Practical fast on-line exact pattern matching algorithms for highly similar sequences

Nadia Ben Nsira Thierry Lecroq Élise Prieur-Gaston

LITIS EA 4108, Normastic FR3638, IRIB, Université de Rouen Normandie, Normandie Université, France

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Big data

- NGS technologies output numerous individual genomes of the same species
- More than 99% similar

Highly similar sequences

- Differ from the reference by: SNVs (SNPs), indels, CNVs, translocations, ...
- Common and non-common parts

Efficient solutions

- Strong need for efficient indexing and pattern matching

Pattern matching

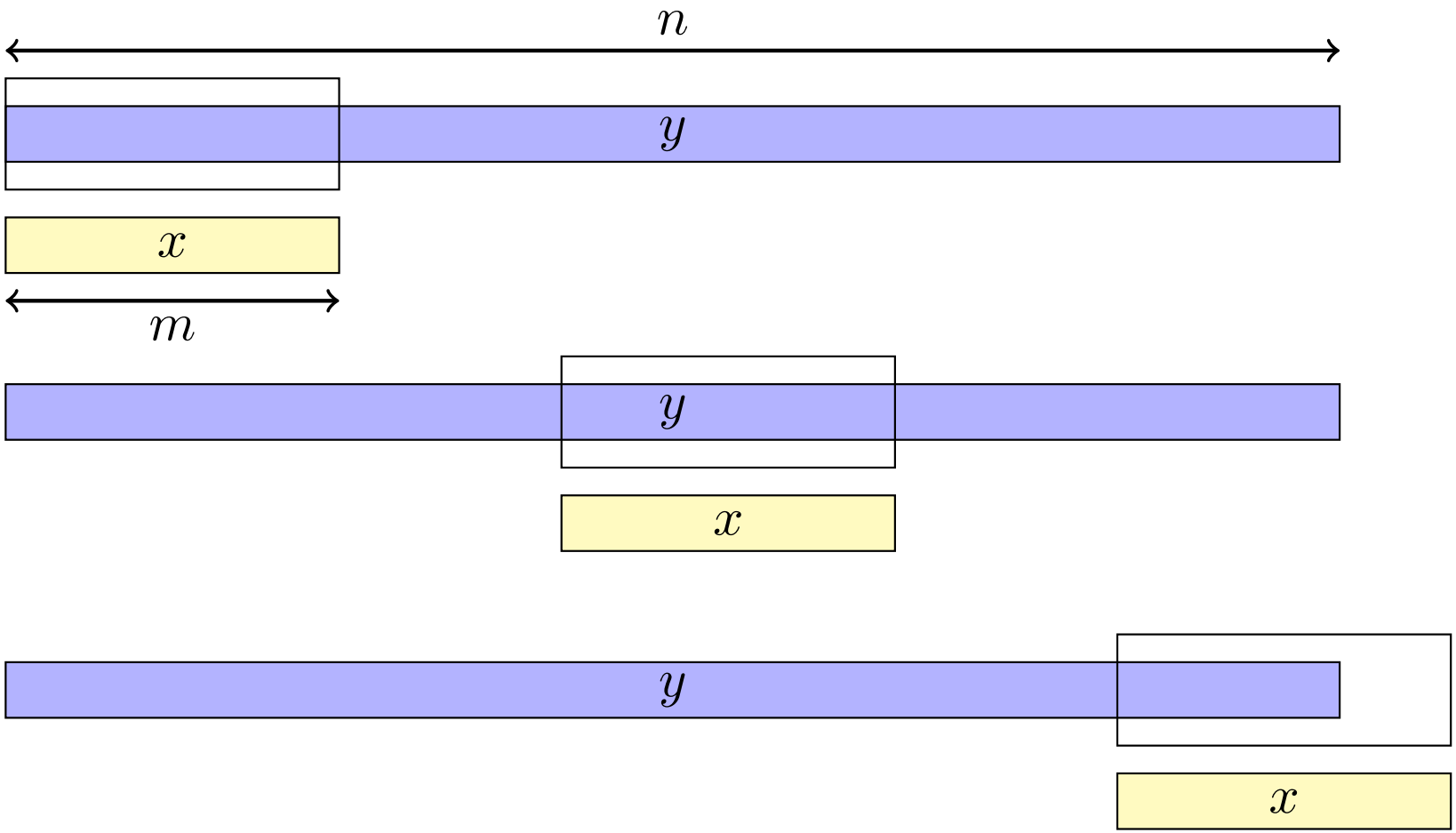
Find one(all the) position(s) of a pattern of length m in a sequence of length n:

