Suffix Trees and Suffix Arrays

Some problems

- Given a pattern P = P[1..m], find all occurrences of P in a text S = S[1..n]
- Another problem:
  - Given two strings $S_1[1..n_1]$ and $S_2[1..n_2]$ find their longest common substring.
    - find i, j, k such that $S_1[i .. i+k-1] = S_2[j .. j+k-1]$ and k is as large as possible.
- Any solutions? How do you solve these problems (efficiently)?

Exact string matching

- Finding the pattern P[1..m] in S[1..n] can be solved simply with a scan of the string S in O(m+n) time. However, when S is very long and we want to perform many queries, it would be desirable to have a search algorithm that could take O(m) time.
- To do that we have to preprocess *S*. The preprocessing step is especially useful in scenarios where the text is relatively constant over time (e.g., a genome), and when search is needed for many different patterns.

Applications in Bioinformatics

- Multiple genome alignment
  - Michael Hohl et al. 2002
  - Longest common substring problem
  - Common substrings of more than two strings
- Selection of signature oligonucleotides for microarrays
  - Kaderali and Schliep, 2002
- Identification of sequence repeats
  - Kurtz and Schleiermacher, 1999

Suffix trees

- Any string of length m can be degenerated into m suffixes.
  - abcdefgh (length: 8)
  - 8 suffixes:
    - h, gh, fgh, efgh, defgh, cdefgh, bcefgh, abcdefgh
- The suffixes can be stored in a suffix-tree and this tree can be generated in O(*n*) time
- A string pattern of length *m* can be searched in this suffix tree in O(*m*) time.
  - Whereas, a regular sequential search would take O(*n*) time.

History of suffix trees

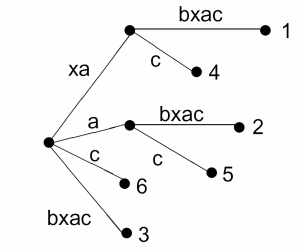
- Weiner, 1973: suffix trees introduced, linear-time construction algorithm
- McCreight, 1976: reduced space-complexity
- Ukkonen, 1995: new algorithm, easier to describe
- In this course, we will only cover a naive (quadratic-time) construction.

Definition of a suffix tree

- Let $S=S[1..n]$ be a string of length n over a fixed alphabet Σ. A suffix tree for S is a tree with n leaves (representing n suffixes) and the following properties:
  - Every internal node other than the root has at least 2 children
  - Every edge is labeled with a nonempty substring of S.
  - The edges leaving a given node have labels starting with different letters.
  - The concatenation of the labels of the path from the root to leaf i spells out the i-th suffix $S[i..n]$ of S. We denote $S[i..n]$ by S_i.

An example suffix tree

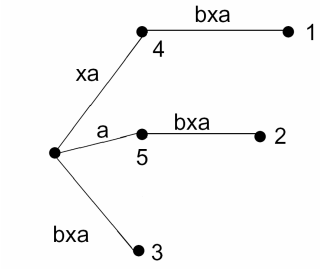
- The suffix tree for string: 1 2 3 4 5 6
  x a b x a c



Does a suffix tree always exist?

What about the tree for xabxa?

- The suffix tree for string: 1 2 3 4 5
  x a b x a



xa an *a* are not leaf nodes.

Problem

- Note that if a suffix is a prefix of another suffix we cannot have a tree with the properties defined in the previous slides.
  - e.g. *xabxa*

The fourth suffix *xa* or the fifth suffix *a* won't be represented by a leaf node.

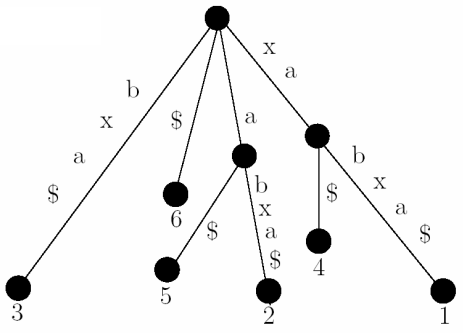
Solution: the terminal character $

- Note that if a suffix is a prefix of another suffix we cannot have a tree with the properties defined in the previous slides.
  - e.g. *xabxa*

The fourth suffix *xa* or the fifth suffix *a* won't be represented by a leaf node.

- Solution: insert a special terminal character at the end such as $. Therefore xa$ will not be a prefix of the suffix xabxa.

