GOETHE UNIVERSITÄT FRANKFURT AM MAIN

Assembly of long, error-prone reads using repeat graphs

Mikhail Kolmogorov, Jeffrey Yuan, Yu Lin and Pavel A. Pevzner

July 5, 2021

Presented by: Johannes Hausmann, Luis Kress

Background

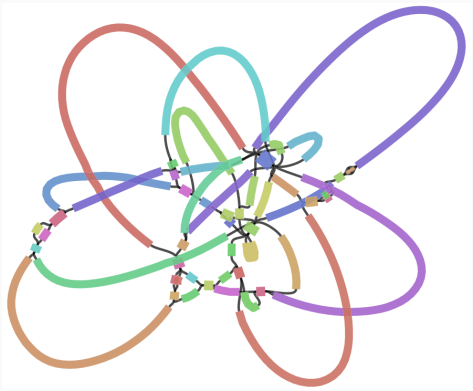
- Assembly: reconstruct target sequence from the reads

Background

- Assembly: reconstruct target sequence from the reads
- Different assemblers, different graph structures

Background

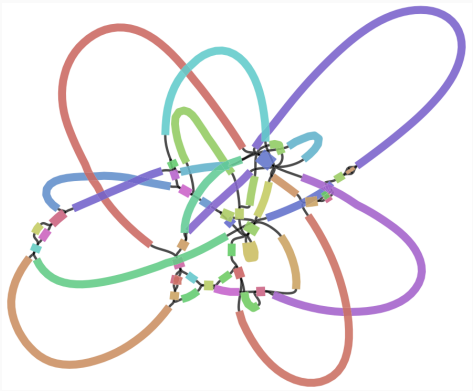
- Assembly: reconstruct target sequence from the reads
- Different assemblers, different graph structures
- Repeats $\rightarrow$ assembly fragmentation



Tangled assembly graph of *E.coli* [1]

Background

- Assembly: reconstruct target sequence from the reads
- Different assemblers, different graph structures
- Repeats $\rightarrow$ assembly fragmentation



Tangled assembly graph of *E.coli* [1]

- Small differences between repeat copies $\rightarrow$ hard to resolve with error-prone reads

Disjointigs

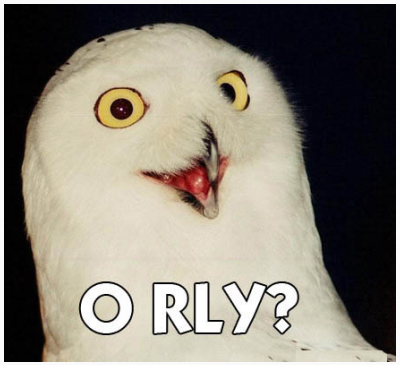
- Most assemblers spend much time on correct contig assembly

Disjointigs

- Most assemblers spend much time on correct contig assembly
- Flye uses a different approach [1]:

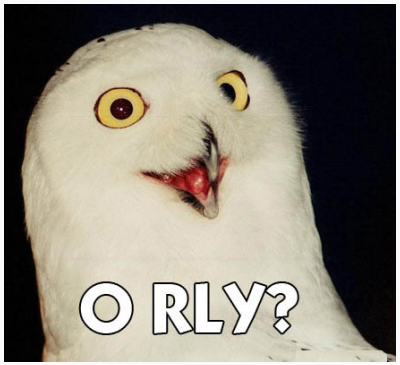
Disjointigs

- Most assemblers spend much time on correct contig assembly
- Flye uses a different approach [1]:
  - we don't care about the correct contig assembly



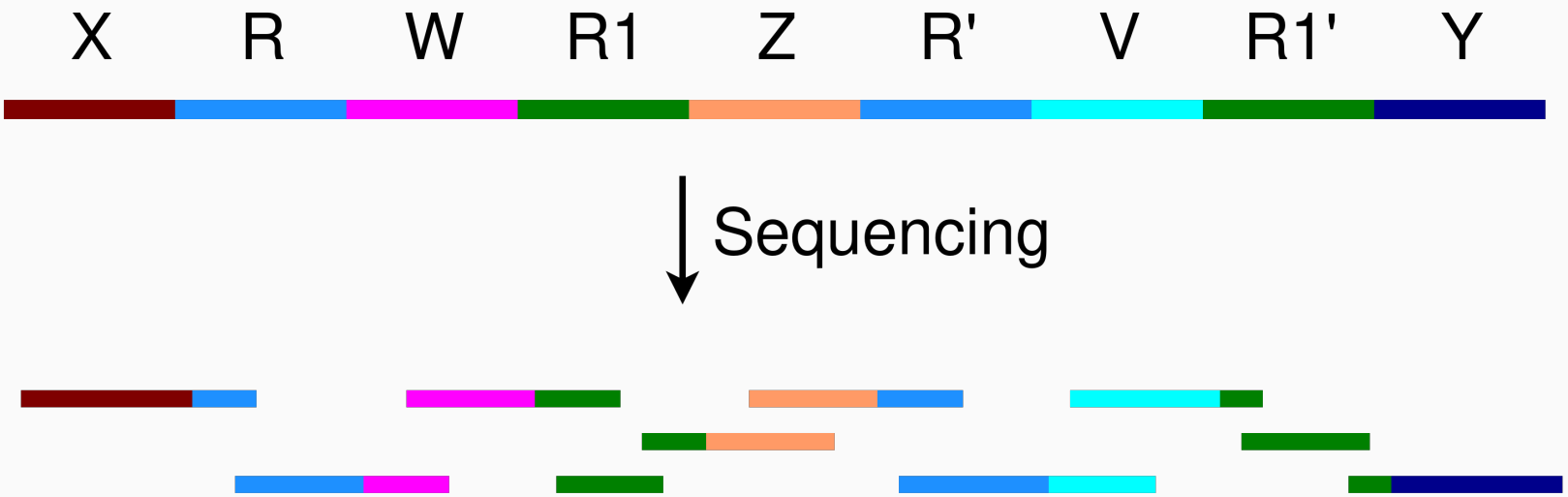
Disjointigs

- Most assemblers spend much time on correct contig assembly
- Flye uses a different approach [1]:
  - we don't care about the correct contig assembly (at least at the initial stage)

