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CSE 421

RNA Secondary Structure, Sequence Alignment

Shayan Oveis Gharan

Sequence Alignment

Sequence Alignment

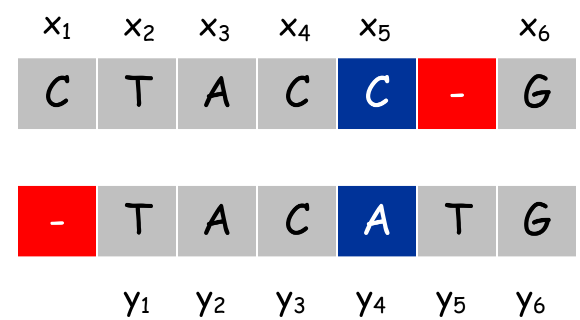
Given two strings $x_1, \dots, x_m$ and $y_1, \dots, y_n$ find an alignment with minimum number of mismatch and gaps.

An alignment is a set of ordered pairs $(x_{i_1}, y_{j_1}), (x_{i_2}, y_{j_2}), \dots$ such that $i_1 < i_2 < \cdots$ and $j_1 < j_2 < \cdots$

Example: `CTACCG` vs. `TACATG`.

Sol: We aligned

x_2-y_1, x_3-y_2, x_4-y_3, x_5-y_4, x_6-y_6.



So, the cost is 3.

DP for Sequence Alignment

Let $OPT(i, j)$ be min cost of aligning $x_1, \dots, x_i$ and $y_1, \dots, y_j$

Case 1: OPT matches x_i, y_j

- Then, pay mis-match cost if $x_i \neq y_j$ + min cost of aligning $x_1, \dots, x_{i-1}$ and $y_1, \dots, y_{j-1}$ i.e., $OPT(i-1, j-1)$

Case 2: OPT leaves x_i unmatched

- Then, pay gap cost for x_i + $OPT(i-1, j)$

Case 3: OPT leaves y_j unmatched

- Then, pay gap cost for y_j + $OPT(i, j-1)$

Bottom-up DP

```
Sequence-Alignment(m, n, x1x2...xm, y1y2...yn) {
   for i = 0 to m
      M[0, i] = i
   for j = 0 to n
      M[j, 0] = j

   for i = 1 to m
      for j = 1 to n
         M[i, j] = min( (xi=yj ? 0:1) + M[i-1, j-1],
                        1 + M[i-1, j],
                        1 + M[i, j-1])
   return M[m, n]
}
```

Analysis: $\Theta(mn)$ time and space.

English words or sentences: m, n $\leq$ 10,..,20.

Computational biology: m = n = 100,000. 10 billions ops OK,
but 40GB array?

Optimizing Memory

If we are not using strong induction in the DP, we just need to use the last (row) of computed values.

```
Sequence-Alignment(m, n, x₁x₂...xₘ, y₁y₂...yₙ) {
  for i = 0 to m
     M[0, i] = i
  for j = 0 to n
     M[j, 0] = j

  for i = 1 to m
     for j = 1 to n
        M[i, j] = min( (xᵢ=yⱼ ? 0:1) + M[i-1, j-1],
                       1 + M[i-1, j],
                       1 + M[i, j-1])
  return M[m, n]
}
```

Just need $i-1, i$ rows to compute M[i,j]

DP with $O(m + n)$ memory

- Keep an Old array containing values of the last row
- Fill out the new values in a New array
- Copy new to old at the end of the loop

```
Sequence-Alignment(m, n, x1x2...xm, y1y2...yn) {
  for i = 0 to m
     O[i] = i
  for i = 1 to m
     N[0]=i                                      M[i-1, j-1]
     for j = 1 to n
        N[j] = min( (xi=yj ? 0:1) + O[j-1],
                    1 + O[j],                    M[i-1, j]
                    1 + N[j-1])                  M[i, j-1]
     for j = 1 to n
        O[j]=N[j]
  return N[n]
}
```

Lesson

Advantage of a bottom-up DP:

It is much easier to optimize the space.

Longest Path in a DAG

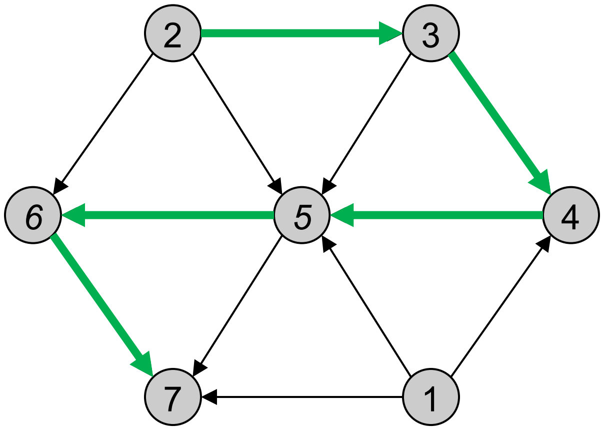
Longest Path in a DAG

Goal: Given a DAG G, find the longest path.

