Quantitative Biology Colloquium Series

Monday, February 8th

11:00 am – 12:00 noon

HN 310

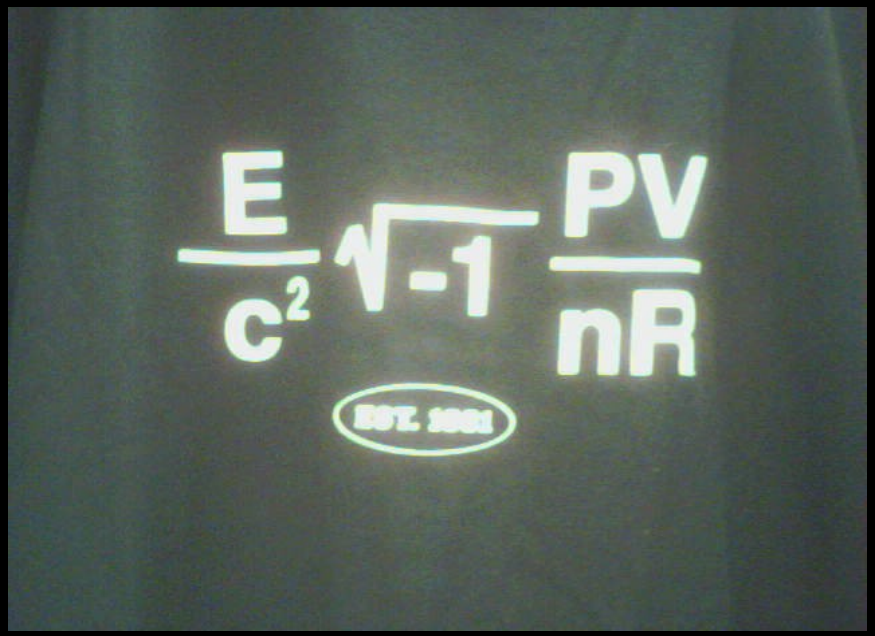
The View from MIT: New Bioinformatics Techniques

Evan Genest, Vincent Xue and Devin Ghamand

Opportunities at M.I.T

MIT Summer Research Program
HST Summer Institute

MIT Facts #1



MIT Facts #2 A Prominent Biology Department

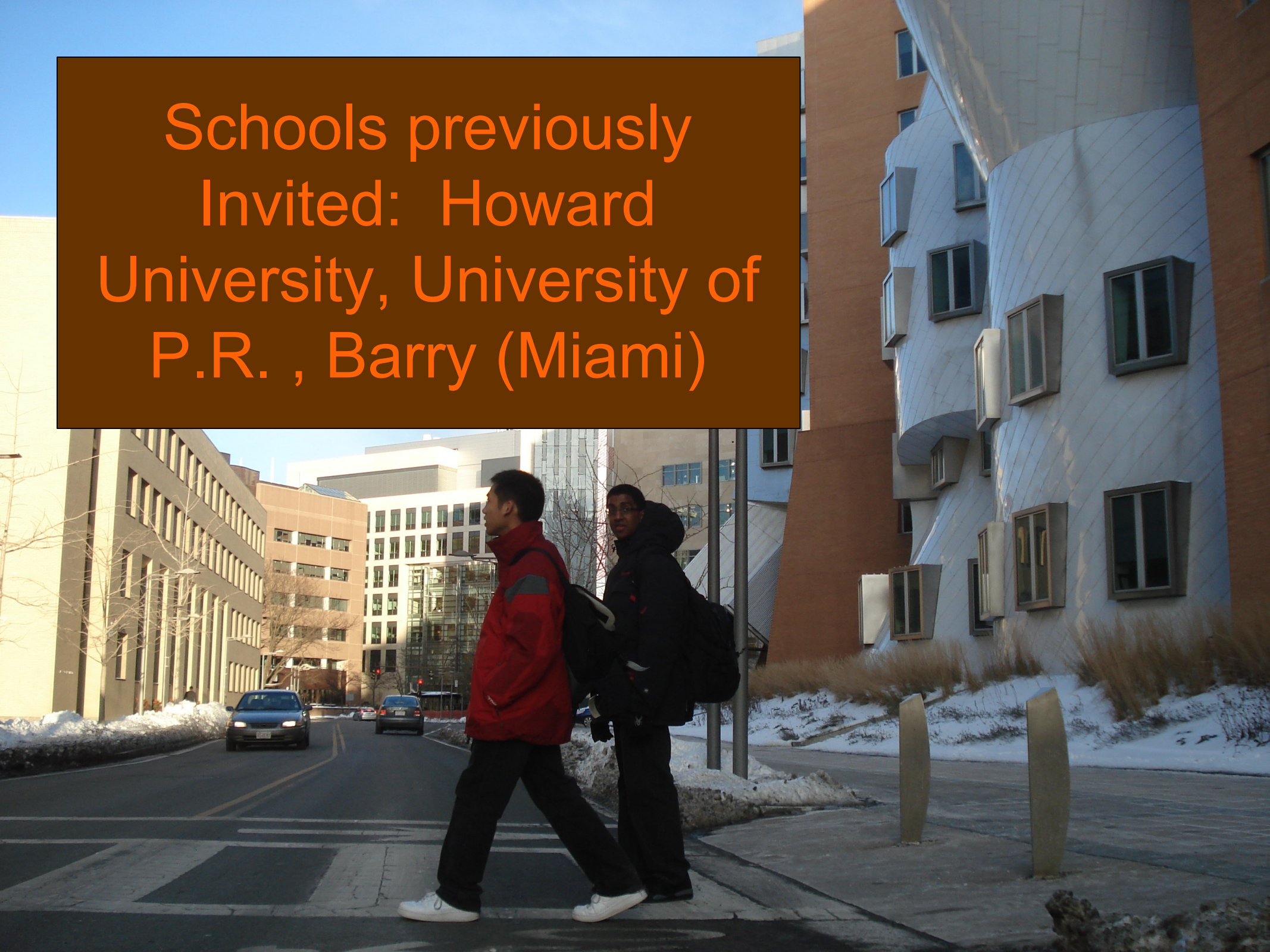
Top Employment Sectors for MIT Graduates

	Undergrads	Masters
Aerospace/defense	5%	7%
Biological science	8%	3%
Computer technologies	19%	20%
Consulting	13%	18%
Finance	14%	15%
Other engineering	12%	9%

The top employers were McKinsey, Microsoft, MIT, Intel, Amazon, and Bain & Company.

Dr. H. Robert Horvitz
Dr. Phillip A. Sharp
Dr. Susumu Tonegawa
Dr. H. Gobind Khorana

MIT #3 – The Smoot


Schools previously Invited: Howard University, University of P.R. , Barry (Miami)

A Different Topic Each Day

KINETICS

9:30 AM- 11:30 AM Professor Bob Sauer: "Binding and Kinetics"
12:30 - 3:00 PM Dr. Caroline Koehrer: “Determining RNA-protein binding constants using filter binding assay and surface plasmon resonance (BIAcore)
3:30- 4:30 PM Dr. Mandana Sassanfar- Journal club

GENETICS

9:00 AM - 9:30 AM Review and discussion
9:30 - 12:00 Professor Chris Kaiser: “Fundamentals of Genetic Analysis.”
1:00 - 3:00 PM Mary Kay Thompson and Jamie Newman: “Using RNAi screens to explore regulatory mechanisms in mammalian cells.”

