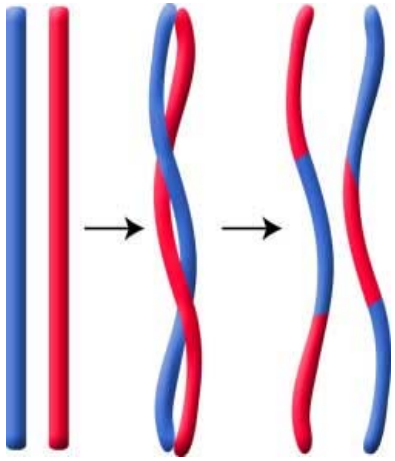
http://pastime.cgu.edu.tw/petang/index.htm



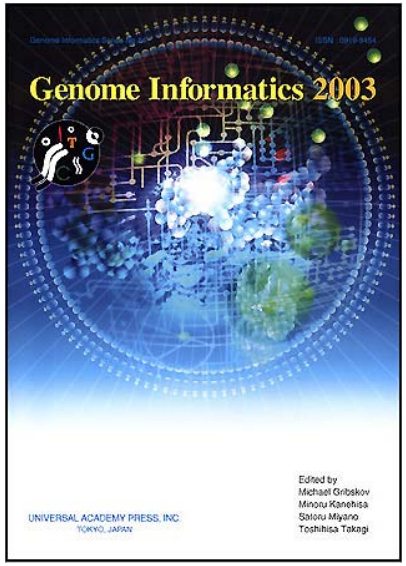
Bioinformatics

Introduction to Systems Biology & Bioinformtics

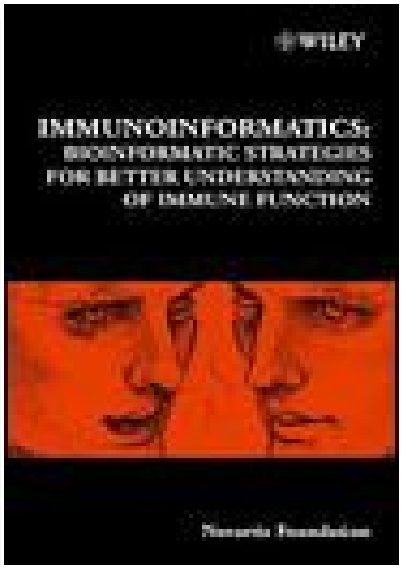
AGTCCGCGAATACAGGCTCGGT AGTCCGCGAATACAGGCTCGGT

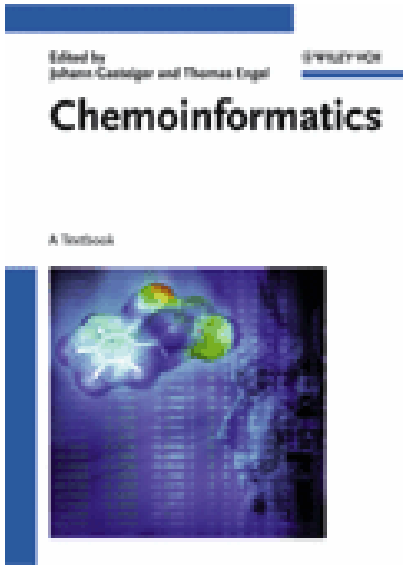
Petrus Tang, Ph.D. (鄧致剛)
Graduate Institute of Basic Medical Sciences
and
Bioinformatics Center, Chang Gung University.
petang@mail.cgu.edu.tw
EXT: 5136

Bio informatics







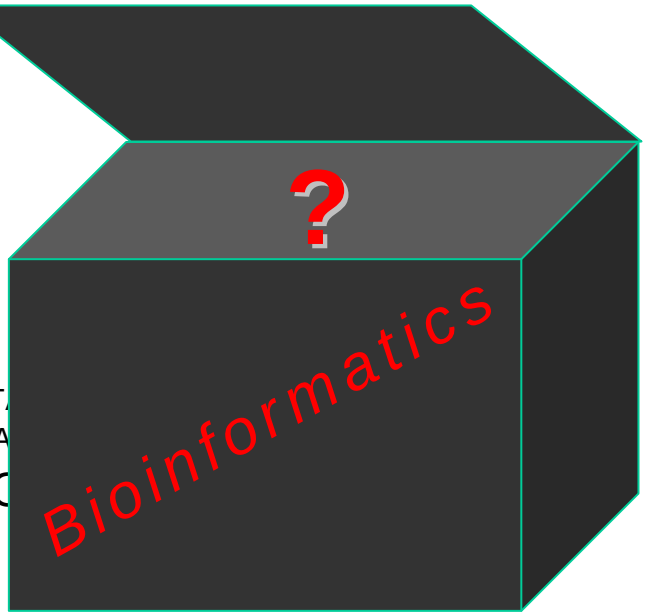


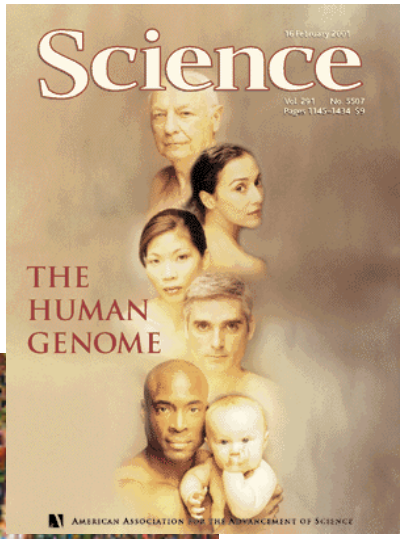
-Omics Mania *biome, cellomics, chronomics, clinomics, complexome, crystallomics, cytomics, degradomics, diagnomics, enzymome, epigenome, expressome, fluxome, foldome, secretome, functome, functomics, genomics, glycomics, immunome, transcriptomics, integromics, interactome, kinome, ligandomics, lipoproteomics, localizome, phenomics, metabolome, pharmacometabonomics, methylome, microbiome, morphome, neurogenomics, nucleome, secretome, oncogenomics, operome, transcriptomics, ORFeome, parasitome, pathome, peptidome, pharmacogenome, pharmacomethylomics, phenomics, phylome, physiogenomics, postgenomics, predictome, promoterome, proteomics, pseudogenome, secretome, regulome, resistome, ribonome, ribonomics, riboproteomics, saccharomics, secretome, somatonome, systeome, toxicomics, transcriptome, translatome, secretome, unknome, vaccinome, variomics...*

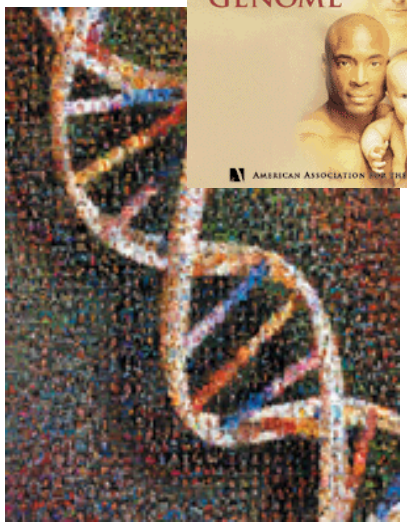
WHAT IS BIOINFORMATICS?

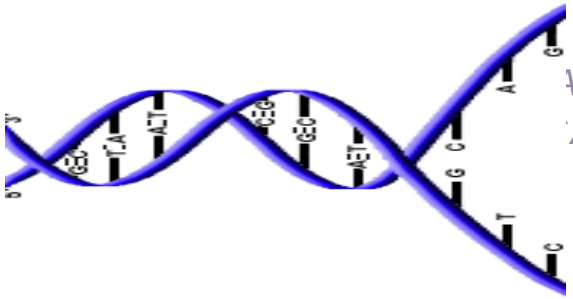


CTAGCTAGCTAGCTA
CTAGCTAGCTAGCTATCGA
CATGCACTAGCTAG





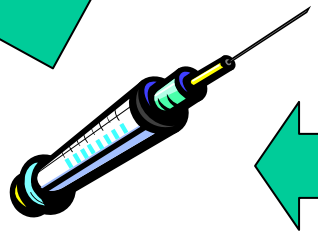


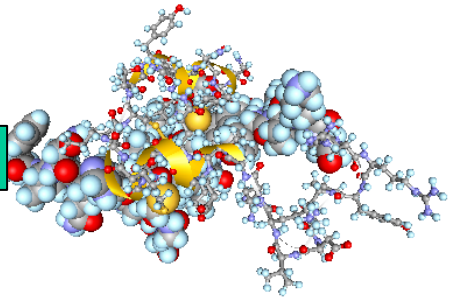


AAATGGCCAATTGATGACCAGAGATTTAGGCCAATTAA
AATGTGAAATGGCCAATTGATGACCAGAGA











Experiment Driven

Hypothesis

↓

Experiments

↓

Results



Information Driven

Experiments

↓

Hypothesis

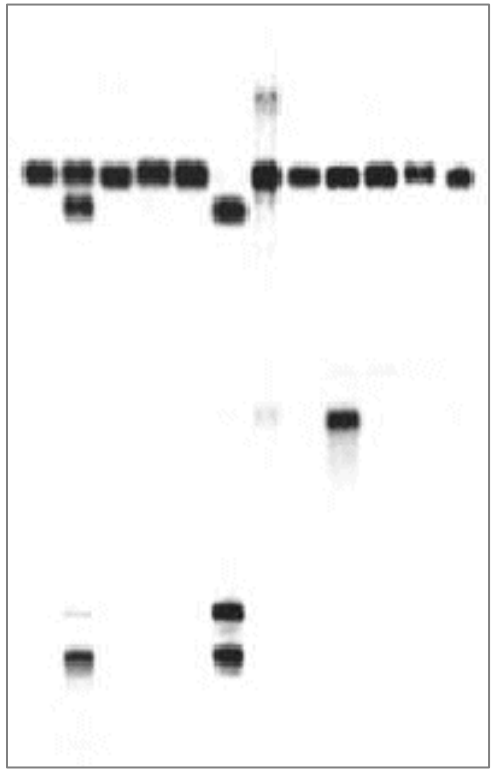
What is Bioinformatics?

- Development of methods & algorithms to organize, integrate, analyze and interpret biological and biomedical data
- Study of the inherent structure & flow of biological information
- Goals of bioinformatics:
  - Identify patterns
  - Classify
  - Make predictions
  - Create models
  - Better utilize existing knowledge

結合生物學、計算機科學與資訊學的技術, 應用於生物化學資料的處理，
將繁瑣無意的資料轉化成有意義、有價值的訊息。

The “old” biology







The most challenging task for a scientist is to get good data

The “new” biology



The most challenging task for a scientist is to make sense of lots of data

Old vs New – What's the difference? (1) Economics

- Miniaturize – less cost
- Multiplex – more data
- Parallelize – save time
- Automate – minimize human intervention
- Thus, you must be able to deal with large amounts of data and trust the process that generated it

What's the difference? (2) Scale

- From gene sequencing (~ 1 KB) to genome sequencing (many MB, even GB)
- From picking several genes for expression studies to analyzing the expression patterns of all genes
- From a catalog of key genes in a few key species to a catalog of all genes in many species
- Analyzing your data in isolation makes less sense when you can make much more powerful statements by including data from others

What's the difference? (3) Logic

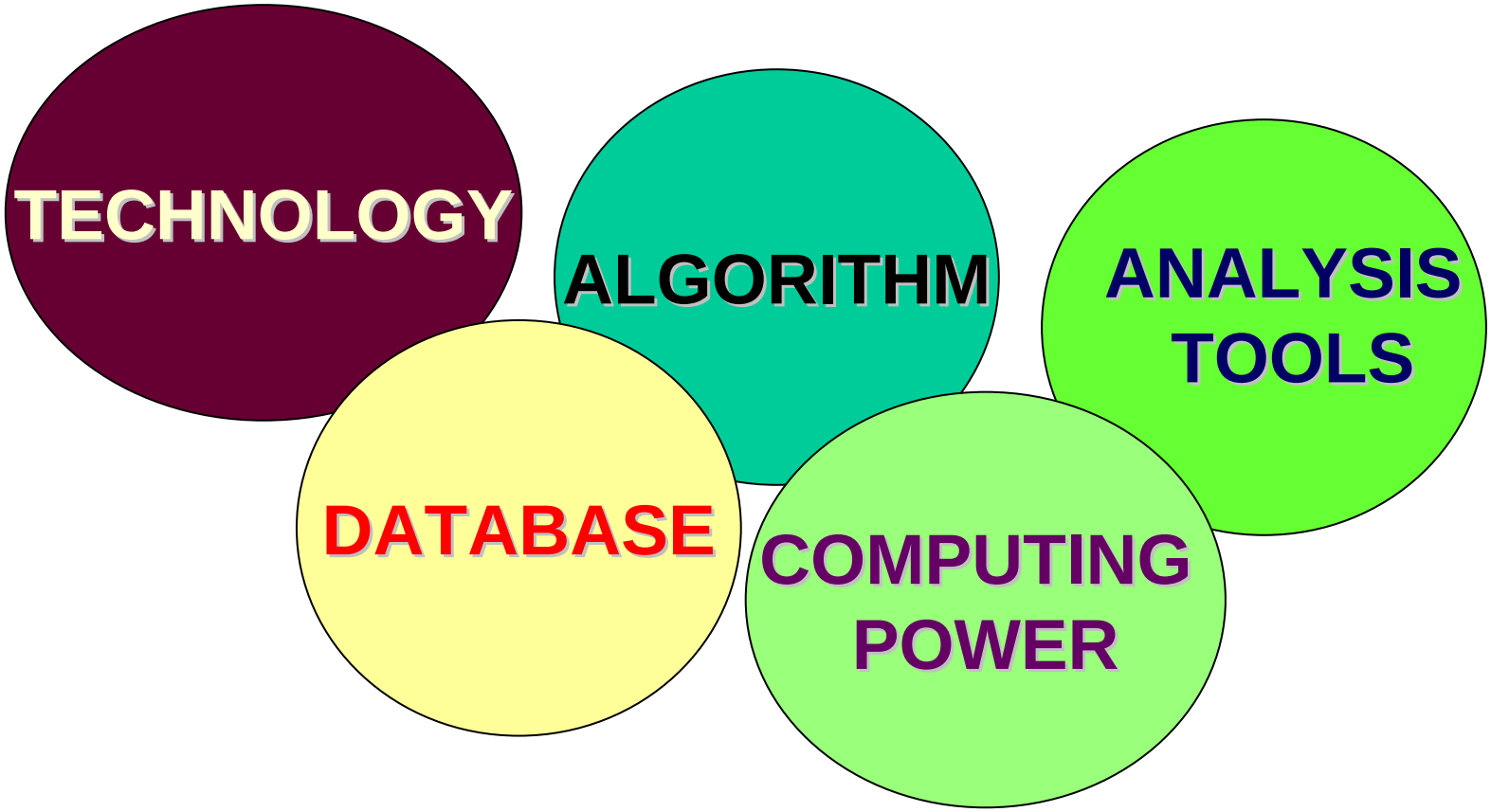
- Hypothesis-driven research to data-driven research
- Expertise-driven approach versus information-driven approach
- Reductionist versus integrationist
- How to answer the question becomes how to question an answer
- Algorithmic approaches for filtering, normalizing, analyzing and interpreting become increasingly important

