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

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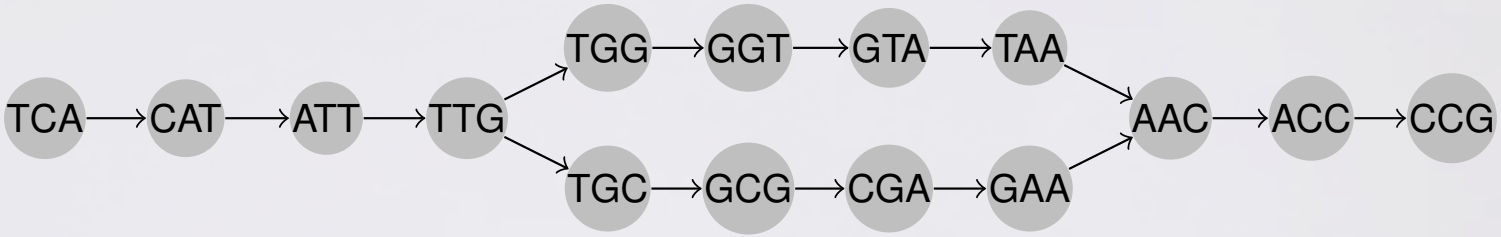
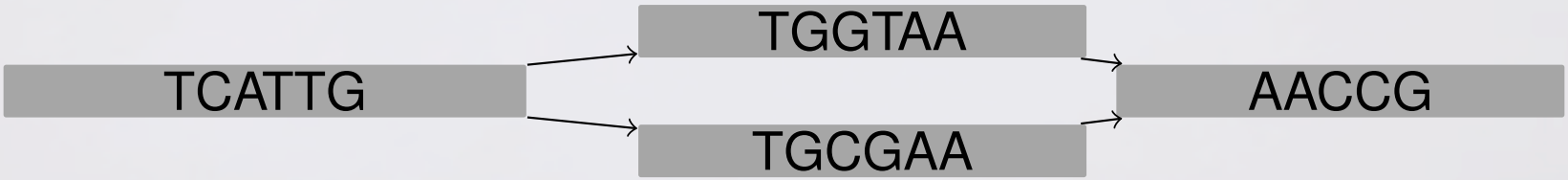
Workshop on Graph Assembly Algorithms for omics data
(adapted from a talk at ISMB 2016)

# Compacted de Bruijn Graph

(non-compacted) de Bruijn graph (nodes = $k$-mers):



