Comp 555 - BioAlgorithms - Spring 2022

- You have until Midnight Thursday to complete PS#6
- Final Study session Thursday April 28 (2:00-3:15)?

Randomized Algorithms

Randomized Algorithms

- Randomized algorithms incorporate random, rather than deterministic, decisions
- Commonly used in situations where no exact and/or fast algorithm is known

- Works for algorithms that behave well on typical data, but poorly in special cases
- Main advantage is that no input can reliably produce worst-case results because the algorithm runs differently each time.

Select

- **Select(L, k)** finds the kth smallest element in L
- Select(L,1) find the smallest…
  - Well known O(n) algorithm

```
minv = HUGE
for v in L:
    if (v < minv):
        minv = v
```

- Select(L, len(L)/2) find the median…
  - How?
  - median = sorted(L)[len(L)/2]   □ O(n logn)
- Can we find medians, or 1st quartiles in O(n)?

Select Recursion

- **Select(L, k)** finds the k^{th} smallest element in **L**
  - Select an element *m* from unsorted list **L** and partition L the array into two smaller lists:

L_{lo} - elements smaller than *m*

and

L_{hi} - elements larger than *m*

if (len(L_{lo}) >= k) then
    Select(L_{lo}, k)
elif (k > len(L_{lo}) + 1) then
    Select(L_{hi}, k – (len(L_{lo}) + 1))
else *m* is the k^{th} smallest element

Example of Select(L, 5)

Given an array: **L =** { 6, 3, 2, 8, 4, 5, 1, 7, 0, 9 }

Step 1: Choose the first element as *m*

L = { 6, 3, 2, 8, 4, 5, 1, 7, 0, 9 }

Our Selection

Example of Select(L,5) (cont'd)

Step 2: Split the array into $\mathbf{L}_{\text{lo}}$ and $\mathbf{L}_{\text{hi}}$

$\mathbf{L}_{lo}$ = { 3, 2, 4, 5, 1, 0 }

L = { 6, 3, 2, 8, 4, 5, 1, 7, 0, 9 }

$\mathbf{L}_{hi}$ = { 8, 7, 9 }

Example of Select(L,5) (cont'd)

<u>Step 3</u>: Recursively call Select on either $\mathbf{L}_{lo}$ or $\mathbf{L}_{hi}$ until len($\mathbf{L}_{lo}$)+1 = k, then return *m*.

len(L_{lo}) > k = 5 □ Select({ 3, 2, 4, 5, 1, 0 }, 5)

m = 3

L_{lo} = { 2, 1, 0 } L_{hi} = { 4, 5 }

k = 5 > len(L_{lo}) +1 □ Select({4, 5 }, 5 - 3 - 1)

m = 4

L_{lo} = { empty }, L_{hi} = { 5 }

k = 1 == len(L_{lo}) + 1 □ return 4

Select Code

```
In [47]: def select(L, k):
             value = L[0]
             Llo = [t for t in L if t < value]
             Lhi = [t for t in L if t > value]
             below = len(Llo) + 1
             if (len(Llo) >= k):
                 return select(Llo, k)
             elif (k > below):
                 return select(Lhi, k - below)
             else:
                 return value

         test = [6, 3, 2, 8, 4, 5, 1, 7, 0, 9]
         print(select(test, 5))

         4
```

- How fast?
- Is it really any better than sorting, and selecting?

Select with Good Splits

- Runtime depends on our selection of *m*:

  - A good selection will split **L** evenly such that

    $|\mathbf{L}_{lo}| = |\mathbf{L}_{hi}| = |\mathbf{L}|/2$

  - The recurrence relation is:

    $T(n) = T(n/2)$

$n + n/2 + n/4 + n/8 + n/16 + \ldots = 2n$ □ $O(n)$

Same as search for minimum

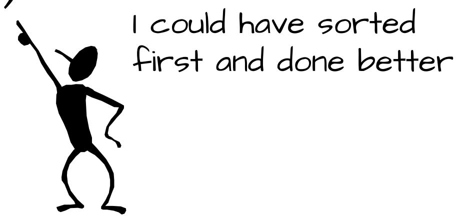
Select with Bad Splits

However, a poor selection will split **L** unevenly and in the worst case, all elements will be greater or less than m so that one Sublist is full and the other is empty.

