A toolkit for *de novo* assembly

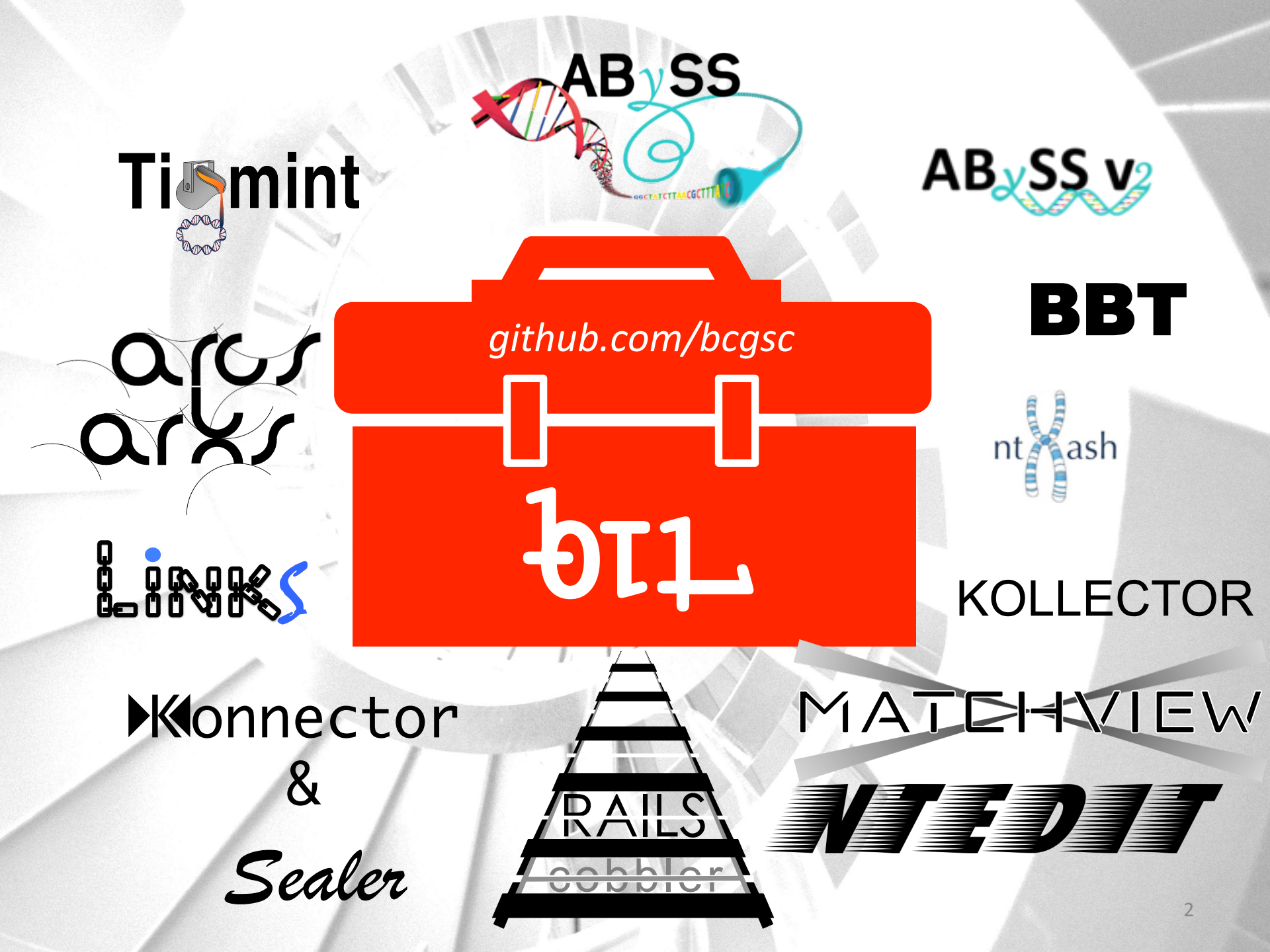
LINKS scaffold graph / *E. coli* K12

René L Warren 03/2019

CANADA'S MICHAEL SMITH GENOME SCIENCES CENTRE

bcgsc

Photo: R. Warren


ABySS
Tigmint
ABySS v2
github.com/bcgsc
BBT
arcs
arks
ntHash
bt2
LINKS
KOLLECTOR
Konnector
&
Sealer
RAILS
cobbler
MATCHVIEW
NTEDIT

Assembly

de novo genome assembly with short reads

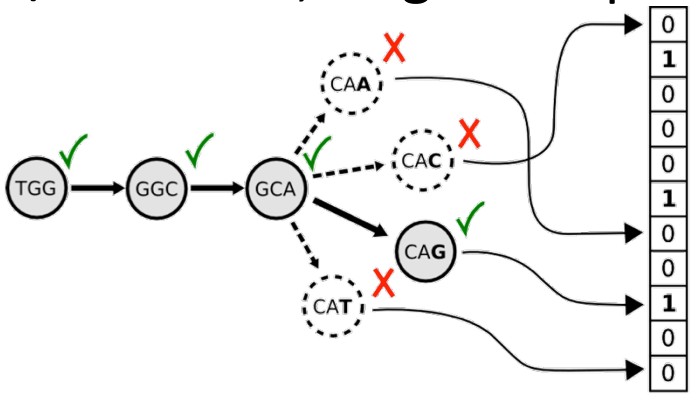
2009 : **Parallel DBG assembler**

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]

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

PLOS

DIDA: Distributed Indexing Dispatched Alignment

Hamid Mohamadi, Benjamin P Vandervalk, Anthony Raymond, Shaun D Jackman, Justin Chu, Clay P Breshears, Inanc Birol

Published: April 29, 2015 • https://doi.org/10.1371/journal.pone.0126409

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

Kollector: transcript-informed, targeted de novo assembly of gene loci

Erdi Kucuk, Justin Chu, Benjamin P. Vandervalk, S. Austin Hammond, René L. Warren ...

