Algorithms to compute string similarity

String Similarity

- Finding differences or edit distance between two sequences can be alternately formulated as finding similarity between two sequences.
- Biologists usually prefer using similarity measures to study relationship between strings.
- Earlier we gave a definition of alignment as follows:
  - **Definition**: Let *v* and *w be* two sequences of length *n* and *m* , respectively , over a finite alphabet ∑. An **alignment** maps the strings *v* and *w* into strings and that may contain indel ('-') characters such that removal of all indel characters leaves *v* and *w* intact.

Similarity using Dynamic Programming-Longest Common Subsequence Problem

If we are interested to find an alignment that maximizes *S*(*n,m*), the number of matched symbols, we can assign a weight of 1 for match and a weight of 0 for both insert and delete operations. The substitution operation is considered as a delete followed by an insert operation. The score table δ consists simply of all diagonal entries to be 1 and rest are 0.The dynamic programming equations will then look like

$$
\begin{array}{l}
S(0,0) \leftarrow 0 \\
\text{for } j = 1 \ \text{ to } \ m \ \text{ do} \\
S(0, j) \leftarrow 0 \qquad\qquad /*\text{insert from w}/* \\
\text{for } \ i = 1 \ \text{ to } \ n \ \text{ do} \\
\{ \ \ S(i,0) \leftarrow 0 \qquad\qquad /*\text{delete from v}/* \\
\quad \text{for } j = 1 \ \text{ to } \ m \ \text{ do} \\
\qquad \text{if } \ v_i = \mathrm{w}_{\mathrm{j}} \ \ \text{match} = S(i-1, j-1) + 1 \\
\qquad S(i, j) \leftarrow \max\{ \ S(i, j-1), \ S(i-1, j), \ \text{match}\} \\
\} \\
\text{write"similarity score is"} \ \ S(n,m)
\end{array}
$$

Dynamic Programming Example

	w		A	T	C	G	T	A	C
v		0	1	2	3	4	5	6	7
	0	0	0	0	0	0	0	0	0
A	1	0							
T	2	0							
G	3	0							
T	4	0							
T	5	0							
A	6	0							
T	7	0							

Initialize *1st* row and *1st* column to be all zeroes.

Or, to be more precise, initialize *0th* row and *0th* *column to be all zeroes.*

LCS via Dynamic Programming :Example

		w	A	T	C	G	T	A	C
v		0	1	2	3	4	5	6	7
	0	0	0	0	0	0	0	0	0
A	1	0	1	1	1	1	1	1	1
T	2	0	1						
G	3	0	1						
T	4	0	1						
T	5	0	1						
A	6	0	1						
T	7	0	1						

$$S_{i,j} = \max \begin{cases} S_{i-1,\, j-1} & \leftarrow \text{value from NW +1, if } v_i = w_j \\ S_{i-1,\, j} & \leftarrow \text{value from North (top)} \\ S_{i,\, j-1} & \leftarrow \text{value from West (left)} \end{cases}$$