SYSTEMS BIOLOGY

9:30 AM -11:15 AM Professor Ernest Frankel: "Introduction to Systems Biology."
12:15 - 2:15 PM Dr. Tatjana Degenhardt " Chromatin Immuno Precipitation-Sequence and microarray analysis"
2:30 - 4:30 PM Dr. Laura Riva: “ChIp Seq analysis using Python.”

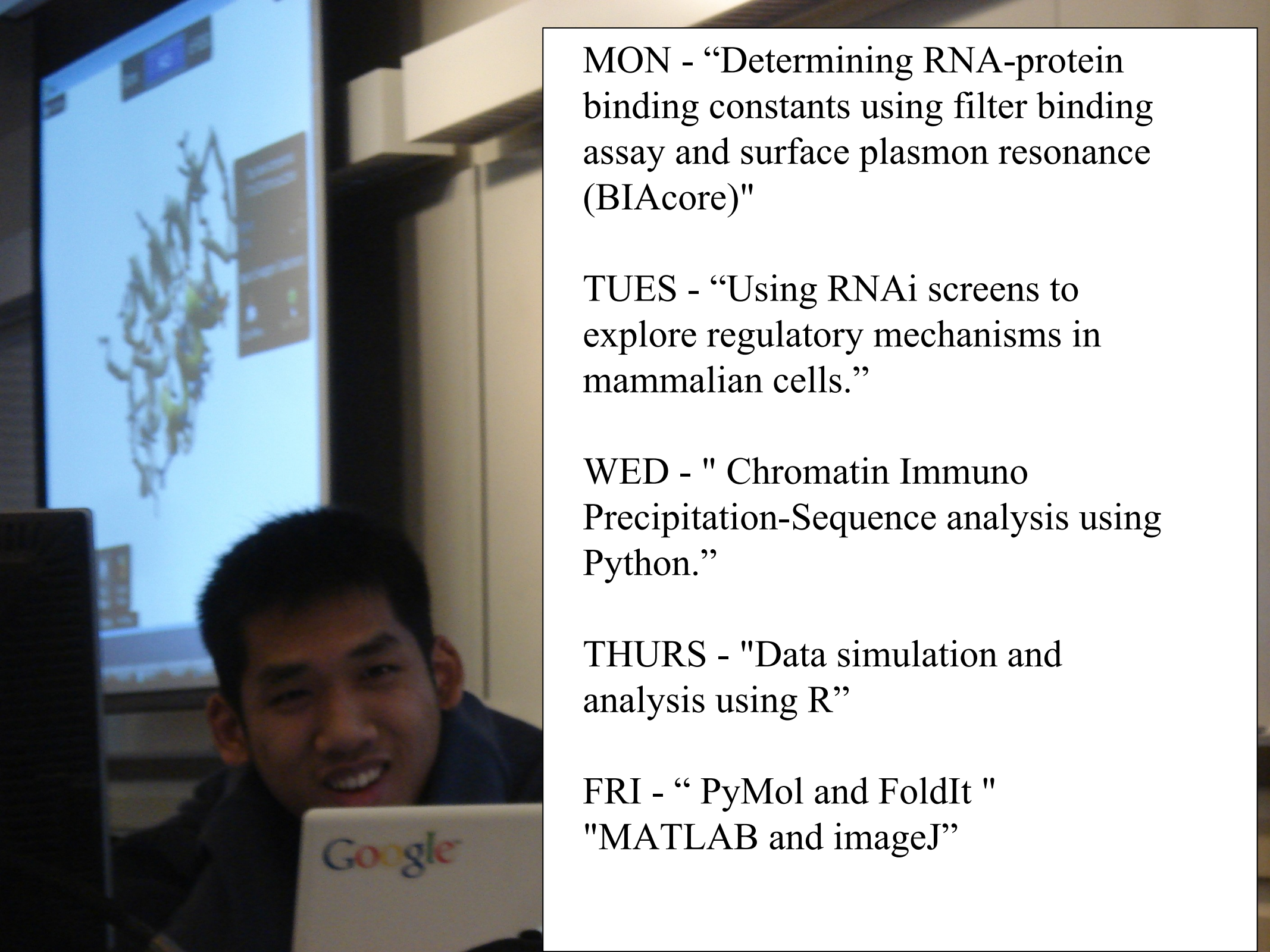
BIOSTATISTICS

9:30 - 11:00 AM Professor Michael Laub: “statistics used in Biology”
11:15 - 12:15 Faculty Lunch with Professor Chris Burge
12:30 - 3:30 PM Noah Spies: "Data simulation and analysis using R”

PROTEIN FOLDING + LOW TECH SYSTEMS BIOLOGY

9:30 -11:30 AM Professor Amy Keating: "Protein Structure and Molecular Modeling"
12:30 - 2:30 PM Dr. Emiko Fire/Christopher Negron/ Orr Ashenberg “Protein 3D Visualization, Folding, and Design with PyMol and FoldIt "
3:00 - 4:45 PM Hyun Youk “Imaging data analysis using MATLAB and imageJ”

Mornings



MON - “Determining RNA-protein binding constants using filter binding assay and surface plasmon resonance (BIAcore)"

TUES - “Using RNAi screens to explore regulatory mechanisms in mammalian cells.”

WED - " Chromatin Immuno Precipitation-Sequence analysis using Python.”

THURS - "Data simulation and analysis using R”

FRI - “ PyMol and FoldIt "
"MATLAB and imageJ”

Evenings we returned to the hotel and did homework

Biochemistry

The study chemical processes in living organisms.
- Includes pathway analysis
- Protein interactions
- Rate Reactions

Lecturers:
- Dr. Robert Sauer
  - Uses biophysical, genetic, structural, and design strategies to study the relationship between the sequence, stability, and three-dimensional structures of proteins.
- Dr. Caroline Koehrer-
  - Lectured on RNA-protein binding constants using filter binding assay and surface plasmon resonance

