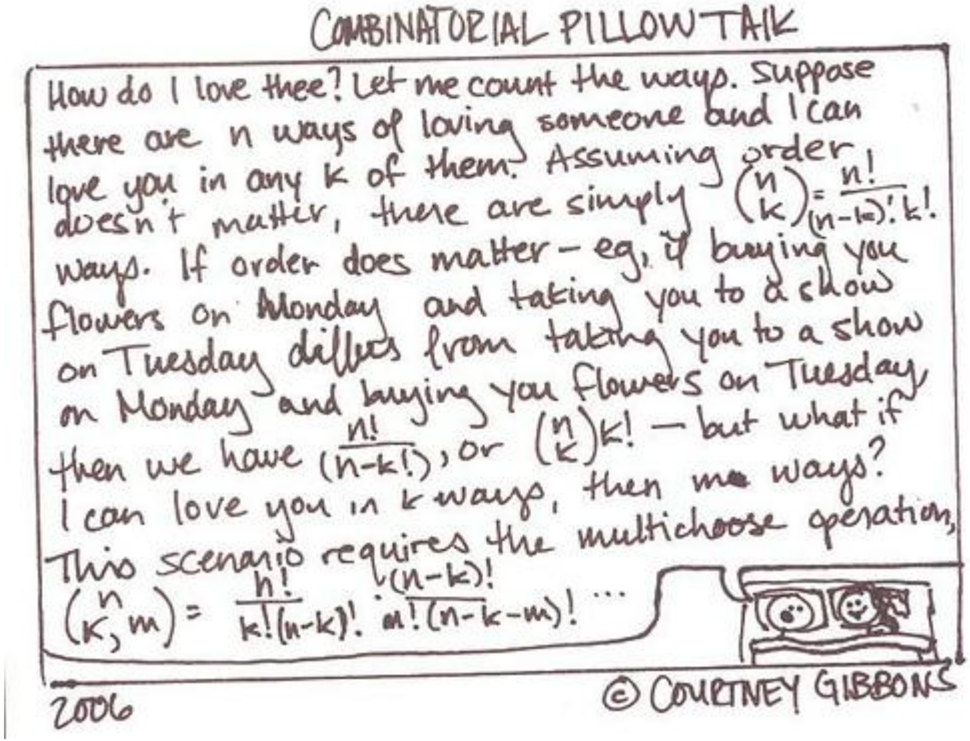
Comp 555 - BioAlgorithms - Spring 2022



- **PROBLEM SET #2 IS DUE NEXT THURSDAY**

Combinatorial Pattern Matching

A Recurring Problem in Sequence Analysis

- Finding patterns within sequences

- Variants on this idea
    - Finding repeated *motifs* amongst a set of strings
    - What are the most *frequent k-mers*
    - How many times does a *specific k-mer* appear

- Fundamental problem: *Pattern Matching*
    - Find all positions of a particular substring in given sequence?

Pattern Matching

The most fundamental of pattern matching problems--
does a pattern, *p*, appear in a text, *t*? And if so, where?

- **Goal:** Find all occurrences of a pattern in a text
- **Input:** Pattern $p = p_1,p_2,\ldots p_n$ and text $t = t_1,t_2,\ldots t_m$
- **Output:** All positions $1 < i < (m – n + 1)$ such that the *n*-letter substring of t starting at i matches p

```
In [2]:  def bruteForcePatternMatching(p, t):
             locations = []
             for i in range(0, len(t)-len(p)+1):
                 if t[i:i+len(p)] == p:
                     locations.append(i)
             return locations

         print(bruteForcePatternMatching("ssi", "imissmissmississippi"))

         [11, 14]
```

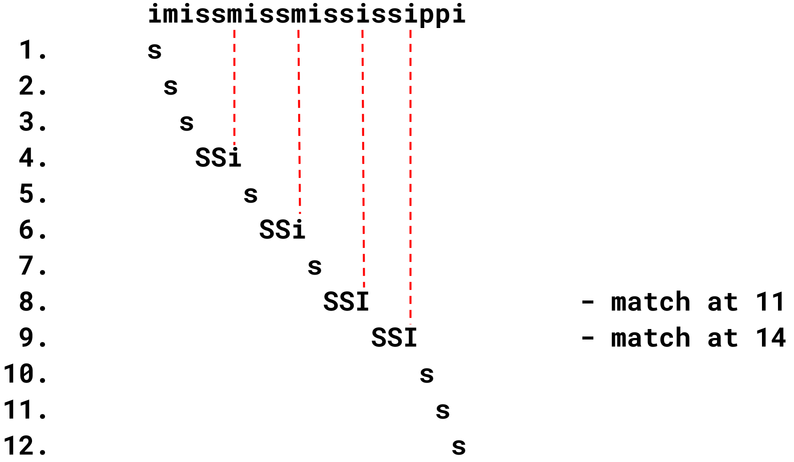
Pattern Matching Performance

- Performance:
    - *m* - length of the text *t*
    - *n* - the length of the pattern *p*
    - Search Loop - executed *O(m)* times (m-n+1)
    - Comparison - *O(n)* symbols compared, t_{j+i} == p_i for i in [0..n]
    - Total cost - *O(mn)* per pattern
- In practice, most comparisons will terminate early. Why?
- But worst-case data examples exist:
    - p = "AAAT"
    - t = "AAAAAAAAAAAAAAAAAAAAAAT"

We can do better!

