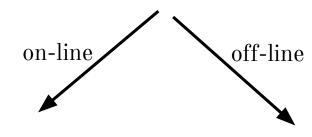
Lesson 3.1

## Recapitulation

Exact string matching algorithms



Boyer-Moore

Multimap (sorted index)

Hash table

Suffix array

Suffix trie

#### Tries

A trie (pronounced "try") is a tree representing a collection of strings with one node per common prefix

Smallest tree such that:

- Each edge is labeled with a character  $c \in \Sigma$
- A node has at most one outgoing edge labeled c, for  $c \subseteq \Sigma$
- Each key is "spelled out" along some path starting at the root

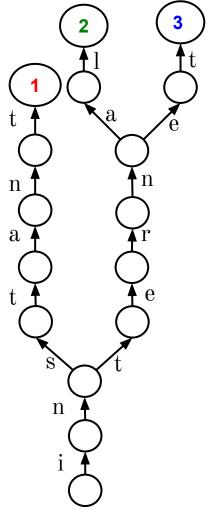
Natural way to represent either a set or a map where keys are strings

## Tries: example

Represent this map with a trie:

key	value
instant	1
internal	2
internet	3

- Each edge is labeled with a character  $c \in \Sigma$
- A node has at most one outgoing edge labeled c, for  $c \subseteq \Sigma$
- Each key is "spelled out" along some path starting at the

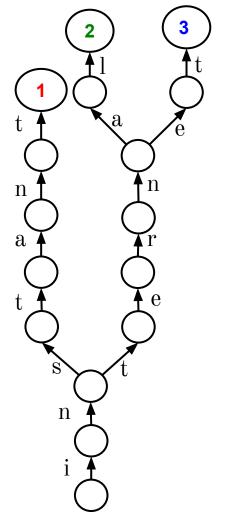


mont

## Tries: example

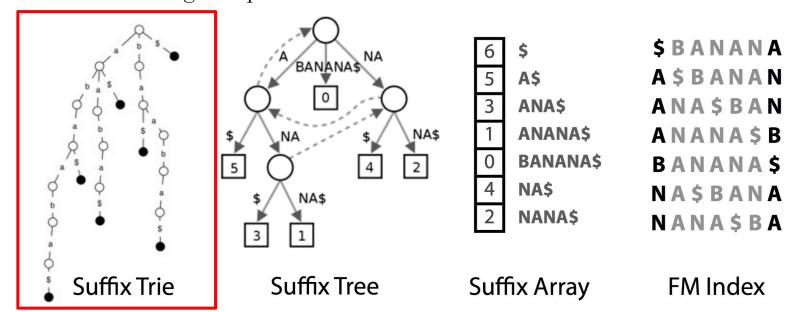
- Checking for presence of a key P, where n = |P|, is O(n) time
- If total length of all keys is N, trie has O(N) nodes

Tries implementation



## Indexing with suffixes

• Until now, our indexes have been based on extracting substrings from T A very different approach is to extract suffixes from T. This will lead us to some interesting and practical index data structures



Build a **trie** containing all **suffixes** of a text T!

```
T = GTTATAGCTGATCGCGGCGTAGCGG$
   GTTATAGCTGATCGCGGCGTAGCGG$
    TTATAGCTGATCGCGGCGTAGCGG$
     TATAGCTGATCGCGGCGTAGCGG$
      ATAGCTGATCGCGGCGTAGCGG$
       TAGCTGATCGCGGCGTAGCGG$
        AGCTGATCGCGGCGTAGCGG$
         GCTGATCGCGGCGTAGCGG$
          CTGATCGCGGCGTAGCGG$
           TGATCGCGGCGTAGCGG$
            GATCGCGGCGTAGCGG$
             ATCGCGGCGTAGCGG$
              TCGCGGCGTAGCGG$
                                n(n+1)/2 chars
               CGCGGCGTAGCGG$
                GCGGCGTAGCGG$
                 CGGCGTAGCGG$
                  GGCGTAGCGG$
                    GCGTAGCGG$
                     CGTAGCGG$
                      GTAGCGG$
                       TAGCGG$
                        AGCGG$
                         GCGG$
                          CGG$
                           GG\$
                            G$
```