The suffix tree for xabxa$



Suffix tree construction

- Start with a root and a leaf numbered 1, connected by an edge labeled *S*$.
- Enter suffixes *S*[2..*n*]$; *S*[3...*n*]$; ... ; *S*[*n*]$ into the tree as follows:
- To insert K_i = *S*[*i*..*n*]$, follow the path from the root matching characters of K_i until the first mismatch at character K_i[*j*] (which is bound to happen)

  (a) If the matching cannot continue from a node, denote that node by *w*

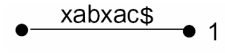
  (b) Otherwise the mismatch occurs at the middle of an edge, which has to be split

Suffix tree construction - 2

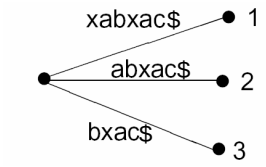
- If the mismatch occurs at the middle of an edge *e* = *S*[*u* ... *v*]
  - let the label of that edge be $a_1...a_l$
  - If the mismatch occurred at character a_k, then create a new node *w*, and replace *e* by two edges S[u ... u+k-1] and S[u+k ... v] labeled by $a_1...a_k$ and $a_{k+1}...a_l$
- Finally, in both cases (a) and (b), create a new leaf numbered *i*, and connect *w* to it by an edge labeled with K_i[*j* ... $|K_i|$]

Example construction

- Let's construct a suffix tree for xabxac$
- Start with:

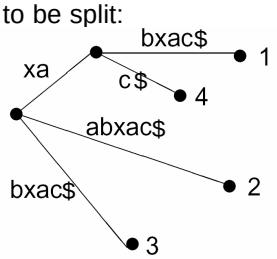


- After inserting the second and third suffix:



Example contd...

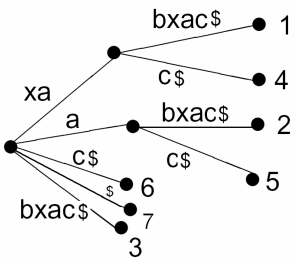
- Inserting the fourth suffix xac$ will cause the first edge to be split:



- Same thing happens for the second edge when ac$ is inserted.

Example contd...

- After inserting the remaining suffixes the tree will be completed:



Complexity of the naive construction

- We need O(*n-i+1*) time for the i^{th} suffix. Therefore the total running time is:

$$\sum_{1}^{n} O(i) = O(n^2)$$

- What about space complexity?
  - Can also take $O(n^2)$ because we may need to store every suffix in the tree separately,
  - e.g., abcdefghijklmn

Storing the edge labels efficiently

- Note that, we do not store the actual substrings $S[i \ldots j]$ of S in the edges, but only their start and end indices (i, j).
- Nevertheless we keep thinking of the edge labels as substrings of S.
- This will reduce the space complexity to $O(n)$

Suffix tree applet

- http://pauillac.inria.fr/~quercia/documents-info/Luminy-98/albert/JAVA+html/SuffixTreeGrow.html

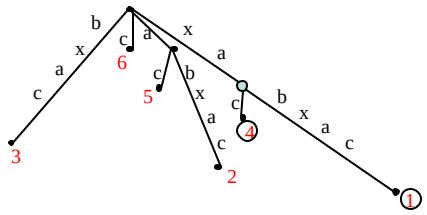
Using suffix trees for pattern matching

- Given S and P. How do we find all occurrences of P in S?
- **Observation.** Each occurrence has to be a prefix of some suffix. Each such prefix corresponds to a path starting at the root.

1. Of course, as a first step, we construct the suffix tree for S. Using the naive method this takes quadratic time, but *linear-time* algorithms (e.g., Ukkonen's algorithm) exist.
2. Try to match P on a path, starting from the root. Three cases:
   (a) The pattern does not match ? P does not occur in T
   (b) The match ends in a node u of the tree. Set $x = u$.
   (c) The match ends inside an edge (v,w) of the tree. Set $x = w$.
3. All leaves below x represent occurrences of P.

Illustration

- T = xabxac
  - suffixes ={xabxac, abxac, bxac, xac, ac, c}
- Pattern P_1: xa
- Pattern P_2: xb



Running Time Analysis

- Search time:
  - O(m+k) where k is the number of occurrences of P in T and m is the length of P
  - O(m) to find match point if it exists
  - O(k) to find all leaves below match point

Scalability

- For very large problems a linear time and space bound is not good enough. This lead to the development of structures such as Suffix Arrays to conserve memory .

Two implementation issues

- Alphabet size
- Generalizing to multiple strings

Effects of alphabet size on suffix trees

- We have generally been assuming that the trees are built in such a way that
  - from any node, we can find an edge in constant time for any specific character in Σ
    - an array of size $|\Sigma|$ at each node
- This takes $\Theta(m|\Sigma|)$ space.

