Dynamic Programming: Edit Distance

Outline

1. DNA Sequence Comparison and CF
2. Change Problem
3. Manhattan Tourist Problem
4. Longest Paths in Graphs
5. Sequence Alignment
6. Edit Distance

Section 1: DNA Sequence Comparison and CF

DNA Sequence Comparison: First Success Story

- Finding sequence similarities with genes of known function is a common approach to infer a newly sequenced gene's function.

- In 1984 Russell Doolittle and colleagues found similarities between a cancer-causing gene and the normal growth factor (PDGF) gene.

Russell Doolittle

http://biology.ucsd.edu/faculty/doolittle.html

Cystic Fibrosis

- **Cystic fibrosis (CF)**: A chronic and frequently fatal disease which produces an abnormally large amount of mucus.
  - Mucus is a slimy material that coats many epithelial surfaces and is secreted into fluids such as saliva.

- CF primarily affects the respiratory systems of children.

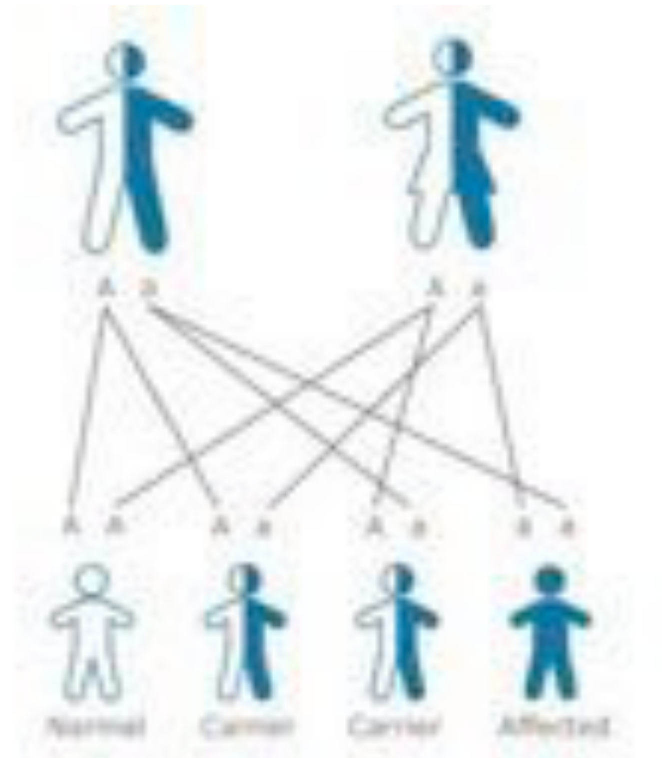
http://www.eradimaging.com/site/article.cfm?ID=327

Cystic Fibrosis: Inheritance

- In the early 1980s biologists hypothesized that CF is a genetic disorder caused by mutations in an unidentified gene.

- Heterozygous carriers are asymptomatic.

- Therefore a person must be homozygously recessive in the CF gene in order to be diagnosed with CF.



http://www.discern-genetics.org/diagram61.php

Cystic Fibrosis: Connection to Other Proteins

- **Adenosine Triphosphate (ATP)**: The energy source of all cell processes.

- ATP binding proteins are present on the cell membrane and act as transport channels.

- In 1989, biologists found a similarity between the cystic fibrosis gene and ATP binding proteins.

- This connection was plausible, given the fact that CF involves sweet secretion with abnormally high sodium levels.

Cystic Fibrosis: Mutation Analysis

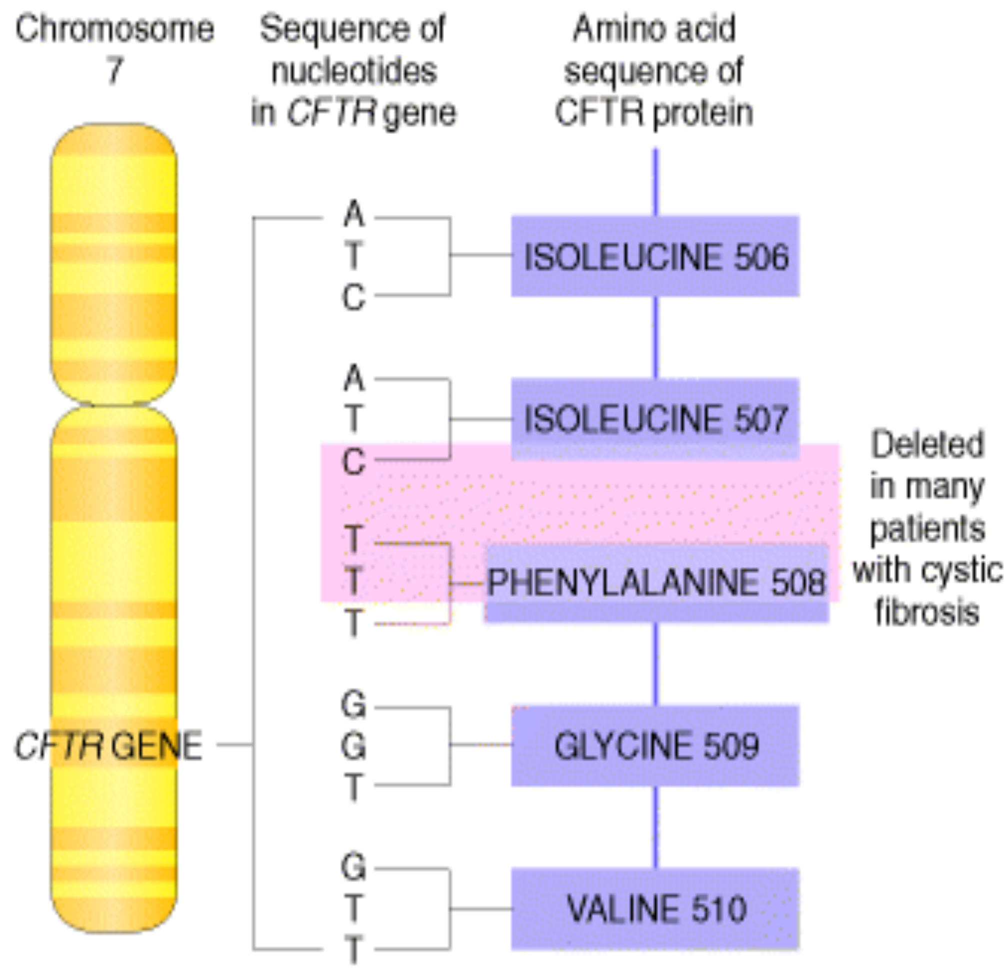
- If a high percentage of CF patients have a given mutation in the gene and the normal patients do not, then this could be an indicator of a mutation related to CF.

- A certain mutation was in fact found in 70% of CF patients, convincing evidence that it is a predominant genetic diagnostics marker for CF.

Cystic Fibrosis and the CFTR Protein

- **CFTR Protein**: A protein of 1480 amino acids that regulates a chloride ion channel.
- CFTR adjusts the "wateriness" of fluids secreted by the cell.
- Those with cystic fibrosis are missing a single amino acid in their CFTR protein (illustrated on following slide).

Cystic Fibrosis and the CFTR Protein



Section 2: The Change Problem

Bring in the Bioinformaticians

- Similarities between a gene with known function and a gene with unknown function allow biologists to infer the function of the gene with unknown function.

- We would like to compute a similarity score between two genes to tell how likely it is that they have similar functions.

- Dynamic programming is a computing technique for revealing similarities between sequences.

- The **Change Problem** is a good problem to introduce the idea of dynamic programming.

Motivating Example: The Change Problem

- Say we want to provide change totaling 97 cents.
- We could do this in a large number of ways, but the quickest way to do it would be:
  - Three quarters = 75 cents
  - Two dimes = 20 cents
  - Two pennies = 2 cents
- Question 1: How do we know that this is quickest?
- Question 2: Can we generalize to arbitrary denominations?

The Change Problem: Formal Statement

- Goal: Convert some amount of money $\boldsymbol{M}$ into given denominations, using the fewest possible number of coins.

- Input: An amount of money $\boldsymbol{M}$, and an array of $\boldsymbol{d}$ denominations $\mathbf{c} = (c_1, c_2, \ldots, c_d)$, in 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

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

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

The Change Problem: Another 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.

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

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

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

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

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

- Lastly, three coins are needed to make change for 7 and 9.

The Change Problem: Recurrence

- This example expresses the following recurrence relation:

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

The Change Problem: Recurrence

- In general, given the denominations ***c***: c_1, c_2, …, c_d, the recurrence relation is:

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

The Change Problem: Pseudocode

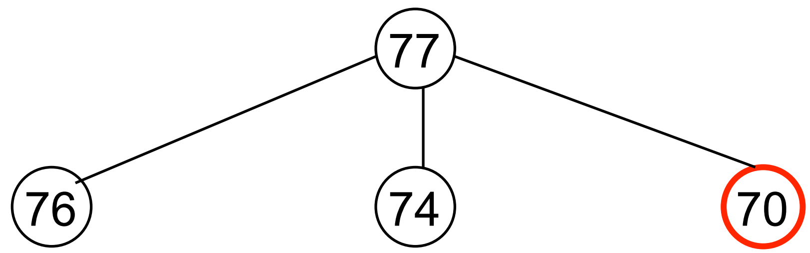
```
RecursiveChange(M,c,d)
   if M = 0
      return 0
  bestNumCoins ← infinity
  for i ← 1 to d
      if M ≥ c_i
         numCoins ← RecursiveChange(M – c_i , c, d)
         if numCoins + 1 < bestNumCoins
            bestNumCoins ← numCoins + 1
  return bestNumCoins
```

The RecursiveChange Tree: Example

- We now will provide the tree of recursive calls if $M = 77$ and the denominations are 1, 3, and 7.
- We will outline all the occurrences of 70 cents to demonstrate how often it is called.

The RecursiveChange Tree

The RecursiveChange Tree



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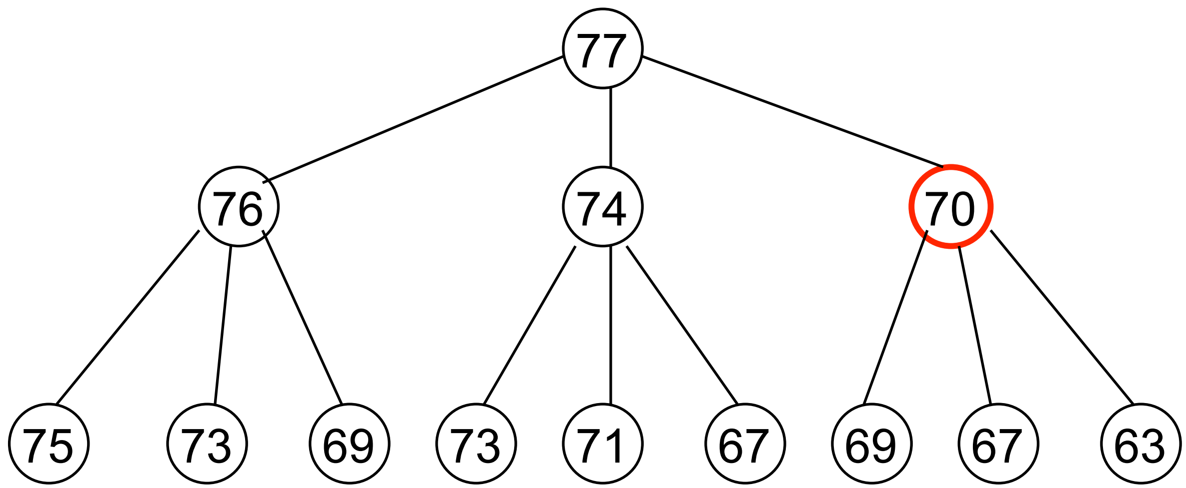

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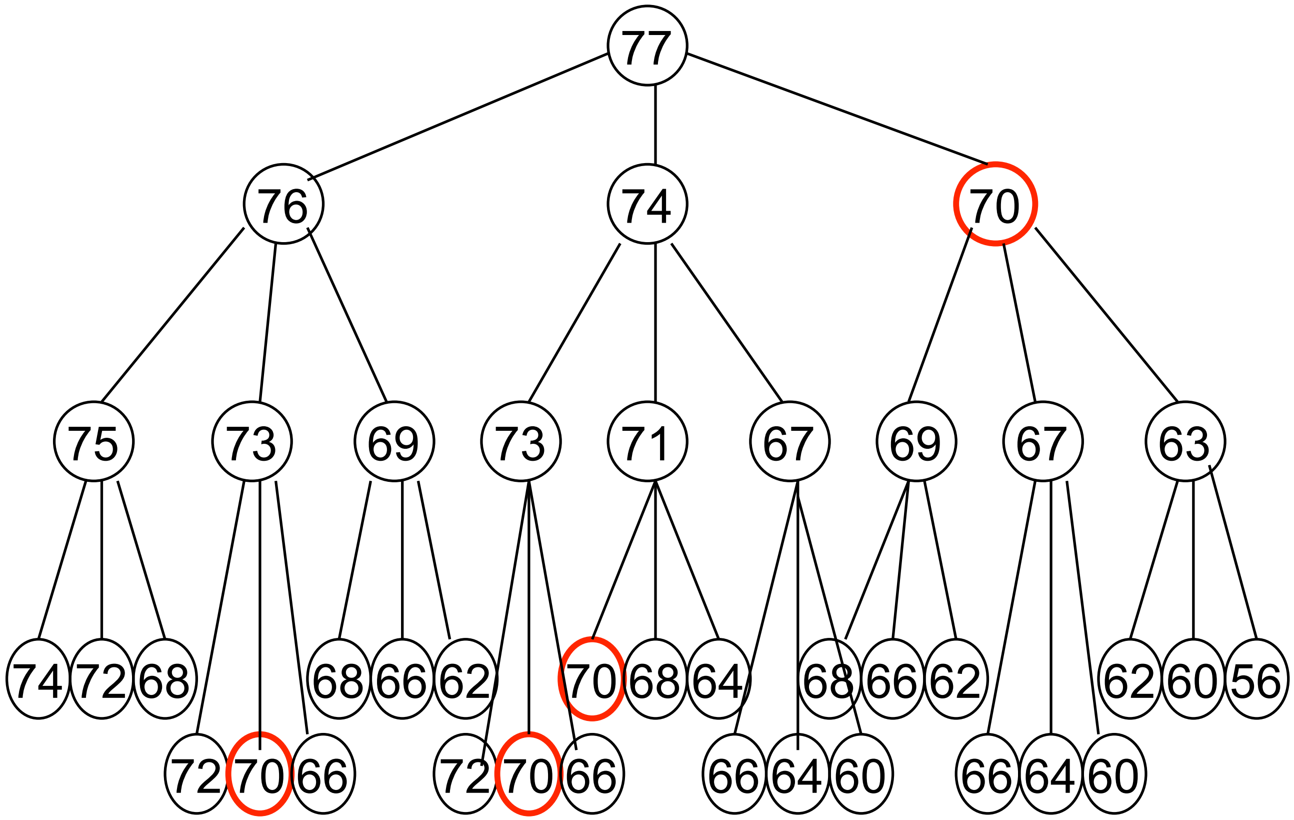

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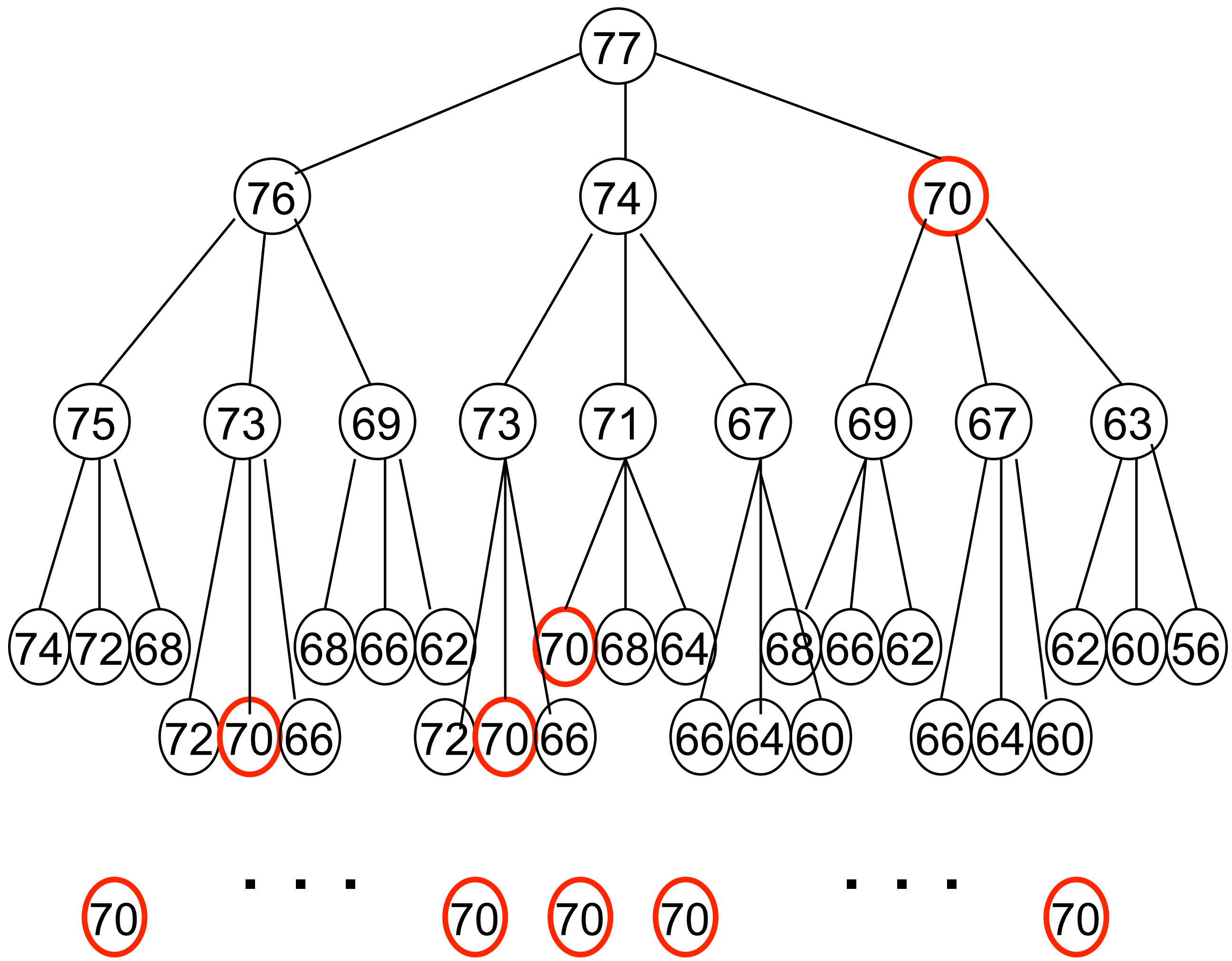

RecursiveChange: Inefficiencies

- As we can see, RecursiveChange recalculates the optimal coin combination for a given amount of money repeatedly.
- For our example of $\boldsymbol{M} = 77$, $\boldsymbol{c} = (1,3,7)$:
  - The optimal coin combination for 70 cents is computed 9 times!

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  - The optimal coin combination for 50 cents is computed billions of times!

