Linear-space sequence alignment

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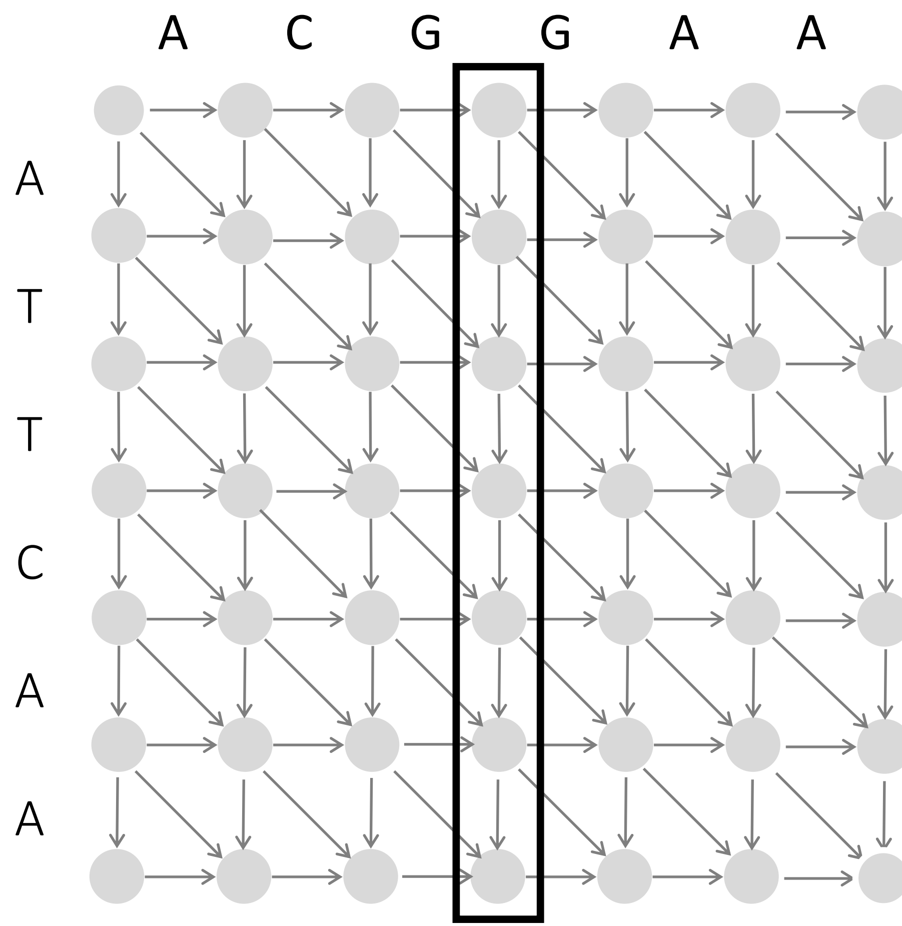
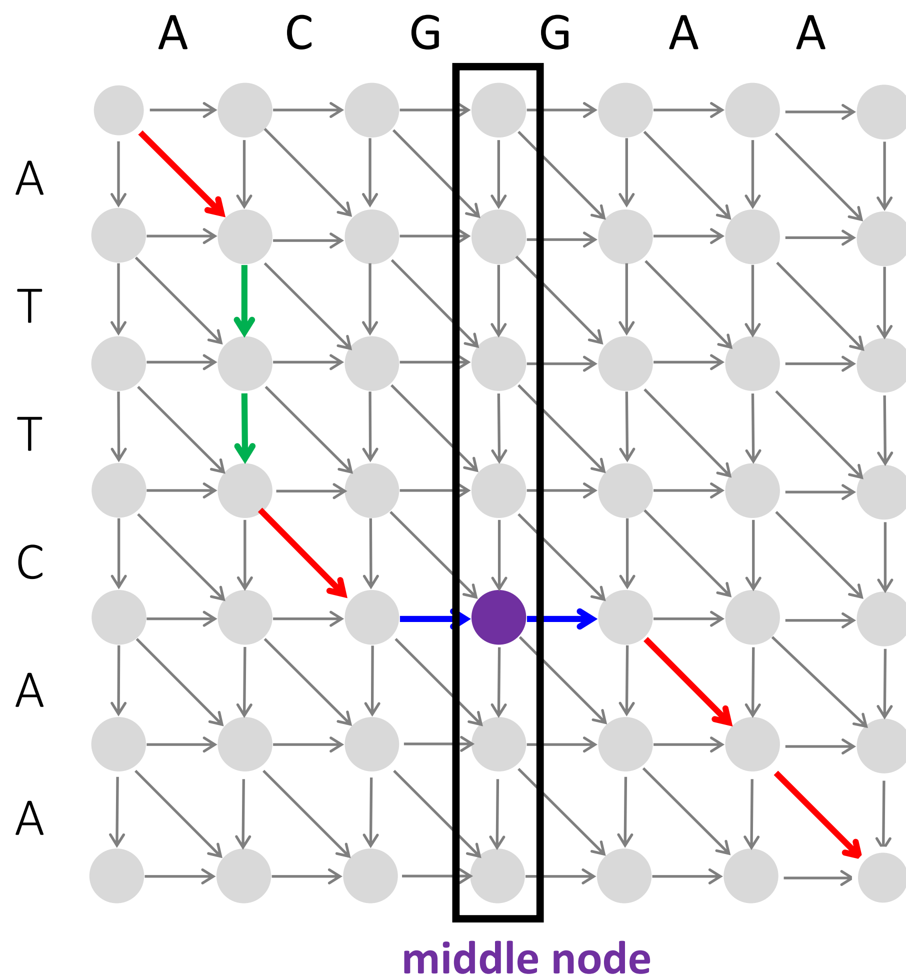
Adapted from Phillip Compeau and Pavel Pevzner. *Bioinformatics Algorithms: An Active Learning Approach*

Middle Column of the Alignment



middle column
(*middle*=#columns/2)

Middle Node of the Alignment

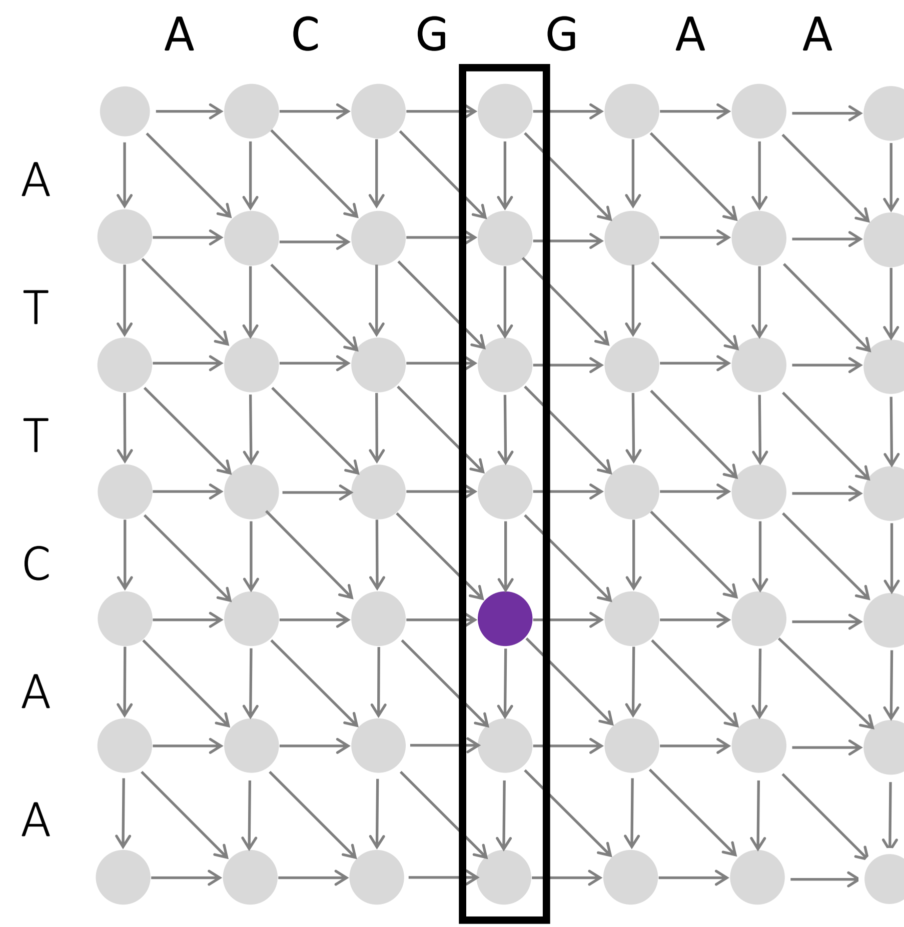


(a node where an optimal alignment path crosses the middle column)

