CSE 421
Intro to Algorithms
Winter 2000

Sequence Alignment

Sequence Alignment

- What
- Why
- A Simple Algorithm
- Complexity Analysis
- A better Algorithm:
  "Dynamic Programming"

Sequence Similarity: What

G G A C C A

T A C T A A G
| : | : | | :
T C C – A A T

Sequence Similarity: Why

- Diff
- RCS
- Molecular Bio

  Similar sequences often have similar origin or function

  Similarity often recognizable after 10^8 –10^9 years

Terminology

- *String:* ordered list of letters TATAAG
- *Prefix:* consecutive letters from front
  empty, T, TA, TAT, ...
- Suffix: … from end
  empty, G, AG, AAG, ...
- *Substring:* … from ends or middle
  empty, TAT, AA, ...
- *Subsequence:* ordered, nonconsecutive
  TT, AAA, TAG, ...

Sequence Alignment

```
a c b c d b        a c – – b c d b
 /  \ |               |     |   |
c a d b d          – c a d b – d –
```

Defn: An *alignment* of strings S, T is a pair of strings S', T' (with spaces) s.t.

(1) |S'| = |T'|, and (|S| = "length of S")

(2) removing all spaces leaves S, T

6.8: “Min_Edit_Distance”

a b b c → delete a → b b c → insert a → b a b c → replace c → b a b b (cost 3)

a b b c → insert b → b a b b c → delete c → b a b b (cost 2)

```
- a b c
  | | |
b a b b -
```


Alignment Scoring

```
a c b c d b        a  c  -  -  b  c  d  b
c a d b d          -  c  a  d  b  -  d  -
                  -1  2 -1 -1  2 -1  2 -1
                   Value = 3*5 + 5*(-1) = +1
```

- The *score* of aligning (characters or spaces) x & y is $\sigma(x,y)$.
- *Value* of an alignment = $\sum_{i=1}^{|S'|} \sigma(S'[i], T'[i])$
- An *optimal alignment:* one of max value

Optimal Alignment: A Simple Algorithm

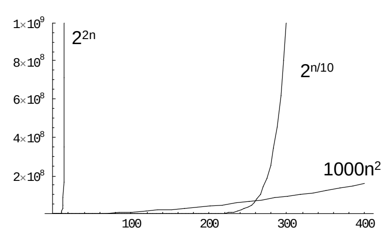
for all subseqs A of S, B of T s.t. |A| = |B| **do**
  align A[i] with B[i], $1 \le i \le |A|$
  align all other chars to spaces
  compute its value
  retain the max
end
output the retained alignment

S = abcd	A = cd
T = wxyz	B = xz
-abc-d	a-bc-d
w--xyz	-w-xyz

Analysis

- Assume |S| = |T| = n
- Cost of evaluating one alignment: $\ge n$
- How many alignments are there: $\ge \binom{2n}{n}$
  pick n chars of S,T together
  say k of them are in S
  match these k to the k *un*picked chars of T
- Total time: $\ge n\binom{2n}{n} > 2^{2n}$, for $n > 3$
- E.g., for n = 20, time is > 2^{40} operations

Polynomial vs Exponential Growth



Optimal Alignment in O(n^2) via “Dynamic Programming”

- Input: S, T, |S| = n, |T| = m
- Output: value of optimal alignment

Easier to solve a “harder” problem:

V(i,j) = value of optimal alignment of S[1], …, S[i] with T[1], …, T[j] for all $0 \le i \le n$, $0 \le j \le m$.

Base Cases

- V(i,0): first i chars of S; all match spaces

$$V(i,0) = \sum_{k=1}^{i} \sigma(S[k],-)$$

- V(0,j): first j chars of T; all match spaces

$$V(0,j) = \sum_{k=1}^{j} \sigma(-,T[k])$$

General Case

Opt align of S[1], …, S[i] vs T[1], …, T[j]:

$$\begin{bmatrix} \sim\sim\sim\sim & S[i] \\ \sim\sim\sim\sim & T[j] \end{bmatrix}, \begin{bmatrix} \sim\sim\sim\sim & S[i] \\ \sim\sim\sim\sim & - \end{bmatrix}, \text{ or } \begin{bmatrix} \sim\sim\sim\sim & - \\ \sim\sim\sim\sim & T[j] \end{bmatrix}$$

Opt align of $S_1 \ldots S_{i-1}$ & $T_1 \ldots T_{j-1}$

$$V(i,j) = \max \begin{Bmatrix} V(i-1,j-1) + \sigma(S[i],T[j]) \\ V(i-1,j) + \sigma(S[i], -) \\ V(i,j-1) + \sigma(-, T[j]) \end{Bmatrix},$$

for all $1 \le i \le n$, $1 \le j \le m$.

Example

Mismatch = -1
Match = 2

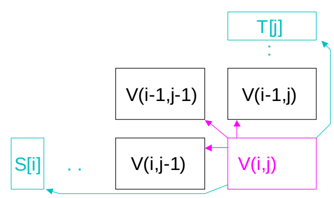
i \ j		0	1	2	3	4	5
			c	a	d	b	d ←T
0		0	-1	-2	-3	-4	-5
1	a	-1	-1	1			
2	c	-2	1				
3	b	-3					
4	c	-4					
5	d	-5					
6	b	-6					

↑S

Time = O(mn)

Calculating One Entry

$$V(i,j) = \max \begin{Bmatrix} V(i-1,j-1) + \sigma(S[i],T[j]) \\ V(i-1,j) + \sigma(S[i], -) \\ V(i,j-1) + \sigma(-, T[j]) \end{Bmatrix}$$



Finding Alignments: Trace Back

i \ j		0	1	2	3	4	5
			c	a	d	b	d ←T
0		0	-1	-2	-3	-4	-5
1	a	-1	-1	1	0	-1	-2
2	c	-2	1	0	0	-1	-2
3	b	-3	0	0	-1	2	1
4	c	-4	-1	-1	-1	1	1
5	d	-5	-2	-2	1	0	3
6	b	-6	-3	-3	0	3	2

↑S

Complexity Notes

- Time = O(mn), (value and alignment)
- Space = O(mn)
- Easy to get value in Time = O(mn) and Space = O(min(m,n))
- Possible to get value *and alignment* in Time = O(mn) and Space = O(min(m,n)) but tricky.