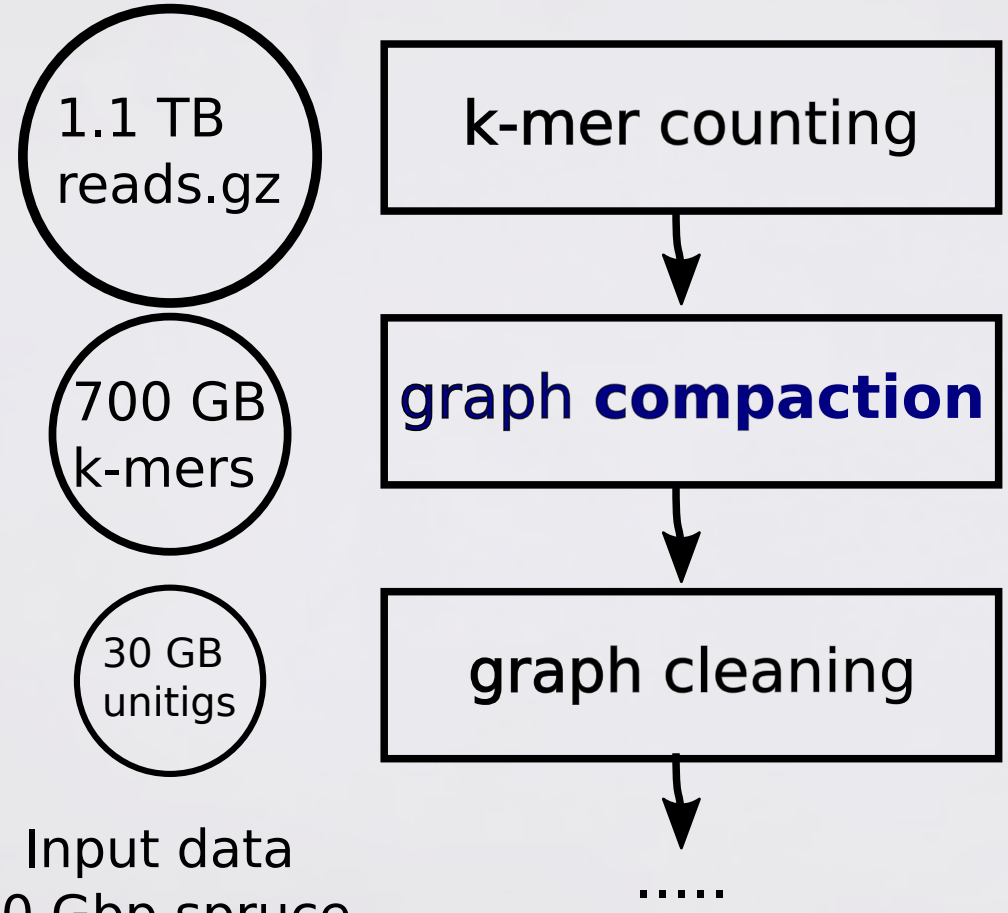

**Compacted** de Bruijn graph:




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

- no loss of information
- less space

# Steps of de Bruijn graph assemblers




Recent progress,
Stand-alone software
(KMC2, DSK2, Jellyfish2)

Integrated in assemblers,
high-memory or slow
**This work**

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)

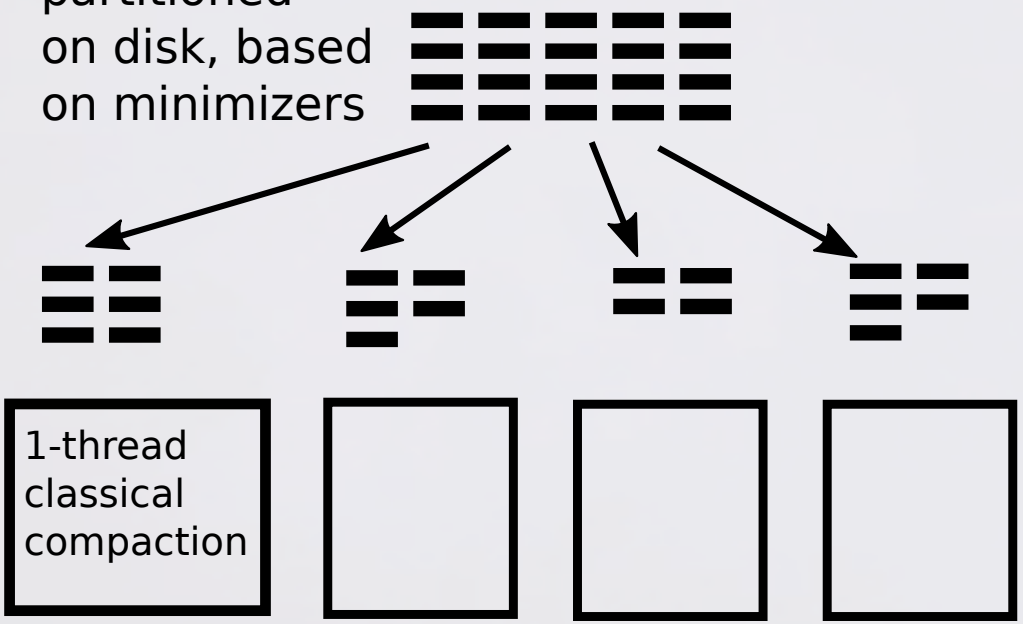
# BCALM 2

Software for *constructing* (not indexing) compacted de Bruijn graphs

Successor of BCALM 1 (single-threaded)

