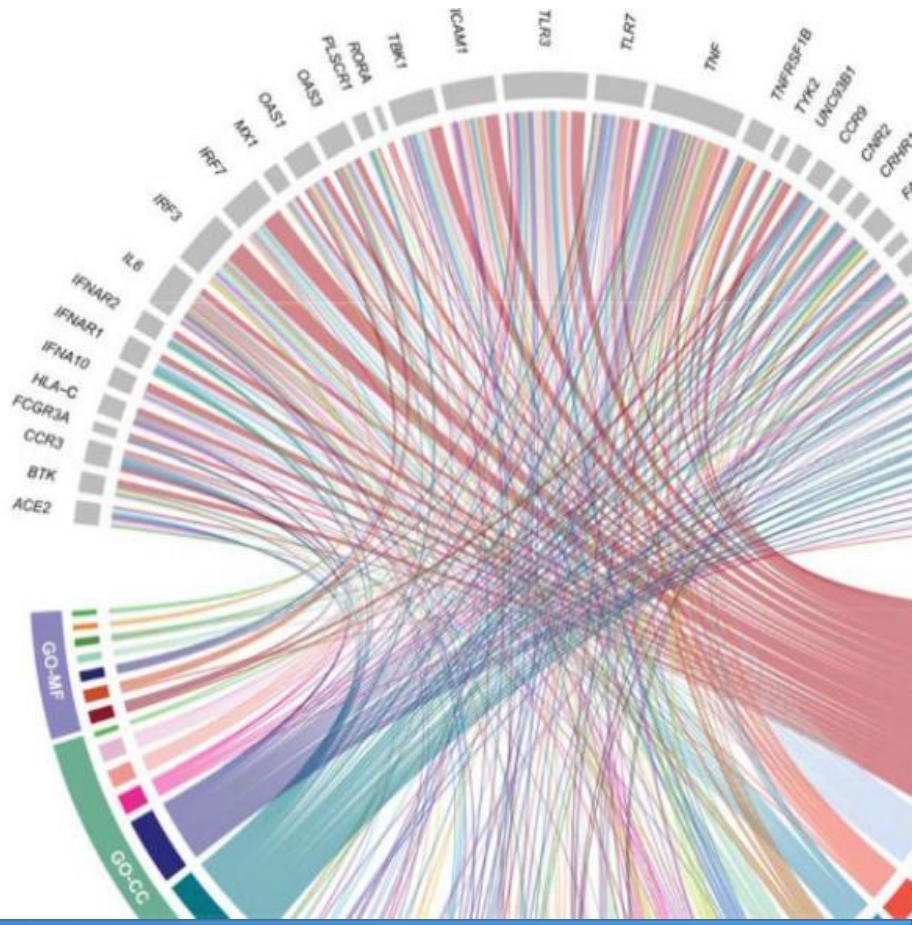
Tècniques i Eines Bioinformàtiques

Approximate String Matching



Santiago Marco-Sola (santiago.marco@upc.edu)

Màster en Enginyeria Informàtica, UPC
Departament of Computer Science
Facultat d'Informàtica de Barcelona (FIB), UPC

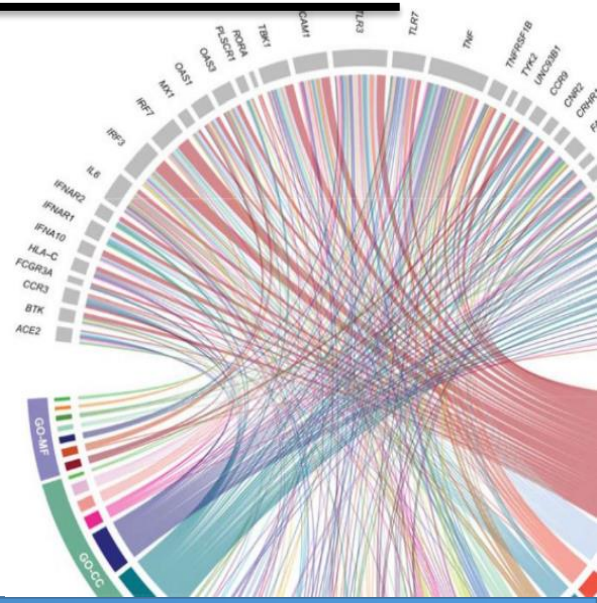
Acknowledgements

Many pictures and materials are taken from **Ben Langmead's course**.

Course heavily inspired in:

- **Genome-Scale Algorithm Design**. Veli Mäkinen, Djamal Belazzougui, Fabio Cunial, Alexandru I. Tomescu. Cambridge University Press.
- **Algorithms on Strings, Trees, and Sequences**. Dan Gusfield. Cambridge University Press.
- **An Introduction to Bioinformatics Algorithms.** Neil C. Jones, Pavel A. Pevzner. MIT Press.

1 Tries


IL6
IFNAP2
IFNAR1
IFNA10
HLA-C
FCGR3A
CCR3
BTK
ACE2
IRF3
IRF7
MX1
OAS1
OAS3
FLSCR1
RDRA
TBK1
ICAM1
TLR7
TNF
TNFRSF1B
TYK2
CCR9
GO:MF
GO:CC

Tries

A trie ("try") is a tree representing a collection of strings (keys):
the smallest tree such that

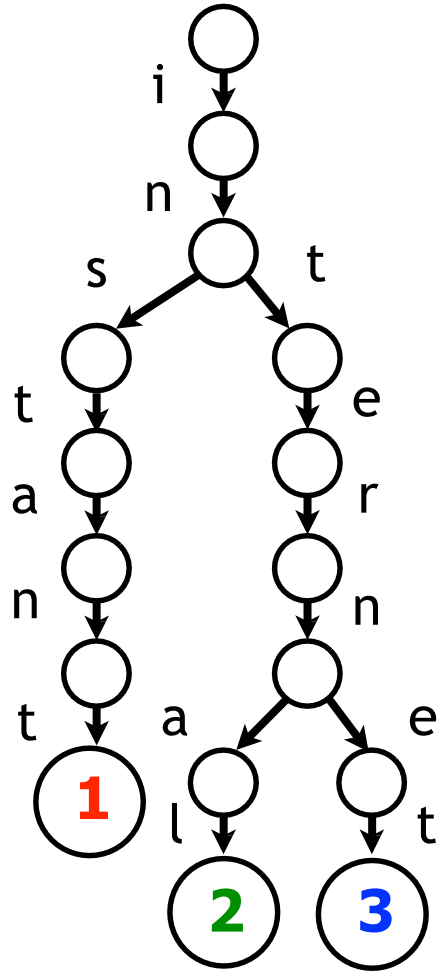
- Each edge is labeled with a character $c \in \Sigma$
- For given node, at most one child edge has label c, for any $c \in \Sigma$
- Each key is "spelled out" along some path starting at root

Helpful for implementing a *set* or *map* when the keys are strings

Tries

Keys: instant, internal, internet

Key	Value
instant	1
internal	2
internet	3



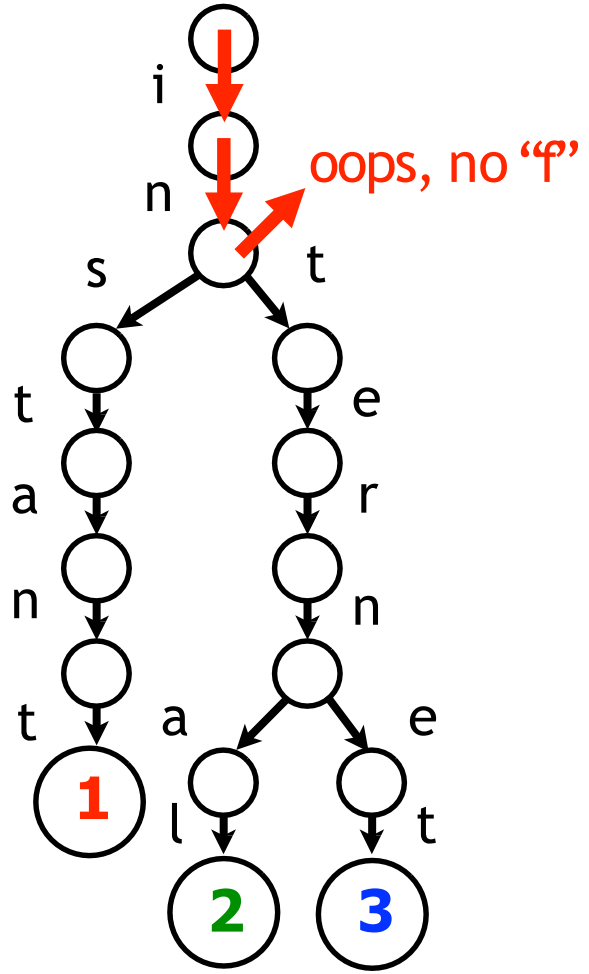
Smallest tree such that:

- Each edge is labeled with a character $c \in \Sigma$
- For given node, at most one child edge has label c, for any $c \in \Sigma$
- Each key is "spelled out" along some path starting at root

Tries

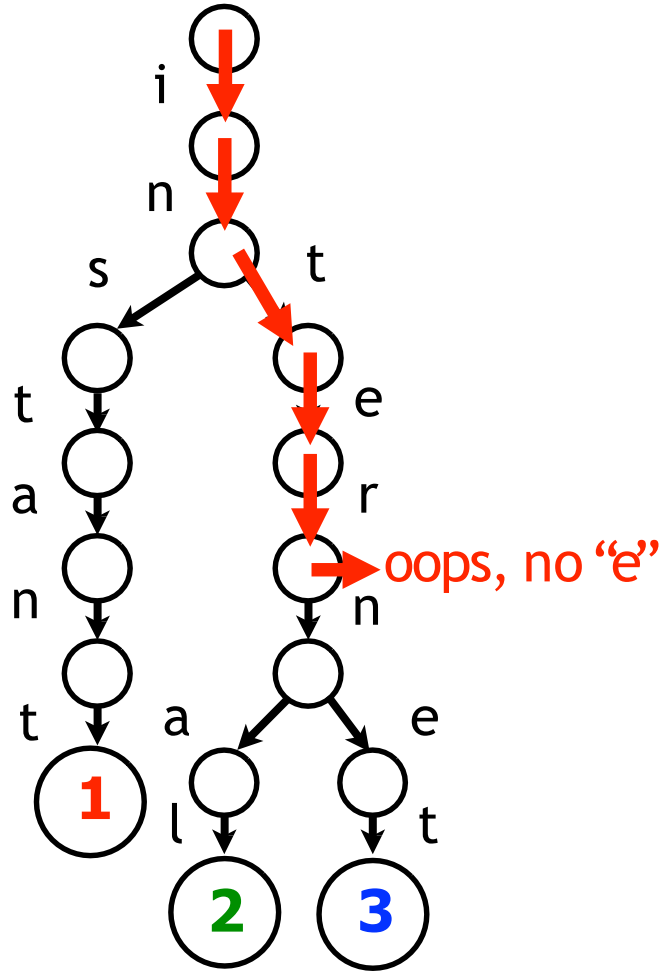
How do we check whether "infer" is in the trie?

Start at root and try to match successive characters of "infer" to edges in trie



Tries

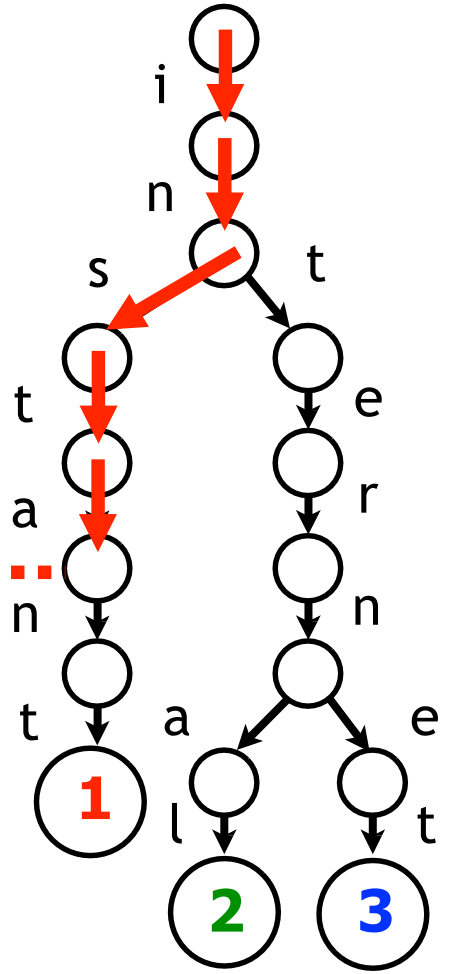
Matching “interesting”



Tries

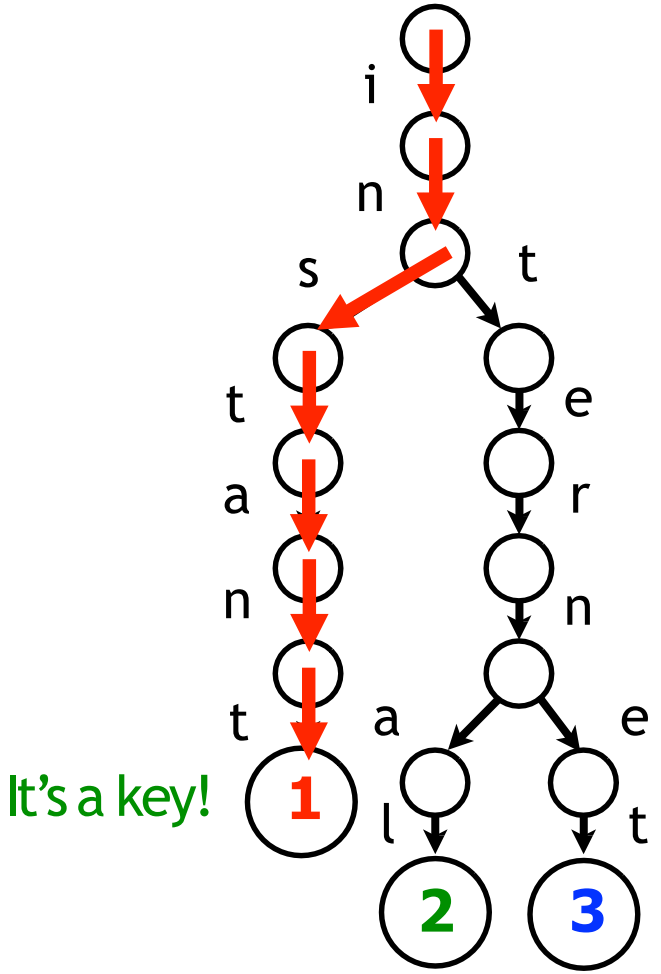
Matching “insta”

No value associated with node, so “insta” wasn’t a key

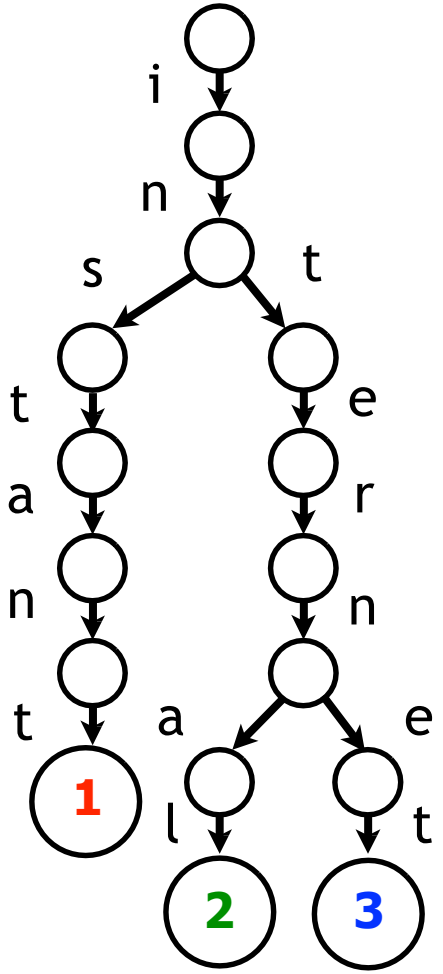


Tries

Matching “instant”



