COMPSCI 311: Introduction to Algorithms

Lecture 14: Dynamic Programming – Sequence Alignment

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slides credit: Dan Sheldon (adapted)

Dynamic Programming Recipe

Step 1: Devise simple recursive algorithm

Flavor: make "first choice",
then recursively solve remaining part of the problem

Step 2: Write recurrence for optimal value

Step 3: Design bottom-up iterative algorithm

- Weighted interval scheduling: first-choice is binary
- Rod-cutting: first choice has n options
- Subset Sum: need to "add a variable" (one more dimension)

Today: similarity between sequences

A Simple Case: Minimum Edit Distance

How many edits to go from PLEASANT to PRESENT ?

Levenshtein distance: an edit is

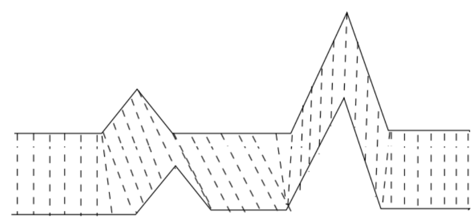
- substituting a letter
- deleting a letter
- inserting a letter

Application: spelling correction

"preffered": (0) proffered (1) preferred (2) referred ...

Dynamic Time Warping

Measure similarity between two temporal sequences



Speech recognition, speaker recognition, gait recognition

Testing embedded systems (sensor response profile,
behavior in given scenario, e.g., braking)

Source: https://en.wikipedia.org/wiki/Dynamic_time_warping

Sequence Alignment: Motivation

- Biologists use genetic similarity to determine evolutionary relationships.
- How do we evaluate if two gene sequences are similar or not, and how similar they are ?
- We *align* them: Needleman-Wunsch algorithm (global alignment)
  Also: Smith-Waterman for local alignment (similar regions), not discussed here
- Need efficiency for long sequences
- Also used in spell-checkers, `diff` program, search engines.

Sequence Alignment: Definition

Example. TAIL vs TALE

- For two strings $X = x_1x_2 \dots x_m, Y = y_1y_2 \dots y_n$, an alignment M is a matching between $\{1, \dots, m\}$ and $\{1, \dots, n\}$.
- M is valid if
  - Matching. Each element appears in at most one pair in M.
  - No crossings. If $(i, j), (k, \ell) \in M$ and $i < k$, then $j < \ell$.
- Cost of M:
  - Gap penalty. For each unmatched character, you pay δ.
  - Alignment cost. For a match (i, j), you pay $C(x_i, y_j)$.
    (in general, depends on the pair of mismatched symbols)

$$\text{cost}(M) = \delta(m + n - 2|M|) + \sum_{(i,j)\in M} C(x_i, y_j).$$

Sequence Alignment: Running Example

Problem. Given strings X, Y gap-penalty δ and cost matrix C, find valid alignment of minimal cost.

Example 1. TAIL vs TALE, $\delta = 0.5$, $C(x,y) = \mathbf{1}[x \neq y]$.

```
TAIL-    I not matched
TA-LE    E not matched
```

Example 2. TAIL vs TALE, $\delta = 5$, $C(x,y) = \mathbf{1}[x \neq y]$.

```
TAIL
TALE
```

Clicker Question 1

Consider the longest common subsequence (LCS) problem: given two sequences of symbols, find the longest (not necessarily contiguous) sequence that belongs to both

A: LCS is a special case of sequence alignment, gap penalty $\delta = 0$, mismatch cost 1 for different symbols

B: LCS is a special case of sequence alignment, gap penalty $\delta = 1$, mismatch cost ∞ for different symbols

C: LCS is a special case of sequence alignment, gap penalty $\delta = 0$, mismatch cost ∞ for different symbols

D: LCS cannot be defined as special case of sequence alignment

Toward an Algorithm

- Try what we did before: Let O be optimal alignment.
  - If $(m,n) \in O$ we can align $x_1 x_2 \dots x_{m-1}$ with $y_1 y_2 \dots y_{n-1}$.
  - If $(m,n) \notin O$ then either x_m or y_n must be unmatched (if both were matched, we'd have a crossing).
- Value $\mathrm{OPT}(m,n)$ of optimal alignment is either:
  - $C(x_m, y_n) + \mathrm{OPT}(m-1, n-1)$, If (m,n) matched
  - $\delta + \mathrm{OPT}(m-1, n)$, If m unmatched
  - $\delta + \mathrm{OPT}(m, n-1)$. If n unmatched

Recurrence

Let $\mathrm{OPT}(i,j)$ be optimal alignment cost of $x_1 x_2 \dots x_i$ and $y_1 y_2 \dots y_j$.

$$\mathrm{OPT}(i,j) = \min \begin{Bmatrix} C(x_i, y_j) + \mathrm{OPT}(i-1, j-1) \\ \delta + \mathrm{OPT}(i-1, j) \\ \delta + \mathrm{OPT}(i, j-1) \end{Bmatrix}$$

And (i,j) is in optimal alignment iff first term is the minimum.