Recall: A directed graph G is a DAG if it has no cycle.

This problem is NP-hard for general directed graphs:

- It has the Hamiltonian Path as a special case



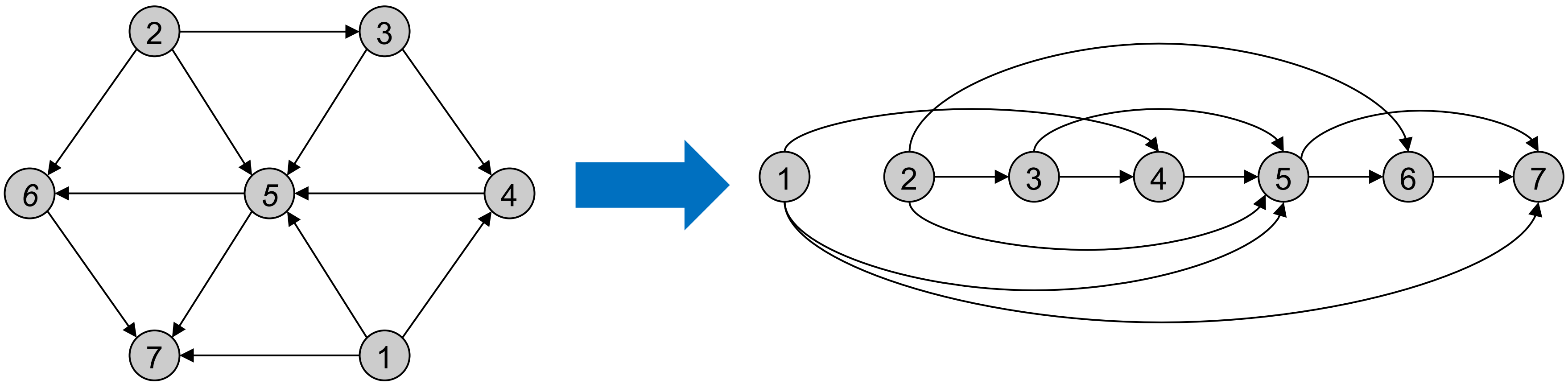
DP for Longest Path in a DAG

Q: What is the right ordering?

Remember, we have to use that G is a DAG, ideally in defining the ordering

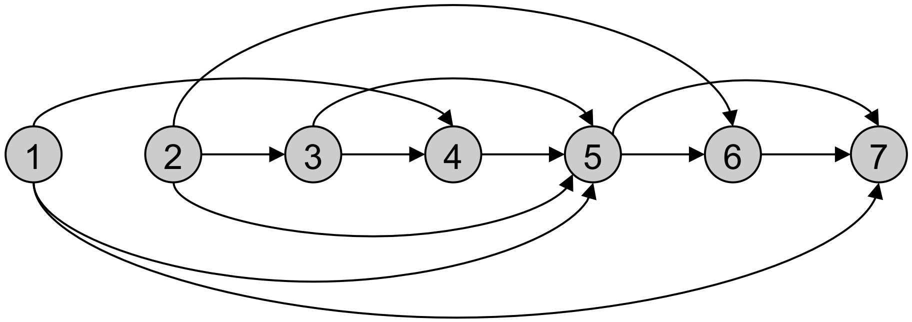
We saw that every DAG has a topological sorting

So, let's use that as an ordering.



DP for Longest Path in a DAG

Suppose we have labelled the vertices such that (i, j) is a directed edge only if $i < j$.



Let $OPT(j)$ = length of the longest path ending at j

Suppose in the longest path ending at j, last edge is (i, j).

Then, none of the $i + 1, \dots, j - 1$ are in this path since topological ordering. So,

$$OPT(j) = OPT(i) + 1.$$

DP for Longest Path in a DAG

Suppose we have labelled the vertices such that (i, j) is a directed edge only if $i < j$.