If we preprocess our pattern we can search more efficiently (*O(n)*).

Example: FindPattern("ssi", "imissmissmississippi"):



```
         imissmissmississippi
 1.      s
 2.       s
 3.        s
 4.         SSi
 5.            s
 6.             SSi
 7.                s
 8.                 SSI             - match at 11
 9.                    SSI          - match at 14
10.                       s
11.                        s
12.                         s
```

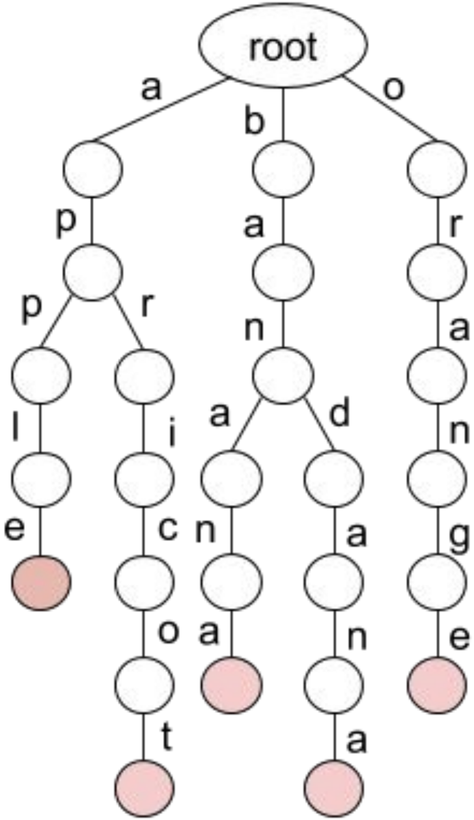
- At steps 4 and 6 after finding the mismatch *"i" ≠ "m"* we can skip over all positions tested because we know that the *suffix* *"sm"* is not a *prefix* of our pattern *"ssi"*.
- Even works for our worst-case example "AAAAT" in "AAAAAAAAAAAAAAT" by recognizing the shared prefixes ("AAA" in "AAAA").
- How about finding multiple patterns [p_1,p_2,...,p_3] in t

A Slight Pivot

- We could analyze the problem of finding a single pattern within a text an come up with the an optimal solution (O(m), size of text or O(n), size of pattern?)
- It is a worthwhile exercise (check out Boyer-Moore string search), but we should consider the following
    a. Generally, the text is far larger than the pattern, m >> n
    b. Generally, the pattern check performs far fewer than n tests at the m - n + 1 positions
    c. Generally, we will search for more than a single pattern, especially if we are looking in a large text. Should we start over for every search?

Keyword Trees

- We can also preprocess the set of pattern strings we are searching for to minimize the number of comparisons
- **Idea:** Combine patterns that share prefixes, to *share* those comparisons
  - Stores a set of keywords in a rooted labeled tree
  - Each edge labeled with a letter from an alphabet
  - All edges leaving a given vertex have distinct labels
  - Leaf vertices are indicated
  - Every keyword stored can be spelled on a path from the root to some leaf vertex
  - Searches are performed by "threading" the target pattern through the tree
- A *Tree* is a special graph as discussed previously
  - One connected component
  - *N* nodes, *N-1* edges, No loops
  - Exactly one path from any.
- A ***Trie*** is a tree that is related to a sequence.
  - Generally, there is a 1-to-1 correspondence between either nodes or edges of the *trie* and a symbol of the sequence



Prefix *Trie* Match

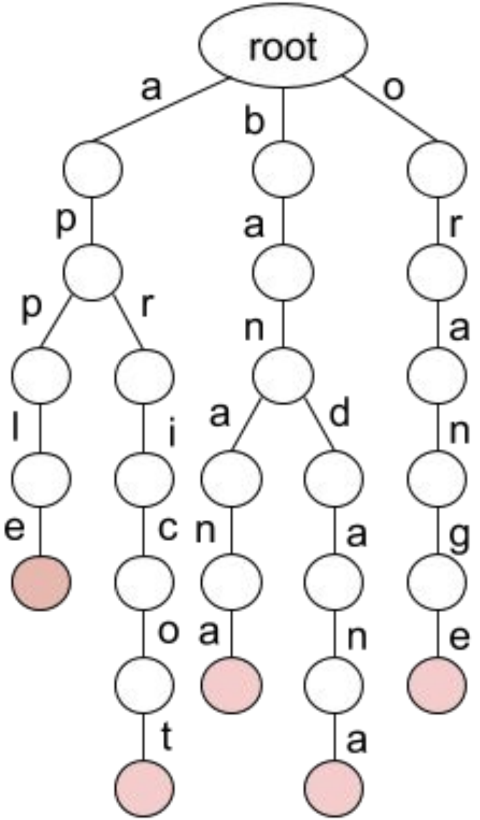
- **Input:** A text *t* and a trie *P* of patterns
- **Output:** True if *t* leads to a leaf in *P*; False otherwise