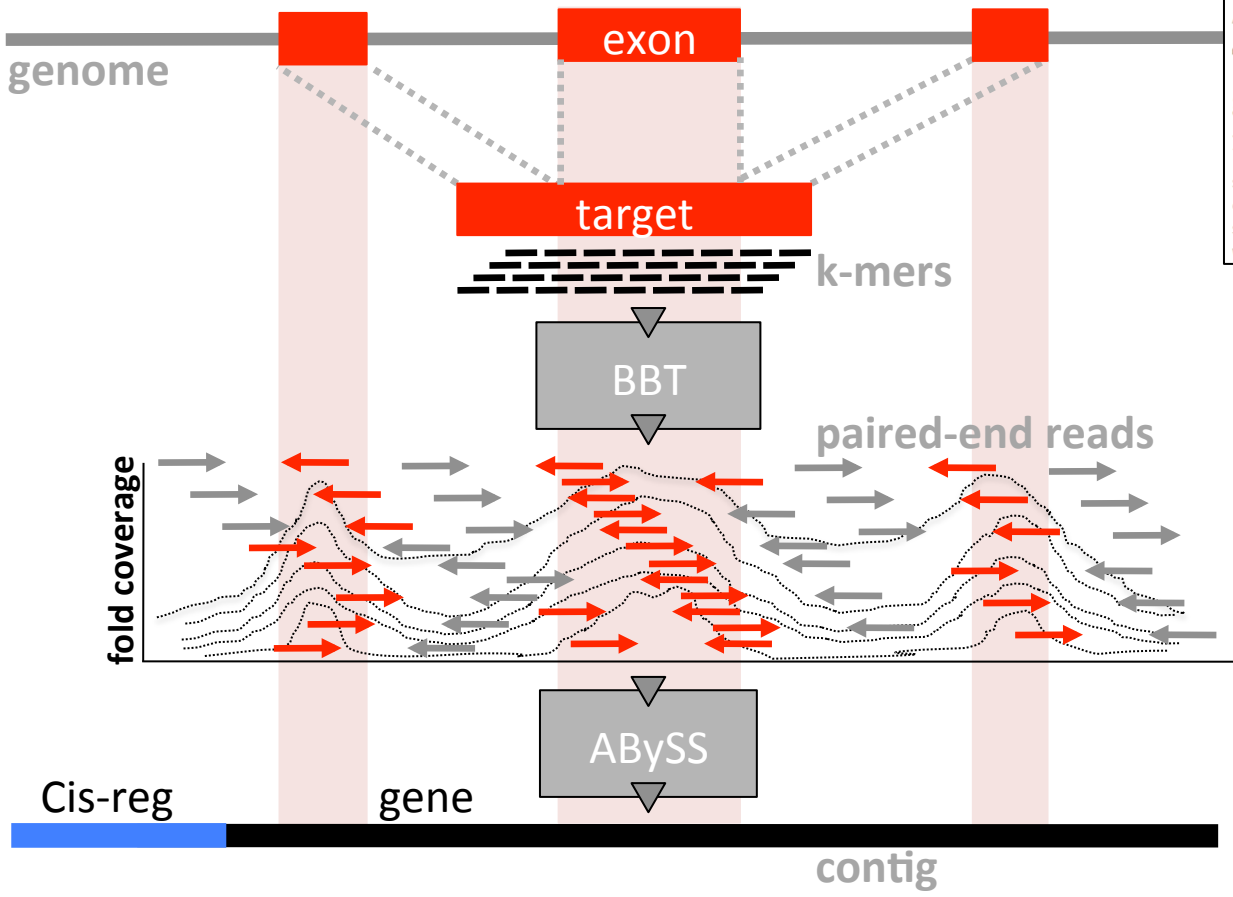
Bioinformatics, Volume 33, Issue 12, 15 June 2017, Pages 1782–1788,

nature COMMUNICATIONS

Article | OPEN | Published: 10 November 2017

The North American bullfrog draft genome provides insight into hormonal regulation of long noncoding RNA

S. Austin Hammond, René L. Warren, Benjamin P. Vandervalk, Erdi Kucuk, Hamza Khan, Ewan A. Gibb, Pawan Pandoh, Heather Kirk, Yongjun Zhao, Martin Jones, Andrew J. Mungall, Robin Coope, Stephen Pleasance, Richard A. Moore, Robert A. Holt, Jessica M. Round, Sara Ohora, Branden V. Walle, Nik Veldhoen, Caren C. Helbing & Inanc Birol

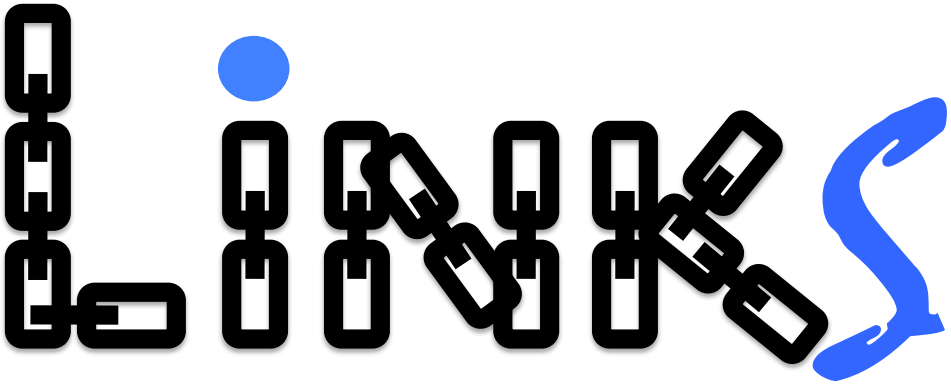


792 K bullfrog transcripts

5 iterations

624 K (~80%) genes reconstructed

Scaffolding



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

(GIGA)n SCIENCE

RESEARCH Open Access

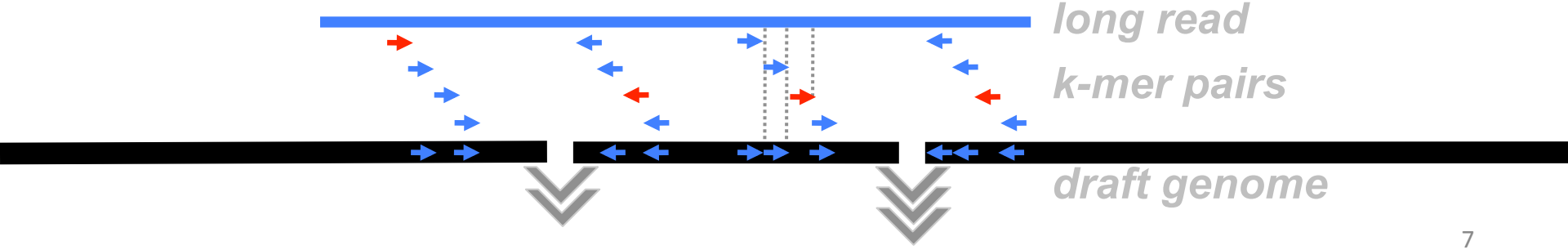
LINKS: Scalable, alignment-free scaffolding of draft genomes with long reads

