Design and Analysis of Algorithms
Dynamic Programming

Si Wu

School of CSE, SCUT

cswusi@scut.edu.cn

TA: 1684350406@qq.com

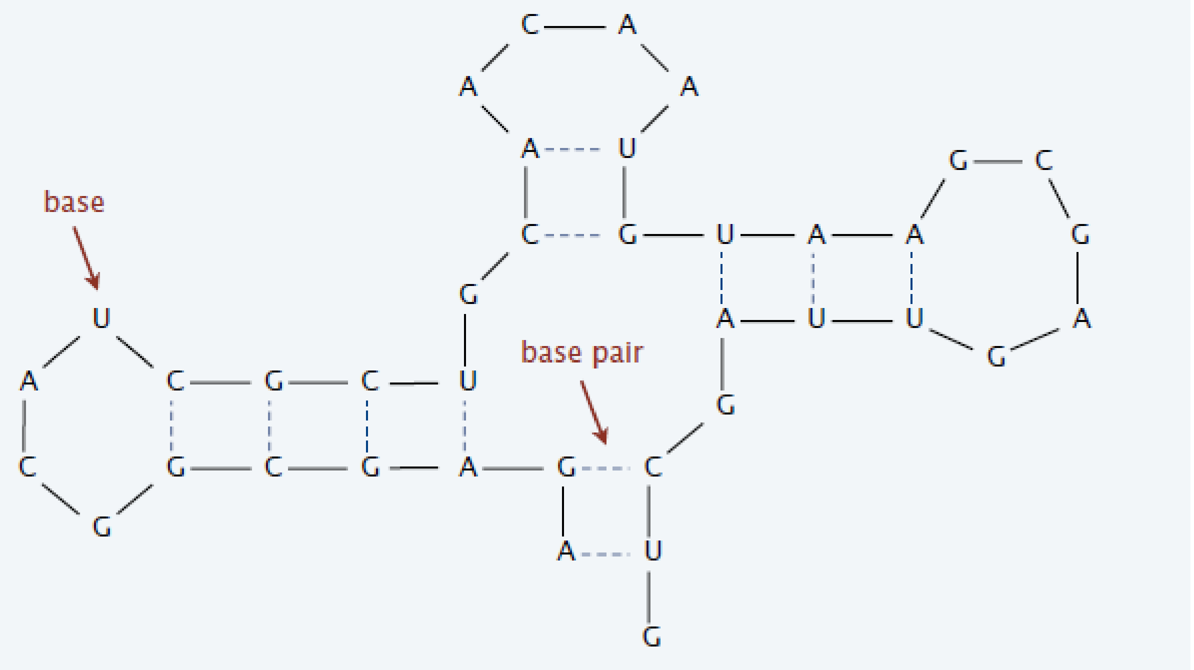
Topics

- **RNA Secondary Structure**
- **Bellman-Ford Algorithm**
- **Sequence Alignment**

RNA Secondary Structure

RNA. String $B = b_1 b_2 \ldots b_n$ over alphabet {A, C, G, U}.

Secondary structure. RNA is single-stranded so it tends to loop back and form base pairs with itself. This structure is essential for understanding behavior of molecule.



RNA secondary structure for GUCGAUUGAGCGAAUGUAACAACGUGGCUACGGCGAGA

RNA Secondary Structure

Secondary structure. A set of pairs $S = \{(b_i, b_j)\}$ that satisfy:

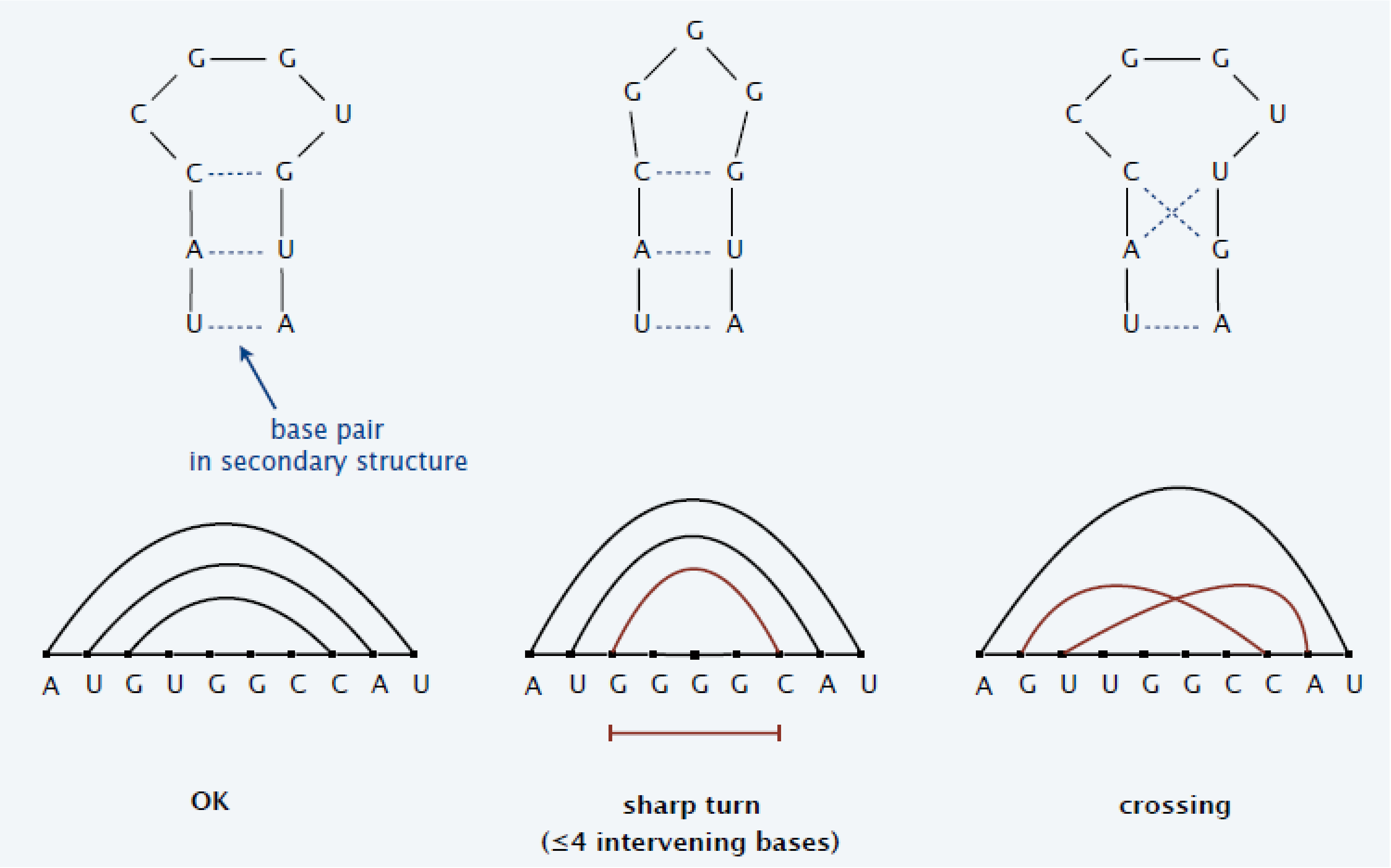
- Each pair in S is a Watson-Crick complement: A-U, U-A, C-G, or G-C.
- The ends of each pair are separated by at least 4 intervening bases. If $(b_i, b_j) \in S$, then $i < j - 4$.
- If (b_i, b_j) and (b_k, b_l) are two pairs in S, then we cannot have $i < k < j < l$.