Divide & Conquer for Sequence Alignment

AlignmentPath(*source, sink*)

find *MiddleNode*

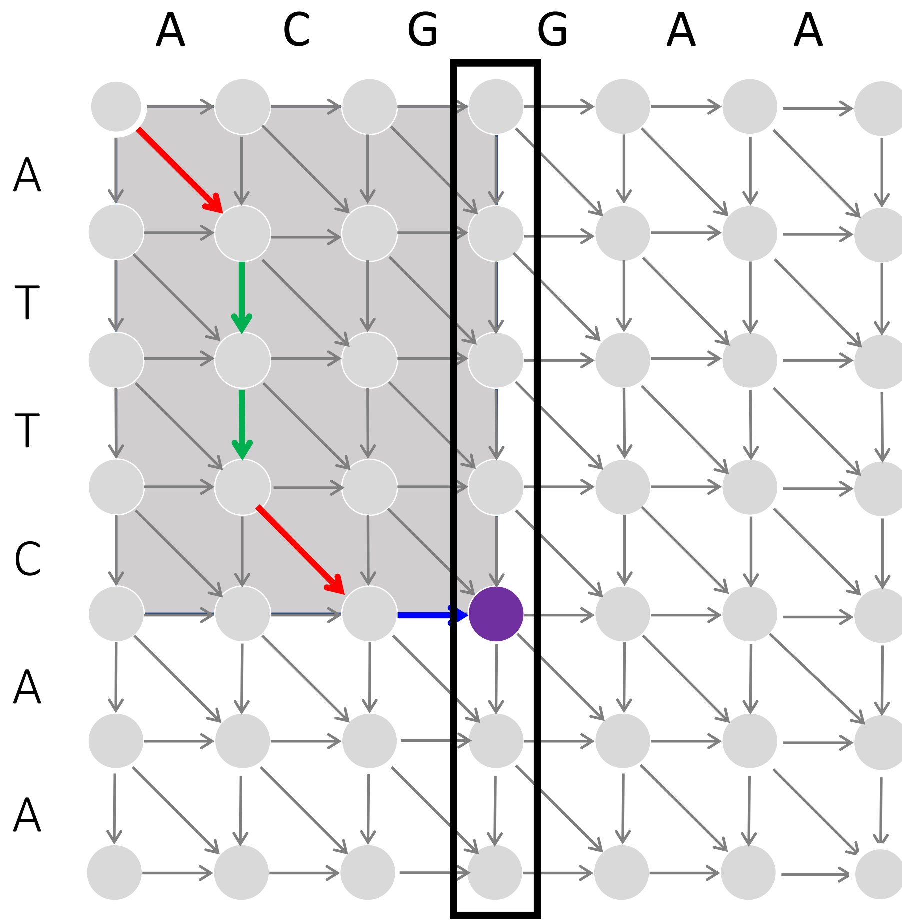


Divide and Conquer Approach to Sequence Alignment

AlignmentPath(*source, sink*)

find *MiddleNode*

AlignmentPath(*source, MiddleNode*)



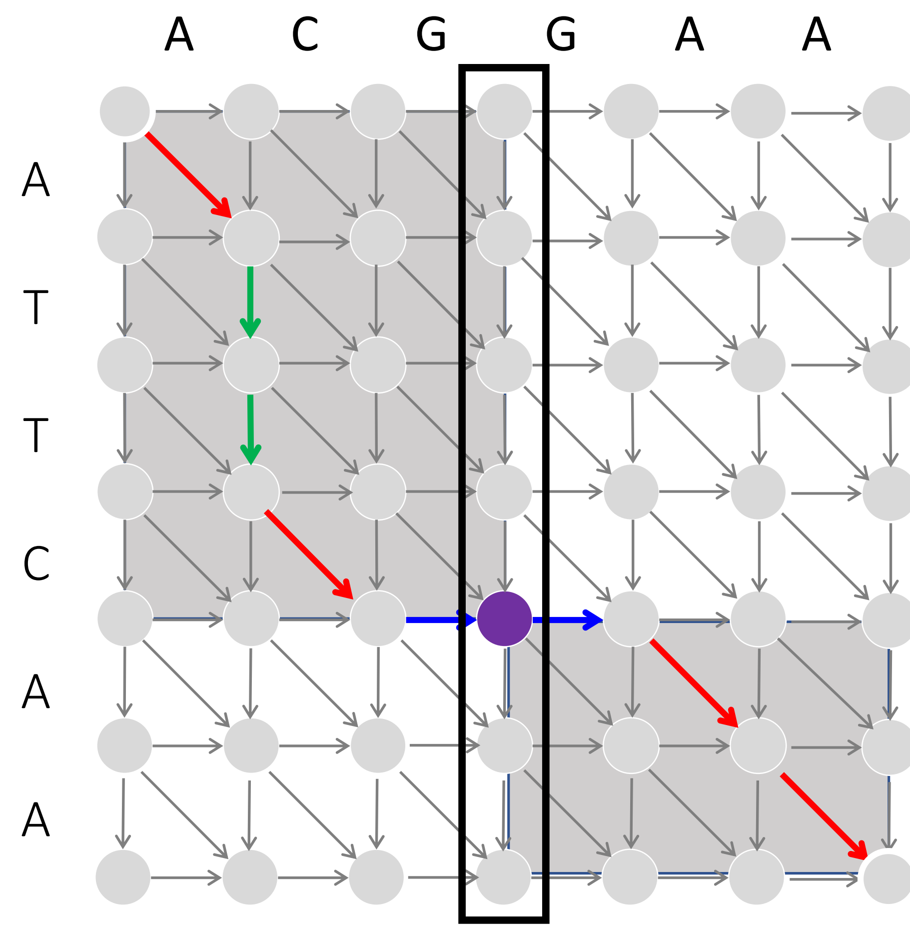
Divide and Conquer Approach to Sequence Alignment

AlignmentPath(*source*, *sink*)

find *MiddleNode*

AlignmentPath(*source*, *MiddleNode*)

AlignmentPath(*MiddleNode*, *sink*)



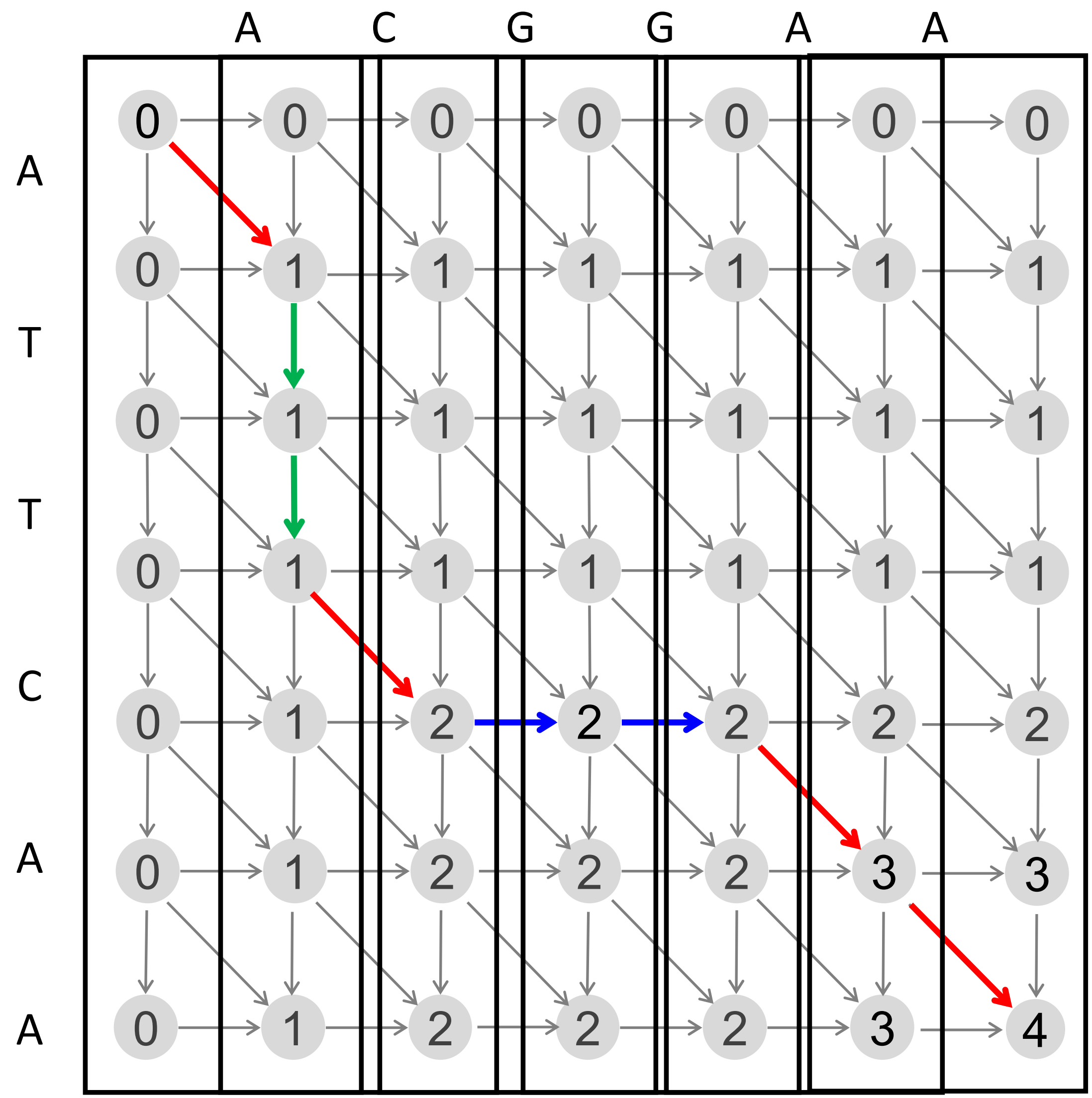
How do we find the middle node in **linear space?**