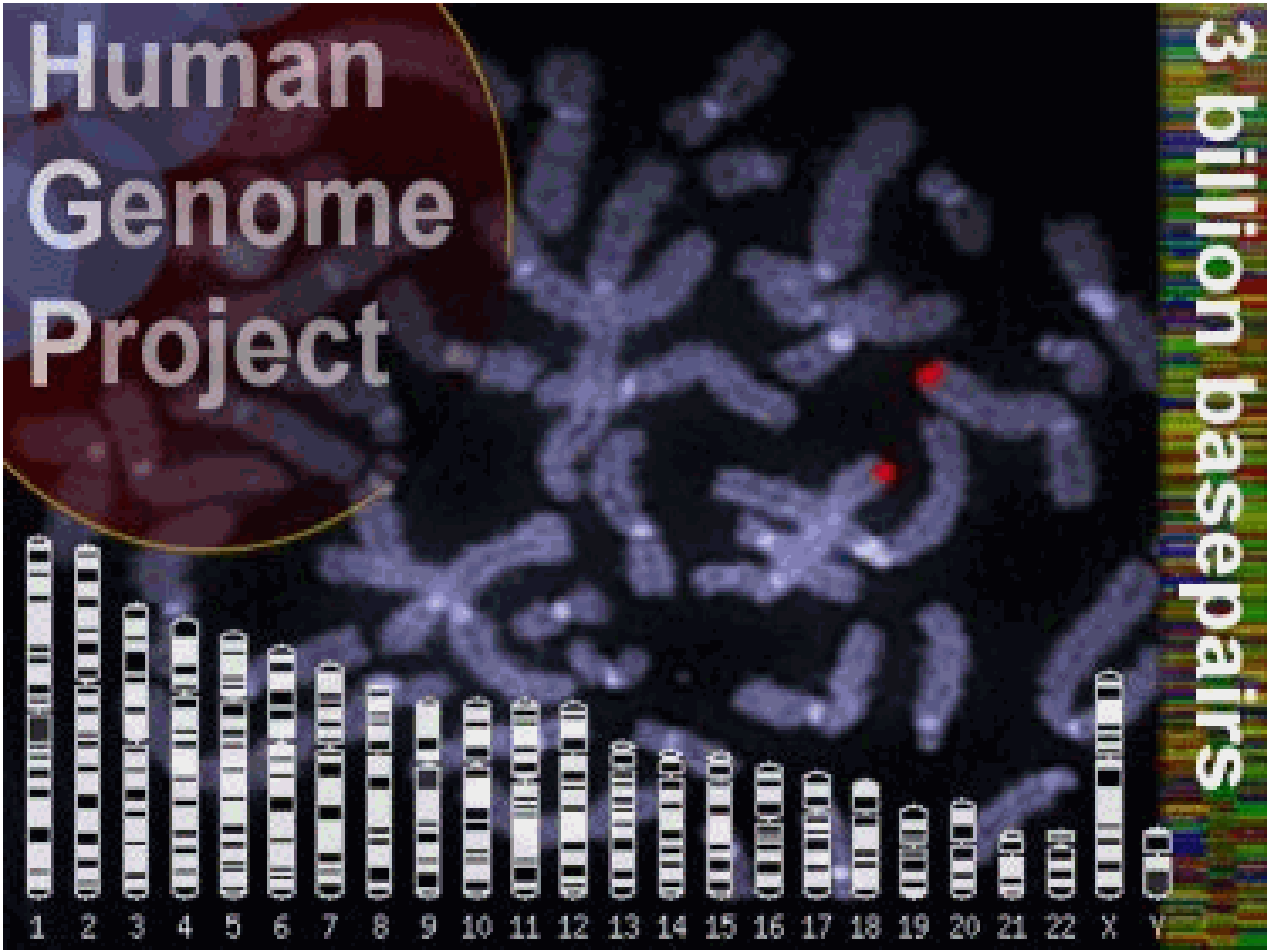
Data-driven Science Done Wrong

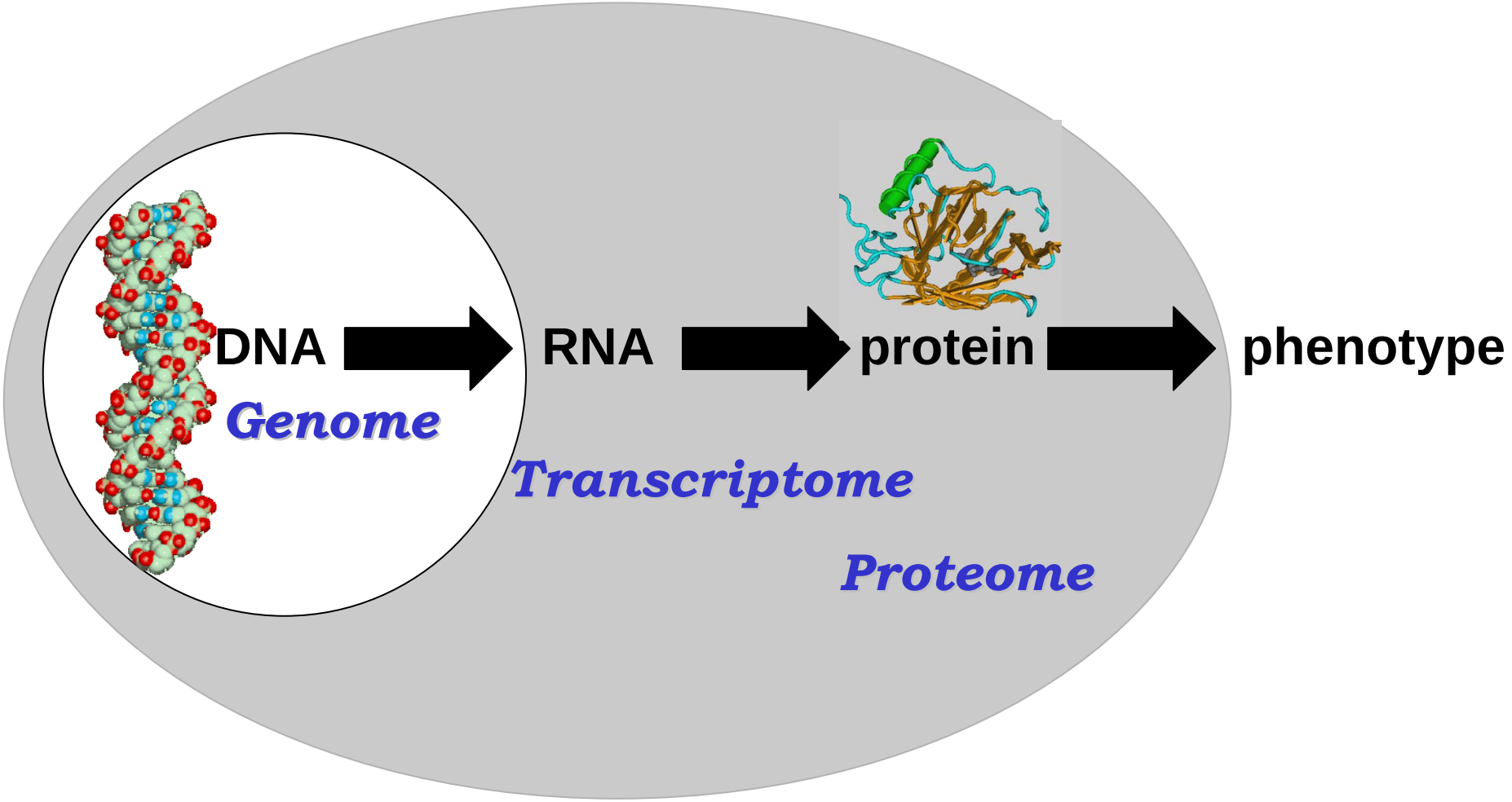
- Must have some hypothesis – data is not the end goal of science
- Finding patterns in the data is where analysis starts, not ends
- Must understand the limits of high-throughput technology (e.g. microarrays measure transcription only, one genome does not tell you about species variation, etc.)
- Must understand or explore the limits of your algorithm



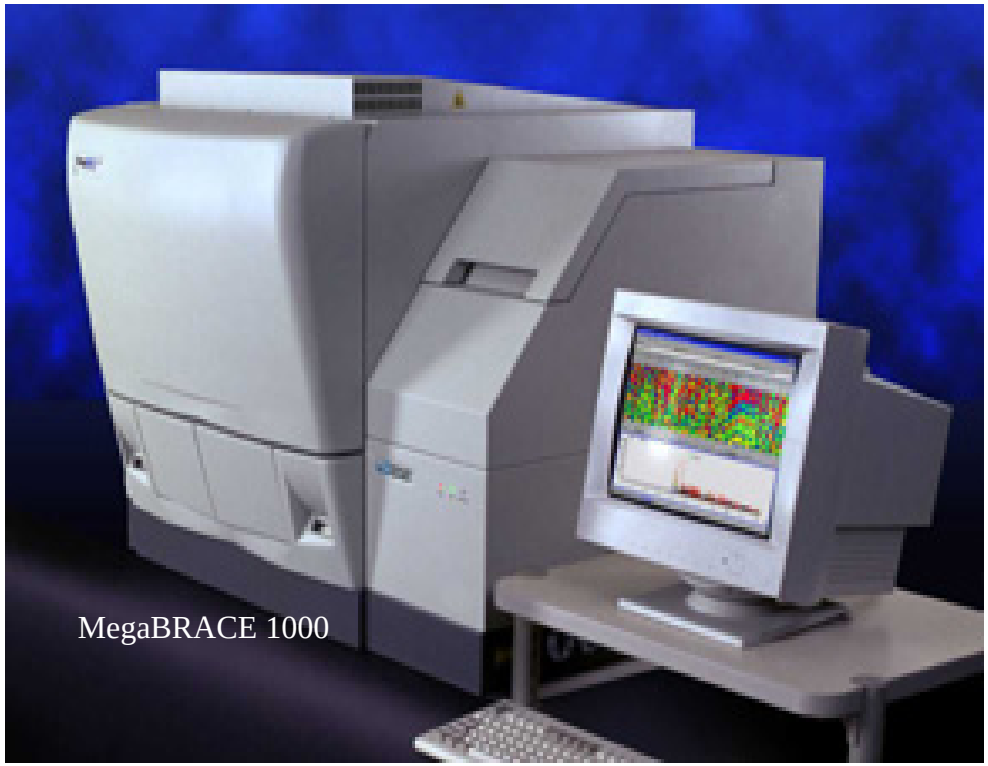
THE COMPONENTS OF BIOINFORMATICS




Human
Genome
Project
3 billion base pairs
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 X Y


DNA
RNA
protein
phenotype
Genome
Transcriptome
Proteome

DNA Sequencing

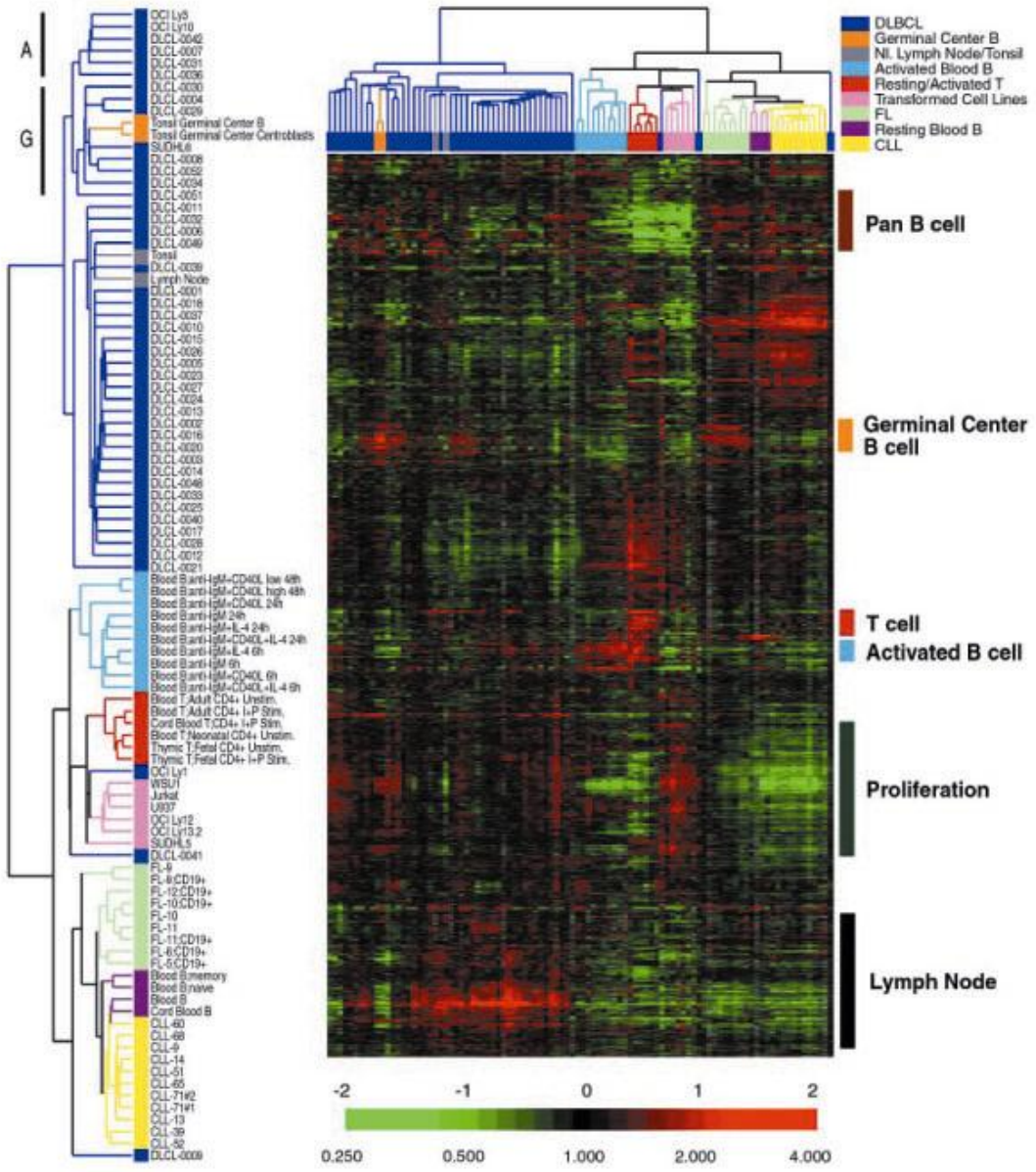




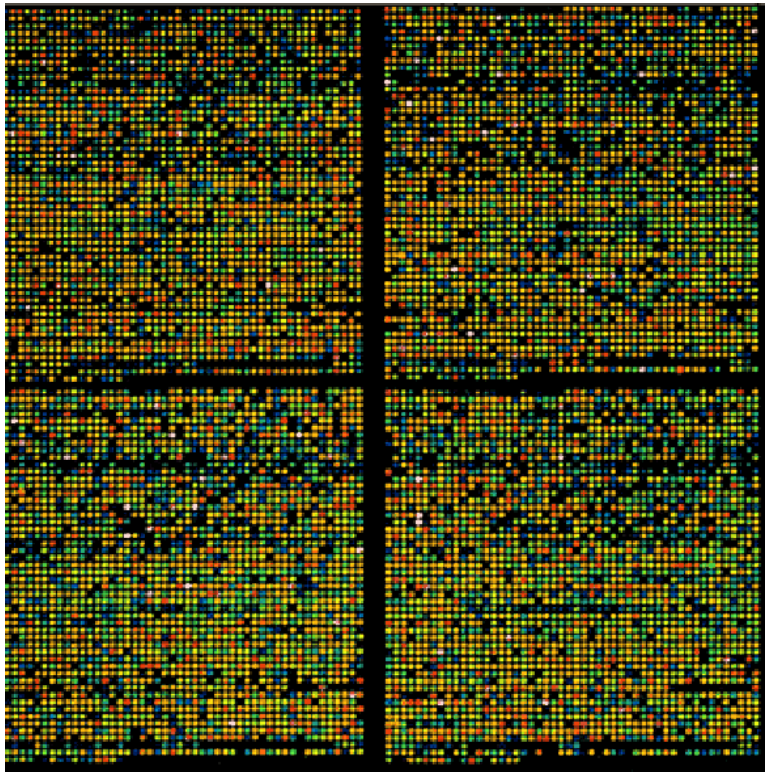
96 DNA sequencing in 2 hrs, approximately 600-800 readable bps per run.