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- For our example of $\boldsymbol{M} = 77$, $\boldsymbol{c} = (1,3,7)$:
  - The optimal coin combination for 70 cents is computed 9 times!
  - The optimal coin combination for 50 cents is computed billions of times!
  - Imagine how many times the optimal coin combination for 3 cents would be calculated…

RecursiveChange: Suggested Improvements

- We're re-computing values in our algorithm more than once.
- Instead, let's save results of each computation for all amounts from 0 to M. This way, we can do a reference call to find an already computed value, instead of re-computing each time.
- The new algorithm will have running time $M*d$, where M is the amount of money and d is the number of denominations.
- This is an example of the method of **dynamic programming**.

The Change Problem: Dynamic Programming

<u>DPChange($\boldsymbol{M,c,d}$)</u>

$\quad bestNumCoins_0 \leftarrow 0$

$\quad$ **for** $\boldsymbol{m} \leftarrow 1$ to $\boldsymbol{M}$

$\qquad bestNumCoins_m \leftarrow$ infinity

$\qquad$ **for** $i \leftarrow 1$ to $\boldsymbol{d}$

$\qquad\quad$ **if** $\boldsymbol{m} \geq c_i$

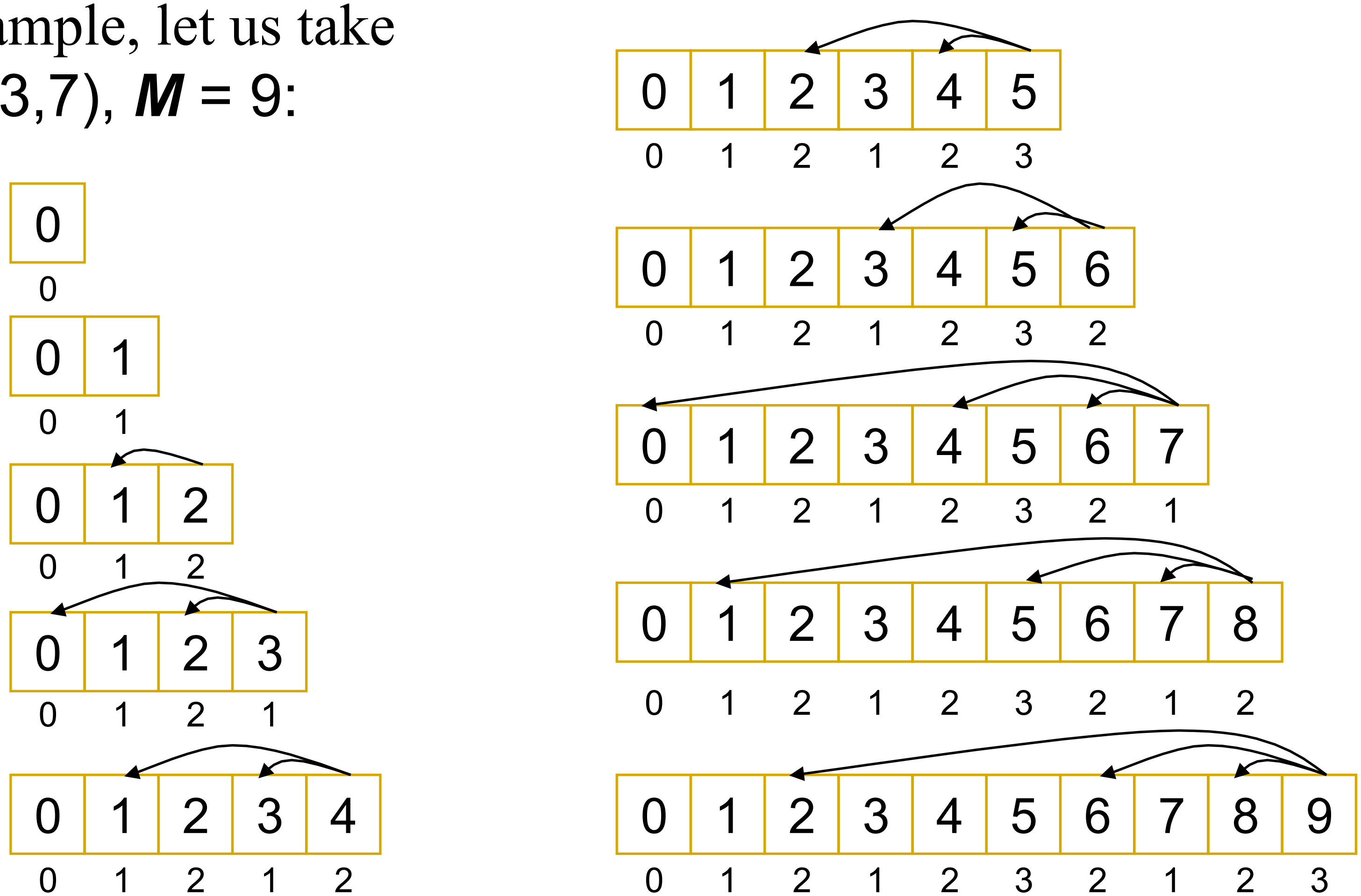
$\qquad\qquad$ **if** $bestNumCoins_{m - c_i} + 1 < bestNumCoins_m$

$\qquad\qquad\quad bestNumCoins_m \leftarrow bestNumCoins_{m - c_i} + 1$

$\quad$ **return** $bestNumCoins_M$

DPChange: Example

- For example, let us take
  $\boldsymbol{c} = (1,3,7)$, $\boldsymbol{M} = 9$:



Quick Note on Dynamic Programming

- You may have noticed that the dynamic programming algorithm provided somewhat resembles the recursive algorithm we already had.

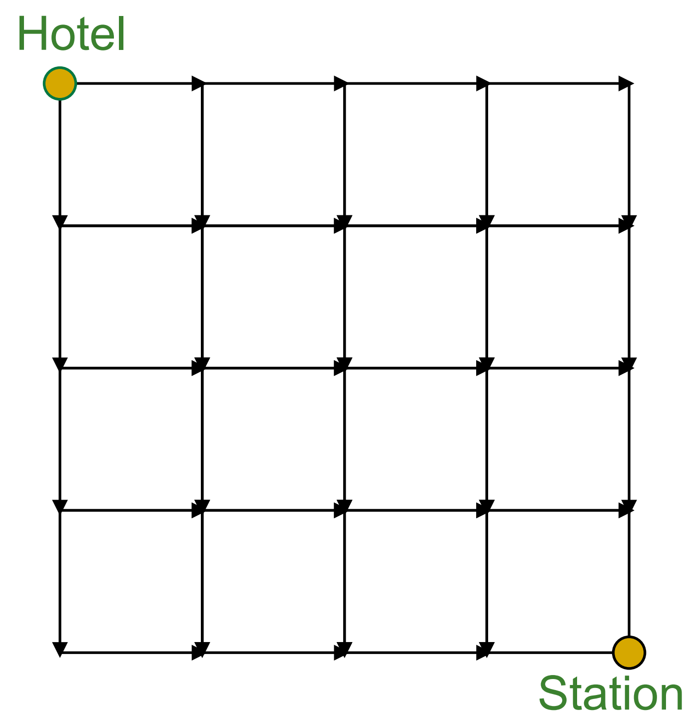
- The difference is that with recursion, we had constant repetition since we proceeded from more complicated sums "down the tree" to less complicated ones.

- With DPChange, we always "build up" from easier problem instances to the desired one, and in so doing avoid repetition.

Section 3: Manhattan Tourist Problem

Additional Example: Manhattan Tourist Problem

- Imagine that you are a tourist in Manhattan, whose streets are represented by the grid on the right.



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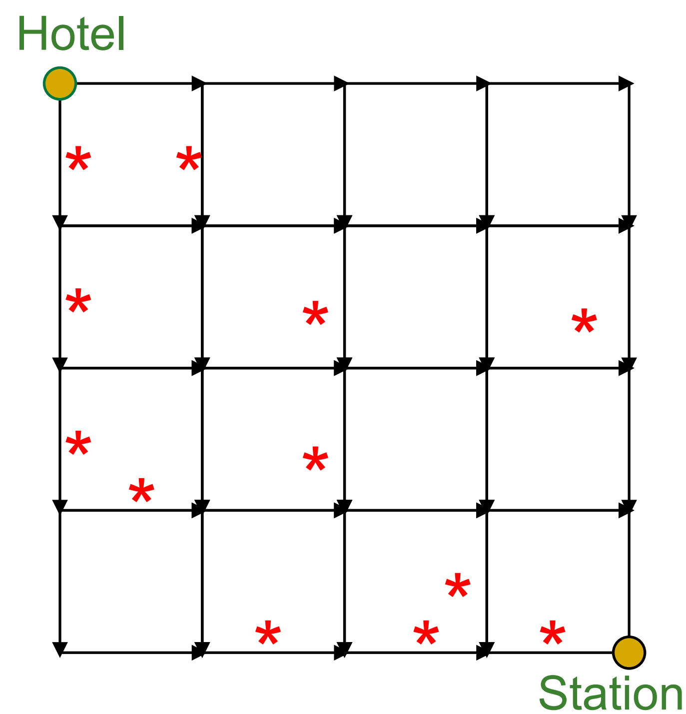
- Imagine that you are a tourist in Manhattan, whose streets are represented by the grid on the right.
- You are leaving town, and you want to see as many attractions (represented by *) as possible.



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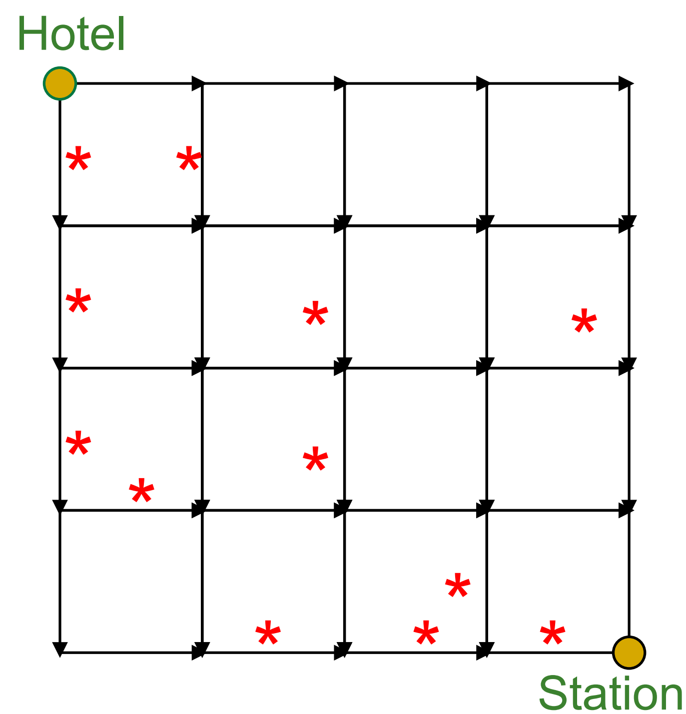

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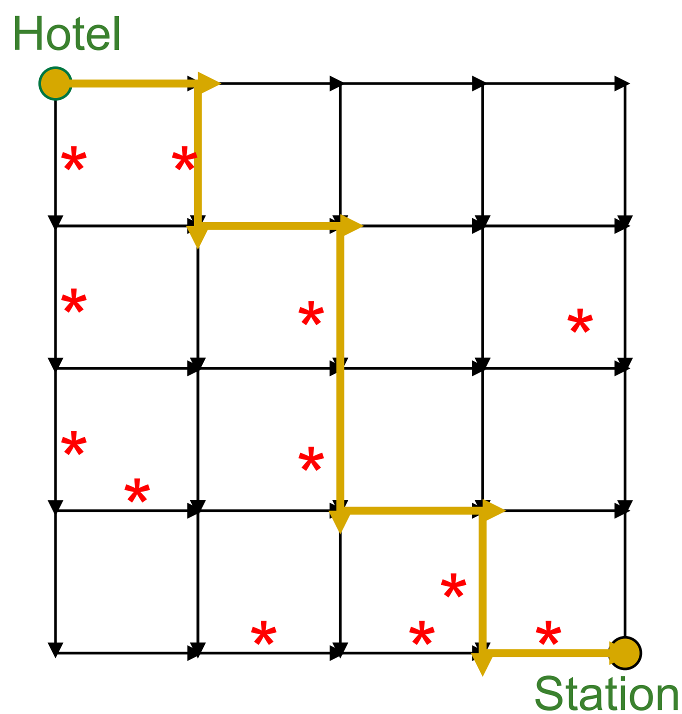

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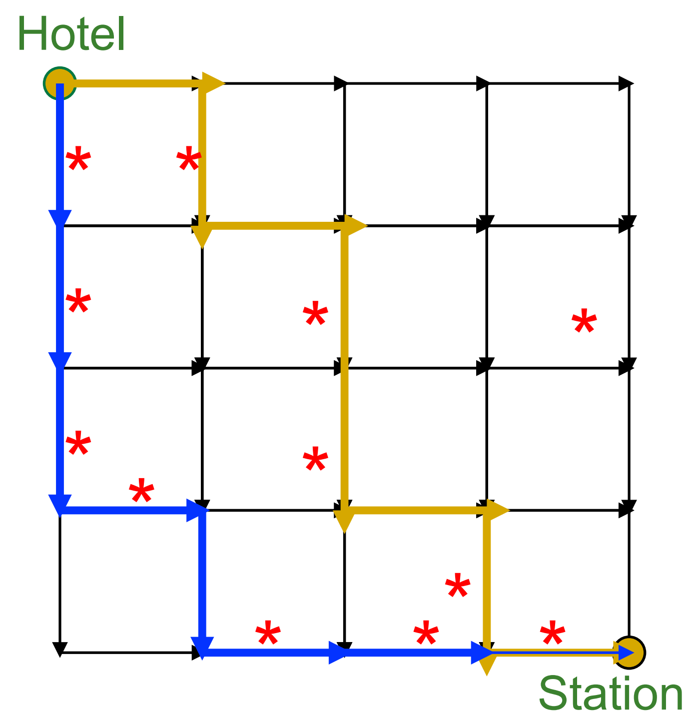


Manhattan Tourist Problem (MTP): Formulation

- 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.*"

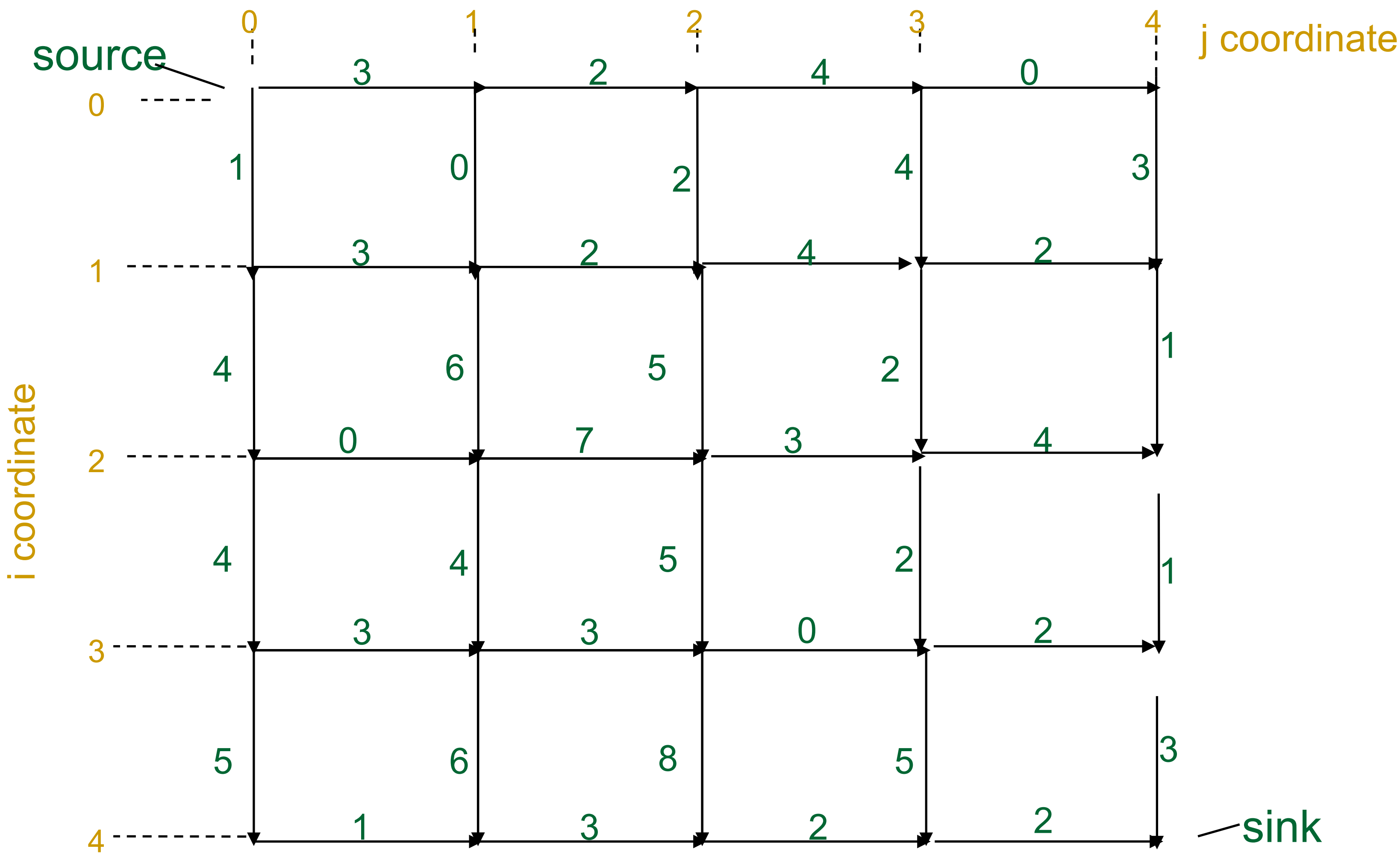
- Output: A longest path in ***G*** from "*source*" to "*sink.*"

MTP Greedy Algorithm

- Our first try at solving the MTP will use a **greedy algorithm**.

- Main Idea: At each node (intersection), choose the edge (street) departing that node which has the greatest weight.