Computing Alignment Score in Linear Space

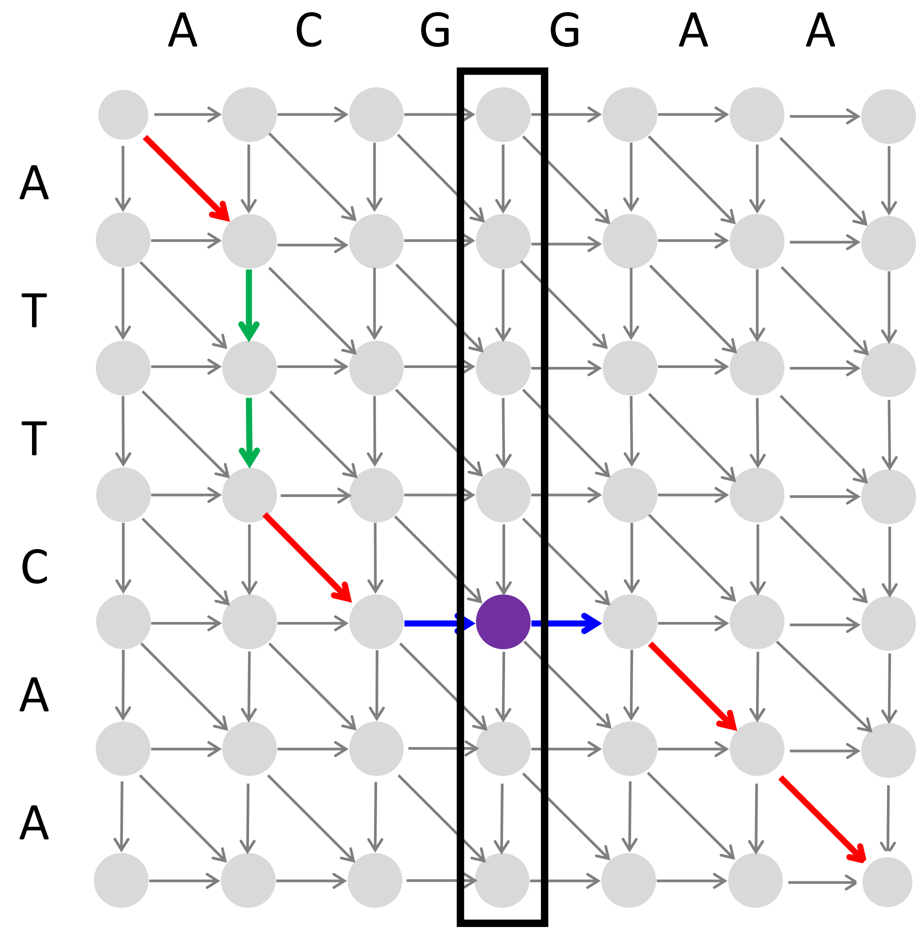
Finding the **longest path** in the alignment graph **requires** storing all backtracking pointers – O(*nm*) memory.

Finding the **length of the longest path** in the alignment graph **does not require** storing any backtracking pointers – O(*n*) memory.

Recycling the Columns in the Alignment Graph



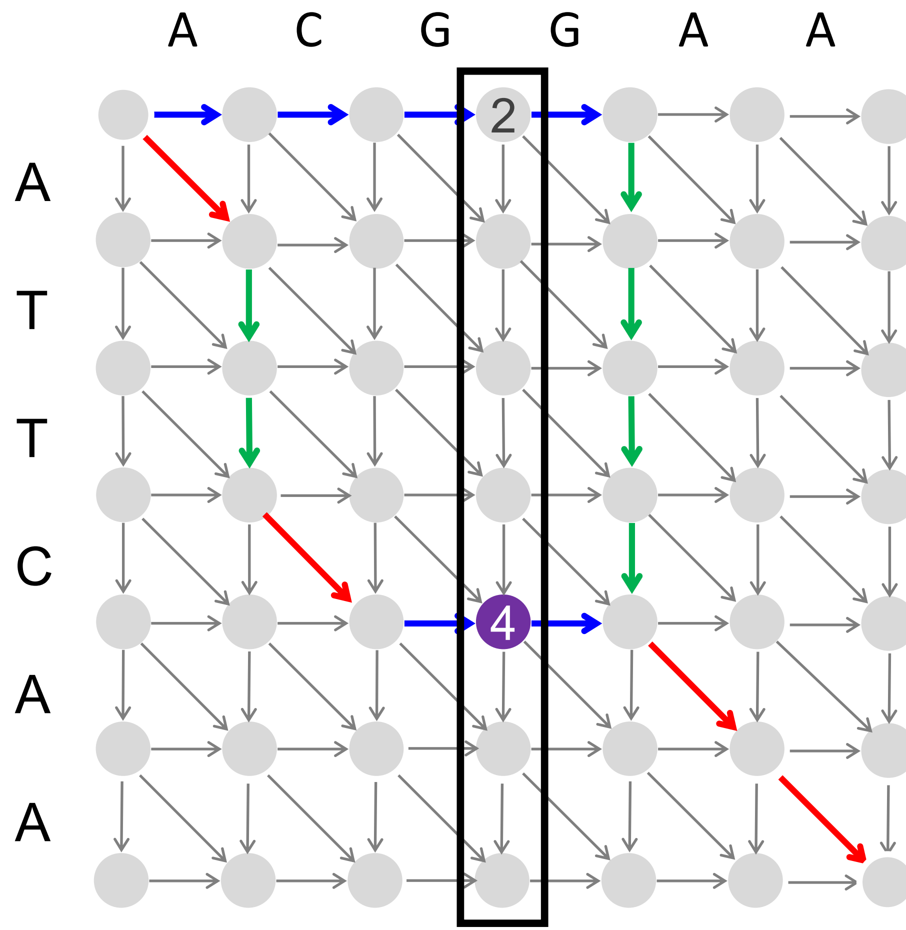
Can We Find the Middle Node without Constructing the Longest Path?



