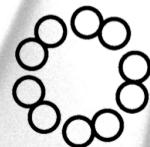


# A toolkit for *de novo* assembly

LINKS scaffold graph / *E. coli* K12

René L Warren, 2018



CANADA'S MICHAEL SMITH  
GENOME  
SCIENCES  
CENTRE

b1

Tig mint

arcs  
arks

LINKS

Konnection

&

Sealer



BBT



KOLLECTOR

MATCHVIEW





# *De novo* Assembly



# *de novo genome assembly with short reads*

GENOME  
RESEARCH  
Resource

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

Jared T. Simpson,<sup>1</sup> Kim Wong, Shaun D. Jackman, Jacqueline E. Schein, Steven J.M. Jones, and İnanç Birol<sup>2</sup>

Journal Article

Assembling the 20 Gb white spruce (*Picea glauca*) genome from whole-genome shotgun sequencing data

[İnanç Birol, Anthony Raymond, Shaun D. Jackman, Stephen Pleasance, Robin Cope ...](#)

*Bioinformatics*, Volume 29, Issue 12, 15 June 2013, Pages 1492–1497,  
<https://doi.org/10.1093/bioinformatics/btt178>

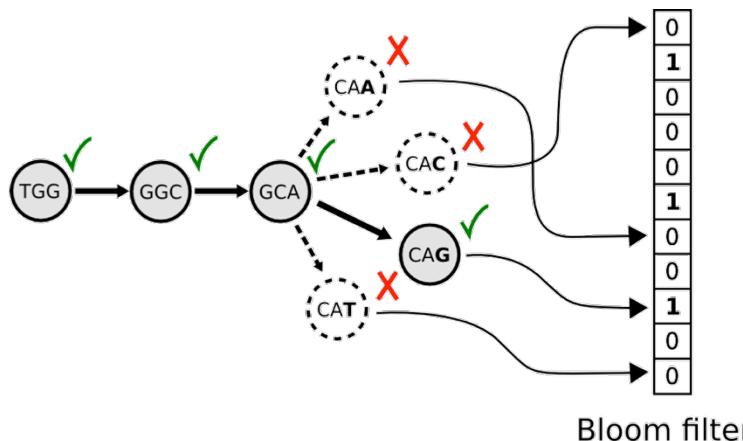
2009 : Parallel DBG assembler

MPI to aggregate memory

Assembled 20Gb spruce genome

2017 : Bloom filter representation

1/10<sup>th</sup> RAM, single computer, scalable to spruce (20Gbp)



GENOME  
RESEARCH  
Method

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

Shaun D. Jackman,<sup>1</sup> Benjamin P. Vandervalk,<sup>1</sup> Hamid Mohamadi, Justin Chu, Sarah Yeo, S. Austin Hammond, Golnaz Jahesh, Hamza Khan, Lauren Coombe, Rene L. Warren, and İnanç Birol

