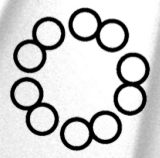
# Scalable solutions for *de novo* genome assembly

5-step

René L Warren 2019



CANADA'S MICHAEL SMITH GENOME SCIENCES CENTRE

Photo: R. Warren

# 1 Assembly


# Short reads *de novo* genome assembly

2009 **Parallel DBG assembler**

- MPI to aggregate memory
- Assembled 20 Gb spruce genome

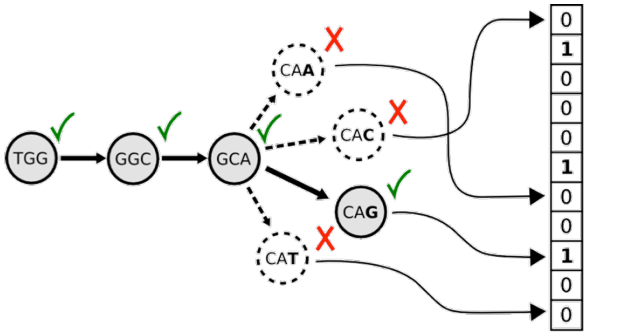
GENOME RESEARCH
Resource

**ABySS: A parallel assembler for short read sequence data**

Jared T. Simpson,[1] Kim Wong, Shaun D. Jackman, Jacqueline E. Schein, Steven J.M. Jones, and İnanç Birol[2]

2017 **Bloom filter representation**

- 1/10th RAM
- Large genomes, single computer




Bloom filter

GENOME RESEARCH
Method

**ABySS 2.0: resource-efficient assembly of large genomes using a Bloom filter**

Shaun D. Jackman,[1] Benjamin P. Vandervalk,[1] Hamid Mohamadi, Justin Chu, Sarah Yeo, S. Austin Hammond, Golnaz Jahesh, Hamza Khan, Lauren Coombe, Rene L. Warren, and Inanc Birol

**https://github.com/bcgsc/abyss**


2
Correction

# Tigmint

Jackman et al. BMC Bioinformatics (2018) 19:393
https://doi.org/10.1186/s12859-018-2425-6