4-path that visits the node (4,middle) In the middle column

***i*-path** – a longest path among paths that visit the *i*-th node in the middle column

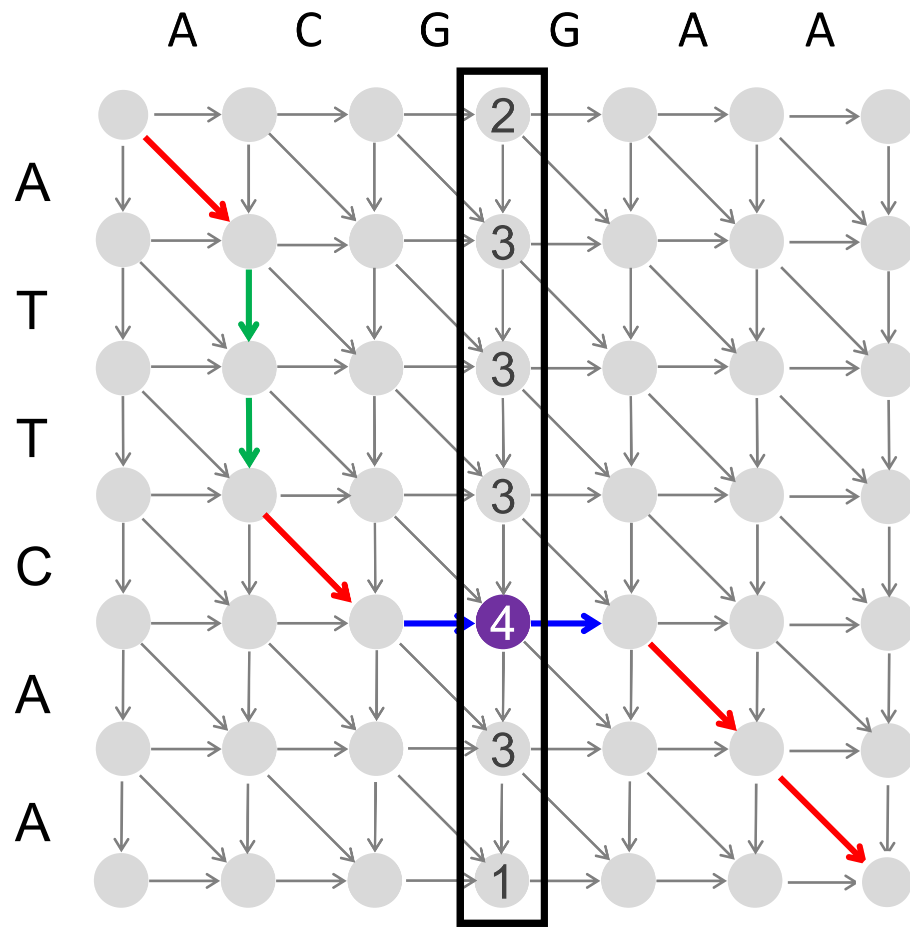
Can We Find The Lengths of All *i*-paths?



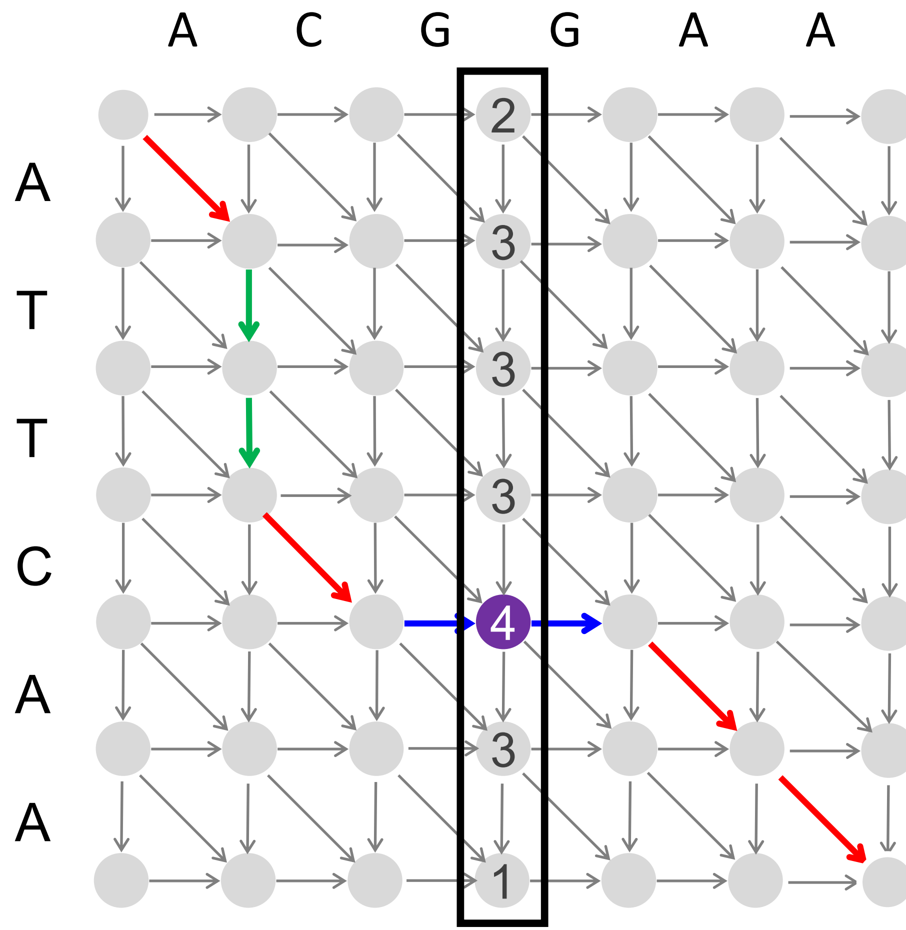
length(i):
length of an *i*-path:

length(0)=2
length(4)=4

Can We Find The Lengths of All *i*-paths?



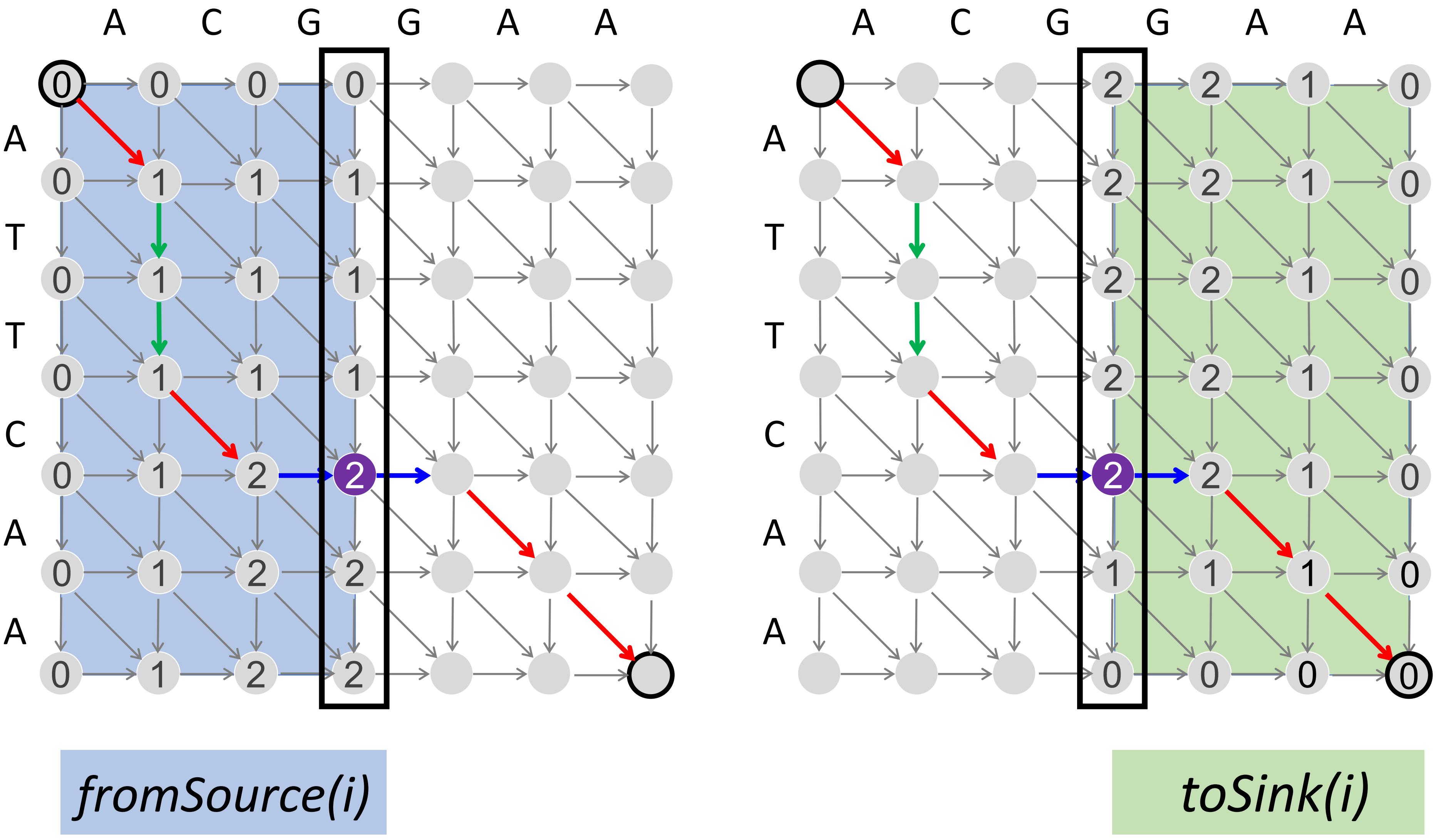
Can We Find The Lengths of *i*-paths?



