CSEP 521 Applied Algorithms Spring 2005

Dynamic Programming
Contiguous Ordering - PQ Trees

Reading

• Chapter 15

Outline for the Evening

- DNA
- Approximate String Matching
- Approximate String Searching
- Dynamic Progamming
- Longest Common Subsequence
- DNA reconstruction
- Contiguous Ordering and PQ-trees

DNA

- DNA is a large molecule that can be abstractly defined as a sequence of symbols from the set, A, C, G, T, called nucleotides.
- The human genome has about 3 billion nucleotides.
 - A huge percentage of the genome is shared by all humans.
 - Some of the variation makes us different.
 - Some of the variation is inconsequential.
 - The human genome is still being discovered.

Approximate Matching

- Two DNA sequences approximately match if one can be transformed into the other by a short sequence of replacements and insertions of gaps.
- Example:

```
-S = AGCATG
```

$$-T = AGATCGT$$

Approximate matching

$$-S' = AG - -CATG$$

$$-T' = A G A T C G T -$$

Applications of Approximate Matching

- DNA string alignment.
 - Given two similar DNA sequences find the best way to align them to the same length.
- DNA database searching.
 - Find DNA sequences that are similar to the query.
- Approximate text matching for searching.
 - agrep in unix
- Spell checking
 - Find the words that most closely match the misspelled word.

Scoring an Approximate Matching

- We need a way of scoring the quality of an approximate matching.
- A scoring function is a mapping σ from {A, C, G, T, -}² to integers.
 - The quantity $\sigma(x,y)$ is the score of a pair of symbols, x and y.
- Example:
 - $-\sigma(x,y) = +2 \text{ if } x=y \text{ and } x \text{ in } \{A,C,G,T\}$
 - $-\sigma(x,y) = -1$ otherwise

Scoring Example

Example:

$$-S' = AG - -CATG$$

 $-T' = AGATCGT -$

- Score = $4 \times 2 + 4 \times (-1) = 4$
- Is this the best match between the two strings with this scoring function?
 - -S = AGCATG
 - -T = AGATCGT

Approximate String Matching Problem

- Input: Two strings S and T in an alphabet Σ and a scoring function σ .
- Output: Two strings S' and T' in the alphabet $\Sigma' = \Sigma$ union {-} with the properties:
 - -S = S' with the -'s removed.
 - -T = T' with the -'s removed.
 - -|S'|=|T'|
 - The score $\sum_{i=1}^{|S'|} \sigma(S'[i], T'[i])$ is maximized.

Algorithms for Approximate String Matching

- O(mn) time and storage algorithm (using dynamic programming) invented by Needleman and Wunch, 1970.
- Fischer and Paterson, 1974, invented a very similar algorithm for computing the minimum edit distance between two strings.

Dynamic Programming for Approximate String Matching

- Assume S has length m and T has length n.
- For all i and j, 0 ≤ i ≤ m and 0 ≤ j ≤ n, we find the maximum score for the sequences S[1..i] and T[1..j].
- The "dynamic program" fills in a (m+1)x(n+1) matrix M in increasing order of i and j with these maximum values.
- Once the dynamic program has completed we can recover the optimal string S' and T' from the matrix M.

Max Score Recurrence

 Define M[i,j] = maximum score for a match between S[1..i] and T[1..j].

$$\begin{split} M[i,0] &= \sum_{k=1}^{i} \sigma(S[k],-) & \text{match of } S[1..i] \text{ with empty string} \\ M[0,j] &= \sum_{k=1}^{j} \sigma(-,T[k]) & \text{match of } T[1..j] \text{ with empty string} \\ M[i,j] &= \max\{ & M[i-1,j-1] + \sigma(S[i],T[j]), \\ M[i-1,j] + \sigma(S[i],-), \\ M[i,j-1] + \sigma(-,T[j]) \} \end{split}$$

Dynamic Program Initialization

S = AGCATG

T = AGATCGT

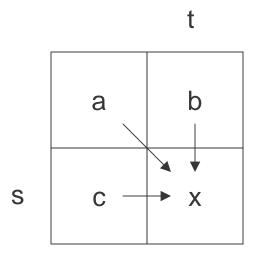
scoring function

+2 for exact match

		0	1	2	3	4	5	6	7
			A	G	A	Т	C	G	T
0		0	-1	-2	-3	-4	-5	-6	-7
1	A	-1							
	G	-2							
3	C	-3							
4	A	-4							
5	Т	-5							
6	G	-6							

Lecture 9 - Dynamic Programming, PQ-trees

The Dynamic Programming Pattern



$$d = a + 2$$
 if $s = t$
 $= a - 1$ otherwise
 $h = c - 1$
 $v = b - 1$
 $x = max(d, h, v)$

Dynamic Program Example (1)

S = AGCATG

T = AGATCGT

scoring function

+2 for exact match

		0	1	2	3	4	5	6	7
			A	G	A	Т	C	G	Т
0		0	-1	-2	-3	-4	-5	-6	-7
1	A	-1	2						
2	G	-2							
3	C	-3							
	A	-4							
5	Т	-5							
6	G	-6							

Lecture 9 - Dynamic Programming, PQ-trees

Dynamic Program Example (2)

S = AGCATG

T = AGATCGT

scoring function

+2 for exact match

		0	1	2	3	4	5	6	7
			A	G	A	Т	C	G	Т
0		0	-1	-2	-3	-4	-5	-6	-7
1	A	-1	2	1					
2	G	-2	1						
3	C	-3							
4	A	-4							
5	Т	-5							
6	G	-6							

Lecture 9 - Dynamic Programming, PQ-trees

Dynamic Program Example (3)

S = AGCATG

T = AGATCGT

scoring function

+2 for exact match

		0	1	2	3	4	5	6	7
			A	G	A	Т	C	G	Т
0		0	-1	-2	-3	-4	-5	-6	-7
1	A	-1	2	1	0				
2	G	-2	1	4					
3	C	-3	0						
	A	-4							
5	Т	-5							
6	G	-6							

Lecture 9 - Dynamic Programming, PQ-trees

Dynamic Program Example (4)

S = AGCATG

T = AGATCGT

scoring function

+2 for exact match

		0	1	2	3	4	5	6	7
			A	G	A	Т	C	G	Т
0		0	-1	-2	-3		-5	-6	-7
1	A	-1	2	1	0	-1	-2	-3	-4
2	G	-2	1	4	3	2	1	0	-1
3	C	-3	0	3	3	2	4	3	2
4	A	-4	-1	2	5	4	3	3	2
5	Т	-5	-2	1	4	7	6	5	
6	G	-6	-3	0	3	6	6		

Lecture 9 - Dynamic Programming, PQ-trees

Dynamic Program Example (5)

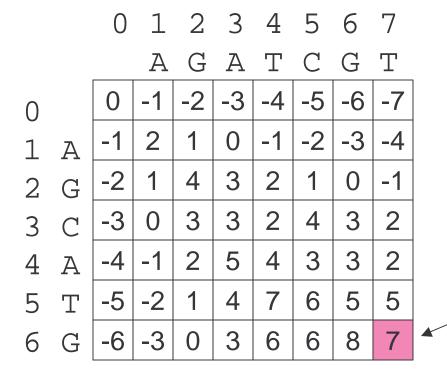
S = AGCATG

T = AGATCGT

scoring function

+2 for exact match

-1 otherwise

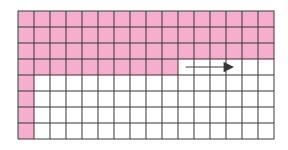


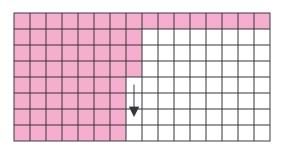
Max score for any matching

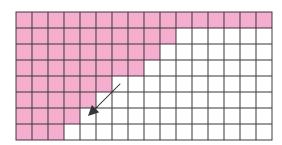
Dynamic Programming Order

By row for i = 1 to m do for j = 1 to n do M[i,j] := ... By column for j = 1 to n do for i = 1 to m do M[i,j] := ...