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

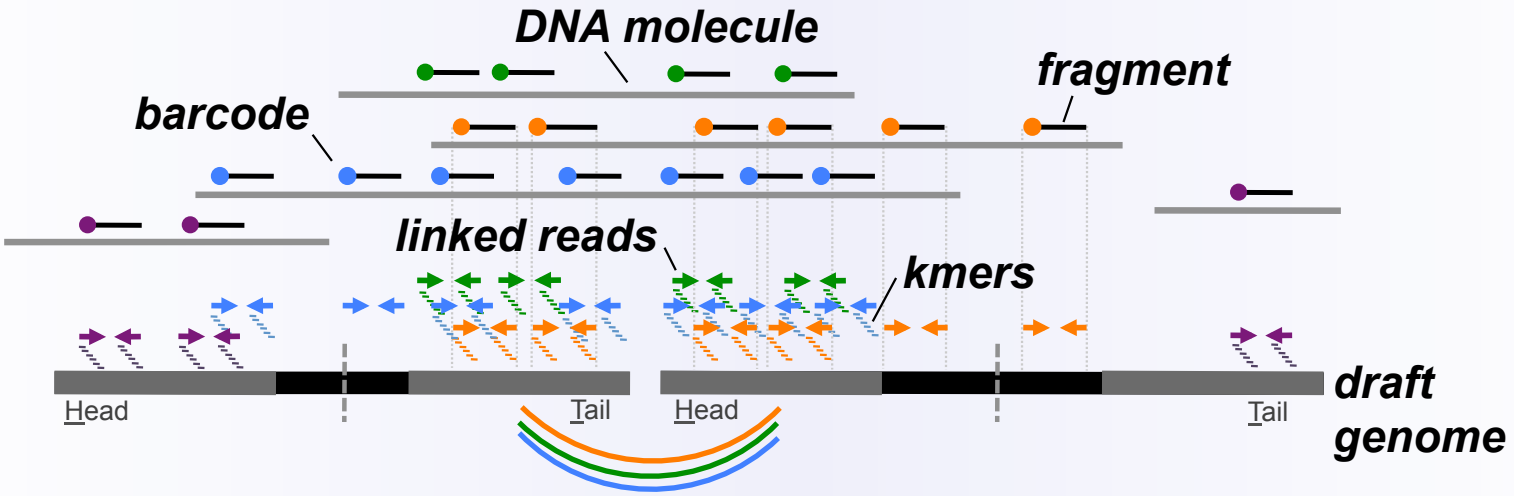
Long read kmer scaffolding

- **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

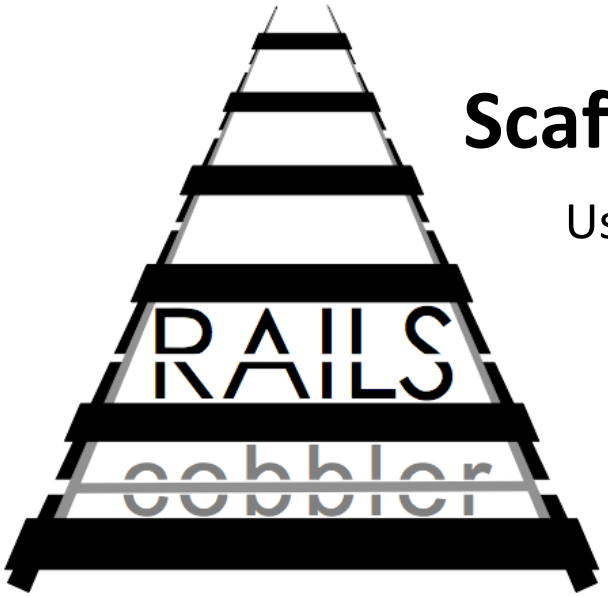
ARKS: chromosome-scale scaffolding of human genome drafts with linked read kmers

