

BWT / eBWT similarity

Giovanna Rosone

University of Pisa, Italy

Dagstuhl Seminar 19241 25 Years of the Burrows-Wheeler Transform

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Measures based on Burrows-Wheeler Transform

Why should we use the (e)BWT?

- The motivation is the clustering effect that the BWT/eBWT produces.
- The (e)BWT places groups symbols with a similar context close together. Such contexts are near in the sorted list!

Intuitive idea

The greater is the number of substrings shared by two strings, the smaller is their "distance"

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We can extend the notion of BWT to a multiset of words in two ways almost equivalents:

- concatenating all strings of the collection separating each string with a distinct end-marker and computing the BWT of the string so obtained
- computing the extended BWT (EBWT) (also known as *multi-string BWT*) of all strings
 - without concatenating the strings belonging to the collection !
 - allowing sets of strings to be removed or added (for instance merge two eBWTs).

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Two variants:

- (circular sorting) eBWT [*Mantaci, Restivo, R. and Sciortino,* 2007]: sorting the conjugates (cyclic rotations) of the input strings by using the lexicographic order on infinite words
 - useful for application where the input strings are circular (for instance mitochondrial dna, ...)
 - the strings in the collection are not ordered.
- (linear sorting) eBWT [Bauer, Cox and R., 2013]: sorting the suffixes of all words by using the usual lexicographic order (but one needs to append an (implicit) distinct end-marker to each string)
 - useful for application where the input strings are linear (for instance books, NGS libraries, . . .)
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Let S be the set of the words that end with the end-markers. We use implicit distinct end markers, i.e. $\$_1 = \$_2 = \$_3 = \$$: we use the position of the words in the collection in order to establish the order relation between two identical suffixes.

cbut(S) is a permutation of the symbols in S, obtained as concatenation of the symbols that (circularly) precede the first symbol of the suffix in the list of its lexicographically sorted suffixes of S.

The use of ordered and distinct "end-marker" symbols makes the multiset of sequences an ordered collection.

So the identical or similar sequences could be distant in the collection.

This can make the difference in the clustering effect!!

C	TT_{3}
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			Collec	tion S			
	0	1	2	3	4	5	6
S_1	G	C	C	Α	Α	C	\$ ₁
S_2	G	Α	G	C	T	C	\$ ₂
S_3	Т	C	G	C	Т	Т	\$3

ebwt(S) is a permutation of the symbols in S, obtained as concatenation of the symbols that (circularly) precede the first symbol of the suffix in the list of its lexicographically sorted suffixes of S.

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S_3	T	C	G	C	Т	Т	\$3

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eBWT	Sorted Suffixes of S
C	\$ ₁
C	\$ ₂
T	\$3
C	AAC ¹
A	$AC\$_1$
G	$AGCTC\$_2$
A	C
T	$C\$_2$
C	CAAC ^{\$1}
G	$CCAAC\$_1$
T	$CGCTT\$_3$
G	$CTC\$_2$
G	$CTT\$_3$
\$2	GAGCTC ^{\$2}
\$1	GCCAAC [§] ₁
Ā	GCTC\$2
C	$GCTT\$_3$
T	T\$3
C	$TC\$_2$
\$3	TCGCTT\$3
Č	TT_{3}
	▶ ▲ ■ ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ●

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S_1	G	C	C	Α	Α	C	\$ ₁
S_2	G	Α	G	C	T	C	\$ ₂
S_3	T	C	G	C	Т	Т	\$3

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C	\$1
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C	AAC ¹
A	$AC\$_1$
G	AGCTC ^{\$2}
A	C ¹
T	$C\$_2$
C	CAAC ¹
\overline{G}	CCAAC ^{\$1}
T	$CGCTT_{3}$
G	CTC\$2
G	$CTT\$_3$
\$2	GAGCTC\$2
\$1	GCCAAC\$1
A	GCTC\$2
C	GCTT\$3
\tilde{T}	T\$3
	TC\$2
\$3	TCGCTT\$3
	TT_{3}
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Example: swapping sequences

EB

BWT	Sorted Suffixes	
Т	\$	
Т	\$	
Т	\$	
Т	ACCACT\$	
G	ACCT\$	
G	ACCT\$	
C	ACT\$	
Т	AGACCT\$	
G	AGACCT\$	
C	CACT	
A	CCACT\$	
A	CCT\$	
Α	CCT\$	
\underline{C}	CT\$	
$\frac{C}{\underline{A}}{\underline{C}}$	CT\$	
C	CT\$	
Α	GACCT\$	
A	GACCT\$	
\$	GAGACCT\$	
C	<i>T</i> \$	
C	T\$	
C	<i>T</i> \$	
\$	TACCACT\$	
\$	TAGACCT\$	

$S = \{ TAGACCT, TACCACT, GAGACCT \}$ $S' = \{ TACCACT, TAGACCT, GAGACCT \}$

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Example: swapping sequences

$\mathsf{S} = \{ TAGA\underline{C}CT, TACC\underline{A}CT, GAGACCT \}$

EBWT	Sorted Suffixes
T	\$
T	\$
T	\$
T	ACCACT
G	ACCT
G	ACCT
C	ACT\$
T	AGACCT
G	AGACCT
C	CACT
A	CCACT
A	CCT\$
A	CCT\$
$\frac{C}{\underline{A}}{\underline{C}}$	CT\$
\underline{A}	CT\$
C	CT\$
A	GACCT
A	GACCT\$
\$	GAGACCT
C	T\$
C	T\$
C	T\$
\$	TACCACT
\$	TAGACCT

$\mathsf{S}' = \{ \underline{TACC\underline{A}CT}, \underline{TAGA\underline{C}CT}, \underline{GAGACCT} \}$

\$
\$
CT\$
CT\$
CT ^{\$}

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Example: swapping sequences

$S = \{ TAGA \underline{C}CT, TACC \underline{A}CT, GAGACCT \}$

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EBWT	Sorted Suffixes	EBWT	Sorted Suffixes
T	\$	T	\$
T	\$	T	\$
T	\$	T	\$
T	ACCACT\$	T	ACCACT\$
G	ACCT\$	G	ACCT\$
G	ACCT\$	G	ACCT\$
C	ACT	C	ACT\$
T	AGACCT\$	T	AGACCT\$
G	AGACCT\$	G	AGACCT\$
C	CACT\$	C	CACT\$
A	CCACT\$	A	CCACT\$
A	CCT\$	A	CCT\$
A	CCT\$	A	CCT\$
$\frac{C}{\underline{A}}{\underline{C}}$	CT\$	A	CT\$
\underline{A}	CT\$	$\frac{A}{C}{C}$	CT\$
	CT\$	\overline{C}	CT\$
A	GACCT\$	A	GACCT\$
A	GACCT\$	A	GACCT\$
\$	GAGACCT\$	\$	GAGACCT\$
C	T\$	C	T
C	T	C	T\$
C	T\$	C	T
\$ \$	TACCACT\$	\$	TACCACT\$
\$	TAGACCT	\$	TAGACCT

Ordered collection: $S = \{TAGA\underline{C}CT, TACC\underline{A}CT, GAGACCT\}$

$\frac{EBWT}{T}$	Suffixes \$	
T	\$	
T	\$	
T	ACCACT\$	In these regions, when the non-\$ suffixes are the same,
G	ACCT\$	In these regions, when the non- φ suffixes are the same,
G	ACCT\$	the ordering of the symbols in eBWT depends on the
C	ACT\$	
T_{α}	AGACCT\$	ordering of the sequences in the collection.
G	AGACCT\$	
A	CACT\$ CCACT\$	
A	CCT\$	
A	CCT\$	
\hat{C}	CT\$	
Α	CT\$	
C	CT\$	
A	GACCT\$	
A	GACCT\$	
\$	GAGACCT\$	Note that the rest of EBWT is unaffected by this change in ordering.
$C \\ C$	T\$ T\$	
C	T	
\$	T^{\bullet}_{ACCACT}	
\$	TAGACCT\$	
Ψ	1110110010	

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Ordered collection: $S = \{ TAGACCT, TACCACT, GAGACCT \}$

$\frac{EBWT}{T}$	Suffixes \$	
T	\$	
T	\$	
G	ACCACT\$	In these regions, when the non-\$ suffixes are the same,
G	ACCT\$	G
C	ACT\$	the ordering of the symbols in eBWT depends on the
	AGACCT\$	and an in a fight a conservation that a collection
Ĝ	AGACCT\$	ordering of the sequences in the collection.
\tilde{c}	CACT\$	
A	CCACT\$	
A	CCT\$	
A	CCT\$	
C	CT\$	
A	CT\$	
C	CT\$	
A	GACCT\$	
A	GACCT\$	
\$	GAGACCT\$	Note that the rest of EBWT is unaffected by this change in ordering.
$C \\ C$	T\$ T\$	
$C \\ C$	7 \$ 7 \$	
\$	TACCACT\$	
ծ Տ	TAGACCT\$	
æ	IAGACCIS	

Ordered collection: $S = \{ TAGACCT, TACCACT, GAGACCT \}$

EBWT	Suffixes	
T	\$	
T	\$	
T	\$	
T	ACCACT\$	In these regions, when the non-\$ suffixes are the same,
G	ACCT\$	3
G	ACCT\$	the ordering of the symbols in eBWT depends on the
C	ACT\$	
T	AGACCT\$	ordering of the sequences in the collection.
G	AGACCT\$	
C	CACT\$	
A	CCACT\$	
A	CCT\$	• BCR can swap the sequences <i>TAGACCT</i> and <i>TACCACT</i> in
A	CCT\$	· · ·
C	CT\$	the ordered collection
A		• by swapping the symbols C and A directly in the EBWT during its
C		
A	GACCT\$	construction [Cox, Bauer, Jakobi and R, 2012]
A	GACCT\$	
\$	GAGACCT\$	Note that the rest of EBWT is unaffected by this change in ordering.
C	T\$	Note that the rest of LBWT is unanected by this change in ordering.
C	T	
C		
\$ \$	TACCACT\$	
\$	TAGACCT\$	

Ordered collection: $S = \{TACCACT, TAGACCT, GAGACCT\}$

$\frac{EBWT}{T}$	Suffixes \$ \$ \$	
T G C T G	ACCACT\$ ACCT\$ ACCT\$ ACT\$ AGACCT\$ AGACCT\$	In these regions, when the non-\$ suffixes are the same, the ordering of the symbols in eBWT depends on the ordering of the sequences in the collection.
C A A A C C C A A \$ C	CACT\$ CCACT\$ CCT\$ CT\$ CT\$ CT\$ GACCT\$ GACCT\$ GACCT\$ T\$	 BCR can swap the sequences <i>TAGACCT</i> and <i>TACCACT</i> in the ordered collection by swapping the symbols C and A directly in the EBWT during its construction [Cox, Bauer, Jakobi and R, 2012] Note that the rest of EBWT is unaffected by this change in ordering.
C C \$ \$	T\$ T\$ TACCACT\$ TAGACCT\$	

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The document array

For simplicity, we use the document array DA(S): a sequence of "colors" that depends on how the suffixes of S are mixed in the sorted list.

DA[i] = h: if *i*-th smallest suffix in the sorted collection belongs to the string S_h

Note that the DA is not necessary, one can use the LF-mapping starting from each \hat{s}_i .

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Collection S							
	0	1	2	3	4	5	6
S_1	G	C	C	Α	Α	C	\$ ₁
S_2	G	Α	G	C	Т	C	\$ ₂
S_3	Т	C	G	C	T	Т	\$3

DA[i] = h: if *i*-th smallest suffix in the sorted collection belongs to the string S_h

Note that the DA is not necessary, one can use the LF-mapping starting from each \hat{s}_i .