\$ 0

DNA: \$ < A < C < G < T)

T = GTTATAGCTGATCGCGGCGTAGCGG\$

GTTATAGCTGATCGCGGCGTAGCGG\$ TTATAGCTGATCGCGGCGTAGCGG\$

TATAGCTGATCGCGGCGTAGCGG\$

ATAGCTGATCGCGGCGTAGCGG\$

First add special terminal character \$ to the end of Ttagctgatcgcggcgtagcggs

\$ is a character that does not appear elsewhere in T,

and we define it to be less than other characters (for

AGCTGATCGCGGCGTAGCGG\$

GCTGATCGCGGCGTAGCGG\$

CTGATCGCGGCGTAGCGG\$

TGATCGCGGCGTAGCGG\$ GATCGCGGCGTAGCGG\$

ATCGCGGCGTAGCGG\$

TCGCGGCGTAGCGG\$

GTAGCGG\$

TAGCGG\$

G\$

\$ enforces a rule we're all used to using: e.g. "as" comes before "ash" in the dictionary.

\$ guarantees no suffix is a prefix of any other suffix.

CGCGGCGTAGCGG\$ GCGGCGTAGCGG\$ CGGCGTAGCGG\$ GGCGTAGCGG\$ GCGTAGCGG\$ CGTAGCGG\$ AGCGG\$ GCGG\$ CGG\$ GG\$

n(n+1)/2 chars

#### Tries

Smallest tree such that:

Each edge is labeled with a character from  $\Sigma$ 

A node has at most one outgoing edge

Each key is "spelled out" along some path starting at the root

T: abaaba T\$: abaaba\$

Each path from root to leaf represents a suffix; each suffix is represented by some path from root to leaf

Would this still be the case if we hadn't added \$?

∢a

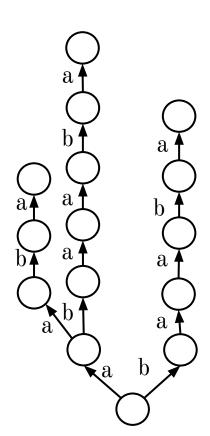
Shortest (non-empty) suffix

T: abaaba T\$: abaaba\$

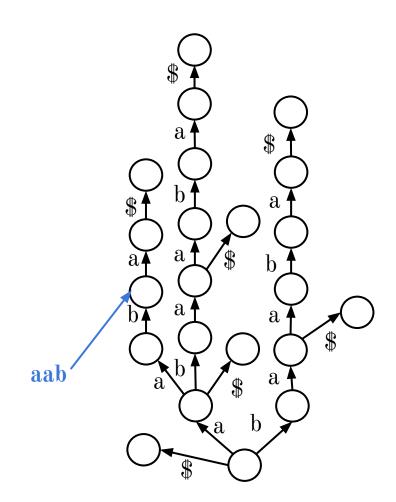
Each path from root to leaf represents a suffix; each suffix is represented by some path from root to leaf

Would this still be the case if we hadn't added \$?

No. Lost suffixes: "aba", "ba", etc.



We can think of nodes as having labels, where the label spells out characters on the path from the root to the node



How do we check whether a string S is a substring of T?

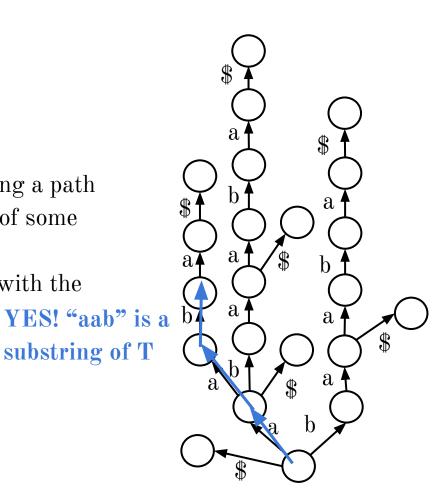
Note: Each of T's substrings is spelled out along a path from the root. I.e., every substring is a prefix of some suffix of T.