For a poor selection, the recurrence relation is

$$T(n) = T(n\text{-}1)$$

In this case, the runtime is $O(n^2)$.



Our dilemma:

$O(n)$ or $O(n^2)$,

depending on the list… or $O(n \log n)$ independent of it

Select Analysis (cont'd)

- Select seems risky compared to Sort
- To improve Select, we need to choose *m* to give good 'splits'
- It can be proven that to achieve O(*n*) running time, we don't need a perfect splits, just reasonably good ones.
- In fact, if both subarrays are at least of size *n/4*, then running time will be O(*n*).
- This implies that half of the choices of *m* make good splitters.

A Randomized Approach

- To improve Select, ***randomly*** select m.
- Since half of the elements will be good splitters, if we choose m at random we will get a 50% chance that m will be a good choice.
- This approach will make sure that no matter what input is received, the expected running time is small.

Randomized Select

```
In [48]: import random

         def randomizedSelect(L, k):
             value = random.choice(L)
             Llo = [t for t in L if t < value]
             Lhi = [t for t in L if t > value]
             below = len(Llo) + 1
             if (len(Llo) >= k):
                 return randomizedSelect(Llo, k)
             elif (k > below):
                 return randomizedSelect(Lhi, k - below)
             else:
                 return value

         test = [6, 3, 2, 8, 4, 5, 1, 7, 0, 9]
         print(randomizedSelect(test, 5))

         4
```

RandomizedSelect Analysis

- Worst case runtime: $O(n^2)$
- ***Expected runtime***: $O(n)$.
- Expected runtime is a good measure of the performance of randomized algorithms, often more informative than worst case runtimes.
- Worst case runtimes are rarely repeated
- RandomizedSelect always returns the correct answer, which offers a way to classify Randomized Algorithms.

Types of Randomized Algorithms

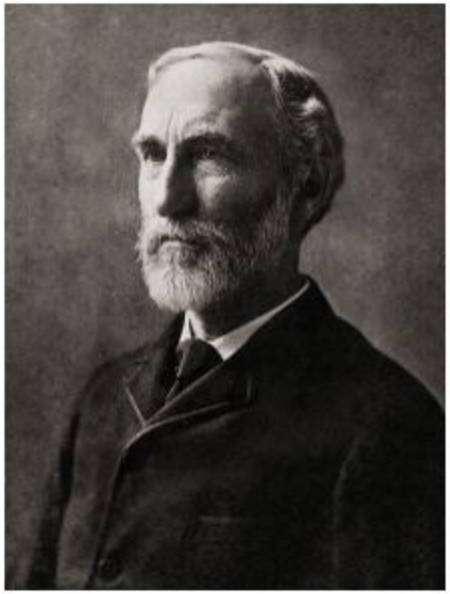
- **Las Vegas Algorithms** – always produce the correct solution (i.e. randomizedSelect)

- **Monte Carlo Algorithms** – do not always return the correct solution.

Of course, Las Vegas Algorithms are always preferred, but they are often hard to come by.

Gibbs Sampling

- RandomProfileMotifSearch is probably not the best way to find motifs. Depends on random guesses followed by a greedy optimization procedure.
- Gibbs Sampling estimates a distribution of each variable in turn, conditional on the current values of the other variables.
- However, we can improve the algorithm by introducing **Gibbs Sampling**, an iterative procedure that discards one *k*-mer's contribution to the profile distribution at each iteration and replaces it with a new one.
- Gibbs Sampling starts out slowly but chooses new *k*-mers with increasing the odds that it will improve the current solution.