DA	eBWT	Sorted Suffixes of S
1	C	\$ ₁
2	C	\$ ₂
3	T	\$ ₃
1	C	$AAC\$_1$
1	A	$AC\$_1$
2	G	$AGCTC\$_2$
1	A	$C\$_1$
2	T	C
1	C	$CAAC\$_1$
1	G	CCAAC ^{\$1}
3	T	$CGCTT\$_3$
2	G	$CTC\$_2$
3	G	$CTT\$_3$
2	\$2	GAGCTC ^{\$2}
1	\$1	GCCAAC ^{\$1}
2	Ā	$GCTC\$_2$
3	C	$GCTT\$_3$
3	T	T\$3
2	C	$TC\$_2$
2	\$3	TCGCTT\$3
3	\tilde{C}	$TT\$_3$

The document array

For simplicity, we use the document array DA(S): a sequence of "colors" that depends on how the suffixes of S are mixed in the sorted list.

Collection S							
	0	1	2	3	4	5	6
S_1	G	C	C	Α	Α	C	\$ ₁
S_2	G	Α	G	C	Т	C	\$2
S_3	Т	C	G	C	T	Т	\$3

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2	C	\$ ₂
3	T	\$ ₃
1	C	AAC ¹
1	A	$AC\$_1$
2	G	AGCTC ^{\$2}
1	A	C ¹
2	T	$C\$_{2}$
1	$T \\ C$	CAAC ¹
1	G	CCAAC ^{\$1}
3	T	$CGCTT\$_3$
2	G	$CTC\$_2$
3	G	$CTT\$_3$
2	\$ ₂	GAGCTC ^{\$2}
1	\$ ₁	GCCAAC ^{\$1}
2	Ā	GCTC ^{\$2}
3	C	$GCTT\$_3$
3	T	$T\$_{3}$
2	C	$T\check{C}\$_2$
2	\$3	TCGCTT\$3
3	Č	$TT\$_{3}$

Projections on two strings

One can compute the eBWT of the whole collection and analyze all pairs at the same time or one can get a projection of the two selected strings.

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In order to remove S_2 , we only need to remove the blue symbols (associated with the suffixes of S_2) in eBWT.

Actually, we don't need to store the colors, for instance the symbols of S_2 can be found by using the LF-mapping starting from $\$_2$

$\begin{array}{c ccccccccccccccccccccccccccccccccccc$			
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$			
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$			
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$			
$\begin{array}{cccccccccccccccccccccccccccccccccccc$			
$\begin{array}{cccccccccccccccccccccccccccccccccccc$			
$\begin{array}{cccccccccccccccccccccccccccccccccccc$			
$\begin{array}{rrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrr$	WE		
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	ne blue		
th the T $CGCTTs_3$ G $CCAACs_1$ T G $CTCs_2$ G $CTTs_3$ T G $CTTs_3$ G $CTTs_3$ s_2 $GAGCTCs_2$ G $CTTs_3$ d to s_1 $GCCAACs_1$ T Ts_3 tance C $GCTTs_3$ S_3 $TCGCTTs_3$ T Ts_3 tance T Ts_3 G TTs_3 T Ts_3 T Ts_3 G TTs_3 G TTs_3 G TTs_3 G TTs_3 G TCs_2 G $GCTTs_3$ G TTs_3 G TTs_3 G TCs_2 G TTs_3 G TTs_3 G TTs_3 G TCs_2 G TTs_3 G TTs_3 G TCS_2 G TTs_3 G TTS_3 G TCS_2 G TTS_3 G TCS_3 G G TCS_3 G T			
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	th the		
$\begin{array}{cccccccccccccccccccccccccccccccccccc$			
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	T.		
$\begin{array}{cccccc} d \ to & \begin{smallmatrix} s_1 & GCCACS_1 & T & T\$_3 \\ & & GCTC\$_2 & & \$_3 & TCGCTT\$_3 \\ tance & C & GCTT\$_3 & C & TT\$_3 \\ & & T & T\$_3 & C & TT\$_3 \\ be & & \begin{smallmatrix} c & & & \\ s_3 & TCGCTT\$_3 \\ & & & \hline \end{array}$			
tance $\begin{array}{cccc} C & GCTT\$_3 & & TCGCTT\$_3 \\ T & T\$_3 & & C & TT\$_3 \end{array}$ be $\begin{array}{cccc} C & TT\$_3 & & C & TT\$_3 \end{array}$	to		
tance T $T_{\$_3}$ \tilde{C} $TT\$_3$ be C $TC\$_2$ $\$_3$ $TCGCTT\$_3$	1 10		
be $\begin{array}{c} T & TC\$_2 \\ \$_3 & TCGCTT\$_3 \end{array}$	tance		
DE \$3 TCGCTT\$3	·		
	be		

Projections on two strings

One can compute the eBWT of the whole collection and analyze all pairs at the same time or one can get a projection of the two selected strings.

Collection S	eBWT	Sorted Suffixes of	s	
0 1 2 3 4 5 6		\$1	<u> </u>	
$S_1 G C C A A C \$_1$	C	\$2		
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	T	\$ ₃		
$S_3 \mid T C G C T T \mid \$_3$	C	AAC ^{\$1}		
	$A \\ G$	$AC\$_1 \\ AGCTC\$_2$		
In order to remove S_2 , we	A	C ^{\$1}		
	T	$C\$_2$		
only need to remove the blue	\overline{C}	CAAC ¹		
	G	$CCAAC\$_1$		
symbols (associated with the	T	$CGCTT\$_3$		
suffixes of S_2) in $eBWT$.	G	$CTC\$_2$		
sumities of D_2 in $eD W I$.	G	$CTT\$_3$		
	\$2 ¢	$GAGCTC\$_2$ $GCCAAC\$_1$		
Actually, we don't need to	$\overset{\$_1}{A}$	GCTC\$2		
	Ĉ	$GCTT\$_3$		
store the colors, for instance	\widetilde{T}	T_{3}^{0}		
the symbols of S_2 can be	C	$TC\$_2$		
the symbols of D ₂ can be	\$3	$TCGCTT\$_3$		
found by using the	C	$TT\$_3$		
LF-mapping starting from $\$_2$.				

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Collection S							
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S_2	G	Α	G	C	Т	C	\$ ₂
S_3	T	C	G	C	Т	Т	\$3

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Actually, we don't need to store the colors, for instance the symbols of S_2 can be found by using the LF-mapping starting from $\$_2$

6 \$1 \$2 \$3 \$3 blue the conce	eBWT C C T C A A C G G C S 2 S 1 A C T C S 3 C S 3 C	$\begin{tabular}{lllllllllllllllllllllllllllllllllll$	<u>fS</u>	eBWT C T C A A C G G T G \$1 C T \$3 C	Sorted Suffixes of S $\$_1$ $\$_3$ $AC\$_1$ $C\$_1$ $CAAC\$_1$ $CCAAC\$_1$ $CGCTT\$_3$ $GCCAAC\$_1$ $GCCTT\$_3$ $GCCTAC\$_1$ $GCTT\$_3$ TCS_3 TCS_3 TCS_3 TCS_3 TCS_3 TCS_3 $TT\$_3$ TCS_3 $TT\$_3$ TCS_3 $TT\$_3$ TCS_3 TCS_3 TS_3 TCS_3 $TT\$_3$ TCS_3	
$\$_2$.			• • • •		▶ < ≣ > ≣ • ୨०	, C

Sequences comparison

Similarity measures based on eBWT can be obtained by using the following property.

Key

Since conjugates/suffixes starting with the same context are close in the sorted list:

The greater is the number of segments shared by u and v, the greater is the mixing of the suffixes of u and v in the sorted list and the greater is the clustering effect in the eBWT.

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First goal

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Similarity measures for comparing DNA genomes

Some measures:

- Mantaci, Restivo, R. and Sciortino, 2007
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- Yang, Zhang, and Wang, 2010

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Takes into account the alternation (mixing) of the colors, i.e. symbols coming from different sequences in the output of eBWT

DA	eBWT	Sorted suffixes
1	C	\$ 1
2	G	\$ ₂
1	$\$_1$	$A \ C \ A \ C \ G \ G \ C \ \$_1$
2	$\$_2$	$A \ C \ A \ C \ G \ G \ G \ \$_2$
1	C	$A \ C \ G \ G \ C \ \$_1$
2	C	$A \ C \ G \ G \ G \ \$_2$
1	G	C $\$_1$
1	A	$C \ A \ C \ G \ G \ C \ \$_1$
2	A	$C A C G G G \$_2$
1	A	$C \ G \ G \ C \ \$_1$
2	A	$C \ G \ G \ G \ \$_2$
2	G	$G \$
1	G	$G \ C \ \$_1$
2	G	$G G \$_2$
1	C	$G \ G \ C \ \$_1$
2	C	$G G G \$_2$

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 $\begin{array}{c} DA \\ (1) \\ 2 \\ 1 \end{array}$ $D_{col}(u, v)$ eBWTSorted suffixes $\begin{array}{ccc} C & \$_1 \\ G & \$_2 \\ \$_1 & A \ C \ A \ C \ G \ G \ C \ \$_1 \end{array}$ 2 1 C A C G G G $\$_2$ 2 $G \qquad C \$_1$ 1 $A \qquad C \ A \ C \ G \ G \ C \$ 2 $A \qquad C \ A \ C \ G \ G \ G \ \$_2$ 1 $A \qquad C \ G \ G \ C \ \$_1$ 2 $A \qquad C \ G \ G \ G \ \$_2$ 2 $G \qquad G \$_2$ $G \qquad G \subset \$_1$ 1 2 $G \qquad G \subseteq S_2$ C $G G C \$_1$ 2 C $G G G \$_2$ BWT/ eBWT similarity June 10 - 14 , 2019

 $D_{col}(u,v) = \sum_{\substack{i=1,\\n_i \neq 0}}^{k} (n_i - 1)$

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 $\mathsf{S} = \{ u = ACACGGC\$_1, v = ACACGGGS_2 \}$

Takes into account the alternation (mixing) of the colors, i.e. symbols coming from different sequences in the output of eBWT

 $D_{col}(u,v)$ DA eBWTSorted suffixes C\$1 2 1 G\$2 $\$_1$ A C A C G G C $\$_1$ 0 2 0 0 $2 \qquad C \qquad A \ C \ G \ G \ G \ \$_2$ 0 $G \qquad C \$_1$ 1 $A \qquad C \ A \ C \ G \ G \ C \ \$_1$ $A \qquad C \ A \ C \ G \ G \ G \ \$_2$ 0 0 $\frac{1}{2}$ $A \qquad C \ G \ G \ C \ \$_1$ $A \qquad C \ G \ G \ G \ \$_2$ $G \qquad G \$_2$ $G \qquad G \subset \$_1$ 2 $G \qquad G \ G \ \$_2$ $C \qquad G \ G \ C \$ 2 C $G G G \$_2$

 $D_{col}(u,v) = \sum_{\substack{i=1,\\n_i \neq 0}}^{k} (n_i - 1)$

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June 10 - 14 , 2019

 $S = \{u = ACACGGC\$_1, v = ACACGGG\$_2\}$

Takes into account the alternation (mixing) of the colors, i.e. symbols coming from different sequences in the output of eBWT

