String Algorithms and Data Structures

Approximate Pattern Matching

CS 199-225

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Learning Objectives

Review exact pattern matching and introduce approximate matching

Formally define a mismatch vs an edit

Discuss strategies for efficient approximate pattern matching…

… With mismatches

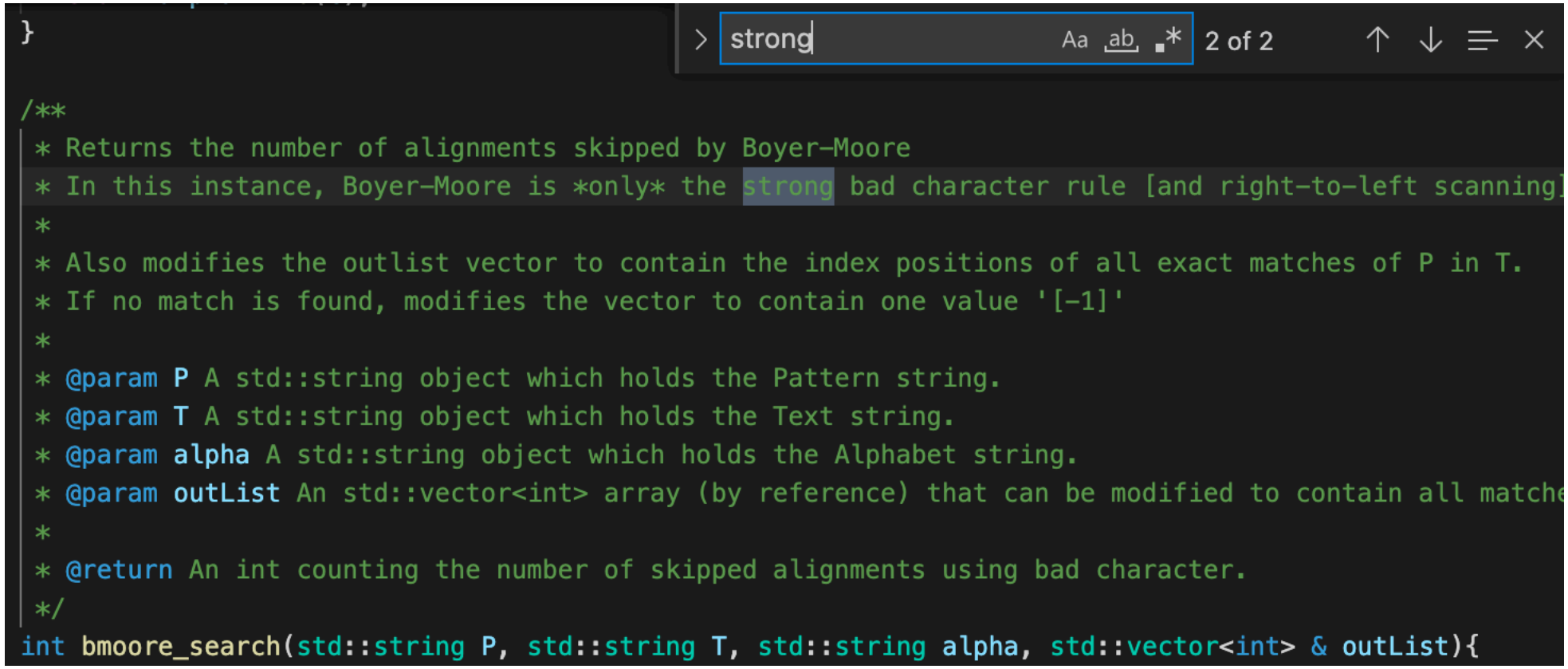
… With edits

Suffix-Based Index Review

	Suffix tree	**Suffix array**	**FM Index**
Time: Does P occur?	$O(n)$	$O(n \log m)$	$O(n)$
Time: Count k occurrences of P	$O(n + k)$	$O(n \log m)$	$O(n)$
Time: Report k locations of P	$O(n + k)$	$O(n \log m + k)$	$O(n + k)$
Space	$O(m)$	$O(m)$	$O(m)$
Needs T?	*yes*	*yes*	*no*
Bytes per input character	>15	~4	~0.5

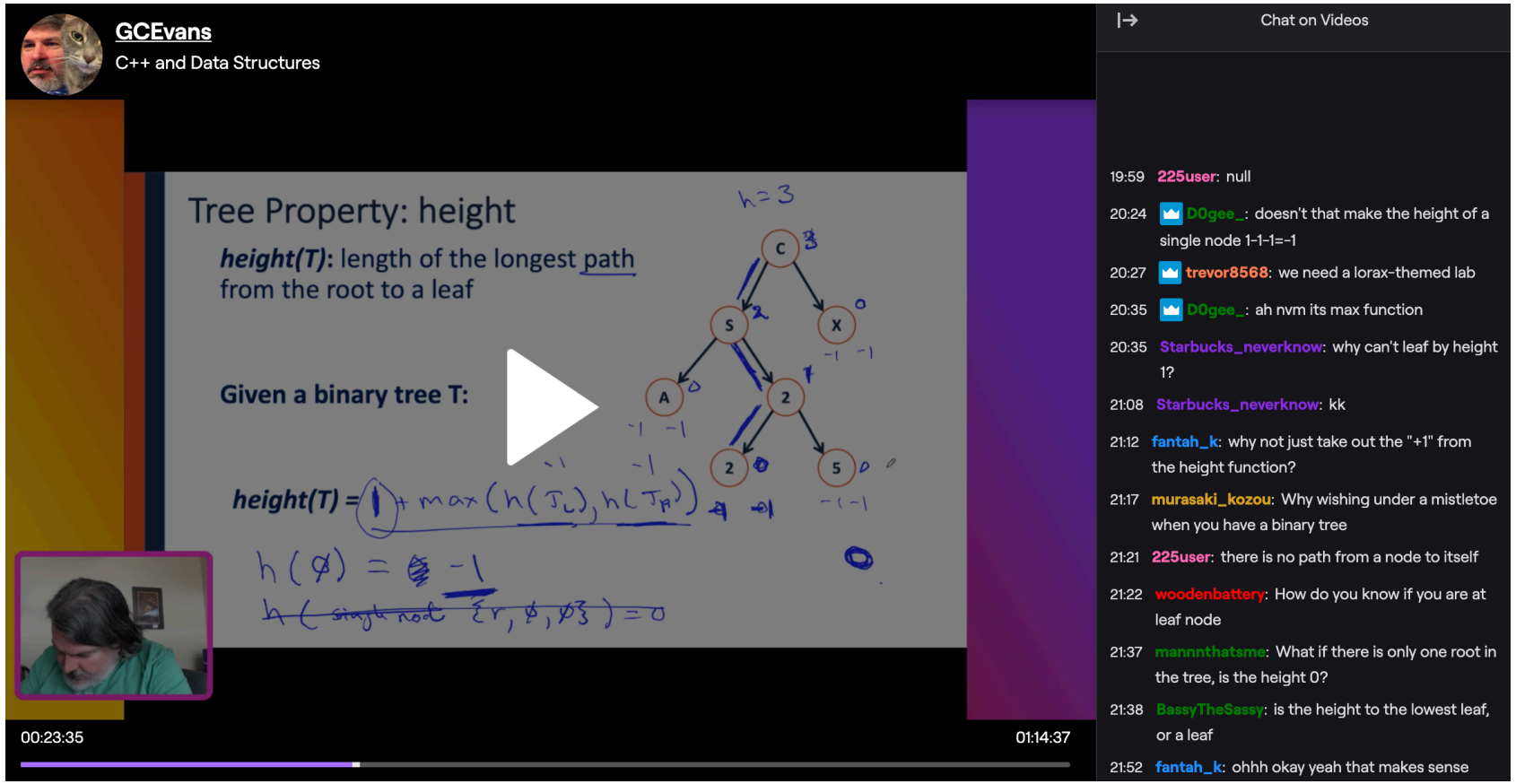
$m = |T|, n = |P|, k =$ # occurrences of P in T

Limitations of exact pattern matching



But what if I was actually trying to look up ‘string’?

Limitations of exact pattern matching



If I ban “bad word”, what happens to “b@d w0rd”?