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

# Parallel compaction, first attempt



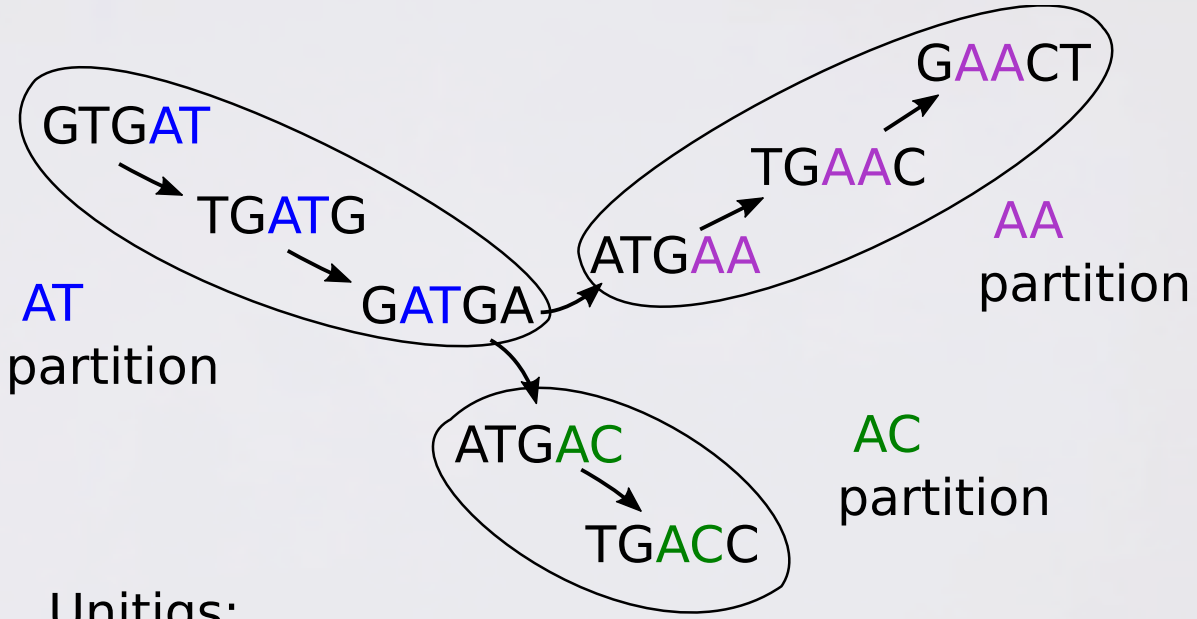

**minimizer** of *s*:
smallest $\ell$-mer in *s*
[Roberts *et al*, 2004]

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

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

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

# Compaction of partitions

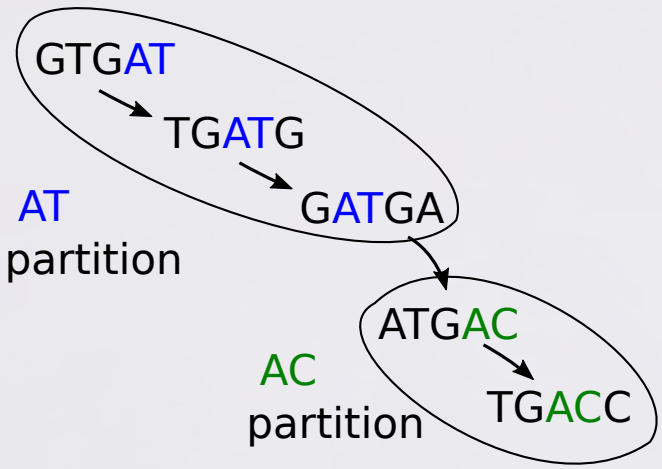



Unitigs:

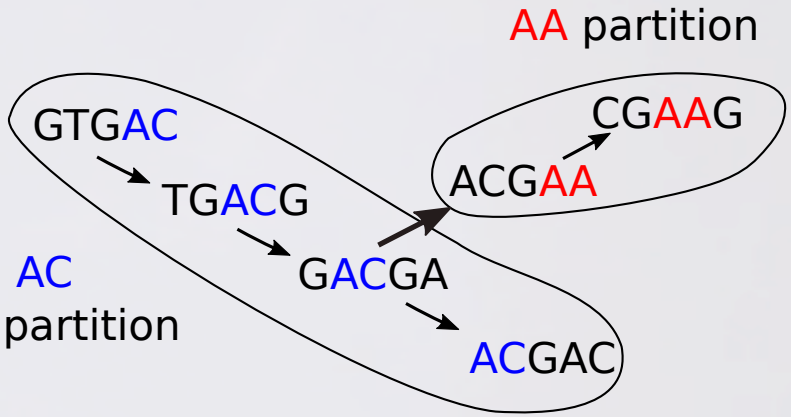
GTGATGA
ATGACC
ATGAACT

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

# Can’t just compact partitions




Real unitig:
GTGATGACC

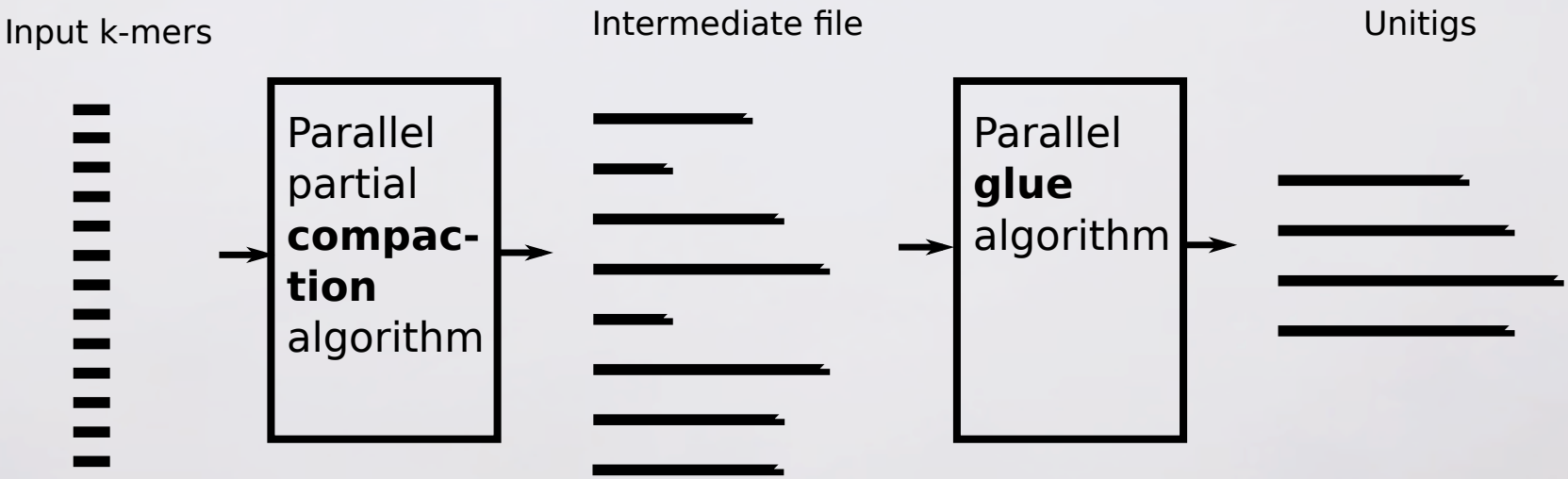



Real unitigs:
GTGACGA
ACGAC
ACGAAG

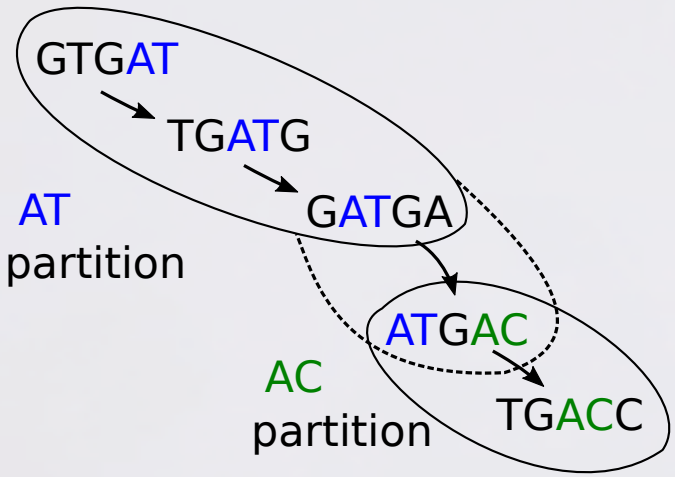
Left: 1 unitig = multiple partitions. (*Merge them?*)
Right: 1 partition = multiple unitigs. (*Split them?*)