- with index $\rightarrow O(m)$
- without index $\rightarrow O(n)$

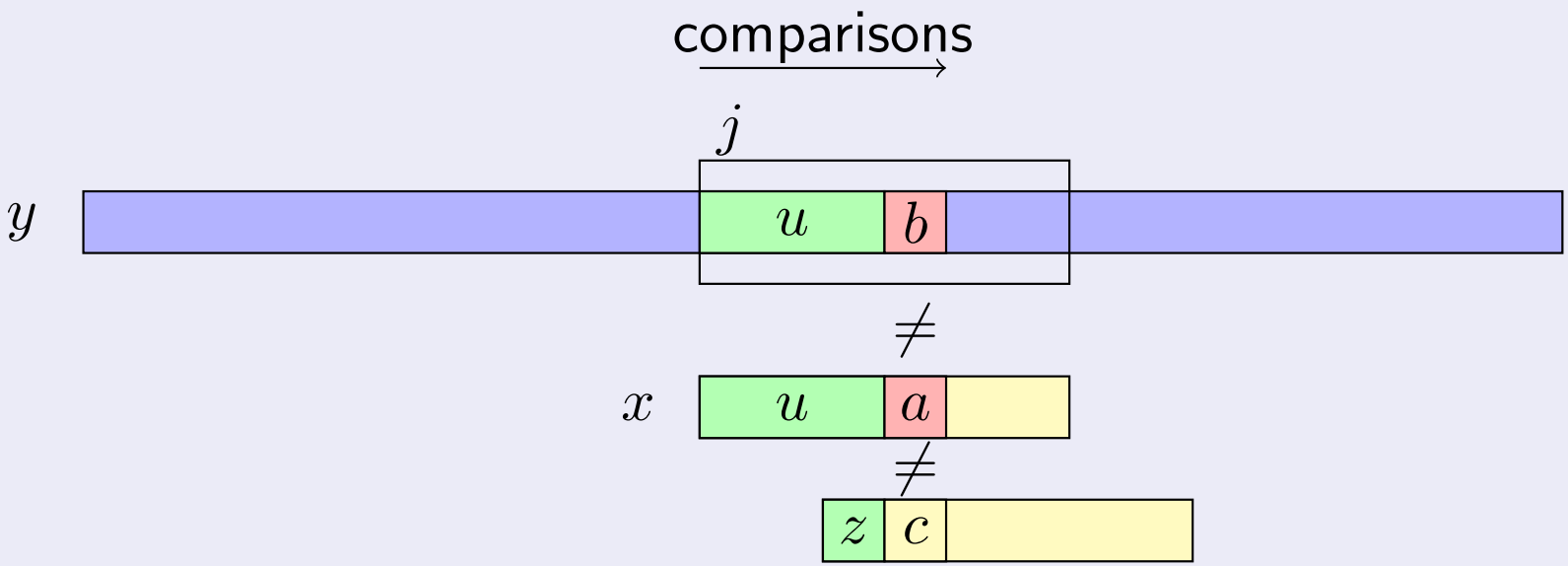
Notations

- finite alphabet Σ
- string $x[0\,..\,m-1]$ on Σ^*
- length $|x| = m$
- $\tilde{x}$ is the reverse of x ($x[m-1]x[m-2]\cdots x[1]x[0]$)
- $x[i\,..\,j]$ is a factor (substring) of x from position i to position j (both inclusive)
- $x[0\,..\,i]$ is a prefix
- $x[i\,..\,m-1]$ is a suffix
- u is a border of x if u is both a prefix and a suffix of x
- *Border*(x) is the longest border of x

