Sequence analysis in linear time and compact space

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Presenting joint work with Djamal Belazzougui, Fabio Cunial, and Juha Kärkkäinen (ESA 2013) and work by Belazzougui (STOC 2014)

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MOTIVATION

Sequence analysis is the process of discovering some common features of one or more strings. For example, *maximal repeat* of a string $T = t_1 t_2 \cdots t_n$ is a substring that appears at least twice and whose left and right extensions appear less times.

- `X` is not right-maximal in `agtcXacgatXat` but `Xa` is.

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- `X` is not right-maximal in `agtcXacgatXat` but `Xa` is.

Maximal unique match (MUM) of two strings A and B is a substring that occurs exactly ones in each string and whose left and right extensions do not appear in both strings.

- `Xa` is a MUM of $A =$ `agtcXa` and $B =$ `cgatXat`.

SOLUTIONS

Suffix tree [Wei73,...] for text of length n from alphabet of size σ:

- $O(n \log n)$ bits
- Myriads of sequence analysis problems in $O(n)$ time

Solutions

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Compressed representations for BWT [GV00,FM00,Sad00,...]

- Kernel of compressed suffix trees
- A few sequence analysis problems in $O(n \log \sigma)$ time

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Compact $O(n \log \sigma)$ bits space and linear time for myriads of problems?

Our ESA 2013 results enhanced with Belazzougui STOC 2014

Compact representations for *bidirectional* BWT:

- $O(n \log \sigma)$ bits
- Many sequence analysis problems in $O(n)$ time

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- Many sequence analysis problems in $O(n)$ time

- Main insights:
  - Conceptual: Visiting suffix tree nodes through suffix link tree $\rightarrow$ No need for LCP array
  - Technical: Avoiding LessThan query on wavelet trees $\rightarrow$ Constant time bidirectional backward step
  - Technical: Index construction in linear time in compact space (Belazzougui, STOC 2014)

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Theoretical / practical replacement of compressed suffix trees?

Our results in detail

Representation	1		2		3
Implementation	1a	1b	2a [CPM 2010]	2b	3
Space (bits)	$n \log \sigma +$ $+n + o(n)$	$n \log \sigma +$ $+o(n \log \sigma)$	$2n \log \sigma +$ $+o(n)$	$2n \log \sigma +$ $+o(n \log \sigma)$	$O(n \log \sigma)$
`isLeftMaximal`	$O(\log \sigma)$	$O(1)$	$O(\log \sigma)$	$O(1)$	$O(1)$
`isRightMaximal`	$O(1)$	$O(1)$	$O(\log \sigma)$	$O(1)$	$O(1)$
`enumerateLeft`	$O(\log \sigma)$	$O(1)$	$O(\log \sigma)$	$O(1)$	$O(1)$
`enumerateRight`			$O(\log \sigma)$	$O(1)$	$O(1)$
`extendLeft`	$O(\log \sigma)$	$O(\sigma)$	$O(\log \sigma)$	$O(\sigma)$	$O(1)$
`extendRight`			$O(\log \sigma)$	$O(\sigma)$	$O(1)$
Applications	MUM, SUS, MR, LB, QP, IPS, IPK		MUM, SUS, MEM, SR, NSR, MAW, IPS, IPK		BBB

SUS: shortest unique substrings; MR: maximal repeats; LB: longest border; QP: quasiperiod; IPS: inner product of substrings; IPK: inner product of k-mers; (N)SR: (near) supermaximal repeats; MAW: minimal absent words; BBB: bidirectional b&b (supported also by Implementation 2a).

RELATED WORK

- Bidirectional BWT [Lametal09,SOG10]:
  - Bidirectional backward step in $O(\sigma)$ time [Lametal09] and in $O(\log \sigma)$ time [SOG10].
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- Avoiding LCP array construction to solve *maximal repeats* [BBO12]:
  - Visiting suffix tree nodes in level-wise order.
  - Analysis uses Weiner links.
  - We improve the space and time and show how to solve many related problems.
  - Our technique extends to *synhronized* search and enables indexing for all-against-all problems.

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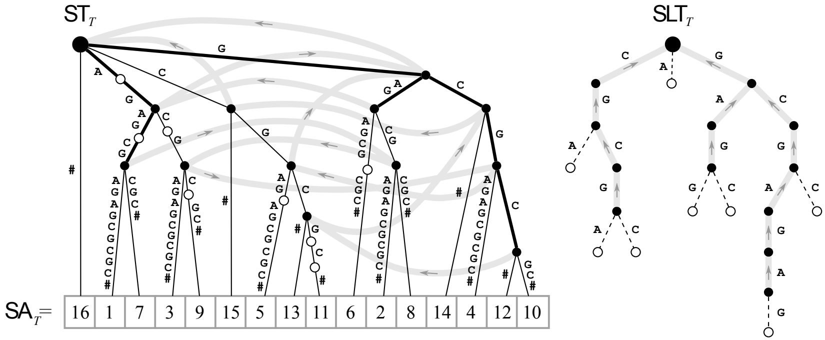
- Alphabet-independent backward search [BN11,BN13]:
  - We extend the technique for bidirectional backward search.