MTP Greedy Algorithm: Example



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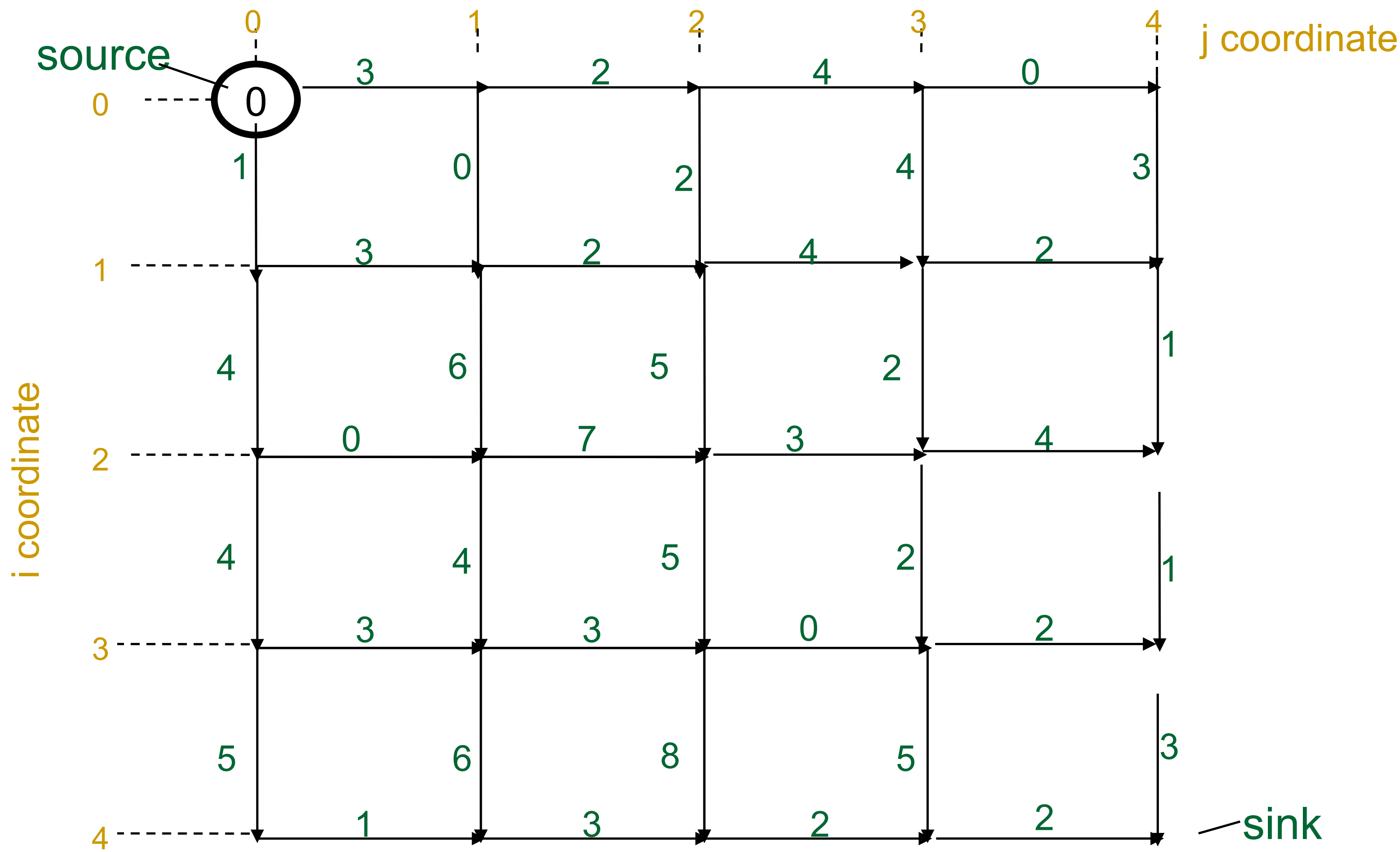

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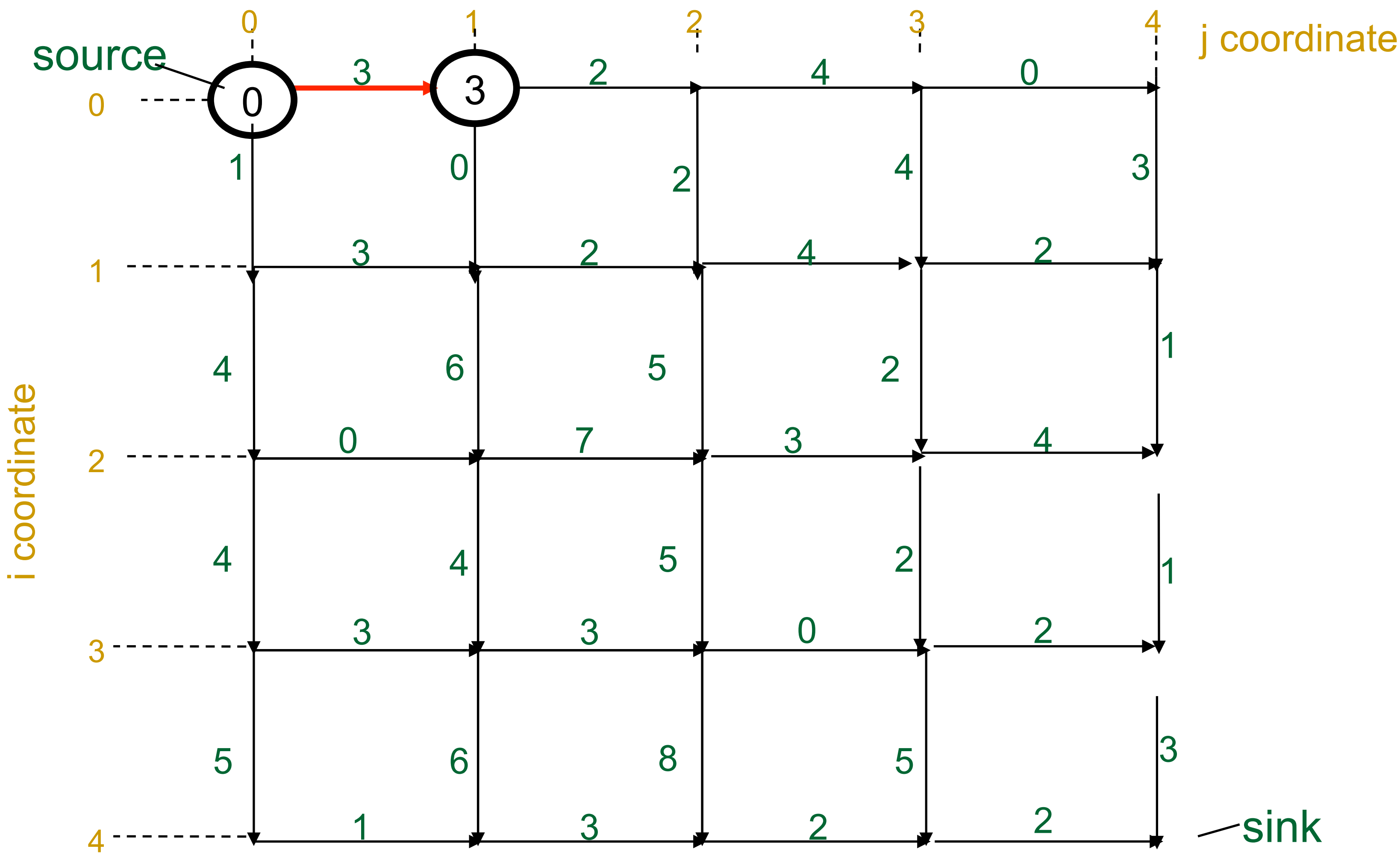

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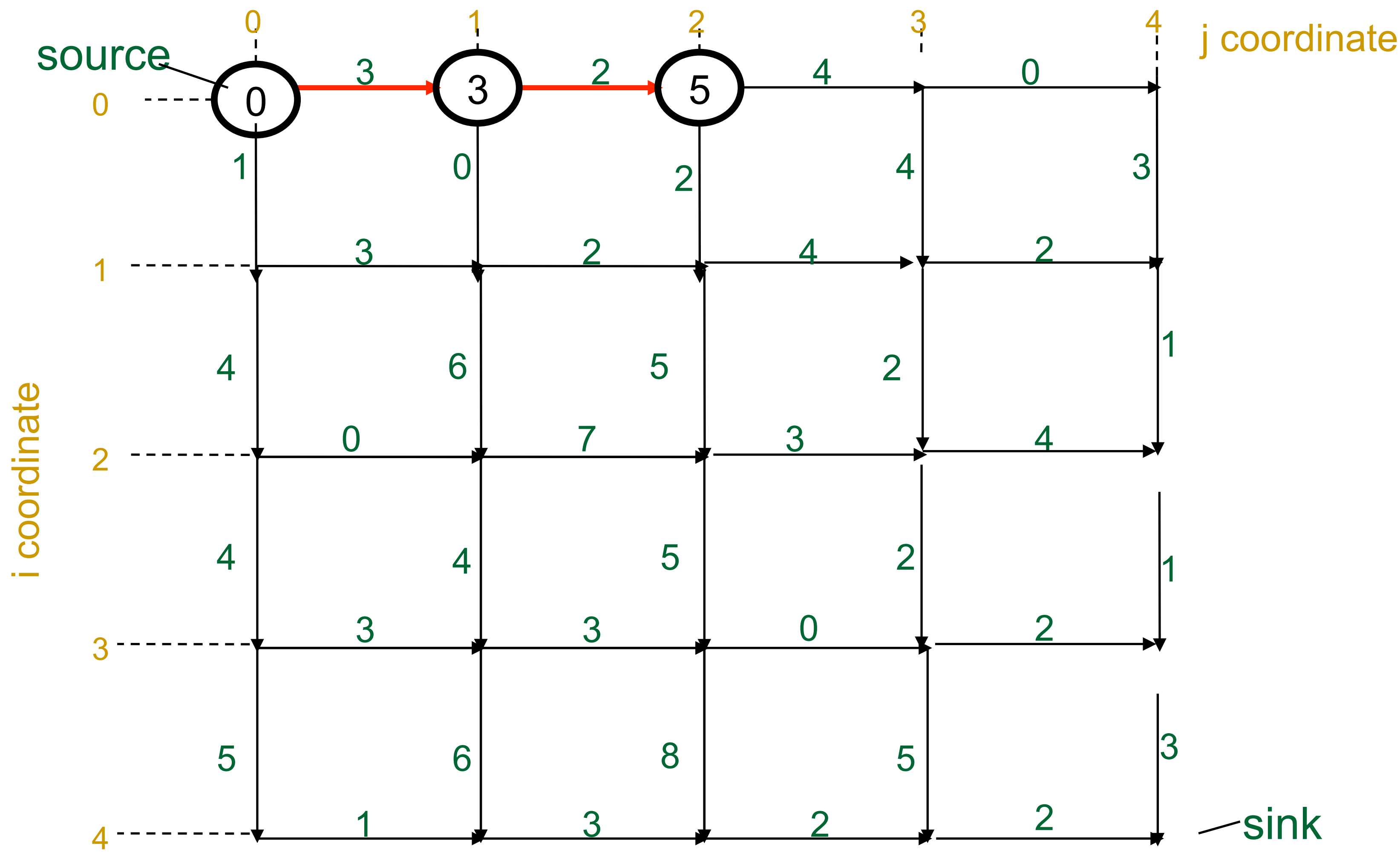

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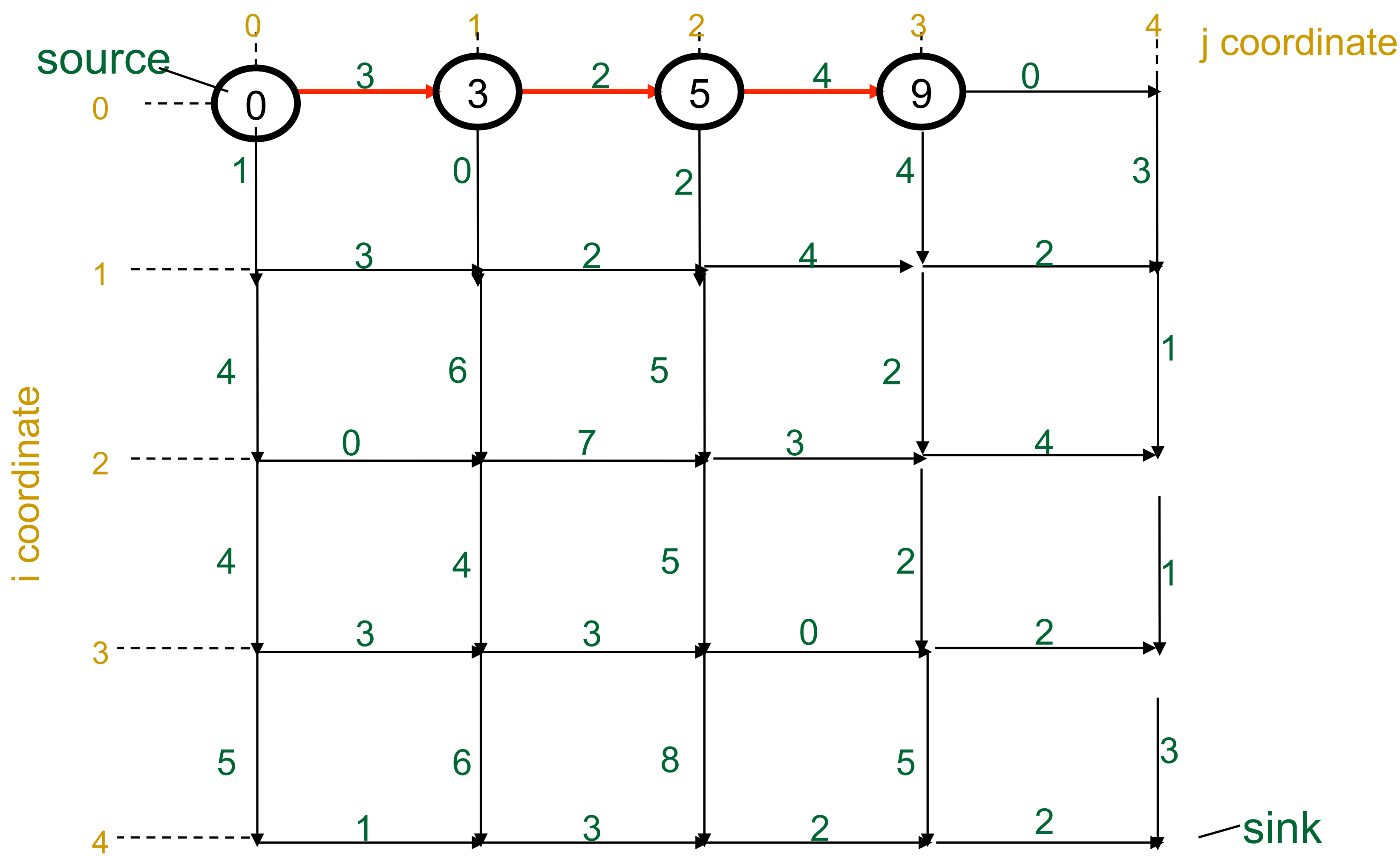

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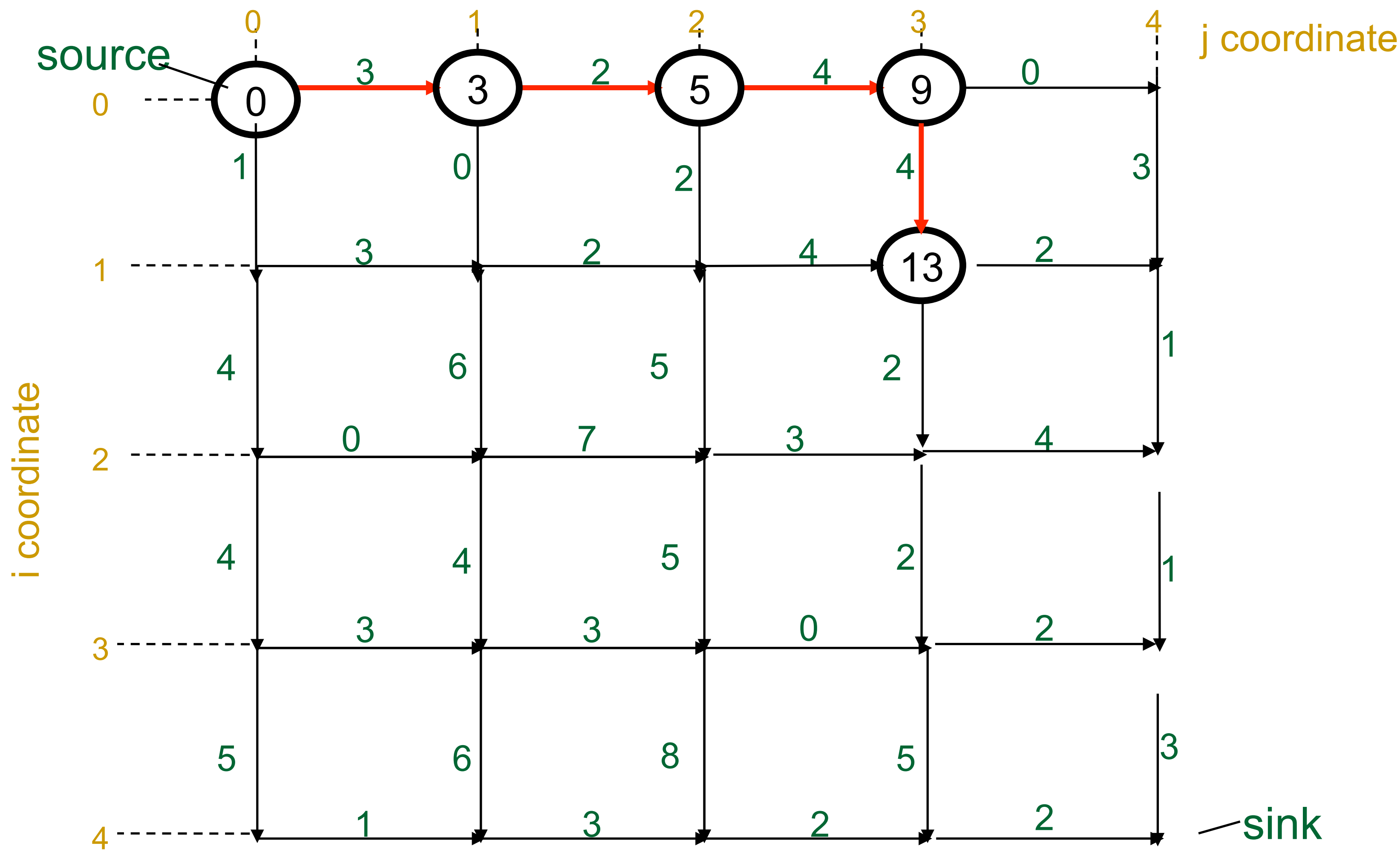

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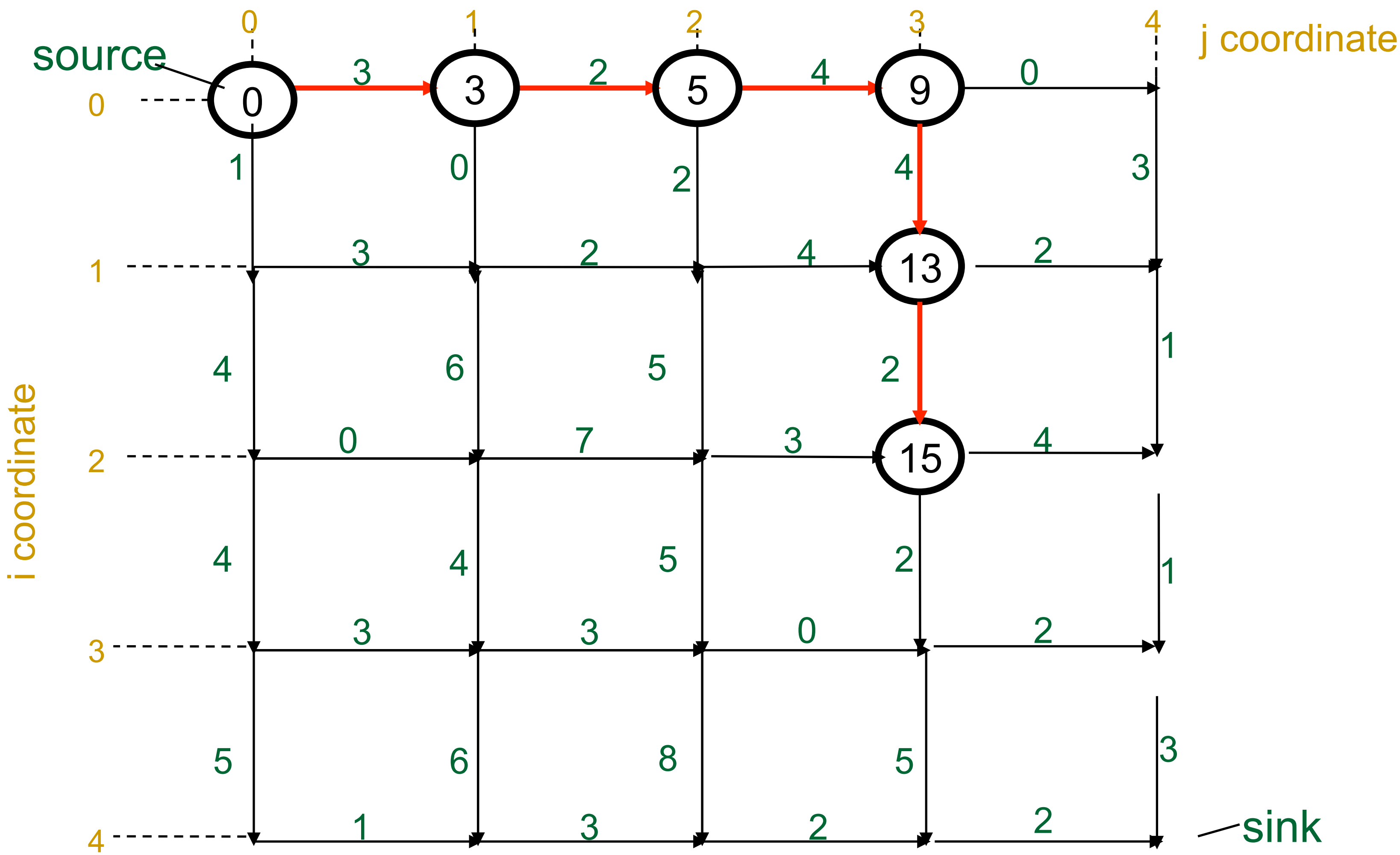