Josiah W Gibbs

How Gibbs Sampling Works

1) Randomly choose starting positions **s** = (s_1,...,s_t) and form the set of *k*-mers associated with these starting positions.
2) Randomly choose one of the *t* sequences.
3) Create a profile **P** from the remaining *t* -1 sequences.
4) For each position in the removed sequence, calculate the probability that the *k*-mer starting at that position was generated by **P**.
5) Choose a new starting position for the selected sequence at random based on the probabilities calculated in step 4.
6) Repeat steps 2-5 until there is no improvement

Gibbs Sampling: an Example

Input:

t = 5 sequences, motif length l = 8

1. GTAAACAATATTTATAGC
2. AAAATTTACCTCGCAAGG
3. CCGTACTGTCAAGCGTGG
4. TGAGTAAACGACGTCCCA
5. TACTTAACACCCTGTCAA

Gibbs Sampling: an Example

1) Randomly choose starting positions, $\boldsymbol{s}=(s_1, s_2, s_3, s_4, s_5)$ in the 5 sequences:

$s_1=7$	`GTAAACAATATTTATAGC`
$s_2=11$	`AAAATTTACCTTAGAAGG`
$s_3=9$	`CCGTACTGTCAAGCGTGG`
$s_4=4$	`TGAGTAAACGACGTCCCA`
$s_5=1$	`TACTTAACACCCTGTCAA`

Gibbs Sampling: an Example

2) Choose one of the sequences at random:

Sequence 2: AAAATTTACCTTAGAAGG

$s_1=7$	GTAAACAATATTTATAGC
$s_2=11$	AAAATTTACCTTAGAAGG
$s_3=9$	CCGTACTGTCAAGCGTGG
$s_4=4$	TGAGTAAACGACGTCCCA
$s_5=1$	TACTTAACACCCTGTCAA

Gibbs Sampling: an Example

2) Choose one of the sequences at random:
Sequence 2: AAAATTTACCTTAGAAGG

$s_1=7$ GTAAACAATATTTATAGC

$s_3=9$ CCGTACTGTCAAGCGTGG

$s_4=4$ TGAGTAAACGACGTCCCA

$s_5=1$ TACTTAACACCCTGTCAA

Gibbs Sampling: an Example

3) Create profile ***P*** from *l*-mers in remaining 4 sequences:

1	A	A	T	A	T	T	T	A
3	T	C	A	A	G	C	G	T
4	G	T	A	A	A	C	G	A
5	T	A	C	T	T	A	A	C
A	1/4	2/4	2/4	3/4	1/4	1/4	1/4	2/4
C	0	1/4	1/4	0	0	2/4	0	1/4
T	2/4	1/4	1/4	1/4	2/4	1/4	1/4	1/4
G	1/4	0	0	0	1/4	0	3/4	0
Consensus String	T	A	A	A	T	C	G	A

Gibbs Sampling: an Example

4) Calculate the $prob(\boldsymbol{a} \mid \boldsymbol{P})$ for every possible 8-mer in the removed sequence:

Strings Highlighted in Red	$prob(\mathbf{a} \mid \mathbf{P})$
AAAATTTACCTTAGAAGG	.000732
AAAATTTACCTTAGAAGG	.000122
AAAATTTACCTTAGAAGG	0
AAAATTTACCTTAGAAGG	0
AAAATTTACCTTAGAAGG	0
AAAATTTACCTTAGAAGG	0
AAAATTTACCTTAGAAGG	0
AAAATTTACCTTAGAAGG	.000183
AAAATTTACCTTAGAAGG	0
AAAATTTACCTTAGAAGG	0
AAAATTTACCTTAGAAGG	0

Gibbs Sampling: an Example

5) Create a distribution of probabilities of k-mers $prob(\boldsymbol{a} \mid \boldsymbol{P})$, and randomly select a new starting position based on this distribution.

A) To create this distribution, divide each probability $prob(\boldsymbol{a} \mid \boldsymbol{P})$ by the total:

Starting Position 1: *prob(* AAAATTTA | P) = .706

Starting Position 2: *prob(* AAATTTAC | P) = .118

Starting Position 8: *prob(* ACCTTAGA | P) = .176

Gibbs Sampling: an Example

B) Select a new starting position at random according to computed distribution:

P(selecting starting position 1):	.706
P(selecting starting position 2):	.118
P(selecting starting position 8):	.176

```
t = random.random()
if (t < .706):
    # use position 1
elif (t < (.706 + .118)):
    # use position 2
else:
    # use position 8
```

Gibbs Sampling: an Example

Assume we select the substring with the highest probability – then we are left with the following new substrings and starting positions.

