Tigmint

Correcting Misassemblies Using Linked Reads From Large Molecules

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RECOMB-Seq 2018-04-20
https://sjackman.ca/tigmint-recomb-slides
Funded by Genome Canada · Genome BC · NIH · NSERC

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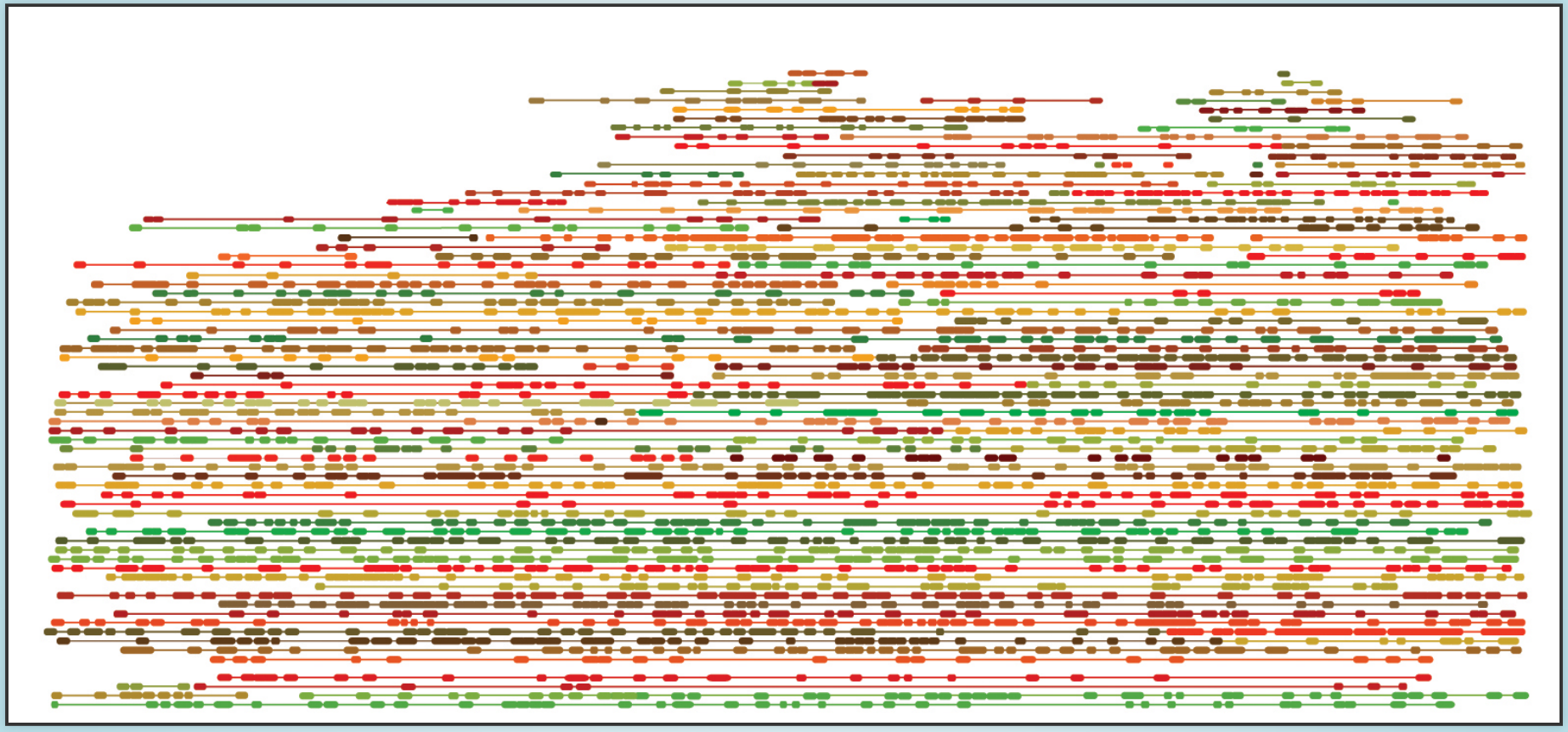
Linked Reads