Alignment: Backtracking

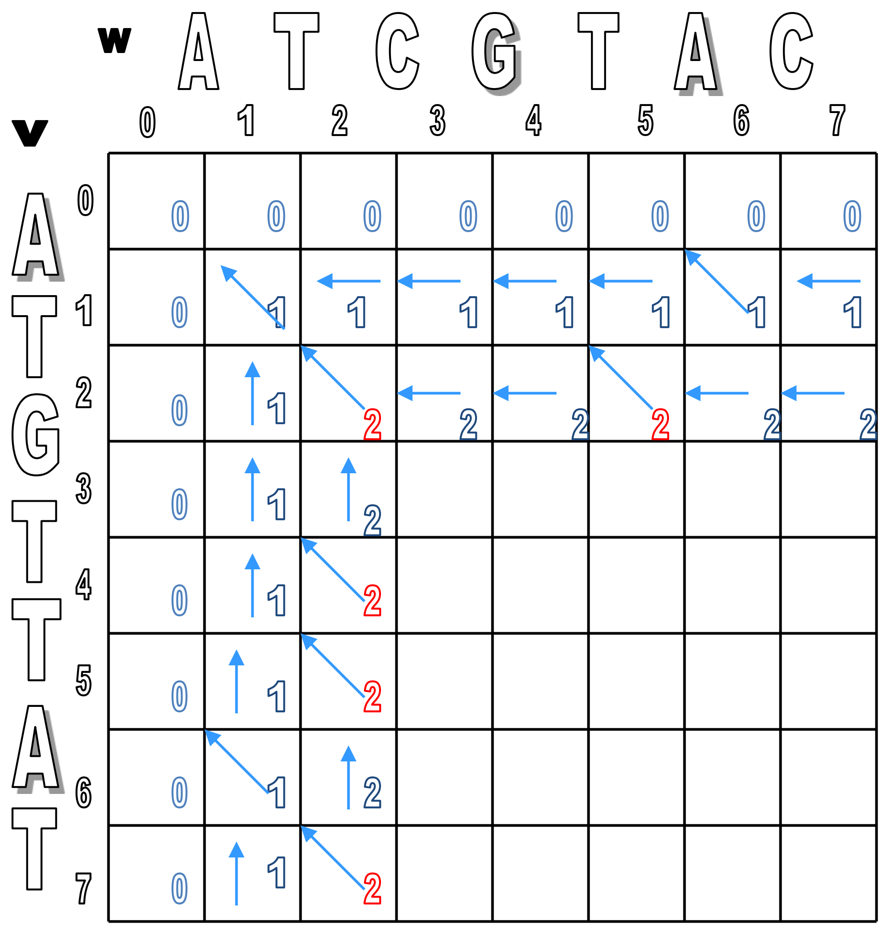
Arrows $\nwarrow \uparrow \leftarrow$ show where the score originated from.

$\uparrow$ if from the top

