A Recurring Problem

- Finding patterns within sequences
- Variants on this idea
  - Finding repeated motifs amoungst a set of strings
  - What are the most frequent k-mers
  - How many time does a specific k-mer appear
- Fundamental problem: *Pattern Matching*
  - Find all positions of a particular substring in given sequence?

Pattern Matching

- **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

```
def bruteForcePatternMatching(p, t):
    locations = []
    for i in xrange(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
  - Comparison - *O(n)* symbols compared
  - Total cost - *O(mn)* per pattern
- In practice, most comparisons terminate early
- Worst-case:
  - `p = "AAAT"`
  - `t = "AAAAAAAAAAAAAAAAAAAAAAT"`

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We can do better!

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

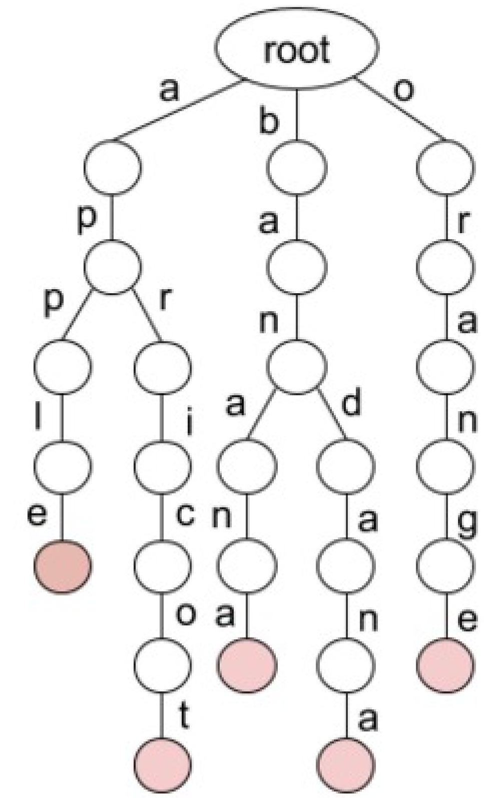
Example:

```
   imissmississippi
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 $i \neq m$ 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 $[p_1, p_2, \ldots, p_3]$ in t

Keyword Trees

- We can preprocess the set of strings we are seeking 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 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



Multiple Pattern Matching

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

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

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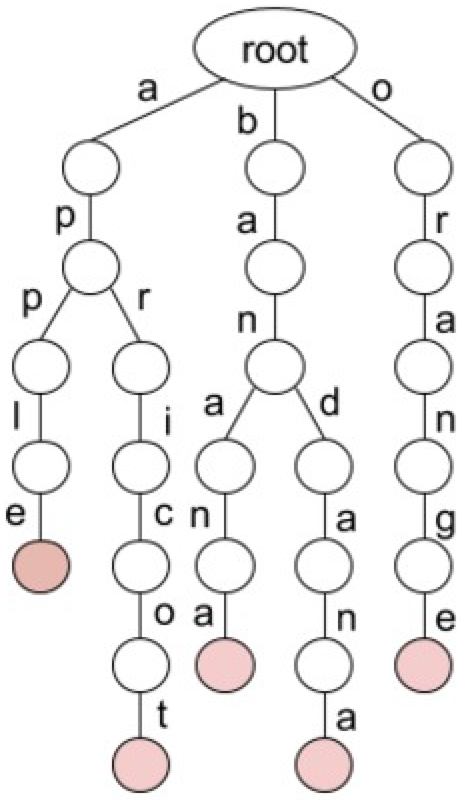
Multiple Pattern Matching Example

