Lossless seeds for searching short patterns with high error rate

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Approximate String Matching

Searching a string that matches a pattern with errors

- pattern of size m
- text of size n
- maximal number of errors: k

Authorized errors

- substitution
- insertion
- deletion

A new algorithm for searching short patterns with high error rate:

- a new kind of seed: 01^*0 seed

Main existing searching methods

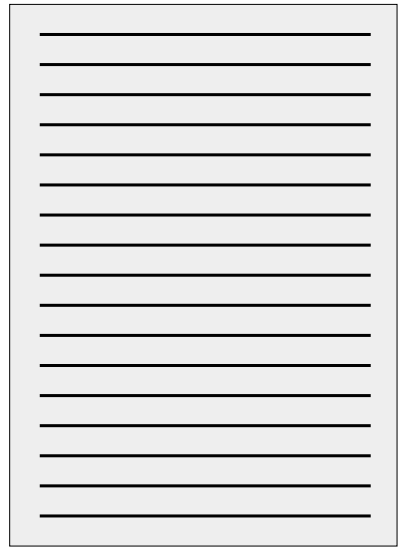
- Neighborhood exploration
- Exact seed filtration
- Hybrid method

Neighborhood Exploration

Pattern

GATTACA

Text



Neighborhood Exploration

Pattern

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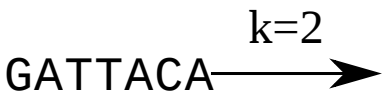
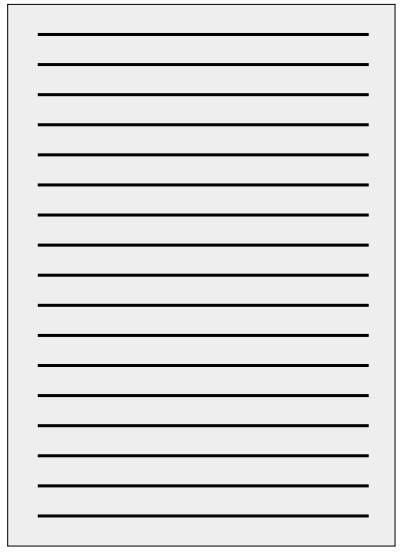
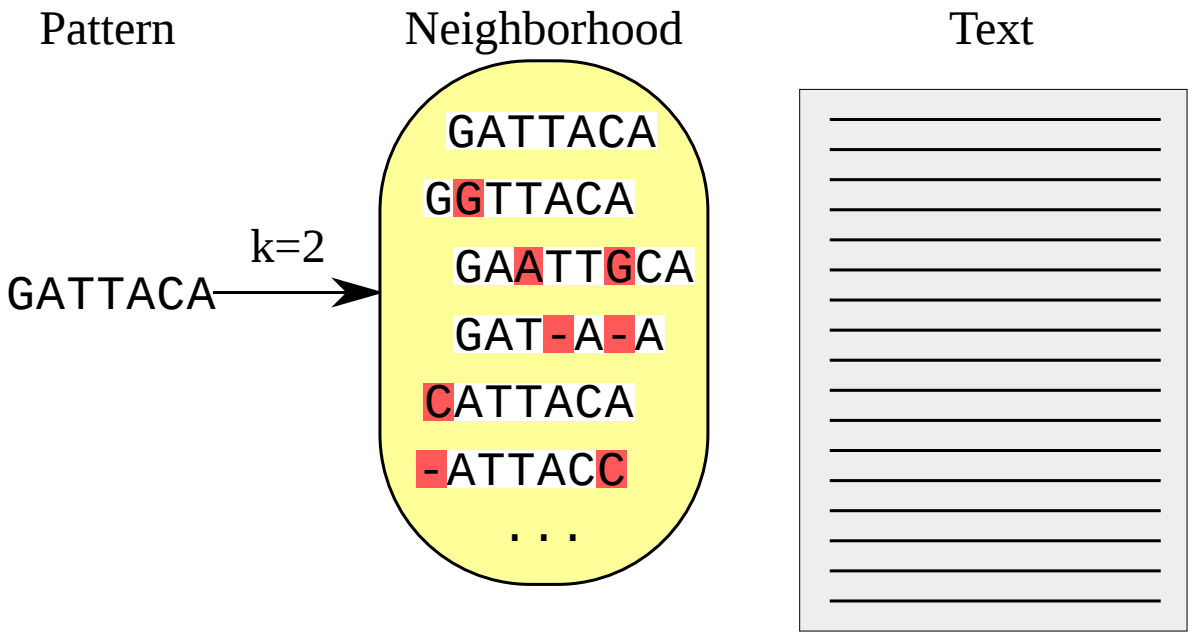




Neighborhood Exploration



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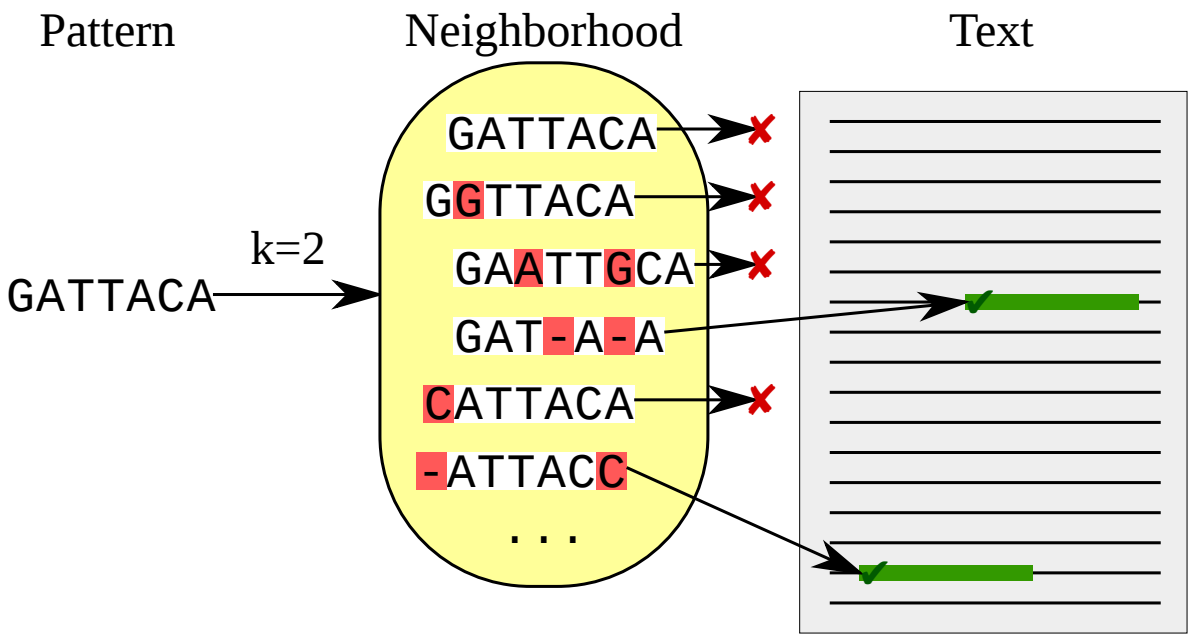

