Computational Biology

Lecture 19

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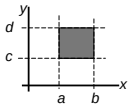
Chaining local alignments

- Having found many maximal matches (local alignments) between x and y with different lengths, we would like to chain them together to maximize the sum of lengths
- Each match x_a, …, x_b and y_c, …, y_d can be represented as a square in two dimensions



- Two squares can be chained if the top left corner of one is below and to the right of the bottom right corner of the other

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Generalizing

- We have rectangles, each with a weight w
- Two rectangles i and j can be in the same chain if the bottom left corner of j is above and to the right of the top right corner of i, we say j follows i in the chain
- We would like to find a chain with maximum weight

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Simple solution

- Construct a directed acyclic graph G:
  - one vertex for each rectangle
  - a directed edge from vertex i to vertex j iff rectangle j can follow rectangle i in some chain
- Let $v(i)$ be the maximum weight of a chain that ends in rectangle i.

Algorithm:

$v(j) \leftarrow w(j)$ for all vertices j

topologically sort G (if i before j, there is no edge (j, i), i.e. i cannot follow j in a chain)

updating v(i) can only affect v(j) for j > i
for all vertices j in order
  $v(j) \leftarrow w(j)$ + max $v(i)$ where edge $e = (i,j)$ exists

the rectangle i with max $v(i)$ is the end of the optimal chain and
we can trace back by keeping pointers

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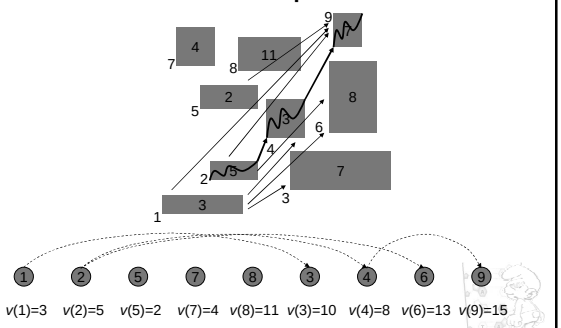
Example



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Running time

- Topological sort can be done in linear time in the number of vertices and edges of G; therefore in $O(n^2)$, where n is the number of rectangles
- Updating v(i) for all i takes $O(n^2)$ time as well
- We would like a better time bound like $O(n\log n)$
- The bound $O(n\log n)$ can be achieve
- We will consider an $O(n\log n)$ time algorithm for the one dimensional problem (rectangles become segments on the x line) and then generalize it for two dimensions

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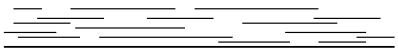
One dimension



- We have n segments
- Let I be the list of all $2n$ left and right end points

```
sort I
V ← 0
for i = 1 to 2n
    if I[i] is left of segment j, set v(j) to w(j) + V      [ entering j ]
    if I[i] is right of segment j, set V to max(v(j), V)    [ exiting j ]
```

- The value of V at the end is the weight of the optimal chain
- The chain itself can be obtained by the now familiar back tracing strategy

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Correctness and time

- When entering a segment j, j has a potential to participate in the chain and contribute a $w(j)$ to the *max* weight computed so far to make it

$$v(j) = V + w(j)$$

- When leaving segment j, $v(j)$ is used as the maximum weight unless a better maximum V has been found before exiting j
- The running time is $O(n \log n)$ dominated by the sorting operation

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Two dimensions

- We will generalize the approach for the one dimension
- Let I be the list of the left and right end points of the rectangles (x coordinates)
- The chaining algorithm processes the entries in I in order (left to right) as in the one dimension case
- But the algorithm must also consider the y coordinates of each rectangle

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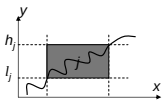
Idea



- As we go through I, we keep a list L of some rectangles that are possible ends for the current chain
- Let l_j be the low y coordinate of rectangle j and h_j be the high y coordinate of rectangle j
- Each rectangle in L will be represented as a triple (h_j, $v(j)$, j) where:
  - h_j: high y coordinate of rectangle j
  - $v(j)$: maximum weight of a chain that ends in rectangle j
  - j: the rectangle