$s_1=7$	GTAAACAATATTTATAGC
$s_2=1$	AAAATTTACCTCGCAAGG
$s_3=9$	CCGTACTGTCAAGCGTGG
$s_4=5$	TGAGTAATCGACGTCCCA
$s_5=1$	TACTTCACACCCTGTCAA

Gibbs Sampling: an Example

6) We iterate the procedure again with the above starting positions until we cannot improve the score any more.

```
In [103]: import numpy

          def Score(seq, i, k, distr):
              return numpy.prod([distr[j][seq[i+j]] for j in range(k)])

          def Profile(DNA, offset, k):
              profile = []
              t = len(DNA)
              for i in range(k):
                  counts = {base : 0.01 for base in "acgt"}
                  for j in xrange(t):
                      counts[DNA[j][offset[j]+i]] += 0.96 / t
                  profile.append(counts)
              return profile
```

Gibbs Sampling in Python

In [92]:
```
def GibbsProfileMotifSearch(seqList, k):
    start = [random.randint(0,len(seqList[t])-k) for t in range(len(seqList))]
    bestScore = 0.0
    noImprovement = 0
    while True:
        remove = random.randint(0,len(seqList)-1)
        start[remove] = -1
        distr = Profile(seqList, k, start)
        score = 0.0
        for t in range(len(seqList)):
            if (start[t] < 0):
                rScore = 0.0
                for i in xrange(len(seqList[remove])-k+1):
                    score = Score(seqList[remove], i, k, distr)
                    if (score > rScore):
                        rStart, rScore = i, score
                score += rScore
                start[t] = rStart
            else:
                score += Score(seqList[t], start[t], k, distr)
        if (score > bestScore):
            bestScore = score
            noImprovement = 0
        else:
            noImprovement += 1
            if (noImprovement > len(seqList)):
                break
    return score, start
```

Gibbs Sampling Performance

In [116]:

```python
random.seed(2020)

seqApprox = [
    'tagtggtcttttgagtgtagatctgaagggaaagtatttccaccagttcggggtcacccagcagggcagggtgacttaat',
    'cgcgactcggcgctcacagttatcgcacgtttagaccaaaacggagttggatccgaaactggagtttaatcggagtcctt',
    'gttacttgtgagcctggttagacccgaaatataattgttggctgcatagcggagctgacatacgagtaggggaaatgcgt',
    'aacatcaggctttgattaaacaatttaagcacgtaaatccgaattgacctgatgacaatacggaacatgccggctccggg',
    'accaccggataggctgcttattaggtccaaaaggtagtatcgtaataatggctcagccatgtcaatgtgcggcattccac',
    'tagattcgaatcgatcgtgtttctccctctgtgggttaacgaggggtccgaccttgctcgcatgtgccgaacttgtaccc',
    'gaaatggttcggtgcgatatcaggccgttctcttaacttggcggtgcagatccgaacgtctctggaggggtcgtgcgcta',
    'atgtatactagacattctaacgctcgcttattggcggagaccatttgctccactacaagaggctactgtgtagatccgta',
    'ttcttacacccttctttagatccaaacctgttggcgccatcttcttttcgagtccttgtacctccatttgctctgatgac',
    'ctacctatgtaaaacaacatctactaacgtagtccggtctttcctgatctgccctaacctacaggtcgatccgaaattcg']

s, m = GibbsProfileMotifSearch(seqApprox, 10)

print(s, m)
for i, j in enumerate(m):
    print(seqApprox[i][j:j+10])
```

```
0.0137569615302 [17, 47, 18, 33, 21, 0, 46, 70, 16, 65]
tagatctgaa
tggatccgaa
tagacccgaa
taaatccgaa
taggtccaaa
tagattcgaa
cagatccgaa
tagatccgta
tagatccaaa
tcgatccgaa
```

Gibbs Sampler in Practice

- Fewer profile searches, *O(n)*, in exchange for updating the profile, *O(kt)*, more often (tradeoff which is easier)
- Gibbs sampling can converge much faster than a fully randomized approach
- Gibbs sampling is more likely to converge to locally optimal motifs rather a fully randomized algorithm.
- Like the fully Randomized Algorithm it must be run with many randomly chosen initial seeds to achieve good results.

Next Time

Andy, the literal Cowboy.