Languages of lossless seeds

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Introduction

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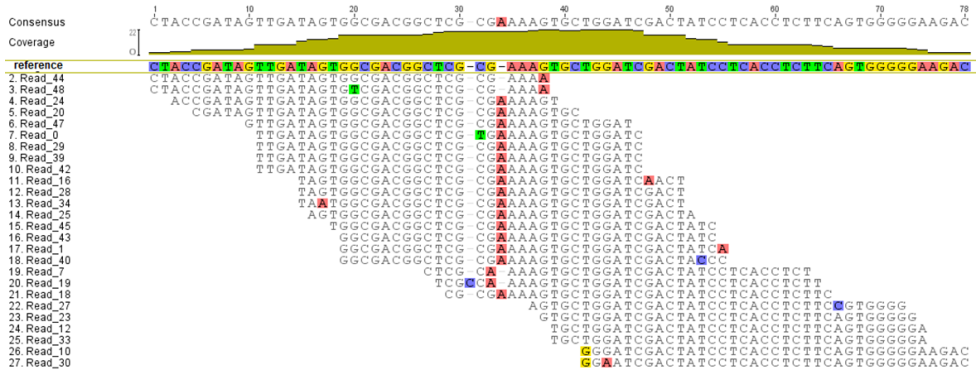

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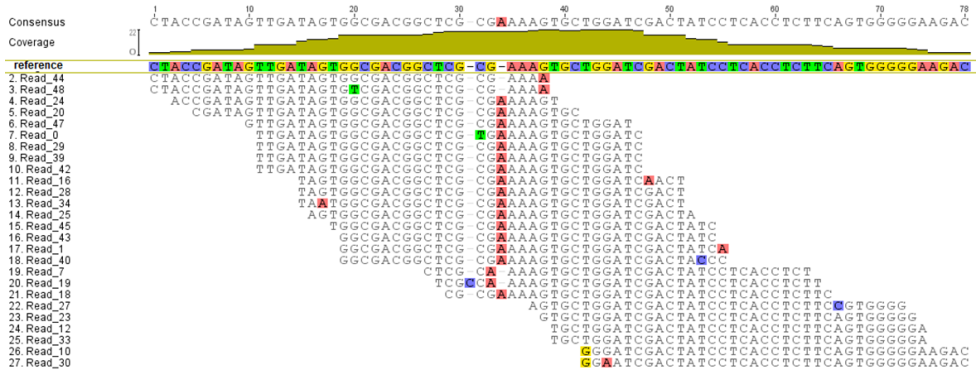

- They are widely used in programs for NEXT-GENERATION SEQUENCING data processing
  - e.g., in short-read mapping