Exact Seed Filtration

Pattern

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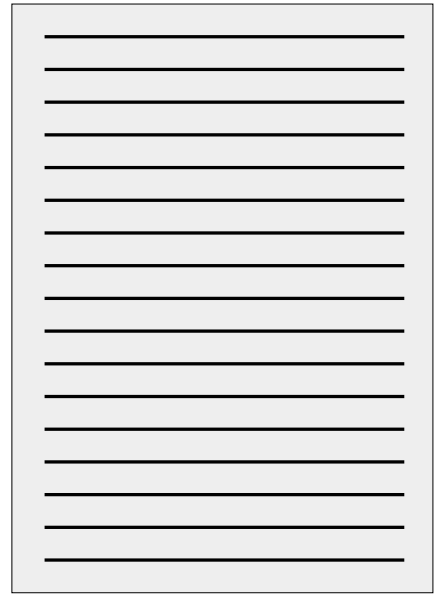

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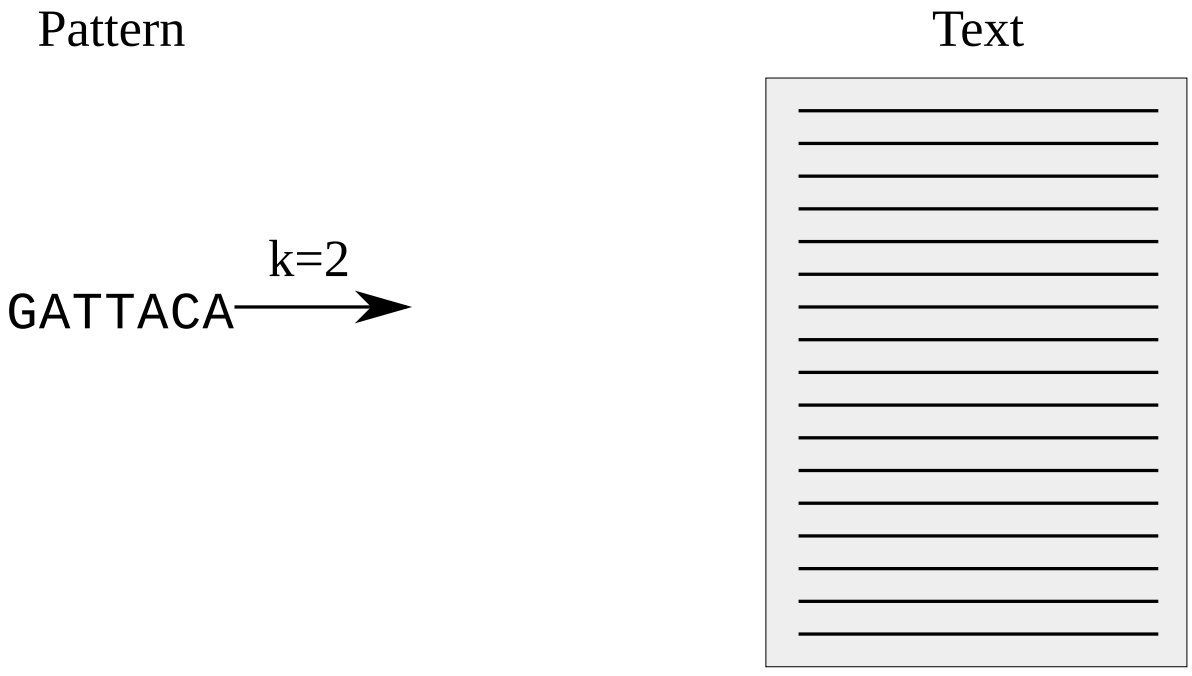
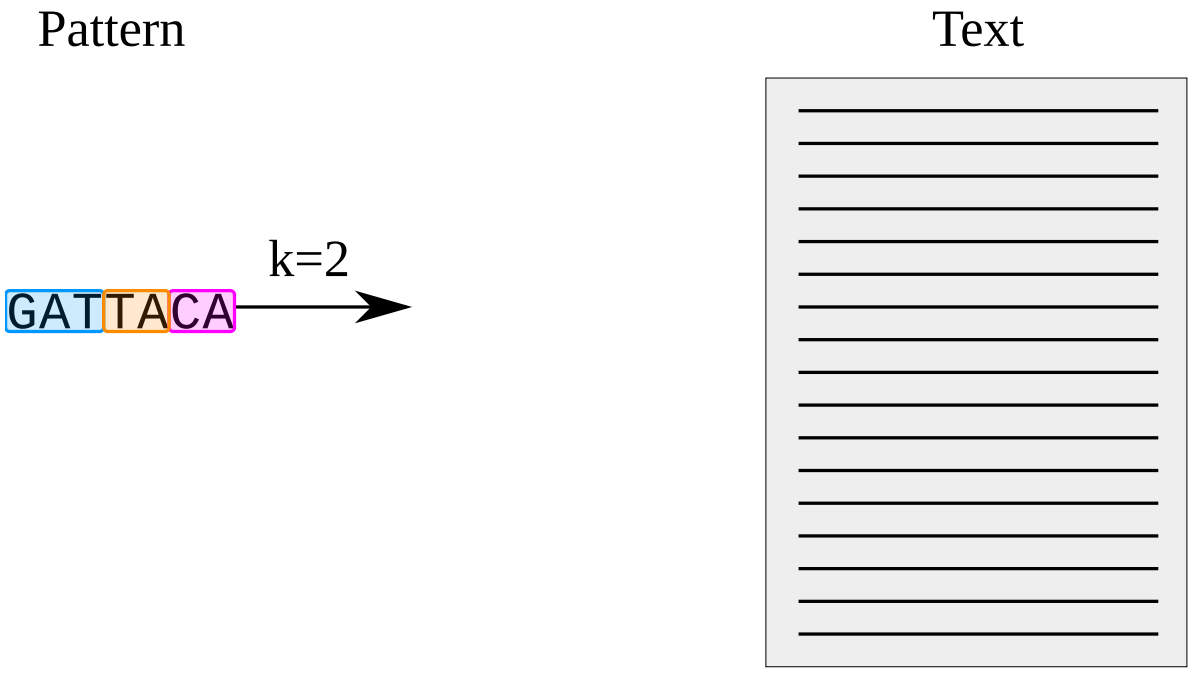


Exact Seed Filtration



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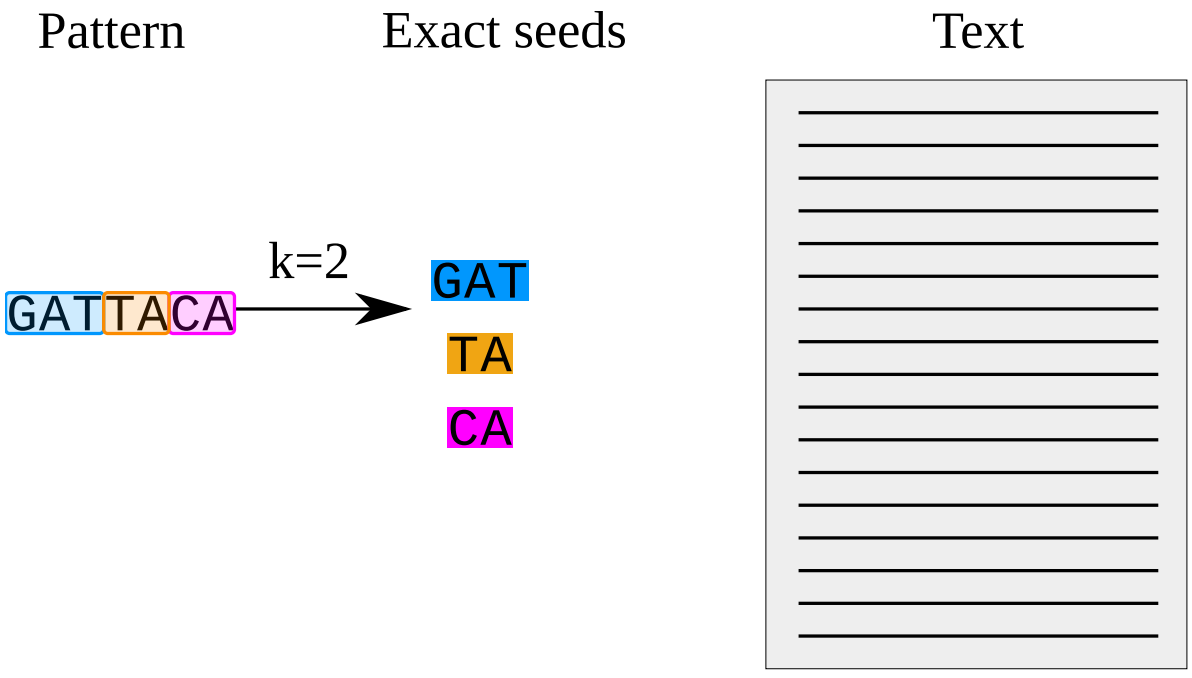