Free energy. Usual hypothesis is that an RNA molecule will form the secondary structure with the minimum total free energy. (approximate by the number of base pairs)

Goal. Given an RNA molecule $B = b_1 b_2 \ldots b_n$, find a secondary structure S that maximizes the number of base pairs.

RNA Secondary Structure

Examples.

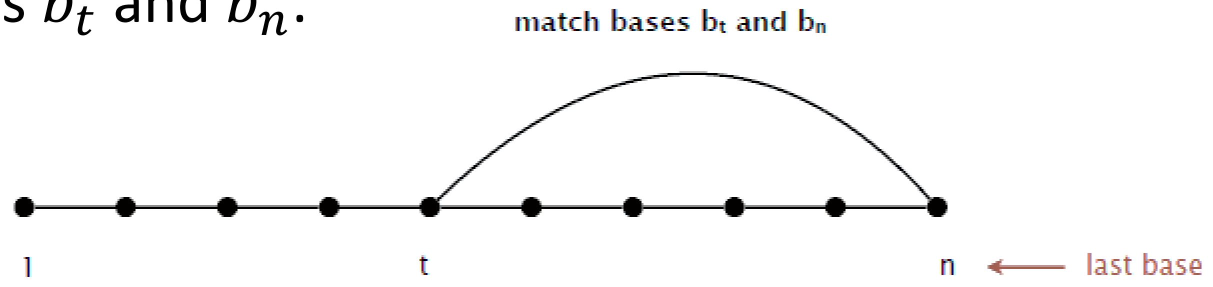


RNA Secondary Structure: Sub-problems

First attempt. $OPT(j)$ = maximum number of base pairs in a secondary of the substring $b_1 b_2 \ldots b_j$.

Goal. $OPT(n)$

Choice. Match bases b_t and b_n.

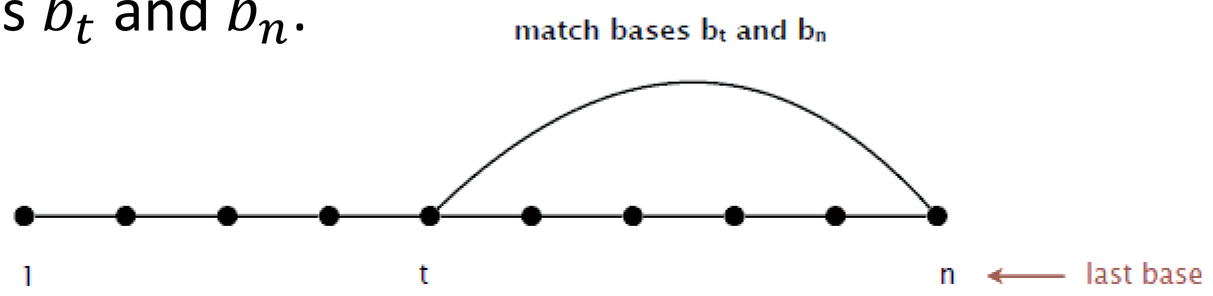


RNA Secondary Structure: Sub-problems

First attempt. $OPT(j)$ = maximum number of base pairs in a secondary of the substring $b_1 b_2 \dots b_j$.

Goal. $OPT(n)$

Choice. Match bases b_t and b_n.



Difficulty. Results in two sub-problems.

- Find secondary structure in $b_1 b_2 \dots b_{t-1}$. ($OPT(t-1)$)
- Find secondary structure in $b_{t+1} b_2 \dots b_{n-1}$. (need more sub-problems)

Dynamic Programming Over Intervals

Notation. $OPT(i, j)$ = maximum number of base pairs in a secondary of the substring $b_i b_{i+1} \dots b_j$.

Case 1. If $i \geq j - 4$.

- $OPT(i, j) = 0$ by no-sharp turns condition.

Case 2. Bases b_j is not involved in a pair.

- $OPT(i, j) = OPT(i, j - 1)$.

Case 3. Bases b_j pairs with b_t for some $i \leq t < j - 4$.

