CAP 5510: Introduction to Bioinformatics
CGS 5166: Bioinformatics Tools

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www.cis.fiu.edu/~giri/teach/BioinfS13.html

Syllabus

- Fundamentals of Biology, Statistics, the Internet, and Bioinformatics
- Databases and Data Integration; Programming with BioPerl and BioPython;
- Sequence Alignment, Multiple Sequence Alignment
- Sequencing; Next Generation Sequencing & Applications
- Discovery, Learning, Prediction & Inference: Nucleotide and Protein Sequences
- Machine Learning: NN, HMM, SOM, SVM, etc.
- Gene Regulation; Regulatory Elements; microRNA; Regulatory networks
- Transcriptomics: Analysis of Gene Expression Data
- Gene Ontology and Pathways; Protein-protein interactions
- Genomics, Proteomics, Comparative Genomics
- Phylogenetic Analysis
- Molecular Structural Analysis: RNA and Proteins
- Genetics and Genome-Wide Association Schemes
- Single Nucleotide Polymorphisms
- Miscellanea: Omics; Alternative Splicing; Epigenetics; Translational bioinformatics; visualization;

Evaluation

- Semester Project (45 %)
- Homework Assignments (20 %)
- Exam (15 %)
- Quizzes (10 %)
- Summary Reports of Interest (5 %)
- Class Participation (5 %)

Course Homepage

http://www.cis.fiu.edu/~giri/teach/BioinfS13.html

- Lecture notes, required reading material, homework, announcements, etc.