Start at the root and follow the edges labeled with the characters of S:

YES! "aab" is a

If we "fall off" the trie (there is no outgoing edge for next character of S) then
 S is not a substring of T

2. If we exhaust S without falling off, S is a substring of T



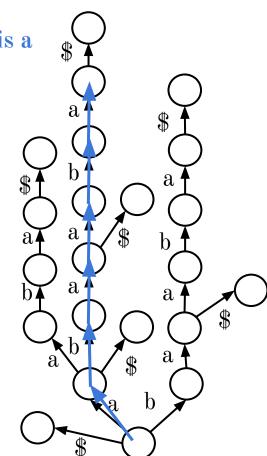
YES! "abaaba" is a substring of T

How do we check whether a string S is a substring of T?

Note: Each of T's substrings is spelled out along a path from the root. I.e., every substring is a prefix of some suffix of T.

Start at the root and follow the edges labeled with the characters of S:

- If we "fall off" the trie (there is no outgoing edge for next character of S) then S is not a substring of T
- 2. If we exhaust S without falling off, S is a substring of T



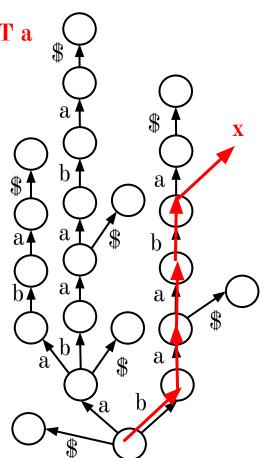
"baabb" is NOT a substring of T

How do we check whether a string S is a substring of T?

Note: Each of T's substrings is spelled out along a path from the root. I.e., every substring is a prefix of some suffix of T.

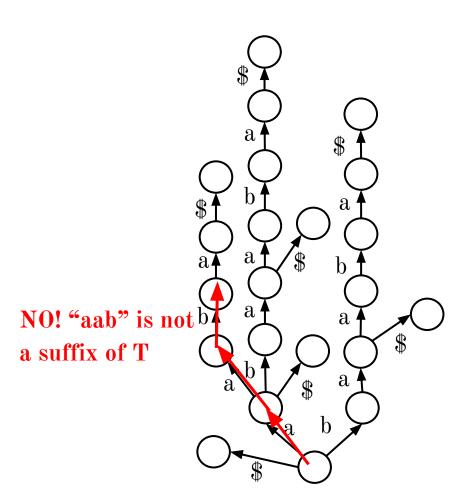
Start at the root and follow the edges labeled with the characters of S:

- If we "fall off" the trie (there is no outgoing edge for next character of S) then
   S is not a substring of T
- 2. If we exhaust S without falling off, S is a substring of T



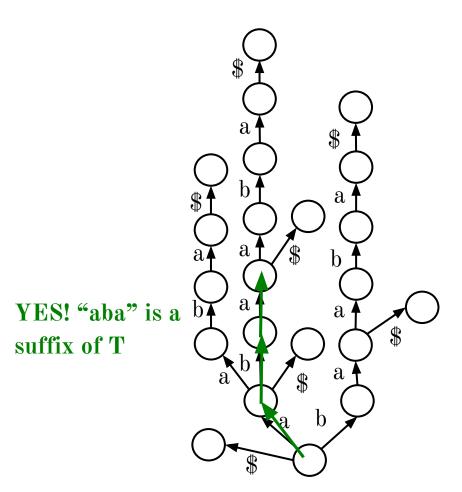
How do we check whether a string S is a suffix of T?

Same procedure as for substring, but additionally check whether the **final node** in the walk has an outgoing edge labeled \$



How do we check whether a string S is a suffix of T?

Same procedure as for substring, but additionally check whether the **final node** in the walk has an outgoing edge labeled \$

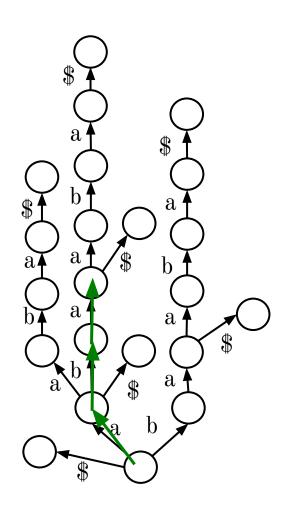


How do we count the number of times a string S occurs as a substring of T?

Follow path corresponding to S. Either we fall off, in which case answer is 0, or we end up at node n and the answer = # of leaf nodes in the subtree rooted at n.