# Strategy

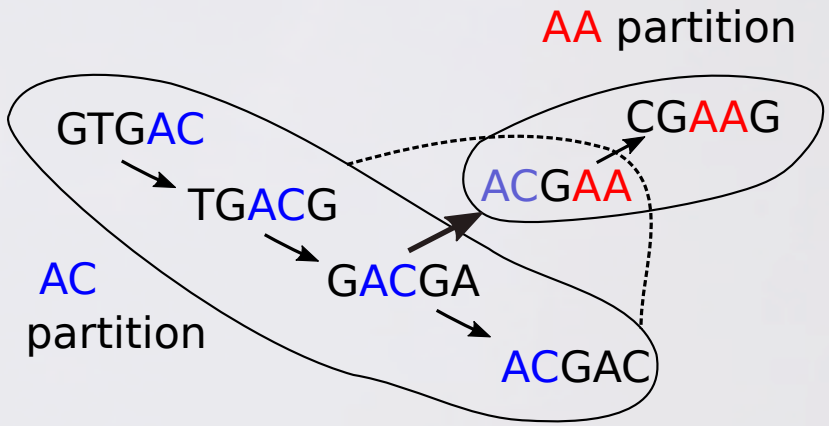
- Put certain $k$-mers into two partitions.
- x is a **doubled kmer** when minimizer($x[1..k-1]$) $\neq$ minimizer($x[2\ldots k]$).

