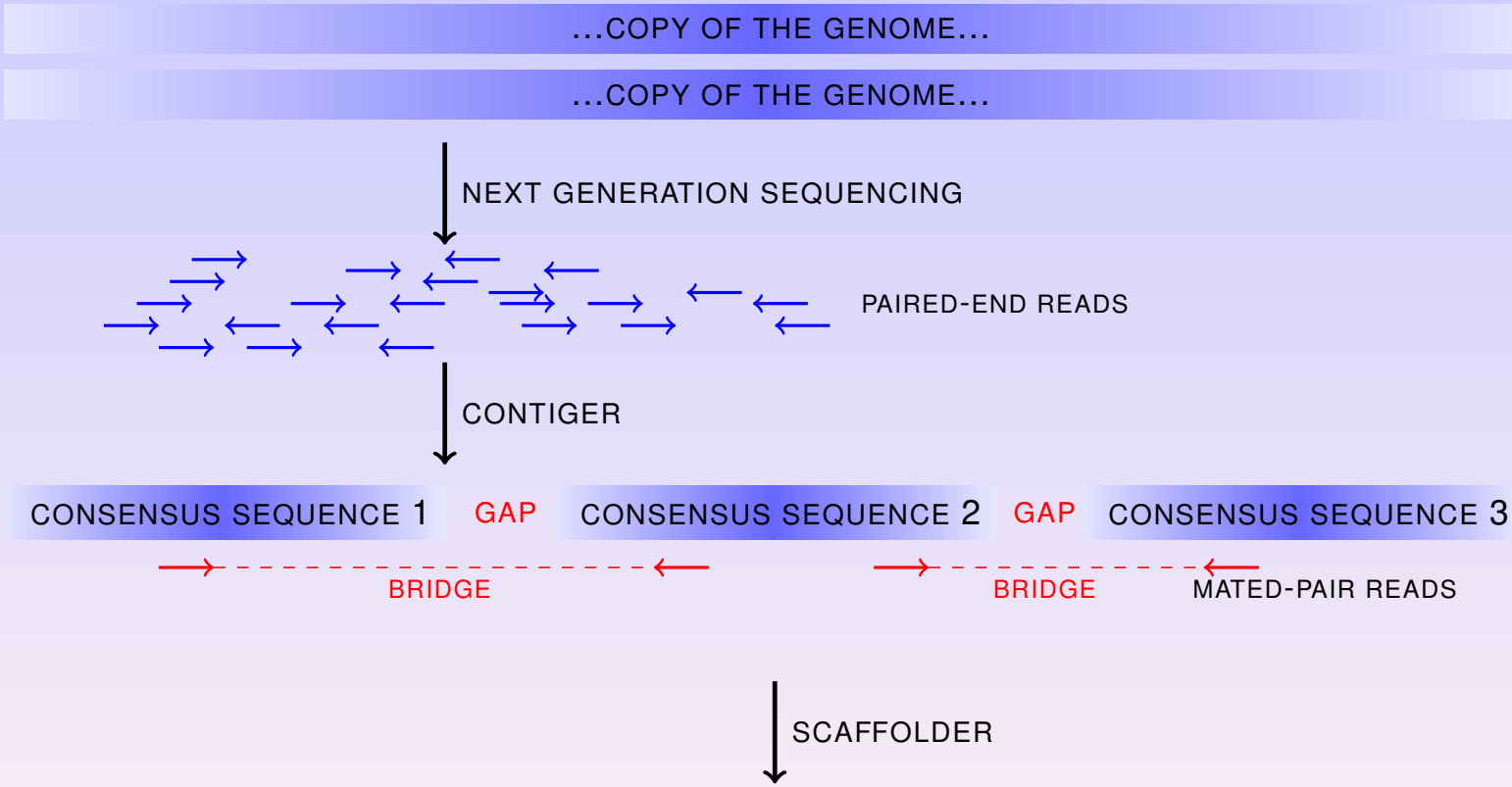
2 GST features
- Scripting for the GST
- GST modeled graph
- Expected solution
- Scaffolding solutions