Approximate Pattern Matching

de bruwn graph

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About 429,000 results (0.59 seconds)

Showing results for de ***bruijn*** graph
Search instead for de bruwn graph

Scholarly articles for **de bruijn graph**

IDBA–a practical iterative **de Bruijn graph de** novo ... - Peng - Cited by 269

... metagenomics assembly via succinct **de Bruijn graph** - Li - Cited by 1244

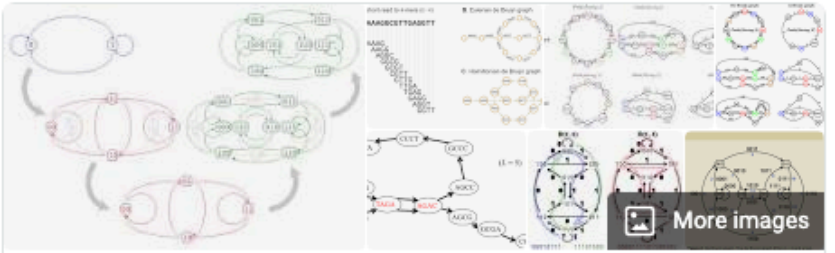
Space-efficient and exact **de Bruijn graph** ... - Chikhi - Cited by 245

en.wikipedia.org › wiki › De_Bruijn_graph

De Bruijn graph - Wikipedia

In **graph** theory, an n-dimensional **De Bruijn graph** of m symbols is a directed **graph** representing overlaps between sequences of symbols. It has m^n vertices, consisting of all possible length-n sequences of the given symbols; the same symbol may appear multiple times in a sequence.

Properties · Dynamical systems



De Bruijn graph

In graph theory, an n-dimensional De Bruijn graph of m symbols is a directed graph representing overlaps between sequences of symbols. It has m^n vertices, consisting of all possible length-n sequences of the given symbols; the same symbol may appear multiple times in a sequence. Wikipedia

Approximate Pattern Matching

```
Score =  248 bits (129), Expect = 1e-63
Identities = 213/263 (80%), Gaps = 34/263 (12%)
Strand = Plus / Plus

Query: 161 atatcaccacgtcaaaggtgactccaactcca---ccactccattttgttcagataatgc 217
           ||||||||||||||||||||||||||||  |     | |   || ||||||||||||||
Sbjct: 481 atatcaccacgtcaaaggtgactccaact-tattgatagtgttttatgttcagataatgc 539

Query: 218 ccgatgatcatgtcatgcagctccaccgattgtgagaacgacagcgacttccgtcccagc 277
           |||||||   ||||||||||||||||||| || |           ||||||||||||
Sbjct: 540 ccgatgactttgtcatgcagctccaccgattttg-g-----------ttccgtcccagc 586

Query: 278 c-gtgcc--aggtgctgcctcagattcaggttatgccgctcaattcgctgcgtatatcgc 334
           |  || |  | ||||||||||||||||||||||||||||||||||||| |||||||||
Sbjct: 587 caatgacgta-gtgctgcctcagattcaggttatgccgctcaattcgctgggtatatcgc 645

Query: 335 ttgctgattacgtgcagctttcccttcaggcggga-----------ccagccatccgtc 382
           ||||||||||||||||||||||||||||||||||           ||||||||||||
Sbjct: 646 ttgctgattacgtgcagctttcccttcaggcgggattcatacagcggccagccatccgtc 705

Query: 383 ctccatatc-accacgtcaaagg 404
            |||||||| ||||||||||||
Sbjct: 706 atccatatcaaccacgtcaaagg 728
```

Approximate Pattern Matching

Input: A text *T*, a pattern *P*, and a distance *d*

Output: All positions in *T* where *P* has at most *d* mismatches or edits

P: word

T: There would have been a time for such a word

Alignment 1:
```
would
word
```

~~Not a match!~~

Distance 2 match!

Alignment 2:
```
word
word
```

Match!

Distance 0 match!

Approximate Pattern Matching

What is the distance between these two strings?

X: `10011`

Y: `00110`

Approximate Pattern Matching

What is the distance between these two strings?

X: 1 0 0 1 1

Y: 0 0 1 1 0

```
X: 1 0 0 1 1
     |   |
Y: 0 0 1 1 0
```

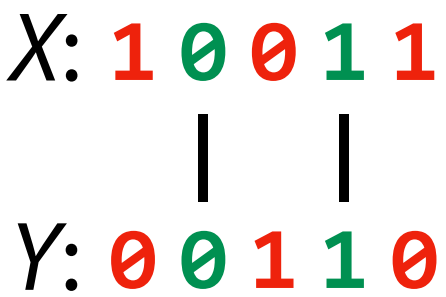
Hamming distance is 3!

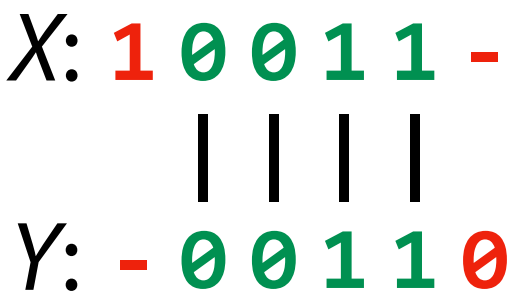
```
X: 1 0 0 1 1 -
     | | | |
Y: - 0 0 1 1 0
```

Edit distance is 2!

Approximate Pattern Matching

How can I describe the relationship between two strings?

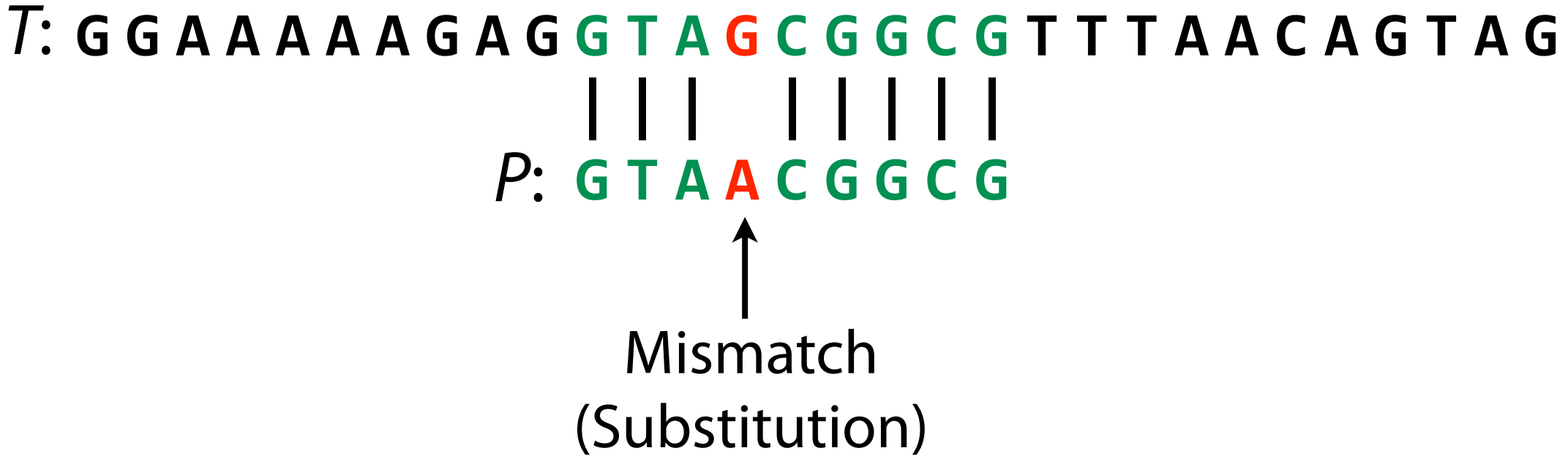




Approximate Pattern Matching

A **substitution** replaces one character with another

Described as the character swap needed to *convert T* to *P*



Hamming Distance

The minimum number of ***substitutions*** to turn one string into another.

```
X: G A G G T A G C G G C G T T
   |   | | | |   | | |   | | |
Y: G T G G T A A C G G G G T T
```

Hamming distance = 3

```
X: T G G C C G C G C A A A A C A G C
   | |   | | | | | | | | | | | |
Y: T G A C C G C G C A A A C A G C T
```

Hamming distance = 6

Hamming Distance

The minimum number of ***substitutions*** to turn one string into another.