1,000,000 bps in 24 hrs.

Microarray

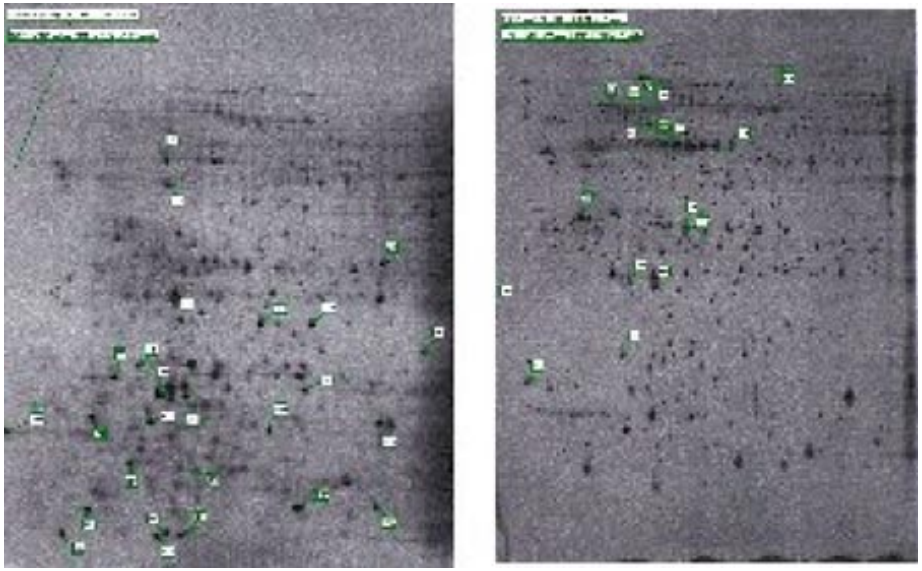


10,000 Clones per slide



http://llmpp.nih.gov/lymphoma/images/figure1.html (1 of 2) [2000/11/14 AM 08:54:21]

Proteomics

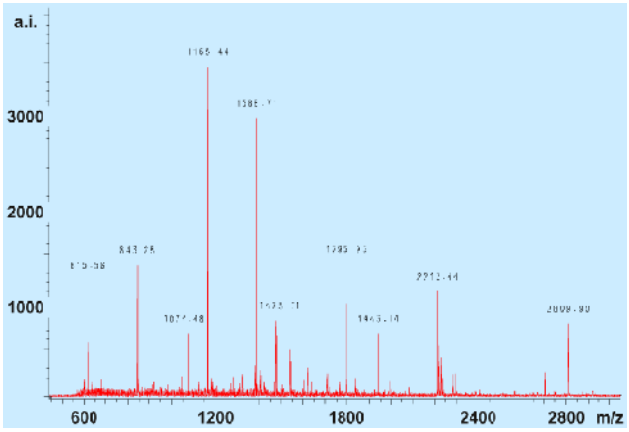


2 Dimensional Electrophoresis gels, differences that are characteristics of the individual starting states recognized by comparison of two protein pattern

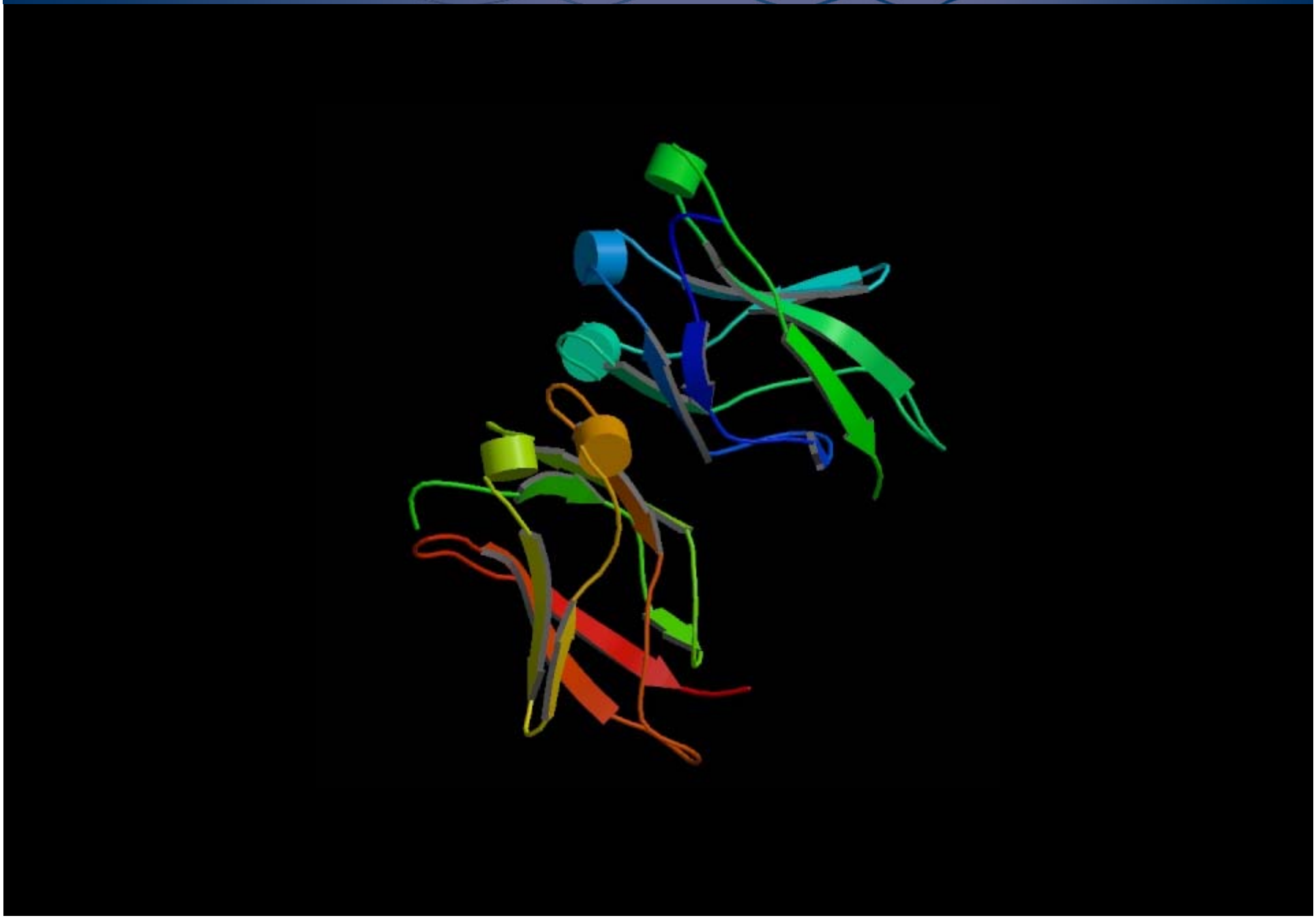
6,000 protein spots per gel

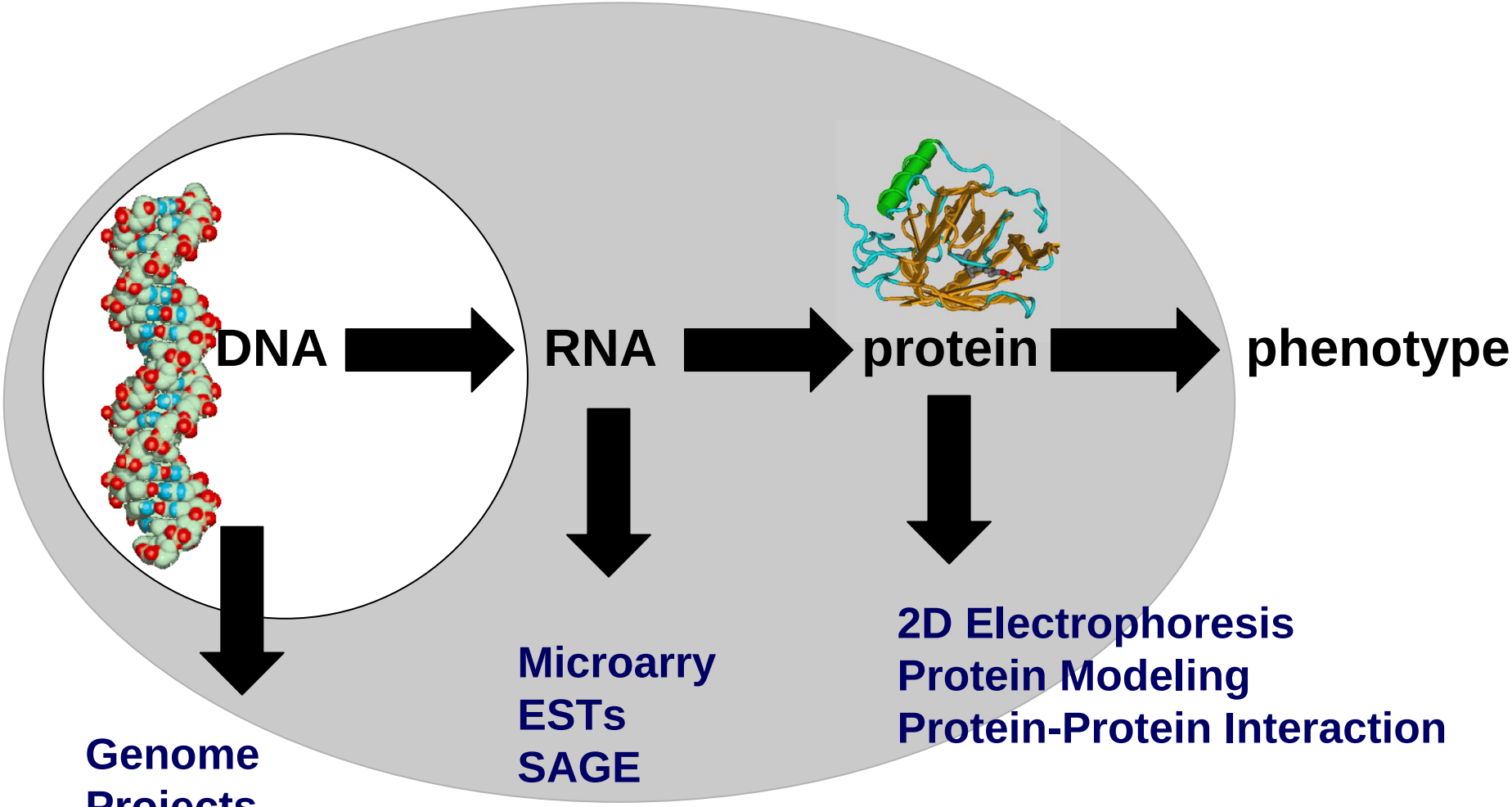


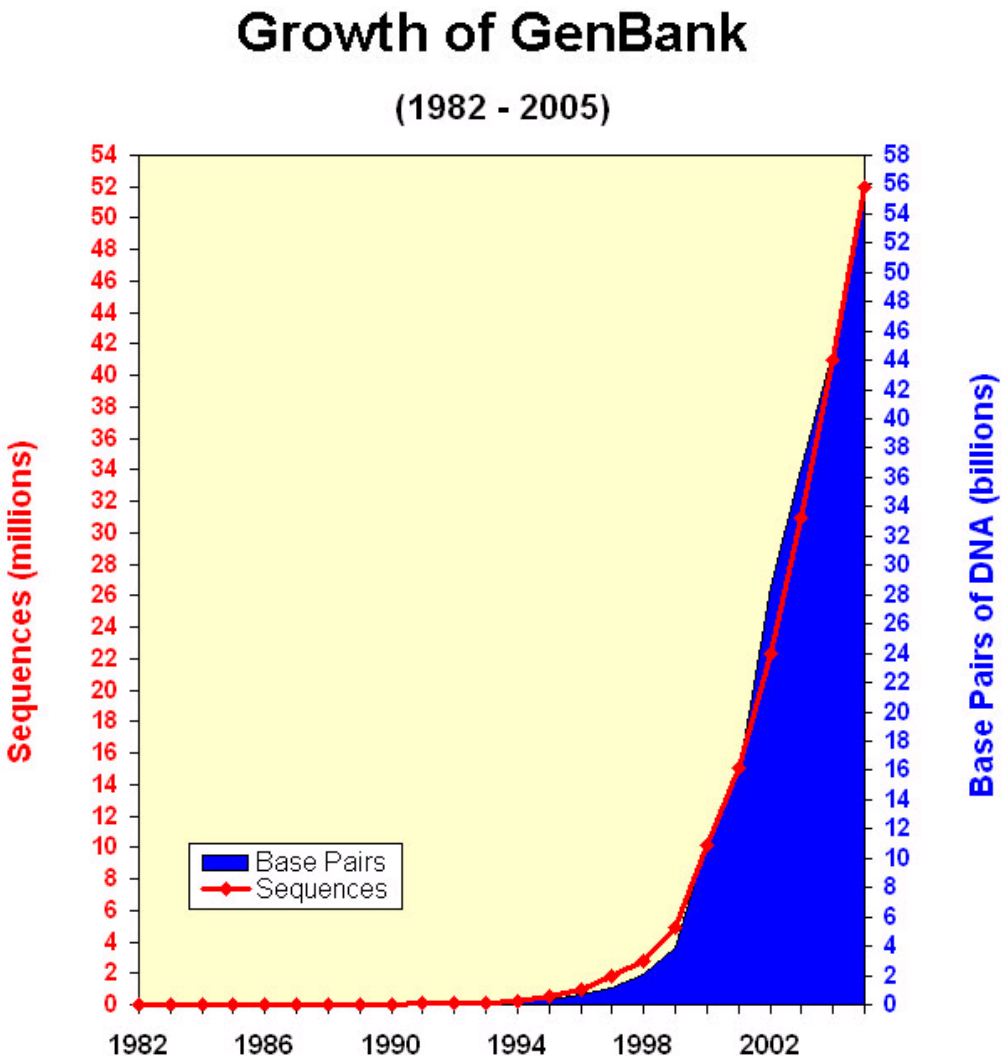
MALDI-MS peptide mass fingerprint, for identification of proteins separated by 2D electrophoresis



3D Modeling




DNA
RNA
protein
phenotype
Genome
Projects
Microarry
ESTs
SAGE
2D Electrophoresis
Protein Modeling
Protein-Protein Interaction