$\leftarrow$ if from the left

$\nwarrow$ if $v_i = w_j$

Backtracking Example



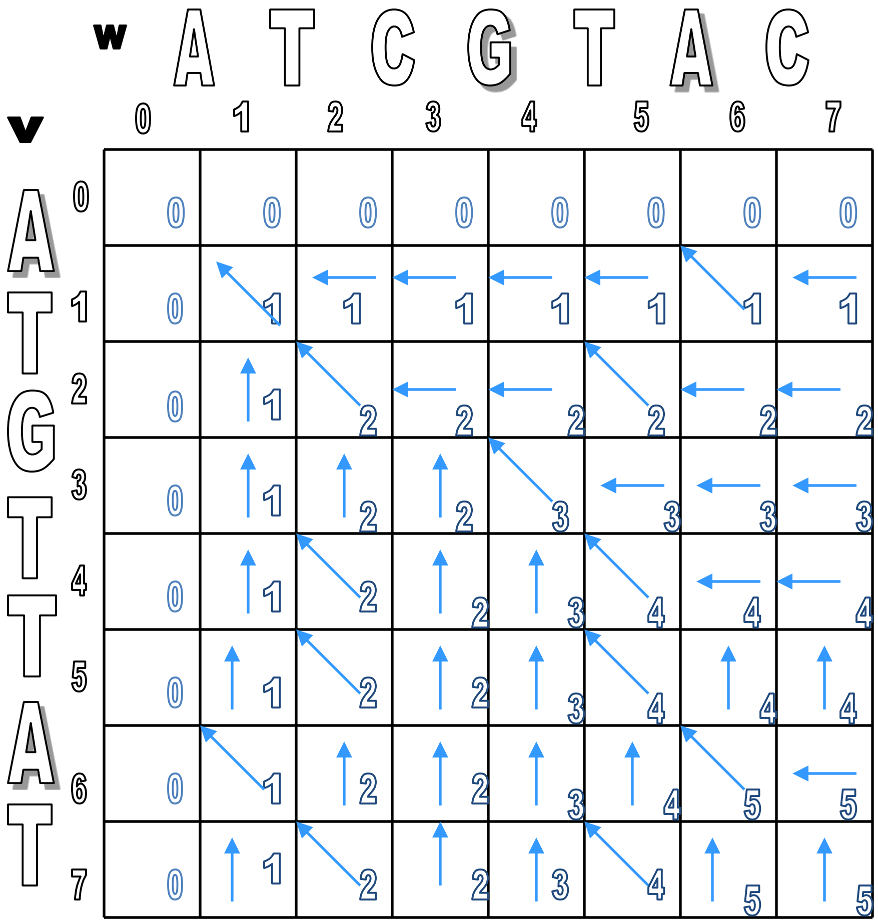
Find a match in row and column 2.