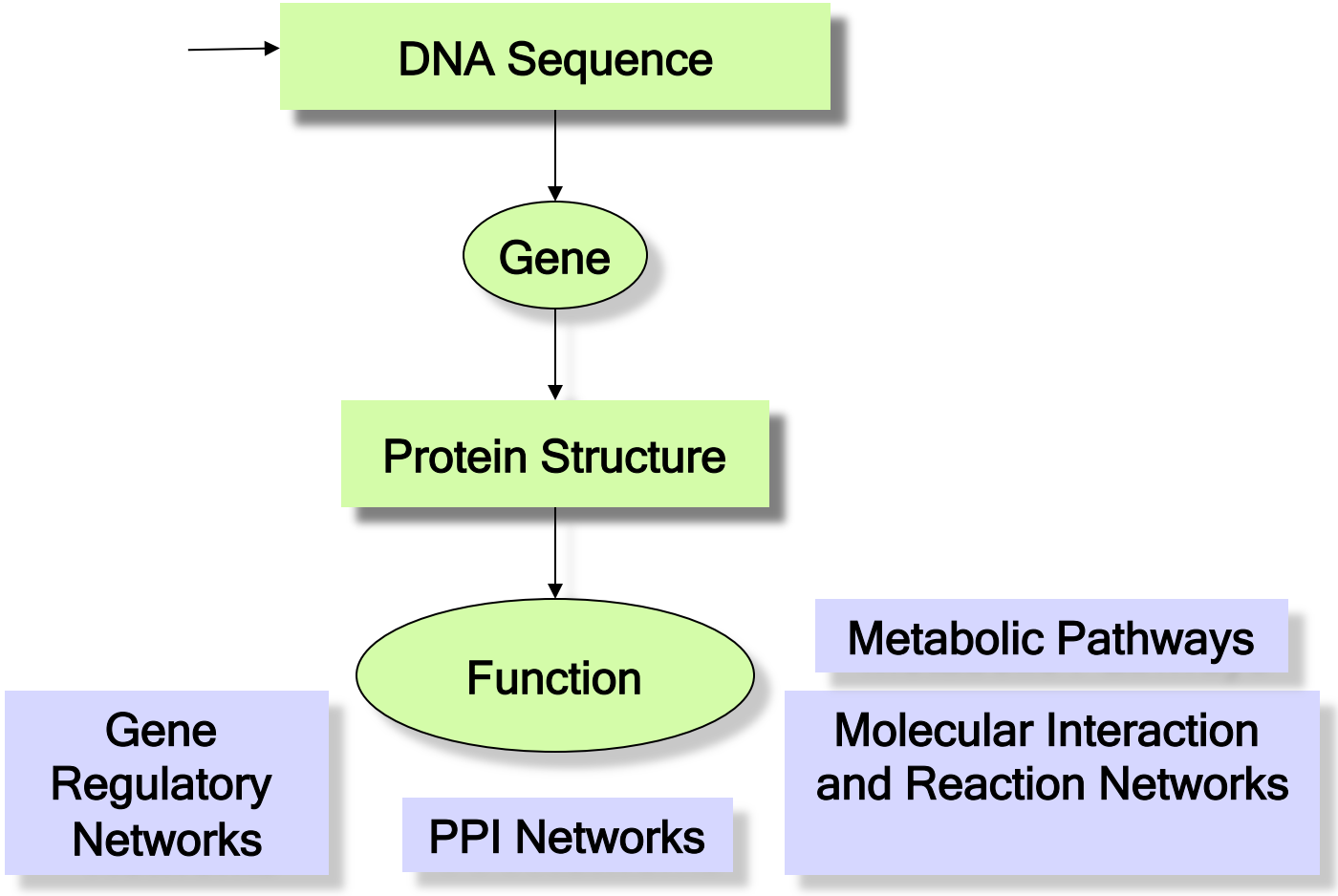
History

- What major world event took place on 26 June, 2000?
- What major discovery was made in 1953?
- 1975: Sanger Sequencing
- 1977: first bacteriophage sequenced
- 1990: HGP initiated

Introduction

1. What is Bioinformatics?
   - Analysis of biological data with computing & statistical tools.
2. The different aspects of Informatics?
   - Data Management (Database Technology, Internet Programming)
   - Data Analysis (Data Mining, Modeling, Statistics)
   - Development of Efficient Algorithms
   - Visualization and Interface Design (HCI, Graphics)
3. How to assist biological research?
   - Build databases for data
   - Build efficient tools for search, retrieval, analysis, & visualization
   - Propose models and efficient tools to verify the model using known data
   - use predicted information to narrow down search
   - propose new experiments based on model or analysis
   - Build smart, hyperlinked, integrated mining environments

Overall Goals



Perspective of Bioinformatics

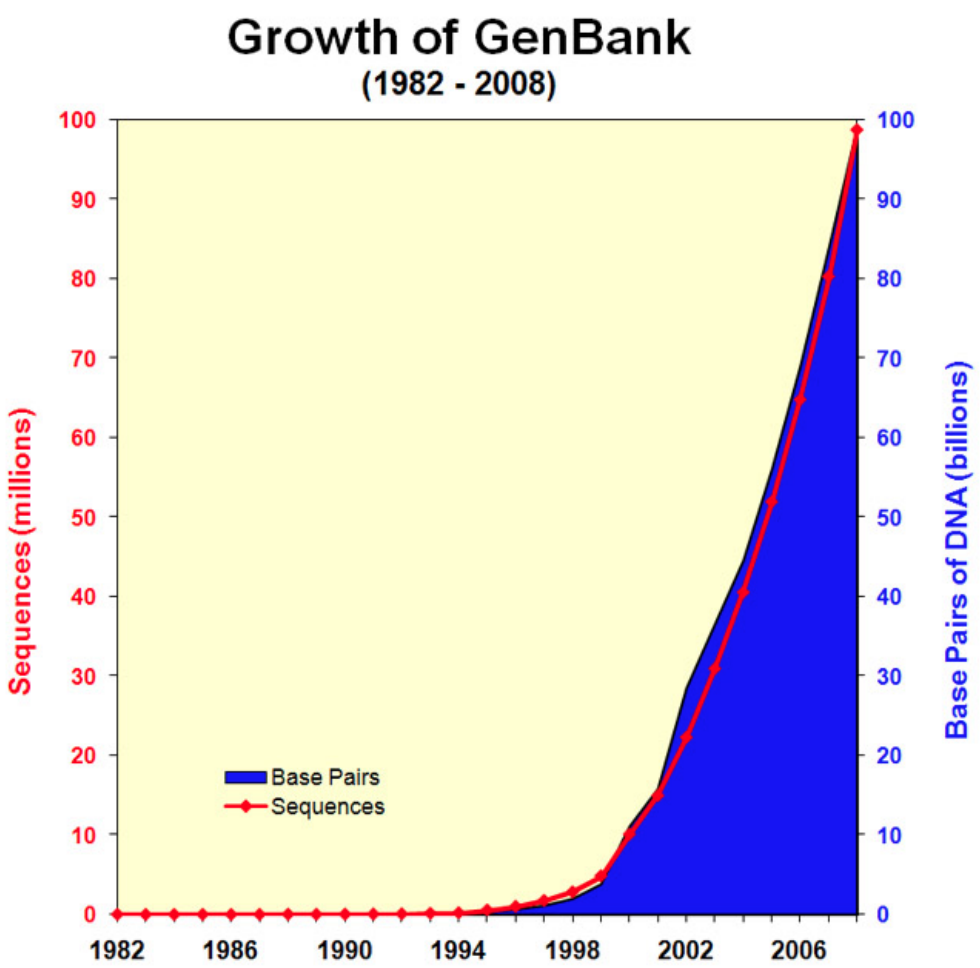
- Study of the cell: DNA, genes, proteins
- Study of the organism: genome, changes over time, over body regions, or over physiological or pathological states
- Study of all life: Tree of Life, Phylogeny, Variations, comparative genomics

