Longest Common Subsequence and Global Sequence Alignment

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Introduction

Reading:

- "Longest Common Subsequence", 15.4 CLRS
- "Text Similarity Testing", 9.4 GT

Look at two dynamic programming algorithms that measure the similarity of two sequences.

Longest common subsequence

Definition

Given a sequence of values $(a_1, a_2, \ldots, a_m)$, a subsequence is a sequence $(a_{i_1}, a_{i_2}, \ldots, a_{i_t})$ where $1 \leq i_1 < i_2 < \ldots i_t \leq m$.

Alternatively,

- () is a subsequence of every sequence.
- $(b_1, \ldots, b_t)$ is a subsequence of $(a_1, \ldots, a_m)$ if there is some i such that $b_t = a_i$ and $(b_1, \ldots, b_{t-1})$ is a subsequence of $(a_1, \ldots, a_{i-1})$.

Problem

Given sequences $(a_1, a_2, \ldots, a_m)$ and $(b_1, b_2, \ldots, b_n)$, find the longest subsequence that is common to both sequences.

Example

The LCS of $(1, 1, 2, 3, 4, 5)$ and $(5, 2, 3, 4, 1, 1)$ is $(2, 3, 4)$.

Optimal substructure

Lemma

Let $(x_1, \ldots, x_t)$ be a LCS of $(a_1, \ldots, a_m)$ and $(b_1, \ldots, b_n)$. Then there is some i, j such that $x_t = a_i = b_j$ and $(x_1, \ldots, x_{t-1})$ is a LCS of $(a_1, \ldots, a_{i-1})$ and $(b_1, \ldots, b_{j-1})$.

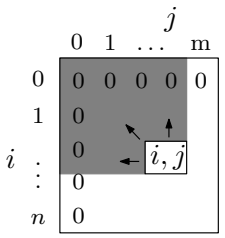
Proof

By definition, there must be some i, j such that $x_t = a_i = b_j$ and $(x_1, \ldots, x_{t-1})$ is a subsequence of $(a_1, \ldots, a_{i-1})$ and $(b_1, \ldots, b_{j-1})$. If some $(w_1, \ldots, w_s)$ is a longer subsequence of $(a_1, \ldots, a_{i-1})$ and $(b_1, \ldots, b_{j-1})$ than $(x_1, \ldots, x_{t-1})$, then $(w_1, \ldots, w_s, x_t)$ is a longer common subsequence of $(a_1, \ldots, a_m)$ and $(b_1, \ldots, b_n)$ than $(x_1, \ldots, x_t)$, a contradiction. □

Data structure

Let $L[i,j]$ be the length of the LCS of $(a_1,\ldots,a_i)$ and $(b_1,\ldots,b_j)$. Then

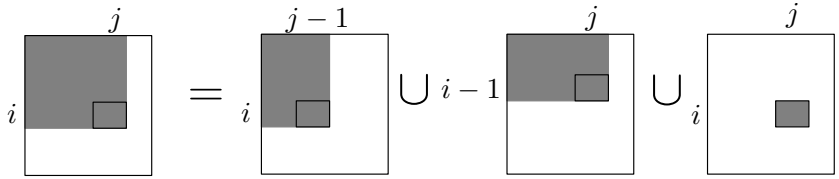
$$L[i,j] = \max_{r\le i, s\le j} \begin{cases} 0 & \text{if } r=0 \text{ or } s=0 \\ L[r-1,s-1]+1 & \text{if } a_r = b_s \\ 0 & \text{otherwise} \end{cases}$$



$L[i,j]$ depends on the values of all of the cells in the shaded region. So fill each row from left-to-right, starting with the top row and proceeding to the bottom.

Each cell in L takes $O(nm)$ time to fill. There are $O(nm)$ cells. So the total runtime is $O(n^2m^2)$.

Redundancy

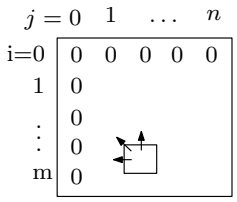


The region being maximized over can be represented by three smaller regions. The maximization of two of the regions are subproblems stored in the table. So

$$L[i,j] = \begin{cases} 0 & \text{if } r=0 \text{ or } s=0 \\ \max\left\{ \begin{array}{l} L[i-1,j-1]+1, \\ L[i-1,j], L[i,j-1] \end{array} \right\} & \text{if } a_i = b_j \\ \max\{L[i-1,j], L[i,j-1]\} & \text{otherwise} \end{cases}$$

Initialization

- zero the left column and bottom row
- $lcs[i,j]$ depends on values left and above, so fill each row left-to-right starting from the top going towards the bottom



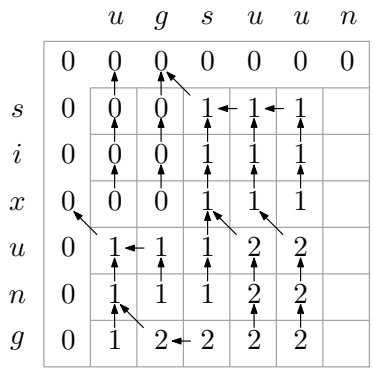

```
Algorithm LCS(A,B)
   int  lcs[A.length+1, B.length+1]
   char backtrack[A.length+1, B.length+1]
   for i ← 0 to A.length do
      lcs[i, 0] ← 0
   for j ← 0 to B.length do
      lcs[0, j] ← 0
```