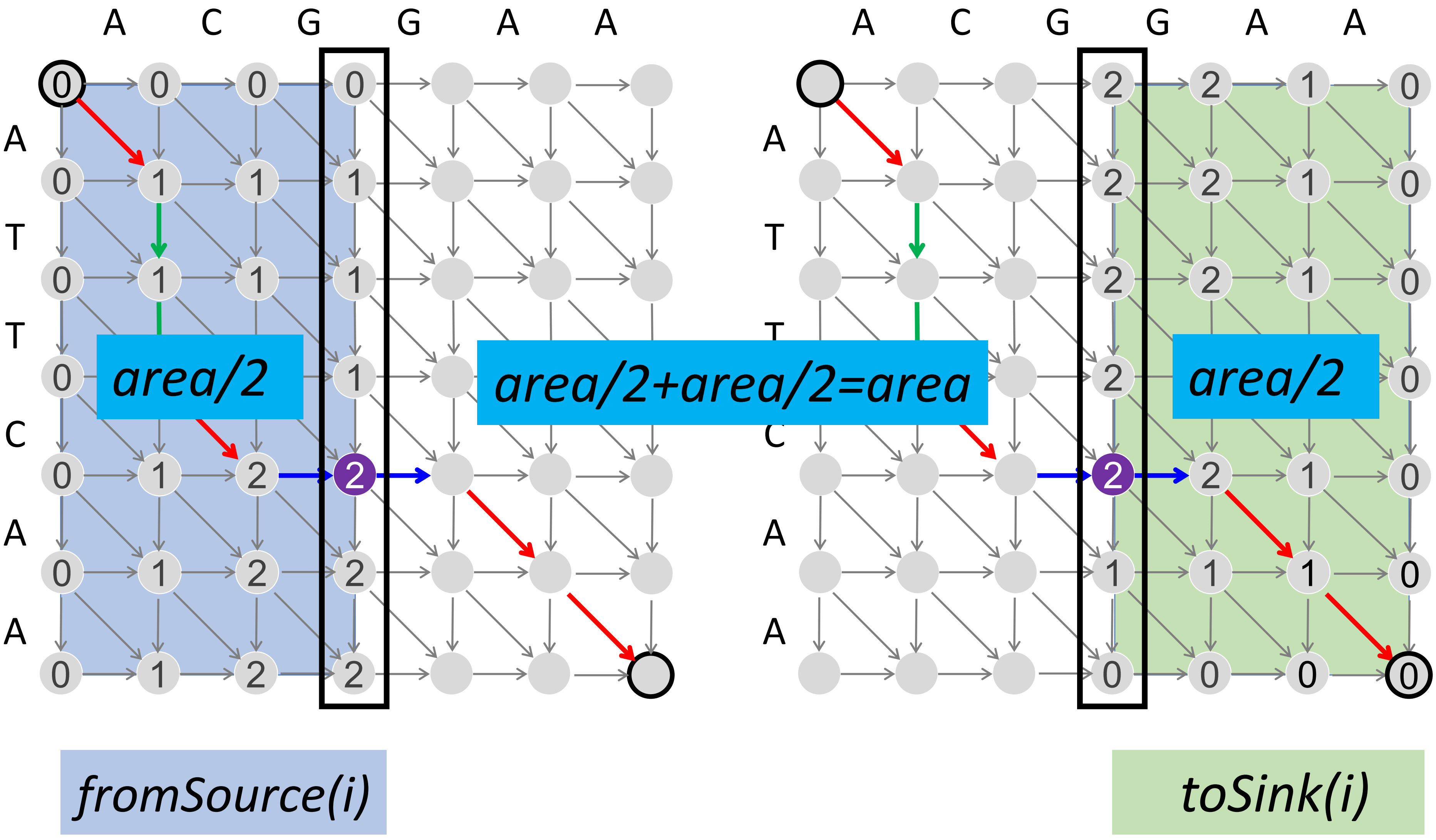
length(i):
length of an *i*-path

length(i)=fromSource(i)+toSink(i)

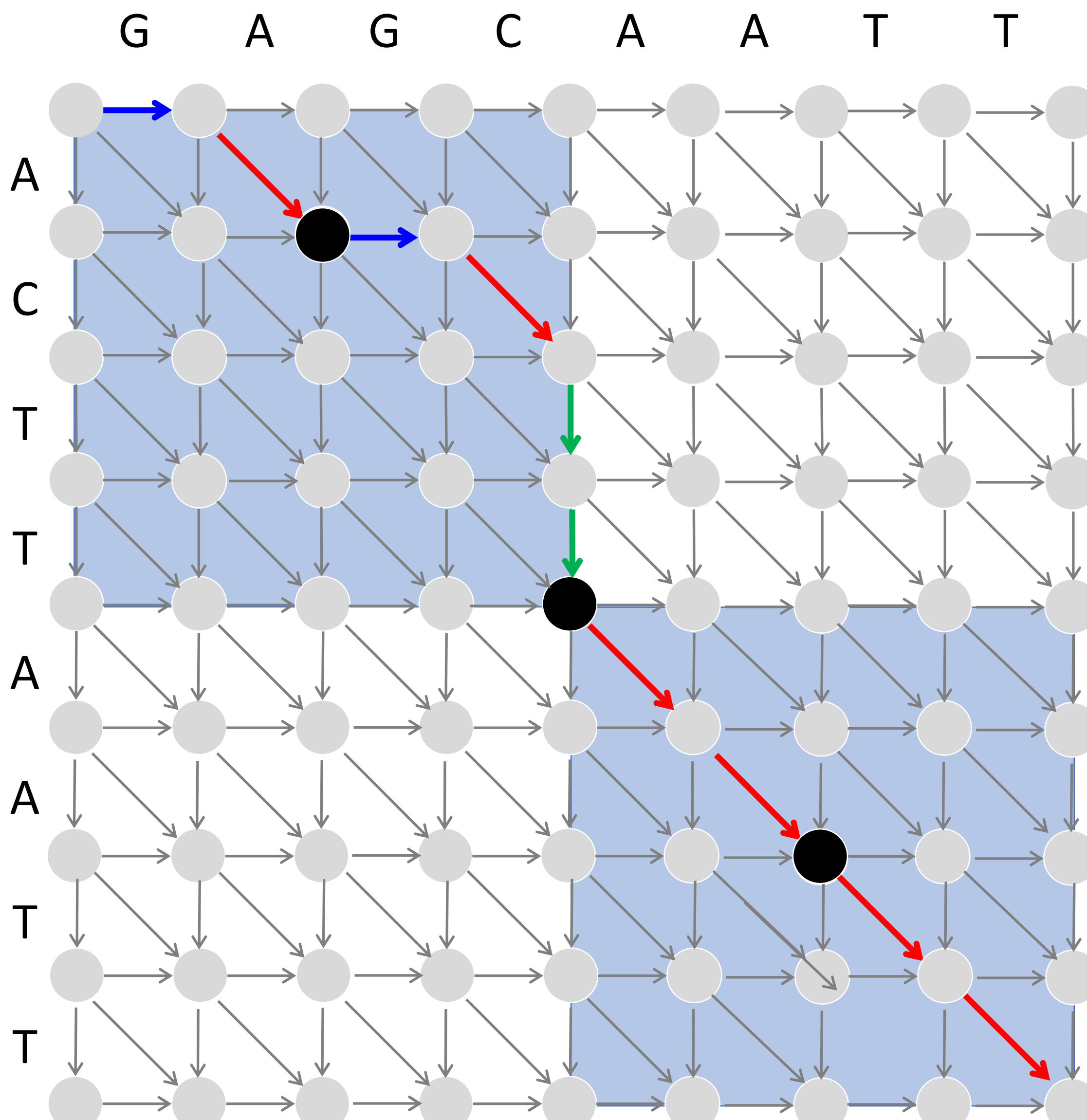
Computing *FromSource* and *toSink*



How Much Time Did It Take to Find the Middle Node ?



Laughable Progress: O(*nm*) Time to Find **ONE** Node!

