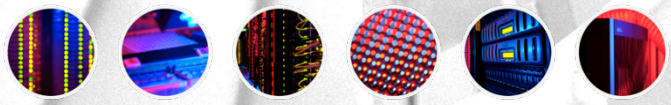
Genome Assembly Toolkit

LINKS scaffold graph / *E. coli* K12

René L Warren

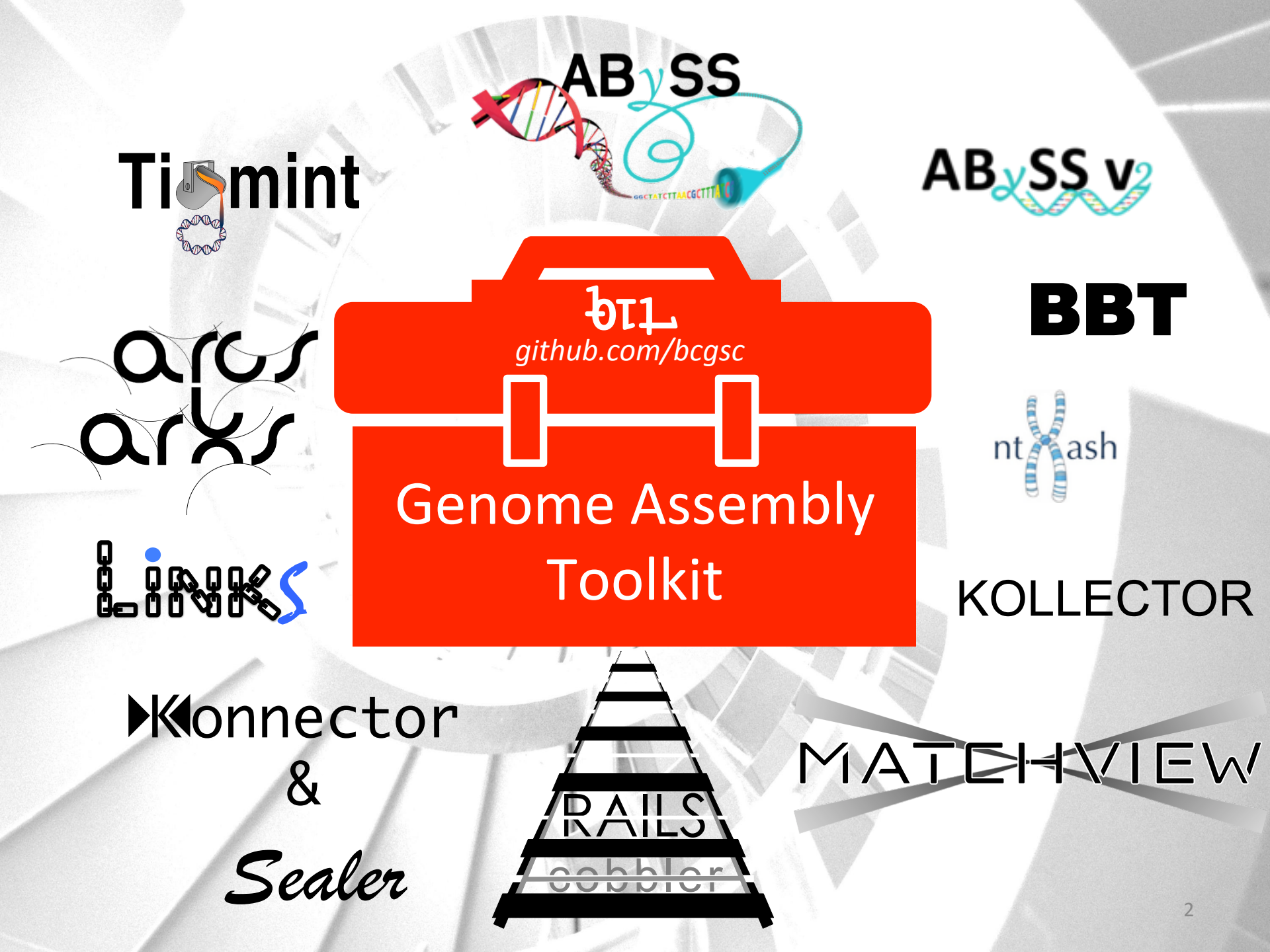
Bioinformatics Technology Lab



CANADA'S MICHAEL SMITH GENOME SCIENCES CENTRE
WWW.BCGSC.CA

2018

Photo: R. Warren


ABySS
Tigmint
ABySS v2
BBT
github.com/bcgsc
Genome Assembly Toolkit
arcs
ntHash
LINKS
KOLLECTOR
Konnector
&
Sealer
RAILS
cobbler
MATCHVIEW