By diagonal



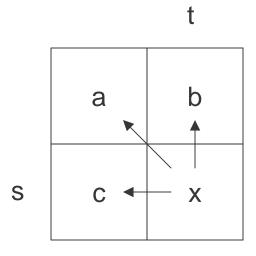




Which order is best?

How to Find the Matching

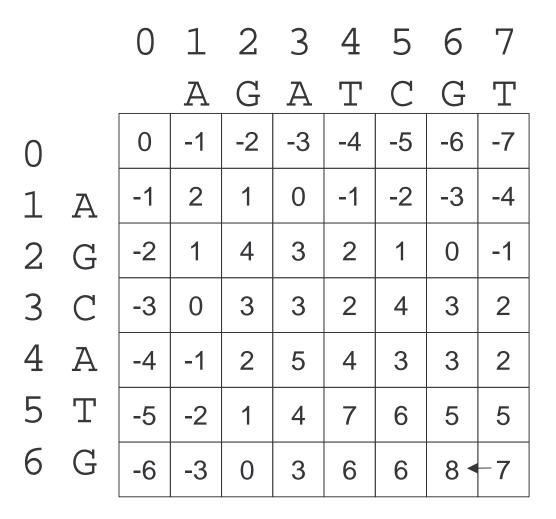
To find S' and T' we build a matching graph.



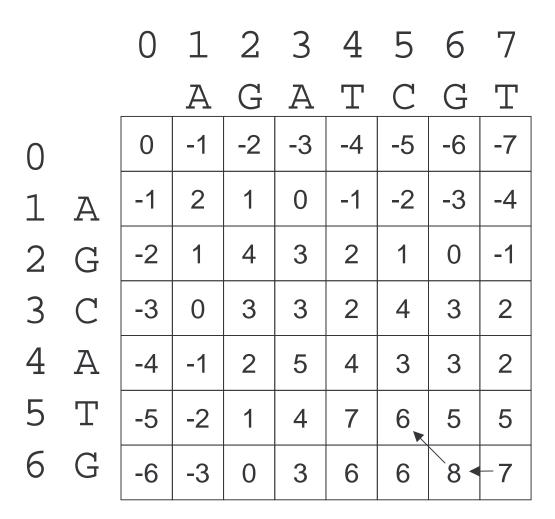
$$x = a + 2$$
 if $s = t$
= $a - 1$ otherwise?
 $x = c - 1$?
 $x = b - 1$?

If the answer is yes, include the corresponding edge.

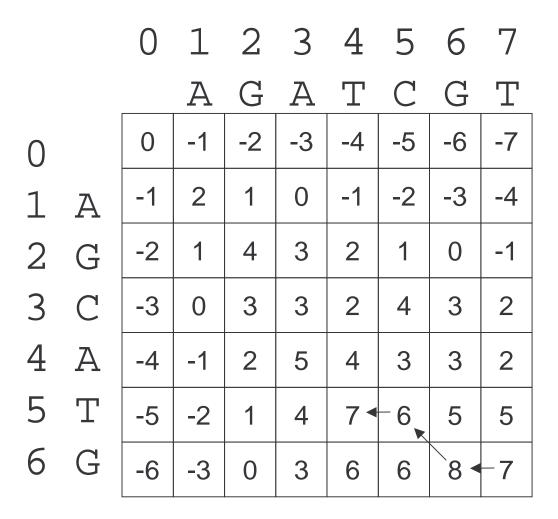
Computing the Matching Graph (1)



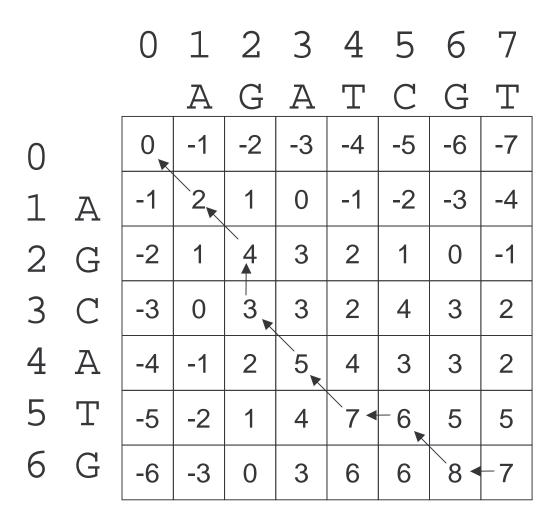
Computing the Matching Graph (2)



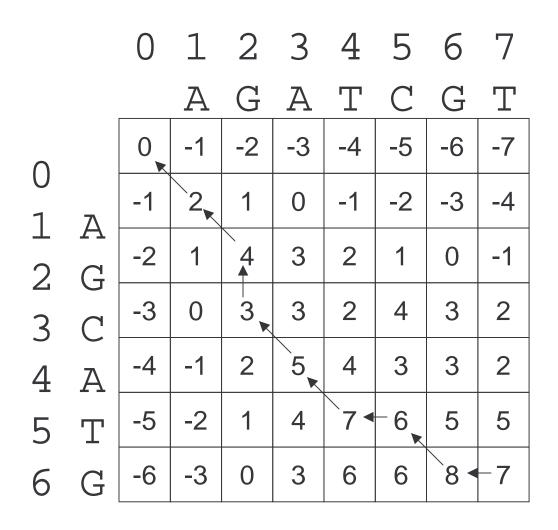
Computing the Matching Graph (3)



Computing the Matching Graph



Computing the Matching Path



Matching Path (0,0) (1,1) (2,2) (3,2) (4,3) (5,4) (5,5) (6,6) (6,7)

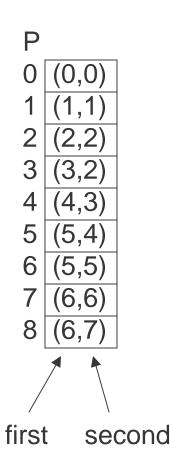
There can be multiple paths

Algorithm to find Matching

- Follow any path in the matching graph starting at (m,n).
- The path will end up at (0,0).
- Output each pair (i,j) visited to make a list of pairs forming a matching path.

Computing the Matching

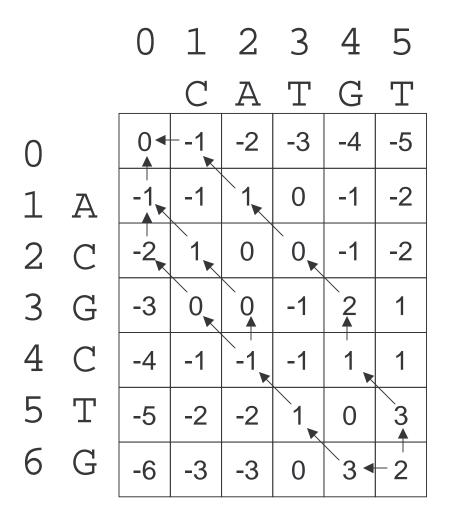
```
p = length of the matching path P
i := 1;
i := 1;
for k = 1 to p do
   if P[k].first = P[k-1].first then
     S'[k] := -;
   else
     S'[k] := S[i];
     i := i + 1;
   if P[k].second = P[k-1].second then
    T'[k] := -;
   else
     T'[k] := T[j];
     j := j + 1;
```



Creating the Matching

P
0 (0,0)
1 (1,1)
2 (2,2)
3 (3,2)
4 (4,3)
5 (5,4)
6 (5,5)
7 (6,6)
8 (6,7)

Example of Multiple Paths



Multiple matching with same score

score =
$$3 \times 2 + 4 \times (-1)$$

= 2

Exercise

- Find an optimal approximate matching for
 - A G T T C
 - -ACTATC

		0	1	2	3	4	5	6
			A	C	Т	A	Т	C
0		0	-1	-2	-3	-4	-5	-6
1	A	-1						
2	G	-2						
3	Т	-3						
4	Т	-4						
5	C	-5						

Lecture 9 - Dynamic Programming, PQ-trees

Approximate String Searching

- Input: Query string Q and target string T in an alphabet Σ and a scoring function σ, and a minimum score r.
- Output: The set of k such that for some i ≤ k score(Q,T[i..k]) ≥ r. That is, an approximate match of some substring of T that ends at index k has a score of at least r.
 - score(X,Y) is the maximum score for all matchings between X and Y.

