

Consensus Strings with Small Maximum Distance and Small Distance Sum

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Consensus String Problems

Input: A set (multi-set) of strings.

Output: A string that is a good **consensus** of the input strings.

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s_3	a	b	c	c	c	c	a
s_4	c	c	c	a	b	c	a
s_5	c	b	c	a	a	c	a
s_6	c	b	c	a	a	c	a
s_7	a	b	b	a	b	a	a
s_8	b	b	c	a	a	c	a

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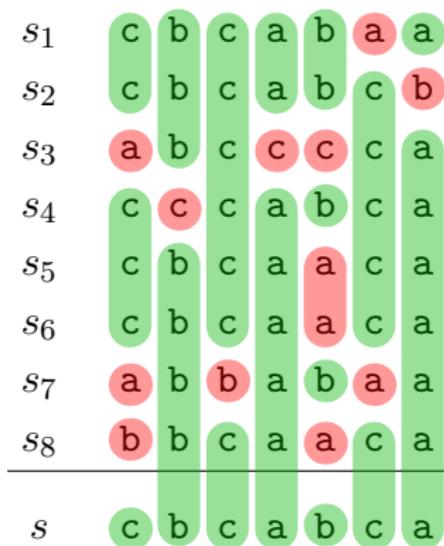
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s_8	b	b	c	a	a	c	a

s	c	b	c	a	b	c	a

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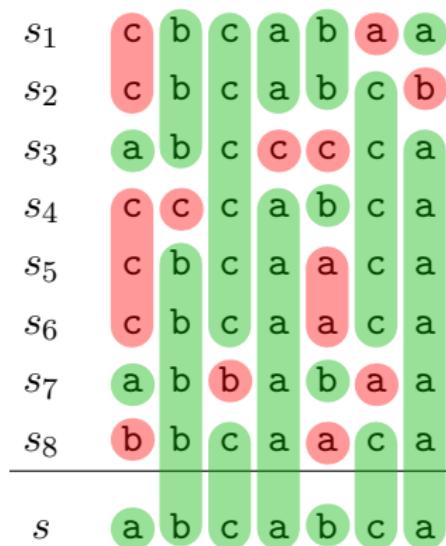
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Basic Notations

Standard string notations:

Σ	finite alphabet
Σ^*	words over Σ
Σ^n	$\{w \in \Sigma^* \mid w = n\}$
$\Sigma^{\leq n}$	$\bigcup_{i=0}^n \Sigma^i$
$d_H(u, v)$	Hamming distance
\preceq	substring relation, $u \preceq v \Leftrightarrow v = xuy$

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For multi-set $S \subseteq \Sigma^\ell$ and $v \in \Sigma^\ell$:

$$\begin{array}{ll} r_H(v, S) = \max\{d_H(v, u) \mid u \in S\} & \text{radius of } S \text{ (w. r. t. } v) \\ s_H(v, S) = \sum_{u \in S} d_H(v, u) & \text{distance sum of } S \text{ (w. r. t. } v) \end{array}$$

The Closest String Problem

(r, s) -CLOSEST STRING

Instance: Multi-set $S = \{s_i \mid 1 \leq i \leq k\} \subseteq \Sigma^\ell$, $\ell \in \mathbb{N}$,
 $d_r, d_s \in \mathbb{N}$.

Question: Is there an $s \in \Sigma^\ell$ with
 $r_H(s, S) \leq d_r$ and $s_H(s, S) \leq d_s$?

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s_1	c b c a b a a	
s_2	c b c a b c b	
s_3	a b c c c c a	$k = 8$
s_4	c c c a b c a	$\ell = 7$
s_5	c b c a a c a	$d_r = 2$
s_6	c b c a a c a	$d_s = 20$
s_7	a b b a b a a	
s_8	b b c a a c a	

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<hr/>							
s	a	b	c	a	b	c	a

$k = 8$
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 $d_r = 2$
 $d_s = 20$

$r_H(s, S) = 2$
 $s_H(s, S) = 16$

The “Substring Variant”

(r, s)-CLOSEST SUBSTRING

Instance: Multi-set $S = \{s_i \mid 1 \leq i \leq k\} \subseteq \Sigma^{\leq \ell}$, $\ell \in \mathbb{N}$,
 $d_r, d_s, m \in \mathbb{N}$.