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



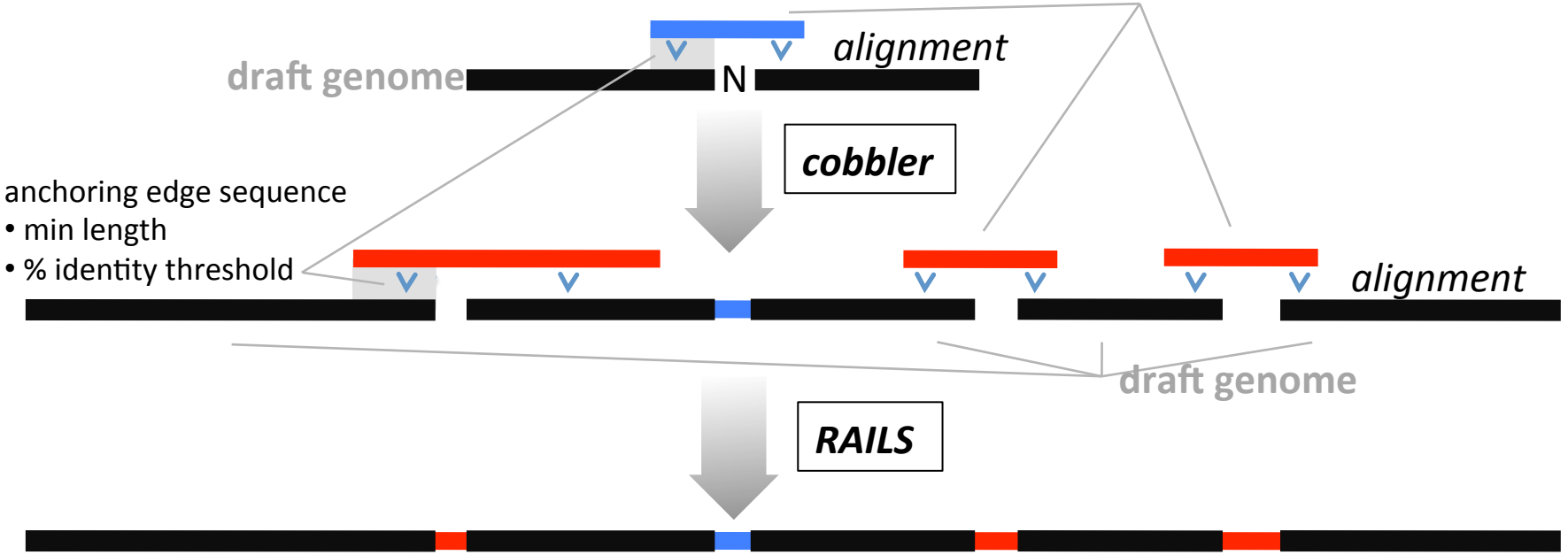
JSS The Journal of Open Source Software

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

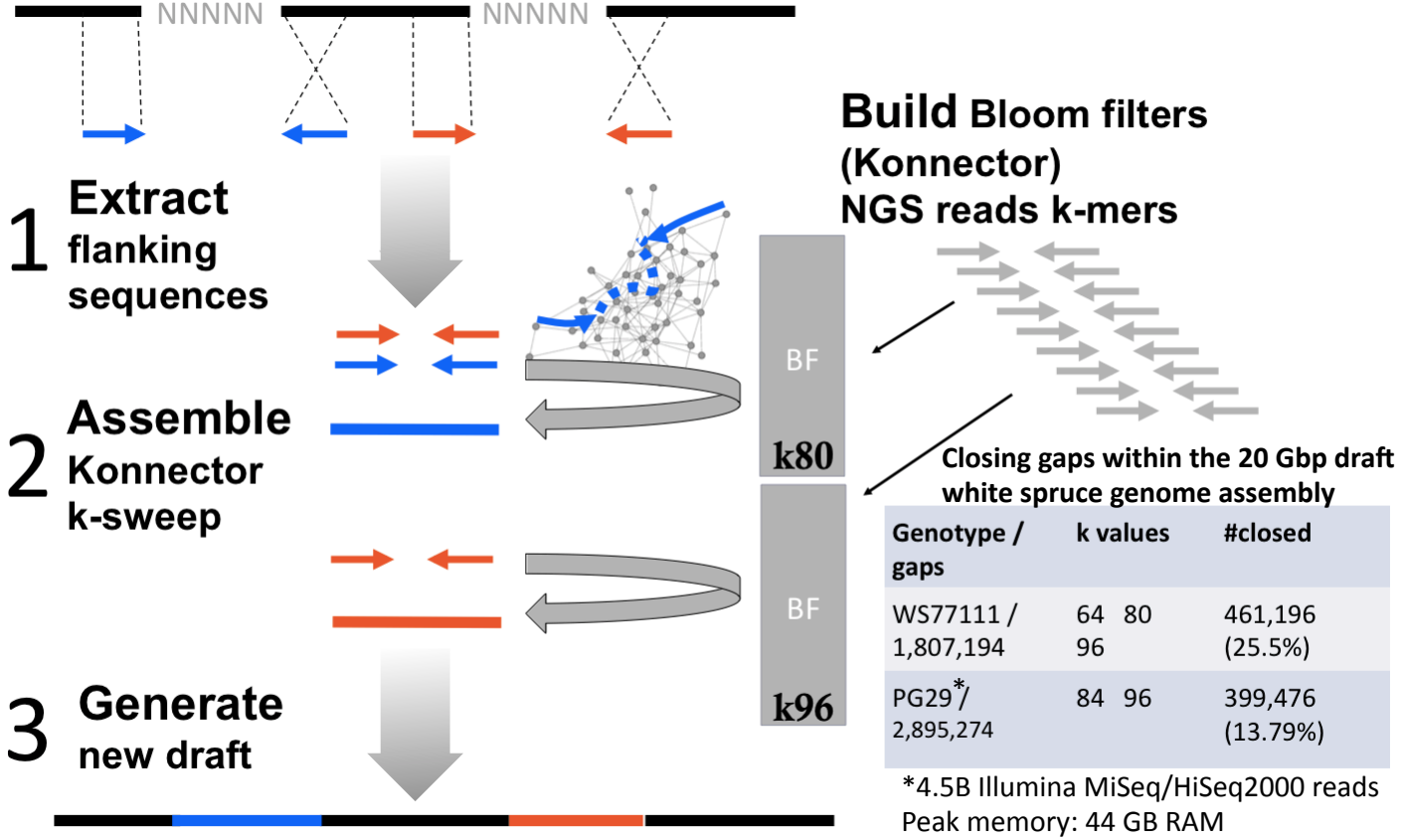
SOFTWARE Open Access

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%)

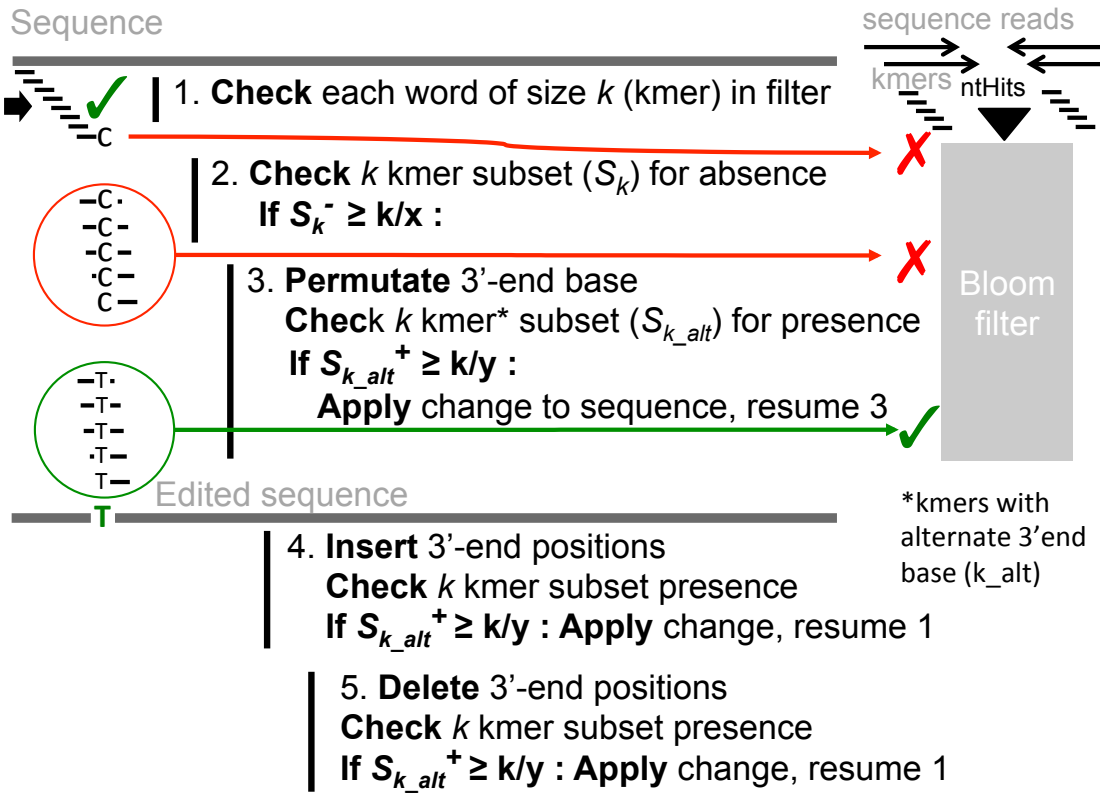
*4.5B Illumina MiSeq/HiSeq2000 reads
Peak memory: 44 GB RAM
Run time: 27h