Tools for Linked Reads

Align linked reads
Lariat (Long Ranger) · EMA
Structural variants
Long Ranger · GROC-SVs · NAIBR · SVenX · Topsorter
Phase variants
Long Ranger
Genome sequence assembly
Supernova
Scaffolding
ARCS · Architect · Fragscaff · Scaff10x

https://github.com/johandahlberg/awesome-10x-genomics

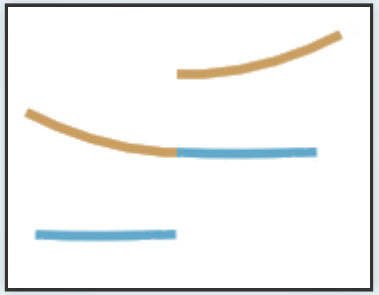
Contigs and scaffolds come to an end due to...

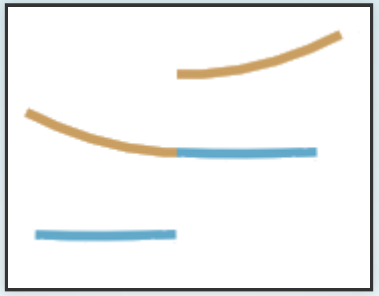
- repeats
- sequencing gaps
- structural variation
- misassemblies

Misassemblies limit contiguity

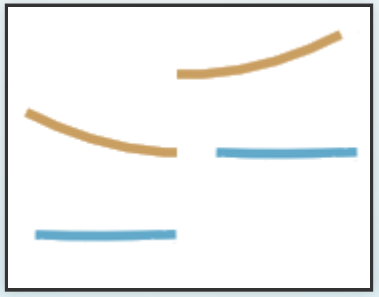
particularly for highly contiguous assemblies.

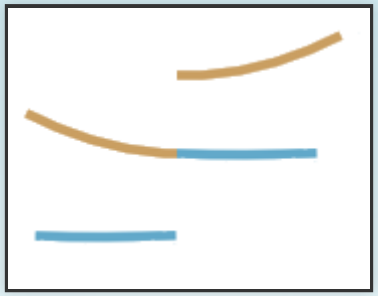
Most scaffolding tools do not correct misassemblies.