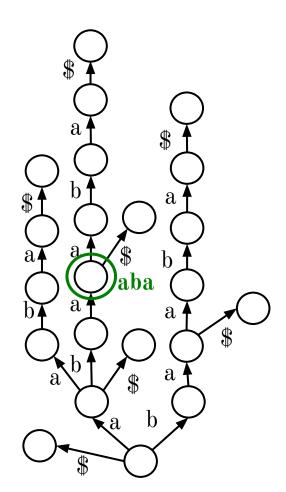
"aba" - 2 occurrences

Leaves can be counted with depth-first traversal.



How do we find the **longest repeated** substring of T?

Find the deepest node with more than one child



How many nodes does the suffix trie have?

Is there a class of string where the number of suffix trie nodes grows linearly with m? Yes: e.g. a string of m a's in a row

T = aaaa

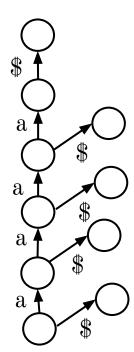
Total nodes:

1 Root

m nodes with incoming a edge

m + 1 nodes with incoming \$ edge

Total: 2m + 2 nodes

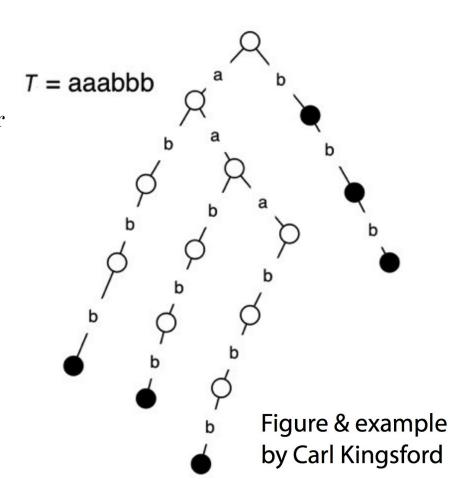


Is there a class of string where the number of suffix trie nodes grows with  $O(m^2)$ ? Yes:  $a^nb^n$ 

#### Total nodes:

- 1 root
- n nodes along "b chain," right
- n nodes along "a chain," middle
- n chains of n "b" nodes hanging off each "a chain" node
- 2n + 1\$ leaves (not shown)

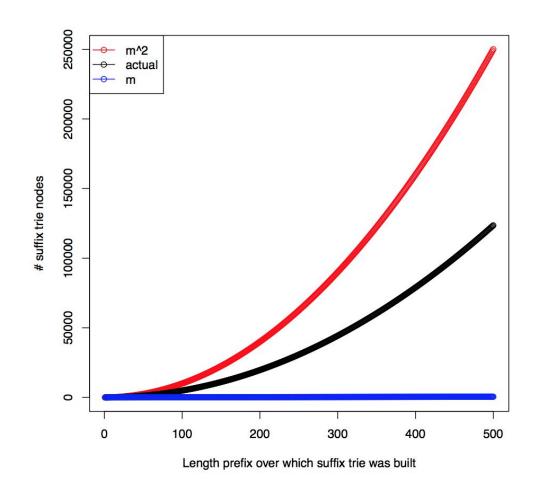
Total:  $n^2 + 4n + 2$  nodes, where m = 2n