 $D_{col}(u, v)$ DA eBWTSorted suffixes C\$1 $\mathbf{2}$ G\$2 $\$_1$ A C A C G G C $\$_1$ 0 2 0 0 C A C G G G $\$_2$ 2 0 $G \qquad C \$_1$ 1 $A \qquad C A C G G C \$_1$ $\mathbf{2}$ $A \qquad C \ A \ C \ G \ G \ S_2$ 0 0 $A \qquad C \ G \ G \ C \ \$_1$ $C G G G S_2$ A 1 G $G \$ $G \qquad G \subset \$_1$ $G \qquad G \ G \ \$_2$ $\mathbf{2}$ C $G G C \$_1$ 2 C $G G G \$_2$ BWT/ eBWT similarity

$$D_{col}(u,v) = \sum_{\substack{i=1, \\ n_i \neq 0}}^k (n_i - 1)$$

 $\mathsf{S} = \{ u = ACACGGC\$_1, v = ACACGGGS_2 \}$

Takes into account the alternation (mixing) of the colors, i.e. symbols coming from different sequences in the output of eBWT

 $D_{col}(u, v)$ DA eBWTSorted suffixes C\$1 $\mathbf{2}$ G\$2 $\$_1$ A C A C G G C $\$_1$ 0 2 0 0 C A C G G G $\$_2$ 2 0 $G \qquad C \$_1$ 1 $A \qquad C A C G G C \$_1$ 1 2 $A \qquad C \ A \ C \ G \ G \ G \ \$_2$ 0 0 $A \qquad C \ G \ G \ C \ \$_1$ $A \qquad C \ G \ G \ G \ \$_2$ $\mathbf{2}$ 1 $G \qquad G \$_2$ $G \qquad G \subset \$_1$ 1 0 $G \qquad G \ G \ \$_2$ $G G C \$_1$ 2 C $G G G \$_2$

$$D_{col}(u, v) = \sum_{\substack{i=1, \\ n_i \neq 0}}^{k} (n_i - 1)$$

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 $\mathsf{S} = \{ u = ACACGGC\$_1, v = ACACGGGS_2 \}$

Takes into account the alternation (mixing) of the colors, i.e. symbols coming from different sequences in the output of eBWT

$D_{col}(u, v)$	DA	eBWT	Sorted suffixes
0	1	C	\$ ₁
0	2	G	\$ ₂
0	1	$\$_1$	$A \ C \ A \ C \ G \ G \ C \ \$_1$
0	2	$\$_2$	$A \ C \ A \ C \ G \ G \ \$_2$
0	1	C	$A \ C \ G \ G \ C \ \$_1$
0	2	C	$A \ C \ G \ G \ G \ \$_2$
1	1	G	C $\$_1$
1	1	A	$C \ A \ C \ G \ G \ C \ \$_1$
0	2	A	$C \ A \ C \ G \ G \ G \ \$_2$
0	1	A	$C \ G \ G \ C \ \$_1$
1	2	A	$C \ G \ G \ G \ \$_2$
1	2	G	G $\$_2$
0	1	G	$G \ C \ \$_1$
0	(2)	G	$G G \$_2$
	Ť	C	$G \ G \ C \ \$_1$
	2	C	$G \ G \ G \ \$_2$

BWT/ eBWT similarity

$$D_{col}(u,v) = \sum_{\substack{i=1, \\ n_i \neq 0}}^{k} (n_i - 1)$$

 $\mathsf{S} = \{ u = ACACGGC\$_1, v = ACACGGGS_2 \}$

Takes into account the alternation (mixing) of the colors, i.e. symbols coming from different sequences in the output of eBWT

$D_{col}(u, v)$	DA	eBWT	Sorted suffixes
0	1	C	\$ ₁
0	2	G	\$ ₂
0	1	$\$_1$	$A \ C \ A \ C \ G \ G \ C \ \$_1$
0	2	$\$_2$	$A \ C \ A \ C \ G \ G \ G \ \$_2$
0	1	C	$A \ C \ G \ G \ C \ \$_1$
0	2	C	$A \ C \ G \ G \ G \ \$_2$
1	1	G	C $\$_1$
1	1	A	$C \ A \ C \ G \ G \ C \ \$_1$
0	2	A	$C A C G G G \$_2$
0	1	A	$C \ G \ G \ C \ \$_1$
1	2	A	$C \ G \ G \ G \ \$_2$
1	2	G	G $\$_2$
0	1	G	$G \ C \ \$_1$
0	2	G	$G G \$_2$
0	(1)	C	$G \ G \ C \ \$_1$
	$\underbrace{}_{2}$	C	$G G G \$_2$

BWT/ eBWT similarity

$$D_{col}(u,v) = \sum_{\substack{i=1,\\n_i \neq 0}}^{k} (n_i - 1)$$

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 $\mathsf{S} = \{ u = ACACGGC\$_1, v = ACACGGGS_2 \}$

Takes into account the alternation (mixing) of the colors, i.e. symbols coming from different sequences in the output of eBWT

 $D_{col}(u, v)$ DA eBWTSorted suffixes \$1 C $\mathbf{2}$ G \$2 $\$_1$ A C A C G G C $\$_1$ 0 $\mathbf{2}$ 0 0 C A C G G G $\$_2$ 2 0 $G \qquad C$ 1 1 $A \qquad C \ A \ C \ G \ G \ C \$ 2 $A \qquad C \ A \ C \ G \ G \ G \ \$_2$ 0 0 $A \qquad C \ G \ G \ C \ \$_1$ $\mathbf{2}$ $A \qquad C \ G \ G \ G \ \$_2$ 2 $G \qquad G \$_2$ $G \qquad G \subset \$_1$ 2 $G \qquad G \subseteq S_2$ 0 C $G G C \$_1$ 0 2 C $G G G \$_2$

BWT/ eBWT similarity

$$D_{col}(u, v) = \sum_{\substack{i=1, \\ n_i \neq 0}}^{k} (n_i - 1)$$

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 $S = \{u = ACACGGC\$_1, v = ACACGGG\$_2\}$

Takes into account the alternation (mixing) of the colors, i.e. symbols coming from different sequences in the output of eBWT

Sorted suffixes $D_{col}(u,v)$ DA eBWTC\$1 2 G \$2 1 $\$_1$ $A \ C \ A \ C \ G \ G \ C$ 0 $\mathbf{2}$ $\$_2$ A C A C G G G $\$_2$ 0 C A C G G C $\$_1$ 1 0 2 C A C G G G $\$_2$ 0 $G \qquad C$ 1 1 $A \qquad C \ A \ C \ G \ G \ C \$ $\mathbf{2}$ $A \qquad C \ A \ C \ G \ G \ G \ \$_2$ 0 0 $A \qquad C \ G \ G \ C \ \$_1$ $\mathbf{2}$ $A \qquad C \ G \ G \ G \ \$_2$ 2 G $G \ \$_2$ $G \qquad G \subset \$_1$ 0 $\mathbf{2}$ $G \qquad G \subseteq S_2$ C $G G C \$_1$ 0 2 C $G G G \$_2$

BWT/ eBWT similarity

$$D_{col}(u,v) = \sum_{\substack{i=1,\\n_i \neq 0}}^k (n_i - 1)$$

In the example:

 $D_{col}(u,v) = 2$

that we can normalize with the lengths of the sequences, so that

$$D_{col}(u,v) = 2/(8+8)$$

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 $\mathsf{S} = \{ u = ACACGGC\$_1, v = ACACGGGS_2 \}$

Compute the expectation or the entropy of the distribution of the alternations of colors

DA	eBWT	Sorted suffixes
1	C	\$ ₁
2	G	\$ ₂
1	$\$_1$	$A C A C G G C \$_1$
2	$\$_2$	$A C A C G G G \$_2$
1	C	$A \ C \ G \ G \ C \ \$_1$
2	C	$A \ C \ G \ G \ G \ \$_2$
1	G	C $\$_1$
1	A	$C \ A \ C \ G \ G \ C \ \$_1$
2	A	$C \ A \ C \ G \ G \ G \ \$_2$
1	A	$C \ G \ G \ C \ \$_1$
2	A	$C \ G \ G \ G \ \$_2$
2	G	$G \ \$_2$
1	G	$G \ C \ \$_1$
2	G	$G G \$_2$
1	C	$G \ G \ C \ \$_1$
2	C	$G \ G \ G \ \$_2$

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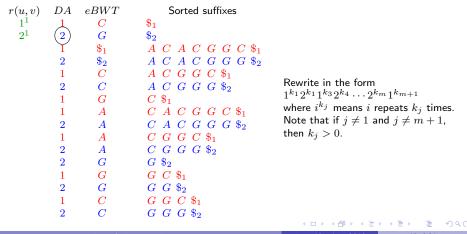
 $\mathsf{S} = \{ u = ACACGGC\$_1, v = ACACGGGS_2 \}$

Compute the expectation or the entropy of the distribution of the alternations of colors

r(u, v)	DA	eBWT	Sorted suffixes	
1^{1}	(1)	C	\$ ₁	
	$\overbrace{2}$	G	\$ ₂	
	1	$\$_1$	$A \ C \ A \ C \ G \ G \ C \ \$_1$	
	2	$$_{2}$	$A \ C \ A \ C \ G \ G \ G \ \$_2$	
	1	C	$A \ C \ G \ G \ C \ \$_1$	
	2	C	$A \ C \ G \ G \ G \ \$_2$	Rewrite in the form $1^{k_1}2^{k_1}1^{k_3}2^{k_4}\cdots 2^{k_m}1^{k_m+1}$
	1	G	C $\$_1$	
	1	A	$C \ A \ C \ G \ G \ C \ \$_1$	where i^{k_j} means <i>i</i> repeats k_j times.
	2	A	$C A C G G G \$_2$	Note that if $j \neq 1$ and $j \neq m+1$,
	1	A	$C \ G \ G \ C \ \$_1$	then $k_j > 0$.
	2	A	$C \ G \ G \ G \ \$_2$	
	2	G	G \$2	
	1	G	$G \ C \ \$_1$	
	2	G	$G G \$_2$	
	1	C	$G \hspace{0.1in} G \hspace{0.1in} C \hspace{0.1in} \$_{1}$	
	2	C	$G \ G \ G \ \$_2$	
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 $\mathsf{S} = \{ u = ACACGGC\$_1, v = ACACGGGS_2 \}$

Compute the expectation or the entropy of the distribution of the alternations of colors



 $\mathsf{S} = \{ u = ACACGGC\$_1, v = ACACGGGS_2 \}$

Compute the expectation or the entropy of the distribution of the alternations of colors

r(u, v)	DA	eBWT	Sorted suffixes	
1^{1}	1	C	\$ ₁	
2^{1}	2	G	$\$_2$	
1^{1}	(1)	$\$_1$	$A \ C \ A \ C \ G \ G \ C \ \$_1$	
	$\underbrace{}_{2}$	$$_{2}$	$A \ C \ A \ C \ G \ G \ G \ \$_2$	
	1	C	$A \ C \ G \ G \ C \ \$_1$	
	2	C	$A \ C \ G \ G \ G \ \$_2$	Rewrite in the form $1^{k_1}2^{k_1}1^{k_3}2^{k_4}\cdots 2^{k_m}1^{k_{m+1}}$
	1	G	C $\$_1$	
	1	A	$C \ A \ C \ G \ G \ C \ \$_1$	where i^{k_j} means <i>i</i> repeats k_j times.
	2	A	$C A C G G G \$_2$	Note that if $j \neq 1$ and $j \neq m+1$,
	1	A	$C \ G \ G \ C \ \$_1$	then $k_j > 0$.
	2	A	$C \ G \ G \ G \ \$_2$	
	2	G	G \$2	
	1	G	$G \ C \ \$_1$	
	2	G	$G G \$_2$	
	1	C	$G \ G \ C \ \$_1$	
	2	C	$G \ G \ G \ \$_2$	
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 $\mathsf{S} = \{ u = ACACGGC\$_1, v = ACACGGGS_2 \}$

