GoldRush-Link: Integrating minimizer-based overlap detection and gap-filling into the ntLink long read scaffolder

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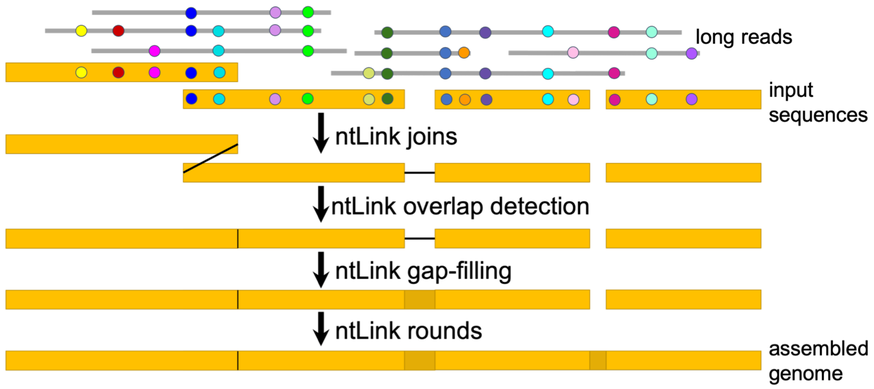
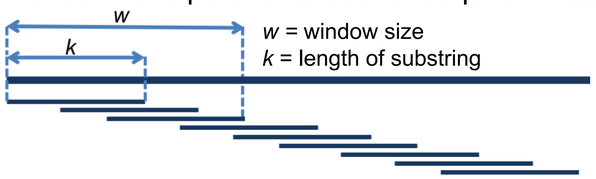
GoldRush-Link

- Essential step in new *de novo* assembler GoldRush
  - Powered by **ntLink**[1] long read scaffolder
- **ntLink** improvements:
  - Overlap detection
  - Gap-filling
  - Liftover-based rounds



Minimizer sketches

Reduce computational cost of sequence data storage and manipulation[2]

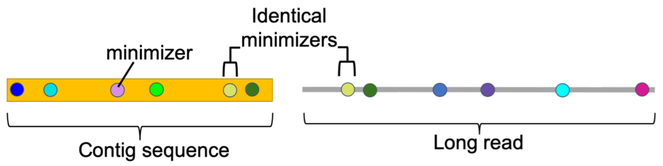


For each window of *w* adjacent *k*-mers:
- Compute hash values of each *k*-mer
- Window's minimizer = smallest hash value

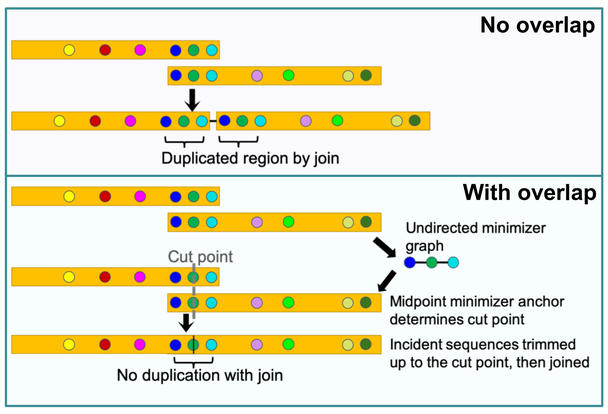
Generates ordered list of minimizers per sequence

Methods

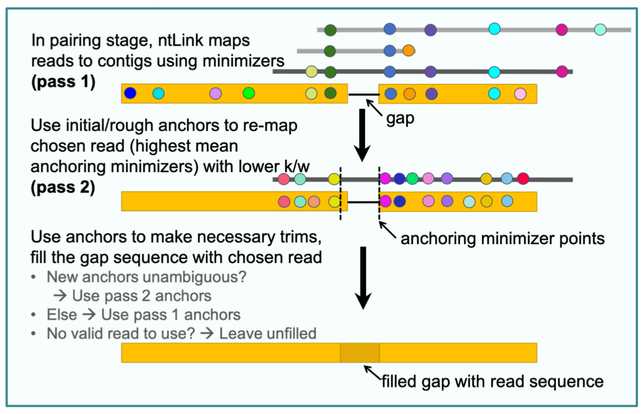
Schematic key:



Overlap detection

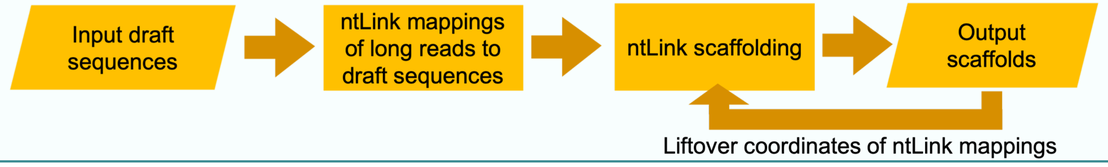


Gap-filling



Liftover-based rounds

- Running additional rounds of ntLink can produce more contiguous final assemblies
- Re-mapping the reads at each round is costly
  → Liftover mapping coordinates after each ntLink round based on scaffold composition