i=2, j=2,5 is a match (T).
j=2, i=4,5,7 is a match (T).

Since $v_i = w_j$, $s_{i,j} = s_{i-1,j-1} + 1$

$s_{2,2} = [s_{1,1} = 1] + 1$
$s_{2,5} = [s_{1,4} = 1] + 1$
$s_{4,2} = [s_{3,1} = 1] + 1$
$s_{5,2} = [s_{4,1} = 1] + 1$
$s_{7,2} = [s_{6,1} = 1] + 1$

Backtracking Example



Continuing with the dynamic programming algorithm gives this result.

LCS: Example

i coords:	0	1	2	2	3	3	4	5	6	7	8
elements of *v*		A	T	--	C	--	T	G	A	T	C
elements of *w*		--	T	G	C	A	T	--	A	--	C
j coords:	0	0	1	2	3	4	5	5	6	6	7

$(0,0) \rightarrow (1,0) \rightarrow (2,1) \rightarrow (2,2) \rightarrow (3,3) \rightarrow (3,4) \rightarrow (4,5) \rightarrow (5,5) \rightarrow (6,6) \rightarrow (7,6) \rightarrow (8,7)$

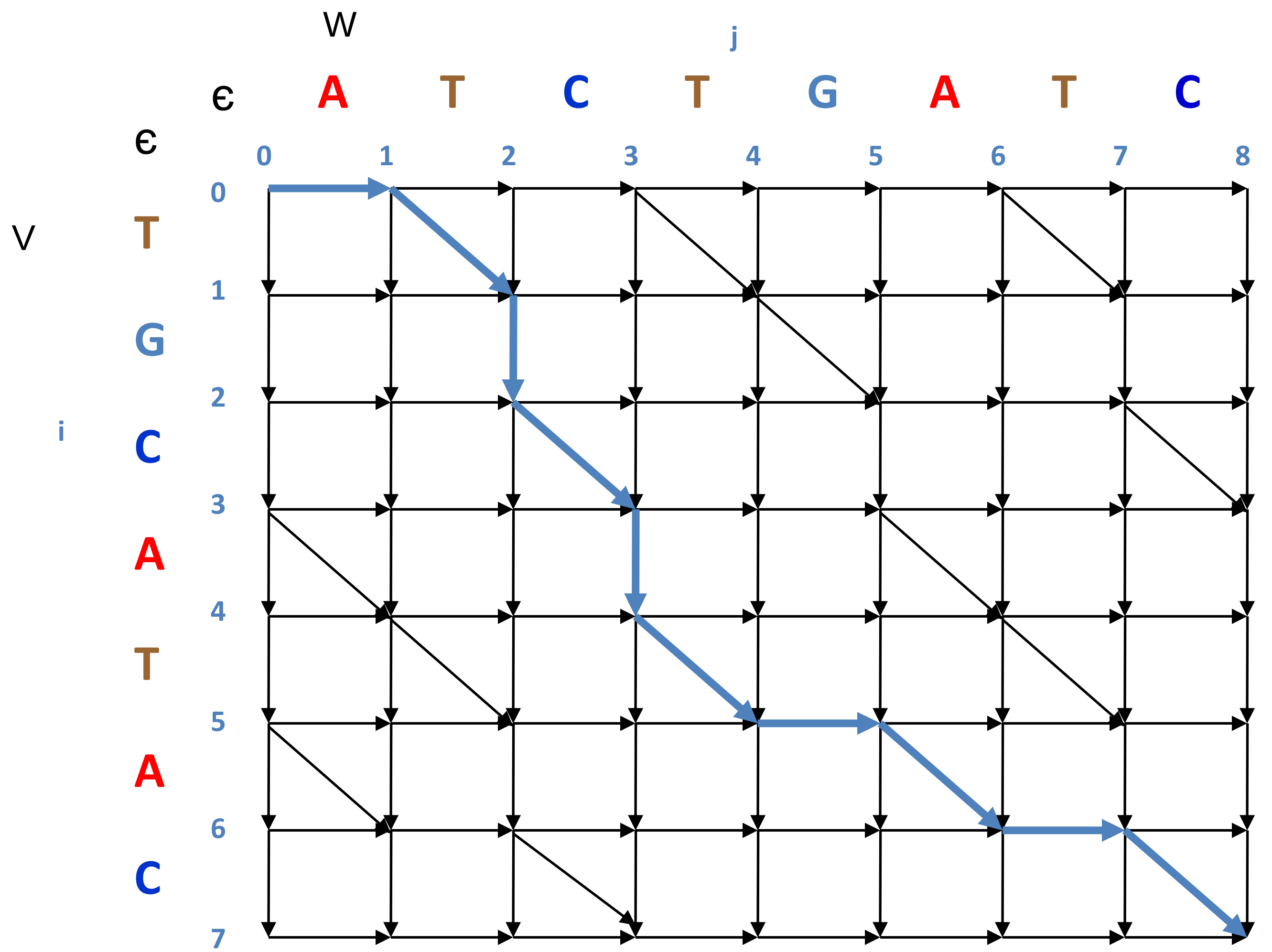
Matches shown in red

positions in *v*: $2 < 3 < 4 < 6 < 8$

positions in *w*: $1 < 3 < 5 < 6 < 7$

Every common subsequence is a path in 2-D grid

Edit Graph for LCS Problem



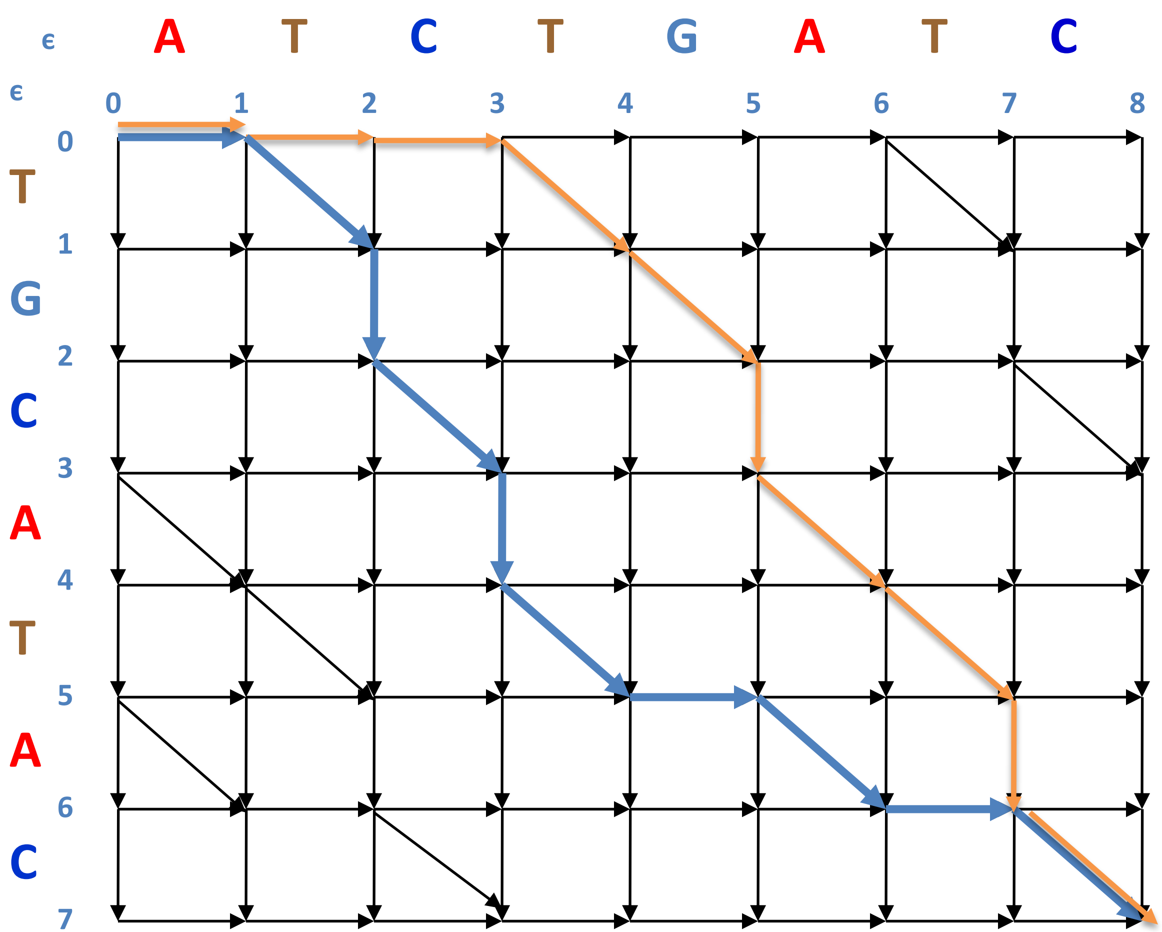
Every path is a common subsequence.

Every diagonal edge adds an extra element to common subsequence

***LCS Problem:** Find a path with maximum number of diagonal edges*

Imagine vertical lines for characters of sequence w and horizontal lines for those of v. This also illustrates an alternate way to represent the “edit graph”.. It is embedded.