De novo Assembly

de novo genome assembly with short reads

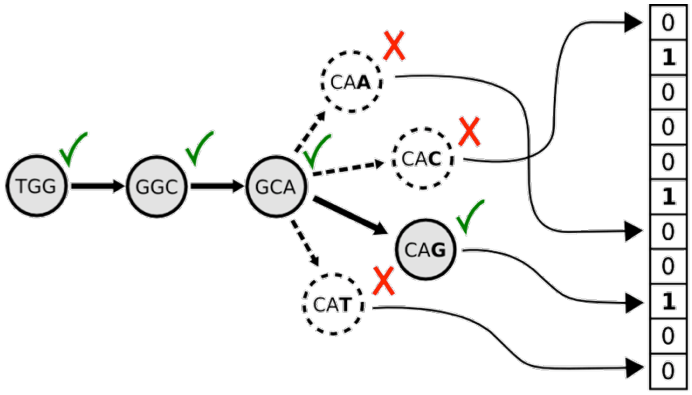
2009: **Parallel DBG assembler**

MPI to aggregate memory

Assembled 20Gb spruce genome

2017: **Bloom filter representation**

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



Bloom filter

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]

Journal Article

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

Inanc Birol, Anthony Raymond, Shaun D. Jackman, Stephen Pleasance, Robin Coope ...

