Introduction to Bioinformatics

CPSC 265

Thanks to Jonathan Pevsner, Ph.D.

Textbooks

Johnathan Pevsner, who I stole most of these slides from (thanks!) has written a textbook, *Bioinformatics and Functional Genomics* (Wiley, 2003). The chapters contain content, lab exercises, and quizzes that were developed in his course over the past six years.

All Pevsner's powerpoints are available at:
http://pevsnerlab.kennedykrieger.org

Several other bioinformatics texts are available:
- Baxevanis and Ouellette
- David Mount
- Durbin et al.

What is bioinformatics?

- Interface of biology and computers
- Analysis of proteins, genes and genomes using computer algorithms and computer databases
- Genomics is the analysis of genomes. The tools of bioinformatics are used to make sense of the billions of base pairs of DNA that are sequenced by genomics projects.

Top ten challenges for bioinformatics

[1] Precise models of where and when transcription will occur in a genome (initiation and termination)

[2] Precise, predictive models of alternative RNA splicing

[3] Precise models of signal transduction pathways; ability to predict cellular responses to external stimuli

[4] Determining protein:DNA, protein:RNA, protein:protein recognition codes

[5] Accurate *ab initio* protein structure prediction

Top ten challenges for bioinformatics

[6] Rational design of small molecule inhibitors of proteins

[7] Mechanistic understanding of protein evolution

[8] Mechanistic understanding of speciation

[9] Development of effective gene ontologies: systematic ways to describe gene and protein function

[10] Education: development of bioinformatics curricula

Source: Ewan Birney, Chris Burge, Jim Fickett

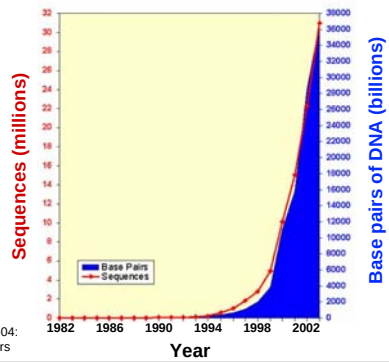

Fig. 2.1
Page 17

There are three major public DNA databases

EMBL ⟷ **GenBank** ⟷ **DDBJ**

Housed at EBI	**Housed at NCBI**	**Housed in Japan**
European Bioinformatics Institute	National Center for Biotechnology Information	

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>100,000 species are represented in GenBank

all species	**128,941**
viruses	**6,137**
bacteria	**31,262**
archaea	**2,100**
eukaryota	**87,147**

Table 2-1
Page 17

The most sequenced organisms in GenBank

Homo sapiens	11.2 billion bases
Mus musculus	7.5b
Rattus norvegicus	5.7b
Danio rerio	2.1b
Bos taurus	1.9b
Zea mays	1.4b
Oryza sativa (japonica)	1.2b
Xenopus tropicalis	0.9b
Canis familiaris	0.8b
Drosophila melanogaster	0.7b

Updated 8-29-05
GenBank release 149.0

Table 2-2
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National Center for Biotechnology Information (NCBI)

www.ncbi.nlm.nih.gov

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www.ncbi.nlm.nih.gov

Fig. 2.5
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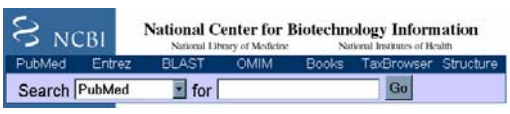