X: G G C C G G C

Y: C C G G G G G

Hamming distance = 5

X: T A T A T A

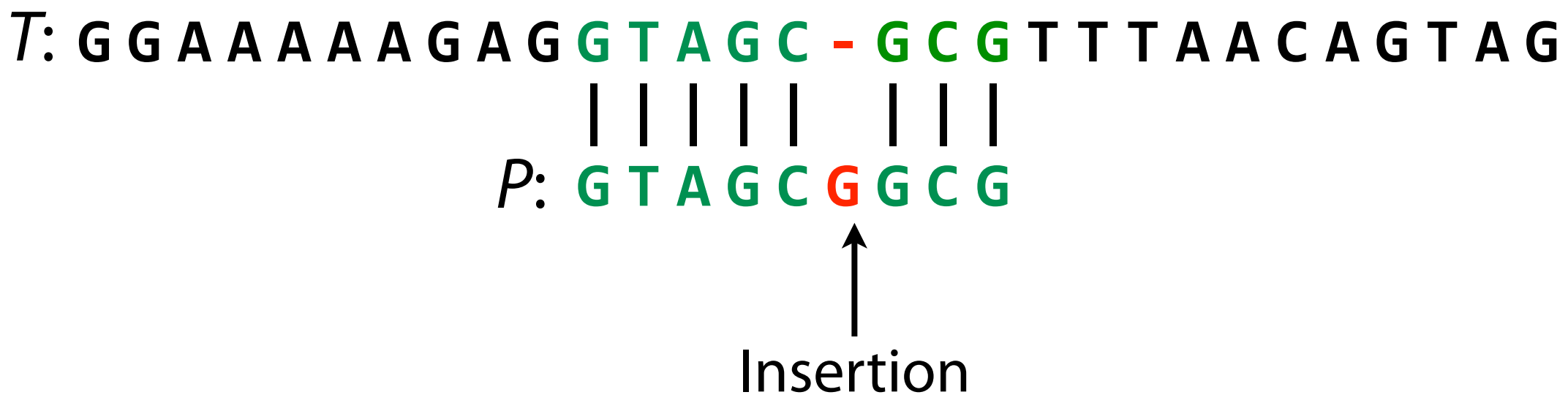
Y: A T A T A T

Hamming distance = 6

Approximate Pattern Matching

An **insertion** adds a character, shifting all other characters back

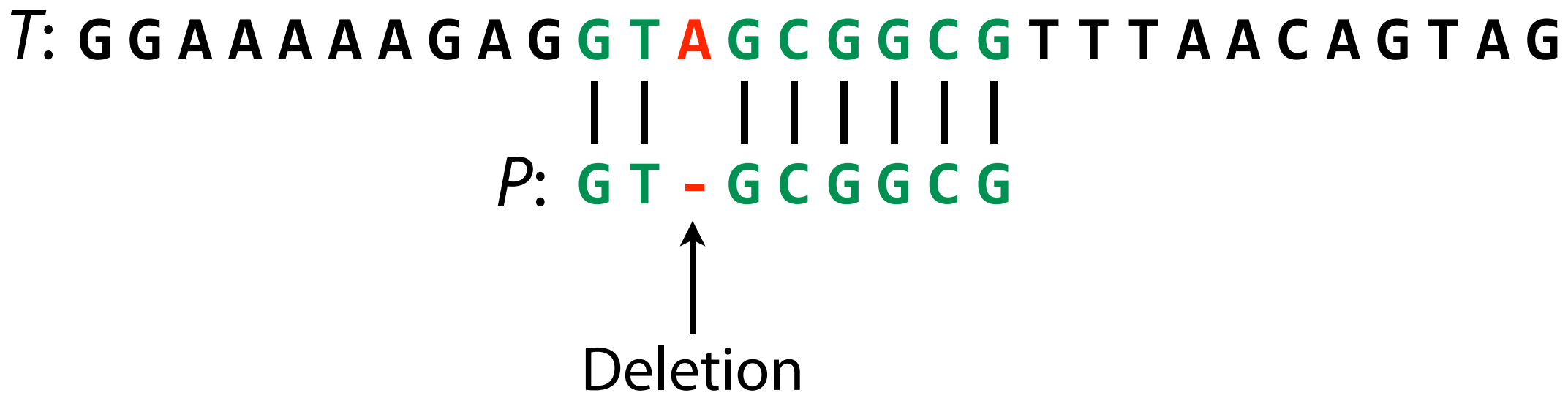
Insertion is relative! What edits *convert T* to *P*



Approximate Pattern Matching

An **deletion** removes a character, shifting all other characters forward

Deletion is relative! What edits *convert T* to *P*



Edit Distance

The minimum number of substitutions, insertions, or deletions (**edits!**) needed to turn one string into another (from X to Y)!

```
X:  T G G C C G C G C A A A A A C A G C -
    | |   | | | | | | | | | |   | | | |
Y:  T G A C C G C G C A A A A - C A G C T
```

Edit distance = 3

```
X:  G C G C T       G C G C T       G G C C T
        | | |       | |     |       |     | |
Y:  - - G C T       G C - - T       G - - C T
```

Edit distance = 2

Edit Distance

The minimum number of substitutions, insertions, or deletions (**edits!**) needed to turn one string into another (from X to Y)!

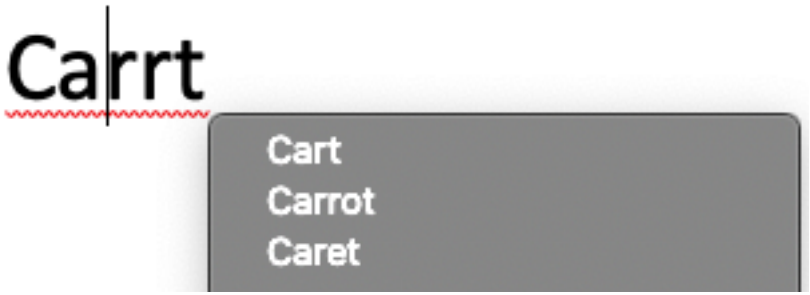
```
X: G G C C G G C       G G C C G G C - -
           | |             | | | |
Y: C C G G G G G       - - C C G G G G
```

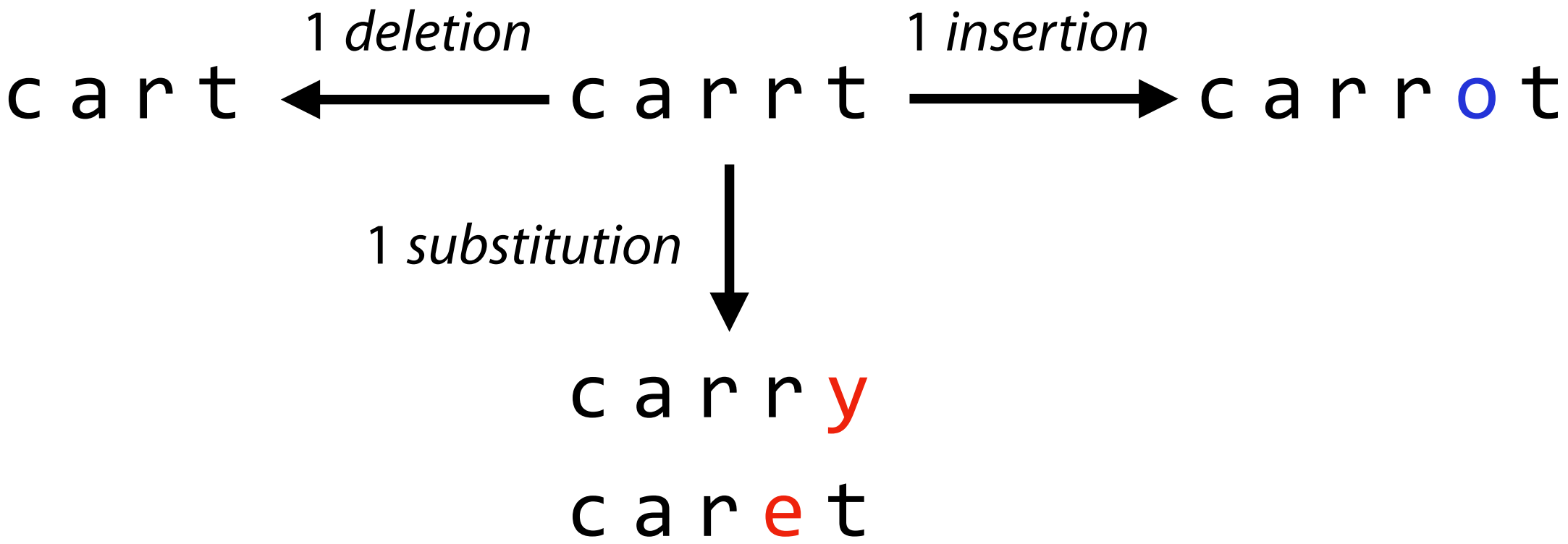
Edit distance = 5

```
X: T A T A T A -
     | | | | |
Y: - A T A T A T
```