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

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

KOLLECTOR

Targeted *de novo* assembly of gene loci

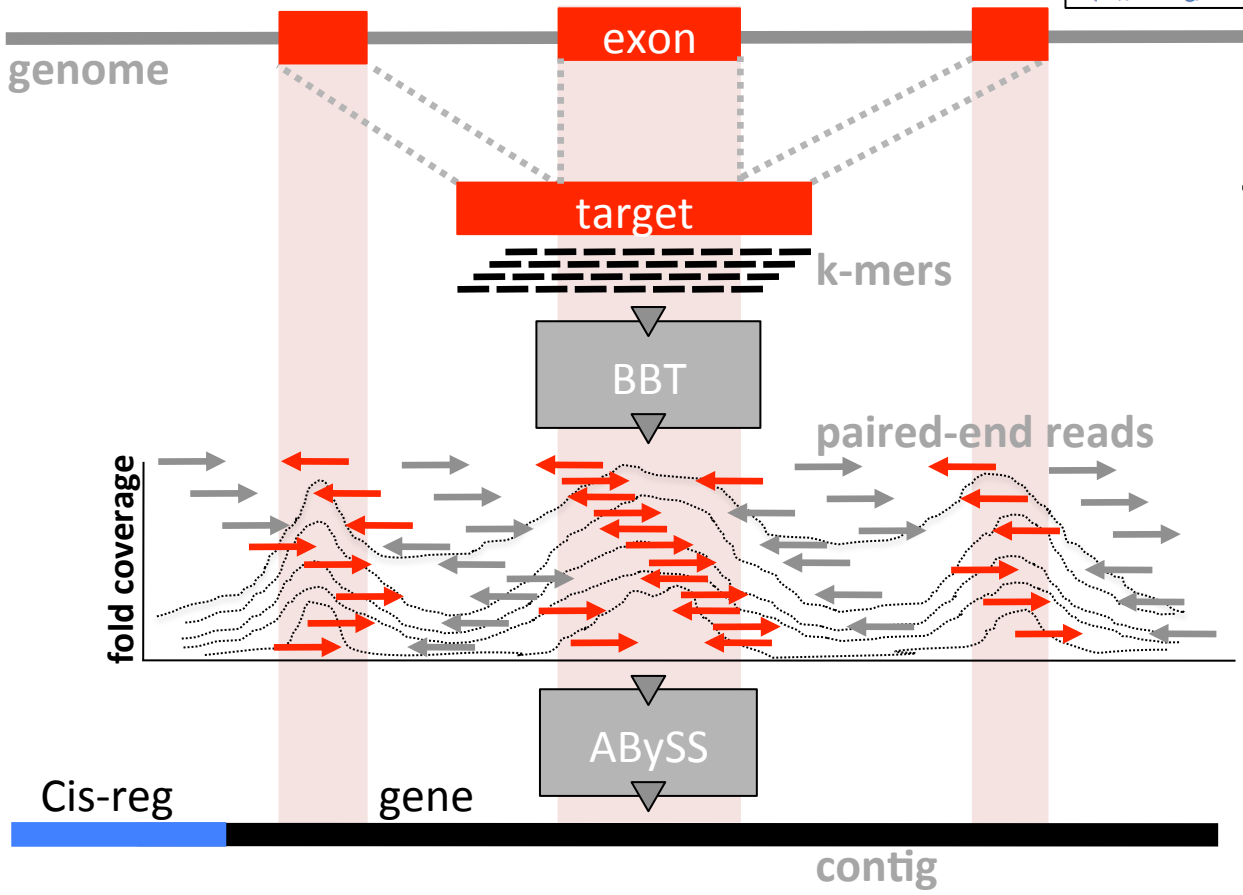
Using a progressive Bloom filter

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

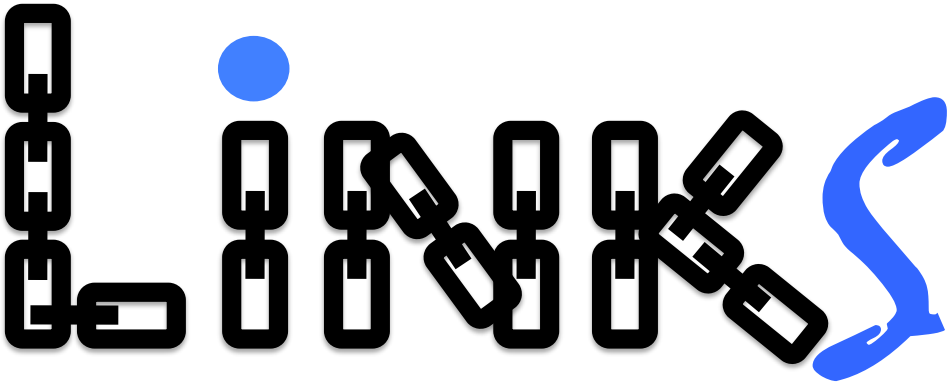


792 K bullfrog transcripts

5 iterations

624 K (79%) genes reconstructed

Scaffolding



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

(GIGA)n SCIENCE

RESEARCH Open Access

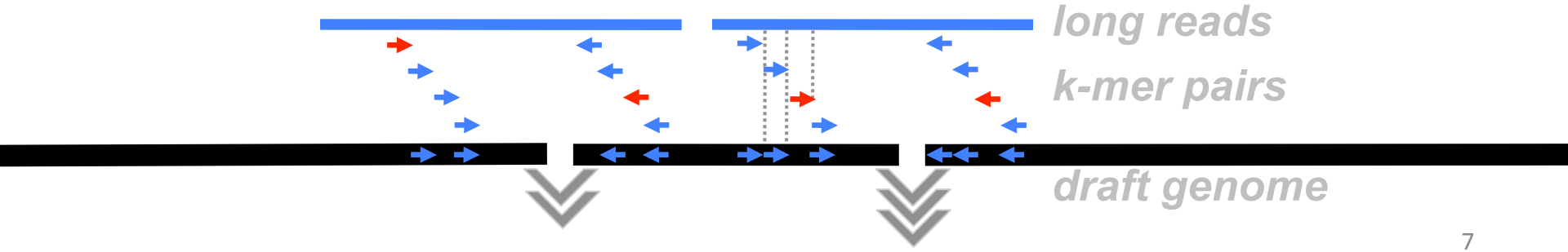
LINKS: Scalable, alignment-free scaffolding of draft genomes with long reads