Sliding window

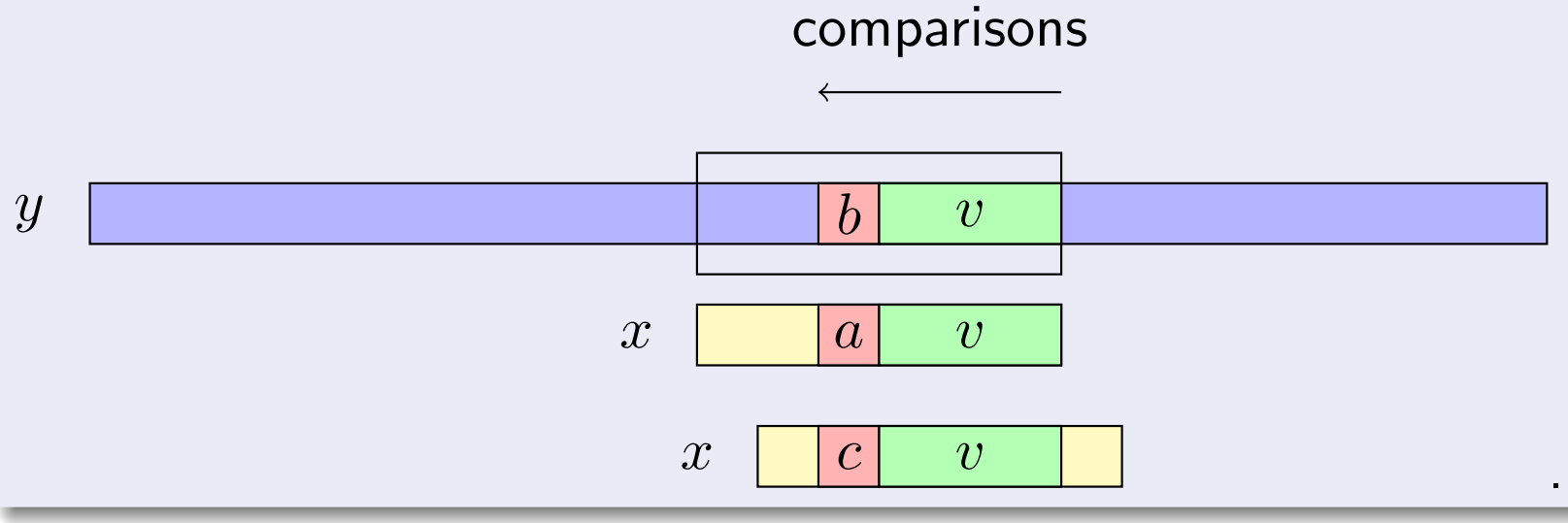


Knuth-Morris-Pratt algorithm (1977)



$k = \min\{\ell \mid x[|Border^{\ell}(u)|] \neq a\}$ and $z = Border^{k}(u)$

Boyer-Moore algorithm (1977)



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2 Search in highly similar sequences

Off-line sith an index

- Huang *et al.* 2010: $O(n + N \log N)$ bits where n is the total length of common parts in one string and N is the total length of non-common parts in all sequences
- Kuruppu *et al.* 2010: Relative Lempel-Ziv index
- Na *et al.* 2018: FM-index of an alignment
- BWBBLE, Huang *et al.* 2013: practical solution

Highly similar sequences

r sequences

	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
y_0	A	T	G	C	T	A	G	C	A	A	G	A	T	A	C	A	G
y_1	A	T	G	C	T	A	G	C	A	A	C	A	T	A	C	A	G
y_2	A	T	G	C	G	A	G	C	A	A	G	A	T	A	C	A	G
y_3	A	T	G	C	T	A	G	C	A	A	C	A	T	A	C	A	T

Highly similar sequences

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	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
y_0	A	T	G	C	T	A	G	C	A	A	G	A	T	A	C	A	G
y_1	A	T	G	C	T	A	G	C	A	A	C	A	T	A	C	A	G
y_2	A	T	G	C	G	A	G	C	A	A	G	A	T	A	C	A	G
y_3	A	T	G	C	T	A	G	C	A	A	C	A	T	A	C	A	T
y	A	T	G	C	{G, T}	A	G	C	A	A	{C, G}	A	T	A	C	A	{G, T}

Highly similar sequences

r sequences

	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
y_0	A	T	G	C	T	A	G	C	A	A	G	A	T	A	C	A	G
y_1	A	T	G	C	T	A	G	C	A	A	C	A	T	A	C	A	G
y_2	A	T	G	C	G	A	G	C	A	A	G	A	T	A	C	A	G
y_3	A	T	G	C	T	A	G	C	A	A	C	A	T	A	C	A	T
y	A	T	G	C	{G, T}	A	G	C	A	A	{C, G}	A	T	A	C	A	{G, T}
					G	A	G	C	A	A	C						

Highly similar sequences

r sequences

	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
y_0	A	T	G	C	T	A	G	C	A	A	G	A	T	A	C	A	G
y_1	A	T	G	C	T	A	G	C	A	A	C	A	T	A	C	A	G
y_2	A	T	G	C	G	A	G	C	A	A	G	A	T	A	C	A	G
y_3	A	T	G	C	T	A	G	C	A	A	C	A	T	A	C	A	T
y	A	T	G	C	{G, T}	A	G	C	A	A	{C, G}	A	T	A	C	A	{G, T}
					G	A	G	C	A	A	C						