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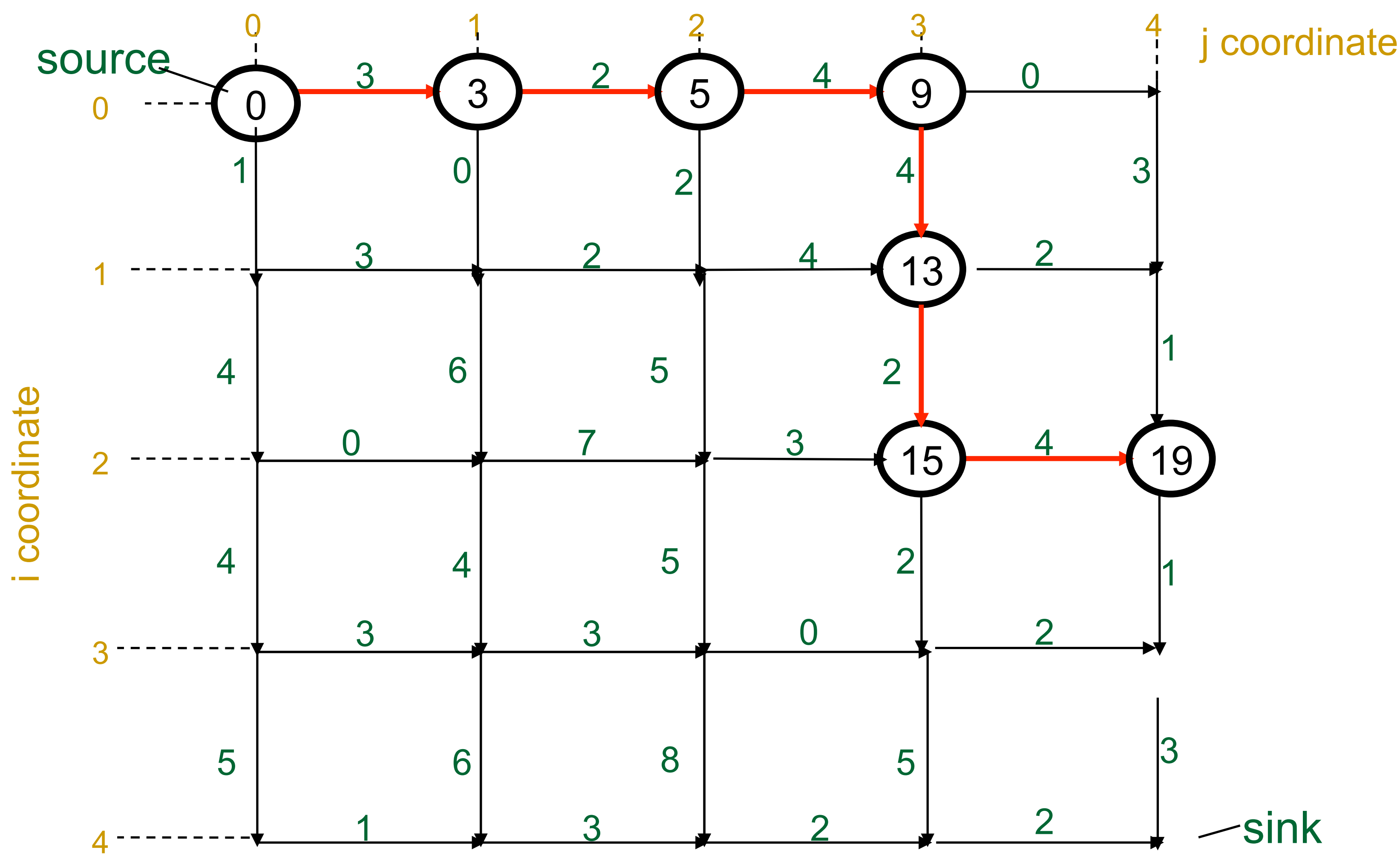

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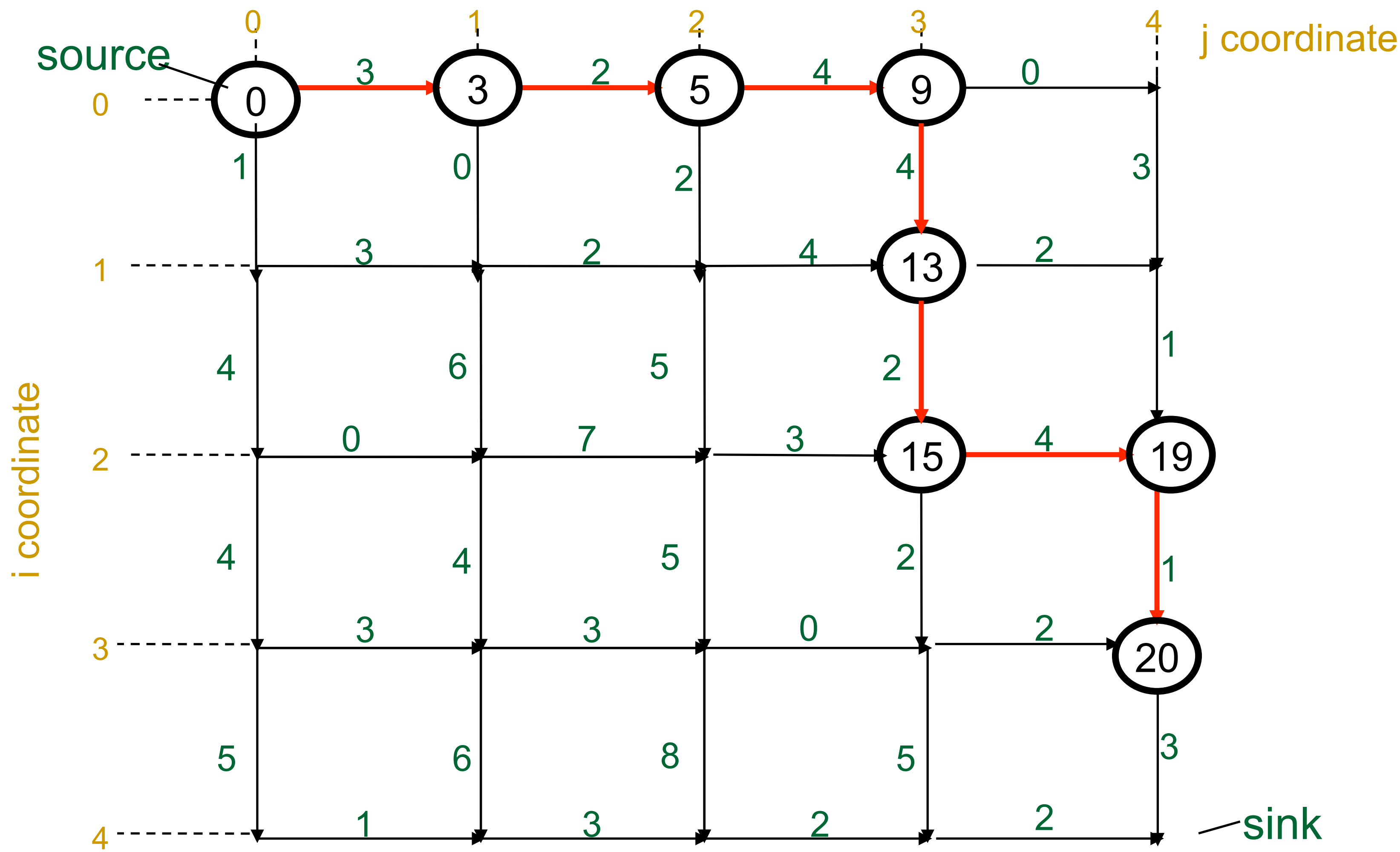

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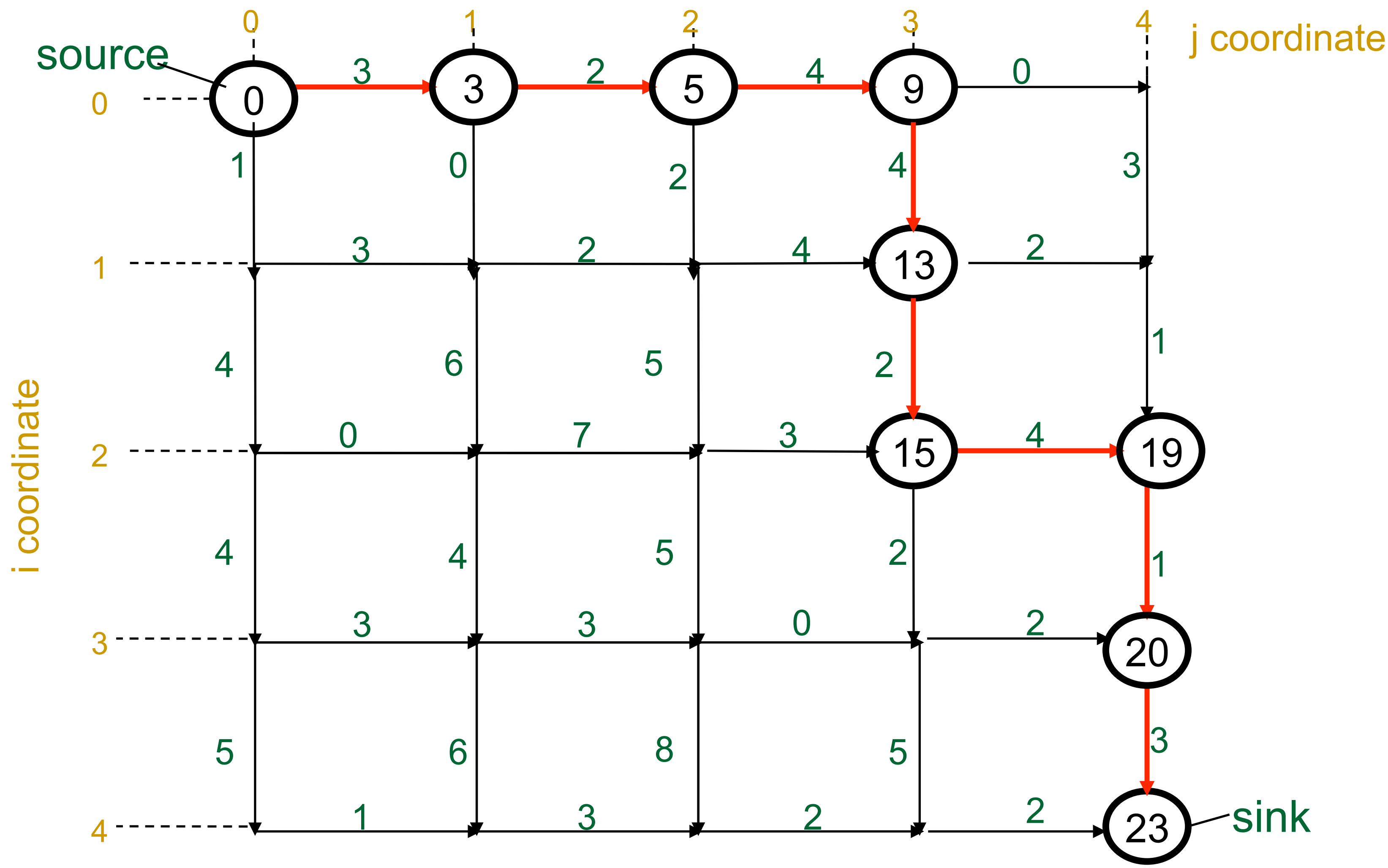
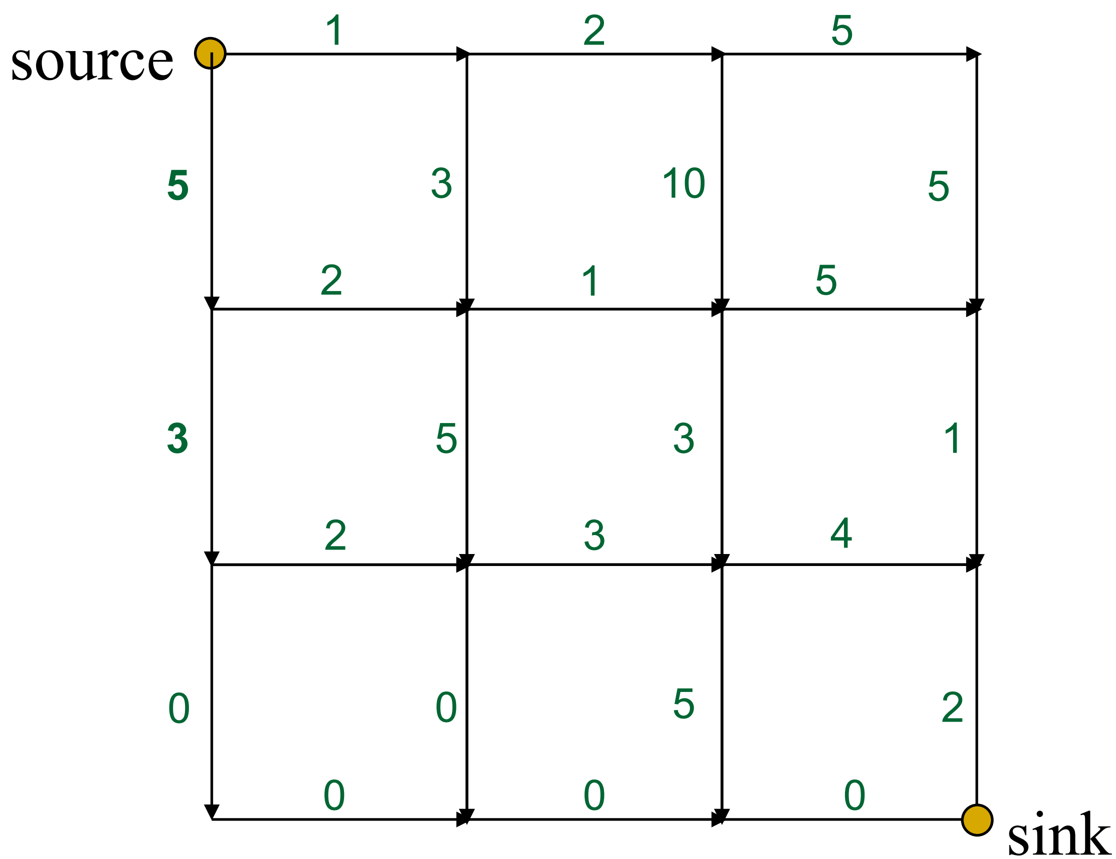


MTP Greedy Algorithm Is Not Optimal



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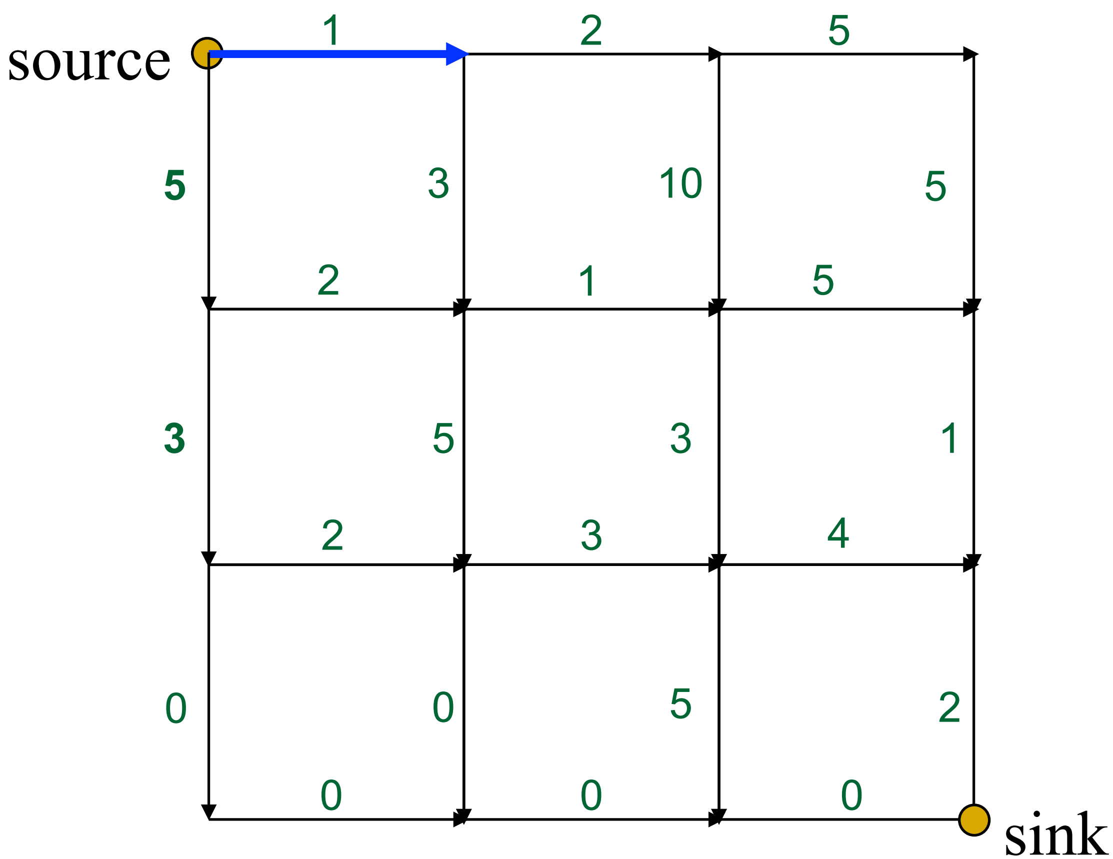