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

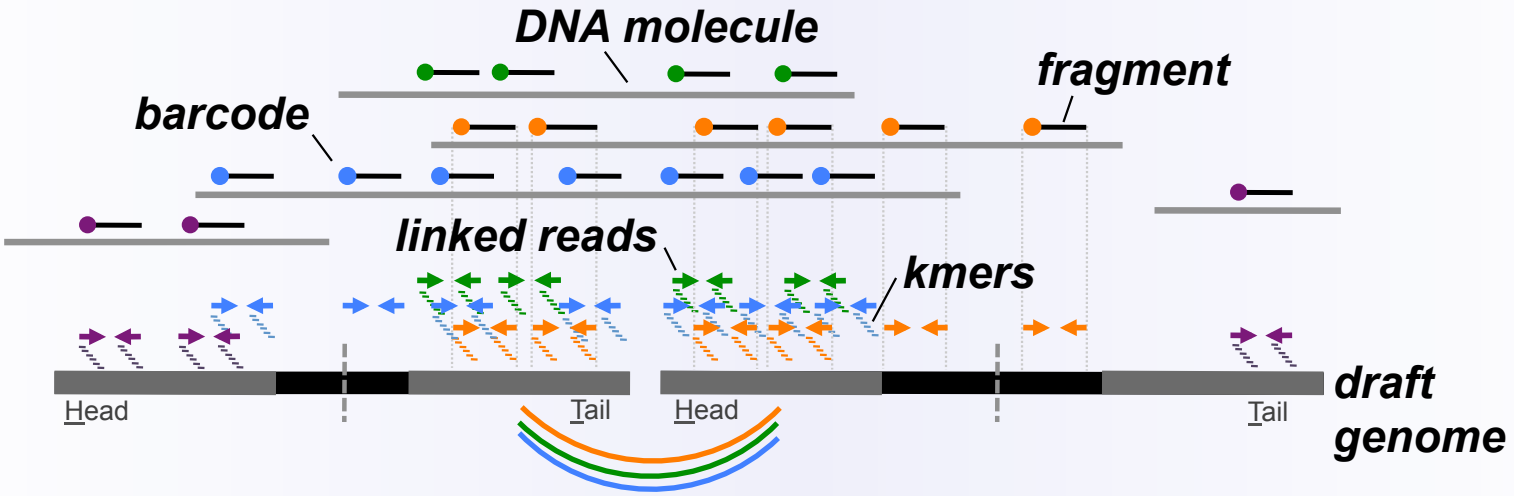
Long read kmer scaffolding

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

≠ length **≠ errors** **⃠ base correction**



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

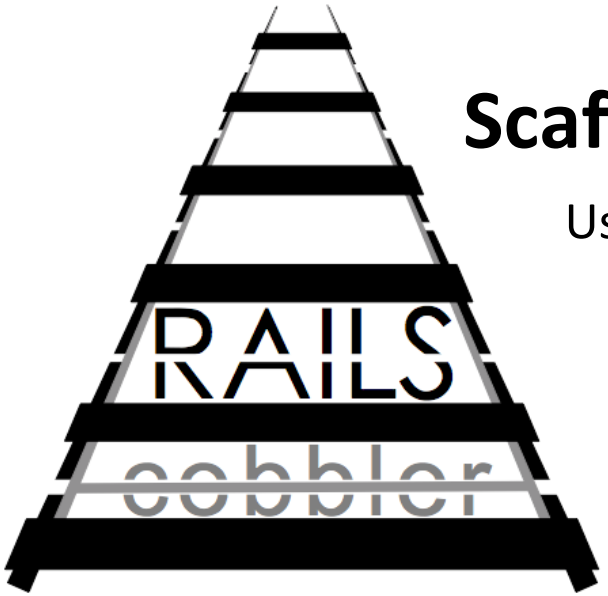
ARKS: chromosome-scale scaffolding of human genome drafts with linked read kmers