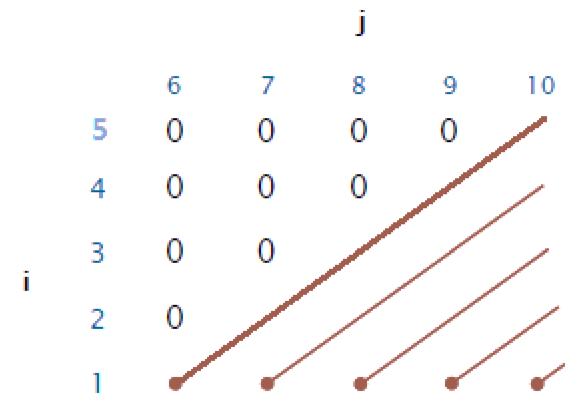
- Non-crossing constraint decouples resulting sub-problems.
- $OPT(i, j) = 1 + \max_t \{OPT(i, t - 1) + OPT(t + 1, j - 1)\}$.

(take max over t such that $i \leq t < j - 4$, b_t and b_j are Watson-Crick complements)

Bottom-Up Dynamic Programming Over Intervals

Q. In which order to solve the sub-problems?

A. Do shortest intervals first.



order in which to solve subproblems

RNA-Secondary-Structure $(n, b_1, b_2, \dots, b_n)$

For $k = 5$ To $n - 1$

  For $i = 1$ To $n - k$

    $j \leftarrow i + k$.

    For each b_t $(i \le t < j - 4)$ paired with b_j

      $T = 1 + M[i, t-1] + M[t+1, j-1]$.

      $M[i, j] \leftarrow \max\{M[i, j-1], T\}$.

Return $M[1, n]$.

RNA Secondary Structure: An Example

RNA sequence. A C C G G U A G U
1 2 3 4 5 6 7 8 9

4	0	0	0	
3	0	0		
2	0			
$i = 1$				
	$j = 6$	7	8	9

Initial values

RNA-Secondary-Structure $(n, b_1, b_2, \dots, b_n)$

For $k = 5$ To $n - 1$
  For $i = 1$ To $n - k$
    $j \leftarrow i + k.$
    For each b_t $(i \le t < j - 4)$ paired with b_j
      $T = 1 + M[i, t-1] + M[t+1, j-1].$
      $M[i, j] \leftarrow \max\{M[i, j-1], T\}.$
Return $M[1, n]$.