Polishing

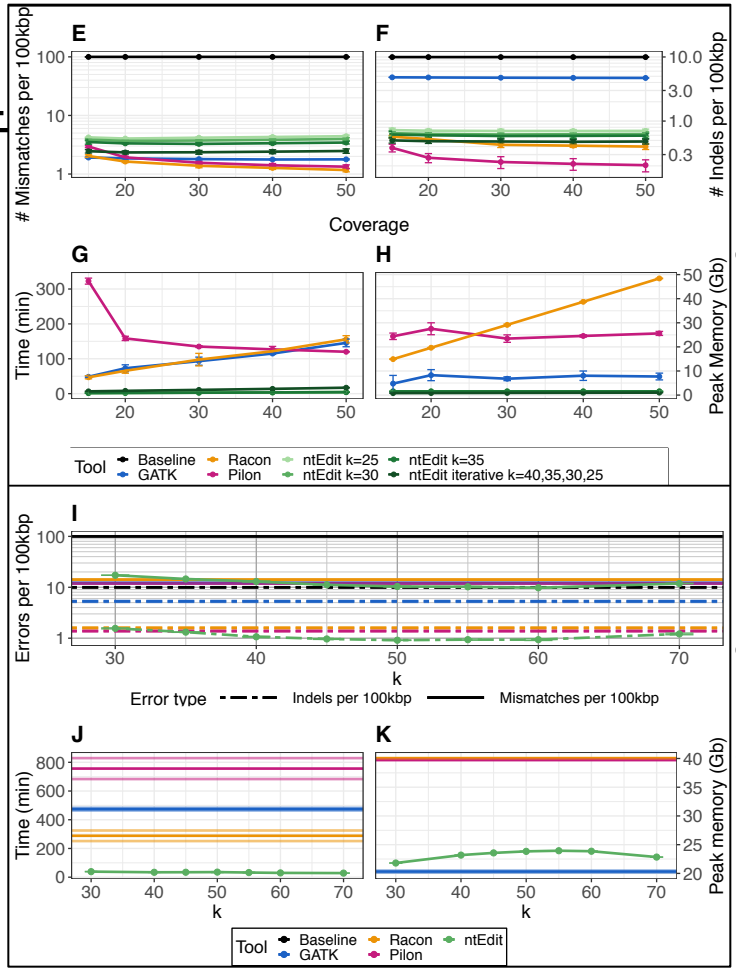
NTEDIT

Quickly fix homozygous errors and "haploidize" pseudo-haploid genome sequences

Approach



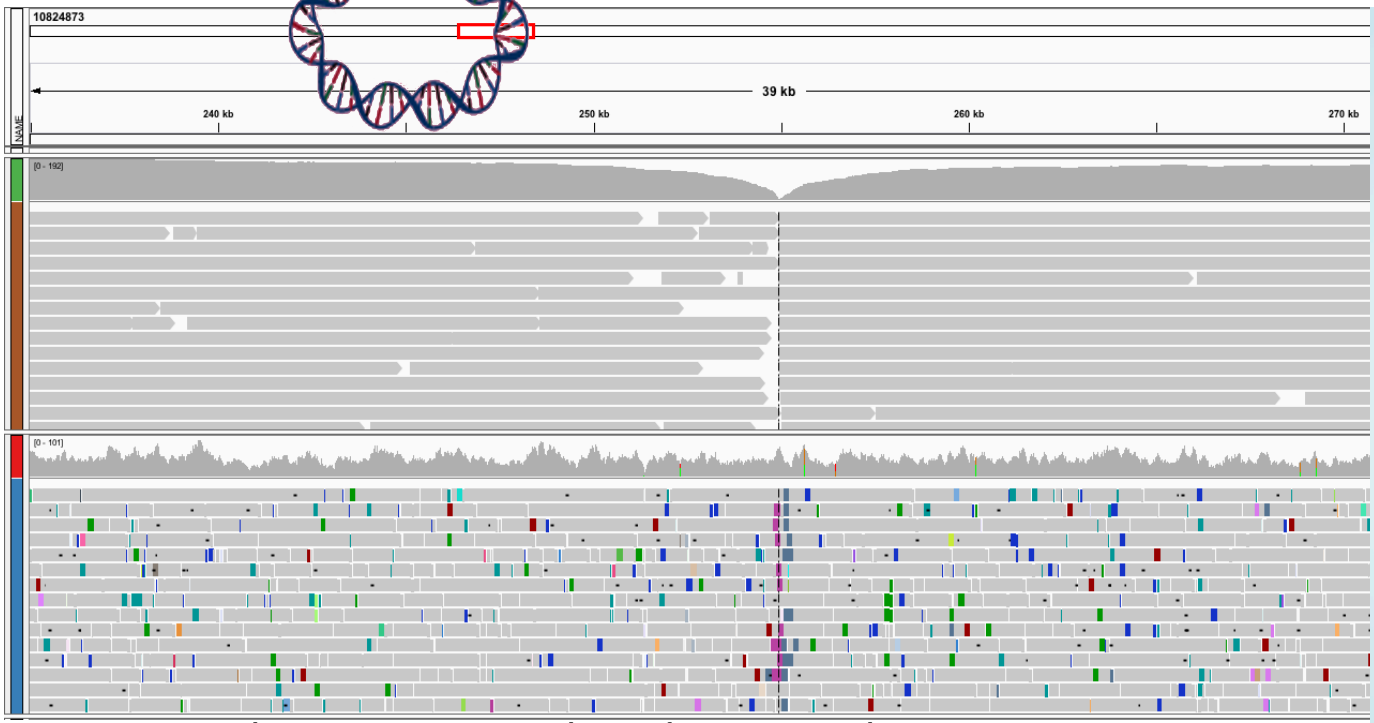
Results




Analysis

Tigmint

misassembly correction with linked reads



IGV screenshot: a Tigmint breakpoint in human genome NA24143

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]

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

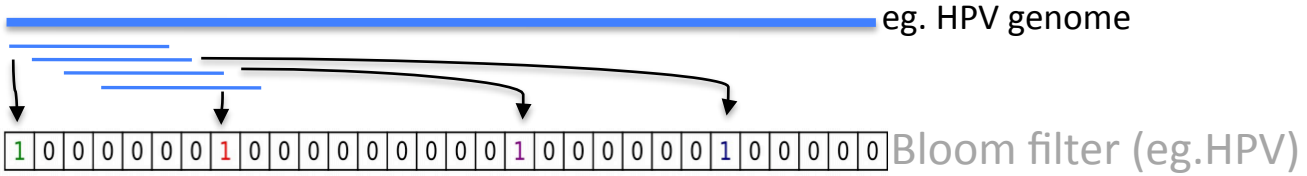