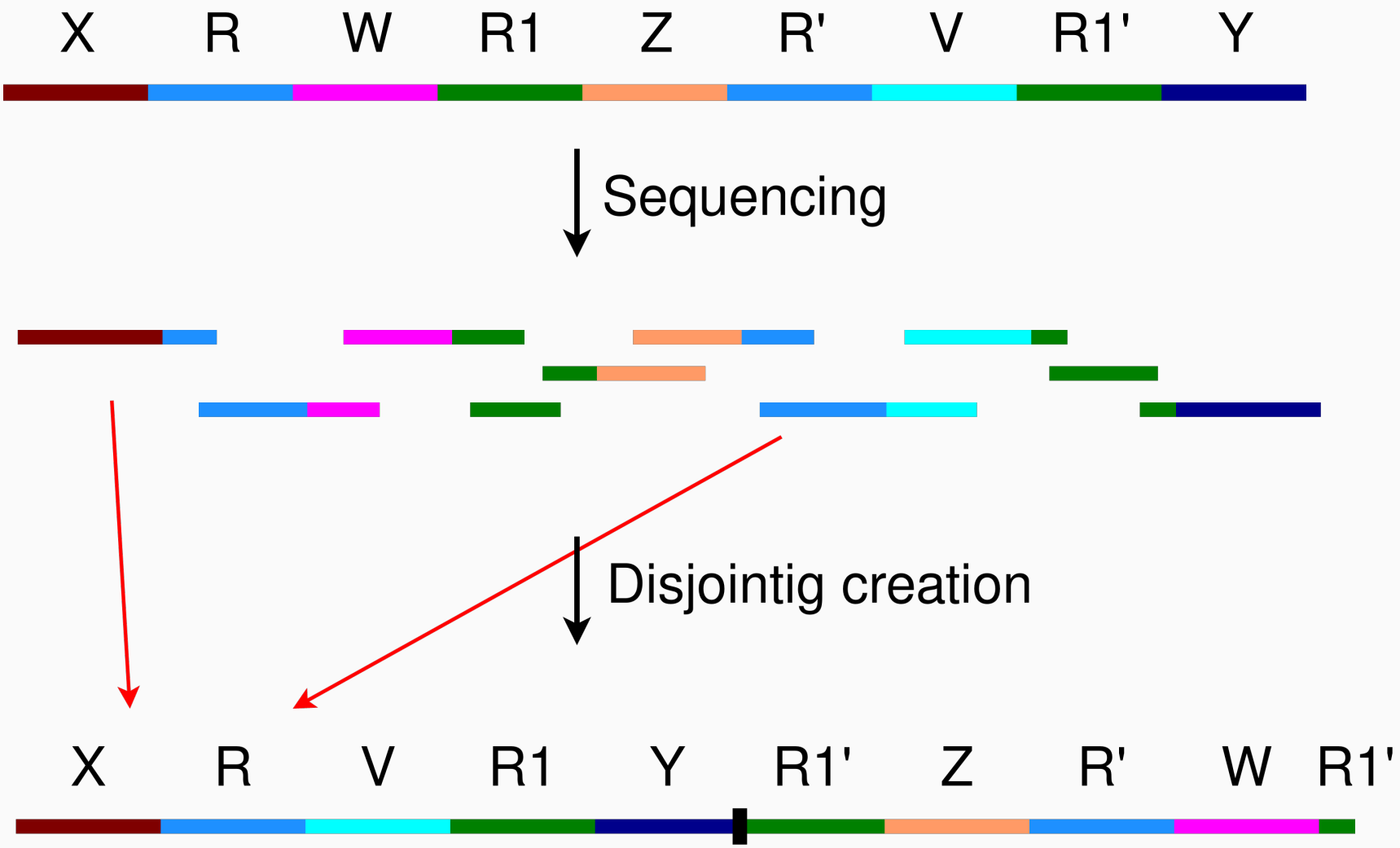


- Generate arbitary paths from overlapping reads $\rightarrow$ Disjointigs

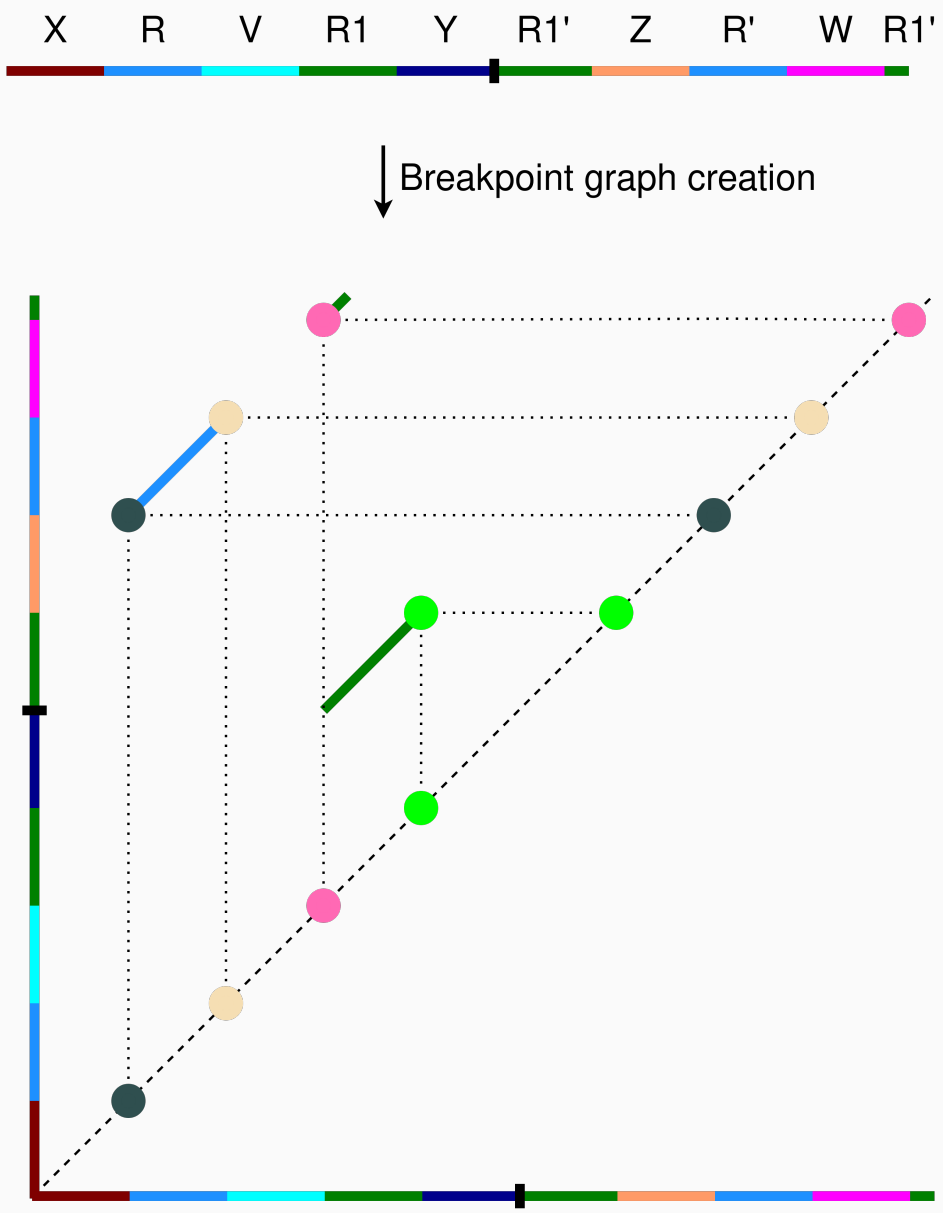
Repeat Graph Creation



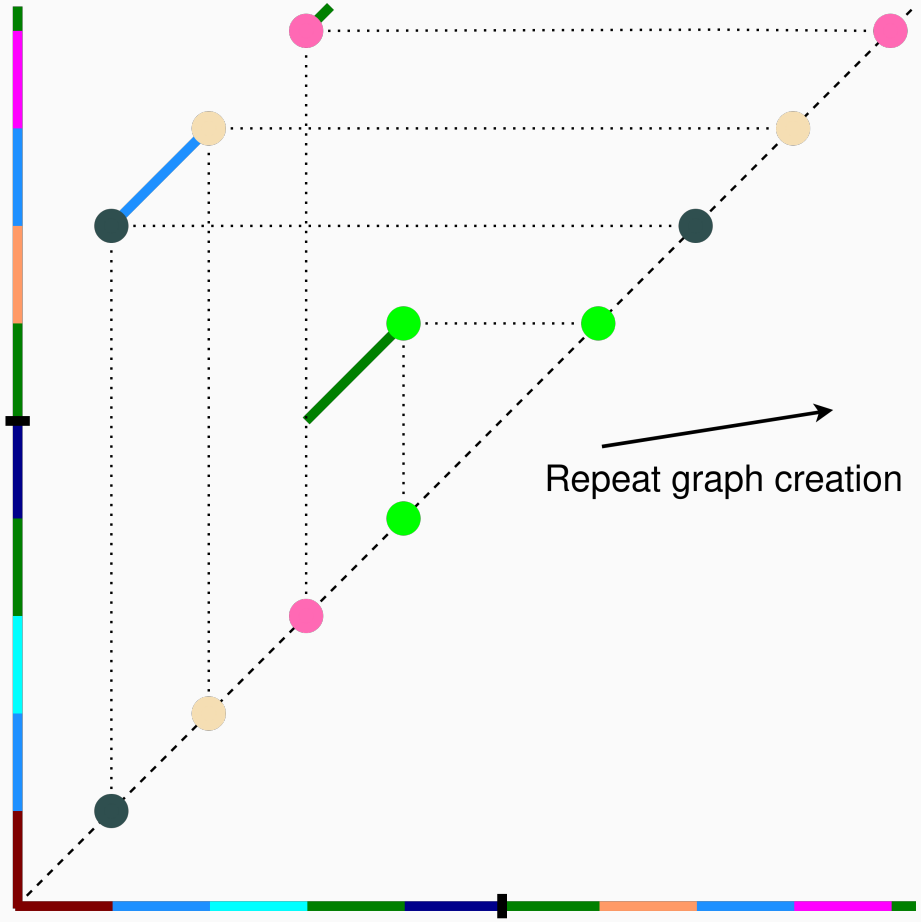
Repeat Graph Creation



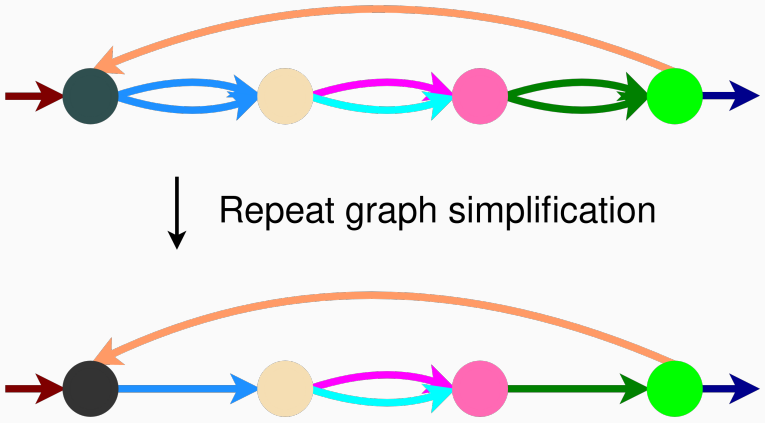
Repeat Graph Creation



Repeat Graph Creation



Repeat graph creation



Results

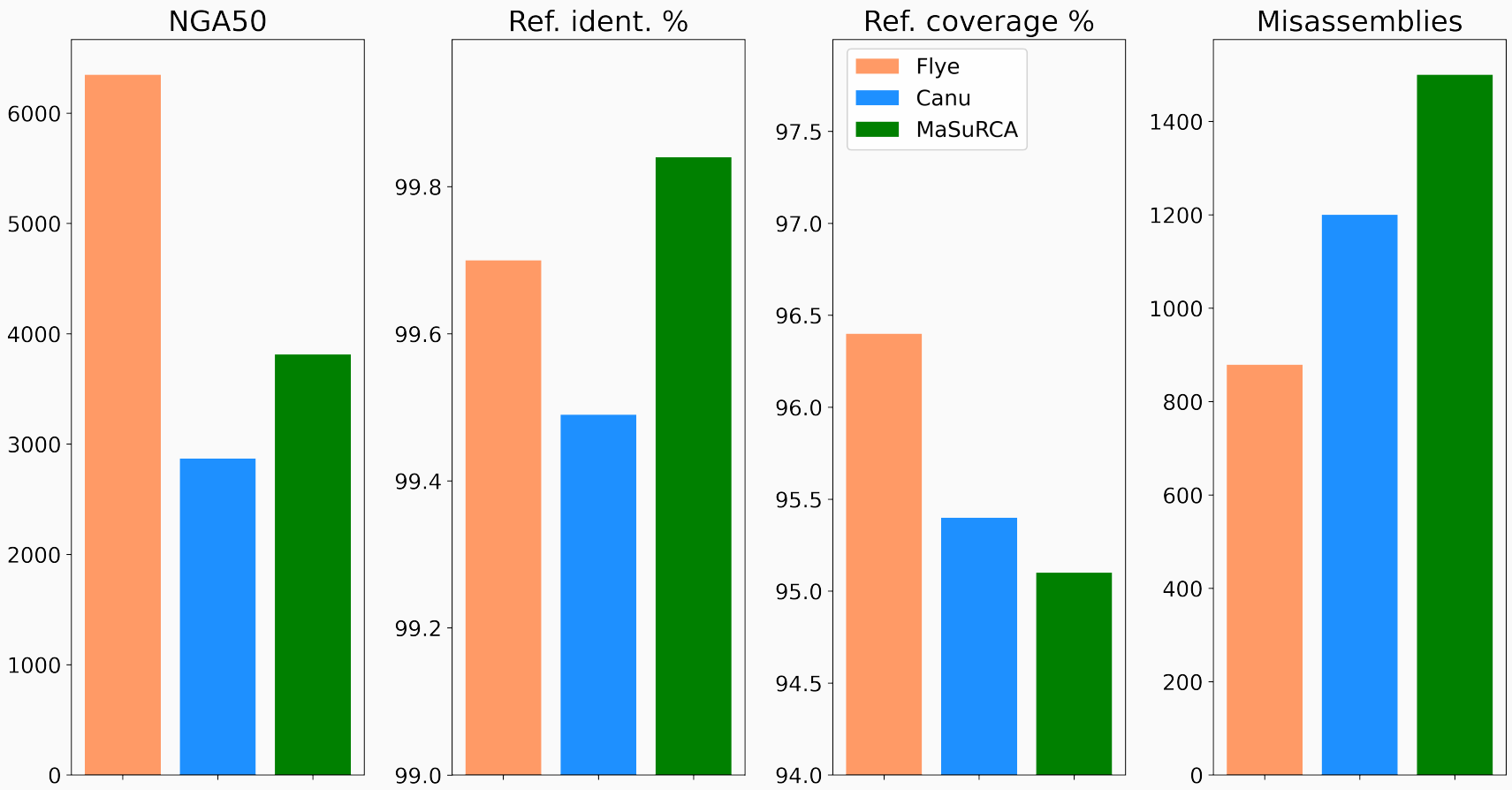


Figure 1: Results for HUMAN testset

Git (presentation and poster)

https://github.com/LKress/ASA

References i


M. Kolmogorov, J. Yuan, Y. Lin, and P. A. Pevzner.
Assembly of long, error-prone reads using repeat graphs.
Nature Biotechnology, 37(5):540–546, May 2019.


Y. Lin, S. Nurk, and P. A. Pevzner.
What is the difference between the breakpoint graph and the de Bruijn graph?
BMC genomics, 15 Suppl 6:S6, 2014.


P. A. Pevzner, P. A. Pevzner, H. Tang, and G. Tesler.
De novo repeat classification and fragment assembly.
Genome Research, 14(9):1786–1796, Sept. 2004.

References ii


B. J. Walker, T. Abeel, T. Shea, M. Priest, A. Abouelliel, S. Sakthikumar, C. A. Cuomo, Q. Zeng, J. Wortman, S. K. Young, and A. M. Earl.
Pilon: an integrated tool for comprehensive microbial variant detection and genome assembly improvement.
PloS One, 9(11):e112963, 2014.