Main loop

```
   for i ← 1 to n do
      for j ← 1 to m do
         lcs[i, j] ← lcs[i − 1, j]
         backtrack[i, j] ←'↑'
         if lcs[i, j − 1] > lcs[i, j] then
            lcs[i, j] ← lcs[i, j − 1]
            backtrack[i, j] ← '←'
         if a_i = b_j and
            lcs[i − 1, j − 1] + 1 > lcs[i, j]
         then
            lcs[i, j] ← lcs[i − 1, j − 1] + 1
            backtrack[i, j] ← '↖'
```

Example

Find the longest common subsequence of (s, i, x, u, n, g) and (u, g, s, u, u, n).



		u	g	s	u	u	n
	0	0	0	0	0	0	0
s	0	0	0	1	1	1	
i	0	0	0	1	1	1	
x	0	0	0	1	1	1	
u	0	1	1	1	2	2	
n	0	1	1	1	2	2	
g	0	1	2	2	2	2	

Global sequence alignment

Given two sequences $X = (a_1, \ldots, a_m)$ and $Y = (b_1, \ldots, b_n)$, we want to figure out how similar they are.

A bit similar to longest common sequence, but:

- we may want to match 2 different letters

  e.g. `AACCATGTC`
  `AAGCATATC`
- we may want to allow gaps (i.e. insertions or deletions)

  e.g. `AGCCGCT_CC`
  `AGC__CTGCC`

Application: DNA sequence alignment

Matching two pieces of DNA

- evolution may have inserted/removed pieces
- some bases (i.e. the letters) may have mutated

Formalization

Definition

A pairwise sequence alignment of X, Y is a pair of sequences X', Y', possibly containing gaps ("-") such that

- X' minus the gaps is X,
- Y' minus the gaps is Y,
- $|X'| = |Y'|$, and
- $X'_i = Y'_i =$ "-" never happens

The score of the alignment X', Y' is

$$\sum_{i=1}^{|X'|} s(X'_i, Y'_i),$$

where s is a score function defined by biologists to tell us how good/bad a mismatch is.

- e.g. $s(A, A) = 8$, $s(*, -) = -\delta$ (gap penalty), etc.

Optimal substructure

Call the prefix of a sequence everything but the last element. Let X', Y' be an optimal sequence alignment. Then X' ends in either a_m or $-$ and Y' ends in either b_n or $-$.

So four cases to consider:

1. X' ends in a_m and Y' ends in b_n: then the prefixes of X', Y' are an optimal alignment of the prefixes of X, Y.
2. X' ends in a_m and Y' ends in $-$: then the prefixes of X', Y' are an optimal alignment of the prefix of X and the whole of Y.
3. X' ends in $-$ and Y' ends in b_n: then the prefixes of X', Y' are an optimal alignment of the whole of X and the prefix of Y.
4. X' and Y' cannot both end in $-$

Data structure

Let $gsa[i,j]$ be the score of the optimal sequence alignment of $(a_1,\ldots,a_i)$ and $(b_1,\ldots,b_j)$. Then

$$gsa[i,j] = \begin{cases} 0 & \text{if } i=j=0 \\ -i\delta & \text{if } i>0, j=0 \\ -j\delta & \text{if } i=0, j>0 \\ \max \begin{cases} gsa[i-1,j-1]+ \\ \quad s(a_i,b_j), \\ gsa[i-1,j]-\delta, \\ gsa[i,j-1]-\delta \end{cases} & \text{if } i>0, j>0 \end{cases}$$

by the optimal substructure, where δ is the gap penalty. We can fill in the table the same way as for the longest common subsequence.

Initialization

```
Algorithm Smith-Wasserman(X,Y)
   int    gsa[X.length+1, Y.length+1]
   string backtrack[X.length+1, Y.length+1]
   for i ← 1 to m do
      gsa[i,0] ← −iδ
      backtrack[i,0] ←'gap in X'
   for j ← 1 to n do
      gsa[0,j] ← −jδ
      backtrack[i,0] ←'gap in Y'
```

Main loop

```
   for i ← 1 to m do
      for j ← 1 to n do
         mscore ← gsa[i−1,j−1] + s(a_i,b_j)
         xscore ← gsa[i−1,j] − δ
         yscore ← gsa[i,j−1] − δ
         if mscore ≥ xscore and mscore ≥ yscore then
            gsa[i,j] ← mscore
            backtrack[i,j] ← 'match'
         else if xscore ≥ yscore then
            gsa[i,j] ← xscore
            backtrack[i,j] ←'gap in X'
         else
            gsa[i,j] ← yscore
            backtrack[i,j] ←'gap in Y'
```

Path recovery

```
   X' ←''
   Y' ←''
   i ← m
   j ← n
   while i > 0 or j > 0 do
      if backtrack[i,j] ='match' then
         X' ← a_i + X'
         Y' ← b_j + Y'
      else if backtrack[i,j] ='gap in X' then
         X' ←'-'+X'
         Y' ← b_j + Y'
      else
         X' ← a_i + X'
         Y' ←'-'+Y'
   return X', Y', gsa[m,n]
```

Example

Let $X = \texttt{GGCAC}$ and $Y = \texttt{GTCCTC}$. Let

$$score(x, y) = \begin{cases} 5 & \text{if } x = y \\ -1 & \text{if } x \neq y, \text{ but } \begin{array}{l} \text{both } x, y \in \{A, T\} \text{ or} \\ \text{both } x, y \in \{G, C\} \end{array} \\ -3 & \text{otherwise} \end{cases}$$

with a gap penalty of -2

		G	T	C	C	T	C
	0	-2	-4	-6	-8	-10	-12
G	-2	5	3	1	-1	-3	-5
G	-4	3	2	2	0	-2	-4
C	-6	1	0	7	7	5	3
A	-8	-1	0	5	5	6	
C	-10	-3	-2	5	10		