Calculating K_D

(1) $$K_D = \frac{[A][B]}{[AB]}$$

$$[A]_{total} = [A] + [AB]$$
$$[B]_{total} = [B] + [AB]$$

(2) $$K_D = \frac{([A]_{total} - [AB])\,[B]}{[AB]}$$

(3) $$K_D = \frac{[A]_{total}[B] - [AB][B]}{[AB]}$$

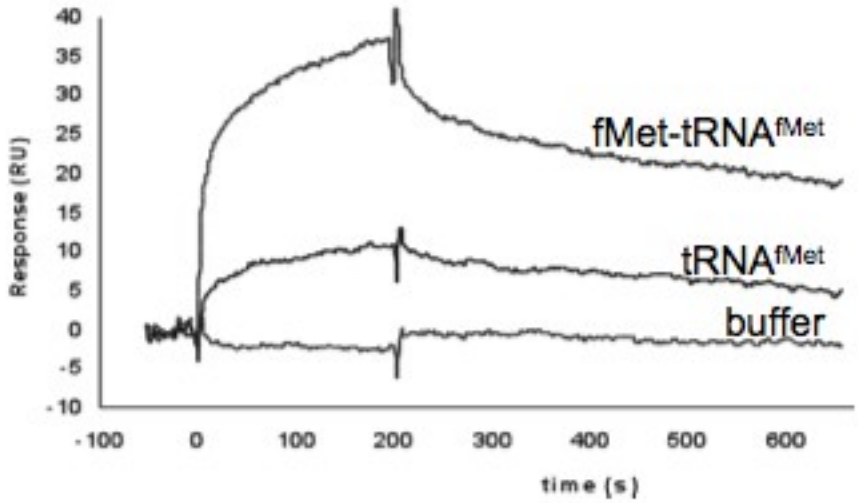
(4) $$K_D = \frac{[A]_{total}[B]}{[AB]} - \frac{[AB][B]}{[AB]}$$

(5) $$K_D = \frac{[A]_{total}[B]}{[AB]} - [B]$$

(6) $$\frac{[AB]}{[A]_{total}} = \frac{[B]}{[B] + K_D}$$

Caroline Koehrer, Ph.D.

Case study:
initiator tRNA – initiation factor IF2 complex



Surface ligand: IF2

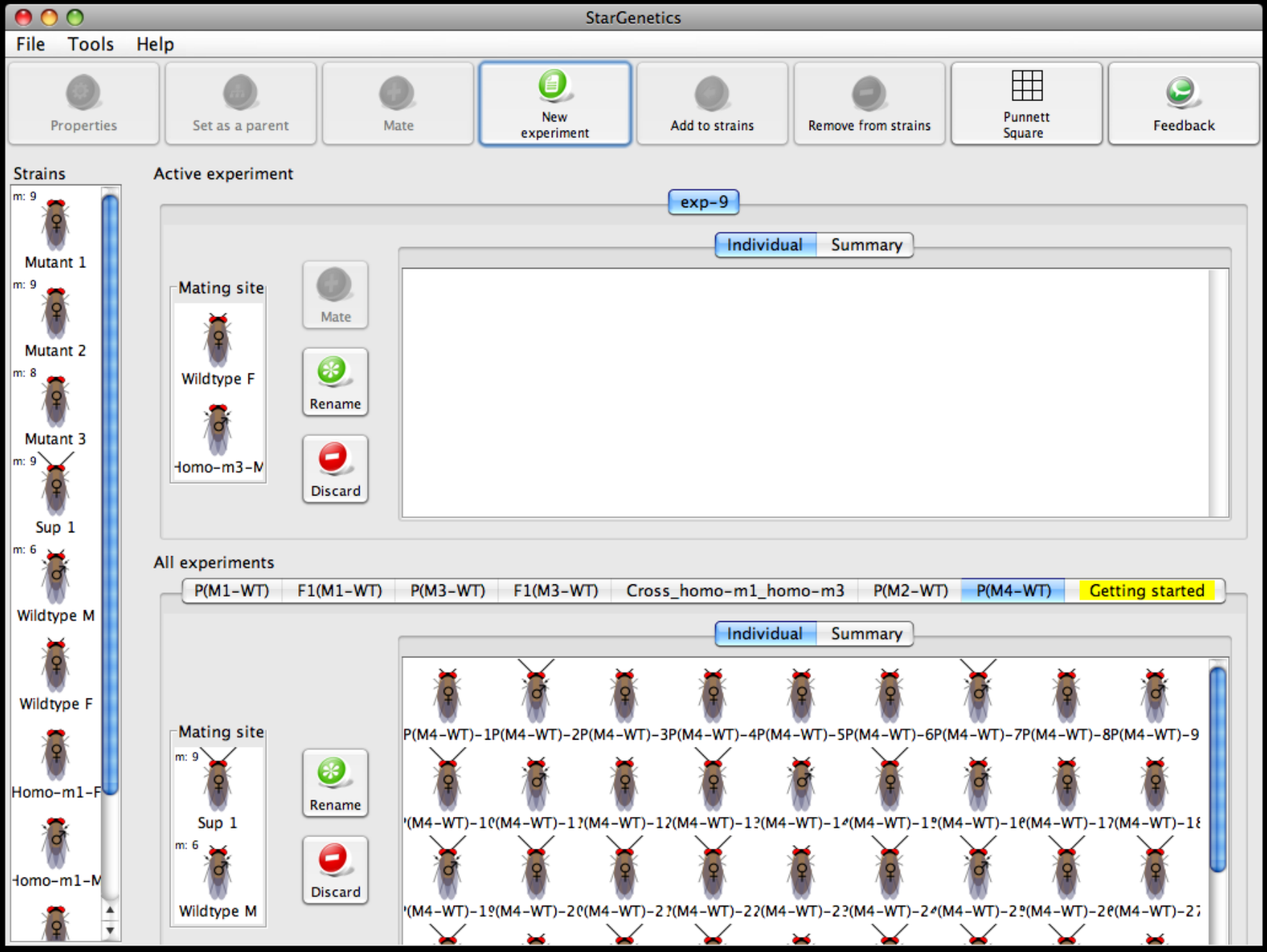
Analyte: fMet-tRNA^{fMet}; tRNA^{fMet}; buffer

