CS481: Bioinformatics Algorithms

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The Change Problem

Goal: Convert some amount of money M into given denominations, using the fewest possible number of coins

Input: An amount of money M, and an array of d denominations $c = (c_1, c_2, \ldots, c_d)$, in a decreasing order of value ($c_1 > c_2 > \ldots > c_d$)

Output: A list of d integers $i_1, i_2, \ldots, i_d$ such that

$$c_1 i_1 + c_2 i_2 + \ldots + c_d i_d = M$$

and $i_1 + i_2 + \ldots + i_d$ is minimal

Change Problem: Example

Given the denominations 1, 3, and 5, what is the minimum number of coins needed to make change for a given value?

Value	1	2	3	4	5	6	7	8	9	10
Min # of coins	1		1		1					

Only one coin is needed to make change for the values 1, 3, and 5

Change Problem: Example (cont'd)

Given the denominations 1, 3, and 5, what is the minimum number of coins needed to make change for a given value?

Value	1	2	3	4	5	6	7	8	9	10
Min # of coins	1	2	1	2	1	2		2		2

However, two coins are needed to make change for the values 2, 4, 6, 8, and 10.

Change Problem: Example (cont'd)

Given the denominations 1, 3, and 5, what is the minimum number of coins needed to make change for a given value?

Value	1	2	3	4	5	6	7	8	9	10
Min # of coins	1	2	1	2	1	2	3	2	3	2

Lastly, three coins are needed to make change for the values 7 and 9

Change Problem: Recurrence

This example is expressed by the following recurrence relation:

$$\textbf{minNumCoins(M)} = \textbf{min of} \begin{cases} \textbf{minNumCoins(M-1) + 1} \\ \textbf{minNumCoins(M-3) + 1} \\ \textbf{minNumCoins(M-5) + 1} \end{cases}$$

Change Problem: Recurrence (cont'd)

Given the denominations c: c_1, c_2, …, c_d, the recurrence relation is:

$$\textbf{minNumCoins}(M) = \min \text{ of } \begin{cases} \textbf{minNumCoins}(M-c_1) + 1 \\ \textbf{minNumCoins}(M-c_2) + 1 \\ \quad\quad\quad\quad \ldots \\ \textbf{minNumCoins}(M-c_d) + 1 \end{cases}$$

Change Problem: A Recursive Algorithm

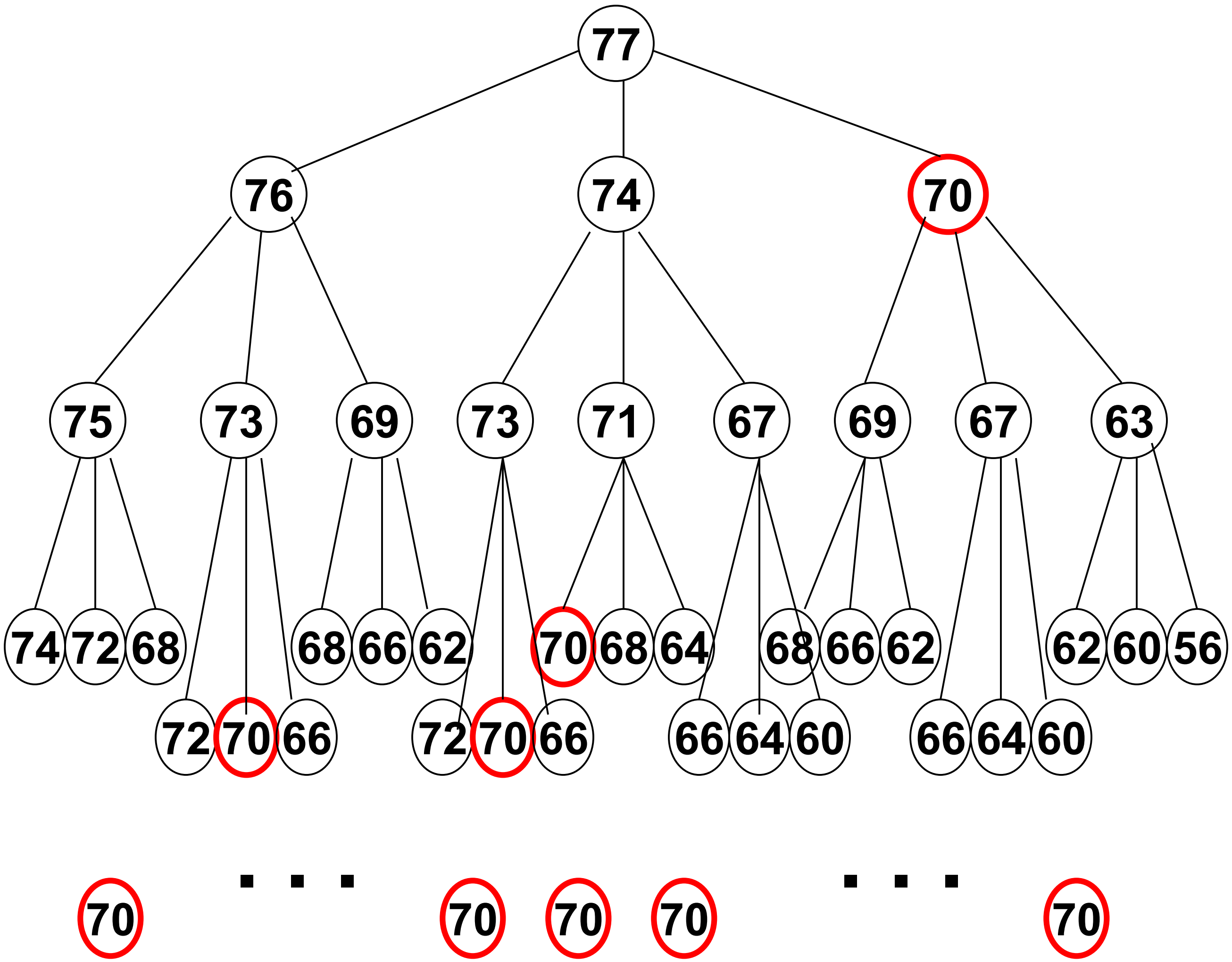
```
RecursiveChange(M,c,d)
   if M = 0
      return 0
   bestNumCoins ← infinity
   for i ← 1 to d
      if M ≥ c_i
         numCoins ← RecursiveChange(M – c_i , c, d)
         if numCoins + 1 < bestNumCoins
            bestNumCoins ← numCoins + 1
   return bestNumCoins
```

RecursiveChange Is Not Efficient

- It recalculates the optimal coin combination for a given amount of money repeatedly

- i.e., ***M*** = 77, ***c*** = (1,3,7):
  - Optimal coin combo for 70 cents is computed **9** times!

The RecursiveChange Tree



We Can Do Better

- We're re-computing values in our algorithm more than once
- Save results of each computation for 0 to ***M***
- This way, we can do a reference call to find an already computed value, instead of re-computing each time
- Running time $M*d$, where ***M*** is the value of money and ***d*** is the number of denominations

The Change Problem: Dynamic Programming

<u>DPChange(M,c,d)</u>
  $\text{bestNumCoins}_0 \leftarrow 0$
  for $m \leftarrow 1$ to M
    $\text{bestNumCoins}_m \leftarrow$ infinity
    for $i \leftarrow 1$ to d
      if $m \geq c_i$
        if $\text{bestNumCoins}_{m - c_i} + 1 < \text{bestNumCoins}_m$
          $\text{bestNumCoins}_m \leftarrow \text{bestNumCoins}_{m - c_i} + 1$
  return bestNumCoins_M

DPChange: Example

0
0

0	1
0	1

0	1	2
0	1	2

0	1	2	3
0	1	2	1

0	1	2	3	4
0	1	2	1	2

0	1	2	3	4	5
0	1	2	1	2	3

0	1	2	3	4	5	6
0	1	2	1	2	3	2

0	1	2	3	4	5	6	7
0	1	2	1	2	3	2	1

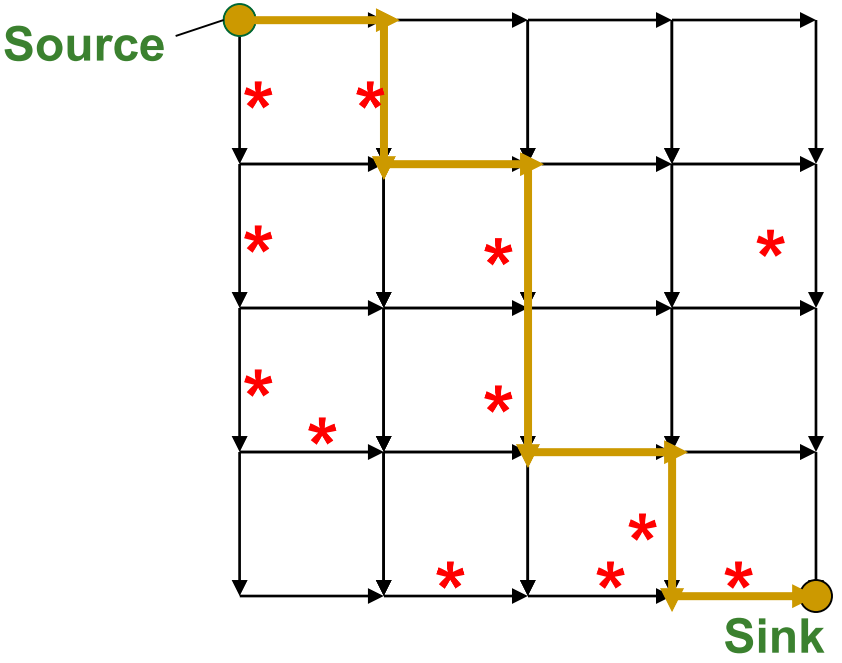
0	1	2	3	4	5	6	7	8
0	1	2	1	2	3	2	1	2

0	1	2	3	4	5	6	7	8	9
0	1	2	1	2	3	2	1	2	3

c = (1,3,7)
M = 9

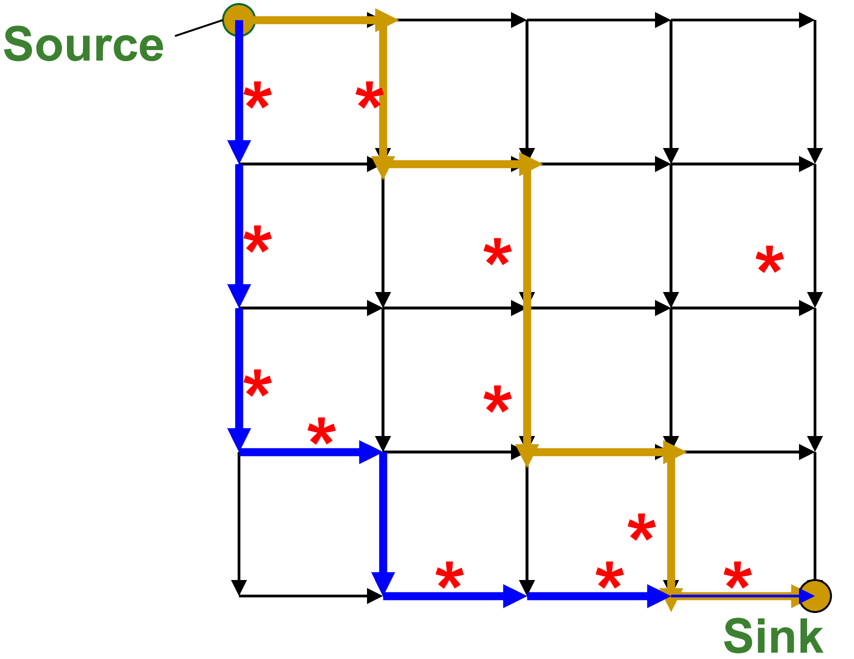
Manhattan Tourist Problem (MTP)

Imagine seeking a path (from source to sink) to travel (only eastward and southward) with the most number of attractions (*) in the Manhattan grid



Manhattan Tourist Problem (MTP)