Built suffix tries for the first 500 prefixes of the lambda phage virus genome

Black curve shows how # nodes increases with prefix length

Suffix trie implementation



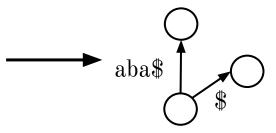
# Suffix Tree

Lesson 3.2

## Suffix trie: making it smaller

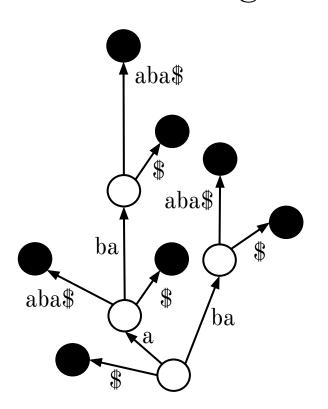
T: abaaba\$ ıb

Idea 1: Coalesce non-branching paths into a single edge with a string label



Reduces # nodes, edges, guarantees internal nodes have >1 child

## Suffix trie: making it smaller

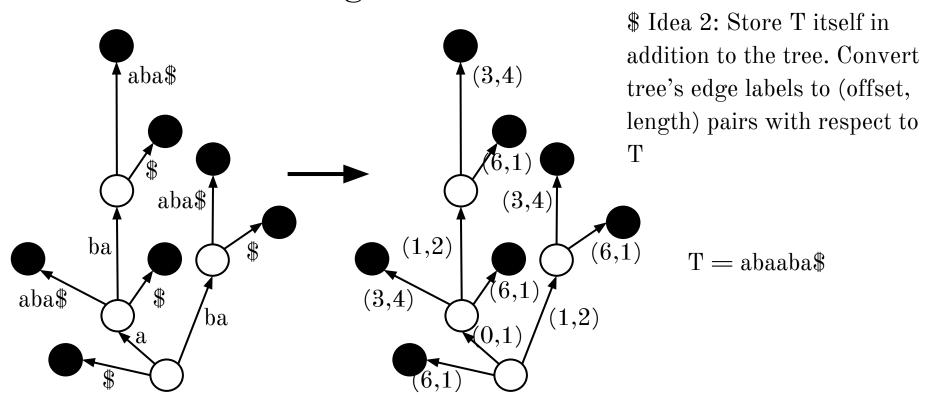


How many leaves? M

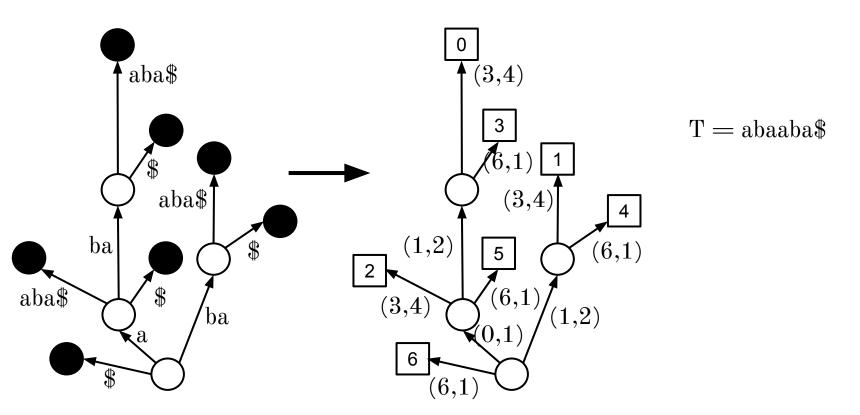
How many non-leaf nodes?  $\leq$  m - 1

 $\leq 2m$  -1 nodes total - O(m) nodes

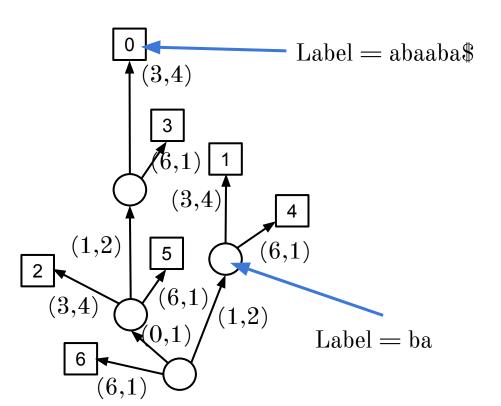
## Suffix trie: making it smaller



## Suffix trie: leaves hold offsets



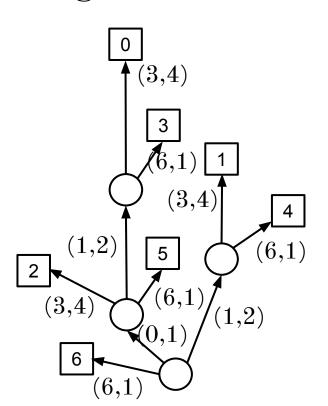
## Suffix trie: labels



T = abaaba

Again, each node's label equals the concatenated edge labels from the root to the node. These aren't stored explicitly

