CSE 421: Algorithms

Winter 2014

Lecture 17: Sequence alignment and Bellman-Ford

Reading:
Sections 6.6-6.10

sequence alignment: edit distance

- **Given:**
  - Two strings of characters $A=a_1\ a_2 \ldots a_n$ and $B=b_1\ b_2 \ldots b_m$
- **Find:**
  - The minimum number of edit steps needed to transform A into B where an edit can be:
  - insert a single character
  - delete a single character
  - substitute one character by another

recursive solutions

- Sub-problems: Edit distance problems for **all prefixes** of A and B that don't include all of both A and B
- Let D(i,j) be the number of edits required to transform $a_1\ a_2 \ldots a_i$ into $b_1\ b_2 \ldots b_j$
- Clearly D(0,0)=0

computing D(n,m)

- Imagine how best sequence handles the last characters a_n and b_m
- Think of $b_1 b_2 \ldots b_m$ as fixed and we want to edit $a_1 a_2 \ldots a_n$. How will the last character become b_m ?

computing D(n,m)

- Imagine how best sequence handles the last characters a_n and b_m
- If best sequence of operations
  - deletes a_n then D(n,m)=
  - inserts b_m then D(n,m)=
  - replaces a_n by b_m then D(n,m)=
  - matches a_n and b_m then D(n,m)=

computing D(n,m)

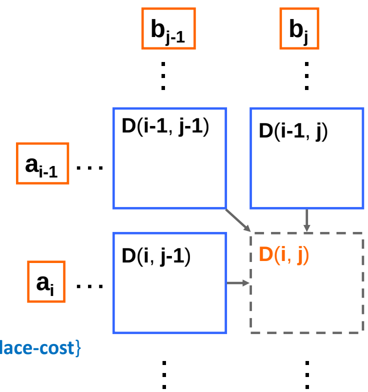
- Imagine how best sequence handles the last characters a_n and b_m
- If best sequence of operations
  - deletes a_n then D(n,m)=D(n-1,m)+1
  - inserts b_m then D(n,m)=D(n,m-1)+1
  - replaces a_n by b_m then D(n,m)=D(n-1,m-1)+1
  - matches a_n and b_m then D(n,m)=D(n-1,m-1)

recursive algorithm D(n,m)

```
if n=0 then
    return (m)
else if m=0 then
    return(n)
else
    if a_n=b_m then
        replace-cost ← 0
    else                          } cost of substitution of a_n by b_m (if used)
        replace-cost ← 1
    endif
    return(min{ D(n-1, m) + 1,
                D(n, m-1) + 1,
                D(n-1, m-1) + replace-cost } )
```

dynamic programming

```
for j = 0 to m; D(0,j) ← j; endfor
for i = 1 to n; D(i,0) ← i; endfor
for i = 1 to n
    for j = 1 to m
        if a_i=b_j then
            replace-cost ← 0
        else
            replace-cost ← 1
        endif
        D(i,j) ← min { D(i-1, j) + 1,
                       D(i, j-1) + 1,
                       D(i-1, j-1) + replace-cost}
    endfor
endfor
```



example run with AGACATTG and GAGTTA

		A	G	A	C	A	T	T	G
	0	1	2	3	4	5	6	7	8
	0								
G	1								
A	2								
G	3								
T	4								
T	5								
A	6								

example run with AGACATTG and GAGTTA

		A	G	A	C	A	T	T	G
	0	1	2	3	4	5	6	7	8
G	1	1	1	2	3	4	5	6	7
A	2								
G	3								
T	4								
T	5								
A	6								

example run with AGACATTG and GAGTTA

		A	G	A	C	A	T	T	G
	0	1	2	3	4	5	6	7	8
G	1	1	1	2	3	4	5	6	7
A	2	1	2	1					
G	3								
T	4								
T	5								
A	6								

example run with AGACATTG and GAGTTA

		A	G	A	C	A	T	T	G
	0	1	2	3	4	5	6	7	8
G	1	1	1	2	3	4	5	6	7
A	2	1	2	1	2	3	4	5	6
G	3	2	1	2	2	3	4	5	5
T	4								
T	5								
A	6								

example run with AGACATTG and GAGTTA

		A	G	A	C	A	T	T	G
	0	1	2	3	4	5	6	7	8
G	1	1	1	2	3	4	5	6	7
A	2	1	2	1	2	3	4	5	6
G	3	2	1	2	2	3	4	5	5
T	4	3	2	2	3	3	3	4	5
T	5	4	3	3	3	4	3	3	4
A	6	5	4	3	4	3	4	4	4

example run with AGACATTG and GAGTTA

		A	G	A	C	A	T	T	G
	0	1	2	3	4	5	6	7	8
G	1	1	1	2	3	4	5	6	7
A	2	1	2	1	2	3	4	5	6
G	3	2	1	2	2	3	4	5	5
T	4	3	2	2	3	3	3	4	5
T	5	4	3	3	3	4	3	3	4
A	6	5	4	3	4	3	4	4	4

example run with AGACATTG and GAGTTA

		A	G	A	C	A	T	T	G
	0	1	2	3	4	5	6	7	8
G	1	1	1	2	3	4	5	6	7
A	2	1	2	1	2	3	4	5	6
G	3	2	1	2	2	3	4	5	5
T	4	3	2	2	3	3	3	4	5
T	5	4	3	3	3	4	3	3	4
A	6	5	4	3	4	3	4	4	4

reading off the operations

- **Follow the sequence and use each color of arrow to tell you what operation was performed.**
- **From the operations can derive an optimal alignment / edit sequence**

