BMI/CS 776
Lecture 1

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2007.01.23

Today

- Introductions
- Course information
- Overview of course topics

My introduction

- Arrived in August
- Departments of Biostatistics & Medical Informatics and Computer Sciences
- Member of the Genome Center of Wisconsin
- Interests in comparative genomics
- Expertise in multiple whole-genome alignment

Your introductions

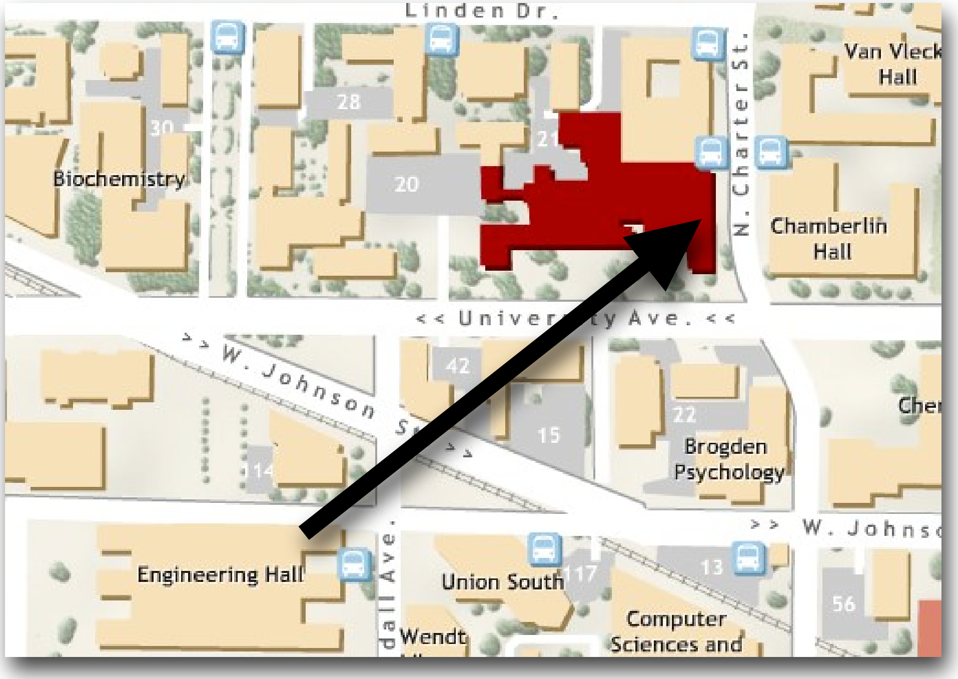
- Name
- Department
- Year
- Interests (academic/research)

Web site

- URL: http://www.biostat.wisc.edu/bmi776/
- Syllabus/Readings/Lectures
- Homeworks/Project
- Email list and archive

Office hours

- Times TBA
- 6720 Medical Sciences Center (MSC)
- Very confusing building
- Best bet: Take elevator near 420 N. Charter St. entrance



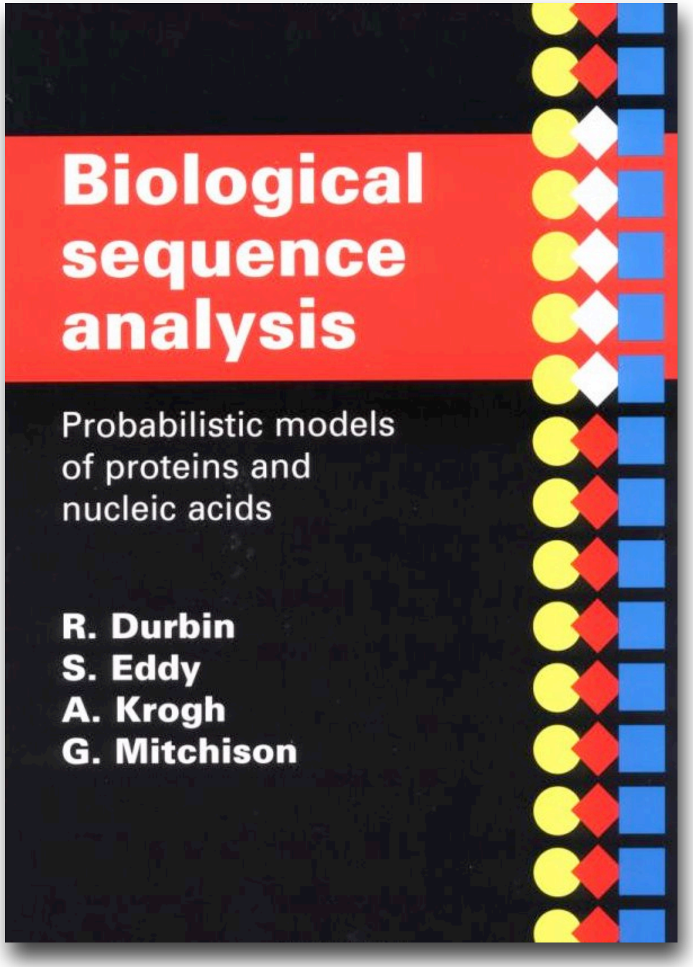
Prerequisites

- BMI/CS 576
- Computer Science: Graphs, Dynamic Programming (at least CS 367)
- Statistics: Probability, Bayesian networks
- Biology: None required, but you must be interested in learning some!