Search Algorithm

We change the previous dynamic program slightly.

$$\begin{split} M[i,0] &= \sum_{k=1}^{i} \sigma(Q[k],-) \\ M[0,j] &= 0 \qquad \text{We don't care where the match begins in T} \\ M[i,j] &= \max \{ \\ &M[i-1,j-1] + \sigma(Q[i],T[j]), \\ &M[i-1,j] + \sigma(Q[i],-), \\ &M[i,j-1] + \sigma(-,T[j]) \} \end{split}$$

Choose all k such that $M[m,k] \ge r$ where m is the length of Q.

Example of Approximate Matching

```
Q = AGTA

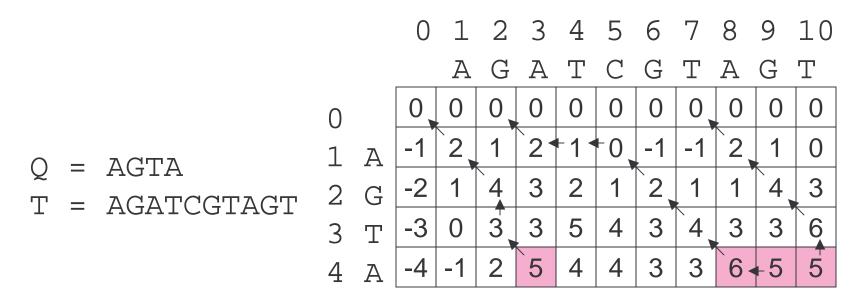
T = AGATCGTAGT r = 5
```

scoring function +2 for exact match -1 otherwise

		0	1	2	3	4	5	6	7	8	9	10
			A	G	A	Т	C	G	Т	A	G	Т
0		0	0	0	0	0	0	0	0	0	0	0
1	A	-1	2	1	2	1	0	-1	-1	2	1	0
2	G	-2	1	4	3	2	1	2	1	1	4	3
3	Т	-3	0	3	3	5	4	3	4	3	3	6
4	A	-4	-1	2	5	4	4	3	3	6	5	5

output is 3, 8, 9, 10

Recovering the Matchings



- O AGTA
- T AG-A 1-3
- O A--GTA
- T ATCGTA 3-8

- Q A--GTA-
- T ATCGTAG 3-9
- Q AGTA
- T AGT- 8-10

Notes on Approximate Matching

- Time complexity O(mn)
- Storage complexity O(mn)
 - Storage in the dynamic program can be reduced to O(m+n) by just keeping the frontier.
 - Recovering the matching can be done in time O(m+n) cleverly.

FASTA and **BLAST**

- Two of best known approximate search algorithms for DNA database searching
- Both use the idea of exclusion search
 - Parameter k for number of possible errors
 - Exact search on k+1 substrings. At least one must succeed

k = 4 search string



- 1. Find all the exact matches for at least one of the strings
- 2. For each such match do an approximate matching

Example

k = 2

AGTTATGCC → AGT TAT GCC

TTAGACGTTCATGACCTAGTTTAGCTATGAGAGTTATG

Dynamic Programming O(mn) Exclusion Search O(sm² + n)

m search string length n database length s number of successes in exact search

Dynamic Programming

- A strategy for designing algorithms.
- A technique, not an algorithm.
- The word "programming" is historical and predates computer programming.
- Ideal when the problem breaks down into recurring small sub-problems.

Longest Common Subsequence

- Longest common subsequence (LCS) problem:
 - Given two sequences x[1..m] and y[1..n], find the longest subsequence which occurs in both (not necessarily contiguous).
 - Example: x = A B C B D A B, y = B D C A B A
 - B C and A A are both subsequences of both
 - What is the LCS? BCAB, BCBA
 - Brute-force algorithm: For every subsequence of x, check if it's a subsequence of y
 - How many subsequences of x are there?
 - What will be the running time of the brute-force alg?

LCS Algorithm

- Brute-force algorithm: 2^m subsequences of x each takes O(n) to search in y: O(n 2^m)
- We can do better: for now, let's only worry about the problem of finding the *length* of the LCS
 - When finished we will see how to backtrack from this solution back to the actual LCS.
- Notice LCS problem has optimal substructure
 - Subproblems: LCS of pairs of *prefixes* of x and y

Finding LCS Length

- Define c[i,j] to be the length of the LCS of X_i =x[1..i] and Y_i=y[1..j]
 - What is the length of LCS of x and y?c[m,n]
- Theorem:

$$c[i,j] = \begin{cases} c[i-1,j-1]+1 & \text{if } x[i]=y[j],\\ max(c[i,j-1],c[i-1,j]) & \text{otherwise} \end{cases}$$

LCS Recurrence

$$c[i,j] = \begin{cases} c[i-1,j-1]+1 & \text{if } x[i] = y[j], \\ max(c[i,j-1],c[i-1,j]) & \text{otherwise} \end{cases}$$

Proof: When calculating c[i,j], there are two cases to consider:

First case: x[i]=y[j]: one more symbol in strings X and Y matches, so the length of LCS X_i and Y_j equals to the length of LCS of smaller strings X_{i-1} and Y_{i-1}, plus 1.

LCS Recurrence

$$c[i,j] = \begin{cases} c[i-1,j-1]+1 & \text{if } x[i] = y[j], \\ max(c[i,j-1],c[i-1,j]) & \text{otherwise} \end{cases}$$

- Second case: x[i] ≠ y[j]
- As symbols don't match, our solution is not improved, and the length of LCS(X_i, Y_j) is the maximum of LCS(X_i, Y_{j-1}) and LCS(X_{i-1}, Y_j)

Why not just take the length of LCS(X_{i-1} , Y_{j-1})?

LCS recursive solution

$$c[i,j] = \begin{cases} c[i-1,j-1]+1 & \text{if } x[i] = y[j], \\ max(c[i,j-1],c[i-1,j]) & \text{otherwise} \end{cases}$$

Why not just take the length of LCS(X_{i-1} , Y_{j-1})?

Answer: Let x=abc y=db

$$c[3,2]=max(c[3,1],c[2,2])=max(0,1)=1$$

$$c[3,2] \neq c[2,1] = 0$$

Exercise: Write the Program

```
    m = length(X) // # of symbols in X
    n = length(Y) // # of symbols in Y
    for i = 1 to m c[i,0] = 0 // special case: Y<sub>0</sub>
    for j = 1 to n c[0,j] = 0 // special case: X<sub>0</sub>
```

Exercise: Create a Dynamic Program

- Design a dynamic program for knapsack problem.
- Input: $(s_1,c_1), (s_2,c_2),..., (s_n,c_n), S$
- Output: find a subset X of $\{1,2,\ldots,n\}$ such that $\sum_{i\in X}s_i\leq S \text{ and }\sum_{i\in X}c_i \text{ is maximized}$
- Hint: For i ≤ n and k ≤ S recursively define

$$c(i,k) = max\{\sum_{j \in X} c_j : X \subseteq \{1,2,...,i\} \text{ and } \sum_{j \in X} s_j = k\}$$

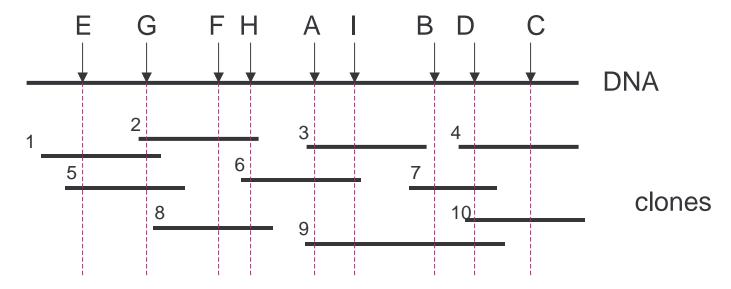
DNA Sequence Reconstruction

- DNA can only be sequenced in relatively small pieces, up to about 1,000 nucleotides.
- By chemistry a much longer DNA sequence can be broken up into overlapping sequences called clones.
 Clones are 10's of thousands of nucleotides long.