Bioinformatics, Volume 30, Issue 23, 1 December 2014, Pages 3402–3404,

Sequence classification with Bloom filters

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

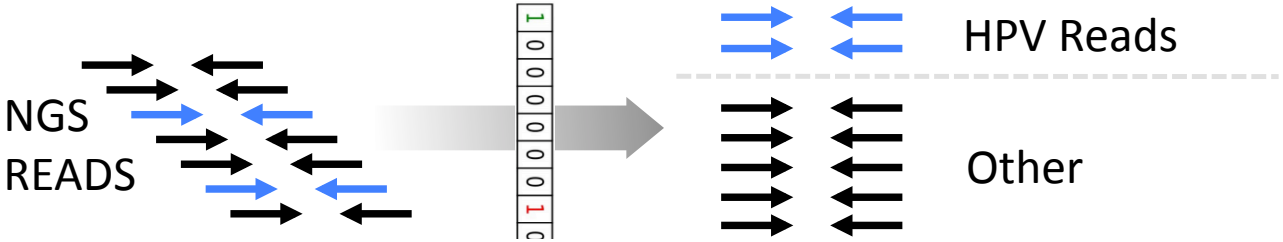
BioBloom-Maker

- 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** MiBF

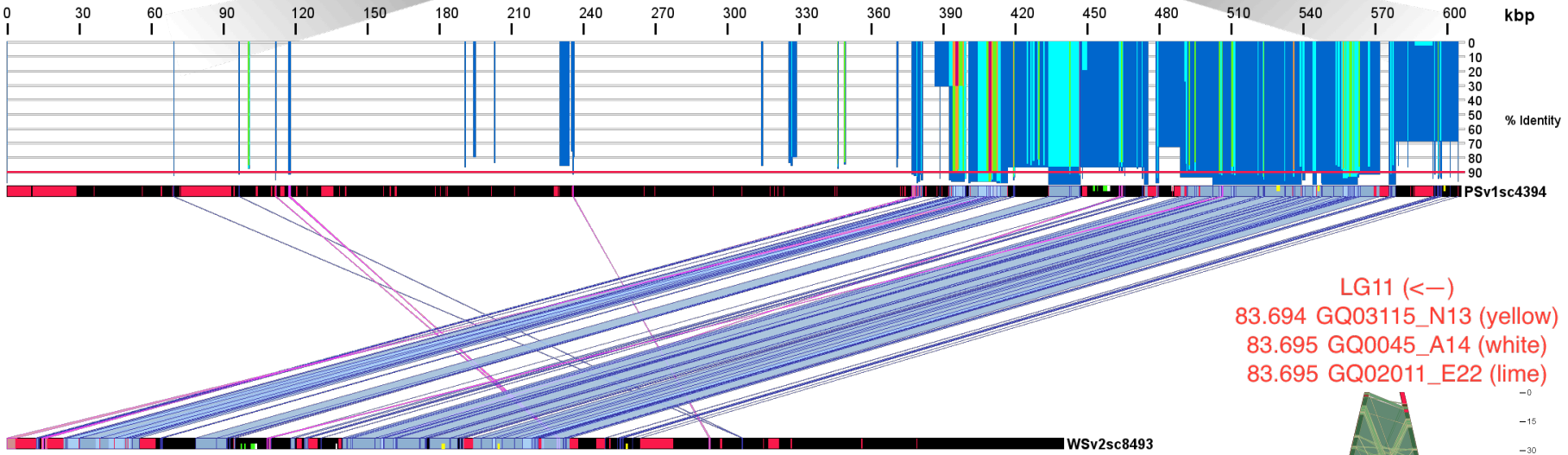


Categorizer

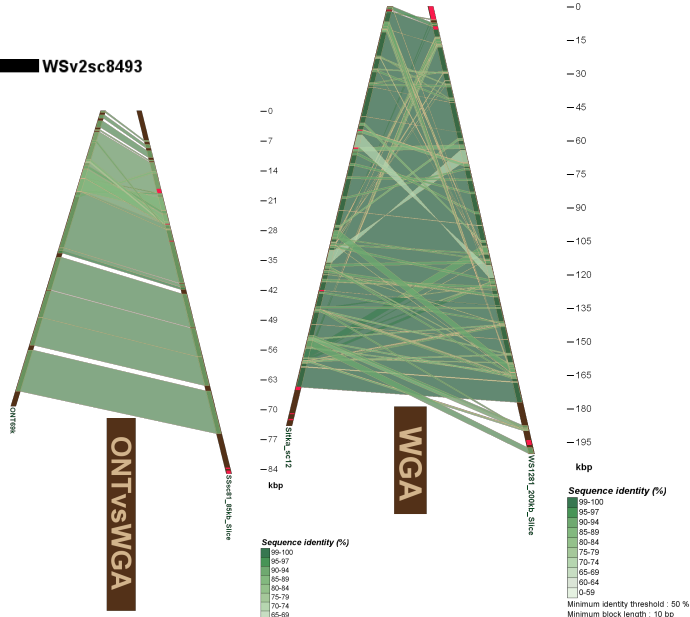
- Bins sequences : **Analysis summary** - hits tally to particular categories