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

Gap-filling

Scaffolding and gap-filling

Uses LINKS scaffolding algorithm



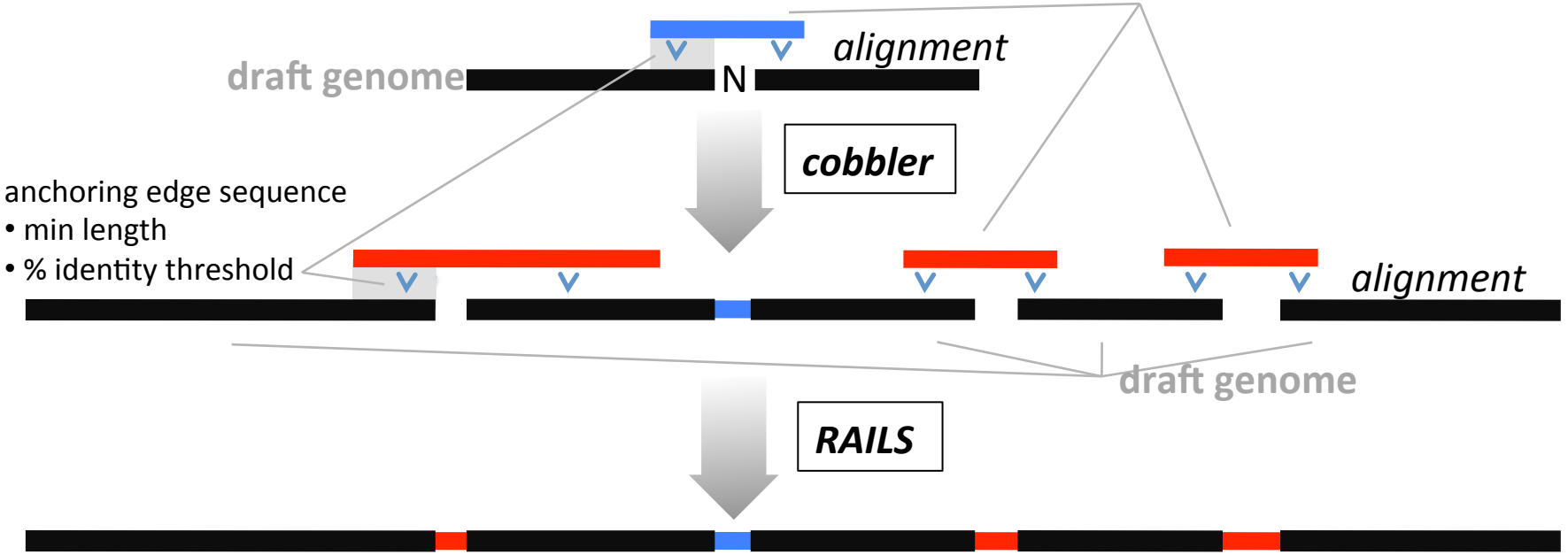
JSS The Journal of Open Source Software

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

long sequences (eg. Draft, Moleculo, Kollector, PacBio, Nanopore)



Gaps filled with sequence from the input with the most anchoring bases to the draft

Sealer

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

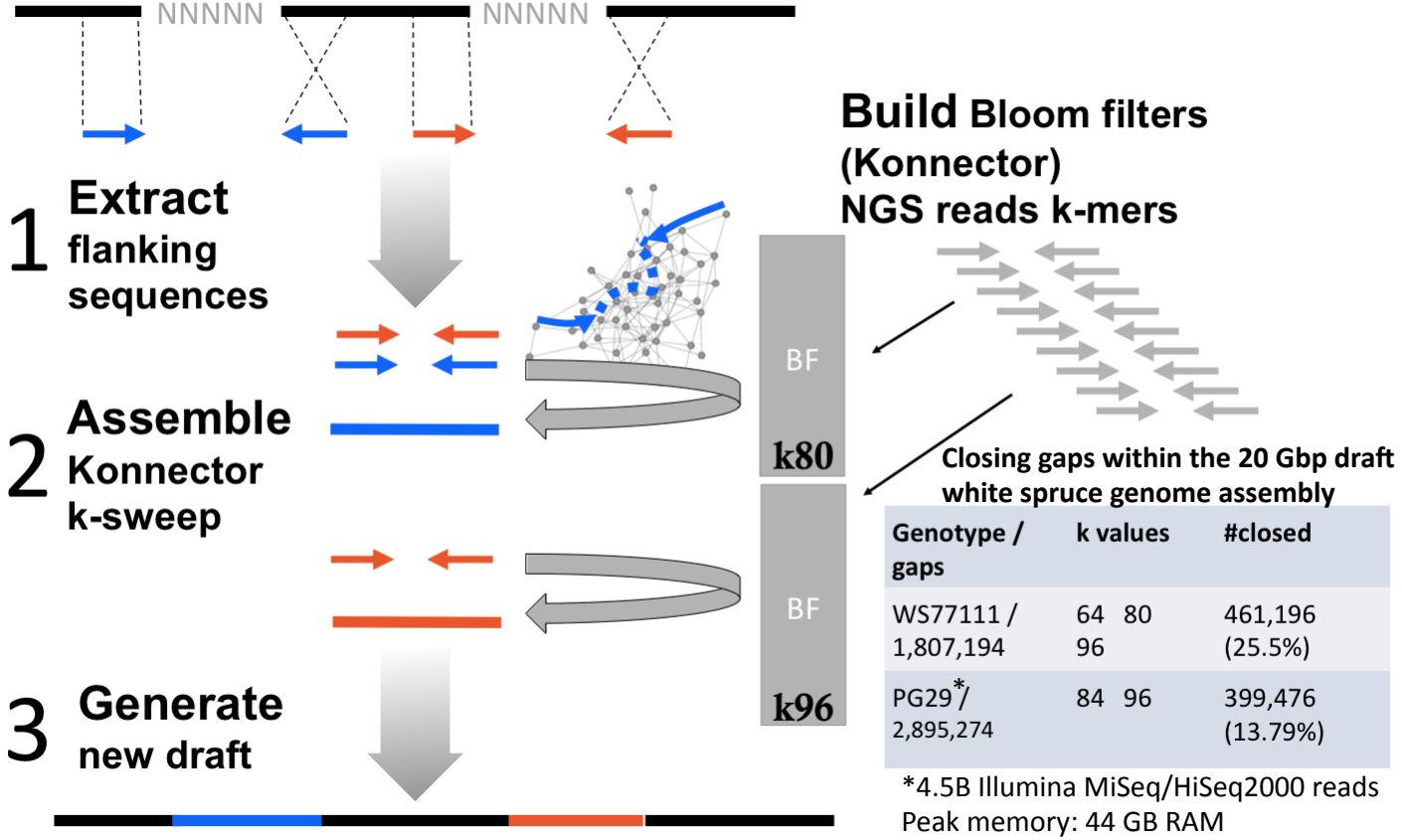
SOFTWARE Open Access

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

Automated genome finishing

- Gap-filler (resolve *N*s)
- Implements Bloom filter de Bruijn graph (Scalable)