Results

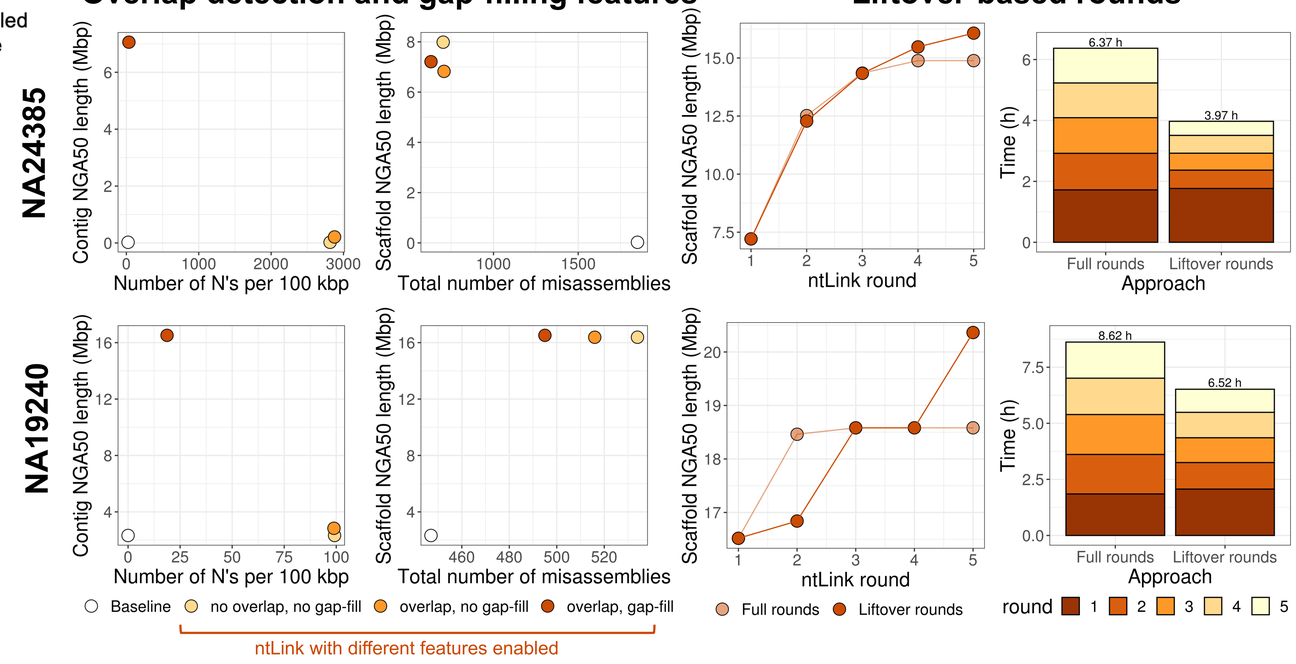
ntLink assemblies using Oxford Nanopore long reads for two human individuals:

Individual	Fold coverage	Baseline assembly
NA24385	67	GoldRush[4] goldtigs
NA19240	49	Shasta[3]

GoldRush goldtigs: Polished, corrected golden path reads
Golden path reads: ~1x read representation of the genome

Overlap detection and gap-filling features

Liftover-based rounds



- Using the overlap and gap-filling features substantially increases the "contig" contiguity
- Both features also reduce the overall number of misassemblies
- Running additional ntLink rounds yields further contiguity gains
- Using the liftover functionality vs. naïve rounds results in higher contiguity and faster runtimes

Conclusions

- Multiple new features were added to the **ntLink** long read scaffolder
  - Overlap detection, gap-filling and liftover-based rounds
- These improvements were made with our *de novo* long read assembler, GoldRush, in mind, but are also applicable to the general usage of **ntLink**

References

1. Coombe L, et al. 2021. LongStitch: high-quality genome assembly correction and scaffolding using long reads. *BMC Bioinformatics* **22**: 2021.06.17.448848.
2. Roberts M, et al. 2004. Reducing storage requirements for biological sequence comparison. *Bioinformatics* **20**: 3363–3369.
3. Shafin K, et al. 2020. Nanopore sequencing and the Shasta toolkit enable efficient de novo assembly of eleven human genomes. *Nat Biotechnol* **38**: 1044–1053
4. Wong J, et al. 2022. GoldRush-Path: a de novo assembler for long reads with linear time complexity. *ISMB HiTSeq talk*.

Software Availability

https://github.com/bcgsc/ntlink
https://github.com/bcgsc/goldrush
conda install -c bioconda ntlink

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