String Distance and Dynamic Programming

Lecture 8

Life is similar

- Life is based on a repertoire of successful structural and interrelated building blocks which are passed around
- The vast majority of proteins are the result of a series of genetic duplications and subsequent modifications
- “Everything in life is so similar that the same genes that work in flies are the ones that work in humans” (Wieschaus, 1995)

Comparison and analogy

- By identifying and comparing related objects we can distinguish variable and conserved features, and thereby determine what is crucial to structure and function
- Biological universality occurs at many levels of details, so we can compare not only the sequence data, but 3D shapes, chemical pathways, morphological features etc.

Why compare biosequences

- The biological sequences encode and reflect higher-level molecular structures and mechanisms
- **In bimolecular sequences (DNA, RNA or protein), high sequence similarity <u>usually</u> implies significant structural and functional similarity**
- A tractable, though partly heuristic way to infer the structure and function of an unknown protein is to search for the similar known proteins at the sequence level

Keep in mind

- There is no one-to-one correspondence between similar sequences and similar structures or between sequences and functions:
  - Similar structures can be obtained from completely unrelated sequences
  - Very similar sequences can produce very different structures depending on the location of a change

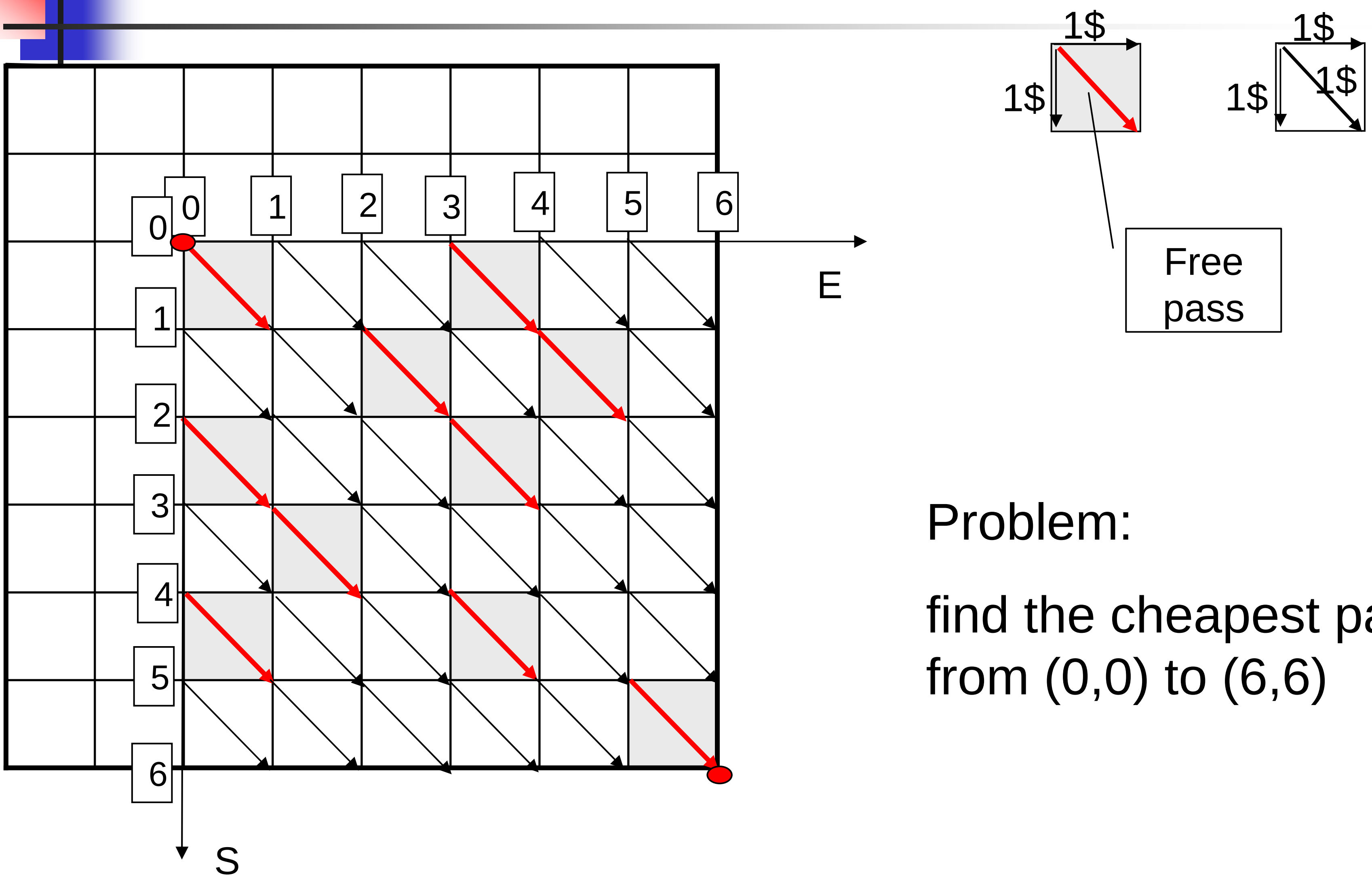
A shift to approximate pattern matching

- Approximate – means some errors are allowed in valid matches
- The shift is accompanied by a shift in technique: *dynamic programming*