Imagine seeking a path (from source to sink) to travel (only eastward and southward) with the most number of attractions (*) in the Manhattan grid



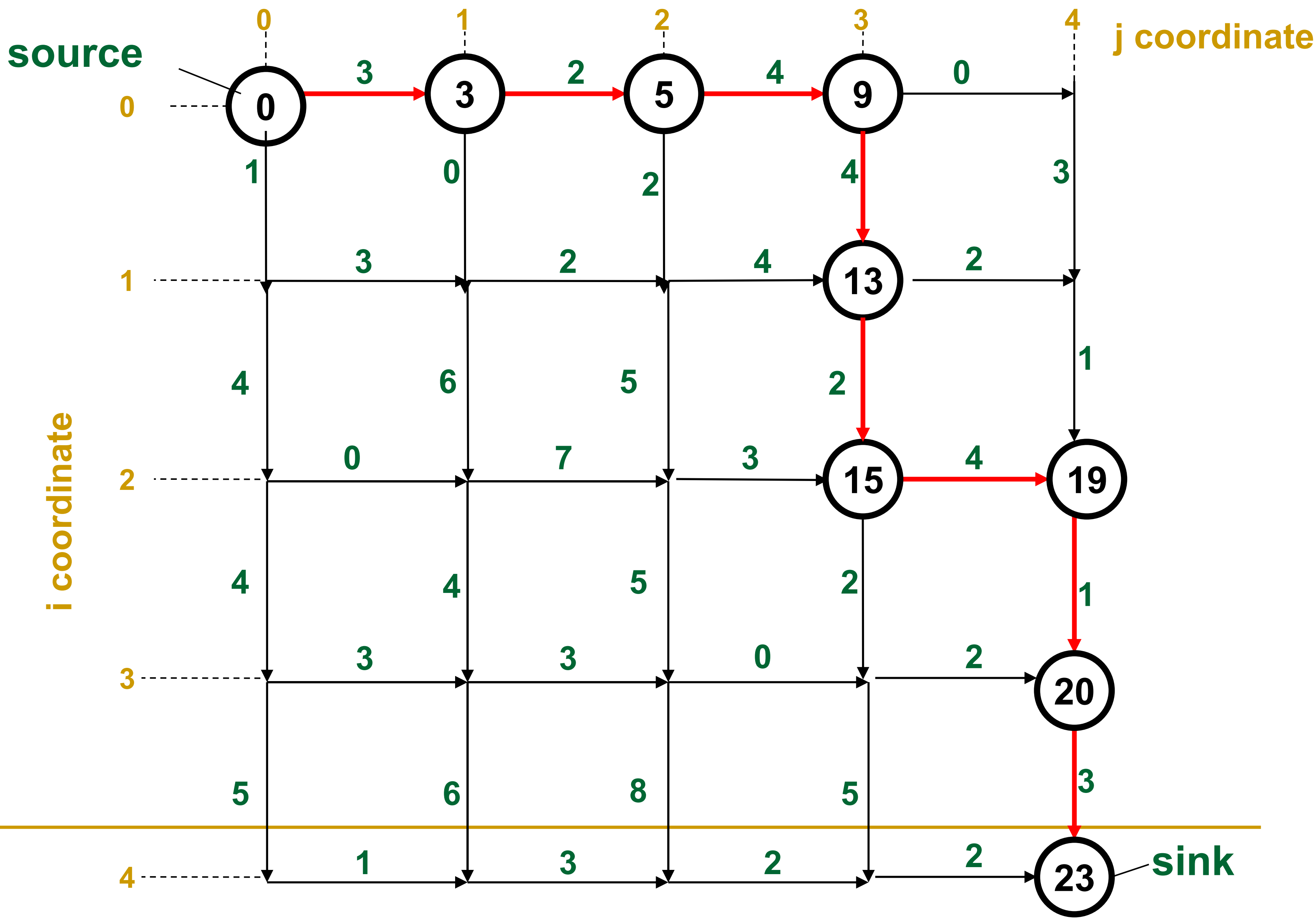
Manhattan Tourist Problem: Formulation

Goal: Find the longest path in a weighted grid.

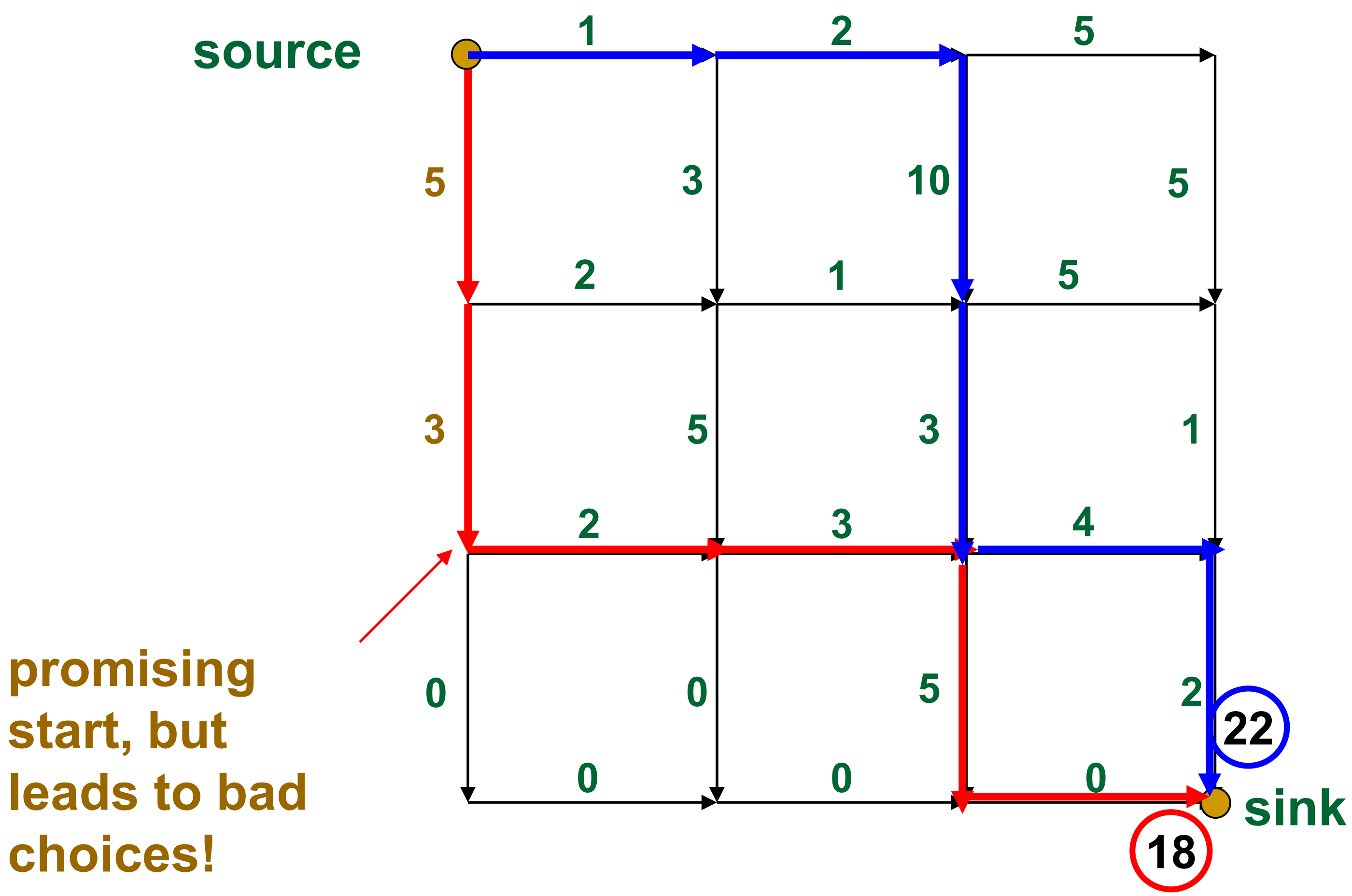
Input: A weighted grid G with two distinct vertices, one labeled "source" and the other labeled "sink"

Output: A longest path in G from "source" to "sink"

MTP: An Example



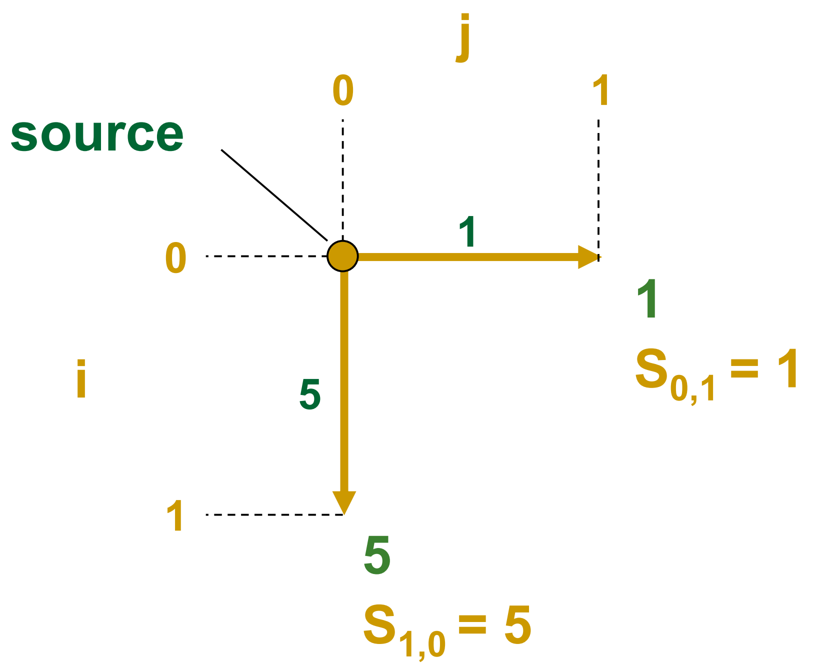
MTP: Greedy Algorithm Is Not Optimal



MTP: Simple Recursive Program

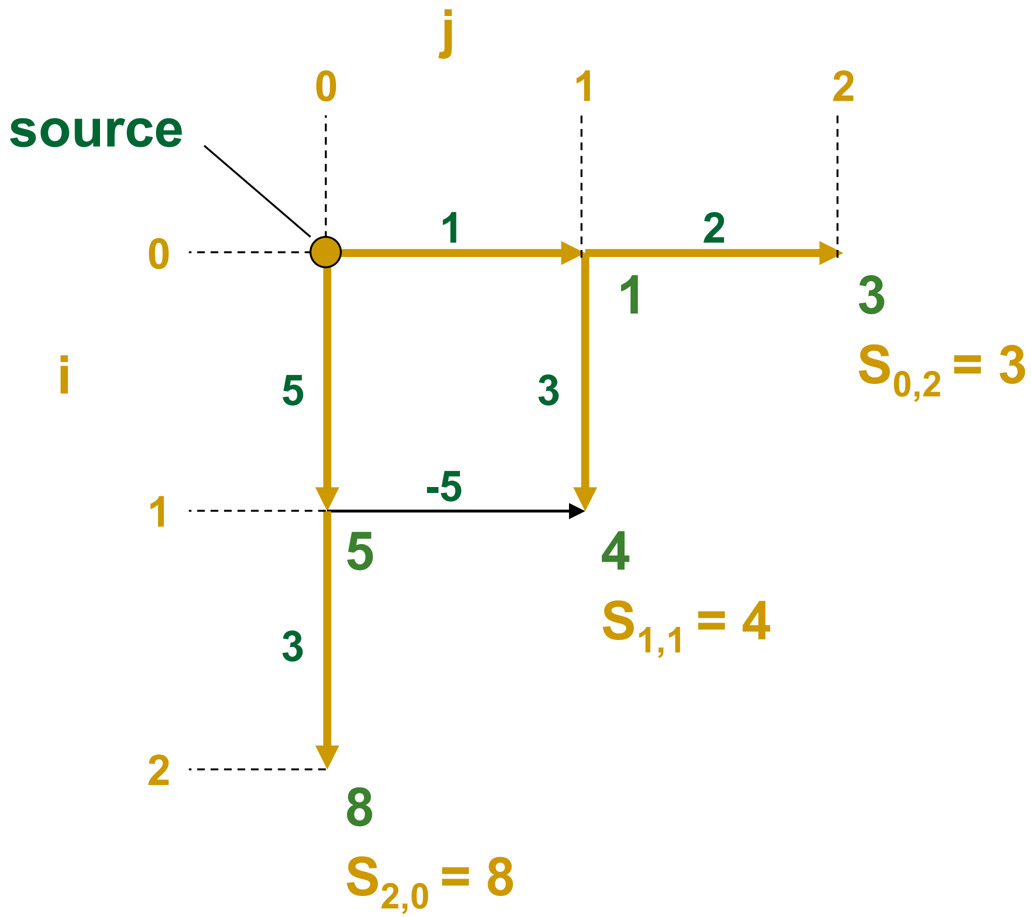
```
MT(n,m)
   if n=0  or m=0
      return MT(n,m)
   x ← MT(n-1,m)+
               length of the edge from (n- 1,m) to (n,m)
   y ← MT(n,m-1)+
               length of the edge from (n,m-1) to (n,m)
   return max{x,y}
```