Relationship Between Edit Distance and LCS Problem



T G C A T A C
A T C T G A T C

- T G C A T - A – C
A T - C - T G A T C

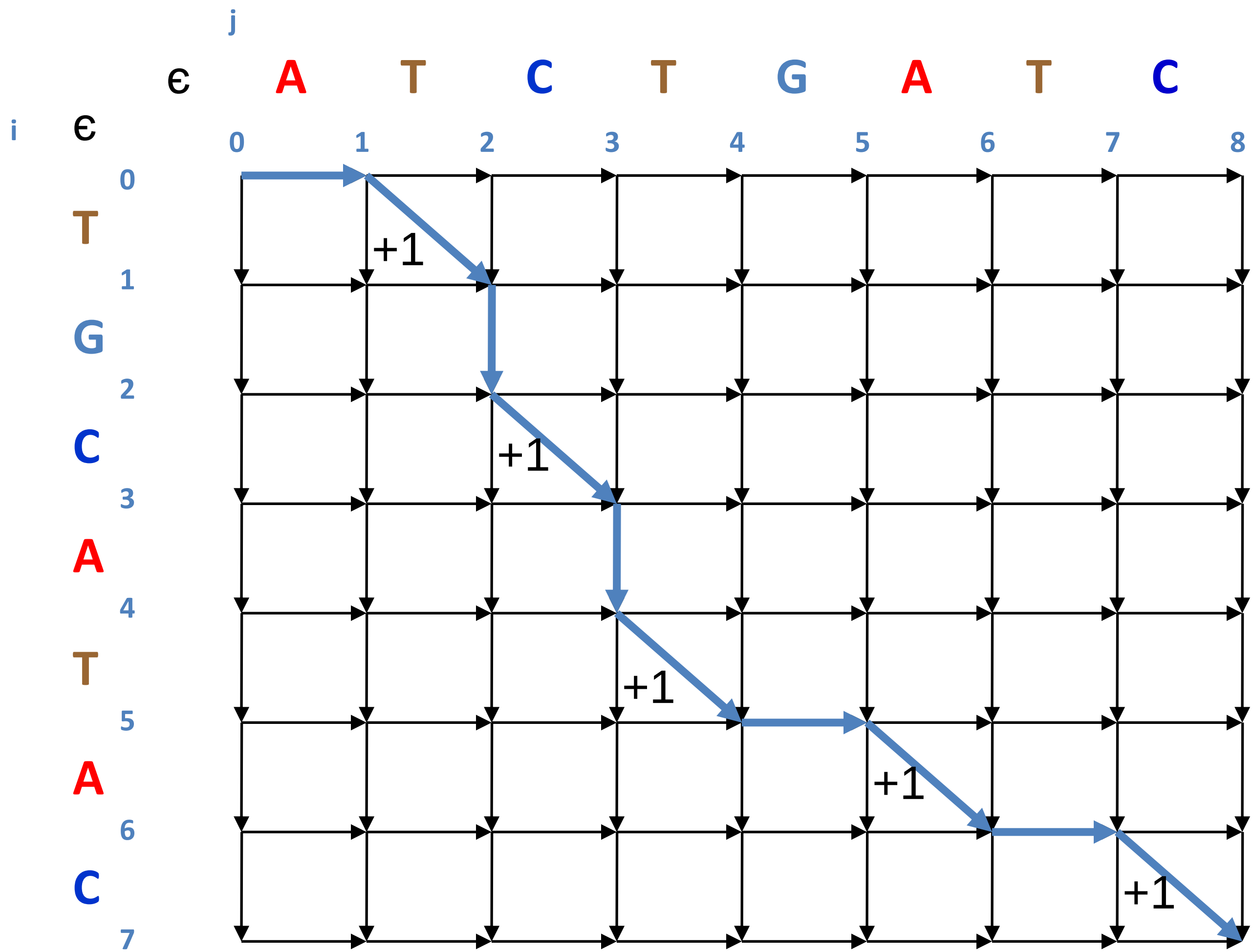
T G C A T A C
A T C T G A T C

- - - T G C A T A C
A T C T G - A T - C

$D=n+m-2L$

$D=7+8-2*5=5$

LCS Edit Graph



Computing LCS

Let $\boldsymbol{v}_i$ = prefix of $\boldsymbol{v}$ of length i: $v_1 \ldots v_i$

and $\boldsymbol{w}_j$ = prefix of $\boldsymbol{w}$ of length j: $w_1 \ldots w_j$

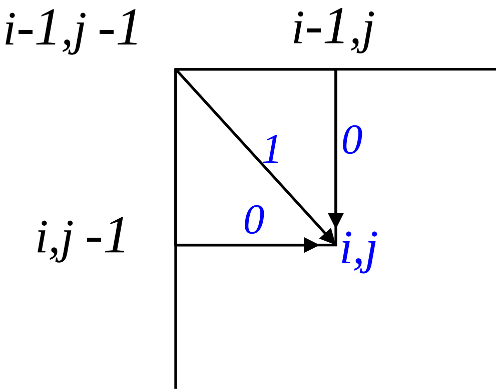
The length of LCS($\boldsymbol{v}_i$,$\boldsymbol{w}_j$) is computed by:

$$s_{i,j} = \max \begin{cases} s_{i-1,j} \\ s_{i,j-1} \\ s_{i-1,j-1} + 1 \text{ if } v_i = w_j \end{cases}$$