SUFFIX TREE, WEINER LINKS, SUFFIX-LINK TREE



Bidirectional BWT

T=xaby$yabx

T^r=xbay$ybax

sorted suffixes of
T# and T^r#

x	#	x	#
y	$yabx#	y	$ybax#
y	abx#	b	ax#
x	aby$yabx#	b	ay$ybax#
a	bx#	y	bax#
a	by$yabx#	x	bay$ybax#
b	x#	a	x#
#	xaby$yabx#	#	xbay$ybax#
b	y$yabx#	a	y$ybax#
$	yabx#	$	ybax#

character preceding each suffix

#<$<a<b<x<y

BIDIRECTIONAL BWT

T=xaby$yabx

	L	
	x	#
	y	$yabx#
[i,j]	y	abx#
[i,j]	x	aby$yabx#
	a	bx#
	a	by$yabx#
	b	x#
	#	xaby$yabx#
	b	y$yabx#
	$	yabx#

T^r=xbay$ybax

	L’	
	x	#
	y	$ybax#
[i’,j’]	b	ax#
[i’,j’]	b	ay$ybax#
	y	bax#
	x	bay$ybax#
	a	x#
	#	xbay$ybax#
	a	y$ybax#
	$	ybax#

- $i' = i = C[\mathtt{a}]$
- $j' = j = C[\mathtt{a}+1] = C[\mathtt{b}] - 1$
- $L_{i\ldots j} = \mathtt{yx}$
- $L'_{i'\ldots j'} = \mathtt{bb}$

BIDIRECTIONAL BWT

T=xaby\$yabx

x #
y \$yabx#
y abx#
x aby\$yabx#
a bx#
a by\$yabx#
b x#
\# xaby\$yabx#
b y\$yabx#
\$ yabx#

T^r=xbay\$ybax

x #
y \$ybax#
b ax#
b ay\$ybax#
y bax#
x bay\$ybax#
a x#
\# xbay\$ybax#
a y\$ybax#
\$ ybax#

- $i' = i + LessThan_{\mathrm{y}}(L_{i\dots j})$
- $j' = i + LessThan_{\mathrm{y}+1}(L_{i\dots j}) - 1$
- $i = C[\mathrm{y}] + rank_{\mathrm{y}}(L_{1\dots i-1}) + 1$
- $j = C[\mathrm{y}] + rank_{\mathrm{y}}(L_{1\dots j})$

MAXIMAL UNIQUE MATCHES (MUMS)

THEOREM

Substring w is a maximal unique match (MUM) *between $s \in \Sigma^*$ and $t \in \Sigma^*$ iff its only occurrences are $s[i, i + |w| - 1]$ and $t[j, j + |w| - 1]$ and extending w left or right looses one of the occurrences. We can discover all the τ maximal unique matches between s and t in $O(|s| + |t|)$ time and $O((|s| + |t|) \log |\Sigma| + \tau \log(|s| + |t|))$ bits of space.*

- For example, on $s =$ `xaby` and $t =$ `yabx` mums are `x`, `y`, `ab`.

ALGORITHM

Algorithm $\texttt{mums}(M, \texttt{bidirectionalBWTindex}, i, j, i', j', I)$

$\texttt{left} = rank_0(I, j) - rank_0(I, i-1);$

$\texttt{right} = rank_1(I, j) - rank_1(I, i-1);$

if $(\texttt{left} == 0$ **or** $\texttt{right} == 0)$

    return ;

if $(!\texttt{bidirectionalBWTindex.rightMaximal}(i', j'))$

    return ;

if $(\texttt{bidirectionalBWTindex.leftMaximal}(i, j)$ **and** $\texttt{left} == 1$ **and** $\texttt{right} == 1)$

    M is a MUM;

for each $c \in \texttt{bidirectionalBWTindex.EnumerateLeft}(i, j)$ **do**

    $(ii, jj, ii', jj') \leftarrow \texttt{bidirectionalBWTindex.extendLeft}(c, i, j, i', j');$

    $\texttt{mums}(cM, \texttt{bidirectionalBWTindex}, ii, jj, ii', jj', I);$

...

