Efficient pattern matching in degenerate strings with the Burrows–Wheeler transform

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Outline

1. Introduction
2. Pattern matching in degenerate strings with the BWT
3. Experiments

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Burrow-Wheeler Transform (BWT)

Definition

Let x be a string built on a finite alphabet Σ.
The BWT of x is defined as the pair (L, h) where L is the last column of the matrix M_x formed by all the sorted cyclic rotations of x and h is the index of x in this matrix.

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$x = \texttt{BANANA}$

1	1	B	A	N	A	N	A
2	2	A	N	A	N	A	B
3	3	N	A	N	A	B	A
4	4	A	N	A	B	A	N
5	5	N	A	B	A	N	A
6	6	A	B	A	N	A	N

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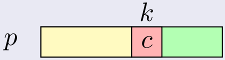
5	5	N	A	B	A	N	A
6	6	A	B	A	N	A	N

	SA						BWT
1	6	A	B	A	N	A	N
2	4	A	N	A	B	A	N
3	2	A	N	A	N	A	B
4	1	B	A	N	A	N	A
5	5	N	A	B	A	N	A
6	3	N	A	N	A	B	A

$BWT(\mathtt{BANANA}) = (\mathtt{NNBAAA}, 4)$

Backward search



Assume

(i, j) is the interval in the SA of a text t of the suffixes of t starting with $p[k+1\,..\,m]$

then

(i', j') is the interval in the SA of t of the suffixes of t starting with $p[k\,..\,m]$

with

$$i' = C[c] + \mathit{rank}_c(\mathit{BWT}, i-1) + 1 \text{ and } j' = C[c] + \mathit{rank}_c(\mathit{BWT}, j)$$

where

$c = p[k]$, $C[c] = \sharp\{i \mid t[i] < c\}$ and
$\mathit{rank}_c(x, i)$ gives the number of occurrences of the letter c in the prefix $x[1\,..\,i]$.

Backward search – example

$\rightarrow$	1	6	A	B	A	N	A	N
	2	4	A	N	A	B	A	N
	3	2	A	N	A	N	A	B
	4	1	B	A	N	A	N	A
	5	5	N	A	B	A	N	A
$\rightarrow$	6	3	N	A	N	A	B	A

$(1, 6)$ is the interval in the SA of BANANA of suffixes starting with ε

Backward search – example

$\rightarrow$	1	6	A	B	A	N	A	N
	2	4	A	N	A	B	A	N
	3	2	A	N	A	N	A	B
	4	1	B	A	N	A	N	A
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$\rightarrow$	1	6	A	B	A	N	A	N
	2	4	A	N	A	B	A	N
$\rightarrow$	3	2	A	N	A	N	A	B
	4	1	B	A	N	A	N	A
	5	5	N	A	B	A	N	A
	6	3	N	A	N	A	B	A

$(6, 6)$ is the interval in the SA of BANANA of suffixes starting with A

Backward search – example

	1	6	A	B	A	N	A	N
$\rightarrow$	2	4	A	N	A	B	A	N
$\rightarrow$	3	2	A	N	A	N	A	B
	4	1	B	A	N	A	N	A
	5	5	N	A	B	A	N	A
	6	3	N	A	N	A	B	A

$(2, 3)$ is the interval in the SA of BANANA of suffixes starting with AN

Backward search – example

	1	6	A	B	A	N	A	N
$\rightarrow$	2	4	A	N	A	B	A	N
$\rightarrow$	3	2	A	N	A	N	A	B
	4	1	B	A	N	A	N	A
	5	5	N	A	B	A	N	A
	6	3	N	A	N	A	B	A

$(2,3)$ is the interval in the SA of BANANA of suffixes starting with AN

	1	6	A	B	A	N	A	N
	2	4	A	N	A	B	A	N
	3	2	A	N	A	N	A	B
	4	1	B	A	N	A	N	A
	5	5	N	A	B	A	N	A
$\Rightarrow$	6	3	N	A	N	A	B	A

$(6,6)$ is the interval in the SA of BANANA of suffixes starting with NAN

Degenerate strings

Definition

Given an alphabet Σ we define a new alphabet Δ_Σ as the non-empty subsets of Σ:
$\Delta_\Sigma = \mathcal{P}(\Sigma) \setminus \{\emptyset\}$
Singletons are called *solid* letters.
Degenerate or *indeterminate* strings on an alphabet Σ are strings of Δ_Σ.