3 Benchmarking workflow for the GST

4 Results
- Large repeats
- Short repeats

5 Perspectives

CONTEXT



IN THE CONTEXT OF HIGH THOUGHPUT SEQUENCING, THE SCAFFOLDING PROCESS IS A DIFFICULT TASK FOR WHICH NO WIDELY ACCEPTED METHODOLOGY EXISTS

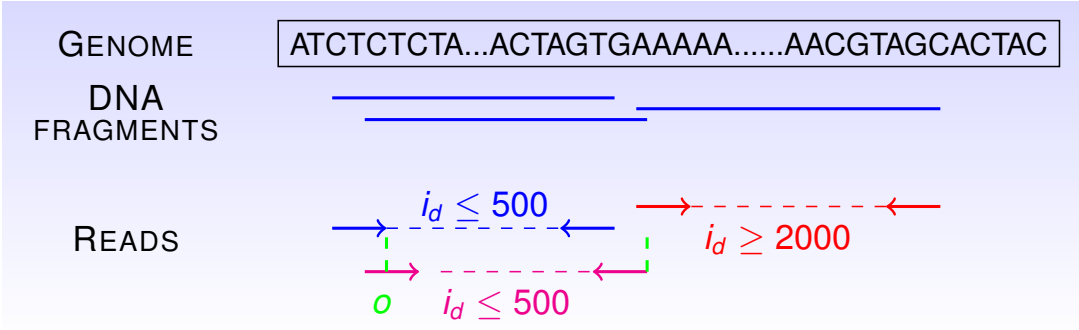
SOME DEFINITIONS

"The *Contig Scaffolding Problem* is to order and orientate the given contigs in a manner that is consistent with as many mate-pairs as possible".

Hudson *et al.* 2002

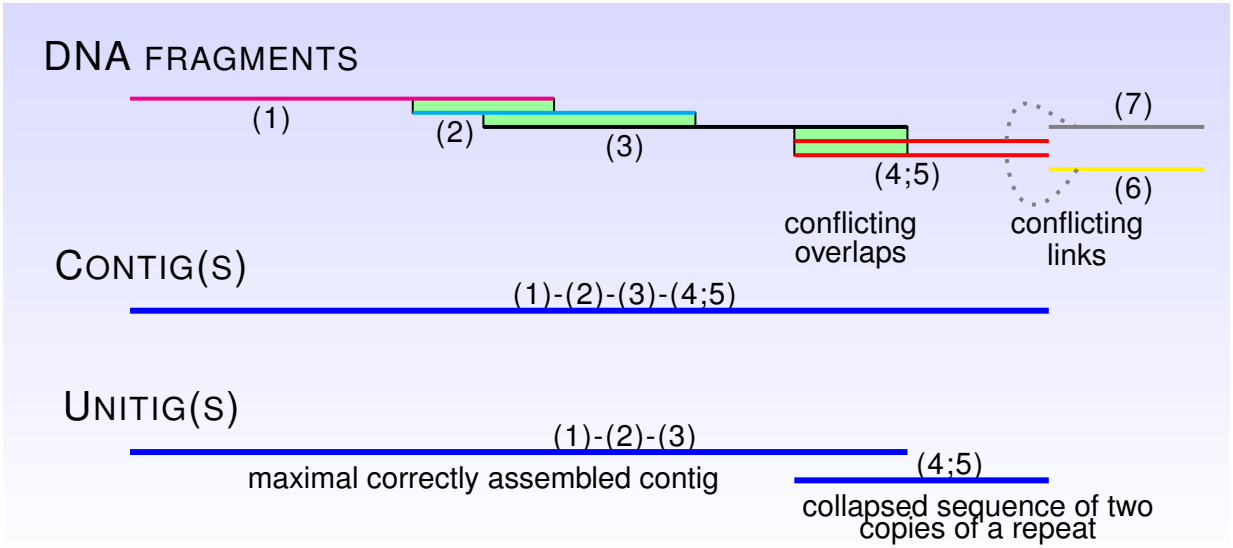
SOME DEFINITIONS

Genome is fragmented, extremities are sequenced ($\mapsto$ reads) . . .



. . . reads are assembled into consensus sequences.

UNITIGS ARE HIGH CONFIDENCE CONTIGS.