## ...and we get: Suffix tree

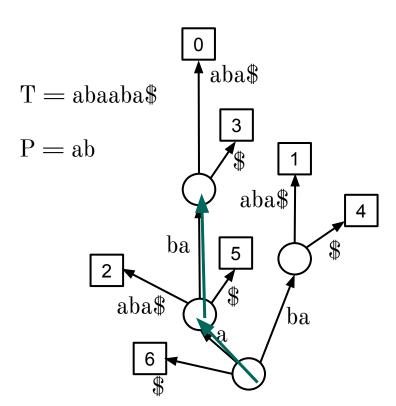


T = abaaba\$

Because edges can have string labels, we must distinguish two notions of "depth"

- Node depth: how many edges we must follow from the root to reach the node
- Label depth: total length of edge labels for edges on path from root to node

- How do we check whether a string
   S is a substring of T?
- Essentially same procedure as for suffix trie, except we have to deal with coalesced edges

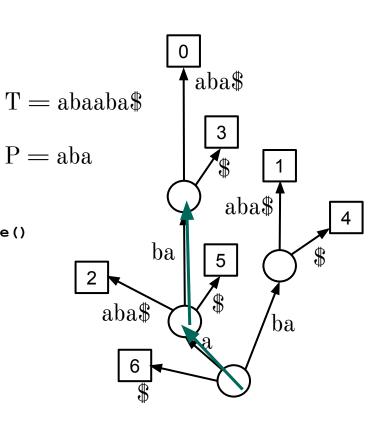


- How do we check whether a string
   S is a suffix of T?
- Essentially same procedure as for suffix trie, except we have to deal with coalesced edges

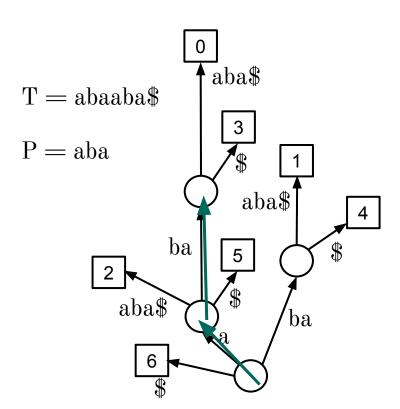
```
Fall_off, ended_in_node = climb_the_tree()
if fall_off:
    substring = False
    suffix = false

Else:
    substring = True
    if ended_in_node:
        suffix = True

Else:
    suffix = False
```



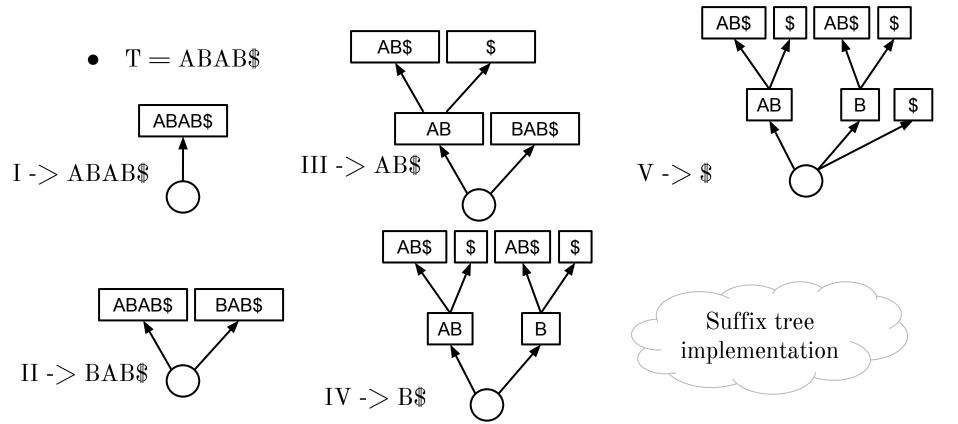
- How do we count the number of times a string S occurs as a substring of T?
- Same procedure as for suffix trie:
   Count the number of branches going out of the node in which we ended following the path
- This is common application of suffix tree: Find all matches of P in T