$\Sigma = \{\mathtt{a}, \mathtt{b}, \mathtt{c}, \mathtt{d}, \mathtt{e}\}$
$t = \{\mathtt{c}, \mathtt{e}\} \cdot \{\mathtt{c}, \mathtt{d}\} \cdot \{\mathtt{a}, \mathtt{b}, \mathtt{c}\} \cdot \{\mathtt{a}, \mathtt{d}\} \cdot \{\mathtt{a}, \mathtt{b}, \mathtt{c}\}$

Pattern matching on degenerate strings

Definition

Given 2 degenerate strings p and t find all the positions $0 \leq j < |t| - |p|$ on t where $p[i] \cap t[i+j] \neq \emptyset$ for $0 \leq i < |p|$.

$p = \{\mathtt{a}\} \cdot \{\mathtt{c}, \mathtt{d}\}$ occurs at positions 3 and 4 in
$t = \{\mathtt{c}, \mathtt{e}\} \cdot \{\mathtt{c}, \mathtt{d}\} \cdot \{\mathtt{a}, \mathtt{b}, \mathtt{c}\} \cdot \{\mathtt{a}, \mathtt{d}\} \cdot \{\mathtt{a}, \mathtt{b}, \mathtt{c}\}$

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Burrows-Wheeler transform on degenerate strings (D-BWT)

Given an order on Δ_Σ denoted by the usual symbol $<$, we can compute the BWT of a degenerate string x in the same way as for a regular string.

$t = \{\mathtt{c}, \mathtt{e}\} \cdot \{\mathtt{c}, \mathtt{d}\} \cdot \{\mathtt{a}, \mathtt{b}, \mathtt{c}\} \cdot \{\mathtt{a}, \mathtt{d}\} \cdot \{\mathtt{a}, \mathtt{b}, \mathtt{c}\}$

$\mathtt{A} = \{\mathtt{a}, \mathtt{b}, \mathtt{c}\}, \mathtt{B} = \{\mathtt{a}, \mathtt{d}\}, \mathtt{C} = \{\mathtt{c}, \mathtt{d}\}, \mathtt{D} = \{\mathtt{c}, \mathtt{e}\}$

$\mathtt{A} < \mathtt{B} < \mathtt{C} < \mathtt{D}$

1	1	D	C	A	B	A
2	2	A	D	C	A	B
3	3	B	A	D	C	A
4	4	A	B	A	D	C
5	5	C	A	B	A	D

1	3	A	B	A	D	B
2	1	A	D	C	A	C
3	4	B	A	D	A	D
4	2	C	A	B	B	A
5	5	D	C	A	C	A

Burrows-Wheeler transform on degenerate strings (D-BWT)

Jacqueline W. Daykin and Bruce Watson
A Text Transformation Scheme for Degenerate Strings
Proceedings of the 2nd International Conference on Algorithms for Big Data, Palermo, Italy, April 07-09, 2014 pp 23–29

Jacqueline W. Daykin and Bruce Watson
Indeterminate String Factorizations and Degenerate Text Transformations
Mathematics in Computer Science **11**(2) (2017) 209–218

BWBBLE

Lin Huang, Victoria Popic and Serafim Batzoglou
Short read alignment with populations of genomes
Bioinformatics **29**(13) (2013) i361–i370

Represent a collection of genomes called *reference multi-genome* and do pattern matching

BWBBLE

SNPs (aka SNVs or substitutions)

4-letter alphabet $\{\mathtt{A}, \mathtt{C}, \mathtt{G}, \mathtt{T}\}$ $\rightarrow$ 16-letter IUPAC encoding $\rightarrow$ 4-bit Gray code (to minimize $\sharp$ separate intervals during the search with the BWT)

Indels (insertions-deletions)

Corresponding sequences padded with surrounding bases (length depending on read length) are concatenated at the end of the reference multi-genome (separated by a special character)

Inversions, translocations and duplications

only both ends of the events are concatenated at the end of the reference multi-genome