RNA Secondary Structure: An Example

RNA sequence. A C C G G U A G U

	A	C	C	G	G	U	A	G	U
	1	2	3	4	5	6	7	8	9

$$\boxed{i \le t < j - 4}$$

4	0	0	0	
3	0	0		
2	0			
i = 1				
j =	6	7	8	9

Initial values

4	0	0	0	0
3	0	0	1	
2	0	0		
i = 1	1			
j =	6	7	8	9

Filling in the values for k = 5

4	0	0	0	0
3	0	0	1	1
2	0	0	1	
i = 1	1	1		
j =	6	7	8	9

Filling in the values for k = 6

4	0	0	0	0
3	0	0	1	1
2	0	0	1	1
i = 1	1	1	1	
j =	6	7	8	9

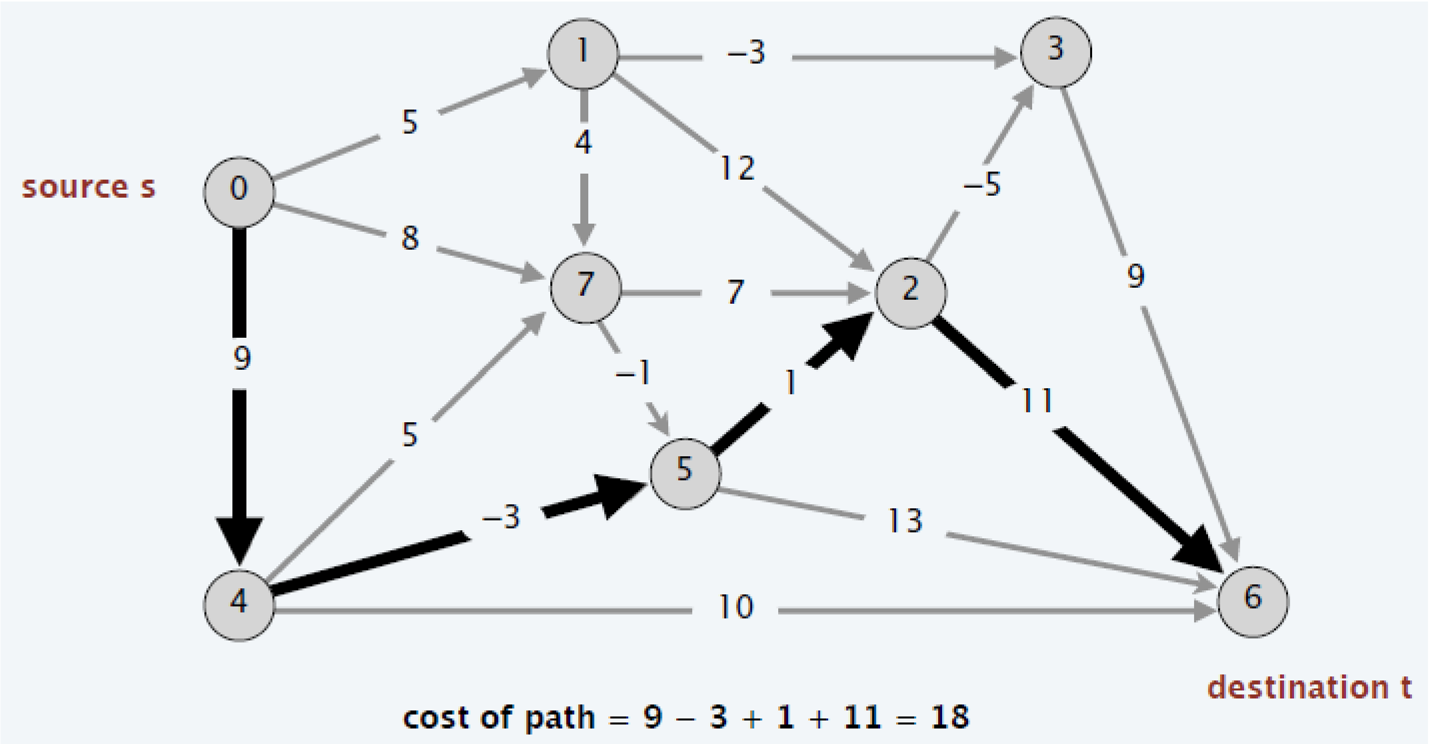
Filling in the values for k = 7

4	0	0	0	0
3	0	0	1	1
2	0	0	1	1
i = 1	1	1	1	2
j =	6	7	8	9

Filling in the values for k = 8

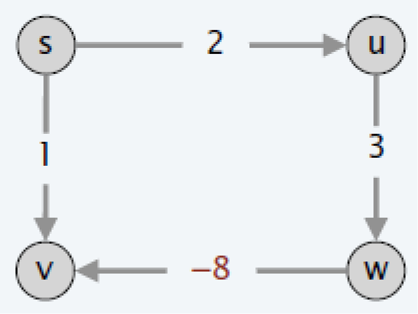
Shortest Paths

Shortest-path problem. Given a digraph $G = (V, E)$, with arbitrary edge weights or cost c_{vw}, find cheapest path from node s to node t.

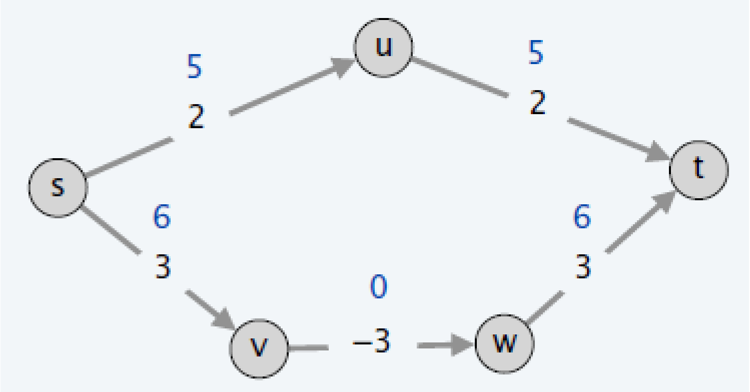


Shortest Paths: Failed Attempts

Dijkstra. May not produce shortest paths when edge weights are negatives.

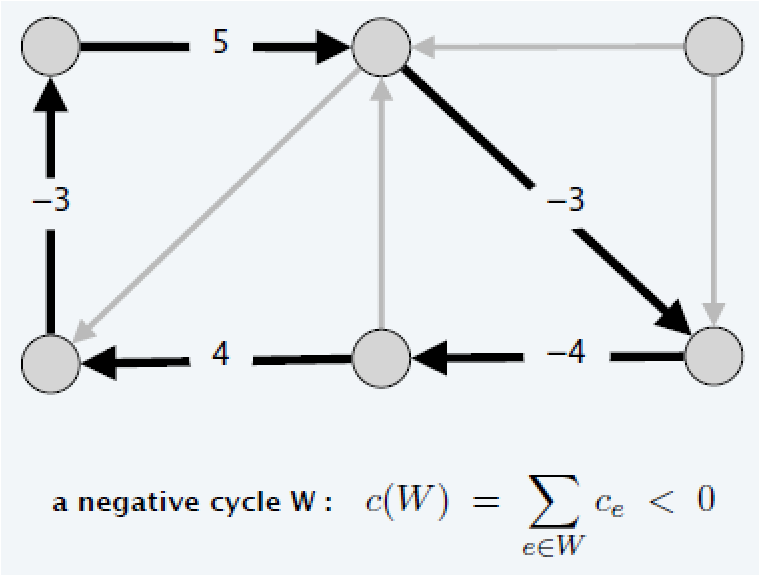


Reweighting. Adding a constant to every edge weight does not necessarily make Dijkstra's algorithm produce shortest paths.



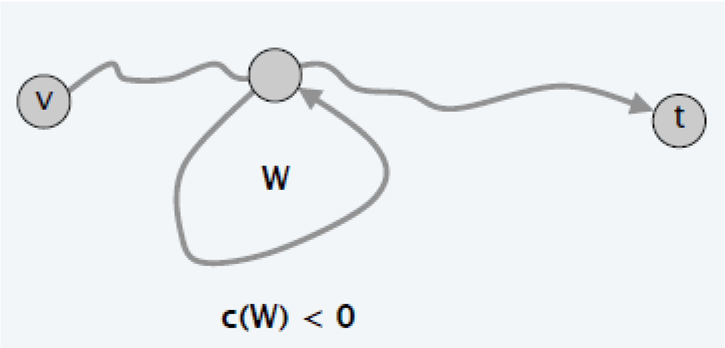
Negative Cycles

Def. A negative cycle is a directed cycle such that sum of its edge weight is negative.



Shortest Paths and Negative Cycles

Lemma 1. If some path from v to t contains a negative cycle, then there does not exist a cheapest path from v to t.

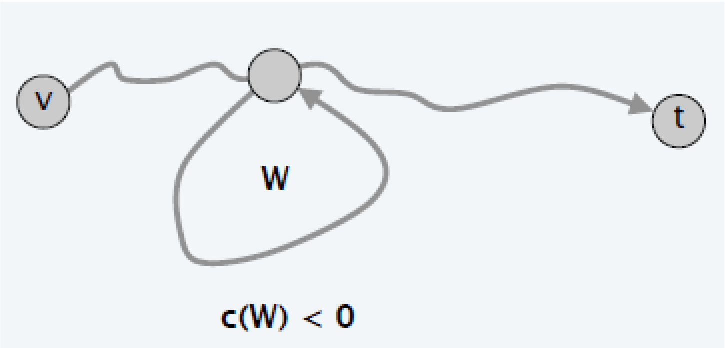


Shortest Paths and Negative Cycles

Lemma 1. If some path from v to t contains a negative cycle, then there does not exist a cheapest path from v to t.