Fig. 2.5
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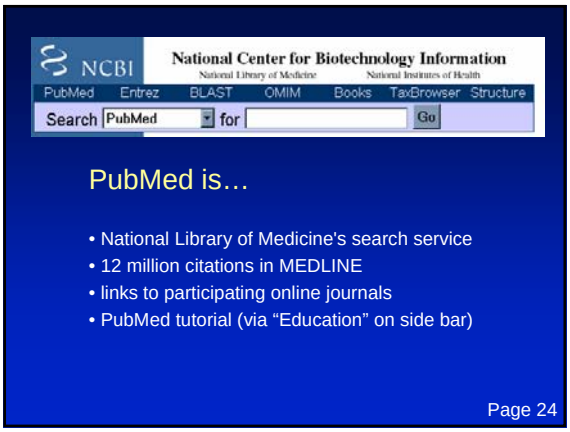
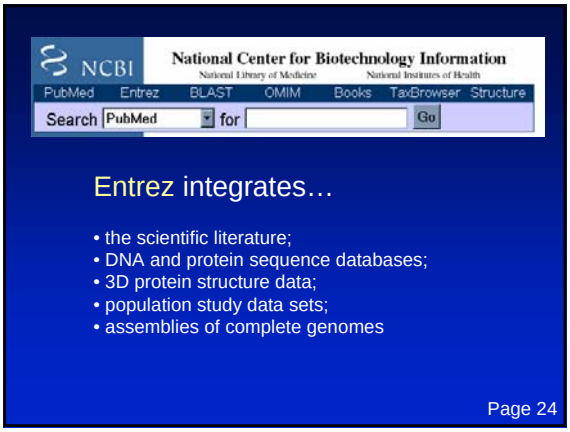
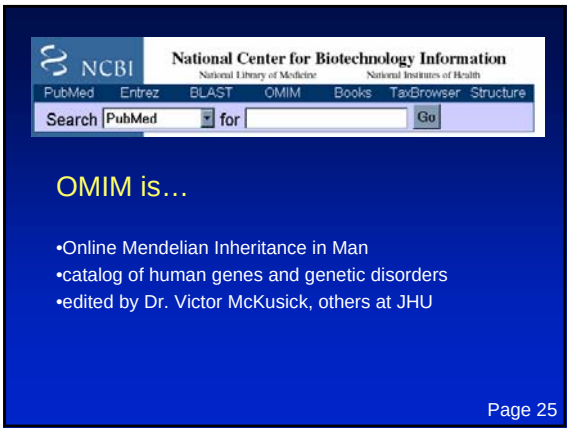

NCBI
National Center for Biotechnology Information
National Library of Medicine
National Institutes of Health
PubMed Entrez BLAST OMIM Books TaxBrowser Structure
Search PubMed for Go
PubMed is…
• National Library of Medicine's search service
• 12 million citations in MEDLINE
• links to participating online journals
• PubMed tutorial (via "Education" on side bar)
Page 24


NCBI
National Center for Biotechnology Information
National Library of Medicine
National Institutes of Health
PubMed Entrez BLAST OMIM Books TaxBrowser Structure
Search PubMed for Go
Entrez integrates…
• the scientific literature;
• DNA and protein sequence databases;
• 3D protein structure data;
• population study data sets;
• assemblies of complete genomes
Page 24


NCBI
National Center for Biotechnology Information
National Library of Medicine
National Institutes of Health
PubMed Entrez BLAST OMIM Books TaxBrowser Structure
Search PubMed for Go
BLAST is…
• Basic Local Alignment Search Tool
• NCBI's sequence similarity search tool
• supports analysis of DNA and protein databases
• 80,000 searches per day
Page 25



OMIM is…

- Online Mendelian Inheritance in Man
- catalog of human genes and genetic disorders
- edited by Dr. Victor McKusick, others at JHU

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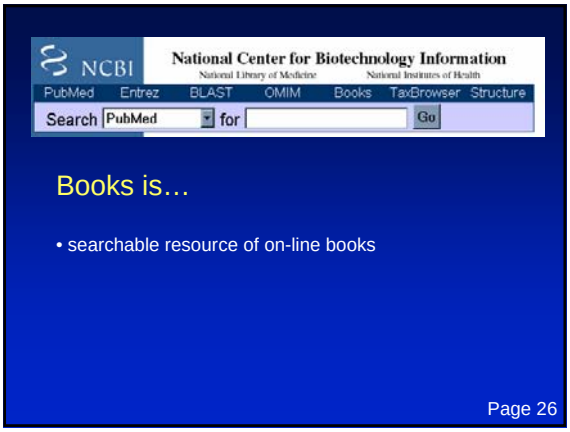