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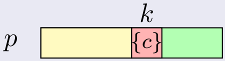
Backward search on the D-BWT: formalization



$$
\begin{aligned}
&\mathit{OneStep}(H, k, C, \mathit{BWT} = (L, h), p) = \\
&(((r, s)) \quad | \quad r = C[c] + \mathit{rank}_c(L, i-1) + 1, \\
&\qquad s = C[c] + \mathit{rank}_c(L, j), \\
&\qquad r \le s,\ (i, j) \in H,\ c \in \Delta_\Sigma \text{ and } c \cap p[k] \ne \emptyset).
\end{aligned}
$$

Let $\mathit{Step}(m, C, \mathit{BWT}, p) = \mathit{OneStep}(\{(1, n)\}, m, C, \mathit{BWT}, p)$ and $\mathit{Step}(i, C, \mathit{BWT}, p) = \mathit{OneStep}(\mathit{Step}(i+1, C, \mathit{BWT}, p), i, C, \mathit{BWT}, p)$ for $1 \le i \le m-1$.

In words, $\mathit{Step}(i, C, \mathit{BWT}, p)$ applies step m through to i of the backward search.
Then $\mathit{Step}(1, C, \mathit{BWT}, p)$ contains the intervals in the SA of t of the suffixes of t starting with p.

Backward search on the D-BWT: correctness

Lemma

The interval $(i, j) \in \mathit{Step}(k, C, \mathit{BWT}, p)$ *if and only if* $p[k..m]$ *is a degenerate prefix of* $M_t[h]$ *for* $i \leq h \leq j$.

Corollary

The interval $(i, j) \in \mathit{Step}(1, C, \mathit{BWT}, p)$ *if and only if* p *is a degenerate prefix of* $M_t[h]$ *for* $i \leq h \leq j$.

Intervals do not overlap

Lemma

The intervals in OneStep$(\{(i, j)\}, k, C, \mathit{BWT}, p)$ *do not overlap.*

Intervals do not overlap

$t = \{c, e\} \cdot \{c, d\} \cdot \{a, b, c\} \cdot \{a, d\} \cdot \{a, b, c\}$
$A = \{a, b, c\}, B = \{a, d\}, C = \{c, d\}, D = \{c, e\}$
$A < B < C < D$
$p = \{c\} \cdot \{d\} \cdot \{b\}$
$b \in A$ and $d \in B, C$

$\rightarrow$	1	3	A	B	A	D	C
$\rightarrow$	2	5	A	D	C	A	B
	3	4	B	A	D	C	A
	4	2	C	A	B	A	D
	5	1	D	C	A	B	A

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$\mathtt{A} < \mathtt{B} < \mathtt{C} < \mathtt{D}$

$p = \{\mathtt{c}\} \cdot \{\mathtt{d}\} \cdot \{\mathtt{b}\}$

$\mathtt{b} \in \mathtt{A}$ and $\mathtt{d} \in \mathtt{B}, \mathtt{C}$

	1	3	A	B	A	D	C
	2	5	A	D	C	A	B
⇒	3	4	B	A	D	C	A
⇒	4	2	C	A	B	A	D
	5	1	D	C	A	B	A

Intervals do not overlap

Lemma

The intervals in OneStep$(\{(i, j), (i', j')\}, k, C, BWT, p)$ *with* $i \leq j < i' \leq j'$ *do not overlap.*

Corollary

Let H *be a set of non-overlapping intervals. The intervals in OneStep*(H, k, C, BWT, p) *do not overlap.*

Intervals do not overlap

$t = \{\mathtt{c}, \mathtt{e}\} \cdot \{\mathtt{c}, \mathtt{d}\} \cdot \{\mathtt{a}, \mathtt{b}, \mathtt{c}\} \cdot \{\mathtt{a}, \mathtt{d}\} \cdot \{\mathtt{a}, \mathtt{b}, \mathtt{c}\}$

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$\mathtt{A} < \mathtt{B} < \mathtt{C} < \mathtt{D}$

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$\mathtt{b} \in \mathtt{A}$, $\mathtt{d} \in \mathtt{B}, \mathtt{C}$ and $\mathtt{c} \in \mathtt{A}, \mathtt{D}$

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$\mathtt{A} < \mathtt{B} < \mathtt{C} < \mathtt{D}$

$p = \{\mathtt{c}\} \cdot \{\mathtt{d}\} \cdot \{\mathtt{b}\}$

$\mathtt{b} \in \mathtt{A}$, $\mathtt{d} \in \mathtt{B},\mathtt{C}$ and $\mathtt{c} \in \mathtt{A},\mathtt{D}$

