Department of Electrical Engineering (ESAT)

Faculty of Engineering
Katholieke Universiteit Leuven

Systems Theory in Systems Biology

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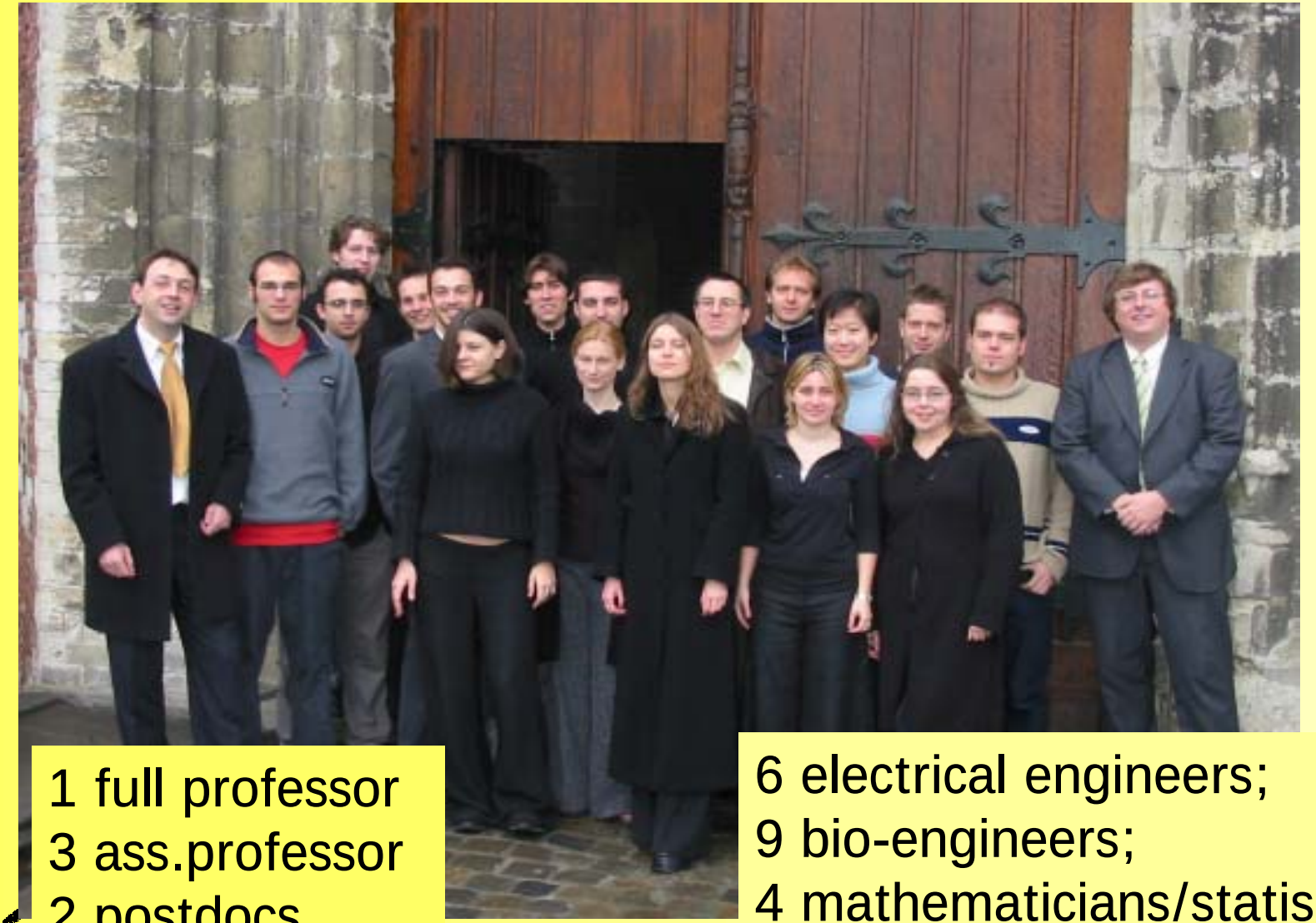
Our team



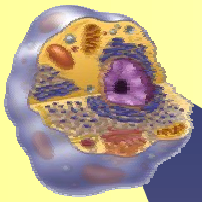
1 full professor
3 ass.professor
2 postdocs
14 phd students