Edit distance = 2

Edit Distance





Edit Distance

```
Score =  248 bits (129), Expect = 1e-63
Identities = 213/263 (80%), Gaps = 34/263 (12%)
Strand = Plus / Plus
```

Substitution

```
Query: 161 atatcaccacgtcaaaggtgactccaactcca---ccactccattttgttcagataatgc 217
           ||||||||||||||||||||||||||||  |     | |   || ||||||||||||||
Sbjct: 481 atatcaccacgtcaaaggtgactccaact-tattgatagtgtttttatgttcagataatgc 539

Query: 218 ccgatgatcatgtcatgcagctccaccgattgtgagaacgacagcgacttccgtcccagc 277
           |||||||   ||||||||||||||||||| || |           ||||||||||||
Sbjct: 540 ccgatgactttgtcatgcagctccaccgattttg-g----------ttccgtcccagc 586
```

Deletion

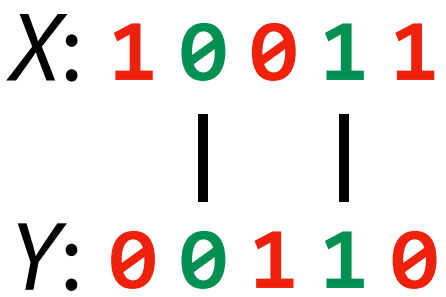
```
Query: 278 c-gtgcc--aggtgctgcctcagattcaggttatgccgctcaattcgctgcgtatatcgc 334
           |  ||  |  | ||||||||||||||||||||||||||||||||||||| |||||||||
Sbjct: 587 caatgacgta-gtgctgcctcagattcaggttatgccgctcaattcgctgggtatatcgc 645

Query: 335 ttgctgattacgtgcagctttcccttcaggcggga----------ccagccatccgtc 382
           ||||||||||||||||||||||||||||||||           ||||||||||||
Sbjct: 646 ttgctgattacgtgcagctttcccttcaggcgggattcatacagcggccagccatccgtc 705
```

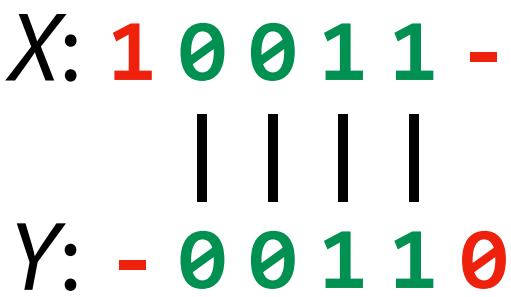
Insertion

```
Query: 383 ctccatatc-accacgtcaaagg 404
           ||||||||  ||||||||||||
Sbjct: 706 atccatatcaaccacgtcaaagg 728
```

Approximate Pattern Matching

How can I describe the relationship between two strings?





Edit string: Describe the changes you would make to X to become Y

Approximate Pattern Matching

Input: A text *T*, a pattern *P*, and a distance *d*

Output: All positions in *T* where *P* has at most *d* mismatches or edits

Hamming Distance: Min number substitutions (mismatches)

Edit Distance: Min number edits (substitution, insertions, deletions)

Approximate Pattern Matching

$\Sigma = 0, 1$ $P = 000$

Hamming Distance 1 strings:

Edit Distance 1 strings:

Approximate Pattern Matching

$\Sigma = 0, 1$ $P = 000$

Hamming Distance 1 strings: 100 010 001

Edit Distance 1 strings:

100 1000 00

010 0100

001 0010

0001

0000

Approximate Pattern Matching

P = abb d = 1

Using ***Hamming*** distance, what are valid approximate matches for P?

Using ***edit*** distance, what are valid approximate matches for P?

A) aba

B) aabb

C) bbb

D) ab

Approximate Pattern Matching

How do we find all approximate matches for a pattern in a text?

P: **word**

T: **There would have been a time for such a word**

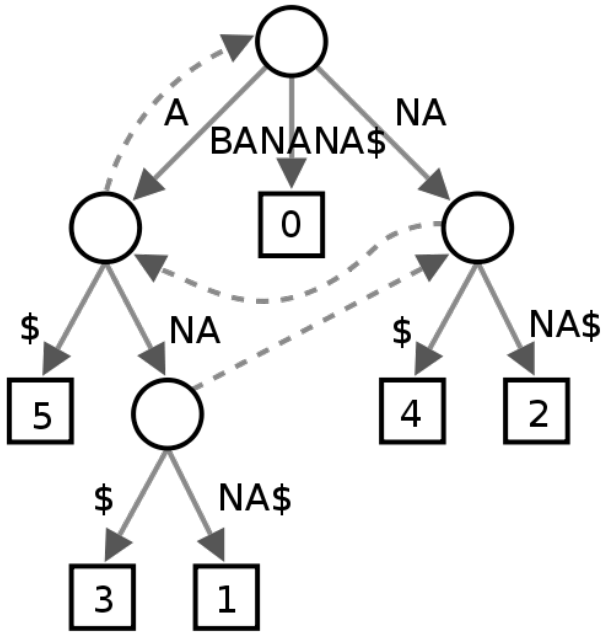
word word word word word word word word word word
word word word word word word word word
word word word word word word word word
word word word word word word word word
word word word word word word word word

Approximate Pattern Matching

How do we find all approximate matches for a pattern in a text?

Can we use our efficient exact pattern matching algorithms?

	A	C	G	T
A	0	0	1	2
C	0	1	0	1
G	0	1	2	0
T	0	1	2	3



6	$
5	A$
3	ANA$
1	ANANA$
0	BANANA$
4	NA$
2	NANA$

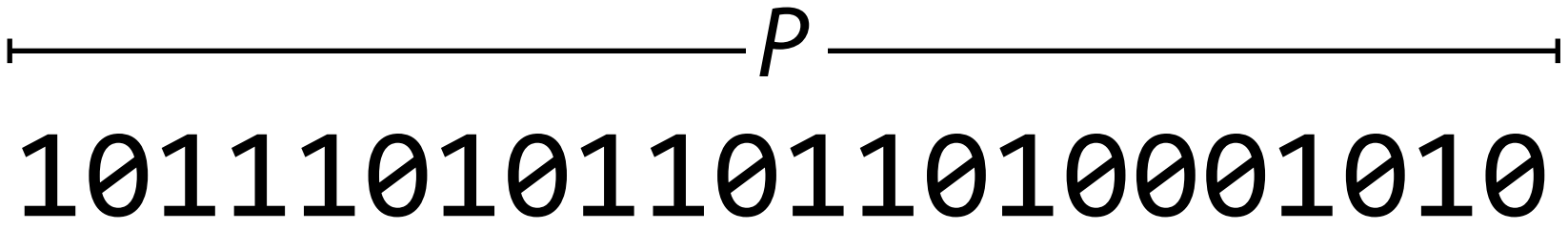
$	**B**	**A**	**N**	**A**	**N**	**A**
A	**$**	**B**	**A**	**N**	**A**	**N**
A	**N**	**A**	**$**	**B**	**A**	**N**
A	**N**	**A**	**N**	**A**	**$**	**B**
B	**A**	**N**	**A**	**N**	**A**	**$**
N	**A**	**$**	**B**	**A**	**N**	**A**
N	**A**	**N**	**A**	**$**	**B**	**A**

Boyer-Moore | Suffix Tree | Suffix Array | FM Index

Approximate Pattern Matching

Can we use our efficient exact pattern matching algorithms?