MTP: Dynamic Programming

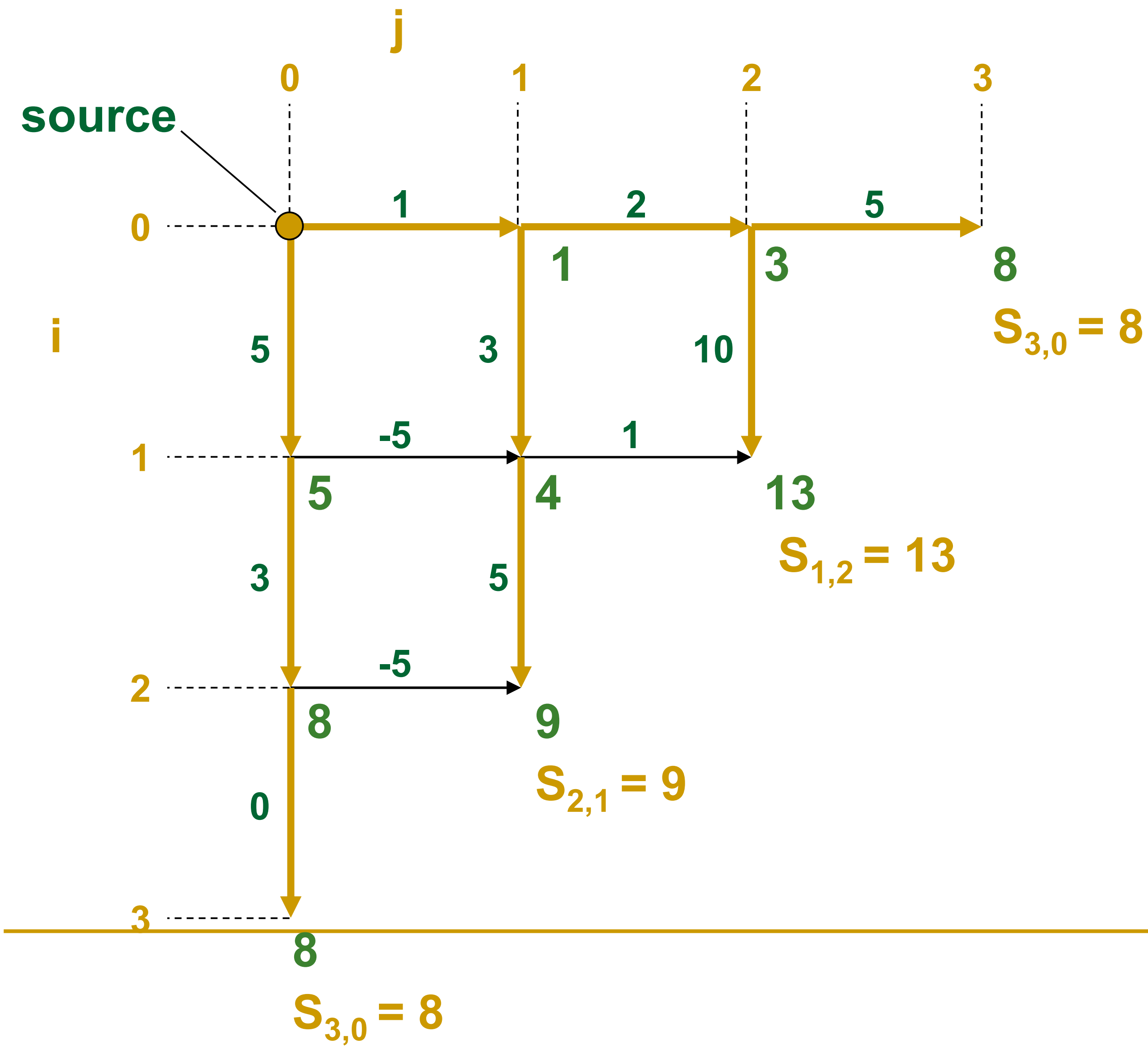


- Calculate optimal path score for each vertex in the graph
- Each vertex's score is the maximum of the prior vertices score plus the weight of the respective edge in between

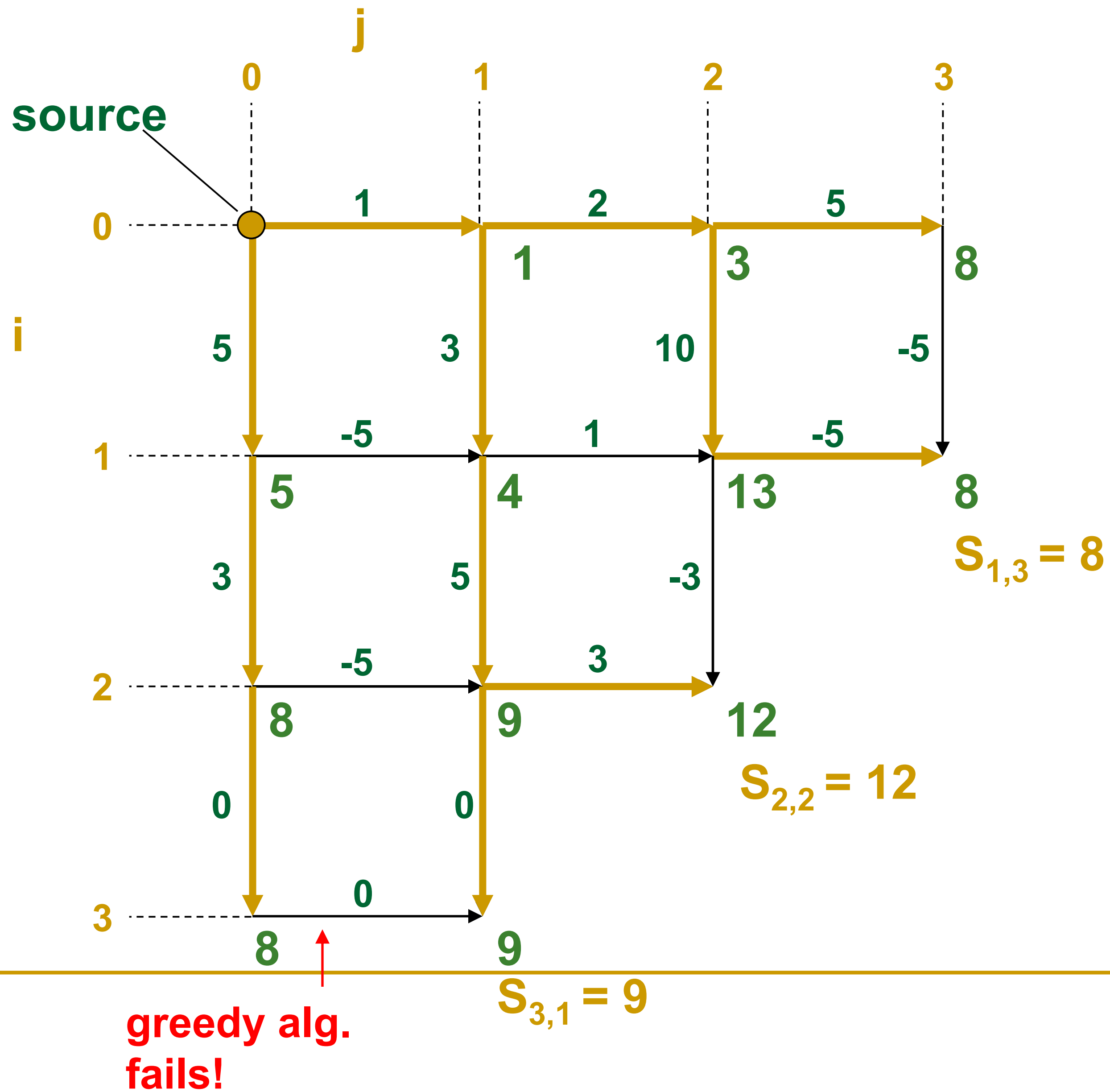
MTP: Dynamic Programming (cont'd)



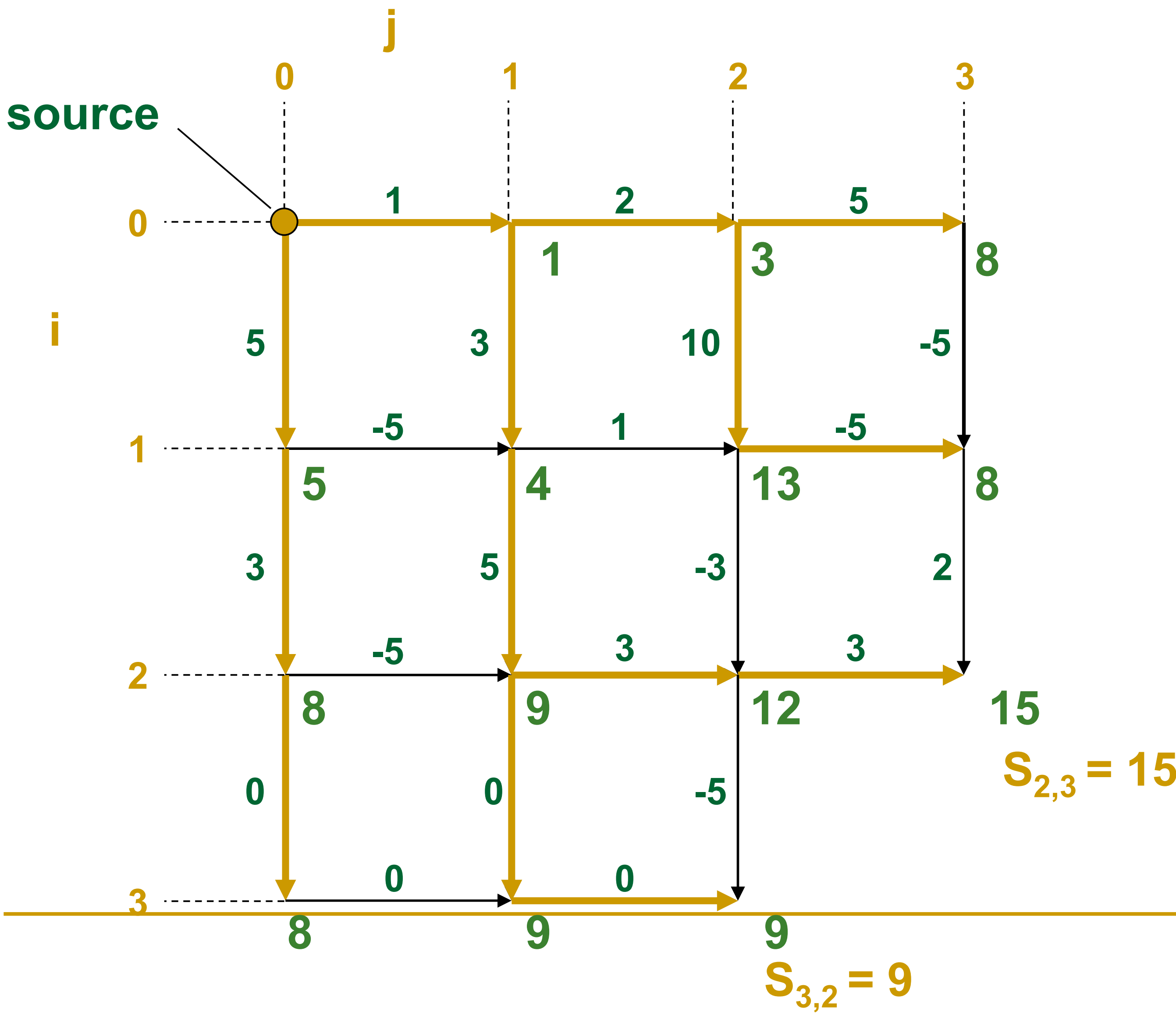
MTP: Dynamic Programming (cont'd)