Let $OPT(j)$ = length of the longest path ending at j

$$OPT(j) = \begin{cases} 0 & \text{If } j \text{ is a source} \\ 1 + \max\limits_{i:(i,j) \text{ an edge}} OPT(i) & \text{o.w.} \end{cases}$$

DP for Longest Path in a DAG

```
Let G be a DAG given with a topological sorting: For all edges
(i,j) we have i<j.

Compute-OPT(j){
   if (in-degree(j)==0)
     return 0
   if (M[j]==empty)
     M[j]=0;
     for all edges (i,j)
       M[j] = max(M[j],1+Compute-OPT(i))
   return M[j]
}
Output max(M[1],…,M[n])
```

Running Time: $O(n+m)$
Memory: $O(n)$
Can we output the longest path?

Outputting the Longest Path

```
Let G be a DAG given with a topological sorting: For all edges
(i,j) we have i<j.
Initialize Parent[j]=-1 for all j.
Compute-OPT(j){
    if (in-degree(j)==0)
      return 0
    if (M[j]==empty)
      M[j]=0;
      for all edges (i,j)
        if (M[j] < 1+Compute-OPT(i))
          M[j]=1+Compute-OPT(i)
          Parent[j]=i
    return M[j]
}
Let M[k] be the maximum of M[1],…,M[n]
While (Parent[k]!=-1)
    Print k
    k=Parent[k]
```

Record the entry that
we used to compute OPT(j)

Longest Increasing Subsequence

Longest Increasing Subsequence

Given a sequence of numbers

Find the longest increasing subsequence

41, 22, 9, 15, 23, 39, 21, 56, 24, 34, 59, 23, 60, 39, 87, 23, 90

41, 22, **9**, **15**, **23**, 39, 21, 56, **24**, **34**, **59**, 23, **60**, 39, **87**, 23, 90

DP for LIS

Let OPT(j) be the longest increasing subsequence ending at j.

Observation: Suppose the OPT(j) is the sequence

$$x_{i_1}, x_{i_2}, \dots, x_{i_k}, x_j$$

Then, $x_{i_1}, x_{i_2}, \dots, x_{i_k}$ is the longest increasing subsequence ending at x_{i_k}, i.e., $OPT(j) = 1 + OPT(i_k)$

$$OPT(j) = \begin{cases} 1 & \text{If } x_j > x_i \text{ for all } i < j \\ 1 + \max_{i: x_i < x_j} OPT(i) & \text{o.w.} \end{cases}$$

Remark: This is a special case of Longest path in a DAG: Construct a graph 1,…n where (i, j) is an edge if $i < j$ and $x_i < x_j$.

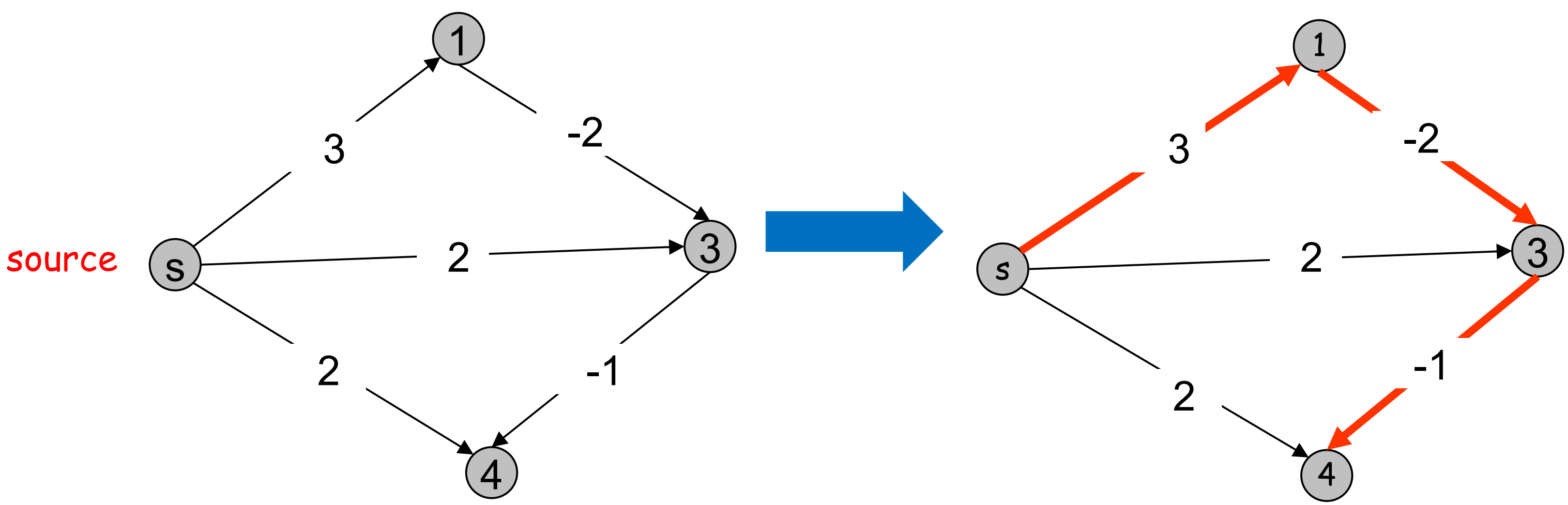
Shortest Paths with Negative Edge Weights

Shortest Paths with Neg Edge Weights

Given a weighted directed graph $G = (V, E)$ and a source vertex s, where the weight of edge (u,v) is $c_{u,v}$

Goal: Find the shortest path from s to all vertices of G.