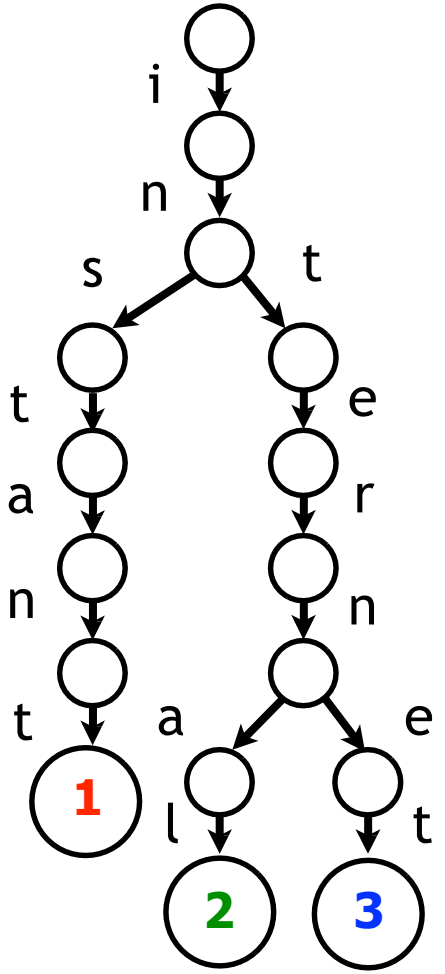
Tries



Checking for presence of key *P*, where $|P| = n$ traverses $\leq$ ***n*** edges

If total length of all keys is *N*, trie has $\leq$ ***N*** edges

Tries



How to represent edges between a node and its children?

Map (from characters to child nodes)

Idea 1: Hash table

Idea 2: Sorted lists

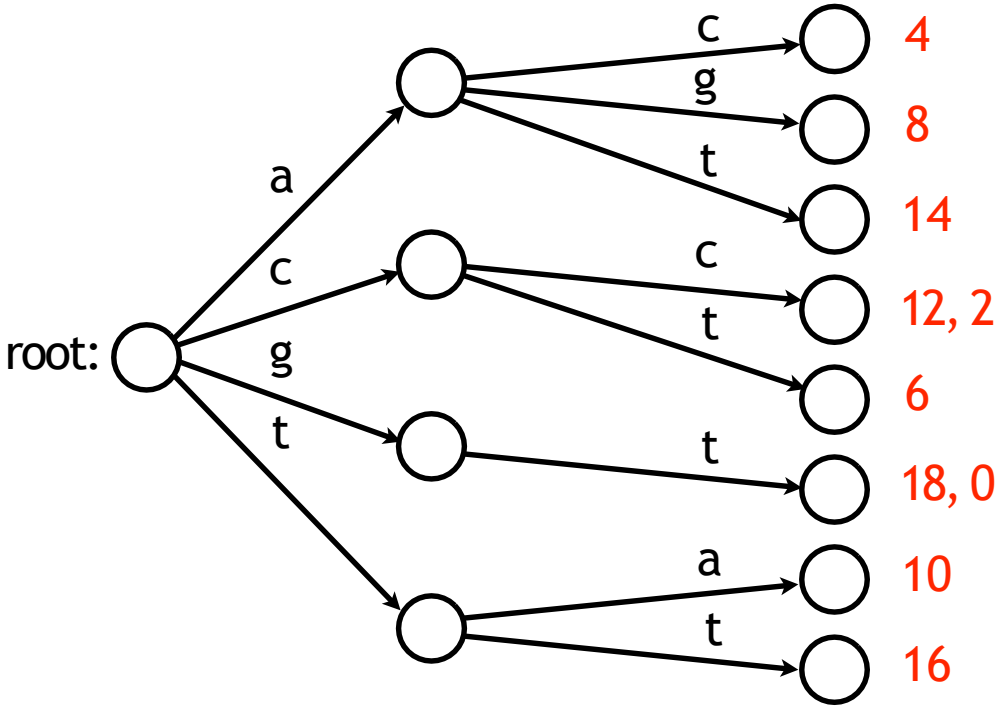
Assuming hash table, it's reasonable to say querying with P, $|P| = n$, is $O(n)$ time

Tries

Could use trie to represent *k*-mer index.
Map *k*-mers to offsets where they occur

Index

ac	4
ag	8
at	14
cc	12
cc	2
ct	6
gt	18
gt	0
ta	10
tt	16



Tries: implementation

Code

```
class TrieMap(object):
    """ Trie implementation of a map.
        Associating keys (strings or other
        sequence type) with values.  Values
        can be any type. """

    def __init__(self, kvs):
        self.root = {}
        # For each key (string)/value pair
        for (k, v) in kvs: self.add(k, v)

    def add(self, k, v):
        """ Add a key-value pair """
        cur = self.root
        for c in k: # for each character
                    # in the string
            if c not in cur:
                cur[c] = {}
            cur = cur[c]
        cur['value'] = v # at the end of
                         # the path, add
                         # the value
```

Code

```
[...]


def query(self, k):
    # Given key, return associated
    # value or None
    cur = self.root
    for c in k:
        if c not in cur:
            return None # key wasn't
                        # in the trie
        cur = cur[c]
    # get value, or None if there's no
    # value associated with this node
    return cur.get('value')
```

Tries: alternatives

Tries aren't the only way to encode sets or maps over strings using a tree.

E.g. ternary search tree:

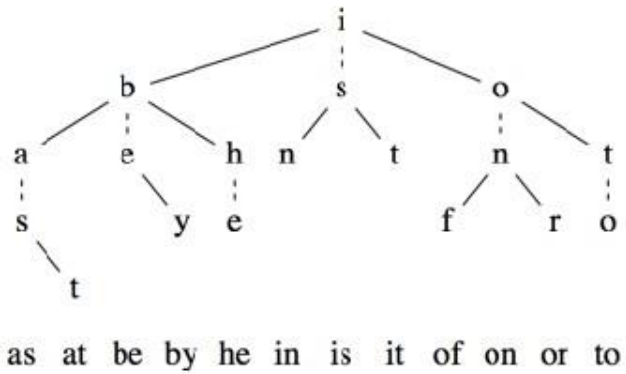
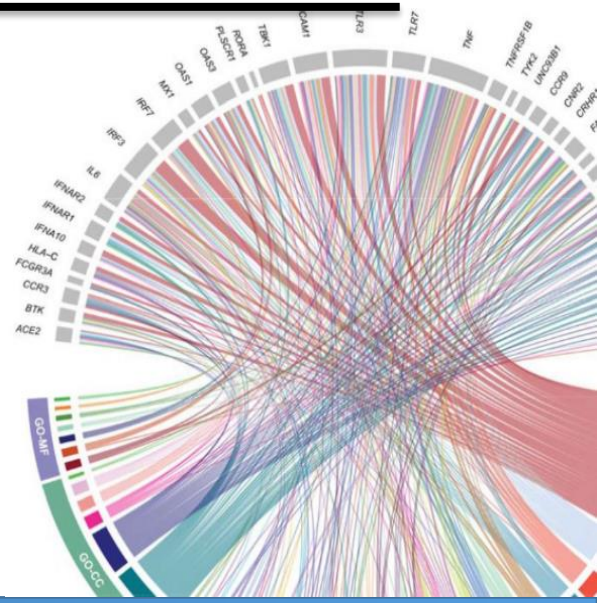


Figure 2. A ternary search tree for 12 two-letter words

Bentley, Jon L., and Robert Sedgewick. "Fast algorithms for sorting and searching strings." *Proceedings of the eighth annual ACM-SIAM symposium on Discrete algorithms*. Society for Industrial and Applied Mathematics, 1997

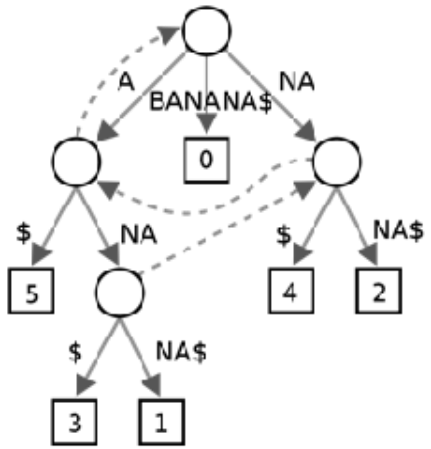
2 Suffix Tries



Indexing with suffixes

We studied indexes built over substrings of *T*

Different approach is to index *suffixes* of *T*. This yields surprisingly economical & practical data structures:



Suffix Tree

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

Suffix Array

$BANANA
A$BANAN
ANA$BAN
ANANA$B
BANANA$
NA$BANA
NANA$BA

FM Index

Suffix trie

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

Suffix trie

First add special *terminal character* **$** to the end of *T*

$ is a character that does not appear elsewhere in *T*, and we define it to be less than other characters (**$** < **A** < **C** < **G** < **T**)

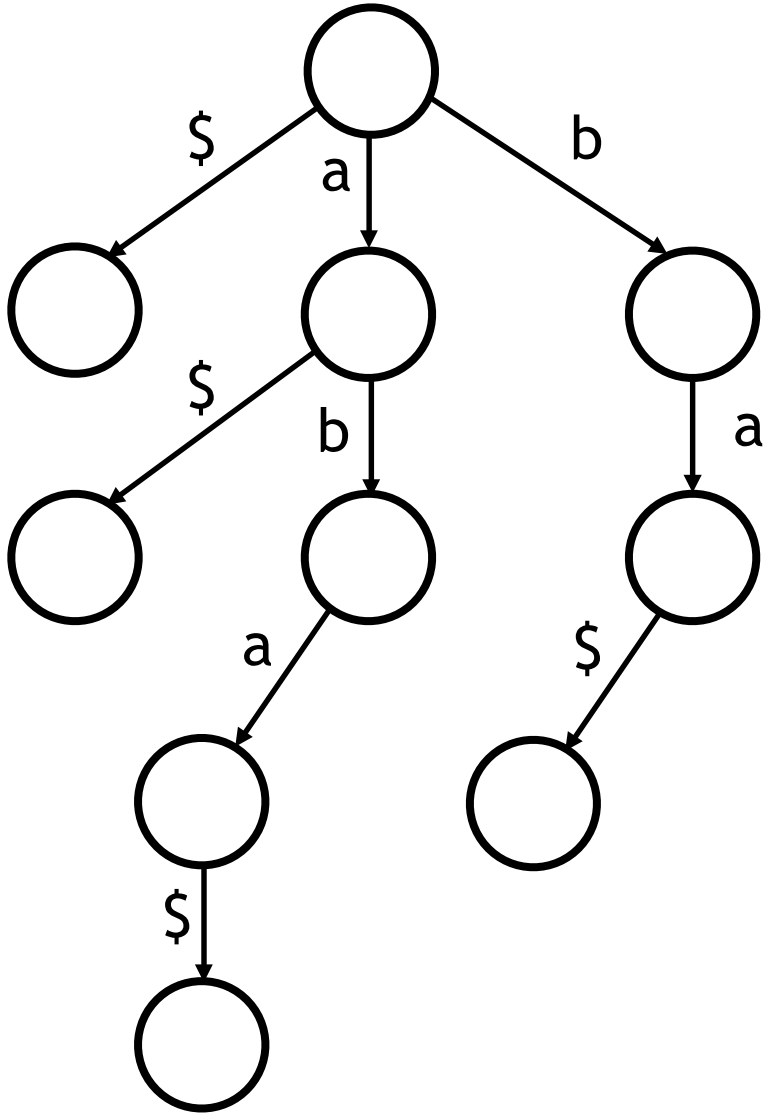
$ enforces a familiar rule: e.g. "as" comes before "ash" in the dictionary.
$ also guarantees no suffix is a prefix of any other suffix.

T: G T T A T A G C T G A T C G C G G C G T A G C G G $
G T T A T A G C T G A T C G C G G C G T A G C G G $
T T A T A G C T G A T C G C G G C G T A G C G G $
T A T A G C T G A T C G C G G C G T A G C G G $
A T A G C T G A T C G C G G C G T A G C G G $
T A G C T G A T C G C G G C G T A G C G G $
A G C T G A T C G C G G C G T A G C G G $
G C T G A T C G C G G C G T A G C G G $
C T G A T C G C G G C G T A G C G G $
T G A T C G C G G C G T A G C G G $
G A T C G C G G C G T A G C G G $
A T C G C G G C G T A G C G G $
T C G C G G C G T A G C G G $
C G C G G C G T A G C G G $
G C G G C G T A G C G G $

Suffix trie

T: aba**$**

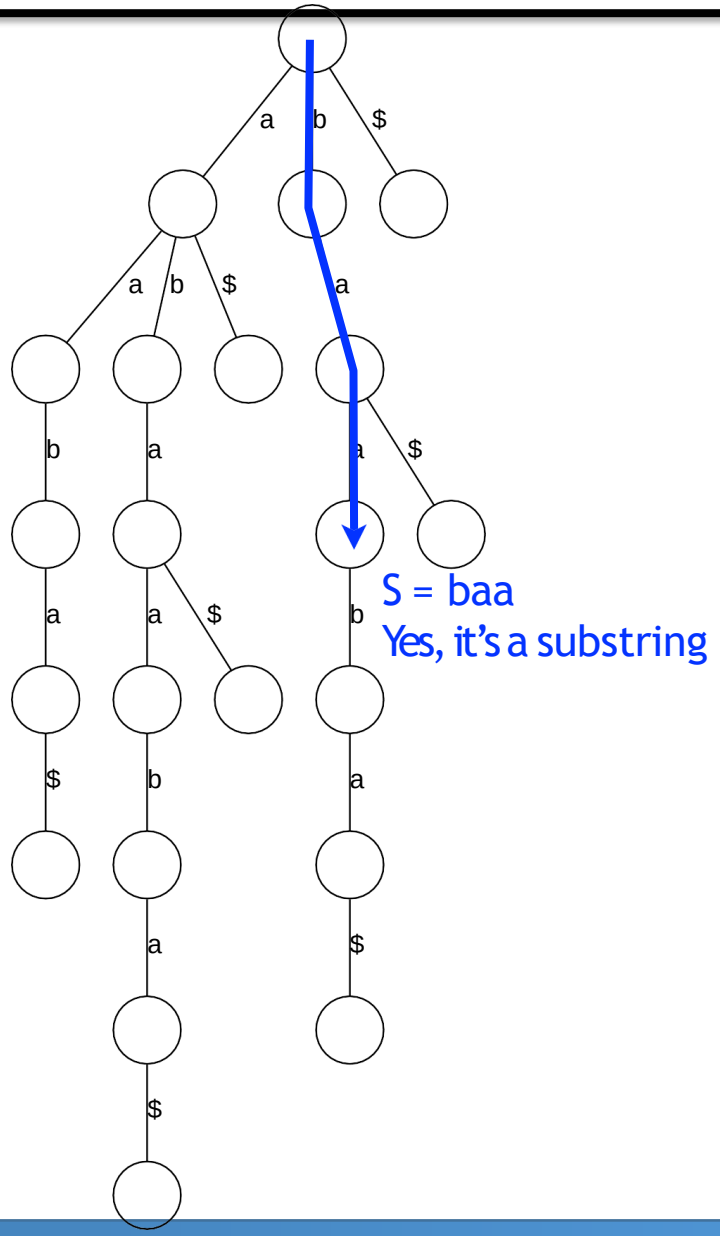
What's the suffix trie?



Suffix trie

- 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.