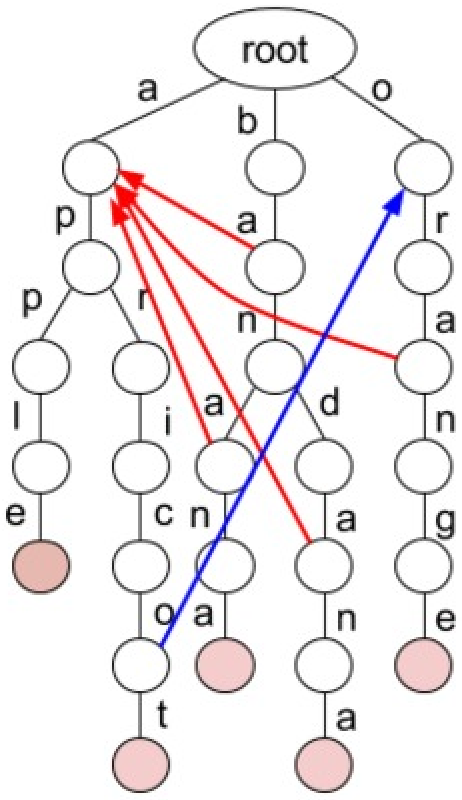
```
multiplePatternMatching("bananapple", P):
 0:  PrefixTrieMatching("bananapple", P) = True
 1:  PrefixTrieMatching("ananapple", P) = False
 2:  PrefixTrieMatching("nanapple", P) = False
 3:  PrefixTrieMatching("anapple", P) = False
 4:  PrefixTrieMatching("napple", P) = False
 5:  PrefixTrieMatching("apple", 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]
```



Improvements

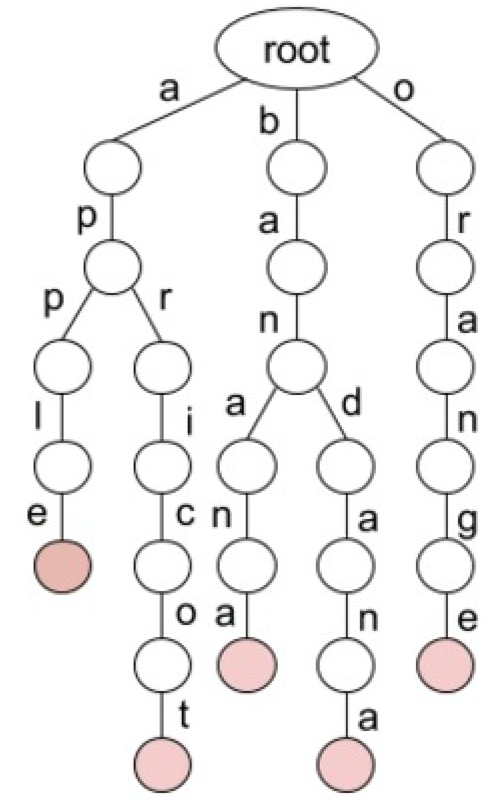
- Based on our previous speed-up
- We can add failure edges to our Trie
- *Aho-Corasick* Algorithm

```
bapple
bap
 apple
```



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 (see pg 353)
- Memory issues
  - Tries require a lot of memory
  - Practical implementation is challenging
  - Genomic reads - millions to billions of
- Patterns typically of length > 100