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

computing edit distance on strings of length m and n

- **Time:**

- **Space:**

saving space

- To compute the distance values we only need the last two rows (or columns)
  - **O**(min(**m**,**n**)) space
- To compute the alignment/sequence of operations
  - seem to need to store all **O**(**mn**) pointers/arrow colors
- Nifty divide and conquer variant that allows one to do this in **O**(min(**m**,**n**)) space and retain **O**(**mn**) time
  - In practice the algorithm is usually run on smaller chunks of a large string, e.g. **m** and **n** are lengths of genes so a few thousand characters
    - Researchers want all alignments that are close to optimal
    - Basic algorithm is run since the whole table of pointers (**2** bits each) will fit in RAM
  - Ideas are neat, though

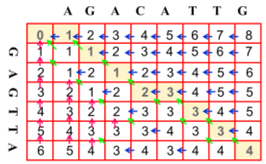
saving space

- Alignment corresponds to a path through the table from lower right to upper left
  - Must pass through the middle column
- Recursively compute the entries for the middle column from the left
  - If we knew the cost of completing each then we could figure out where the path crossed
  - Problem
    - There are **n** possible strings to start from.
  - Solution
    - Recursively calculate the right half costs for each entry in this column using alignments starting at the other ends of the two input strings!
  - Can reuse the storage on the left when solving the right hand problem

saving space

		A	G	A	C	A	T	T	G
	0	1	2	3	4	5	6	7	8
G	1	1	1	2	3	4	5	6	7
A	2	1	2	1	2	3	4	5	6
G	3	2	1	2	2	3	4	5	5
T	4	3	2	2	3	3	3	4	5
T	5	4	3	3	3	4	3	3	4
A	6	5	4	3	4	3	4	4	4

recurrence



$$T(m,n) \le cmn + T\left(q, \frac{n}{2}\right) + T\left(m-q, \frac{n}{2}\right)$$
$$T(m,1) \le cm$$
$$T(1,n) \le cn$$

shortest paths with negative edge weights

- **Dijsktra's algorithm failed with negative-cost edges**
  - **What can we do in this case?**
  - **Negative-cost cycles could result in shortest paths with length -∞**
- **Suppose no negative-cost cycles in G**
  - **Shortest path from s to t has at most n-1 edges**

    If not, there would be a repeated vertex which would create a cycle that could be removed since cycle can't have negative cost

shortest paths with negative edge weights

- **We want to grow paths from s to t based on the # of edges in the path**
- **Let Cost(s,t,i)=cost of minimum-length path from s to t using up to i hops.**

  - **Cost(v,t,0) =** $\begin{cases} 0 \text{ if } v=t \\ \infty \text{ otherwise} \end{cases}$

  - **Cost(v,t,i) =**

shortest paths with negative edge weights

- **We want to grow paths from s to t based on the # of edges in the path**
- **Let Cost(s,t,i)=cost of minimum-length path from s to t using up to i hops.**

  - **Cost(v,t,0) =** $\begin{cases} 0 \text{ if } v=t \\ \infty \text{ otherwise} \end{cases}$

  - **Cost(v,t,i) = min{ Cost(v,t,i-1),** $\min_{(v,w)\in E}(c_{vw}+\text{Cost}(w,t,i-1))$ **}**

Bellman-Ford

- Observe that the recursion for **Cost(s,t,i)** doesn't change **t**
  - Only store an entry for each **v** and **i**
    - Termed OPT(**v**,**i**) in the text
- Also observe that to compute OPT(*,**i**) we only need OPT(*,**i-1**)
  - Can store a current and previous copy in O(**n**) space.

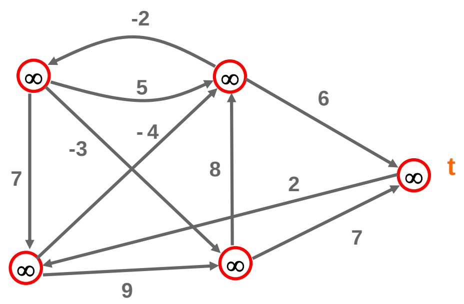
Bellman-Ford

ShortestPath(G,s,t)
    for all **v**∈**V**
        OPT[**v**]←∞
    OPT[**t**]←**0**
    for **i**=**1** to **n**-**1** do
        for all **v**∈**V** do
            OPT'[**v**]←$\min_{(v,w)\in E}$ (c_{vw}+**OPT**[**w**])
        for all **v**∈**V** do
            OPT[**v**]←min(**OPT'**[**v**],**OPT**[**v**])