Pf.

If there exists such a cycle W, then can build a $v \to t$ path of arbitrarily negative weight by detouring around cycle as many times as desired.

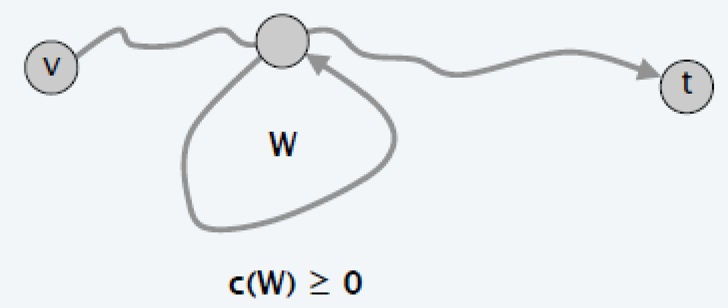


Shortest Paths and Negative Cycles

Lemma 2. If G has no negative cycles, then there exists a cheapest path from v to t that is simple (i.e. does not repeat nodes), and hence has at most $\leq n - 1$ edges.

Pf.

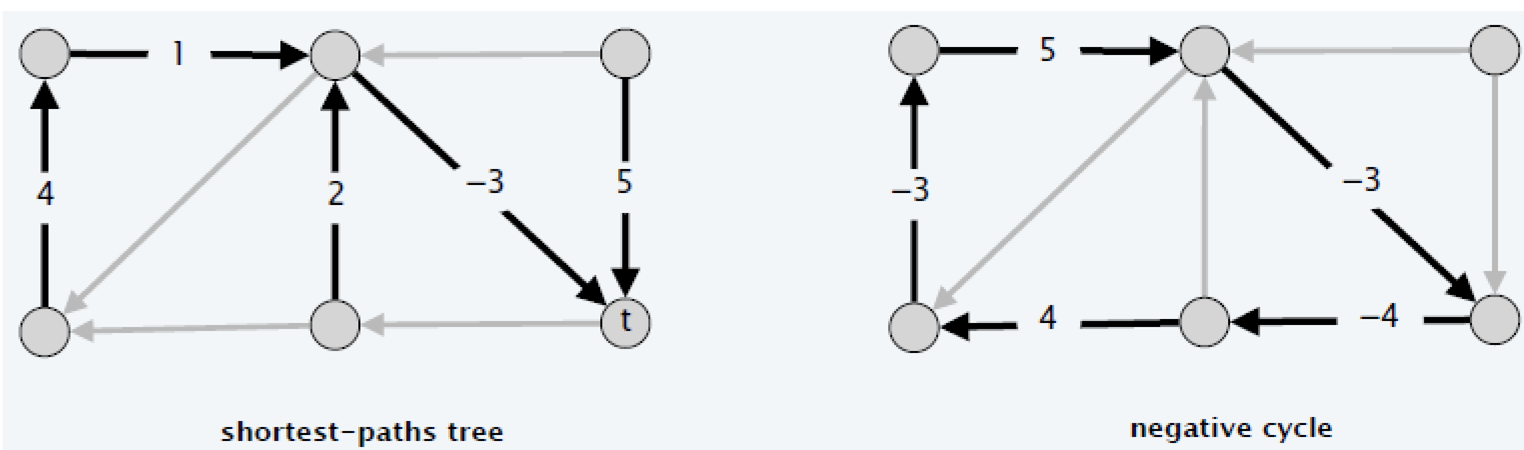
- Consider a cheapest $v \rightarrow t$ path P that uses the fewest edges.
- If P contains a cycle W, can remove portion of P corresponding to W without increasing the cost.



Shortest Paths and Negative-Cycles Problems

Single-destination shortest-paths problem. Given a digraph $\mathrm{G} = (V, E)$ with edge weights c_{vw}, and no negative cycles and a distinguished note t, find cheapest $v \rightarrow t$ path for each node v.

Negative-cycle problem. Given a digraph $\mathrm{G} = (V, E)$ with edge weights c_{vw}, find a negative cycle (if one exists).



Shortest Paths: Dynamic Programming

Def. $OPT(i, v)$ = cost of shortest $v \to t$ path that uses $\leq i$ edges.

- Case 1: Cheapest $v \to t$ path uses $\leq i - 1$ edges.
  - $OPT(i, v) = OPT(i - 1, v)$.
- Case 2: Cheapest $v \to t$ path uses exactly i edges.
  - If (v, w) is the first edge, then OPT uses (v, w), and then selects best $w \to t$ path using $\leq i - 1$ edges.

$$OPT(i, v) = \begin{cases} \infty & if\ i = 0 \\ \min\left\{OPT(i-1, v), \min\limits_{(v,w)\in E}\{OPT(i-1, w) + c_{vw}\}\right\} & otherwise \end{cases}$$

Observation. If no negative cycles, $OPT(n - 1, v)$ = cost of cheapest $v \to t$ path.