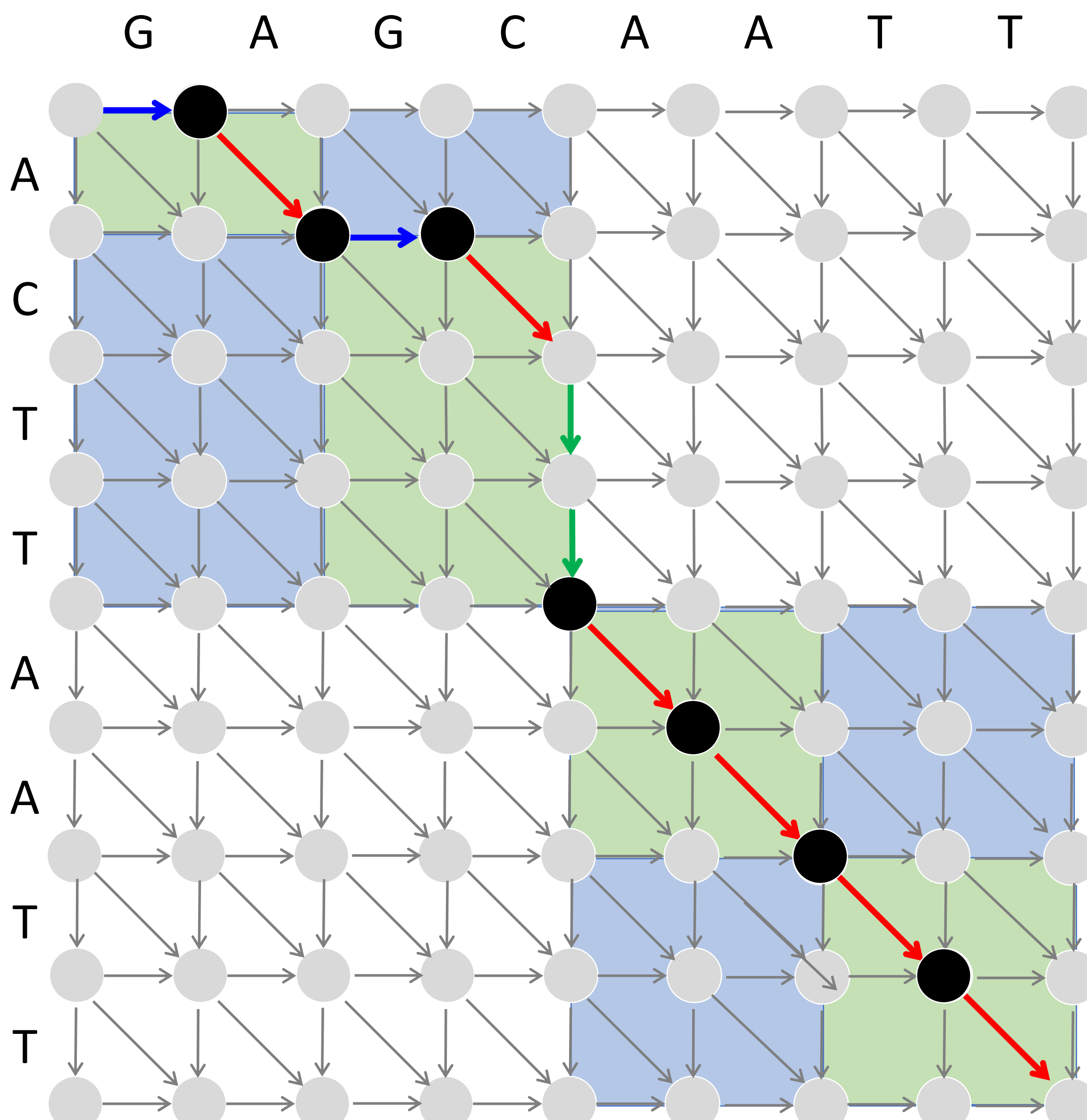


Each subproblem can be conquered in time proportional to its area:

area/4+area/4=
area/2

How much time would it take to conquer 2 subproblems?

Laughable Progress: O(*nm+nm/2*) Time to Find **THREE** Nodes!

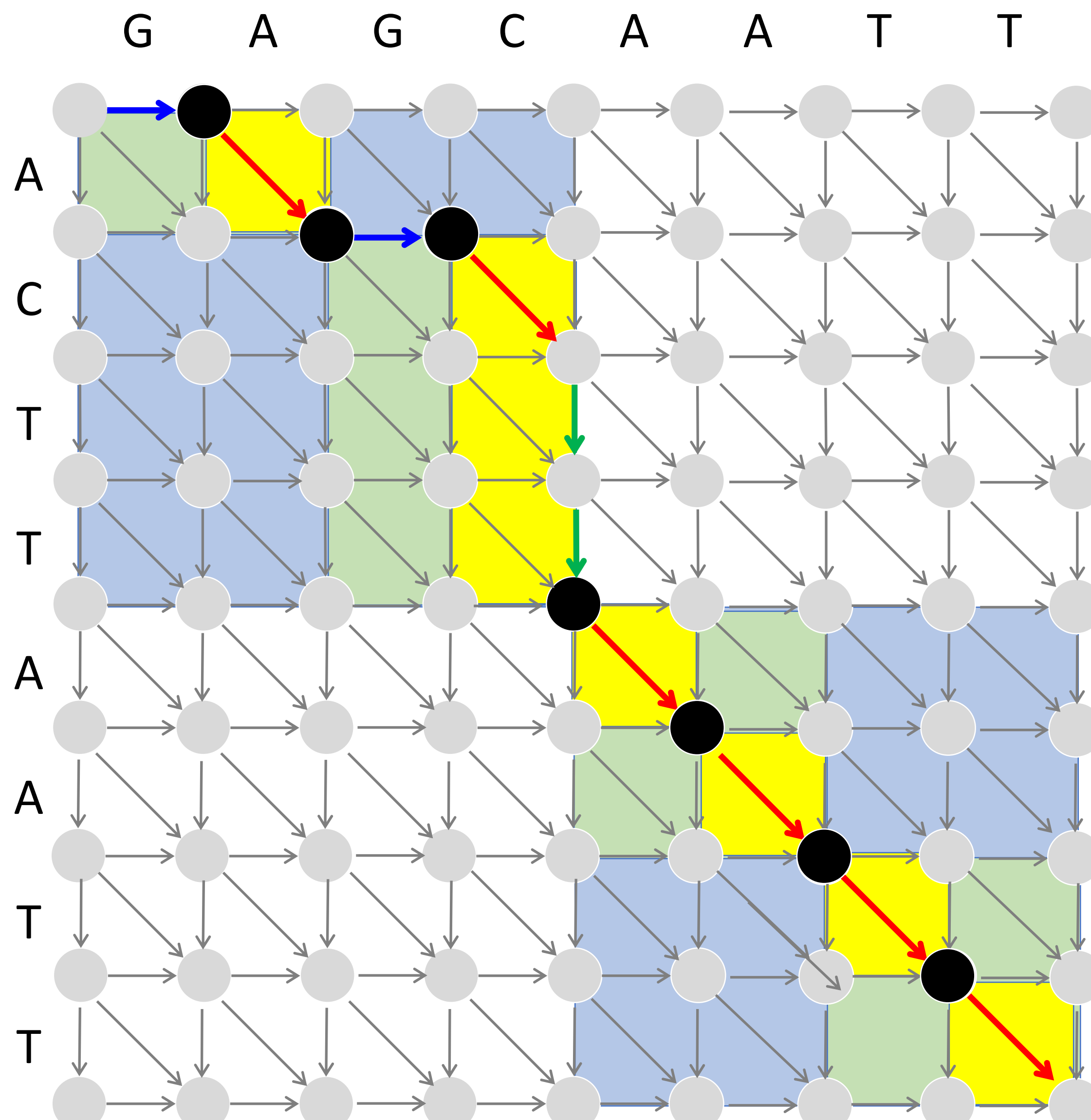


Each subproblem can be conquered in time proportional to its area:

area/8+area/8=
area/4

How much time would it take to conquer 4 subproblems?