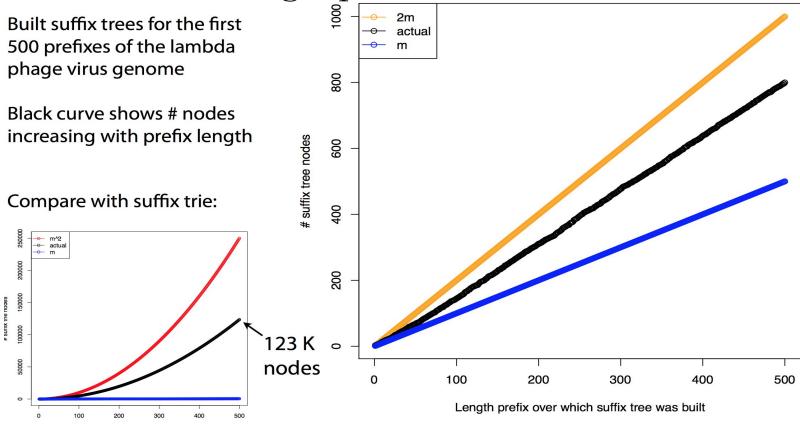
## Suffix tree: building

- Naive method 1: build a suffix trie, then coalesce non-branching paths and relabel edges
- Naive method 2: build a single-edge tree representing only the longest suffix, then augment to include the 2nd-longest, then augment to include 3rd-longest, etc
- Both are O(m2) time, but first uses O(m<sup>2</sup>) space while second uses O(m)

## Suffix tree: building Naive method 2



Suffix tree: building - performance



## Suffix tree: building

- Ukkonen's algorithm O(m) time and space:
  Ukkonen, Esko. "On-line construction of suffix trees."
  Algorithmica 14.3 (1995): 249-260
- Has online property: if T arrives one character at a time, algorithm efficiently updates suffix tree upon each arrival
- We won't cover it here; see Gusfield Ch. 6 for details

# Approximate string matching

Lesson 3.3

## Genome sequence alignment requires approximate

#### Read

CTCAAACTCCTGACCTTTGGTGATCCACCCGCCTNGGCCTTC

#### Reference

GATCACAGGTCTATCACCCTATTAACCACTCACGGGAGCTCTCCATGCATTTGGTATTTTT CGTCTGGGGGGTATGCACGCGATAGCATTGCGAGACGCTGGAGCCGGAGCACCCTATGTC ACAATTGAATGTCTGCACAGCCACTTTCCACAGACATCATAACAAAAATTTCCACCA ACAAAGAACCCTAACACCAGCCTAACCAGATTTCAAATTTTATCTTTTGGCGGTATGCAC CCCCGAACCAACCAAACCCCAAAGACACCCCCCACAGTTTATGTAGCTTACCTCCTCAAA GCAATACACTGACCCGCTCAAACTCCTGGATTTTTGGATCCACCCAGCGCCTTTGGCCTAAA CTAGCCTTTCTATTAGCTCTTAGTAAGATTACACATGCAAGCATCCCCGTTCCAGTGAGT TCACCCTCTAAATCACCACGATCAAAAGGAACAAGCATCAAGCACGCAGCAATGCAGCTC AAAACGCTTAGCCTAGCCACACCCCCACGGGAAACAGCAGTGATTAACCTTTAGCAATAA ACGA A AGTTTA ACTA AGCTA TACTA ACCCCA GGGTTGGTCA ATTTCGTGCCAGCCACCGC GGTCACACGATTAACCCAAGTCAATAGAAGCCGGCGTAAAGAGTGTTTTAGATCACCCCC TCCCCAATAAAGCTAAAACTCACCTGAGTTGTAAAAAACTCCAGTTGACACAAAATAGAC TACGAAAGTGGCTTTAACATATCTGAACACACAATAGCTAAGACCCAAACTGGGATTAGA TACCCCACTATGCTTAGCCCTAAACCTCAACAGTTAAATCAACAAAACTGCTCGCCAGAA CACTACGAGCCACAGCTTAAAACTCAAAGGACCTGGCGGTGCTTCATATCCCTCTAGAGG AGCCTGTTCTGTAATCGATAAACCCCGATCAACCTCACCACCTCTTGCTCAGCCTATATA CCGCCATCTTCAGCAAACCCTGATGAAGGCTACAAAGTAAGCGCAAGTACCCACGTAAAG ACGTTAGGTCAAGGTGTAGCCCATGAGGTGGCAAGAAATGGGCTACATTTTCTACCCCAG AAAACTACGATAGCCCTTATGAAACTTAAGGGTCGAAGGTGGATTTAGCAAGTAAACTAAG AGTAGAGTGCTTAGTTGAACAGGGCCCTGAAGCGCGTTACACCCCCCGTCACCCTCCTC AAGTATACTTCAAAGGACATTTAACTAAAACCCCTACGCATTTATATAGAGGAGACAAGT CGTAACCTCAAACTCCTGCCTTTGGTGATCCACCCGCCTTGGCCTACCTGCATAATGAAG GCCCCAAACCCACTCCACCTTACTACCAGACAACCTTAGCCAAACCATTTACCCAAATAA AGTATAGGCGATAGAAATTGAAACCTGGCGCAATAGATATAGTACCGCAAGGGAAAGATG GGCCTACTTCACAAAGCGCCTTCCCCCGTAAATGA