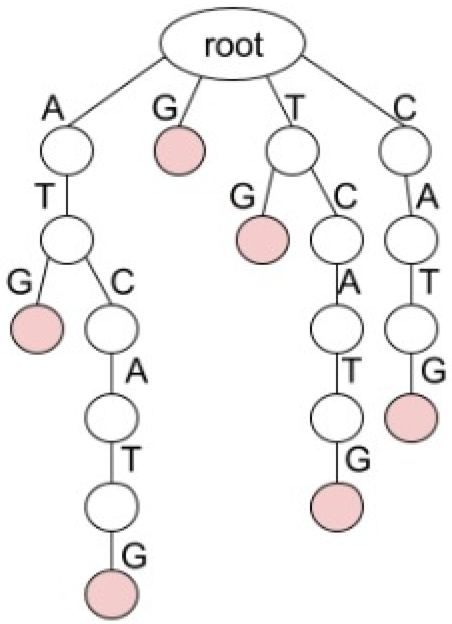


Another Twist

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

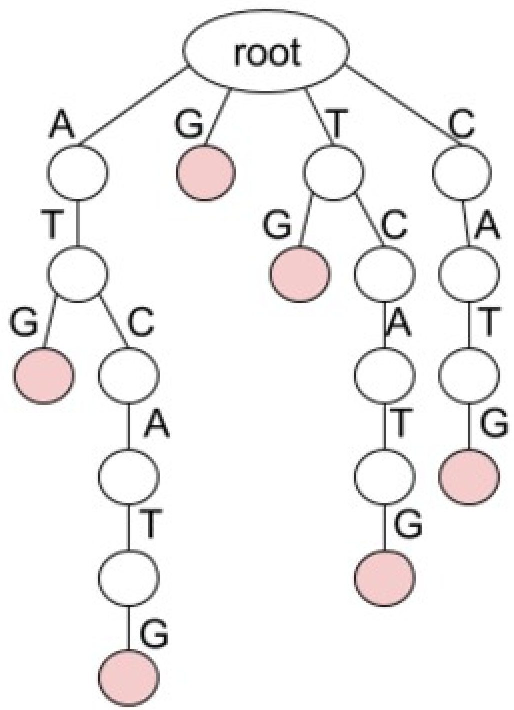
```
Example: ACATG
           CATG
            ATG
             TG
              G
```

- The resulting keyword tree:
- A *Suffix Trie*

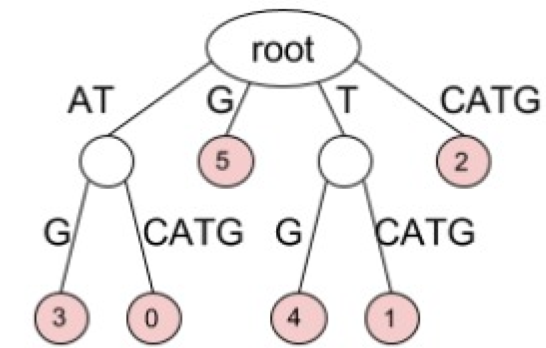


Suffix Tree

A *compressed* Suffix Trie

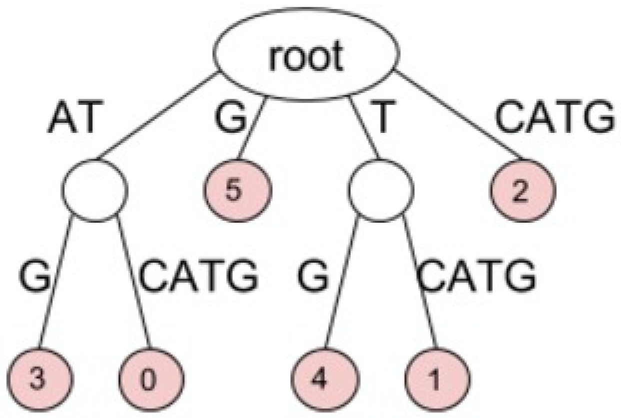


- Combines nodes with in and out degree 1
- Edges are text substrings
- All internal nodes have at least 3 edges
- All leaf nodes are labeled with an index



Uses for Suffix Trees

- Suffix trees hold all suffixes of a text, T
  - i.e., ATCGC: ATCGC, TCGC, CGC, GC, C
- 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