General Information

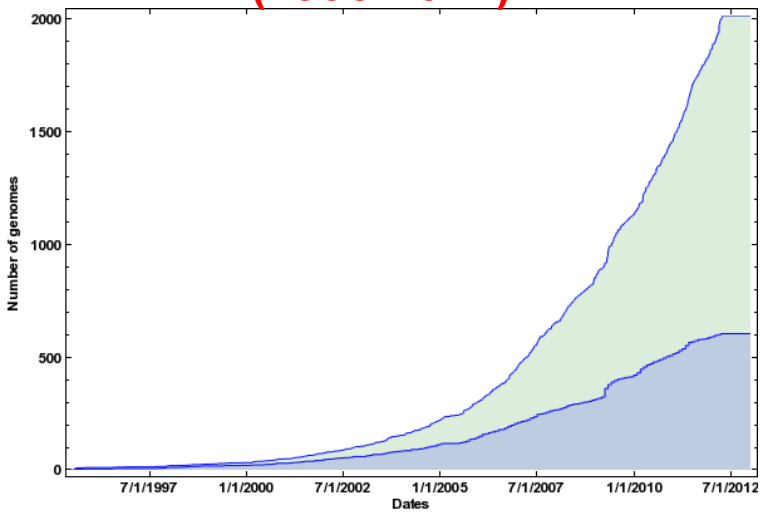
- GenBank Release 157/175/193 (Dec 2006/09/12) contains over 64/112/161 million sequence entries totaling over 69/110/126 Gb from over 2,500/?/9000 organisms [http://www.ncbi.nlm.nih.gov] (Storage: ~600 GBytes uncompressed)
- Human Genome has ~3 billion bp with 32,000+ genes.
- 435/624/3880 complete microbial genomes sequenced (684/914/12847 more in progress)
- 2540/3250 Viral genomes (300bp - 300Kb) (1st 1978: Simian virus; 5Kb).
- 22/180 complete eukaryotic genomes sequenced (175/613 more in progress):

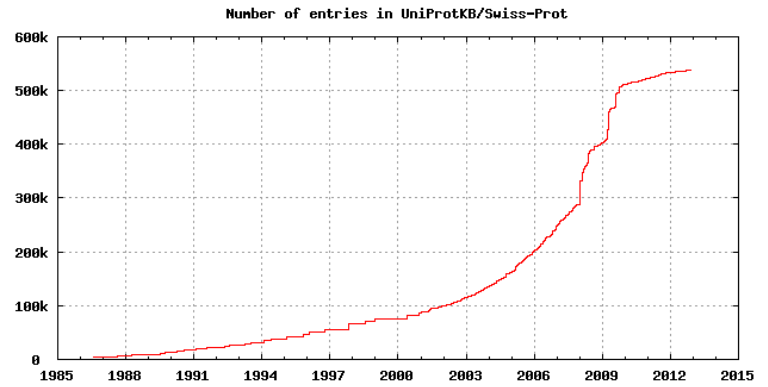
  Caenorhabditis elegans, *Arabidopsis thaliana*, *Saccharomyces cerevisiae*, *Mus musculus*, *Homo sapiens*, *Oryza sativa*, *Plasmodium falciparum*, *Drosophila melanogaster*, *Anopheles gambiae*, *Macaca mulatta*, *Bos taurus*, *Felis catus*, *Gallus gallus*
- Swiss-Prot Release 51.3/54.7/2012_11 (Dec'06/Jan'08/Nov 2012): 250K/333K/550K entries; 91/120/191 million amino acids.

Growth of Sequence Databases



Microbial Genome Growth (1995-2012)





SwissProt Growth (1985-2012)