Related courses

- Botany 563
  - Phylogenetic Analysis of Molecular Data
  - Taught by Professor David Baum
- Computer Science 838
  - Advanced Natural Language Processing
  - Taught by Professor Jerry Zhu

Required text



Biological sequence analysis

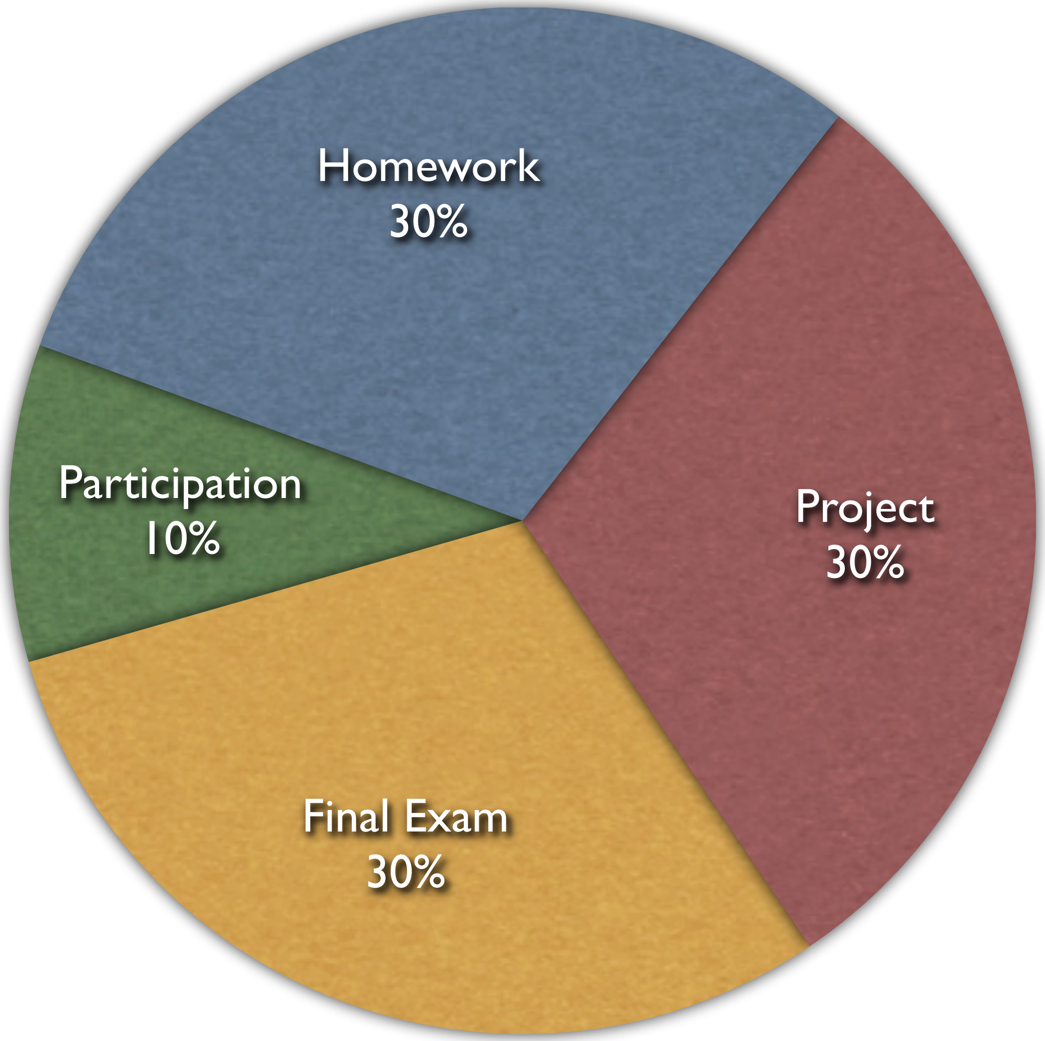
Probabilistic models of proteins and nucleic acids

R. Durbin
S. Eddy
A. Krogh
G. Mitchison

Reading

- Reading assignments for each lecture
- Types of reading
  - From textbook
  - Research articles
  - Notes passed out in class (better come!)