# KOLLECTOR

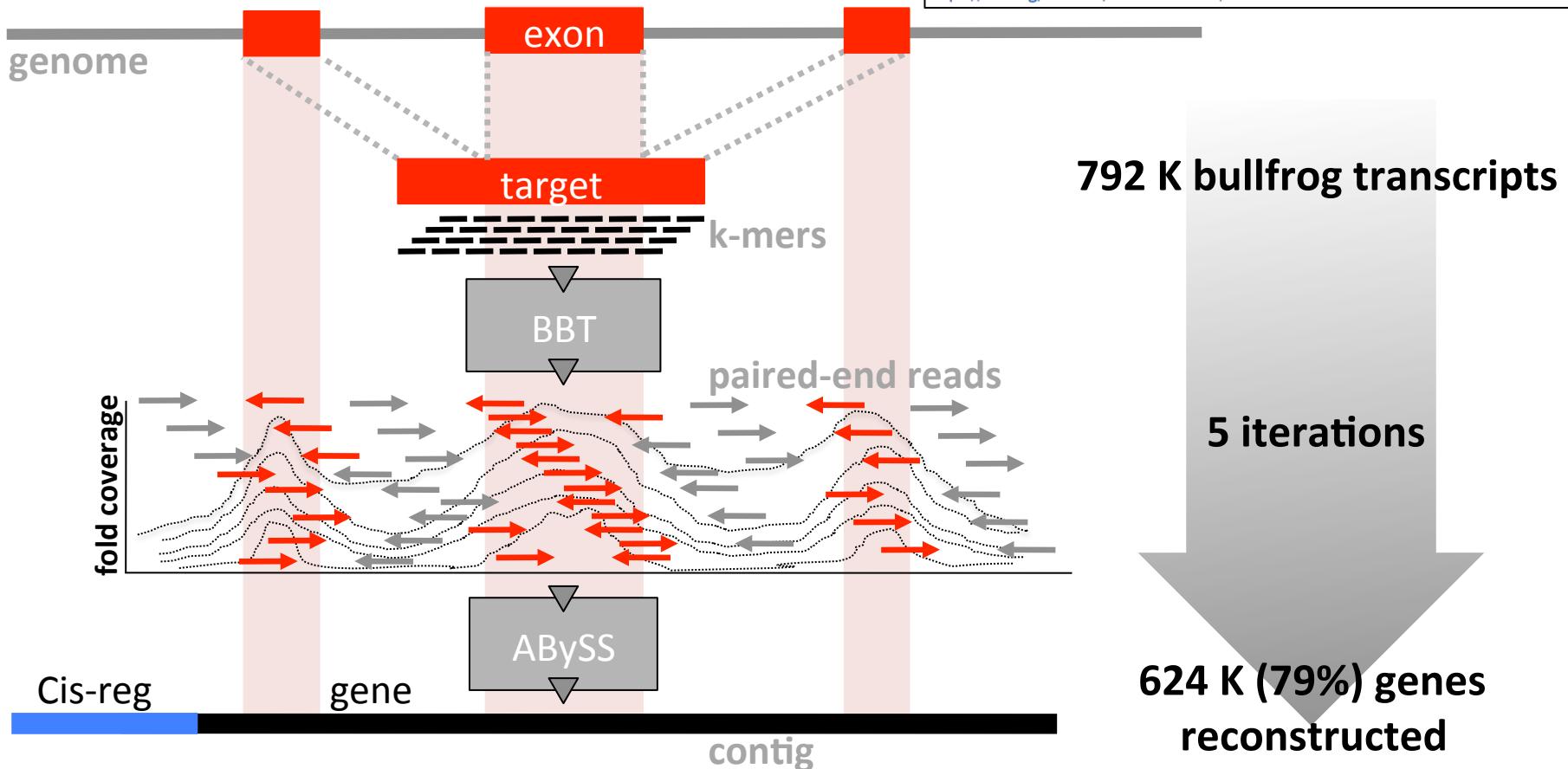
## Targeted *de novo* assembly of gene loci

Using a progressive Bloom filter

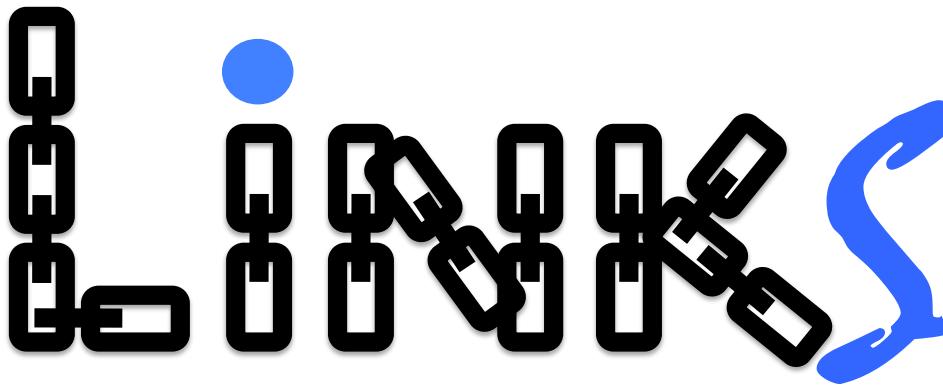
Journal Article

Kollector: transcript-informed, targeted de novo assembly of gene loci [@](#)  
Erdi Kucuk, Justin Chu, Benjamin P. Vandervalk, S. Austin Hammond, René L. Warren ...

Bioinformatics, Volume 33, Issue 12, 15 June 2017, Pages 1782–1788,  
<https://doi.org/10.1093/bioinformatics/btx078>



