Compacting de Bruijn graphs from sequencing data quickly and in low memory

Rayan Chikhi (CNRS)

joint work with A. Limasset (ENS Rennes), P. Medvedev (Penn State)

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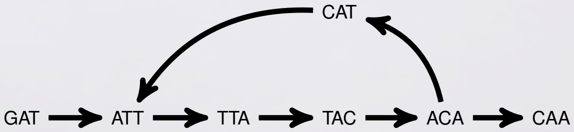
de Bruijn Graph

```
sequence:   GATTACATTACAA
  k-mers:   GAT
   (k=3)     ATT
              TTA
               ...
```

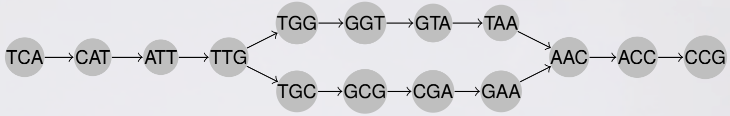
nodes: k-mers (words of length k)
edges: exact suffix-prefix overlaps of length $k-1$



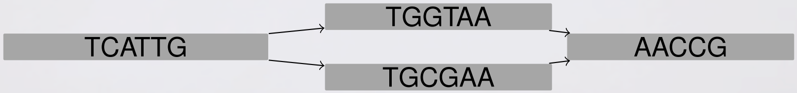
- assembly of genomes, metagenomes
- variant calling
- RNA-seq assembly & quantification

Compacted de Bruijn Graph

non-compacted de Bruijn graph:



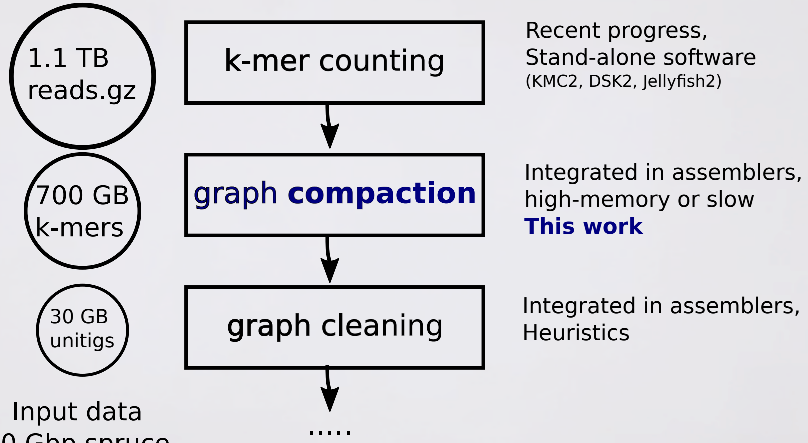
Compacted de Bruijn graph:



Each non-branching path becomes a single node (*unitig*).

- no loss of information
- less space

Steps of de Bruijn graph assemblers



1.1 TB reads.gz
k-mer counting
Recent progress, Stand-alone software (KMC2, DSK2, Jellyfish2)
700 GB k-mers
graph **compaction**
Integrated in assemblers, high-memory or slow
This work
30 GB unitigs
graph cleaning
Integrated in assemblers, Heuristics
.....

Input data
20 Gbp spruce
[Birol 2013]

- computationally intensive
- bottlenecks at early stages

20 Gbp spruce and 22 Gbp pine

Previous assemblies

- spruce: 2 days, 1380 cores, 4.3 TB RAM [Birol 2013]
- pine: 3 months, 32 cores, 0.8 TB RAM [Zimin 2014]

This work:
improve performance by **orders of magnitude** (up to compaction step)

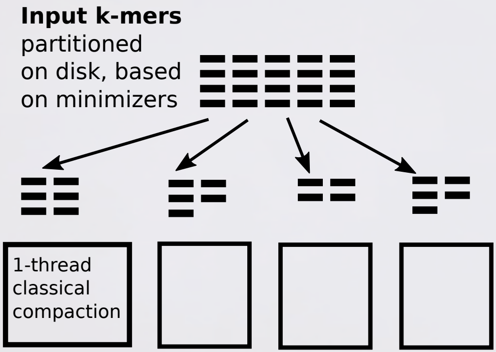
BCALM 2

Software for constructing and compacting de Bruijn graphs

Successor of BCALM 1 (single-threaded)

Parallel graph compaction is non-trivial, let’s see why..

