COMPSCI 311: Introduction to Algorithms

Lecture 16: Dynamic Programming – Sequence Alignment

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Dynamic Programming Recipe

Step 1: Devise simple recursive algorithm

- Flavor: make "first choice", then recursively solve subproblem

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)
- Now: similarity between sequences

Sequence Alignment

Example. TAIL vs TALE

For two strings $X = x_1 x_2 \dots x_m, Y = y_1 y_2 \dots y_n$, 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 $C(x_i, y_j)$.

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

Sequence Alignment

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

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

Example 2. TAIL vs TALE, $\delta = 10$, $C(x,y) = \mathbf{1}[x \neq y]$.

Example Recap

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

```
TAIL-    I not matched (gap)
TA-LE    E not matched (gap)
```

Example 2. TAIL vs TALE, $\delta = 10$, $C(x,y) = \mathbf{1}[x \neq y]$.

```
TAIL
TALE
```

Applications

Genomics

- Biologists use genetic similarity to determine evolutionary relationships.
- Genetic similarity = cost of aligning DNA sequences

Spell-checkers, `diff` program, search engines.

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

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Consider the longest common subsequence (LCS) problem: given two strings X and Y, find the longest substring (not necessarily contiguous) common to both. Is LCS a special case of sequence alignment?

A. Yes, with gap penalty $\delta = 0$ and alignment cost $\mathbf{1}[x \neq y]$

B. Yes, with gap penalty $\delta = 1$, and alignment cost ∞ if $x \neq y$, else 0

C. Yes, with gap penalty $\delta = 0$, and alignment cost ∞ if $x \neq y$, else 0

D. No

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Suppose we try to align X = "banana" with Y = "ana". Assume $\delta > 0$ and the cost of a match is zero. In an optimal alignment:

A. Y will match the first occurrence of "ana" in X.

B. Y will match the second occurrence of "ana" in X.

C. Y may match any occurrence of "ana" in X.

D. The optimal alignment depends on values of δ and the mismatch cost.

Toward an Algorithm

Let O be optimal alignment. Is pair (m, n) matched in O?

- If $(m, n) \in O$ we can align $x_1 x_2 ... x_{m-1}$ with $y_1 y_2 ... y_{n-1}$.
- If $(m, n) \notin O$ then either x_m or y_n must be unmatched (by no crossing).

Value $\mathrm{OPT}(m, n)$ of optimal alignment is one of:

- $C(x_m, y_n) + \mathrm{OPT}(m-1, n-1)$, 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 $x_1 x_2 ... x_i$ and $y_1 y_2 ... y_j$.

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

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

Base case?

- $\mathrm{OPT}(0, j) = j\delta$ align $X = \emptyset$ to $Y = y_1 \dots y_j$
- $\mathrm{OPT}(i, 0) = i\delta$ similar

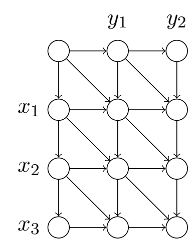
Sequence Alignment Pseudocode

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**
      $v_1 = C(x_i, y_j) + M[i-1, j-1]$
      $v_2 = \delta + M[i-1, j]$
      $v_3 = \delta + M[i, j-1]$
      $M[i, j] \leftarrow \min\{v_1, v_2, v_3\}$

- Blue = recurrence, rest = DP "boilerplate"
- Running time? $\Theta(mn)$
- Example. TALE and TAIL, $\delta = 1, C(x, y) = 2 \cdot \mathbf{1}[x \neq y]$.

Sequence Alignment

- Recovering optimal matching: store each choice, trace back.
- Related to shortest path in weighted directed graph.



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

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Dijkstra's algorithm runs in $O(|E| \log |V|) \implies O(mn \log(mn))$ time for a graph with $\Theta(mn)$ nodes and edges. Sequence alignment takes only $O(mn)$ time. What can we conclude?

A. We could use dynamic programming to compute shortest paths in any graph asymptotically faster than Dijkstra's algorithm.

B. By the multiplicativity property of big-O, the $\log |V|$ factor is dominated by $|E|$, so Dijkstra's running time is $O(|E|) = O(mn)$.

C. The graph in sequence alignment is a special case where we can compute shortest paths faster.

D. Dijkstra's algorithm only works on undirected graphs.

Can We Use Less Space?

We've focused on **time** complexity, but **space** matters too!

Two sequences of length 10^5: $mn = 10^{10}$ (10 GB)

for $j = 1, \ldots, n$ **do**
  for $i = 1, \ldots, m$ **do**
    $v_1 = C(x_i, y_j) + M[i-1, j-1]$
    $v_2 = \delta + M[i-1, j]$
    $v_3 = \delta + M[i, j-1]$
    $M[i, j] \leftarrow \min\{v_1, v_2, v_3\}$

Can we save space?

- Computing column $M[\cdot, j]$ only needs $M[\cdot, j-1]$
  $\implies$ keep just two columns (currrent, previous)
  $\implies$ linear space $O(m+n)$
- But: can only compute cost, not recover alignment!

Sequence Alignment in Linear Space

Hirschberg's algorithm: clever combination of DP and divide-and-conquer

Goal: find shortest path from $(0,0) \to (m,n)$

Board work

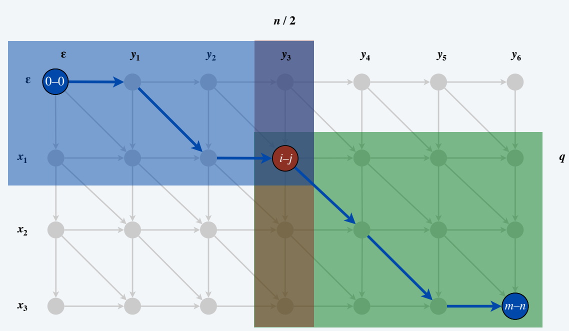
1. $\mathrm{OPT}(i,j) = f(i,j) =$ length of shortest path from $(0,0) \to (i,j)$
2. For any j, can compute $f(\cdot, j)$ in $O(mn)$ time and $O(m+n)$ space
3. Let $g(i,j) =$ length of shortest path from $(i,j) \to (m,n)$
4. For any j, can compute $g(\cdot, j)$ in $O(mn)$ time and $O(m+n)$ space
5. **Key idea:** find *one* node on shortest path. Fix $j = n/2$ and find q to maximize
$$f(q, n/2) + g(q, n/2)$$
$\implies$ node $(q, n/2)$ is on shortest path.
6. Recursively find shortest-path from $(0,0) \to (q, n/2)$
7. Recursively find shortest-path from $(q, n/2) \to (m,n)$.
8. Time $T(m,n) = T(q, n/2) + T(m-q, n/2) + O(mn)$. Solves to $O(mn)$ (recursion tree)

Space still $O(m+n)$.

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.



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slide credit: Kevin Wayne / Pearson

Sequence Alignment: Summary

Align sequences X, Y

- Binary choice
- Recurse on prefixes
- $O(mn)$ time
- $O(m+n)$ space: more subtle
  - DP + Divide and Conquer

More sequences:

- RNA secondary structure
- match max. # of bases
- problem substructure:
  over *intervals*