Application of Konnector



Closing gaps within the 20 Gbp draft white spruce genome assembly

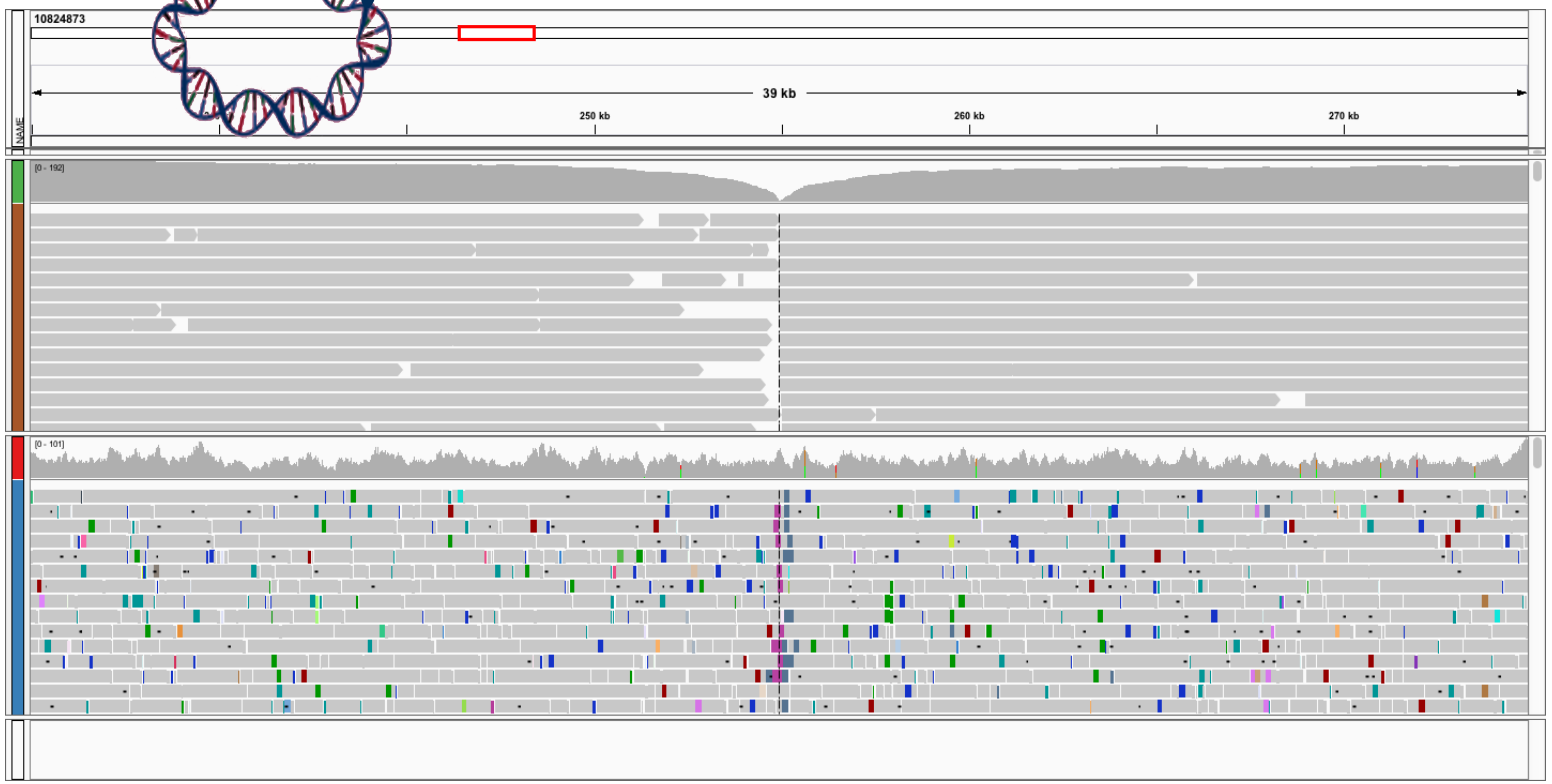
Genotype / gaps	k values	#closed
WS77111 / 1,807,194	64 80 96	461,196 (25.5%)
PG29*/ 2,895,274	84 96	399,476 (13.79%)

*4.5B Illumina MiSeq/HiSeq2000 reads
Peak memory: 44 GB RAM
Run time: 27h

Misassembly Correction & Assessment

Tigmint

Linked read misassembly correction



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.