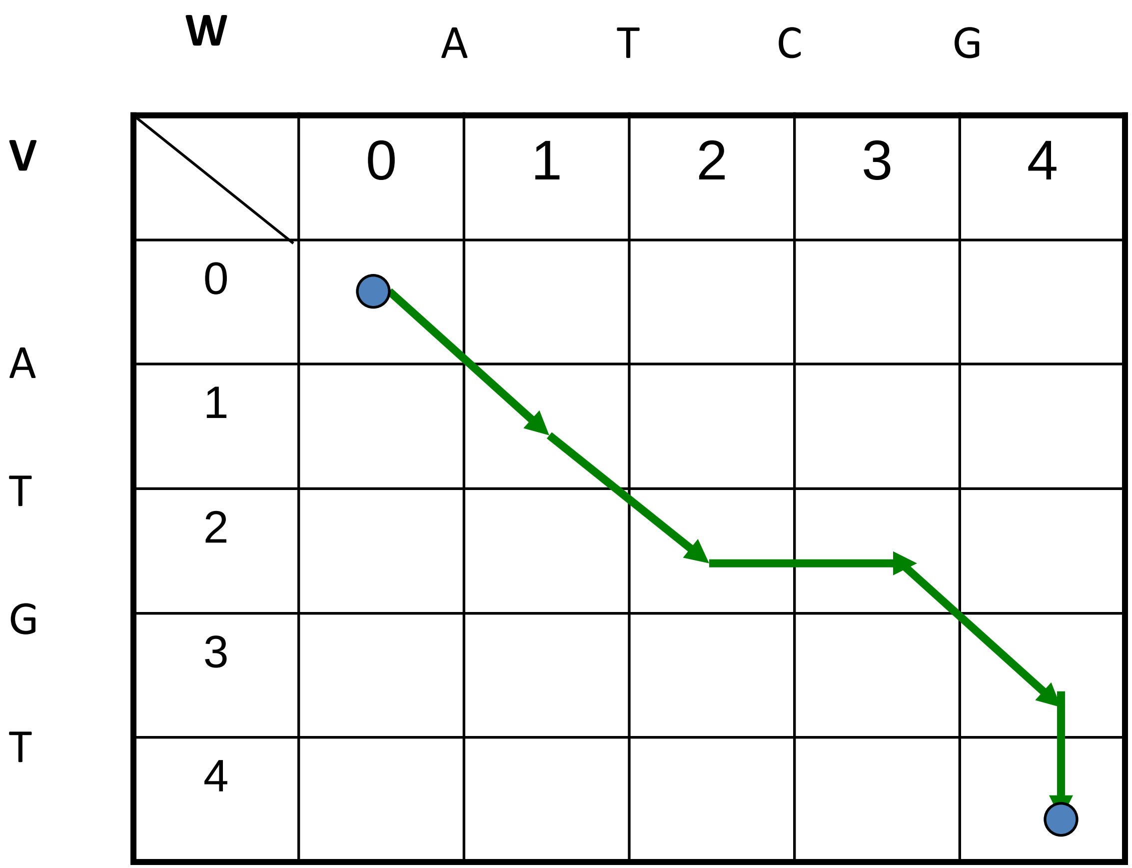
(It is the same definition that we presented earlier but shows that LCS has its own dynamic programming formulation independent of sequence alignment problem)

Computing LCS (cont'd)

$$s_{i,j} = \text{MAX} \begin{cases} s_{i-1,j} + 0 \\ s_{i,j-1} + 0 \\ s_{i-1,j-1} + 1, \quad \text{if } v_i = w_j \end{cases}$$



Every Path in the Grid Corresponds to an Alignment: Another Example




```
0 1 2  2 3 4

V =  A T -  G T
     |  |      |
W=   A T C G –

 0 1 2  3 4 4
```

LCS Runtime

- It takes O(*nm*) time to fill in the *nxm* dynamic programming matrix.