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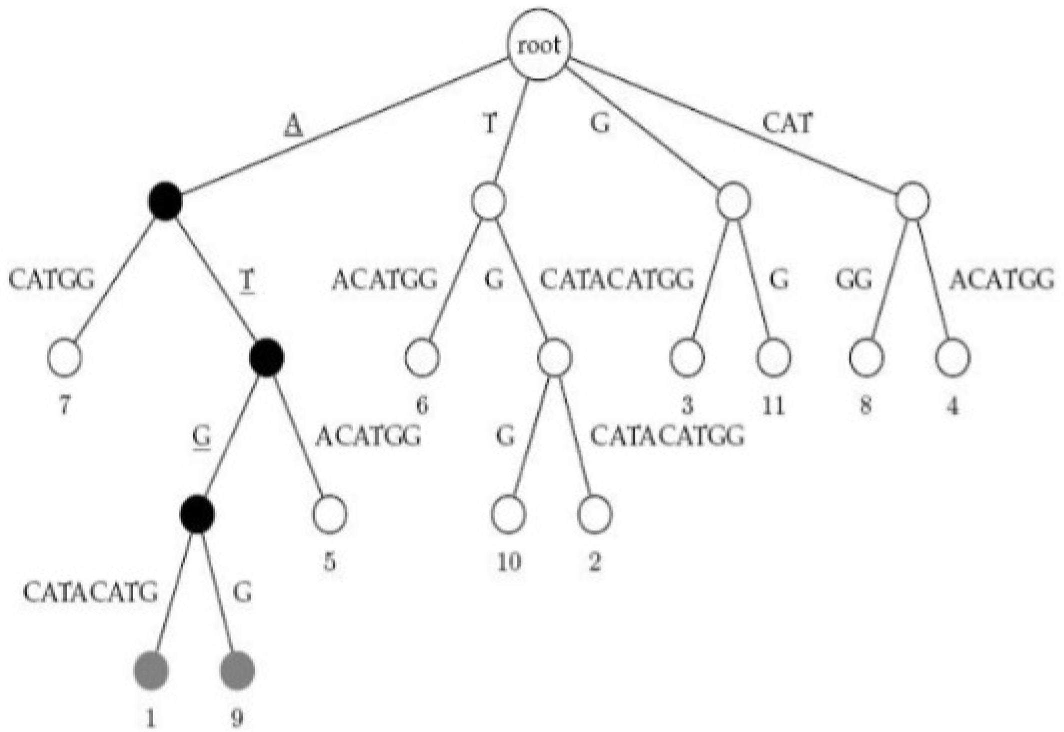
Suffix Tree Examples

- What is the string represented in the suffix tree?
- What letter occurs most frequently?
- How many times doaes "ATG" appear, and where?
- How long is the longest repeated k-mer?



First Previous Next Notebook

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

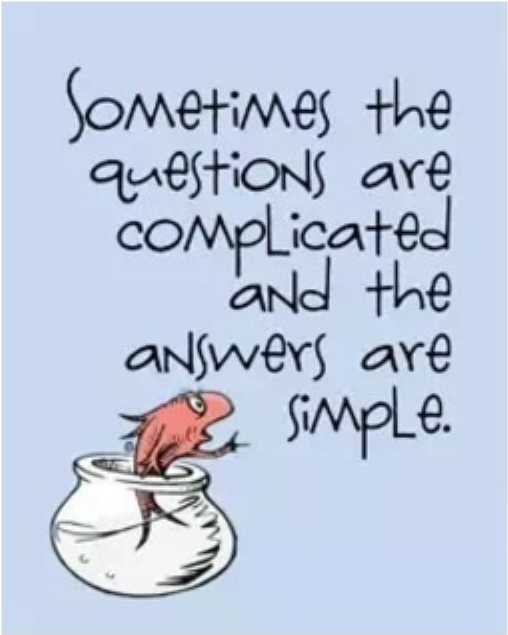
Substring Searching

- Is there some other data structure to gain efficent 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 searchs there is some advantage to performing a sort first and amortizing its cost over many searchs
- For strings *suffixes* are interesting *items*. Why?

```
Suffixes: panamabananas       Sorted Suffixes:  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 orginal string? How?
- How many times does "ana" appear in the string?
- What is the most/least frequent letter in the orginal string?
- What is the most frequent two-letter substring in the orginal string?

Properties of a Naive sorted suffix implementation

- Size of the sorted list if the given string has a length of n? $O(n^2)$
- Cost of the sort? $O(n^2 log(n))$
- Practical for big n
- 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:

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

When sorted it is simply:

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

Its arg sort is:

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

- The i^{th} element in the arg sort is the *index* of the i^{th} element from the orginal list when sorted.
- Thus, `[A[i] for i in argsort(A)] == sorted[A]`

Code for Arg Sorting

```
def argsort(input):
    return sorted(range(len(input)), cmp=lambda i,j: 1 if input[i] >= input[j] else -1)

A = [7,2,4,3,1,5,0,6]
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]
[0, 1, 2, 3, 4, 5, 6, 7]

[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