$\Rightarrow$	1	3	A	B	A	D	C
	2	5	A	D	C	A	B
	3	4	B	A	D	C	A
	4	2	C	A	B	A	D
$\Rightarrow$	5	1	D	C	A	B	A

Consecutive intervals can merge

Lemma

$\textit{Merge}(\textit{OneStep}(((i,j),(j+1,j')),k,C,\textit{BWT},p)) = \textit{OneStep}(((i,j')),k,C,\textit{BWT},p).$

Consecutive intervals can merge

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$\mathtt{b} \in \mathtt{A}$, $\mathtt{d} \in \mathtt{B}, \mathtt{C}$ and $\mathtt{c} \in \mathtt{A}, \mathtt{D}$

	1	3	A	B	A	D	C
	2	5	A	D	C	A	B
$\rightarrow$	3	4	B	A	D	C	A
$\rightarrow$	4	2	C	A	B	A	D
	5	1	D	C	A	B	A

Consecutive intervals can merge

$t = \{\mathsf{c},\mathsf{e}\} \cdot \{\mathsf{c},\mathsf{d}\} \cdot \{\mathsf{a},\mathsf{b},\mathsf{c}\} \cdot \{\mathsf{a},\mathsf{d}\} \cdot \{\mathsf{a},\mathsf{b},\mathsf{c}\}$

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$\mathtt{A} < \mathtt{B} < \mathtt{C} < \mathtt{D}$

$\mathsf{b} \in \mathtt{A}$, $\mathsf{d} \in \mathtt{B},\mathtt{C}$ and $\mathsf{c} \in \mathtt{A},\mathtt{D}$

$\Rightarrow$	1	3	A	B	A	D	C
	2	5	A	D	C	A	B
	3	4	B	A	D	C	A
	4	2	C	A	B	A	D
$\Rightarrow$	5	1	D	C	A	B	A

Pattern matching in conservative degenerate strings

A degenerate string is said to be *conservative* if its number of non-solid letters is upper-bounded by a fixed positive constant q.

Theorem

Let t be a conservative degenerate string over a constant size alphabet. Let the number of degenerate letters of t be bounded by a constant q. Then given the BWT of t, all the intervals in the BWT of occurrences of a pattern p of length m can be detected in time $O(qm^2)$.

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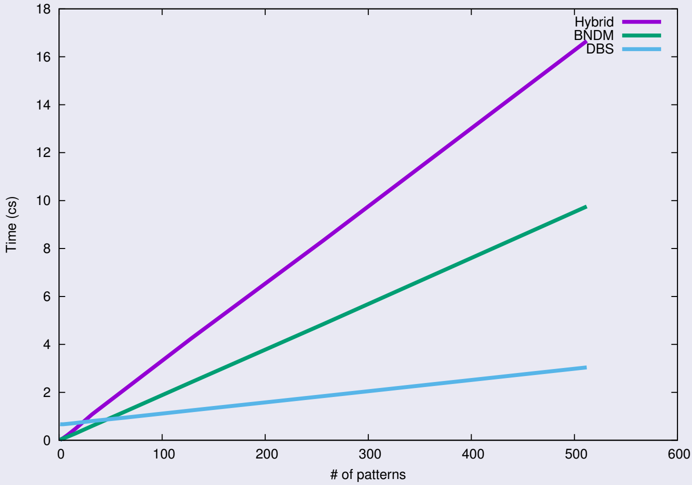
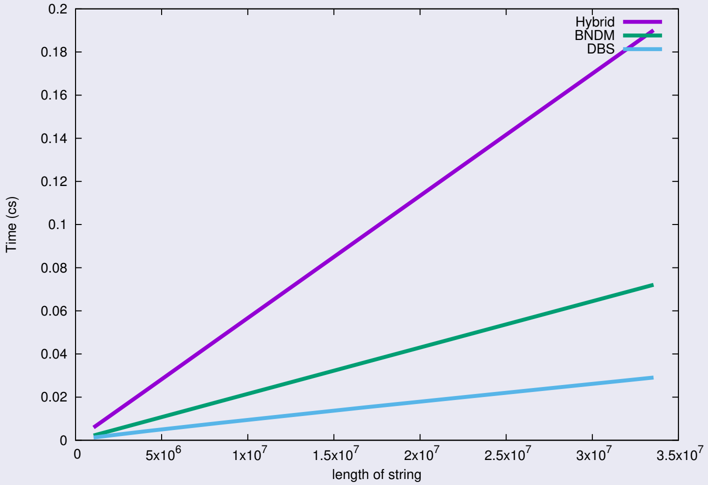
Experiments