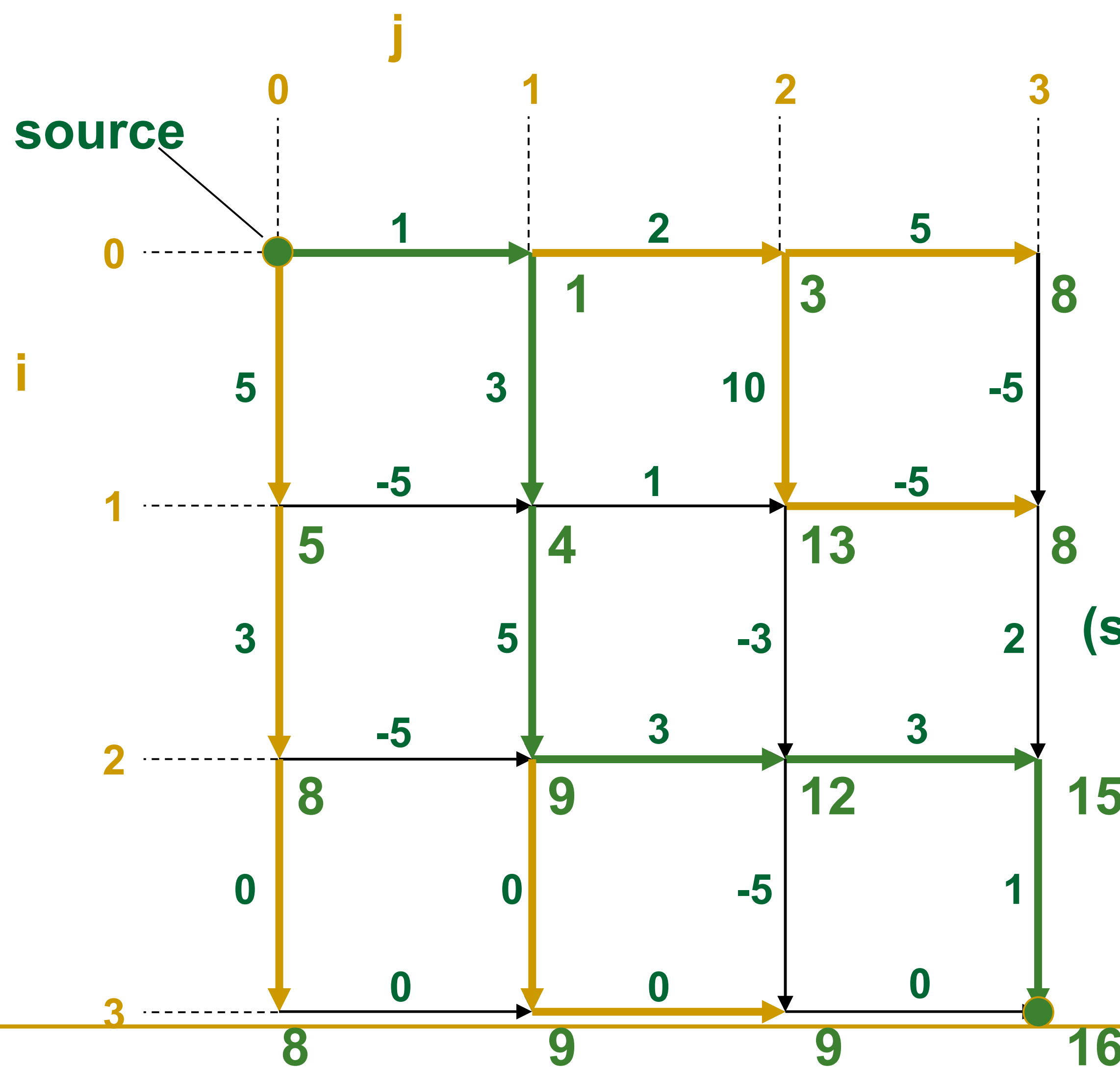
MTP: Dynamic Programming (cont'd)



MTP: Dynamic Programming (cont'd)



MTP: Dynamic Programming (cont'd)



Done!

(showing all back-traces)

$S_{3,3} = 16$

MTP: Recurrence

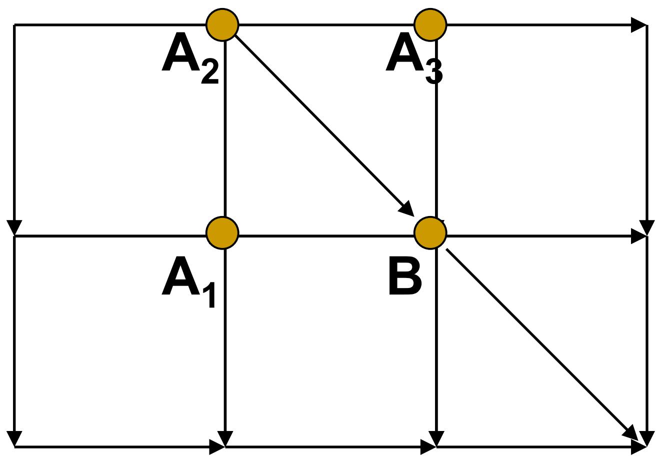
Computing the score for a point (i,j) by the recurrence relation:

$$s_{i,j} = \max \begin{cases} s_{i-1,j} + \text{weight of the edge between } (i-1, j) \text{ and } (i, j) \\ s_{i,j-1} + \text{weight of the edge between } (i, j-1) \text{ and } (i, j) \end{cases}$$

The running time is n x m for a n by m grid

(n = # of rows, m = # of columns)

Manhattan Is Not A Perfect Grid



What about diagonals?

- The score at point B is given by:

$$s_B = \max \text{ of } \begin{cases} s_{A1} + \text{weight of the edge } (A_1, B) \\ s_{A2} + \text{weight of the edge } (A_2, B) \\ s_{A3} + \text{weight of the edge } (A_3, B) \end{cases}$$

Manhattan Is Not A Perfect Grid (cont'd)

Computing the score for point x is given by the recurrence relation:

$$s_x = \max_{\text{of}} \begin{cases} s_y + \text{weight of vertex } (y, x) \text{ where} \\ y \in \text{Predecessors}(x) \end{cases}$$

- Predecessors (x) – set of vertices that have edges leading to x

- The running time for a graph G(V, E) (V is the set of all vertices and E is the set of all edges) is O(E) since each edge is evaluated once

Traveling in the Grid

- The only hitch is that one must decide on the order in which visit the vertices
- By the time the vertex x is analyzed, the values s_y for all its predecessors y should be computed – otherwise we are in trouble.
- We need to traverse the vertices in some order
- Since Manhattan is not a perfect regular grid, we represent it as a DAG

Longest Path in DAG Problem

- Goal: Find a longest path between two vertices in a weighted DAG
- Input: A weighted DAG G with source and sink vertices
- Output: A longest path in G from source to sink

Longest Path in DAG: Dynamic Programming

- Suppose vertex v has indegree 3 and predecessors $\{u_1, u_2, u_3\}$
- Longest path to v from source is:

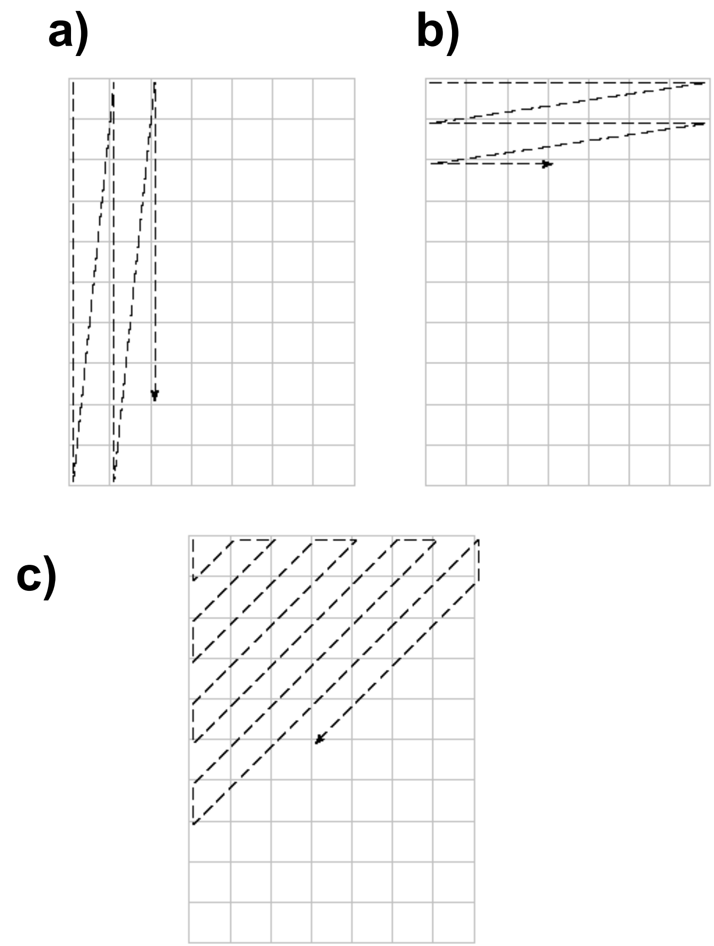
$$s_v = \max \text{ of } \begin{cases} s_{u_1} + \text{weight of edge from } u_1 \text{ to } v \\ s_{u_2} + \text{weight of edge from } u_2 \text{ to } v \\ s_{u_3} + \text{weight of edge from } u_3 \text{ to } v \end{cases}$$

<u>In General</u>:

$$s_v = \max_u \; (s_u + \text{weight of edge from } u \text{ to } v)$$

Traversing the Manhattan Grid

- **3 different strategies:**
  - **a) Column by column**
  - **b) Row by row**
  - **c) Along diagonals**