We show a connection between

- lossless seeds
- symbolic dynamics
- formal languages

Text filtration – general principle

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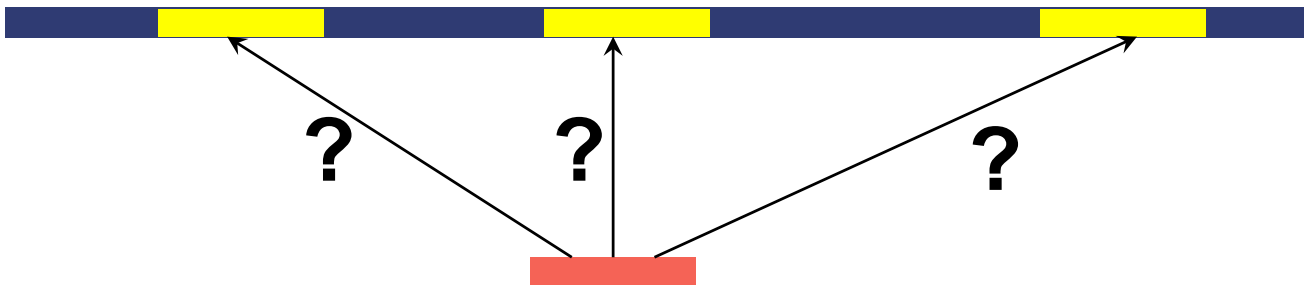
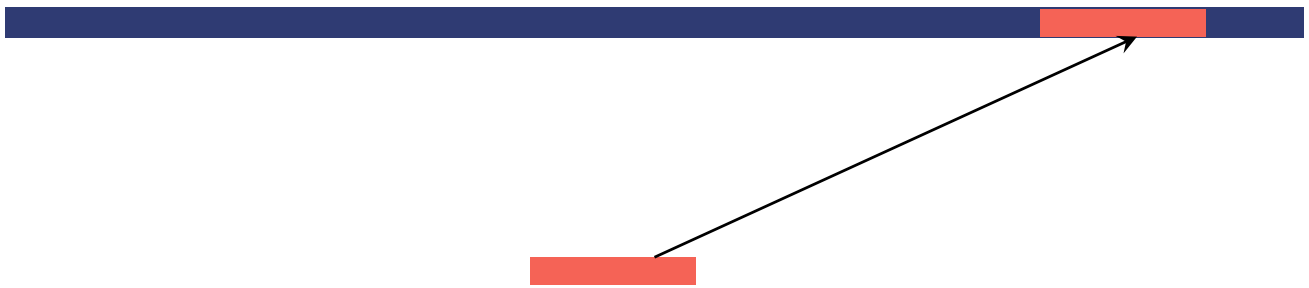
Potential matches



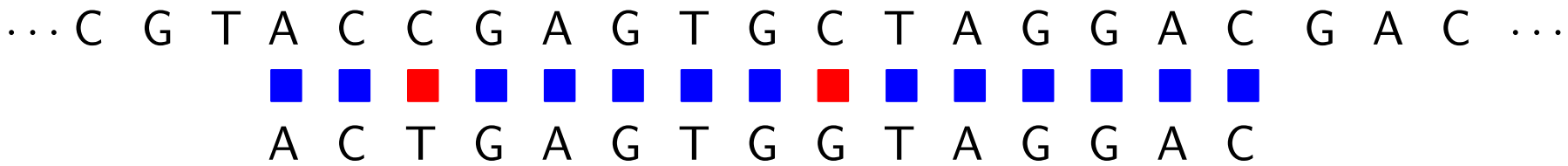
Text filtration – general principle

True matches



Gapless similarities

Similarities can be defined through **Hamming distance**



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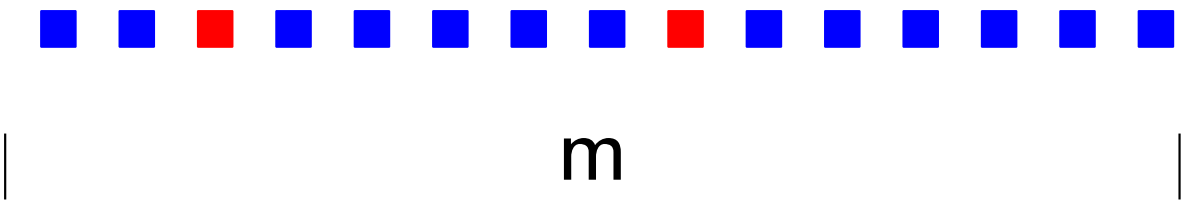

(m, k)-**problem**

m: length of compared strings
k: number of allowed mismatches

Seeds

Principle of lossless seeds

Two strings of the same length m in Hamming distance $\leq k$ must share some patterns – so-called **seeds**

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Seeds can be: continuous vs. spaced, lossy vs. lossless

Lossless seeds

Example ($(15, 2)$-problem)

Seeds solving this problem are, e.g.:

- `#####`
- `##-#--##-#`

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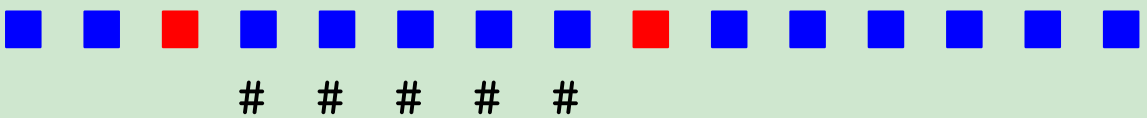