For Hamming distance (mismatches), we can!



Approximate Pattern Matching

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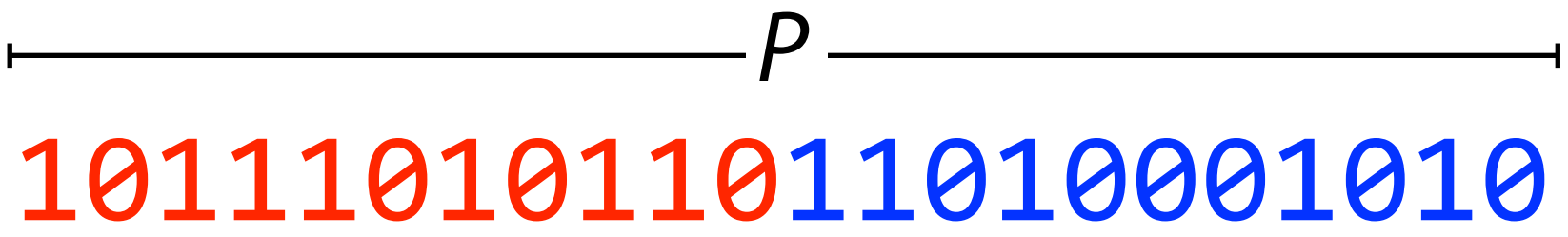

Approximate Pattern Matching

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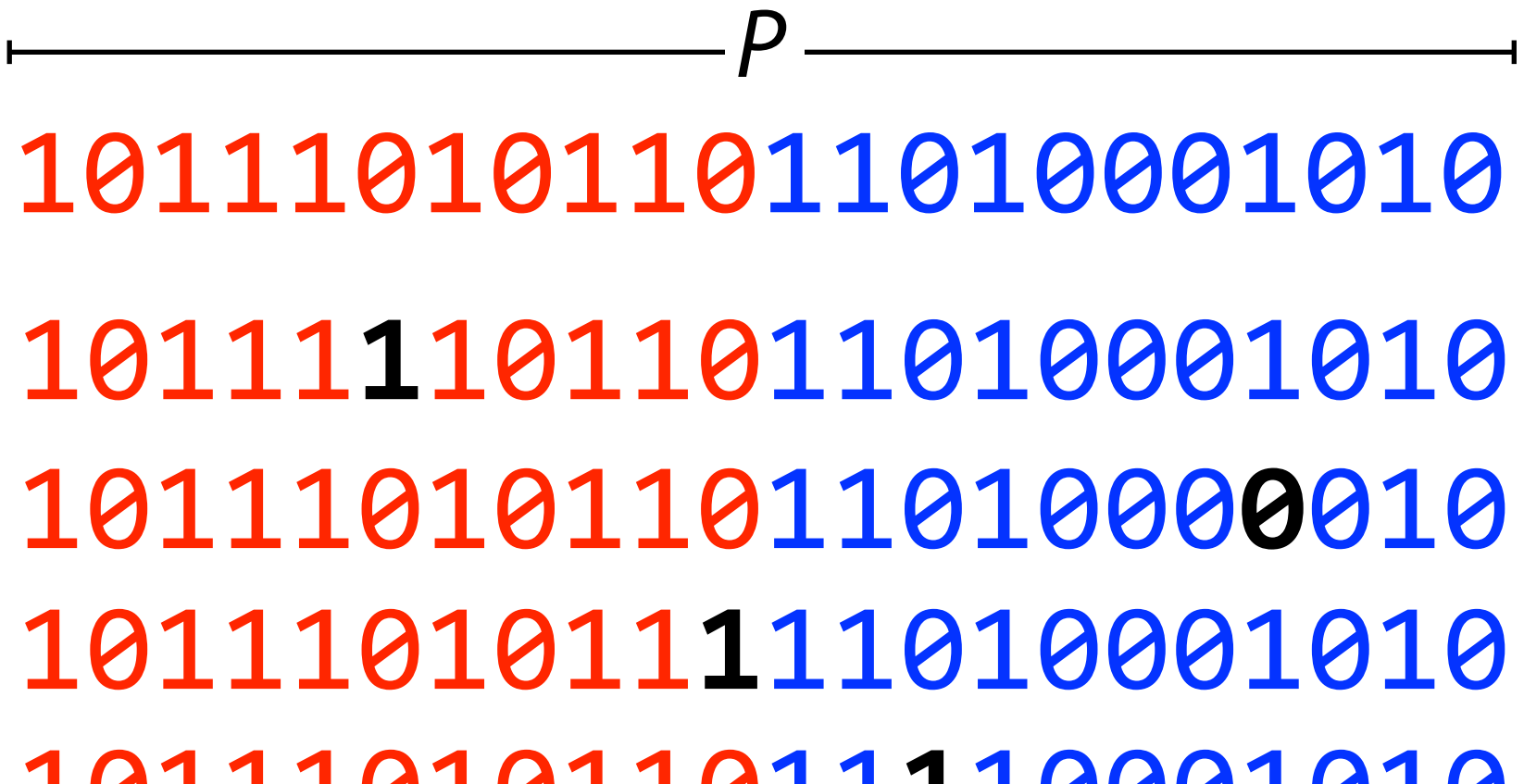
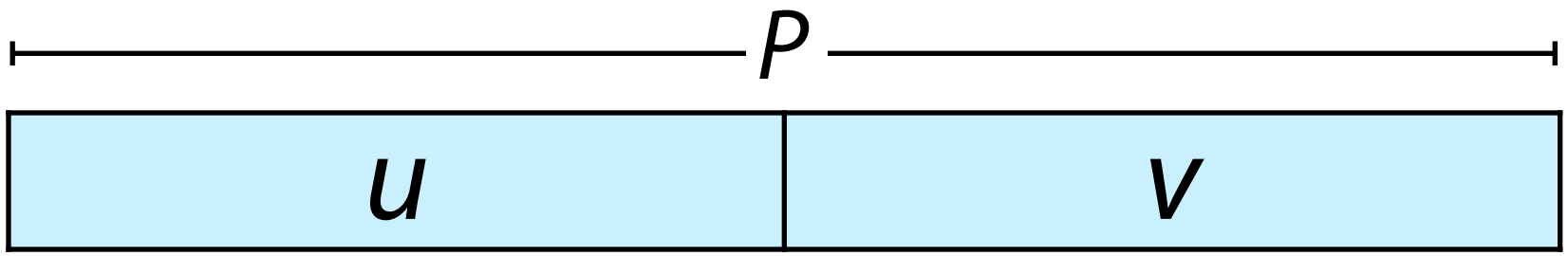


Approximate Pattern Matching

Can we use our efficient exact pattern matching algorithms?

For Hamming distance (mismatches), we can!

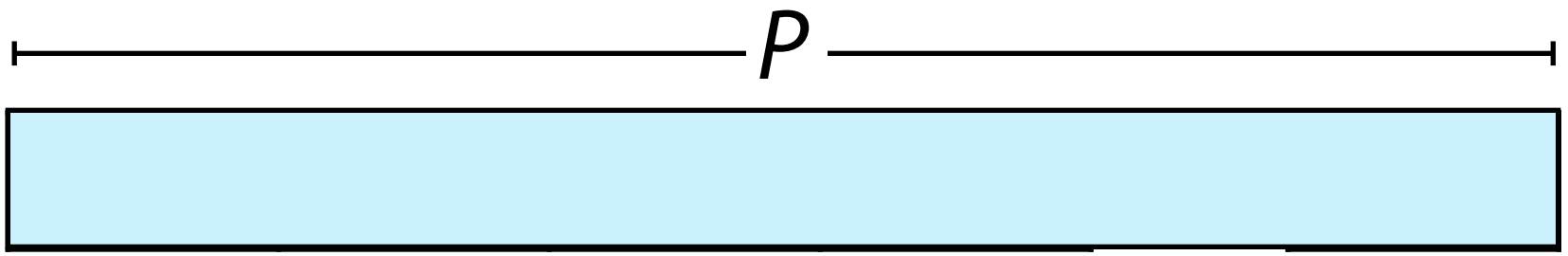


If *P* occurs in *T* with 1 mismatch, then *u* or *v* has no mismatch

We can search for *u* and *v* in T as a proxy for *P*!