Question: Is there an $s \in \Sigma^m$,
multi-set $S' = \{s'_i \mid s'_i \preceq s_i, 1 \leq i \leq k\} \subseteq \Sigma^m$ with
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s_1	a a c b c a b a a	
s_2	b c b c a b c b	$k = 8$
s_3	a a b c c	$\ell = 11$
s_4	c c c a b c a c	$m = 4$
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s_7	a a b b a b a a	$r_H(s, S') = 1$
s_8	b b c a a c a c c b	$s_H(s, S') = 7$
<hr/>	s	a b c a

The “Outlier Variant”

(r, s)-CLOSEST STRING WITH OUTLIERS

Instance: Multi-set $S = \{s_i \mid 1 \leq i \leq k\} \subseteq \Sigma^\ell$, $\ell \in \mathbb{N}$,
 $d_r, d_s, t \in \mathbb{N}$.

Question: Is there an $s \in \Sigma^\ell$,
 $S' \subseteq S$ with $|S'| = k - t$ with
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$s_8 \quad b \ b \ c \ a \ a \ c \ a$

$$k = 8$$

$$\ell = 7$$

$$t = 2$$

$$d_r = 2$$

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<hr/>								
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s_5	c	b	c	a	a	a	c	a
s_6	c	b	c	a	a	a	c	a
<hr/>								
s_8	b	b	c	a	a	c	a	
s	c	b	c	a	b	c	a	

$k = 8$
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 $t = 2$
 $d_r = 2$
 $d_s = 8$

$r_H(s, S) = 2$
 $s_H(s, S) = 7$

The “r- and s-Variants”

(r)-CLOSEST STRING:

(s)-CLOSEST STRING:

(r, s)-CLOSEST STRING without d_s bound

(r, s)-CLOSEST STRING without d_r bound

Likewise for substring- and outlier-variants.

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The (r)- and (s)-variants are intensively investigated:

our terminology	common in literature
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(r)-CLOSEST SUBSTRING	CLOSEST SUBSTRING
(s)-CLOSEST SUBSTRING	CONSENSUS PATTERNS

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(s)-CLOSEST SUBSTRING	CONSENSUS PATTERNS

Hardness

All these problems are **NP-hard**
(except (s)-CLOSEST STRING, which is trivial).

Parameters

k	number of input strings
ℓ	length of input strings
d_r	radius bound
d_s	distance sum bound
$ \Sigma $	alphabet size
m	substring length ((r, s)-CLOSEST SUBSTRING)
t	number of outliers ((r, s)-CLOSEST STRING-WO)
$k - t$	number of inliers ((r, s)-CLOSEST STRING-WO)

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Notation:

(r, s) -CLOSEST STRING(p_1, p_2, \dots) means (r, s) -CLOSEST STRING parameterised by p_1, p_2, \dots

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fixed-parameter tractable: \exists algorithm with running time $f(k) \times p(|x|)$ for recursive f and polynomial p (x is input and k the parameter).

$\mathsf{W}[1]$ -hardness \Rightarrow *not* fixed parameter tractable.

State of the Art

Previous literature:

(r)-CLOSEST STRING

(s)-CLOSEST STRING

(r)-CLOSEST SUBSTRING

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((s)-CLOSEST SUBSTRING(ℓ, m))

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Our Contribution:

(r, s)-CLOSEST STRING

(r, s)-CLOSEST SUBSTRING

(s)-CLOSEST SUBSTRING(ℓ, m)

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(r, s)-CLOSEST SUBSTRING

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(r)-CLOSEST STRING-WO

(s)-CLOSEST STRING-WO

(r, s)-CLOSEST STRING-WO

Results for (r, s) -CLOSEST STRING

k	d_r	d_s	$ \Sigma $	ℓ	Result
p	—	—	—	—	FPT
—	p	—	—	—	FPT
—	—	p	—	—	FPT
—	—	—	2	—	NP-hard
—	—	—	—	p	FPT

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—	—	—	2	—	NP-hard
—	—	—	—	p	FPT

Branching Algorithm

Fpt-branching algorithm for (r)-CLOSEST STRING(d_r):¹

$$d_r = 2$$

s_1	c	b	c	a	b	a	a
s_2	c	b	c	a	b	c	b
s_3	a	b	c	c	c	c	a
s_4	c	c	c	a	b	c	a
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s_6	c	b	c	a	a	c	a
s_7	a	b	b	a	b	a	a
s_8	b	b	c	a	a	c	a

s	a	b	c	a	b	c	a
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¹Gramm, Niedermeier, Rossmanith, Algorithmica, 2003.