Shortest Paths: Implementation

Shortest-Paths (V, E, c, t)

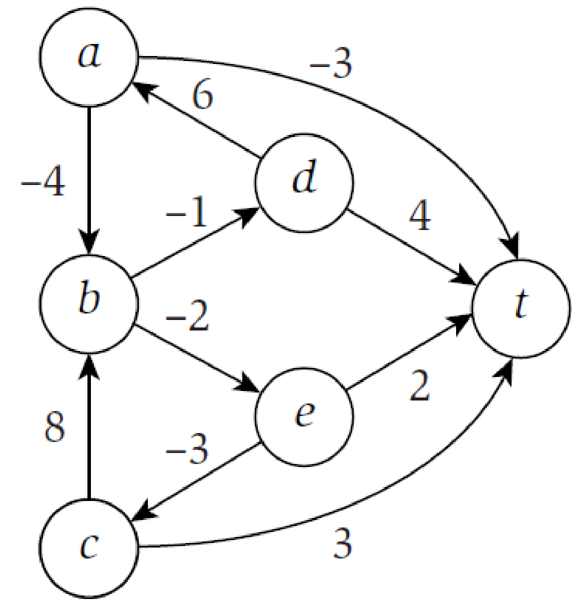
For each node $v \in V$
  $M[0, v] \leftarrow \infty.$

$M[0, t] \leftarrow 0.$

For $i = 0$ To $n - 1$
  For each node $v \in V$
    $M[i, v] \leftarrow M[i - 1, v].$
   For each edge $(v, w) \in E$
     $M[i, v] \leftarrow \min\{M[i, v], M[i - 1, w] + c_{vw}\}.$

Shortest Paths: An Example

Ex. Considering the following directed graph, find a shortest path from each node to t.



Shortest-Paths (V, E, c, t)

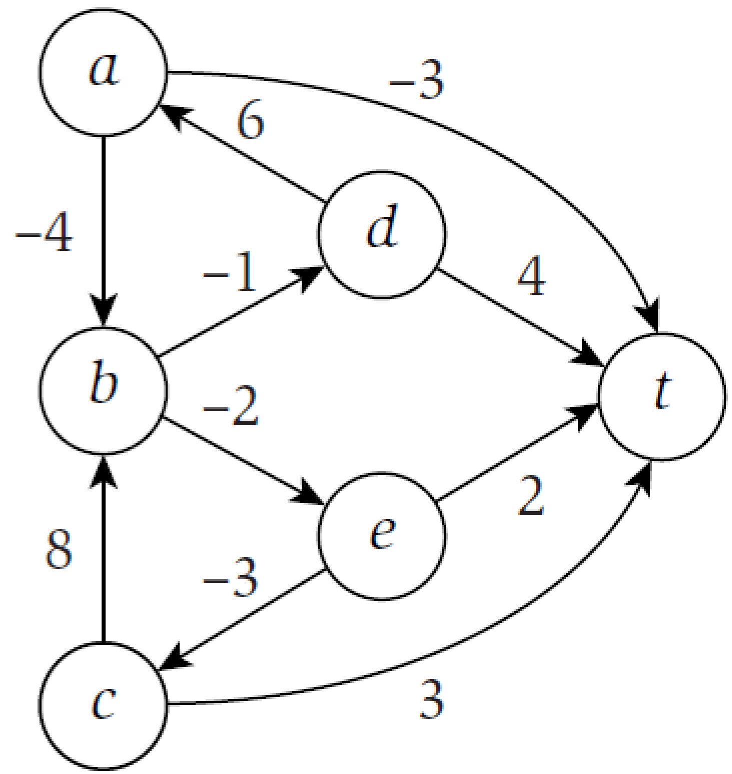
For each node $v \in V$
  $M[0, v] \leftarrow \infty$.
$M[0, t] \leftarrow 0$.
For $i = 0$ To $n - 1$
  For each node $v \in V$
    $M[i, v] \leftarrow M[i-1, v]$.
    For each edge $(v, w) \in E$
      $M[i, v] \leftarrow \min\{M[i, v], M[i-1, w] + c_{vw}\}$.

	0	1	2	3	4	5
t						
a						
b						
c						
d						
e						

Shortest Paths: An Example

Ex. Considering the following directed graph, find a shortest path from each node to t.

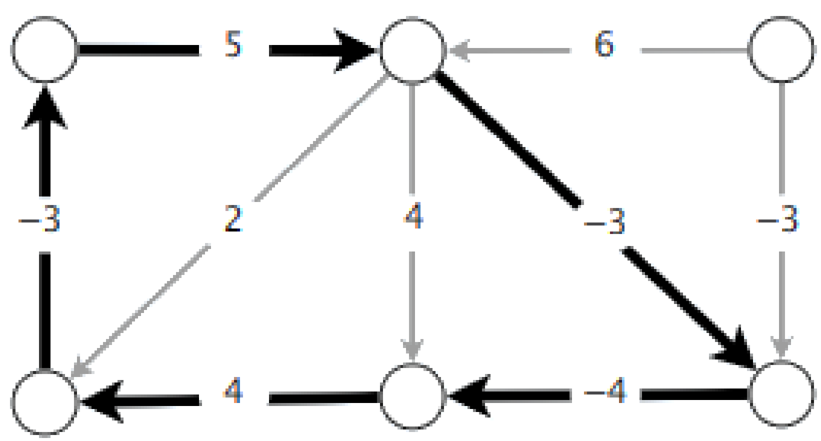
	0	1	2	3	4	5
t	0	0	0	0	0	0
a	∞	−3	−3	−4	−6	−6
b	∞	∞	0	−2	−2	−2
c	∞	3	3	3	3	3
d	∞	4	3	3	2	0
e	∞	2	0	0	0	0



Each row corresponds to the shortest path from a node to t, as we allow the path to use an increasing number of edges