R. Grossi, C. S. Iliopoulos, C. Liu, N. Pisanti, S. P. Pissis, A. Retha, G. Rosone, F. Vayani, L. Versari

On-Line Pattern Matching on Similar Texts

28th Combinatorial Pattern Matching (CPM), Warsaw, Poland (2017) 9:1–9:14

Highly similar sequences

r sequences

	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
y_0	A	T	G	C	T	A	G	C	A	A	G	A	T	A	C	A	G
y_1	A	T	G	C	T	A	G	C	A	A	C	A	T	A	C	A	G
y_2	A	T	G	C	G	A	G	C	A	A	G	A	T	A	C	A	G
y_3	A	T	G	C	T	A	G	C	A	A	C	A	T	A	C	A	T

$$y_0 \text{ et } Z = ((\{2\}, 4, \mathtt{G}), (\{1, 3\}, 10, \mathtt{C}), (\{3\}), 16, \mathtt{T})$$

For highly similar sequences

Hamming distance

For $u, v \in A^*$ such that $|u| = |v|$:

$$\mathit{Ham}(u, v) = \sharp\{i \mid u[i] \neq v[i]\}$$

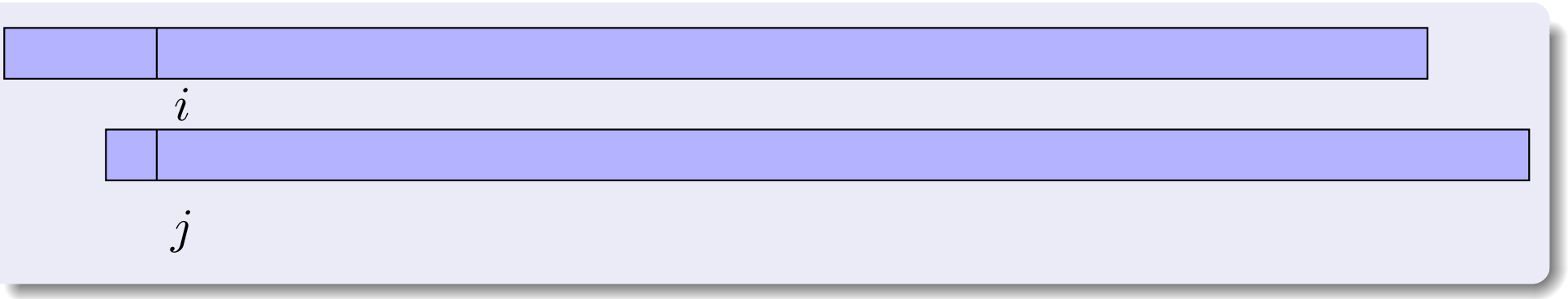
Longest Common Extension

For $x \in A^*$ and $0 \leq i \leq j \leq |x| - 1$:

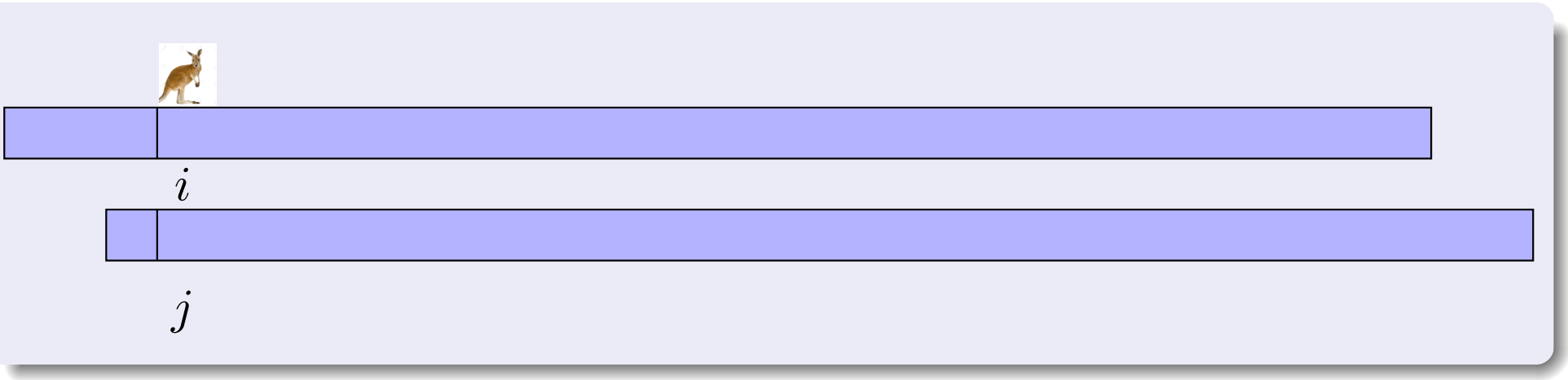
$$LCE_x^k(i, j) = \max\{\ell \mid \mathit{Ham}(x[i \,..\, i + \ell - 1], x[j \,..\, j + \ell - 1]) \leq k\}$$