Books is…

- searchable resource of on-line books

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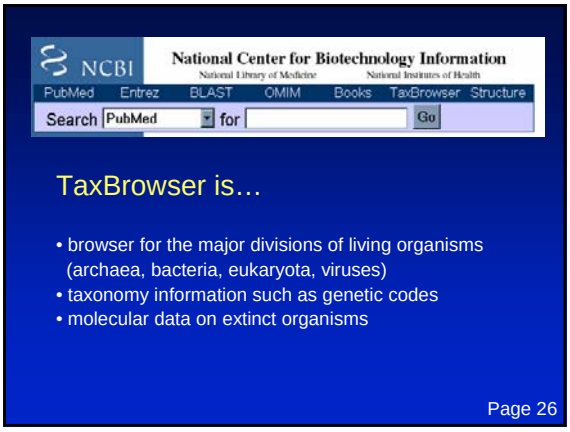

TaxBrowser is…

- browser for the major divisions of living organisms (archaea, bacteria, eukaryota, viruses)
- taxonomy information such as genetic codes
- molecular data on extinct organisms

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Structure site includes…

- Molecular Modelling Database (MMDB)
- biopolymer structures obtained from the Protein Data Bank (PDB)
- Cn3D (a 3D-structure viewer)
- vector alignment search tool (VAST)

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Accessing information on molecular sequences

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Accession numbers are labels for sequences

NCBI includes databases (such as GenBank) that contain information on DNA, RNA, or protein sequences.
You may want to acquire information beginning with a query such as the name of a protein of interest, or the raw nucleotides comprising a DNA sequence of interest.

DNA sequences and other molecular data are tagged with accession numbers that are used to identify a sequence or other record relevant to molecular data.

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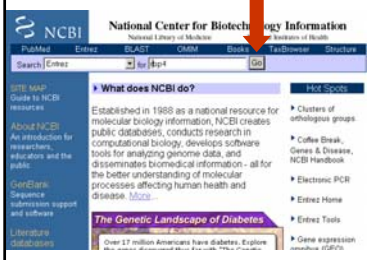
From the NCBI home page, type "lectin" and hit "Go"



revised
Fig. 2.7
Page 29

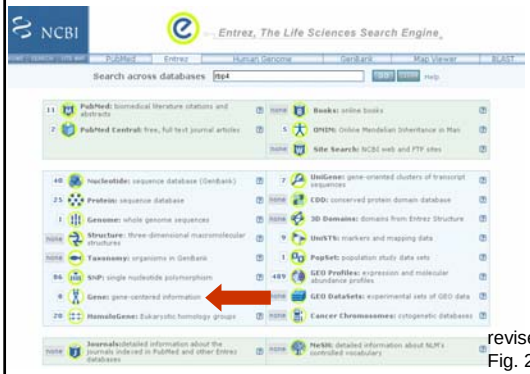


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Fig. 2.7
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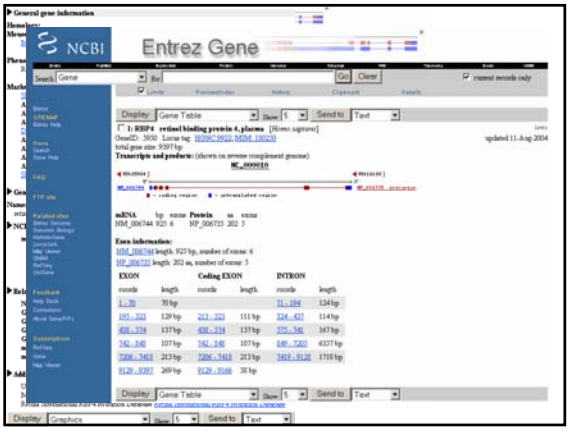

Fig. 2.9
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FASTA format

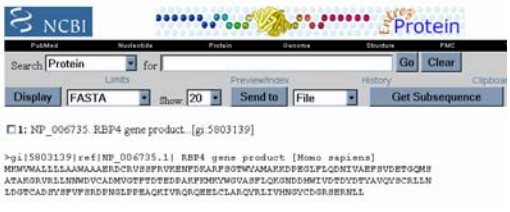

Fig. 2.10
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PubMed at NCBI to find literature information

PubMed is the NCBI gateway to MEDLINE.

MEDLINE contains bibliographic citations and author abstracts from over 4,600 journals published in the United States and in 70 foreign countries.

It has 12 million records dating back to 1966.