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Entering a rectangle

- When we enter a rectangle k, k has a potential to contribute $w(k)$ to the weight of the chain
- Rectangle k has to be chained to one of the rectangles in L to extend the chain
- We look for the rectangle j in L that is closest to k (in the y dimension) with $h_j < l_k$
- We set $v(k) = w(k) + v(j)$
- Is $v(k)$ computed as above the maximum weight of a chain ending in rectangle k? Let's see…

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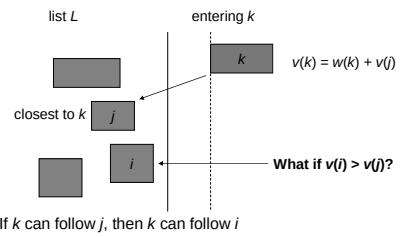
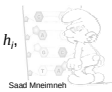
Computing $v(k)$



If k can follow j, then k can follow i

Therefore we need to make sure that if $v(i) \geq v(j)$ and $h_j \geq h_i$, rectangle j is not in the list L



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Restrictive rectangle

If
- $v(i) \geq v(j)$ and
- $h_j \geq h_i$

then we say that rectangle *j* is *more restrictive* than rectangle *i*

If
- $i \in L$ and
- *j* is more restrictive than *i*

then $j \notin L$

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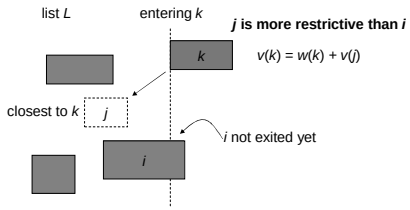
But what if…



but here *k* cannot follow *i and j should be used !*

make sure *i* is inserted in *L* only when we exit *i*

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Exiting a rectangle

- When we exit a rectangle *k*, we insert it in *L* only if *k* is not more restrictive than some $j \in L$
- Moreover, after we insert *k*, we delete from *L* all *j* that are more restrictive than *k*
- Therefore, *L* satisfies the following:

  If $h_i < h_j \Leftrightarrow v(i) < v(j)$

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Therefore…

The value of $v(k)$ is computed correctly as

$$v(k) = w(k) + v(j)$$

where $j \in L$ is closest to k with $h_j < l_k$ because:

- j is not more restrictive than any $i \in L$
- k can follow j because $j \in L$ means that j ends before k starts
- all j that end before k starts where considered for L

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Algorithm

$L \leftarrow \phi$
for i = 1 to $2n$

begin

if $I[i]$ is left of rectangle k [entering k]
then find highest $h_j < l_k$ in L
$v(k) = w(k) + v(j)$

if $I[i]$ is right of rectangle k [exiting k]
then find highest $h_j \leq h_k$ in L
if $v(k) > v(j)$
then insert k in L
delete all entries j from L with $h_j \geq h_k$ and $v(j) \leq v(k)$

end

The maximum $v(j)$ in L is the value of the maximum weight chain
The chain can be obtained by a back tracing strategy

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Analysis

- Sorting I takes $O(n \log n)$ time
- Keep L as a balanced binary search tree sorted by h_j, e.g. AVL tree
- **Searching *L***:
  - Either for highest $h_j < l_k$ or for highest $h_j \leq h_k$ takes $O(\log n)$ time
  - The total time of search is $O(n \log n)$
- **Inserting in *L***:
  - Insertion operation takes $O(\log n)$ time
  - The time needed for all insertions is $O(n \log n)$

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Analysis (cont.)

- **Deleting from *L***:
  - All entries to be deleted start just after (h_k, $v(k)$, k) and are successive because L is sorted by increasing order of $v(j)$
  - Therefore, successively examine L starting after (h_k, $v(k)$, k) until the first (h_j, $v(j)$, j) with $v(j) > v(k)$ is found
  - Successor operation takes $O(\log n)$ time
  - Deletion operation takes $O(\log n)$ time
  - The total time needed for all deletions is $O(n \log n)$

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