Genetic Sequence Data Bank Aug 15 2006, Release 155.0

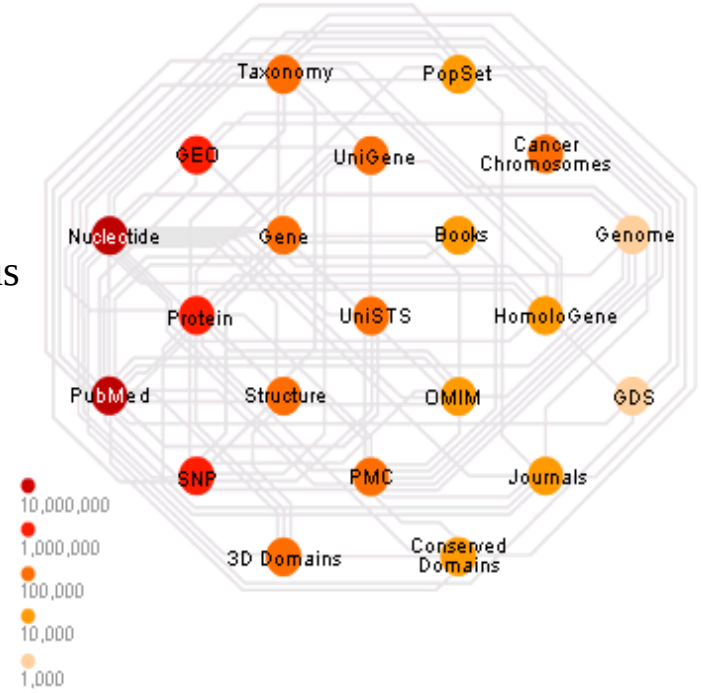
65,369,091,950 bases, from
61,132,599 reported sequences

Homo sapiens
12,385,903,706 bases from
10,649,134 sequences

Expressed sequence tags
7,893,983

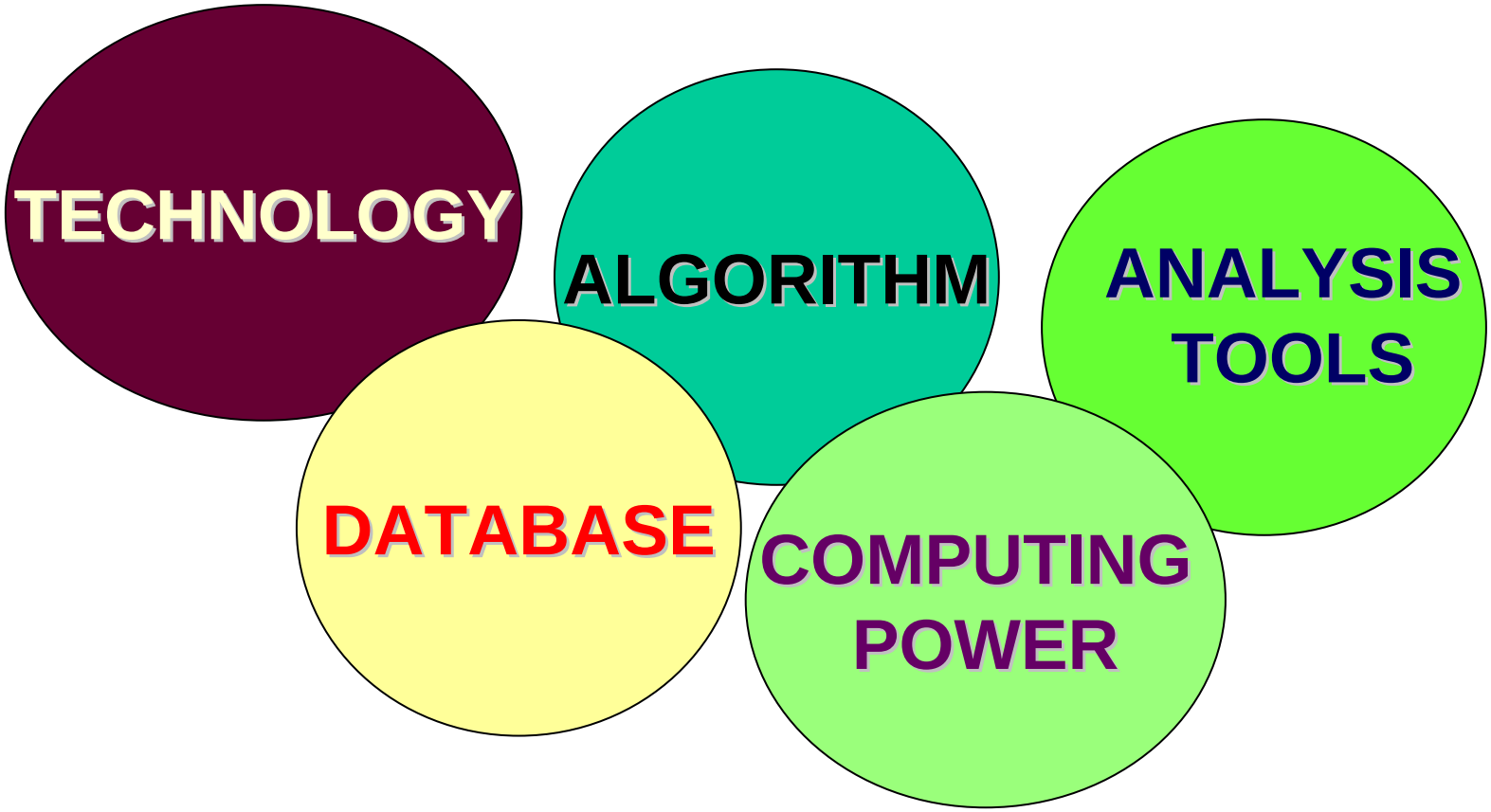
Recent years have seen an explosive growth in biological data. Large sequencing projects are producing increasing quantities of nucleotide sequences. The contents of nucleotide databases are doubling in size approximately every 14 months. The latest release of GenBank (V.139) exceeded two billion base pairs. Not only the size of sequence data is rapidly increasing, but also the number of characterized genes from many organisms and protein structures doubles about every two years. To cope with this great quantity of data, a new scientific discipline has emerged: ***bioinformatics, biocomputing or computational biology***

Entries	Bases	Species
10649134	12385903706	Homo sapiens
6753652	8049817803	Mus musculus
1267882	5747965742	Rattus norvegicus
1663937	3566605068	Bos taurus
1287702	2540551749	Danio rerio
2499723	1998269811	Zea mays
1149146	1500985768	Oryza sativa
226213	1251961979	Strongylocentrotus purpuratus
1236899	1075752229	Sus scrofa
1175934	961525020	Xenopus tropicalis
1426915	893771790	Canis familiaris
655519	845341580	Drosophila melanogaster
800633	770627209	Gallus gallus
1198209	758043364	Arabidopsis thaliana
209185	691252171	Pan troglodytes
868038	507883206	Triticum aestivum
397437	468939096	Medicago truncatula
784170	465881813	Sorghum bicolor
69335	463195893	Macaca mulatta
696319	421330392	Ciona intestinalis





THE COMPONENTS OF BIOINFORMATICS



The International Nucleotide Sequence Database Collaboration



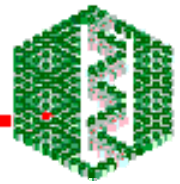
GenBank: *http://www.ncbi.nlm.nih.gov/*
National Center for Biotechnology Information (NCBI)



DDBJ: *http://www.ddbj.nig.ac.jp/*
National Institute of Genetics (NIG)

EMBL: *http://www.ebi.ac.uk*
European Bioinformatics Institute (EBI)

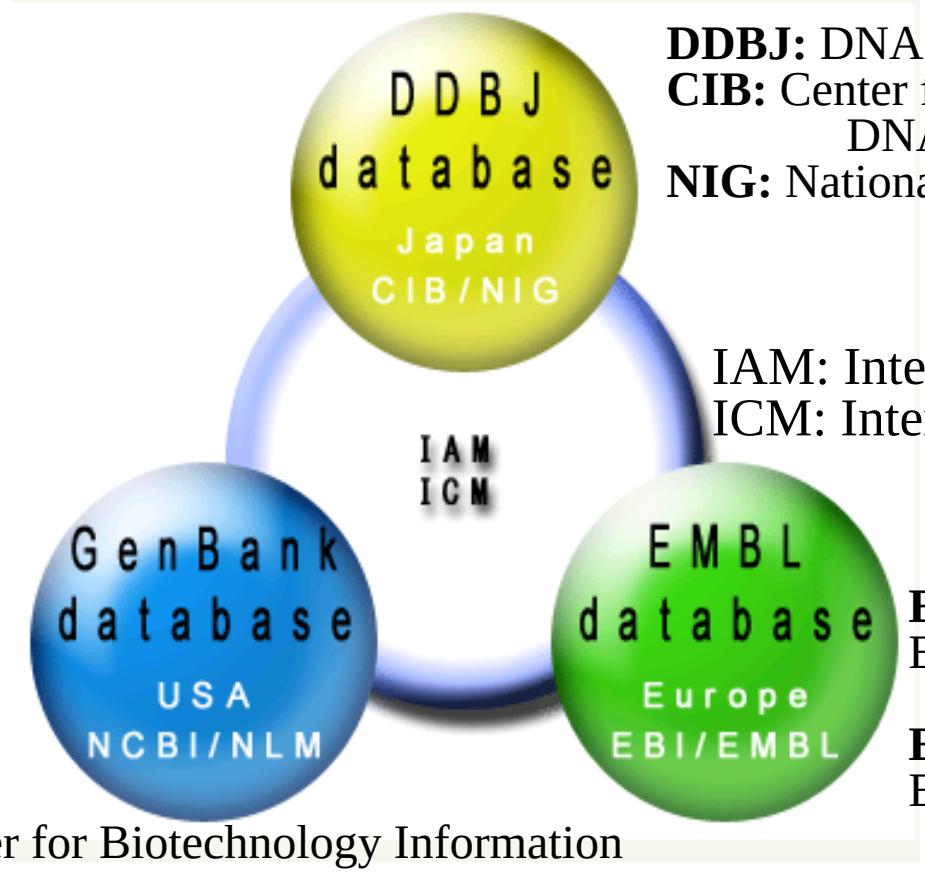






ExPASy: *http://tw.expasy.org*
Expert Protein Analysis System

GenBank/EMBL/DDBJ International Nucleotide Sequence Database



DDBJ: DNA Data Bank of Japan
CIB: Center for Information Biology and DNA Data Bank of Japan
NIG: National Institute of Genetics

IAM: International Advisory Meeting
ICM: International Collaborative Meeting

EMBL:
European Molecular Biology Laboratory
EBI:
European Bioinformatics Institute

NCBI:
National Center for Biotechnology Information
NLM:
National Library of Medicine

Protein Databases

Protein Information Resources (PIR) *http://pir.georgetown.edu/*



In 1988, The Protein Information Resource (PIR), established a cooperative effort with the Munich Information Center for Protein Sequences (MIPS) and the Japan International Protein Information Database (JIPID) , produces the PIR-International . Protein Sequence Database (PIR-PSD) -- a comprehensive, non-redundant, expertly annotated, fully classified and extensively cross-referenced protein sequence database in the public domain. The PIR-PSD, PIR-NREF, iProClass and other PIR auxiliary databases provide an integration of sequences, functional, and structural information to support genomics and proteomics research
The PIR-PSD, Current Release 71.04, March 01, 2002, Contains 283153 Entries

SWISSPROT *http://www.ebi.ac.uk/swissprot/*



The SWISS-PROT Protein Knowledgebase is an annotated protein sequence database established in 1986. It is maintained collaboratively by the Swiss Institute for Bioinformatics (SIB) and the European Bioinformatics Institute (EBI).

Protein Databases

ExPASY Molecular Biology Server *http://tw.expasy.org*



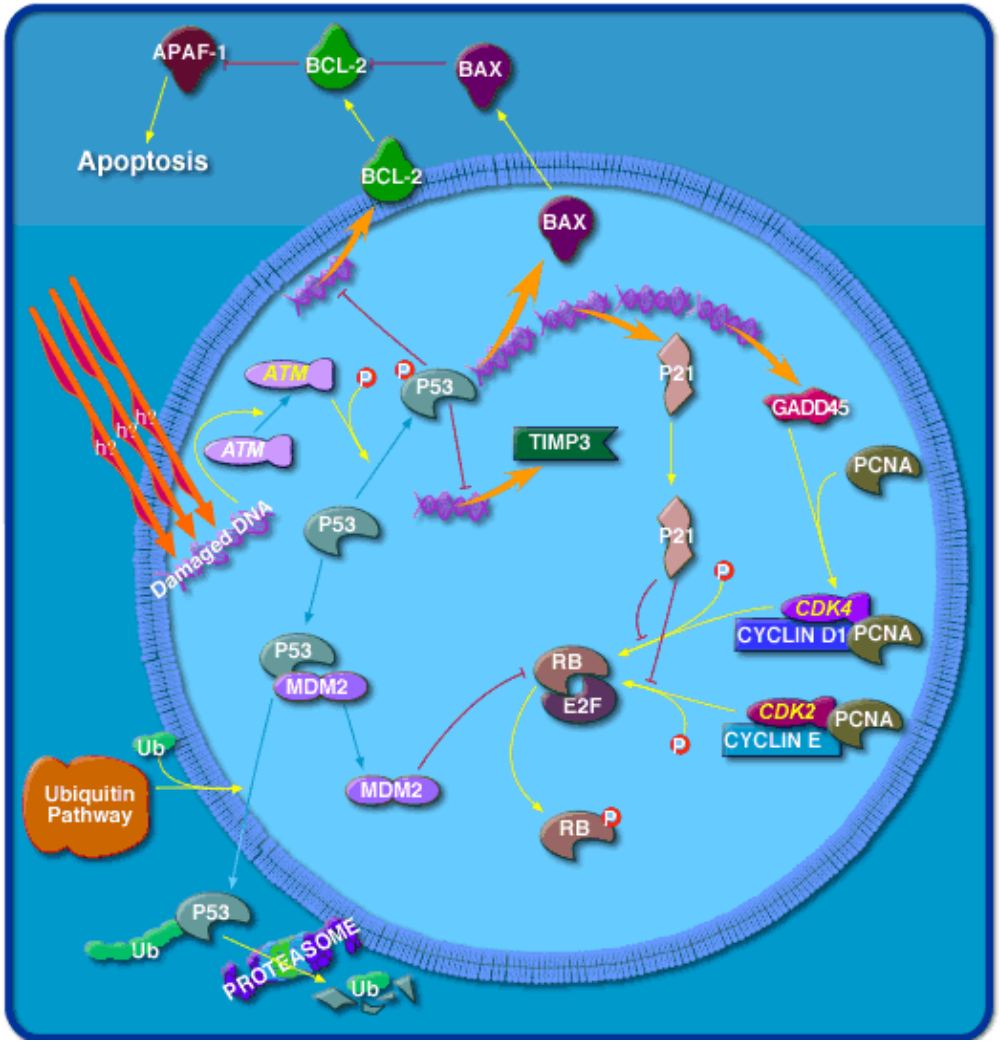
The ExPASy (**Ex**pert **P**rotein **A**nalysis **Sy**stem) proteomics server of the Swiss Institute of Bioinformatics (SIB) is dedicated to the analysis of protein sequences and structures as well as 2-D PAGE

Protein Data Bank *http://www.rcsb.org*

PROTEIN DATA BANK

The Protein Data Bank (PDB) is operated by Rutgers, The State University of New Jersey; the San Diego Supercomputer Center at the University of California, San Diego; and the National Institute of Standards and Technology -- three members of the Research Collaboratory for Structural Bioinformatics (RCSB). The PDB is supported by funds from the National Science Foundation, the Department of Energy, and two units of the National Institutes of Health: the National Institute of General Medical Sciences and the National Library of Medicine.