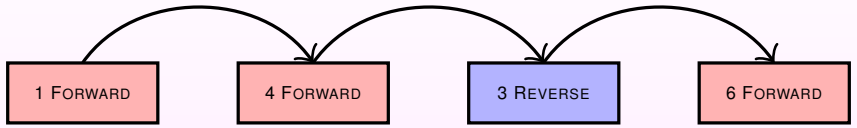
Order and orient

Mated-pair read $\mapsto$ bridge between contigs
Several correctly mapped reads $\mapsto$ link between contigs
High-confidence overlap $\mapsto$ link between contigs
All linkage information $\mapsto$ order and orient contigs

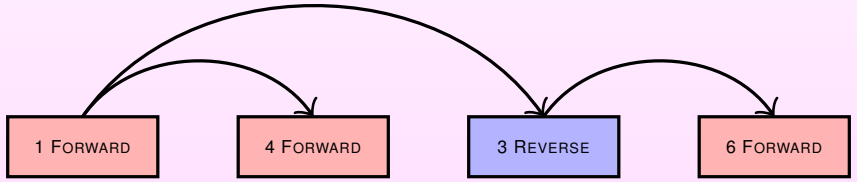
Conflicting links can and will exist.

CHALLENGING PROBLEM

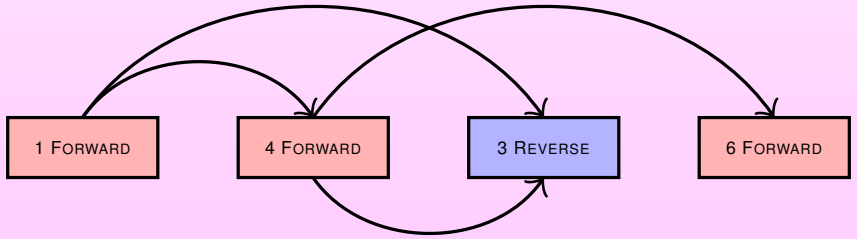
What would you do in these situations?



EASY PATH



LINK COVERAGE?



HEURISTICS...

GENSCALE SCAFFOLDING TOOLS FEATURES

SEVERAL TOOLS MODEL THE PROBLEM DIFFERENTLY.

→ common features:

- model the scaffolding problem as a graph
- use unitigs instead of contigs to better compute coverage
- use unitig coverages to duplicate nodes representing unitigs
- unitig orientations are represented by separate nodes

→ differences:

- **weighted path model** focuses solely on order and orientation
- **distance based model** incorporates link length information
- **flow model** accepts intervals for unitig coverage and link length