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s_6	c b c a a c a
s_7	a b b a b a a
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<hr/>	
s	a b c a b c a

$$s' = \mathbf{c b c a b a a}$$

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$s_7 \quad a \ b \ b \ a \ b \ a \ a$

$s_8 \quad b \ b \ c \ a \ a \ c \ a$

$$s' = \textcolor{red}{c \ b \ c \ a \ b \ a \ a}$$

$s \quad a \ b \ c \ a \ b \ c \ a$

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Extended Branching Algorithm

Goal: Extend branching algorithm to (r, s) -CLOSEST STRING-WO(d_r, t).

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Choice of outliers can be added to the branching (t is a parameter).²

General branching similar:

branch by $d_r + 1$ mismatches between candidate and input string.

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General branching similar:

branch by $d_r + 1$ mismatches between candidate and input string.

Main problem: What is a good initial candidate string?

some input string \rightsquigarrow how do we satisfy d_s bound?

some string with low distance sum \rightsquigarrow how to bound depth of branching?

²Boucher and Ma, BMC Bioinformatics, 2011.

Extended Branching Algorithm

Majority string s_m :

pick a most frequent symbol in each column.

Example:

s_1	d	b	a	b	b	b	b
s_2	d	a	a	b	c	c	d
s_3	d	a	a	b	c	c	d
s_4	a	a	c	c	c	c	d
s_5	a	a	c	b	c	c	d
s_6	a	c	a	b	d	b	d
<hr/>							
s_m	d	a	a	b	c	c	d

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Example:

Lemma

$$r_H(s, S) \leq d_r \Rightarrow d_H(s_m, s) \leq 2d_r.$$

s_1	d	b	a	b	b	b	b
s_2	d	a	a	b	c	c	d
s_3	d	a	a	b	c	c	d
s_4	a	a	c	c	c	c	d
s_5	a	a	c	b	c	c	d
s_6	a	c	a	b	d	b	d
<hr/>							
s_m	d	a	a	b	c	c	d

Extended Branching Algorithm

Majority string s_m :

pick a most frequent symbol in each column.

Example:

s_1	d	b	a	b	b	b	b
s_2	d	a	a	b	c	c	d
s_3	d	a	a	b	c	c	d
s_4	a	a	c	c	c	c	d
s_5	a	a	c	b	c	c	d
s_6	a	c	a	b	d	b	d
<hr/>							
s_m	d	a	a	b	c	c	d

Lemma

$$r_H(s, S) \leq d_r \Rightarrow d_H(s_m, s) \leq 2d_r.$$

Problem: Outliers!

Extended Branching Algorithm

Majority string s_m :

pick a most frequent symbol in each column.

Example:

$t = 2$

s_1	d	b	a	b	b	b	b
s_2	d	a	a	b	c	c	d
s_3	d	a	a	b	c	c	d
s_4	a	a	c	c	c	c	d
s_5	a	a	c	b	c	c	d
s_6	a	c	a	b	d	b	d
<hr/>							
s_m	d	a	a	b	c	c	d

Lemma

$$r_H(s, S) \leq d_r \Rightarrow d_H(s_m, s) \leq 2d_r.$$

Problem: Outliers!

Extended Branching Algorithm

Refined majority string s_m^\diamond :

\exists symb. with at least as many occ. as
majority symbol minus $t \Rightarrow$ use \diamond .

Example:

$$t = 2$$

s_1	d	b	a	b	b	b	b
s_2	d	a	a	b	c	c	d
s_3	d	a	a	b	c	c	d
s_4	a	a	c	c	c	c	d
s_5	a	a	c	b	c	c	d
s_6	a	c	a	b	d	b	d

Lemma

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Problem: Outliers!

$$s_m^\diamond \quad \diamond \ a \ \diamond \ b \ c \ \diamond \ d$$

Extended Branching Algorithm

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s_5	a	a	c	b	c	c	d
s_6	a	c	a	b	d	b	d
<hr/>							
s_m^\diamond	\diamond	a	\diamond	b	c	\diamond	d

Lemma

$$r_H(s, S) \leq d_r \Rightarrow d_H(s_m, s) \leq 2d_r.$$

Problem: Outliers!
Disputed columns.

Extended Branching Algorithm

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Example:

$$t = 2$$

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s_2	d	a	a	b	c	c	d
s_3	d	a	a	b	c	c	d
s_4	a	a	c	c	c	c	d
s_5	a	a	c	b	c	c	d
s_6	a	c	a	b	d	b	d
<hr/>							
s_m^\diamond	\diamond	a	\diamond	b	c	\diamond	d

Lemma

$$r_H(s, S) \leq d_r \Rightarrow d_H(s_m, s) \leq 2d_r.$$

Problem: Outliers!

Disputed columns.

Lemma

If the instance has a solution,
then #disp. columns $\leq 4d_r$.