- 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 -- i.e. there is no outgoing edge for next character of S, then S is not a substring of T
  - If we exhaust S without falling off, S is a substring of T

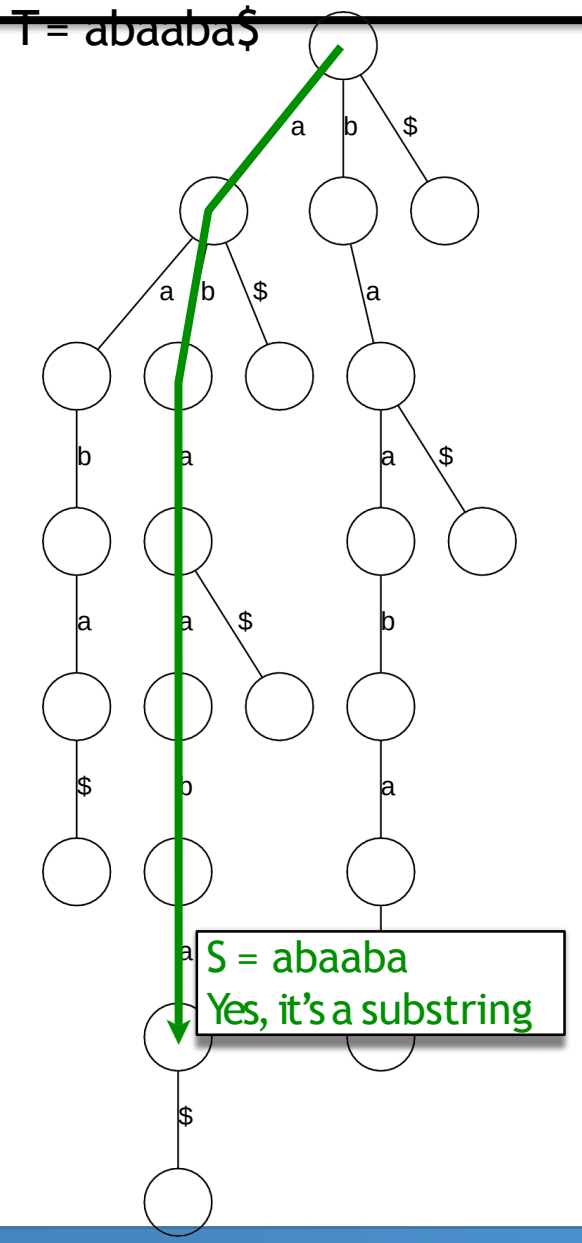


S = baa
Yes, it's a substring

Suffix trie

- 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.

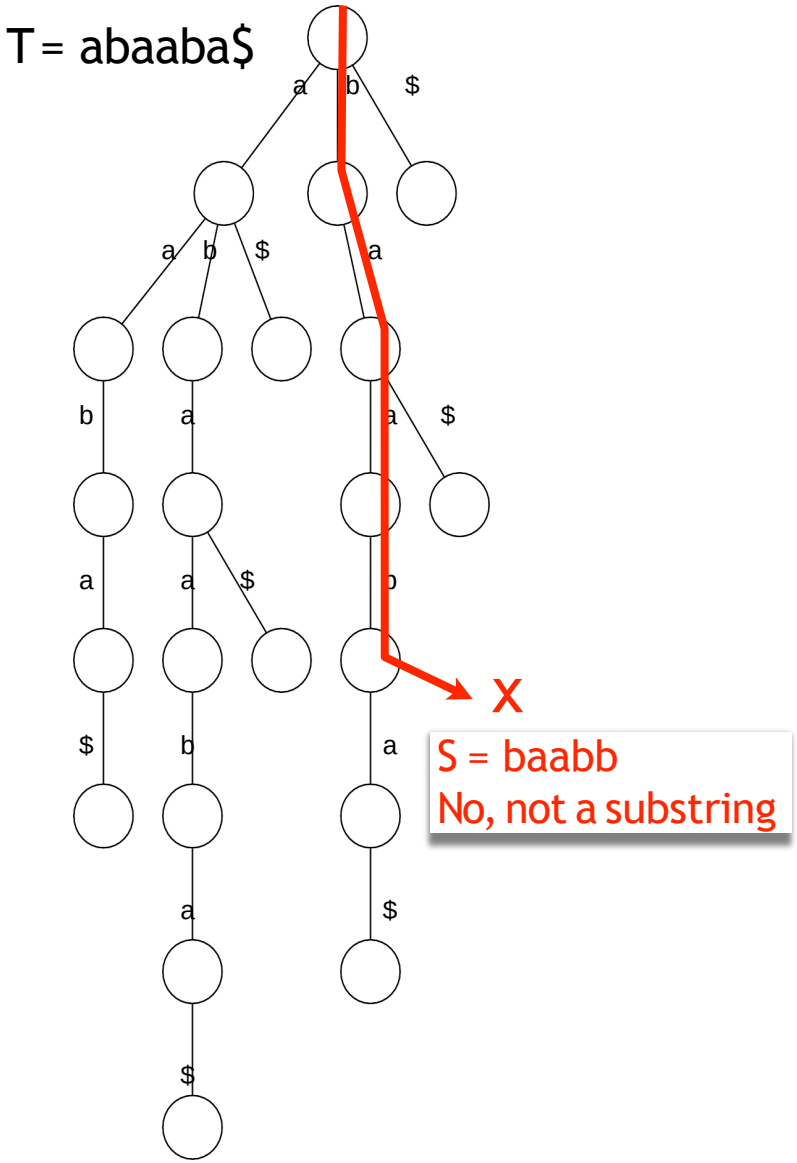
- Every substring is a prefix of some suffix of T.
  - Start at the root and follow the edges labeled with the characters of S
  - If we "fall off" the trie -- i.e. there is no outgoing edge for next character of S, then S is not a substring of T
  - If we exhaust S without falling off, S is a substring of T



Suffix trie

- 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.

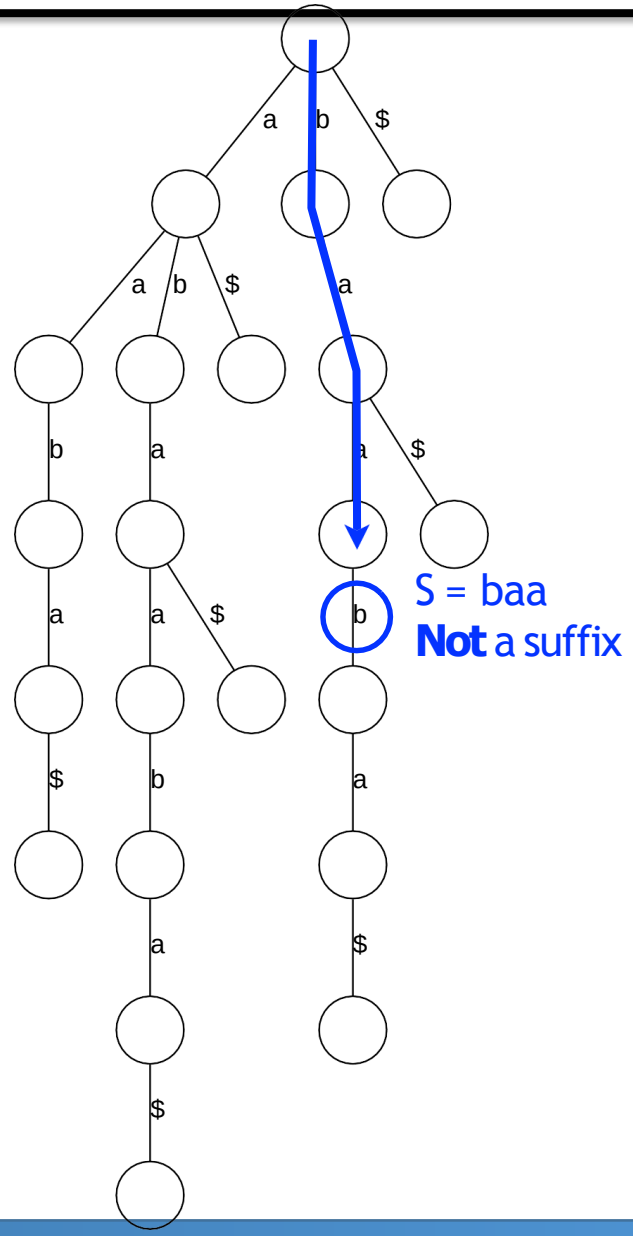
- Every substring is a prefix of some suffix of T.
  - Start at the root and follow the edges labeled with the characters of S
  - If we "fall off" the trie -- i.e. there is no outgoing edge for next character of S, then S is not a substring of T
  - If we exhaust S without falling off, S is a substring of T