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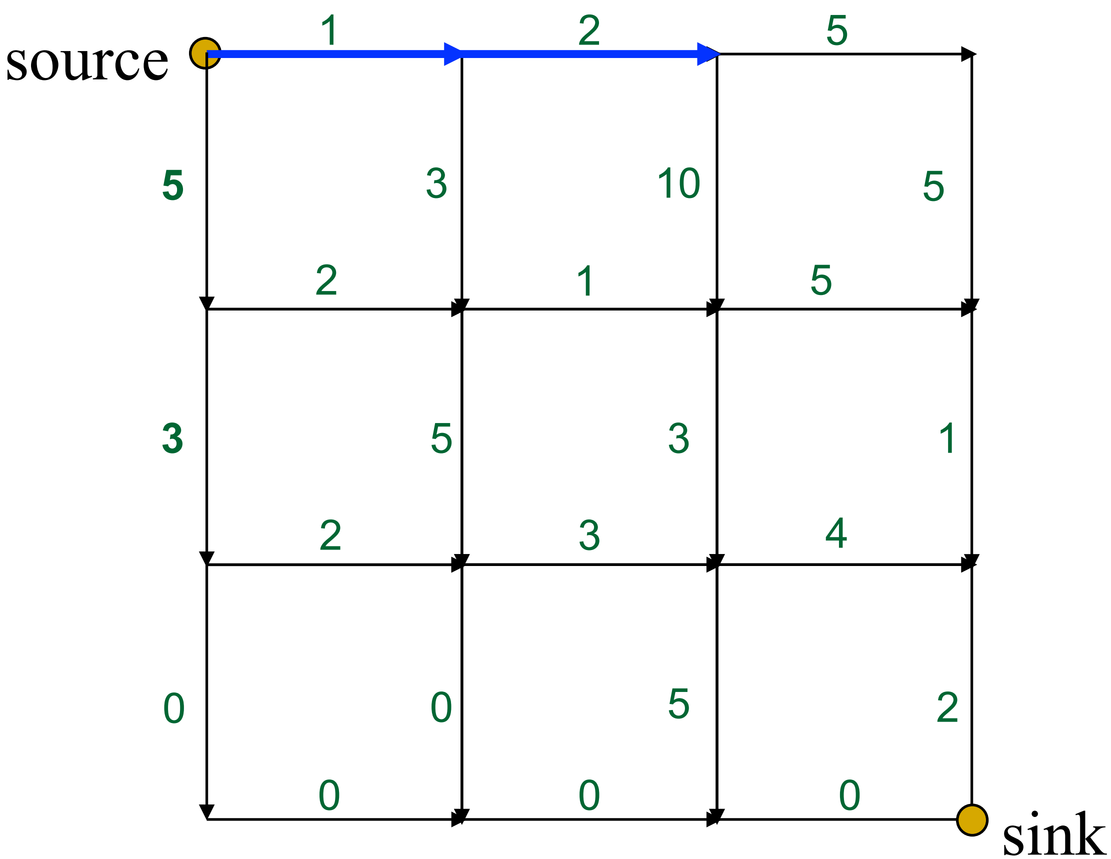

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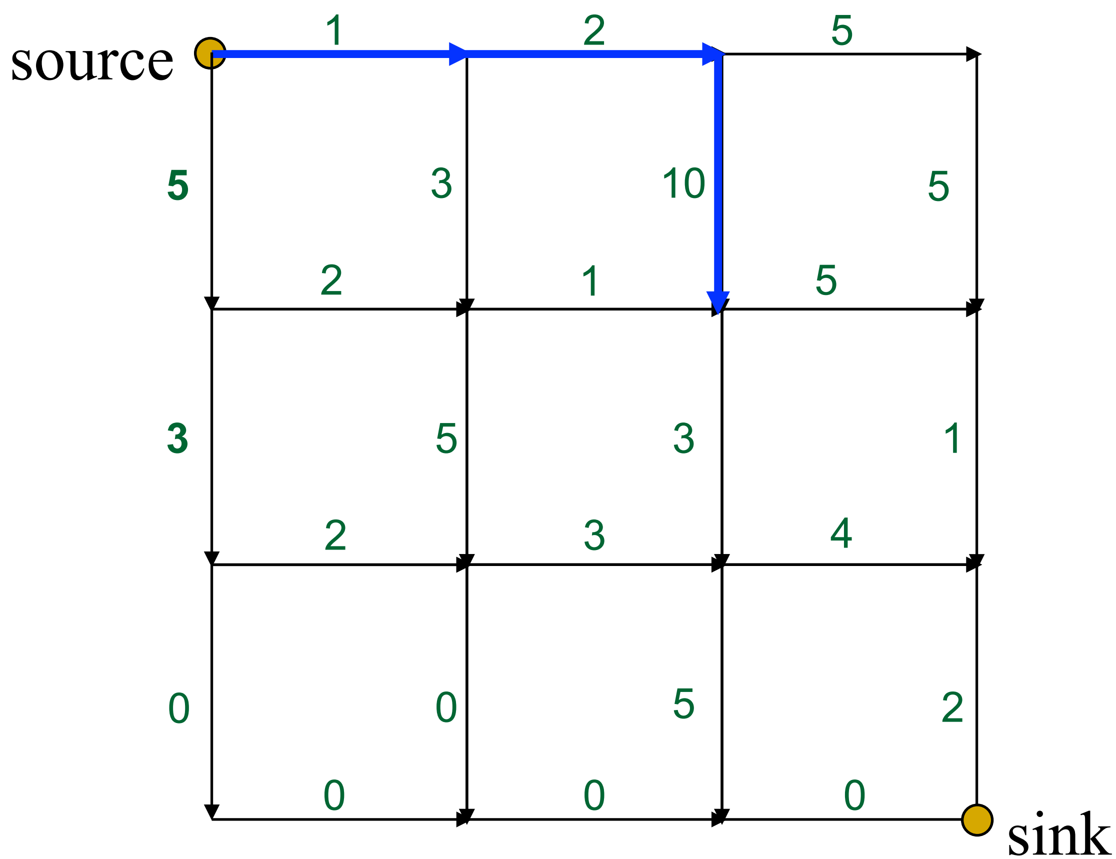

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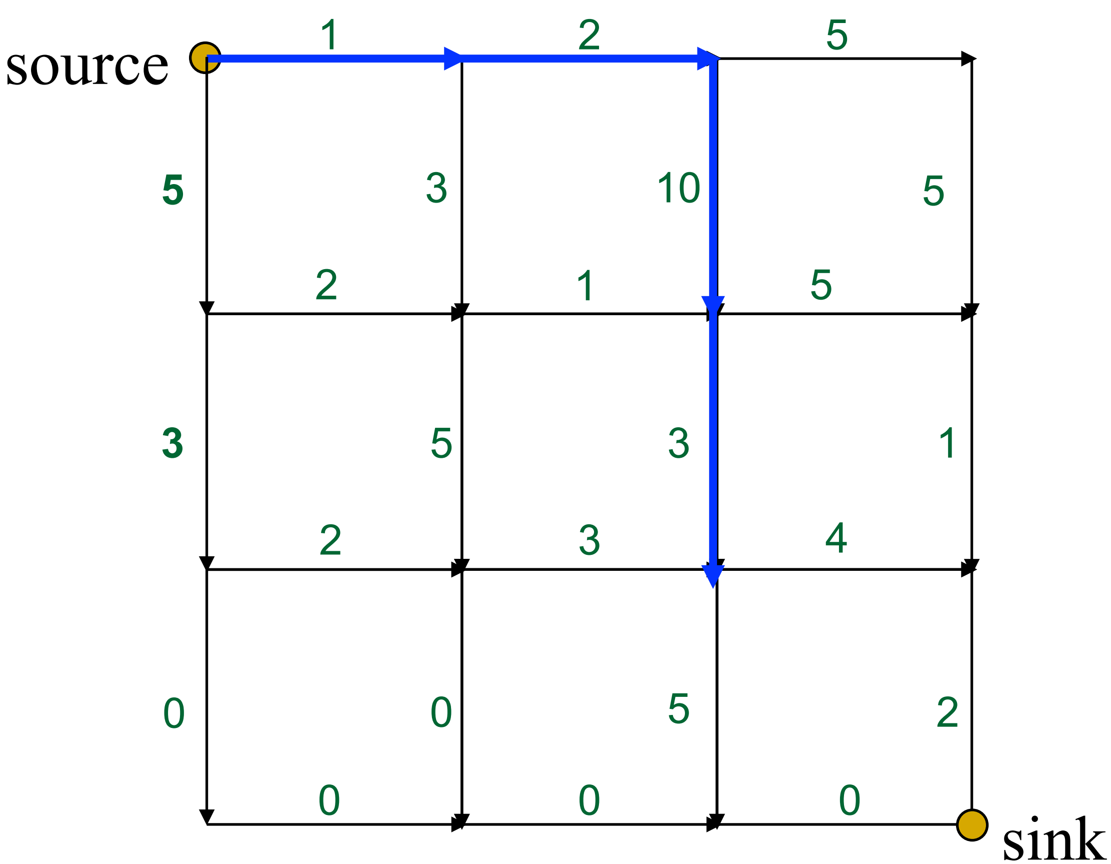

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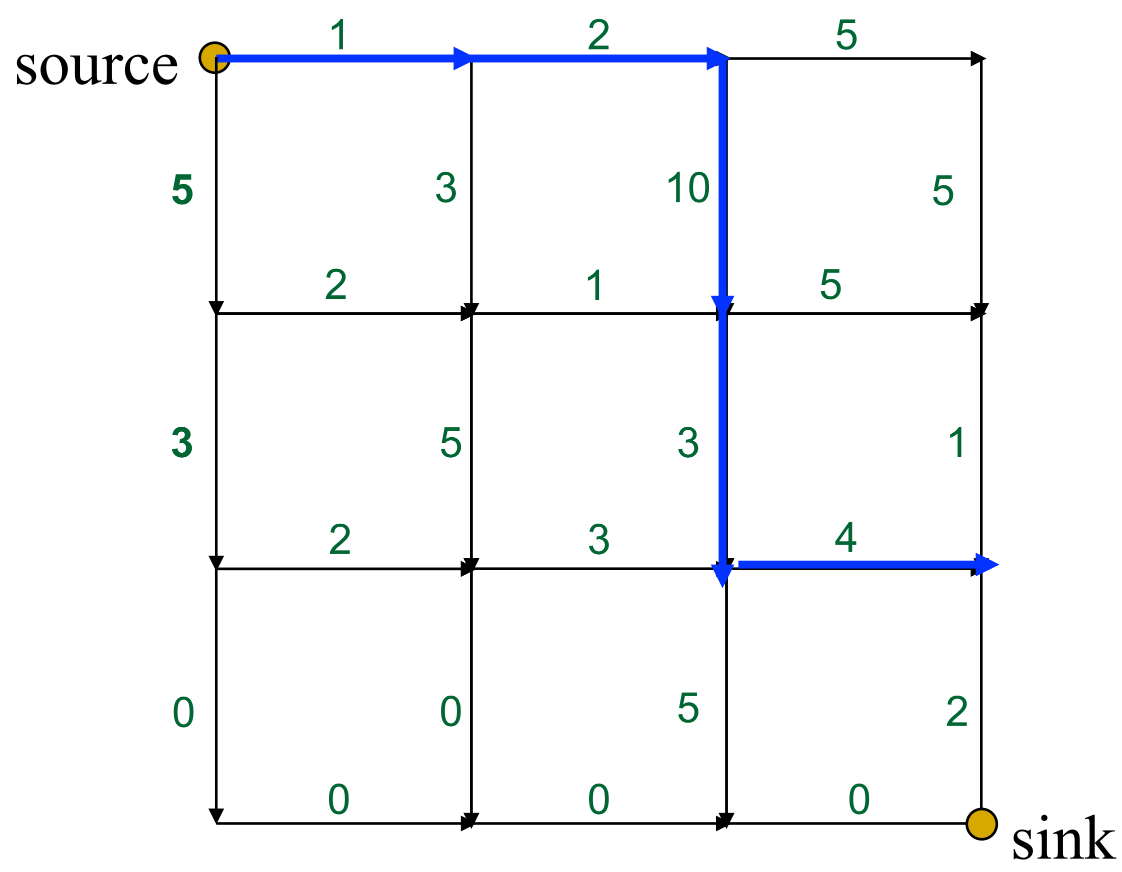

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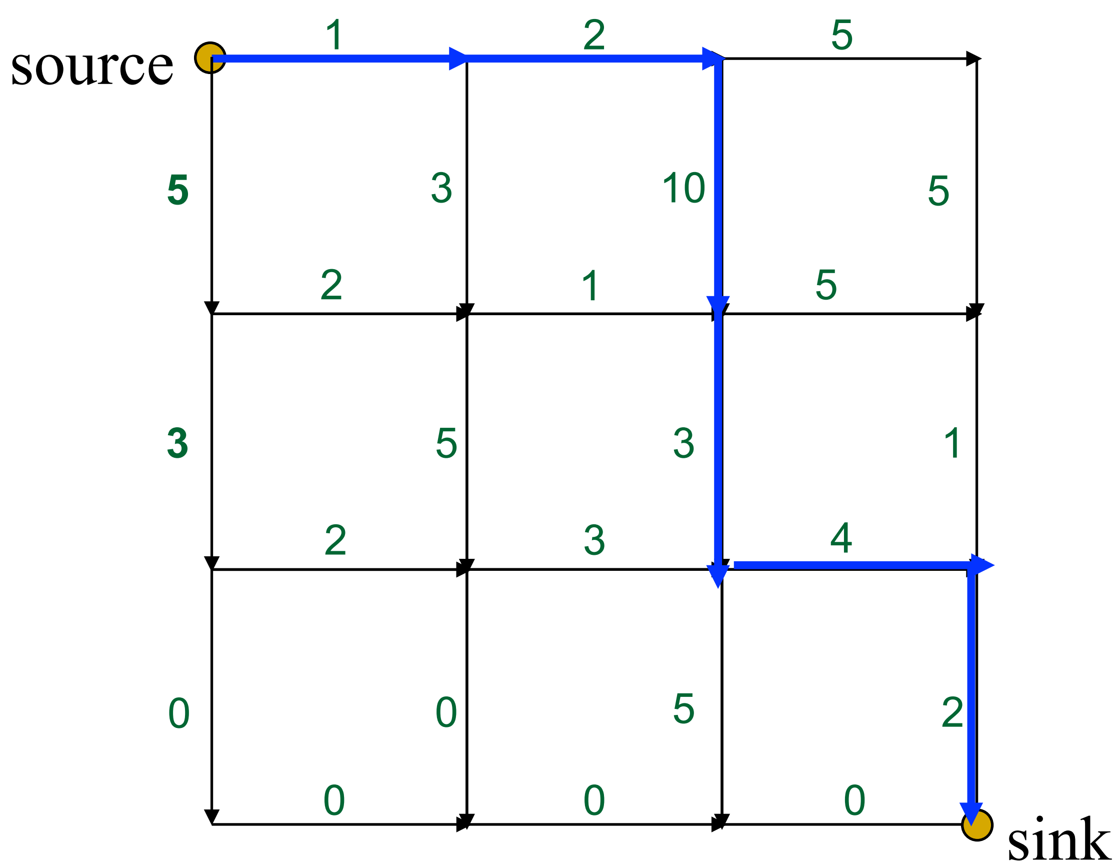

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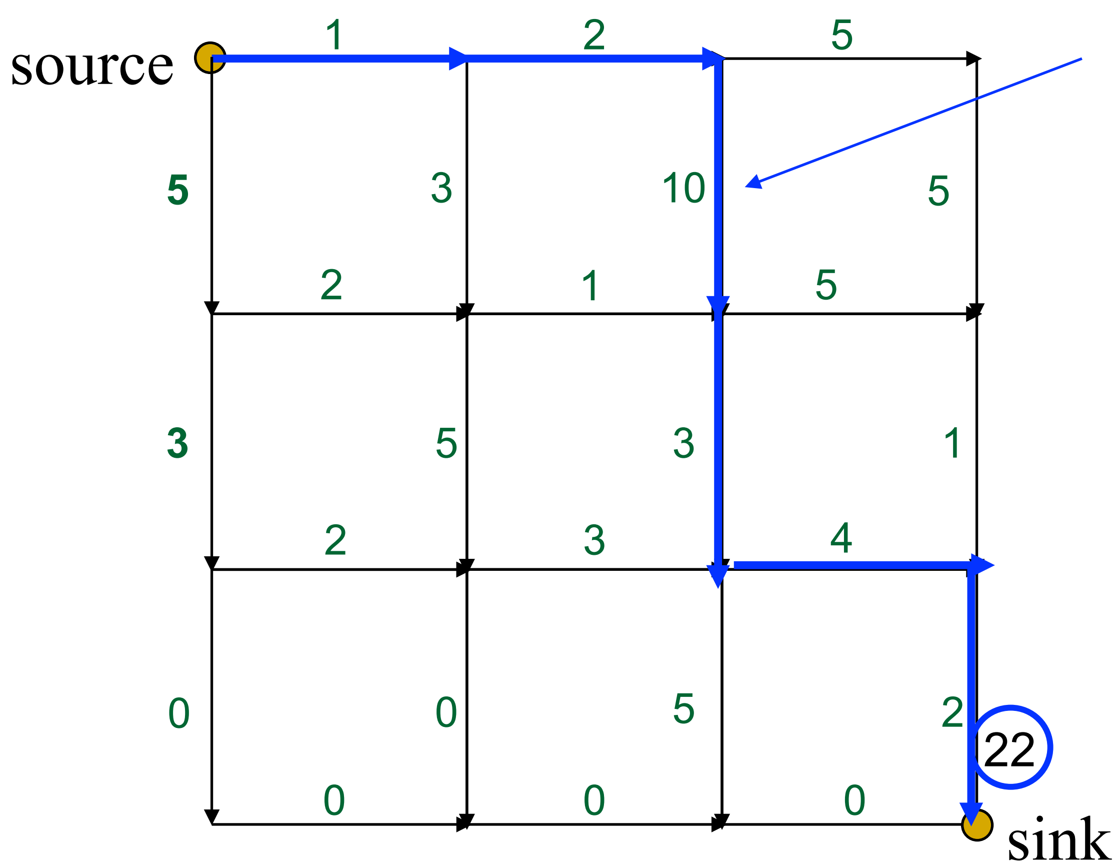

This weight heavily influences the choice of optimal path.