What is output for:

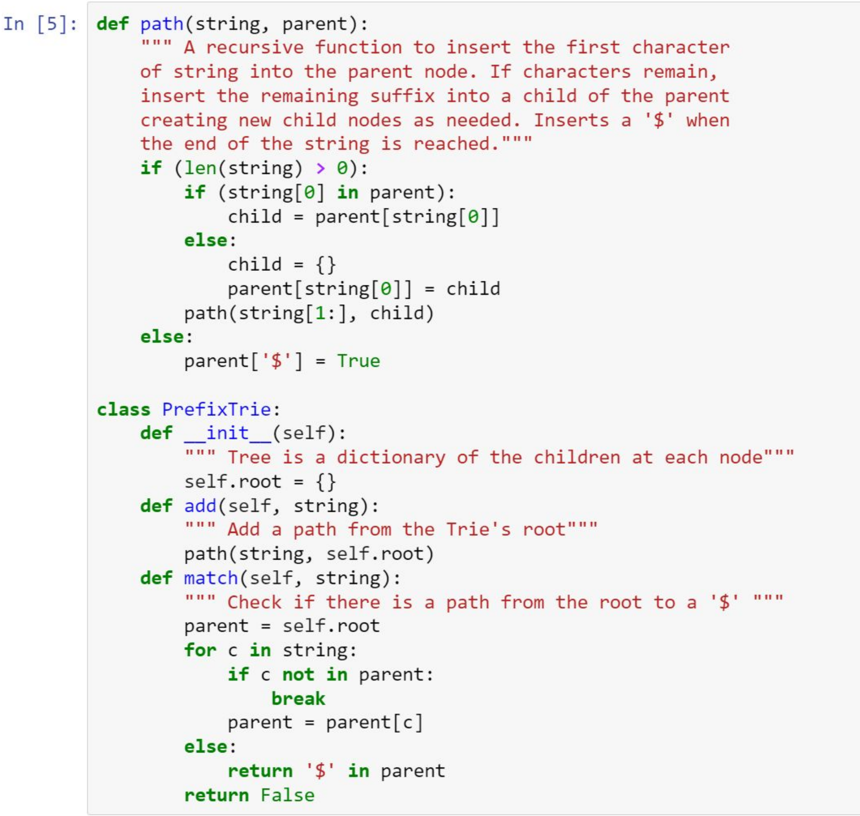
- *apple*
- *band*
- *april*

Performance:

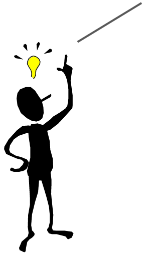
- O(m n_{max}) - m is the length of the text, *t*
  n_{max} - is the longest pattern in the tree



Prefix *Trie* code

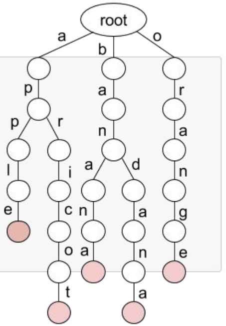


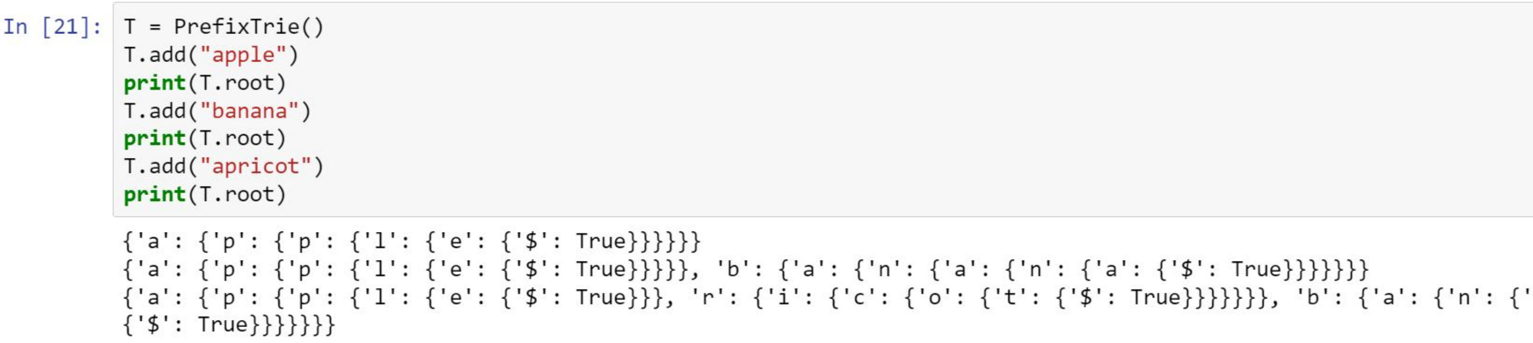
```
In [5]: def path(string, parent):
            """ A recursive function to insert the first character
            of string into the parent node. If characters remain,
            insert the remaining suffix into a child of the parent
            creating new child nodes as needed. Inserts a '$' when
            the end of the string is reached."""
            if (len(string) > 0):
                if (string[0] in parent):
                    child = parent[string[0]]
                else:
                    child = {}
                    parent[string[0]] = child
                path(string[1:], child)
            else:
                parent['$'] = True

        class PrefixTrie:
            def __init__(self):
                """ Tree is a dictionary of the children at each node"""
                self.root = {}
            def add(self, string):
                """ Add a path from the Trie's root"""
                path(string, self.root)
            def match(self, string):
                """ Check if there is a path from the root to a '$' """
                parent = self.root
                for c in string:
                    if c not in parent:
                        break
                    parent = parent[c]
                else:
                    return '$' in parent
                return False
```