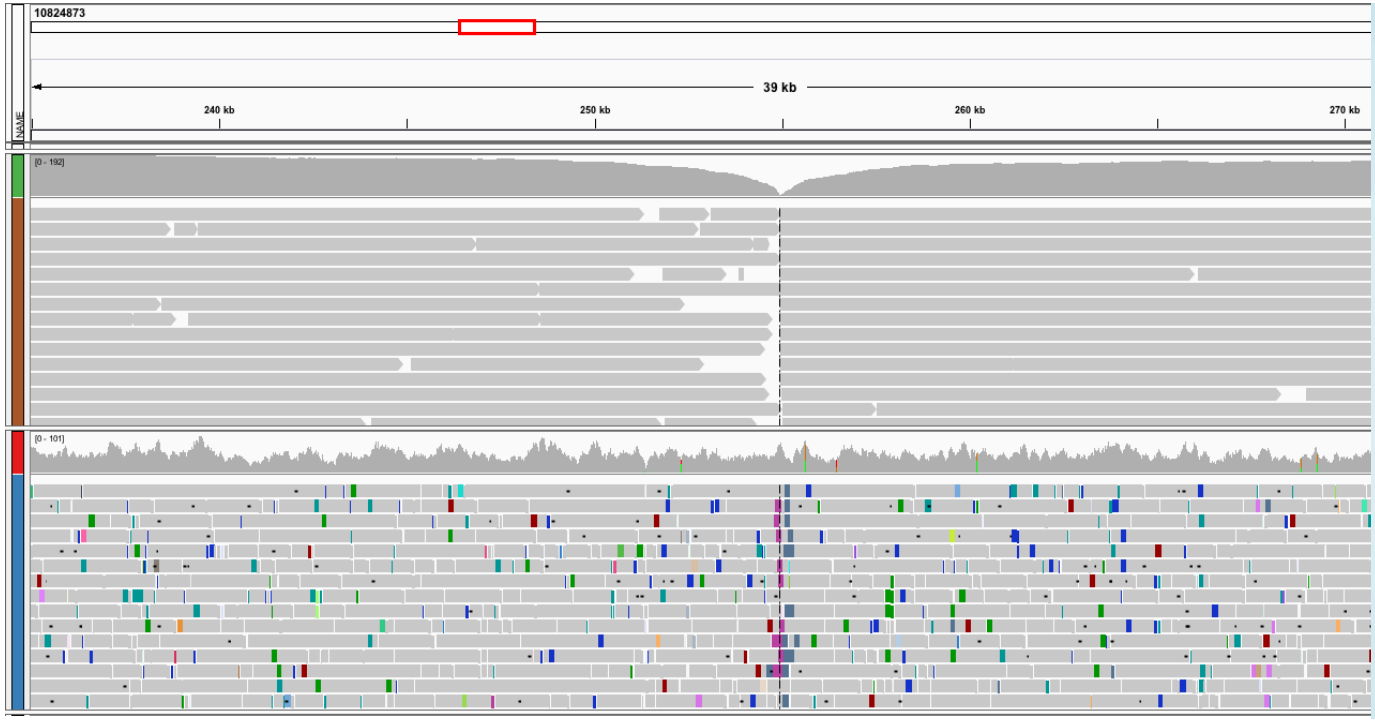
BMC Bioinformatics

SOFTWARE Open Access

## Tigmint: correcting assembly errors using linked reads from large molecules

Shaun D. Jackman[1*], Lauren Coombe[1], Justin Chu[1], Rene L. Warren[1], Benjamin P. Vandervalk[1], Sarah Yeo[1], Zhuyi Xue[1], Hamid Mohamadi[1], Joerg Bohlmann[2], Steven J.M. Jones[1] and Inanc Birol[1]

## Linked reads misassembly correction




Correct misassemblies

Scaffold

*IGV screenshot: Tigmint breakpoint in human genome NA24143*

**https://github.com/bcgsc/tigmint**


3
Scaffolding

# LINKS

Warren *et al. GigaScience* (2015) 4:35
DOI 10.1186/s13742-015-0076-3

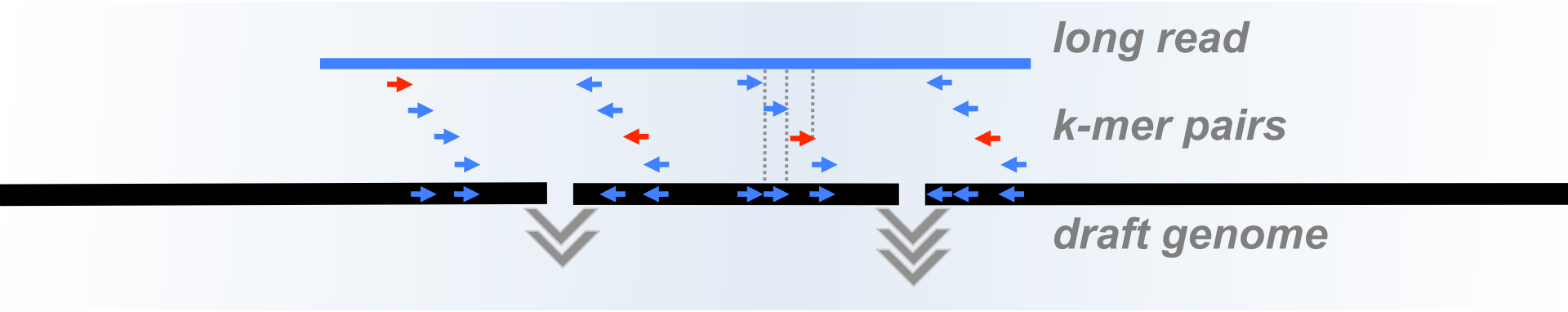
(GIGA)n SCIENCE

RESEARCH Open Access

LINKS: Scalable, alignment-free scaffolding of draft genomes with long reads

René L. Warren*, Chen Yang, Benjamin P. Vandervalk, Bahar Behsaz, Albert Lagman, Steven J. M. Jones and Inanç Birol