ALIGNMENT

Alignment: 2 row representation

Given 2 DNA sequences v and w:

v : ATCTGAT m = 7
w : TGCATA n = 6

Alignment : 2 * k matrix (k > m, n)

letters of v	A	T	--	G	T	T	A	T	--
letters of w	A	T	C	G	T	--	A	--	C

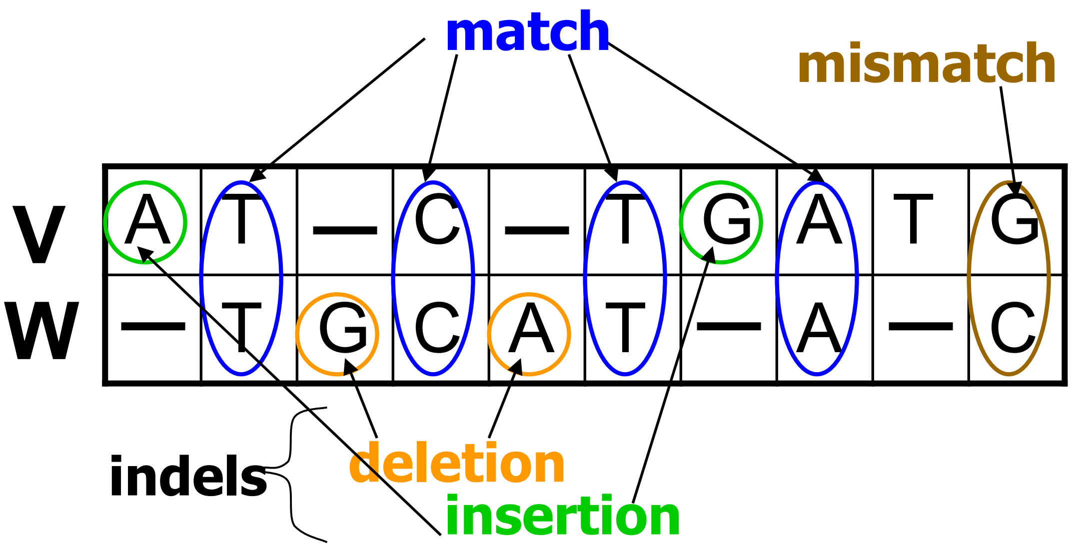
5 matches	2 insertions	2 deletions

Aligning DNA Sequences

V = ATCTGATG **n = 8**

W = TGCATAC **m = 7**

4 matches
1 mismatch
2 insertions
3 deletions



Longest Common Subsequence (LCS) – Alignment without Mismatches

- Given two sequences

$$v = v_1\ v_2 \ldots v_m \text{ and } w = w_1\ w_2 \ldots w_n$$

- The LCS of v and w is a sequence of positions in

$$v\text{: } 1 \le i_1 < i_2 < \ldots < i_t \le m$$

and a sequence of positions in

$$w\text{: } 1 \le j_1 < j_2 < \ldots < j_t \le n$$

such that i_t -th letter of v equals to j_t-letter of w and t is maximal

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

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

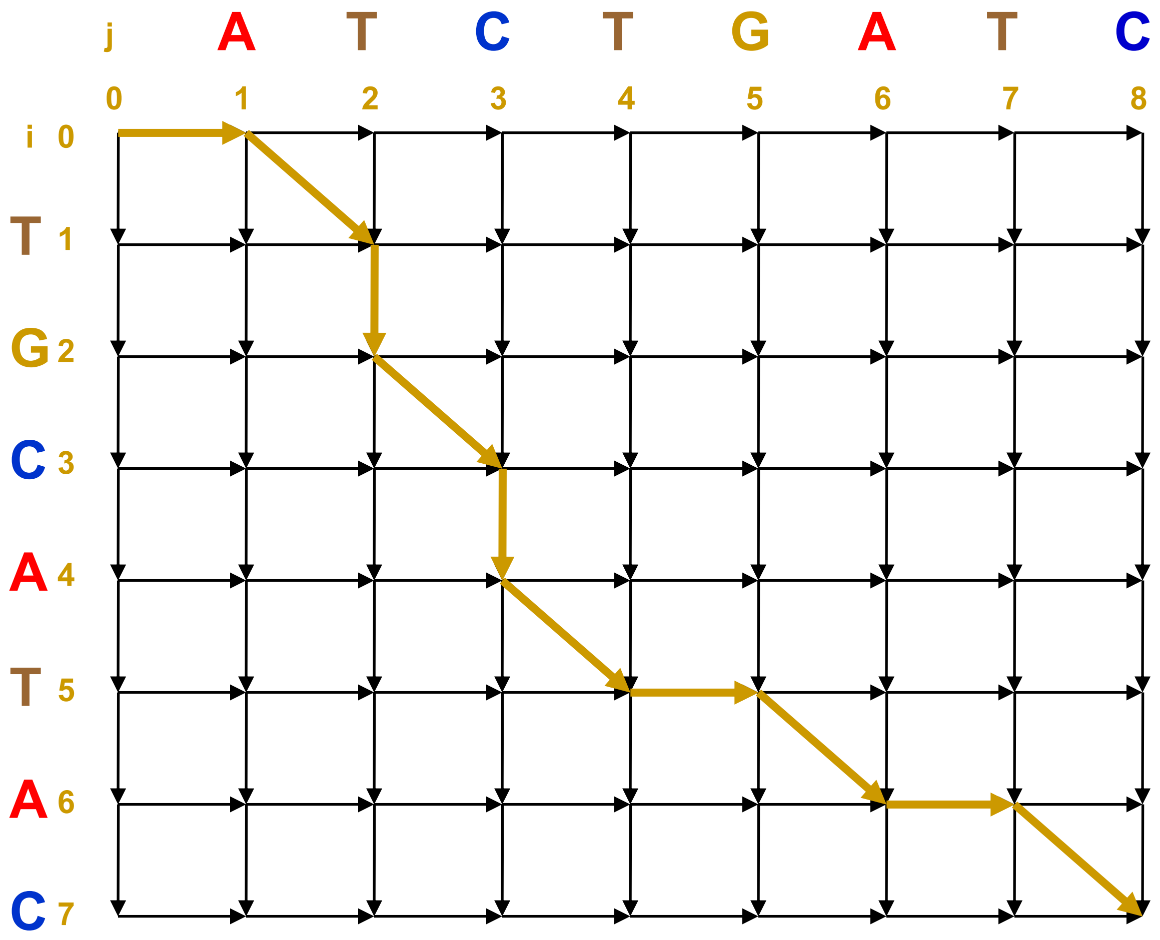
Matches shown in red

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

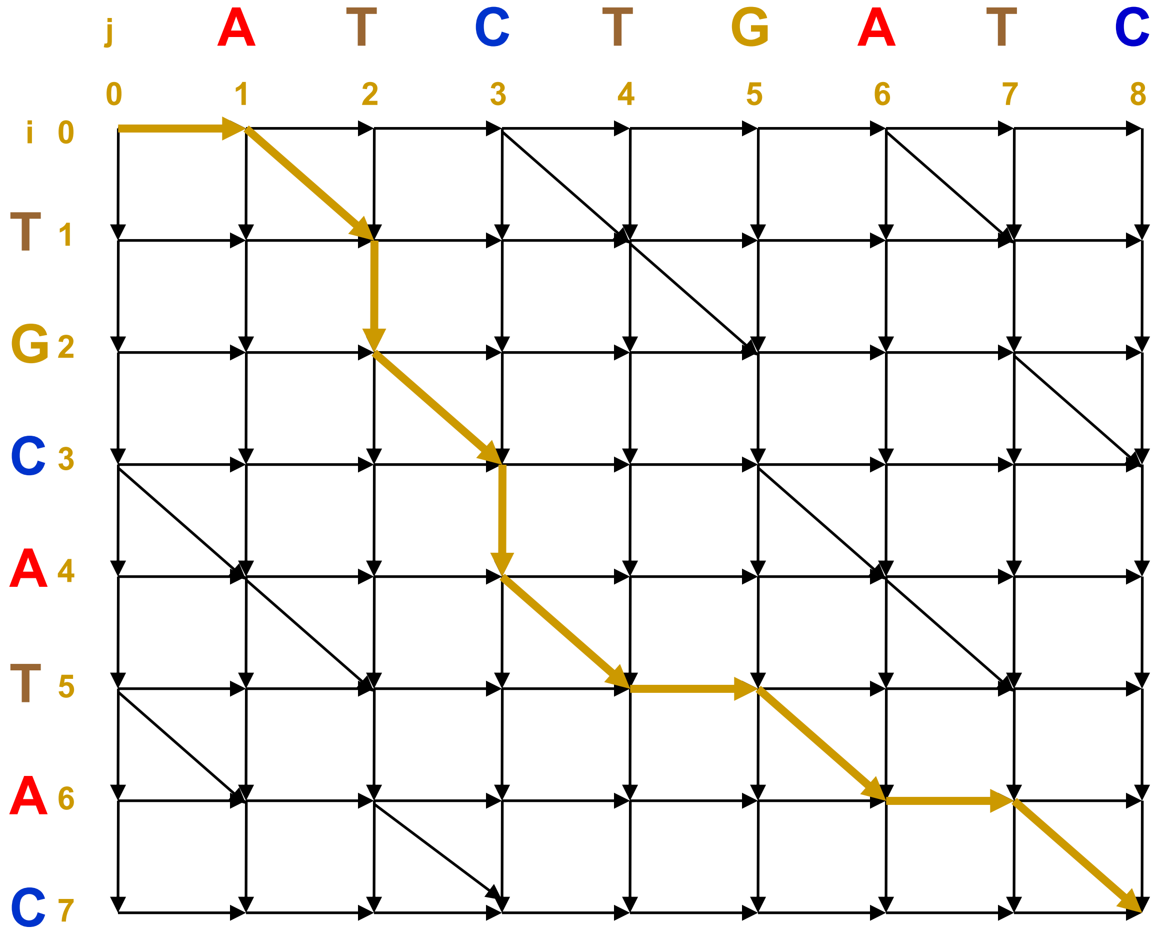
positions in w: $1 < 3 < 5 < 6 < 7$

Every common subsequence is a path in 2-D grid

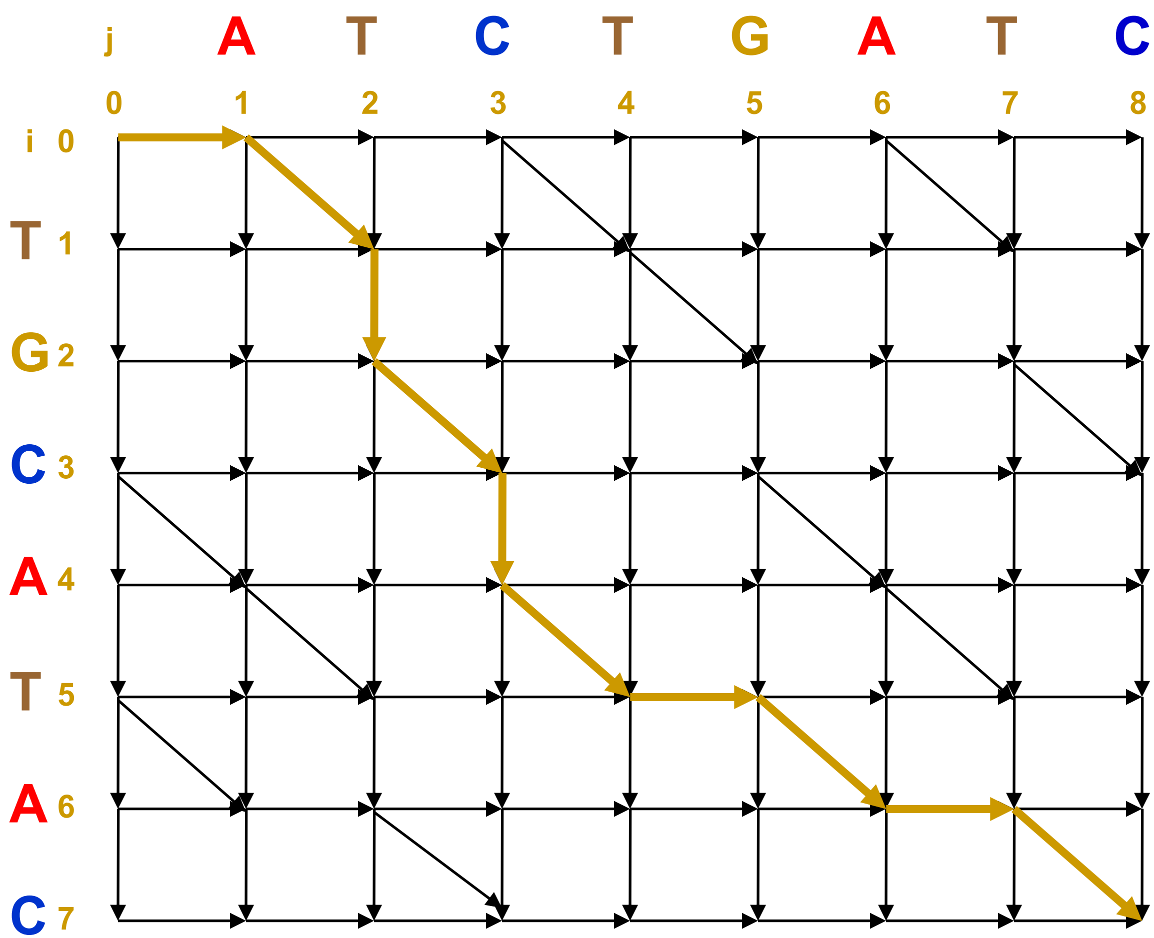
LCS Problem as Manhattan Tourist Problem