Dynamic programming

The main tool in approximate pattern matching

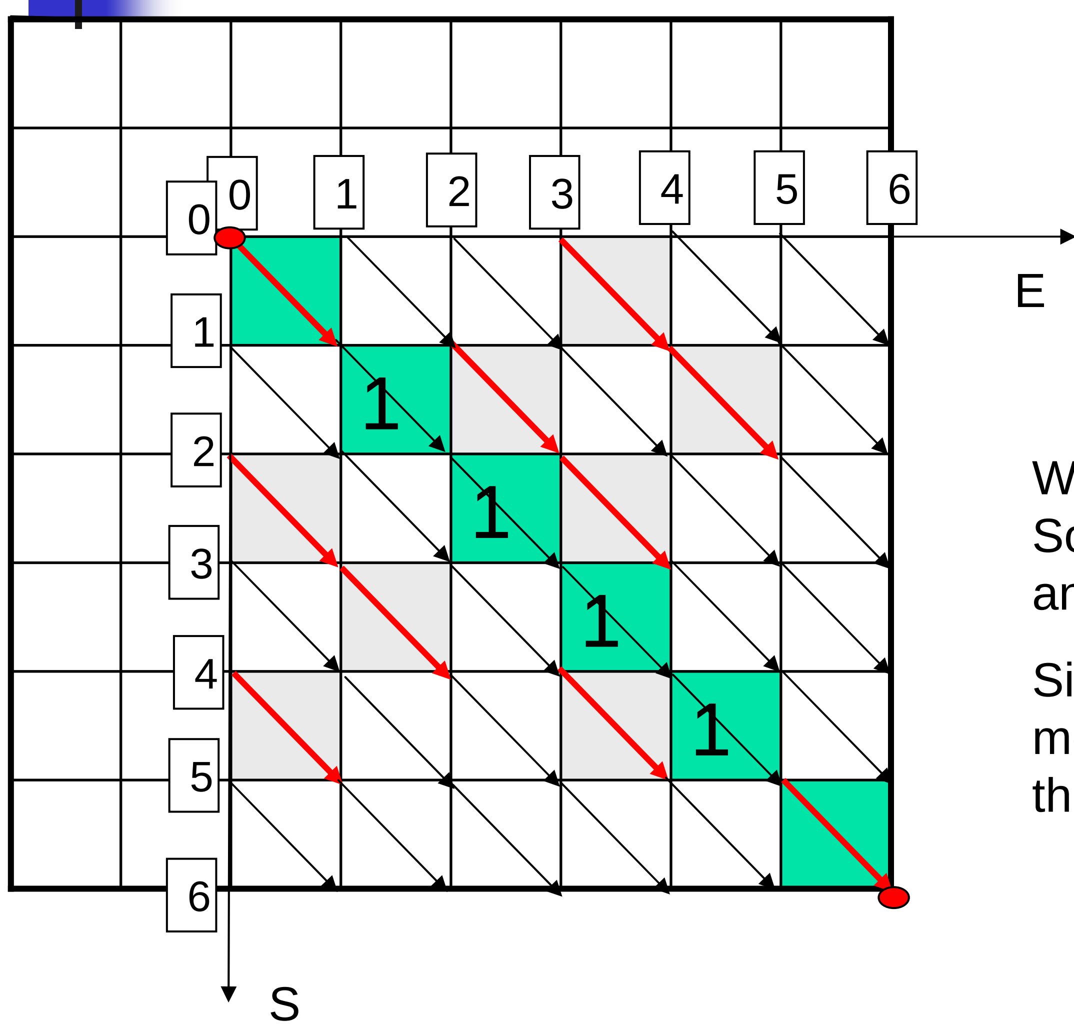
The cheapest path

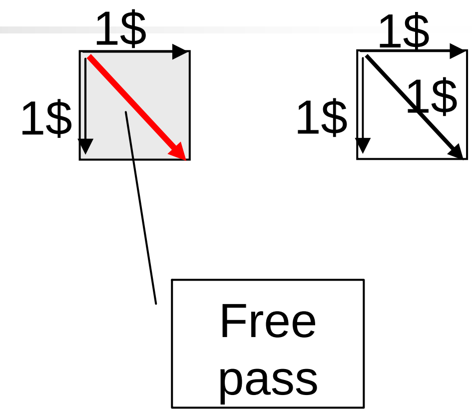


Problem:

find the cheapest path from (0,0) to (6,6)

The path without a map

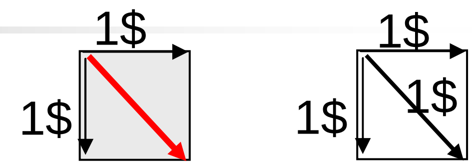


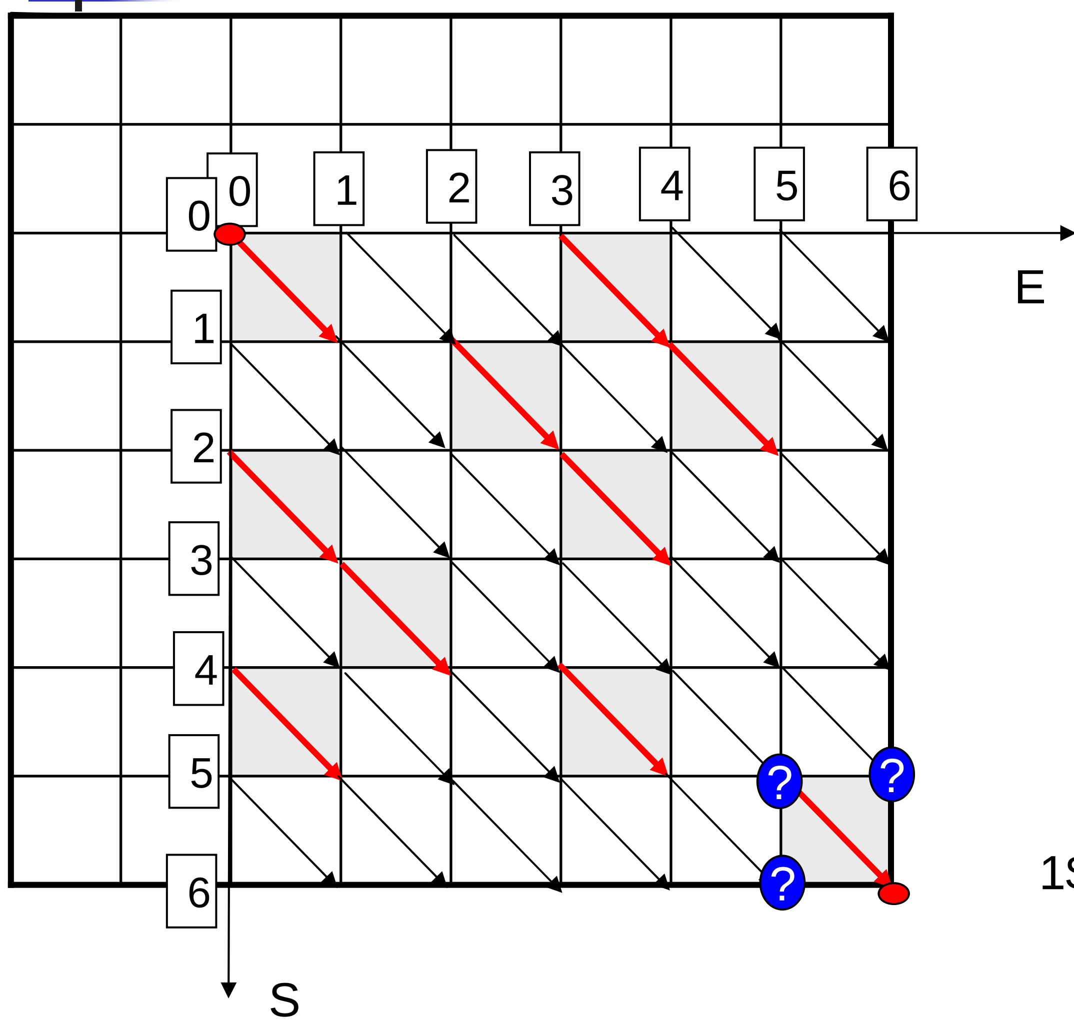


We will always choose the South-East direction (diagonal), and we will pay 4$

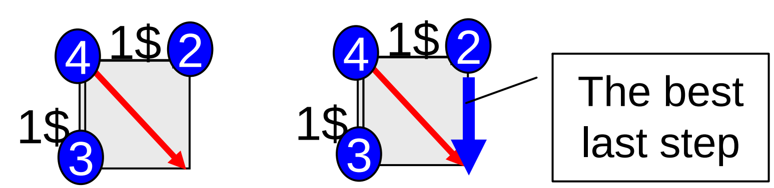
Since we don’t know that if we move strictly East or South, there are more free-pass cells