GOETHE UNIVERSITÄT FRANKFURT AM MAIN

Assembly of long, error-prone reads using repeat graphs

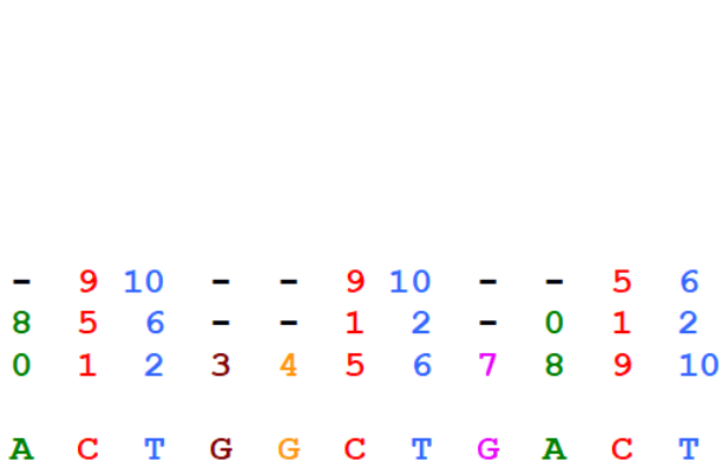
Mikhail Kolmogorov, Jeffrey Yuan, Yu Lin and Pavel A. Pevzner

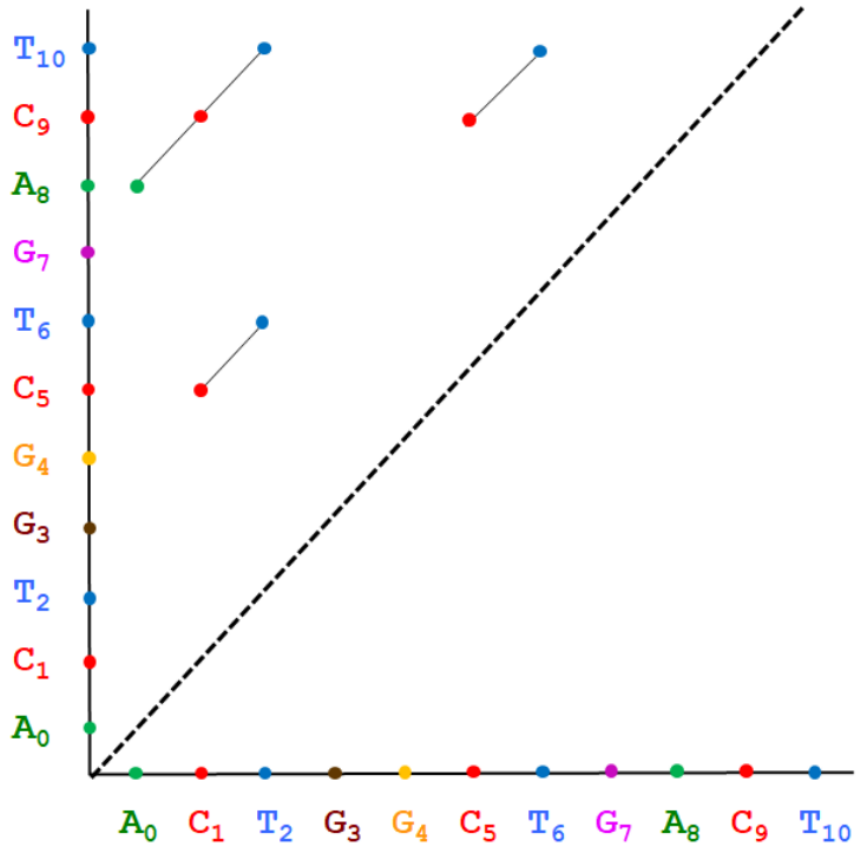
July 5, 2021

Presented by: Johannes Hausmann, Luis Kress

Appendix

Dot plot creation





Dot plot creation [1]

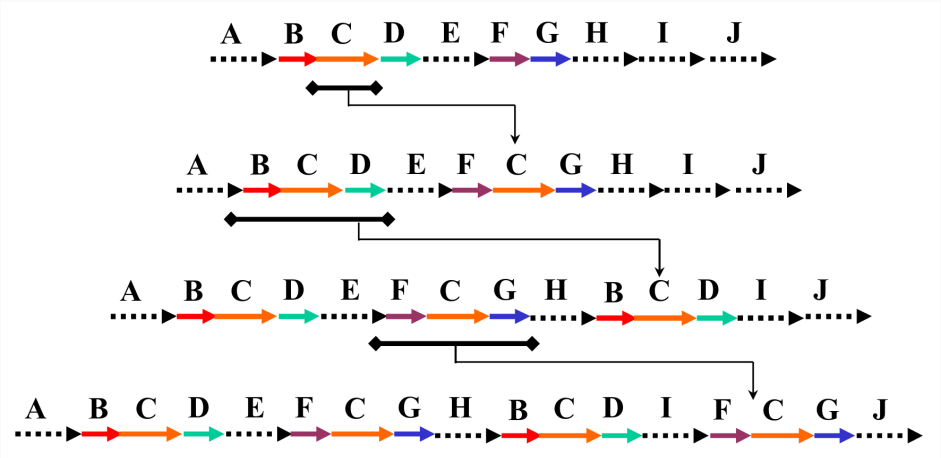
Repeat graphs

- generalization of de Bruijn graphs
- structure
- creation
  - from disjointigs = random walk of reads on the repeat graph
  - means the repeat graph hasn't to be known
  - set of disjointigs of a genome is complete if each k+1-mer from the genome is present in a disjointig from this set $\rightarrow$ repeat graph conctruction of complete set of disjointigs same result as repeat graph construction of the genome