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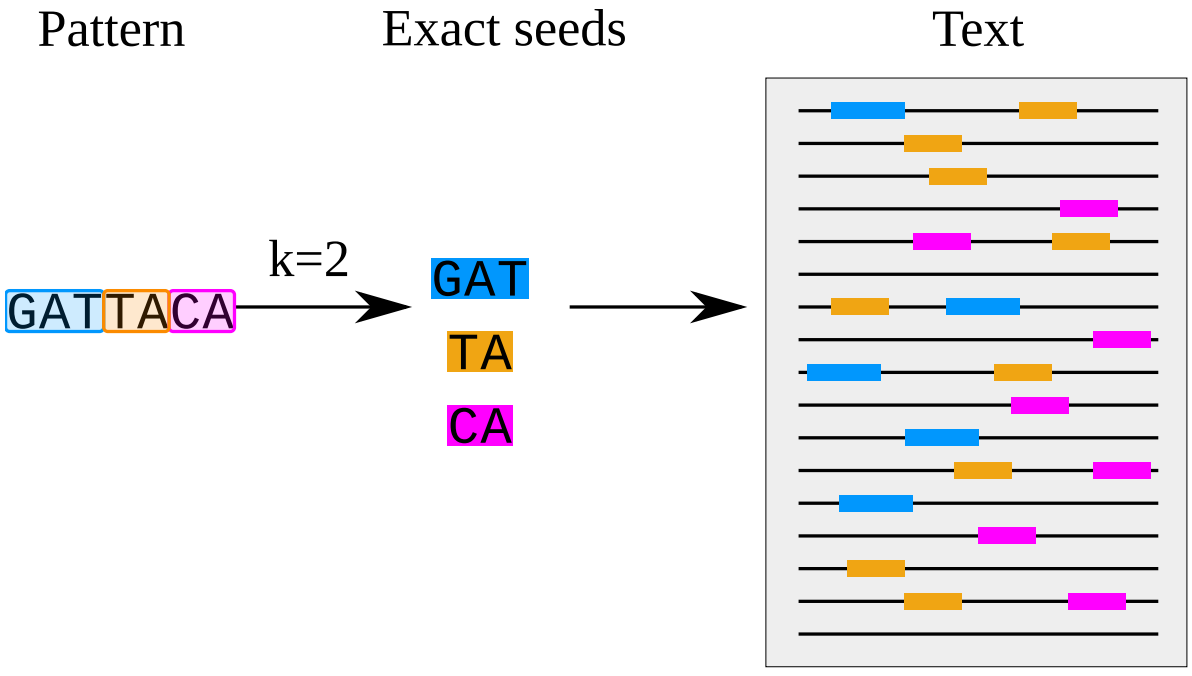

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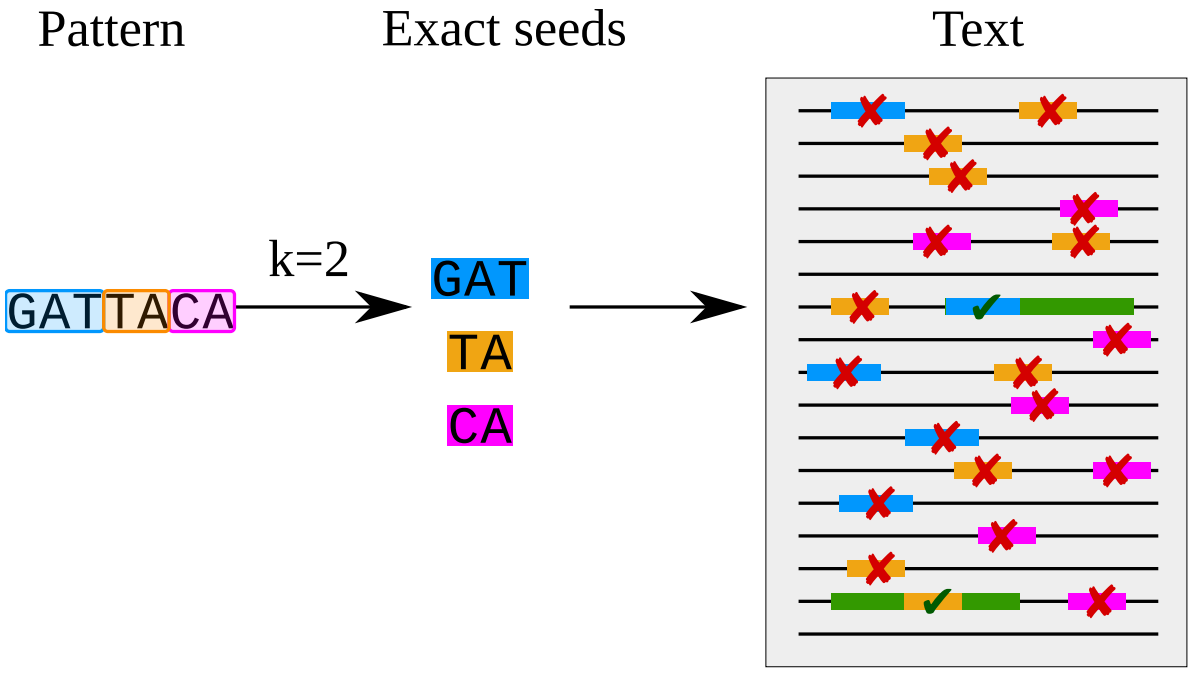
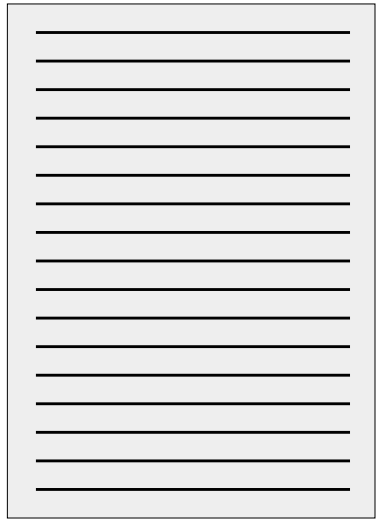