Sub-problems approach

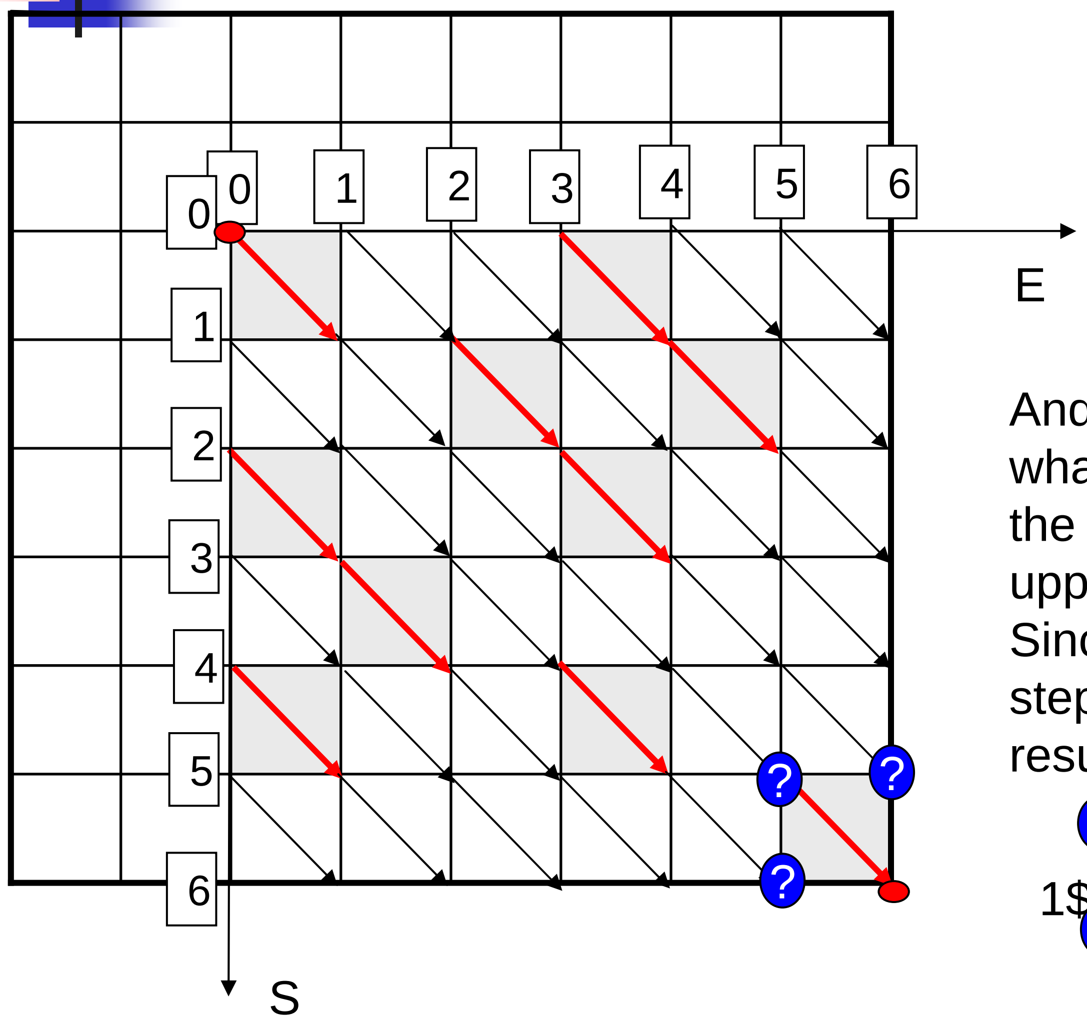


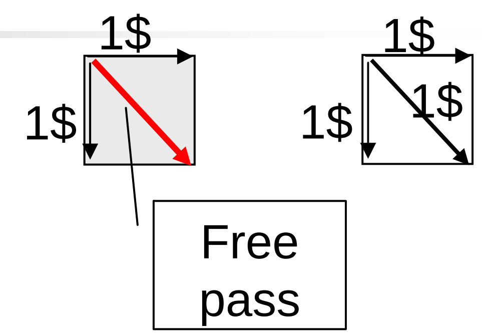


If we knew the cheapest paths
from (0,0) to (5,5)
from (0,0) to (6,5)
from (0,0) to (5,6)
we could choose the best last step to the destination:
For example, if:

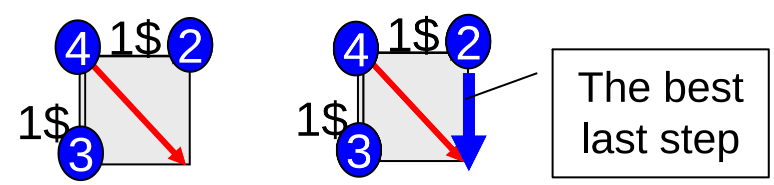


The sub-problems approach

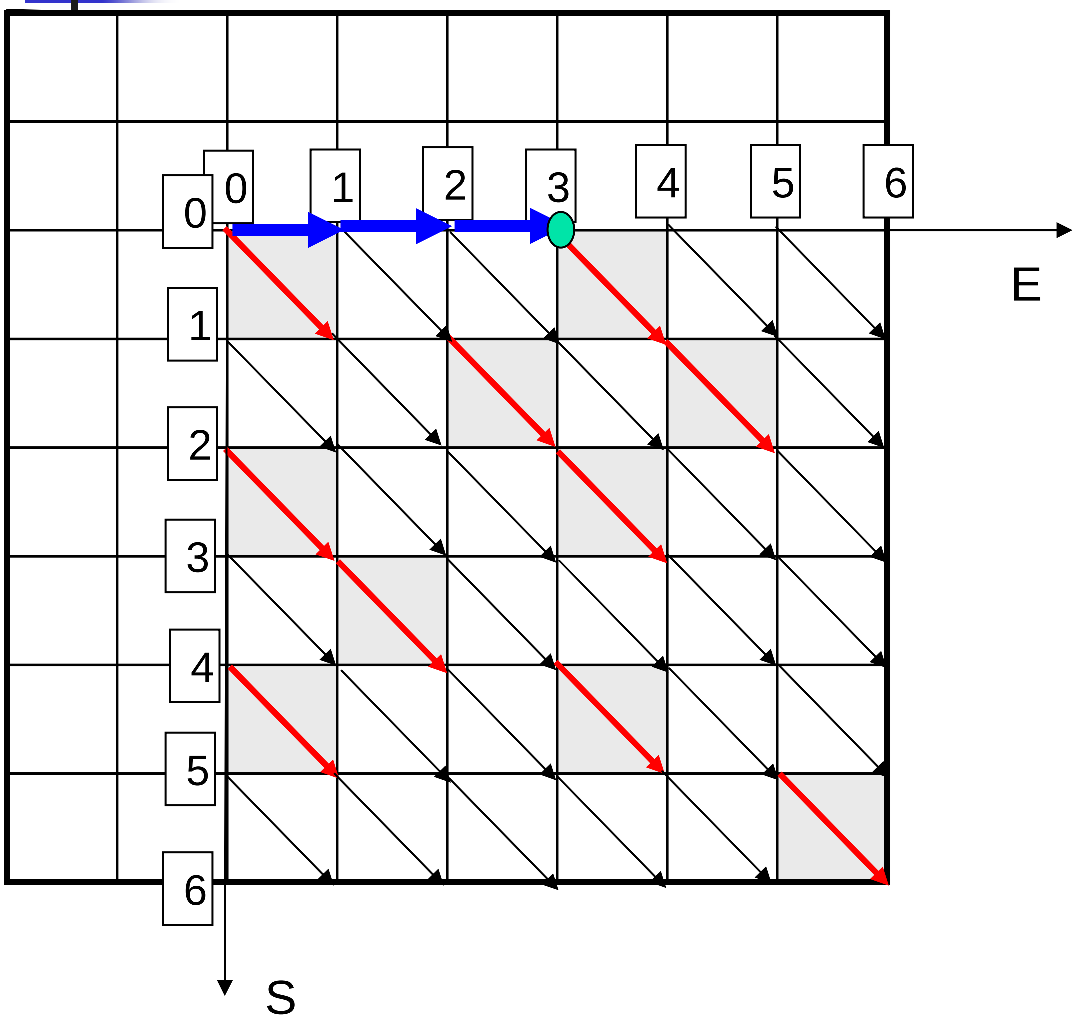




And this is true for any cell – what path to chose depends on the cheapest paths to the left, upper, and upper-left corner. Since we are choosing only 1 step, we can take the min of the result



The recurrence relation – base condition



When i=0, there is no cheaper way of going from (0,0) to (0,j) than to pay j $ - heading strictly to the right (East)

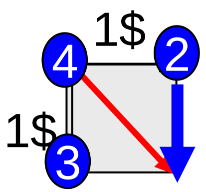
The same for j=0.