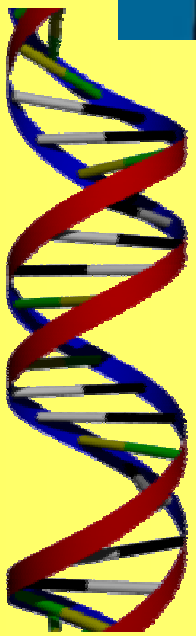
6 electrical engineers;
9 bio-engineers;
4 mathematicians/statisticians
1 medical doctor

Contents

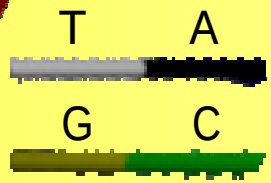
Biology

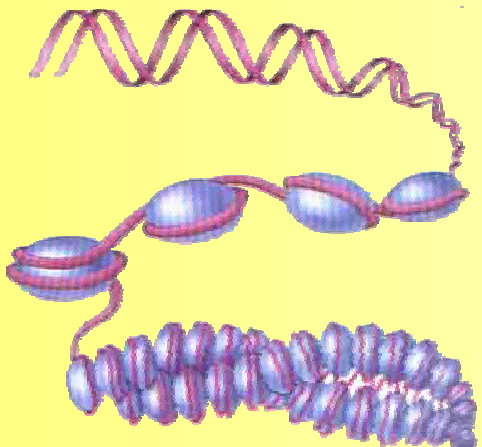
1.000.000 cell types
100.000.000.000.000 cells

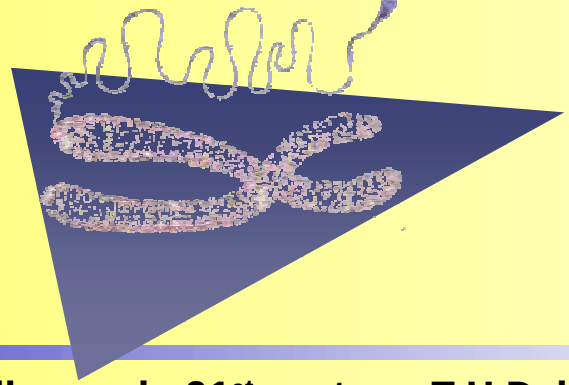




3.201.762.515 bp







Double helix of DNA

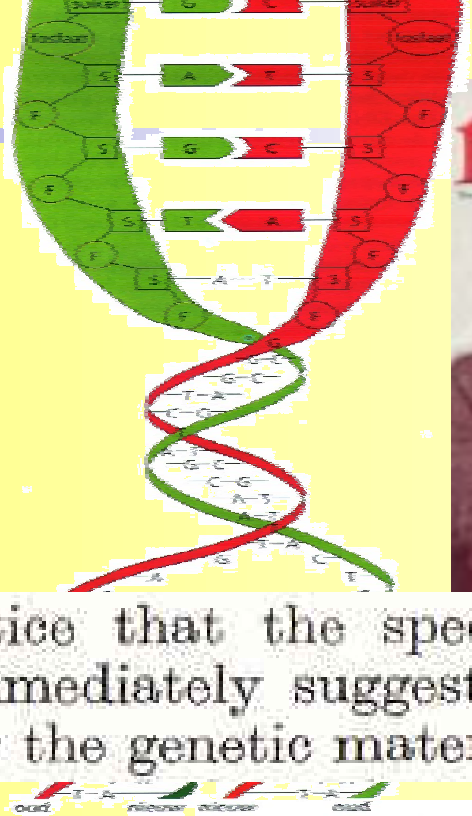

original papers

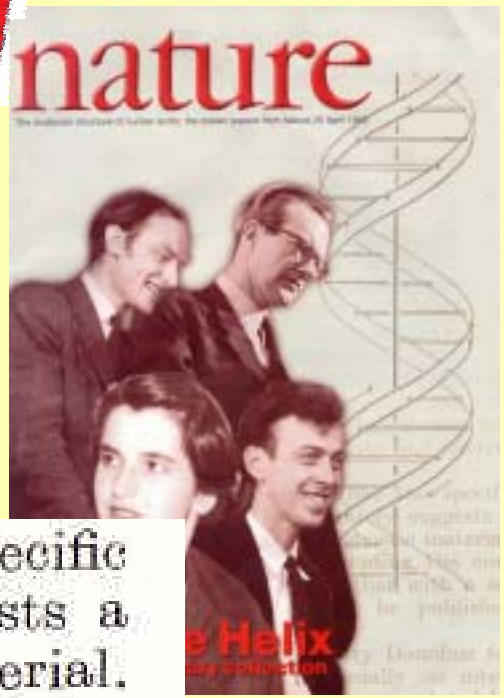
April 25, 1953 NATURE

MOLECULAR STRUCTURE OF NUCLEIC ACIDS

A Structure for Deoxyribose Nucleic Acid

nature




nature

It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material.