More compact representation

- We may try to be more compact taking only O(m) space.
  - At each node, have pointers to only the edges that are needed
- This slows down the search time
- How much?
  - typically the minimum of O(log m) or O(log $|\Sigma|$) with a binary tree representation.
- This effects both suffix tree construction time and later searching time against the suffix tree.

Generalized suffix trees

- Build a suffix tree for a set of strings $S = \{S_1, \ldots, S_z\}$
- Some issues
- Nodes in tree may corresponds to substrings of potentially multiple strings S_i
  - compact edge labels: need 3 fields (start position, stop position, string)
  - leaf labels now a set of pairs indicating starting position and string

Longest common substring problem

- Build a generalized suffix tree for $S_1\$_1S_2\$_2$. Here $\$_1$ and $\$_2$ are different new symbols not occurring in S_1 and S_2.
- Mark every internal node of the tree with {1}, {2}, or {1,2} depending on whether its path label is a substring of S_1 and/or S_2.
- Find the *internal* node which is labeled by {1,2} and has the largest "*string depth*".
- Example: (with the applet)
  - pessimist%mississippi$

Selecting probes for microarrays

- Wikipedia: **Oligonucleotides** are short sequences of nucleotides (RNA or DNA), typically with twenty or fewer base pairs.
- Given a set of genomic sequences, the problem is to identify at least one signature oligonucleotide (probe) for each sequence. These probes must hybridize to only the desired sequence. The algorithm produces a GST from the reverse compliment of all the genomic sequences (candidate probe sequences). Using the GST, the algorithm identifies all common substrings and rejects these regions because probes designed in them would not be specific to a single genomic sequence. Criteria such as probe length are used to further prune this tree.
- http://www.zaik.uni-koeln.de/bioinformatik/arraydesign.html.en

Suffix arrays

- Suffix arrays were introduced by Manber and Myers in 1993
- More space efficient than suffix trees
- A suffix array for a string x of length *m* is an array of size *m* that specifies the lexicographic ordering of the suffixes of x.

Suffix arrays

Example of a suffix array for acaaacatat$

0	aaacatat$	3
1	aacatat$	4
2	acaaacatat$	1
3	acatat$	5
4	atat$	7
5	at$	9
6	caaacatat$	2
7	catat$	6
8	tat$	8
9	t$	10
10	$	11

Suffix array construction

- Naive in place construction
  - Similar to insertion sort
  - Insert all the suffixes into the array one by one making sure that the new inserted suffix is in its correct place
  - Running time complexity:
    - O(m^2) where *m* is the length of the string
- Manber and Myers give a O(*m* log *m*) construction in their 1993 paper.

Suffix arrays

- O(*n*) space where *n* is the size of the database string
- Space efficient. However, there's an increase in query time
- Lookup query
  - Binary search
  - O(m log n) time; m is the size of the query
  - Can reduce time to O(m + log n) using a more efficient implementation

Searching for a pattern in Suffix Arrays

```
find(Pattern P in SuffixArray A):
   i = 0
   lo = 0, hi = length(A)
   for 0<=i<length(P):
      Binary search for x,y
      where P[i]=S[A[j]+i] for lo<=x<=j<y<=hi
      lo = x, hi = y
   return {A[lo],A[lo+1],...,A[hi-1]}
```

Search example

- Search *is* in *mississippi$*

Examine the pattern letter by letter, reducing the range of occurrence each time.

First letter *i*: occurs in indices from 0 to 3

So, pattern should be between these indices.

Second letter *s*: occurs in indices from 2 to 3

Done.
Output: issippi$ and ississippi$

0	11	i$
1	8	ippi $
2	5	issippi $
3	2	ississippi $
4	1	mississippi $
5	10	pi$
6	9	ppi $
7	7	sippi $
8	4	sissippi $
9	6	ssippi $
10	3	ssissippi $
11	12	$

Suffix Arrays

- It can be built very fast.
- It can answer queries very fast:
  - How many times ATG appears?
- Disadvantages:
  - Can't do approximate matching
  - Hard to insert new stuff (need to rebuild the array) dynamically.

Useful links

- http://pauillac.inria.fr/~quercia/documents-info/Luminy-98/albert/JAVA+html/SuffixTreeGrow.html
- http://home.in.tum.de/~maass/suffix.html
- http://homepage.usask.ca/~ctl271/857/suffix_tree.shtml
- http://homepage.usask.ca/~ctl271/810/approximate_matching.shtml
- http://www.cs.mcgill.ca/~cs251/OldCourses/1997/topic7/
- http://dogma.net/markn/articles/suffixt/suffixt.htm
- http://www.csse.monash.edu.au/~lloyd/tildeAlgDS/Tree/Suffix/