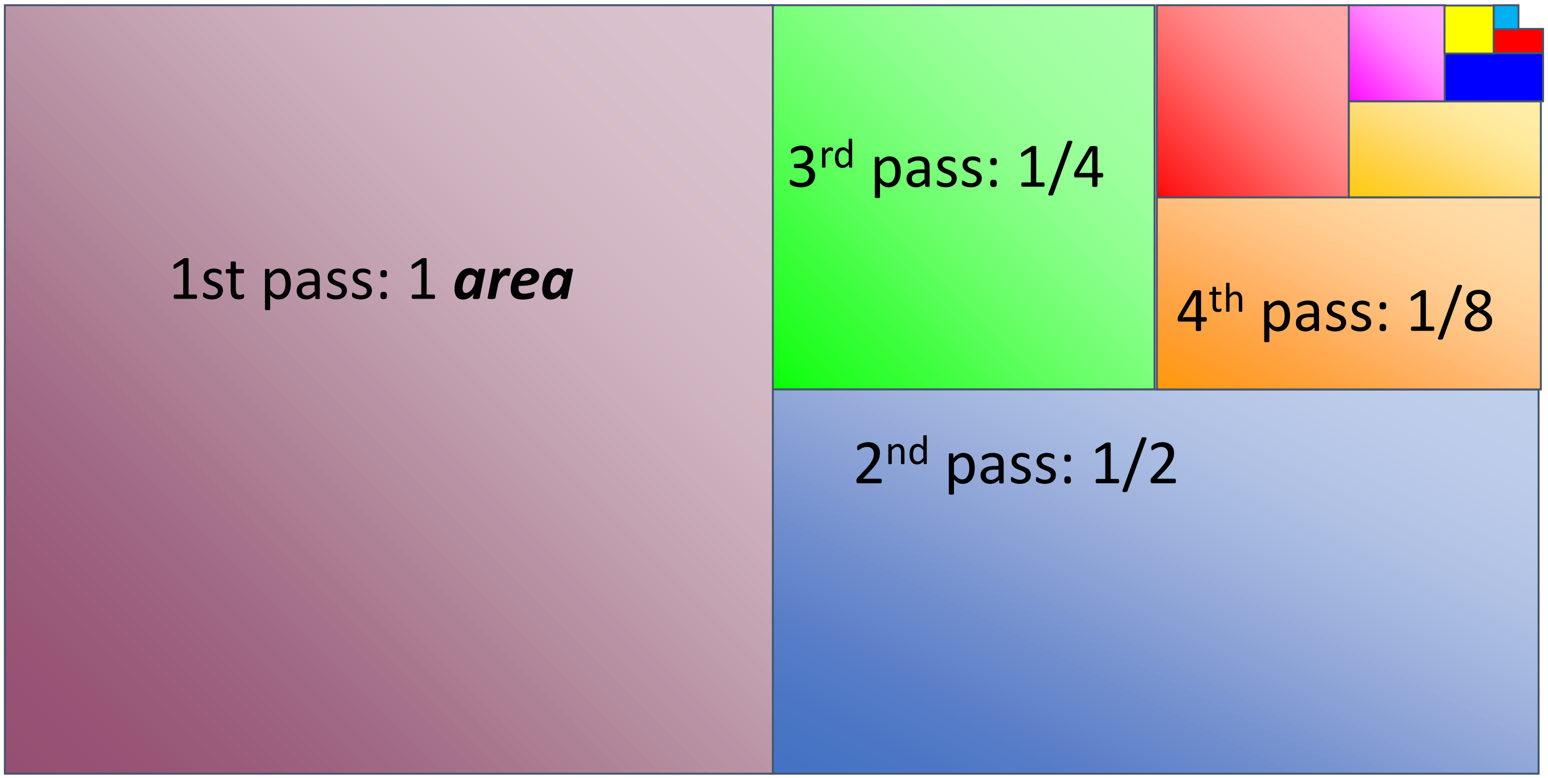
O($nm+nm/2+nm/4$) Time to Find **NEARLY ALL** Nodes!



area+
area/2
+area/4
+area/8
+area/16
....
+area/2^{lgn}

How much time would it take to conquer ALL subproblems?

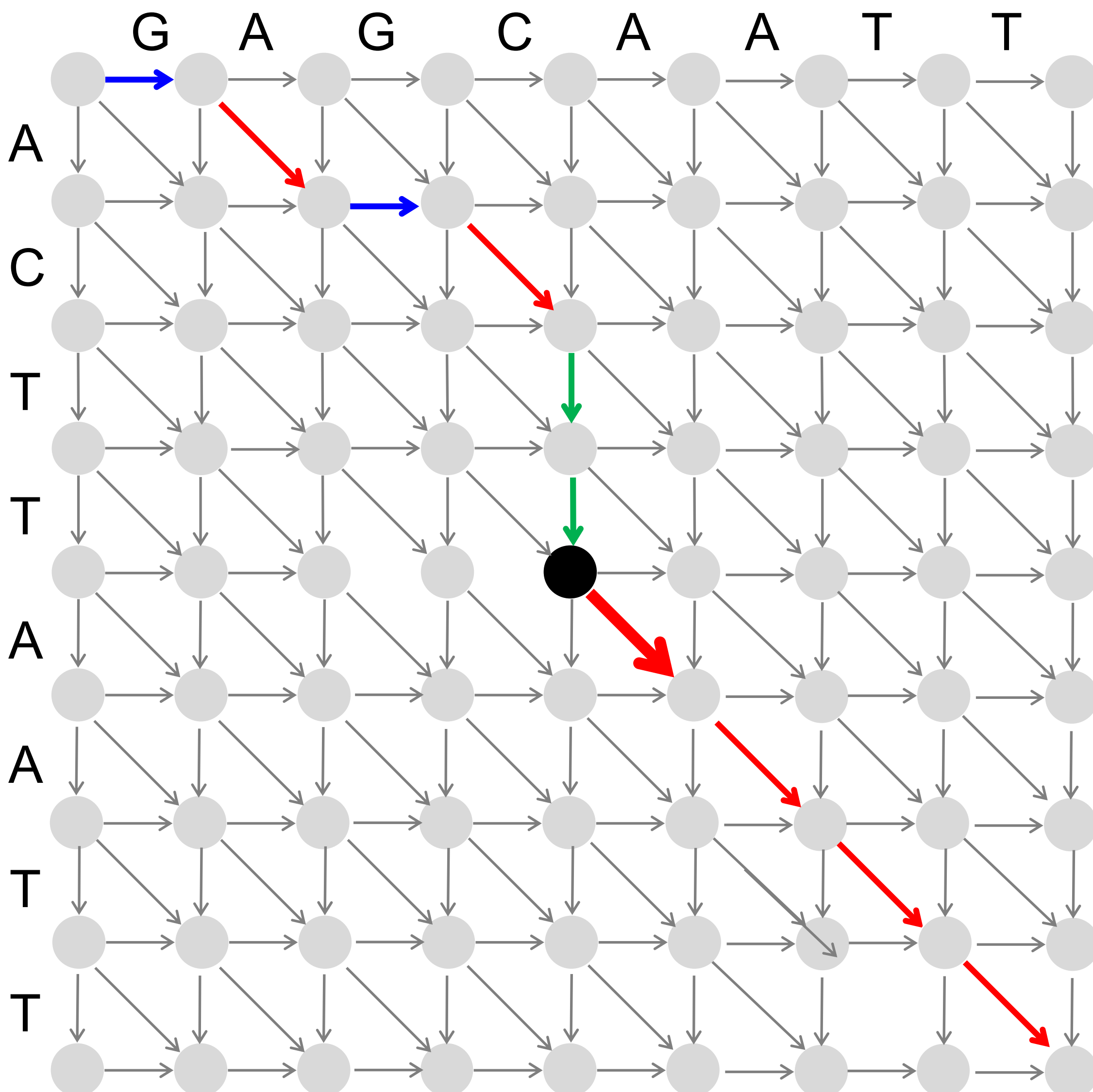
Total Time: ***area(1+1/2+1/4+1/8+1/16+…)***



$$1 + \frac{1}{2} + \frac{1}{4} + \cdots + \frac{1}{2^{\lg n}} = \frac{1 - \frac{1}{2n}}{1 - \frac{1}{2}} = 2 - \frac{1}{n} \ < \ 2$$

Still O(mn)!