Edit Graph for LCS Problem



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

Computing LCS

Let v_i = prefix of v of length i: $v_1 \ldots v_i$

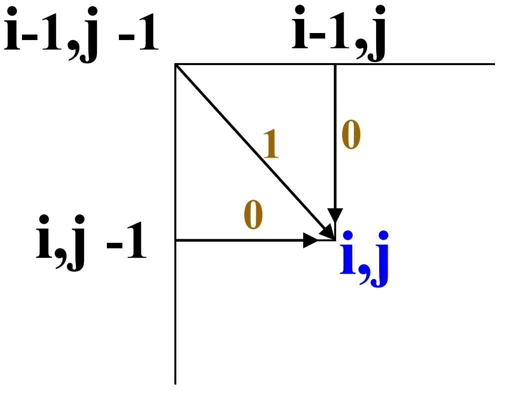
and w_j = prefix of w of length j: $w_1 \ldots w_j$

The length of LCS(v_i,w_j) is computed by:

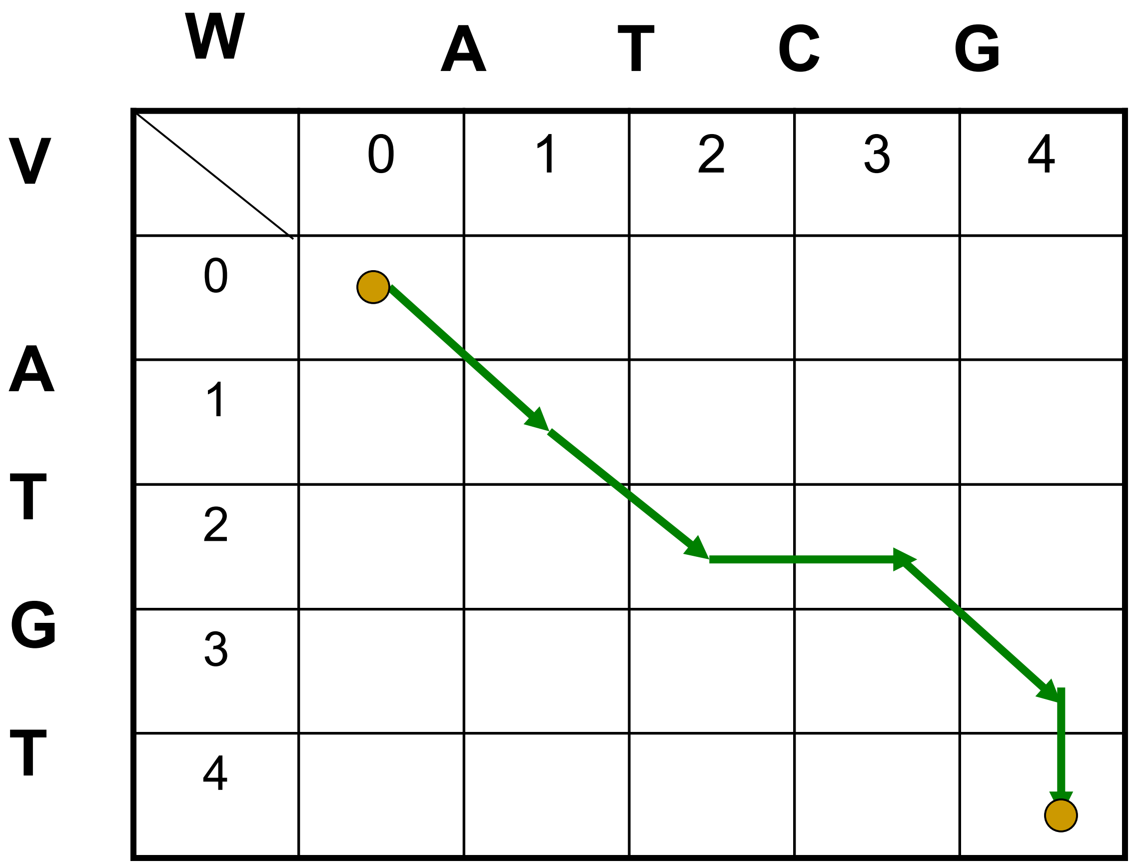
$$s_{i,j} = \max \begin{cases} s_{i-1,\,j} \\ s_{i,\,j-1} \\ s_{i-1,\,j-1} + 1 \quad \text{if } v_i = w_j \end{cases}$$

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




```
      0 1 2 2 3 4
V =   A T - G T
      | |   |
W=    A T C G –
      0 1 2 3 4 4
```

DISTANCE BETWEEN STRINGS

Aligning Sequences without Insertions and Deletions: Hamming Distance

Given two DNA sequences v and w :

v : A T A T A T A T
w : T A T A T A T A

- **The Hamming distance: $d_H(v, w) = 8$ is large but the sequences are very similar**

Aligning Sequences with Insertions and Deletions

By shifting one sequence over one position:

```
v : ATATATAT--
w : --TATATATA
```

- **The edit distance: $d_H(v, w) = 2$.**
- **Hamming distance neglects insertions and deletions in DNA**

Edit Distance

Levenshtein (1966) introduced edit distance between two strings as the minimum number of elementary operations (insertions, deletions, and substitutions) to transform one string into the other

d(v,w) = MIN number of elementary operations
to transform v $\rightarrow$ w

Edit Distance vs Hamming Distance

Hamming distance always compares i-th letter of v with i-th letter of w

V = ATATATAT

| | | | | | | | |

W = TATATATA

Hamming distance:

d(v, w)=8

Computing Hamming distance is a trivial task.

Edit Distance vs Hamming Distance

Hamming distance always compares i-th letter of v with i-th letter of w

V = ATATATAT

W = TATATATA

Just one shift

Make it all line up

Edit distance may compare i-th letter of v with j-th letter of w

V = - ATATATAT

W = TATATATA

Hamming distance:

d(v, w)=8

Computing Hamming distance is a trivial task

Edit distance:

d(v, w)=2

Computing edit distance is a non-trivial task

Edit Distance vs Hamming Distance

Hamming distance always compares i-th letter of v with i-th letter of w

```
V  = ATATATAT
      | | | | | | | |
W  = TATATATA
```

Hamming distance:

d(v, w)=8

Edit distance may compare i-th letter of v with j-th letter of w

```
V  = - ATATATAT
       | | | | | | |
W  = TATATATA
```

Edit distance:

d(v, w)=2

(one insertion and one deletion)

How to find what j goes with what i ???

Edit Distance: Example

TGCATAT → ATCCGAT in 5 steps

TGCATAT	→	(delete last T)
TGCATA	→	(delete last A)
TGCAT	→	(insert A at front)
ATGCAT	→	(substitute C for 3rd G)
ATCCAT	→	(insert G before last A)
ATCCGAT		(Done)

Edit Distance: Example

TGCATAT → ATCCGAT in 5 steps

TGCATAT → (delete last T)
TGCATA → (delete last A)
TGCAT → (insert A at front)
ATGCAT → (substitute C for 3rd G)
ATCCAT → (insert G before last A)
ATCCGAT (Done)

What is the edit distance? 5?

Edit Distance: Example (cont'd)

TGCATAT → ATCCGAT in 4 steps

TGCATAT → (insert A at front)

ATGCATAT → (delete 6th T)

ATGCATA → (substitute G for 5th A)

ATGCGTA → (substitute C for 3rd G)

ATCCGAT (Done)

Edit Distance: Example (cont'd)

TGCATAT → ATCCGAT in 4 steps

TGCATAT → (insert A at front)

ATGCATAT → (delete 6th T)

ATGCATA → (substitute G for 5th A)

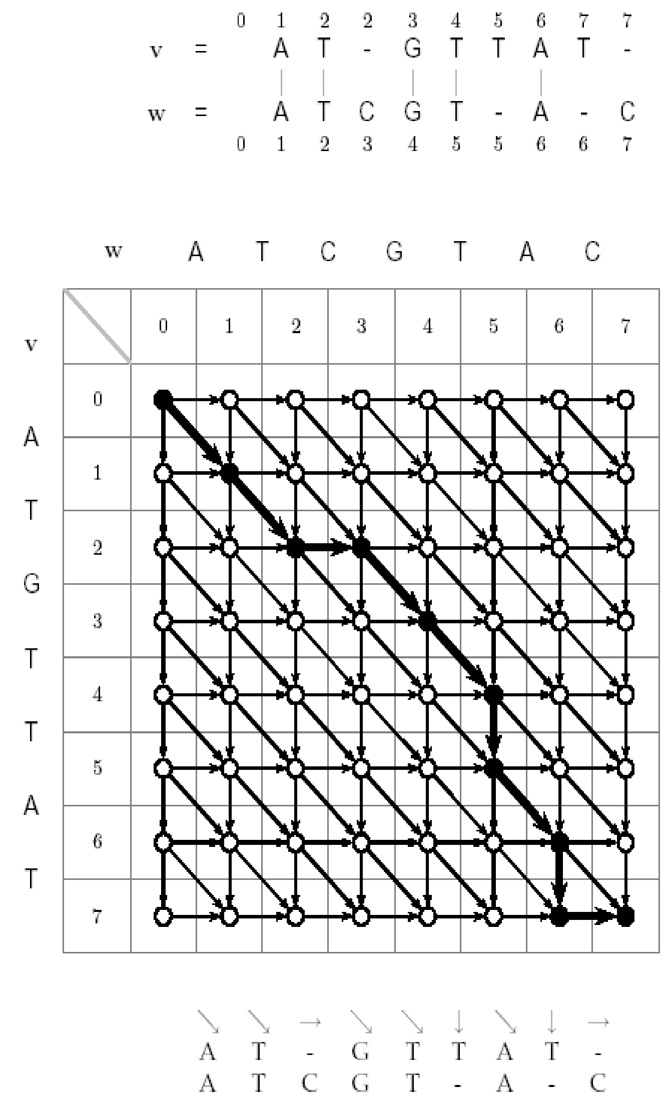
ATGCGTA → (substitute C for 3rd G)

ATCCGAT (Done)

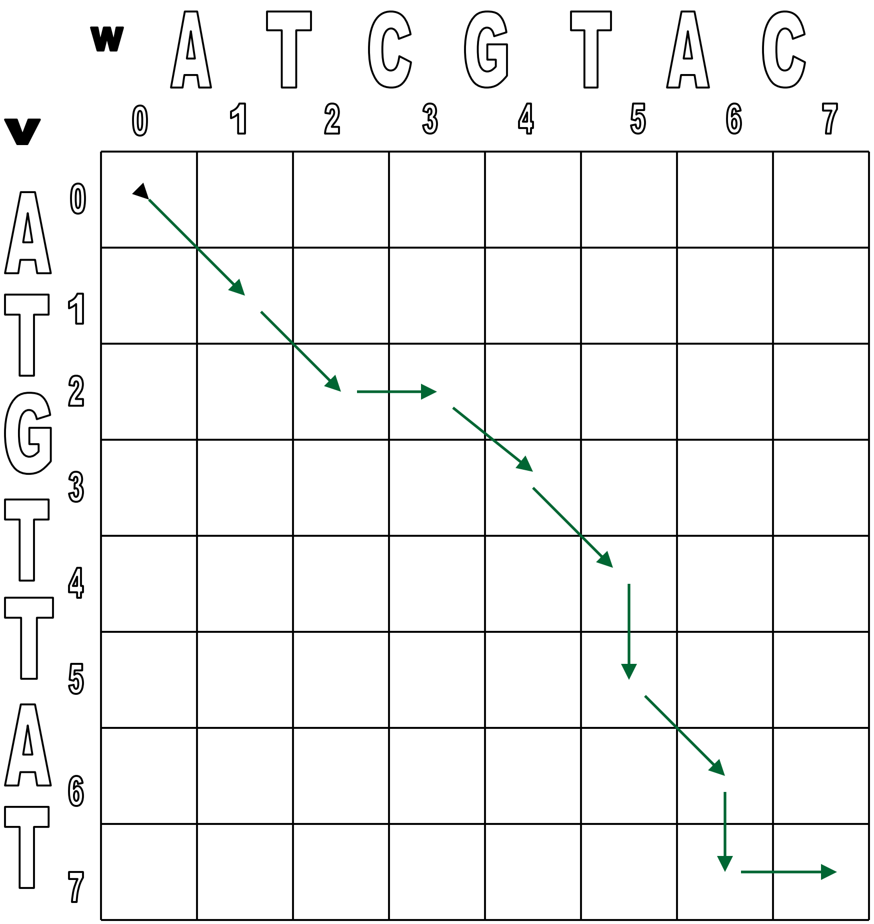
Can it be done in 3 steps???