$\texttt{bidirectionalBWTindex}, I \leftarrow \texttt{constructIndex}(s\$t);$

$\texttt{mums}(\texttt{""}, 0, |s| + |t|, 0, |s| + |t|, I);$

ALGORITHM

Algorithm `mums`$(M,$ `bidirectionalBWTindex`$, i, j, i', j', I)$

`left` $= rank_0(I, j) - rank_0(I, i-1)$;
`right` $= rank_1(I, j) - rank_1(I, i-1)$;
if (`left` $== 0$ **or** `right` $== 0$)
  return ;
if (!`bidirectionalBWTindex.rightMaximal`(i', j'))
  return ;
if (`bidirectionalBWTindex.leftMaximal`(i, j) **and** `left` $== 1$ **and** `right` $== 1$)
  M is a MUM;
Recursion with each possible cM...

```
 1234567890
 xaby$yabx
0987654321
         [a]
SA   10 5 7 2 8 3 9 1 4 6
I     1 0 1 0 1 0 1 0 0 1
SA’  10 5 8 3 7 2 9 1 4 6
         [a]
```

ALGORITHM

Algorithm `mums`(M, `bidirectionalBWTindex`, i, j, i', j', I)
(1) `left` $= rank_0(I, j) - rank_0(I, i-1)$;
(2) `right` $= rank_1(I, j) - rank_1(I, i-1)$;
(3) **if** (`left` $== 0$ **or** `right` $== 0$)
(4) **return** ;
(5) **if** (!`bidirectionalBWTindex.rightMaximal`(i', j'))
(6) **return** ;
(7) **if** (`bidirectionalBWTindex.leftMaximal`(i, j) **and** `left` $== 1$ **and** `right` $== 1$)
(8) M is a MUM;
(9) Recursion with each possible cM...

```
 1234567890
 xaby$yabx
0987654321
                [b]
SA   10 5 7 2 8 3 9 1 4 6
I     1 0 1 0 1 0 1 0 0 1
SA'  10 5 8 3 7 2 9 1 4 6
                [b]
```

ALGORITHM

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(1) `left` $= rank_0(I, j) - rank_0(I, i-1)$;
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 1234567890
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0987654321
         [ab]
SA   10 5 7 2 8 3 9 1 4 6
I     1 0 1 0 1 0 1 0 0 1
SA'  10 5 8 3 7 2 9 1 4 6
              [ba]
```

ANALYSIS

- Number of recursion steps can be bounded by the amount of explicit and implicit Weiner links in suffix tree, which is linear.
- Claimed space bound follows, except for the use of stack:
  - Must use explicit stack, and push the largest interval first; this guarantees $O(\log n)$ depth.
- Bitvector I can be dropped using *synchronized* bidirectional search on two indexes built on s and t separately.

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- See the ESA 2013 paper for more involved applications.

Bidirectional step in $O(1)$?

- Bidirectional step requires to count how many symbols smaller than a given symbol there are in a given BWT range (LessThan query).
  - This can be supported by *wavelet tree* in $O(\log \sigma)$ time.
- We show that LessThan query cannot be supported faster than $O(\log \sigma / \log \log n)$ unless using superlinear space.
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- We show that LessThan query cannot be supported faster than $O(\log \sigma / \log \log n)$ unless using superlinear space.
- However, our algorithms need LessThan query only on ranges corresponding to suffix tree nodes.
- It turns out that $O(1)$ time is possible in this restricted setting.

BIDIRECTIONAL STEP IN $O(1)$

- We extend the technique by Belazzougui and Navarro [BN11,BN13] that supports backward step in constant time for suffix tree node ranges.
- Some ideas:

```
ACGATCGACGAGCTA[CGAGCTAGC]GATCGGCATACGCCGATCGTAC
            C...C
              A...A
           G.....G
             T.......T
```

- There is a representation taking $O(n \log \log \sigma)$ bits that supports partial rank queries in constant time (Belazzougui 2014).
- *Monotone minimal perfect hash function* is required for sorting to derive LessThan answers for maintaining bidirectional BWT range.
- Hashing can be avoided if navigation is *unidirectional*.
- Deterministic linear time construction of BWT and unidirectional BWT index in compact space.
- Most analyses in deterministic linear time.

Discussion

- The techniques also give $O(n)$ time and compact space construction for compressed suffix trees (see Belazzougui, STOC 2014).

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- However, bidirectional or unidirectional BWT index functionality is required to obtain $O(n)$ time sequence analysis on top of such compressed suffix tree.
- There remains a class of sequence analysis tasks that can be solved in $O(n \log^{\epsilon} n)$ time using compressed suffix trees, for which bidirectional BWT index is not sufficient.

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- Mäkinen, Belazzougui, Cunial, and Tomescu. *Genome-scale algorithm design: Biological sequence analysis in the era of high-throughout sequencing*. Cambridge University Press. To appear early 2015.