Inserts the first character into the given parent, creating a child if needed to insert the next character into, continues until there is nothing left to insert then it adds a "$"

Prefix *Trie* code





In [21]:
```python
T = PrefixTrie()
T.add("apple")
print(T.root)
T.add("banana")
print(T.root)
T.add("apricot")
print(T.root)
```

```
{'a': {'p': {'p': {'l': {'e': {'$': True}}}}}}
{'a': {'p': {'p': {'l': {'e': {'$': True}}}}}, 'b': {'a': {'n': {'a': {'n': {'a': {'$': True}}}}}}}
{'a': {'p': {'p': {'l': {'e': {'$': True}}}, 'r': {'i': {'c': {'o': {'t': {'$': True}}}}}}}, 'b': {'a': {'n': {'a': {'n': {'a':
{'$': True}}}}}}}
```

In [22]:
```python
# Build Tree
T.add("bandana")
T.add("orange")

# Dump and use it
print(T.root)
print(T.match('orange'))
print([T.match(v) for v in ['apple', 'banana', 'apricot', 'orange', 'band', 'april', 'bandana', 'bananapple']])
```

```
{'a': {'p': {'p': {'l': {'e': {'$': True}}}, 'r': {'i': {'c': {'o': {'t': {'$': True}}}}}}}, 'b': {'a': {'n': {'a': {'n': {'a':
{'$': True}}}, 'd': {'a': {'n': {'a': {'$': True}}}}}}}, 'o': {'r': {'a': {'n': {'g': {'e': {'$': True}}}}}}}
True
[True, True, True, True, False, False, True, False]
```

Multiple Pattern Matching

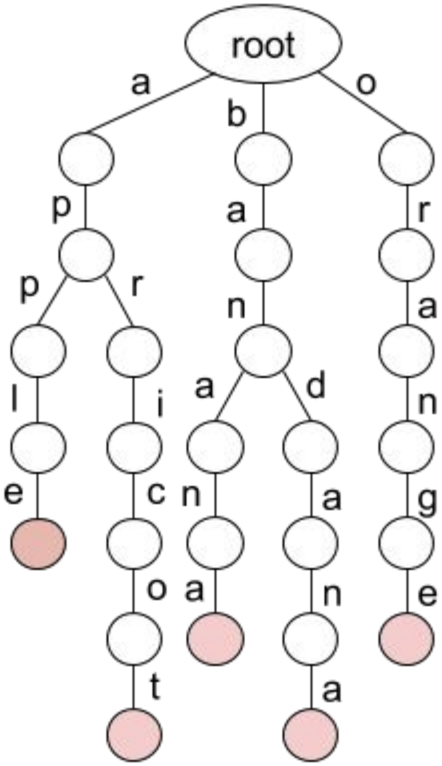
Suppose that we have a long string, *t*, like a genome, and we want to find if any of the strings in a previously constructed prefix trie, *P*, appear within it.

- *t* - the text to search through
- *P* - the trie of patterns to search for

```
def multiplePatternMatching(t, P):
    locations = []
    for i in range(0, len(t)):
        if PrefixTrieMatch(t[i:], P):
            locations.append(i)
    return locations
```

Multiple Pattern Matching Example

```
multiplePatternMatching(“bananapple”, P):
 0:  PrefixTrieMatching(“bananapple”, P) = True
 1:  PrefixTrieMatching(“ananapple”, P) = False
 2:  PrefixTrieMatching(“nanapple”, P) = False
 3:  PrefixTrieMatching(“anapple”, P) = False
 4:  PrefixTrieMatching(“napple”, P) = False
 5:  PrefixTrieMatching(“apple”, P) = True
 6:  PrefixTrieMatching(“pple”, P) = False
 7:  PrefixTrieMatching(“ple”, P) = False
 8:  PrefixTrieMatching(“le”, P) = False
 9:  PrefixTrieMatching(“e”, P) = False

locations = [0, 5]
```