- Why O(*nm*)? The pseudocode consists of a nested “for” loop inside of another “for” loop to set up a *nxm* matrix.

Similarity Definition Generalized

- We enlarge the alphabet ∑ to ∑' including the space symbol '-'. Then for any two characters *x* and *y* in ∑', we define a *score* or *value* obtained by aligning *x* against *y*. For a given alignment of *S1* and *S2,* let S'_1 and S'_2 denote the strings after the chosen insertion of spaces. And let *k* denote the equal length of these two strings. Then value *V* of alignment between S'_1 and S'_2 is defined as

$$\sum_{i=1}^{k} \delta(S_1^{'}(i), S_2^{'}(i))$$

where δ is the **value or score** associated with the pair of symbols S'_1 (i) and S'_2(i).

Maximization Problem

- In string similarity problems, the value of δ is usually set greater than zero for matched symbols and less than zero for symbol pairs that do not match or when a symbol is aligned with a '-' character.
- This reduces the problem to the problem of maximization of V for all possible alignments.

Dynamic Programming Solution

- Let $V(i, j)$ be the optimal alignment of prefixes $S_1[1...i]$ and $S_2[1...j]$.
- Basis:

$$V(0, j) = \sum_{k=1}^{j} \delta(-, S_2(k))$$

$$V(i,0) = \sum_{k=1}^{i} \delta(S_1(k),-)$$

$$V(0,0) = 0$$

Dynamic Programming Solution

- recurrence relation is:

$$V(i,j) = \max[V(i-1,j-1) + \delta(S_1(i), S_2(j)), \quad \leftarrow \text{replacement}$$

$$V(i-1,j) + \delta(S_1(i), -), \quad \leftarrow \text{deletion}$$

$$V(i,j-1) + \delta(-, S_2(j))] \quad \leftarrow \text{insertion}$$

The value of the optimal alignment is given by $V(n,m)$

Like for the computation of the edit distance, we can use a bottom-up method to compute the alignment matrix. The complexity is *O(nm)* since at each point we perform 3 comparisons, 3 look-up operations and 3 additional operations.

Dynamic Programming Solution

When mismatches are penalized by a constant -μ, indels are penalized by some other constant -σ and matches are rewarded with +1, the recurrence relation is

$$V(i,j) = \max[V(i-1,j-1) - \mu \text{ if } v_i \neq w_j, \quad \longleftarrow \quad \text{mismatch}$$
$$V(i-1,j-1) + 1 \text{ if } v_i = w_j \quad \longleftarrow \quad \text{match}$$
$$V(i-1,j) - \sigma, \quad \longleftarrow \quad \text{deletion}$$
$$V(i,j-1) - \sigma] \quad \longleftarrow \quad \text{insertion}$$

The value of the optimal alignment is given by *V*(*n,m*) which equals

#matches – μ.#mismatches – σ.#indels

Note, the LCS problem is the Global Alignment problem with μ=0 and σ=0

Like for the computation of the edit distance, we can use a bottom-up method to compute the alignment matrix. The complexity is *O(nm)* since at each point we perform 3 comparisons, 3 look-up operations and 3 additional operations.

Maximum similarity path

- By setting up suitable pointers, once the matrix is computed, we can obtain a trace for the optimal alignment by constructing any path from the cell (n,m) to the cell (0,0).

- Also, the problem can be formulated as finding a ***maximum weighted path*** in a ***weighted acyclic graph*** similar to one discussed earlier. (In general, computing a longest path in arbitrary graph is NP complete).

Computation time and Storage

- The weights of the edges must correspond to specific values of *s* for the pair of symbols. The algorithm takes $O(nm)$ space.
- This is quite expensive if the sequences are large.
- If one were interested only in the value of the alignment and not obtaining a trace, this could easily be done by keeping only the last two rows of the matrix to compute the next row.
- This will need only $O(n+m)$ space. Is it possible to reconstruct an alignment using only linear space?