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Seed design

- We are given $m > k > 0$, a typical task is to find seeds solving the (m, k)-problem
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  - we want to reach the **maximal possible** weight
- Designed seeds are then **used as parameters** in the programs
  - they are designed for a specific task

Spaced seeds – articles overview

- **Introduced:**
  [Burkhardt and Kärkkäinen, 2001, Burkhardt and Kärkkäinen, 2002]
- **Asymptotic properties:** [Kucherov et al., 2005, Farach-Colton et al., 2007]
- **Complexity:** [Nicolas and Rivals, 2005, Nicolas and Rivals, 2008]
- **Seed design:** [Kucherov et al., 2005], [Lin et al., 2008], [Chen et al., 2009], [Egidi and Manzini, 2011, Egidi and Manzini, 2014b], [Egidi and Manzini, 2013], [B., 2013], [Egidi and Manzini, 2014a]
- **Generalizations:**
  - Seed families: [Kucherov et al., 2005]
  - Vector seeds: [Brejová et al., 2005]
  - Subset seeds: [Noé and Kucherov, 2005]
- **Programs which use them** (examples): ZOOM [Lin et al., 2008], PerM [Chen et al., 2009], Shrimp2 [David et al., 2011]
- **List of all papers:** [Noé, 2014]

An important issue – structural properties of lossless seeds

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- Can be optimal seeds obtained from short patterns in any case?

Conjecture [B., 2013]

Fix m. For every $0 < s < m$, a seed of length s solving the $(m, 2)$-problem with highest possible weight can be obtained from a cyclic seed[a] of length at most $\ell + 1$.

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To find the structure – **approach based on subshifts** – seeds form languages of certain sofic subshifts

Parameters

Fixed params	**Object of study**
m and k	seeds solving the (m, k)-problem
ℓ and k	seeds Q solving $(\lvert Q\rvert + \ell, k)$-problems

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Asymptotic relations between ℓ and m for optimal seeds

Theorem

For a fixed positive k, optimal seeds must satisfy $\ell \in \Theta(m^{\frac{k}{k+1}})$

Subshifts – notation

$\mathcal{A} = \{\#, -\}$	**seed alphabet**
$\mathbf{w}$	a **bi-infinite word** (from $\mathcal{A}^{\mathbb{Z}}$)
$\mathbf{w}[m, n]$	**factor** $\mathbf{w}_m \mathbf{w}_{m+1} \cdots \mathbf{w}_n$ of the bi-infinite word $\mathbf{w}$
σ	**shift operation**, $(\sigma(\mathbf{u}))_i = \mathbf{u}_{i+1}$
S_X	**subshift** of all bi-infinite words over $\mathcal{A}$, which do not contain any word from X as a factor (X: set of finite words)
$\oplus$	**"seed OR"**

```
-#--###-#
    ⊕
##--#-##-
    =
##--#####
```

Approach based on subshifts

The main idea: Fix ℓ and k, find subshifts of the full shift $\mathcal{A}^{\mathbb{Z}}$ with seeds as languages.

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Theorem

Let:

- m *and* k *be positive integers,*
- Q *be a seed such that* $|Q| < m$,
- $\ell := m - |Q|$,
- $\mathbf{w} := \cdots --|Q--\cdots$.