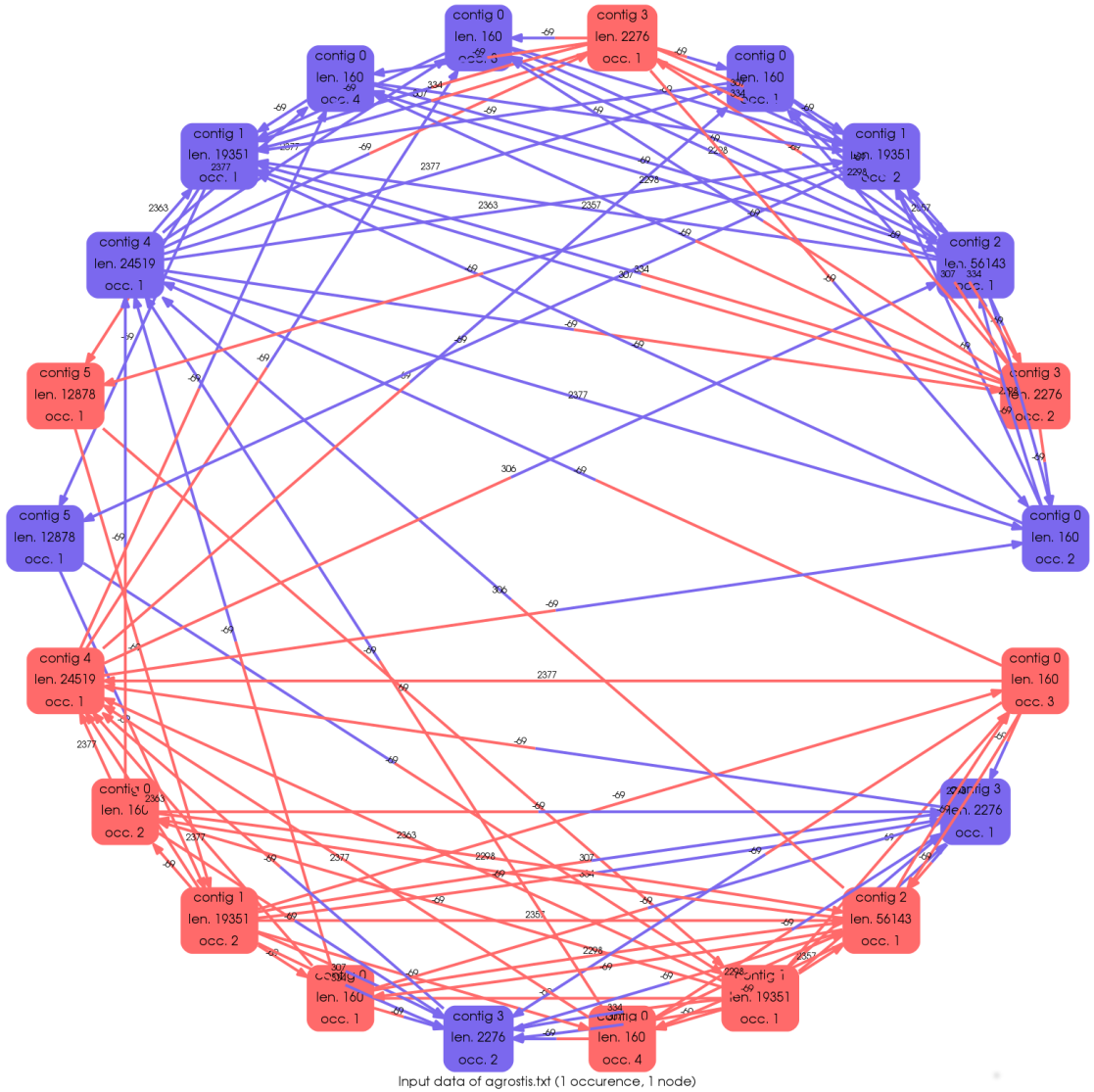
HANDLING THE MODELED GRAPHS

Automated ways to control the input data and validate the scaffolding solution:

- a script to visualize input data and GST solutions: `graph_generator.py`
- a script to inspect the features of the modeled input graph: `graph_inspector.py`
- a script to automatically detect correctly solved instances: `graph_comparator.py`

GST MODELED GRAPH

Agrostis stolonifera chpl. genome input data graph



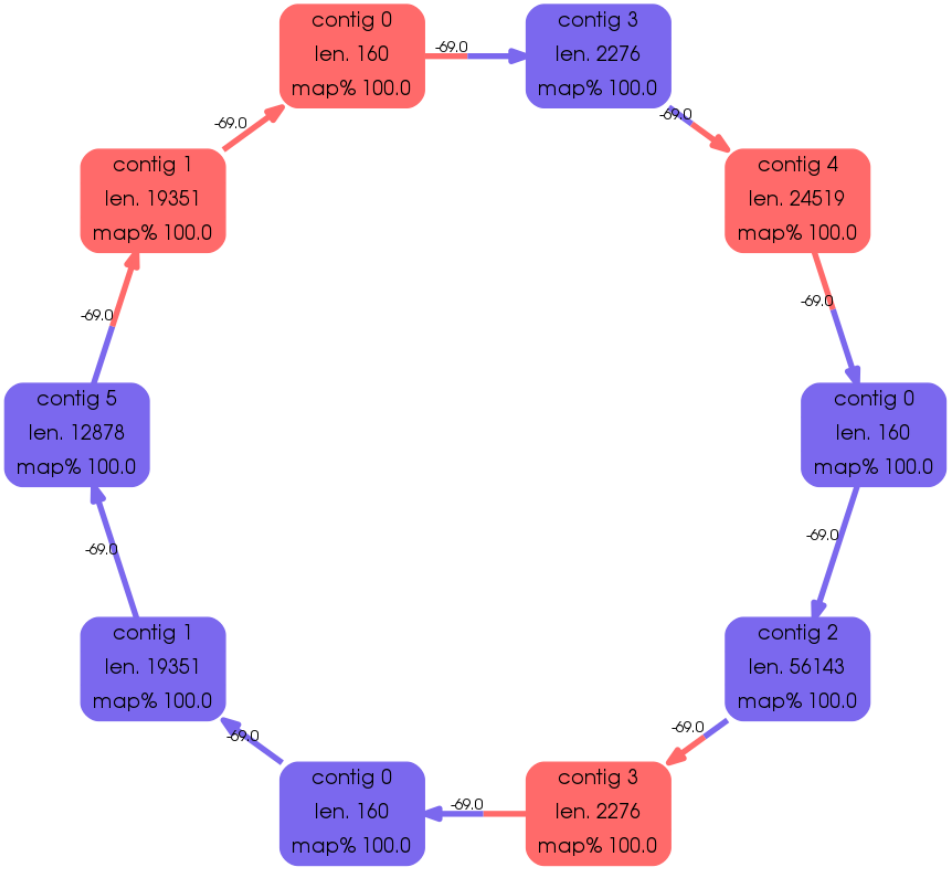
Input data of agrostis.txt (1 occurence, 1 node)

