Space-efficient merging of succinct de Bruijn graphs

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Joint work with
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Outline

1. Introduction to de Bruijn graphs
2. Succinct representation of de Bruijn graphs
3. Merging succinct de Bruijn graphs

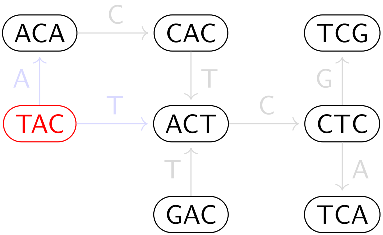
de Bruijn graphs (dBGs)

Definitions:

- Given a collection of strings $\mathcal{S}$, a *de Bruijn* graph of order k is a directed graph containing:
  - a node v for every **unique** k**-mer** $v[1]\ldots v[k]$ in $\mathcal{S}$.
  - an edge (u, v) with label $v[k]$ if there is a $(k+1)$**-mer** $u[1]\ldots u[k]v[k]$ in $\mathcal{S}$.

Example:

- $\mathcal{S} = \{$TACACT, TACTCA, GACTCG$\}$



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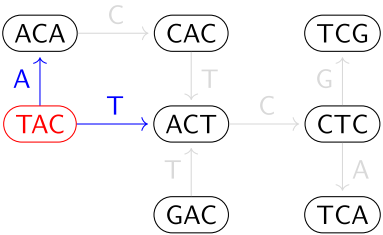

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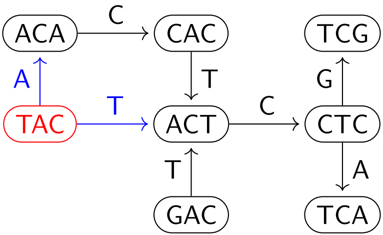

Comments

- Sometimes colors are assigned to (groups of) strings so edges are colored
- At the core it is a data structure supporting existential queries on k-mers, and the retrieval of "overlapping" k-mers
- Compressed suffix trees and bidirectional FM-indices support more operations using slightly more space

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Succinct representation of dBGs:

BOSS*:

- Bowe *et al.* in [WABI 2012] introduced a succinct representation for dBGs using space $m(\log \sigma + 2) + o(m)$ bits, where $m = |E|$.
- Each edge is represented by its symbol plus 2 bits
- Additional rank/select data structures to support efficient navigation
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*for the authors' initials

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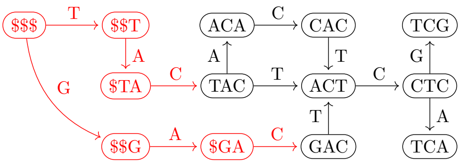
- $\mathcal{S} = \{$\$\$\$TACACT, \$\$\$TACTCA, \$\$\$GACTCG$\}$



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*For convenience, we add k copies of a symbol \$ at the beginning of each string s_i.

Succinct representation of dBGs:

BOSS:

- Nodes v_i are sorted by their **reversed labels** $\overleftarrow{v_i}$, and we list the symbols in the outgoing edges obtaining array W
- In array last we mark the position of the **last outgoing edge** of each node.
- In array W we mark (with a $^\bullet$) the symbols associated to the **2nd, 3rd, . . .** edge entering in a node.

Nodes	W
\$ \$ \$	G
	T
A C A	C
T C A	#
\$ G A	C
\$ T A	C
C A C	T
G A C	T
T A C	A
	T
C T C	A
	G
\$ \$ G	A
T C G	#
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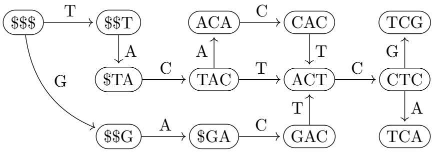
A C T	C



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1	.	T
1	A C A	C
1	T C A	#
1	$ G A	C
1	$ T A	C
1	C A C	T
1	G A C	T
0	T A C	A
1	.	T
0	C T C	A
1	.	G
1	$ $ G	A
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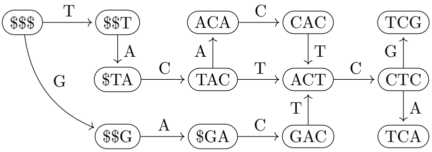

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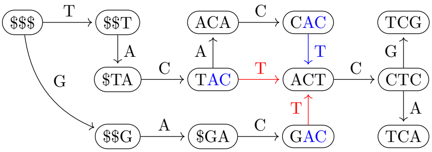

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1	C
1	#
1	C
1	C
1	T
1	T$^\bullet$
0	A
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1	G
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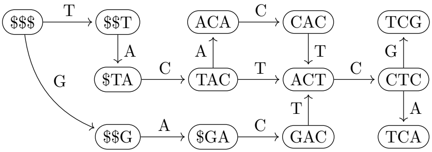