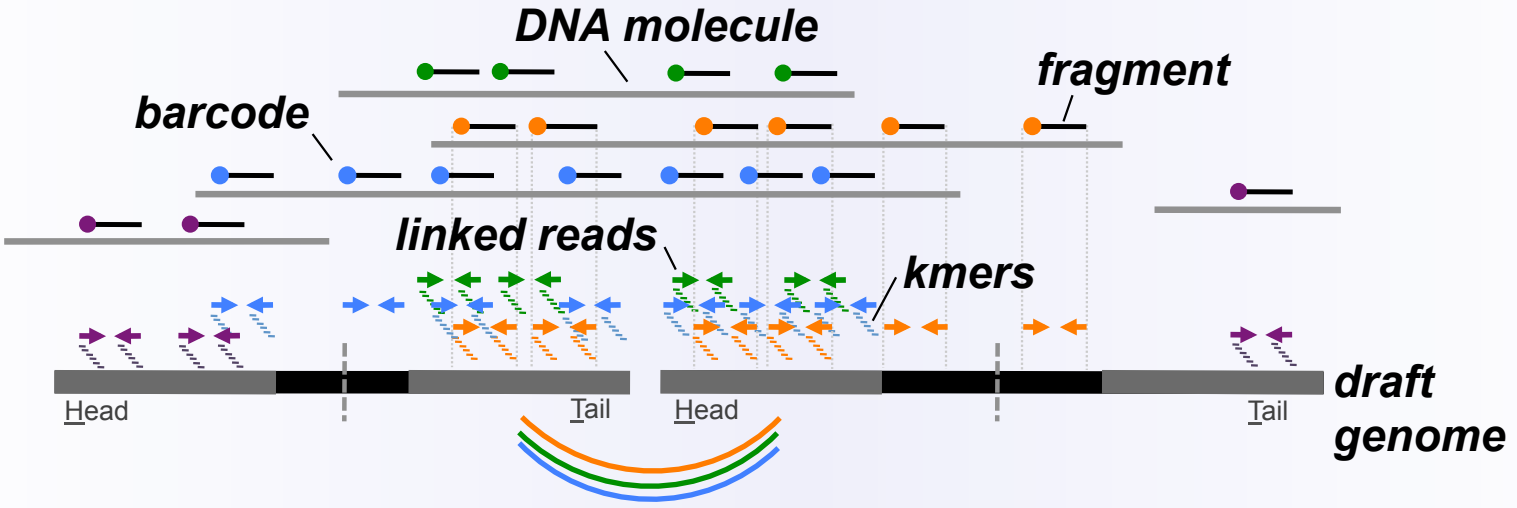
## Long read kmer scaffolding




- **Scaffolder** — order & orient sequences
- ***k-mer* based** — no alignments, error tolerant = no error corrections
- **Vast k-mer space** — no fragment length limitations
- **Versatile** — long-reads, draft sequences, MPET

**https://github.com/bcgsc/links**

# Linked read scaffolding




**ARCS: scaffolding genome drafts with linked reads**

Sarah Yeo, Lauren Coombe, René L Warren ✉, Justin Chu, Inanç Birol Author Notes

*Bioinformatics*, Volume 34, Issue 5, 1 March 2018, Pages 725–731,
https://doi.org/10.1093/bioinformatics/btx675

https://github.com/bcgsc/arcs

Coombe *et al. BMC Bioinformatics* (2018) 19:234
https://doi.org/10.1186/s12859-018-2243-x

