BioInformatics and Computational Molecular Biology

### Course Website http://BioInformatics.uchc.edu

What is Bioinformatics

Bioinformatics upgrades the information content of biological measurements. "Discovery" WHAT KIND OF MEASUREMENTS?

- SEQUENCE
- PHYSIOLOGIC
- EXPRESSION
- STRUCTURE

*Where do these data come from?* Computational Molecular Biology

- Strings
  - nucleotides
  - amino acids
  - Sequence reads
- Gene expression
  - Large data arrays

# Kinds of problems we will study: Homology/Alignment

- How similar is the *catfish* Somatostasin Precursor
- mpstriqcal allaval svcsvsgapsdaklrqflqrsilapsvkqeltryttlaellaelaqaenevlds sdevsraaesegarlemera agpmlaprerkagcknffwktftsc

### to the human Somatostatin Precursor

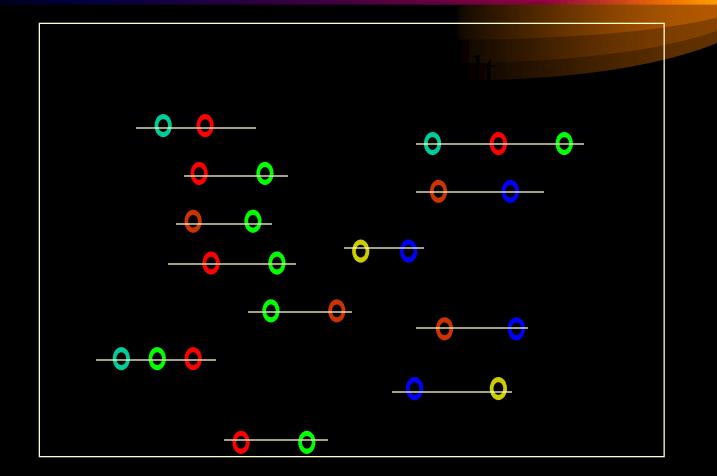
mlscrlqcalaalcivlalggvtgapsdprlrqflqkslaatgkqelakyflaellsepnqtendalepedlpqaaeqde mrlelqrsansnpamaprerkagcknffwktftsc

# Kinds of problems we will study: Phylogeny

Given corresponding regions of DNA in the gene causing cell wall permeability, can we determine which of the bacteria is most likely the ancestor and what the lineage is?

Bacterium A	ACGTAC
Bacterium B	ACTTTG
Bacterium C	ACTATG
Bacterium D	AGGTAG

Kinds of problems we will study: Constructing a genome *de novo* Mapping/Fragment Assembly



## Kinds of problems we will study: Gene-finding

Given this sequence of bases, can we find a substring which is a gene?

*Kinds of problems we will study: Gene-expression in large data arrays* 

# An example from the M.I.T. Lab of G. Stephanopoulos

7000 gene expression levels provided among24 different tissues-some normal, somediseased. No labels for the genes.

The task: Discover ways that the gene expression levels (numbers) can be viewed so as to give insight into their function or tissue of origin.