Detecting Negative Cycles

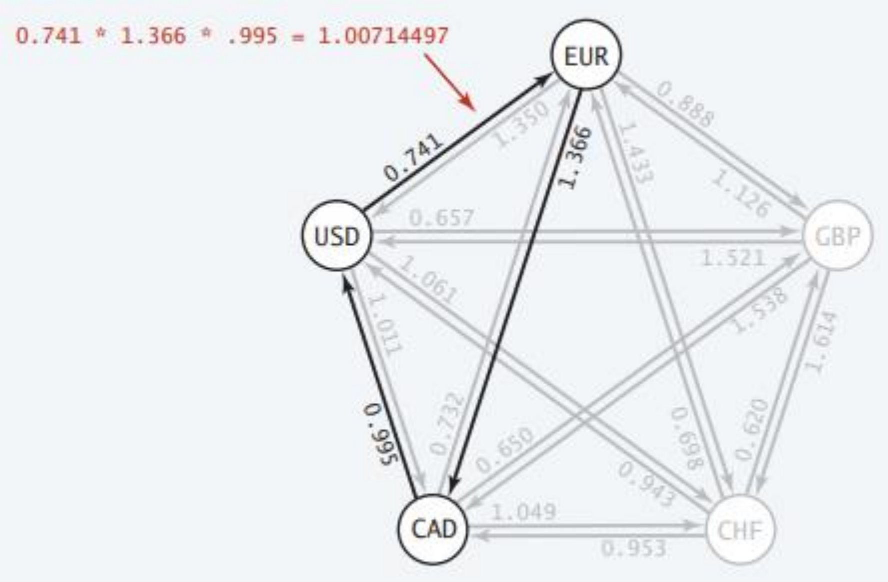
Negative cycle detection problem: Given a digraph $G(V, E)$, with edge lengths ℓ_{vw}, find a negative cycle (if one exists).



Detecting Negative Cycles: Application

Currency conversion: Given n currencies and exchange rates between pairs of currencies, is there an arbitrage opportunity?

Remark. Fastest algorithm very valuable!



Detecting Negative Cycles

Lemma 1. If $OPT(n, v) = OPT(n-1, v)$ for every node v, then no negative cycles.
Pf. The $OPT(n, v)$ values have converged $\Longrightarrow$ shortest $v \rightarrow t$ path exists.

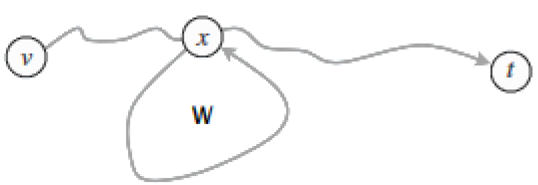
Lemma 2. If $OPT(n, v) < OPT(n-1, v)$ for some node v, then (any) shortest $v \rightarrow t$ path of length $\leq n$ contains a cycle W. Moreover W is a negative cycle.

Detecting Negative Cycles

Lemma 2. If $OPT(n, v) < OPT(n-1, v)$ for some node v, then (any) shortest $v \to t$ path of length $\leq n$ contains a cycle W. Moreover W is a negative cycle.

Pf. [by contradiction]

- Since $OPT(n, v) < OPT(n-1, v)$, we know that shortest $v \to t$ path P has exactly n edges.
- The path P must contain a repeated note x.
- Let W be any cycle in P.
- Deleting W yields a $v \to t$ path with $< n$ edges $\Longrightarrow W$ is a negative cycle.



c(W) < 0

String Similarity

Q. How similar are two strings?

Ex. ocurrance & occurrence.

o	c	u	r	r	a	n	c	e	–
o	c	c	u	r	r	e	n	c	e

6 mismatches, 1 gap

o	c	–	u	r	r	a	n	c	e
o	c	c	u	r	r	e	n	c	e

1 mismatch, 1 gap

o	c	–	u	r	r	–	a	n	c	e
o	c	c	u	r	r	e	–	n	c	e

0 mismatches, 3 gaps

Edit Distance

Edit distance.

- Gap penalty δ; mismatch penalty α_{pg}.
- Cost = sum of gap and mismatch penalties.

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

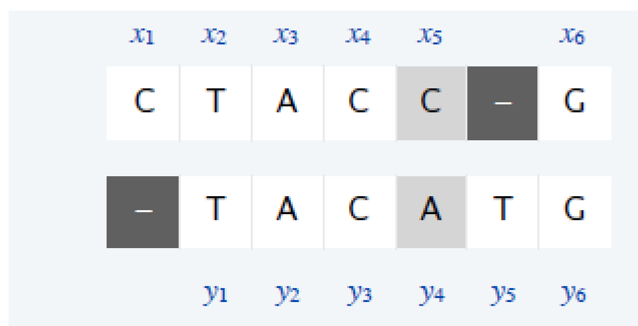
$$\text{cost} = \delta + \alpha_{CG} + \alpha_{TA}$$

Applications. Speech recognition, computational biology,…

Sequence Alignment

Goal. Given two strings $x_1 x_2 \dots x_m$ and $y_1 y_2 \dots y_n$ find a min-cost alignment.

Def. An alignment M is a set of ordered pairs $x_i - y_j$ such that each item occurs in at most one pair and no crossings ($x_i - y_j$ and $x_h - y_k$ cross if $i < h$, but $j > k$).



an alignment of CTACCG and TACATG:

$M = \{ x_2–y_1, x_3–y_2, x_4–y_3, x_5–y_4, x_6–y_6 \}$

Sequence Alignment

Goal. Given two strings $x_1 x_2 \ldots x_m$ and $y_1 y_2 \ldots y_n$ find a min-cost alignment.

Def. An alignment M is a set of ordered pairs $x_i - y_j$ such that each item occurs in at most one pair and no crossings ($x_i - y_j$ and $x_h - y_k$ cross if $i < h$, but $j > k$).

Def. The cost of an alignment M is:

$$cost(M) = \underbrace{\sum_{(x_i, y_j) \in M} \alpha_{x_i y_j}}_{\text{mismatch}} + \underbrace{\sum_{i: x_i \; unmatched} \delta + \sum_{j: y_j \; unmatched} \delta}_{\text{gap}}$$

Sequence Alignment: Problem Structure

Def. $OPT(i, j) =$ min cost of aligning prefix strings $x_1 x_2 \dots x_i$ and $y_1 y_2 \dots y_j$.
Goal. $OPT(m, n)$.