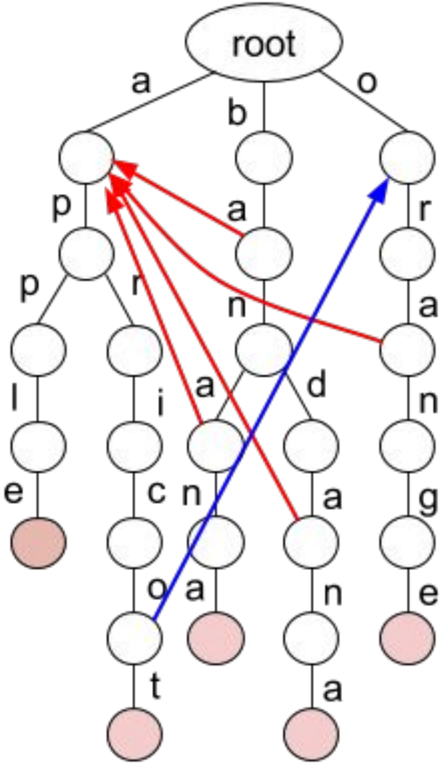
This process is called "threading" the text through the tree

Trie Improvements

- Based on our previous speed-up
- We can add failure edges to our Trie
  Add an edge to any *prefix* from the root
  that matches a *suffix* on our failed path
- *Aho-Corasick* Algorithm

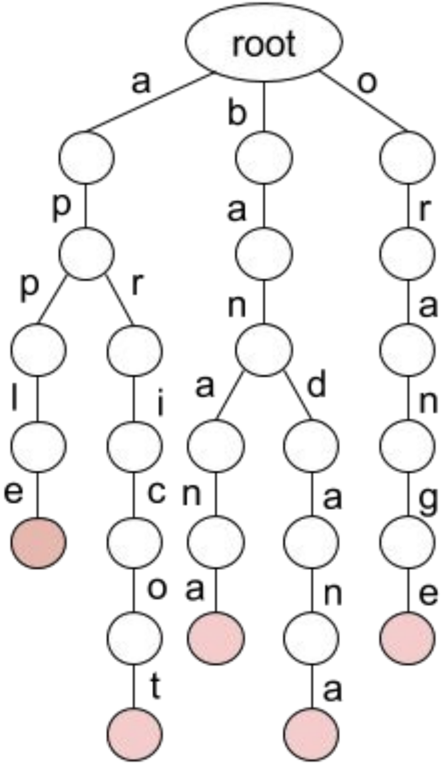
How it works

```
bapple          apricorange
bap             apricor
 apple                orange
     *                     *
```



Multiple Pattern Matching Performance

- m - len(t)
- d - max depth of P (longest pattern in P)
- O(md) to find all patterns
- Can be decreased further to O(m) using Aho-Corasick Algorithm
    - Add links for pattern suffixes that match text prefixes
- Pattern matching data structure is query specific

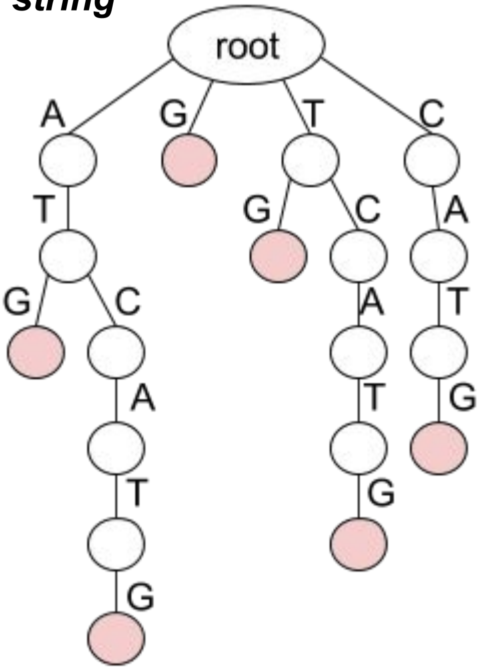


***Idea:** Rather than building a search data structure for indexing the prefixes of search patterns, what if we built one for indexing every suffix of the **text**.*

Now for a Twist

- What if our list of keywords were simply all ***suffixes*** of a ***single given string***

```
Example: ATCATG
          TCATG
           CATG
            ATG
             TG
              G
```

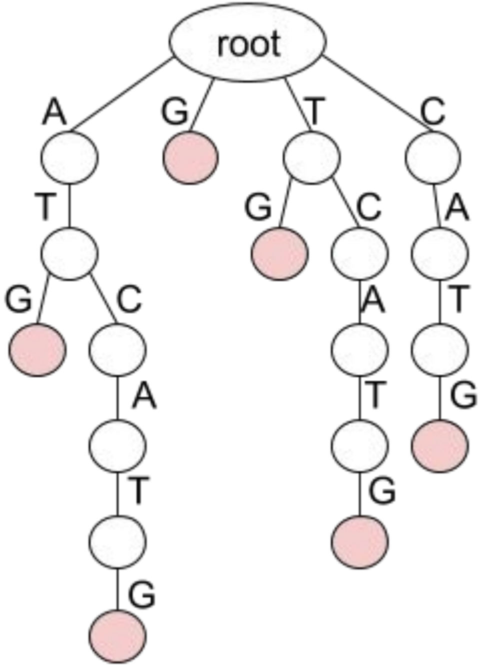


  - The resulting keyword tree:
  - A **Suffix Trie**
  - How would you find "CAT"
  - It is a prefix of one of our suffixes
  - If there is a path for our entire pattern, we know which suffix it came from
  - Try "AT"

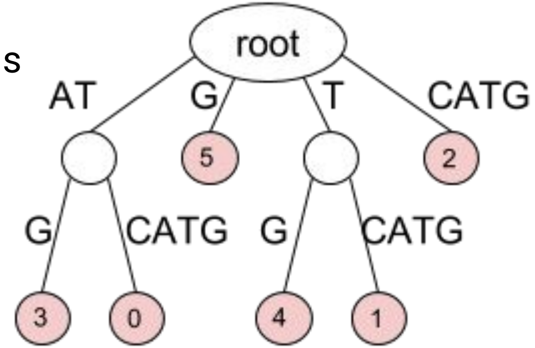
What advantages might this approach have?