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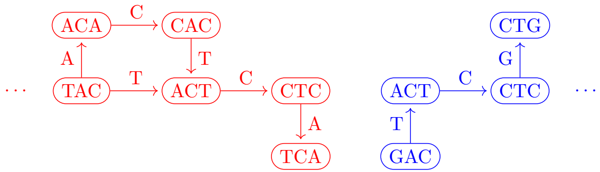
Merging de Bruijn graphs

- Suppose we are given the BOSS representation of two de Bruijn graphs G_0 and G_1 for the collections of strings $\mathcal{C}_0$ and $\mathcal{C}_1$
- We want to compute the BOSS for $\mathcal{C}_{01} = \mathcal{C}_0 \cup \mathcal{C}_1$ directly, that is, without decoding G_0 and G_1.
- Working space is a major issue, since it limits the size of the largest graph we can build

Example:

$\mathcal{S}_1 = \{\$\$\$\text{TACACT}, \$\$\$\text{TACTCA}\} \cup \{\$\$\$\text{GACTCG}\}$



Merging de Bruijn Graphs

Merging BOSS representations

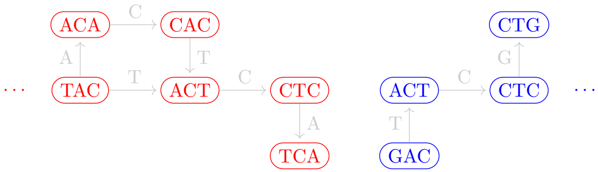
- Tasks:
  1. Merge the nodes in G_0 and G_1 according the order of their k-mers,

$$\overleftarrow{v_1} \prec \cdots \prec \overleftarrow{v_{n_0}} \qquad \text{and} \qquad \overleftarrow{w_1} \prec \cdots \prec \overleftarrow{w_{n_1}}$$

  2. Recognize when two nodes in G_0 and G_1 refer to the same k-mer, and

$$\overleftarrow{v_i} \ ?= \overleftarrow{w_j}$$

  3. Properly merge and update W and last.



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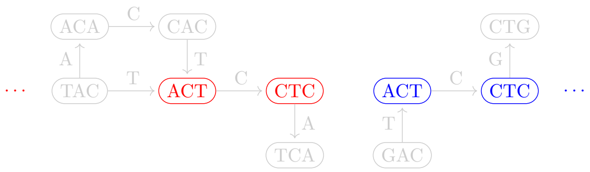

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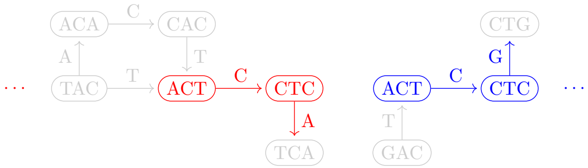

Observation:

- Order preserving bijection between the symbols in *W* and *Nodes*...
- ... excluding those marked with •
- We get the last symbol of each node (first in the ordering)

last	Nodes	W
0	? ? $	G
1	.	T
1	? ? A	C
1	? ? A	$
1	? ? A	C
1	? ? A	C
1	? ? C	T
1	? ? C	T•
0	? ? C	A
1	.	T•
0	? ? C	A
1	.	G
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1	? ? G	$
1	? ? T	A
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1	? ? C	T$^\bullet$
0	? ? C	A
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1	? ? C	$T^{\bullet}$
0	? ? C	A
1	.	$T^{\bullet}$
0	? ? C	A
1	.	G
1	? ? G	A
1	? ? G	\$
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Previous approach (Muggli et al. Bioinformatics '19)

- Recover labels columnwise right to left.
- Do this for both dbGs and simultaneously merge nodes
- Working space: $2(|V|\log\sigma + |E| + |V|)$ bits

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Our approach: induced sorting

- Merge nodes according to the rightmost h symbols for $h = 1, 2, \dots, k$
- At each iteration edge labels are used to refine the merging
- Inspired by Holt and McMillan [Bioinformatics 2014, ACM-BCB 2014]

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1	? G A	C		? G A
1	? ? T A	C•		? C A C
0	? ? A C	A	→	? T C C
1	.	T•		.
0	? ? A C	A		? ? A C
1	.	T•		.
0	? ? T C	A		? ? T C
1	.	C		.
1	? ? \$ G	A		? ? \$ G
1	? ? C G	#		? ? C G
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1	? ? C G	#		? ? C G
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1	? ? A T	C		? C A T

H&M Merging algorithm

- The H&M algorithm merges BWTs by progressively larger contexts.
- Very nice feature: only $2n$ bits working space (for Z^{h-1} and Z^h).