# **Scaffolding**



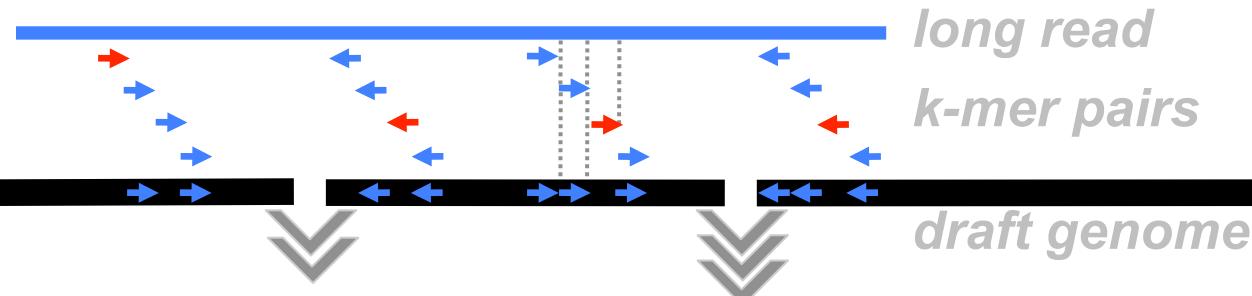
## LINKS: Scalable, alignment-free scaffolding of draft genomes with long reads

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

# Long read kmer scaffolding

- **Scaffolder** : order & orient sequences
  - ***k*-mer based** : no alignments
  - **Vast k-mer space** : no fragment length limitation
  - **Versatile** : long-reads, draft sequences, MPET

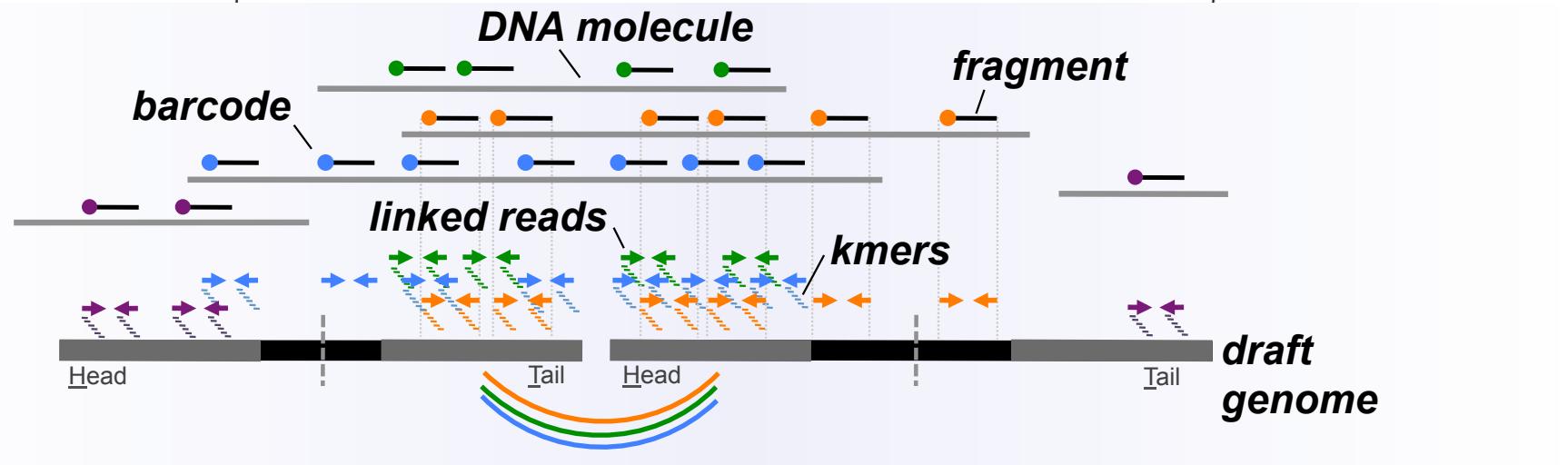
**# length**      **# errors**      **🚫 base correction**



# arcs

# arks

## Linked read scaffolding



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

BMC Bioinformatics

### 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>

SOFTWARE

Open Access

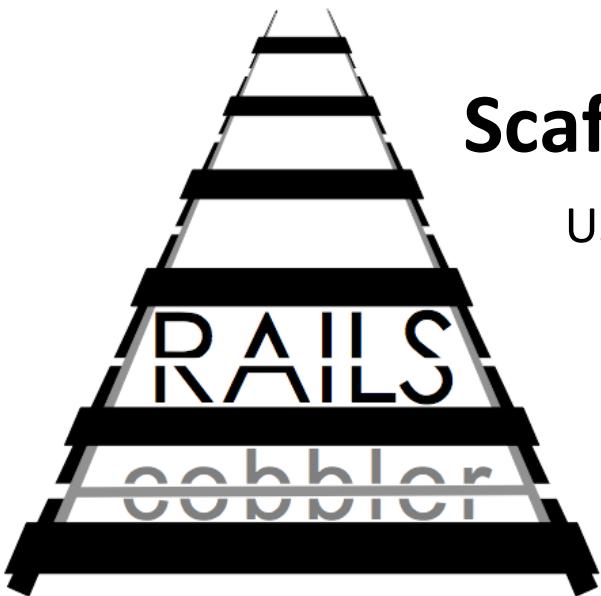
### ARKS: chromosome-scale scaffolding of human genome drafts with linked read kmers