Suffix Tree

A *compressed* Suffix Trie



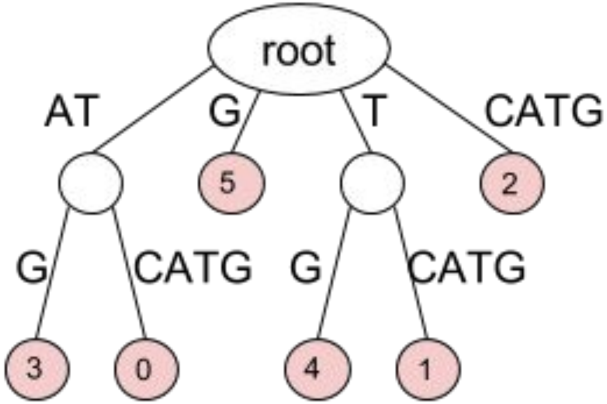
- Combine nodes with in and out degree 1
- Make edges of these substrings
- All internal nodes have at least 3 edges
- Leaf nodes are labeled with the suffix indices



```
012345
ATCATG
```

Uses for Suffix Trees

- Suffix trees hold all suffixes of a text, T
    - i.e., ATCATG: ATCATG, TCATG, CATG, ATG, TG, G
- Can be built in O(m) time for text of length m
- To find any pattern P in a text:
    - Build suffix tree for text, O(m), m=|T|
    - Thread the pattern through the suffix tree
    - Can find pattern in O(n) time! (n=|P|)
- O(|T|+|P|) time for "Pattern Matching Problem" (better than Naïve O(|P||T|)
- Build suffix tree and lookup pattern
- Multiple Pattern Matching in O(|T|+k|P|)

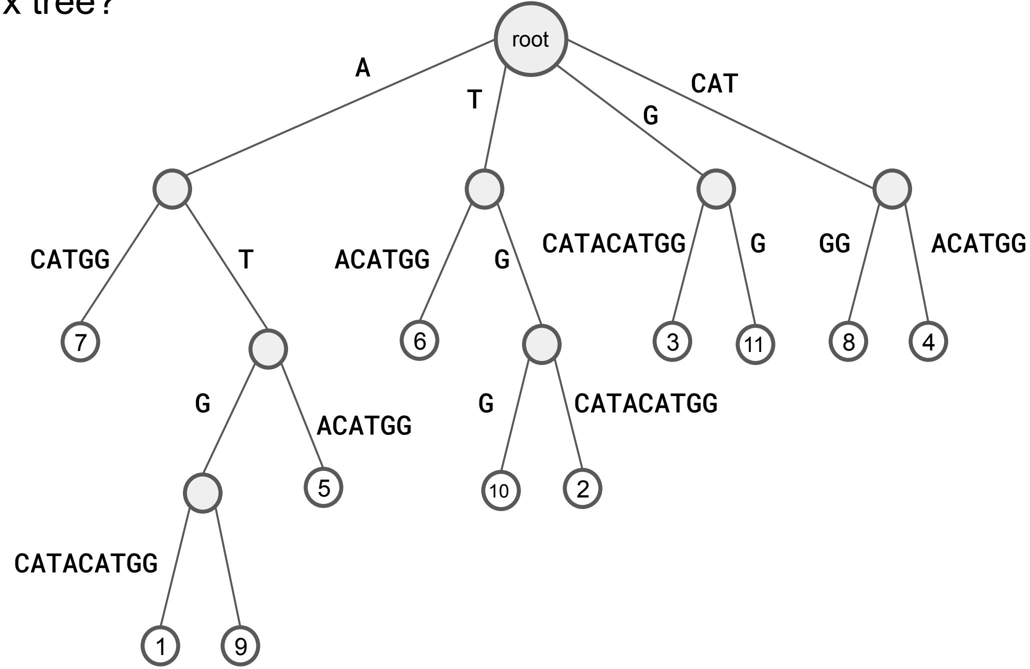


Suffix Tree Overhead

- Input: text of length m
- Computation
    - O(m) to compute a suffix tree
    - Does not require building the suffix trie first
- Memory
    - O(m) - nodes are stored as offsets and lengths
- Huge hidden constant, best implementations
- Requires about 20*m bytes
- 3 GB human genome = 60 GB RAM