BWT	suffixes
b	$
c	ab$
$	abcab$
a	b$
a	bcab$
b	cab$

S_1 = abcab$

+

BWT	suffixes
c	#
#	aabcabc
c	abc#
a	abcabc#
a	bc#
a	bcabc#
b	c#
b	cabc#

S_2 = aabcabc#

=

BWT	suffixes
b	$
c	#
#	aabcabc
c	ab$
c	abc#
$	abcab$
a	abcabc#
a	b$
a	bc#
a	bcab$
a	bcabc#
b	c#
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Z	BWT	
0	b	$
0	c	ab$
0	$	abcab$
0	a	b$
0	a	bcab$
0	b	cab$
1	c	#
1	#	aabcabc
1	c	aabc#
1	a	abcabc#
1	a	bc#
1	a	bcabc#
1	b	c#
1	b	cabc#

h=1

Z	BWT	
0	b	$
1	c	#
0	c	ab$
0	$	abcab$
1	#	aabcabc
1	c	abc#
1	a	abcabc#
0	a	b$
0	a	bcab$
1	a	bc#
1	a	bcabc#
0	b	cab$
1	b	c#
1	b	cabc#

h=2

Z	BWT	
0	b	$
1	c	#
1	#	aabcabc
0	c	ab$
0	$	abcab$
1	c	abc#
1	a	abcabc#
0	a	b$
0	a	bcab$
1	a	bc#
1	a	bcabc#
1	b	c#
0	b	cab$
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h=3

Z	BWT	
0	b	$
1	c	#
1	#	aabcabc
0	c	ab$
0	$	abcab$
1	c	abc#
1	a	abcabc#
0	a	b$
0	a	bcab$
1	a	bc#
1	a	bcabc#
1	b	c#
0	b	cab$
1	b	cabc#

dBG vs BWT Merging

- For dBGs we know the merging takes exactly k iterations (good)
- After the merging duplicate nodes have to be deleted (bad, extra work)

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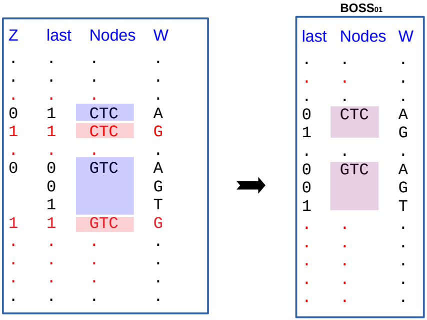
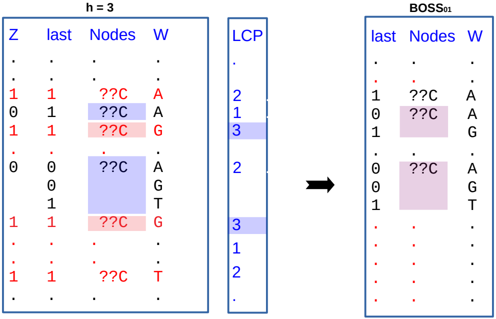


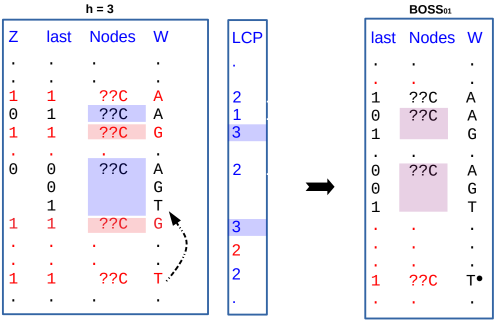
dBG vs BWT Merging

We can find duplicate nodes using right-to-left LCP values,



dBG vs BWT Merging

We can find duplicate nodes using right-to-left LCP values, that are also useful for finding which symbols in W should be marked with $\bullet$



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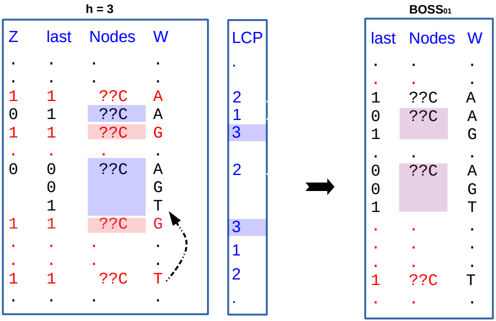

Summing up

- With a modified H&M algorithm we co-lexicographically merge the nodes using only $2|V|$ bits of working space
- Using a trick from Egidi *et al.* [Spire '17], we compute the LCP values to detect duplicate nodes and correctly mark symbols in W
  - We can maintain only LCP values modulo 4 and only use additional $2|V|$ bits of working space
  - If we store the exact LCP values we get the Variable Order de Bruijn graph

Conclusions

- Algorithm for merging two of more BOSS succinct representations of de Bruijn graphs
- Cost: $\mathcal{O}(|E| + |V| \cdot k)$ time, where E and V are edges and vertices of the new graph, as in Muggli *et al.*
- Working space: $4|V|$ bits $+ \mathcal{O}(\sigma)$ words, less than Muggli *et al.*
- In external memory we can arrange the working space into 2σ distinct files so that all data is accessed sequentially
- We can support Variable Order and Colored variants.