# String Algorithms and Data Structures <br> Approximate Pattern Matching 

CS 199-225
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Brad Solomon


Department of Computer Science

## 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 $k$ <br> occurrences of $P$ | $O(n+k)$ | $O(n \log m)$ | $O(n)$ |
| Time: Report $k$ <br> 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 | $n o$ |
| Bytes per input <br> character | $>15$ | $\sim 4$ | $\sim 0.5$ |

$$
m=|T|, n=|P|, k=\# \text { occurrences of } P \text { in } T
$$

## Limitations of exact pattern matching

```
strong
Aa ab, * 2 of 2
    \imath \equiv}
/**
* Returns the number of alignments skipped by Boyer-Moore
* In this instance, Boyer-Moore is *only* the strong bad character rule [and right-to-left scanning
* Also modifies the outlist vector to contain the index positions of all exact matches of P in T.
* If no match is found, modifies the vector to contain one value '[-1]'
*
* @param P A std::string object which holds the Pattern string.
* @param T A std::string object which holds the Text string.
* @param alpha A std::string object which holds the Alphabet string.
* @param outList An std::vector<int> array (by reference) that can be modified to contain all matche
* @return An int counting the number of skipped alignments using bad character.
*/
int bmoore_search(std::string P, std::string T, std::string alpha, std::vector<int> & outList){
```

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



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
$\bigcirc$ 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 $\mathrm{m}^{\mathrm{n}}$ 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 $\mathrm{m}^{\mathrm{n}}$ 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
    |I||||| ||||||||||
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: word Alignment 2: word

## Not a match! <br> Distance 2 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?

$$
X: 10011
$$

Y: 00110

$$
\begin{aligned}
& X: 10011 \\
& \text { Y: } 00110
\end{aligned}
$$

Hamming distance is 3 !

$$
\begin{aligned}
& \text { X: } 10011 \text { - } \\
& \text { | | | | } \\
& \text { Y: - 00110 }
\end{aligned}
$$

Edit distance is 2 !

## Approximate Pattern Matching

How can I describe the relationship between two strings?

$$
\begin{aligned}
& X: 10011 \\
& \text { | | } \\
& \text { Y: } 00110
\end{aligned}
$$

$$
\begin{aligned}
& \text { X: } 10011 \text { - } \\
& \text { | | | | } \\
& \text { Y: - 00110 }
\end{aligned}
$$

## Approximate Pattern Matching

A substitution replaces one character with another
Described as the character swap needed to convert $T$ to $P$

T: G G A A A A A G A G G T A G C G G C G T T T A ACAGTAG


Mismatch
(Substitution)

## Hamming Distance

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


Hamming distance $=3$

X: TGGCCGCGCAAAAACAGC
|| ||||||||
Y: TGACCGCGCAAAACAGCT

Hamming distance $=6$

## Hamming Distance

The minimum number of substitutions to turn one string into another.
X: G G C C G G C | |
Hamming distance $=5$
$Y:$ C C G G G G G

X: TATATA
Hamming distance $=6$
Y: ATATAT

## Approximate Pattern Matching

An insertion adds a character, shifting all other characters back Insertion is relative! What edits convert $T$ to $P$

T: G G A A A A A G A G G T A G C - G C G T T T A ACAGTAG

$$
\begin{aligned}
& \text { |||||||| } \\
& P: \text { G T A G C G G C G } \\
& \uparrow \\
& \text { Insertion }
\end{aligned}
$$

## Approximate Pattern Matching

An deletion removes a character, shifting all other characters forward Deletion is relative! What edits convert $T$ to $P$

T: G G A A A A A G A G G T A G C G G C G T T T A ACAGTAG

## || |||||| <br> $P:$ G T-GC G G C G <br> $\uparrow$

Deletion

## Edit Distance

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

```
X: TGGCCGCGCAAAAACAGC -
    || |||||||||| ||||
Edit distance \(=3\)
```

Y: TGACCGCGCAAAA-CAGCT


G G C 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

$Y: ~ C C G G G G G$

Y: - ATATAT

## G G C C G G C - -



Edit distance $=5$

-     - C C G G G G G

X: TATATA-


Edit distance $=2$

## Edit Distance

## Carrt

Cart
Carrot
Caret

## $\mathrm{Cart} \stackrel{1 \text { deletion }}{\longleftrightarrow} \mathrm{Carrt} \xrightarrow{1 \text { insertion }} \mathrm{Carrot}$ <br> 1 substitution <br> carry <br> caret