Hybrid Method

Pattern

GATTACA

Text



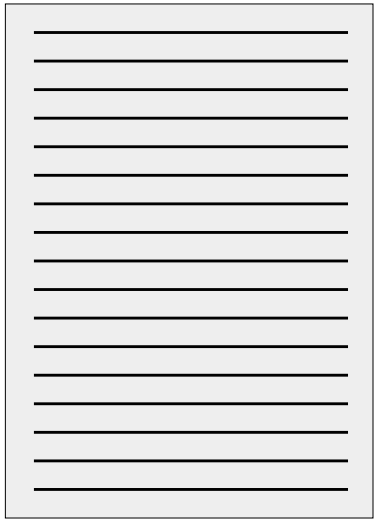
Hybrid Method

Pattern

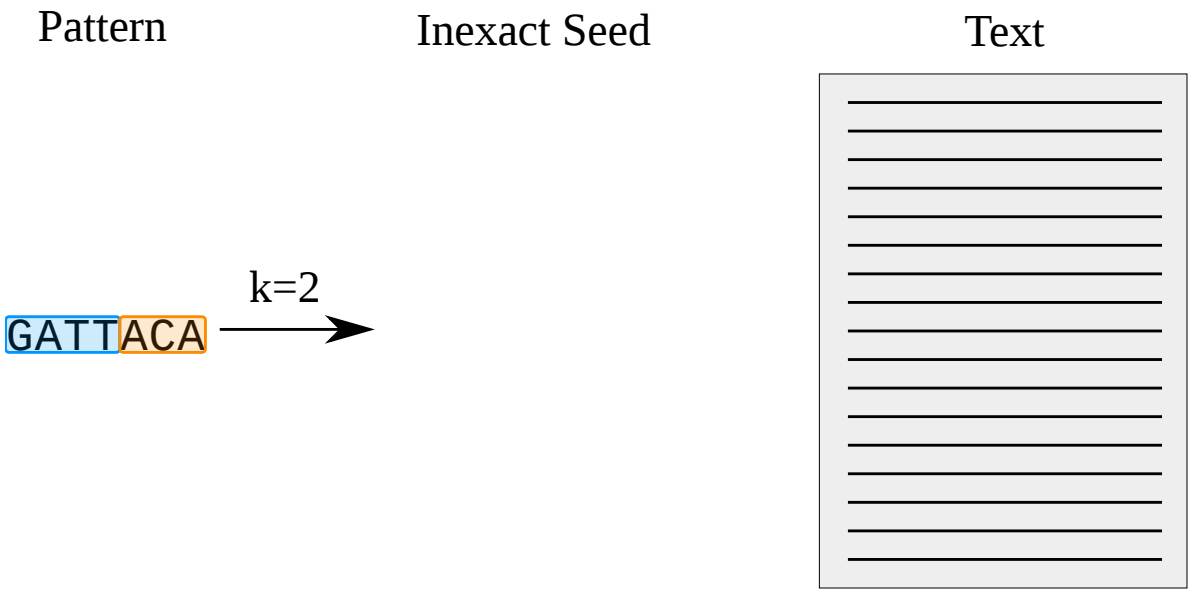
GATTACA

k=2

Text



Hybrid Method



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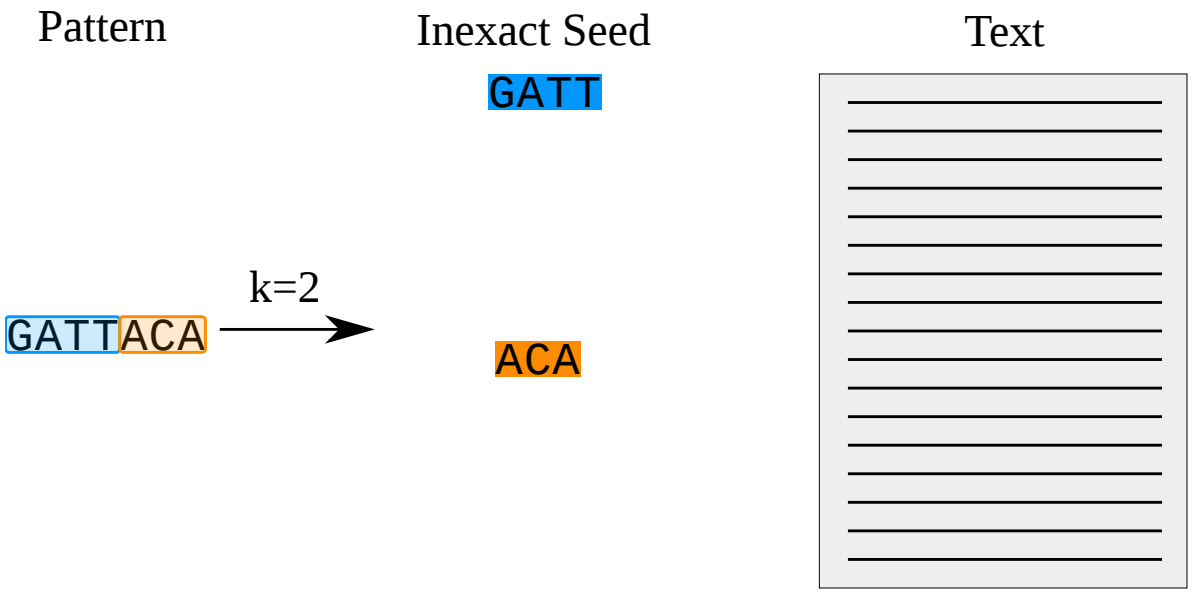

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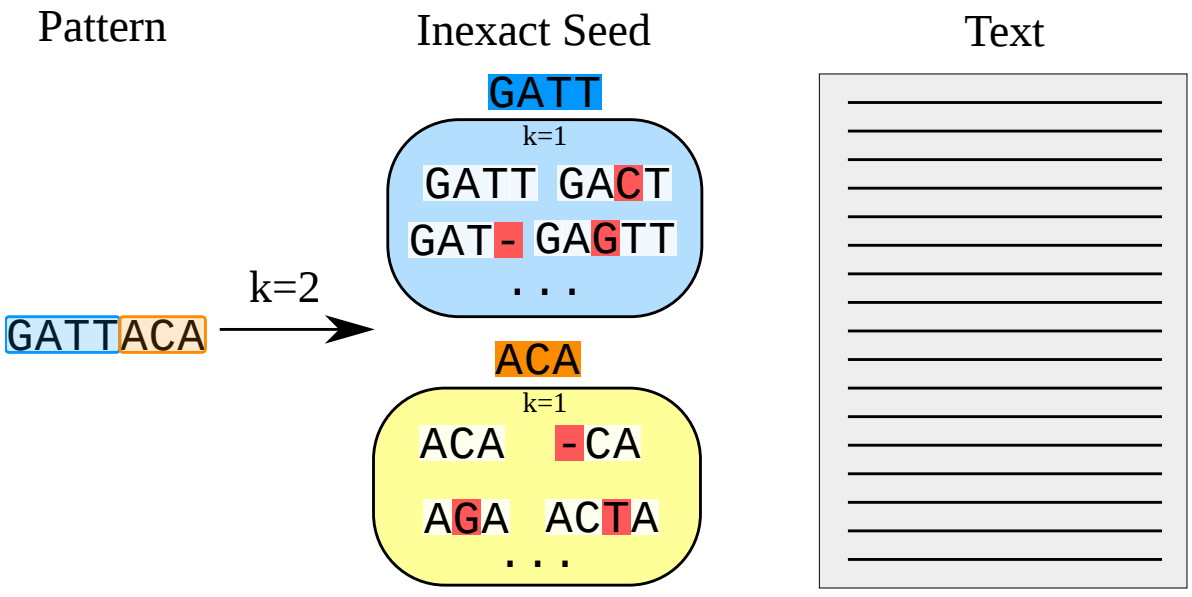

