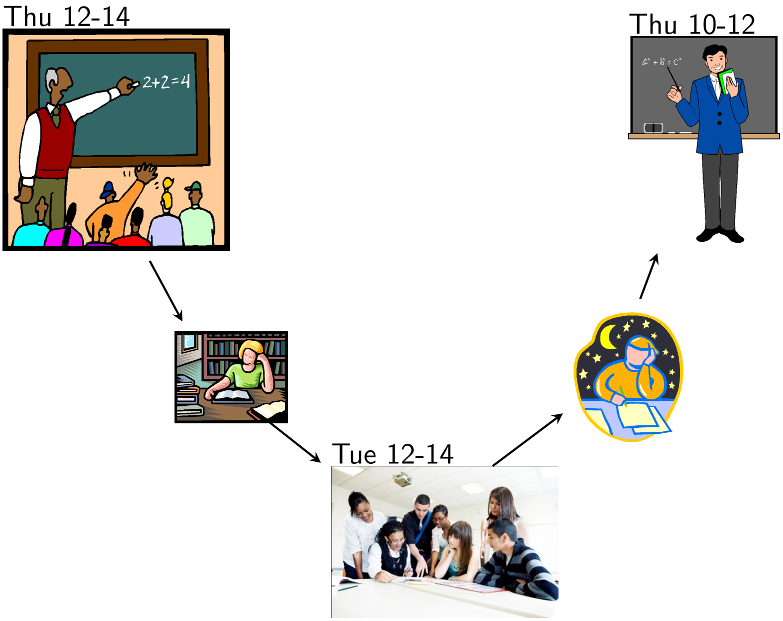
582670 Algorithms for Bioinformatics

Lecture 1: Primer to algorithms and molecular biology

4.9.2012

Course format

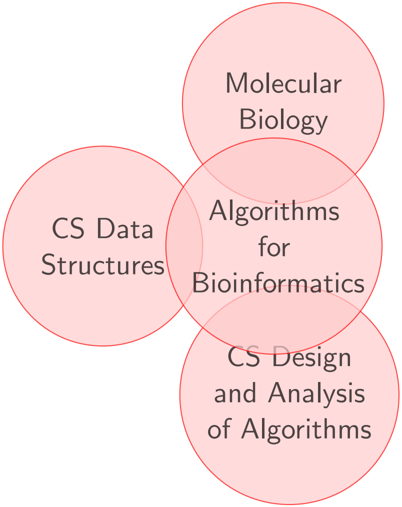


Grading

- Exam 48 points
- Exercises 12 points
  - 30% $\implies$ 1
  - 85% $\implies$ 12
- Grading $\sim 30 \implies 1$, $\sim 50 \implies 5$ (depending on difficulty of exam)
- Tuesday study group is mandatory!
  (Inform beforehand if you cannot attend)

Course overview

- Introduction to algorithms in the context of molecular biology
- Targeted for
  - biology and medicine students
  - first year bioinformatics students
  - CS / Math / Statistics students thinking of specializing in bioinformatics
- Some programming skills required
  - We will use Python in this course
- Not as systematic as other CS algorithm courses, emphasis on learning some design principles and techniques with the biological realm as motivation



Molecular Biology
CS Data Structures
Algorithms for Bioinformatics
CS Design and Analysis of Algorithms

Algorithms *for* Bioinformatics

- State-of-the-art algorithms <u>in</u> bioinformatics are rather involved
- Instead, we study toy problems motivated by biology (but not too far from reality) that have clean and introductory level algorithmic solutions
- The goal is to arouse interest to study the real advanced algorithms in bioinformatics!
- We avoid statistical notions to give algorithmic concepts the priority
- Continue to further bioinformatics course to learn the practical realm

Algorithm

Well-defined problem Solution to problem

$$\text{input} \longrightarrow \text{output}$$

$$\underbrace{\to\to\to\ \ldots \qquad\qquad\qquad\qquad \to}_{\text{number of steps: } f(\text{size of input})}$$

Homework:
Find out what the following algorithm running time notions mean:

$$f(n) \in O(n), f(n) \in o(n), f(n) \in \Omega(n), f(n) \in \omega(n), f(n) \in \Theta(n)$$

Algorithms in Bioinformatics

Weakly defined problem   Solution to problem

$$\text{input} \longrightarrow \text{output=input'} \longrightarrow \text{output'=input''} \longrightarrow \text{output'''}$$

- Reasons:
  - Biological problems usually too difficult to be solved algorithmically
  - Problem modelling leads to statistical notions $\Longrightarrow$ general local optimization algorithms necessary
- Problematic for CS theory:
  - optimal solutions to subproblems do not necessarily lead to best global solution