The base condition:

if i=0 then COST(i,j)=j

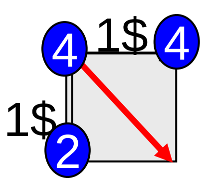
if j=0 then COST(i,j)=i

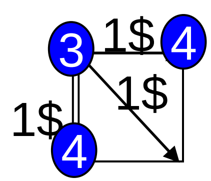
The recurrence relation (for i>0 and j>0)

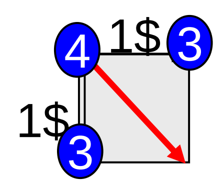


$$COST(i,j)=\min \begin{cases} COST(i-1,j)+1 \\ COST(i,j-1)+1 \\ COST(i-1,j-1)+DIAGONAL(i,j) \end{cases}$$

For each case, what is the best move?



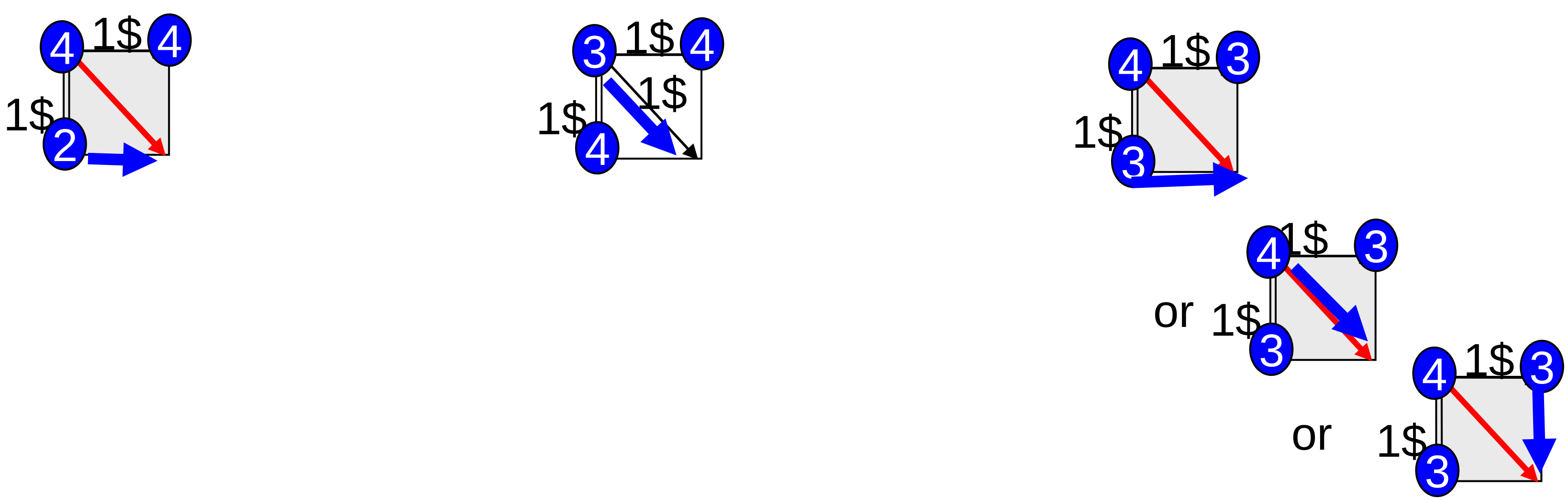




The recurrence relation

$$
COST(i,j) = \min \begin{cases} COST(i-1,j)+1 \\ COST(i,j-1)+1 \\ COST(i-1,j-1)+DIAGONAL(i,j) \end{cases}
$$

The best moves:



The top-down (usual) recursion

$$COST(i,j)=\min \begin{cases} COST(i-1,j)+1 \\ COST(i,j-1)+1 \\ COST(i-1,j-1)+DIAGONAL(i,j) \end{cases}$$

algorithm cheepestCost (**array** *diagonalCost, N*, *M*)

return *cost* (*N*, *M*)

algorithm *cost* (*i*, *j*)

if *i*=0 **then**

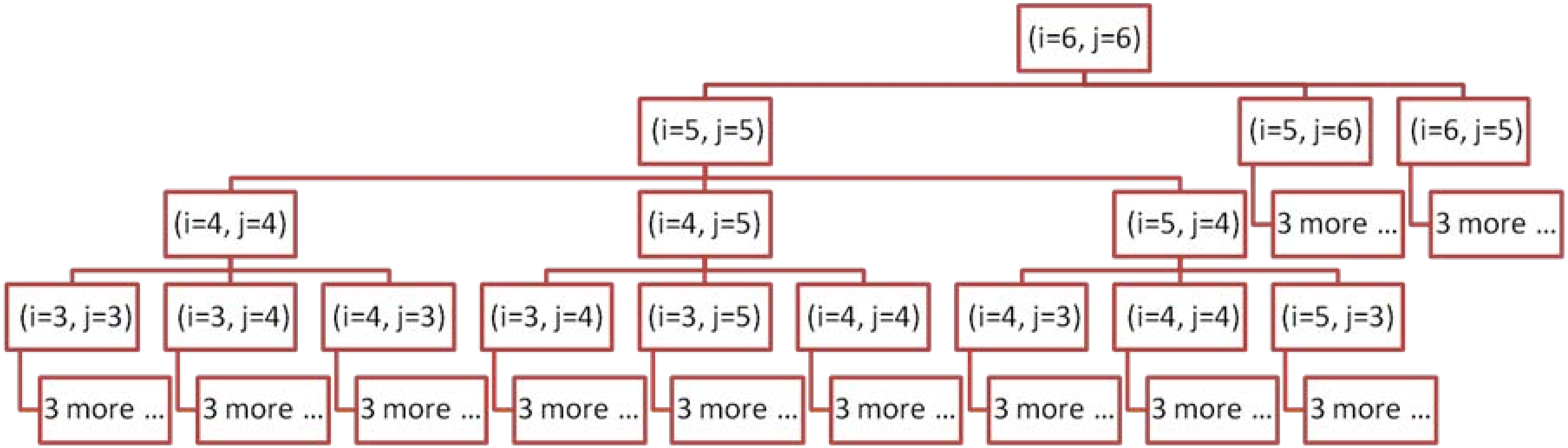
return *j*

if *j*=0 **then**

return *i*

return min (***cost*** (*i*-1, *j*) +1, ***cost*** (*i*, *j*-1)+1, ***cost*** (*i*-1, *j*-1)+*diagonalCost* [*i*] [*j*])