BMC Bioinformatics

SOFTWARE Open Access

**ARKS: chromosome-scale scaffolding of human genome drafts with linked read kmers**

Lauren Coombe†, Jessica Zhang†, Benjamin P. Vandervalk, Justin Chu, Shaun D. Jackman, Inanc Birol and René L. Warren*

https://github.com/bcgsc/arks

# 4 Gap-filling

# Scaffolding and gap-filling with long reads

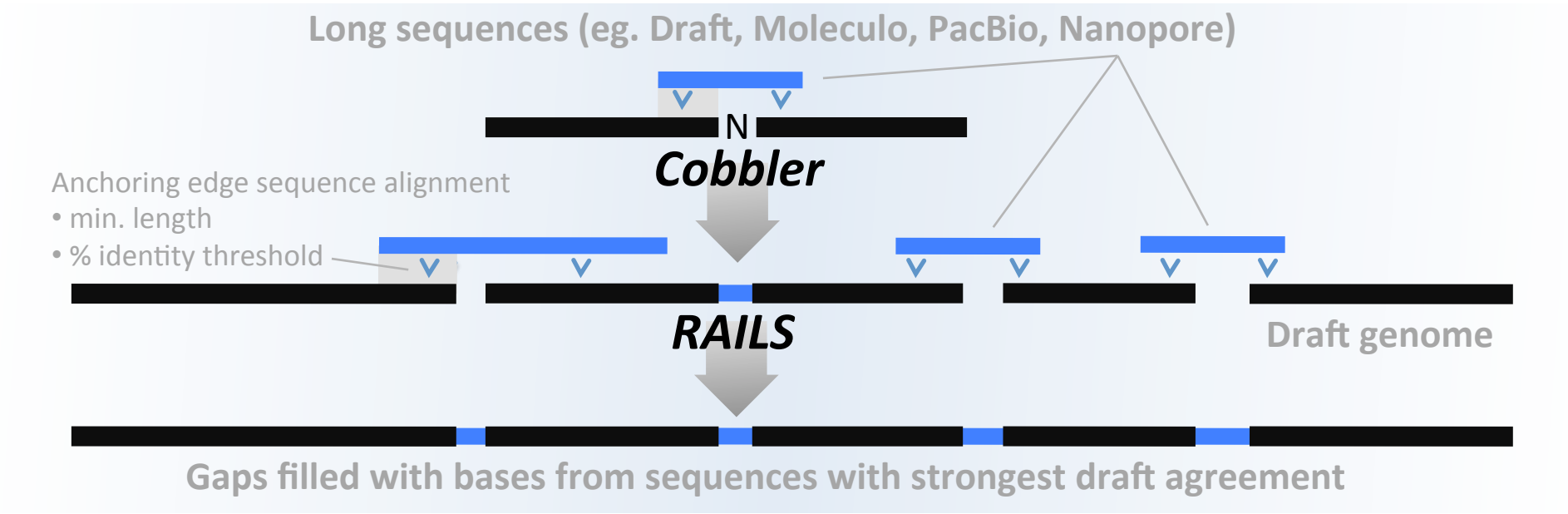
Uses LINKS scaffolding algorithm

JSS The Journal of Open Source Software

RAILS and Cobbler: Scaffolding and automated finishing of draft genomes using long DNA sequences

Rene L Warren[1] 2016

1 BC Cancer Agency, Genome Sciences Centre, Vancouver, BC, Canada




https://github.com/bcgsc/rails

# Sealer

## Gap filling with short reads

Vandervalk *et al. BMC Medical Genomics* 2015, **8**(Suppl 3):S1
http://www.biomedcentral.com/1755-8794/8/S3/S1