$$\sum nodes = \sum cov. \times 2$$

unitig	len	cov
1	19351	[2, 2]
0	160	[2, 4]
3	2276	[2, 2]
2	56143	[1, 1]
5	12878	[1, 1]
4	24519	[1, 1]

EXPECTED SOLUTION

Agrostis stolonifera chpl. genome expected solution



Golden standard / mapping solution of agrostis.txt (1 occurence, 1 node)

→USE UNITIGS THE RIGHT NUMBER OF TIMES IN THE CORRECT ORIENTATION

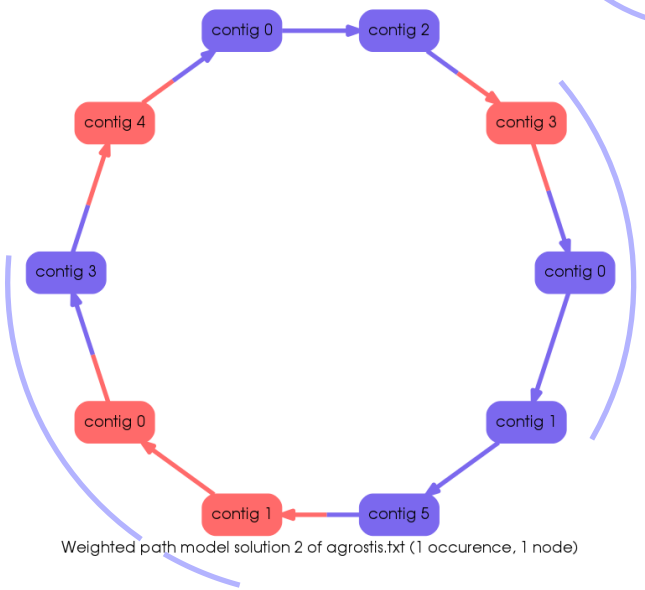
→ORDER UNITIGS TO OBTAIN AN UNINTERRUPTED CIRCULAR PATH

unitig	orient.	occ.
1	reverse	1
1	forward	1
3	reverse	1
3	forward	1
0	reverse	1
0	forward	2

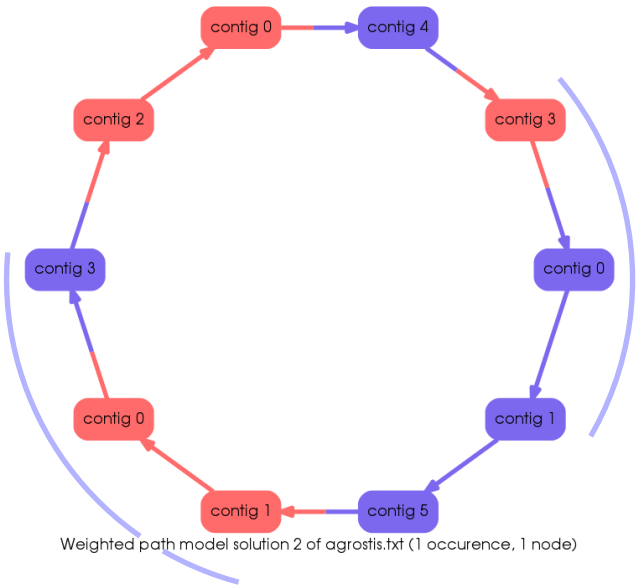
SCAFFOLDING SOLUTIONS

Agrostis stolonifera chpl. genome scaffolding solutions

UNITIGS FORMING THE INVERTED REPEATED SEQUENCE OF THE CHLOROPLASTIC GENOME ARE DUPLICATED.