# Partitions with doubled *k*-mers



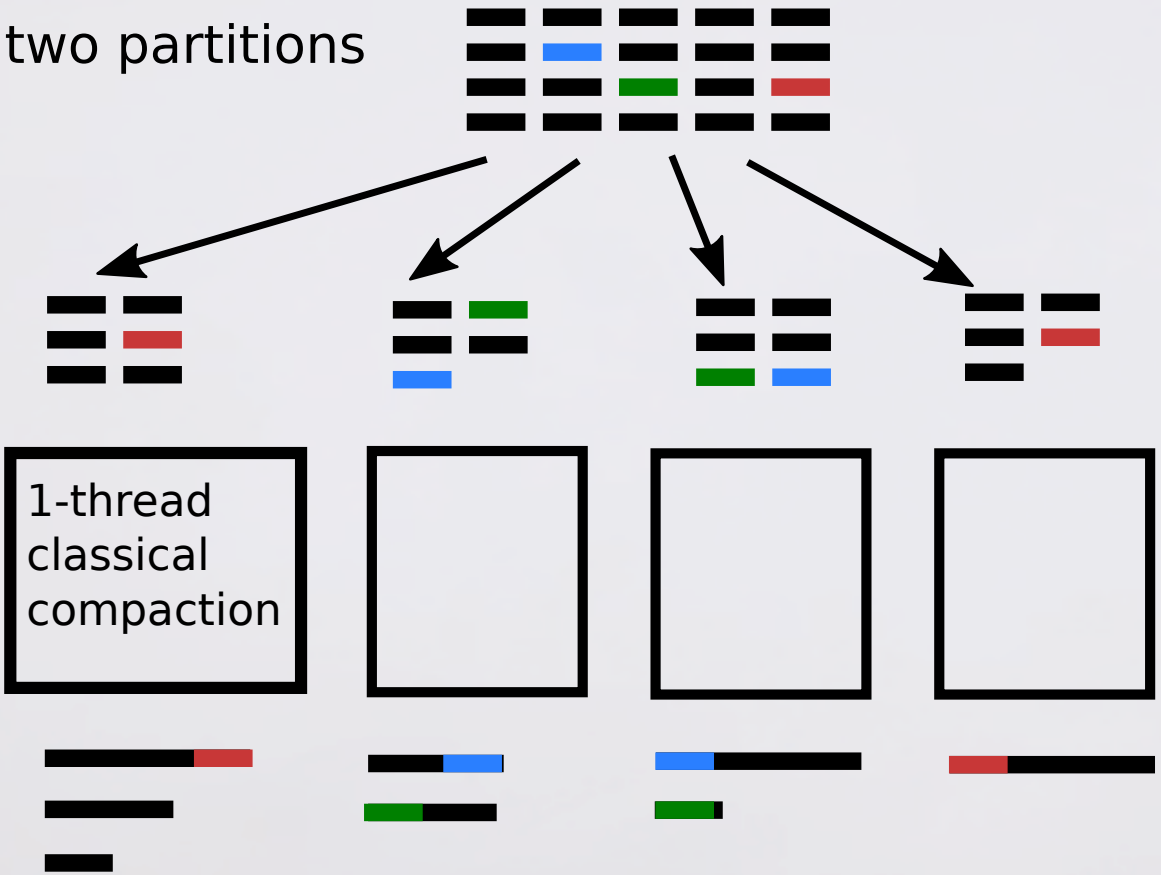

Compacted partitions:
GTGATGAC
ATGACC




Compacted partitions:
GTGACGA
ACGAC
ACGAA
ACGAAG

# BCALM 2's partial compaction module

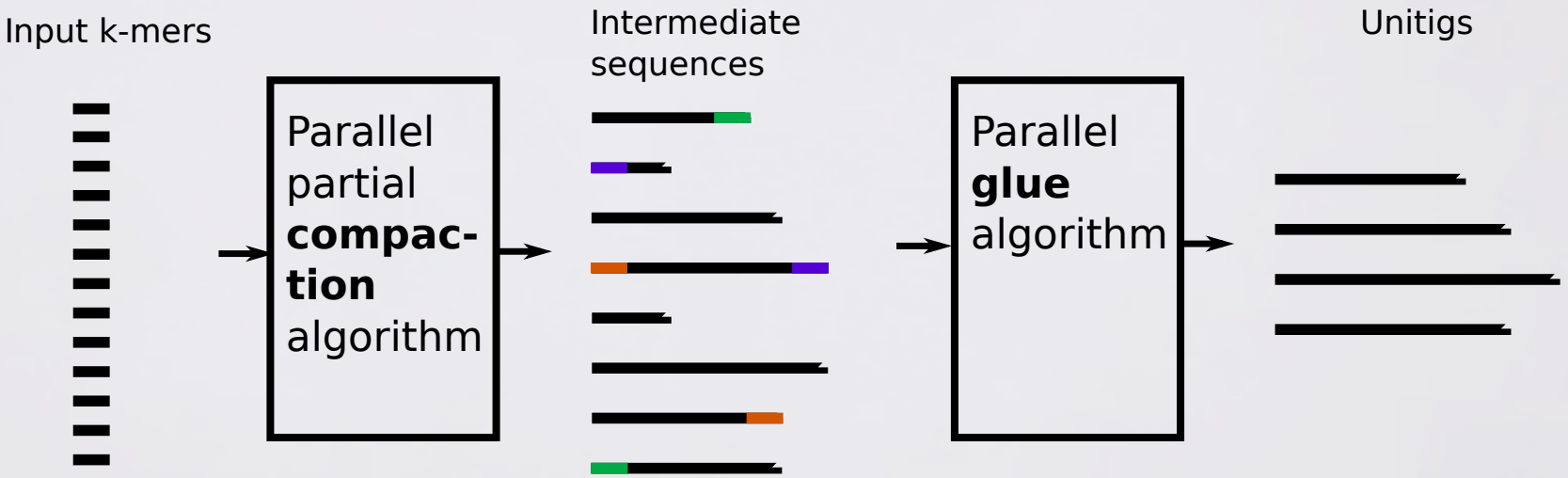
**Doubled kmers**
are inserted in
two partitions




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

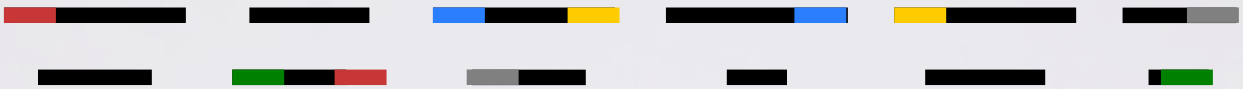
**Lemma** 2:
Gluing together
strings with
matching
doubled *k*-mers
yield unitigs.

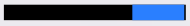
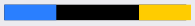
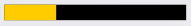
# Big picture


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

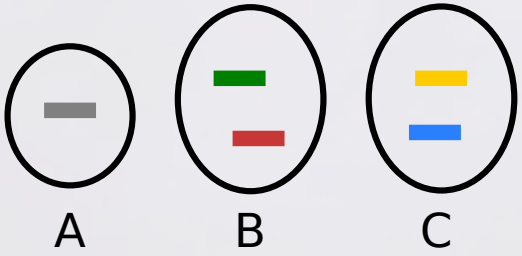
# BCALM 2's glue module

Input sequences

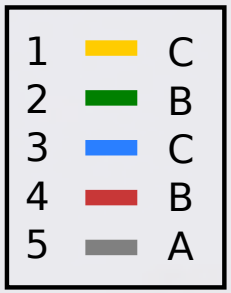


Cannot load all sequences in memory. Need again to partition.
Would like to have  ,  and  in the same partition.