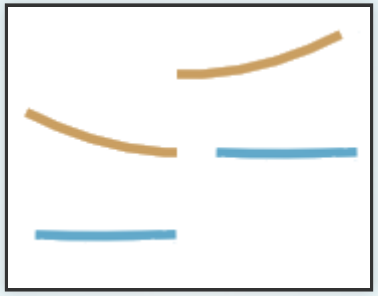


Correct misassemblies

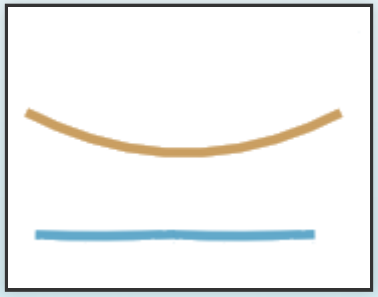




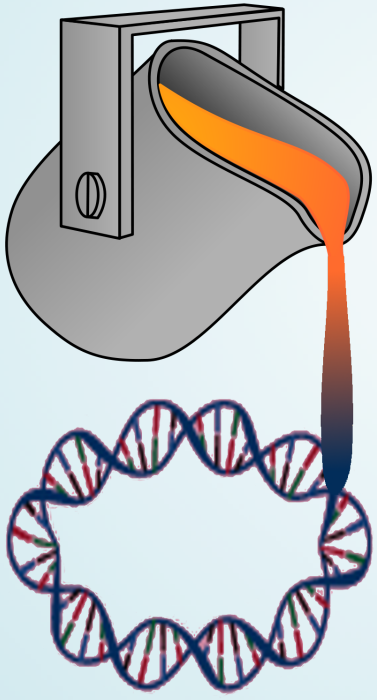
Correct misassemblies



Scaffold



Tigmint

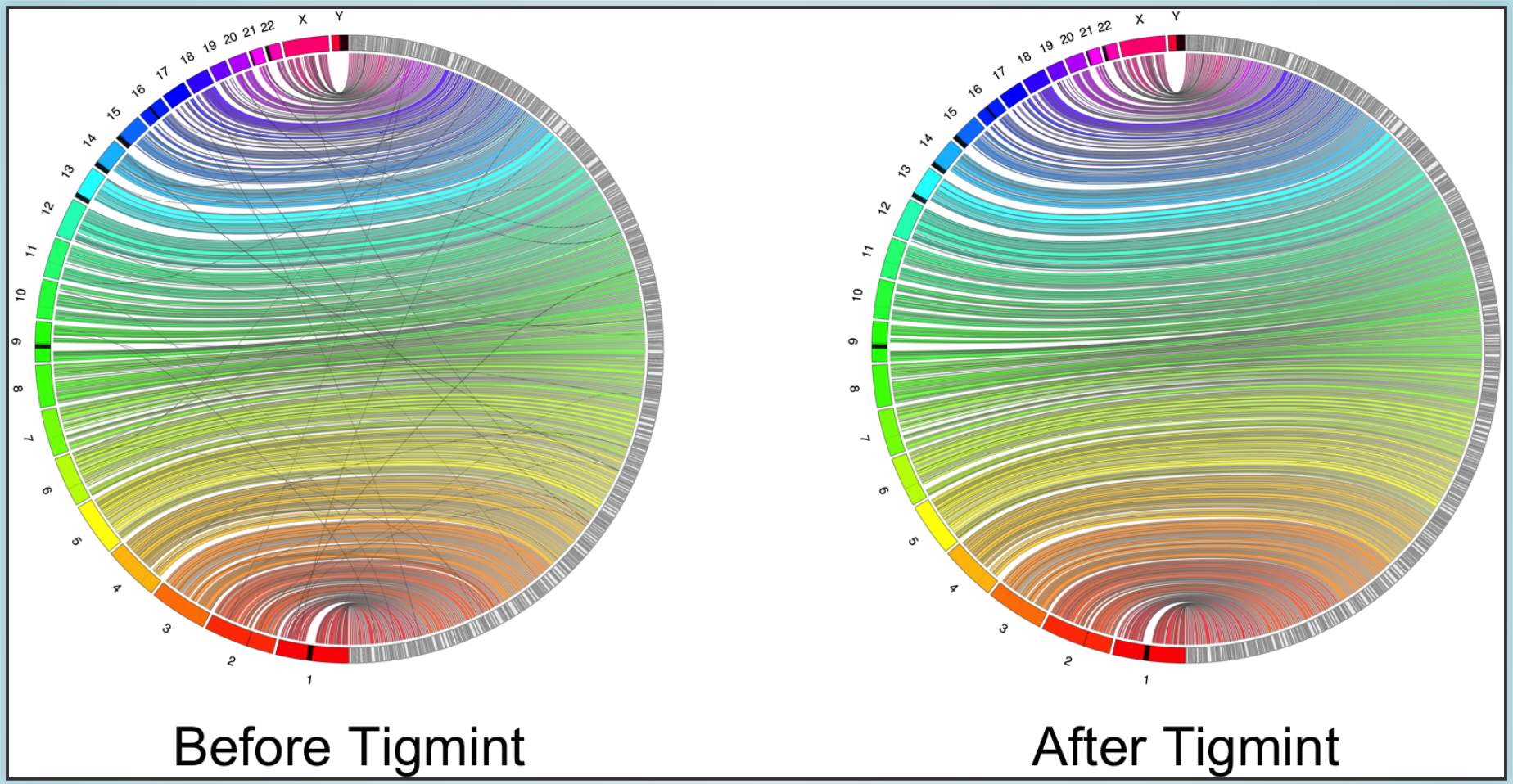


https://github.com/bcgsc/tigmint

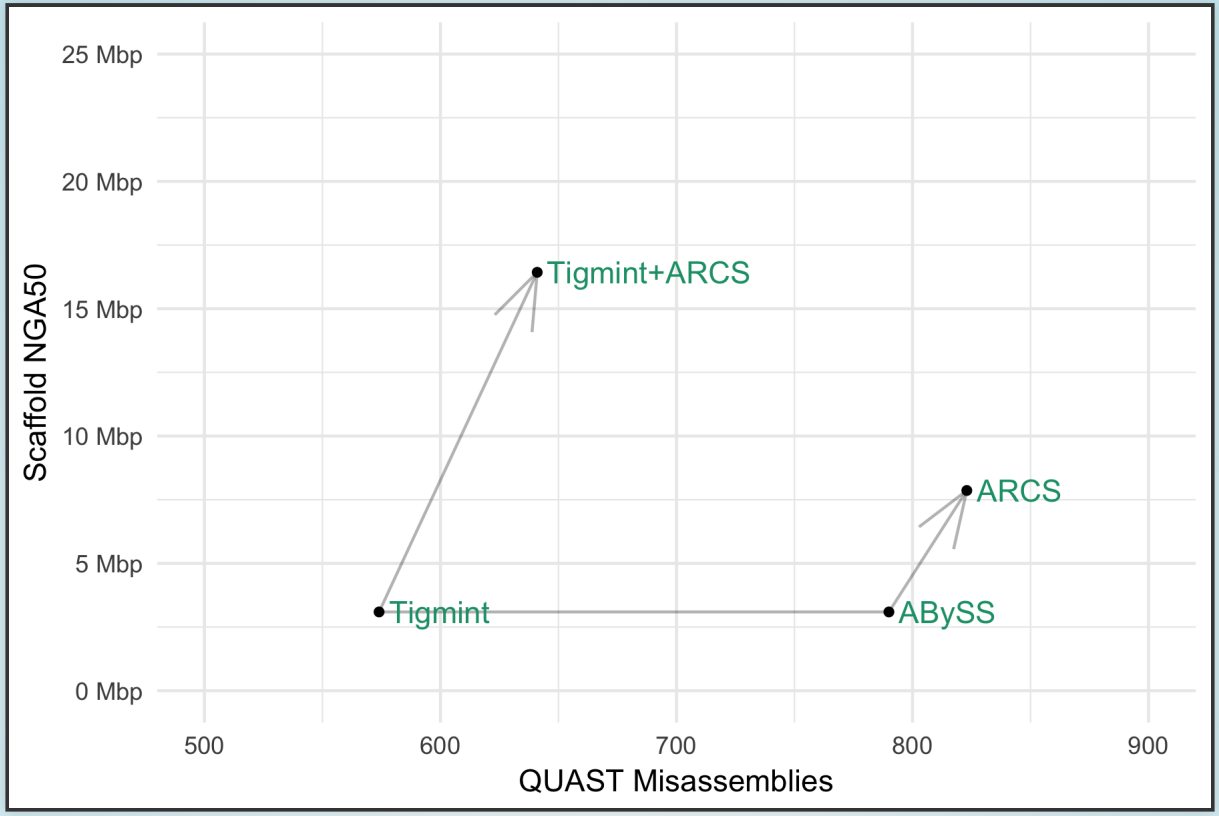
Method

- Map reads to the assembly
- Group reads within *d* bp of each other (*d* = 50 kbp)
- Infer start and end coordinates of molecules
- Construct an interval tree of the molecules
- Each *w* bp region ought to be spanned by *n* molecules (*w* = 1 kbp, *n* = 20)
- Identify regions with fewer than *n* spanning molecules
- Cut sequences at regions with insufficient coverage