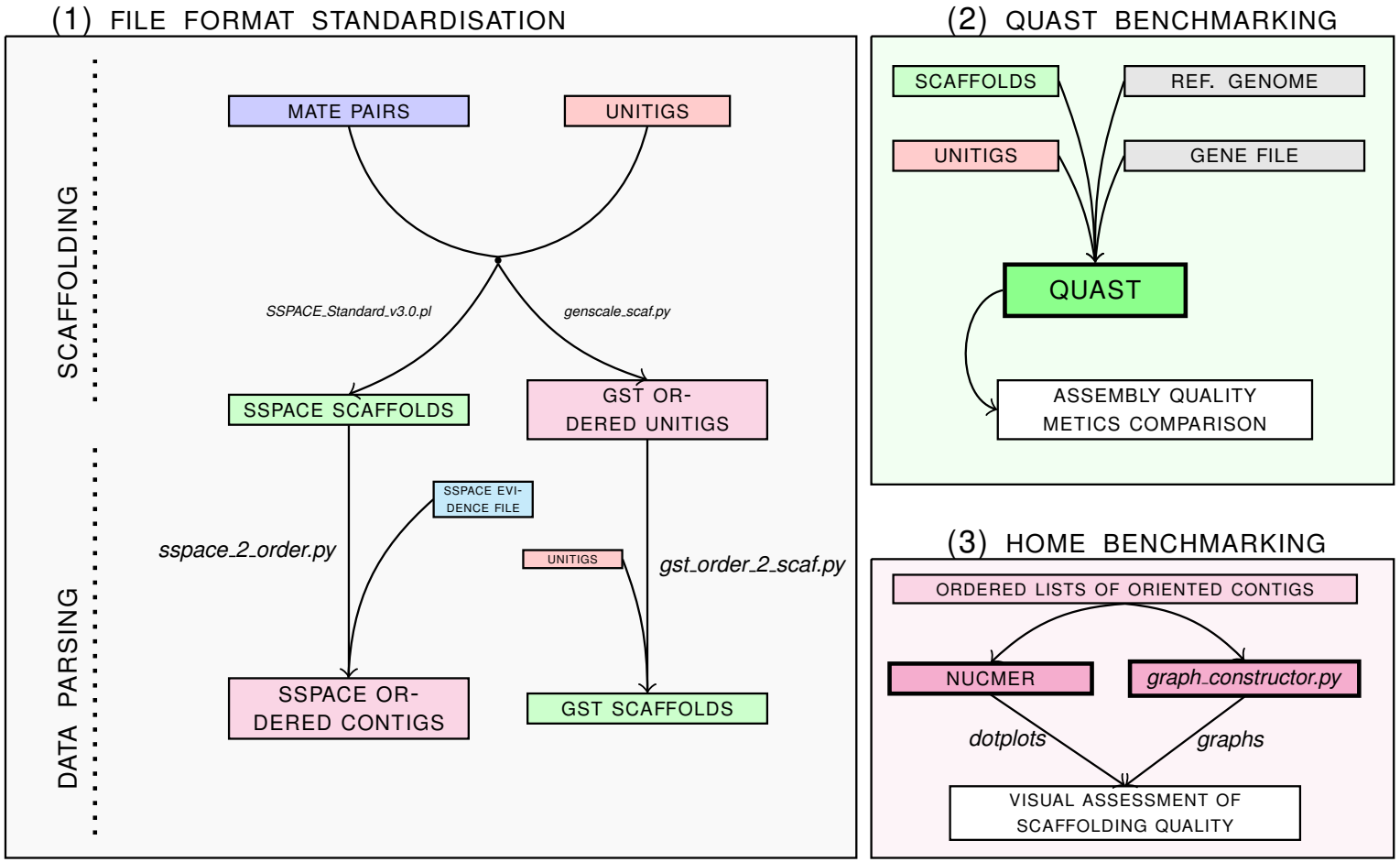
Weighted path model solution 2 of agrostis.txt (1 occurence, 1 node)



Weighted path model solution 2 of agrostis.txt (1 occurence, 1 node)

BENCHMARKING WORKFLOW FOR THE GST

SOLUTIONS FOUND WITH THE GENSCALE TOOLS ARE BENCHMARKED AGAINST THE SSPACE PUBLISHED SCAFFOLDER.