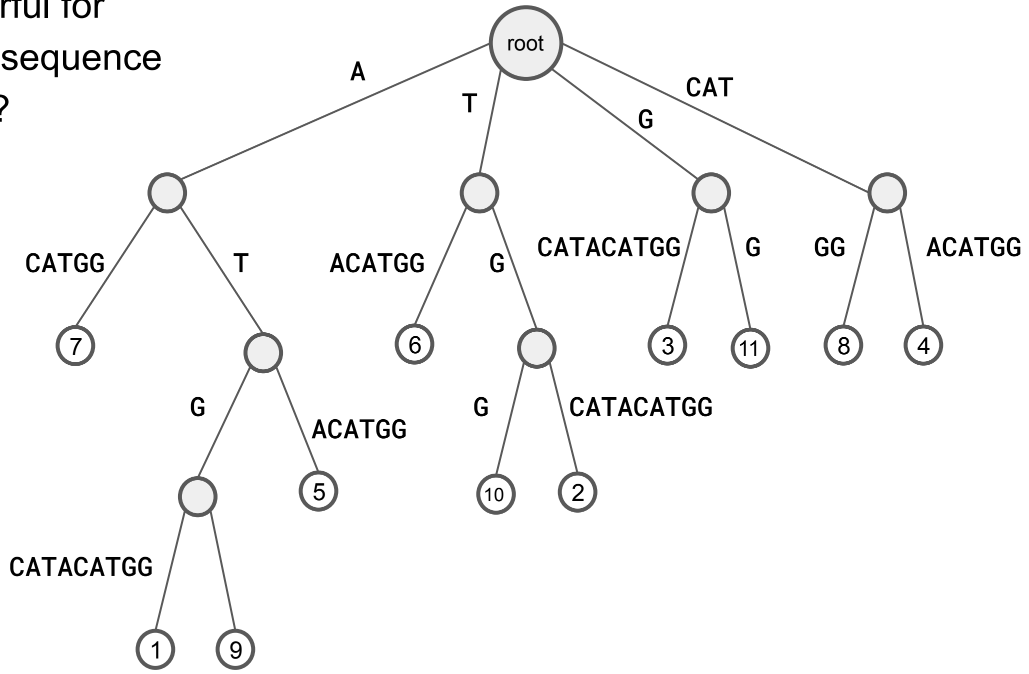
Suffix Tree Examples

- What is the string represented in the suffix tree?
  Find path that leads to "1"
- What letter occurs most frequently?
  Find edge from the root leads to the most leafs
- How many times does "ATG" appear, and where?
  Match "ATG" to tree and count the number of leafs from that path
- How long is the longest repeated k-mer?
  Find longest path leading to two leafs



Suffix Trees: Theory vs. Practice

- In theory, suffix trees are extremely powerful for making a variety of queries concerning a sequence
  - What is the shortest unique substring?
  - How many times does a given string appear in a text?
- Despite the existence of linear-time construction algorithms, and O(m) search times, suffix trees are still rarely used for genome-scale searching
- Large storage overhead



Substring Searching

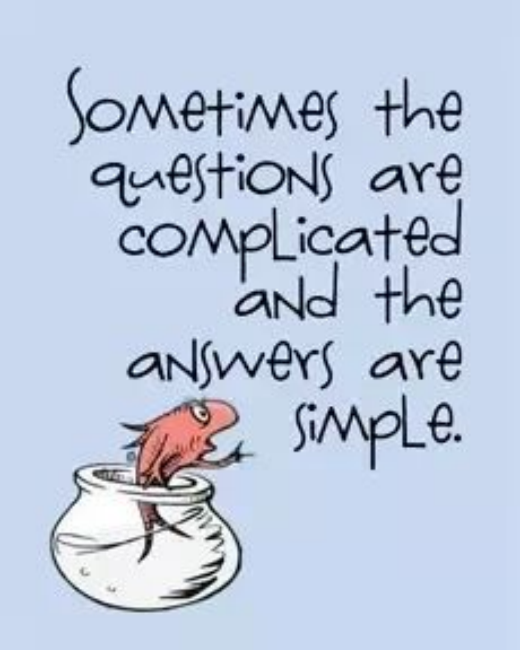
- Is there some other data structure to gain efficient access to all of the suffixes of a given string with less overhead than a suffix tree?
- Some things we know
  - Searching an unordered list of items with length *n* generally requires *O(n)* steps
  - However, if we sort our items first, then we can search using *O(log(n))* steps
  - Thus, if we plan to do frequent searches there is some advantage to performing a sort first and amortizing its cost over many searches
- For strings *suffixes* are interesting *items*. Why?

Suffixes:	**Sorted Suffixes:**
`panamabananas`	`abananas`
`anamabananas`	`amabananas`
`namabananas`	`anamabananas`
`amabananas`	`ananas`
`mabananas`	`anas`
`abananas`	`as`
`bananas`	`bananas`
`ananas`	`mabananas`
`nanas`	`namabananas`
`anas`	`nanas`
`nas`	`nas`
`as`	`panamabananas`
`s`	`s`

Questions you can ask

Is there any use for a list of sorted suffixes?

```
Sorted Suffixes:  abananas
                  amabananas
                  anamabananas
                  ananas
                  anas
                  as
                  bananas
                  mabananas
                  namabananas
                  nanas
                  nas
                  panamabananas
                  s
```



- Does the substring "nana" appear in the original string?
- How many times does "ana" appear in the string?
- What is the most/least frequent letter in the original string?
- What is the most frequent two-letter substring in the original string?