Grading



Participation

- Very small class
- Keys to participation
  - Show up to class!
  - Do the assigned reading
  - Don’t be afraid to ask questions

Homework

- Programming
  - Implement algorithms from course
  - Analyze real data
  - Preferred languages: C, C++, Java, & Python
- Written problems
  - Algorithm simulation
  - Proofs

Project

- Goals:
  - Develop a new model/algorithm
  - Implement it
  - Apply to a meaningful data set

Milestones	
March 9	Proposal
April 13	Progress Report
May 4	Final report

Final exam

- Monday, May 14, 2007, 7:25-9:25 PM
- Cumulative
- Open book/notes, no memorization required

Computer accounts

- BMI UNIX machines
  - No lab, login remotely via SSH
  - May need VPN if off campus network
  - Machines: mi1.biostat.wisc.edu, mi2.biostat.wisc.edu
- Need UNIX help? Try CS1000 from DoIT

Major topics

- Biology of nucleic acids
- Modeling of nucleotide evolution
- Finding elements in genomes
- Genome alignment
- RNA structure and discovery
- Analysis of cellular networks

Plan of attack

- All things DNA-related before Spring break
- RNA, cellular networks, and other topics after the break

Course goals

- We will have been successful if...
  - You are aware of and understand the most important problems in computational molecular biology
  - You have an understanding of the models and algorithms that are currently used for these problems.

Course theme

"Nothing in biology makes sense except in the light of evolution."
- Theodosius Dobzhansky

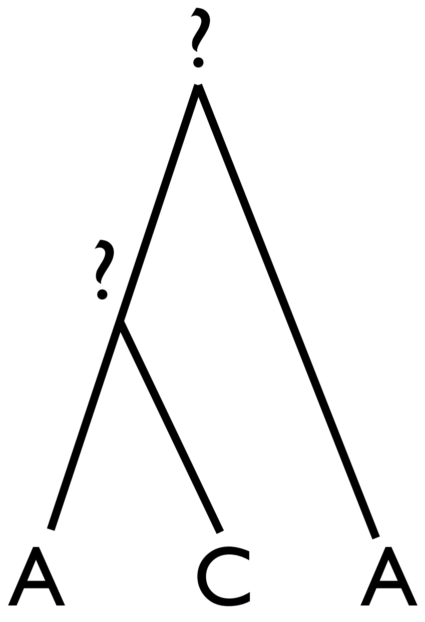
- Evolution as a **tool** in deciphering the genome
- "Comparative" models
- Combine **within** genome models with **between** genome models

Biology of nucleic acids

- How does DNA replicate and mutate?
- How do we define evolutionary relationships between DNA positions?
- How do we represent and classify such relationships?
- Key concepts: homology, tree theory

Modeling of nucleotide evolution

- How do we model the evolution of a set of sequences from an ancestral sequence?
- How can we use such models to infer trees?
- How might we reconstruct ancestral sequences?
- Key concepts: Markov models, Poisson processes, Rate matrices, Maximum likelihood, Bayesian analysis

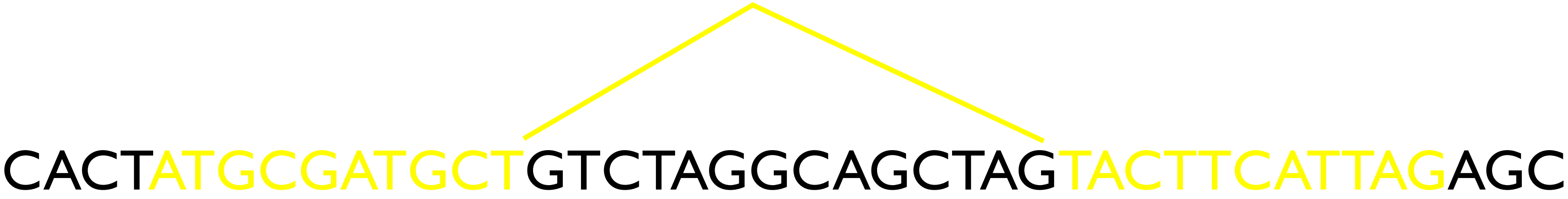


Motif finding

CTATCGTAGCGACTGCTACTCGATACTAGCT
CACTAGTCCATGCTTGCTAGGCAGTCGTAGC
CGATCGGGATTAAGTCGAAGCTCGCAAACCA
CGCAATTCGATGCTCACATGAGCATTGGGCC
CATCGTATGGCTCAAGTCGATCCTAGGACGA

- How can we find common (degenerate) patterns in a set of functionally similar sequences?
- Key concepts: Hidden Markov models, Gibbs sampling, Expectation-Maximization

Gene finding



CACTATGCGATGCTGTCTAGGCAGCTAGTACTTCATTAGAGC

- How do we find gene structures in the genomes of... Prokaryotes? Eukaryotes?
- Can we use comparative genomics to increase the accuracy of our predictions?
- Key concepts: Generalized HMMs, higher-order Markov models, Pair HMMs.