BBT

Bio Bloom Tools

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

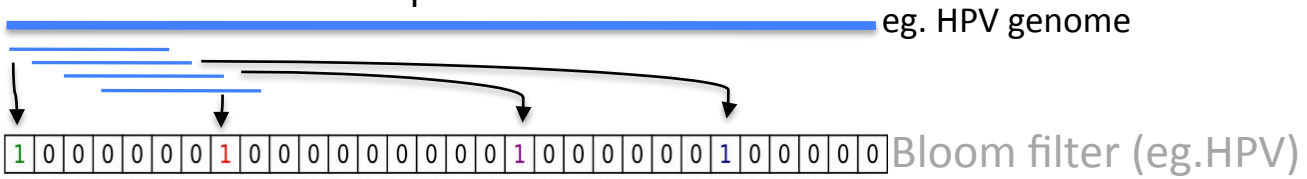
Bioinformatics, Volume 30, Issue 23, 1 December 2014, Pages 3402–3404,

Sequence classification with Bloom filters

Sequence filtering ***contaminant screening*** ***pathogen discovery***

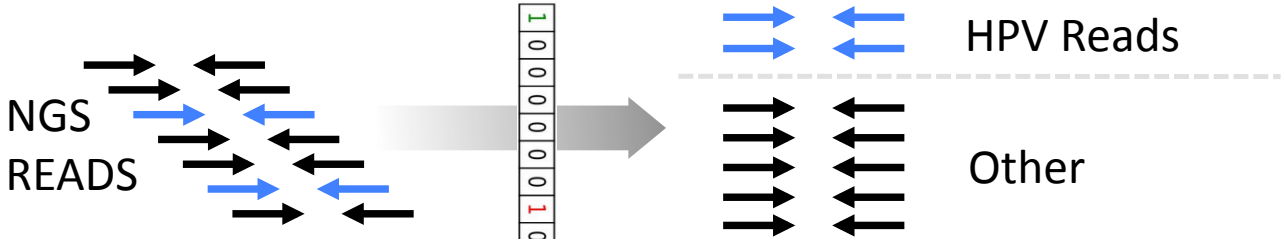
BioBloom-Maker

- 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

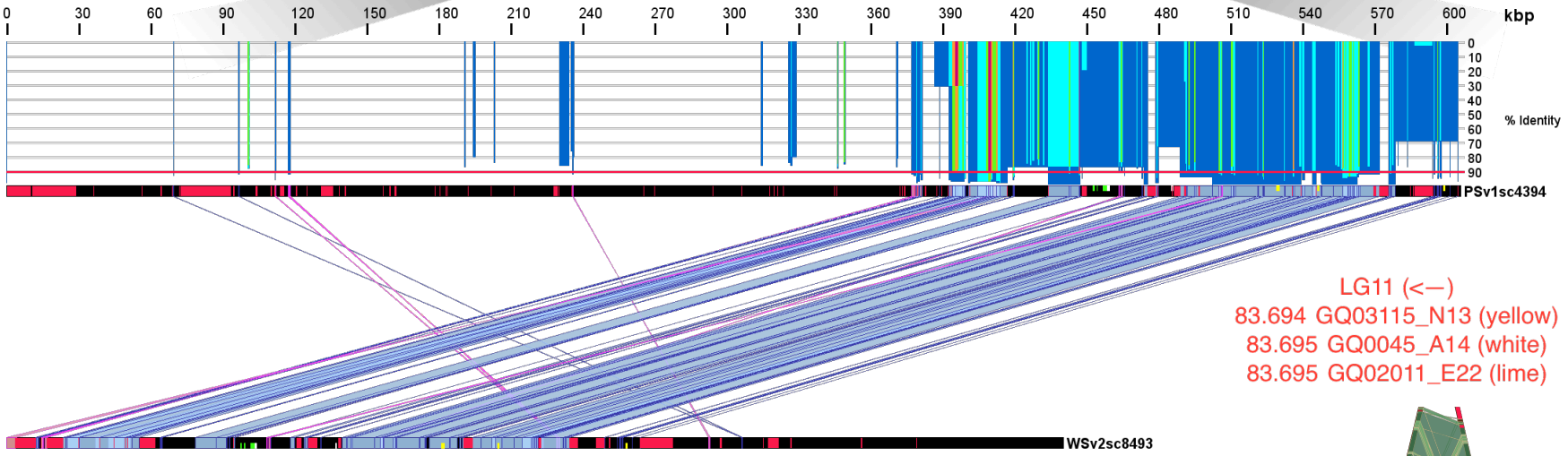


Categorizer

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



MATCHVIEW



LG11 (<—)
83.694 GQ03115_N13 (yellow)
83.695 GQ0045_A14 (white)
83.695 GQ02011_E22 (lime)