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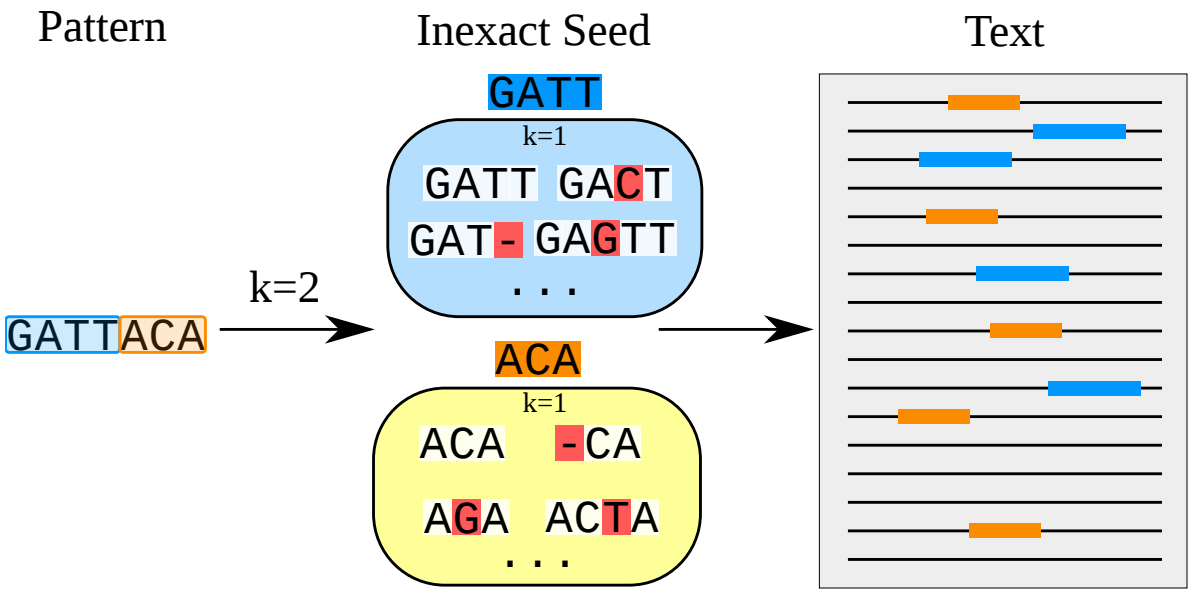

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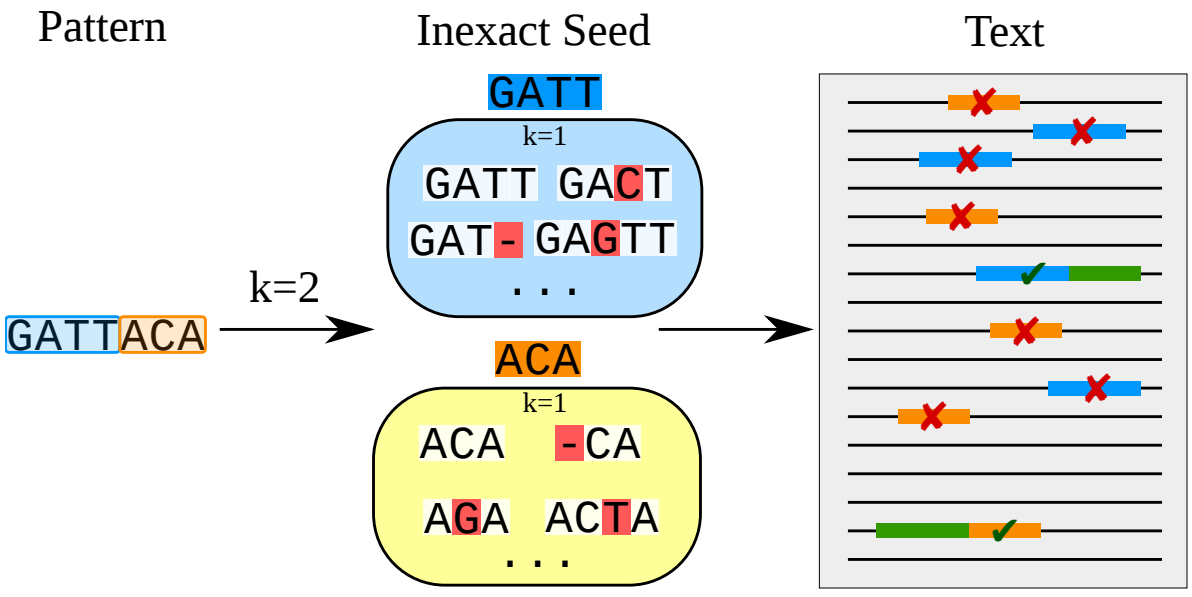

A New Kind of Hybrid Method

A new approximate seed: the 01^*0 seed

Suitable for short patterns and high error rate

$2 \times 4 > 1 \times 5$?

Example: $m = 20$ and $k = 3$

$2 \times 4 > 1 \times 5$?

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4 parts of size 5
1 exact part

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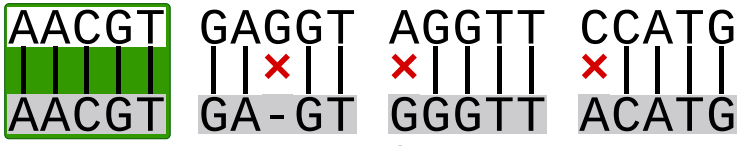

4 parts of size 5
1 exact part

5 parts of size 4
2 exact parts

Distribution of Errors Between Exact Parts

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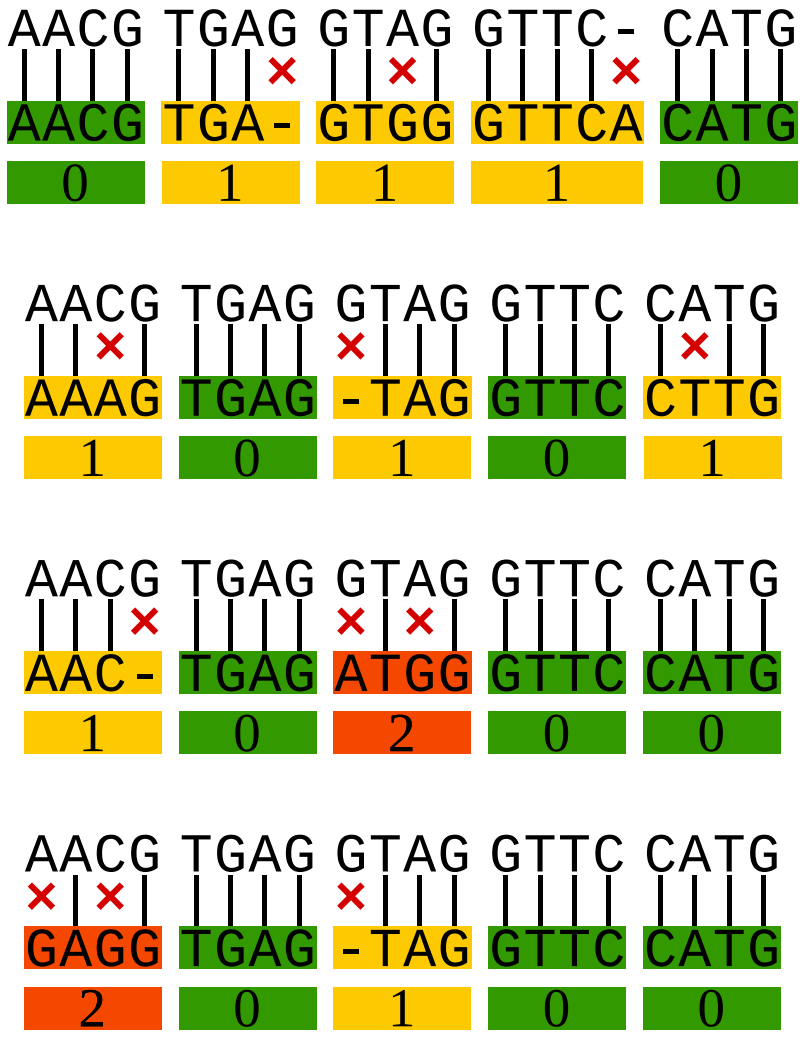

