CAP 5510: Introduction to Bioinformatics
CGS 5166: Bioinformatics Tools

Giri Narasimhan

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http://www.cs.fiu.edu/~giri/teach/BioinfS15.html
Office ECS 254 (and EC 2474); Phone: x-3748
Office Hours: By Appointment Only

Jan 12, 2015

Presentation Outline

General Information

- Course Webpage: `http://www.cs.fiu.edu/~giri/teach/BioinfS15.html`
    - Lecture Slides
    - Announcements
    - Reading Material
    - Homework
    - VISIT OFTEN!
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- Phone: x-3748; Email: giri@cis.fiu.edu
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- Extra 1 credit for CGS 5166 students

Core Syllabus

- Fundamentals of Biology, Statistics, & Bioinformatics
- Databases; Data Integration; BioPerl & BioPython;
- Sequence Alignment, Multiple Sequence Alignment
- Sequencing; Next Generation Sequencing & Applications
- Discovery, Learning, Prediction & Inference
- Machine Learning: NN, HMM, SOM, SVM, etc.
- Gene Regulation; Regulatory Elements; & 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
- Misc.: Omics; Alt. Splicing; Epigenetics; Visualization;

Evaluation

Category	Percentage
Semester Project	45%
Homework Assignments	20%
Exam	15%
Quizzes	10%
Summary Reports of Interest	5%
Class Participation	5%

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Some History . . .

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  - 1975 – Sanger Sequencing
  - 1977 – first bacteriophage sequenced
  - 1978 – Dayhoff's *Atlas of Protein Sequence and Structure*
  - 1980s – EMBL, GenBank, SWISSProt, and DDBJ
  - 1990 – HGP initiated
  - Oct, 2013 – first Bioinformatics Nobel Prize (Chemistry) to Karplus, Warshel, and Levitt for computer models for xomplec chemical processes.

Algorithms and Hardware

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Quantum Computing	Showed that some problems can be solved more efficiently on a quantum computer

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Presentation Outline

Broad Goals of Bioinformatics

DNA Sequence

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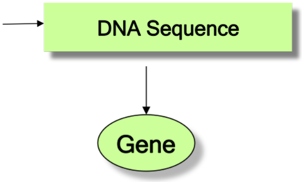
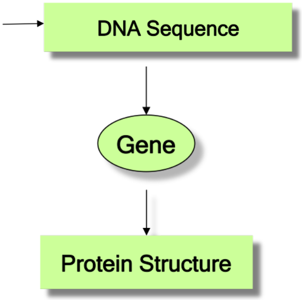


DNA Sequence

Gene

Broad Goals of Bioinformatics



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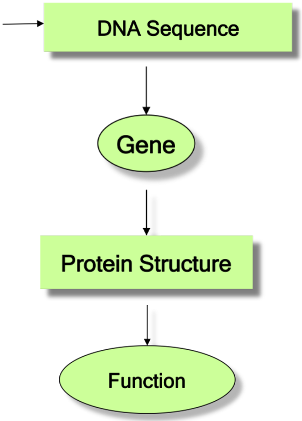

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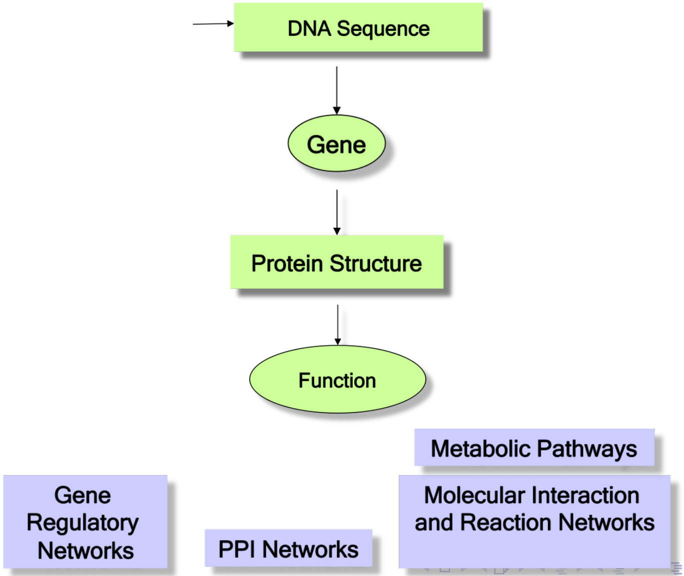
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Metabolic Pathways

Gene Regulatory Networks

PPI Networks

Molecular Interaction and Reaction Networks

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- **All life:** Tree of life, phylogeny, variations, comparative studies

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- UniProtKB/Swiss-Prot Release 54.7/2012_11/**2015_01** (Jan08/Nov'12/**Jan'15**): 333K/530K/**550K** entries; 120/191/**194** million amino acids.