## 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
\(||||||||||||||||||||||||||||||||||||||||||||||||||\mid\)
Sbjct: 481 atatcaccacgtcaaaggtgactccaact-tattgatagtgttttatgttcagataatgc 539
Query: 218 ccgatgatcatgtcatgcagctccaccgattgtgagaacgacagcgacttccgtcccagc 277
\(||l| l||||||||||||||||||||||||||||||||||\mid\)
Sbjct: 540 cogatgactttgtcatgcagctccaccgattttg-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
\(\||1| 1| || | l|l| l|l| l \mid l\)
Sbjct: 706 atccatatcaaccacgtcaaagg 728
```


## Approximate Pattern Matching

How can I describe the relationship between two strings?

$$
\begin{aligned}
& X: 10011 \\
& Y: 001 \mid
\end{aligned}
$$



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

$\Sigma=0,1 \quad \mathrm{P}=000$

Hamming Distance 1 strings:

Edit Distance 1 strings:

Approximate Pattern Matching
$\Sigma=0,1 \quad \mathrm{P}=000$

Hamming Distance 1 strings: $100 \quad 010 \quad 001$

| Edit Distance 1 strings: | 100 | 1000 | 00 |
| :--- | :--- | :--- | :--- |
|  | 010 | 0100 |  |
|  | 001 | 0010 |  |
|  |  | 0001 |  |
|  |  | 0000 |  |

## Approximate Pattern Matching

$P=\mathrm{abb} \quad d=1$

Using Hamming distance, what are valid approximate matches for P?
Using edit distance, what are valid approximate matches for P?
A) $a b a$
B) $a \mathrm{abb}$
C) bbb
D) $a b$

## 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

## 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 |
| $\mathbf{C}$ | 2 |  |  |
| C | 0 | 1 | 0 |

Boyer-Moore


\$ B A N A N A A \$ B ANAN ANA\$BAN ANANA\$B BANANA\$ NA\$BANA NANA\$BA

## Approximate Pattern Matching

Can we use our efficient exact pattern matching algorithms?
For Hamming distance (mismatches), we can!


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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 $p_{0}, p_{1}, \ldots, p_{k}$ 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 $p_{0}, p_{1}, \ldots, p_{k}$ 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
$v: \quad$ 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
$v: \quad r d$ word 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
$T$ : AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
$P$ : ВВВААА
$T$ : AABAAAAAAAAAAAAAABBBAAAAAAAAAAAABAAAAA

## 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


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

## Approximate Pattern Matching in Genomics

Partition Seed: Length ~40
CTCAAACTCCTGACCTTTGGTGATCCACCCGCCTAGGCCTTC
T: Length 3 billion

GATCACAGGTCTATCACCCTATTAACCACTCACGGGAGCTCTCCATGCATTTGGTATTTT CGTCTGGGGGGTATGCACGCGATAGCATTGCGAGACGCTGGAGCCGGAGCACCCTATGTC GCAGTATCTGTCTTTGATTCCTGCCTCATCCTATTATTTATCGCACCTACGTTCAATATT