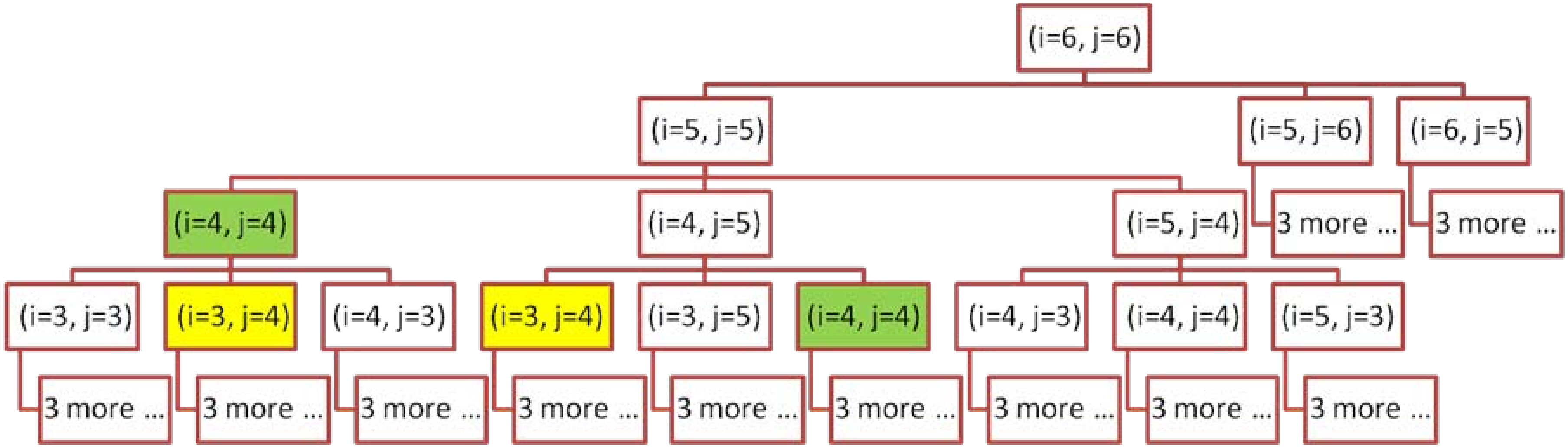
The recursion tree



$O(3^N)$?

But there are only N*M different combinations

The recursion tree



$O(3^N)$?

We call the recursive function multiple times with the same parameters

Dynamic programming steps

- The recurrence relation
- The bottom-up computation
- The traceback

Dynamic programming I

- **The recurrence relation**
- The bottom-up computation
- The traceback

The recurrence relation

The base condition:

if i=0 then COST(i,j)=j
if j=0 then COST(i,j)=i

The main relation (for i>0 and j>0)

$$COST(i,j)=\min \begin{cases} COST(i-1,j)+1 \\ COST(i,j-1)+1 \\ COST(i-1,j-1)+DIAGONAL(i,j) \end{cases}$$