Parallel compaction, first attempt



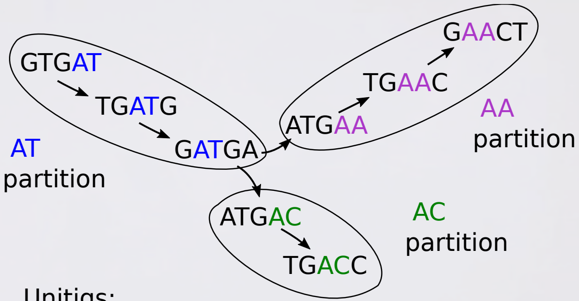
minimizer of *s*:
smallest ℓ-mer in *s*
[Roberts *et al*, 2004]

e.g. ($\ell = 2$, lexicographical order)

```
TGACGGG
 GACGGGT
  ACGGGTC
   CGGGTCA
    GGGTCAG
     GGTCAGA
```

Frequency ordering
$\rightarrow$ better repartition.
[RECOMB'14]

Compaction of partitions

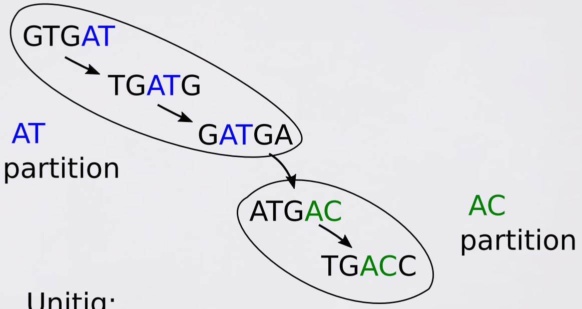


Unitigs:

GTGATGA
ATGACC
ATGAACT

k-mers are partitioned w.r.t minimizer.
In this case, compacting all partitions returns exactly all the unitigs.

Compaction of partitions (2)

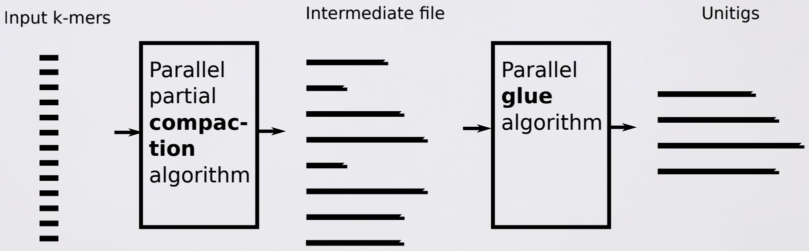


Unitig:

GTGATGACC

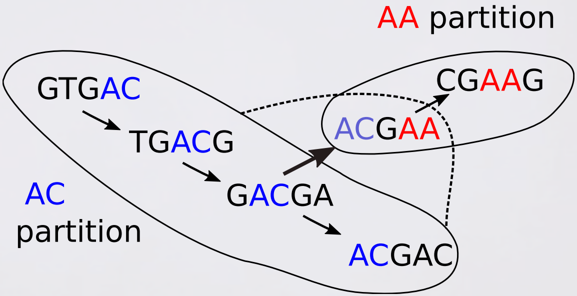
This case indicates that partitions contain sub-strings of unitigs.
Those substrings need to be later merged.

2-step strategy


Input k-mers
Parallel partial **compaction** algorithm
Intermediate file
Parallel **glue** algorithm
Unitigs

Simple partitioning is not enough

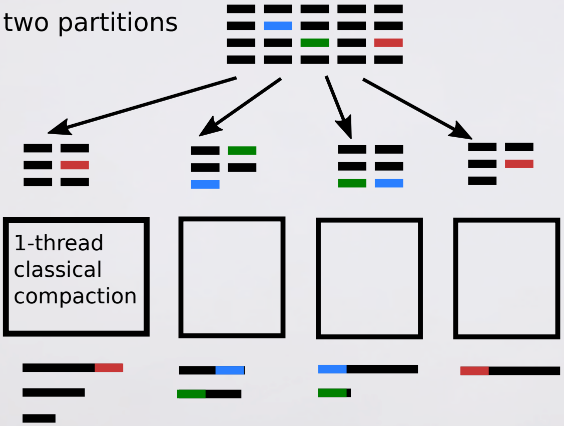
Compacting partitions may create false unitigs (due to missing edges).



- A simple fix: put certain *k*-mers into two partitions.
- x is a **doubled kmer** when minimizer($x[1..k-1]$) $\neq$ minimizer($x[2 \dots k]$).

BCALM 2’s partial compaction module

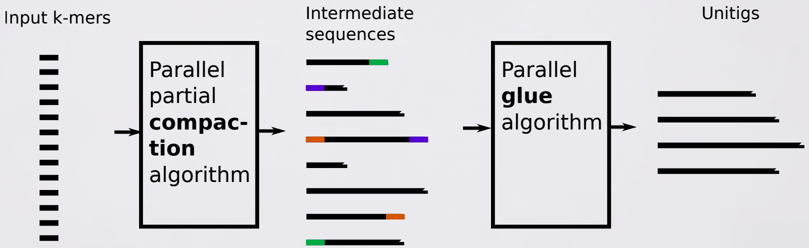
Doubled kmers are inserted in two partitions



Lemma 1: doubled *k*-mers appear as prefixes or suffixes of compacted strings.