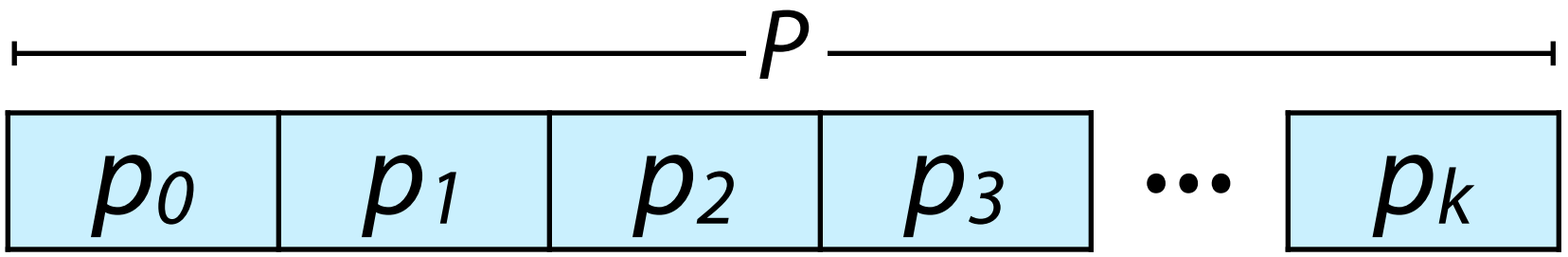
Approximate Pattern Matching

If *P* occurs in *T* with up to *k* mismatches…



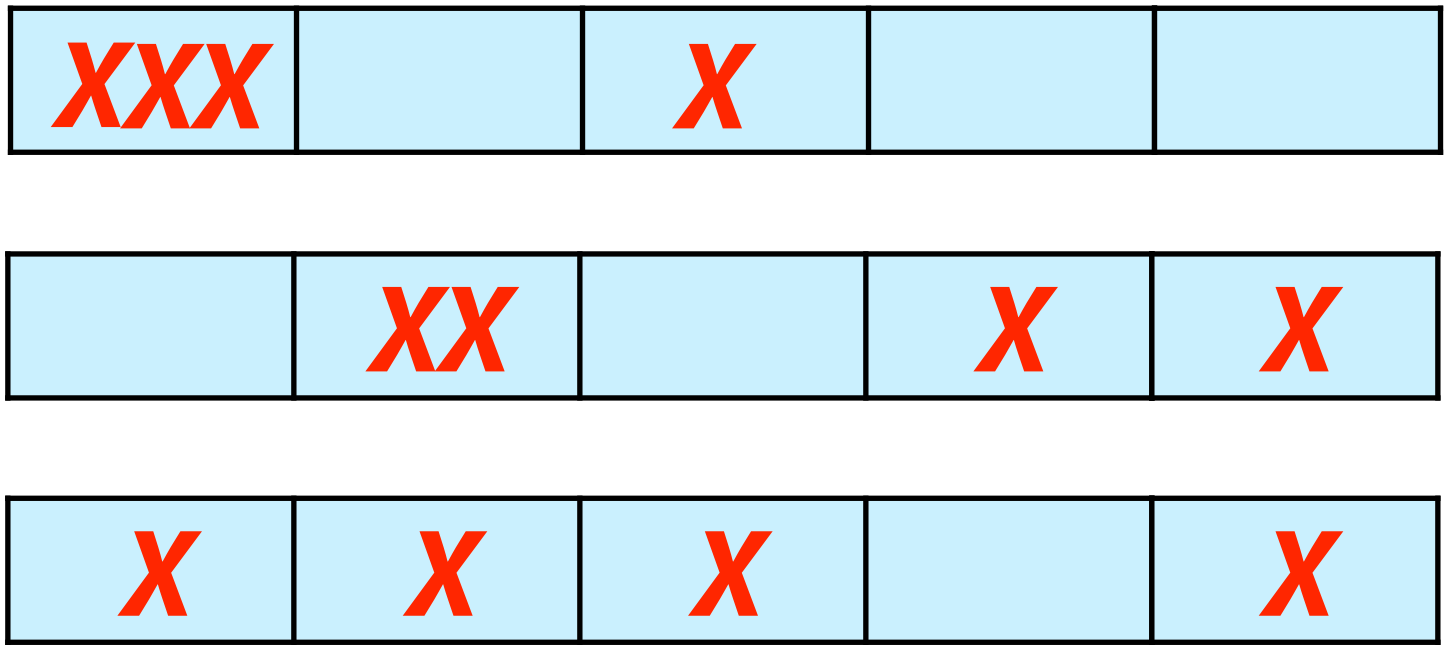
Approximate Pattern Matching

If *P* occurs in *T* with up to *k* mismatches, then if we split P into *k+1* partitions, at least one of p_0, p_1, ..., p_k must appear with 0 mismatches.



Approximate Pattern Matching

If *P* occurs in *T* with up to *k* mismatches, then if we split P into *k+1* partitions, at least one of p_0, p_1, ..., p_k must appear with 0 mismatches.



5 partitions
4 mismatches (*X*)

Approximate Pattern Matching

Pigeonhole principle: A direct relationship between containers and objects from either perspective below.

k+1 pigeons, *k* holes?

At least one hole has two pigeons!

k pigeons, *k+1* holes?

At least one hole is empty!

Approximate Pattern Matching

Pigeonhole principle lets us use exact matching algorithms:

P: **`word`**

T: **`There would have been a time for such a word`**

Approximate Pattern Matching

Pigeonhole principle lets us use exact matching algorithms:

P: **word**

T: **There would have been a time for such a word**

u: **wo** wo wo

v: **rd** rd

1) Given *k* allowed mismatches, break the pattern up into *k+1* partitions

What do we do with these partial matches?

Approximate Pattern Matching

P: **word**

T: **There would have been a time for such a word**

u: **wo** **word** **word**

v: **rd** **word**

1) Given *k* allowed mismatches, break the pattern up into *k+1* partitions

2) Count mismatches in the remaining characters in the alignment

3) Return all matches (but don't duplicate!)

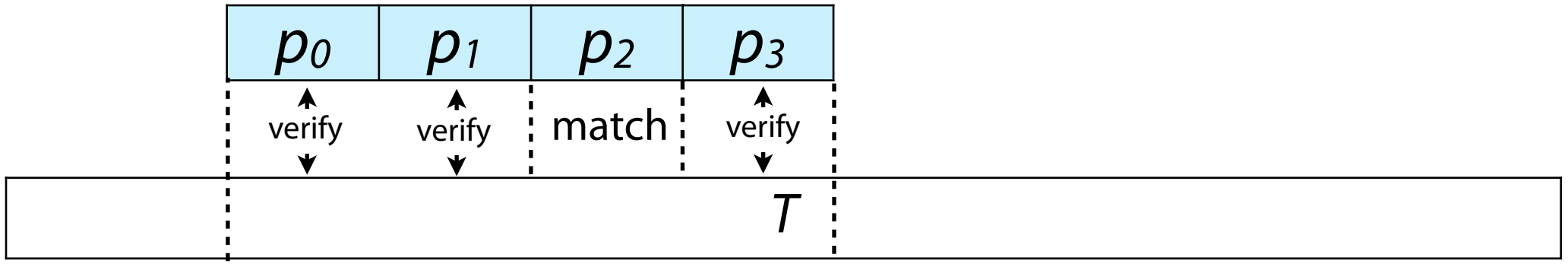
Approximate Pattern Matching

P: **CATS**

T: **THE CART WAS CARRIED BY THE CATS**

Approximate Pattern Matching

Counting mismatches requires verifying non-matching partitions



CATS

THE CART WAS CARRIED BY THE CATS

Approximate Pattern Matching

Seed and Extend: Using the pigeonhole principle to search a large text for exact matches and validating only these matches

Pros:

Cons:

Approximate Pattern Matching

P: **AAAAAA**

T: **AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA**

P: **BBBAAB**

T: **AABAAAAAAAAAAAAAABBBAAAAAAAAAAAAABAAAAA**

Approximate Pattern Matching

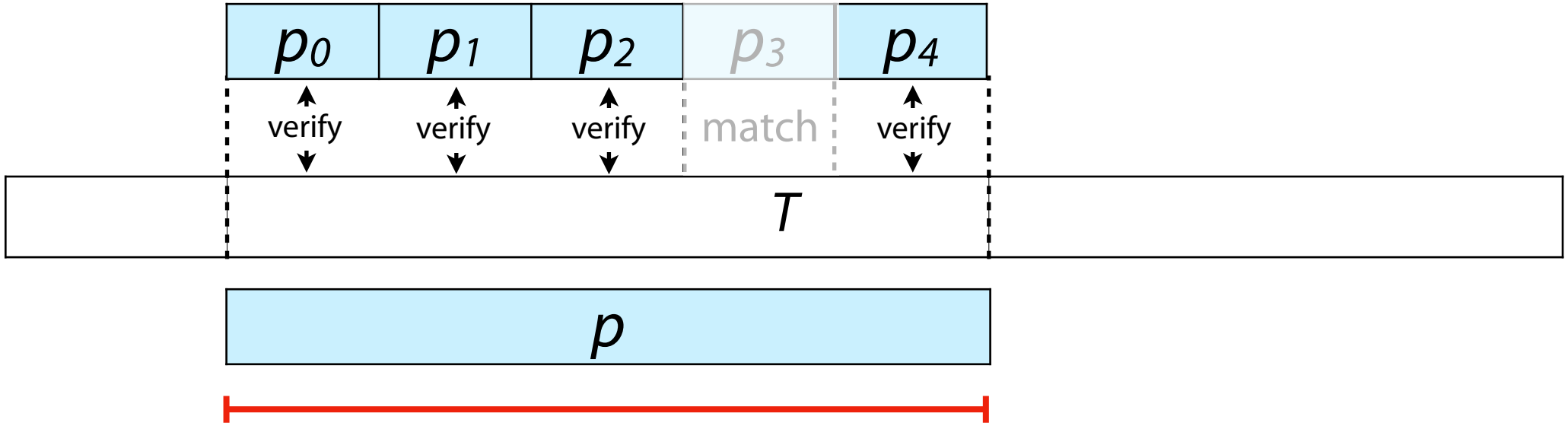
As a ***heuristic***, seed and extend reduces the overall search space

T: **There would have been a time for such a word**

word

word

word



Only consider mismatches while verifying a seed hit

Approximate Pattern Matching

As a ***heuristic***, seed and extend reduces the overall search space

T: **There would have been a time for such a word**

word

word

word

Consider the likelihood of seeing 'wo' or 'rd' **by chance**:

256 characters : $\frac{1}{256}^2 = 0.000015$

Approximate Pattern Matching in Genomics

Partition Seed: Length ~40

`CTCAAACTCCTGACCTTTGGTGATCCACCCGCCTAGGCCTTC`

T: Length 3 billion

Likelihood of random seed string:

$$\frac{1}{4}^{40} = 8.27e-25$$

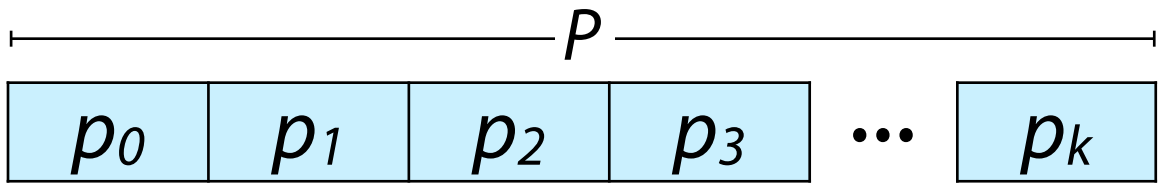
# of times seed will occur by chance in T:

Likelihood * (~ length)

$$2.48e-15$$

Approximate Pattern Matching

"Seed and extend" approach to pattern matching



Pros:

Reuse exact matching algs

Works for Hamming and edit distance*

As a heuristic, reduces search space

Cons:

Slow for large *k*

small partitions matching many times by chance

k+1 exact matching problems, one per partition

* we don't know how to do edit distance verification yet

Approximate Pattern Matching

If *P* occurs in *T* with up to *k* mismatches, then if we split P into *k+1* partitions, at least one of $p_0, p_1, ..., p_k$ must appear with 0 mismatches.

$P =$ A A A A A A A A $\quad d = 3$

How many partitions?

What is the characters in each partition(s)?

$T =$ ... B B B B B B A A B B B B B B ...

Approximate Pattern Matching

If *P* occurs in *T* with up to *k* mismatches, then if we split P into *k+1* partitions, at least one of $p_0, p_1, ..., p_k$ must appear with 0 mismatches.

$P =$ A B A C A A B A $\quad d = 3$

How many partitions?

What is the characters in each partition(s)?

$T =$ ... B B B B A B A A B A B B B B ...

Approximate Pattern Matching

If P occurs in T with up to k mismatches, then if we split P into $k+1$ partitions, at least one of $p_0, p_1, ..., p_k$ must appear with 0 mismatches.

$P =$ B A A A A A $\qquad\qquad d = 1$

$T =$ ... B B B B B B A A A A A B A A ...

Assignment 10: a_pigeon

Learning Objective:

Preprocess text into kmers and a hash table

Use pigeonhole principle to perform approximate matching

Consider: Do the partitions need to be contiguous runs of characters? Do they need to all be the same length?

`kmerMap text_to_kmer_map(string & T, int k)`

Input:

`string & T`: The input text — can be very large this week!

`int k`: The fixed size for each kmer (substring)

Output:

`kmerMap`: `unordered_map<string, vector<int>>`

T: **aaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaa** $k = 4$

aaaa aaaa aaaa aaaa aaaa aaaa aaaa aaaa aaaa
aaaa aaaa aaaa aaaa aaaa aaaa aaaa aaaa
aaaa aaaa aaaa aaaa aaaa aaaa aaaa aaaa
aaaa aaaa aaaa aaaa aaaa aaaa aaaa aaaa
aaaa aaaa aaaa aaaa aaaa aaaa aaaa aaaa

```
vector<Seed> partitionPattern(string P, int np)
```

Input:

`string P`: The input pattern — can be large this week!

`int np`: The number of non-overlapping partitions to split P

Output:

`vector<Seed>` : Vector of partitioned strings and their index

```
typedef std::pair<std::string, int> Seed;
```

P: **`ABCDEFGH`** *np = 2* **`{ {ABCD, 0}, {EFGH, 4} }`**

`vector<int> approximate_search(fname, P, mm)`

Input:

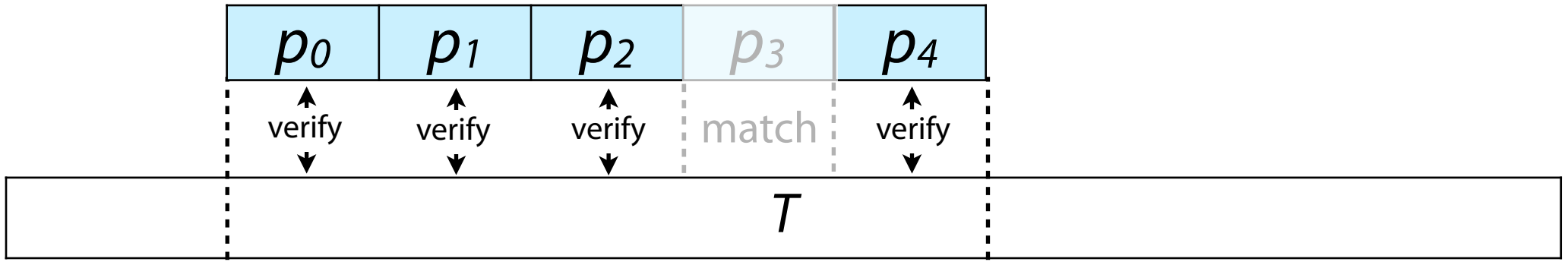
`string fname`: The file storing the text T

`string P`: The pattern text

`int mm`: The number of allowed mismatches

Output:

`vector<int>`: The index positions in T of all approximate matches

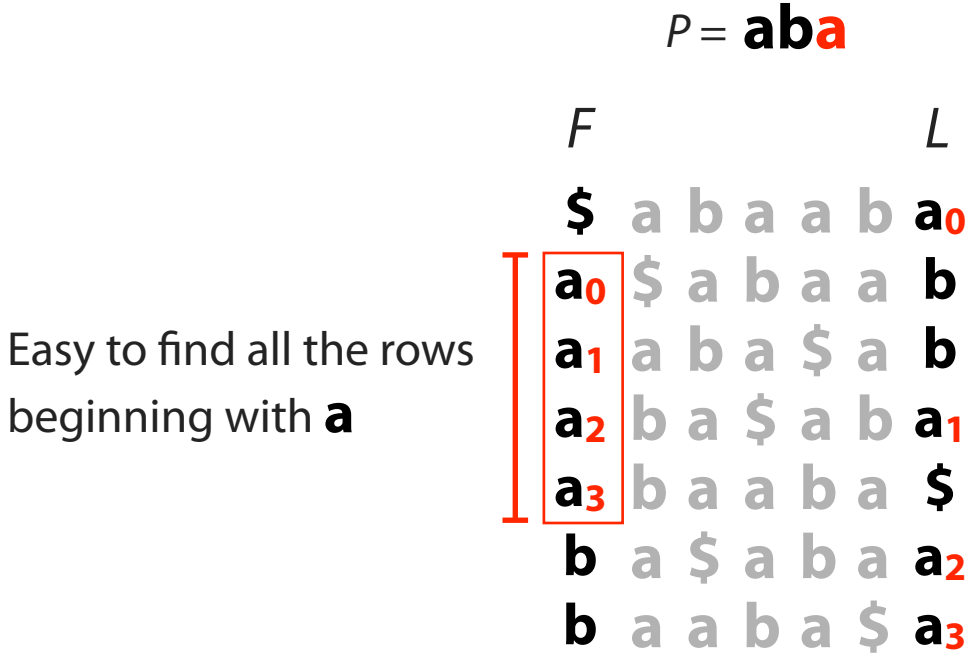


Bonus Slides

FM Index w/ mismatches

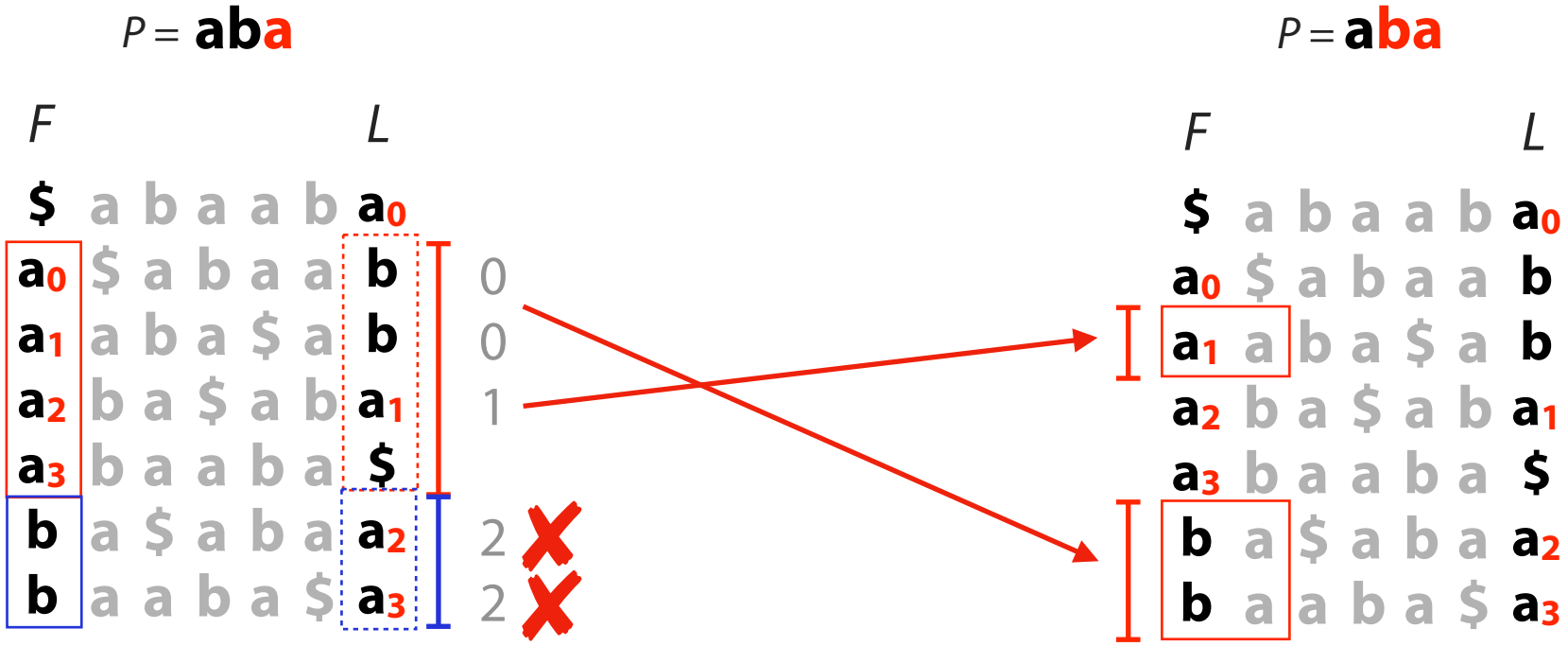
Start with shortest suffix, then match successively longer suffixes

Keep track of mismatches for each suffix



FM Index w/ mismatches

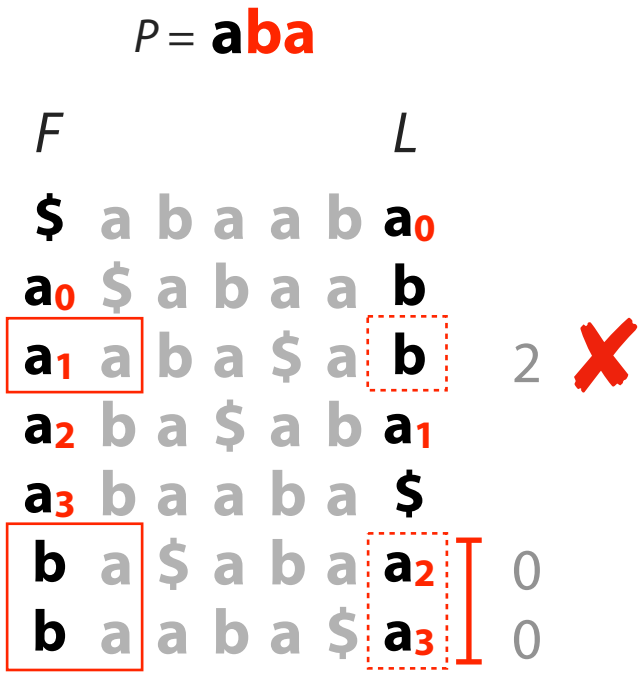
We have rows beginning with **a**, now we want rows beginning with **ba**

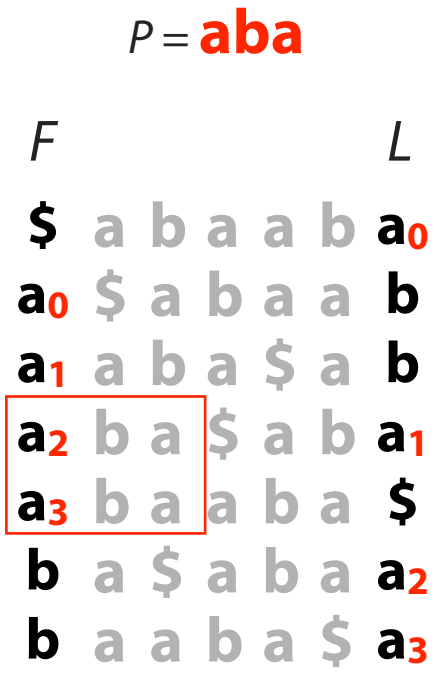


No longer have just one search range!

FM Index w/ mismatches

We have rows beginning with **ba**, now we seek rows beginning with **aba**





Only works for Hamming Distance (mismatches)!