Metabolic & Signalling Pathways



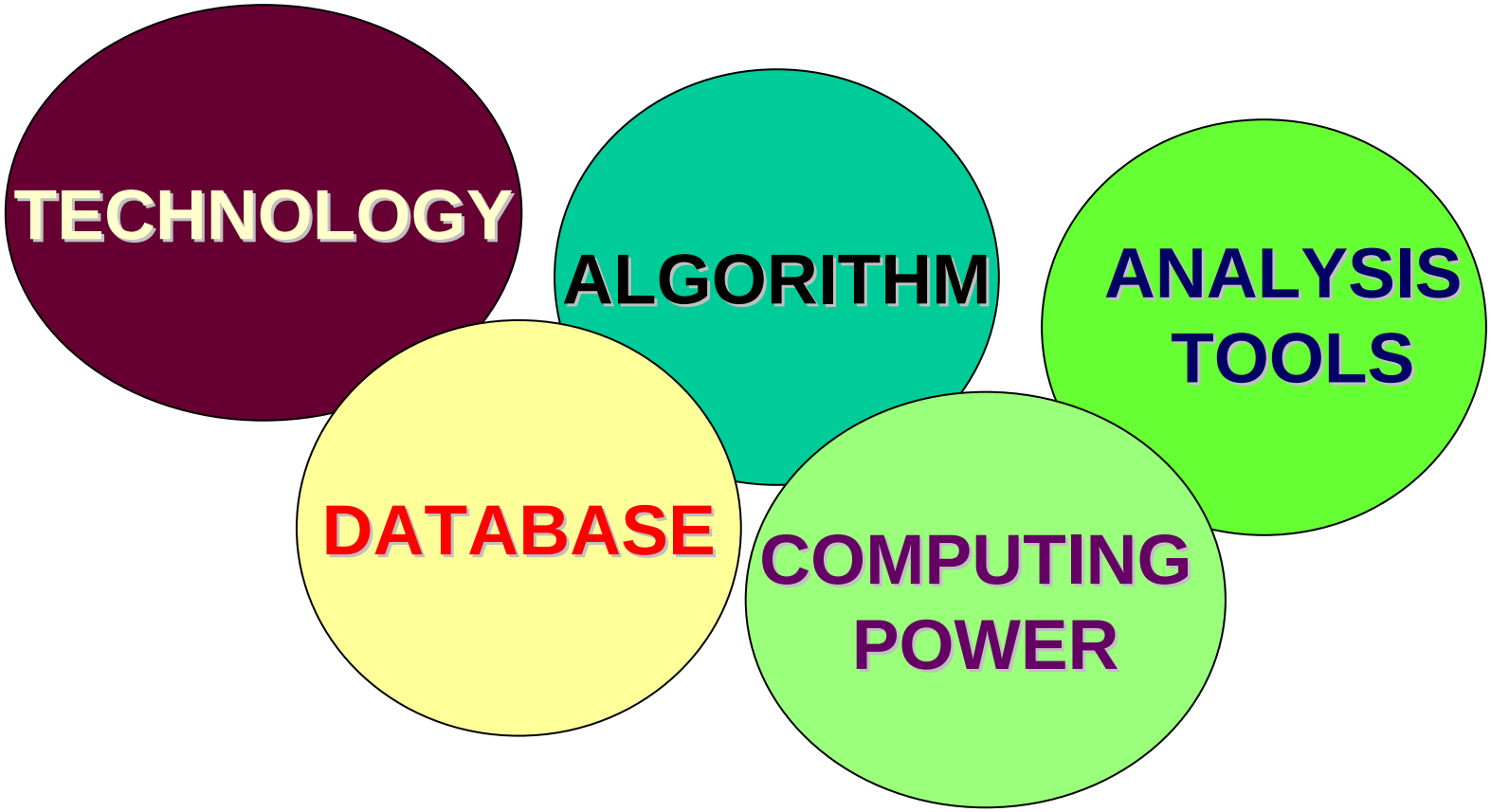
Biocarta
(*http://biocarta.com*)

Kyto Encyclopedia of Genes &Genomes
http://www.genome.ad.jp/kegg/

The Cancer Genome Anatomy Project (CGAP) *http://cgap.nci.nih.gov/*



THE COMPONENTS OF BIOINFORMATICS





BIOINFORMATICS ANALYSIS TOOLS

- $ Vector NTI suite, Omiga, DNAsis
- $ Staden Package, EMBOSIS, BLAST, FASTA

On line analysis tools



http://bioinfo.nhri.org.tw/

生物資訊 Bioinformatics

國家衛生研究院巨分子序列分析服務

巨分子序列分析服務 GCG

在 Unix 系統下以 Command Mode 進行核酸或蛋白質的序列分析。
(telnet://bioinfo.nhri.org.tw)

巨分子序列分析服務 SeqWeb

連線至 SeqWEB 以瀏覽器進行核酸或蛋白質的序列分析。
(http://bioinfo.nhri.org.tw/)

EMBOSS

連線至 SeqWEB 以瀏覽器進行核酸或蛋白質的序列分析
(http://srs.nchc.org.tw/EMBOSS/)

Smith-Waterman 快速序列搜尋系統 GenWEB

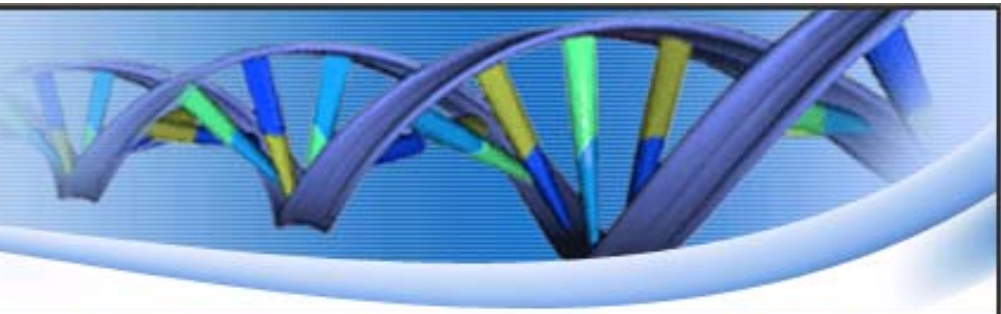
直接連線至 GenWeb 以瀏覽器進行核酸或蛋白質的快速序列搜尋。以特殊設計的硬體加速序列搜尋的速度，可進行 Smith-Waterman 及 FrameSearch 等搜尋功能。
(http://sw.nhri.org.tw/cgi-bin/genweb/bin/login.cgi)

ExPASy (Expert Protein Analysis System)

連線至 ExPASy 以瀏覽器進行蛋白質的序列分析。
(http://tw.expasy.org)



國家衛生研究院
TBI生物資訊核心設施



SEARCH

Go!!

powered by Google 站內搜尋

- GCG
- EMBOSS
- BLAST
- FTP Server
- PDA
- Discussion group
- Site Map
- GMBD Core TBI

HOME

最新消息 | 分析工具 | 資料庫 | 課程訊息 | 常見問題 | 帳號申請 | 全球網站

最新消息

國家衛生研究院生物資訊服務，提供**新版 Wisconsin Package**：(含 **GCG 11.1**與 **SeqWeb 3.1**) 上線使用，詳情請參考 新版公告。(公佈日期 2006/07/03)

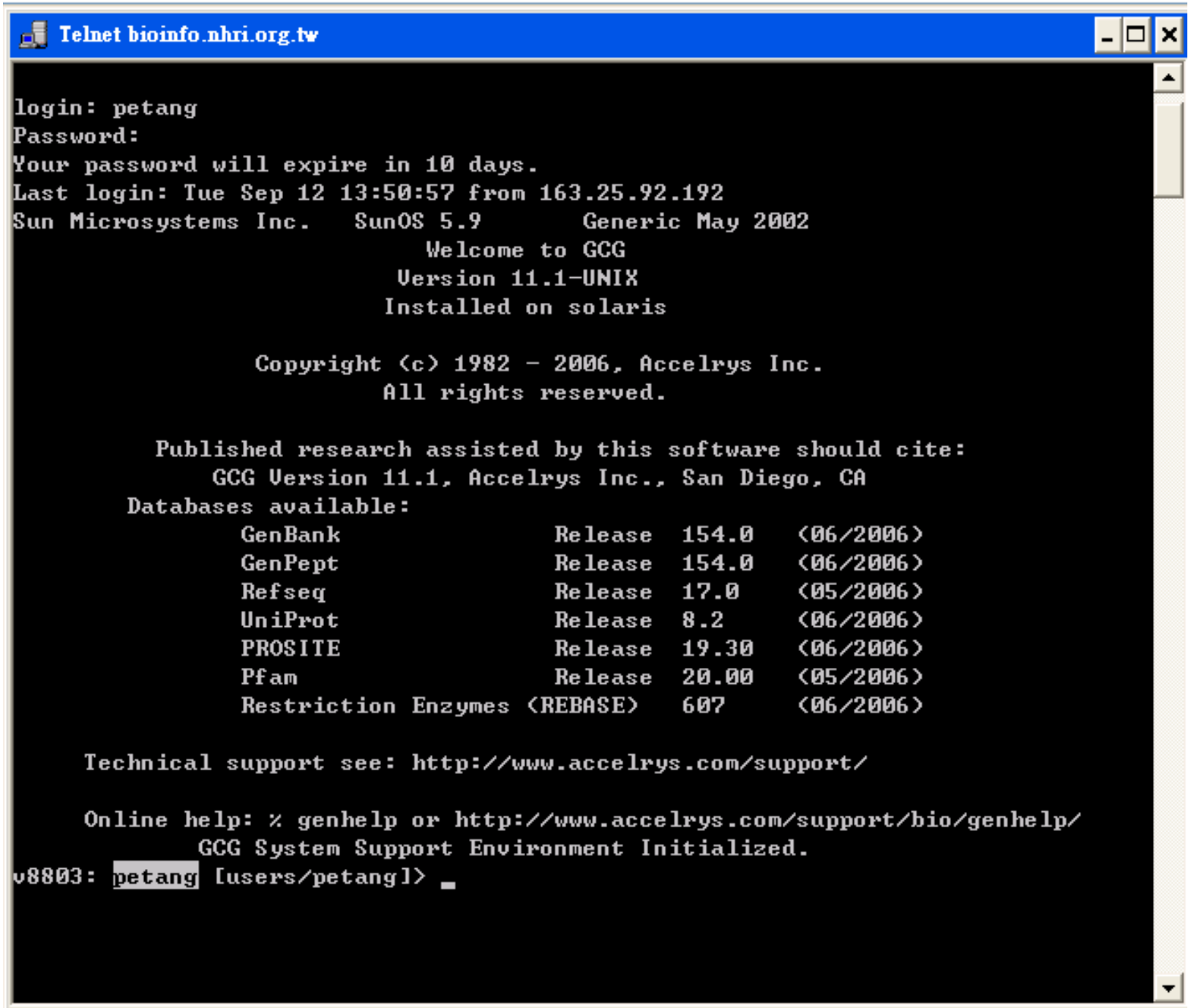
國家衛生研究院「研究資源2006系列活動」，將在 9/20-21 於「中研院生命科學圖書館電腦教室」，舉辦 **JEMBOSS基礎課程**，報名截止，請見學員名單！ (公佈日期 2006/09/18)

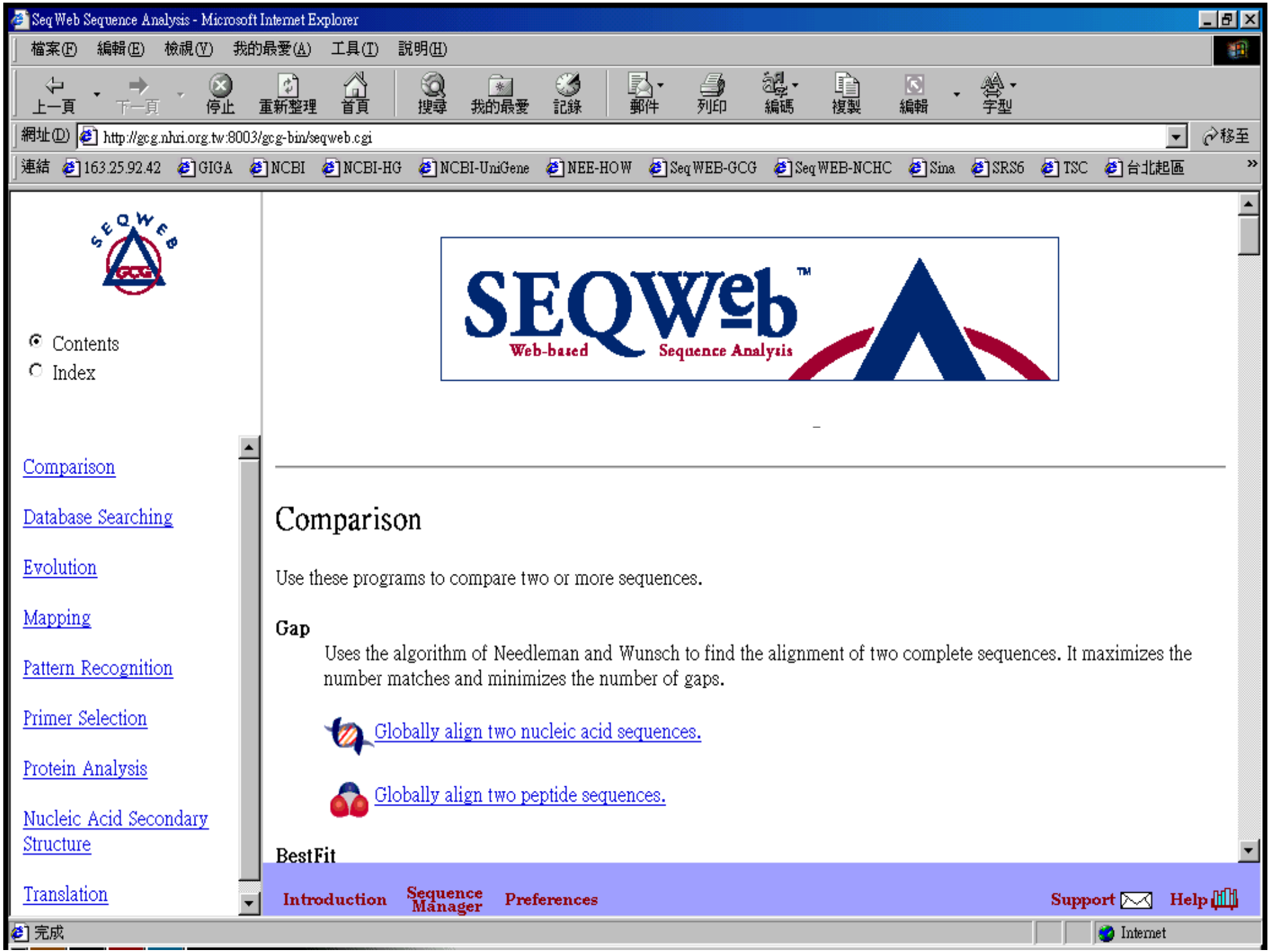
「**基因體研究之分析方法研習會**」，影音內容上線，請進入議程網頁後點選**Video圖示**，即可線上觀看演講內容！ 本項活動由基因體醫學國家型科技計畫支持。 (公佈日期 2006/08/31)

國家衛生研究院 GCG 程式及資料庫更新至 **2006-4** 版！請見詳細內容！(公佈日期 2006/08/30)

國立中興大學、國立陽明大學、教育部顧問室、國科會生命科學推動中心、生物資訊與系統生物學教學資源中心、與台灣生物資訊學會，將於 **2006年9月12日至15日**，假**「中興大學圖書館國際會議廳」**舉辦 2006台灣生物資訊研討會 (Symposium and Workshop of Bioinformatics in Taiwan 2006)， 請見大會網址！(公佈日期 2006/08/16)