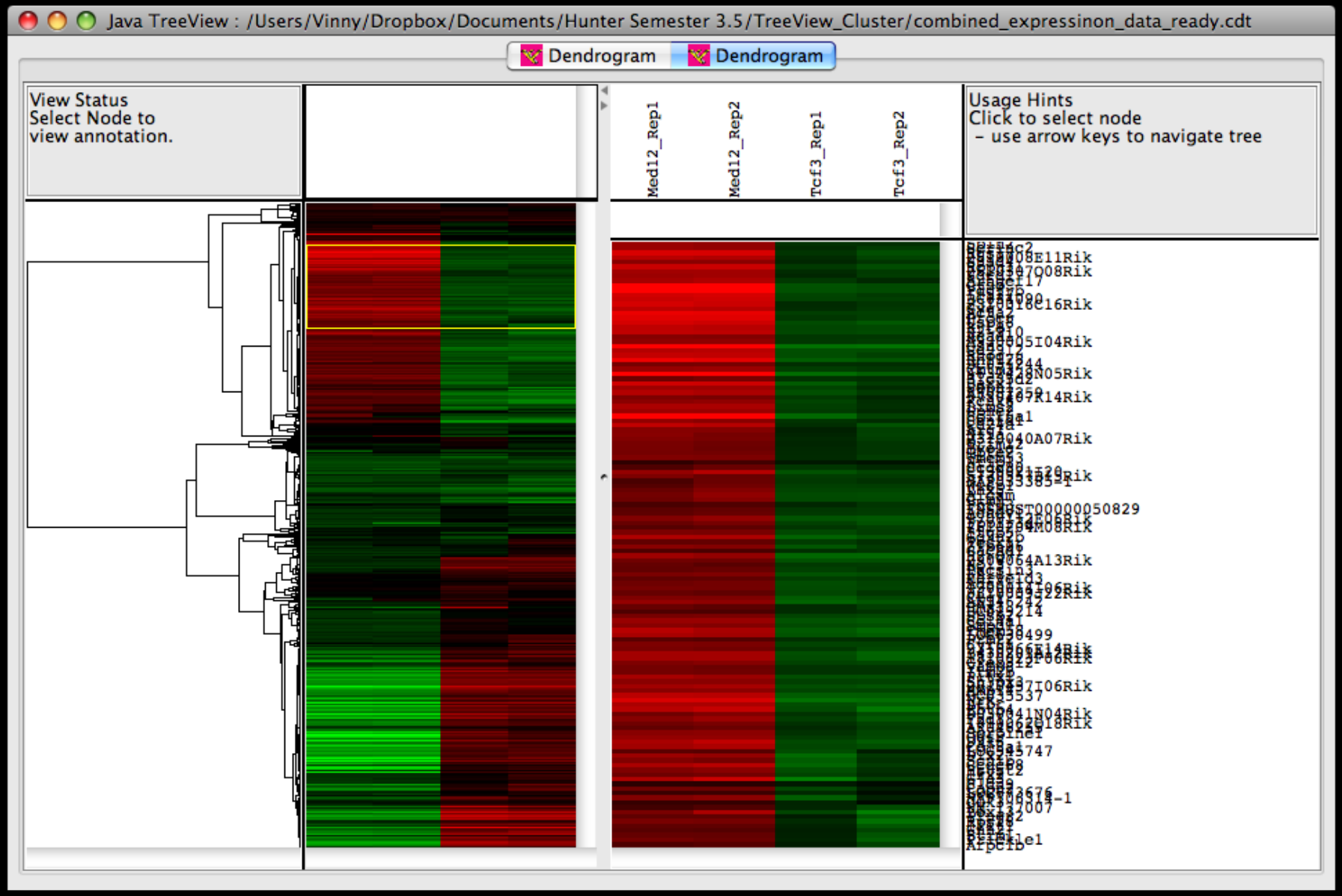
[Mayer, Koehrer et al., 2003: Anticodon Sequence Mutants of Escherichia coli Initiator tRNA: Effects of Overproduction of Aminoacyl-tRNA Synthetases, Methionyl-tRNA Formyltransferase, and Initiation Factor 2 on Activity in Initiation.]

Genetics

The study of heredity
Terminology: Dominance, Recessive, Epistasis

Lecturers
- Chris Kaiser
  - Uses combined genetic, biochemical and cell biological methods to gain an understanding of the molecular mechanisms that are underlie protein folding and intracellular trafficking in yeast S. cerevisiae
- Mary K. Thompson: Graduate student, Ph.D. program in Biology, Gilbert Lab
- Jamie Newman: Graduate student, Ph.D. program in Biology Young Lab, Whitehead Institute


StarGenetics
File
Tools
Help
Properties
Set as a parent
Mate
New experiment
Add to strains
Remove from strains
Punnett Square
Feedback
Strains
m: 9
Mutant 1
m: 9
Mutant 2
m: 8
Mutant 3
m: 9
Sup 1
m: 6
Wildtype M
Wildtype F
Homo-m1-F
Homo-m1-M
Active experiment
exp-9
Individual
Summary
Mating site
Wildtype F
Homo-m3-M
Mate
Rename
Discard
All experiments
P(M1-WT)
F1(M1-WT)
P(M3-WT)
F1(M3-WT)
Cross_homo-m1_homo-m3
P(M2-WT)
P(M4-WT)
Getting started
Individual
Summary
Mating site
m: 9
Sup 1
m: 6
Wildtype M
Rename
Discard
P(M4-WT)-1P(M4-WT)-2P(M4-WT)-3P(M4-WT)-4P(M4-WT)-5P(M4-WT)-6P(M4-WT)-7P(M4-WT)-8P(M4-WT)-9


Java TreeView : /Users/Vinny/Dropbox/Documents/Hunter Semester 3.5/TreeView_Cluster/combined_expressinon_data_ready.cdt
Dendrogram
Dendrogram
View Status
Select Node to
view annotation.
Med12_Rep1
Med12_Rep2
Tcf3_Rep1
Tcf3_Rep2
Usage Hints
Click to select node
- use arrow keys to navigate tree

Systems Biology

Purpose:

Discover molecular changes in an unbiased way.
Determine the functional consequences of these changes

Methods:

- High throughput measurement
  - microarray
  - RNAi screening
  - Imaging - mass spectroscopy
  - chIP seq
- Computational analysis
  - Differential equations models
  - Fishing for information
  - Visualizing data in an effective way

Ernest Frankel

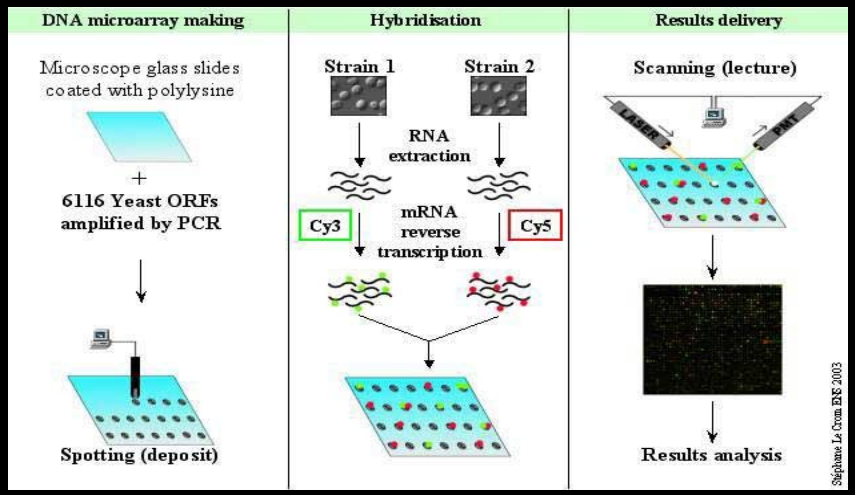
Systems Biology

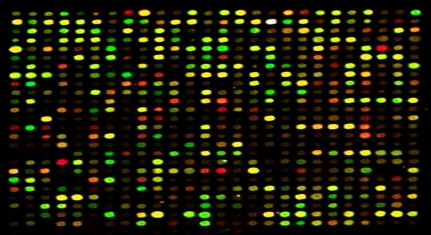
Lecturers:

- Ernest Frankel
  - Develops computational and experimental approaches to search for new therapeutic strategies for diseases.
    - currently focus on the study of cancer, neurodegenerative diseases and diabetes.
- Dr. Tatjana Degenhardt
  - Postdoctoral Associate, Frankel Lab
- Dr. Laura Riva
  - Postdoctoral Associate, Frankel Lab

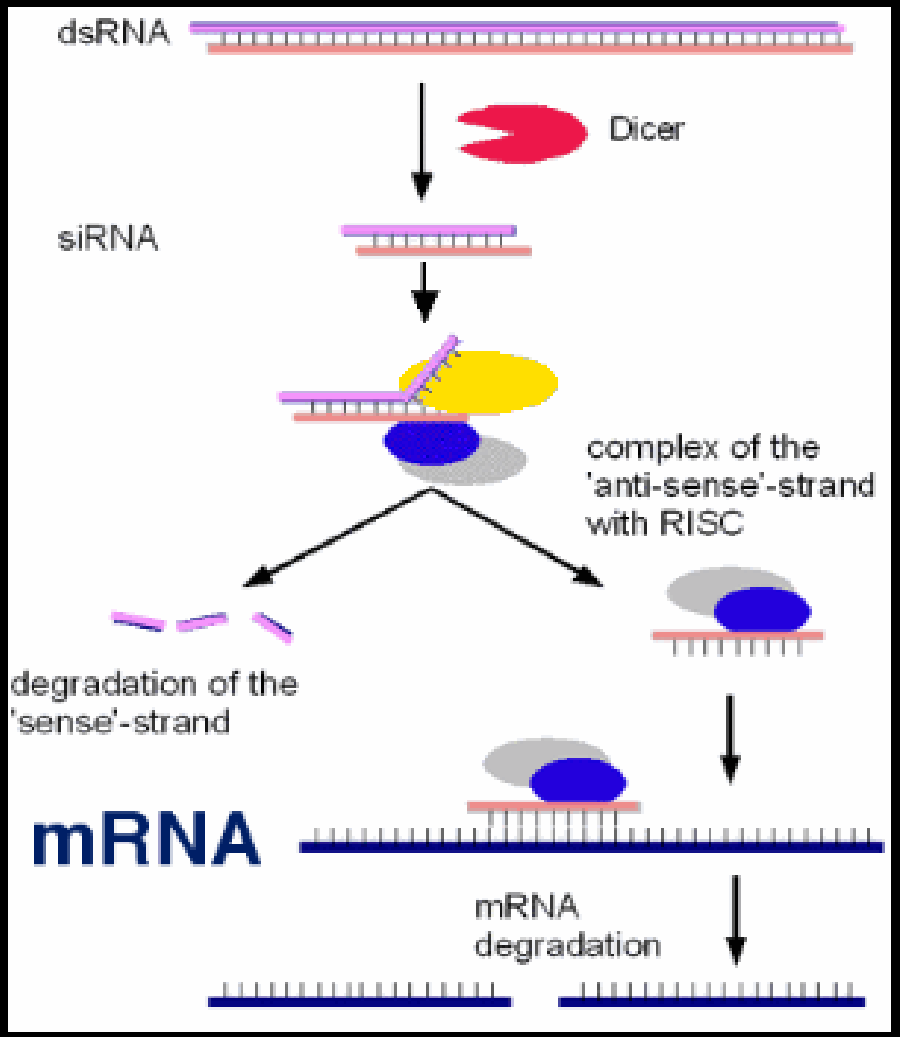
Methods For High Throuput Analysis

Microarray





RNAi Screening

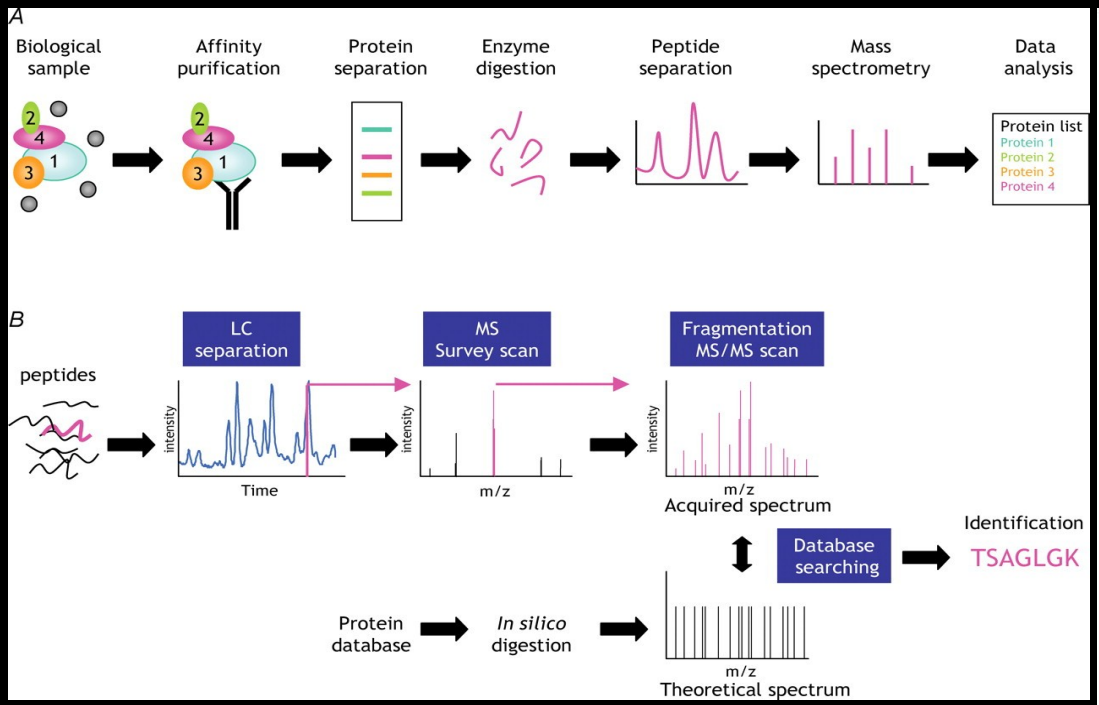


http://transcriptome.ens.fr/sgdb/presentation/principle.php

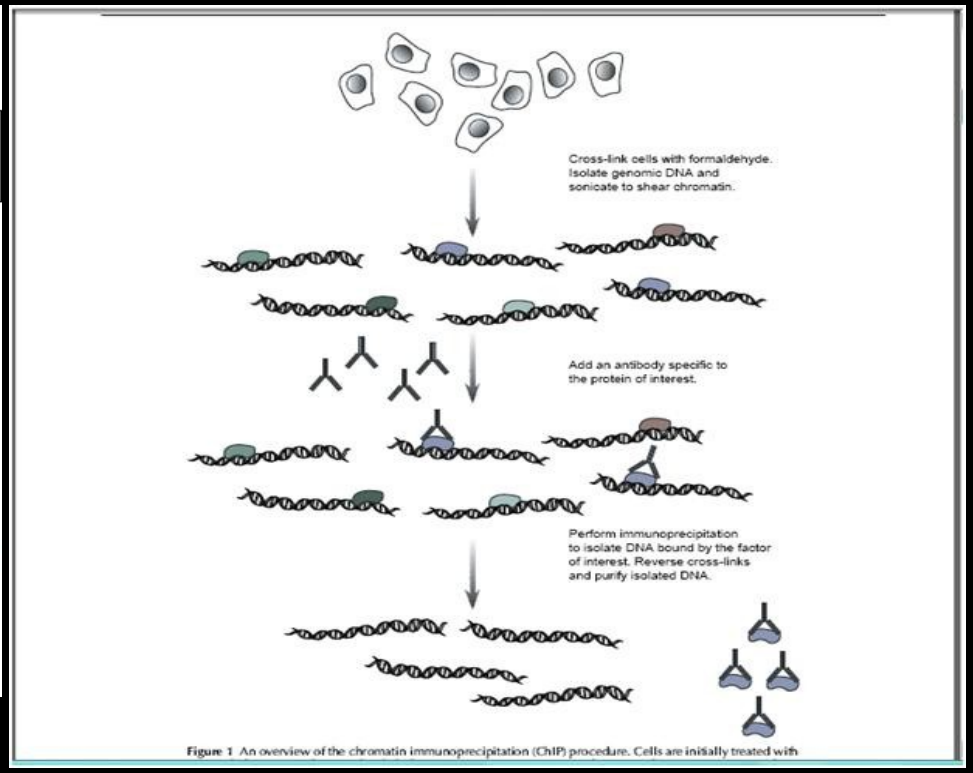
http://hades1.bioquant.uniheidelberg.de/rnai.html

Methods For High Throuput Analysis

Mass Spectroscopy



Chromatin immunoprecipitation(chIP) sequencing



http://jp.physoc.org/content/563/1/11/F1.large.jpg

Computational Analysis

- Differential Equation Models
- Fishing for Information
- Visualizing data in a useful way
  - UCSC Genome Browser
  - Panther Database
  - DAVID
  - oPOSSUM

Python Scripting

```
#!/usr/bin/env python

import string, sys

# If no arguments were given, print a helpful message
if len(sys.argv)==1:
    print 'arguements not provided'
    sys.exit(0)

# Loop over the arguments
for i in sys.argv[1:]:
file = open(i)
line=file.read()
temp=line.upper()
# Transcribe
temp=temp.replace('A','U')
temp=temp.replace('G','Z')
temp=temp.replace('C','G')
temp=temp.replace('Z','C')
temp=temp.replace('T','A')
print temp
```

Biostatistics:

Using Statistics to solve questions in Biology

Lectures:

- Michael T. Laub-
  - Works to understand how cells process information, make decisions, and control their own behavior
- Noah Spies
  - PhD Student (Bartel Lab)

Protein Modeling and Computational Biology

How does the primary structure of a protein take on its shape?

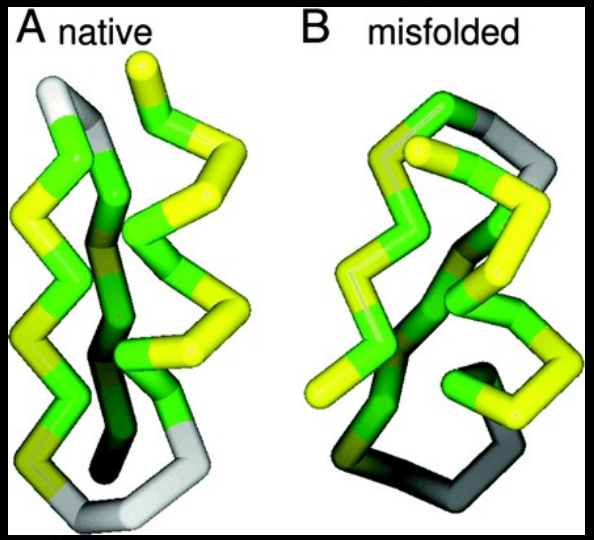
Lecturers:

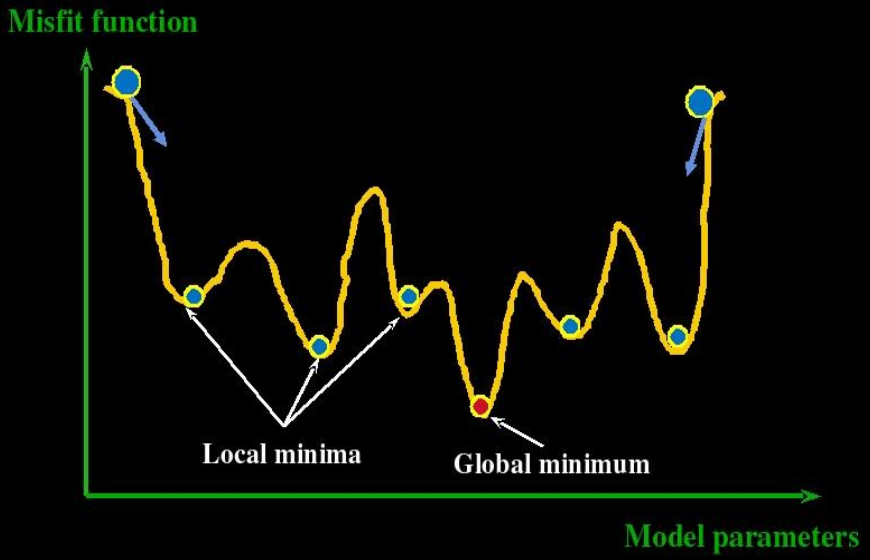
- Dr. Emiko Fire, Postdoctoral Fellow, Department of Biology
- Christopher Negron- PhD student, Computer and System Biology Graduate Program
- Orr Ashenberg- PhD student, Computer and System Biology Graduate Program
- Hyun Youk - PhD student, Physics Program

Pymol.org

Pymol.org

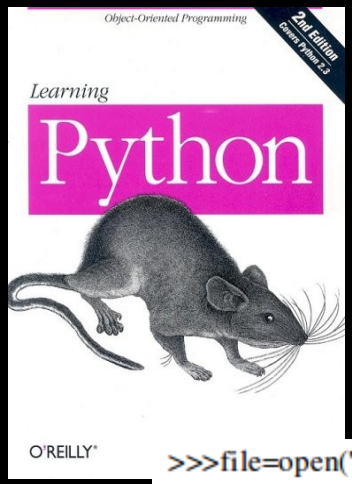
Fold–It ; a human-based supplement to avoid local minima in computer based protein folding (A collaboration at the Univ of Washington between the Baker Biochemistry Lab and Dept of Computer Science