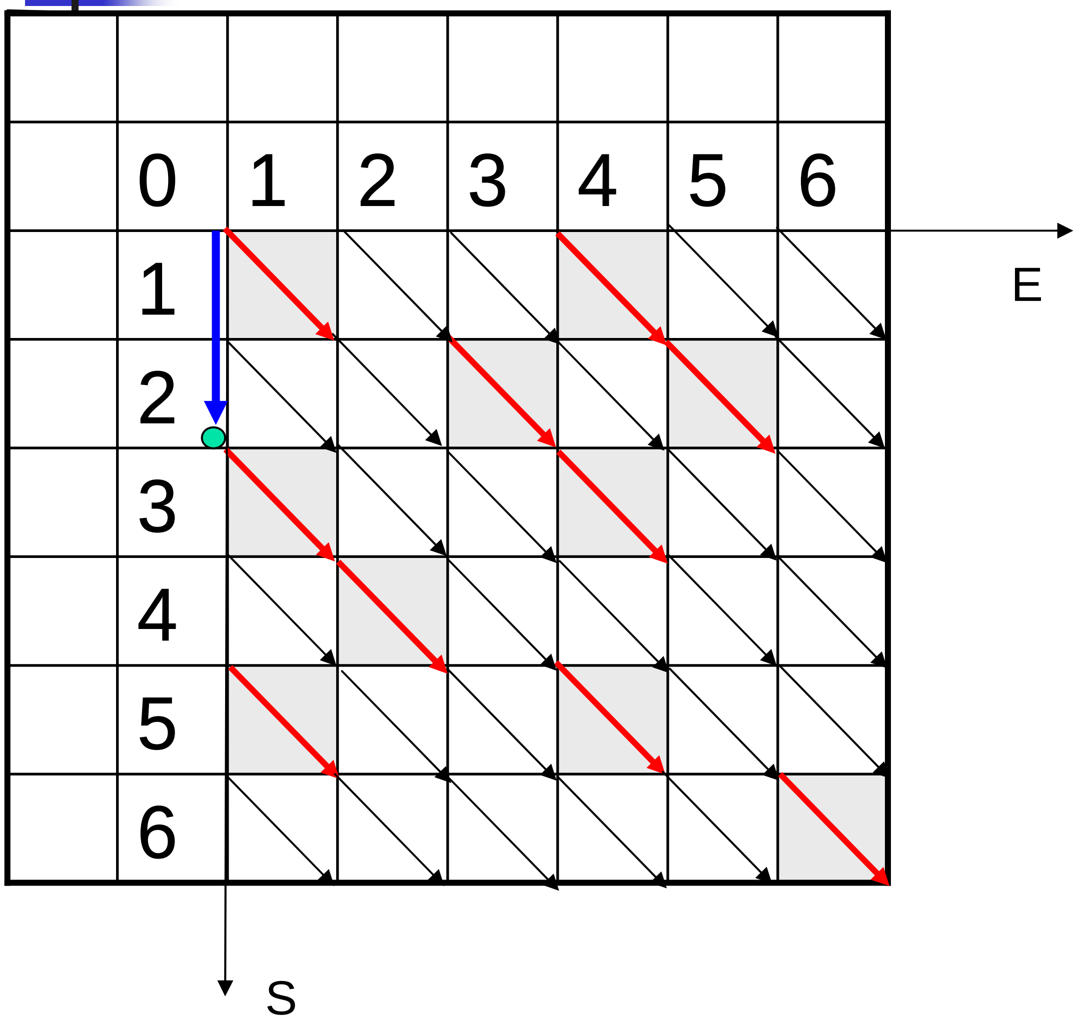
Dynamic programming II

- The recurrence relation
- **The bottom-up computation**
- The traceback

The bottom-up computation

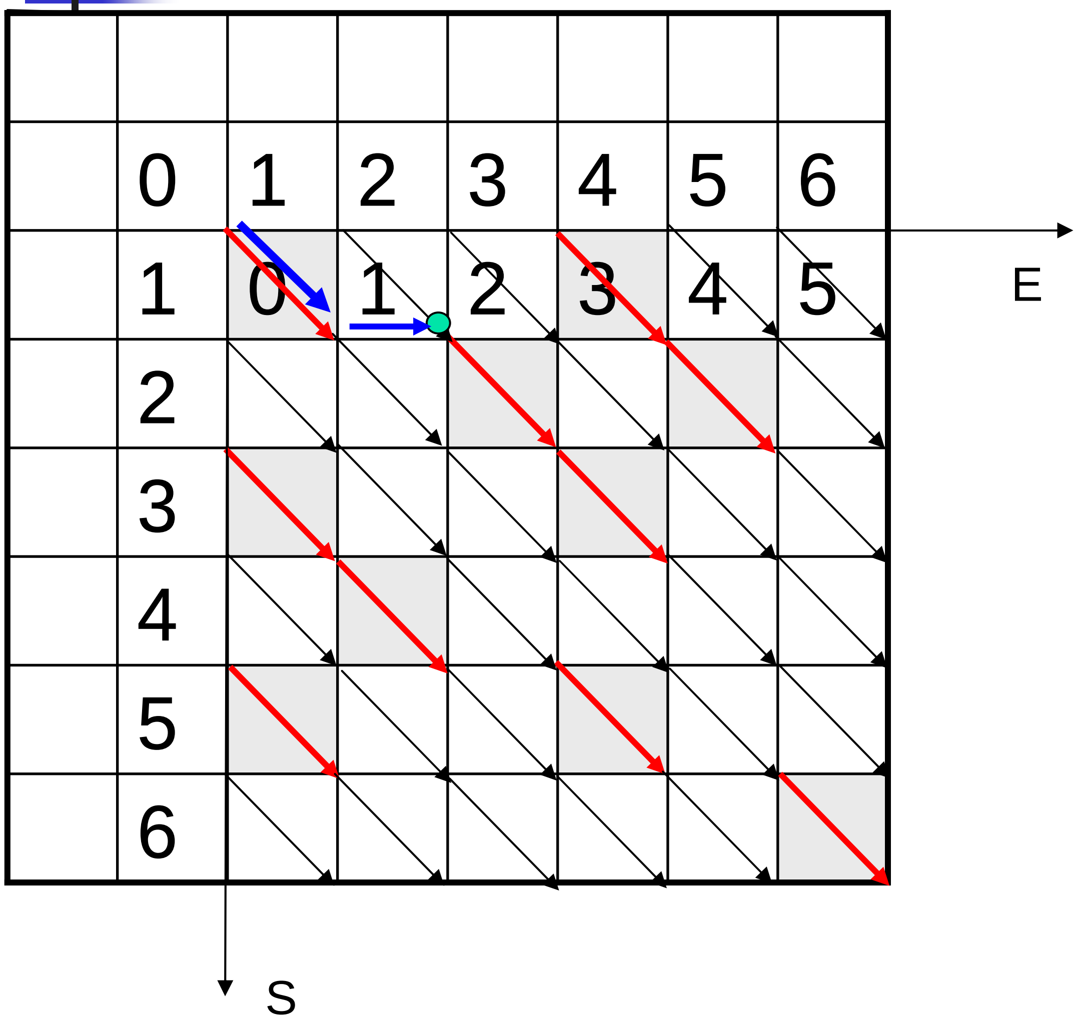
- Fill in the best values for each cell of the N*M table starting from the lowest values
- First, compute the basic values of recursion – for i=0 and for j=0
- Apply recursion relation for computing the value of each cell from the lowest numbers of i and j to the largest
- At the end, we will have the cost of the best path in the cell (N,M)

Fill values for i=0 and for j=0 (the base recursion condition)



There is no cheaper way of going to the point (2,0) than paying 2 $

Fill values for i=1 (from left to right)



Cell(1,2)=1

since the cheapest possible way is to continue the free path through the cell (1,1)

Fill in the entire table (left-to-right top-down)

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

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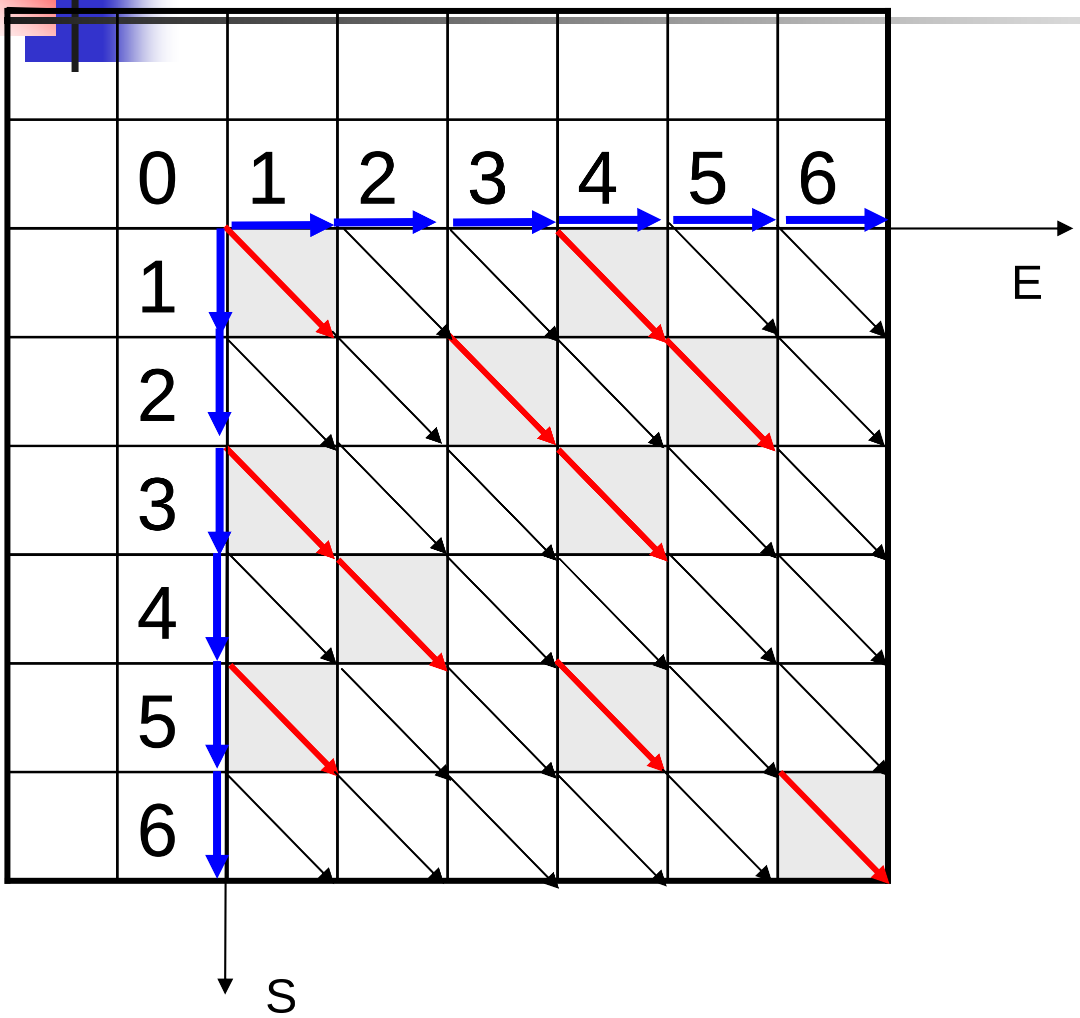
The cheapest possible path costs 3$

But what is this path?