Sequence differences occur because of...

- 1. Sequencing errors
- 2. Natural variation

... 3 billion nucleotides long reference genome...
...and we have to deal with repetitive sequences

## Approximate string matching

Looking for places where a P matches T with up to a certain number of mismatches or edits. Each such place is an approximate match.

A mismatch is a single-character substitution (variation) - SNV:

T: GGAAAAAGAGGTAGCGGCGTTTAACAGTAG

P: GTAACGGCG

An edit is a single-character substitution or gap (insertion or deletion):

T: GGAAAAAGAGGTAGC-GCGTTTAACAGTAG (insertion)

P: GTAGCGGCG

T: GGAAAAAGAGGTAGCGGCGTTTAACAGTAG (deletion)

P: GTAGC-GCG

## Hamming and edit distance

For two same-length strings X and Y, **hamming** distance is the minimum number of single-character substitutions needed to turn one into the other:

X: GAGGTAGCGGCGTTTAAC

Y: GTGGTAACGGGGTTTAAC

Hamming distance = 3

**Edit** distance (Levenshtein distance): minimum number of edits required to turn one into the other:

X: TGGCCGCGCAAAAACAGC

Edit distance = 2

Y: TGACCGCGCAAAA- CAGC

What would be the Hamming distance here?

## Approximate matching

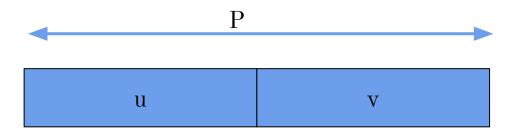
Adapting the naive algorithm with configurable Hamming distance:

```
def naiveApproximate(p, t, maxHammingDistance=1):
   occurrences = []
   for i in range(len(t) - len(p) + 1): # for all alignments
       nmm = 0
                            # for all characters
       for j in range(len(p)):
          nmm += 1
                                      # mismatch
              if nmm > maxHammingDistance:
                 break
                                        # exceeded maximum distance
       if nmm <= maxHammingDistance:</pre>
          # approximate match; return pair where first element is the
          # offset of the match and second is the Hamming distance
          occurrences.append((i, nmm))
   return occurrences
```

Instead of stopping upon first mismatch, stop when maximum distance is exceeded

## Approximate matching

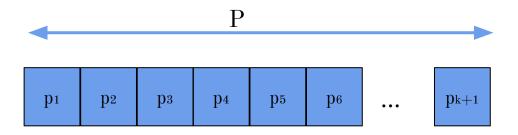
Mission: apply exact matching algorithms to approximate matching problems!



If P occurs in T with 1 edit, then u or v appears with no edits (u and v are two non-overlapping substrings of P)

## Approximate matching

Mission: apply exact matching algorithms to approximate matching problems!



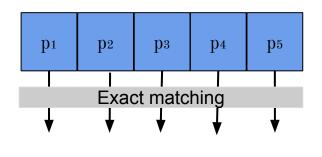
If P occurs in T with up to k edits, at least one of p1, p2, ..., pk+1 must appear with 0 edits

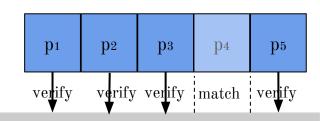
## Pigeonhole principle

If n items are put into m containers, with n > m, then at least one container must contain more than one item (Dirichlet's principle).



## Pigeonhole principle





#### References