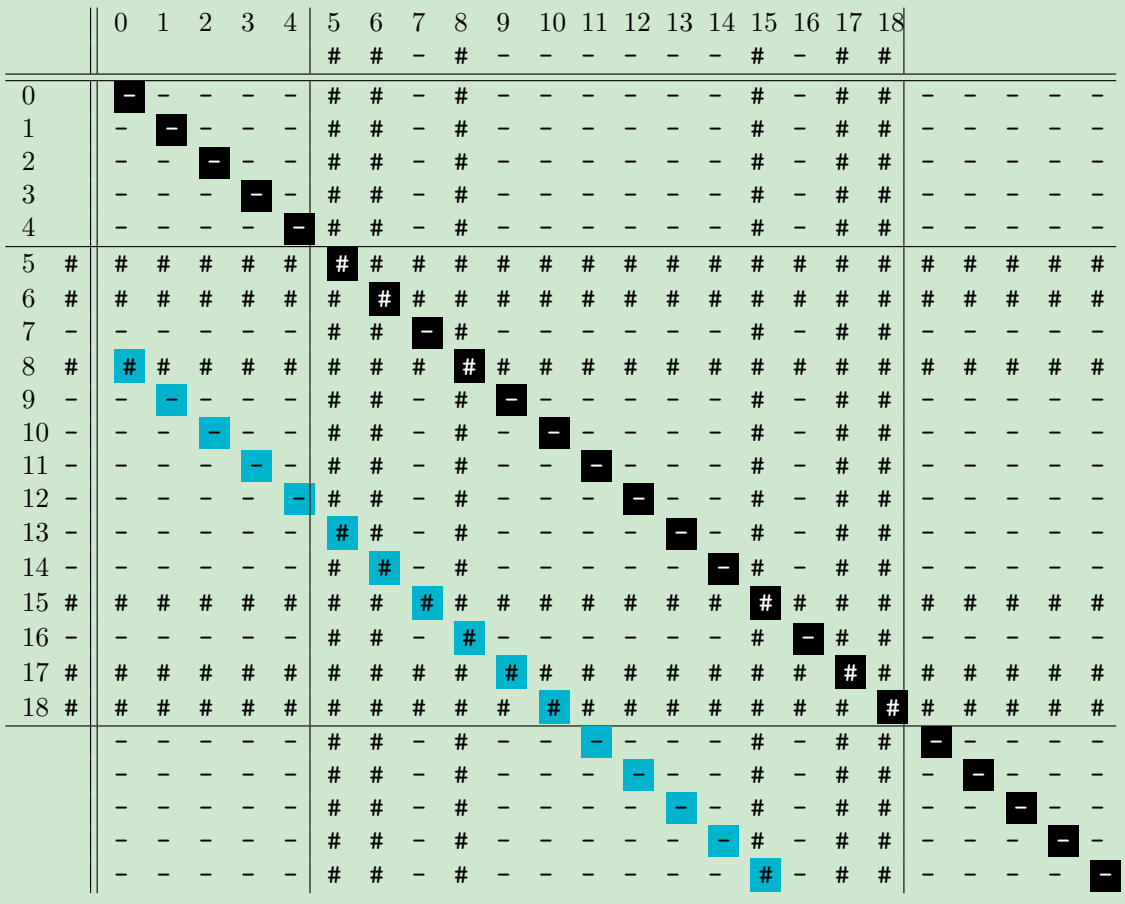
The seed Q *does not solve the* (m, k)*-problem if and only if*

$$(\oplus(\sigma^{i_1}(\mathbf{w}), \ldots, \sigma^{i_k}(\mathbf{w}))[0, \ell] = \#^{\ell+1}.$$

for some integers $i_1, \ldots, i_k$.

$(m, 2)$-problems – Laser method [B., 2013]

Example ($(19, 2)$-problem, $Q =$ ##–#––––––#–##)



The bi-infinite word $\oplus(\sigma^5(\mathbf{w}), \sigma^{13}(\mathbf{w})$

$(m, 2)$-problems – Laser method [B., 2013]

Example ($(19, 2)$-problem, $Q =$ ##–#––––––#–##)