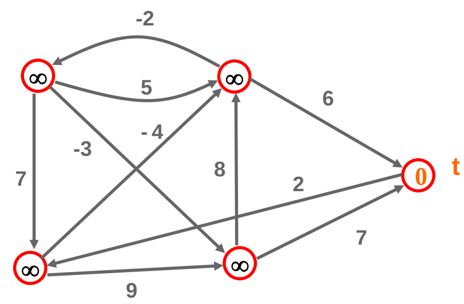
    return **OPT**[**s**]

O(**mn**) time

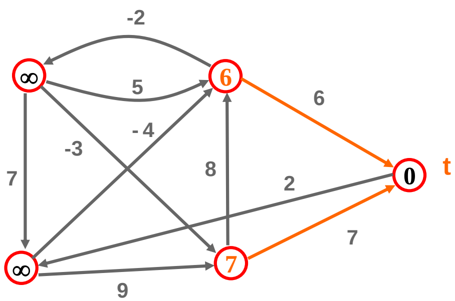
Bellman-Ford



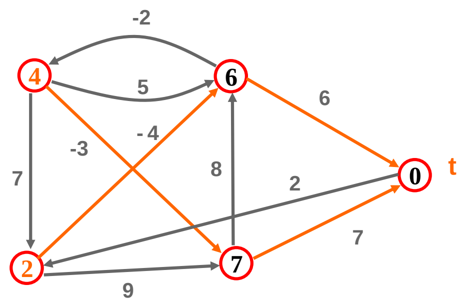
Bellman-Ford



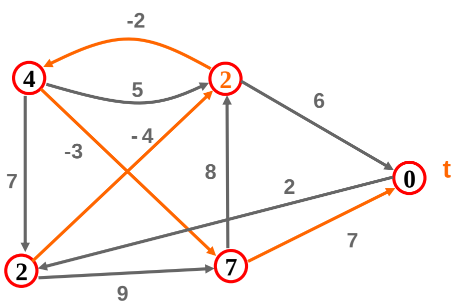
Bellman-Ford



Bellman-Ford



Bellman-Ford



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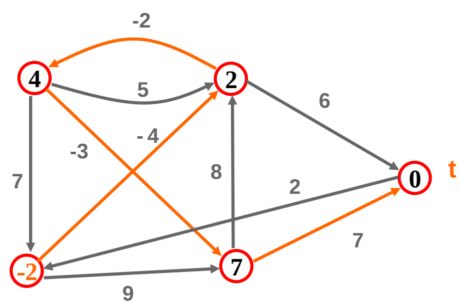

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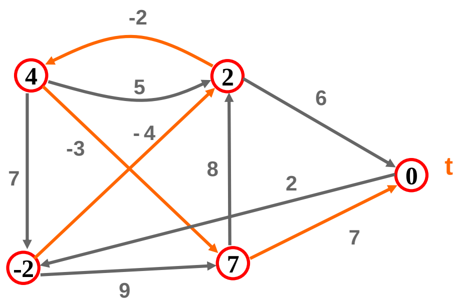
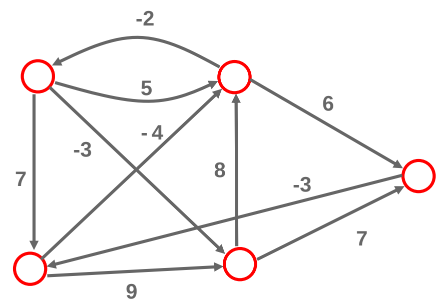


negative cycles



negative cycles

- **Claim:** There is a negative-cost cycle that can reach **t** iff for some vertex $v \in V$, $\mathrm{Cost}(v,t,n) < \mathrm{Cost}(v,t,n-1)$
- **Proof:**

negative cycles

- **Claim:** There is a negative-cost cycle that can reach **t** iff for some vertex $v \in V$, $\mathrm{Cost}(v,t,n) < \mathrm{Cost}(v,t,n-1)$
- **Proof:**
  - We already know that if there aren't any then we only need paths of length up to **n-1**
  - For the other direction
    - The recurrence computes **Cost(v,t,i)** correctly for **any** number of hops **i**
    - The recurrence reaches a fixed point if for every $v \in V$, $\mathrm{Cost}(v,t,i)=\mathrm{Cost}(v,t,i-1)$
    - A negative-cost cycle means that eventually some **Cost(v,t,i)** gets smaller than any given bound
      - Can't have a negative cost cycle if for every $v \in V$, $\mathrm{Cost}(v,t,n)=\mathrm{Cost}(v,t,n-1)$

last details

- Can run algorithm and stop early if the OPT and OPT' arrays are ever equal
  - Even better, one can update only neighbors **v** of vertices **w** with OPT'[w]≠OPT[w]
- Can store a successor pointer when we compute OPT
  - Homework assignment

- By running for **n** steps we can find some vertex **v** on a negative cycle and use the successor pointers to find the cycle