Compute the expectation or the entropy of the distribution of the alternations of colors

r(u, v)	DA	eBWT	Sorted suffixes	
1^{1}	1	C	\$ ₁	
2^{1}	2	G	\$ ₂	
1^{1}	1	$\$_1$	$A \ C \ A \ C \ G \ G \ C \ \$_1$	
2^{1}	(2)	$$_{2}$	$A \ C \ A \ C \ G \ G \ G \ \$_2$	
	Ĭ	C	$A \ C \ G \ G \ C \ \$_1$	
	2	C	$A \ C \ G \ G \ G \ \$_2$	Rewrite in the form $1^{k_1}2^{k_1}1^{k_3}2^{k_4}\cdots 2^{k_m}1^{k_m+1}$
	1	G	C $\$_1$	
	1	A	$C \ A \ C \ G \ G \ C \ \$_1$	where i^{k_j} means <i>i</i> repeats k_j times.
	2	A	$C A C G G G \$_2$	Note that if $j \neq 1$ and $j \neq m+1$,
	1	A	$C \ G \ G \ C \ \$_1$	then $k_j > 0$.
	2	A	$C \ G \ G \ G \ \$_2$	
	2	G	G $\$_2$	
	1	G	$G \ C \ \$_1$	
	2	G	$G G \$_2$	
	1	C	$G \ G \ C \ \$_1$	
	2	C	$G \ G \ G \ \$_2$	
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 $\mathsf{S} = \{ u = ACACGGC\$_1, v = ACACGGGS_2 \}$

Compute the expectation or the entropy of the distribution of the alternations of colors

r(u, v)	DA	eBWT	Sorted suffixes	
1^{1}	1	C	\$ ₁	
2^{1}	2	G	\$ ₂	
1^{1}	1	\$ 1	$A \ C \ A \ C \ G \ G \ C \ \$_1$	
2^{1}	2	$\$_2$	$A \ C \ A \ C \ G \ G \ G \ \$_2$	
1^{1}	(1)	C	$A \ C \ G \ G \ C \ \$_1$	
	$\underbrace{}_{2}$	C	$A \ C \ G \ G \ G \ \$_2$	Rewrite in the form $1^{k_1}2^{k_1}1^{k_3}2^{k_4}\cdots 2^{k_m}1^{k_m+1}$
	1	G	C $\$_1$	
	1	A	$C \ A \ C \ G \ G \ C \ \$_1$	where i^{k_j} means <i>i</i> repeats k_j times.
	2	A	$C A C G G G \$_2$	Note that if $j \neq 1$ and $j \neq m+1$,
	1	A	$C \ G \ G \ C \ \$_1$	then $k_j > 0$.
	2	A	$C \ G \ G \ G \ \$_2$	
	2	G	G $\$_2$	
	1	G	$G \ C \ \$_1$	
	2	G	$G G \$_2$	
	1	C	$G \ G \ C \ \$_1$	
	2	C	$G \ G \ G \ \$_2$	
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 $\mathsf{S} = \{ u = ACACGGC\$_1, v = ACACGGGS_2 \}$

r(u, v)	DA	eBWT	Sorted suffixes	
1^{1}	1	C	\$ ₁	
2^{1}	2	G	\$ ₂	
1^{1}	1	\$ 1	$A \ C \ A \ C \ G \ G \ C \ \$_1$	
2^{1}	2	$\$_2$	$A \ C \ A \ C \ G \ G \ G \ \$_2$	
1^{1}	1	C	$A \ C \ G \ G \ C \ \$_1$	
2^{1}	(2)	C	$A \ C \ G \ G \ G \ \$_2$	Rewrite in the form $1^{k_1}2^{k_1}1^{k_3}2^{k_4}\cdots 2^{k_m}1^{k_m+1}$
	Ĭ	G	C $\$_1$	
	1	A	$C \ A \ C \ G \ G \ C \ \$_1$	where i^{k_j} means <i>i</i> repeats k_j times.
	2	A	$C A C G G G \$_2$	Note that if $j \neq 1$ and $j \neq m+1$,
	1	A	$C \ G \ G \ C \ \$_1$	then $k_j > 0$.
	2	A	$C \ G \ G \ G \ \$_2$	
	2	G	G $\$_2$	
	1	G	$G \ C \ \$_1$	
	2	G	$G G \$_2$	
	1	C	$G \ G \ C \ \$_1$	
	2	C	$G \ G \ G \ \$_2$	
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 $\mathsf{S} = \{ u = ACACGGC\$_1, v = ACACGGGS_2 \}$

r(u, v)	DA	eBWT	Sorted suffixes	
1^{1}	1	C	\$ ₁	
2^{1}	2	G	\$ ₂	
1^{1}	1	$\$_1$	$A \ C \ A \ C \ G \ G \ C \$	
2^{1}	2	$\$_2$	$A \ C \ A \ C \ G \ G \ \mathfrak{G} \ \mathfrak{g}_2$	
1^{1}	1	C	$A \ C \ G \ G \ C \ \$_1$	
2^{1}	2	C	$A \ C \ G \ G \ G \ \$_2$	Rewrite in the form
1^{2}	(1)	G	C $\$_1$	$1^{k_1}2^{k_1}1^{k_3}2^{k_4}\cdots 2^{k_m}1^{k_{m+1}}$
1-	1	A	$C \hspace{0.1in} A \hspace{0.1in} C \hspace{0.1in} G \hspace{0.1in} G \hspace{0.1in} C \hspace{0.1in} \$_{1}$	where i^{k_j} means i repeats k_j times.
	2	A	$C \ A \ C \ G \ G \ \mathfrak{G} \ \mathfrak{g}_2$	Note that if $j \neq 1$ and $j \neq m+1$,
	1	A	$C \ G \ G \ C \ \$_1$	then $k_j > 0$.
	2	A	$C \ G \ G \ G \ \$_2$	
	2	G	G $\$_2$	
	1	G	$G \ C \ \$_1$	
	2	G	$G \ G \ \$_2$	
	1	C	$G \hspace{0.1in} G \hspace{0.1in} C \hspace{0.1in} \$_{1}$	
	2	C	$G \ G \ G \ \$_2$	
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 $\mathsf{S} = \{ u = ACACGGC\$_1, v = ACACGGGS_2 \}$

r(u, v)	DA	eBWT	Sorted suffixes	
1^{1}	1	C	\$ ₁	
2^{1}	2	G	\$ ₂	
1^{1}	1	$\$_1$	$A \ C \ A \ C \ G \ G \ C \ \$_1$	
2^{1}	2	$\$_2$	$A \ C \ A \ C \ G \ G \ G \ \$_2$	
1^{1}	1	C	$A \ C \ G \ G \ C \ \$_1$	
2^{1}	2	C	$A \ C \ G \ G \ G \ \$_2$	Rewrite in the form
1^{2}	1	G	C $\$_1$	$1^{k_1}2^{k_1}1^{k_3}2^{k_4}\cdots 2^{k_m}1^{k_{m+1}}$
	1	A	$C \hspace{0.1in} A \hspace{0.1in} C \hspace{0.1in} G \hspace{0.1in} G \hspace{0.1in} C \hspace{0.1in} \$_{1}$	where i^{k_j} means i repeats k_j times.
2^{1}	(2)	A	$C A C G G G \$_2$	Note that if $j \neq 1$ and $j \neq m+1$,
	ĭ	A	$C \ G \ G \ C \ \$_1$	then $k_j > 0$.
	2	A	$C \ G \ G \ G \ \$_2$	
	2	G	$G \$	
	1	G	$G \ C \ \$_1$	
	2	G	$G G \$_2$	
	1	C	$G \hspace{0.1in} G \hspace{0.1in} C \hspace{0.1in} \$_{1}$	
	2	C	$G G G \$_2$	
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 $\mathsf{S} = \{ u = ACACGGC\$_1, v = ACACGGGS_2 \}$

r(u, v)	DA	eBWT	Sorted suffixes	
1^{1}	1	C	\$ ₁	
2^{1}	2	G	\$ ₂	
1^{1}	1	$\$_1$	$A \ C \ A \ C \ G \ G \ C \ \$_1$	
2^{1}	2	$\$_2$	$A \ C \ A \ C \ G \ G \ G \ \$_2$	
1^{1}	1	C	$A \ C \ G \ G \ C \ \$_1$	
2^{1}	2	C	$A \ C \ G \ G \ G \ \$_2$	Rewrite in the form $1^{k_1}2^{k_1}1^{k_3}2^{k_4}\cdots 2^{k_m}1^{k_m+1}$
1^{2}	1	G	C $\$_1$	
	1	A	$C \ A \ C \ G \ G \ C \ \$_1$	where i^{k_j} means i repeats k_j times.
2^{1}	2	A	$C A C G G G \$_2$	Note that if $j \neq 1$ and $j \neq m+1$,
1^{1}	(1)	A	$C \ G \ G \ C \ \$_1$	then $k_j > 0$.
	$\underbrace{}_{2}$	A	$C \ G \ G \ G \ \$_2$	
	2	G	$G \ \$_2$	
	1	G	$G \ C \ \$_1$	
	2	G	$G G \$_2$	
	1	C	$G \ G \ C \ \$_1$	
	2	C	$G \ G \ G \ \$_2$	
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 $\mathsf{S} = \{ u = ACACGGC\$_1, v = ACACGGGS_2 \}$

Compute the expectation or the entropy of the distribution of the alternations of colors

r(u, v)	DA	eBWT	Sorted suffixes	
1^1	1	C	\$ ₁	
2^{1}	2	G	\$ ₂	
1^{1}	1	$\$_1$	$A \ C \ A \ C \ G \ G \ C \$	
2^{1}	2	$\$_2$	$A \ C \ A \ C \ G \ G \ G \ \$_2$	
1^{1}	1	C	$A \ C \ G \ G \ C \ \$_1$	
2^{1}	2	C	$A \ C \ G \ G \ G \ \$_2$	Rewrite in the form
1^{2}	1	G	C $\$_1$	$1^{k_1}2^{k_1}1^{k_3}2^{k_4}\cdots 2^{k_m}1^{k_{m+1}}$
1	1	A	$C \ A \ C \ G \ G \ C \ \$_1$	where i^{k_j} means i repeats k_j times.
2^{1}	2	A	$C \ A \ C \ G \ G \ \mathfrak{G} \ \mathfrak{g}_2$	Note that if $j \neq 1$ and $j \neq m+1$,
1^{1}	1	A	$C \ G \ G \ C \ \$_1$	then $k_j > 0$.
2^{2}	(2)	A	$C \ G \ G \ G \ \$_2$	
2	2	G	$G \$	
	1	G	$G \ C \ \$_1$	
	2	G	$G G \$_2$	
	1	C	$G \ G \ C \ \$_1$	
	2	C	$G G G \$_2$	
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 $\mathsf{S} = \{ u = ACACGGC\$_1, v = ACACGGGS_2 \}$

r(u, v)	DA	eBWT	Sorted suffixes	
1^{1}	1	C	\$ ₁	
2^{1}	2	G	\$ ₂	
1^{1}	1	$\$_1$	$A \ C \ A \ C \ G \ G \ C \ \$_1$	
2^{1}	2	$\$_2$	$A \ C \ A \ C \ G \ G \ G \ \$_2$	
1^{1}	1	C	$A \ C \ G \ G \ C \ \$_1$	
2^{1}	2	C	$A \ C \ G \ G \ G \ \$_2$	Rewrite in the form $1^{k_1}2^{k_1}1^{k_3}2^{k_4}\cdots 2^{k_m}1^{k_m+1}$
1^{2}	1	G	C $\$_1$	
	1	A	$C \ A \ C \ G \ G \ C \ \$_1$	where i^{k_j} means <i>i</i> repeats k_j times.
2^{1}	2	A	$C \ A \ C \ G \ G \ \mathfrak{G} \ \mathfrak{g}_2$	Note that if $j \neq 1$ and $j \neq m+1$,
1^{1}	1	A	$C \ G \ G \ C \ \$_1$	then $k_j > 0$.
2^{2}	2	A	$C \ G \ G \ G \ \$_2$	
	2	G	G $\$_2$	
1^{1}	(1)	G	$G \ C \ \$_1$	
	$\widetilde{2}$	G	$G G \$_2$	
	1	C	$G \ G \ C \ \$_1$	
	2	C	$G G G \$_2$	
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 $\mathsf{S} = \{ u = ACACGGC\$_1, v = ACACGGGS_2 \}$