		0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18					
							#	#	–	#	–	–	–	–	–	–	#	–	#	#					
0		–	–	–	–	–	#	#	–	#	–	–	–	–	–	–	#	–	#	#	–	–	–	–	–
1		–	–	–	–	–	#	#	–	#	–	–	–	–	–	–	#	–	#	#	–	–	–	–	–
2		–	–	–	–	–	#	#	–	#	–	–	–	–	–	–	#	–	#	#	–	–	–	–	–
3		–	–	–	–	–	#	#	–	#	–	–	–	–	–	–	#	–	#	#	–	–	–	–	–
4		–	–	–	–	–	#	#	–	#	–	–	–	–	–	–	#	–	#	#	–	–	–	–	–
5	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#
6	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#
7	–	–	–	–	–	–	#	#	–	#	–	–	–	–	–	–	#	–	#	#	–	–	–	–	–
8	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#
9	–	–	–	–	–	–	#	#	–	#	–	–	–	–	–	–	#	–	#	#	–	–	–	–	–
10	–	–	–	–	–	–	#	#	–	#	–	–	–	–	–	–	#	–	#	#	–	–	–	–	–
11	–	–	–	–	–	–	#	#	–	#	–	–	–	–	–	–	#	–	#	#	–	–	–	–	–
12	–	–	–	–	–	–	#	#	–	#	–	–	–	–	–	–	#	–	#	#	–	–	–	–	–
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14	–	–	–	–	–	–	#	#	–	#	–	–	–	–	–	–	#	–	#	#	–	–	–	–	–
15	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#
16	–	–	–	–	–	–	#	#	–	#	–	–	–	–	–	–	#	–	#	#	–	–	–	–	–
17	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#	#
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		–	–	–	–	–	#	#	–	#	–	–	–	–	–	–	#	–	#	#	–	–	–	–	–

$\Longrightarrow$ Q does not solve the problem

Extending seeds to bi-infinite words

Definition

w is (ℓ, k)-valid $\iff$ $\forall i_1, \ldots, i_k \in \mathbb{Z}$:

$$(\oplus(\sigma^{i_1}(\mathbf{w}), \ldots, \sigma^{i_k}(\mathbf{w}))[0, \ell] \neq \#^{\ell+1}.$$

Important property: Every factor Q of **w** solves the $(|Q| + \ell, k)$-problem.

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A bi-infinite word **w** is (ℓ, k)-valid $\iff$ all its k factors $u^{(1)}, \ldots, u^{(k)}$ of length $\ell + 1$ satisfy $\mathrm{C}_k^{\ell}(u^{(1)}, \ldots, u^{(k)})$

Example

Example ($\ell = 5$, $k = 2$)

- $Q^{(1)} =$ ##–#–– solves the $(11, 2)$-problem
- $Q^{(2)} =$ ––#–## solves the $(11, 2)$-problem
- $Q^{(3)} =$ ##–#––––––––––#–## does not solve the $(25, 2)$-problem
  - because $\neg \mathrm{C}^{\frac{5}{2}}(Q^{(1)}, Q^{(2)})$
    - reason: $Q^{(1)} \oplus Q^{(2)} =$ ###### $= \#^{\ell+1}$

Generating sets

Definition

For given positive integers ℓ and k, a subset G of $\mathcal{A}^{\ell+1}$ is called (ℓ, k)-**generating set** if the following conditions are satisfied:

1. for all $v^{(1)}, \ldots, v^{(k)} \in G$, it holds $\mathrm{C}_k^{\ell}(v^{(1)}, \ldots, v^{(k)})$;
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Definition

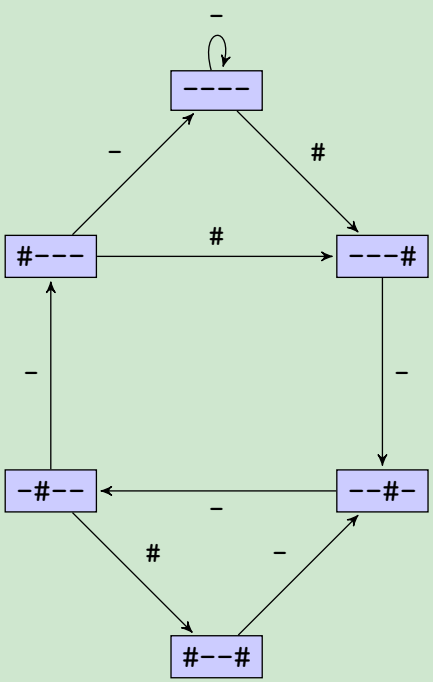
A seed Q is **generated** by an (ℓ, k)-generating set G if it is a factor of some bi-infinite word from $S_{\mathcal{A}^{\ell+1} \setminus G}$.