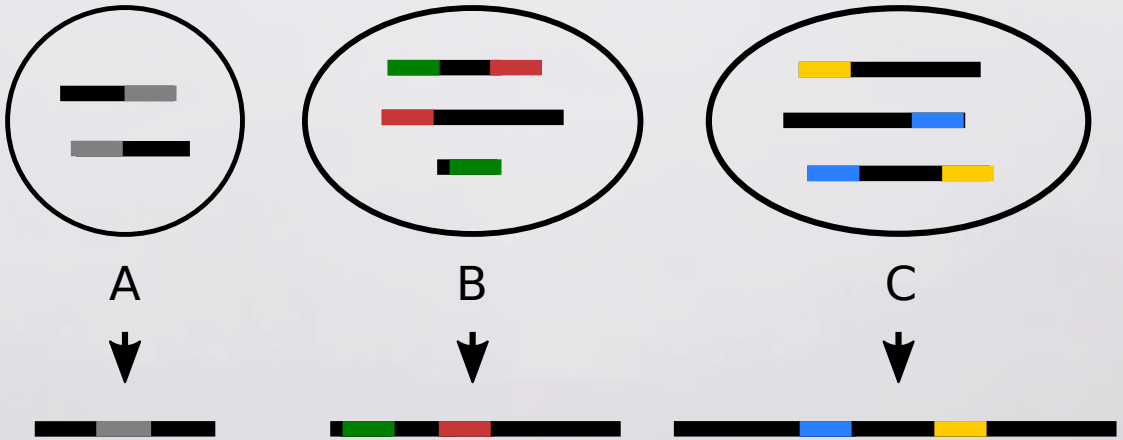
**Union-find**
of doubled kmers




Minimal perfect
hash table

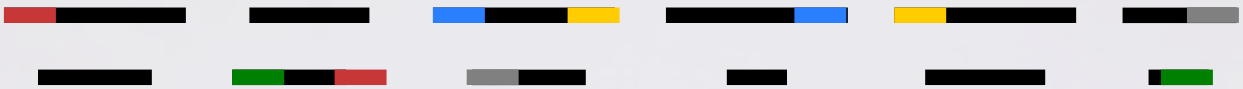


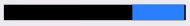
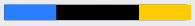
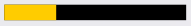

Sequences of
each U-F class
are loaded
and glued
in parallel.