The Alignment Grid

- Every alignment path is from source to sink



Alignment as a Path in the Edit Graph



0 1 2 2 3 4 5 6 7 7

A T _ G T T A T _

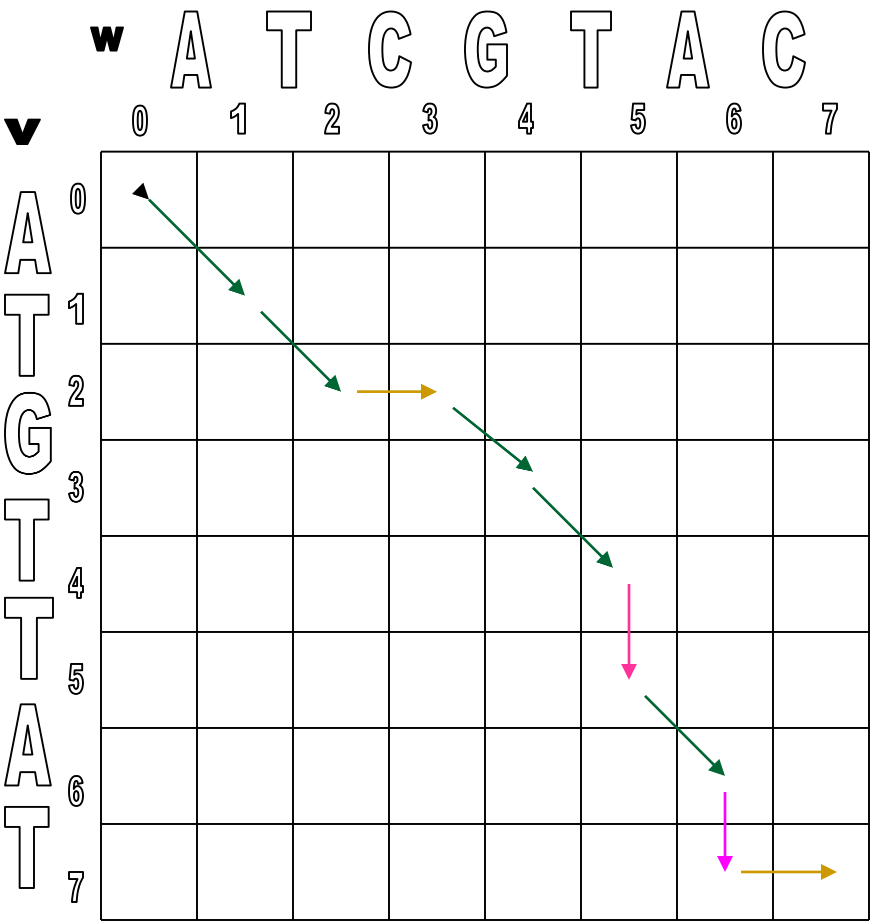
A T C G T _ A _ C

0 1 2 3 4 5 5 6 6 7

- Corresponding path -

(0,0) , (1,1) , (2,2), (2,3), (3,4), (4,5), (5,5), (6,6), (7,6), (7,7)

Alignments in Edit Graph (cont'd)

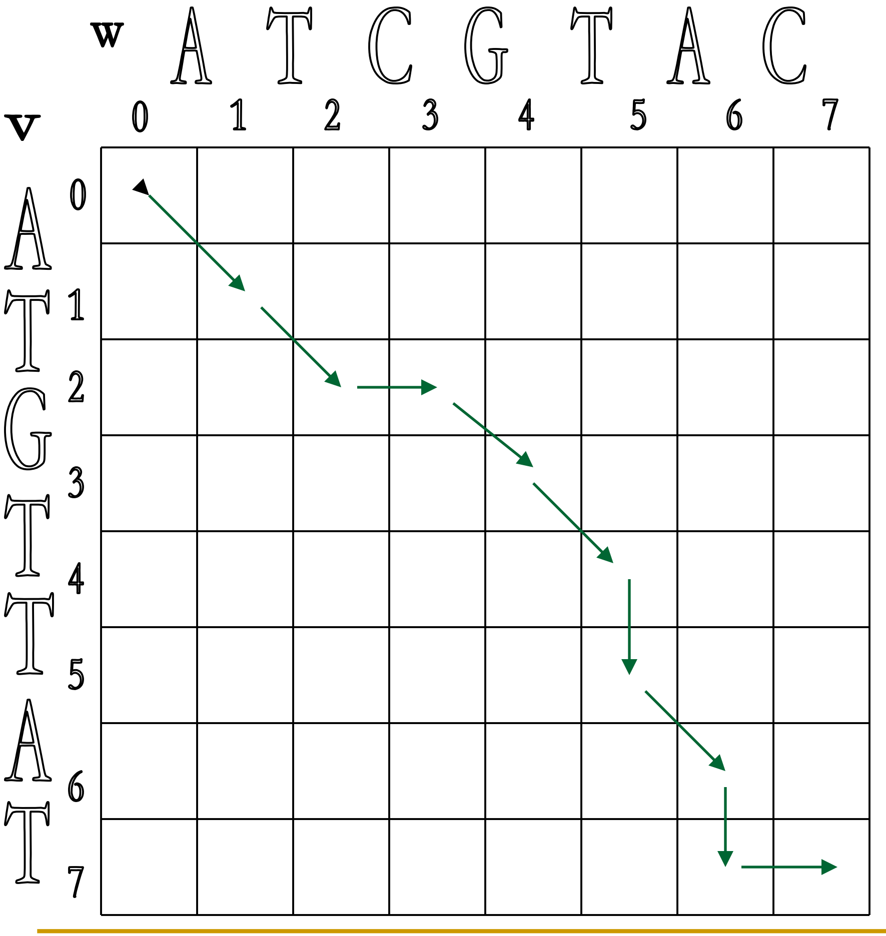


and represent indels in v and w with score 0.

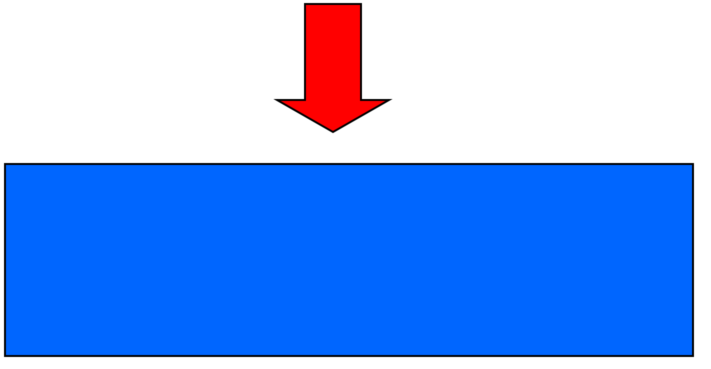
represent matches with score 1.

- The score of the alignment path is 5.

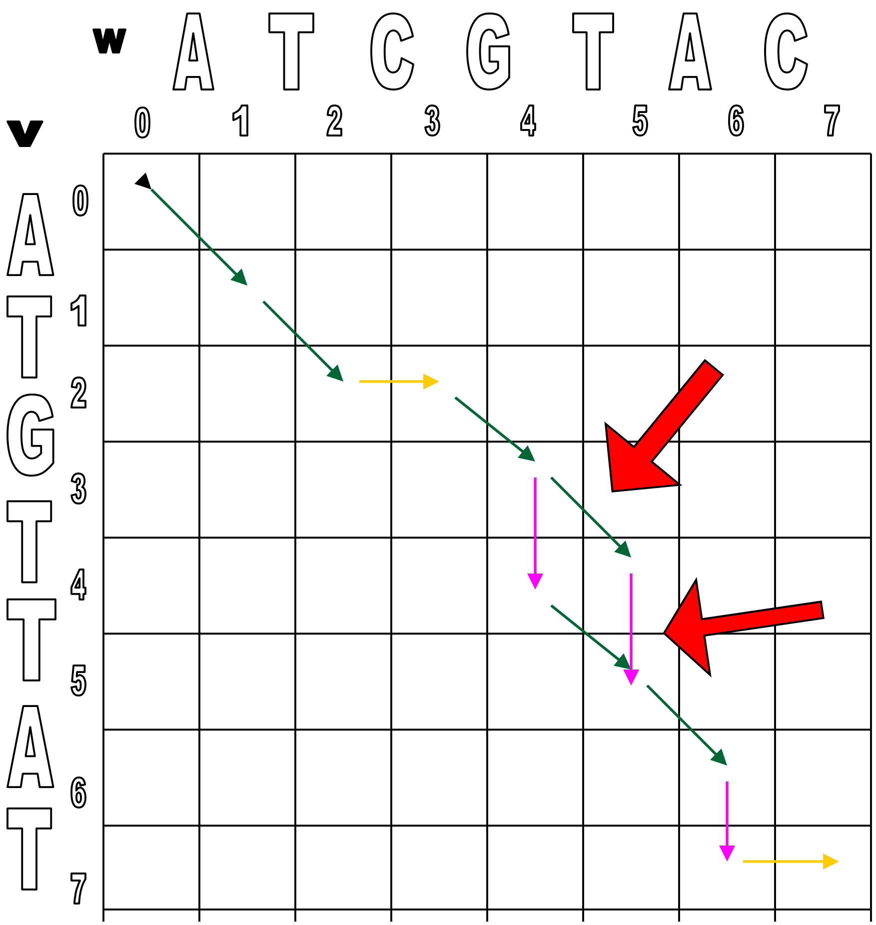
Alignment as a Path in the Edit Graph



Every path in the edit graph corresponds to an alignment:



Alignment as a Path in the Edit Graph



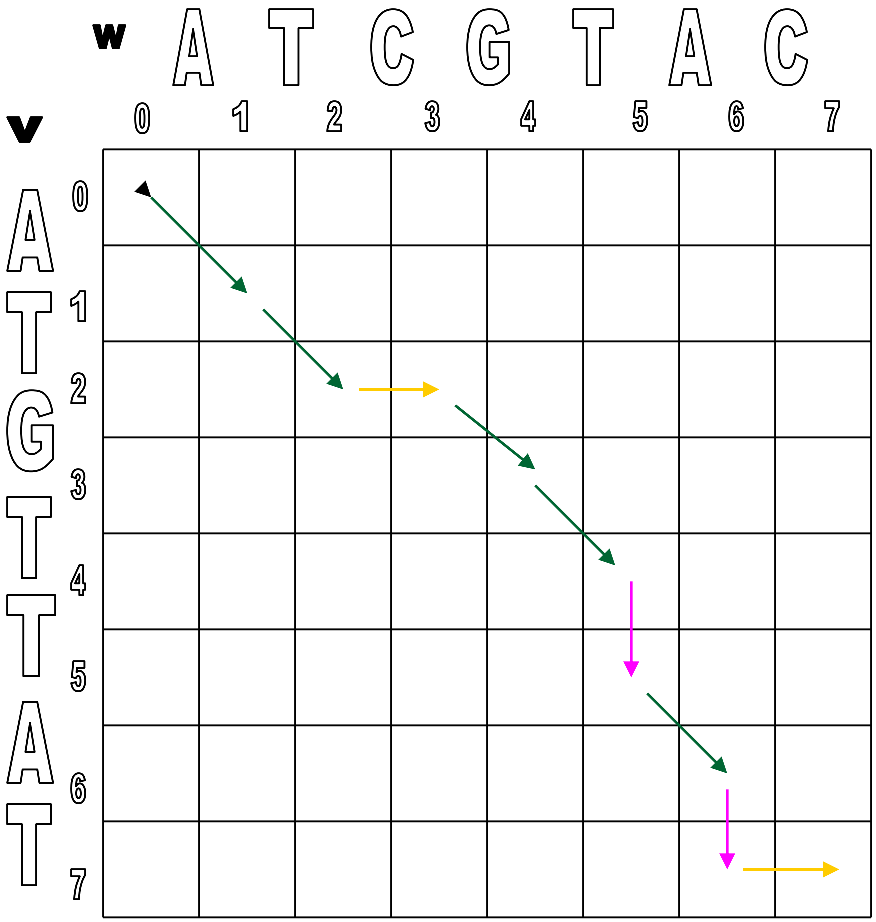
Old Alignment

```
     0122345677
v=   AT_GTTAT_
w=   ATCGT_A_C
     0123455667
```

New Alignment

```
     0122345677
v=   AT_GTTAT_
w=   ATCG_TA_C
     0123445667
```

Alignment as a Path in the Edit Graph



0122345677

v= AT_GTTAT_

w= ATCGT_A_C

0123455667

(0,0) , (1,1) , (2,2), (2,3), (3,4), (4,5), (5,5), (6,6), (7,6), (7,7)

Alignment: Dynamic Programming

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

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.