Kangaroo jumps

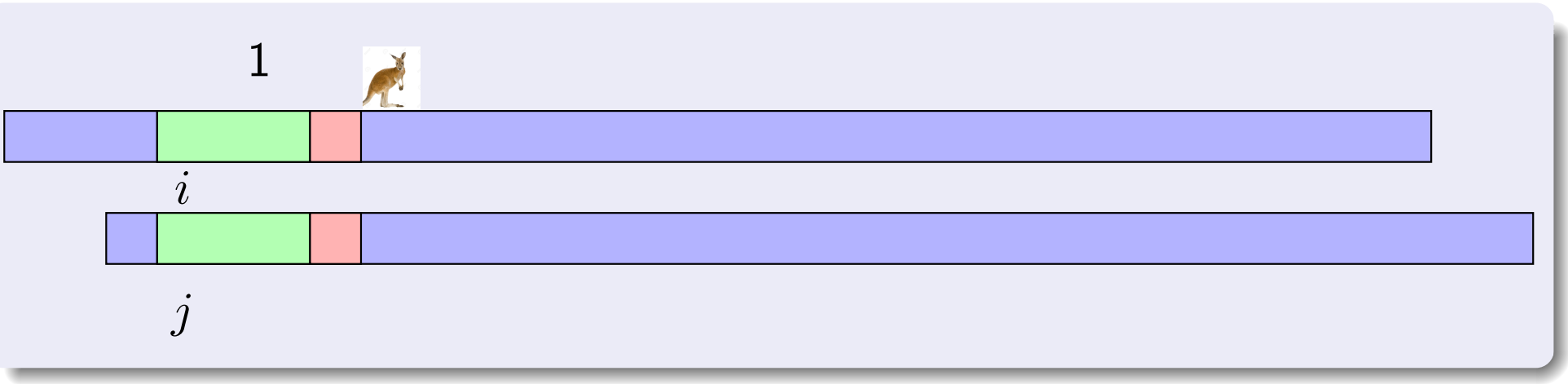
Kangaroo jumps



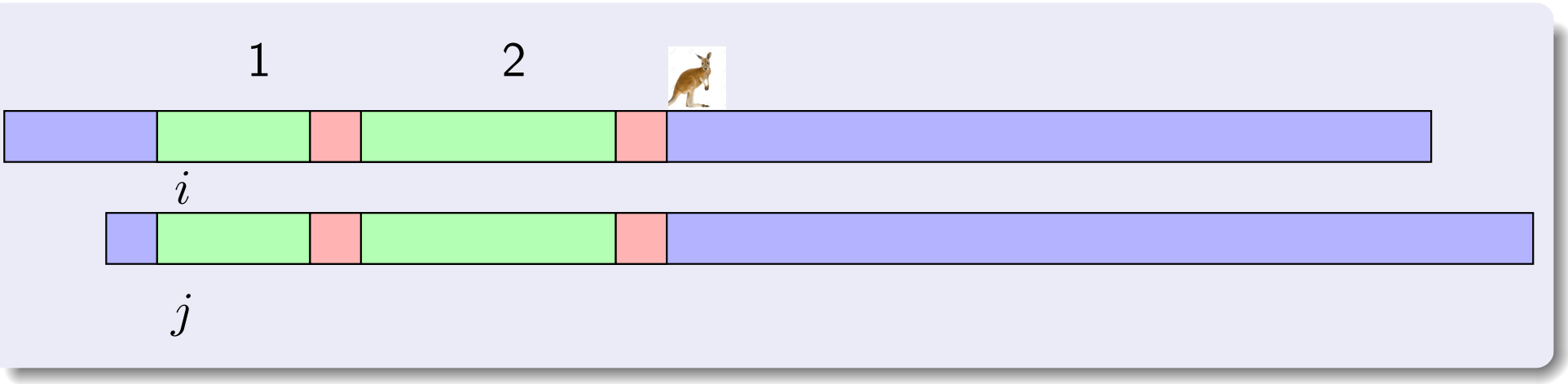
Kangaroo jumps



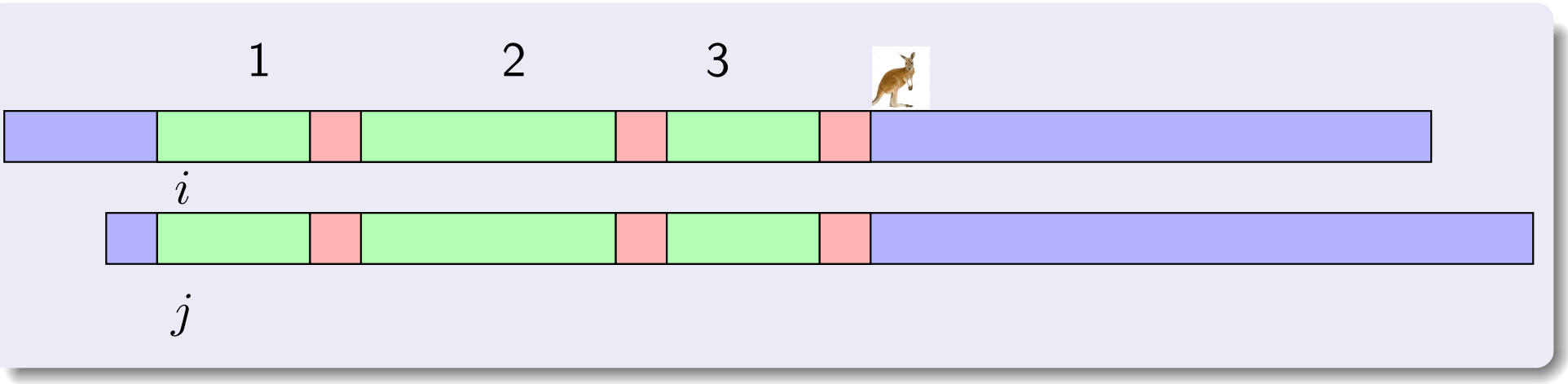
Kangaroo jumps



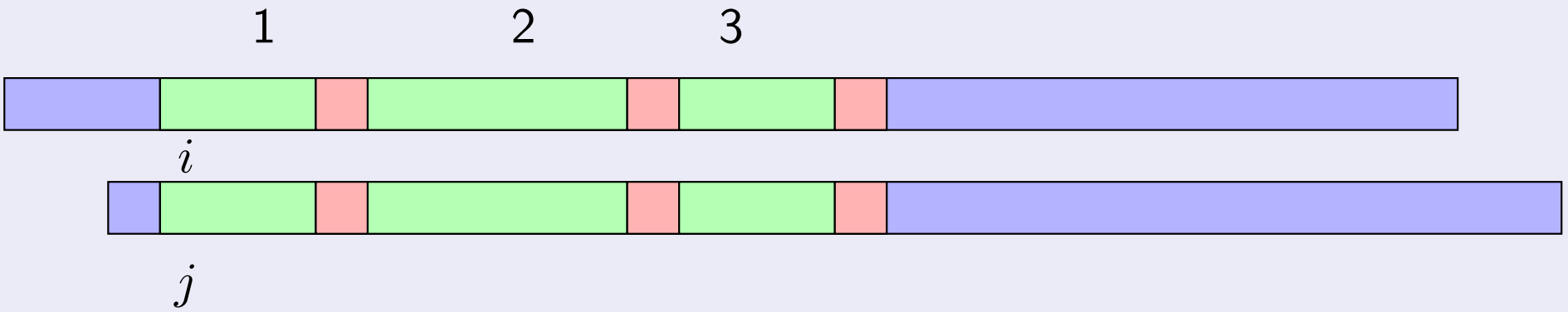
Kangaroo jumps



Kangaroo jumps



Kangaroo jumps



$LCE_x^k(i,j)$ can be computed in $O(k)$ time after $O(n)$ preprocessing time

References

Restriction: 1 variation on a window of size m

Adaptations of KMP and BM without LCE by adapting the shift functions

N. Ben Nsira, T. Lecroq and M. Elloumi

A fast Boyer-Moore type pattern matching algorithm for highly similar sequences

International Journal of Data Mining and Bioinformatics **13**(3) (2015) 266-288

N. Ben Nsira, T. Lecroq and M. Elloumi

On-line String Matching in Highly Similar DNA Sequences

Mathematics in Computer Science **11**(2) (2017) 113–126

2 variants

- relaxing the restriction from 1 to k variations in a window of size m
- searching for a finite set of patterns (still with 1 variation in a window of size m

Single pattern with at most k variations

Applying the Landau-Vishkin algorithm as a filter

Searching with k mismatches in $O(kn)$
When $\mathit{Ham}(x, y_0[j \,..\, j+\ell-1]) = \ell \leq k$

- $\ell = 0$: an exact occurrence of the pattern has been found in y_0 and all the other sequence that do not have a variation comparing to y_0 between position j and position $j + m - 1$ both included.
- $\ell > 0$: let $W = \{i_0, \ldots, i_{\ell-1}\}$ be the set of the ℓ positions such that $y_0[j + i_p] \neq x[i_p]$ with $0 \leq p < \ell$. Then x occurs exactly in y_h if:
  - $(\mathcal{G}, j + i_p, x[i_p]) \in Z$ with $g \in \mathcal{G}$ for all $0 \leq p < \ell$;
  - $\nexists\, (\mathcal{G}, h, c) \in Z$ such that $h \notin W$.