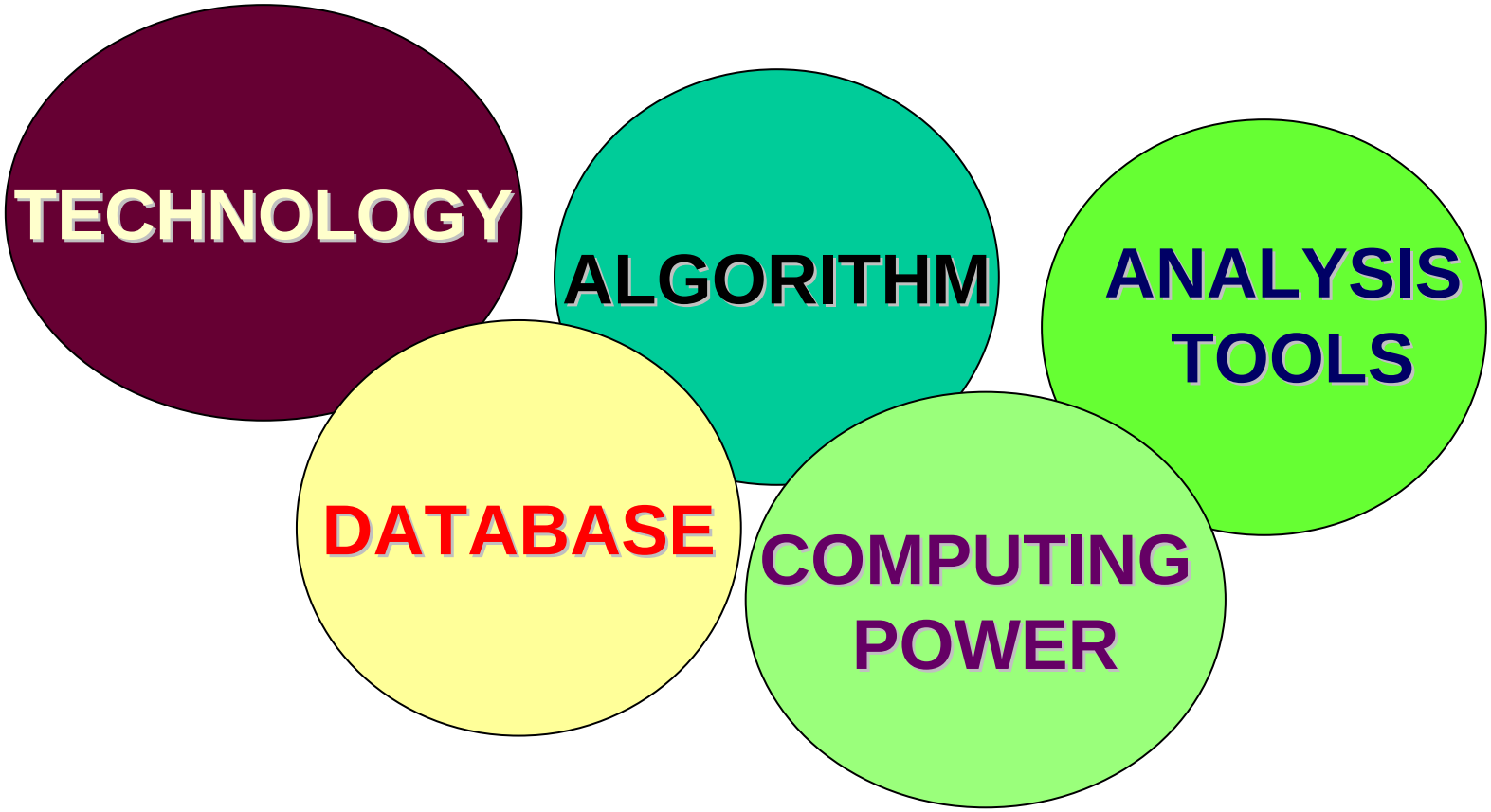
GMBD 基因體醫學生技研發生物資訊核心教育訓練課程，將在 8/14-15 於「中研院生命科學圖書館電腦教室」，舉辦 **巨分子序列分析基礎課程**，學員名單公佈，請參考名單


Telnet bioinfo.nhri.org.tw
login: petang
Password:
Your password will expire in 10 days.
Last login: Tue Sep 12 13:50:57 from 163.25.92.192
Sun Microsystems Inc.   SunOS 5.9   Generic May 2002
Welcome to GCG
Version 11.1-UNIX
Installed on solaris
Copyright (c) 1982 - 2006, Accelrys Inc.
All rights reserved.
Published research assisted by this software should cite:
GCG Version 11.1, Accelrys Inc., San Diego, CA
Databases available:
GenBank Release 154.0 (06/2006)
GenPept Release 154.0 (06/2006)
Refseq Release 17.0 (05/2006)
UniProt Release 8.2 (06/2006)
PROSITE Release 19.30 (06/2006)
Pfam Release 20.00 (05/2006)
Restriction Enzymes (REBASE) 607 (06/2006)
Technical support see: http://www.accelrys.com/support/
Online help: % genhelp or http://www.accelrys.com/support/bio/genhelp/
GCG System Support Environment Initialized.
v8803: petang [users/petang]>


Seq Web Sequence Analysis - Microsoft Internet Explorer
檔案(F) 編輯(E) 檢視(V) 我的最愛(A) 工具(T) 說明(H)
上一頁 下一頁 停止 重新整理 首頁 搜尋 我的最愛 記錄 郵件 列印 編碼 複製 編輯 字型
網址(D) http://gcg.nhri.org.tw:8003/gcg-bin/seqweb.cgi
移至
連結 163.25.92.42 GIGA NCBI NCBI-HG NCBI-UniGene NEE-HOW Seq WEB-GCG Seq WEB-NCHC Sina SRS6 TSC 台北起區
SEQWeb
GCG
Contents
Index
Comparison
Database Searching
Evolution
Mapping
Pattern Recognition
Primer Selection
Protein Analysis
Nucleic Acid Secondary Structure
Translation
SEQWeb™
Web-based Sequence Analysis
Comparison
Use these programs to compare two or more sequences.
Gap
Uses the algorithm of Needleman and Wunsch to find the alignment of two complete sequences. It maximizes the number matches and minimizes the number of gaps.
Globally align two nucleic acid sequences.
Globally align two peptide sequences.
BestFit
Introduction
Sequence Manager
Preferences
Support
Help
完成
Internet



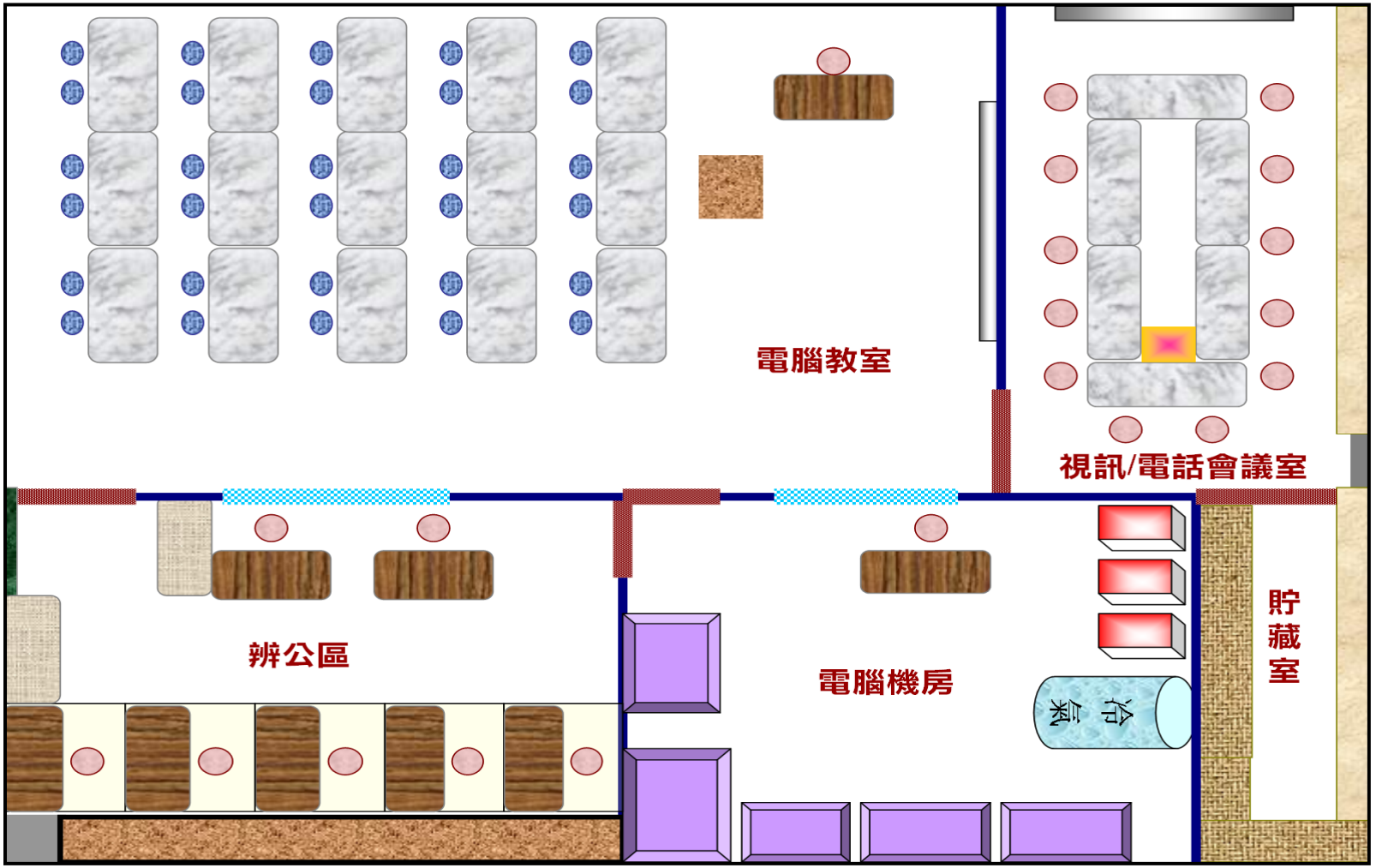
THE COMPONENTS OF BIOINFORMATICS



長庚生物資訊中心
bioinfo.cgu.edu.tw

設備

醫學大樓9樓0917



長庚生物資訊中心

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設備

COMPUTER	CPU	NO.	MEMMORY
SunFire 6800	Sparc 750 MHz	24	48 GB
Sun V60 Cluster	Xeon 2.8 GHz	20	20 GB
IBM X336 Cluster	Xeon 3.2 GHz	14	14 GB
IBM X225 Cluster	Xeon 2.4 GHz	2	1.5GB
HP DL580G3 Cluster	Xeon 3.0 GHz	16	16 GB
LunuxWorX Cluster	Xeon 2.4 GHz	8	8 GB
IBM Z-pro Graphic Station	Xeon 3.2 GB x 2	2	3 GB
教學電腦	P4 2.4 GHz	15	512 MB
教學電腦	P4 3.2 GHz	15	1 GB

ITEMS	SPECIFICATION	NO
Proware RAID System	250 GB x 16 (4 TB)	1
Petastor Fibre RAID System	400 GB x 16 (6.4 TB x 4)	4
Proware NAS System	80 GB x 8 (640 GB)	1
Brocad silkworm 2G Fibre switch	12 ports	1
UPS	10 KVA	1
UPS	30 KVA	2
Video Conference System	Centura	50
Telephone Conference System	Polycom sound station	1

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設備

InforMax™ Invitrogen™ life science software [*Vector NTI Advanced Server*]
[*GENOMAX High-Throughout Sequence Analysis System*]

PARACEL [*Paracel BLAST*] [*Paracel TranscriptAssembler*]

[*Bioinformatics Linux Cluster*]
[*Expression Sequence Tag Analysis Pipeline*]

[*Protein Sequence Analysis Pipeline*]

Tripos [*Protein Modeling & Docking System*]
[*Lead Compound Database*]



emboss [*The European Molecular Biology Open Software Suite*]

LION [*Sequence Retrieval System*]

GeneGo [*MetaCore: PPI Network*]

Genedata solutions in-silico [*Expressionist*]