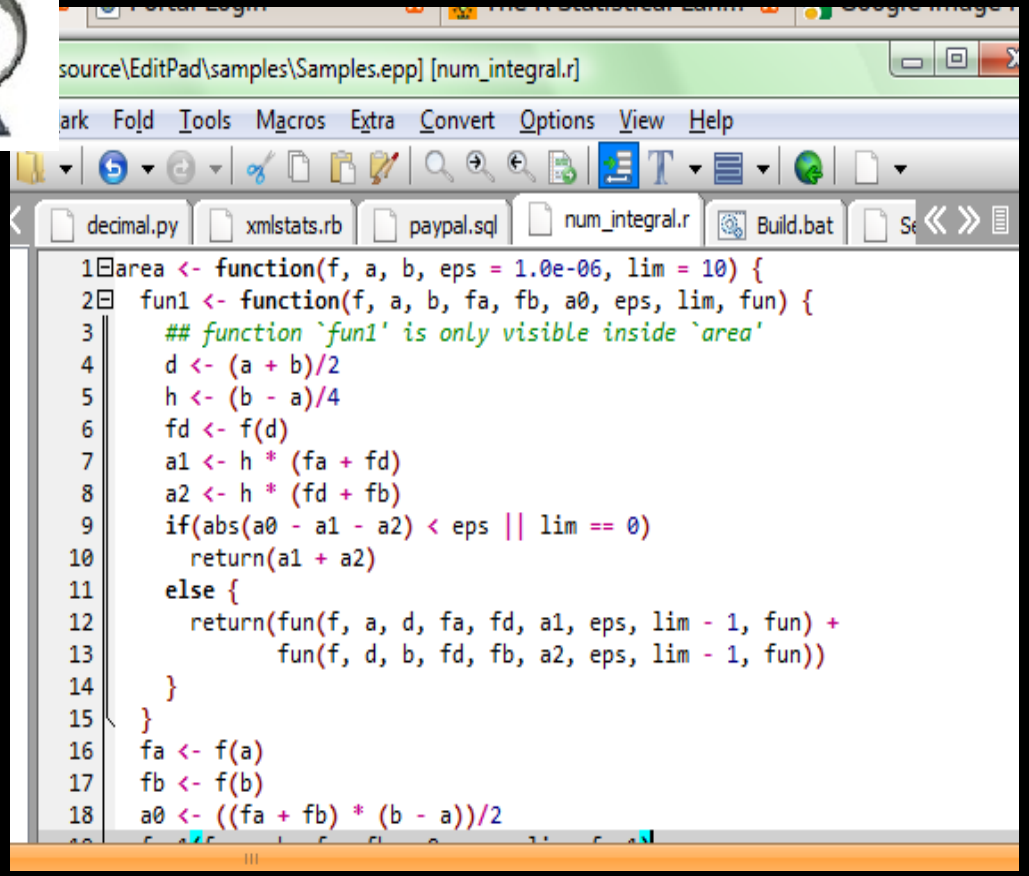


Foldit
Pull Mode
Score:
7789
of 8420
Sheets and Ladders
Rubber Bands are free!
Make as many as you want.
Next
Shake Sidechains
Wiggle All
Freeze Protein
Remove Bands
Disable Bands
Reset Puzzle
Actions
Undo
Menu
Chat - Puzzle Levels
auto show
Chat - Global
auto show

Wednesday + Thursday: Computing (for systems biology problems)



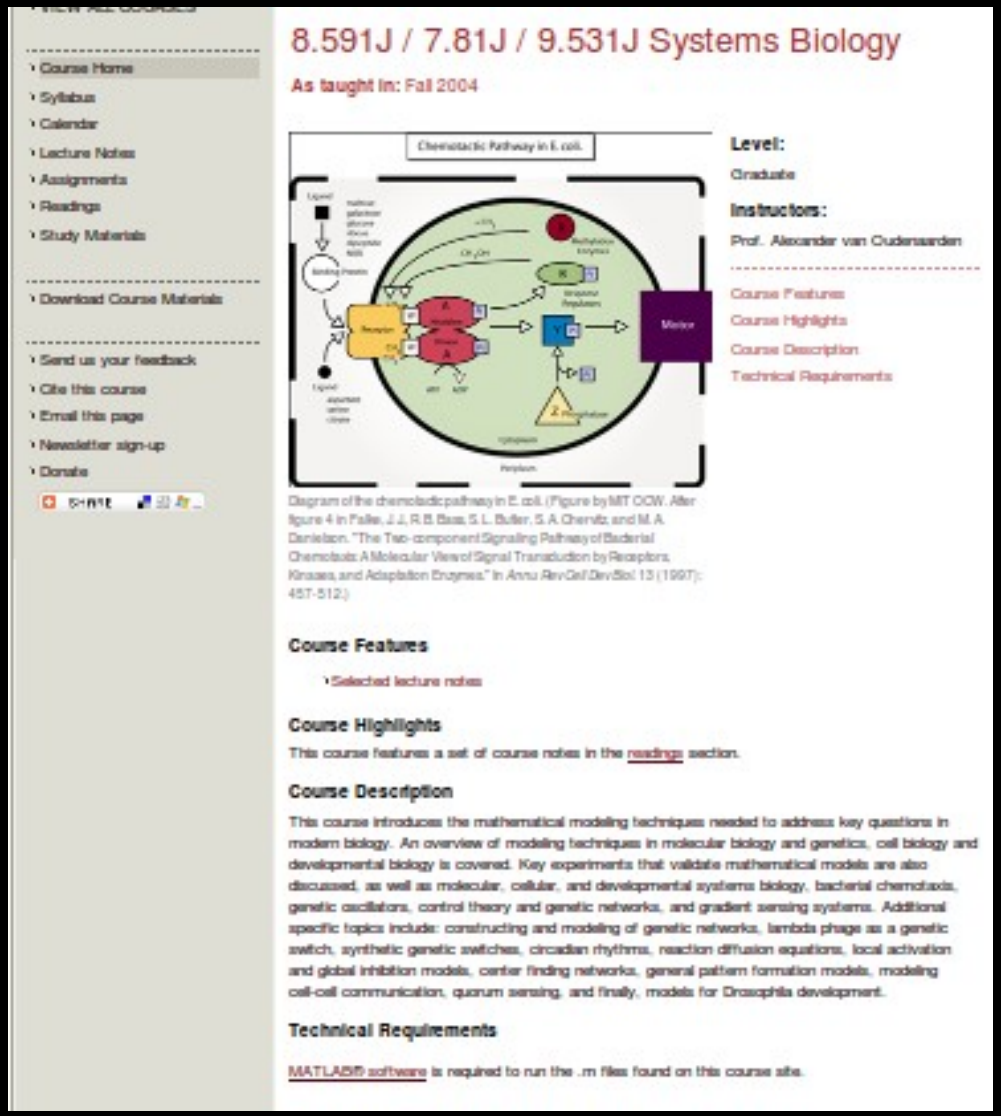

```
>>>file=open('myfirstfile','w') #create file ('w'=write)
>>>file.write('This is my first python file\n')# write string
   into file
>>>file.close()          #close file
>>>file=open('myfirstfile', 'r') #open an existing file
   ('r'=read)
>>>lines=file.readlines() #read entire file into list of line
   strings
>>>lines
['This is my first python file\n']
>>>file.close() #close file
```




```
area <- function(f, a, b, eps = 1.0e-06, lim = 10) {
  fun1 <- function(f, a, b, fa, fb, a0, eps, lim, fun) {
    ## function `fun1' is only visible inside `area'
    d <- (a + b)/2
    h <- (b - a)/4
    fd <- f(d)
    a1 <- h * (fa + fd)
    a2 <- h * (fd + fb)
    if(abs(a0 - a1 - a2) < eps || lim == 0)
      return(a1 + a2)
    else {
      return(fun(f, a, d, fa, fd, a1, eps, lim - 1, fun) +
             fun(f, d, b, fd, fb, a2, eps, lim - 1, fun))
    }
  }
  fa <- f(a)
  fb <- f(b)
  a0 <- ((fa + fb) * (b - a))/2
```