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



# ***Gap-filling***



# Scaffolding and gap-filling

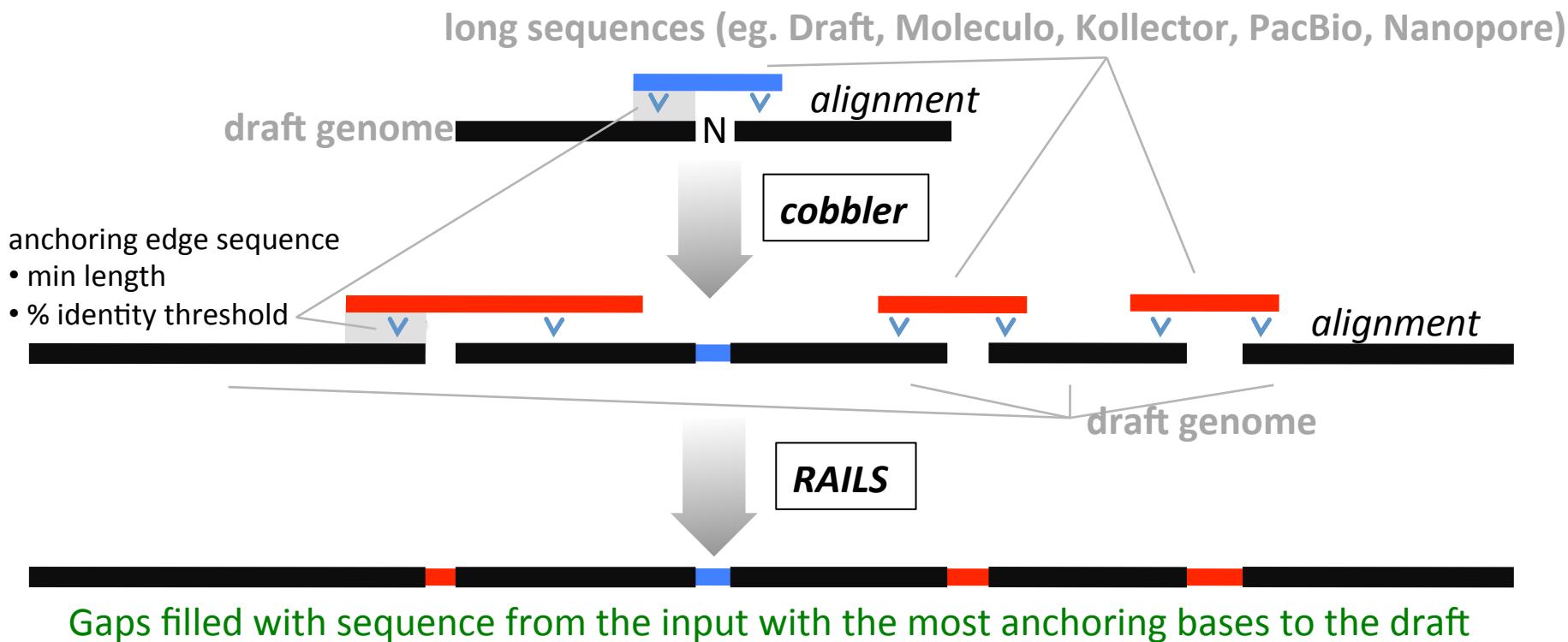
Uses LINKS scaffolding algorithm



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

Rene L Warren<sup>1</sup> 2016

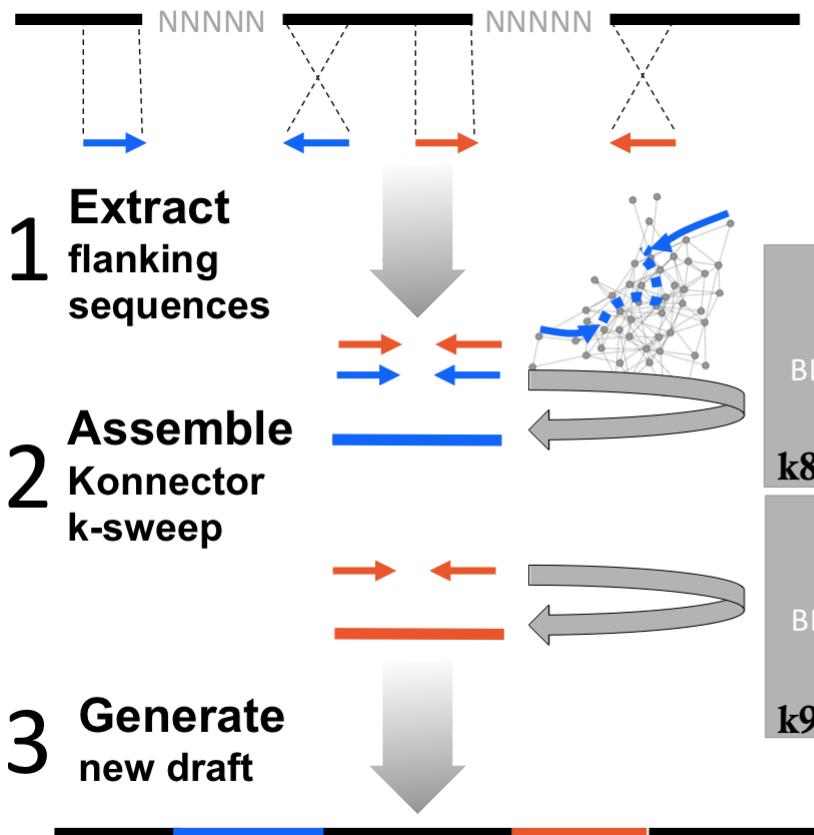
<sup>1</sup> BC Cancer Agency, Genome Sciences Centre, Vancouver, BC, Canada



# Sealer

## Automated genome finishing

- Gap-filler (resolve Ns)
- Implements Bloom filter de Bruijn graph (Scalable)



RESEARCH

Open Access

Konnecter 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



SOFTWARE

Open Access

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



## Application of Konnecter

Build Bloom filters  
(Konnecter)  
NGS reads k-mers

Closing gaps within the 20 Gbp draft white spruce genome assembly

Genotype / gaps	k values	#closed
WS77111 / 1,807,194	64 80 96	461,196 (25.5%)
PG29*/ 2,895,274	84 96	399,476 (13.79%)