Suffix trie

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

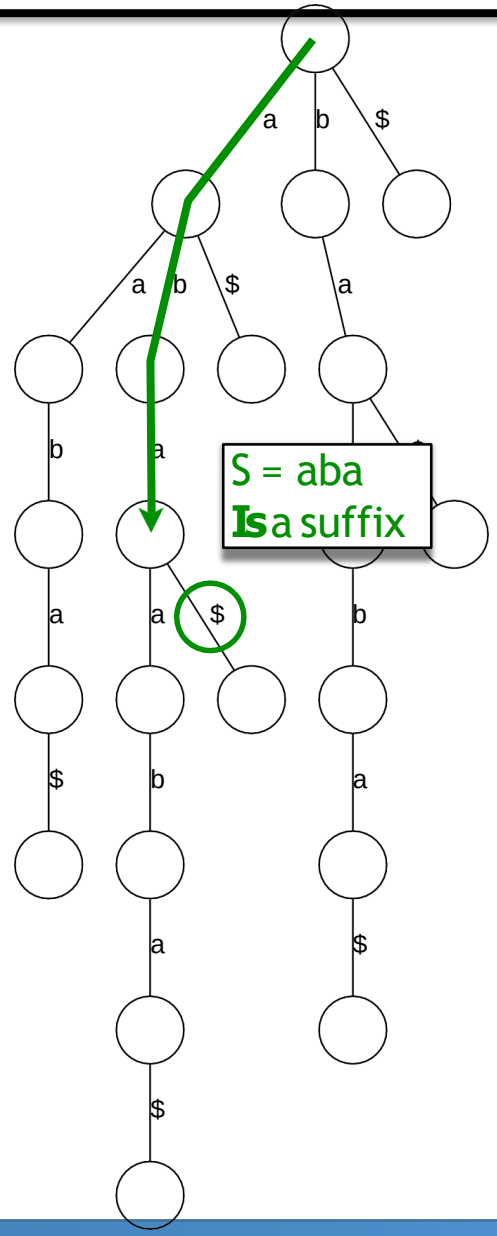
Same procedure as for substring, but additionally check terminal node for **$** child



Suffix trie

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

Same procedure as for substring, but additionally check terminal node for **$** child

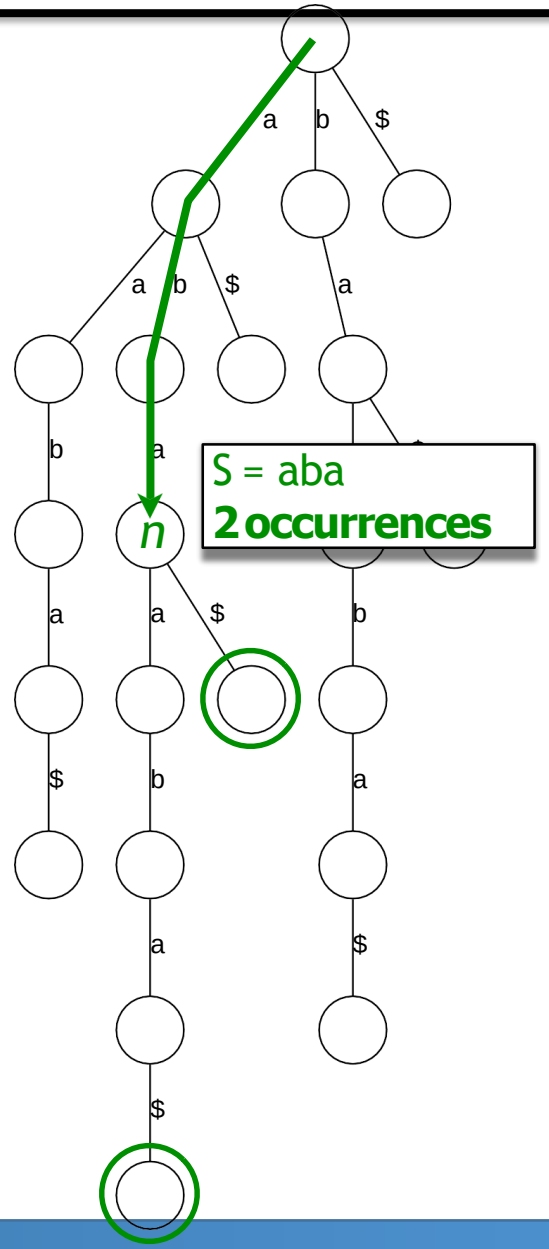


Suffix trie

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

Follow path labeled with *S*. If we fall off, answer is 0. If we end up at node *n*, answer equals # of leaves in subtree rooted at *n*.

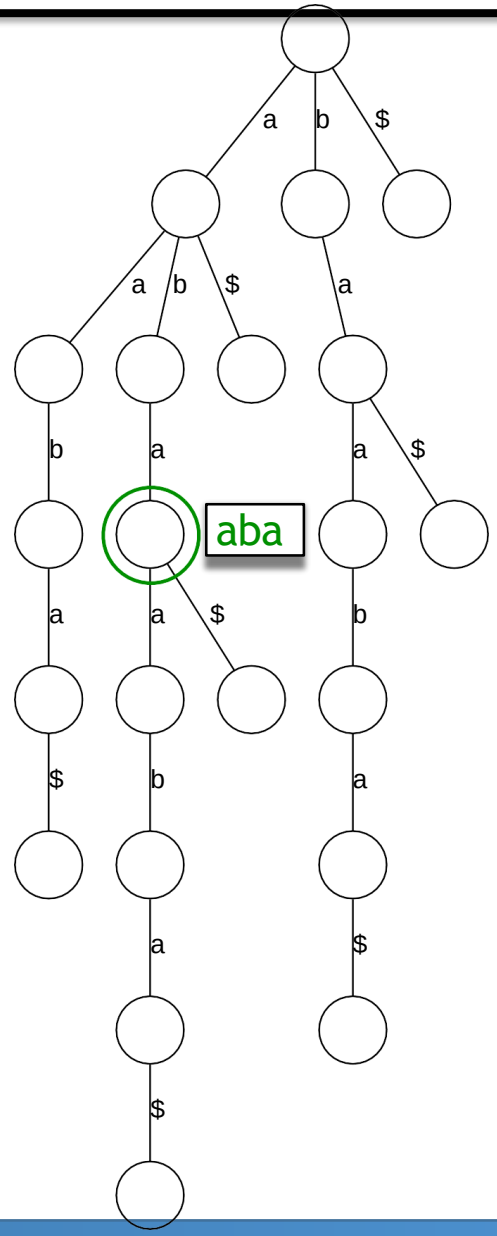
Leaves can be counted with depth-first traversal.



Suffix trie

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

Find the deepest node with more than one child



Suffix trie

How does the suffix trie grow with $|T| = m$?

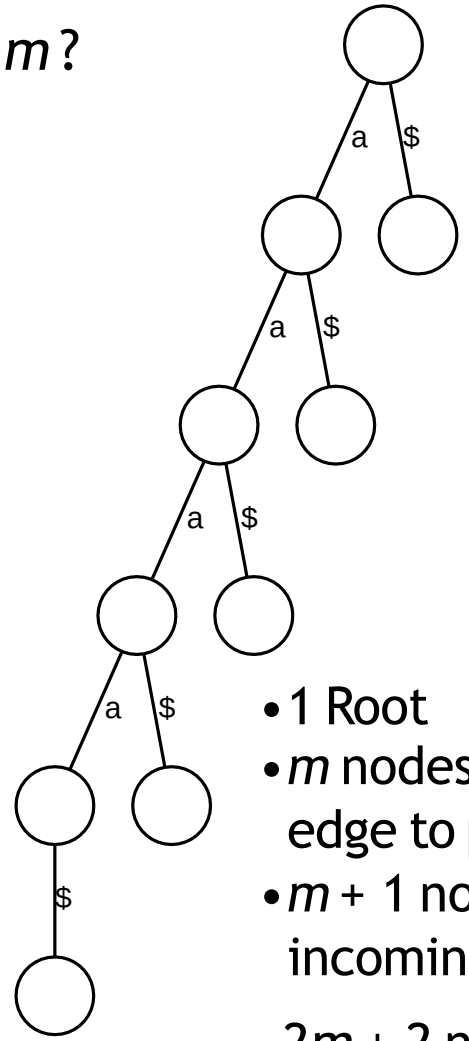
Suffix trie

How does the suffix trie grow with $|T| = m$?

Is there a class of string where the number of suffix trie nodes grows linearly with m?

Yes: a string of m a's in a row (a^m)

T = aaaa$



- 1 Root
- m nodes with "a" edge to parent
- $m + 1$ nodes with incoming **$** edge

$2m + 2$ nodes

Suffix trie

T = aaabbb$

How does the suffix trie grow with $|T| = m$?

Is there a class of string where the number of suffix trie nodes grows with m^2?