MIT Open Course Ware

[http://ocw.mit.edu/]



- Course Home
- Syllabus
- Calendar
- Lecture Notes
- Assignments
- Readings
- Study Materials

- Download Course Materials

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- Donate

8.591J / 7.81J / 9.531J Systems Biology

As taught in: Fall 2004

Chemotactic Pathway in E. coli.

Level:

Graduate

Instructors:

Prof. Alexander van Oudenaarden

Course Features
Course Highlights
Course Description
Technical Requirements

Diagram of the chemotactic pathway in E. coli. (Figure by MIT OCW. After figure 4 in Falke, J.J., R.B. Bass, S.L. Butler, S.A. Chervitz, and M.A. Danielson. "The Two-component Signaling Pathway of Bacterial Chemotaxis: A Molecular View of Signal Transduction by Receptors, Kinases, and Adaptation Enzymes." In *Annu. Rev. Cell. Dev. Biol.* 13 (1997): 457-512.)

Course Features

- Selected lecture notes

Course Highlights

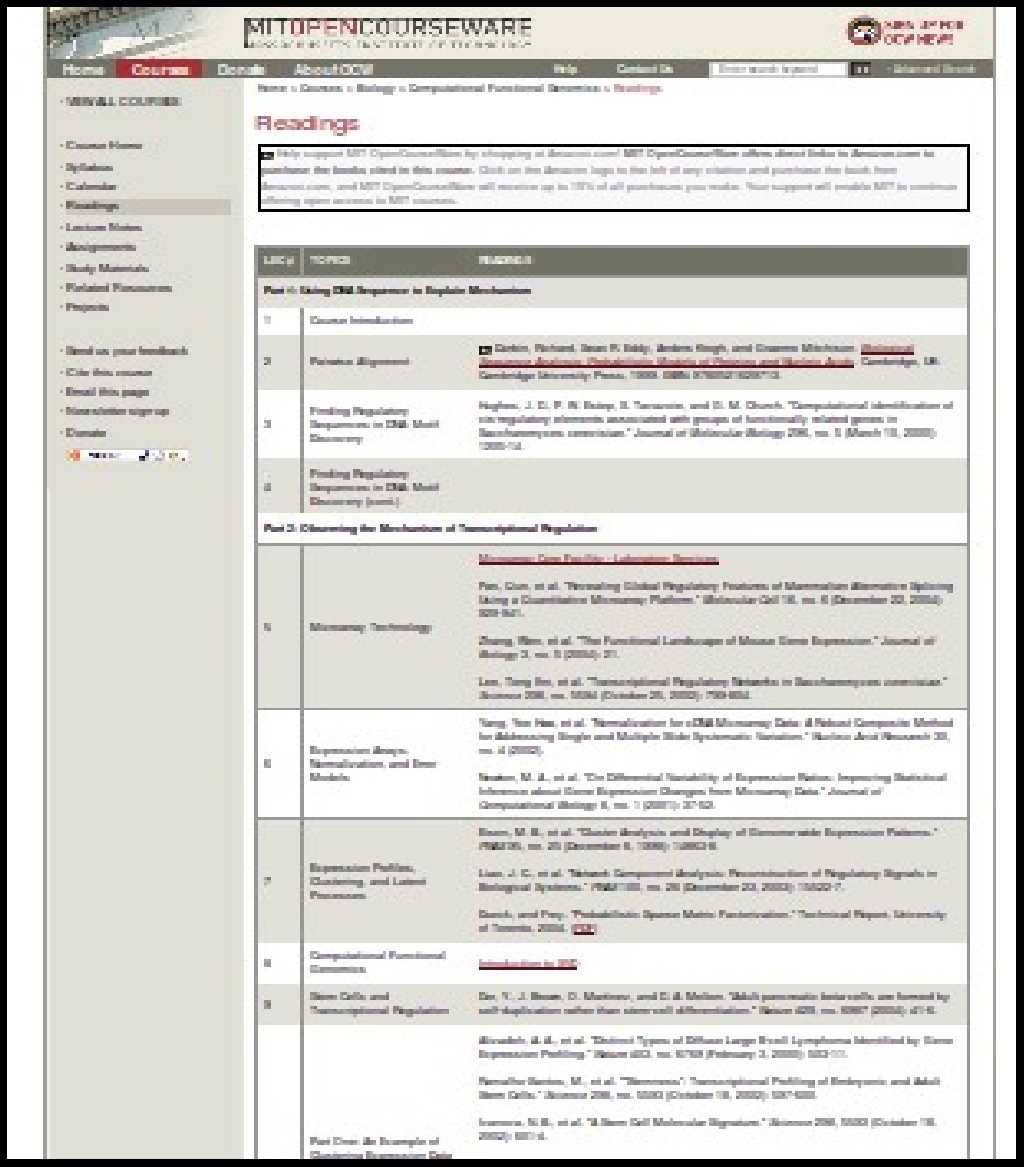
This course features a set of course notes in the readings section.

Course Description

This course introduces the mathematical modeling techniques needed to address key questions in modern biology. An overview of modeling techniques in molecular biology and genetics, cell biology and developmental biology is covered. Key experiments that validate mathematical models are also discussed, as well as molecular, cellular, and developmental systems biology, bacterial chemotaxis, genetic oscillators, control theory and genetic networks, and gradient sensing systems. Additional specific topics include: constructing and modeling of genetic networks, lambda phage as a genetic switch, synthetic genetic switches, circadian rhythms, reaction diffusion equations, local activation and global inhibition models, center finding networks, general pattern formation models, modeling cell-cell communication, quorum sensing, and finally, models for Drosophila development.

Technical Requirements

MATLAB® software is required to run the .m files found on this course site.



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Readings

Opportunities at M.I.T

MIT Summer Research Program
HST Summer Institute

Teaching style at M.I.T.

Acknowledgements:
Mandana Sassanfar
Hunter QuBi Grant (NIH)
Veronica Lichman