\*4.5B Illumina MiSeq/HiSeq2000 reads

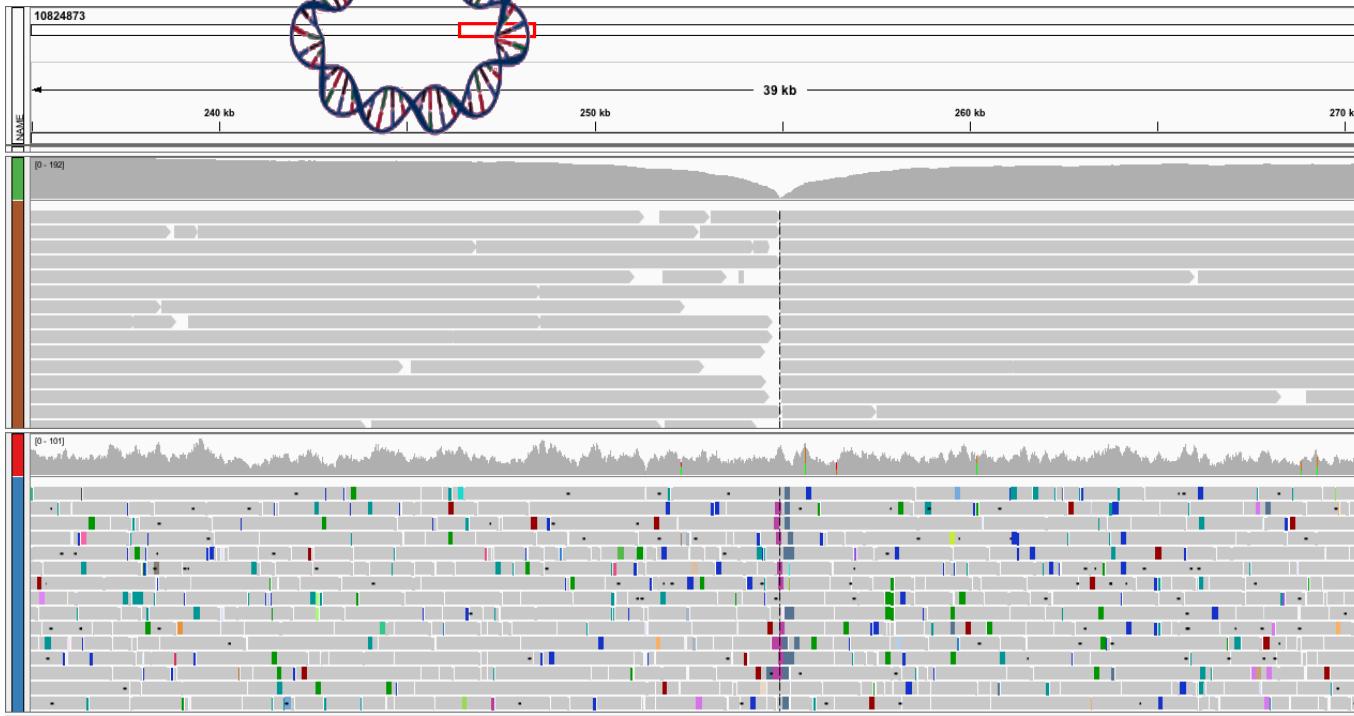
Peak memory: 44 GB RAM

Run time: 27h

# *Misassembly Correction & Assessment*

# Tigmint

Linked read  
misassembly  
correction



Correct misassemblies



Scaffold



*IGV screenshot: a Tigmint breakpoint in human genome NA24143*

Pre-print: Jackman et al., “Tigmint: Correcting Assembly Errors Using Linked Reads From Large Molecules”, bioRxiv, <https://doi.org/10.1101/304253>.

# Bio Bloom Tools

## Sequence classification with Bloom filters

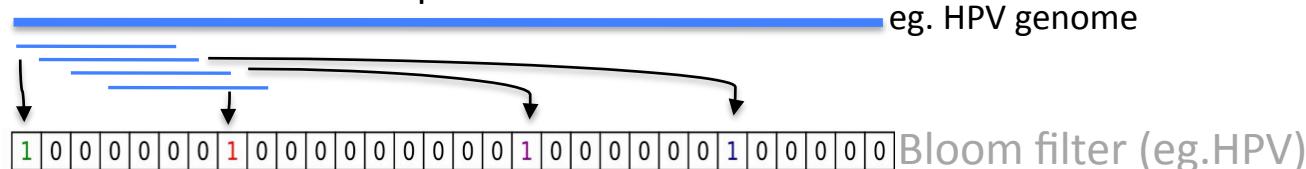
*Sequence filtering*

*contaminant screening*

*pathogen discovery*

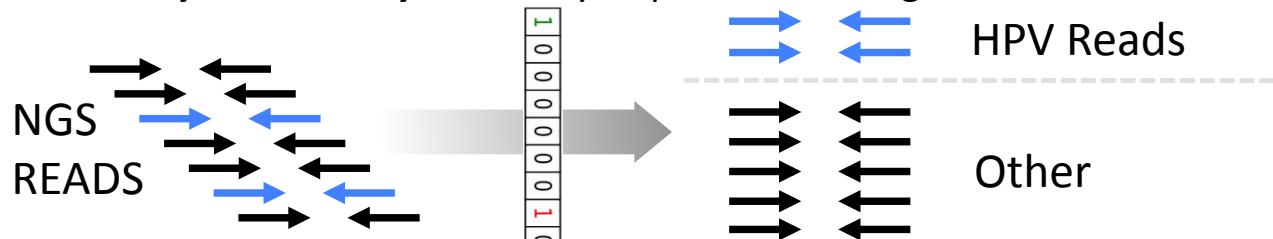
### BioBloom-Maker

- Build filters : **Re-usable** loadable binary file, human readable text file from input sequences
- Customizable : **Flexible** adjust k score threshold FPR #hash functions
- Multi-filter : **Concurrent** BloomMap