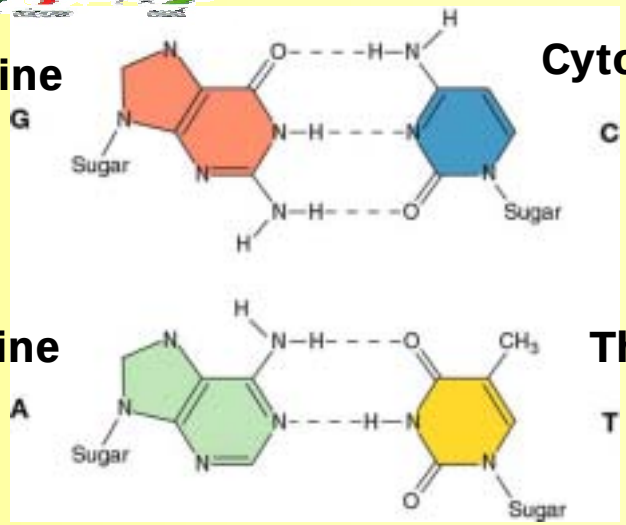

helix at 50

YEARS

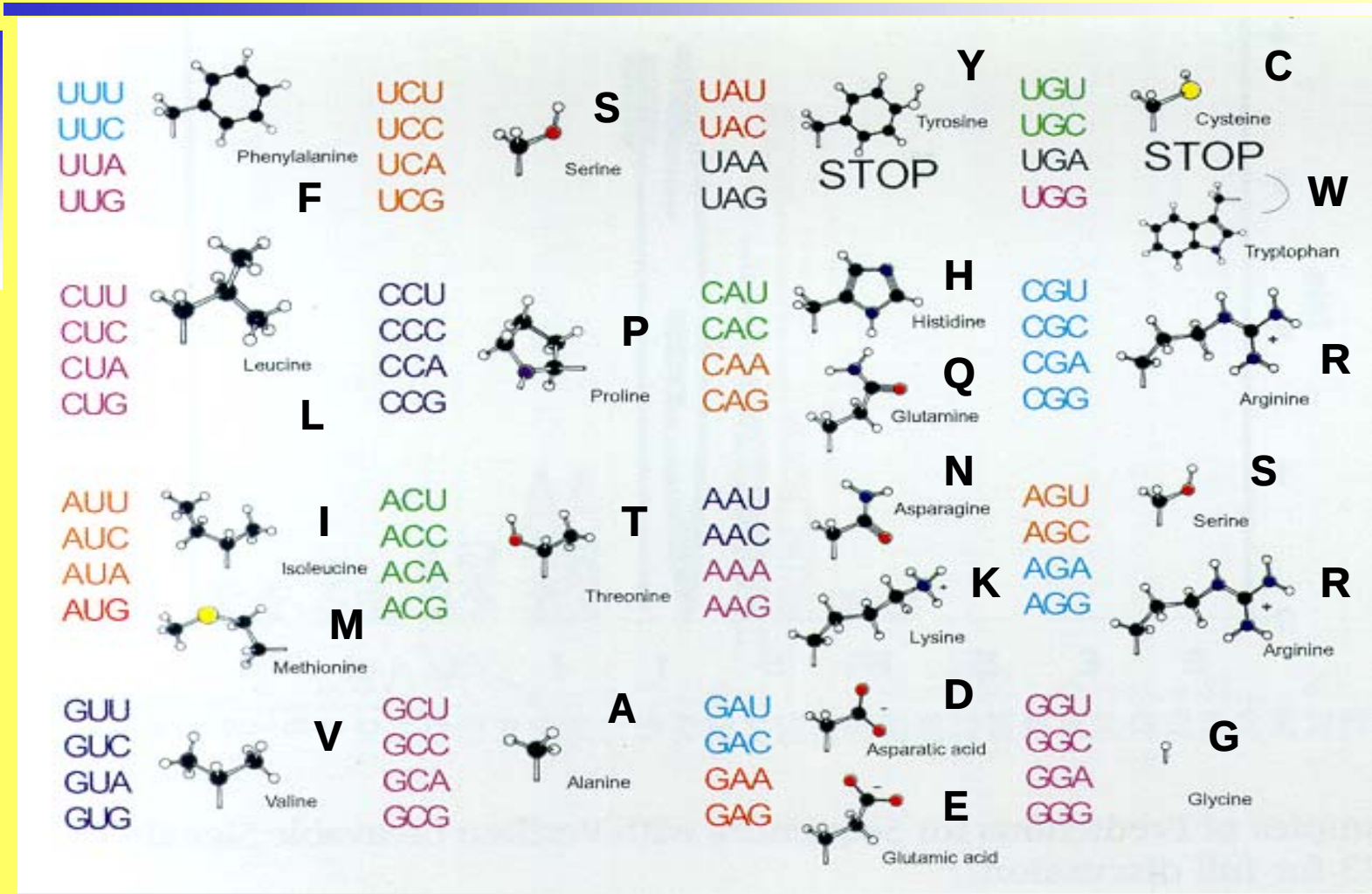
Bismuth-209
Nature's heaviest stable isotope declared unstable