http://www.ncbi.nlm.nih.gov/genbank/genbankstats-2008/

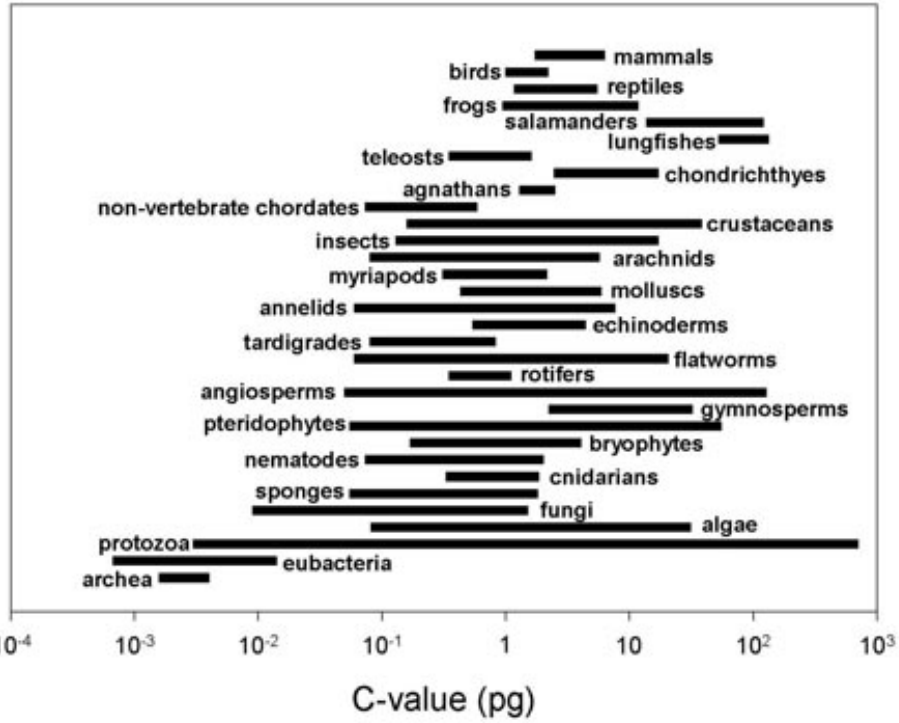
Genome Sizes

Organism	Size	Date	Est. # genes
HIV type 1	9.2 Kb	1997	9
H. influenzae	1.8 Mb	1995	1,740
M. genitalium	0.58 Mb	1998	525
E. coli	4.7 Mb	1997	4,000
S. cerevisiae	12.1 Mb	1996	6,034
C. elegans	97 Mb	1998	19,099
A. thaliana	100 Mb	2000	25,000
D. melanogaster	180 Mb	2000	13,061
M. musculus	3 Gb	2002	~30,000
H. sapiens	3 Gb	2001	32,000+

Short Homework: Curious Facts

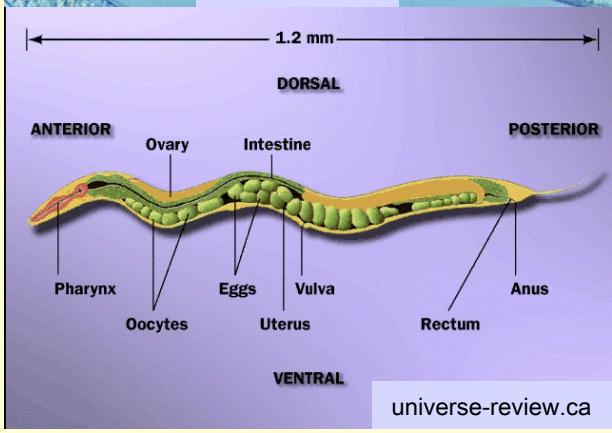
- What is interesting about the following organisms?
  - *Paris japonica, Protopterus aethiopicus, Encephaltozoon intestinalis, Ameoba dubia, Arabidopsis lyrata*
- Ferrari of the virus world?
- 1001 Genomes Project
- App: LeafSnap

Gregory, T.R. (2004a). Macroevolution, hierarchy theory, and the C-value enigma. *Paleobiology* 30: 179-202.

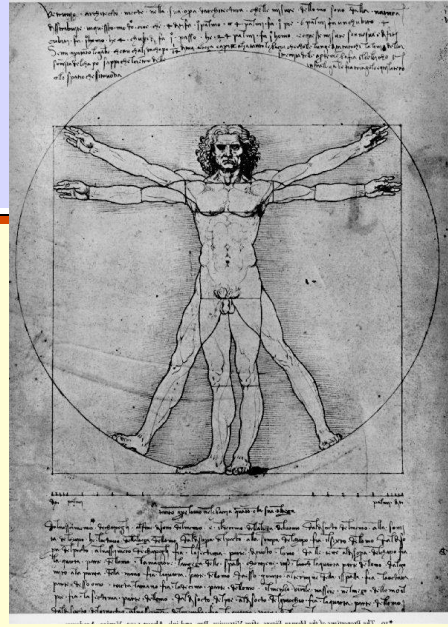


Caenorhabditis Elegans

- Entire genome – 1998; 8 year effort
- 1st animal; 2nd eukaryote (after yeast)
- Nematode (phylum)
- Easy to experiment with; Easily observable
- 97 million bases; 20,000 genes;
- 12,000 with known function; 6 Chromosomes;
- GC content 36%
- 959 cells; 302-cell nervous system
- 36% of proteins common with human
- 15 Kb mitochondrial genome
- Results in ACeDB
- 25% of genes in operons
- Important for HGP: technology, software, scale/efficiency
- 182 genes with alternative splice variants



Homo sapiens



- Sequenced – 2001; 15 year effort
- 3 billion bases, 500 gaps
- Variable density of Genes, SNPs, CpG islands
- ~ 1.1% of genome codes for proteins; 99%?
- ~ 40-48% of the genome consists of repeat sequences
- ~ 10 % of the genome consists of repeats called ALUs
- ~ 5 % of the genome consists of long repeats (>1 Kb)
- 223 genes common with bacteria that are missing from worm, fly or yeast.