BMC Medical Genomics

RESEARCH Open Access

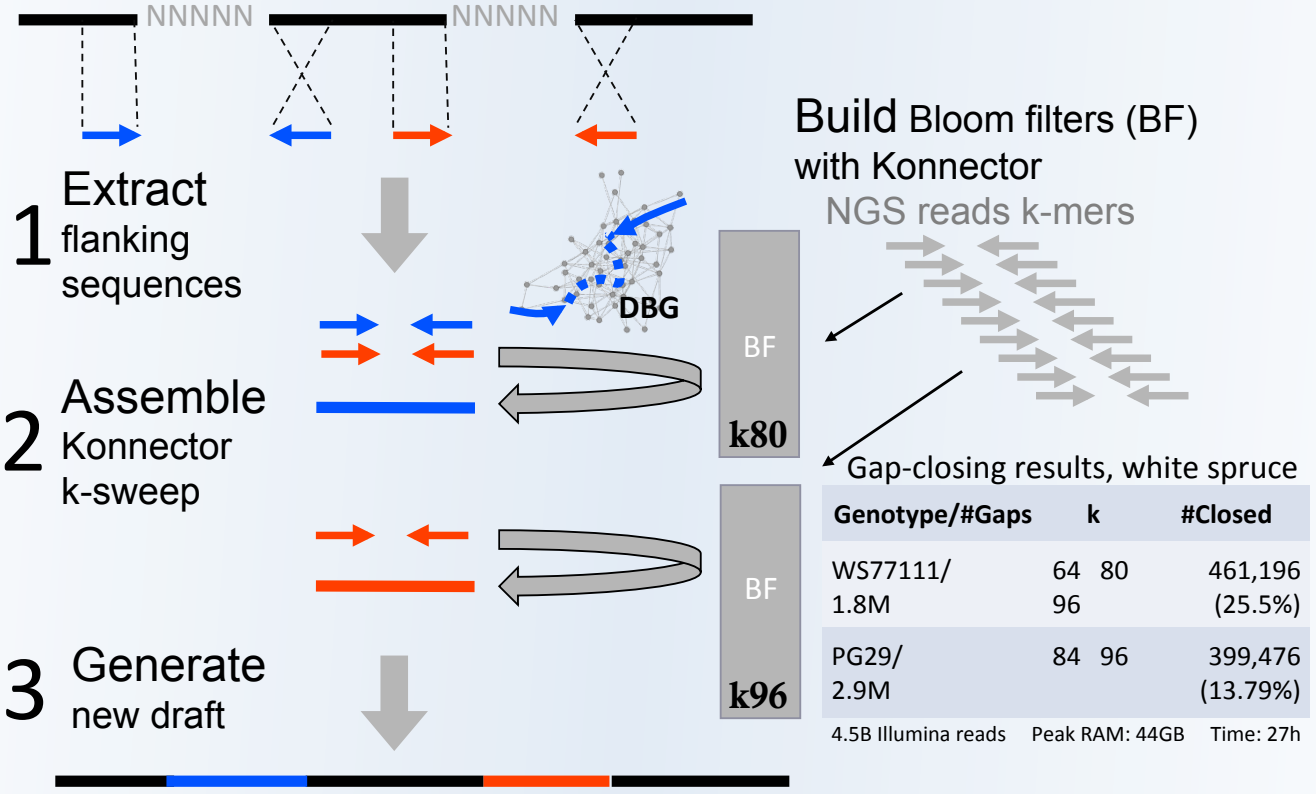
Konnector v2.0: pseudo-long reads from paired-end sequencing data

Paulino *et al. BMC Bioinformatics* (2015) 16:230
DOI 10.1186/s12859-015-0663-4

BMC Bioinformatics

SOFTWARE Open Access

Sealer: a scalable gap-closing application for finishing draft genomes




Gap-closing results, white spruce

| Genotype/#Gaps | k | #Closed |
|---|---|---|
| WS77111/ 1.8M | 64 80 96 | 461,196 (25.5%) |
| PG29/ 2.9M | 84 96 | 399,476 (13.79%) |