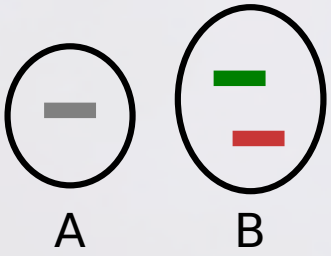
# BCALM 2's glue module

Input sequences



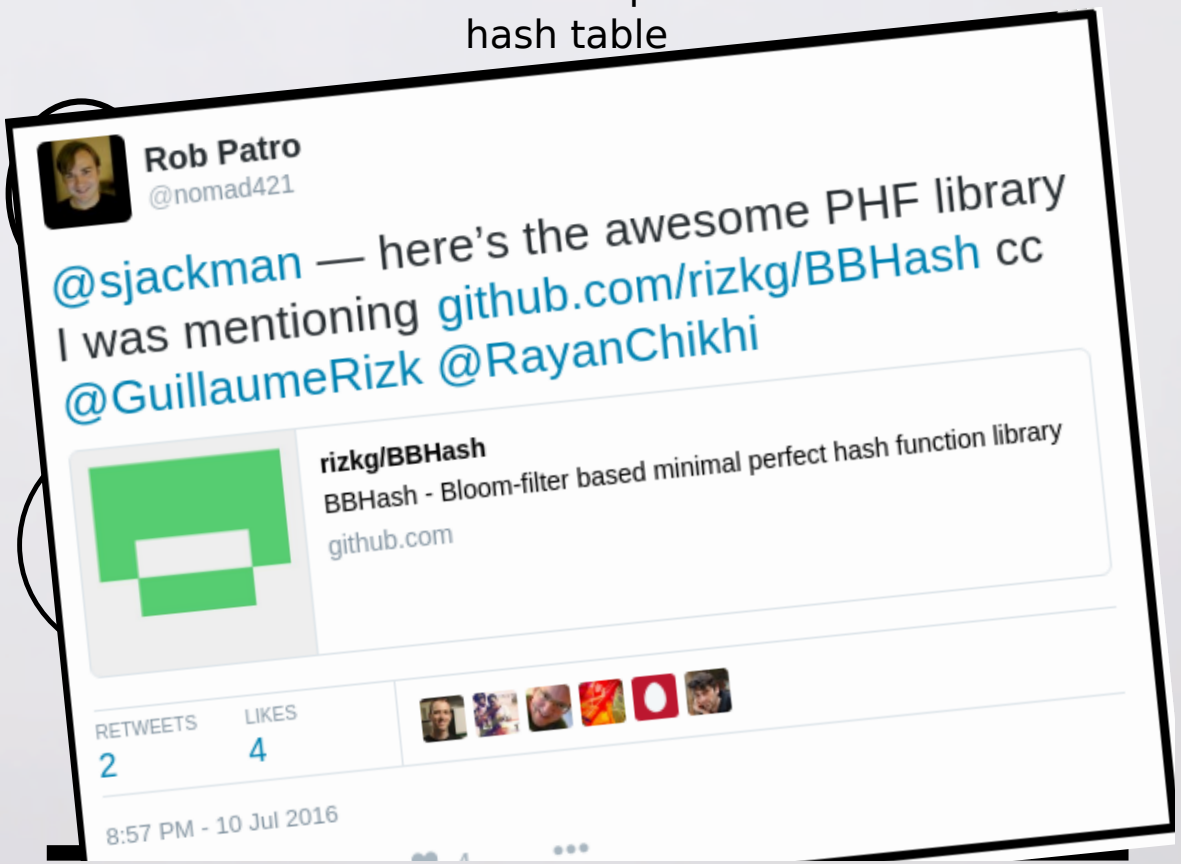
Cannot load all sequences in memory. Need again to partition.
Would like to have  ,  and  in the same partition.

**Union-find**
of doubled kmers




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

Minimal perfect hash table



# 20 Gbp spruce and 22 Gbp pine

Previously,
spruce: 2 days, 1380 cores, 4.3 TB RAM (Abyss) [Birol 2013]
pine: 4 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: 2 days, $\leq$ 30 GB memory, DSK 2

# Human dataset

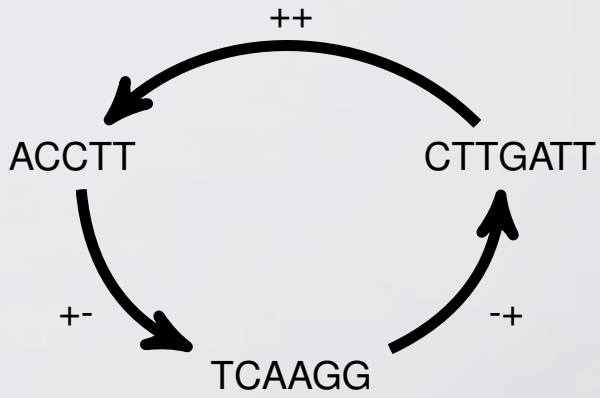
| Human NA18507 | Bcalm 2 | Bcalm 1 | ABySS-P 1.9 |
|---|---|---|---|
| Time | **2 h** | 13 h | 6.5 h |
| Memory | **2.8 GB** | 43 MB | 89 GB |

54 GB compressed reads
$k = 55$, abundance cut-off 7, 16 threads
$k$-mer counting time included in BCALM 1&2: 46 mins, 2 GB memory, DSK 2
Meraculous: 16 hours, $\leq$ 1 TB [Georganas 2014]

# Output in GFA format

- FASTG
- **GFA**
- GFA2

```
H   VN:Z:1.0
S   11  ACCTT
S   12  TCAAGG
S   13  CTTGATT
L   11  +   12  -   4M
L   12  -   13  +   5M
L   11  +   13  +   3M
P   14  11+,12-,13+ 4M,5M
```



# Conclusion

Compacting de Bruijn graphs:

- from **reads** to the **unitig graph**
- efficient
  - 1 hour, 2 GB memory per genome Gbp
- designed as a **small module** for *other* tools (through GFA)
- 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
- C++ library: `http://gatb.inria.fr`