Sequence Alignment – Why?

>gi|12643549|sp|O18381|PAX6_DROME Paired box protein Pax-6 (Eyeless protein)
MRNLPCLGTAGGSGLGGIAGKPSPTMEAVEASTASHRHSTSSYFATTYYHLTDDECHSGVNQLGGVFVGG
RPLPDSTRQKIVELAHSGARPCDISRILQVSNGCVSKILGRYYETGSIRPRAIGGSKPRVATAEVVSKIS
QYKRECPSIFAWEIRDRLLQENVCTNDNIPSVSSINRVLRNLAAQKEQQSTGSGSSSTSAGNSISAKVSV
SIGGNVSNVASGSRGTLSSSTDLMQTATPLNSSESGGASNSGEGSEQEAIYEKLRLLNTQHAAGPGPLEP
ARAAPLVGQSPNHLGTRSSHPQLVHGNHQALQQHQQQSWPPRHYSGSWYPTSLSEIPISSAPNIASVTAY
ASGPSLAHSLSPPNDIESLASIGHQRNCPVATEDIHLKKELDGHQSDETGSGEGENSNGGASNIGNTEDD
QARLILKRKLQRNRTSFTNDQIDSLEKEFERTHYPDVFARERLAGKIGLPEARIQVWFSNRRAKWRREEK
LRNQRRTPNSTGASATSSSTSATASLTDSPNSLSACSSLLSGSAGGPSVSTINGLSSPSTLSTNVNAPTL
GAGIDSSESPTPIPHIRPSCTSDNDNGRQSEDCRRVCSPCPLGVGGHQNTHHIQSNGHAQGHALVPAISP
RLNFNSGSFGAMYSNMHHTALSMSDSYGAVTPIPSFNHSAVGPLAPPSPIPQQGDLTPSSLYPCHMTLRP
PPMAPAHHHIVPGDGGRPAGVGLGSGQSANLGASCSGSGYEVLSAYALPPPPMASSSAADSSFSAASSAS
ANVTPHHTIAQESCPSPCSSASHFGVAHSSGFSSDPISPAVSSYAHMSYNYASSANTMTPSSASGTSAHV
APGKQQFFASCFYSPWV

>gi|6174889|PAX6_HUMAN Paired box protein (Oculorhombin) (Aniridia, type II protein)
MQNSHSGVNQLGGVFVNGRPLPDSTRQKIVELAHSGARPCDISRILQVSNGCVSKILGRYYETGSIRPRA
IGGSKPRVATPEVVSKIAQYKRECPSIFAWEIRDRLLSEGVCTNDNIPSVSSINRVLRNLASEKQQMGAD
GMYDKLRMLNGQTGSWGTRPGWYPGTSVPGQPTQDGCQQQEGGGENTNSISSNGEDSDEAQMRLQLKRKL
QRNRTSFTQEQIEALEKEFERTHYPDVFARERLAAKIDLPEARIQVWFSNRRAKWRREEKLRNQRRQASN
TPSHIPISSSFSTSVYQPIPQPTTPVSSFTSGSMLGRTDTALTNTYSALPPMPSFTMANNLPMQPPVPSQ
TSSYSCMLPTSPSVNGRSYDTYTPPHMQTHMNSQPMGTSGTTSTGLISPGVSVPVQVPGSEPDMSQYWPR
LQ

Drosophila Eyeless vs. Human Aniridia

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Query: 57   HSGVNQLGGVFVGGRPLPDSTRQKIVELAHSGARPCDISRILQVSNGCVSKILGRYYETG 116
            HSGVNQLGGVFV GRPLPDSTRQKIVELAHSGARPCDISRILQVSNGCVSKILGRYYETG
Sbjct: 5    HSGVNQLGGVFVNGRPLPDSTRQKIVELAHSGARPCDISRILQVSNGCVSKILGRYYETG 64

Query: 117 SIRPRAIGGSKPRVATAEVVSKISQYKRECPSIFAWEIRDRLLQENVCTNDNIPSVSSIN 176
            SIRPRAIGGSKPRVAT EVVSKI+QYKRECPSIFAWEIRDRLL E VCTNDNIPSVSSIN
Sbjct: 65   SIRPRAIGGSKPRVATPEVVSKIAQYKRECPSIFAWEIRDRLLSEGVCTNDNIPSVSSIN 124