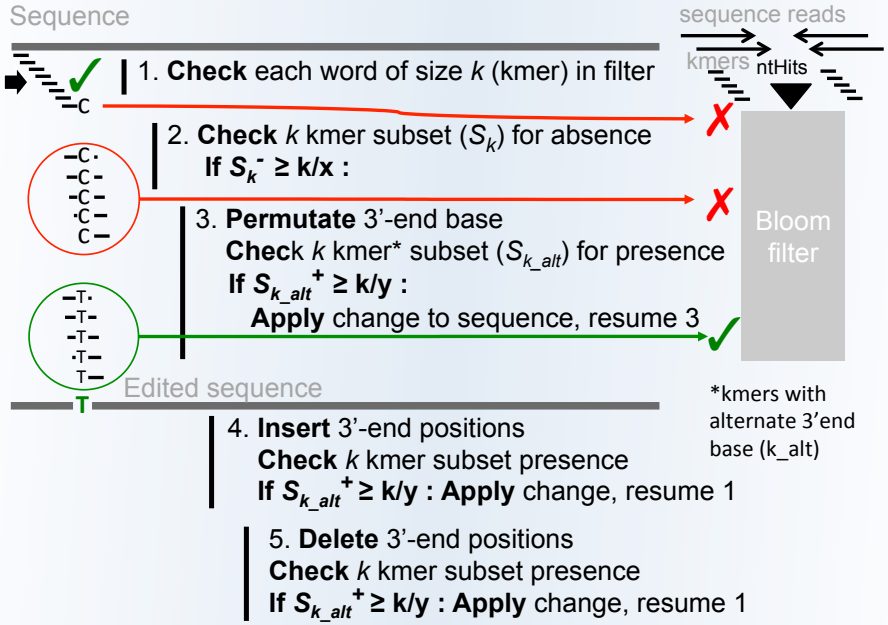
4.5B Illumina reads  Peak RAM: 44GB  Time: 27h

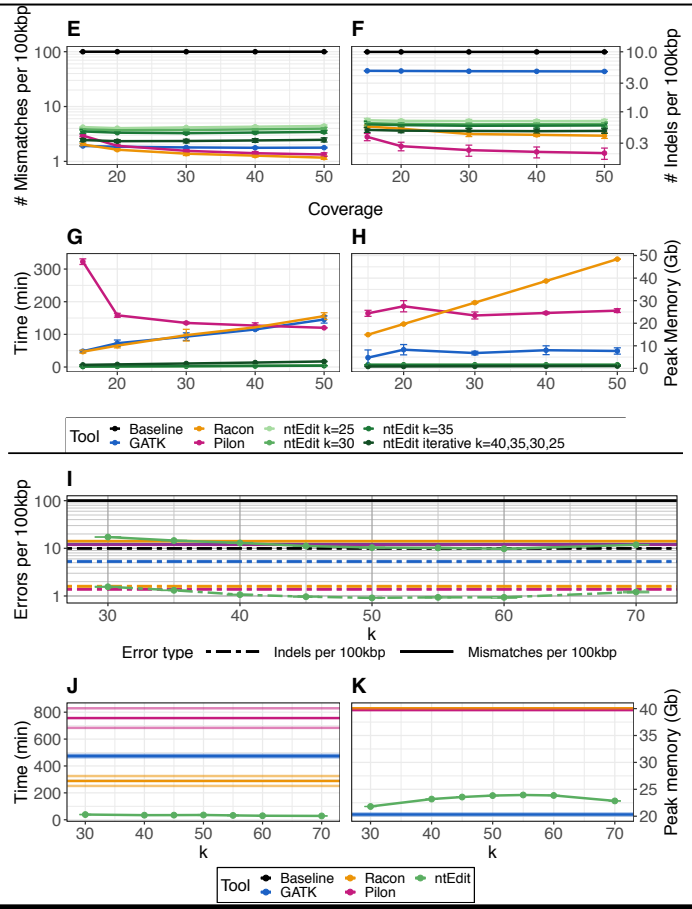
**https://github.com/bcgsc/abyss/tree/master/Sealer**