Case 1. $OPT(i, j)$ includes $x_i - y_j$.
Pay mismatch for $x_i - y_j$ + min cost of aligning $x_1 x_2 \dots x_{i-1}$ and $y_1 y_2 \dots y_{j-1}$.

Case 2a. $OPT(i, j)$ leaves x_i unmatched.
Pay gap for x_i + min cost of aligning $x_1 x_2 \dots x_{i-1}$ and $y_1 y_2 \dots y_j$.

Sequence Alignment: Problem Structure

Def. $OPT(i,j)$ = min cost of aligning prefix strings $x_1 x_2 \ldots x_i$ and $y_1 y_2 \ldots y_j$.
Goal. $OPT(m,n)$.

Case 2b. $OPT(i,j)$ leaves y_j unmatched.
Pay gap for y_j + min cost of aligning $x_1 x_2 \ldots x_i$ and $y_1 y_2 \ldots y_{j-1}$.

$$OPT(i,j) = \begin{cases} j\delta & if\ i = 0 \\ min \begin{cases} \alpha_{x_i y_j} + OPT(i-1, j-1) \\ \delta + OPT(i-1, j) \\ \delta + OPT(i, j-1) \end{cases} & otherwise \\ i\delta & if\ j = 0 \end{cases}$$

Sequence Alignment: Bottom-Up Algorithm

Sequence-Alignment $(m, n, x_1, \ldots, x_m, y_1, \ldots, y_n, \delta, \alpha)$

For $i = 0$ To m
$\quad M[i, 0] \leftarrow i\delta.$
For $j = 0$ To n
$\quad M[0, j] \leftarrow j\delta.$

For $i = 1$ To m
$\quad$ For $j = 1$ To n

$$M[i, j] \leftarrow \min\{\alpha[x_i, y_j] + M[i-1, j-1], \delta + M[i-1, j], \delta + M[i, j-1]\}.$$

Return $M[m, n]$.

Sequence Alignment: An Example

Ex. Align the words *mean* and *name*. Assume that $\delta = 2$; matching a vowel with a different vowel, or a consonant with a different consonant, costs 1; while matching a vowel, or a consonant with each other costs 3.

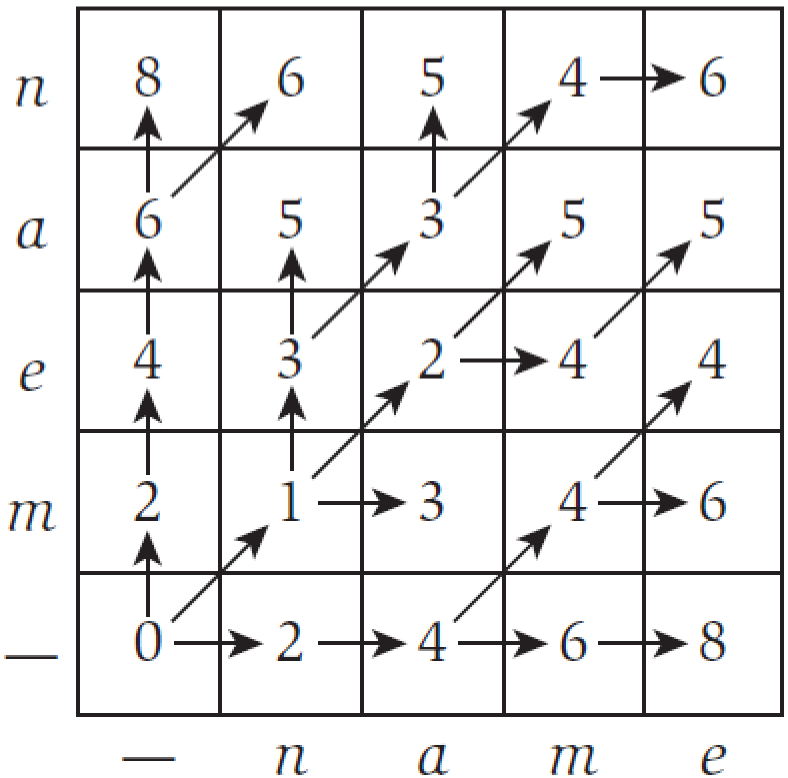
Sequence-Alignment $(m, n, x_1, \ldots, x_m, y_1, \ldots, y_n, \delta, \alpha)$

For $i = 0$ To m
 $M[i, 0] \leftarrow i\delta.$
For $j = 0$ To n
 $M[0, j] \leftarrow j\delta.$
For $i = 1$ To m
 For $j = 1$ To n
  $M[i, j] \leftarrow \min\{\alpha[x_i, y_j] + M[i-1, j-1],$
   $\delta + M[i-1, j], \delta + M[i, j-1]\}.$
Return $M[m, n]$.

n					
a					
e					
m					
-					
	-	**n**	**a**	**m**	**e**

Sequence Alignment: An Example

Ex. Align the words *mean* and *name*. Assume that $\delta = 2$; matching a vowel with a different vowel, or a consonant with a different consonant, costs 1; while matching a vowel, or a consonant with each other costs 3.



$$M[i,j] \leftarrow \min\{\alpha[x_i, y_j] + M[i-1, j-1], \\ \delta + M[i-1, j], \delta + M[i, j-1]\}$$

By following arrows backward from node (4,4), we can trace back to construct the alignment.

Dynamic Programming Summary

Outline.

- Define a collection of subproblems (typically, only a polynomial number of subproblems).
- Solution to original problem can be computed from subproblems.
- Natural ordering of subproblems from “smallest” to “largest” that enables determining a solution to a subproblem from solutions to smaller subproblems.

Techniques.

- Binary choice: weighted interval scheduling.
- Multiway choice: segmented least squares.
- Adding a new variable: knapsack problem.
- Intervals: RNA secondary structure.