Compute the expectation or the entropy of the distribution of the alternations of colors

r(u, v)	DA	eBWT	Sorted suffixes	
1^{1}	1	C	$\$_1$	
2^{1}	2	G	\$ ₂	
1^{1}	1	$\$_1$	$A \ C \ A \ C \ G \ G \ C \ \$_1$	
2^{1}	2	$\$_2$	$A \ C \ A \ C \ G \ G \ \mathfrak{G} \ \mathfrak{g}_2$	
1^{1}	1	C	$A \ C \ G \ G \ C \ \$_1$	
2^{1}	2	C	$A \ C \ G \ G \ G \ \$_2$	Rewrite in the form
1^{2}	1	G	C $\$_1$	$1^{k_1}2^{k_1}1^{k_3}2^{k_4}\cdots 2^{k_m}1^{k_{m+1}}$
	1	A	$C \ A \ C \ G \ G \ C \ \$_1$	where i^{k_j} means <i>i</i> repeats k_j times.
2^{1}	2	A	$C A C G G G \$_2$	Note that if $j \neq 1$ and $j \neq m+1$,
1^{1}	1	A	$C \ G \ G \ C \ \$_1$	then $k_j > 0$.
2^{2}	2	A	$C \ G \ G \ G \ \$_2$	
	2	G	G $\$_2$	
1^{1}	1	G	$G \ C \ \$_1$	
2^{1}	(2)	G	$G G \$_2$	
	ĭ	C	$G \ G \ C \ \$_1$	
	2	C	$G \ G \ G \ \$_2$	
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 $\mathsf{S} = \{ u = ACACGGC\$_1, v = ACACGGGS_2 \}$

Compute the expectation or the entropy of the distribution of the alternations of colors

r(u, v)	DA	eBWT	Sorted suffixes	
1^{1}	1	C	\$ ₁	
2^{1}	2	G	\$ ₂	
1^{1}	1	$\$_1$	$A \ C \ A \ C \ G \ G \ C \ \$_1$	
2^{1}	2	$\$_2$	$A \ C \ A \ C \ G \ G \ G \ \$_2$	
1^{1}	1	C	$A \ C \ G \ G \ C \ \$_1$	
2^{1}	2	C	$A \ C \ G \ G \ G \ \$_2$	Rewrite in the form $1^{k_1}2^{k_1}1^{k_3}2^{k_4}\cdots 2^{k_m}1^{k_m+1}$
1^{2}	1	G	C $\$_1$	
	1	A	$C \ A \ C \ G \ G \ C \ \$_1$	where i^{k_j} means <i>i</i> repeats k_j times.
2^{1}	2	A	$C A C G G G \$_2$	Note that if $j \neq 1$ and $j \neq m+1$,
1^{1}	1	A	$C \ G \ G \ C \ \$_1$	then $k_j > 0$.
2^{2}	2	A	$C \ G \ G \ G \ \$_2$	
	2	G	G \$2	
1^{1}	1	G	$G \ C \ \$_1$	
2^{1}	2	G	$G G \$_2$	
1^{1}	(1)	C	$G \ G \ C \ \$_1$	
	$\overbrace{2}$	C	$G \ G \ G \ \$_2$	
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 $\mathsf{S} = \{ u = ACACGGC\$_1, v = ACACGGGS_2 \}$

r(u, v)	DA	eBWT	Sorted suffixes	
1^{1}	1	C	$\$_1$	
2^{1}	2	G	\$ ₂	
1^{1}	1	$\$_1$	$A \ C \ A \ C \ G \ G \ C \$	
2^{1}	2	$\$_2$	$A \ C \ A \ C \ G \ G \ \$_2$	
1^{1}	1	C	$A \ C \ G \ G \ C \ \$_1$	
2^{1}	2	C	$A \ C \ G \ G \ G \ \$_2$	Rewrite in the form
1^{2}	1	G	C $\$_1$	$1^{k_1}2^{k_1}1^{k_3}2^{k_4}\cdots 2^{k_m}1^{k_{m+1}}$
1	1	A	$C \ A \ C \ G \ G \ C \ \$_1$	where i^{k_j} means i repeats k_j times.
2^{1}	2	A	$C \ A \ C \ G \ G \ \mathfrak{G} \ \mathfrak{g}_2$	Note that if $j \neq 1$ and $j \neq m+1$,
1^{1}	1	A	$C \ G \ G \ C \ \$_1$	then $k_j > 0$.
2^{2}	2	A	$C \ G \ G \ G \ \$_2$	
2	2	G	$G \ \$_2$	
1^{1}	1	G	$G \ C \ \$_1$	
2^{1}	2	G	$G G \$_2$	
1^{1}	1	C	$G \ G \ C \ \$_1$	
2^{1}	(2)	C	$G \ G \ G \ \$_2$	
	\bigcirc			▲□▶ ▲□▶ ▲□▶ ▲□▶ ▲□ ◇�(

In the example:

$$r = 1^{k_1} 2^{k_1} 1^{k_3} 2^{k_4} \cdots 2^{k_m} 1^{k_{m+1}}$$

where i^{k_j} means i repeats k_j times. If t_{k_j} is the number of k_j

$$t_1 = 12$$
 (12 times 1^1 or 2^1) and $t_2 = 2$ (2 times 2^2 or 2^2).

 $s = t_1 + t_2 + \dots + t_{k_j} + \dots + t_{\max(|u|,|v|)}$

$$s = 12 + 2 = 14$$

 $r = 1^{1}2^{1}1^{1}2^{1}1^{2}2^{1}$

The Burrow-Wheeler similarity distribution (BWSD) of u and v is

$$P\{k_j = k\} = \frac{t_k}{s}$$
 for $k = 1, 2, 3, \dots$

$$P\{k_j = 1\} = \frac{11}{14} \text{ and } P\{k_j = 2\} = \frac{2}{14}$$

$$r = 1^{k_1} 2^{k_1} 1^{k_3} 2^{k_4} \cdots 2^{k_m} 1^{k_{m+1}}$$

In the example:

 $r = 1^1 2^1 1^1 2^1 1^1 2^1 1^2 2^1 1^1 2^2 1^1 2^1 1^1 2^1$

where i^{k_j} means i repeats k_j times. If t_{k_j} is the number of k_j

So

$$t_1 = 12 \text{ (12 times } 1^1 \text{ or } 2^1 \text{) and}$$

 $t_2 = 2 \text{ (2 times } 2^2 \text{ or } 2^2 \text{).}$

 $s = t_1 + t_2 + \dots + t_{k_j} + \dots + t_{\max(|u|,|v|)} \qquad s = 12 + 2 = 14$

The Burrow-Wheeler similarity distribution (BWSD) of u and v is

$$P\{k_j = k\} = \frac{t_k}{s}$$
 for $k = 1, 2, 3, \dots$

$$P\{k_j = 1\} = \frac{11}{14} \text{ and } P\{k_j = 2\} = \frac{2}{14}$$

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$$\mathsf{S} = \{u = ACACGGC\$_1, v = ACACGGG\$_2\}$$

In the example:

$$r(u,v) = 1^{1}2^{1}1^{1}2^{1}1^{2}2^{1}1^{2}2^{1}1^{1}2^{2}1^{1}2^{1}1^{1}2^{1}$$

 $t_1 = 12$ (12 times 1^1 or 2^1) and $t_2 = 2$ (2 times 2^2 or 2^2). The Burrow-Wheeler similarity distribution (BWSD) of u and v is

$$P(k_j = 1) = rac{12}{14}$$
 and $P(k_j = 2) = rac{2}{14}$

Yang et al. defined the following measures between u and v:

- $D_M(u,v) = E(k_j) 1$, where $E(k_j)$ is the expectation of BWSD(u,v).
- $D_E(u,v) = -\sum_{k \ge 1, t_k \ne 0} (t_k/s) \log_2(t_k/s)$ is the Shannon entropy of BWSD(u,v).

Properties of D_{col} and BWSD (D_M and D_E)

 D_{col} and BWSD (D_M and D_E) are symmetric. The similarity between u and v is equal to the similarity between v and u.

Differences between two eBWT transformations

Now, we consider two conjugates words $u = GAGCTC(\$_1)$ and $v = GCTCGA(\$_2)$

D_{col}	eBWT	Conjugates sorted		D_{col}	eBWT	Suffixes sorted
				0	C	$\$_1$
				1	A	\$ ₂
0	G	$A \ G \ C \ T \ C \ G$		1	G	$A \ \$_2$
0	G	$A \ G \ C \ T \ C \ G$		1	G	$A \ G \ C \ T \ C $ $\$_1$
0	T	C G A G C T		1	T	C $\$_1$
0	T	$C \ G \ A \ G \ C \ T$		0	T	$C \ G \ A \ \$_2$
0	G	C T C G A G	\neq	0	G	C T C
0	G	$C \ T \ C \ G \ A G$		1	G	$C T C G A \$_2$
0	C	$G \ A \ G \ C \ T C$		1	C	$G A \$_2$
0	C	$G \ A \ G \ C \ T C$		1	$\$_1$	G A G C T C
0	A	$G \ C \ T \ C \ G \ A$		T	A	$G \ C \ T \ C $ $\$_1$
0	A	$G \ C \ T \ C \ G \ A$		0	$\$_2$	$G \ C \ T \ C \ G \ A $ $\$_2$
0	C	$T \ C \ G \ A \ G \ C$		0	C	$T C \$_1$
0	C	$T \ C \ G \ A \ G \ C$		0	C	$T \ C \ G \ A $

If the eBWT obtained by sorting the conjugates is used then

• If u is a conjugate of v, then $D_{col}(u, v) = 0$, $D_M(u, v) = 0$ and $D_E(u, v) = 0$

• If u' is a conjugate of u and v' is a conjugate of v, then $D_{col}(u, v) = D_{col}(u', v')$, $D_M(u, v) = D_M(u', v')$ and $D_E(u, v) = D_E(u', v')$.

They are similarity measures for conjugacy classes.

Properties of D_{col} and BWSD (D_M and D_E)

It is not always true that if $D_{col}(u,v) = 0$, $D_M(u,v) = 0$ and $D_E(u,v) = 0$ then u = v or they are conjugates.

Example

Let u = aabc and v = abbc. Although the two sequences are not conjugates, $D_{col}(u, v) = 0$

$D_{col}(u, v)$	DA	eBWT	со	njug	ates	sorted	,
0	0	c	a	a	b	c	$D_{k}(x,y) = \sum_{k=1}^{k} (x,y)$
0	1	c	a	\boldsymbol{b}	\boldsymbol{b}	\boldsymbol{c}	$D_{col}(u,v) = \sum (n_i - 1)$
0	0	a	a	b	c	a	i=1,
0	1	a	\boldsymbol{b}	\boldsymbol{b}	c	a	$n_i eq 0$
0	0	a	b	c	a	a	
0	1	b	\boldsymbol{b}	c	\boldsymbol{a}	\boldsymbol{b}	
0	0	b	c	a	a	b	
0	1	b	c	\boldsymbol{a}	\boldsymbol{b}	\boldsymbol{b}	$D_{col}(u,v) = 0$

Idea: use the symbols in the eBWT!