Single pattern with at most k variations

$r = 2$ and $k = 2$

	0	1	2	3	4	5	6	7	8	9	10	
y_0	A	C	C	T	A	C	G	A	C	T	A	
x			C	T	A	C	T	T				$j = 2$ and $W = (4, 5)$
x						C	T	A	C	T	T	$j = 5$ and $W = (1, 5)$
y_1	A	C	C	T	A	C	T	A	C	T	T	$Z = (((\{1\}, 6, \mathtt{T}), (\{1\}, 10, \mathtt{T}))$

Single pattern with at most k variations

$r = 2$ and $k = 2$

	0	1	2	3	4	5	6	7	8	9	10	
y_0	A	C	C	T	A	C	G	A	C	T	A	
x			C	T	A	C	T	T				$j = 2$ and $W = (4, 5)$
x						C	T	A	C	T	T	$j = 5$ and $W = (1, 5)$
y_1	A	C	C	T	A	C	T	A	C	T	T	$Z = (((\{1\}, 6, \mathtt{T}), (\{1\}, 10, \mathtt{T}))$

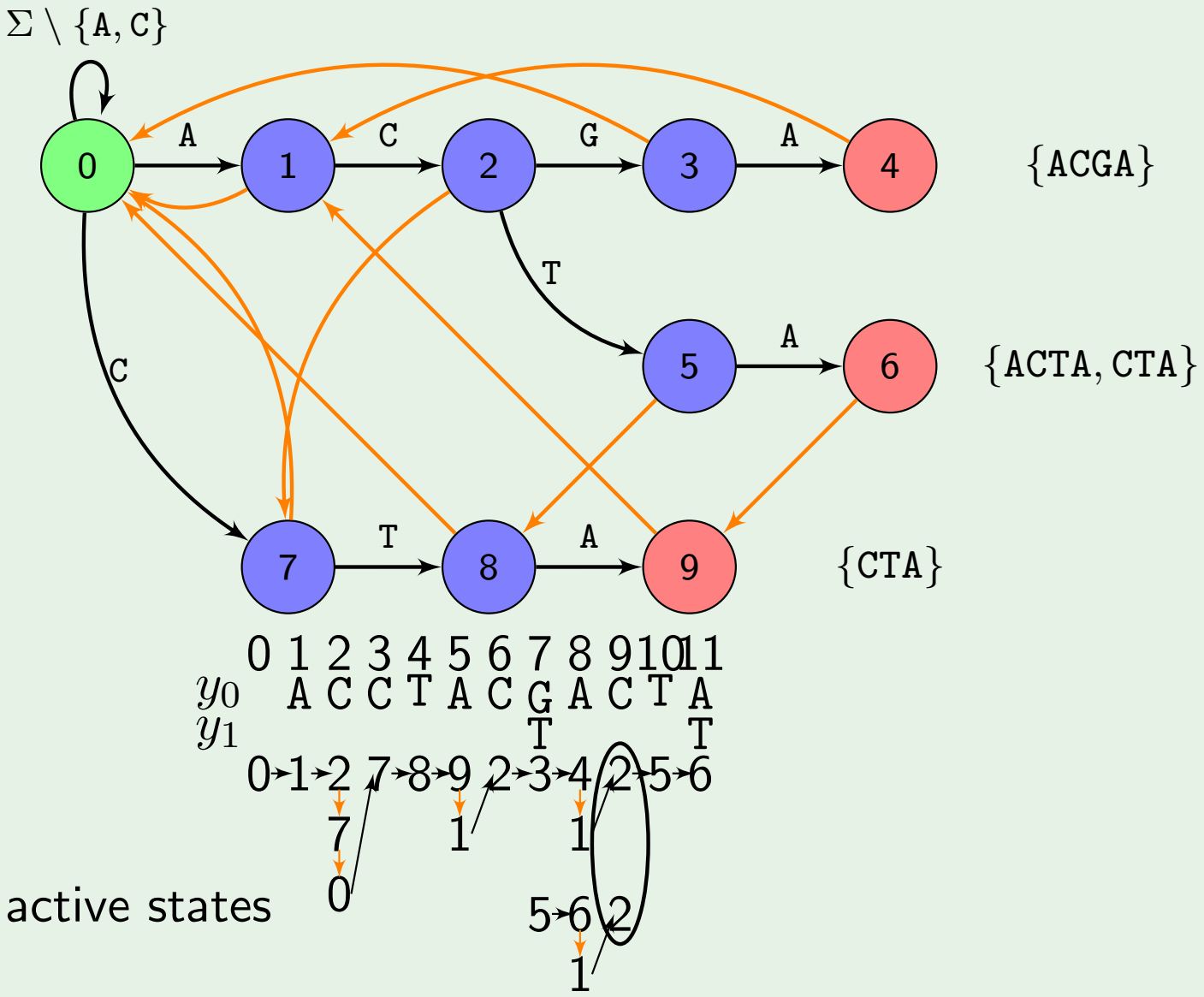
Our solution runs in time $O(knr)$

Multiple patterns with at most 1 variation

- Build a classical trie of the patterns
- Scan the highly similar sequences with at most 2 active states