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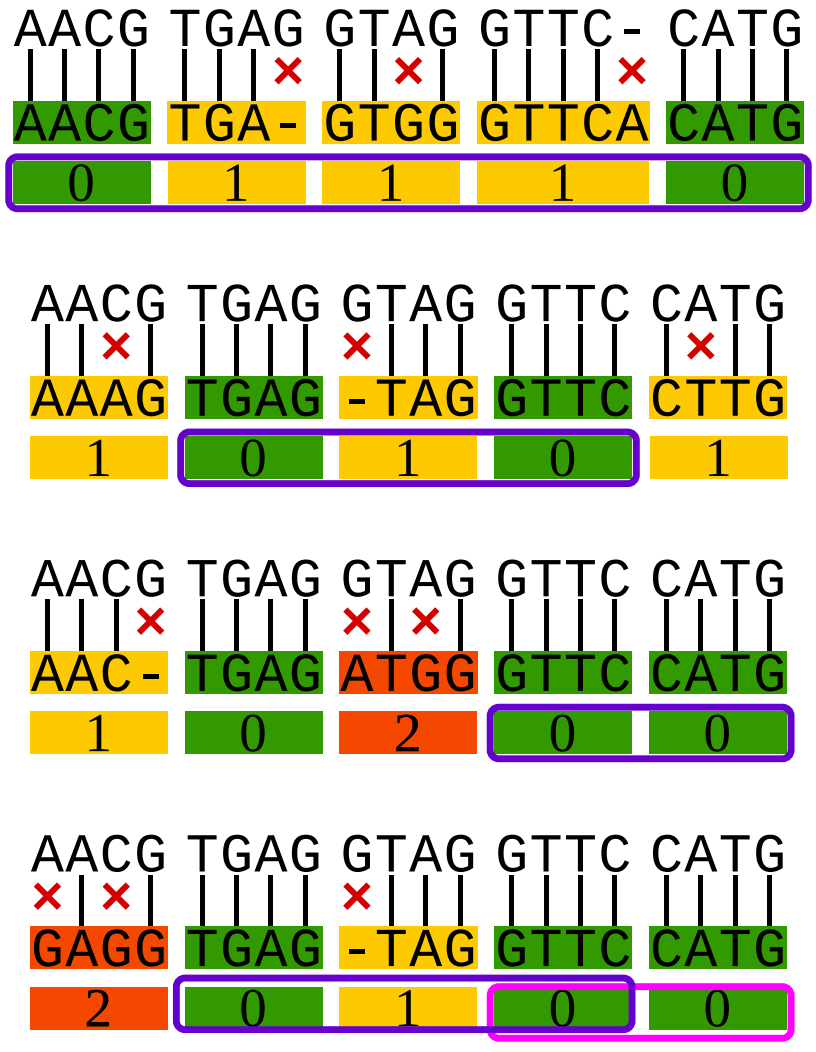

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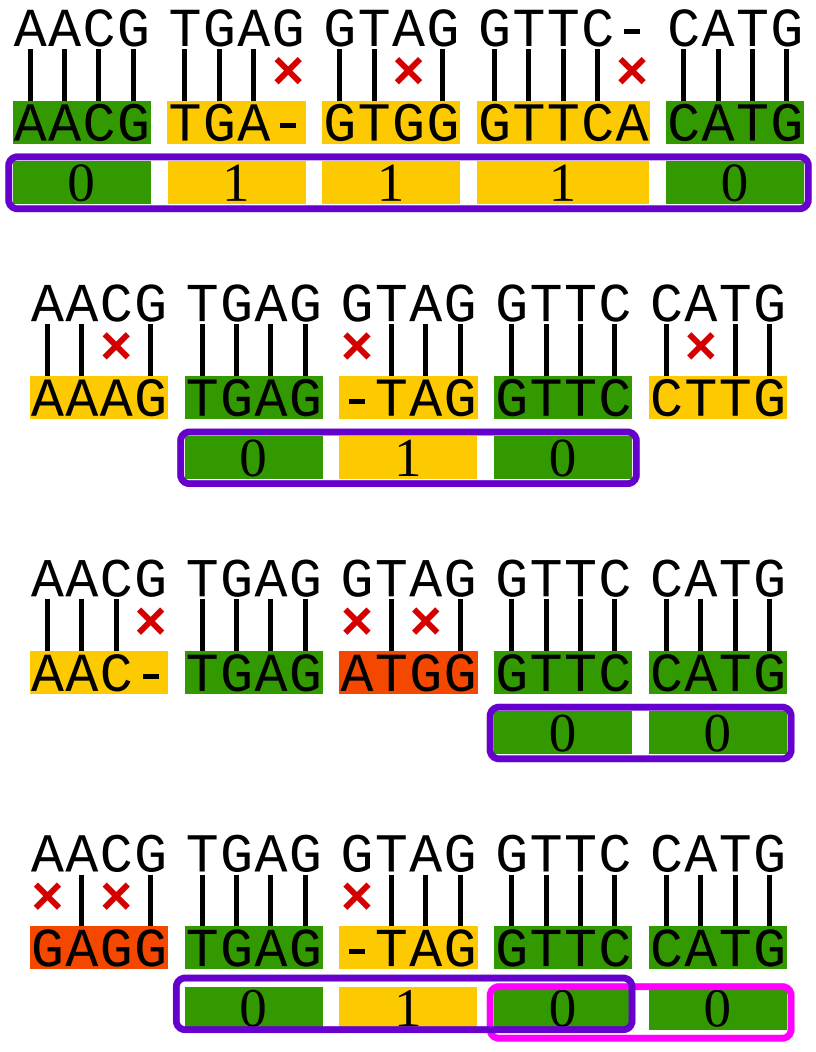
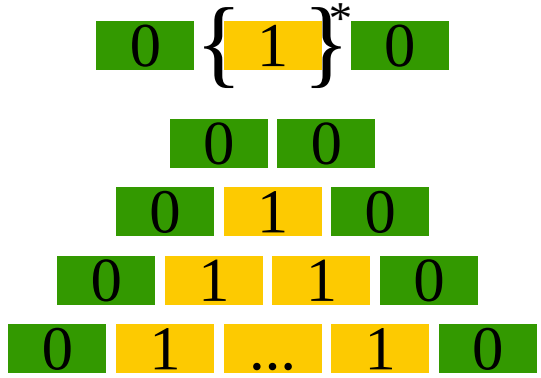


the 01*0 Seed

Definition

A 01*0 seed is a pair of exact parts surrounding 0 or more parts with exactly 1 error.