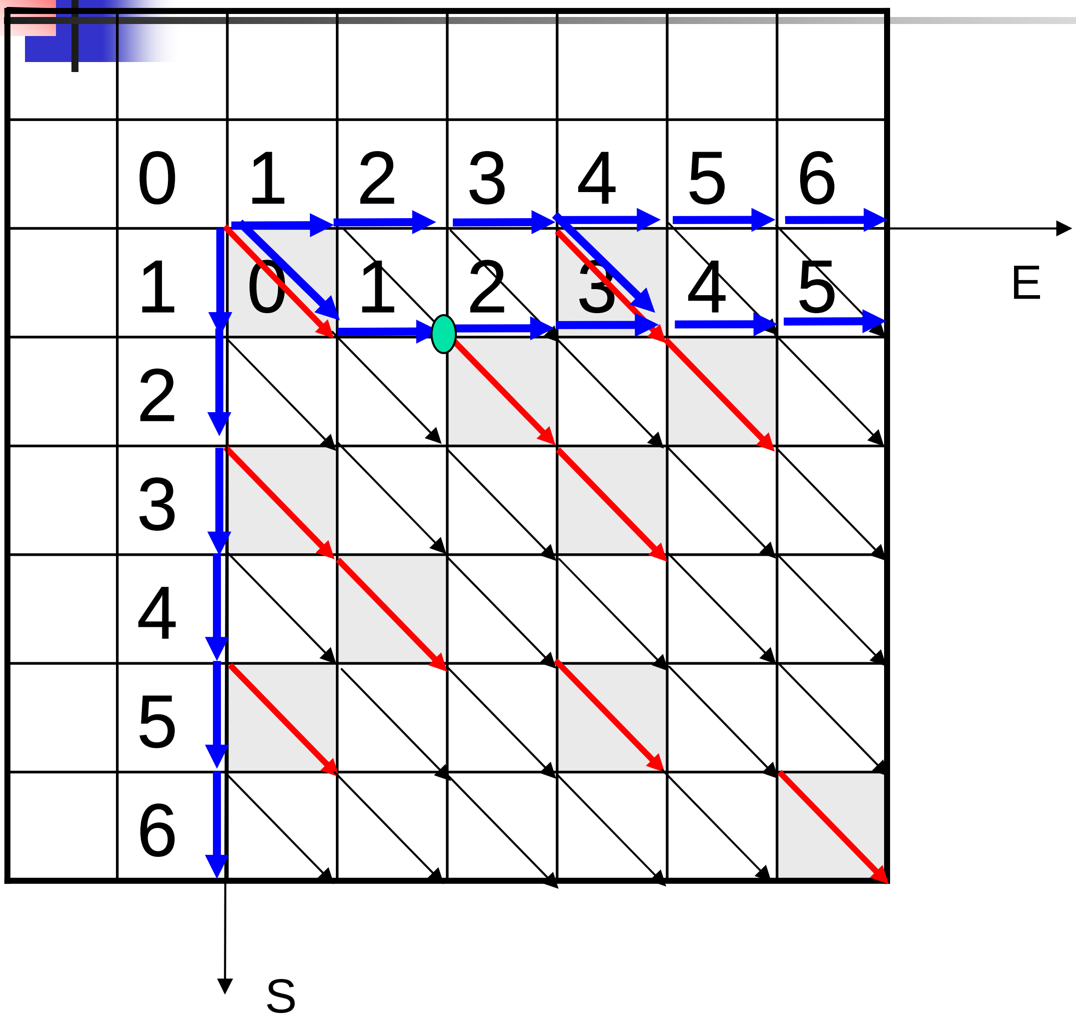
Dynamic programming III

- The recurrence relation
- The bottom-up computation
- **The traceback**

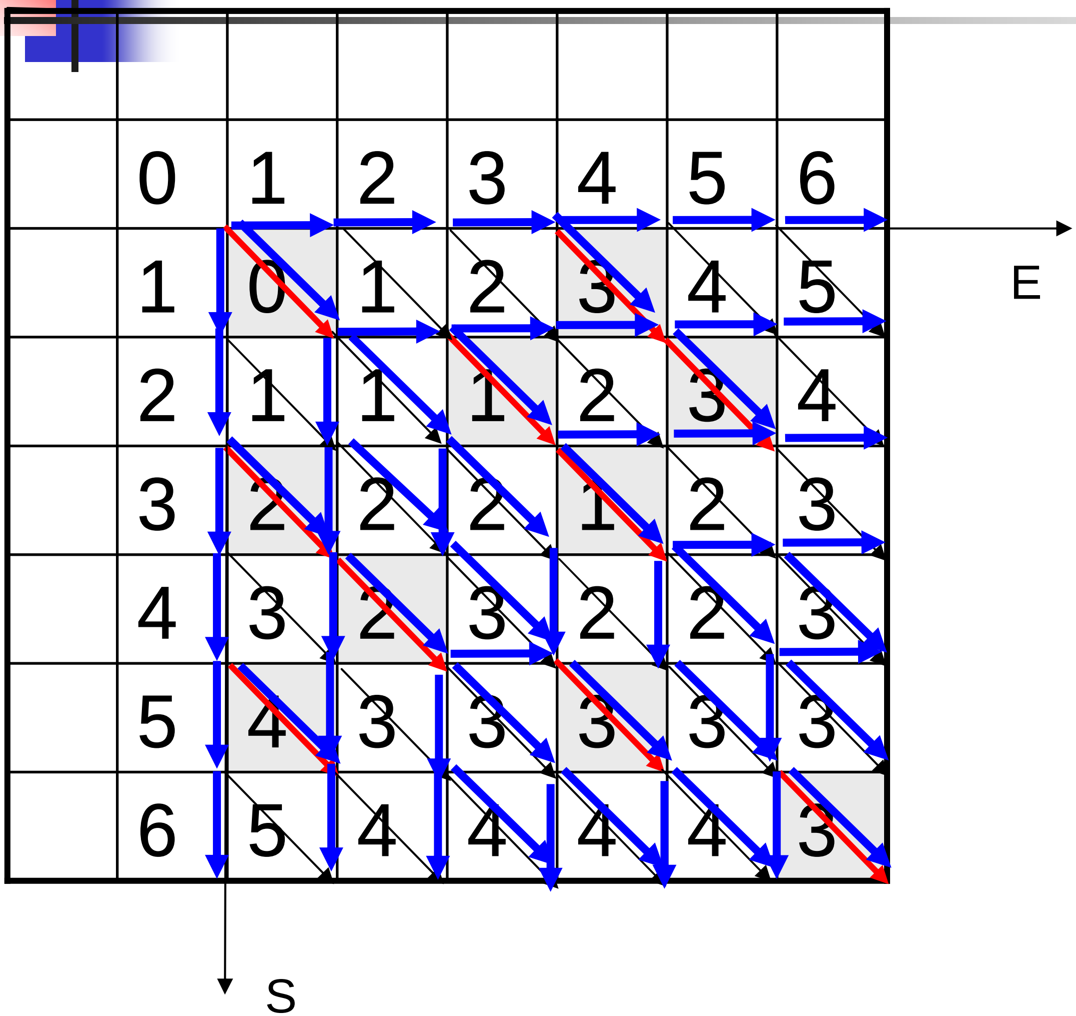
Keeping track of the source



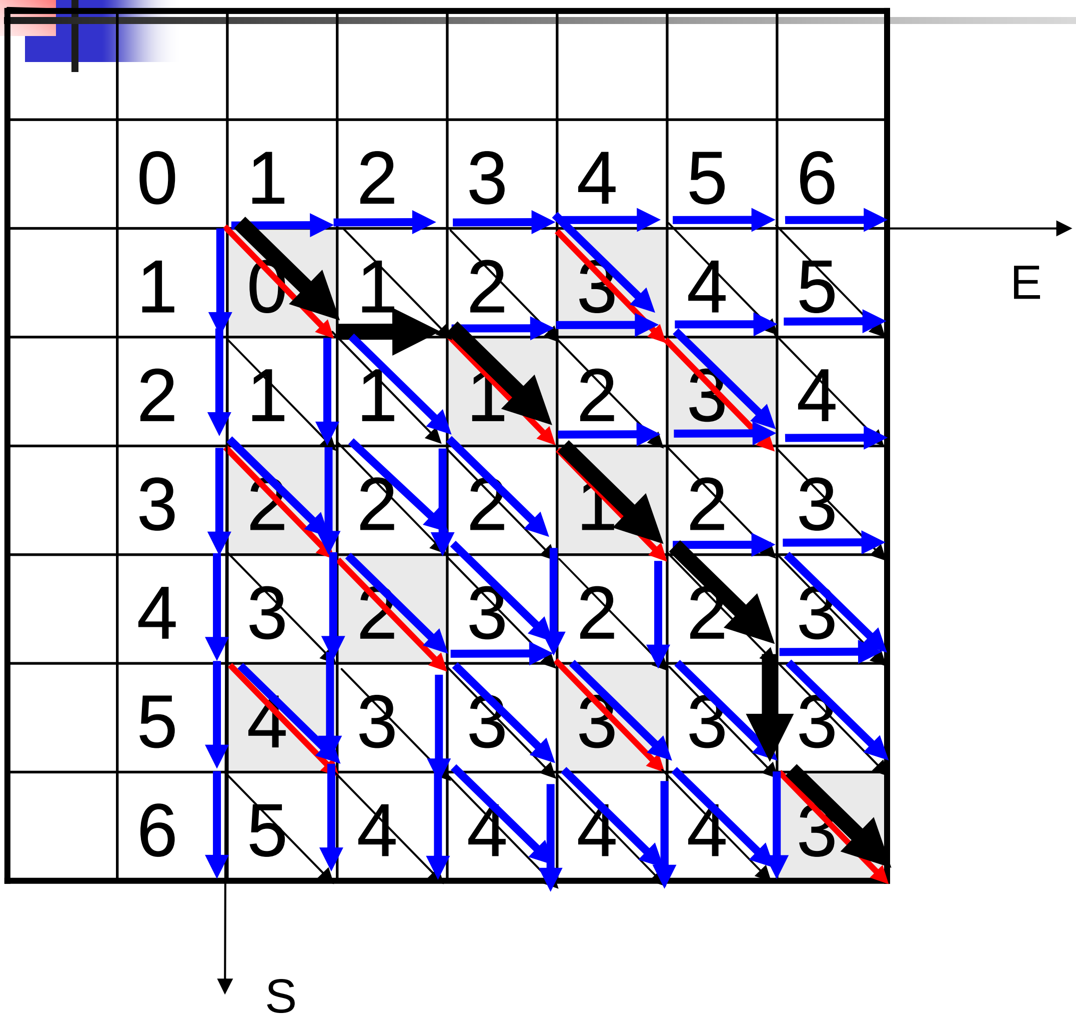
Keeping track of the source



Keeping track of the source



Trace back – how did we get the path with the cost 3



Complexity of the DP algorithm

- 2 nested loops: O(NM)

Edit distance

String dissimilarity

Edit Operations

- We can transform the second string S2 into the first string S1 by applying a sequence of edit operations on S2 :
  - Deleting 1 symbol
  - Inserting 1 symbol
  - Replacing 1 symbol

S1	a	c	t			a	t	g
S2	a		t	a	c	a		g

Insert c

Delete a, c

Insert t

In total, 4 edit operations

String alignment

- An *alignment* of 2 strings is obtained by first inserting spaces (gaps), either into or at the end of both strings, and then placing the 2 resulting strings one above the other, so that every character or space in either string is opposite a single character or space in the other string

alignment

S1	a	c	t	-	-	a	t	g
S2	a	-	t	a	c	a	-	g