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Properties of D_{col} and BWSD (D_M and D_E)

It is not always true that if $D_{col}(u,v) = 0$, $D_M(u,v) = 0$ and $D_E(u,v) = 0$ then u = v or they are conjugates.

Example

Let u = aabc and v = abbc. Although the two sequences are not conjugates, $D_{col}(u, v) = 0$

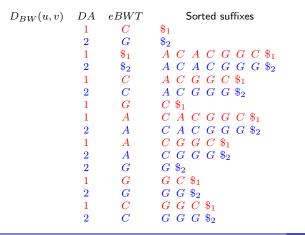
$D_{col}(u, v)$	DA	eBWT	со	njug	ates	sorted	,
0	0	c	a	a	b	c	\mathcal{D} () $\sum_{k=1}^{k}$ (1)
0	1	c	a	\boldsymbol{b}	\boldsymbol{b}	c	$D_{col}(u,v) = \sum (n_i - 1)$
0	0	a	a	b	c	a	i=1,
0	1	a	\boldsymbol{b}	\boldsymbol{b}	c	a	$n_i eq 0$
0	0	a	b	c	a	a	
0	1	b	\boldsymbol{b}	c	\boldsymbol{a}	\boldsymbol{b}	
0	0	b	c	a	a	b	
0	1	\boldsymbol{b}	c	a	\boldsymbol{b}	b	$D_{col}(u,v) = 0$

Idea: use the symbols in the eBWT!

Similarity measure: based on clustering [Mantaci, Restivo, R. and Sciortino, 2008]

Based on differences of the frequencies of the colors in the blocks of the same symbol!

 $S = \{u = ACACGGC\$_1, v = ACACGGG\$_2\}$



Similarity measure: based on clustering [Mantaci, Restivo, R. and Sciortino, 2008]

Based on differences of the frequencies of the colors in the blocks of the same symbol!

 $\mathsf{S} = \{ u = ACACGGC\$_1, v = ACACGGG\$_2 \}$

$D_{BW}(u,v)$	DA	eBWT	Sorted suffixes	
	1	C	\$ 1	
	2	G	\$ ₂	
	1	$\$_1$	$A \ C \ A \ C \ G \ G \ C \ \$_1$	
	2	$\$_2$	$A \ C \ A \ C \ G \ G \ G \ \$_2$	
	1	C	$A \ C \ G \ G \ C \$	
	2	C	$A \ C \ G \ G \ G \ \$_2$	
	1	G	$C \$	
	1	Α	$C \ A \ C \ G \ G \ C \ \$_1$	
	2	A	$C \ A \ C \ G \ G \ G \ \$_2$	
	1	A	$C \ G \ G \ C \ \$_1$	
	2	A	$C \ G \ G \ G \ \$_2$	
	2	G	$G \$	
	1	G	$G \ C \ \$_1$	
	2	G	$G \ G \ \$_2$	
	1	C	$G \ G \ C \ \$_1$	
	2	C	$G G G \$_2$	-

Based on differences of the frequencies of the colors in the blocks of the same symbol!

 $\mathsf{S} = \{ u = ACACGGC\$_1, v = ACACGGG\$_2 \}$

$D_{BW}(u,v)$	$DA \\ 1$	eBWT	Sorted suffixes \$1	We sum the differences between the number of symbols coming from u and from v in each block.
	2	\widetilde{G}	\$ ₂	
	1	$\$_1$	$A C A C G G C \$_1$	k
	2	$\$_2$	$A C A C G G G \$_2$	$D_{BW}(u,v) = \sum_{i=1}^{n} c_i(u) - c_i(v) .$
	1	C	$A \ C \ G \ G \ C \$_1$	$D_{BW}(u, v) = \sum_{i=1}^{i} c_i(u) - c_i(v) .$
	2	C	$A \ C \ G \ G \ G \ \$_2$	<i>i</i> —1
	1	G	C $\$_1$	
	1	A	$C A C G G C \$_1$	
	2	A	$C A C G G G \$_2$	
	1	A	$C \ G \ G \ C \ \$_1$	
	2	A	$C \ G \ G \ G \ \$_2$	
	2	G	G $\$_2$	
	1	G	$G \ C \ \$_1$	
	2	G	$G \ G \ \$_2$	
	1	C	$G \ G \ C \$	
	2	C	$G G G \$_2$	<ロ> <局> < 国> < 国> < 国> < 国> < 国

Based on differences of the frequencies of the colors in the blocks of the same symbol!

 $\mathsf{S} = \{ u = ACACGGC\$_1, v = ACACGGG\$_2 \}$

$D_{BW}(u,v)$	DA	eBWT	Sorted suffixes	number of syn
1	1	\mathcal{C}	\$ ₁	and from v in
1	2	(G)	\$2	
	1	$\$_1$	$A C A C G G C \$_1$	
	2	$\$_2$	$A C A C G G G \$_2$	$D_{BW}(u,v)$
	1	C	$A C G G C \$_1$	$D_{BW}(u, v)$
	2	C	$A \ C \ G \ G \ G \ \$_2$	
	1	G	$C \$	
	1	A	$C A C G G C \$_1$	
	2	A	$C A C G G G \$_2$	
	1	A	$C \ G \ G \ C \ \$_1$	
	2	A	$C \ G \ G \ G \ \$_2$	
	2	G	$G \$	
	1	G	$G \ C \ \$_1$	
	2	G	$G \ G \ \$_2$	
	1	C	$G \ G \ C \$	
	2	C	$G G G \$_2$	< • > < #

We sum the differences between the mbols coming from ueach block

$$D_{BW}(u,v) = \sum_{i=1}^{k} |c_i(u) - c_i(v)|.$$

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Based on differences of the frequencies of the colors in the blocks of the same symbol!

 $\mathsf{S} = \{ u = ACACGGC\$_1, v = ACACGGG\$_2 \}$

$D_{BW}(u,v)$	DA	eBWT	Sorted suffixes	number
1	1	C	\$ ₁	and from
1	2	G	\$ ₂	
0	1	(\$1)	$A C A C G G C \$_1$	
0	2	<u>\$</u> 2	$A C A C G G G \$_2$	D_{BW}
	1	C	$A \ C \ G \ G \ C $ $\$_1$	2 DW
	2	C	$A C G G G \$_2$	
	1	G	$C \ \$_1$	
	1	A	$C A C G G C \$_1$	
	2	A	$C A C G G G \$_2$	
	1	A	$C \ G \ G \ C \ \$_1$	
	2	A	$C G G G \$_2$	
	2	G	G $\$_2$	
	1	G	$G \ C \ \$_1$	
	2	G	$G G \$_2$	
	1	C	$G \ G \ C \ \$_1$	
	2	C	$G G G \$_2$	< □

We sum the differences between the number of symbols coming from u and from v in each block.

$$D_{BW}(u,v) = \sum_{i=1}^{k} |c_i(u) - c_i(v)|.$$

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Based on differences of the frequencies of the colors in the blocks of the same symbol!

 $\mathsf{S} = \{ u = ACACGGC\$_1, v = ACACGGG\$_2 \}$

$D_{BW}(u,v)$	DA	eBWT	Sorted suffixes	numb
1	1	C	\$1	and fi
1	2	G	\$2	
0	1	$\$_1$	$A C A C G G C \$_1$	
0	2	$\$_2$	$A C A C G G G \$_2$	D_E
0	1	$\left(\right)$	$A \ C \ G \ G \ C \ \$_1$	
	2	\bigcirc	$A C G G G \$_2$	
	1	G	C $\$_1$	
	1	A	$C A C G G C \$_1$	
	2	A	$C A C G G G \$_2$	
	1	A	$C \ G \ G \ C \ \$_1$	
	2	A	$C \ G \ G \ G \ \$_2$	
	2	G	$G \ \$_2$	
	1	G	$G \ C \ \$_1$	
	2	G	$G G \$_2$	
	1	C	$G \ G \ C \ \$_1$	
	2	C	$G G G S_2$	•

We sum the differences between the number of symbols coming from u and from v in each block.

$$D_{BW}(u,v) = \sum_{i=1}^{k} |c_i(u) - c_i(v)|.$$

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Based on differences of the frequencies of the colors in the blocks of the same symbol!

 $\mathsf{S} = \{ u = ACACGGC\$_1, v = ACACGGG\$_2 \}$

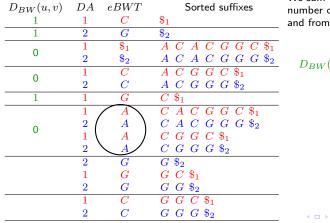
$D_{BW}(u,v)$	DA	eBWT	Sorted suffixes
1	1	C	\$1
1	2	G	\$ ₂
0	1	$\$_1$	$A C A C G G C \$_1$
0	2	$\$_2$	$A C A C G G G \$_2$
0	1	C	$A \ C \ G \ G \ C \ \$_1$
0	2	\underline{C}	$A \ C \ G \ G \ G \ \$_2$
1	1	(G)	$C \ \$_1$
	1	Ă	$C \ A \ C \ G \ G \ C \ \$_1$
	2	A	$C A C G G G \$_2$
	1	A	$C \ G \ G \ C \ \$_1$
	2	A	$C \ G \ G \ G \ \$_2$
	2	G	$G \$
	1	G	$G \ C \ \$_1$
	2	G	$G G \$_2$
	1	C	$G \ G \ C \ \$_1$
	2	C	$G G G \$_2$

We sum the differences between the number of symbols coming from u and from v in each block.

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We sum the differences between the number of symbols coming from u and from v in each block.

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$D_{BW}(u,v)$	DA	eBWT	Sorted suffixes	numbe
1	1	C	\$ ₁	and fr
1	2	G	\$2	
0	1	$\$_1$	$A C A C G G C \$_1$	
	2	$\$_2$	$A C A C G G G \$_2$	D_B
0	1	C	$A \ C \ G \ G \ C \ \$_1$	- D
	2	C	$A C G G G \$_2$	
1	1	G	C \$1	
	1	A	$C \ A \ C \ G \ G \ C \ \$_1$	
0	2	A	$C A C G G G \$_2$	
	1	A	$C G G C \$_1$	
	2	A	$\begin{array}{cccc} C & G & G & G & \$_2 \\ \hline \end{array}$	
	2	$\left(\begin{array}{c} G \\ G \end{array}\right)$	G $\$_2$	
1	1	$\begin{pmatrix} G \\ G \end{pmatrix}$	$G C \$_1$	
	2	\underline{G}	$\frac{G \ G \ \$_2}{C \ C \ C \ \clubsuit}$	
	1	C	$\begin{array}{cccc} G & G & C & \$_1 \\ G & G & G & \clubsuit \end{array}$	
	2	U	$G G G \$_2$	< C

We sum the differences between the number of symbols coming from u and from v in each block.

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$D_{BW}(u,v)$	DA	eBWT	Sorted suffixes	number
1	1	C	\$1	and fron
1	2	G	\$2	
0	1	$\$_1$	$A C A C G G C \$_1$	
0	2	$\$_2$	$A C A C G G G \$_2$	D_{BW}
0	1	C	$A \ C \ G \ G \ C \$	2 DW
	2	C	$A C G G G \$_2$	
1	1	G	$C \ \$_1$	
	1	A	$C A C G G C \$_1$	
0	2	A	$C A C G G G \$_2$	
Ū	1	A	$C \ G \ G \ C \ \$_1$	
	2	A	$C \ G \ G \ G \ \$_2$	
	2	G	G $\$_2$	
1	1	G	$G \ C \ \$_1$	
	2	G	$G G \$_2$	
0	1	$\left(\begin{array}{c} \mathcal{O} \end{array} \right)$	$G \ G \ C \ \$_1$	
	2	\bigcirc	$G G G \$_2$	< D)

BWT/ eBWT similarity

We sum the differences between the number of symbols coming from u and from v in each block.

$$D_{BW}(u,v) = \sum_{i=1}^{k} |c_i(u) - c_i(v)|.$$

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We sum the differences between the

Similarity measure: based on clustering [Mantaci, Restivo, R. and Sciortino, 2008]

Based on differences of the frequencies of the colors in the blocks of the same symbol!