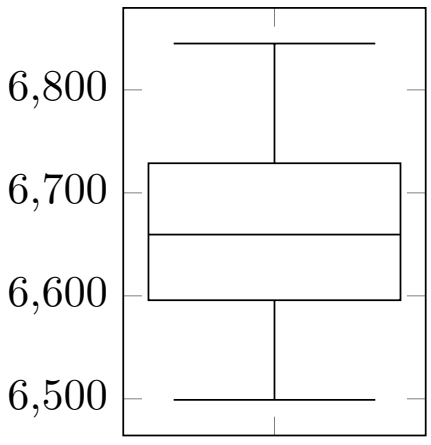


Lemma

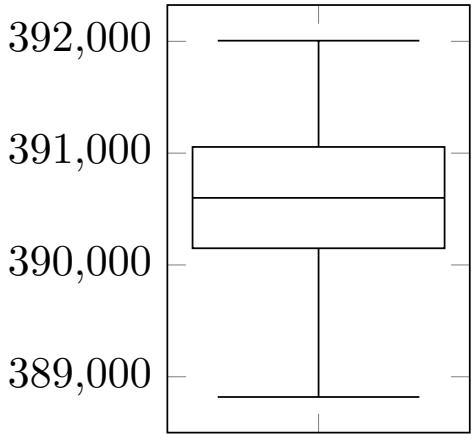
It always exists when the pattern is partitioned in at least $k + 2$ parts.

Good Filtration Efficiency

- larger exact part: 2×4 characters instead of 5 for a classic exact seed filtration
- uniform distribution of errors: 1 error by inner part



01*0 seed



exact seed (5 parts of size 4)

number of candidates per pattern

random DNA strings, 100 patterns, $m = 20$, $k = 3$, $n = 10^8$

Implementation: Bwolo

Indexed text:

- many patterns
- FM-Index

Seeds are generated and searched at the same time in the index

Extension:

1. in the index with a controlled number of errors
2. in the on-line text

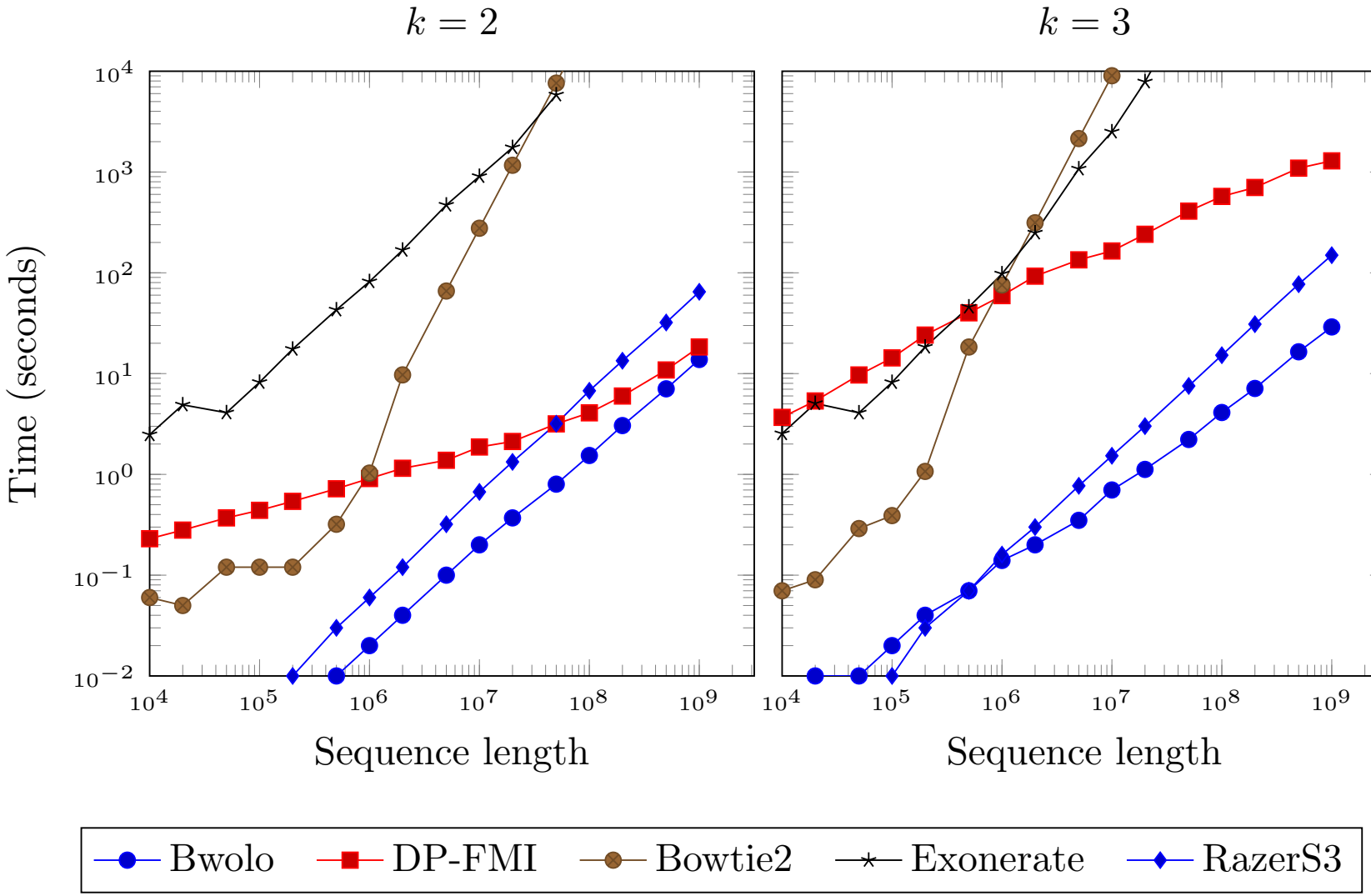
Technically:

- C++
- Seqan library (`www.seqan.de`)

Results – tools

Tool	Index	Method	Detail
Bwolo	FM-Index	Hybrid	01^*0 seeds and extension in index, verification in on-line text
Exonerate	on-line	Neighborhood	Dynamic programming
RazerS3	on-line	Exact Seed	Bit parallel algorithm for the verification step
DP-FMI	FM-Index	Neighborhood	Dynamic programming, in-house implementation
Bowtie2	FM-Index	Exact Seed	Seed filtration in index, verification in on-line text

Bernoulli Sequences



Alphabet: DNA
Text: 10^4 – 10^9 characters

100 patterns of length 20

Simulated Reads on Human Genome

	10,000 Reads		10^7 Reads	
	Time (s)	Memory(Mo)	Time (s)	Memory(Mo)
Bwolo	97	6,522	55,493	9,054
RazerS3	502	6,469	467,413	152,045
Bowtie2	156,164	8,260	-	-

From Schbath *et al.* Journal of Computational Biology (2012).

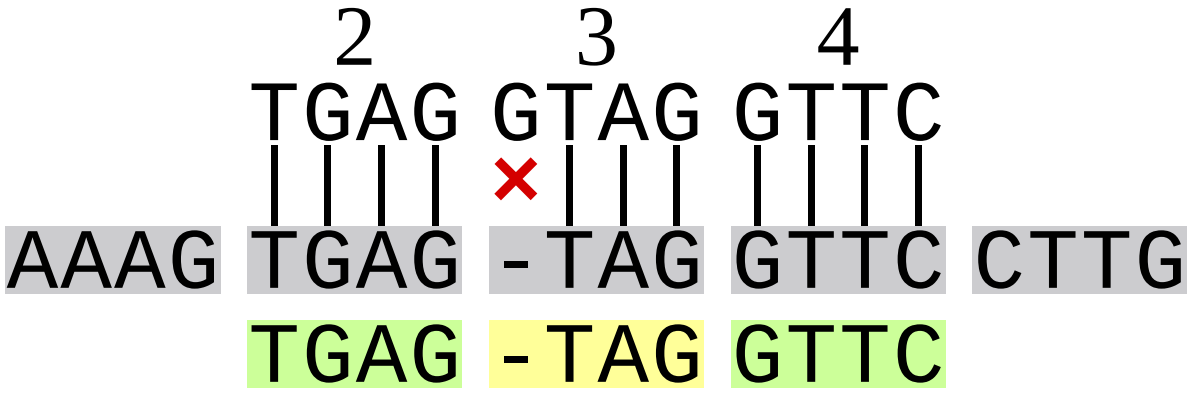
- $n = 2.7 \times 10^9$
- $m = 40$, extracted from the text
- $k = 3$