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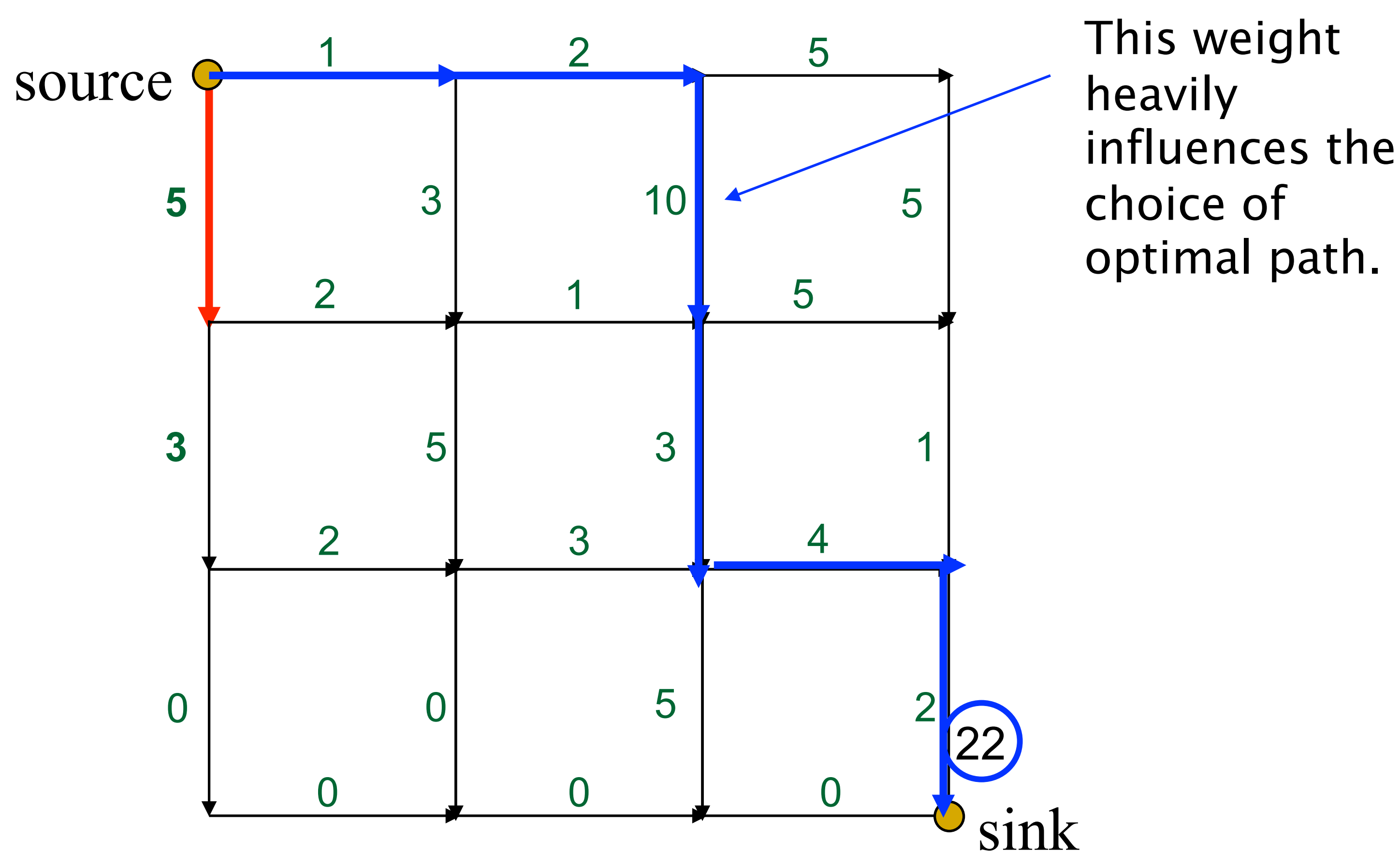

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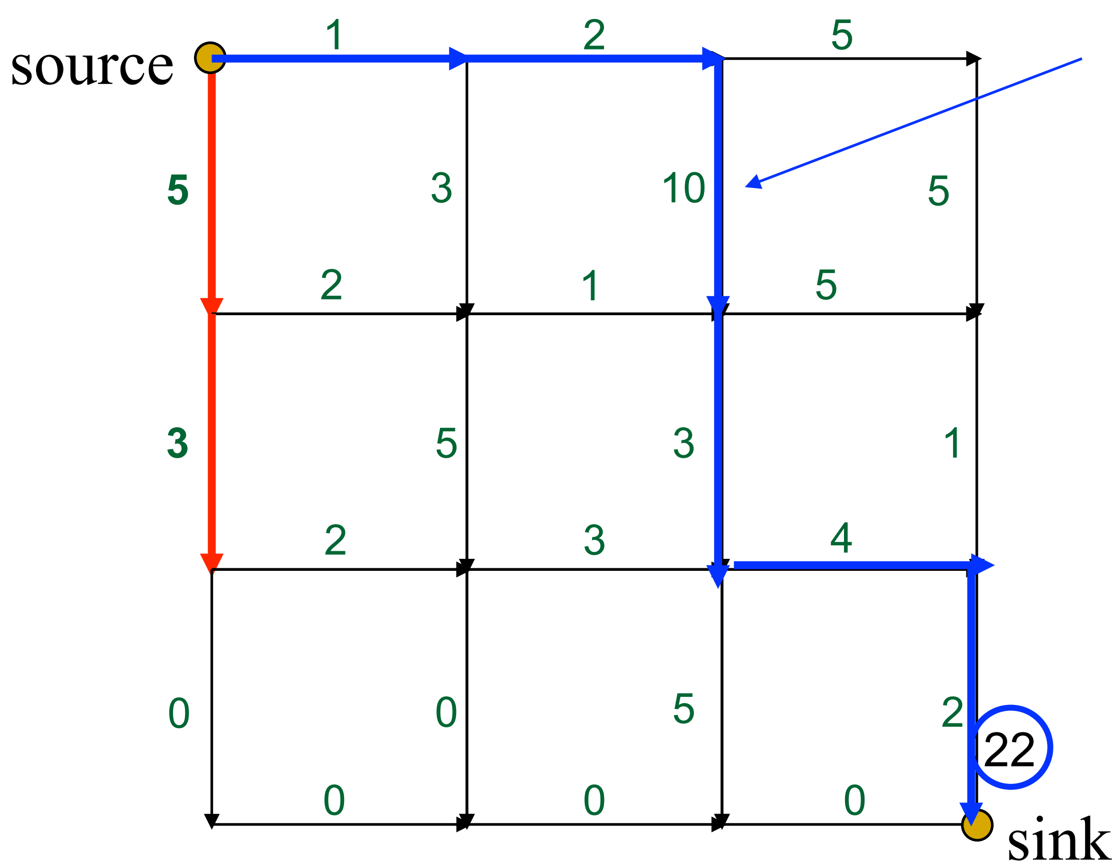

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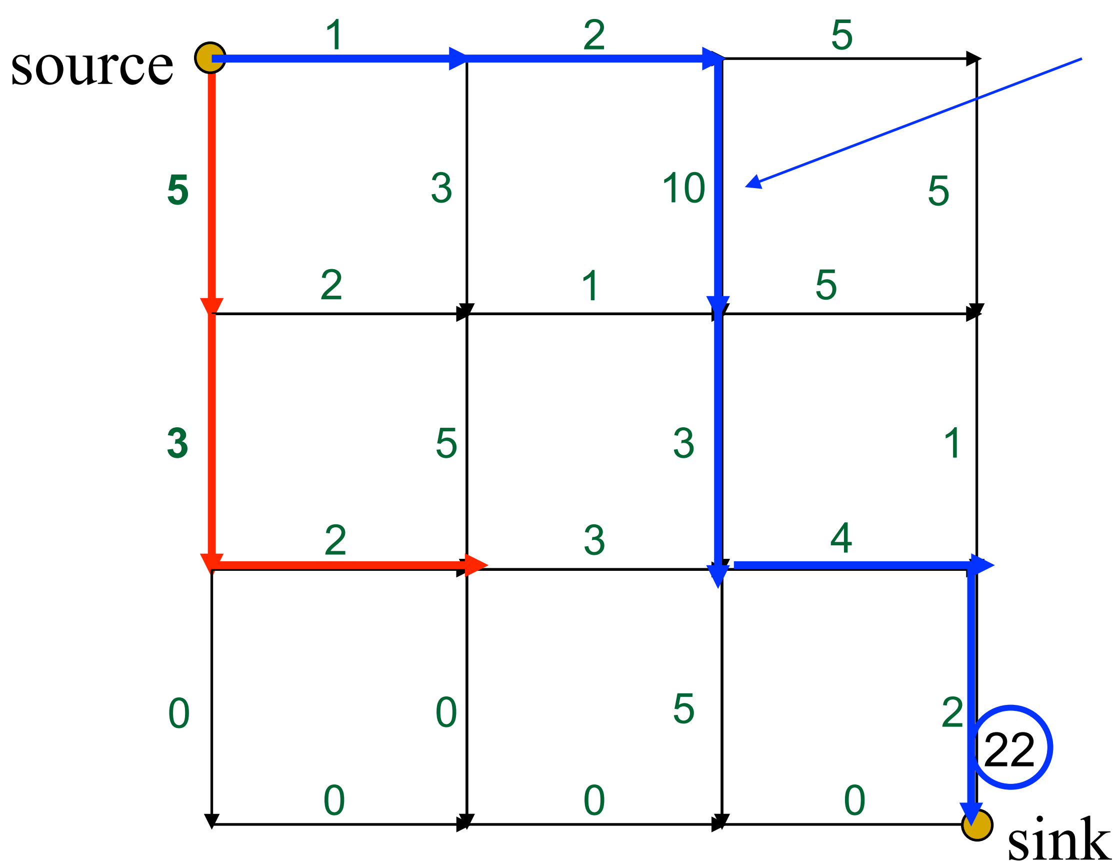

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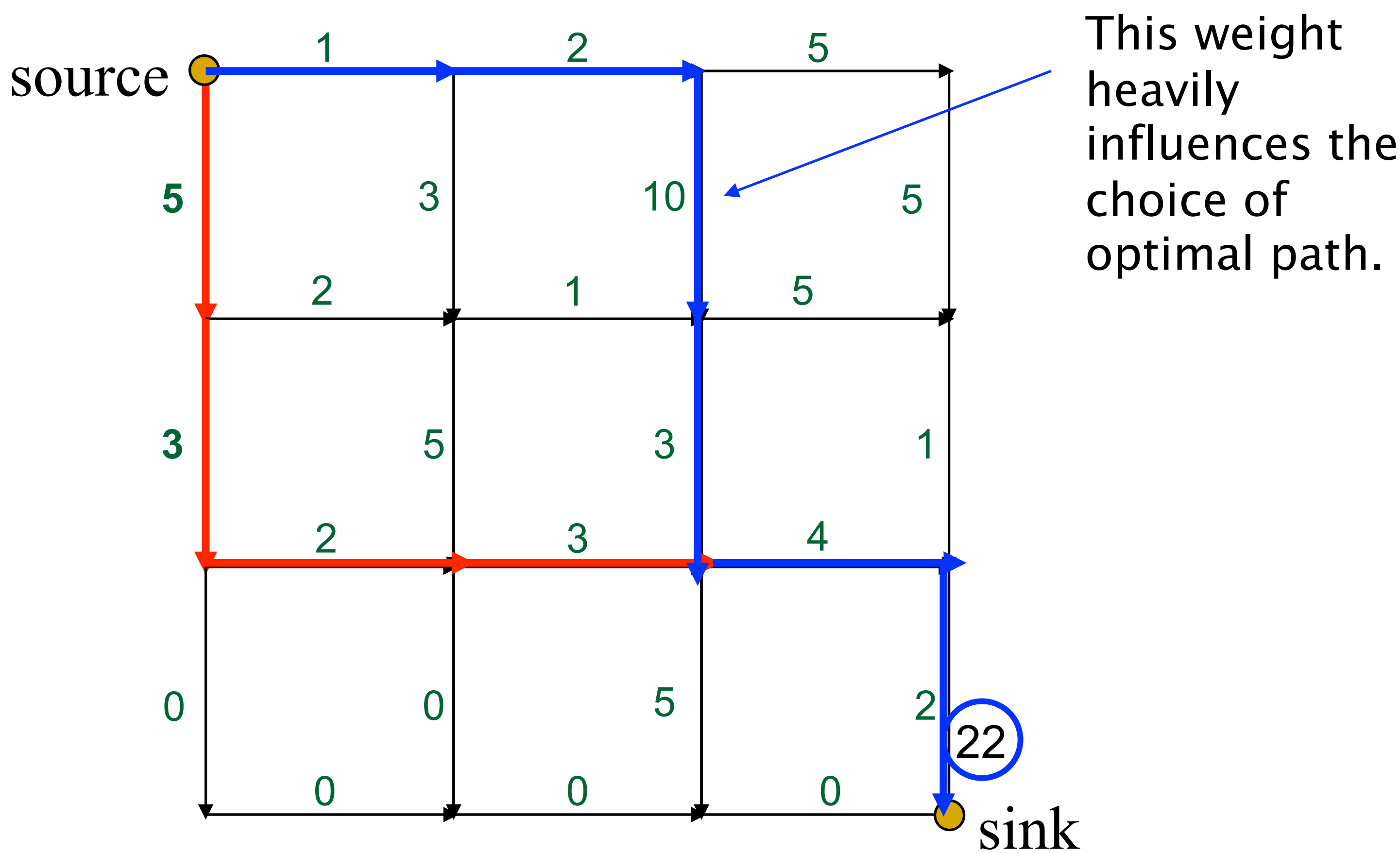

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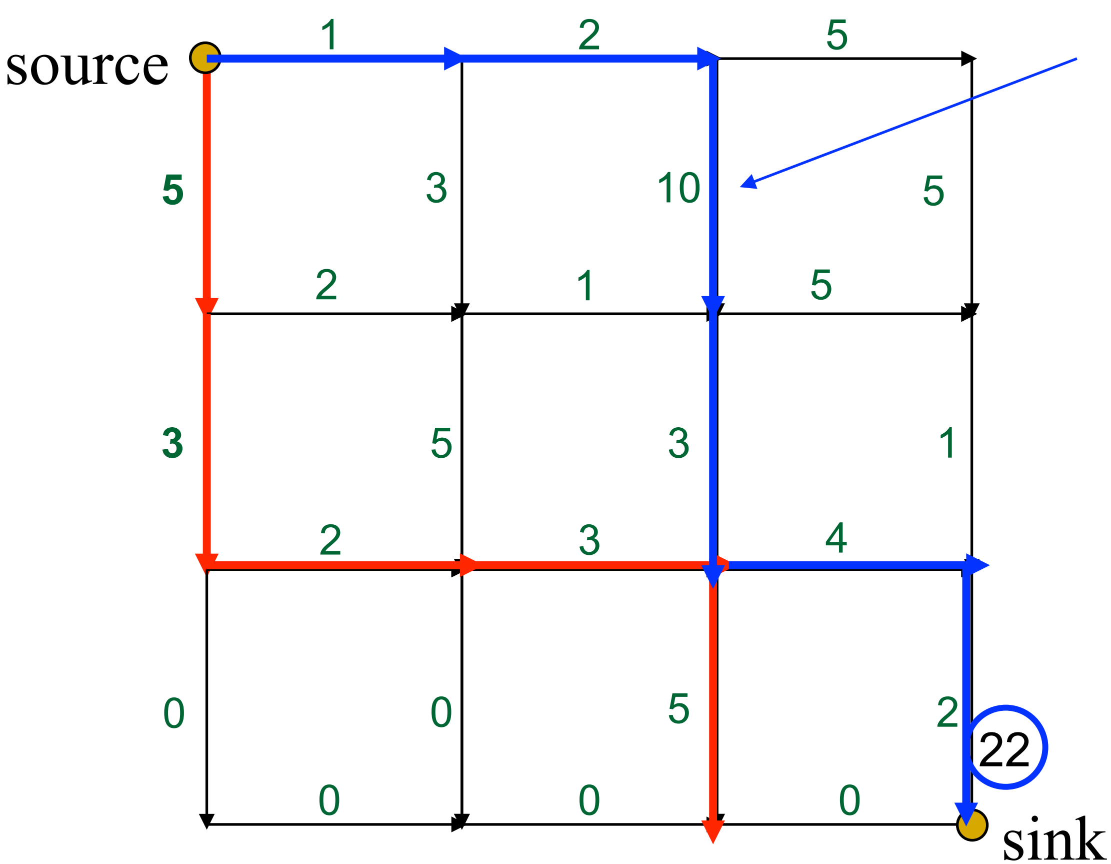

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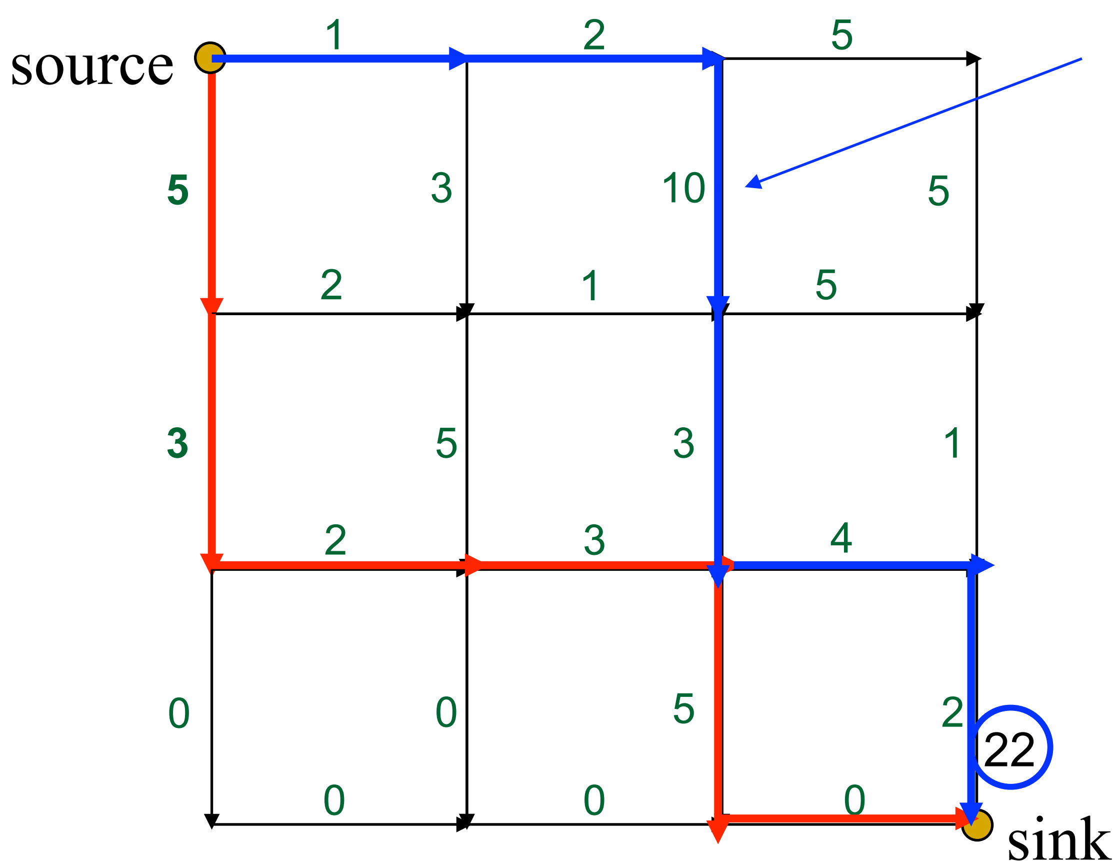