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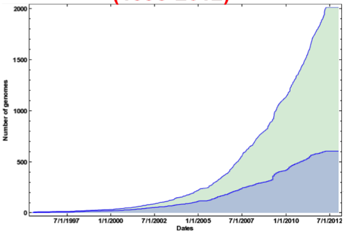
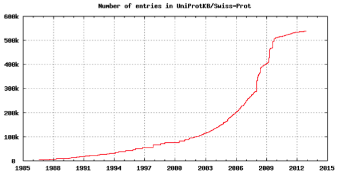
- Microbial and SwissProt growth:

Microbial Genome Growth (1995-2012)





SwissProt Growth (1985-2012)

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- Read more at: `http://www.the-scientist.com/?articles.list/tagNo/2416/tags/whole-genome-sequencing/`

And the Genome Sizes . . .

Organism	Size	Date	No. of Genes (est.)
HIV Type I	9.2 Kb	1997	9
M. genitalium	0.58 Mb	1998	525
H. influenzae	1.8 Mb	1995	1,740
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

Presentation Outline

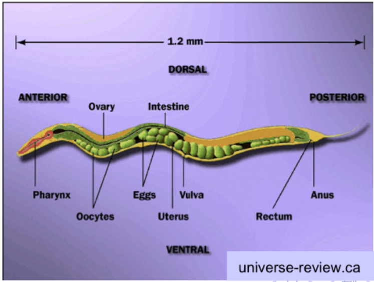
Short Homework

- What is the C-value of an organism? What is its relationship to the genome size? Read aboutthe *C-value enigma* in:
  - Gregory, TR (2004). “Macroevolution, hierarchy theory, and the C-value enigma”. *Paleobiology* **30**:179-202. or
  - Gregory TR (2001). ”Coincidence, coevolution, or causation? DNA content, cell size, and the C-value enigma”. *Biological Reviews* **76**(1): 65101
- Name at least one organims whose genome is considerably larger than that of humans. How big is that genome?
- What is the *Ferrari of the virus world* and why is it called so?
- What is the *1000 Genomes* project? Look at: `http://www.nature.com/nature/focus/1000genomes/`
- What is *antibiotic resistance* and why is it a public health crisis? What is the name of a new antibiotic reported in *Nature* in 2015 that kills pathogens without detectable