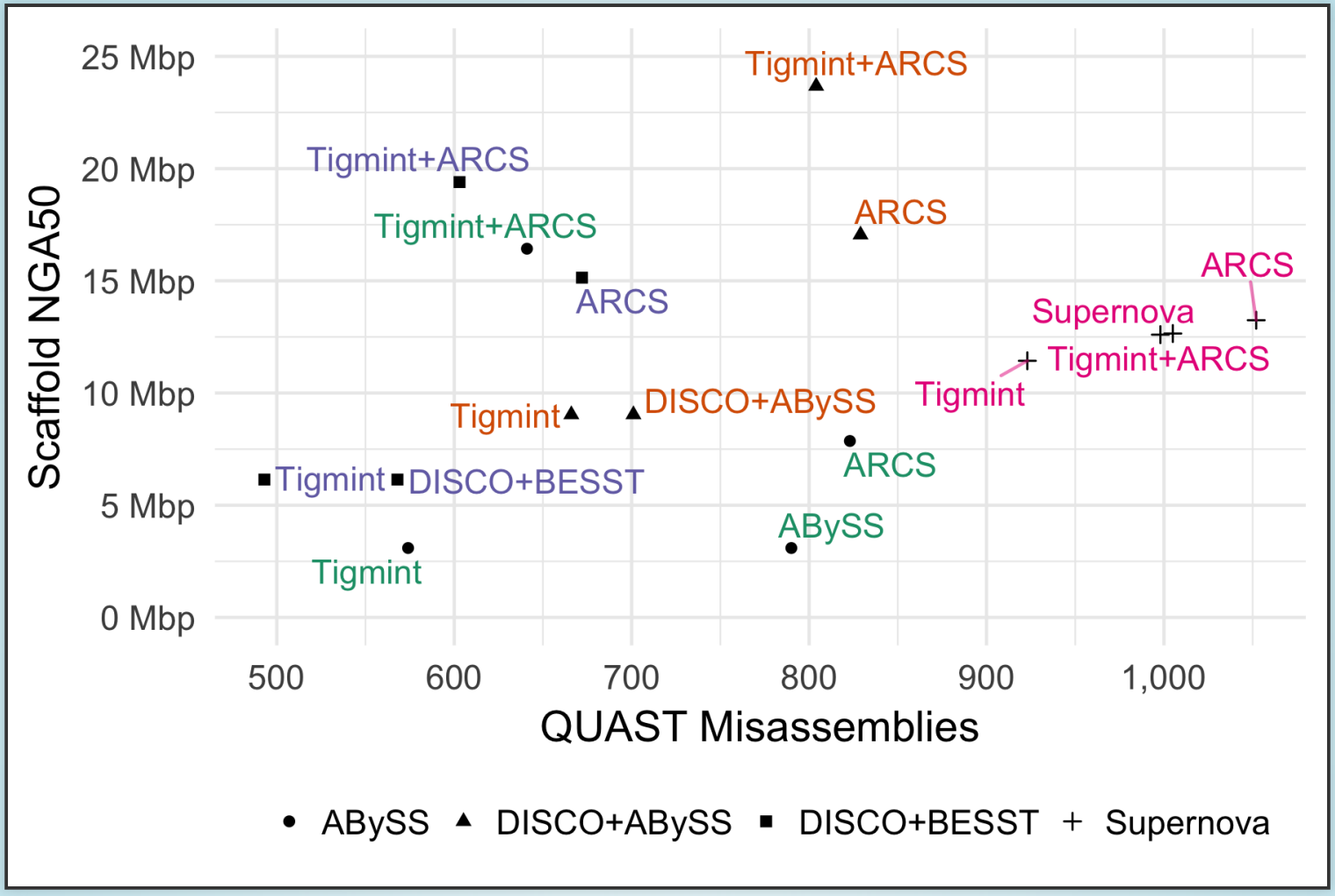
Tracks from top to bottom
molecule coverage, molecules, read coverage, reads