Difference repeat graph de Bruijn graph

- A-Bruijn graph (alignments) generalizes the de Bruijn graph
- "We thus argue that the time has come to explain that the breakpoint graphs and the de Bruijn graphs are two identical data structures (if one ignores a cosmetic difference between them) as they both represent specific instances of a general notion of the A-Bruijn graph introduced in [2]. The A-Bruijn graphs are based on representing genomes as sets of labeled paths and further gluing identically labeled edges (breakpoint graphs) or vertices (de Bruijn graphs) in the resulting paths." [3]
- de Bruijn graphs need correct bases
- otherwise tangled graph

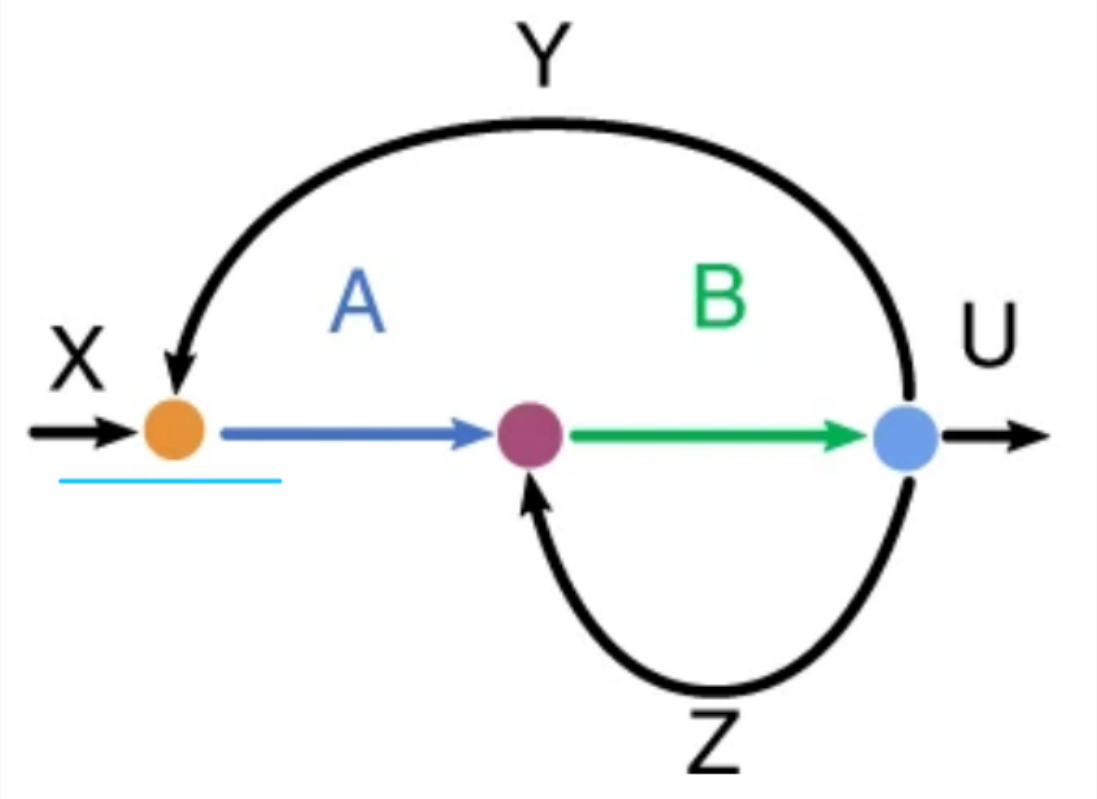
Segmental duplications



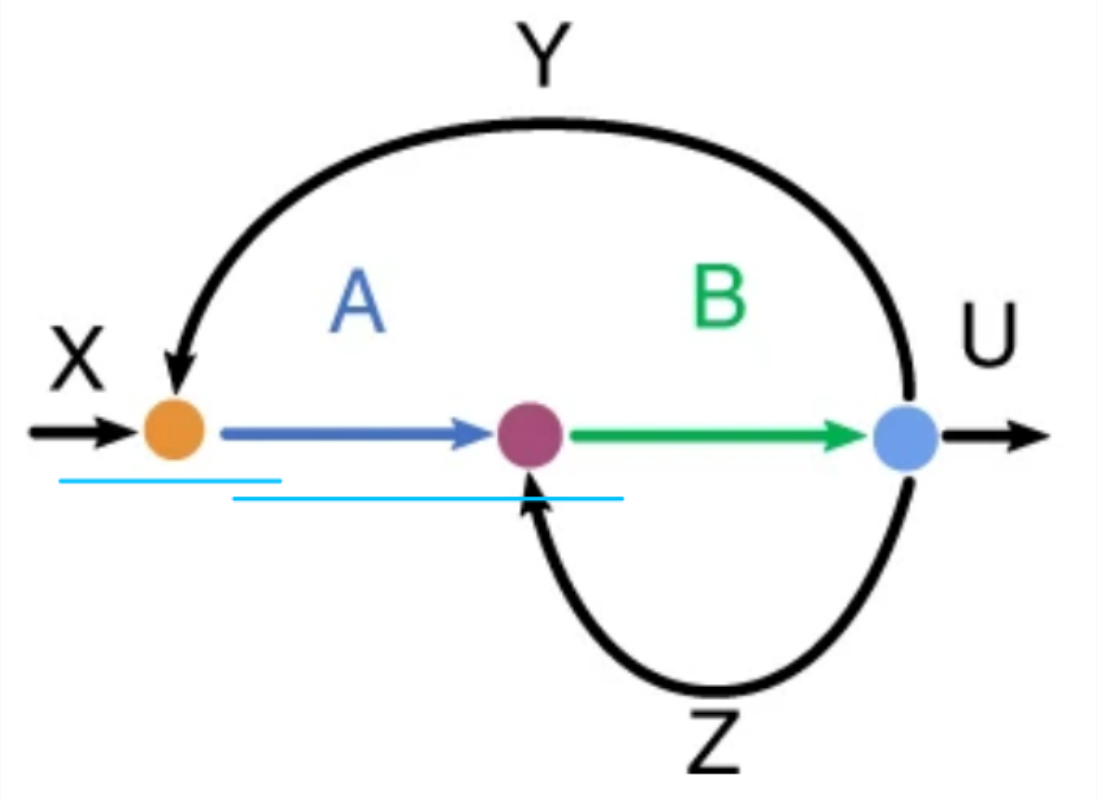
Segmental Duplications [3]