		DNA
 - -		clones

Tagging the Clones

 By chemistry the clones can be tagged by identifying a region of the DNA uniquely.



Each clone is then tagged correspondingly.

Problem to Solve

 Given a set of tagged clones, find a consistent ordering of the tags that determines a possible ordering of the DNA molecule.

clone tag

1.
$$\{E, G\}$$
 output

2. $\{F, G, H\}$

3. $\{A, I\}$

4. $\{C, D\}$

5. $\{E, G\}$

6. $\{A, H, I\}$

7. $\{B, D\}$

8. $\{F, H\}$

9. $\{A, B, D, I\}$

10. $\{C, D\}$

Contiguous Ordering Solutions

Contiguous ordering problem

U = {A, B, C, D, E, F, G, H, I} S = {{E, G} {F, G, H} {A, I}

 $\{C,\,D\}$

 $\{E, G\}$

 $\{A, H, I\}$

{B, D}

 $\{F, H\}$

{A, B, D, I} {C, D}} Solution

EGFHAIBDC ———————

Alternate Solutions

interchange I and A

reversal

EGFHIABDC

CDBIAHFGE

CDBAIHFGE

Linear Time Algorithm

- Booth and Lueker, 1976, designed an algorithm that runs in time O(n+m+s).
 - n is the size of the universe, m is the number of sets, and s is the sum of the sizes of the sets.
- It requires a novel data structure called the PQ tree that represents a set of orderings.
- PQ trees can also be used to test whether an undirected graph is planar.

PQ Trees

PQ trees are built from three types of nodes

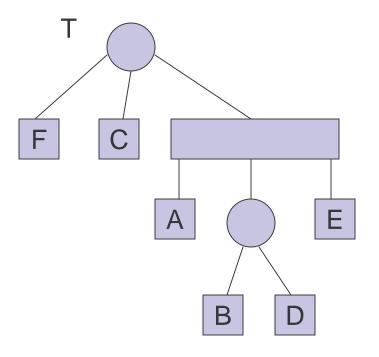
P node Q node leaf

Children can be reordered.

Children can be reversed.

Each leaf has a unique label.

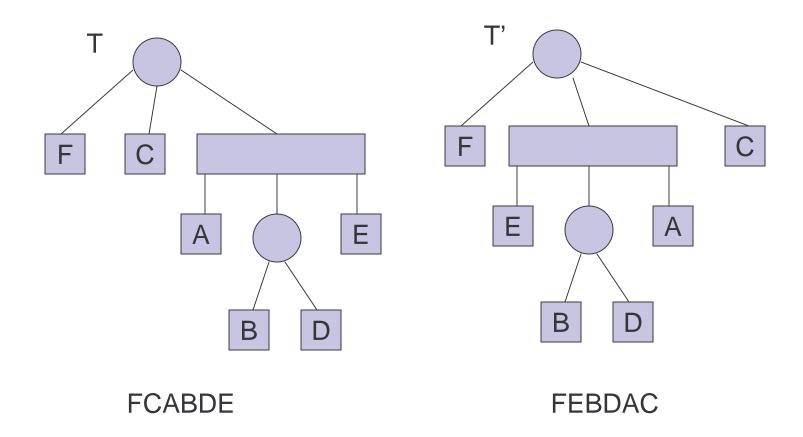
Example PQ-Tree



The frontier of T defines the ordering F(T) = FCABDE, just read the leaves left to right.

T' is equivalent to T if T can be transformed into T by reordering the children of P nodes and reversing the children of Q nodes.

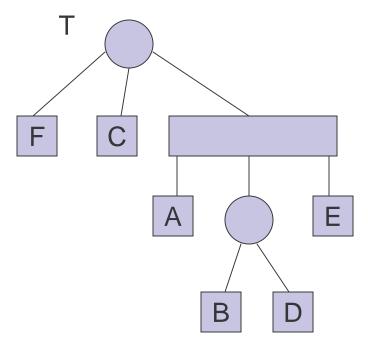
Equivalent PQ Trees



Orderings Defined by a PQ Tree

Given a PQ tree T the orderings defined by T is

$$- PQ(T) = \{F(T') : T' \text{ is equivalent to } T\}$$



There are $6 \times 2 \times 2 = 24$ distinct orderings in PQ(T).

Generally, if a PQ tree T has q Q node and p P nodes with number of children $c_1, c_2, ..., c_p$, then the number of orderings in PQ(T) is $2^q c_1! c_2! ... c_p!$.

$$n! = 1 \times 2 \times ... \times n$$

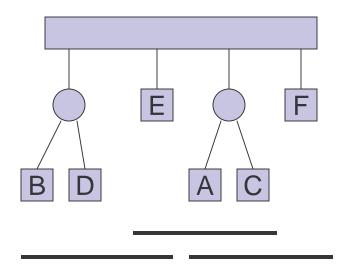
PQ Tree Solution for the Contiguous Ordering Problem

- Input: A universe U and a set S = {S₁, S₂, ..., S_m} of subsets of U.
- Output: A PQ tree T with leaves U with the property that PQ(T) is the set of all orderings of U where each set in S is contiguous in the ordering.

Example Solution

$$U = \{A,B,C,D,E,F\}$$

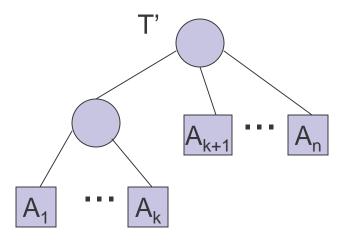
 $S = \{\{A,C,E\}, \{A,C,F\}, \{B,D,E\}\}$



There are 8 orderings that are possible in keeping each of these sets contiguous.

PQ Tree Restriction

- Let $U = \{A_1, A_2, ..., A_n\}$, $S = \{A_1, A_2, ..., A_k\}$, and T a PQ tree.
- We will define a function Restrict with the following properties:
 - Restrict(T,S) is a PQ tree.
 - PQ(Restrict(T,S)) = PQ(T) intersect PQ(T') where



Lecture 9 - Dynamic Programming, PQ-trees

High Level PQ tree Algorithm

- Input is $U = \{A_1, A_2, ..., A_n\}$, and subsets $S_1, S_2, ..., S_m$ of U.
- Initialization:
 - T = P node with children $A_1, A_2, ..., A_n$
- Calculate m restrictions:
 - for j = 1 to m do $T := Restrict(T,S_i)$
- At the end of iteration k:
 - PQ(T) = the set of ordering of U where each set S_1 , S_2 , ..., S_k are contiguous.

Marking Nodes

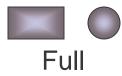
- Given a set S and PQ tree T we can mark nodes either full or partial.
 - A leaf is full if it is a member of S.
 - A node is full if all its children are full.
 - A node is partial if either it has both full and nonfull children or it has a partial child.
 - A node is doubly partial if it has two partial children.

Marks of Nodes

Mark the leaves in S full.

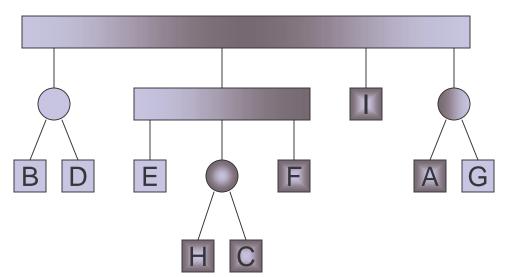
Bottom up mark the nodes full or partial.