Conclusion and Perspectives

- New elegant and efficient seeding approach: trade-off between filtration and search time
- Application to approximate pattern matching: `http://bioinfo.lifl.fr/bwolo`
- Average-case time complexity analysis ?
- Many possible evolutions:
  - application in bioinformatics
  - indexed patterns
  - very suitable for bit parallel algorithms
  - homology search, alignment

Merci

Extension of the Seed on One Side

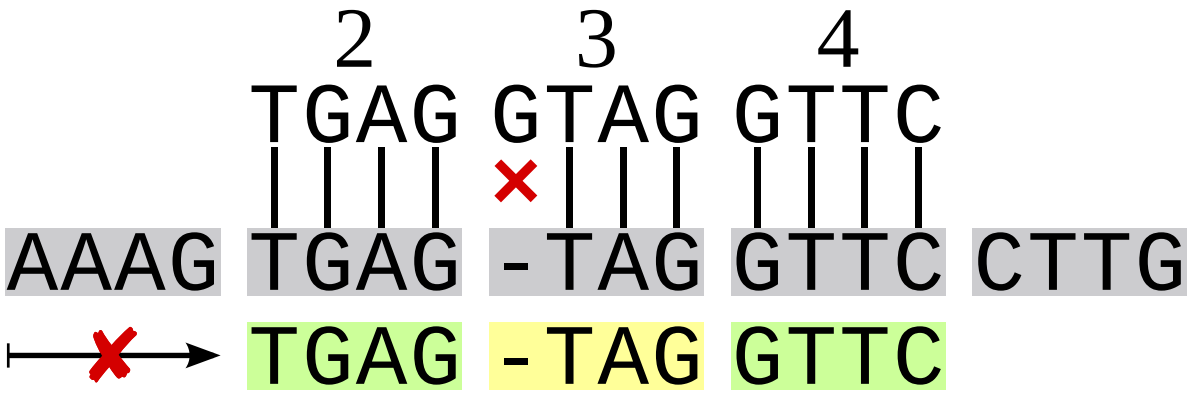


Finding no sub-seed before part 2 means there are errors in previous parts.

Extension on one side (either left or right of the 01^*0 seed) needs only as much error as there are parts on that side.

Extension on one side may be done before verification step.

Extension of the Seed on One Side



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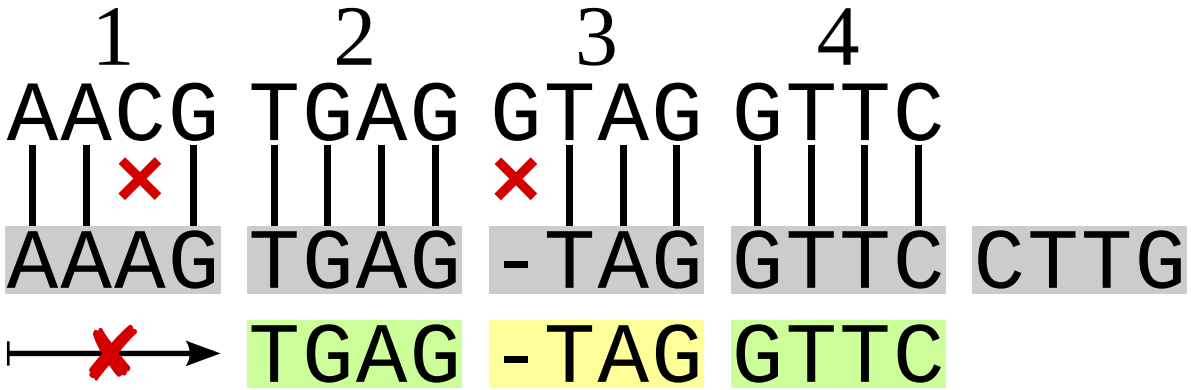

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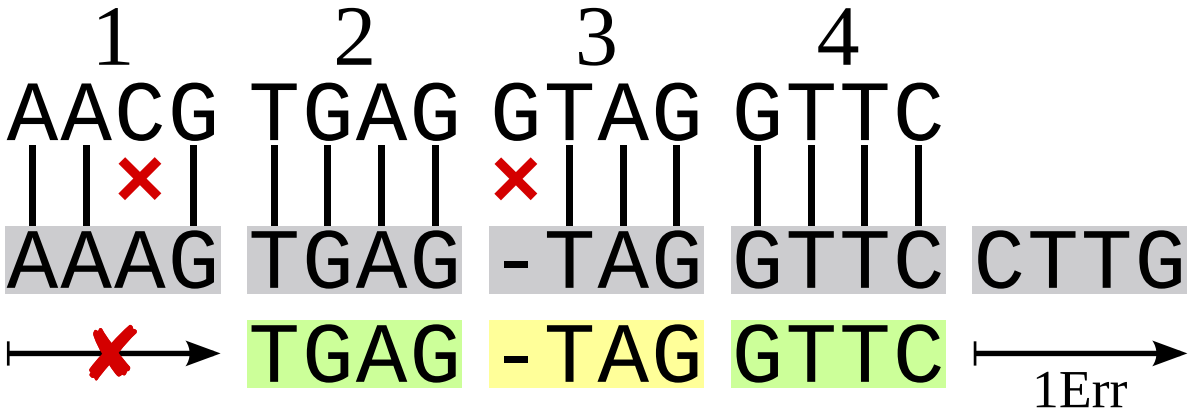

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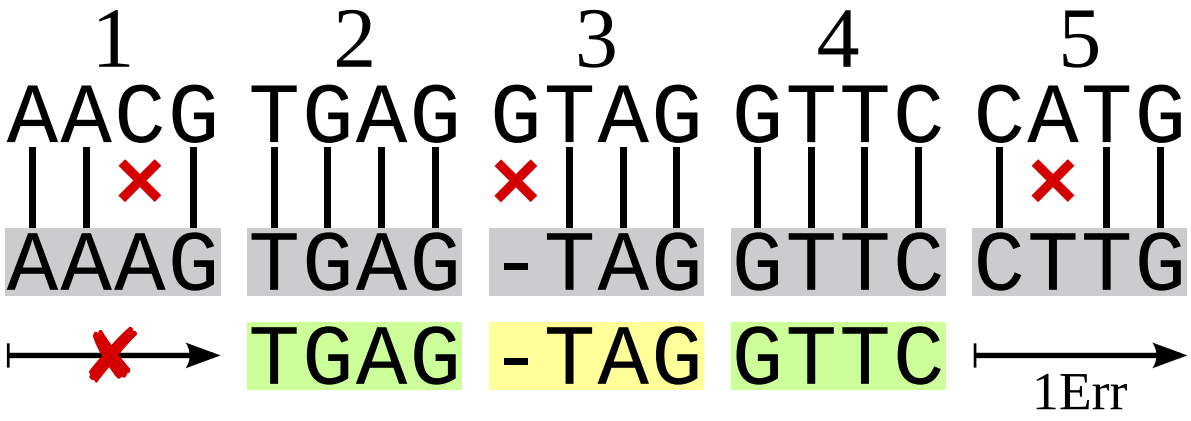

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