ACAGGCGAACATACTTACTAAAGTGTGTTAAT ACAGGCGAACATACTTACTAAAGTGTGTTAAT ${ }^{-1}$ AGGACATAATAATA AACCCCCCCTCCCCCGCTTCTGGCCAC ACAAAGAACCCTAACACCAGCCTAAC TTTTAACAGTCACCCCCCAACTAAC CTCATCAATACAACCCCCGCCCAT CCCCGAACCAACCAAACCCCAAAG GCAATACACTGACCCGCTCAAACT CTAGCCTTTCTATTAGCTCTTAGT TCACCCTCTAAATCACCACGATCAん AAAACGCTAGCCTAGCCACACCCC ACGAAAGTTTAACTAAGCTATACTAA TCCCCAATAAAGCTAAAACTCACCTGAG TACGAAAGTGGCTTTAACATATCTGAACACA TACCCCACTATGCTTAGCCCTAAACCTCAACAGTTAAATCAACAAAAC CACTACGAGCCACAGCTTAAAACTCAAAGGACCTGGCGGTGCTTCATATC AGCCTGTTCTGTAATCGATAAACCCCGATCAACCTCACCACCTCTTGCTCA CCGCCATCTTCAGCAAACCCTGATGAAGGCTACAAAGTAAGCGCAAGTACCCAC ACGTTAGGTCAAGGTGTAGCCCATGAGGTGGCAAGAAATGGGCTACATTTTCTAC AAAACTACGATAGCCCTTATGAAACTTAAGGGTCGAAGGTGGATTTAGCAGTAAACT AGTAGAGTGCITAGTTGAACAGGGCCCTGAAGCGCGTACACACCGCCCGTCACCCTCCT AGTAACCTCAAACTCCTGCCTTTGGTGATCCACCCGCCTTGGCCTACCTGCATACAAG AAGCACCCAACTTACACTTAGGAGATTTCAACTTAACTTGACCGCTCTGAGCTAAACCTA AAGCACCCAACTTACACTTAGGAGATTTCAACTTAACTTGACCGCTCTGAGCTAAACCTA AGTATAGGCGATAGAAATTGAAACCTGGCGCAATAGATATAGTACCGCAAGGGAAAGATG AAAAATTATAACCAAGCATAATATAGCAAGGACTAACCCCTATACCTTCTGCATAATGAA TTAACTAGAAATAACTTTGCAAGGAGAGCCAAAGCTAAGACCCCCGAAACCAGACGAGCT ACCTAAGAACAGCTAAAAGAGCACACCCGTCTATGTAGCAAAATAGTGGGAAGATTTATA GGTAGAGGCGACAAACCTACCGAGCCTGGTGATAGCTGGTTGTCCAAGATAGAATCTTAG TTCAACTTTAAATTTGCCCACAGAACCCTCTAAATCCCCTTGTAAATTTAACTGTTAGTC

## Likelihood of random seed string:


\# of times seed will occur by chance in T :

Likelihood * (~ length)
$2.48 e-15$

## 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 $p_{0}, p_{1}, \ldots, p_{k}$ must appear with 0 mismatches.
$P=$ AAAAAAAA $\quad d=3$

How many partitions?

What is the characters in each partition(s)?
$T=\ldots$ B B B B B B A A 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 $p_{0}, p_{1}, \ldots, p_{k}$ must appear with 0 mismatches.
$P=$ ABACAABA $\quad d=3$

How many partitions?

What is the characters in each partition(s)?
$T=\ldots$ B B B B A B A A 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 $p_{0}, p_{1}, \ldots, p_{k}$ must appear with 0 mismatches.

$$
P=\text { B A A A A A } \quad d=1
$$

$T=\ldots$ B B B B B B 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: aaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaaa
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 $n p=2\{\{A B C D, 0\},\{E F G H, 4\}\}$
vector<int> approximate_search(fname, P, mm) Input:
string fname: The file storing the text T
string $\mathbf{P}$ :The pattern text
int mm :The number of allowed mismatches
Output:
vector<int> : The index positions in T of all approximate matches


## FM Index w/ mismatches

Start with shortest suffix, then match successively longer suffixes
Keep track of mismatches for each suffix

$$
\begin{aligned}
& P=\mathbf{a b a} \\
& \begin{array}{ccccc}
F & & L \\
\text { Easy to find all the rows } \\
\text { beginning with } \mathbf{a}
\end{array} \begin{array}{cccccc}
\mathbf{\$} & \mathrm{a} & \mathrm{~b} & \mathrm{a} & \mathrm{a} & \mathrm{~b} \\
\mathbf{a}_{0}
\end{array}
\end{aligned}
$$

## FM Index w/ mismatches

We have rows beginning with $\mathbf{a}$, now we want rows beginning with ba

$$
P=\mathbf{a b a} \quad P=\mathbf{a b a}
$$



No longer have just one search range!

## FM Index w/ mismatches

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

$$
P=\mathbf{a b a}
$$

$$
P=\mathbf{a b a}
$$

| $F$ |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- |



Only works for Hamming Distance (mismatches)!