 $\mathsf{S} = \{ u = ACACGGC\$_1, v = ACACGGG\$_2 \}$

$D_{BW}(u,v)$	DA	eBWT	Sorted suffixes	number of symbols coming from u
1	1	C	\$1	and from v in each block.
1	2	G	\$ ₂	
0	1	$\$_1$	$A C A C G G C \$_1$	k
0	2	$\$_2$	$A C A C G G G \$_2$	$D_{BW}(u,v) = \sum_{i=1}^{n} c_i(u) - c_i(v) .$
0	1	C	$A \ C \ G \ G \ C \ \$_1$	$D_{BW}(u, v) = \sum_{i=1}^{i=1} c_i(u) - c_i(v) .$
0	2	C	$A \ C \ G \ G \ G \ \$_2$	<i>i</i> —1
1	1	G	C $\$_1$	In the example:
	1	A	$C A C G G C \$_1$	8
0	2	A	$C A C G G G \$_2$	$D_{BW}(u,v) = \sum_{i=1}^{8} c_i(u) - c_i(v) = 4$
0	1	A	$C \ G \ G \ C \ \$_1$	$\sum BW(\alpha, c) \sum_{i=1}^{n} c_i(\alpha) - c_i(c) = 1$
	2	A	$C G G G \$_2$	v=1
	2	G	$G \ \$_2$	that we can normalize with the
1	1	G	$G \ C \ \$_1$	lengths of the sequences, so that
	2	G	$G G \$_2$	3
0	1	C	$G \ G \ C \$	$D_{BW}(u,v) = 4/(8+8)$
	2	C	$G G G \$_2$	ふって 叫 ・山 ・ 山 ・ 雪 ・ ・ 雪 ・ くしゃ
	E	BWT/ eBWT	similarity	June 10 - 14 , 2019 20 / 31

Properties

D_{BW}(u, v) = D_{BW}(v, u), i.e. the measure D_{BW} is symmetric.
D_{BW}(u, v) = 0 if and only if u = v.

Moreover, if the eBWT obtained by sorting the conjugates is used then

- If u is a conjugate of v, then $D_{BW}(u, v) = 0$
- If u' is a conjugate of u and v' is a conjugate of v, then $D_{BW}(u,v) = D_{BW}(u',v').$

Therefore, D_{BW} is a distance measure for conjugacy classes.

Observation: different measures

$$S = \{u = ACACGGC\$_1, v = ACACGGG\$_2\}$$

DA	eBWT	Sorted suffixes
1	C	\$ ₁
2	G	\$ ₂
1	$\$_1$	$A \ C \ A \ C \ G \ G \ C \ \$_1$
2	$\$_2$	$A \ C \ A \ C \ G \ G \ G \ \$_2$
1	C	$A \ C \ G \ G \ C \ \$_1$
2	C	$A \ C \ G \ G \ G \ \$_2$
1	G	C $\$_1$
1	A	$C \ A \ C \ G \ G \ C \ \$_1$
2	A	$C A C G G G \$_2$
1	A	$C \ G \ G \ C \ \$_1$
2	A	$C \ G \ G \ G \ \$_2$
2	G	$G \$
1	G	$G \ C \ \$_1$
2	G	$G G \$_2$
1	C	$G \ G \ C \ \$_1$
2	C	$G G G \$_2$

By changing the partition, one can obtain different similarity measures.

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Biological applications

Biological applications based on these eBWT similarity measures:

- for building the phylogenetic tree of mitochondrial dna: [Mantaci et al. 2007, 2008], [Yang, Chang and Zhang, 2010]
- Protein comparison: Yang, Chang, Zhang and Wang, 2010: based on measure defined in [Yang, Chang and Zhang, 2010]
- Expressed sequence tags: Ng, Phon-Amnuaisuk, Ho: based on measure defined in [Mantaci et al. 2007], a window-based similarity comparison is used.

Second goal: Metagenomics

Metagenomics is the study of genetic material collected from the environment



[Illustration: Spencer Phillips, EMBL-EBI]

Aim to explore the relations between the microbes and their habitats

Applications. Clinical microbiology, plant-microbe interactions, monitoring pollution, sustainability, ecology, ...

Goal: Identify the taxon of each short read

BWT/ eBWT similarity

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[Illustration: Spencer Phillips, EMBL-EBI]

Aim to explore the relations between the microbes and their habitats

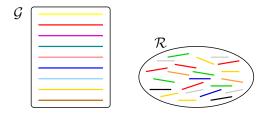
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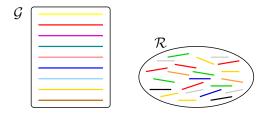
Metagenomic Classification problem



- $\mathcal{R} = \{r_1, \dots, r_{|\mathcal{R}|}\}$ metagenome (collection of short reads)
- $\mathcal{G} = \{g_1, \dots, g_{|G|}\}$ reference genomes (collection of long sequences)
- $\mathcal{S} = \mathcal{R} \cup \mathcal{G}$ multi-set of biological sequences

Goal: to assign each read r_i in \mathcal{R} to a unique genome g_j in \mathcal{G} by reading $eBWT(\mathcal{S}), DA(\mathcal{S}), LCP(\mathcal{S}).$

Metagenomic Classification problem



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- $\mathcal{S} = \mathcal{R} \cup \mathcal{G}$ multi-set of biological sequences

Goal: to assign each read r_i in \mathcal{R} to a unique genome g_j in \mathcal{G} by reading $eBWT(\mathcal{S}), DA(\mathcal{S}), LCP(\mathcal{S}).$

Minimum LCP value $\alpha = 3$

 $r_i = N \underline{GGCGTA}CCA\$_i$

 $g_j{=}TTATTTTGGCGG\underline{GGCGTA}TGTATTAGTTT\$_j$

i	LCP	eBWT	Sorted suffixes	٨
1	0	A	\$ _i	A
2	0	T	\$ _j	in
3	0	C	$\check{A}\$_i$	
4	1	T	$ACCA\$_i$	
5	1	T	$AGTTT\$_j$	
6	1	T	$ATGTATTAGTTT\$_i$	
7	2	T	$ATTAGTTT\$_i$	
8	0	C	$CA\$_i$	C.
9	1	A	$CCA\$_i$	-
10	1	G	$CGGGGGCGTA\$_i$	
11	2	G	$CGTACCA\$_i$	
12	4	G	$CGTATGAT \dots $	
13	1	T	$CTTTTGGCG \dots \$_j$	n
14	0	G	$GCGGGGGCGT \dots \hat{s}_j$	e
15	3	G	$GCGTACCA\$_i$	n
16	5	G	$GCGTATGTAA \dots \$_j$	e_{\perp}
÷.,				
÷.,	1	1	1	

BWT/ eBWT similarity

An $\alpha\text{-cluster}\ \mathcal{C}_\alpha$ of $eBWT(\mathcal{S})$ is any pair of indices (pS,pE) such that

- $\bullet \ LCP[pS] < \alpha \ \text{and} \ LCP[pE+1] < \alpha, \\$
- $LCP[k] \ge \alpha, pS < k \le pE$,
- $DA[s] \in \mathcal{R}$ and $DA[t] \in \mathcal{G}$, $pS \le s, t \le pE$.

 $\mathcal{C}_{\alpha}(r_i, g_j) = \{$

$$Sim_{r}[g] = \sum_{x \in C_{\alpha}} \sum_{a \in \Sigma} \min(n_{r}, n_{g})$$

 $Sim_{\mathbf{r}_i}[g_j] =$

 n_r =number of indices s in x such that eBWT[s] = a and DA[s] = r, n_g =number of indices t in x such that eBWT[t] = a and DA[t] = g.

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Minimum LCP value $\alpha = 3$

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i	LCP	eBWT	Sorted suffixes	
1	0	A	\$ _i	
2	0	T	\$ _j	
3	0	C	$A\$_i$	
4	1	T	$ACCA\$_i$	
5	1	T	$AGTTT\$_i$	
6	1	T	ATGTATTAGTTT\$ _i	
7	2	T	$ATTAGTTT$_{i}$	
8	0	C	$CA\$_i$	•
9	1	A	$CCA\$_i$	
10	1	G	$CGGGGGCGTA\$_i$	
11	2	G	$CGTACCA\$_i$	
12	4	\bigcirc	$CGTATGAT \dots \$_i$	
13	1	T	CTTTTGGCG\$ _i	,
14	0	G	$GCGGGGGCGT \dots \mathring{s}_i$	
15	3	G	$GCGTACCA\$_i$	
16	5	G	$GCGTATGTAA \dots \$_j$	
÷	1		:	
1.	1.1	1.1	1	

An α -cluster C_{α} of eBWT(S) is any pair of indices (pS, pE) such that

- $LCP[pS] < \alpha$ and $LCP[pE+1] < \alpha$,
- $LCP[k] \ge \alpha, pS < k \le pE$,
- $DA[s] \in \mathcal{R}$ and $DA[t] \in \mathcal{G}$, $pS \le s, t \le pE$.

 $C_{\alpha}(r_i, g_j) = \{(11, 12),$

$$Sim_r[g] = \sum_{x \in \mathcal{C}_{lpha}} \sum_{a \in \Sigma} \min(n_r, n_g)$$

 $Sim_{r_i}[g_j] = 1 + \dots =$

 n_r =number of indices s in x such that eBWT[s] = a and DA[s] = r, n_g =number of indices t in x such that eBWT[t] = a and DA[t] = g.

Minimum LCP value $\alpha = 3$

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i	LCP	eBWT	Sorted suffixes
1	0	Α	$\$_i$
2	0	T	\$ _j
3	0	C	$A\$_i$
4	1	T	$ACCA\$_i$
5	1	T	$AGTTT\$_j$
6	1	T	ATGTATTAGTTT\$ _i
7	2	T	$ATTAGTTT$_{i}$
8	0	C	$CA\$_i$
9	1	A	$CCA\$_i$
10	1	G	$CGGGGGCGTA \dots \$_i$
11	2	G	CGTACCA\$ _i
12	4	G	$CGTATGAT \dots \$_i$
13	1	T	CTTTTGGCG ^{\$} _j
14	0	G	$GCGGGGGCGT \dots \$_i$
15	3 (G	$GCGTACCA\$_i$
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÷			:
÷.,	1.1	1.1	1

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- $DA[s] \in \mathcal{R}$ and $DA[t] \in \mathcal{G}$, $pS \le s, t \le pE$.