Extended Branching Algorithm

Refined majority string s_m^\diamond :

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Example:

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s_4	a	a	c	c	c	c	d
s_5	a	a	c	b	c	c	d
s_6	a	c	a	b	d	b	d
<hr/>							
s_m^\diamond	\diamond	a	\diamond	b	c	\diamond	d

Lemma

$$r_H(s, S) \leq d_r \Rightarrow d_H(s_m, s) \leq 2d_r.$$

Problem: Outliers!

Disputed columns.

Lemma

If the instance has a solution,
then #disp. columns $\leq 4d_r$.

Algorithm:

start with s_m^\diamond

branch over $d_r + 1$ mismatches
(or declare outlier)

depth bound: $6d_r + t$.

Results for (r, s) -CLOSEST SUBSTRING

ℓ	k	m	d_r	d_s	$ \Sigma $	Result
—	—	p	—	—	p	FPT
p	p	—	—	—	—	FPT
p	—	—	—	p	—	FPT
p	—	—	—	—	p	FPT
p	—	p	p	—	—	W[1]-hard
—	p	—	p	p	p	W[1]-hard
—	p	p	p	p	—	W[1]-hard

Results for (r, s) -CLOSEST SUBSTRING

ℓ	k	m	d_r	d_s	$ \Sigma $	Result
—	—	p	—	—	p	FPT
p	p	—	—	—	—	FPT
p	—	—	—	p	—	FPT
p	—	—	—	—	p	FPT
p	—	p	p	—	—	W[1]-hard
—	p	—	p	p	p	W[1]-hard
—	p	p	p	p	—	W[1]-hard

(r, s) -CLOSEST SUBSTRING(ℓ, m)

Theorem

(s) -CLOSEST SUBSTRING(ℓ, m) is W[1]-hard.

(r, s)-CLOSEST SUBSTRING(ℓ, m)

Theorem

(s)-CLOSEST SUBSTRING(ℓ, m) is W[1]-hard.

Reduction from multi-coloured clique:

Let $G = (V, E)$ be a graph with partition $V = V_1 \cup \dots \cup V_{k_c}$ such that every V_i , $1 \leq i \leq k_c$, is an independent set.

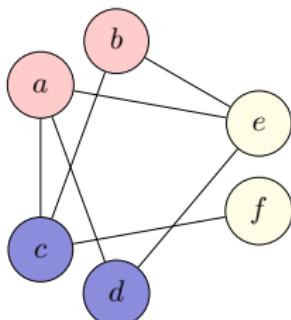
(r, s)-CLOSEST SUBSTRING(ℓ, m)

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Reduction from multi-coloured clique:

Let $G = (V, E)$ be a graph with partition $V = V_1 \cup \dots \cup V_{k_c}$ such that every V_i , $1 \leq i \leq k_c$, is an independent set.



Repeat
 $N = 36$
times

$\mathcal{V}_1 :$	\$	a	c	e	
$\mathcal{V}_2 :$	\$	b	d	f	
$\mathcal{E}_1 :$	\$	◊	a	c	◊
$\mathcal{E}_2 :$	\$	◊	a	d	◊
$\mathcal{E}_3 :$	\$	◊	a	◊	e
$\mathcal{E}_4 :$	\$	◊	b	c	◊
$\mathcal{E}_5 :$	\$	◊	b	◊	e
$\mathcal{E}_6 :$	\$	◊	◊	c	f
$\mathcal{E}_7 :$	\$	◊	◊	d	e

$s : \quad \$ \quad a \quad d \quad e$

Result for the Outlier Variants

Theorem

(s)-CLOSEST STRING-WO($d_s, \ell, k - t$) is W[1]-hard.

Result for the Outlier Variants

Theorem

(s)-CLOSEST STRING-WO($d_s, \ell, k - t$) is W[1]-hard.

We know (r)-CLOSEST STRING-WO($t = 0, |\Sigma| = 2$) is NP-hard, but . . .

Open Problem

- (r)-CLOSEST STRING-WO($|\Sigma|, k - t$),
- (r)-CLOSEST STRING-WO($|\Sigma|, d_r$),
- (r)-CLOSEST STRING-WO($|\Sigma|, d_r, k - t$).

Result for the Outlier Variants

(r, s) -CLOSEST STRING-wo($\ell, |\Sigma|$) $\in \text{FPT}$ (trivial).

Theorem

(r, s) -CLOSEST STRING-wo($\ell, |\Sigma|, d_r, d_s, (k - t)$) does not admit a polynomial kernel unless $\text{coNP} \subseteq \text{NP/Poly}$.

Thank you very much for your attention.