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

JSS The Journal of Open Source Software

Visualizing genome synteny with xmatchview

René L. Warren[1] 2018

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

xmatchview-conifer

Additional bcgsc Technologies

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 linked read
	ConnectTig	: Nanopore-short read hybrid *de novo* assembler
Analysis	**PAVfinder**	: Structural variant finder (genomes/transcriptomes)
	AMPlify	: Antimicrobial peptide assessment 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**	: *De novo* exon annotation, splice graph construction
	Trans-ABySS	: Transcriptome Assembler with short reads
	RNA-Bloom	: Resource-efficient transcriptome assembler
	KLEAT	: Analysis of Alternative Poly-Adenylation
	TransNanoSim	: Transcript nanopore read simulator
Data structure	**miBF/BBT2**	: Multi-Index Bloom Filters
Algorithms	**ntHash**	: Fast nucleotide sequence hashing
	ntCard	: Sequencing data cardinality estimator
	ntHits	: Sequencing data repeat detection

https://github.com/bcgsc

ntPack

Funded Projects Landscape

	Granting Agency	Subject	Years	
*	Genome BC	Characterization and analysis of amphibian host defence peptides as potential antibiotics	10/2017 – 03/2019	AMPlify, AMPassayDB
*	NIH	De Novo Assembly Tools: Research with Unbiased Engines-Renewal (DNA-TRUER)	09/2017 – 07/2021	*de novo* assembly Tools, incl. ABySS2, TAILR, ConnectTig, etc
	NIH	De Novo Assembly Tools: Research with Unbiased Engines (DNA-TRUE)	03/2014 – 01/2017	
*	Genome BC	Automation of the Clinical Bioinformatics Pipeline at the Centre for Clinical Genomics	04/2017 – 03/2020	TAP
	Genome Canada	New bioinformatics for new sequencing technologies: Genome characterization and variation detection using long reads	10/2016 – 09/2018	TransNanosim, RNA-Bloom
*	Genome Canada	Spruce-Up: Advanced spruce genomics for productive and resilient forests	10/2016 – 09/2020	ABySS-LR, gNavigator, XMVc
*	CIHR	Development of an automated end-to-end next generation sequencing assay to detect all classes of genetic variant in a single diagnostic test	04/2016 – 03/2019	PAVfinder
	NIH	Pan-cancer survey of candidate non-coding RNA transcripts on the cloud using a targeted de novo assembly approach	01/2016 – 08/2016	TASR-KLEAT
	Genome Canada	Methods and Technology Development at the Sequencing Platform at the BC Cancer Agency Genome Sciences Centre	10/2015 – 09/2017	ntPack, Konnector RAILS
	BC Cancer Foundation	Next Generation Bioinformatics for Clinical Genomics: using de novo assembly in personalized medicine	06/2015 – 06/2016	RNA-Bloom
	Genome BC	Advanced Assembly Assessment and Annotation	10/2014 – 03/2016	ABySS-Bloom, Kollector
	Genome Canada	SMarTForests: Spruce Marker Technologies for Sustainable Forestry	07/2011 – 09/2015	DIDA, LINKS

*active

Translational Aspect


Robert Warren, 1979

nature COMMUNICATIONS

Article | OPEN | Published: 10 November 2017

The North American bullfrog draft genome provides insight into hormonal regulation of long noncoding RNA

S. Austin Hammond, René L. Warren, Benjamin P. Vandervalk, Erdi Kucuk, Hamza Khan, Ewan A. Gibb, Pawan Pandoh, Heather Kirk, Yongjun Zhao, Martin Jones, Andrew J. Mungall, Robin Coope, Stephen Pleasance, Richard A. Moore, Robert A. Holt, Jessica M. Round, Sara Ohora, Branden V. Walle, Nik Veldhoen, Caren C. Helbing & Inanc Birol


René Warren, 2007

genes

MDPI

Article

The Genome of the Beluga Whale (*Delphinapterus leucas*)

Steven J. M. Jones [1,2,3,*], Gregory A. Taylor [1], Simon Chan [1], René L. Warren [1], S. Austin Hammond [1], Steven Bilobram [1], Gideon Mordecai [4,5], Curtis A. Suttle [4,5,6,7], Kristina M. Miller [8], Angela Schulze [8], Amy M. Chan [4,5], Samantha J. Jones [1,3], Kane Tse [1], Irene Li [1], Dorothy Cheung [1], Karen L. Mungall [1], Caleb Choo [1], Adrian Ally [1], Noreen Dhalla [1], Angela K. Y. Tam [1], Armelle Troussard [1], Heather Kirk [1], Pawan Pandoh [1], Daniel Paulino [1], Robin J. N. Coope [1], Andrew J. Mungall [1], Richard Moore [1], Yongjun Zhao [1], Inanc Birol [1,3], Yussanne Ma [1], Marco Marra [1,3] and Martin Haulena [9]