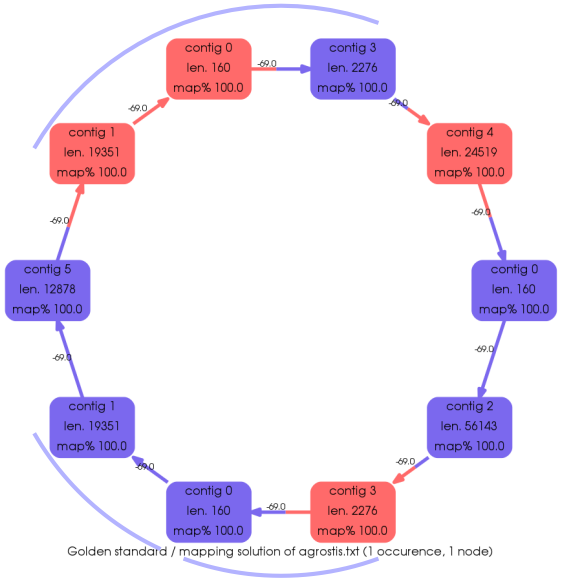
Results

Using the benchmark workflow the following conclusions were drawn:

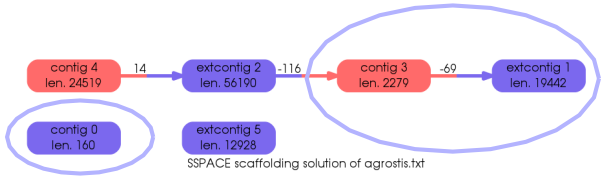
- Genomes with big repeated regions are solved a lot better with GSTs than with SSPACE
- Small repeats are very challenging to assemble because too many conflicting links exists and GST can not take a decision or is too slow
- The GST models processing the link sequence length information perform worse than those focusing only on ordering and orientating

LARGE REPEATS - CHLOROPLASTIC GENOMES

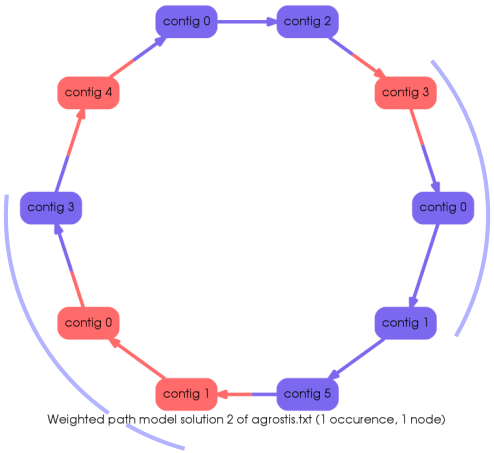
EXCELLENT RESULTS ARE OBTAINED FOR DATA SETS WITH LARGE REPEATS AND A SMALL NUMBER OF UNITIGS.



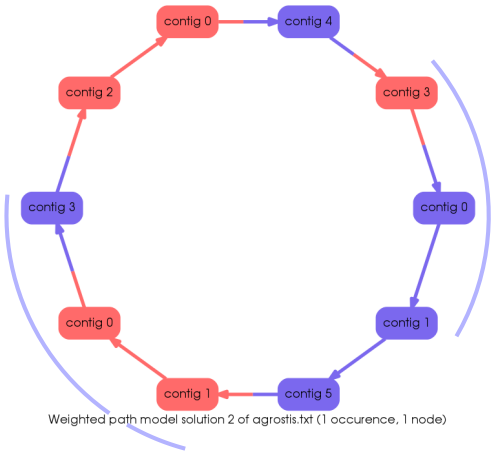
Golden standard / mapping solution of agrostis.txt (1 occurence, 1 node)