### Categorizer

- Bins sequences : **Analysis summary** - hits tally to particular categories

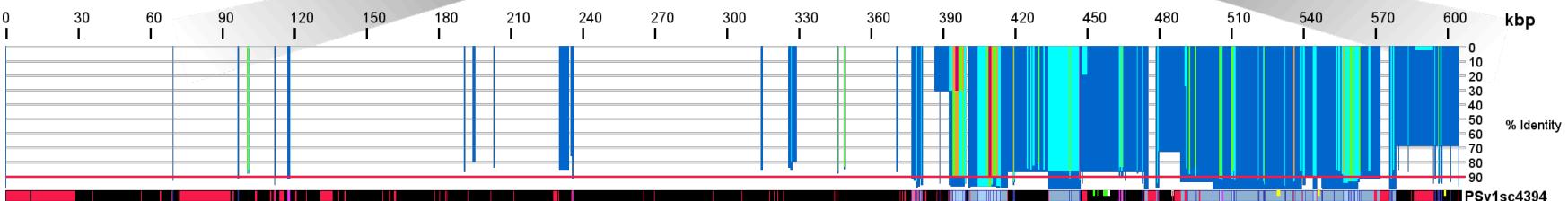


**BioBloom tools: fast, accurate and memory-efficient host species sequence screening using bloom filters**

Justin Chu , Sara Sadeghi, Anthony Raymond, Shaun D. Jackman, Ka Ming Nip, Richard Mar, Hamid Mohamadi, Yaron S. Butterfield, A. Gordon Robertson, Inanç Birol   
Author Notes

*Bioinformatics*, Volume 30, Issue 23, 1 December 2014, Pages 3402–3404,

# MATCHVIEW



LG11 (<--)  
 83.694 GQ03115\_N13 (yellow)  
 83.695 GQ0045\_A14 (white)  
 83.695 GQ02011\_E22 (lime)



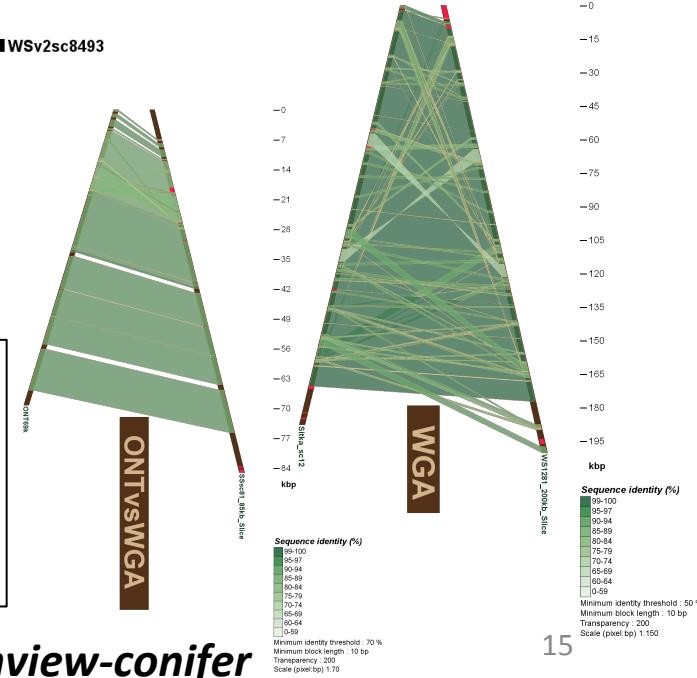
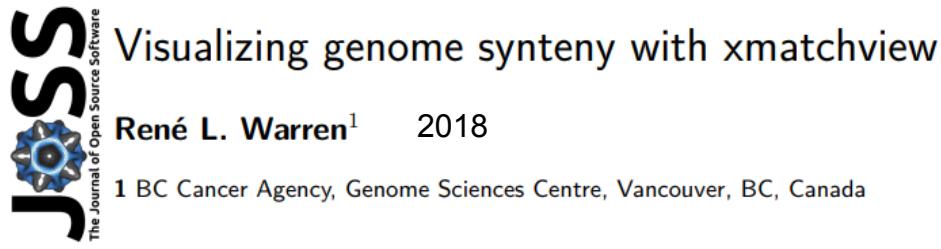
## Legend

- Frequency Repeated**
- Single copy
  - 2X
  - 3X
  - 4X
  - 5X and over

Mismatch threshold : 10 %  
 Minimum Block Length : 10 bp  
 Scale (pixel:bp) 1:300

## Collinear Blocks

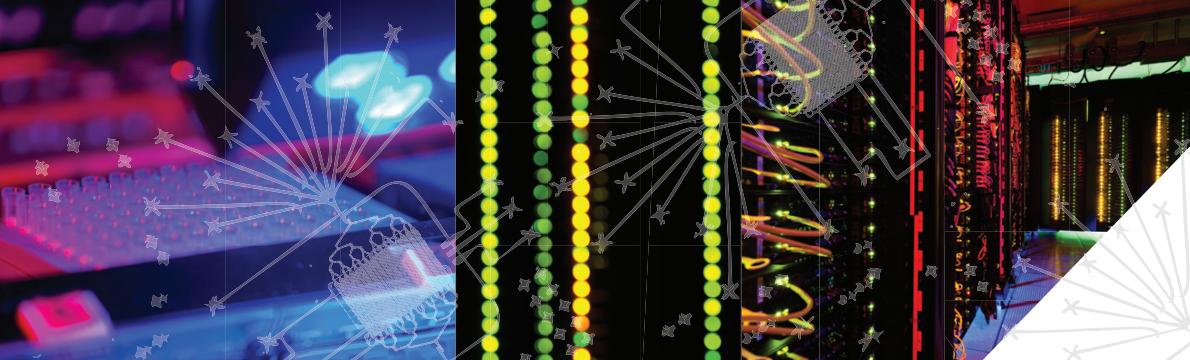
- Direct
  - Inverted
- Other**
- Mismatch threshold
  - Sequence features
  - Ambiguous bases (Ns)