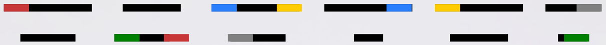
Lemma 2: Gluing together strings with matching doubled *k*-mers yield unitigs.

Big picture


Input k-mers
Parallel partial **compaction** algorithm
Intermediate sequences
Parallel **glue** algorithm
Unitigs

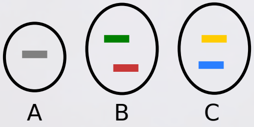
BCALM 2's glue module

Input sequences



Cannot load all sequences in memory. Need again to partition.
Would like to have , and in the same partition.

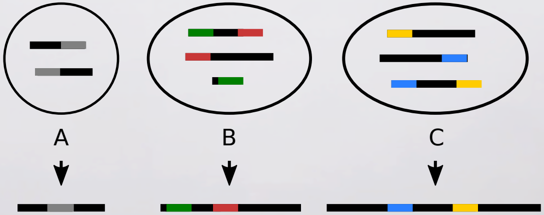
Union-find
of doubled kmers



Minimal perfect
hash table

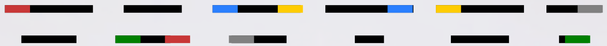
1	🟨	C
2	🟩	B
3	🟦	C
4	🟥	B
5	▨	A

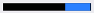
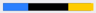
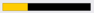
Sequences of
each U-F class
are loaded
and glued
in parallel.



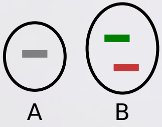
BCALM 2’s glue module

Input sequences



Cannot load all sequences in memory. Need again to partition.
Would like to have ,  and  in the same partition.

Union-find
of doubled kmers



Minimal perfect
hash table

Sequences of
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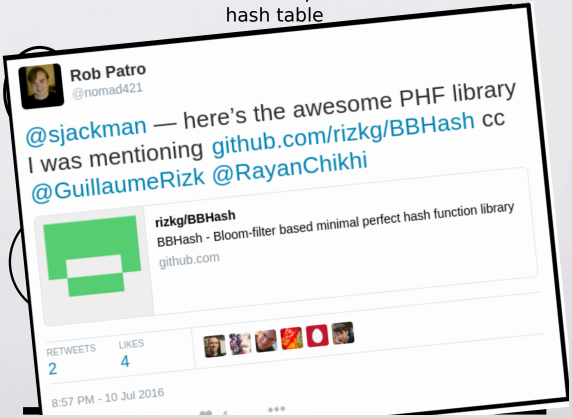

Rob Patro
@nomad421

@sjackman — here’s the awesome PHF library I was mentioning github.com/rizkg/BBHash cc @GuillaumeRizk @RayanChikhi

rizkg/BBHash
BBHash - Bloom-filter based minimal perfect hash function library
github.com

RETWEETS 2
LIKES 4

8:57 PM - 10 Jul 2016

20 Gbp spruce and 22 Gbp pine

Previously,
spruce: 2 days, 1380 cores, 4.3 TB RAM (Abyss) [Birol 2013]
pine: 3 months, 32 cores, 0.8 TB RAM (MaSuRCA) [Zimin 2014]

BCALM 2	Pine	Spruce
Time	8 h 25 m	8 h 52 m
Memory	17 GB	31 GB
Unitigs	30.5 Gbp	56.0 Gbp
#	257 M	580 M

1.1/1.2 TB compressed reads
$k = 61$, abundance cut-off 7, 8/16 threads (pine/spruce)
k-mer counting time not included: 1 day, $\leq$ 40 GB memory, DSK 2

Human dataset

Human NA18507	Bcalm 2	Bcalm 1	ABySS-P 1.9
Time	**2 h**	13 h	6.5 h
Memory	**2.8 GB**	43 MB	89 GB

54 GB compressed reads
$k = 55$, abundance cut-off 3, 16 threads
k-mer counting time included in BCALM 1&2: 46 mins, 2 GB memory, DSK 2
Meraculous: 16 hours, ≤ 1 TB [Georganas 2014]

Conclusion

Compacting de Bruijn graphs:

- efficient
  - 2 days for spruce, vs few CPU-years other methods
  - 2 hours for human
  - 2 GB memory per genome Gbp
- useful module for Illumina assemblers
- unitigs to replace *k*-mers in some applications

Observations:

- bottleneck becomes *k*-mer counting again
- not a data structure (construction algorithm, no queries)

Contact:

- @RayanChikhi, @pashadag, @NP_Malfoy on Twitter