Alignment

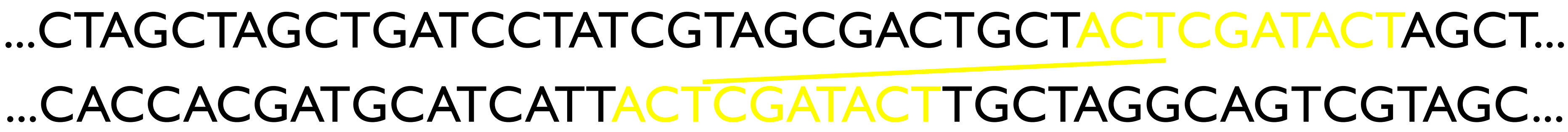
- What is the meaning of sequence alignment?
- How do we align...
    - a pair of short sequences?
    - a pair of long sequences?
    - multiple sequences?
    - whole genomes?

```
CGCCTCGGGT
CGCC---GGT
CACCTAGTAC
CGCTACTTGC
CG--TCTTGC
CGTAGCTTTC
```

Alignment concepts

- Alignment combinatorics
- Statistical alignment
- Pair Hidden Markov Models
- Local alignment and statistics (Karlin-Altschul theorem)
- Parametric alignment

Pattern matching



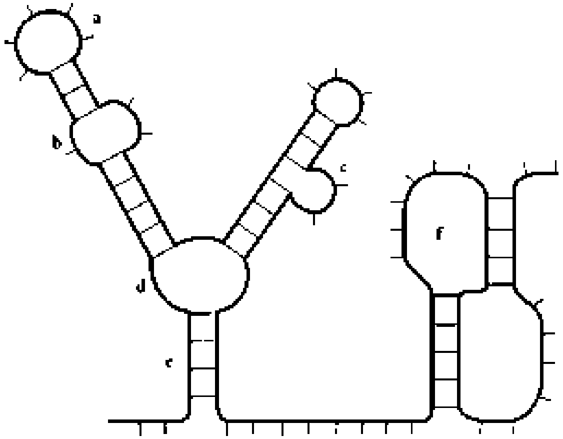
...CTAGCTAGCTGATCCTATCGTAGCGACTGCTACTCGATACTAGCT...

...CACCACGATGCATCATTACTCGATACTTGCTAGGCAGTCGTAGC...

- How can we quickly identify highly-similar substrings in sets of large sequences?
- Key concepts: Suffix trees/arrays, locality-sensitive hashing, q-gram filtration, randomized matching

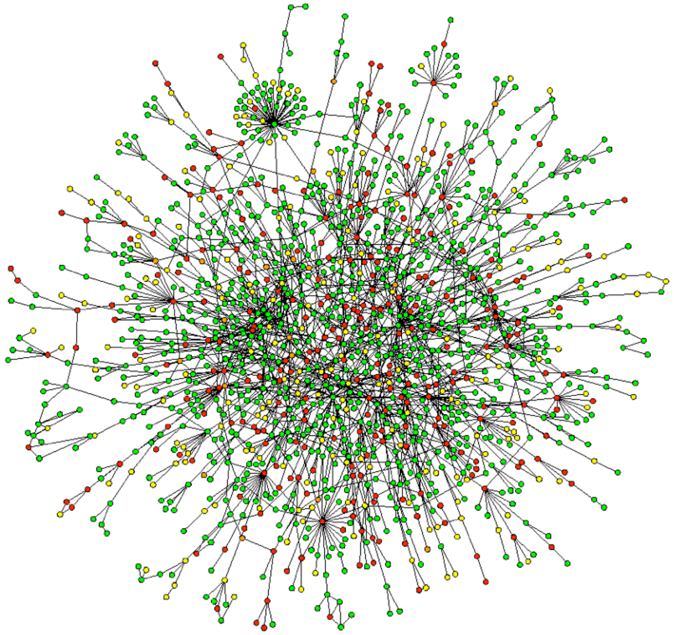
RNA

- How can we predict the secondary structure of RNA?
- How can we locate RNAs of a given structure within a genome?
- Key concepts: Energy minimization, Stochastic context free grammars



Cellular Networks

- How can we infer and represent interactions between cellular components?
- How can we determine important functional modules within networks?
- Key concepts: Graph theory, Inference of Bayesian networks



Next time

- Topic: “The trees of life”
- Assignments:
  - Do assigned readings (check Web site)
  - Log in to BMI machines and change password (use command “passwd”)
- First homework to be assigned on Thursday