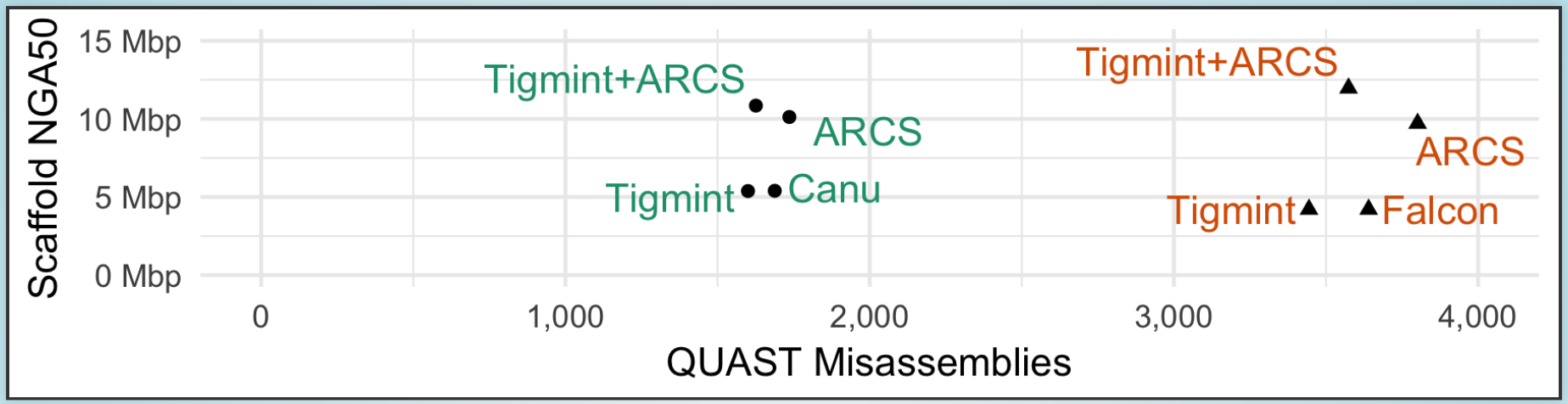
https://github.com/JustinChu/JupiterPlot



- Assemble human HG004 with PE, MP, and linked reads
- Scaffolding with ARCS improved NGA50 from 3 to 8 Mbp
- Tigmint reduced misassemblies by 216 (27% reduction)
- Tigmint + ARCS improved NGA50 over five-fold to 16 Mbp



Note: Supernova used only linked reads, others PE+MP+LR.



Corrects and improves long read assemblies too!

Sequencing	**Nanopore**	**PacBio**
Assembler	Canu	Falcon
NGA50 before Tigmint + ARCS	5.4 Mbp	4.2 Mbp
NGA50 after Tigmint + ARCS	10.9 Mbp	12.0 Mbp
Improvement	2.0x	2.9x

Time and Memory

`bwa mem` Map reads to assembly
5½ hours, 17 GB RAM, 48 threads
`tigmint-molecule` Group reads into molecules
3¼ hours, 0.08 GB RAM, 1 thread
`tigmint-cut` Identify misassemblies and cut sequences
7 minutes, 3.3 GB RAM, 48 threads

Conclusion

Scaffolding after correcting with Tigmint yields an assembly both more correct and more contiguous.

Linked reads permit cost-effective assembly of large genomes using high-throughput sequencing.

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Posters

- SEQ-7 **Tigmint**: Correcting Assembly Errors Using Linked Reads From Large Molecules
- SEQ-6 **ARKS**: chromosome-scale human genome scaffolding with linked read kmers
- SEQ-10 **ONTig**: Contiguating Genome Assembly using Oxford Nanopore Long Reads
- SEQ-8 **Multi-Index Bloom Filters**: A probabilistic data structure for sensitive multi-reference sequence classification with multiple spaced seeds