The members of S will become contiguous.





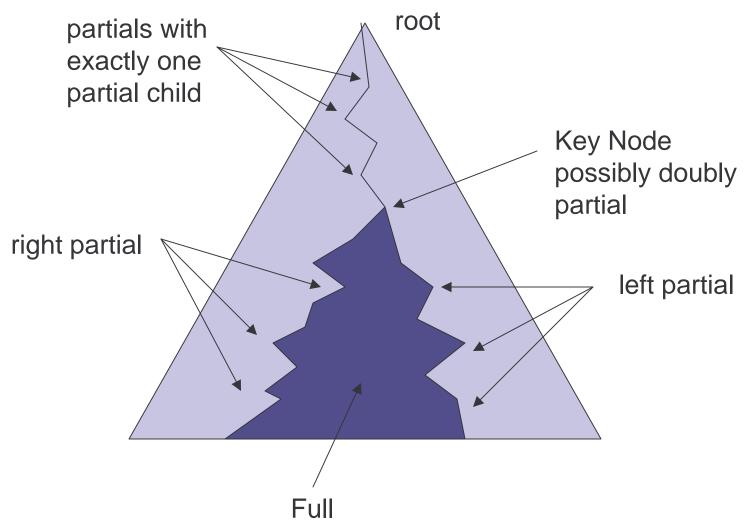








Structure of the Marked PQ Tree

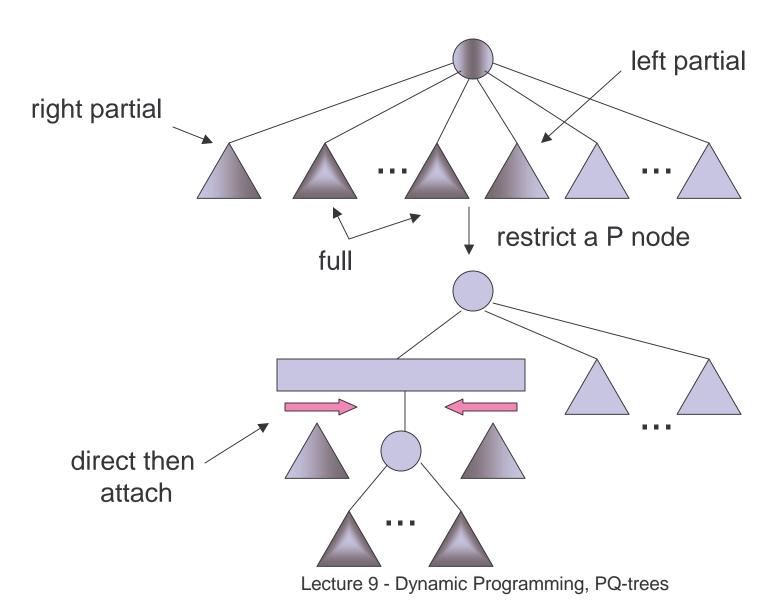


Lecture 9 - Dynamic Programming, PQ-trees

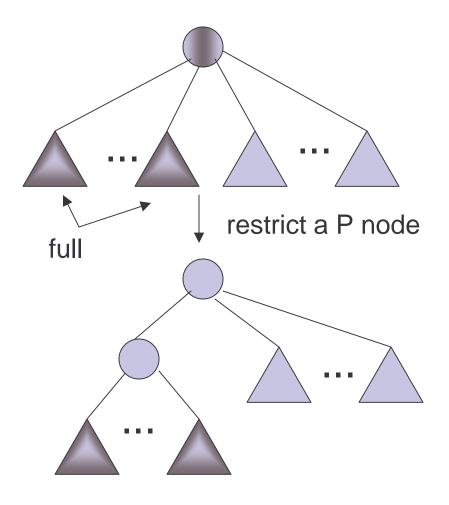
Restrict(T,S)

- Mark the full and partial nodes from the bottom up.
 - In the process the marked leaves become contiguous.
- Locate the key node.
 - Deepest node with the property that all the full leaves are descendents of the node.
- Restrict the key node.
 - In the process of restricting the key node we will have to recursively direct partial nodes.
 - Directing a node returns a sequence of nodes.

Restricting a P Node with Partial Children

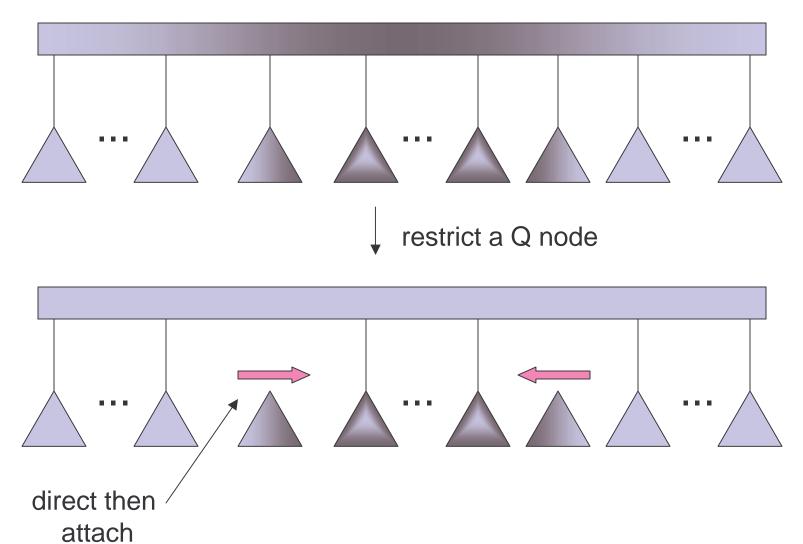


Restricting a P node with no Partial Children

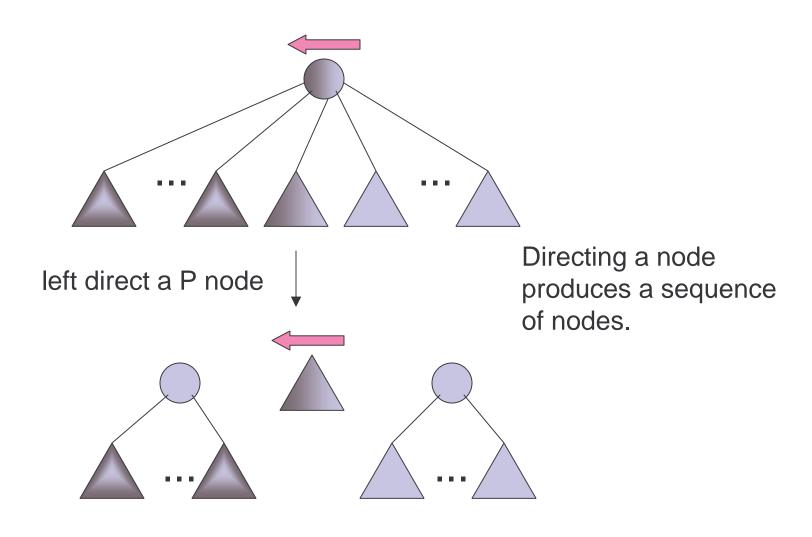


Lecture 9 - Dynamic Programming, PQ-trees

Restricting a Q node

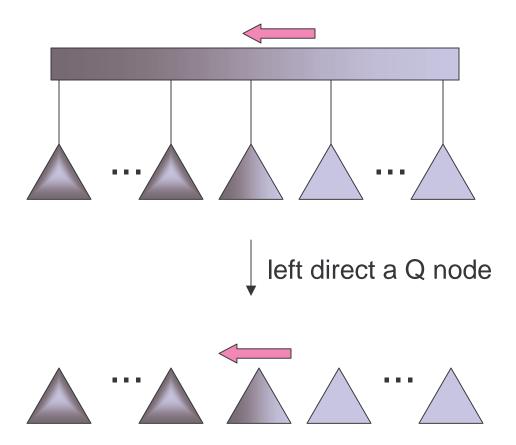


Directing a P Node



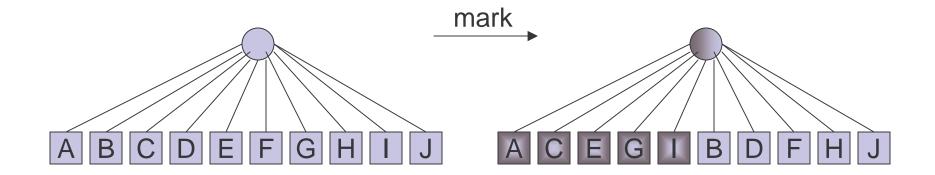
Lecture 9 - Dynamic Programming, PQ-trees