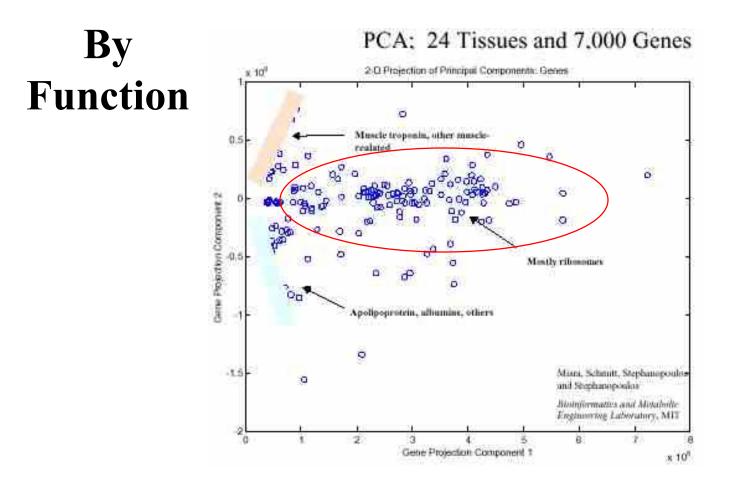
### **STRATEGY**

1. Arrange/transform the data into 'natural' clusters

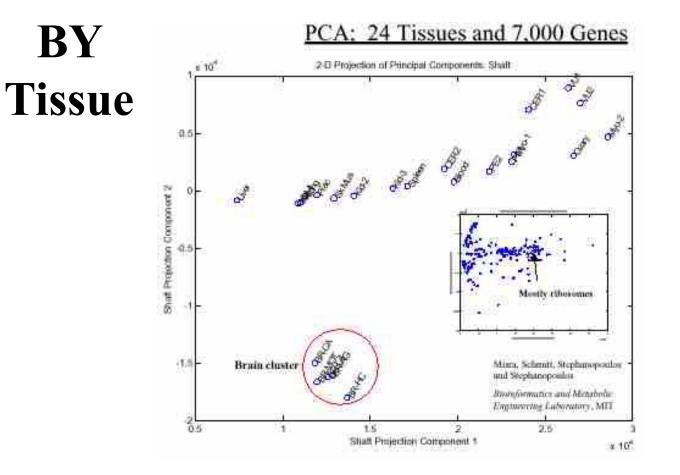
Reduce the *dimension* of the data by identifying and reducing *correlated data* Reveal the labels to see if the clustering

2. Reveal the labels to see if the clustering made sense

#### Principal Component Analysis



### Principal Component Analysis



### ANOTHER EXAMPLE

### Golub,TR, Slonim, DK, Tamayo, P *et al.* SCIENCE 286:531-37,1999

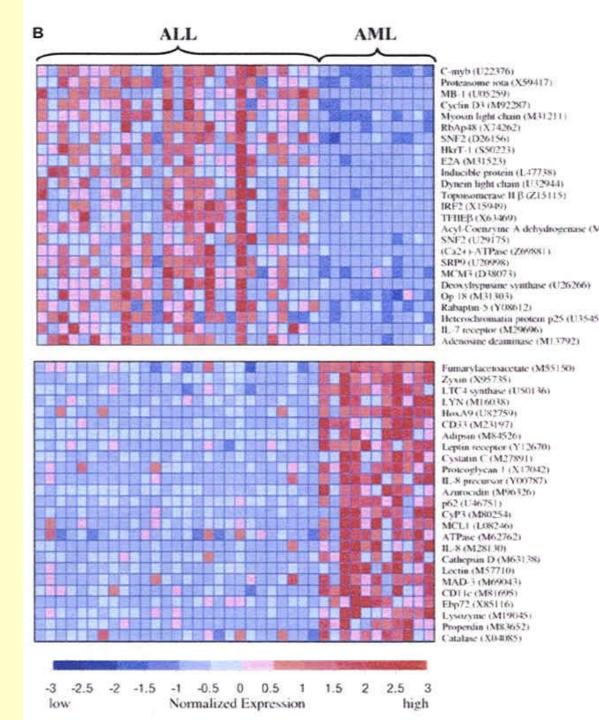
Molecular Classification of Cancer: Class Discovery and Class Prediction by Gene Expression Monitoring Golub,TR, Slonim, DK, Tamayo, P *et al.* SCIENCE 286:531-37,1999

- 38 Marrow Samples
  - 11 Acute Myelocytic Leukemia
  - 27 Acute Lymphocytic Leukemia
- Probes (cDNA's) for 6817 different Human Genes were arranged in a Gene Chip (microarray). The marrow sample caused each cDNA to react with a measurable level (expression level)
- Gene expression levels for each gene were measured in each tissue sample

### Golub,TR, Slonim, DK, Tamayo, P *et al.* SCIENCE 286:531-37,1999

- The preliminary technique, neighborhood analysis, implicated 1100 genes as related to the two tissue types, AML and ALL
- 50 'Best' were used
- Given a 2 class model, the 50 genes classified 36/38 samples accurately. 2 were 'uncertain'

Golub,TR, Slonim, DK, Tamayo, P *et al.* SCIENCE 286:531-37,1999



### Golub,TR, Slonim, DK, Tamayo, P *et al.* SCIENCE 286:531-37,1999

- Self-organizing map applied to the data
  2 classes found -slightly less accurate than Neighborhood Analysis
- SOM applied using 4 class model. SOM found 3 classes accurately:
  - AML
  - B-cell ALL
  - T-cell ALL

So, what exactly is Bioinformatics?

For sure, it is the application of analytical tools to analyze data and set the foundation for discovery

- Pattern Recognition
- AI
- ANN
- Probabilistic Models
- Machine learning
- Optimization
- Dynamic Programming

Using computational methods, we are going to study...

- The Genome
  - How to assemble fragments
  - How to identify genes
- Genes
  - Relation to other genes in other species
  - How are they transcribed
    - RNA structure prediction
  - How do they respond to the environment
    - Gene expression

# Using computational methods, we are going to study...

- Protein Structure
  - Identification
  - -Folding
  - Comparison
    - Primary structure homology
    - Secondary structure: Motifs
    - Tertiary structure homology