The Middle Edge

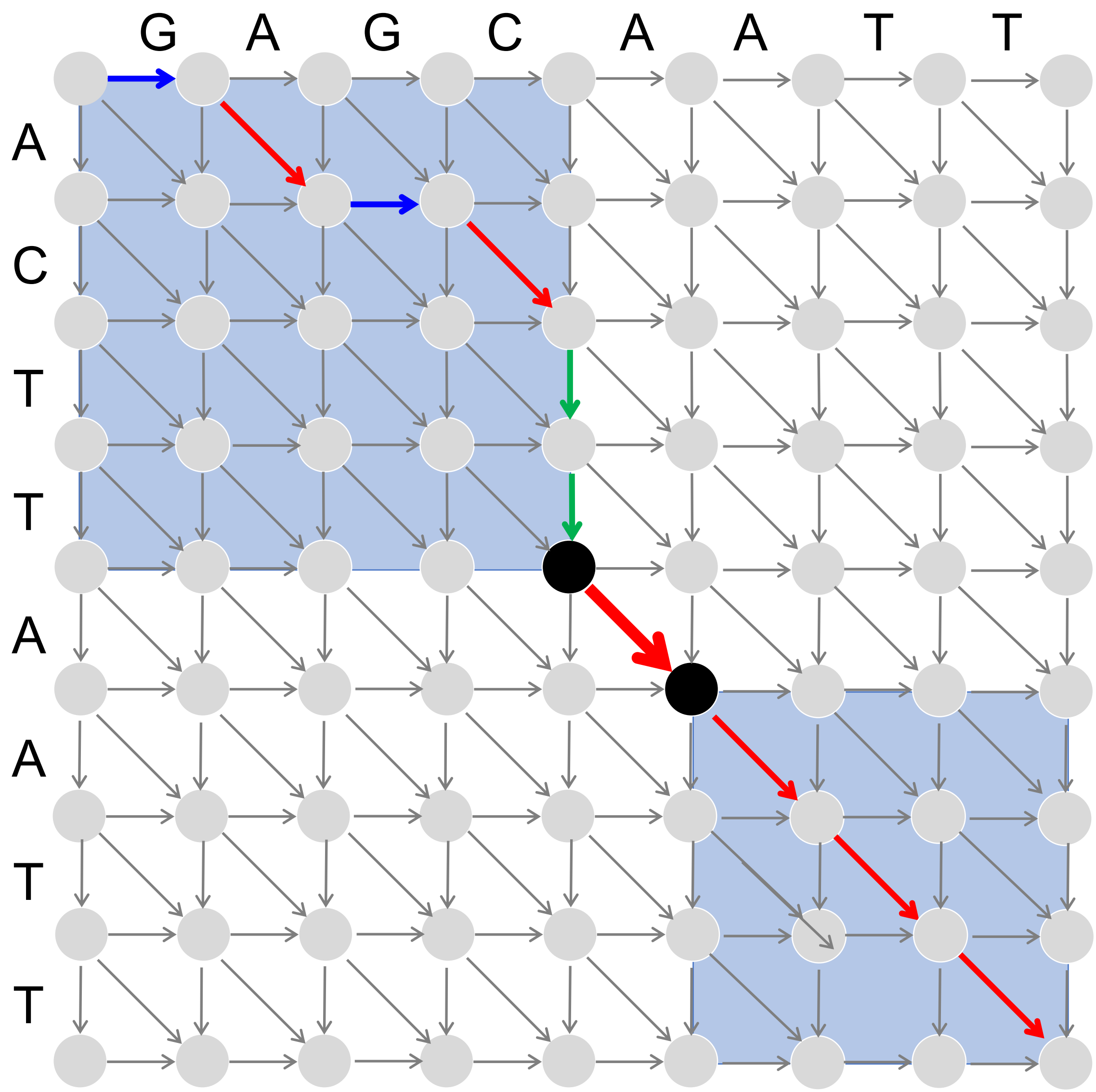


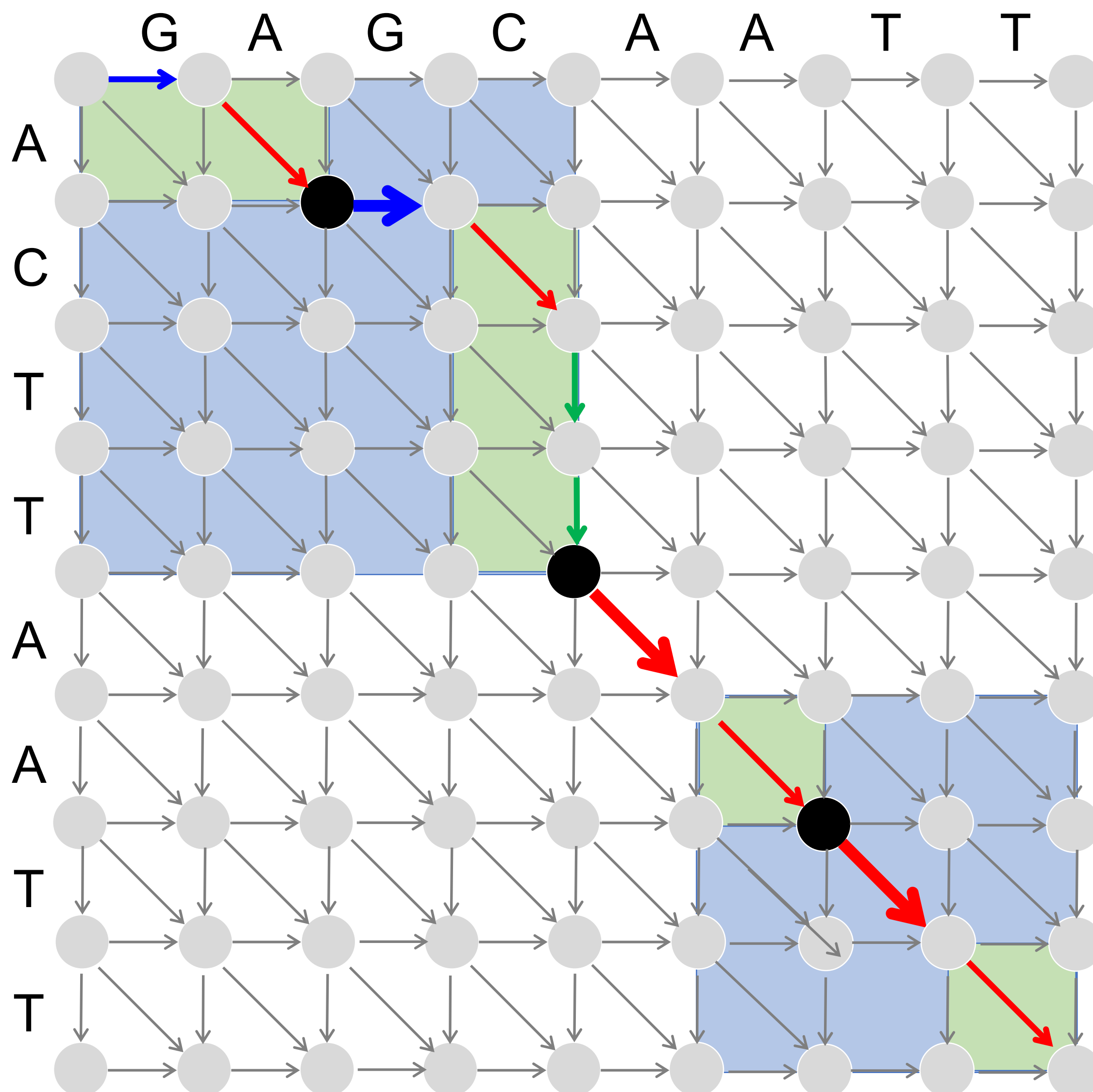
Middle Edge: an edge in an optimal alignment path starting at the middle node

The Middle Edge Problem

Middle Edge in Linear Space Problem. Find a middle edge in the alignment graph in linear space.

- **Input:** Two strings v and w and matrix ***score***.
- **Output:** A middle edge in the alignment graph of these strings (as defined by the matrix ***score***).


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


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

Middle node and edge

- MiddleNodeEdge(v, w, top, bottom, left, right)
  - Finds the middle node and edge between

    $v_{top+1},\ldots,v_{bottom}$ and

    $w_{left+1}, \ldots, w_{right}$
  - mid <- $\lfloor (left+right)/2 \rfloor$
  - Apply linear-space dynamic programming with column reuse to get scores for aligning at the mid column:

    $v_{top+1},\ldots,v_{bottom}$ and $w_{left+1}, \ldots, w_{mid}$
  - Apply linear-space dynamic programming with column reuse to get scores for aligning at the mid column:

    $v_{bottom},\ldots, v_{top+1}$ and $w_{right}, \ldots, w_{mid}$
  - Identify both middle node and middle edge
  - Return (middleNode, middleEdge)

Recursive **LinearSpaceAlignment**

LinearSpaceAlignment(v, w, *top,bottom,left,right*)
  if *left = right*
    return alignment formed by *bottom-top* edges "↓"
  (midNode, midEdge) ← **MiddleNodeEdge***(v, w, top,bottom,left,right)*
  middle ← $\lfloor$*(left+right)/2*$\rfloor$
  LinearSpaceAlignment*(v, w, top,midNode,left,middle)*
  output *midEdge*
  if *midEdge = "→"* **or** *midEdge = "↘"*
    middle ← middle+1
  if *midEdge = "↓"* **or** *midEdge = "↘"*
    midNode ← midNode+1
  LinearSpaceAlignment*(v, w, midNode,bottom,middle,right)*