Adult stem cells
Hybrid cells pose problems

The first stars
Inside the element factories



Genetic (almost) universal code: codons



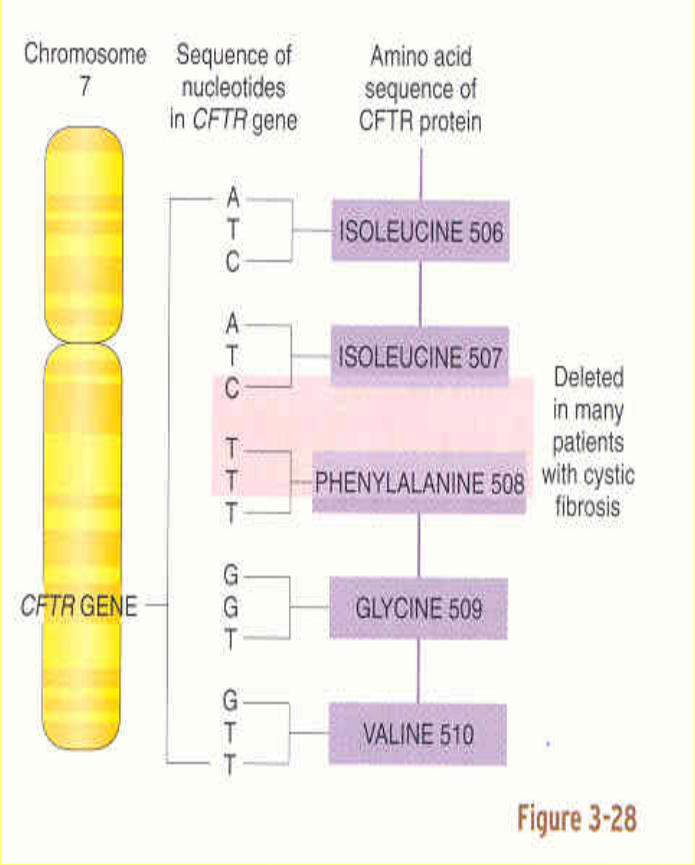
T in DNA
U in RNA

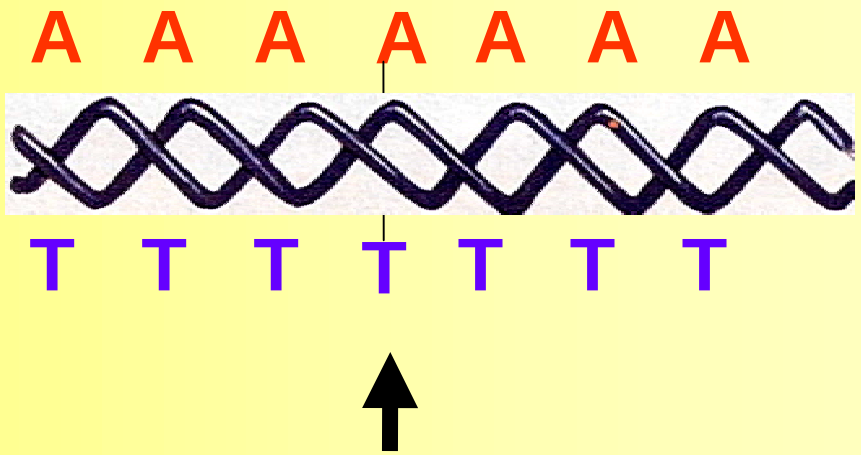
-20 amino acids
-64 codons: Redundancy - robustness