- Segmental duplications are duplicated blocks of genomic DNA typically ranging in size from 1-200 kb (IHGSC 2001)
- They often contain sequence features such as high-copy repeats and gene sequences with intron-exon structure.

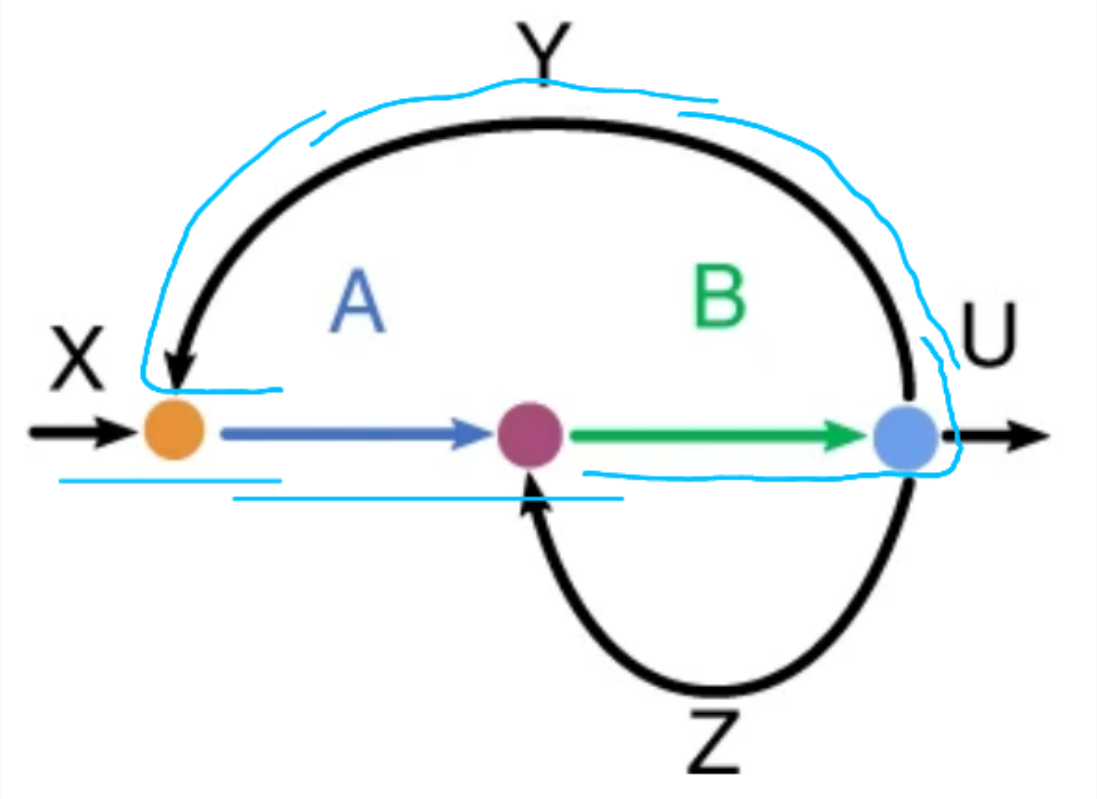
Disjointig creation



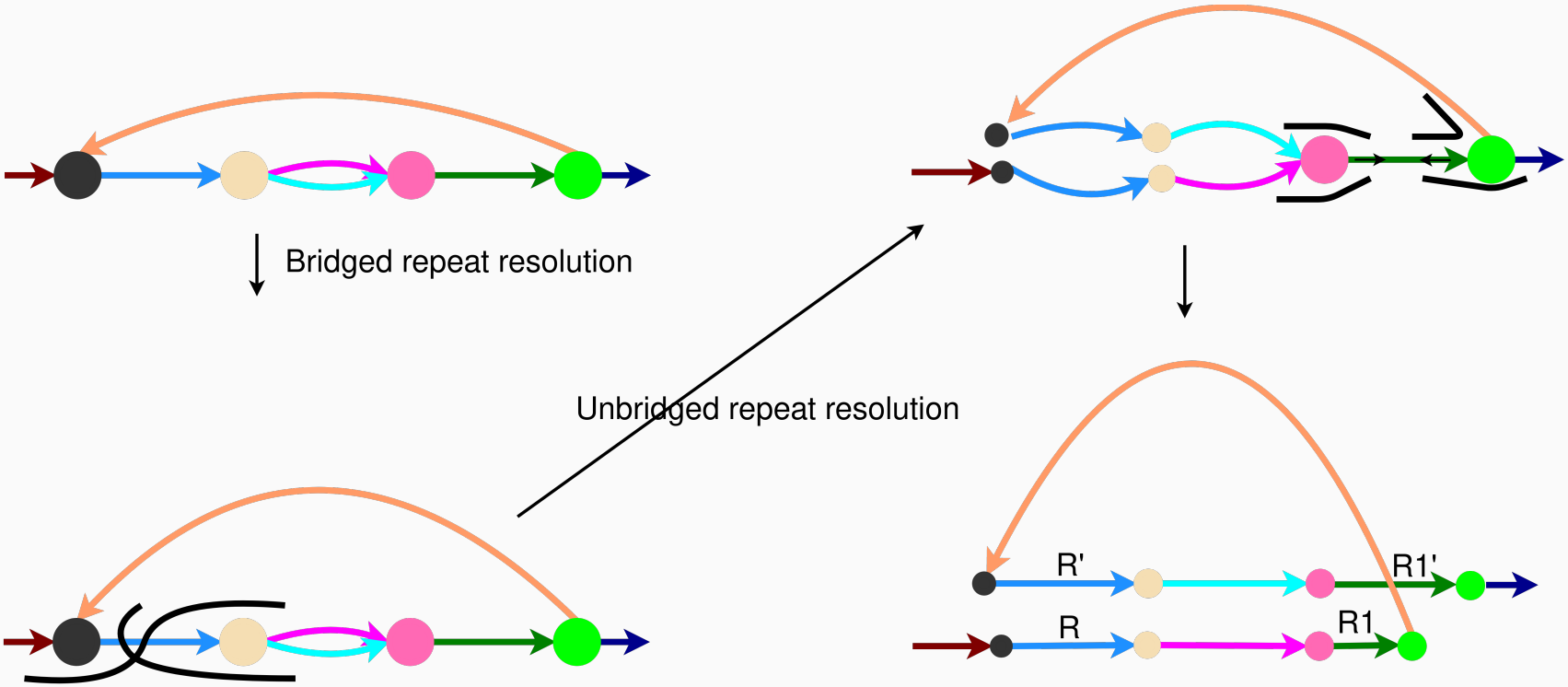
Disjointig creation



Disjointig creation



Repeat resolution



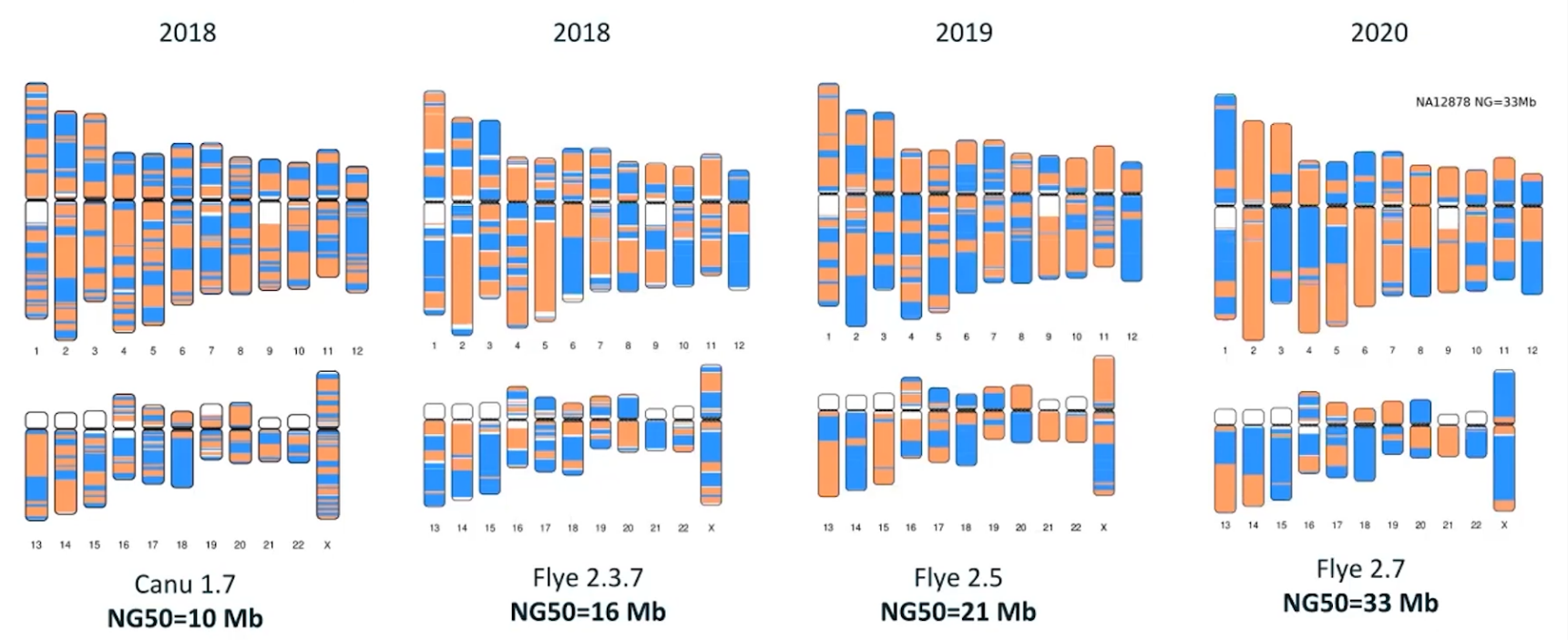
Repeat resolution of the given example [1]

Repeat resolution

"Pilon is a software tool which can be used to automatically improve draft assemblies or to find variation among strains, including large event detection. Pilon requires as input a FASTA file of the genome along with one or more BAM files of reads aligned to the input FASTA file. Pilon uses read alignment analysis to identify inconsistencies between the input genome and the evidence in the reads. It then attempts to make improvements to the input genome, including" [4]:

- Single base differences
- Small indels
- Larger indel or block substitution events
- Gap filling
- Identification of local misassemblies, including optional opening of new gaps

Contigity improvement



Contigity improvements (M. Kolmogorov, personal communication, 29.07.2021)

- colors are contigs $\rightarrow$ change in color means fragmentation