# b1L Projects

<b>Visualization</b>	<b>ABySS-explorer</b>	: Visualizing assembly graphs
<b>QC</b>	<b>gNAVIGATOR</b>	: Assembly completeness (cDNA) and QC (genetic map)
<b>De novo assembly</b>	<b>ABYSS-LR</b>	: Linked read <i>de novo</i> assembler
	<b>TAILR</b>	: Targeted, hybrid <i>de novo</i> assembler informed by linked read
	<b>ONTig</b>	: Nanopore-short read hybrid <i>de novo</i> assembler
<b>Analysis</b>	<b>PAVfinder</b>	: Structural variant finder (genomes/transcriptomes)
	<b>AMPlify</b>	: Antimicrobial peptide discovery with deep learning
<b>Comparative</b>	<b>ABYSS-Bloom</b>	: Comparative genomics with kmer Bloom filters
<b>Reads</b>	<b>NanoSim</b>	: Nanopore read simulator, models on experimental data
	<b>DIDA</b>	: Distributed Indexing & alignment on a compute farm
<b>RNA</b>	<b>Chop-Stitch</b>	: <i>De novo</i> exon annotation, splice graph construction
	<b>Trans-ABYSS</b>	: Transcriptome Assembler with short reads
	<b>RNA-Bloom</b>	: Resource-efficient transcriptome assembler
	<b>KLEAT</b>	: Analysis of APA events using transcriptomes
	<b>TransNanoSim</b>	: Nanopore transcriptome simulator
<b>Data structure</b>	<b>miBF/BBT2</b>	: Multi-Index Bloom Filters
<b>Algorithms</b>	<b>ntHash</b>	: Fast nucleotide sequence hashing
	<b>ntCard</b>	: Sequencing data cardinality estimator
	<b>ntHit</b>	: Sequencing data repeat detection

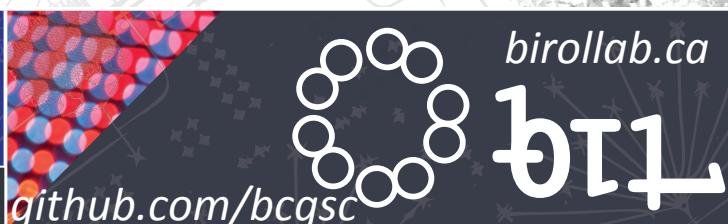
<https://github.com/bcgsc>



# CANADA'S MICHAEL SMITH GENOME SCIENCES CENTRE

A leading international centre for genomics and bioinformatics research committed to advancing knowledge of cancer-related diseases, improving human health through disease prevention, diagnosis and therapeutic approaches, and realizing social and economic benefits of genomics research.

>2 PETABASES SEQUENCED • A HUMAN GENOME EVERY 15 MINUTES • HIGH-PERFORMANCE COMPUTING



AFFILIATIONS BC Cancer Research Center • BC Cancer Agency • BC Cancer Foundation • Genome BC • Simon Fraser University • University of British Columbia • Genome Sciences Institute

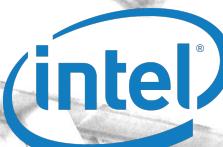
**Lauren Coombe | Austin Hammond | Ben Vandervalk | Zhuyi Xue | Readman Chiu  
Darcy Sutherland | Jessica Zhang | Jeffrey Tse | Justin Chu | Shaun Jackman  
Kristina Gagalova | Chen Yang | Saber Hafezqorani | Golnar Sheikhshab  
Ka Ming Nip | Yee Fay Lim | Chenkai Li | Hamid Mohamadi  
Rene Warren ([rwarren@bcgsc.ca](mailto:rwarren@bcgsc.ca)) | Sinead Aherne | Inanc Birol  
Tony Raymond | Daniel Paulino | Sarah Yeo | Erdi Kucuk | Hamza Khan**



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