Multiple patterns with at most 1 variation

$X = \{\texttt{ACGA}, \texttt{ACTA}, \texttt{CTA}\}$ and $r = 2$ sequences

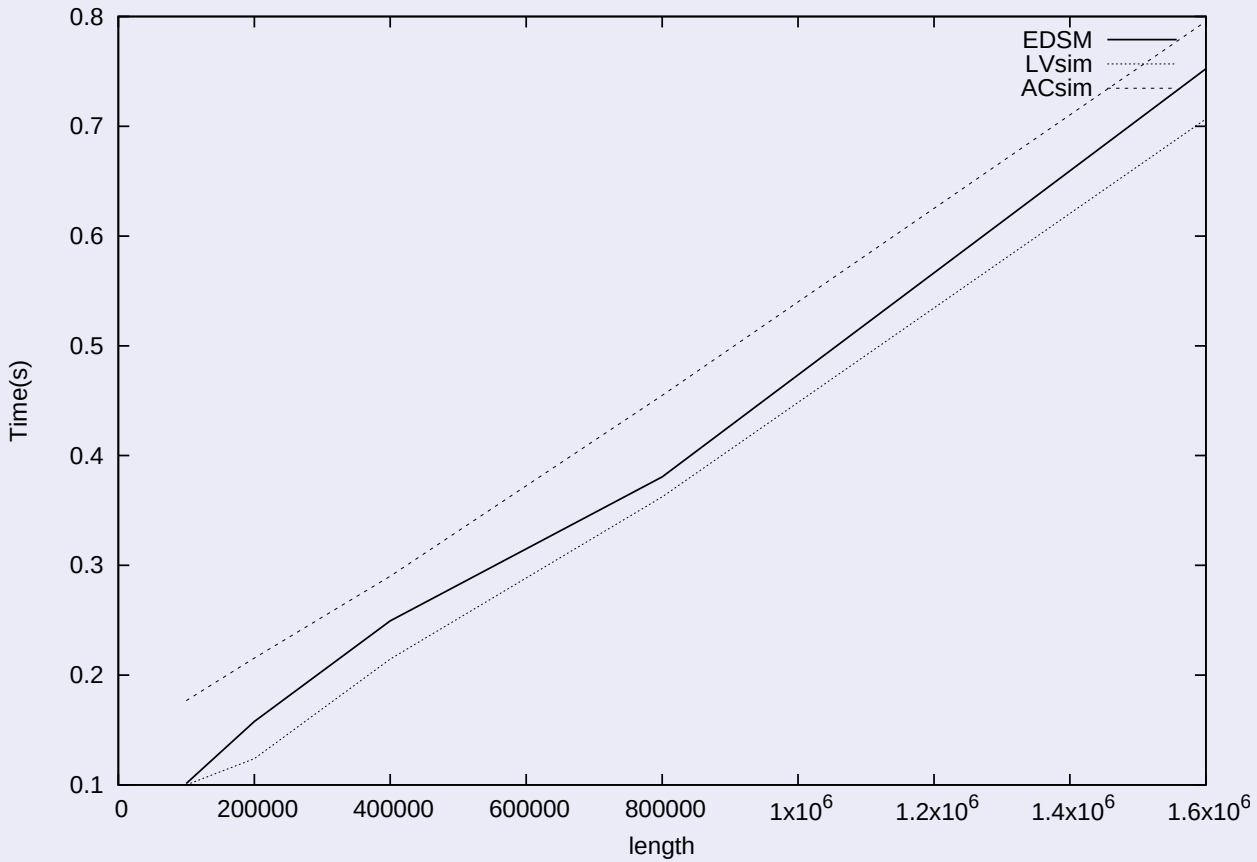


Multiple patterns with at most 1 variation

Our solution runs in time $O(n)$ for the searching phase and in time $O(s)$ for the preprocessing phase where $s = \sum |x|$ for all $x \in X$

Experiments

Similar sequences of different lengths with patterns of length 16



Perspectives

- Do more experiments
- Adapt other pattern matching techniques
- Relax the restrictions
- Adaptive analysis

Thank you for your attention!