Degenerate patterns of length 8 in a solid string of length 5MB, $\sigma = 4$



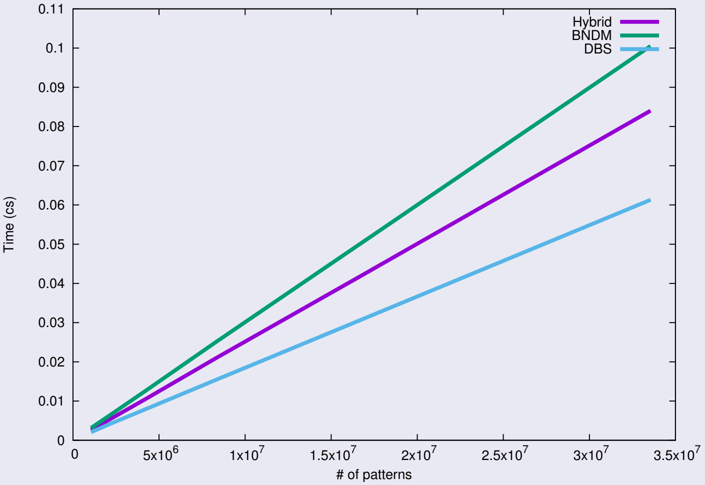
Experiments

One degenerate pattern of length 8 in a conservative degenerate string



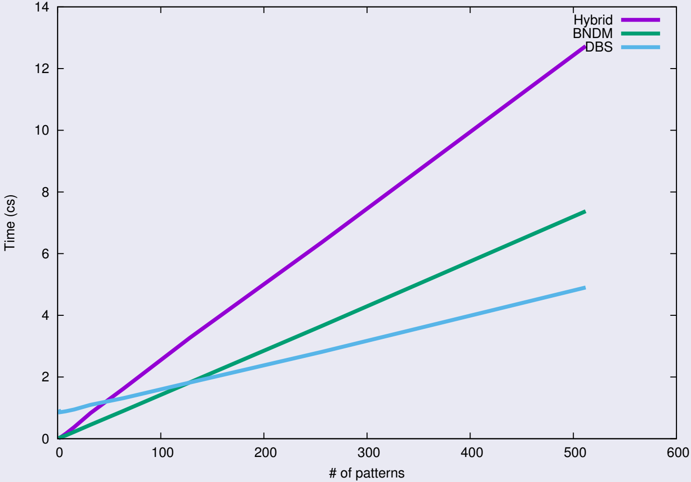
Experiments

Degenerate patterns of length 8 in a solid string, $\sigma = 4$



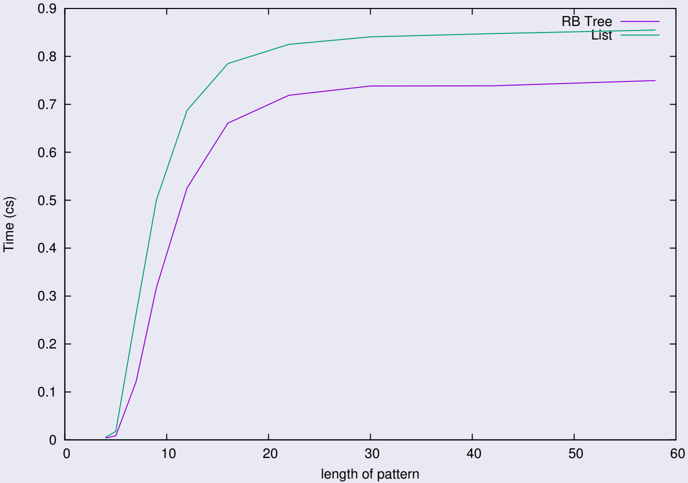
Experiments

Degenerate patterns of length 8 in a solid string, $\sigma = 8$



Experiments

Intervals



Perspectives

- Average case analysis
- Efficient data structure for handling intervals
- Using different order on the alphabet
- ...

Thank you for your attention!