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Tigmint

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Slides

https://sjackman.ca/tigmint-recomb-slides

Markdown source code

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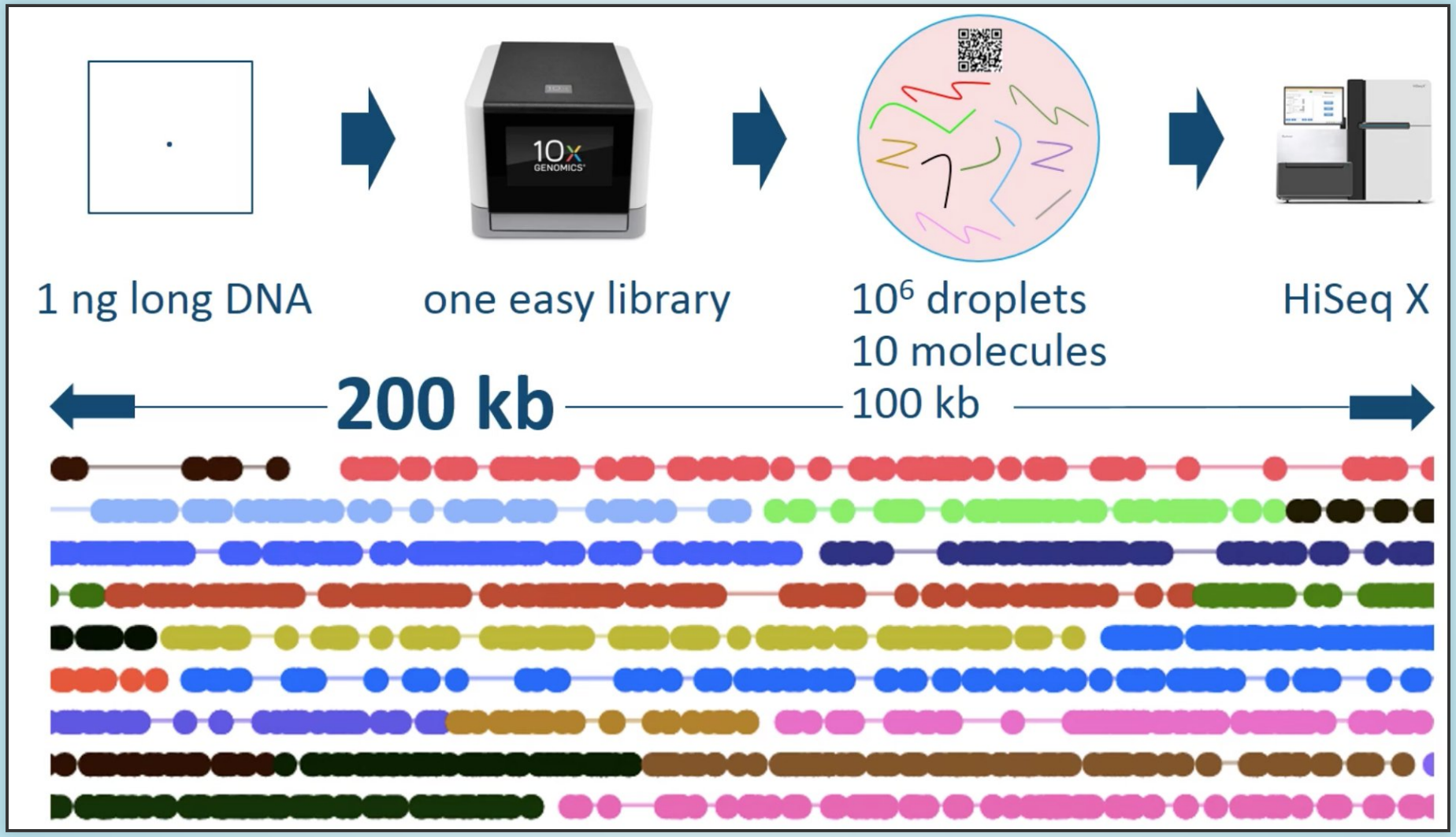
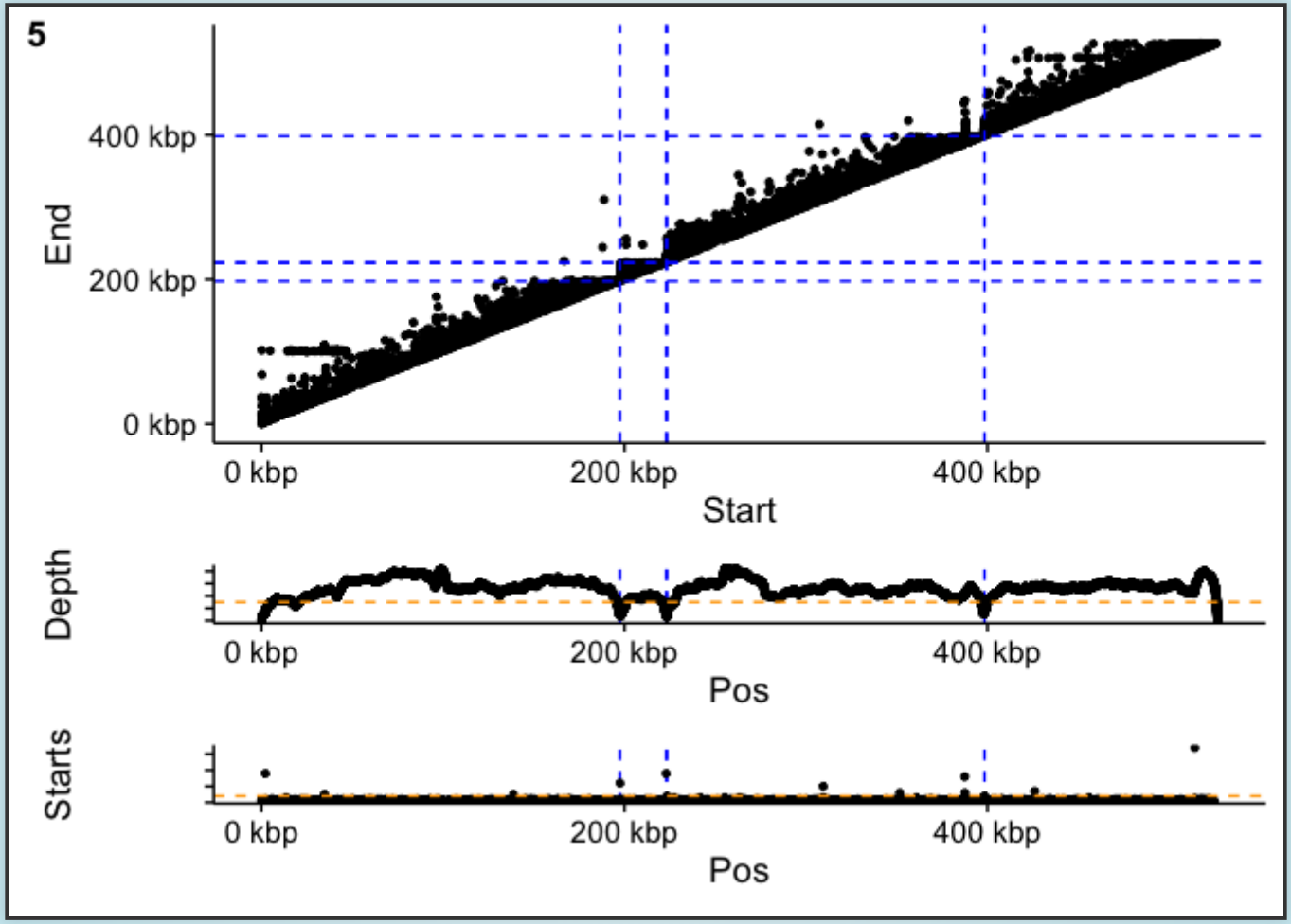
Supplementary Slides

10x Genomics Linked Reads



Scatter Plot



Graph of 10 kbp segments sharing barcodes