# 5 Polishing

# NTEDIT

## Fast genome polishing with short reads




*C. elegans*

*H. Sapiens* chr21

- Human and spruce genomes in 4 and 25 minutes
- Fix frameshift errors in nanopore/pacbio assemblies

**ntEdit: scalable genome sequence polishing**

2019

René L Warren, Lauren Coombe, Hamid Mohamadi, Jessica Zhang, Barry Jaquish, Nathalie Isabel, Steven JM Jones, Jean Bousquet, Joerg Bohlmann, Inanç Birol

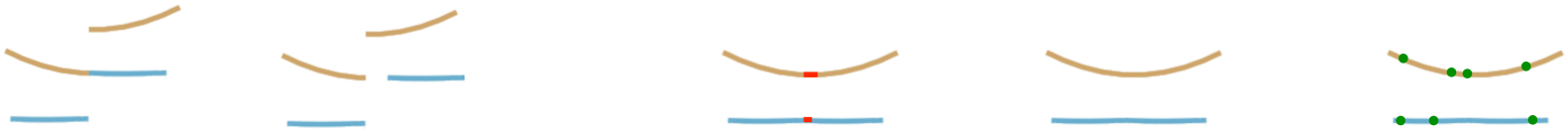
**doi:** https://doi.org/10.1101/565374

bioRxiv THE PREPRINT SERVER FOR BIOLOGY

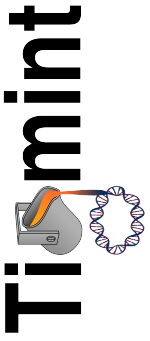
CSH Cold Spring Harbor Laboratory

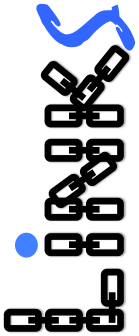
https://github.com/bcgsc/ntedit

# Scalable solutions for genome assembly



Assembly | Correction | Scaffolding | Gap-filling | Polishing

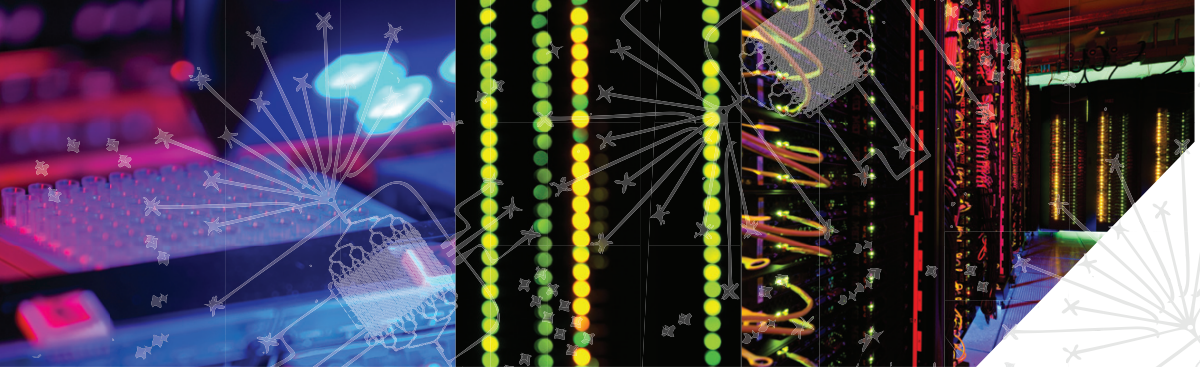








| Read Technology | | | | | | |
|---|---|---|---|---|---|---|
| Short | ● | | | | ● | ● |
| Linked | ● | ● | | ● | ○ | ○ |
| Long | | | ● | ● | | |

Illumina, SMS drafts (Nanopore/PacBio), etc.



CANADA'S MICHAEL SMITH

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