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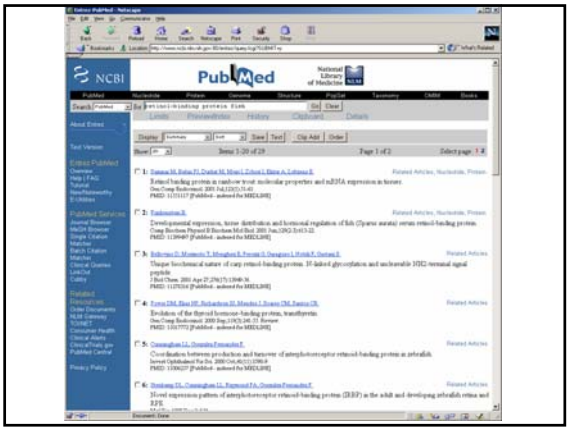

BLAST

BLAST searching is fundamental to understanding the relatedness of any favorite query sequence to other known proteins or DNA sequences.

Applications include
- identifying homologs (orthologs and paralogs)
- discovering new genes or proteins
- discovering variants of genes or proteins
- investigating expressed sequence tags (ESTs)
- exploring protein structure and function

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Four components to a BLAST search

(1) Choose the sequence (query)

(2) Select the BLAST program

(3) Choose the database to search

(4) Choose optional parameters

Then click “BLAST”

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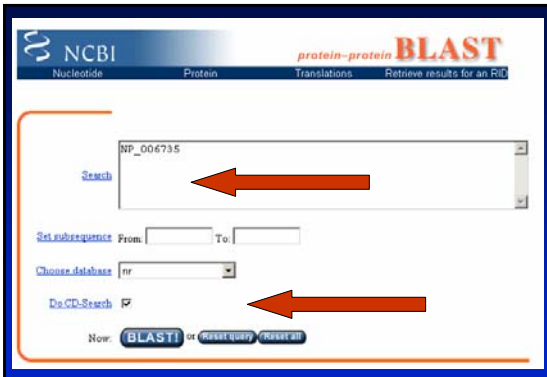

Fig. 4.1
page 89

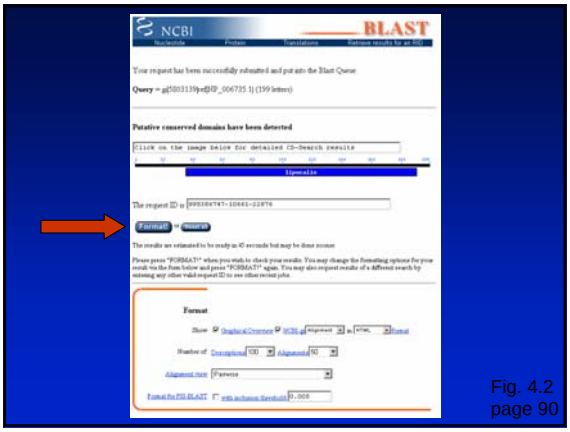

Fig. 4.2
page 90

Step 1: Choose your sequence

Sequence can be input in FASTA format or as accession number

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Example of the FASTA format for a BLAST query

Fig. 2.10
page 32

Step 2: Choose the BLAST program

Step 2: Choose the BLAST program

blastn (nucleotide BLAST)

blastp (protein BLAST)

tblastn (translated BLAST)

blastx (translated BLAST)

tblastx (translated BLAST)

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Choose the BLAST program

Program	Input		Database
blastn	DNA	1	DNA
blastp	protein	1	protein
blastx	DNA	6	protein
tblastn	protein	6	DNA
tblastx	DNA	36	DNA

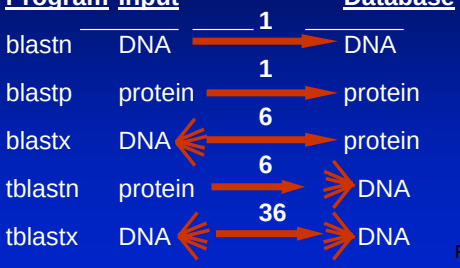

Fig. 4.3
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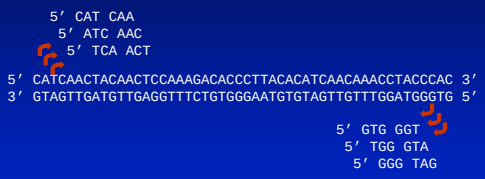
DNA potentially encodes six proteins