Directing a Q Node



Example (1)

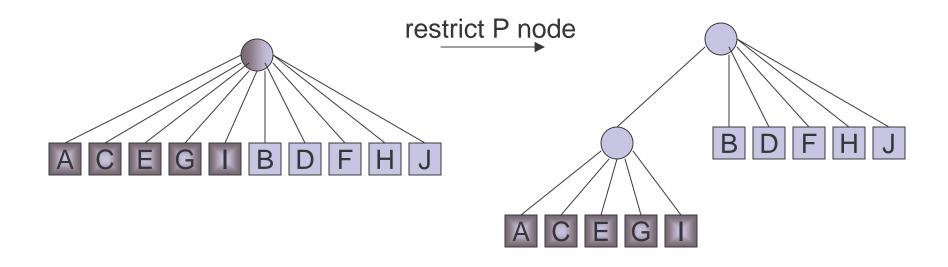
 $U = \{A,B,C,D,E,F,G,H,I,J\}$ $S_1 = \{A,C,E,G,I\}$



Example (2)

$$U = \{A,B,C,D,E,F,G,H,I,J\}$$

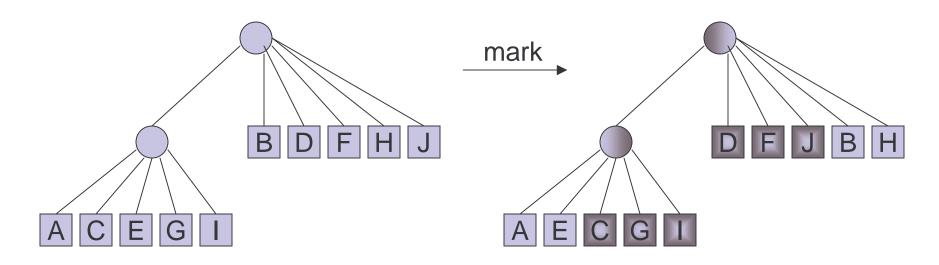
$$S_1 = \{A,C,E,G,I\}$$



special case because no partial child.

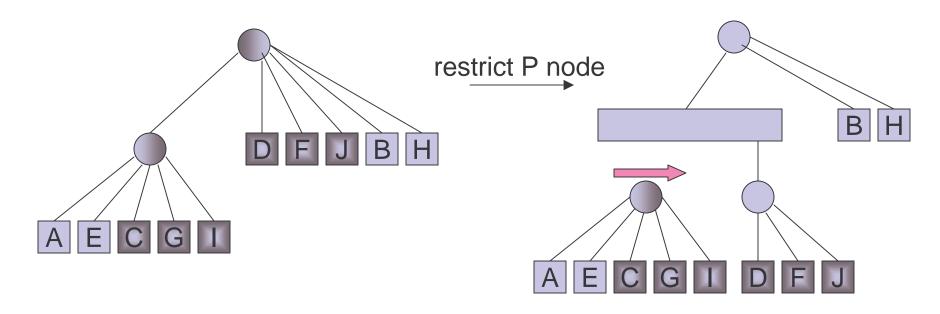
Example (3)

 $U = \{A,B,C,D,E,F,G,H,I,J\}$ $S_2 = \{C,D,F,G,I,J\}$



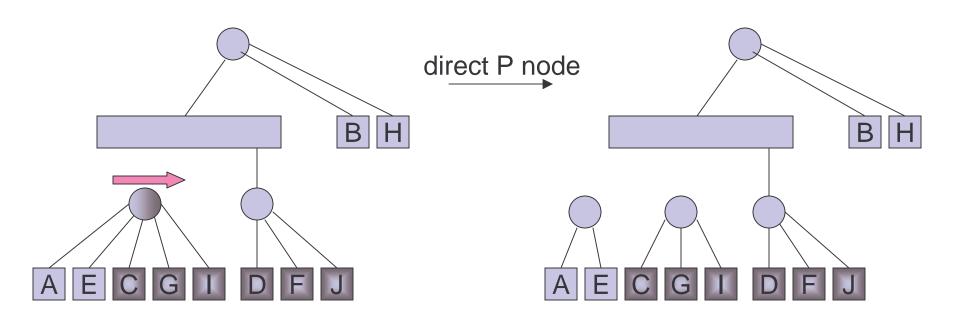
Example (4)

 $U = \{A,B,C,D,E,F,G,H,I,J\}$ $S_2 = \{C,D,F,G,I,J\}$



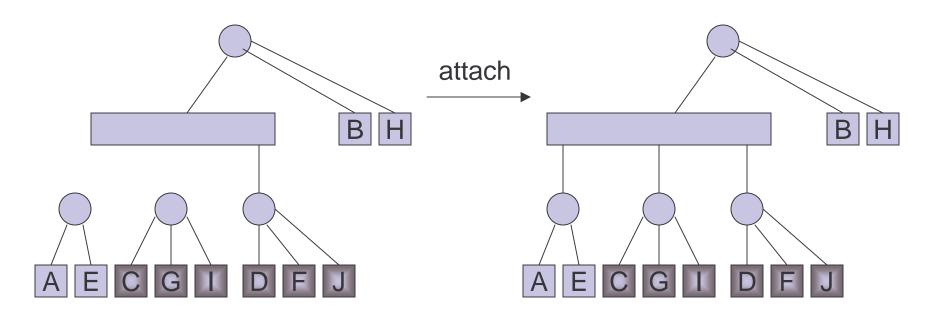
Example (5)

 $U = \{A,B,C,D,E,F,G,H,I,J\}$ $S_2 = \{C,D,F,G,I,J\}$

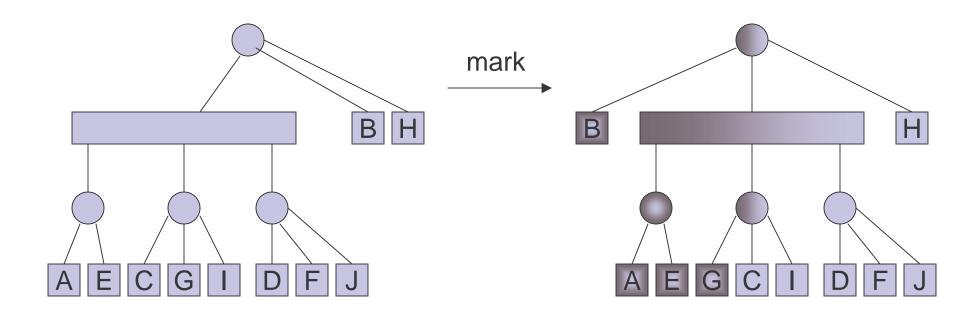


Example (6)