4 gaps,

no mismatches

Edit distance

- The *edit distance* between two strings is defined as the minimum number of edit operations needed to transform one string into another

S1	a	c	t	a	t		g
S2	a		t	a	c	a	g

Insert c

Replace c by t

Delete a

In total, 3 edit operations

Optimal alignment

- An optimal alignment is obtained from the calculation of the edit distance

Optimal alignment

S1	a	c	t	a	t	-	g
S2	a	-	t	a	c	a	g

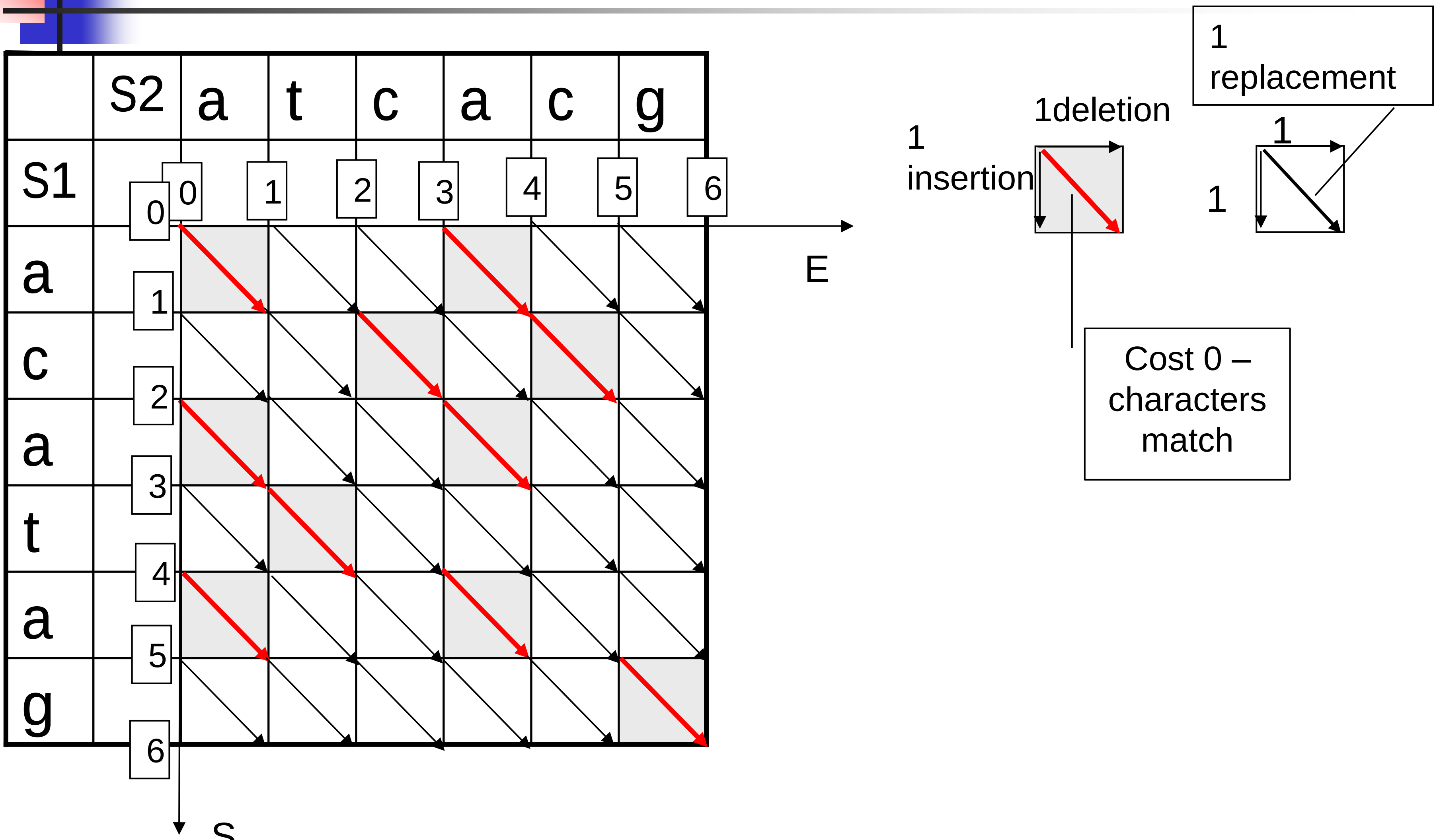
2 gaps,

1 mismatch

The edit distance problem

- Compute the edit distance between two strings along with a sequence of the operations which describe the transformation

Analogy with the cheapest path



The dynamic programming solution to the edit distance problem

- Trivially follows from the solution for the cheapest path:
  - If we moved strictly down in the grid, we inserted 1 symbol into S2
  - If we moved strictly to the right, we deleted 1 symbol from S2
  - If we moved by diagonal of cost 0, we matched the corresponding characters
  - If we moved by diagonal of cost 1, we replaced one symbol in S2 with the corresponding symbol in S1