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Step 3: choose the database

nr = non-redundant (most general database)
dbest = database of expressed sequence tags
dbsts = database of sequence tag sites
gss = genomic survey sequences
htgs = high throughput genomic sequence

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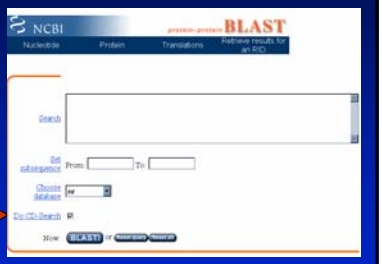
Step 4a: Select optional search parameters



CD search

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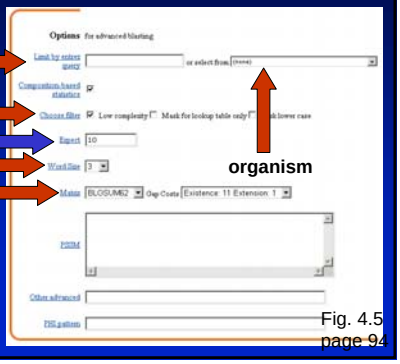
Step 4a: Select optional search parameters



Entrez!

Filter

Expect

Word size

Scoring matrix

organism

Fig. 4.5
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BLAST: optional parameters

You can...
- choose the organism to search
- turn filtering on/off
- change the substitution matrix
- change the expect (e) value
- change the word size
- change the output format

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Fig. 4.6
page 95

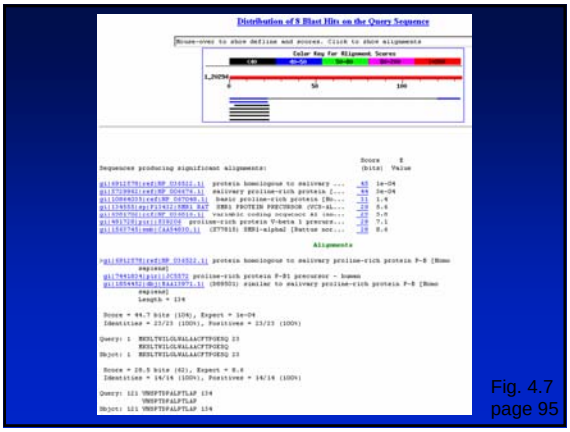

Fig. 4.7
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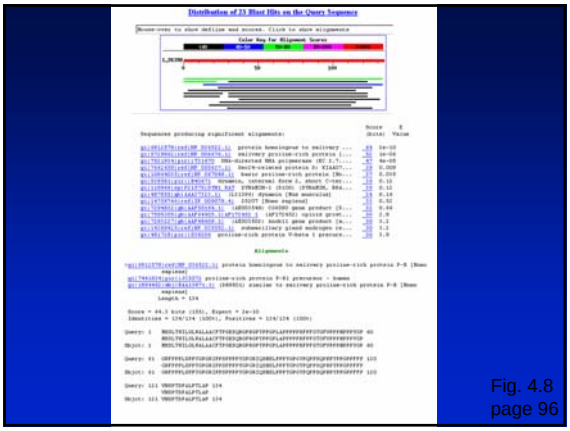

Fig. 4.8
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Step 4b: optional formatting parameters

Alignment view

Descriptions

Alignments

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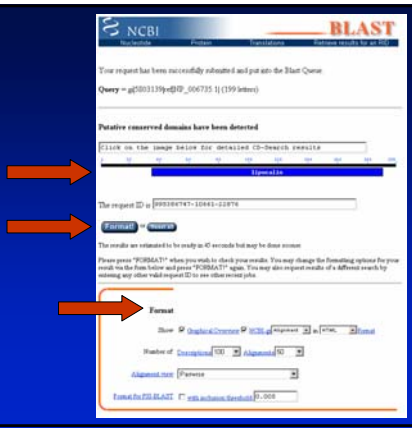

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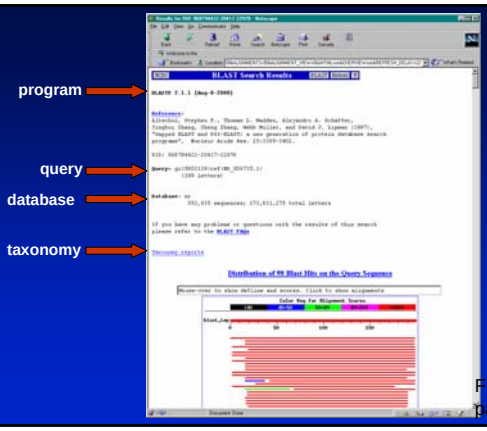