Recall that Dikjstra's Algorithm fails when weights are negative

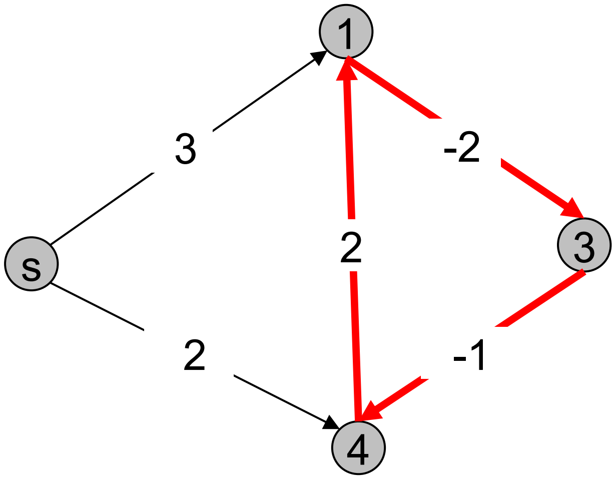


Impossibility on Graphs with Neg Cycles

Observation: No solution exists if G has a negative cycle.

This is because we can minimize the length by going over the cycle again and again.

So, suppose G does not have a negative cycle.



DP for Shortest Path

Def: Let $OPT(v, i)$ be the length of the shortest s - v path with at most i edges.

Let us characterize $OPT(v, i)$.

Case 1: $OPT(v, i)$ path has less than i edges.

- Then, $OPT(v, i) = OPT(v, i - 1)$.

Case 2: $OPT(v, i)$ path has exactly i edges.

- Let $s, v_1, v_2, \dots, v_{i-1}, v$ be the $OPT(v, i)$ path with i edges.
- Then, $s, v_1, \dots, v_{i-1}$ must be the shortest s - v_{i-1} path with at most $i - 1$ edges. So,
$$OPT(v, i) = OPT(v_{i-1}, i - 1) + c_{v_{i-1}, v}$$

DP for Shortest Path

Def: Let $OPT(v, i)$ be the length of the shortest s - v path with at most i edges.

$$OPT(v,i) = \begin{cases} 0 & \text{if } v = s \\ \infty & \text{if } v \neq s, i = 0 \\ \min\left(OPT(v, i-1), \min\limits_{u:(u,v)\text{ an edge}} OPT(u, i-1) + c_{u,v}\right) & \end{cases}$$

So, for every v, $OPT(v, ?)$ is the shortest path from s to v.

But how long do we have to run?

Since G has no negative cycle, it has at most $n-1$ edges. So, $OPT(v, n-1)$ is the answer.

Bellman Ford Algorithm

```
for v=1 to n
   if v ≠ s then
      M[v,0]=∞
M[s,0]=0.

for i=1 to n-1
   for v=1 to n
      M[v,i]=M[v,i-1]
      for every edge (u,v)
         M[v,i]=min(M[v,i], M[u,i-1]+c_{u,v})
```

Running Time: $O(nm)$

Can we test if G has negative cycles?

Bellman Ford Algorithm

```
for v=1 to n
   if v ≠ s then
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M[s,0]=0.

for i=1 to n-1
   for v=1 to n
      M[v,i]=M[v,i-1]
      for every edge (u,v)
         M[v,i]=min(M[v,i], M[u,i-1]+c_{u,v})
```

Running Time: $O(nm)$

Can we test if G has negative cycles?

Yes, run for i=1…2n and see if the M[v,n-1] is different from M[v,2n]

DP Techniques Summary

Recipe:

- Follow the natural induction proof.
- Find out additional assumptions/variables/subproblems that you need to do the induction
- Strengthen the hypothesis and define w.r.t. new subproblems

Dynamic programming techniques.

- Whenever a problem is a special case of an NP-hard problem an ordering is important:
- Adding a new variable: knapsack.
- Dynamic programming over intervals: RNA secondary structure.

Top-down vs. bottom-up:

- Different people have different intuitions
- Bottom-up is useful to optimize the memory