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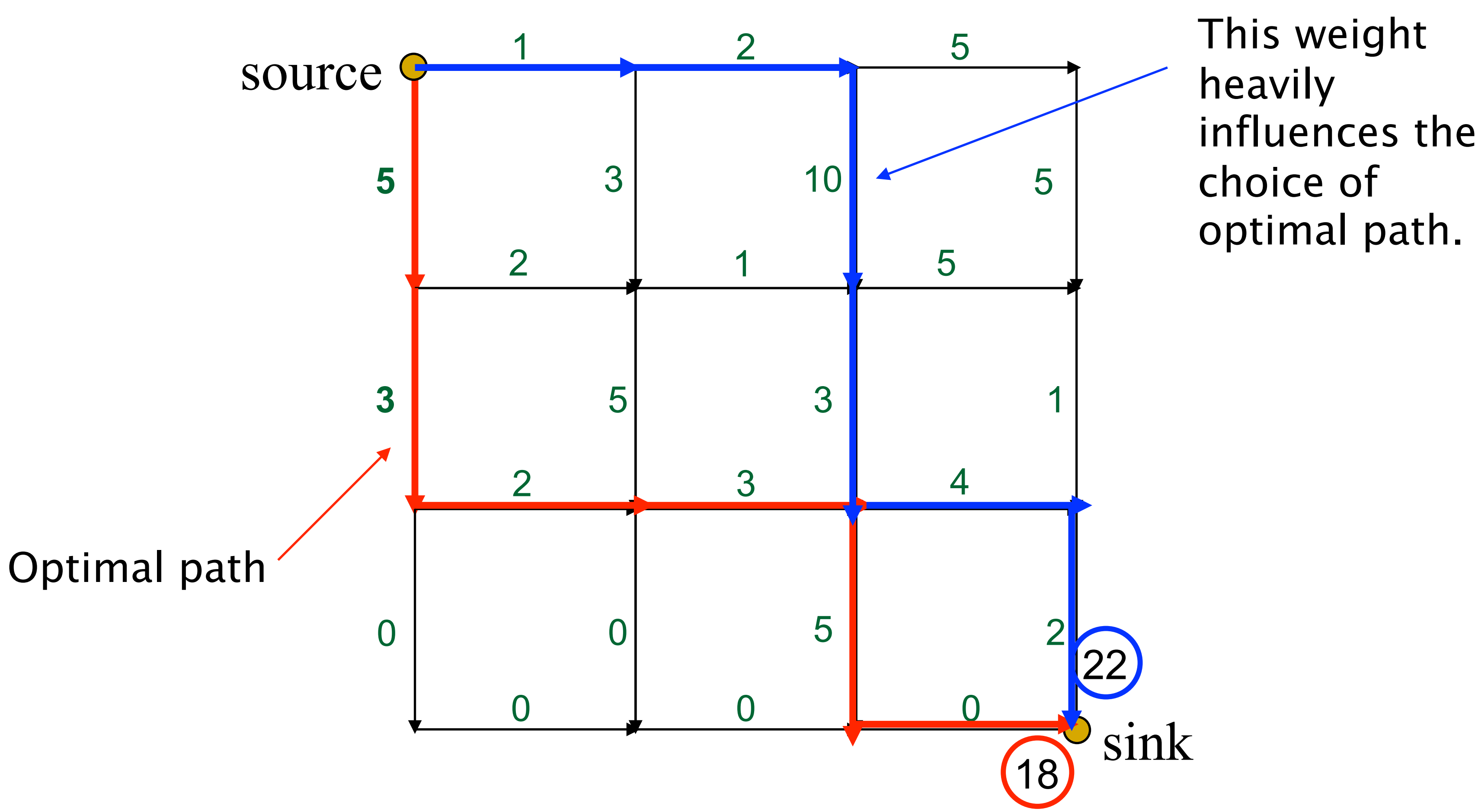


MTP: Simple Recursive Program

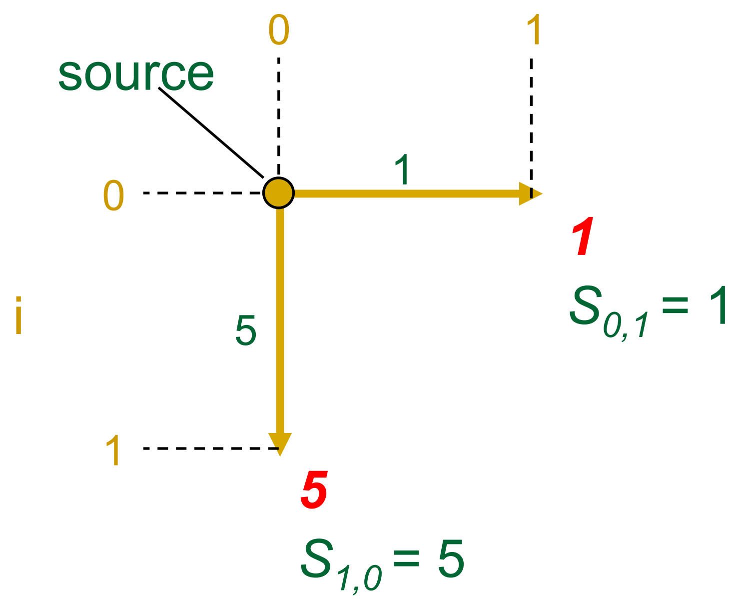
```
MT(n,m)
  if n=0 or m=0
    return MT(n,m)
  x ← MT(n-1,m)+
            length of the edge from (n- 1,m) to (n,m)
  y ← MT(n,m-1)+
            length of the edge from (n,m-1) to (n,m)
  return max{x,y}
```

MTP: Simple Recursive Program

1. **MT**(n,m)
2. **if** $n=0$ or $m=0$
3. **return** $MT(n,m)$
4. $x \leftarrow MT(n-1,m) +$ length of the edge from $(n-1,m)$ to (n,m)
5. $y \leftarrow MT(n,m-1) +$ length of the edge from $(n,m-1)$ to (n,m)
6. **return** $max\{x,y\}$

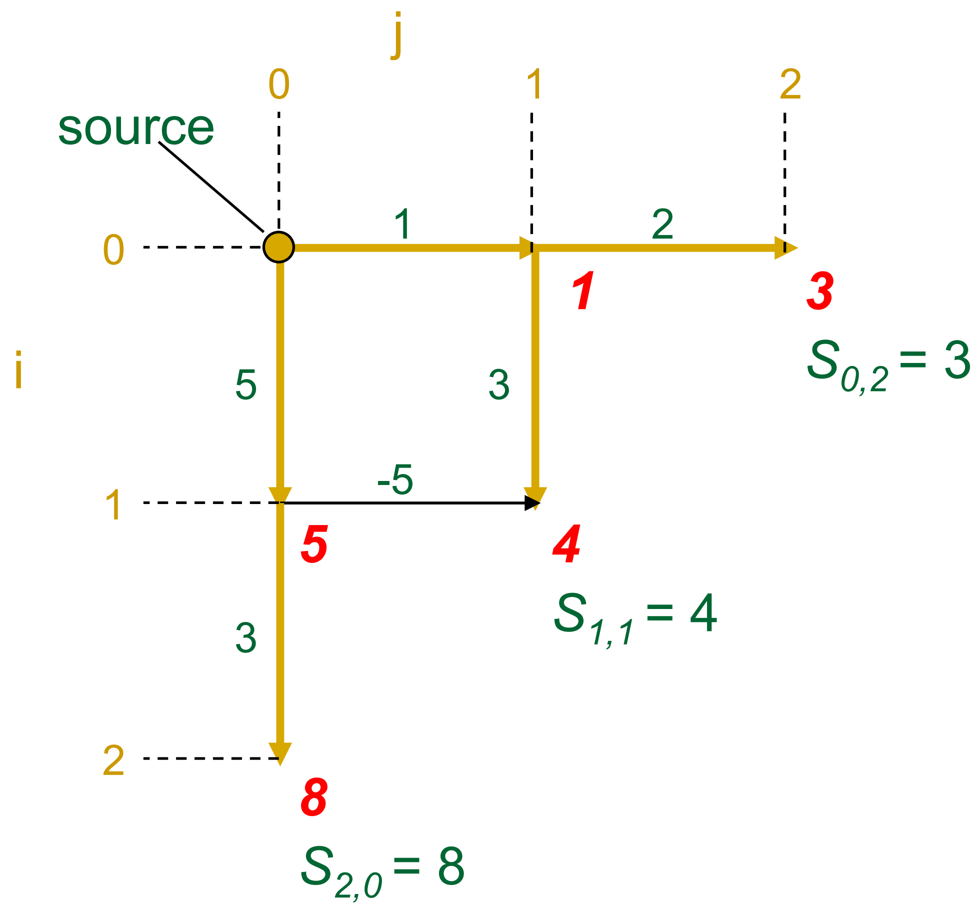
- **What's wrong with this approach?**

MTP: Dynamic Programming



- We calculate the optimal path score for each vertex in the graph.
- A given vertex's score is the maximum sum of incoming edge weight and prior vertex's score (along that incoming edge).

MTP: Dynamic Programming



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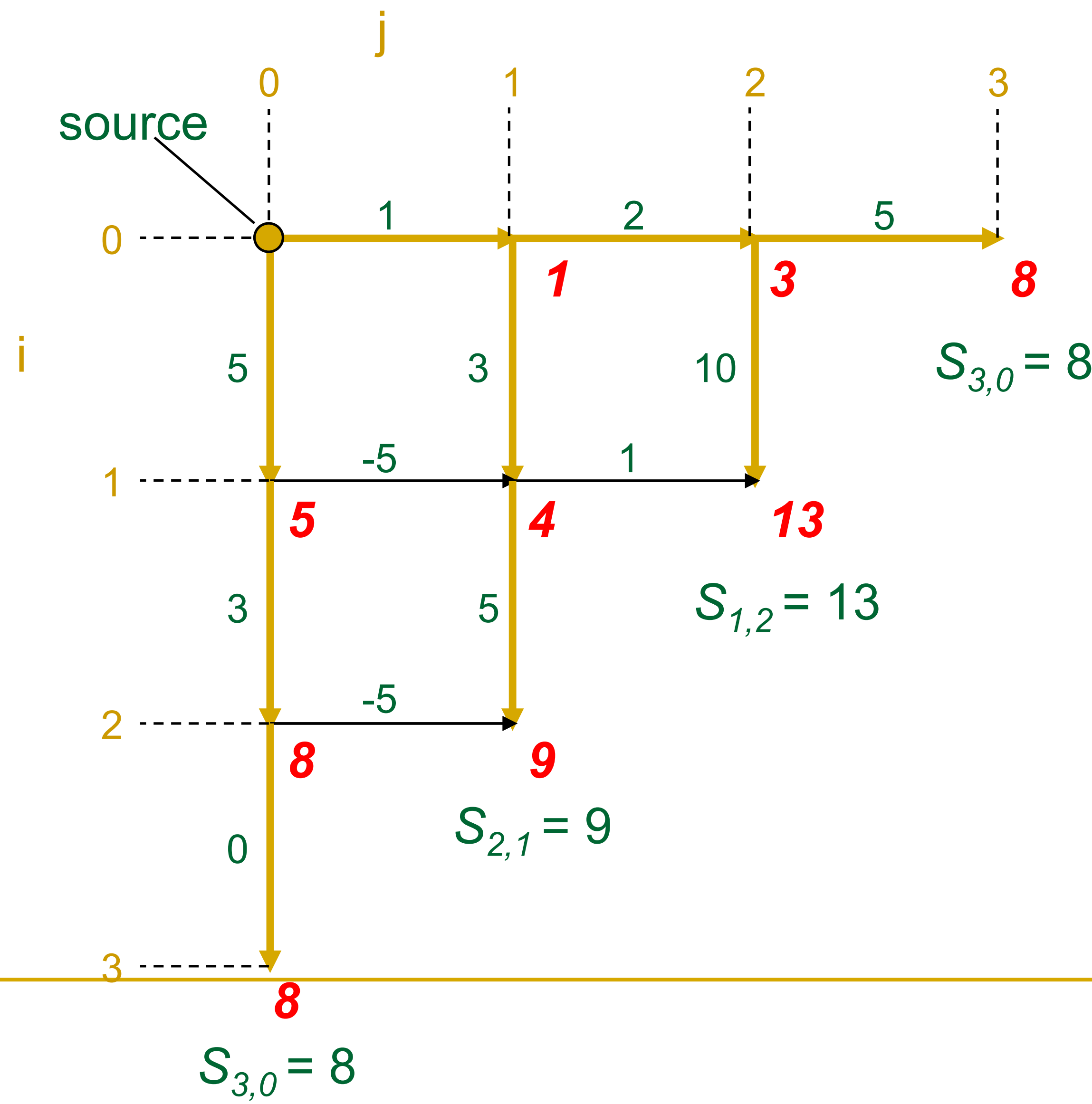

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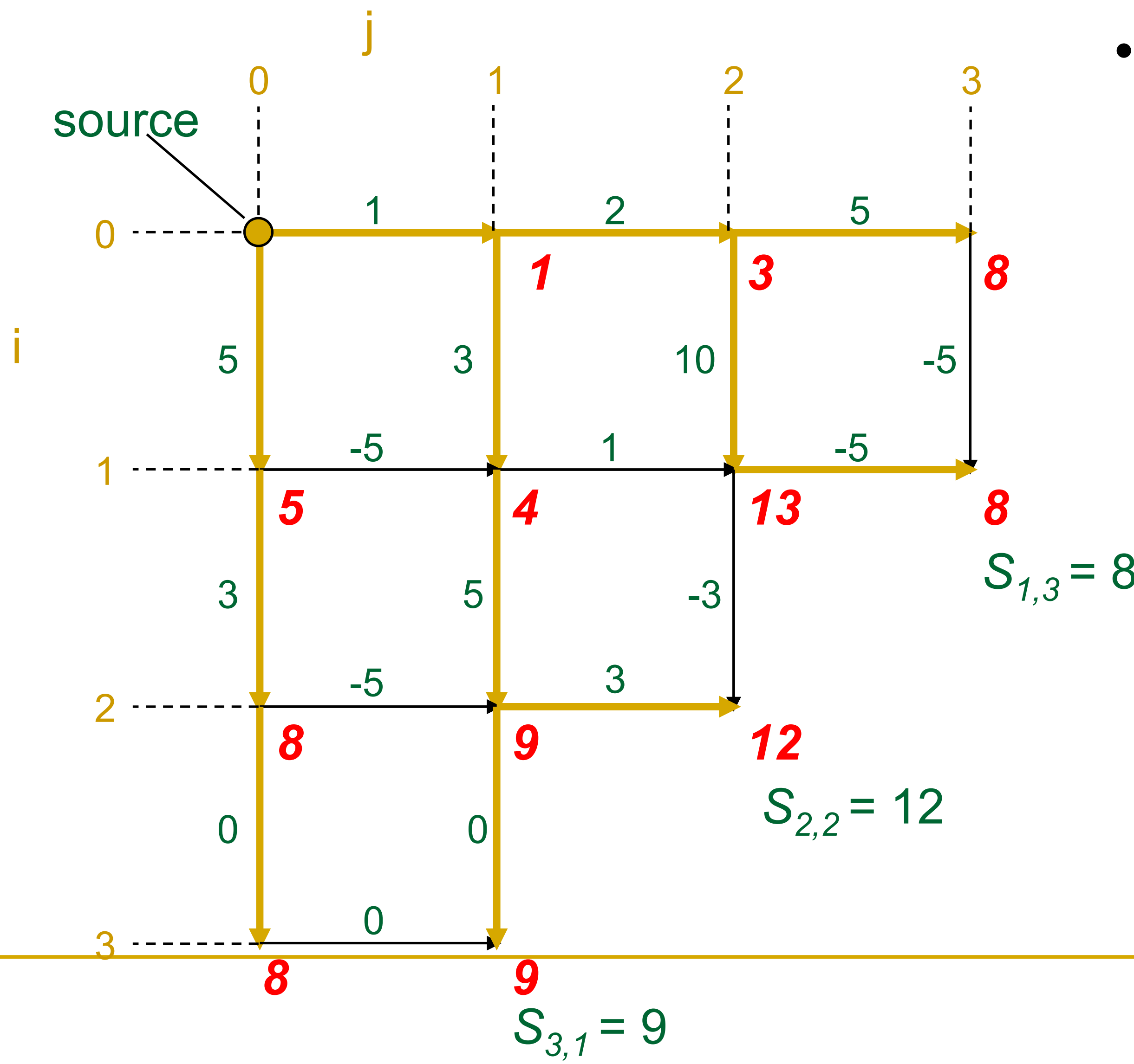

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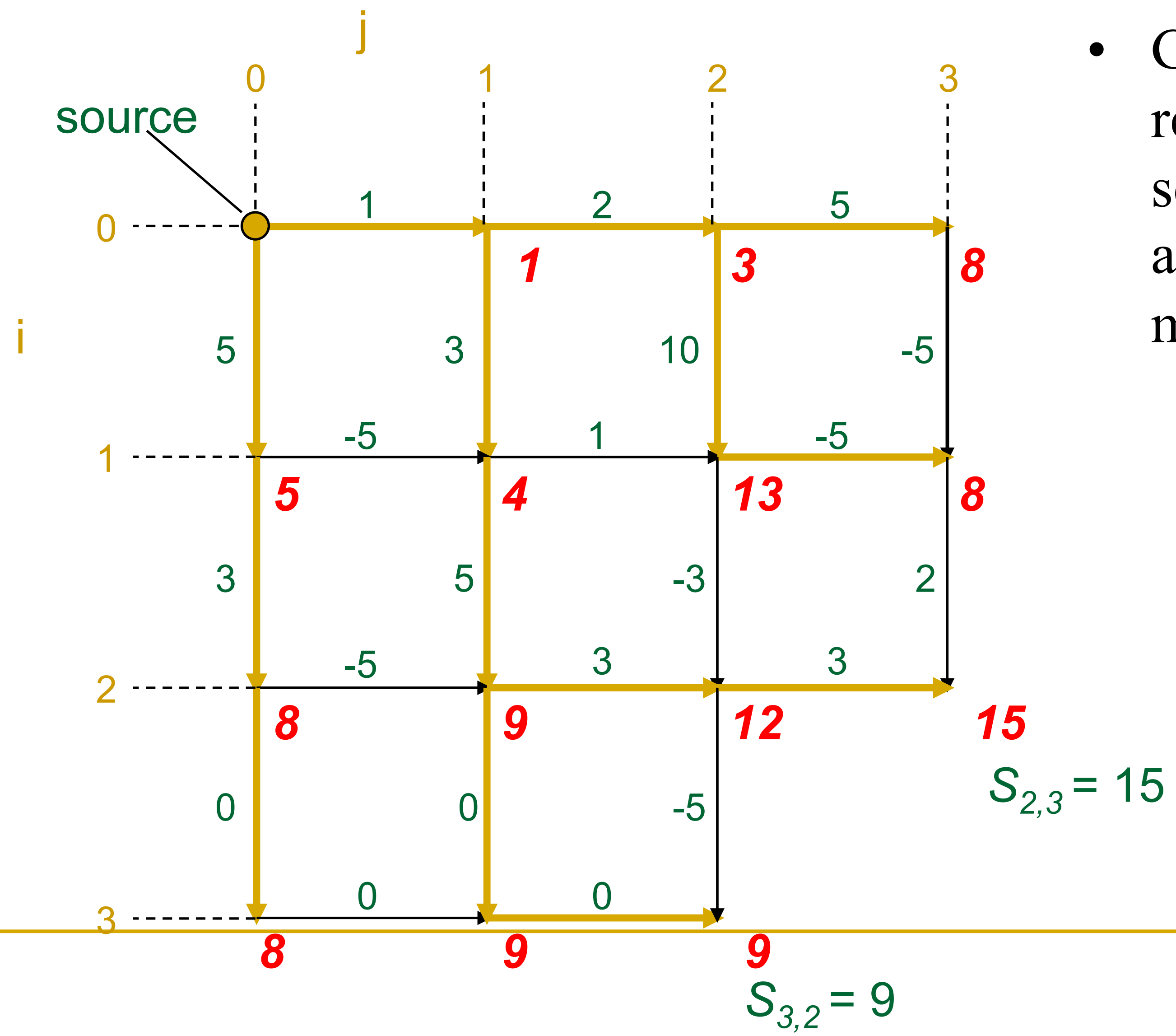