Noémie Warren, 2017

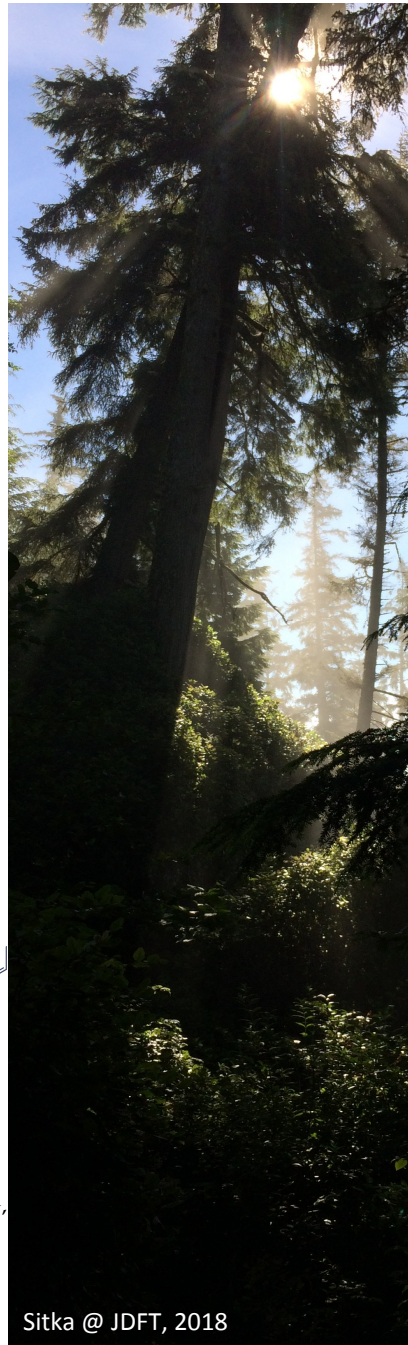
genes

MDPI

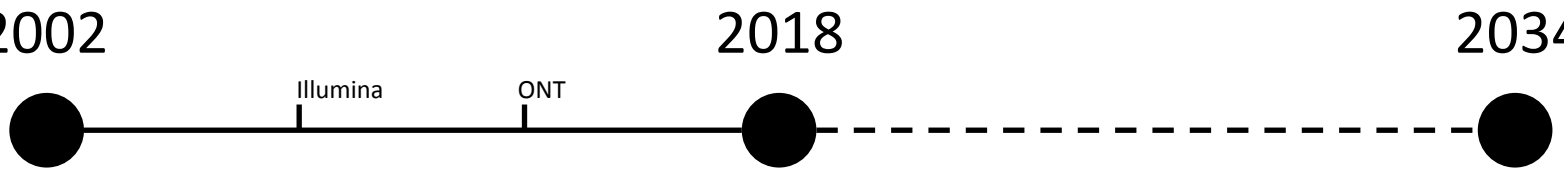
Article

The Genome of the Northern Sea Otter (*Enhydra lutris kenyoni*)

Samantha J. Jones [1,2], Martin Haulena [3], Gregory A. Taylor [1], Simon Chan [1], Steven Bilobram [1], René L. Warren [1], S. Austin Hammond [1], Karen L. Mungall [1], Caleb Choo [1], Heather Kirk [1], Pawan Pandoh [1], Adrian Ally [1], Noreen Dhalla [1], Angela K. Y. Tam [1], Armelle Troussard [1], Daniel Paulino [1], Robin J. N. Coope [1], Andrew J. Mungall [1], Richard Moore [1], Yongjun Zhao [1], Inanc Birol [1,2], Yussanne Ma [1], Marco Marra [1,2] and Steven J. M. Jones [1,2,4,*]


Sitka @ JDFT, 2018

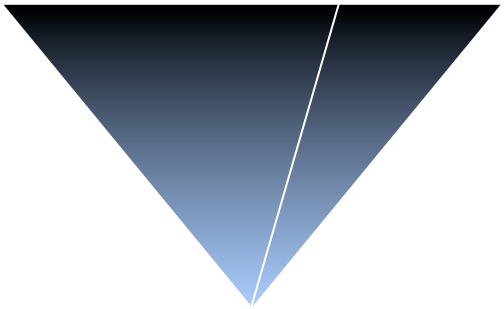
Perspective

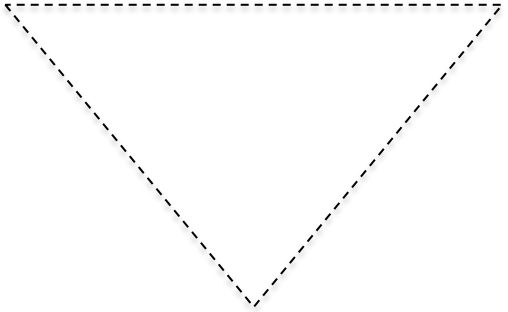


1 x 10 Mbp
bacterial genome

4 x 20 Gbp
conifer genomes ++

?

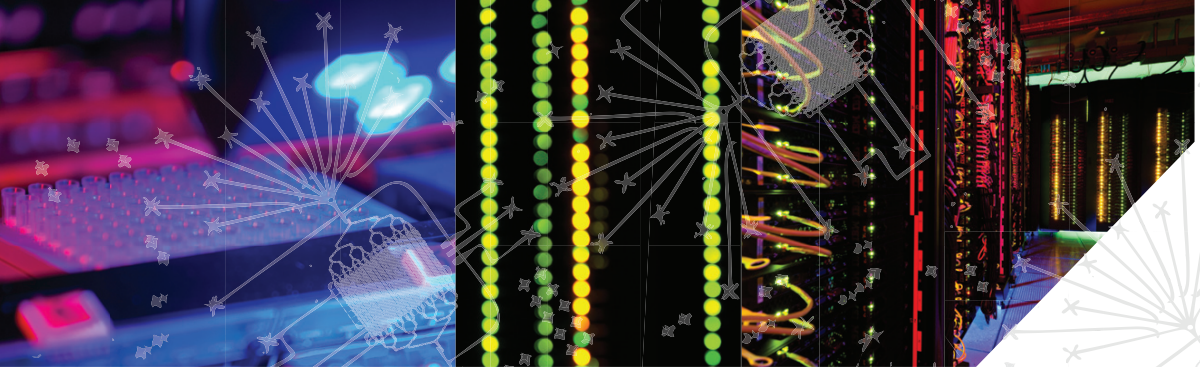




- Illumina/HT Sequencing
- Long read sequencing
- Advances in comp. sci.
- **Bioinformatics R&D**

?

Opportunities



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

birollab.ca

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

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Justin Chu | Shaun Jackman | Chen Yang | Kristina Gagalova | Ka Ming Nip
Golnar Sheikhshab | Saber Hafezqorani | Chenkai Li | Yee Fay Lim | Figali Taho
Amirhossein Afshinfard | Readman Chiu | Hamid Mohamadi
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Tony Raymond | Daniel Paulino | Sarah Yeo | Erdi Kucuk | Hamza Khan

BC CANCER NIH GenomeBritishColumbia GenomeCanada intel *John Jambor Knowledge Fund*

Photo: R. Warren