SSPACE scaffolding solution of agrostis.txt



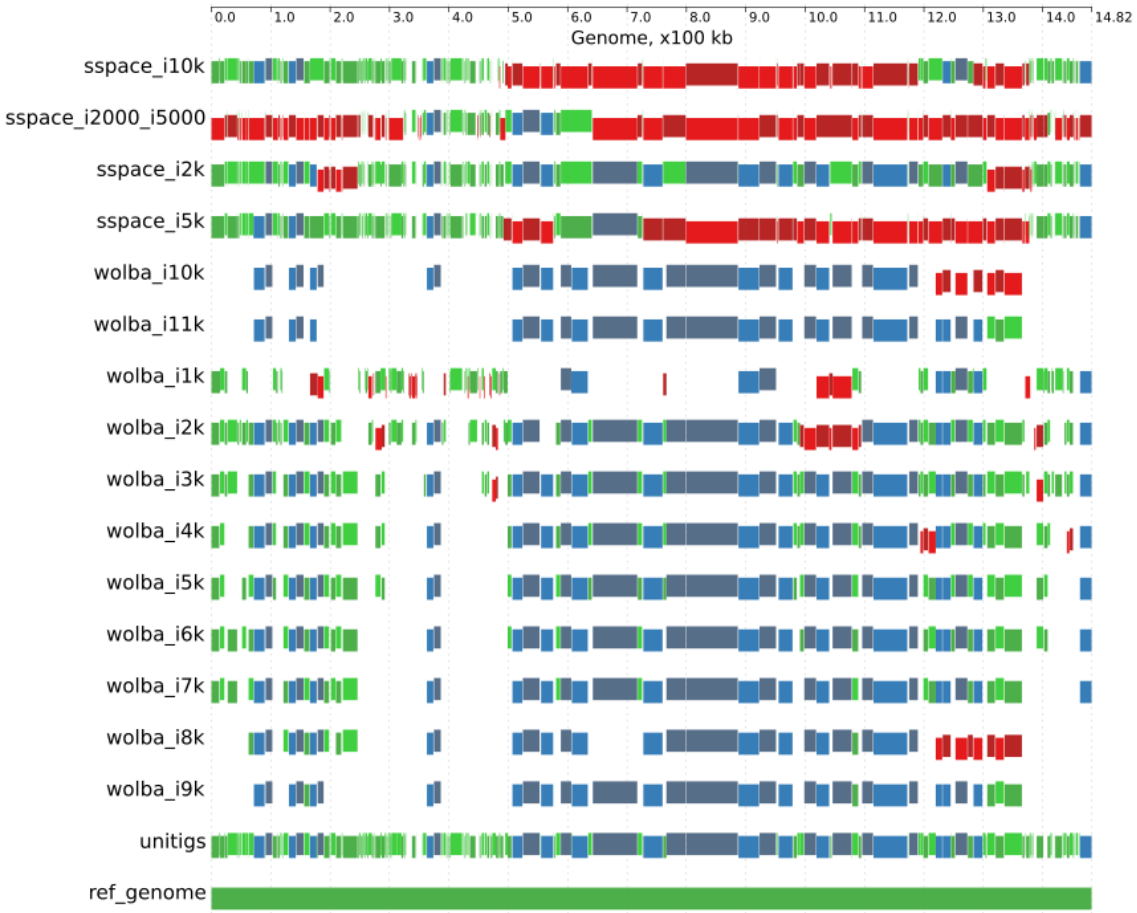
Weighted path model solution 2 of agrostis.txt (1 occurence, 1 node)



Weighted path model solution 2 of agrostis.txt (1 occurence, 1 node)

Short repeats - bacterial genomes

Small repeats are problematic starting from the unitig building step.
The Wolbachia Endosymbiont organism possesses 444 unitigs and only 138 are longer than 1000 base pairs.



PERSPECTIVES

DEVELOP - TEST - BENCHMARK

- Find strategies which solve more challenging data
  $\rightarrow$ flow model in development
- Benchmark against other tools trying to solve repeated regions
- Test the GST with real data
- Test the GST with other genome sequencing data types

THANK YOU FOR YOU ATTENTION

SCAFFOLDING: SAFETY COMES FIRST