Clicker Question 2

Suppose we try to align "banana" with "ana" (occurs twice). The optimal alignment should be with

A: the first match

B: the second match

C: any of the matches

D: depends on the gap and letter mismatch penalties

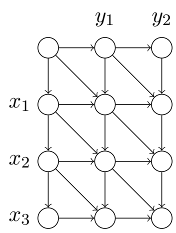
Sequence Alignment Pseudocode

align(X,Y)
  Initialize M[0..m,0..n] = null.
  M[i,0] = $i\delta$, M[0,j] = $j\delta$ for all i, j.
  for $j = 1, \dots, n$ **do**
    for $i = 1, \dots, m$ **do**
      $v_1 = C(x_i, y_j) + M[i-1, j-1]$.
      $v_2 = \delta + M[i-1, j]$.
      $v_3 = \delta + M[i, j-1]$.
      M[i,j] $\leftarrow \min\{v_1, v_2, v_3\}$.

Example. TALE and TAIL, $\delta = 1, C(x,y) = 2 \cdot \mathbf{1}[x \neq y]$.

Sequence Alignment

- Running time is $O(mn)$.
- Computing optimal matching is easy.
- Related to shortest path in weighted directed graph.



Graph has $\sim mn$ nodes and $\sim 3mn$ edges.

Clicker Question 3

Dijkstra's shortest-path algorithm runs in $O(|E| \log |V|)$.

Sequence alignment runs in $O(mn)$ on a graph with $O(mn)$ nodes and edges.

What can we derive from here?

A: We could do shortest paths faster with dynamic programming

B: The $\log |V|$ does not matter compared to $O(|E|)$

C: The graph in sequence alignment is a special case

D: Dijkstra's algorithm works on undirected graphs

Can We Use Less Space?

So far we've focused on **time** complexity

But **space** matters too!

Two sequences of length 10^5 each: 10^{10} (10 GB)

$$\mathrm{OPT}(i,j) = \min \begin{Bmatrix} C(x_i, y_j) + \mathrm{OPT}(i-1, j-1) \\ \delta + \mathrm{OPT}(i-1, j) \\ \delta + \mathrm{OPT}(i, j-1) \end{Bmatrix}$$

Computing column $C(\cdot, j)$ only requires column $C(\cdot, j-1)$
$\Rightarrow$ can keep only two columns (curr, prev), linear space

But: can only compute cost, not recover alignment!

Sequence Alignment in Linear Time

Hirschberg's algorithm: Divide and Conquer

Approach problem from both ends: forward and backward

Denote: $f(i,j)$ = cost of shortest path from $(0,0)$ to (i,j) in alignment graph (solution so far)

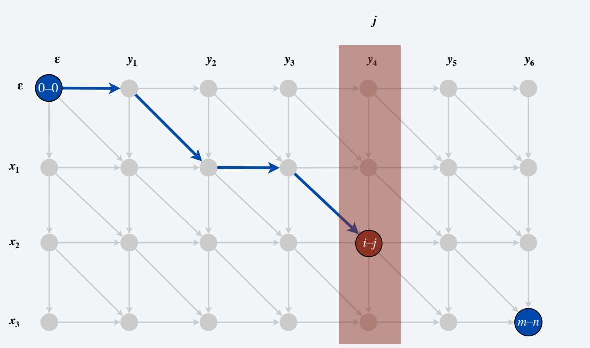
Define $g(i,j)$ = cost of shortest path from (i,j) to (m,n)

$$g(i,j) = \min \begin{Bmatrix} C(x_{i+1}, y_{j+1}) + \mathrm{OPT}(i+1, j+1) \\ \delta + g(i+1, j) \\ \delta + g(i, j+1) \end{Bmatrix}$$

Same recurrence, but going backward $\Rightarrow$ meet in the middle

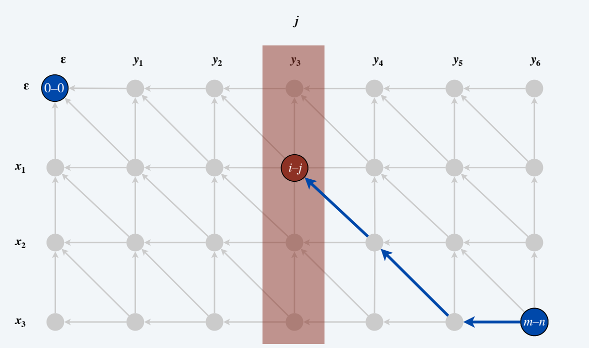
Hirschberg's algorithm

Edit distance graph.
- Let $f(i,j)$ denote length of shortest path from $(0,0)$ to (i,j).
- Lemma: $f(i,j) = OPT(i,j)$ for all i and j.
- Can compute $f(\cdot, j)$ for any j in $O(mn)$ time and $O(m+n)$ space.