Properties of a sorted “suffix array”

- Size of the sorted list if the given text has a length of *m*? $O(m^2)$
- Cost of the sort? $O(m^2 \log(m))$
- Not practical for big *m*
- There are many ways to sort
  - What is an “*in place*” sort?
  - What is a “*stable*” sort?
  - What is an “*arg*” *sort*?

Arg Sorting

consider the list:

`[72,27,45,36,18,54,9,63]`

When sorted it is simply:

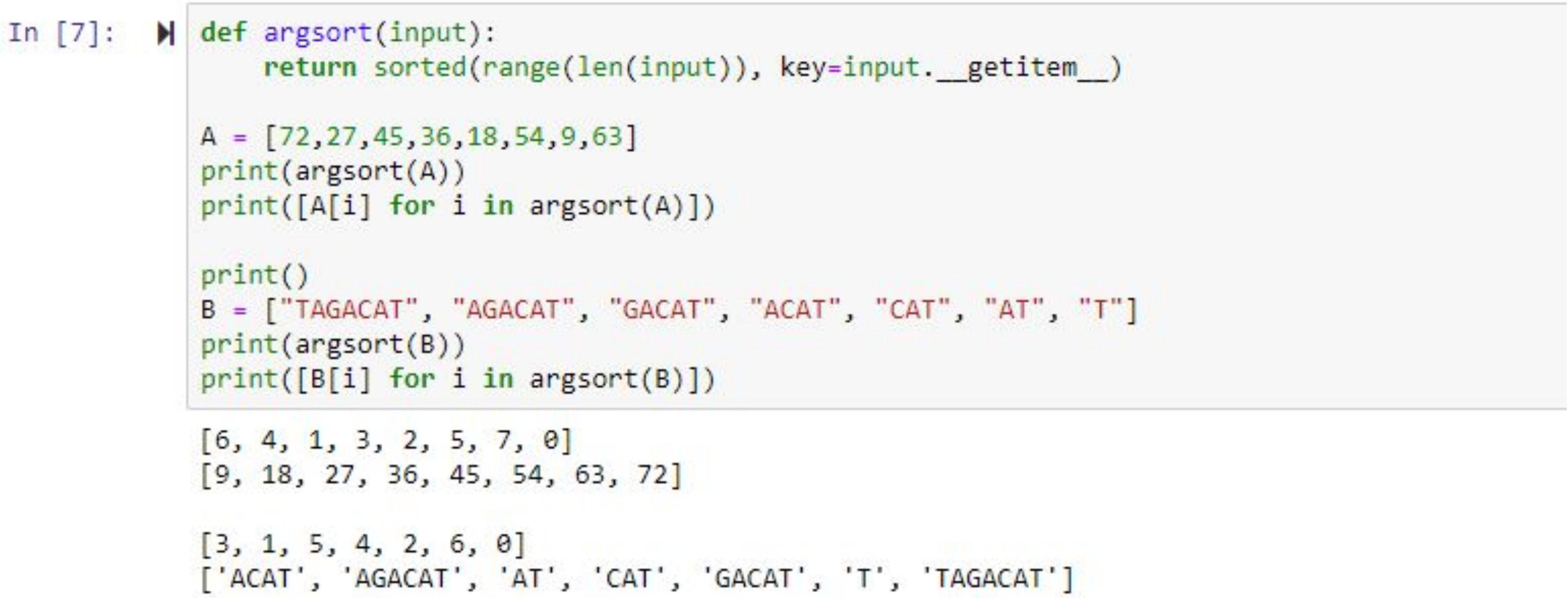
`[9,18,27,36,45,54,63,72]`

Its “arg” sort is:

`[6,4,1,3,2,5,7,0]`

- The *ith* element in the arg sort is the *index* of the *ith* element from the original list when sorted.
- Thus, [A[i] for i in argsort(A)] == sorted(A)

Code for Arg Sorting



In [7]:

```python
def argsort(input):
    return sorted(range(len(input)), key=input.__getitem__)

A = [72,27,45,36,18,54,9,63]
print(argsort(A))
print([A[i] for i in argsort(A)])

print()
B = ["TAGACAT", "AGACAT", "GACAT", "ACAT", "CAT", "AT", "T"]
print(argsort(B))
print([B[i] for i in argsort(B)])
```

```
[6, 4, 1, 3, 2, 5, 7, 0]
[9, 18, 27, 36, 45, 54, 63, 72]

[3, 1, 5, 4, 2, 6, 0]
['ACAT', 'AGACAT', 'AT', 'CAT', 'GACAT', 'T', 'TAGACAT']
```

Next Time

- We'll see how arg sorting can be used to simplify representing our sorted list of suffixes
- Suffix arrays
- Burrows-Wheeler Transforms
- Applications in sequence alignment