Query: 177 RVLRNLAAQKEQ 188
            RVLRNLA++K+Q
Sbjct: 125 RVLRNLASEKQQ 136
```

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Query: 417 TEDDQARLILKRKLQRNRTSFTNDQIDSLEKEFERTHYPDVFARERLAGKIGLPEARIQV 476
           +++ Q RL LKRKLQRNRTSFT +QI++LEKEFERTHYPDVFARERLA KI LPEARIQV
Sbjct: 197 SDEAQMRLQLKRKLQRNRTSFTQEQIEALEKEFERTHYPDVFARERLAAKIDLPEARIQV 256

Query: 477 WFSNRRAKWRREEKLRNQRR 496
           WFSNRRAKWRREEKLRNQRR
Sbjct: 257 WFSNRRAKWRREEKLRNQRR 276
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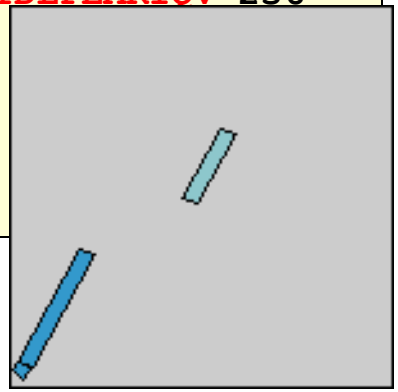


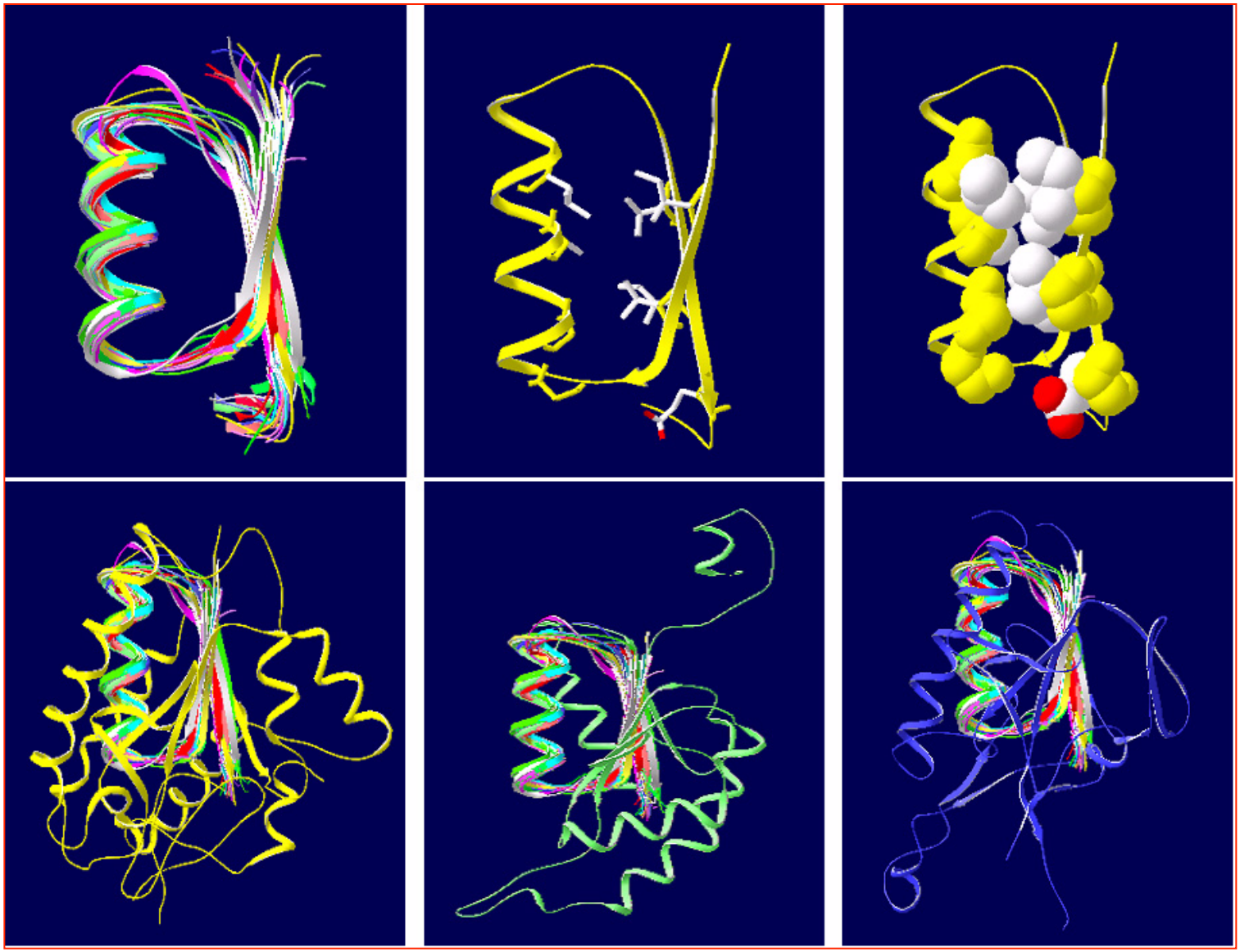
E-Value = 2e-31

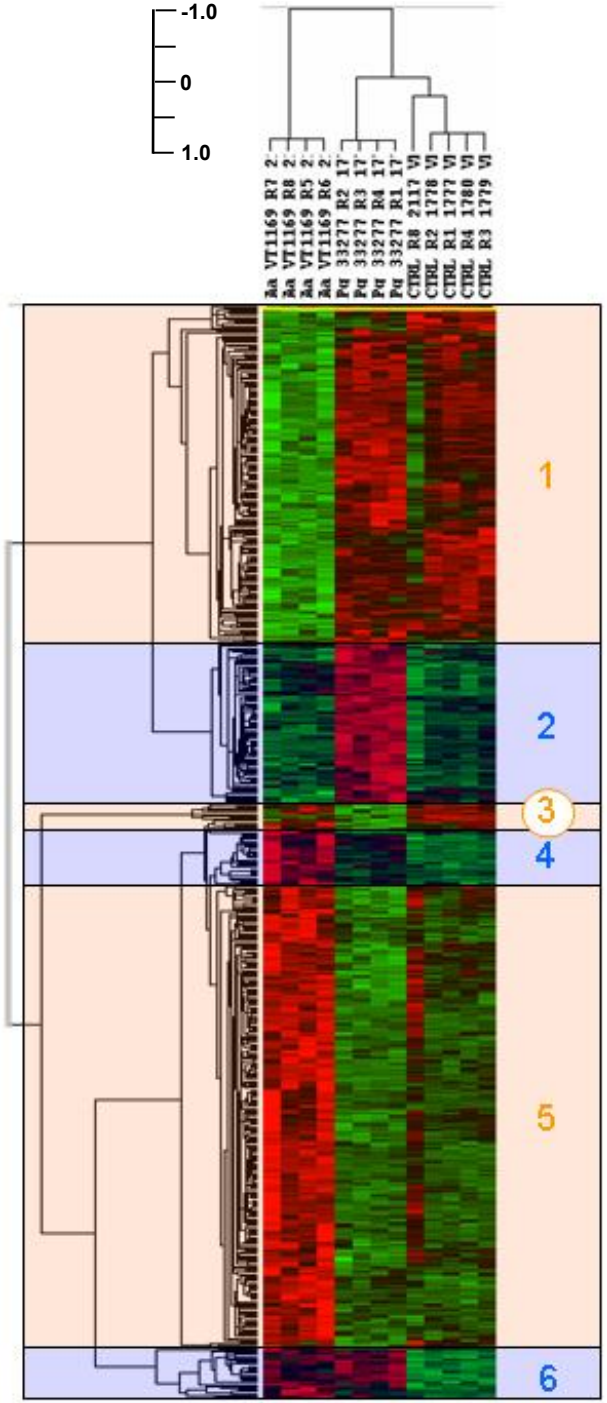
Motif Detection in Protein Sequences

- MTDKMQSLALAPVGNLDSYIRAANAWPMLSADEERALAEKLHYHGDLEAA
  KTLILSHLRFVVHIARNYAGYGLPQADLIQEGNIGLMKAVRRFNPEVGVR
  LVSFAVHWIKAEIHEYVLRNWRIVKVATTKAQRKLFFNLRKTKQRLGWFN
  QDEVEMVARELGVTSKDVREMESRMAAQDMTFDLSSDDDSDSQPMAPVLY