Yes: $a^n b^n$ where $2n = m$

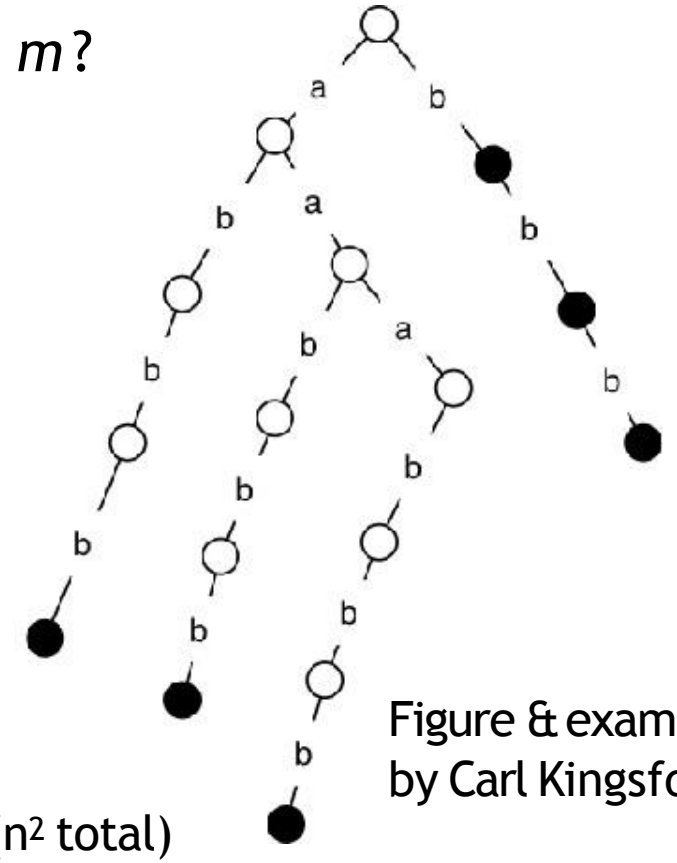


Figure & example by Carl Kingsford

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

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

Suffix trie: upper bound on size: idea 1

Recall our function for build building a suffix trie

```
def __init__(self, t):
    """ Make suffix trie from t """
    t += '$'
    self.root = {}
    for i in range(len(t)):
        cur = self.root
        for c in t[i:]:
            if c not in cur:
                cur[c] = {}
            cur = cur[c]
```

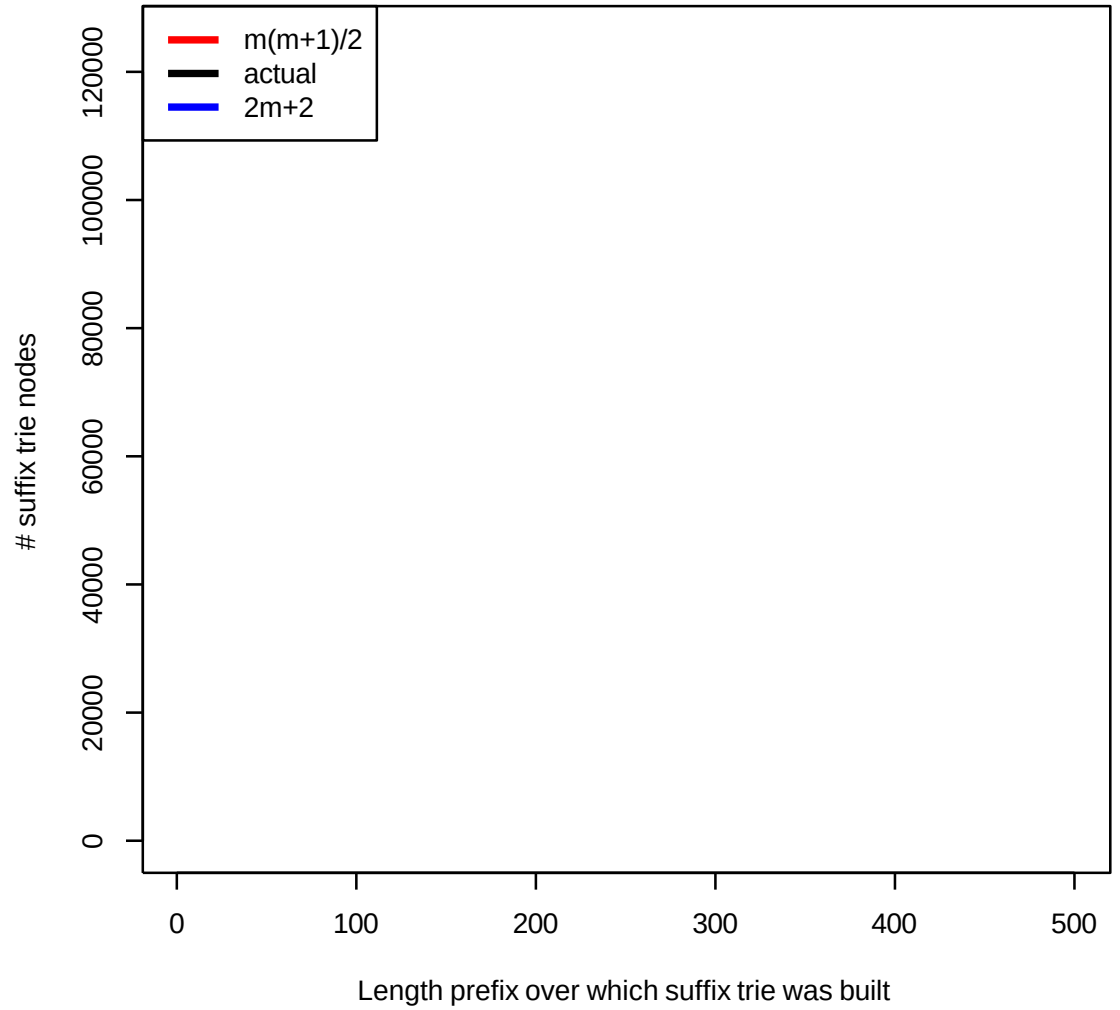
Adds 1 node, runs at most $m(m+1)/2$ times

```
GTTATAGCTGATCGCGGCGTAGCGG$
GTTATAGCTGATCGCGGCGTAGCGG$
 TTATAGCTGATCGCGGCGTAGCGG$
  TATAGCTGATCGCGGCGTAGCGG$
   ATAGCTGATCGCGGCGTAGCGG$
    TAGCTGATCGCGGCGTAGCGG$
     AGCTGATCGCGGCGTAGCGG$
      GCTGATCGCGGCGTAGCGG$
       CTGATCGCGGCGTAGCGG$
        TGATCGCGGCGTAGCGG$
         GATCGCGGCGTAGCGG$
          ATCGCGGCGTAGCGG$
           TCGCGGCGTAGCGG$
            CGCGGCGTAGCGG$
             GCGGCGTAGCGG$
              CGGCGTAGCGG$
               GGCGTAGCGG$
                GCGTAGCGG$
                 CGTAGCGG$
                  GTAGCGG$
                   TAGCGG$
                    AGCGG$
                     GCGG$
                      CGG$
                       GG$
                        G$
                         $
```