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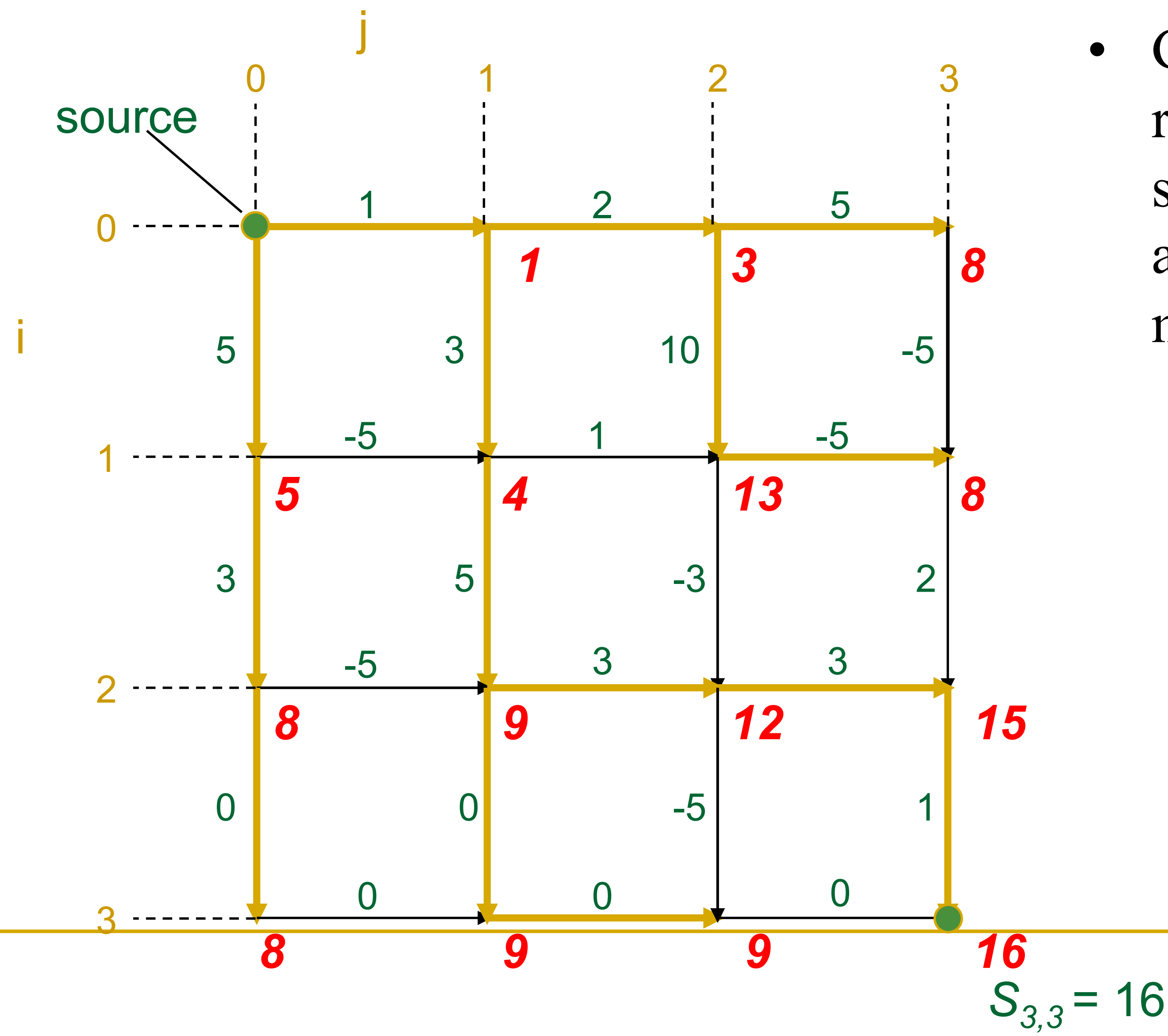
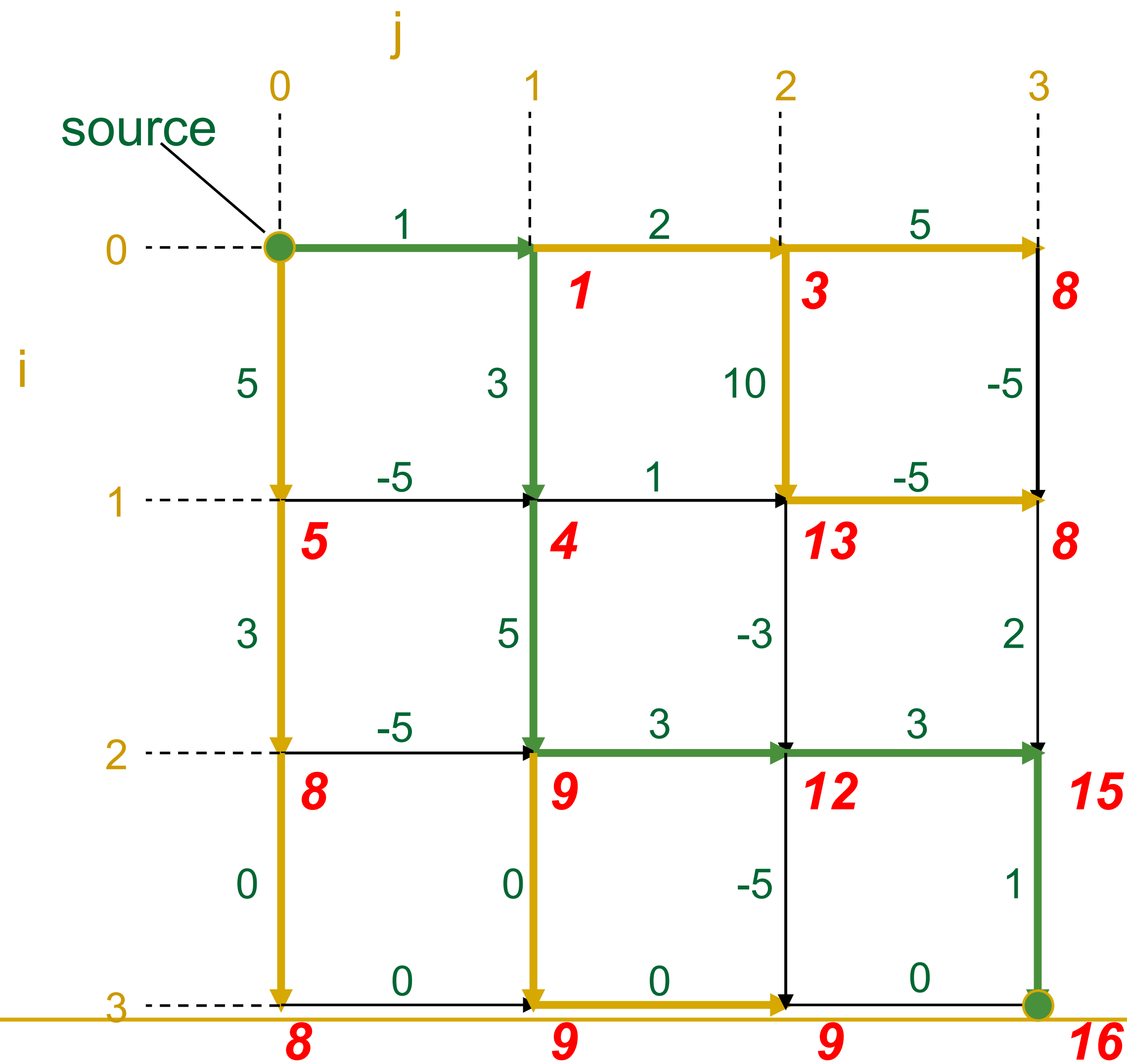
MTP: Dynamic Programming



- Gold edges represent edges selected by the algorithm as maximal.

MTP: Dynamic Programming



- Gold edges represent edges selected by the algorithm as maximal.
- Once we reach the sink, we backtrack along gold edges to the source to find the optimal (green) path.

MTP: Running Time with Dynamic Programming

- The score $s_{i,\,j}$ for a point *(i,j)* is given by the recurrence:

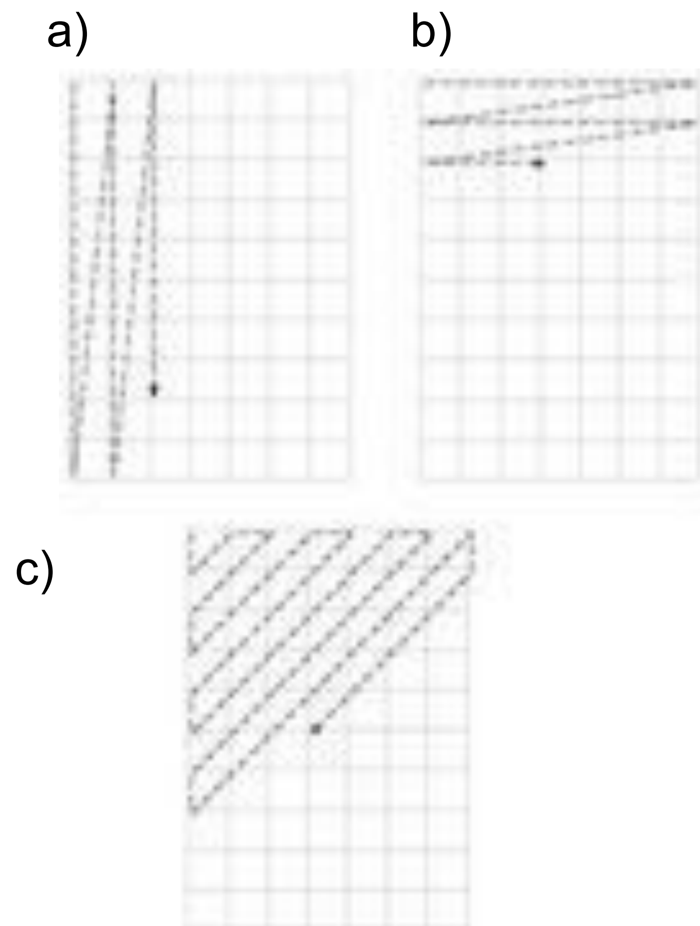
$$s_{i,j} = \max \begin{cases} s_{i-1,j} + \text{weight of edge between } (i-1, j) \text{ and } (i, j) \\ s_{i,j-1} + \text{weight of edge between } (i, j-1) \text{ and } (i, j) \end{cases}$$

- The running time is ***n x m*** for an ***n*** by ***m*** grid.
    - (***n*** = # of rows, ***m*** = # of columns)

Traversing the Manhattan Grid

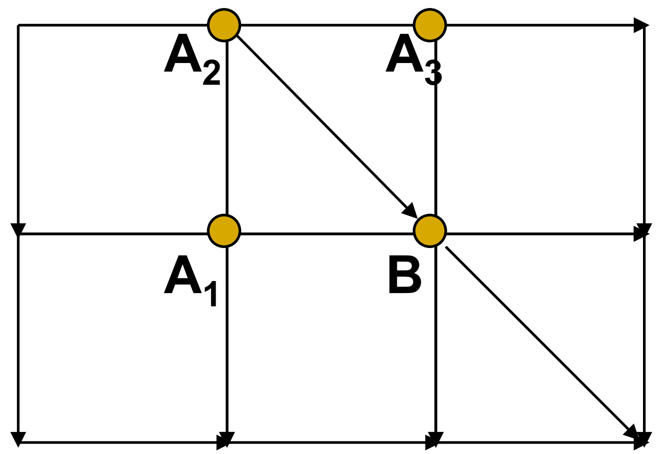
- So that we don't repeat ourselves, we need a strategy for actually traversing through the Manhattan grid to calculate the distances.

- Three common strategies:
  a) Column by column
  b) Row by row
  c) Along diagonals



Manhattan Is Not a Rectangular Grid

- What about diagonals?



- The score at point **B** is given by the recurrence:

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

Section 4:
Longest Path in a Graph

Recursion for an Arbitrary Graph

- We would like to compute the score for point ***x*** in an arbitrary graph.

- Let *Predecessors*(***x***) be the set of vertices with edges leading into ***x***. Then the recurrence is given by:

$$s_x = \max_{y \text{ in } Predecessors(x)} \left\{ s_y + \text{ weight of vertex } (y, x) \right\}$$

- The running time for a graph with ***E*** edges is O(***E***), since each edge is evaluated once.

Recursion for an Arbitrary Graph: Problem

- The only hitch is that we must decide on the order in which we visit the vertices.

- By the time the vertex x is analyzed, the values s_y for all its predecessors y should already be computed.

- If the graph has a cycle, we will get stuck in the pattern of going over and over the same cycle.

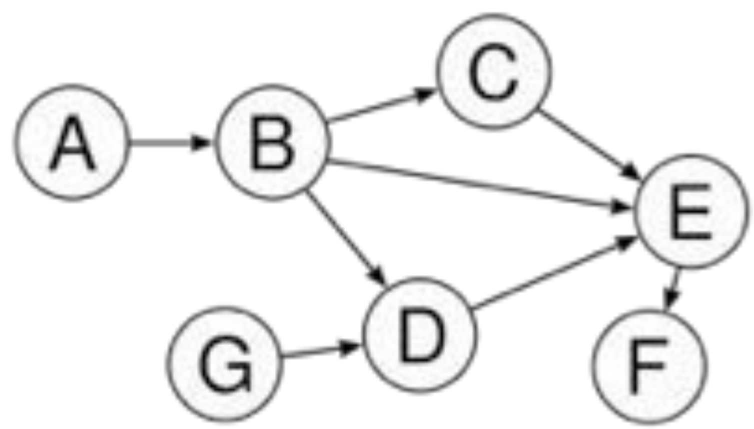
- In the Manhattan graph, we escaped this problem by requiring that we could only move east or south. This is what we would like to generalize…

Some Graph Theory Terminology

- **Directed Acyclic Graph** (DAG): A graph in which each edge is provided an orientation, and which has no cycles.
  - We represent the edges of a DAG with directed arrows.

- In the following example, we can move along the edge from B to C, but not from C to B.

- Note that BCE does not form a cycle, since we cannot travel from B to C to E and back to B.



http://commons.wikimedia.org/wiki/File:Directed_acyclic_graph.svg

Some Graph Theory Terminology

- **Topological Ordering**: A labeling of the vertices of a DAG (from 1 to n, say) such that every edge of the DAG connects a vertex with a smaller label to a vertex with a larger label.

- In other words, if vertices are positioned on a line in an increasing order, then all edges go from left to right.

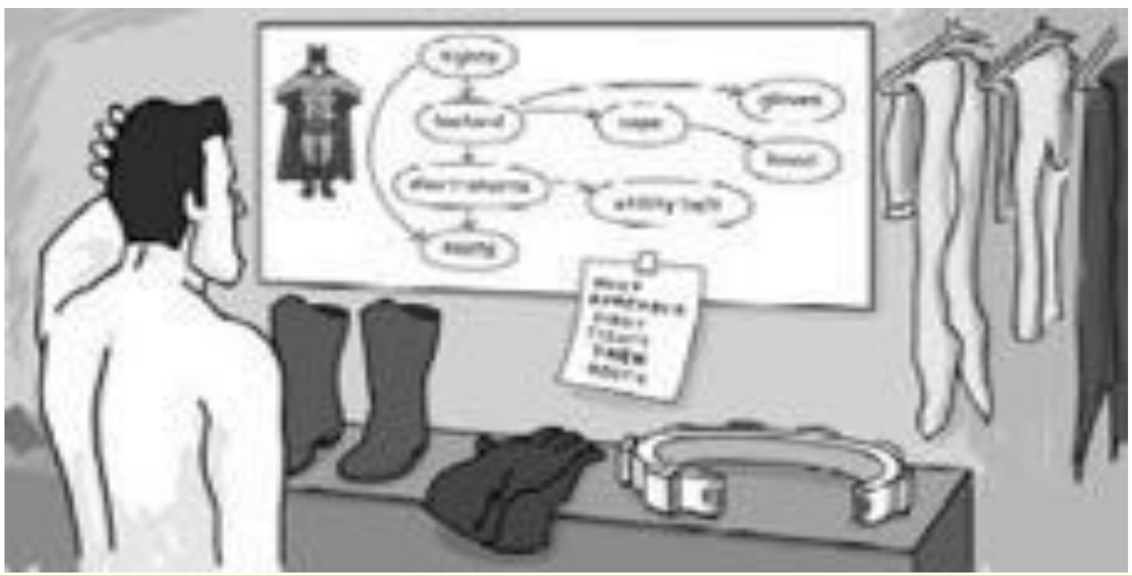
- **Theorem**: Every DAG has a topological ordering.

- What this means: Every DAG has a source node (1) and a sink node (n).

Topological Ordering: Example

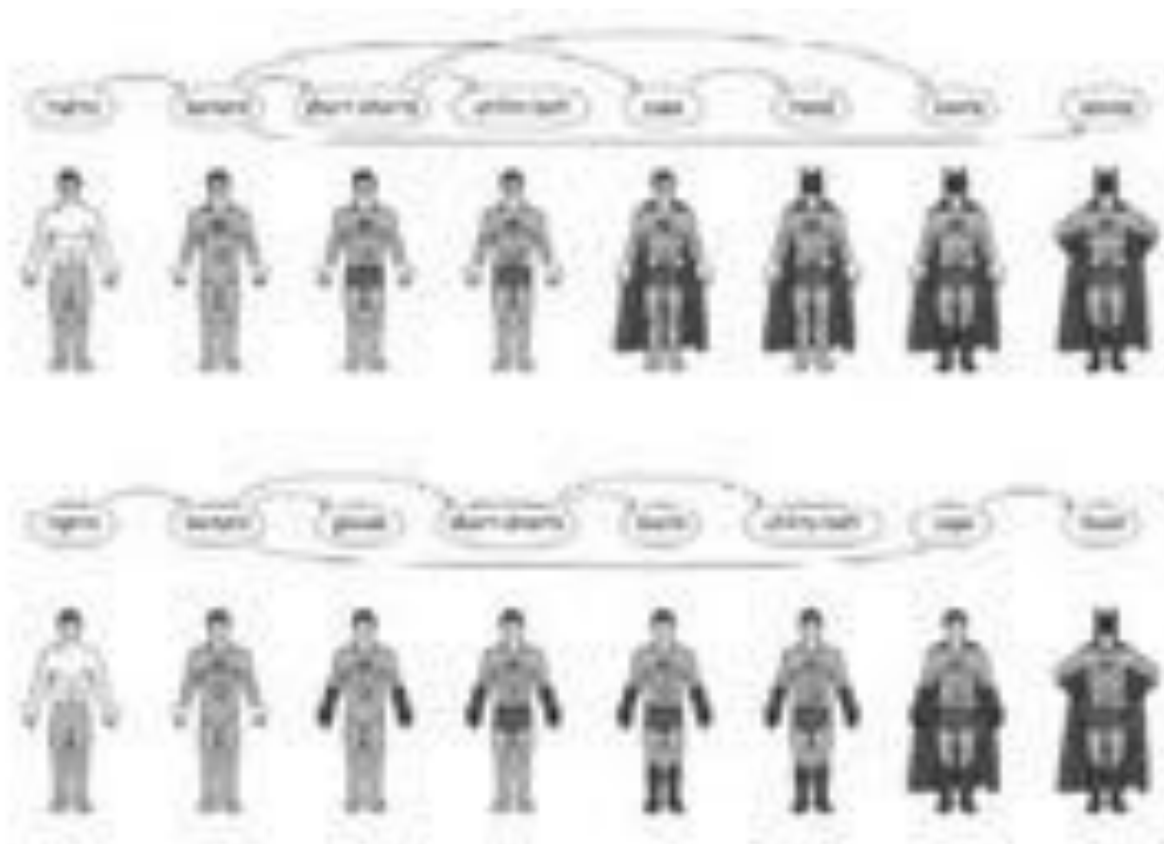
- A superhero’s costume can be represented by a DAG: he can’t put his boots on before his tights!

- He also would like an understandable representation of the graph, so that he can dress quickly.



Topological Ordering: Example

- Here are two different topological orderings of his DAG:



Longest Path in a DAG: Formulation

- 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.
- **Note**: Now we know that we can apply a topological ordering to ***G***, and then use dynamic programming to find the longest path in ***G.***