  LQDKSSNFADGIEDDNWEEQAANRLTDAMQGLDERSQDIIRARWLDEDNK
  STLQELADRYGVSAERVRQLEKNAMKKLRAAIEA

- MTDKMQSLALAPVGNLDSYIRAANAWPMLSADEERALAEKLHYHGDLEAA
  KTLILSHLRFVVHIARNYAGYGLPQADLIQEGNIGLMKAVRRFNPEVGVR
  LVSFAVHWIKAEIHEYVLRNWRIVKVATTKAQRKLFFNLRKTKQRLGWFN
  QDEVEMVARELGVTSKDVREMESRMAAQDMTFDLSSDDDSDSQPMAPVLY
  LQDKSSNFADGIEDDNWEEQAANRLTDAMQGLDERSQDIIRARWLDEDNK
  STLQELADRYGVSAERVRQLEKNAMKKLRAAIEA

Patterns in Protein Structures

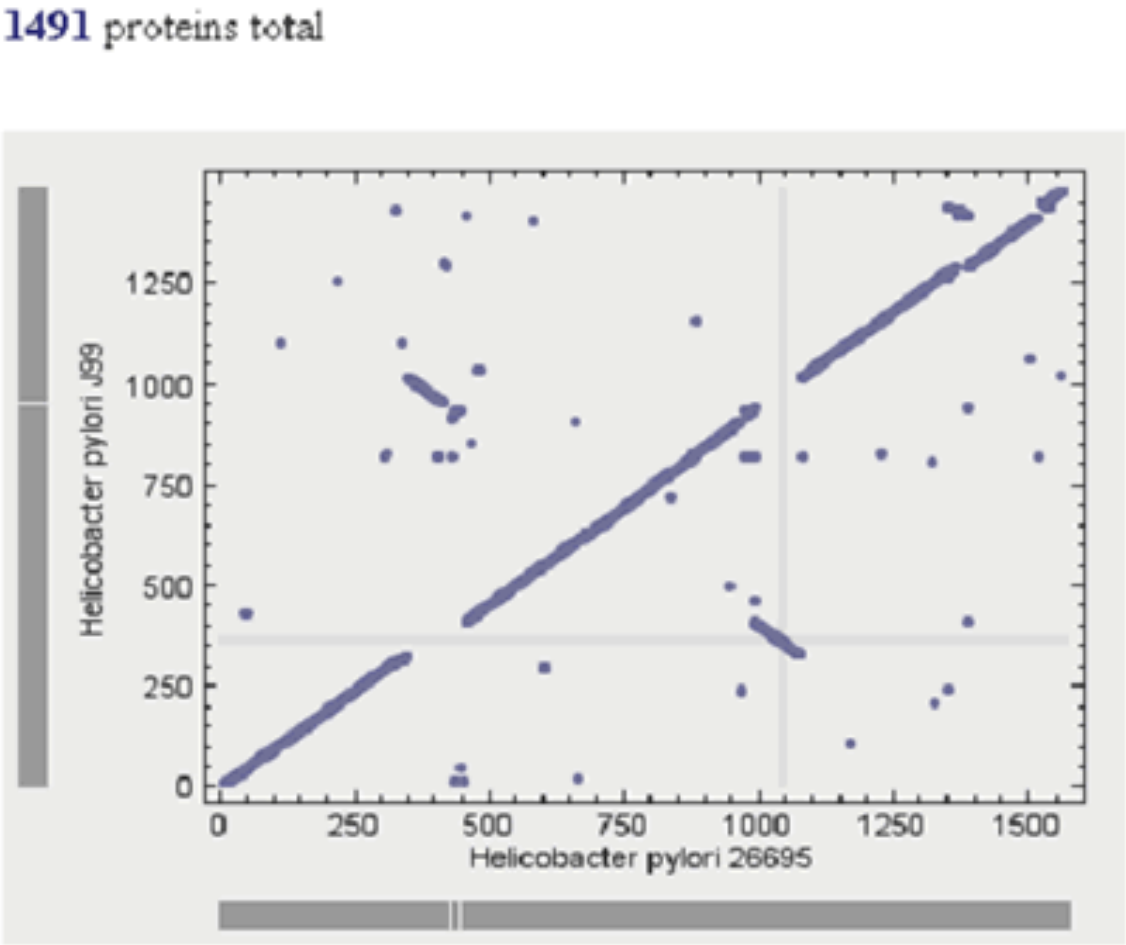




Microarray Analysis

Different patterns of gene expression of oral epithelial IHGK cells upon co-culture with A. actinomycetemcomitans or P. gingivalis.

Tools: GenePlot



Comparison of proteins from two strains of Helicobacter Pylori, 26695 and J99. Each point represents a pair of proteins from the two organisms showing a symmetrical best BLAST score; the coordinates of each point correspond to the position of the protein genes in the 2 genomes. Note the juxtaposition and inversion of two segments of the genome between the two strains.

SIDS

- 18000 Amish people in Pennsylvania
- Mostly intermarried due to religious doctrine
- rare recessive diseases occurred with high frequencies.
- SIDS: 3000 deaths/year (US); 21 deaths (Amish community)
- Many research centers failed to identify cause
- Collaboration between Affymetrix, TGEN & Clinic for special children solved the problem in 2 months
- Studied 10000 SNPs using microarray technology
- Their experiments showed that all the sick infants had two mutant copies of a specific gene, and their parents were carriers of the mutant gene.
- Conclusion: Disease caused by 2 abnormal copies of TSPYL gene
- Identified genes expressed in key organs (brainstem,testes)
- http://www.affymetrix.com/community/wayahead/modern_miracle.affx