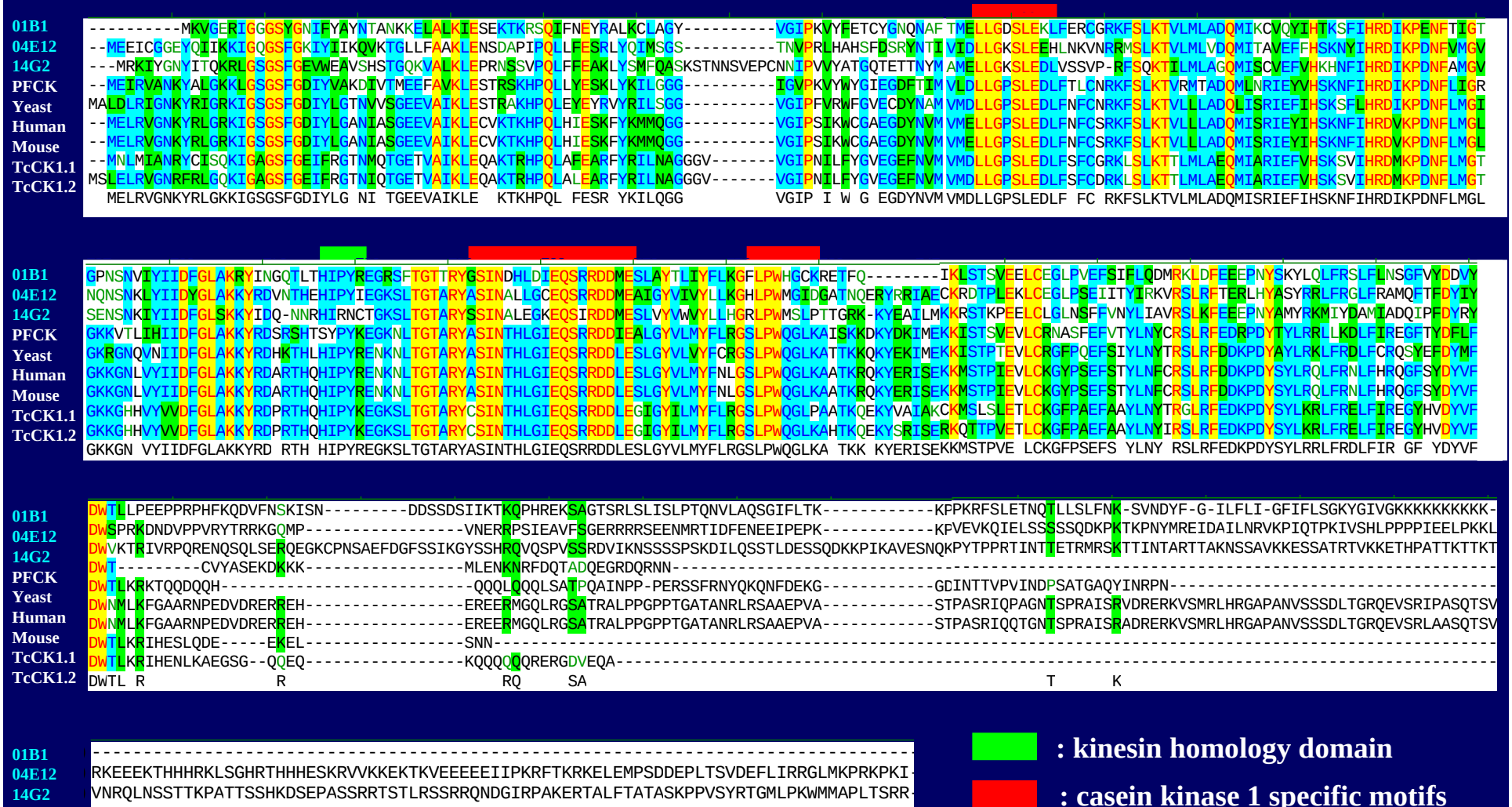
Steps to Identify a Gene

- Gene-Search
- Protein-Search
- Annotation

Full length ORF of *TvEST-14G2*

```
  -2          …AGATGCGAAAAA TCTACGGCAA TTACATTACG CAGAAGCGTC TCGGTTCAGG
                 AAGTTTCGGA GAGGTTTGGG AAGCTGTCAG TCATTCGACC GGACAAAAGG
 101             TTGCTCTCAA ATTAGAGCCC CGAAACTCTA GTGTTCCACA ATTATTTTTC
                 GAAGCCAAGC TATACTCAAT GTTTCAGGCT TCAAAATCCA CAAATAATAG
 201             TGTAGAACCA TGCAACAACA TTCCAGTTGT TTATGCGACT GGTCAAACAG
                 AGACAACTAA CTACATGGCC ATGGAATTAC TTGGCAAGTC TCTGGAAGAT
 301             TTAGTTTCAT CGGTCCCTAG ATTTTCCCAA AAGACAATAT TAATGCTTGC
                 CGGACAAATG ATTTCCTGTG TTGAATTCGT TCACAAACAT AATTTTATTC
 401             ACCGCGACAT CAAGCCAGAT AATTTTGCGA TGGGAGTCAG TGAGAACTCA
                 AACAAAATTT ATATTATCGA TTTTGGACTT TCCAAGAAGT ACATTGACCA
 501             AAATAATCGT CATATTAGAA ATTGCACAGG AAAATCACTT ACCGGAACCG
                 CAAGATATTC ATCAATTAAT GCGCTCGAAG GAAAGGAACA GTCTATAAGA
 601             GATGACATGG AATCTTTGGT ATATGTCTGG GTTTATTTAC TTCATGGACG
                 TCTTCCTTGG ATGAGCTTAC CTACAACAGG CCGCAAGAAG TATGAGGCCA
 701             TTTTAATGAA GAAGAGATCA ACGAAACCCG AAGAATTATG TTTAGGACTT
                 AATAGTTTCT TTGTAAACTA CTTAATAGCA GTTCGCTCAT TGAAATTTGA
 801             AGAAGAACCA AATTACGCGA TGTACAGGAA AATGATATAC GACGCAATGA
                 TTGCTGATCA AATTCCTTTT GATTATCGCT ATGATTGGGT CAAAACGAGA
 901             ATTGTTCGCC CACAACGTGA AAACCAATCA CAGTTGTCCG AACGTCAAGA
                 AGGAAAATGT CCAAACTCAG CTGAGTTTGA TGGTTTCTCC TCCATCAAAG
1001             GATATTCTTC GCACAGACAA GTACAAAGCC CCGTTTCATC TAGAGATGTC
                 ATTAAGAACA GTAGTTCAAG TCCATCAAAG GATATTTTGC AATCATCAAC
1101             CCTTGATGAA TCATCTCAAG ATAAAAAGCC AATCAAAGCT GTCGAATCGA
                 ATCAGAAACC ATATACACCG CCACGTACAA TTAATACTAC CGAAACAAGA
1201             ATGAGATCAA AGACTACAAT CAATACTGCA AGAACAACAG CAAAGAACTC
                 TTCGGCAGTT AAGAAAGAAT CGTCAGCAAC AAGGACTGTT AAGAAAGAAA
1301             CACATCCTGC AACTACAAAA ACAACAAAAA CTGTAAATAG ACAATTGAAC
                 TCTTCTACAA CGAAACCGGC AACTACGAGC TCTCACAAAG ACTCAGAACC
1401             GGCTTCATCA AGACGTACAT CAACTCTACG TTCAAGTCGC CGCCAAAATG
                 ACGGAATTCG CCCTGCAAAG GAAAGAACTG CGCTTTTCAC AGCTACAGCC
1501             AGTAAGCCTC CGGTATCTTA CCGTACTGGA ATGCTTCCGA AATGGATGAT
                 GGCTCCTCTC ACATCTCGTC GCTGAAATAT ATTTTTTATA TTATTTATTT
1601             TTTTCTTTTT CTATCTGTAT ATTAAATGTA TTTCTATATT ATTAAAAAAA
```

Amino Acid Sequence Comparison



Similarity of Various CK1s from Different Species

	TvEST-04E12	TvEST-14G2	TvEST-01B1	*T. cruzi* CK1.1	*T. cruzi* CK1.2	PFCK	Yeast CK1	Mouse CK1	Human CK1
TvEST-04E12	100	32	32	34	34	34	37	37	37
TvEST-14G2		100	24	24	23	24	24	26	25
TvEST-01B1			100	47	47	48	48	38	38
T. cruzi CK1.1				100	23	73	24	61	61
T. cruzi CK1.2					100	74	70	63	63
PFCK						100	69	62	62
Yeast CK1							100	69	67
Mouse CK1								100	99
Human CK1									100

3-D Structure of TvEST-14G2 and other CK1s



```
  1  MRKIYGNYIT QKRLGSGSFG EVWEAVSHST GQKVALKLEP RNSSVPQLFF
 51  EAKLYSMFQA SKSTNNSVEP CNNIPVVYAT GQTETTNYMA MELLGKSLED
101  LVSSVPRFSQ KTILMLAGQM ISCVEFVHKH NFIHRDIKPD NFAMGVSENS
151  NKIYIIDFGL SKKYIDQNNR HIRNCTGKSL TGTARYSSIN ALEGKEQSIR
201  DDMESLVYVW VYLLHGRLPW MSLPTTGRKK YEAILMKKRS TKPEELCLGL
251  NSFFVNYLIA VRSLKFEEEP NYAMYRKMIY DAMIADQIPF DYRYDWVKTR
301  IVRPQRENQS QLSERQEGKC PNSAEFDGFS SIKGYSSHRQ VQSPVSSRDV
351  IKNSSSSPSK DILQSSTLDE SSQDKKPIKA VESNQKPYTP PRTINTTETR
401  MRSKTTINTA RTTAKNSSAV KKESSATRTV KKETHPATTK TTKTVNRQLN
451  SSTTKPATTS SHKDSEPASS RRTSTLRSSR RQNDGIRPAK ERTALFTATA
501  SKPPVSYRTG MLPKWMMAPL TSRR
```

TVEST-14G2



TcCK1.1



TcCK1.2



PfCK1



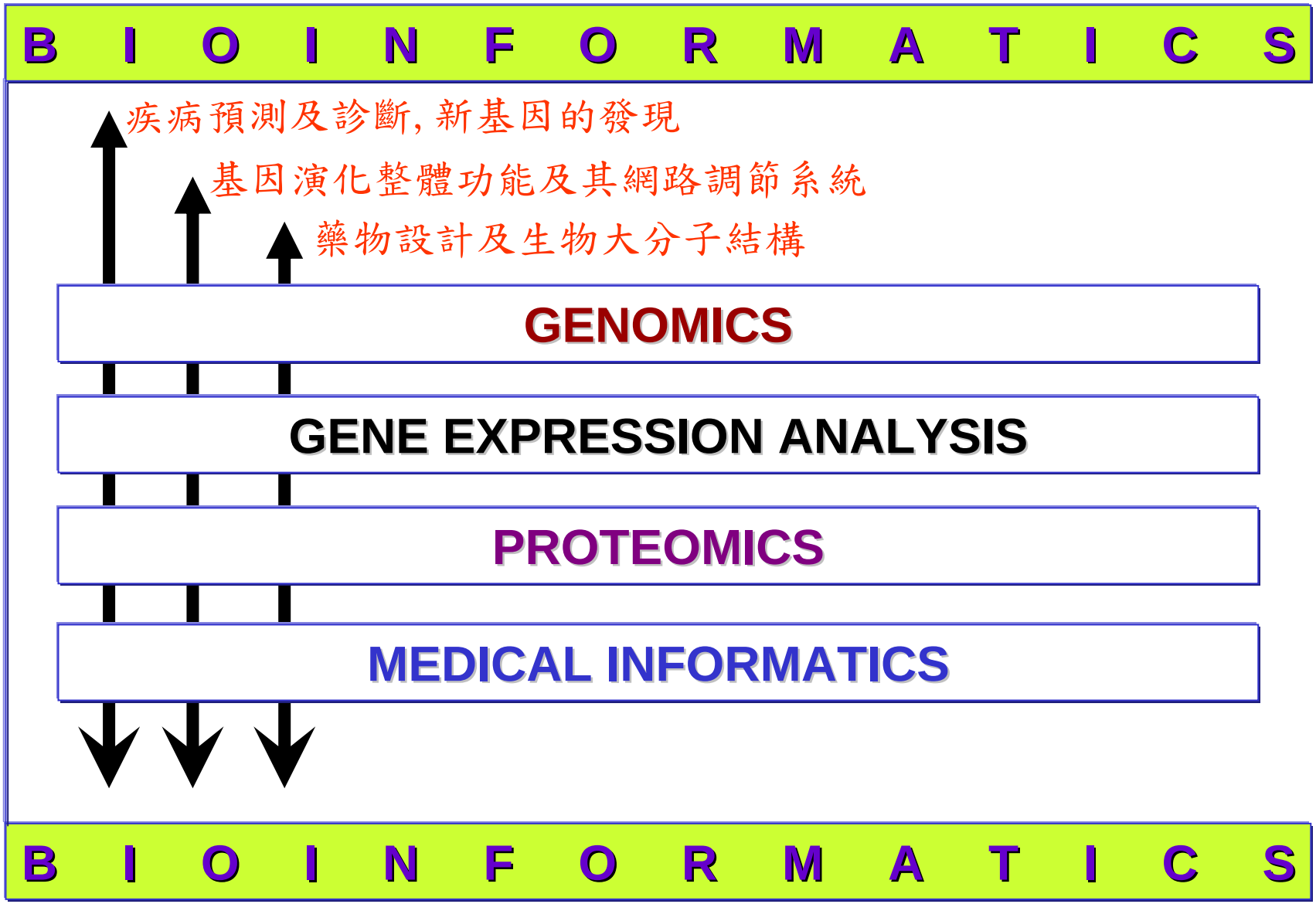
Yeast CK1



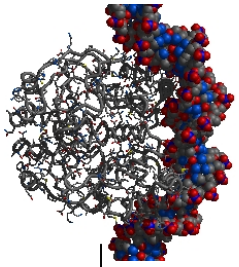
Mouse CK1



Human CK1-δ


B I O I N F O R M A T I C S
疾病預測及診斷, 新基因的發現
基因演化整體功能及其網路調節系統
藥物設計及生物大分子結構
GENOMICS
GENE EXPRESSION ANALYSIS
PROTEOMICS
MEDICAL INFORMATICS
B I O I N F O R M A T I C S

Focuses in Bioinformatics

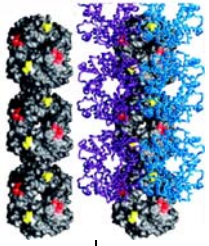


Perturbation
Environment
Medication
Genetic Engineering

Dynamic Response
Gene Expression
Protein Expression

BioChip

Virtual Cell



Analysis

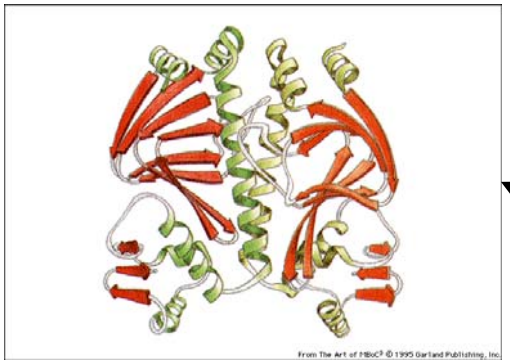
DataBase
Genotype/Phenotype

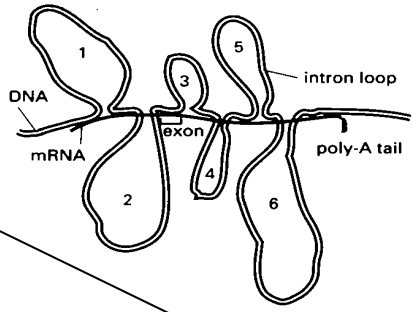
Biology
Molecular Biology
Bio Chemistry
Genetics