Presentation Outline

Caenorhabditis Elgeans: the model worm

www.ucl.ac.uk

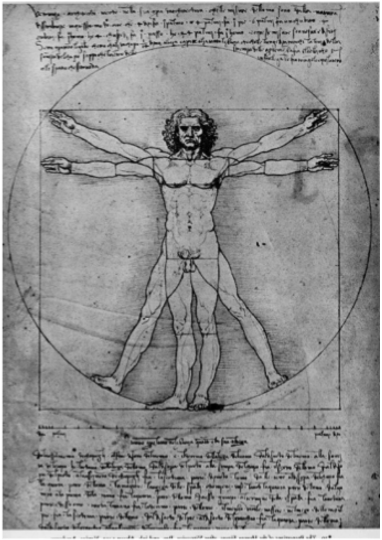


universe-review.ca

Caenorhabditis Elgeans: the model worm

- 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

H. sapiens



H. 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;
- 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.

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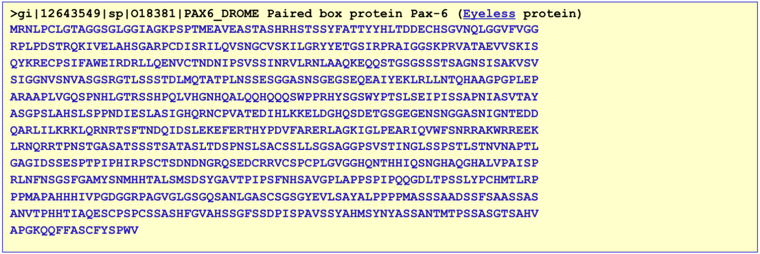
Sequence Alignment



```
>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
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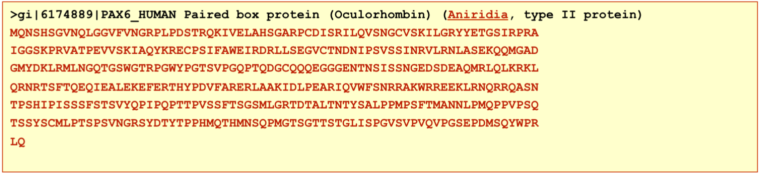
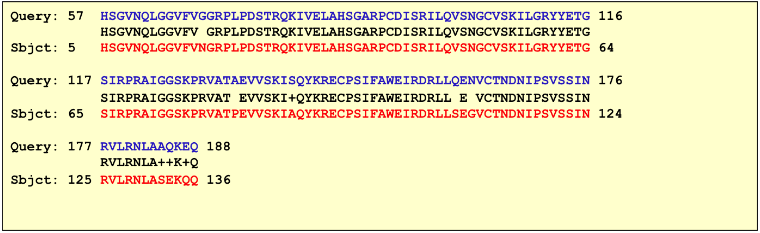


```
>gi|6174889|PAX6_HUMAN Paired box protein (Oculorhombin) (Aniridia, type II protein)
MQNSHSGVNQLGGVFVNGRPLPDSTRQKIVELAHSGARPCDISRILQVSNGCVSKILGRYYETGSIRPRA
IGGSKPRVATPEVVSKIAQYKRECPSIFAWEIRDRLLSEGVCTNDNIPSVSSINRVLRNLASEKQQMGAD
GMYDKLRMLNGQTGSWGTRPGWYPGTSVPGQPTQDGCQQQEGGGENTNSISSNGEDSDEAQMRLQLKRKL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