Algorithms in Bioinformatics

Plenty of important subproblems where algorithmic techniques have been vital:

- Fragment assembly $\Longrightarrow$ human genome
- Design of microarrays $\Longrightarrow$ gene expression measurements
- Sequence comparison $\Longrightarrow$ comparative genomics
- Phylogenetic tree construction $\Longrightarrow$ evolution modeling
- Genome rearrangements $\Longrightarrow$ comparative genomics, evolution
- Motif finding $\Longrightarrow$ gene regulatory mechanism
- Biomolecular secondary structure prediction $\Longrightarrow$ function
- Analysis of high-throughput sequencing data $\Longrightarrow$ genomic variations in populations

Course prerequisites

- Programming skills
- High-school level biology++
  - Molecular genetics reading group recommended to be taken in parallel
  - To avoid overlap with other bioinformatics courses, we do not cover any more biology than is necessary to motivate the problems

Outline

Programming in this Course

- We will use Python
- What we need (on this course):
  - Built-in data types
  - Syntax for control flow statements
  - Function definitions
- What we can omit (i.e. software engineering):
  - Standard library, OOP, exceptions, I/O, etc.

Assignment

Pseudocode

```
$b \leftarrow 2$
$a \leftarrow b$
```

Python

```
b = 2
a = b
print a
```

Arithmetic

Pseudocode

```
DIST $(x_1, y_1, x_2, y_2)$
1. $dx \leftarrow (x_2 - x_1)^2$
2. $dy \leftarrow (y_2 - y_1)^2$
3. return $\sqrt{dx + dy}$
```

Python

```python
from math import sqrt


def dist(x1, y1, x2, y2):
    dx = pow(x2-x1, 2)
    dy = pow(y2-y1, 2)
    return sqrt(dx+dy)


print dist(0, 0, 3, 4)
```

Conditional

Pseudocode

```
MAX ($a$, $b$)
1 if ($a < b$)
2       return $b$
3 else
4       return $a$
```

Python

```
def MAX(a, b):
    if a < b:
        return b
    else:
        return a

print MAX(1,99)
```

for loops

Pseudocode

```
SumIntegers ($n$)
1 $sum \leftarrow 0$
2 for $i \leftarrow 1$ to $n$
3     $sum \leftarrow sum + i$
4 return $sum$
```

Python

```
def SUMINTEGERS(n):
    sum = 0
    for i in range(1,n+1):
        sum = sum + i
    return sum

print SUMINTEGERS(10)
```

while loops

Pseudocode

```
AddUntil ($b$)
1 $i \leftarrow 1$
2 $total \leftarrow i$
3 while $total \leq b$
4     $i \leftarrow i + 1$
5     $total \leftarrow total + i$
6 return $i$
```

Python

```
def ADDUNTIL(b):
    i = 1
    total = i
    while total <= b:
        i = i + 1
        total = total + i
    return i

print ADDUNTIL(25)
```

Recursion

Pseudocode

$$F(n) = \begin{cases} 0, & \text{when } n = 0 \\ 1, & \text{when } n = 1 \\ F(n-1) + F(n-2), & \text{otherwise} \end{cases}$$

Python

```
def RECURSIVEFIBONACCI(n):
    if n == 0:
        return 0
    elif n == 1:
        return 1
    else:
        a = RECURSIVEFIBONACCI(n-1)
        b = RECURSIVEFIBONACCI(n-2)
        return a+b

print RECURSIVEFIBONACCI(8)
```

Strings

Python

```
s='Hello'

s[0] = 'C'     # error: str
s.append('!') # is immutable

s = s + '!'

s = s[:5]

s = s.upper()
```

Output

```
Hello




Hello!

Hello

HELLO
```

Lists

Python

```
l = [0] * 3

l[0] = 1     # list is mutable

l = range(1,4)

l.append('four')

l = [2**i for i in range(6)]
```

Output

```
[0,0,0]

[1,0,0]

[1,2,3]

[1,2,3,'four']

[1,2,4,8,16,32]
```

List access

Pseudocode

```
FIBONACCI ($n$)
1 $F_0 \leftarrow 0$
2 $F_1 \leftarrow 1$
3 for $i \leftarrow 2$ to $n$
4       $F_i \leftarrow F_{i-1} + F_{i-2}$
5 return $F_n$
```

Python

```
def FIBONACCI(n):
    F = [0]*(n+1)
    F[0] = 0
    F[1] = 1
    for i in range(2,n+1):
        F[i] = F[i-1] + F[i-2]
    return F[n]

print FIBONACCI(8)
```

Immutable vs Mutable

Immutable (int, str, ...)

```
a = 2
b = a
b = b + 1     # does not change a

s = 'Hello'
t = s
t = t + '!'   # does not change s
```

Mutable (list, set, dict, ...)

```
l = [0]
m = l
m = m + [1]    # changes also l

l = [0]
m = l[:]       # shallow copy of l
m = m + [1]    # does not change l
```

Pass arguments by reference? - No.