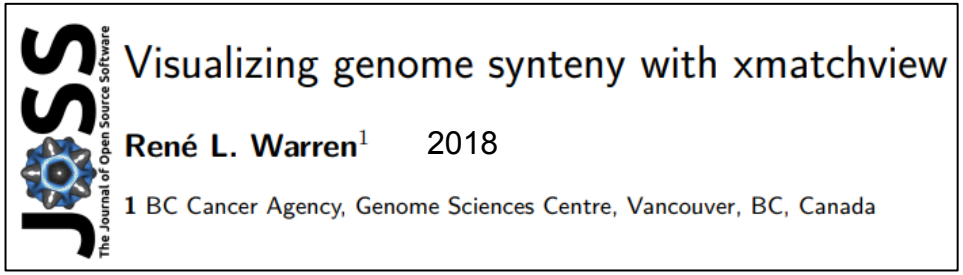
Legend

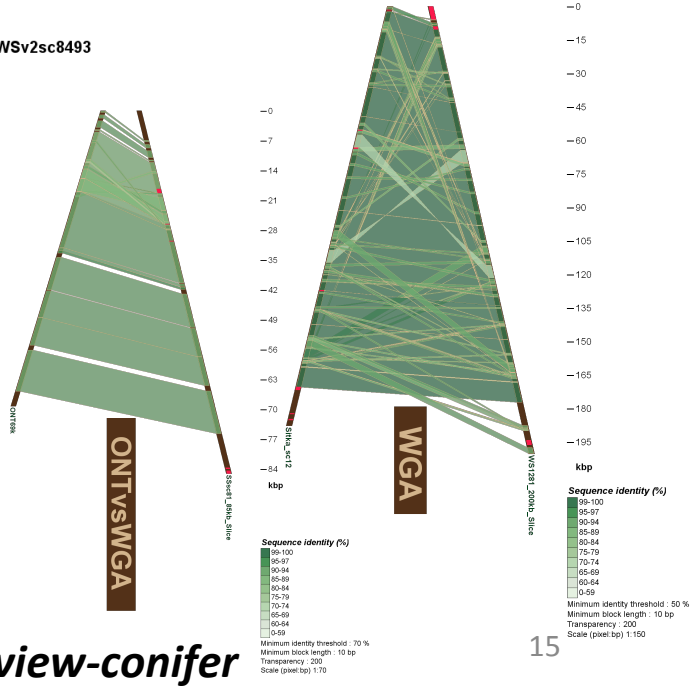
Frequency Repeated
- Single copy
- 2X
- 3X
- 4X
- 5X and over

Collinear Blocks
- Direct
- Inverted

Other
- Mismatch threshold
- Sequence features
- Ambiguous bases (Ns)

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



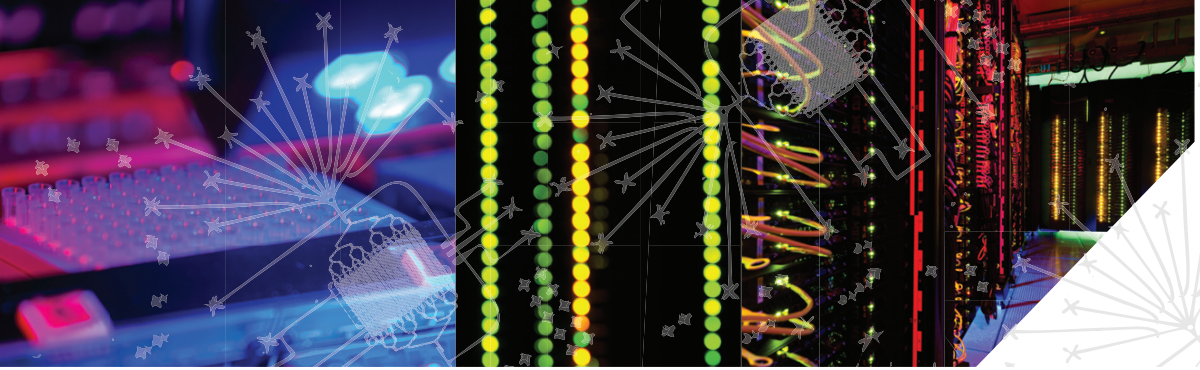


xmatchview-conifer

bt1 Projects

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

https://github.com/bcgsc



CANADA'S MICHAEL SMITH

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Photo: R. Warren