 $U = \{A,B,C,D,E,F,G,H,I,J\}$ $S_2 = \{C,D,F,G,I,J\}$



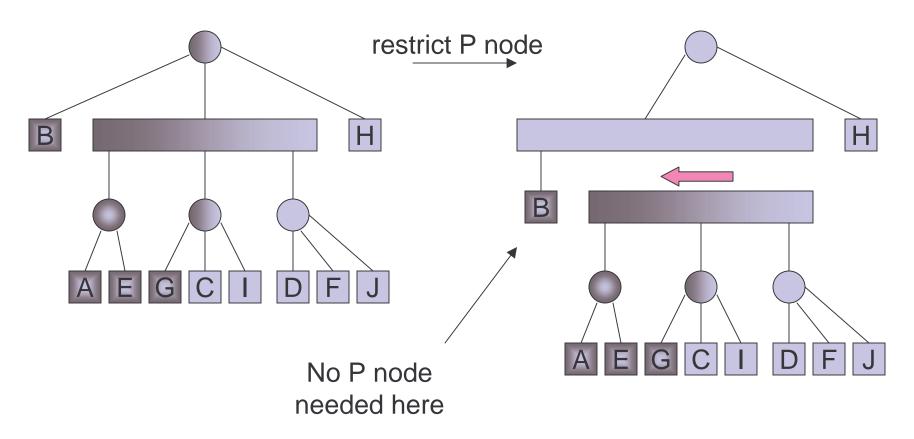
Example (7)



Example (8)

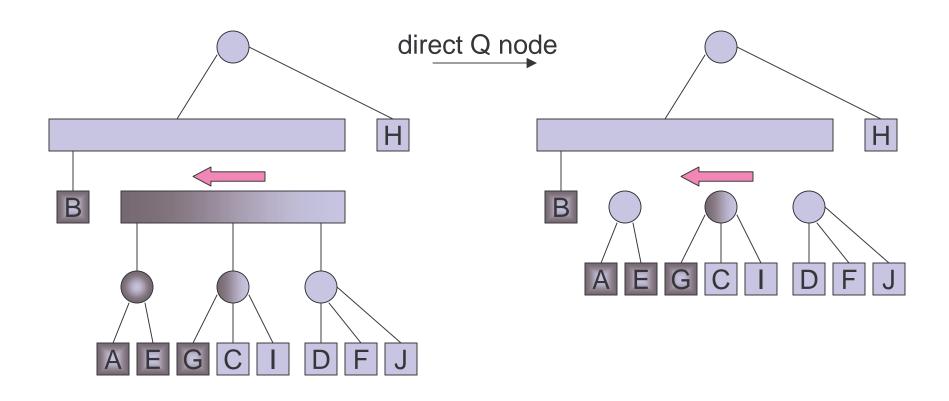
$$U = \{A,B,C,D,E,F,G,H,I,J\}$$

$$S_3 = \{A,B,E,G\}$$

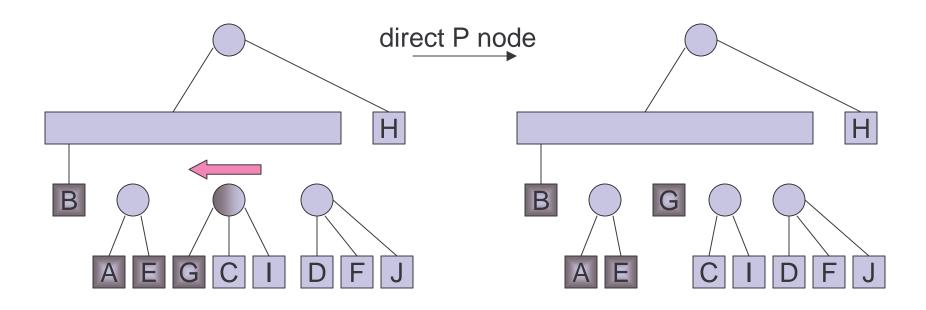


Lecture 9 - Dynamic Programming, PQ-trees

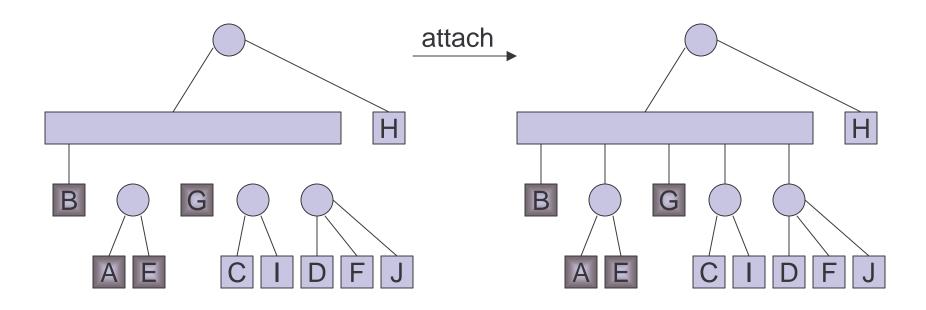
Example (9)



Example (10)



Example (11)

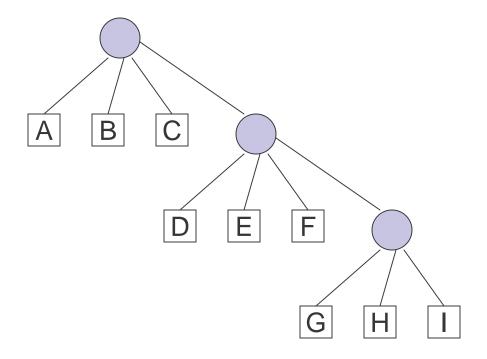


Example (12)

```
U = \{A,B,C,D,E,F,G,H,I,J\}
S_1 = \{A,C,E,G,I\}
S_2 = \{C,D,F,G,I,J\}
S_3 = \{A, B, E, G\}
                                                                 Н
                            В
                                        G
```

Exercise

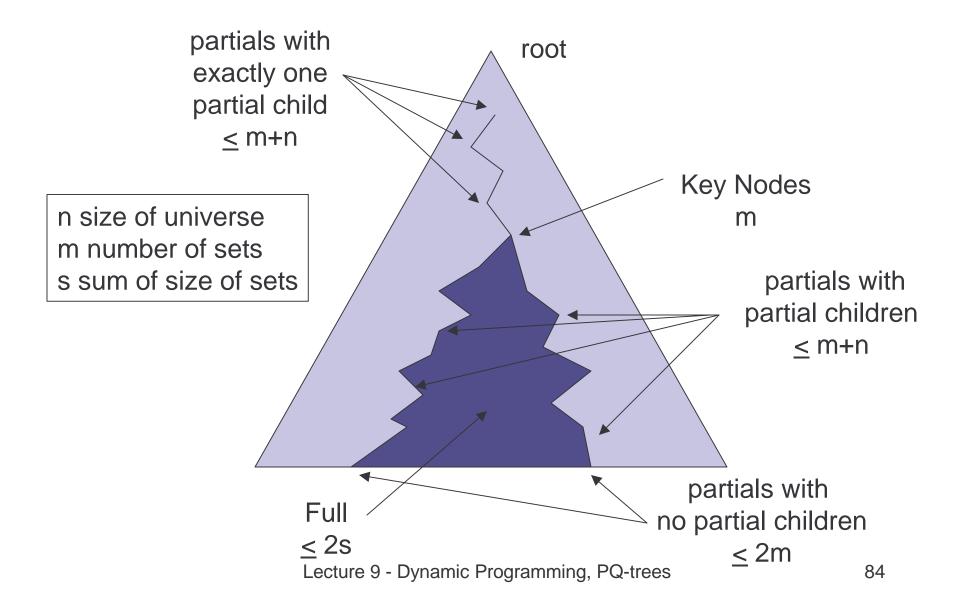
Restrict with to make {A,B,D,E,G} contiguous



Linear Number of Nodes Processed

- Let n be the size of the universe, m the number of sets, and s the sum of the sizes of the sets.
 - Number of full nodes processed ≤ 2s.
 - Number of key nodes processed = m.
 - Number of partial nodes with partial children processed below the key node ≤ m + n.
 - Number of partial nodes with no partial children ≤ 2m.
 - Number of partial nodes processed above the key node < m + n.