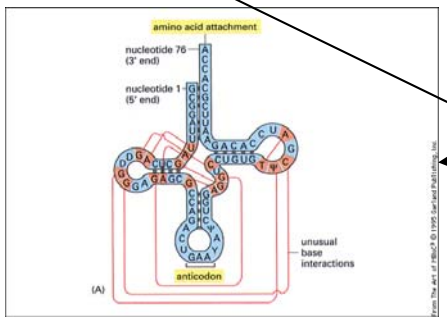
Symbolic
Algorithms/
Computing

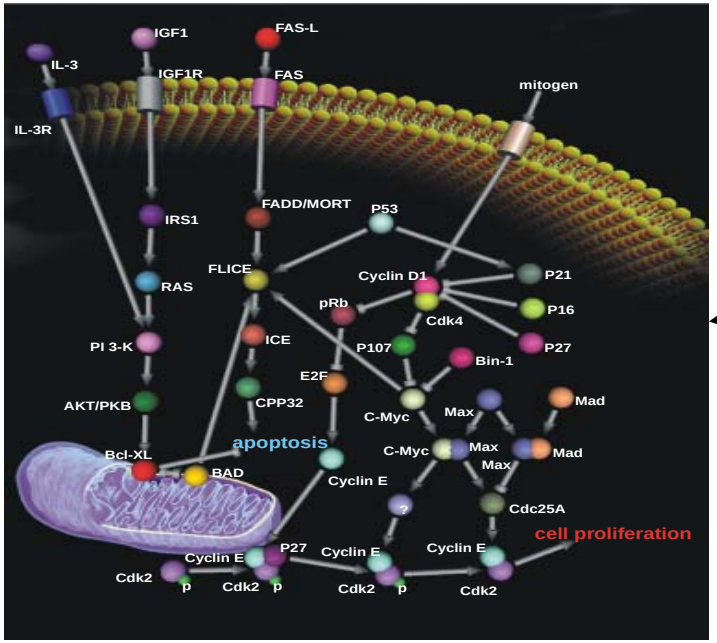
Genome Sequencing

Goals Leading Toward Predictive Biology









Gene Sequence Data

Gene Identification

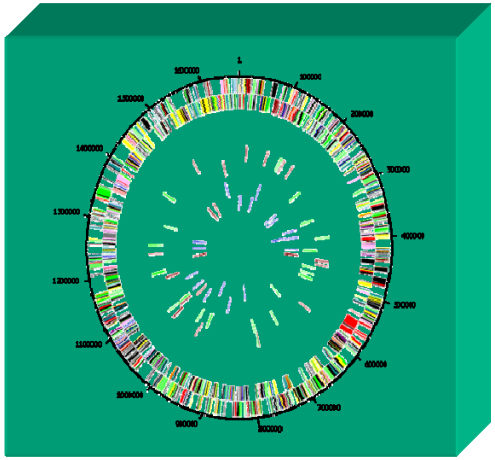
Structure Prediction

Protein Circuit & Regulatory Network Discovery

Biosimulation

Reconstructing Cellular Functions





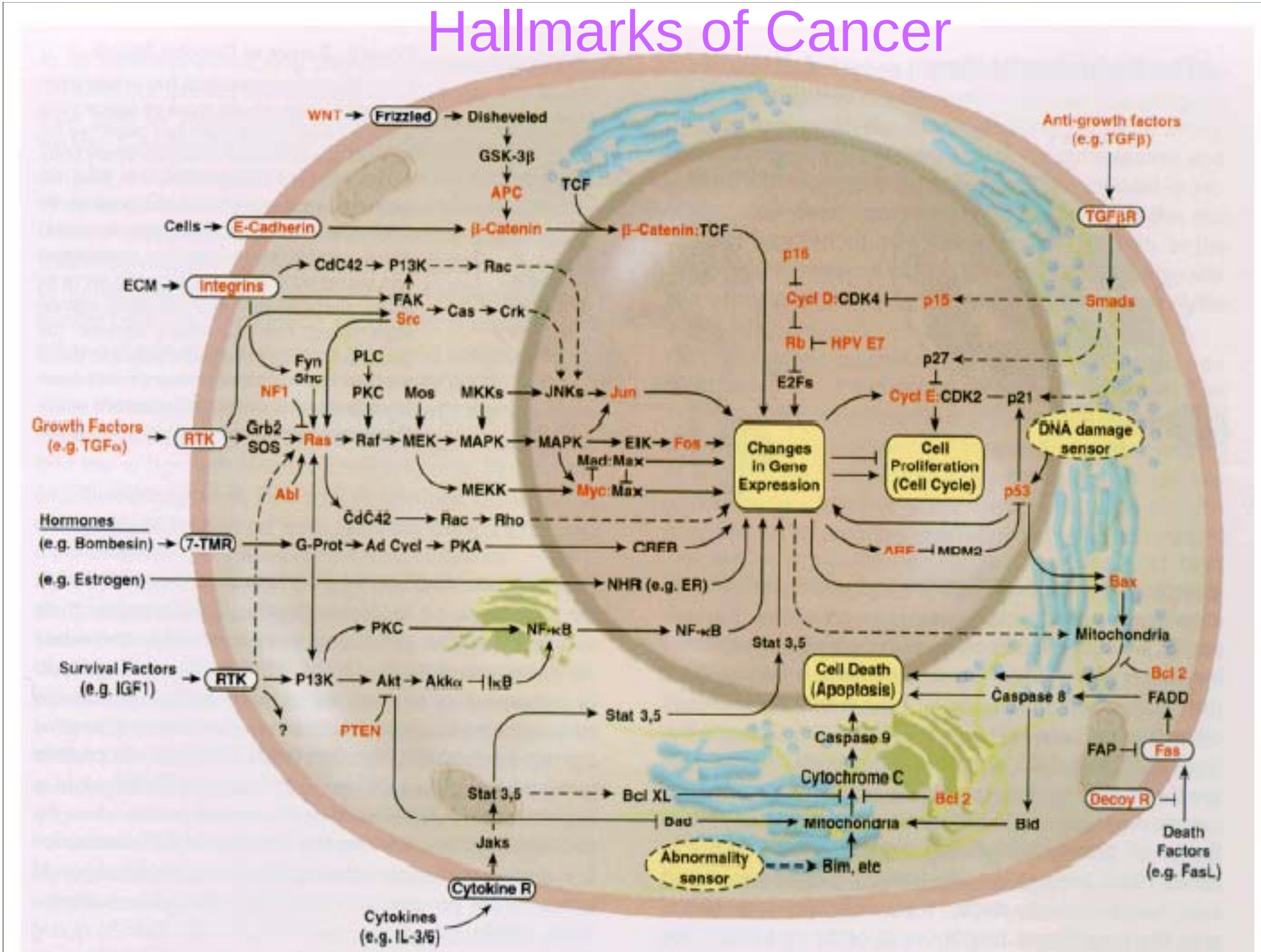
Reductionistic Approach
(Genome Sequencing, DNA arrays, proteomics)

Integrative Approach
(Bioinformatics, Systems Science, modeling & simulation)

20th Century Biology

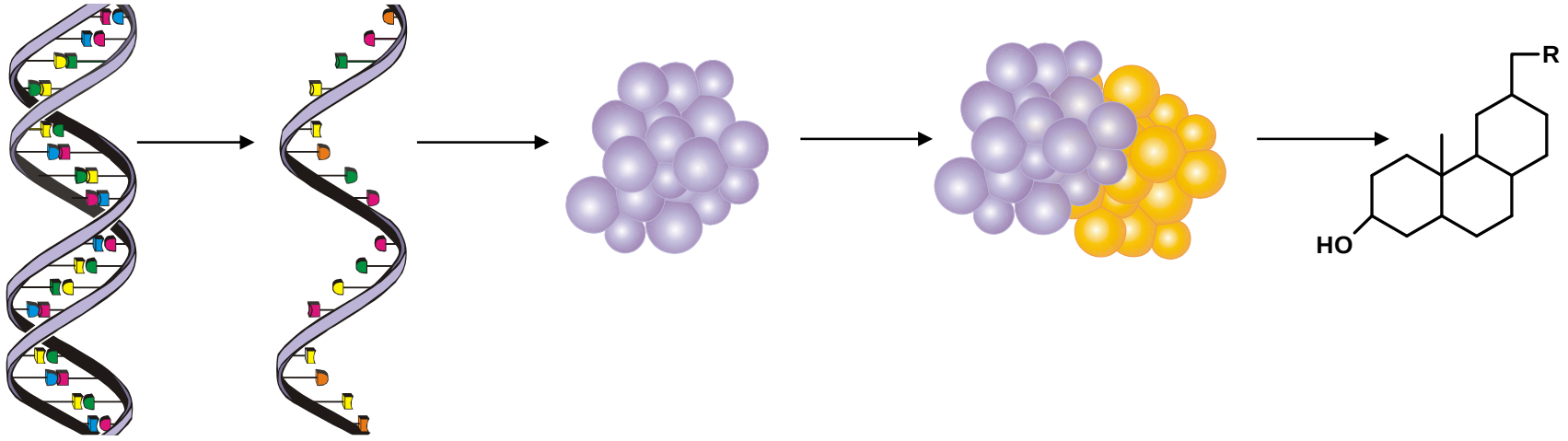
21th Century Biology

Hallmarks of Cancer



D. Hanahan and R. A. Weinberg. Cell., 100(1):57–70 Review, 2000.

SYSTEMS BIOLOGY



Genomics

Proteomics

Metabolomics

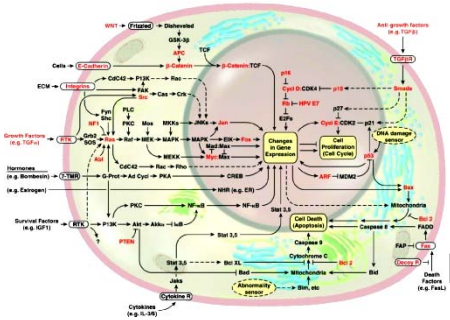
Transcriptomics

Functional Proteomics/Genomics

Systems Biology

Platform for Systems Biology

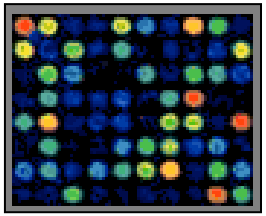
- Objective is to link gene response, protein activity, metabolite dynamics to disease and interventions



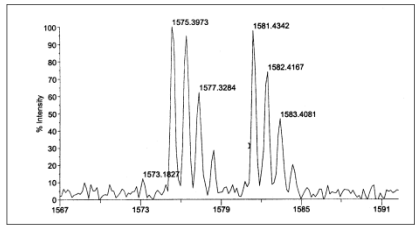
Complex Cellular Samples
bodyfluids, tissue

Dynamics
i.e. environmental + time

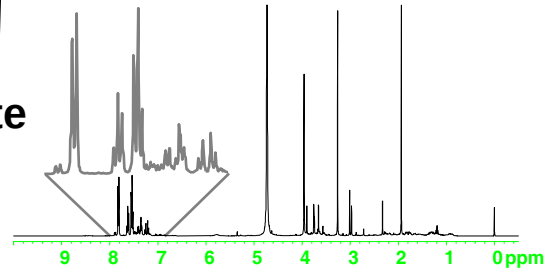
Gene



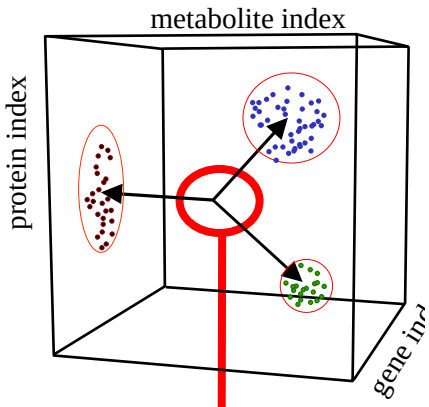
Protein



Metabolite



Quantitative Comparisons



BioSystematics™

Targets Biomarkers

Systems biology and emerging properties





One framework for Systems Biology

1. The components. ***Discover all*** of the genes in the genome and the subset of genes, proteins, and other small molecules constituting the pathway of interest. If possible, define an initial ***model*** of the molecular interactions governing pathway function (how?).

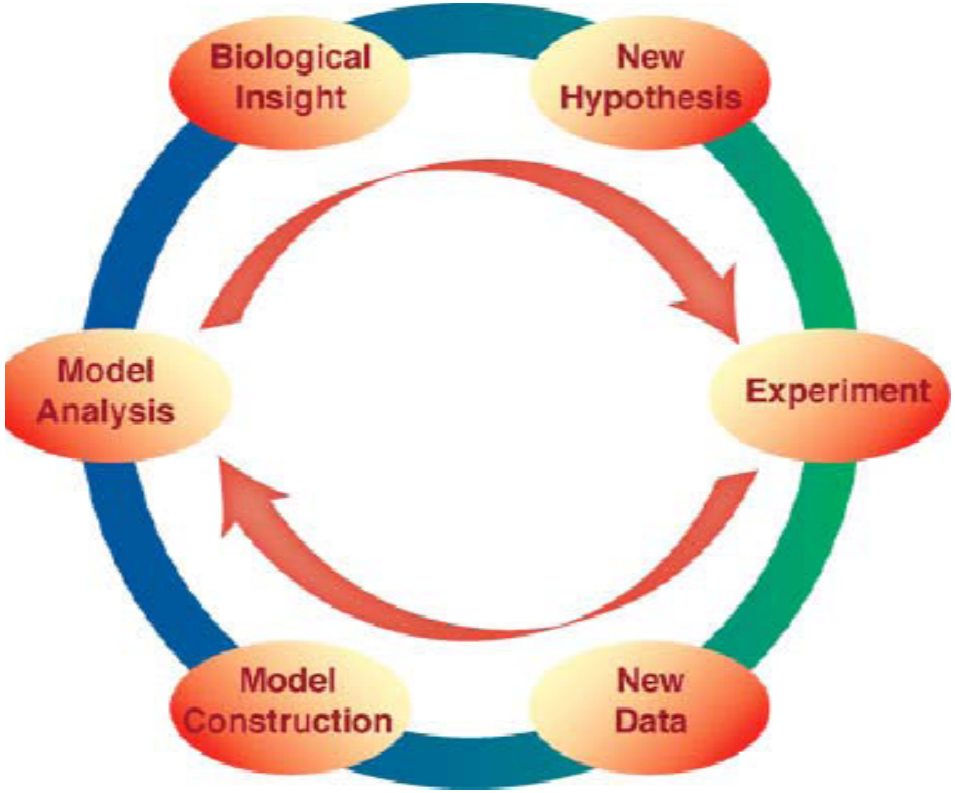
2. Pathway perturbation. Perturb each pathway component through a series of ***genetic*** or ***environmental*** manipulations. Detect and quantify the corresponding ***global*** cellular response to each perturbation.

One framework for Systems Biology

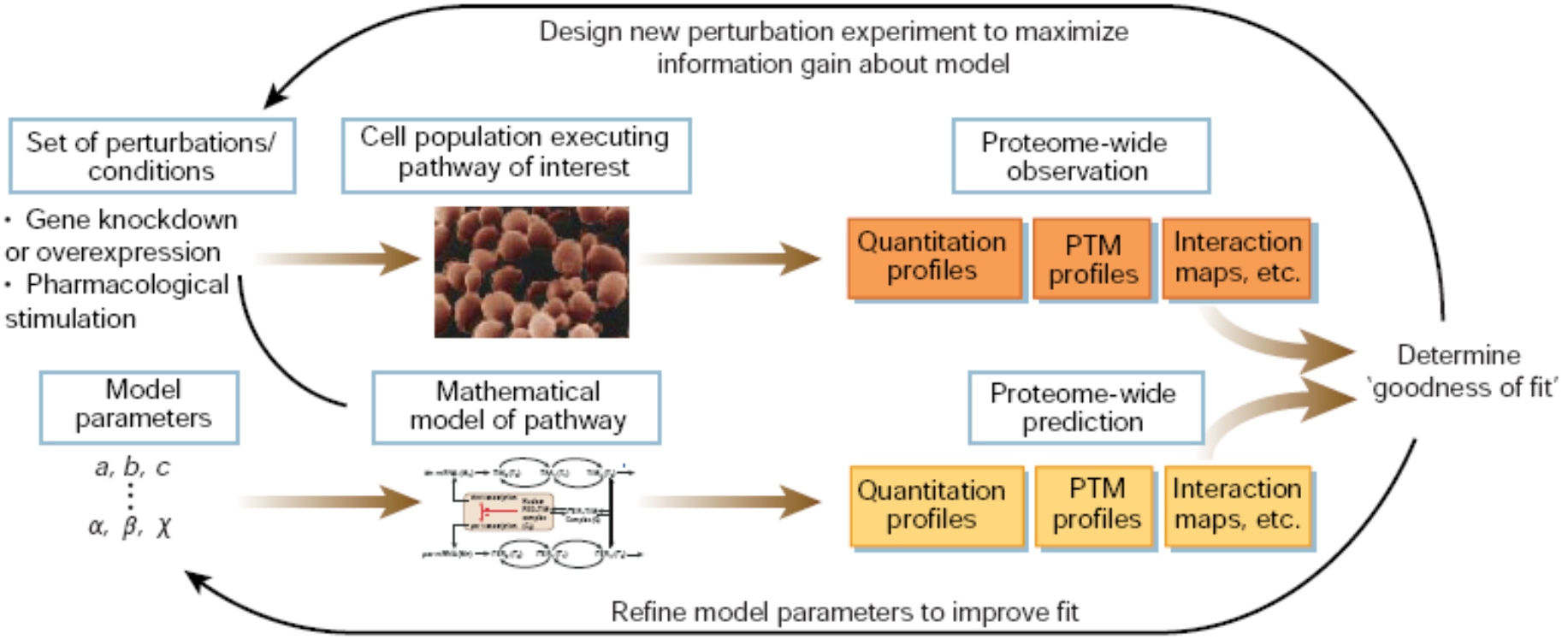
3. Model Reconciliation. ***Integrate*** the observed mRNA and protein responses with the current, pathway-specific model and with the global network of protein-protein, protein-DNA, and other known physical interactions.

4. Model verification/expansion. Formulate new ***hypotheses*** to explain observations not predicted by the model. Design additional perturbation experiments to test these and iteratively repeat steps (2), (3), and (4).

From model to experiment and back again



Systems biology paradigm



Aebersold R, Mann M, *Nature*, 2003.