Fig. 4.9
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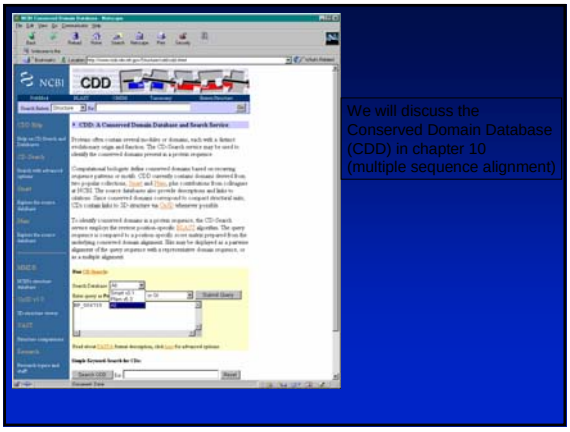

We will discuss the Conserved Domain Database (CDD) in chapter 10 (multiple sequence alignment)

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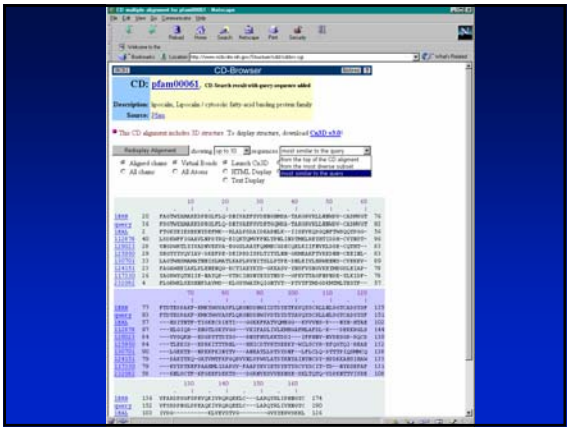
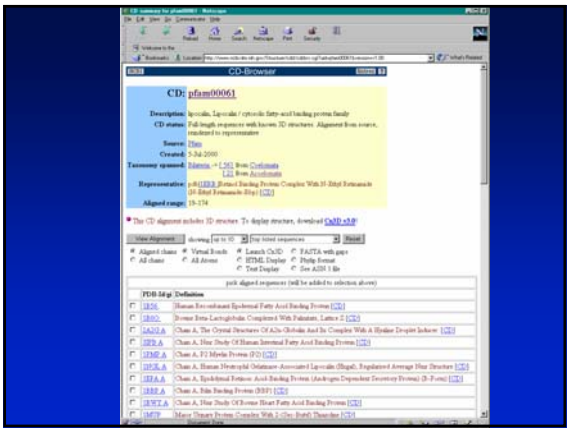




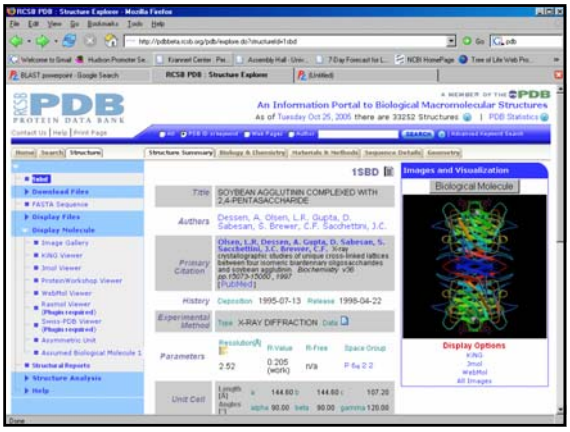
Protein 3D structure

- NCBI – Structure

Unlike mostly everything else, NCBI is not the best

- http://pdbbeta.rcsb.org/pdb/Welcome.do

(latest version of SDSC PDB site)



So now you can

- Find any sequence in the database
- Find relevant publications
- Match DNA to protein sequence
- Find database matches to DNA or protein
- Find conserved domains in protein
- Find the 3D structure of a protein

Without doing any experiments!