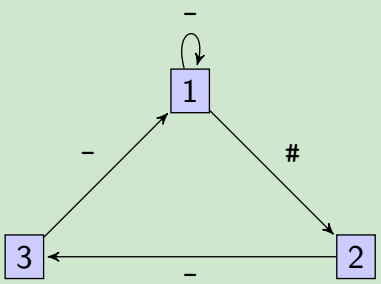
Recognizing automata

Example ($k = 2$, $\ell = 3$)

Generating set $G = \{----, \#---, -\#--, --\#-, ---\#, \#--\#\}$

Automaton from de-Bruijn graph ...and after minimization.





Words from $S_{\mathcal{A}^{\ell+1} \setminus G}$ are bi-infinite paths in such graphs

The main result

Theorem

For given ℓ and k, the set of all (ℓ, k)-valid bi-infinite words is a sofic subshift.

The main result

For given positive ℓ and k:

- Every (ℓ, k)-valid bi-infinite word is generated by some (ℓ, k)-generating set.
- Set of bi-infinite words generated by the same (ℓ, k)-generating set is a subshift of finite type.
- There exist only finitely many (ℓ, k)-generating sets.

$\Downarrow$ $\Downarrow$ $\Downarrow$ $\Downarrow$ $\Downarrow$

Theorem

For given ℓ and k, the set of all (ℓ, k)-valid bi-infinite words is a sofic subshift.

How to find generating sets

1. $k = 1$: The only simple case.

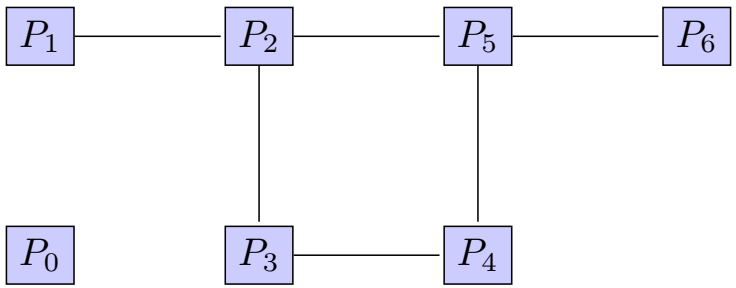
Lemma

Let ℓ and k be positive integers. The unique (ℓ, k)-generating set is the set $\mathcal{A}^{\ell+1} \setminus \{\#^{\ell+1}\}$

2. $k = 2$: $(m, 2)$-generating sets $=$ maximal (w.r.t. to inclusion) independent sets of a graph constructed from the relation C_2^{ℓ}

3. $k > 2$: we would need hypergraphs

Example - $(5,2)$-generating sets search



$P_0 = \{$------ ; -----# , ----#- , ---#-- , --#--- , -#---- , #----- ;
----## , ---##- , --##-- , -##--- , ##---- ;
---#-# , --#-#- , -#-#-- , #-#--- ;
--#--# , -#--#- , #--#-- ; -#---# , #---#- ;
#---## ; ##---# ; #----# $\}$,

$P_1 = \{$#--#-# $\}$, $P_2 = \{$--##-# , -##-#- , ##-#-- $\}$,

$P_3 = \{$-##--# , ##--#- $\}$, $P_4 = \{$-#--## , #--##- $\}$,

$P_5 = \{$--#-## , -#-##- , #-##-- $\}$, $P_6 = \{$#-#--# $\}$.

Concluding remarks

- Every (ℓ, k)-generating set corresponds to a subshift of finite type
- The subshift of all (ℓ, k)-valid bi-infinite words is sofic
- For given ℓ and k, the set of seeds Q solving $(|Q| + \ell, k)$-problems is a regular language
- Cycles in its recognizing automaton correspond to cyclic seeds from [Kucherov et al., 2005]
- For a fixed k, the relation between m and ℓ for optimal seed is $\ell \in \Theta(m^{\frac{k}{k+1}}) \implies$ when $m \to +\infty$, then $\ell \to +\infty$, too

Thank you for your attention!

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