Immutable (int, str, ...)

```
def ADDONE(x,y):
    x = x + 1    # x and y
    y = y + 1    # are local

# return a tuple instead
def ADDONE(x,y):
    return x+1, y+1

x,y = ADDONE(x,y)
```

Mutable (list, set, dict, ...)

```
def CLEAR(l):
    l = []    # l is local


# any mutable can still be
# changed in place, e.g.:
def CLEAR(l):
    l[:] = []
```

Multidimensional lists

Python

```
l = [[0] * 2] * 3  # Caution!
                   # You probably
                   # do not want
                   # do this!!!
l[0][0] = 1



# This is safe:
l = [[0]*2 for i in range(3)]

l[0][0] = 1
```

Output (print l)

```
[[0, 0], [0, 0], [0, 0]]

[[1, 0], [1, 0], [1, 0]]

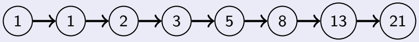


[[0, 0], [0, 0], [0, 0]]

[[1, 0], [0, 0], [0, 0]]
```

pointers: deque

Idea



Python (collections.deque)

```
from collections import deque

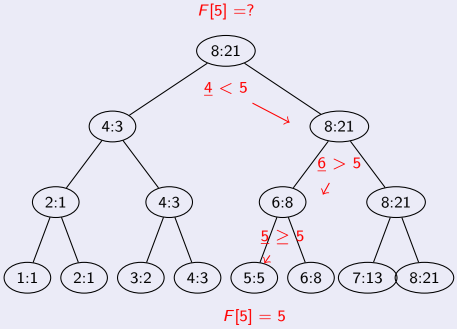

def FIBONACCI(n):
    F = deque()
    F.append(0)
    F.append(1)
    for i in range(2,n+1):
        F.append(F[n-1]+F[n-2])
    return F[n]


print FIBONACCI(8)
```

pointers: trees

Idea

Store max key and max value of each subtree to the nodes



Python

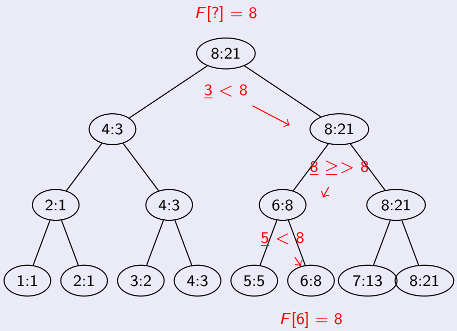
- No built in data type (several external libraries exist)
- For many purposes hash-based dictionary type `dict` is enough:
  - Stores (key, value) pairs so that value associated with a key can be retrieved efficiently (average constant time)
  - Does not support retrieval by value

```
fib = {0:0, 1:1, 2:1, 3:2, 4:3,
       5:5, 6:8, 7:13, 8:21}
print fib[8]
```

pointers: trees

Idea

Store max key and max value of each subtree to the nodes



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       5:5, 6:8, 7:13, 8:21}
print fib[8]
```

Large(r) data sets

- For mutable strings, use e.g.
  - `array.array('c', 'Hello')`
  - `bytearray('Hello')`
- `list` uses a lot of memory ($\sim$ 16 bytes per `int`)
- For homogeneous data, use e.g.
  - `array.array('l', [1,2,3,4])`
  - `numpy.array([1,2,3,4])`

Helpful links

- `http://openbookproject.net/thinkcs/python/english2e/` (Programming tutorial for those who have no programming experience)
- `http://docs.python.org/tutorial/`
- `http://docs.python.org/library/`
- `http://wiki.python.org/moin/BeginnersGuide/`
- `http://wiki.python.org/moin/TimeComplexity/`
- `http://docs.scipy.org/doc/` (NumPy documentation)

Outline

Group 1 (students with biology background)

- One of the fundamental and most deeply studied algorithmic problems is sorting. Before coming to the study group familirize yourself with the problem (e.g. using Wikipedia) and be ready to explain the idea of couple of well-known sorting algorithms like *insertion sort*, *quicksort*, *merge sort*, and *radix sort*.
- At study group, try to understand the running time $O()$-notion of different sorting algorithms:
  - What happens if you are sorting a set of DNA sequences into lexicographic order instead of integers?
  - What if the set of DNA sequences consists of *suffixes* of one DNA sequence?

Group 2 (students with CS background)

- Study the slides “molecular biology primer” (found on course web site) before coming to the study group.
- At study group, be ready to explain the material just using the “molecular biology cheat sheet”.