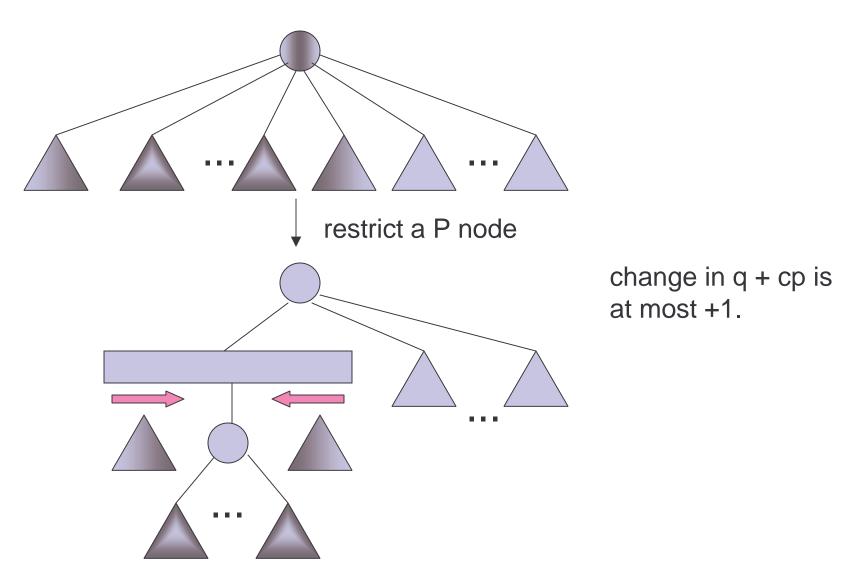
Number of Processed Nodes Amortized



Partials with Partial Children Below the Key Node

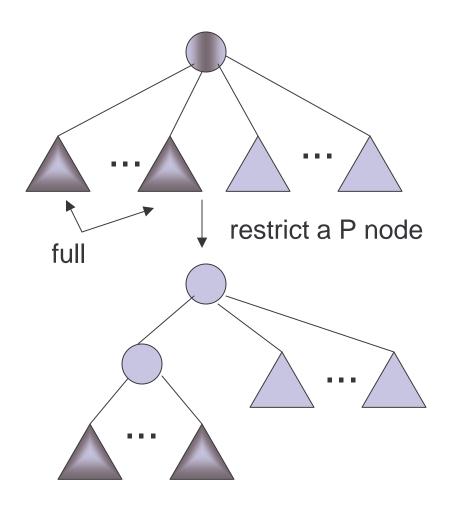
- Amortized complexity argument.
- Consider the quantities:
 - q = number of Q nodes,cp = number of children of P nodes.
 - We examine the quantity x = q + cp
 - x is initially n and never negative.
 - Each restrict of a key node increases x by at most 1.
 - Each direct of a partial node with a partial child decreases x by at least 1.
 - Since there are m restricts of a key node then there are most n + m directs of partials with partial children.

Restricting a P Node with Partial Children



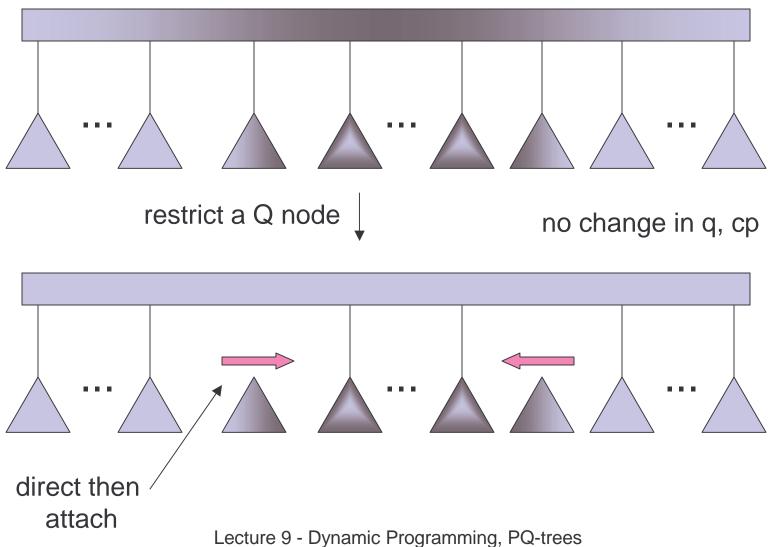
Lecture 9 - Dynamic Programming, PQ-trees

Restricting a P node with no Partial Children

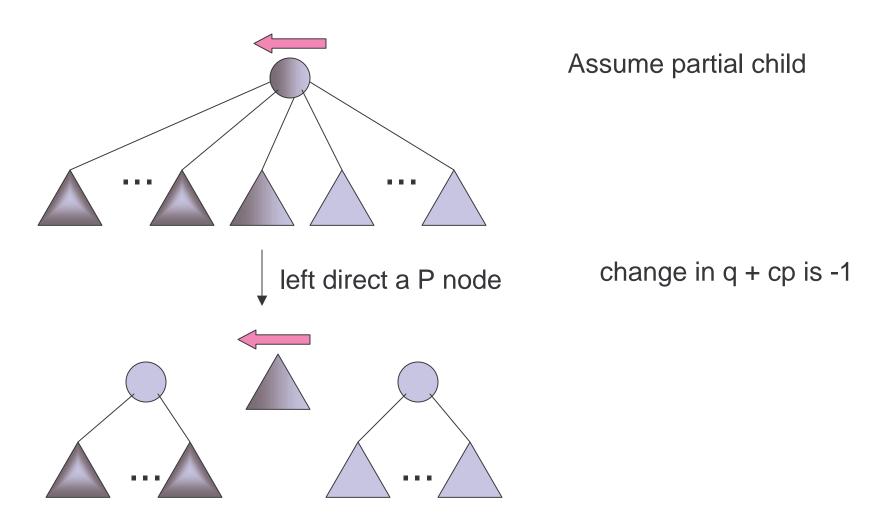


change in q + cp is exactly +1.

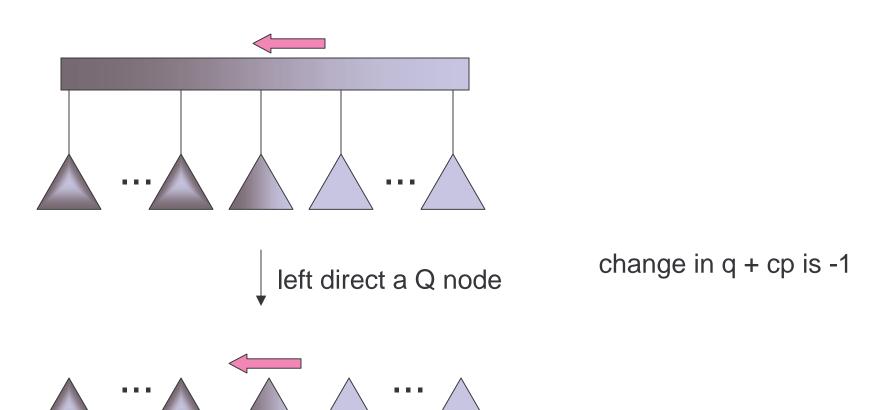
Restricting a Q node



Directing a P Node



Directing a Q Node

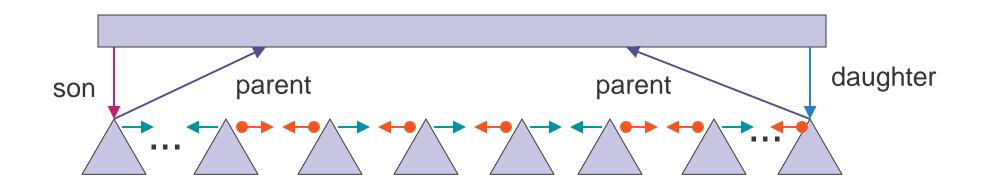


PQ Tree Notes

- In algorithmic design only a linear number of nodes are ever processed.
- Designing the data structures to make the linear time processing a reality is very tricky.
- PQ trees solve the idealized DNA ordering problem.
- In reality, because of errors, the DNA ordering problem is NP-hard and other techniques are used.

Example of Data Structure Trick

Linking the children of a Q node







Linking of siblings can be in any order. Middle children don't know parents. End children know parents.