Suffix trie: actual growth

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

Black curve shows how # nodes increases with prefix length

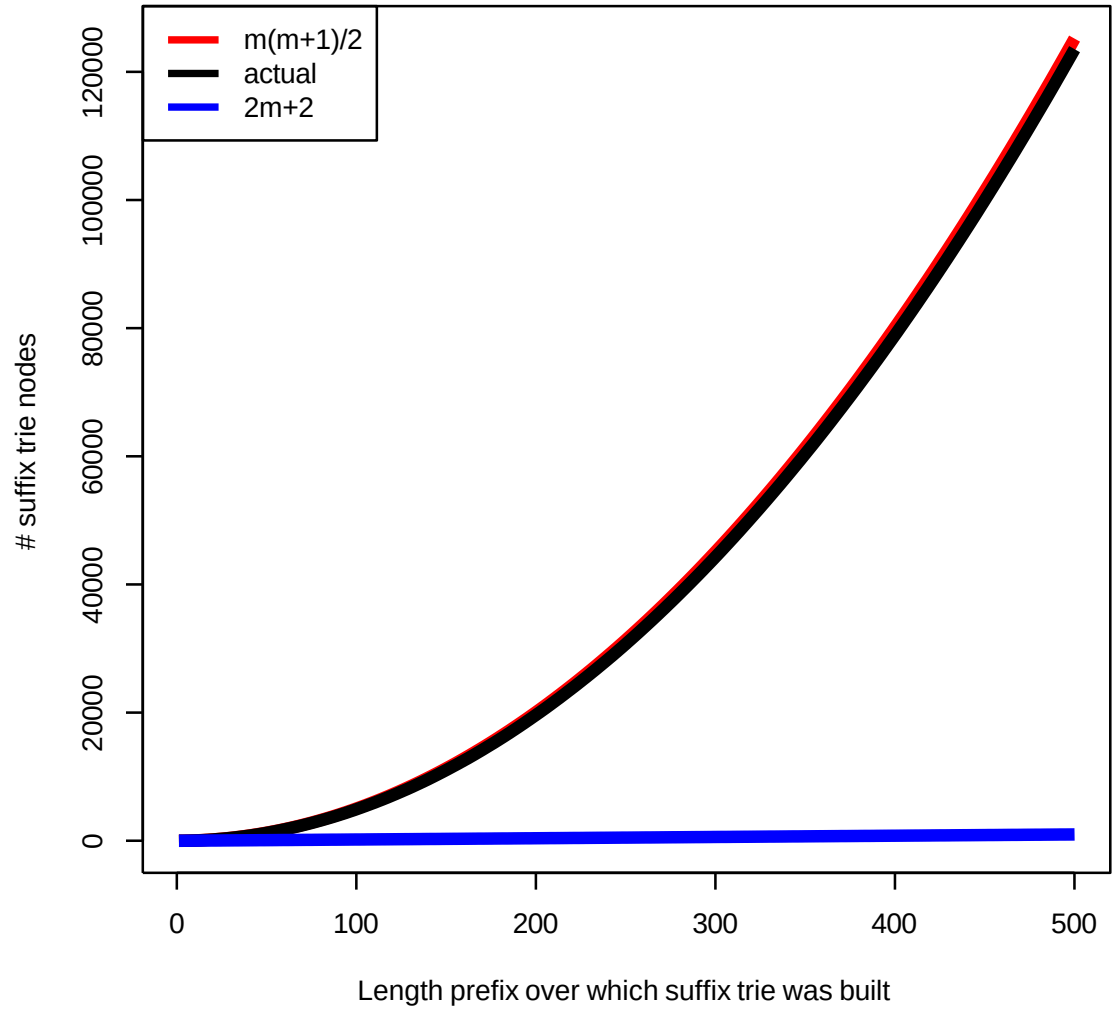


Suffix trie: actual growth

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

Black curve shows how # nodes increases with prefix length

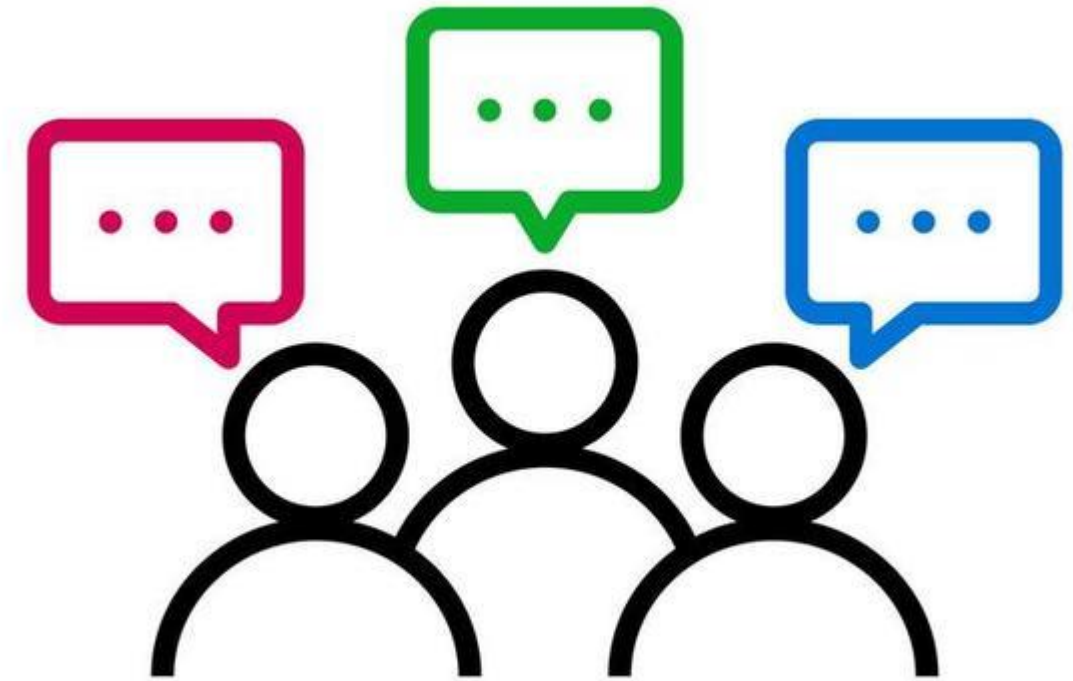
Actual growth *much* closer to worst case than to best!



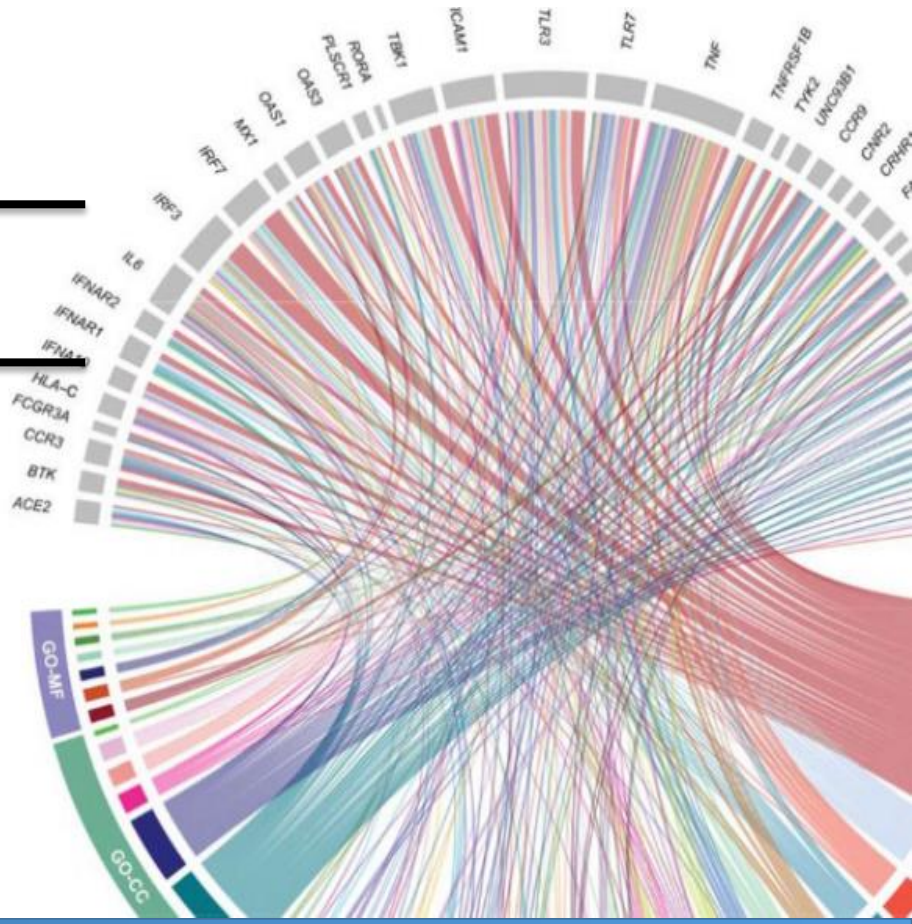
Exercise

Trie Exact Search

- Implement a program that constructs a suffix tree from a given reference and queries an input sequence.



Exercises


ICAM1
TLR3
TLR7
TNF
TNFRSF1B
TYK2
UNC93B1
CCR9
CNR2
TBK1
RORA
PLSCR1
OAS3
OAS1
MX1
IRF7
IRF3
IL6
IFNAR2
IFNAR1
HLA-C
FCGR3A
CCR3
BTK
ACE2
GO-MF
GO-CC