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						

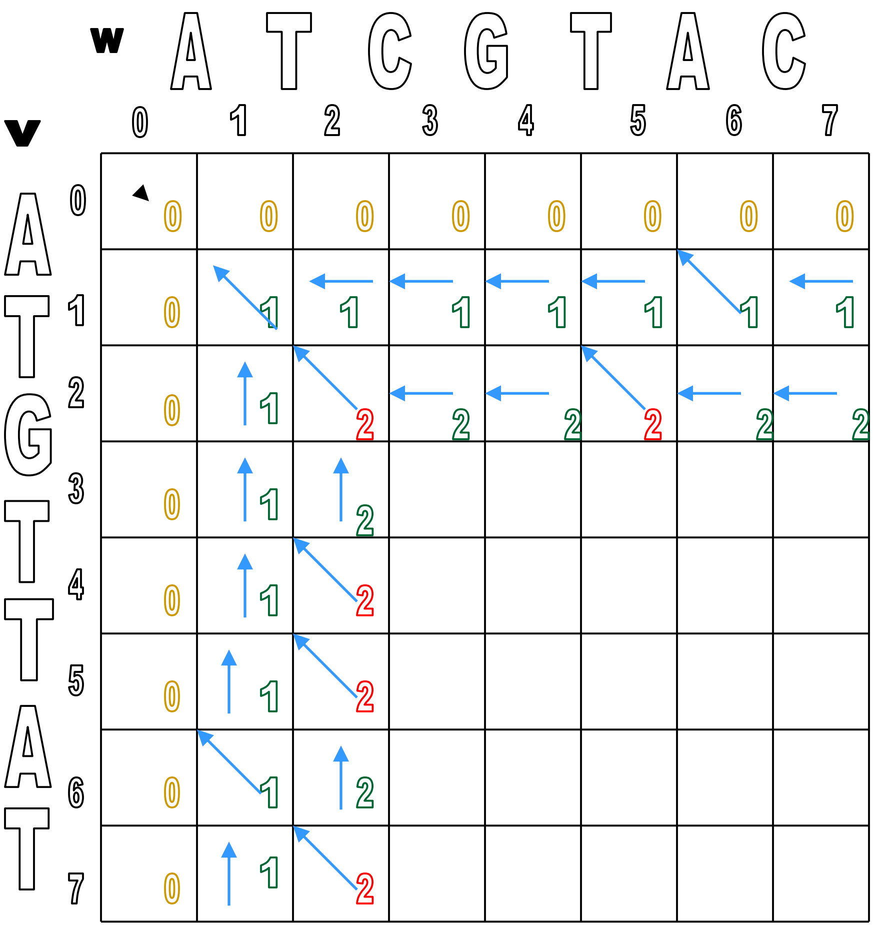
$$S_{i,j} = \max \begin{cases} S_{i-1,\, j-1} & \leftarrow \text{value from NW +1, if } v_i = w_j \\ S_{i-1,\, j} & \leftarrow \text{value from North (top)} \\ S_{i,\, j-1} & \leftarrow \text{value from West (left)} \end{cases}$$

Alignment: Backtracking

Arrows ↖ ↑ ← show where the score originated from.

- ↑ if from the top
- ← if from the left
- ↖ if $v_i = w_j$

Backtracking Example



Find a match in row and column 2.

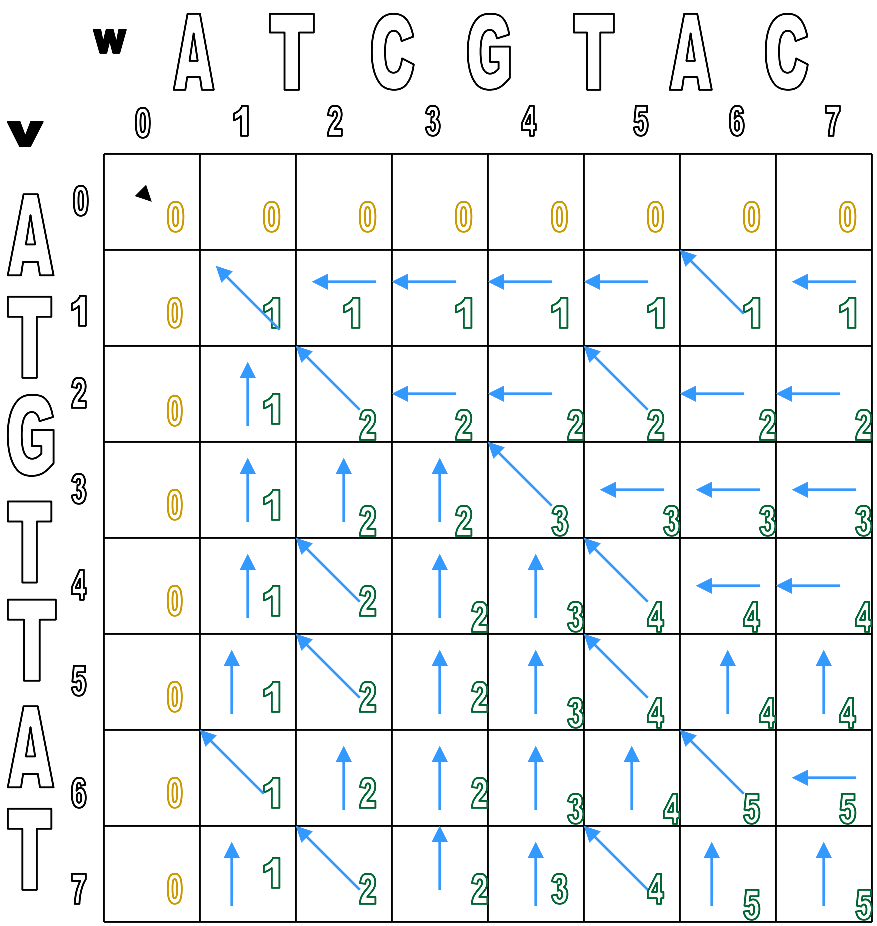
i=2, j=2,5 is a match (T).

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.

Alignment: Dynamic Programming

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

Alignment: Dynamic Programming

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

This recurrence corresponds to the Manhattan Tourist problem (three incoming edges into a vertex) with all horizontal and vertical edges weighted by zero.

LCS Algorithm

<u>Levenshtein(v,w)</u>

for $i \leftarrow 1$ to n

$\quad s_{i,0} \leftarrow 0$

for j $\leftarrow$ 1 to m

$\quad s_{0,j} \leftarrow 0$

for $i \leftarrow 1$ to n

$\quad$ **for** $j \leftarrow 1$ to m

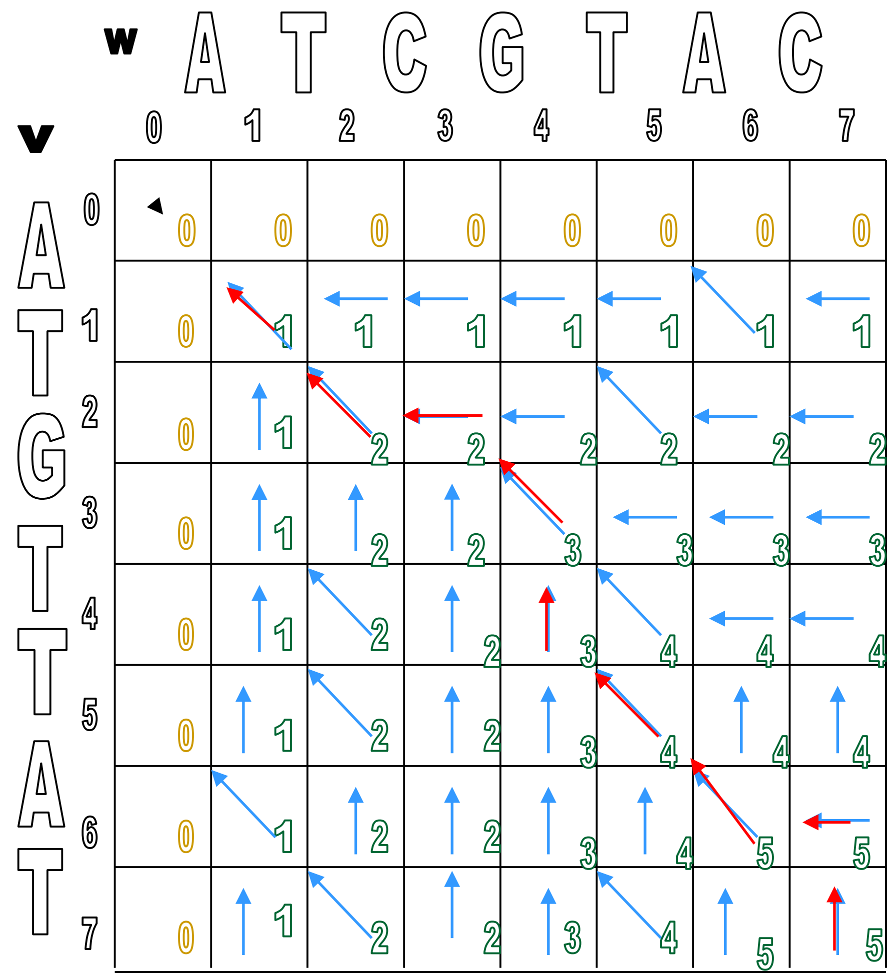
$$s_{i,j} \leftarrow \max \begin{cases} s_{i-1,j} \\ s_{i,j-1} \\ s_{i-1,j-1} + 1, \text{ if } v_i = w_j \end{cases}$$

$$b_{i,j} \leftarrow \begin{cases} \text{“} \uparrow \text{“} & \textbf{if } s_{i,j} = s_{i-1,j} \\ \text{“} \leftarrow \text{“} & \textbf{if } s_{i,j} = s_{i,j-1} \\ \text{“} \nwarrow \text{“} & \textbf{if } s_{i,j} = s_{i-1,j-1} + 1 \end{cases}$$

return $(s_{n,m}, \boldsymbol{b})$

Now What?

- LCS(v,w) created the alignment grid
- Now we need a way to read the best alignment of v and w
- Follow the arrows backwards from sink



Printing LCS : Backtracking

```
PrintLCS (b,v,i,j)
    if  i = 0 or j = 0
        return
    if b_{i,j} = "↖"
        PrintLCS (b,v,i-1,j-1)
        print v_i
    else
        if b_{i,j} = "↑"
            PrintLCS (b,v,i-1,j)
        else
            PrintLCS (b,v,i,j-1)
```

LCS Runtime

- It takes O(nm) time to fill in the $n \cdot m$ dynamic programming matrix.