Hirschberg's algorithm

Edit distance graph.
- Let $g(i,j)$ denote length of shortest path from (i,j) to (m,n).
- Can compute $g(\cdot, j)$ for any j in $O(mn)$ time and $O(m+n)$ space.



How to Divide and Conquer ?

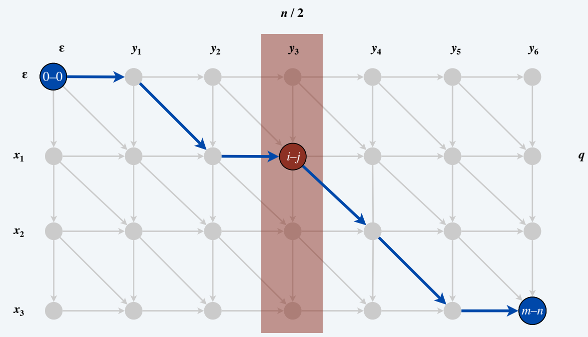
Fact 1 The length of the shortest path through any point (i, j) from $(0, 0)$ to (m, n) is $f(i, j) + g(i, j)$
(shortest path has optimal substructure)

$\Rightarrow$ can split in two parts at some point (i, j) – which ?

Fact 2 Fix a column k, $0 < k < n$ and minimize $f(q, k) + g(q, k)$ over all $0 \leq q \leq m$.
Then the shortest path from $(0, 0)$ to (m, n) passes through (q, k).

Hirschberg's algorithm

Observation 2. let q be an index that minimizes $f(q, n/2) + g(q, n/2)$.
Then, there exists a shortest path from $(0, 0)$ to (m, n) that uses $(q, n/2)$.

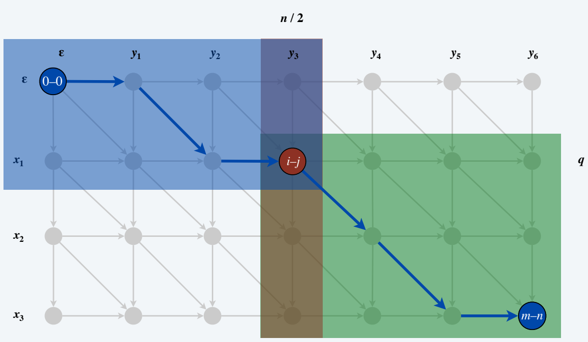


slide credit: Kevin Wayne / Pearson

Hirschberg's algorithm

Divide. Find index q that minimizes $f(q, n/2) + g(q, n/2)$; save node i–j as part of solution.

Conquer. Recursively compute optimal alignment in each piece.



slide credit: Kevin Wayne / Pearson

Hirschberg's Linear-Space Algorithm

```
align(X,Y)
  if m < 2 or n < 2 then solve directly
  Compute f(:, n/2) and g(:, n/2) in linear space
  Find q minimizing f(q, n/2) + g(q, n/2).
  Store pair (q, n/2)                        ▷ part of alignment
  align(X[0:q], Y[0:n/2])
  align(X[q+1:m], Y[n/2+1:n])                ▷ reuse memory
```

What is the recurrence for memory usage?

$f(:, n/2)$ and $g(:, n/2)$ are $O(m)$ each, discarded after finding q.

Splitting in half on larger of m, n (above: assumed n) needs space $O(\min(m, n))$

Complexity Analysis

Recurrence

$O(mn)$ work to build array of alignment costs

$T(m, n) \leq c \cdot mn + T(q, n/2) + T(m - q, n/2)$

Two-dimensional recurrence, don't know q.

Intuition: simplified case $m = n$ and assuming $q = n/2$,
we get $T'(n) \leq cn^2 + 2T'(n/2)$, for $T'(n) = T(n, n)$
This solves to $T'(n) = O(n^2)$

Can guess $T(m, n) \leq k \cdot mn$, prove by induction

Sequence Alignment: Summary

Problem structure: simple

Memory requirement: more subtle

DP + Divide and Conquer

More sequences:
RNA secondary structure

match maximum number of bases

problem substructure:
over *intervals*