 $C_{\alpha}(r_i, g_j) = \{(11, 12), (14, 16), \dots \}$

$$Sim_r[g] = \sum_{x \in \mathcal{C}_{lpha}} \sum_{a \in \Sigma} \min(n_r, n_g)$$

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i	LCP	eBWT	Sorted suffixes	А
1	0	Α	\$ _i	
2	0	T	\$ _j	in
3	0	C	$A\$_i$	
4	1	T	$ACCA\$_i$	
5	1	T	$AGTTT\$_i$	
6	1	T	$ATGTATTAGTTT\$_i$	
7	2	T	$ATTAGTTT$_i$	
8	0	C	$CA\$_i$	C.
9	1	A	$CCA\$_i$	- (
10	1	G	$CGGGGGCGTA \dots $	
11	2	G	$CGTACCA\$_i$	
12	4	G	$CGTATGAT \dots \$_i$	
13	1	T	CTTTTGGCG\$ _i	n
14	0	G	$GCGGGGGCGT \dots \mathring{s}_i$	el
15	3	G	$GCGTACCA\$_i$	n
16	5	G	$GCGTATGTAA \dots \$_j$	e^{1}
÷.,	1.1	1	1	

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- $LCP[k] \ge \alpha, pS < k \le pE$,
- $DA[s] \in \mathcal{R}$ and $DA[t] \in \mathcal{G}$, $pS \le s, t \le pE$.

 $C_{\alpha}(r_i, g_j) = \{(11, 12), (14, 16), \dots \}$

$$Sim_r[g] = \sum_{x \in \mathcal{C}_{lpha}} \sum_{a \in \Sigma} \min(n_r, n_g)$$

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> $Sim_{r_i}[g_j] = 1 + 1 + \dots$ June 10 - 14 , 2019 26

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i	LCP	eBWT	Sorted suffixes
1	:	1	:
17	1	\dot{T}	$GGCGGGGGCG \dots $
18		Ň	GGCGTACCA ^{\$i}
19	6	G	$GGCGTATGTAT \dots $
20	2	G	$GGGCGTAT \dots $
21	3	C	$GGGGCGTAT \dots \$_j$
22	1	C	$GTACCA\$_i$
23	3	C	$GTATGTA \dots \$_j$
24	4	C	$GTATTA \dots \$_j$
25	2	A	$GTTT\$_j$
26	0	$\$_i$	$NGGCGTACCA\$_i$
27	0	T	$T\$_j$
28	1	G	$TACCA\$_i$
29	2	T	$TAGTTT\$_j$
1	1	1	:
			• • • • • • • • • • • • • • • • • • •

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- $LCP[pS] < \alpha$ and $LCP[pE+1] < \alpha$,
- $LCP[k] \ge \alpha$, $pS < k \le pE$,
- $DA[i] \in \mathcal{R} \text{ and } DA[j] \in \mathcal{G},$ $pS \leq i, j \leq pE.$

 $C_{\alpha} = \{(11, 12), (14, 16),$

$$Sim_r[g] = \sum_{x \in \mathcal{C}_{\alpha}} \sum_{a \in \Sigma} \min(n_r, n_g)$$

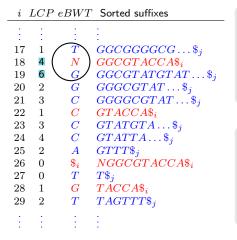
 $Sim_{r}[g] = 1 + 1 +$

 n_r =number of indices i in x such that eBWT[i] = a and DA[i] = r, n_g =number of indices i' in x such that eBWT[i'] = a and DA[i'] = g.

Minimum LCP value $\alpha = 3$

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 $C_{\alpha} = \{(11, 12), (14, 16), (17, 19), \}$

$$Sim_{r}[g] = \sum_{x \in \mathcal{C}_{\alpha}} \sum_{a \in \Sigma} \min(n_{r}, n_{g})$$

 n_r =number of indices i in x such that eBWT[i] = a and DA[i] = r, n_g =number of indices i' in x such that eBWT[i'] = a and DA[i'] = g.

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 $g_j{=}TTATTTTGGCGG\underline{GGCGTA}TGTATTAGTTT\$_j$

i	LCP	eBWT	Sorted suffixes
:	:	:	:
17	1	T	$GGCGGGGGCG \dots $
18	4	Ň	GGCGTACCA ^{\$} _i
19	6	G	$GGCGTATGTAT \dots $
20	2	G	$GGGCGTAT \dots $
21	3	C	$GGGGCGTAT \dots \$_j$
22	1 /	\overline{C}	$GTACCA\$_i$
23	3	C	$GTATGTA \dots \$_j$
24	4	<u> </u>	$GTATTA \dots \$_j$
25	2	A	$GTTT\$_j$
26	0	$\$_i$	$NGGCGTACCA\$_i$
27	0	T	$T\$_j$
28	1	G	$TACCA\$_i$
29	2	T	$TAGTTT\$_j$
1	:	:	:
	· •	· ·	+

An $\alpha\text{-cluster}\ \mathcal{C}_\alpha$ of $eBWT(\mathcal{S})$ is any pair of indices (pS,pE) such that

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- $C_{\alpha} = \{(11, 12), (14, 16), (17, 19), (22, 24)\}$

$$Sim_{r}[g] = \sum_{x \in \mathcal{C}_{\alpha}} \sum_{a \in \Sigma} \min(n_{r}, n_{g})$$

 n_r =number of indices i in x such that eBWT[i] = a and DA[i] = r, n_g =number of indices i' in x such that eBWT[i'] = a and DA[i'] = g.

 $Sim_{r}[g] = 1 + 1 + 1 + 1 = 4$

The read r_i is

- assigned to g_j if g_j is the only genome such that $Sim_{r_i}[g_j] \sim \max_g Sim_{r_i}[g]$ and $Sim_{r_i}[g_j] > \beta$.
- not classified if $\max_{g} Sim_{r_i}[g] \leq \beta$.
- ambiguous if $\max_{g} Sim_{r_i}[g] > \beta$, but there exist at least two genomes g_p and g_q s.t. $Sim_{r_i}[g_p] \sim Sim_{r_i}[g_q] \sim \max_{g} Sim_{r_i}[g_q]$

Example

Let $\alpha = 3$ and $\beta = 0.4$. Suppose the α -similarity between r_i and g_1 , g_2 , g_3 , g_4 , g_5 is $Sim_{r_i}[g_1] = 0.5$, $Sim_{r_i}[g_2] = 0$, $Sim_{r_i}[g_3] =$, $Sim_{r_i}[g_4] = 0.2$, $Sim_{r_i}[g_5] = 0$.

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The read r_i is

• assigned to g_j if g_j is the only genome such that $Sim_{r_i}[g_j] \sim \max_g Sim_{r_i}[g]$ and $Sim_{r_i}[g_j] > \beta$.

• not classified if $\max_{g} Sim_{r_i}[g] \leq \beta$.

• ambiguous if $\max_g Sim_{r_i}[g] > \beta$, but there exist at least two genomes g_p and g_q s.t. $Sim_{r_i}[g_p] \sim Sim_{r_i}[g_q] \sim \max_g Sim_{r_i}[g_p]$

Example

Let $\alpha = 3$ and $\beta = 0.4$. Suppose the α -similarity between r_i and g_1 , g_2 , g_3 , g_4 , g_5 is $Sim_{r_i}[g_1] = 0.5$, $Sim_{r_i}[g_2] = 0$, $Sim_{r_i}[g_3] = 0.8$, $Sim_{r_i}[g_4] = 0.2$, $Sim_{r_i}[g_5] = 0$.

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The read r_i is

- assigned to g_j if g_j is the only genome such that $Sim_{r_i}[g_j] \sim \max_g Sim_{r_i}[g]$ and $Sim_{r_i}[g_j] > \beta$.
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Example

Let $\alpha = 3$ and $\beta = 0.4$. Suppose the α -similarity between r_i and g_1 , g_2 , g_3 , g_4 , g_5 is $Sim_{r_i}[g_1] = 0.5$, $Sim_{r_i}[g_2] = 0$, $Sim_{r_i}[g_3] = 0.8$, $Sim_{r_i}[g_4] = 0.2$, $Sim_{r_i}[g_5] = 0$. $\Rightarrow r_i$ is assigned to g_3 .

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Metagenomics

Step 2: Classification

The read r_i is

- assigned to g_j if g_j is the only genome such that $Sim_{r_i}[g_j] \sim \max_g Sim_{r_i}[g]$ and $Sim_{r_i}[g_j] > \beta$.
- not classified if $\max_{g} Sim_{r_i}[g] \leq \beta$.
- ambiguous if $\max_{g} Sim_{r_i}[g] > \beta$, but there exist at least two genomes g_p and g_q s.t. $Sim_{r_i}[g_p] \sim Sim_{r_i}[g_q] \sim \max_{g} Sim_{r_i}[g]$

Example

Let $\alpha = 3$ and $\beta = 0.4$. Suppose the α -similarity between r_i and g_1 , g_2 , g_3 , g_4 , g_5 is $Sim_{r_i}[g_1] = 0.4$, $Sim_{r_i}[g_2] = 0$, $Sim_{r_i}[g_3] = 0.34$, $Sim_{r_i}[g_4] = 0.2$, $Sim_{r_i}[g_5] = 0$.

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The read r_i is

- assigned to g_j if g_j is the only genome such that $Sim_{r_i}[g_j] \sim \max_g Sim_{r_i}[g]$ and $Sim_{r_i}[g_j] > \beta$.
- not classified if $\max_{g} Sim_{r_i}[g] \leq \beta$.
- ambiguous if $\max_{g} Sim_{r_i}[g] > \beta$, but there exist at least two genomes g_p and g_q s.t. $Sim_{r_i}[g_p] \sim Sim_{r_i}[g_q] \sim \max_{g} Sim_{r_i}[g]$

Example

Let $\alpha = 3$ and $\beta = 0.4$. Suppose the α -similarity between r_i and g_1 , g_2 , g_3 , g_4 , g_5 is $Sim_{r_i}[g_1] = 0.5$, $Sim_{r_i}[g_2] = 0$, $Sim_{r_i}[g_3] = 0.5$, $Sim_{r_i}[g_4] = 0.2$, $Sim_{r_i}[g_5] = 0$. $\Rightarrow r_i$ is ambiguous.

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Preliminary experiments

- Positive and negative control datasets designed in [Lindgreen et al., 2016].
- Reference database \mathcal{G} : 930 genomes from 686 species

	CLARK-S	LightMetaEbwt	LightMetaEbwt	Centrifuge	Centrifuge			
setA2	-highconf	$\alpha \ 16 \beta \ 0.25$	$\alpha \ 16 \beta \ 0.35$	-min-hitlen 16	-min-hitlen 22			
SEN (%)	93.03	92.93	92.48	95.65	93.01			
PREC (%)	99.06	99.81	99.83	97.64	99.66			
F1 (%)	95.95	96.24	96.01	96.63	96.22			
setB2								
SEN (%)	92.84	93.78	93.25	95.53	92.94			
PREC (%)	99.11	99.62	99.64	97.68	99.69			
F1 (%)	95.87	96.61	96.34	96.59	96.20			
setA2Ran								
TN	5,726,336	5,726,294	5,726,357	150,971	5,712,085			
FP	22	64	1	5,575,387	14,273			
SPEC (%)	99.99	99.99	100.00	2.64	99.75			
setB2Ran								
TN	5,406,642	5,406,601	5,406,658	141,994	5,393,260			
FP	17	58	1	5,264,665	13,399			
SPEC (%)	99.99	99.99	100.00	2.63	99.75			
SEN = prop	SEN = proportion of the actual positives identified by the method.							

SEN = proportion of the actual positives identified by the method.

 $\ensuremath{\text{PREC}}\xspace = \ensuremath{\text{proportion}}\xspace$ of positives that are correctely identified by the method.

 $\textbf{SPEC} = \textbf{proportion of actual negatives that are correctely identified as such is a such in the second second$

Open Problems

Open problem

Prove whether some similarity measure based on eBWT is an approximation of Block Edit Distance.

The described "distance" are not a metric because neither it does obeys the triangle inequality.

Open problem

Define a new distance that is a metric.

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Define a new distance that is a metric.

Thank you!

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