Drosophila Eyeless vs. Human Aniridia



```
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
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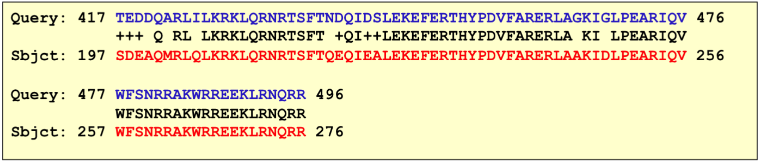

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Query: 417 TEDDQARLILKRKLQRNRTSFTNDQIDSLEKEFERTHYPDVFARERLAGKIGLPEARIQV 476
           +++ Q RL LKRKLQRNRTSFT +QI++LEKEFERTHYPDVFARERLA KI LPEARIQV
Sbjct: 197 SDEAQMRLQLKRKLQRNRTSFTQEQIEALEKEFERTHYPDVFARERLAAKIDLPEARIQV 256

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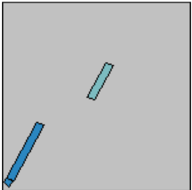


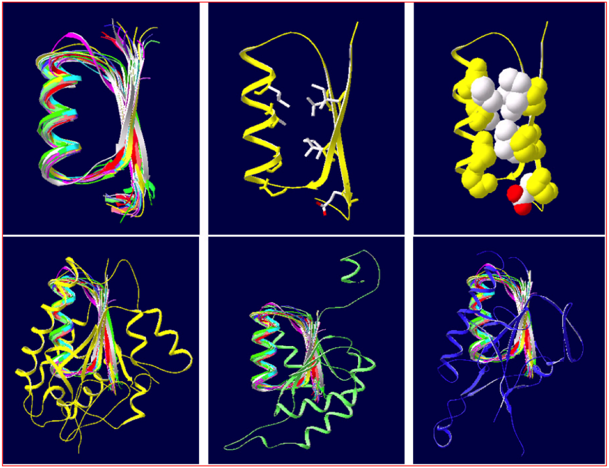
Motif Detection in Protein Sequences

☐ MTDKMQSLALAPVGNLDSYIRAANAWPMLSADEERALAEKLHYHGDLEAA
KTLILSHLRFVVHIARNYAGYGLPQADLIQEGNIGLMKAVRRFNPEVGVR
LVSFAVHWIKAEIHEYVLRNWRIVKVATTKAQRKLFFNLRKTKQRLGWFN
QDEVEMVARELGVTSKDVREMESRMAAQDMTFDLSSDDDSDSQPMAPVLY
LQDKSSNFADGIEDDNWEEQAANRLTDAMQGLDERSQDIIRARWLDEDNK
STLQELADRYGVSAERVRQLEKNAMKKLRAAIEA

☐ MTDKMQSLALAPVGNLDSYIRAANAWPMLSADEERALAEKLHYHGDLEAA
KTLILSHLRFVVHIARNYAGYGLPQADLIQEGNIGLMKAVRRFNPEVGVR
LVSFAVHWIKAEIHEYVLRNWRIVKVATTKAQRKLFFNLRKTKQRLGWFN
QDEVEMVARELGVTSKDVREMESRMAAQDMTFDLSSDDDSDSQPMAPVLY
LQDKSSNFADGIEDDNWEEQAANRLTDAMQGLDERSQDIIRARWLDEDNK
STLQELADRYGVSAERVRQLEKNAMKKLRAAIEA

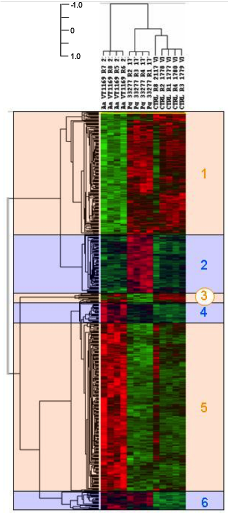
[G. Narasimhan, et al., “Mining Protein Sequences for Motifs,” *J. of Comput Biol*, **9**(5):707-720, 2002.]

Patterns in Protein Structures



[T. Milledge, et al., "Sequence Structure Patterns: Discovery and Applications," *Proc 6th Symposium on Comput Biol & Genome Informatics (CBG)*, 1282-1285, 2005.]

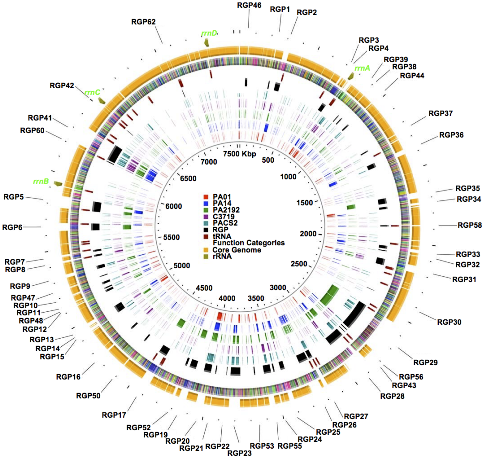
Microarray Analysis



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

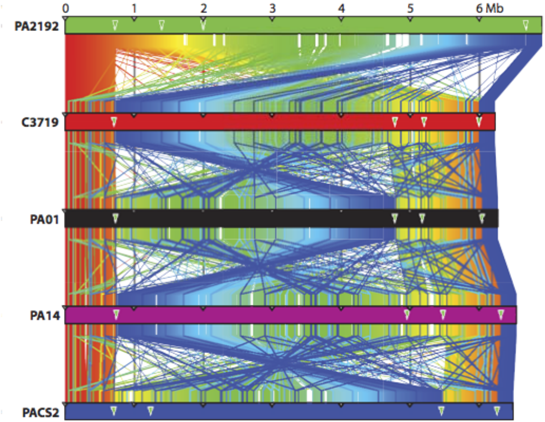
[M. Handfield, et al., "Distinct Expression Profiles Characterize Oral Epithelium-Microbiota Interactions," *Cellular Microbiol*, **7**(6):811-823, 2005.]

Tools: CGView for Comparative Genomics



[K. Mathee, et al., "Dynamics of Pseudomonas aeruginosa genome evolution," *Proc Natl Acad of Sciences (PNAS)*,

Tools: Murasaki for Comparative Genomics



[K. Mathee, et al., "Dynamics of Pseudomonas aeruginosa genome evolution," *Proc Natl Acad of Sciences (PNAS)*,

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- Conclusion: Disease caused by 2 abnormal copies of TSPYL gene & is expressed in key organs (brainstem,testes) `http://www.affymetrix.com/community/wayahead/modern_miracle.affx`