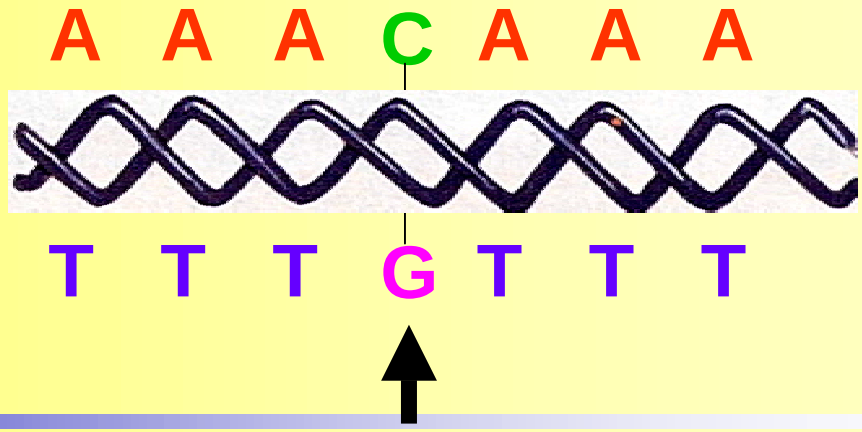
Stop=UAA,UAG,UGA
Start=AUG

SNP: Single Nucleotide Polymorphism

11 million SNPs / 3 billion nucleotides







Monogenic diseases
-1983: Huntington
-1986: Muscular distrophy
-1989: Cystic-fibrosis

HGP: sequencing


articles

Initial sequencing and analysis of the human genome

articles


The Sequence of the Human Genome

February 16, 2001

The genome

.....ACACATTAAATCTTATATGCTAAAACTAGGTCTCGTTTTAGGGATGTTTATAA
CCATCTTTGAGATTATTGATGCATGGTTATTGGTTAGAAAAAATATACGCTTGTTTTTCTTTCCT
AGGTTGATTGACTCATACATGTGTTTCATTGAGGAAGGAACTTAACAAAACTGCACTTTTTTCA
ACGTCACAGCTACTTTAAAAGTGATCAAAGTATATCAAGAAAGCTTAATATAAAGACATTTGTT
TCAAGGTTTCGTAAGTGCACAATATCAAGAAGACAAAAATGACTAATTTTGTTTTCAGGAAGC
ATATATATTACACGAACACAAATCTATTTTTGTAATCAACACCGACCATGGTTCGATTACACAC
ATTAAATCTTATATGCTAAAACTAGGTCTCGTTTTAGGGATGTTTATAACCATCTTTGAGATTAT
TGATGCATGGTTATTGGTTAGAAAAAATATACGCTTGTTTTTCTTTCCTAGGTTGATTGACTCAT
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GCTTGTTTTTCTTTCCTAGGTTGATTGACTCATACATGTGTTTCATTGAGGAAGGAACTTAACA
AAACTGCACTTTTTTCAACGTCACAGCTACTTTAAAAGTGATCAAAGTATATCAAGAAAGCTTA
ATATAAAGACATTTGTTTCAAGGTTTCGTAAGTGCACAATATCAAGAAG.....
.....

Humane Genome

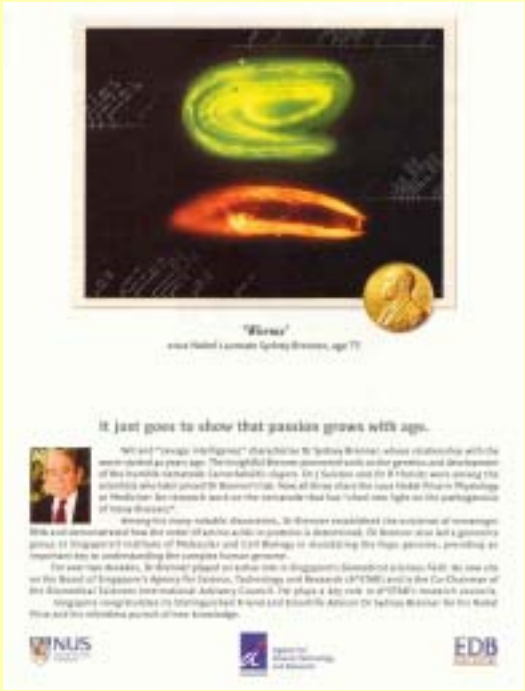
- +/- 30 000 genes of 60 – 120 kB;
- only 3 % DNA = gene (exon: codes for protein);
- rest = intergenic (introns, regulatory elements, see later);
- Each person's genome is 99.8 % identical to everyone else's;

… also other organisms…

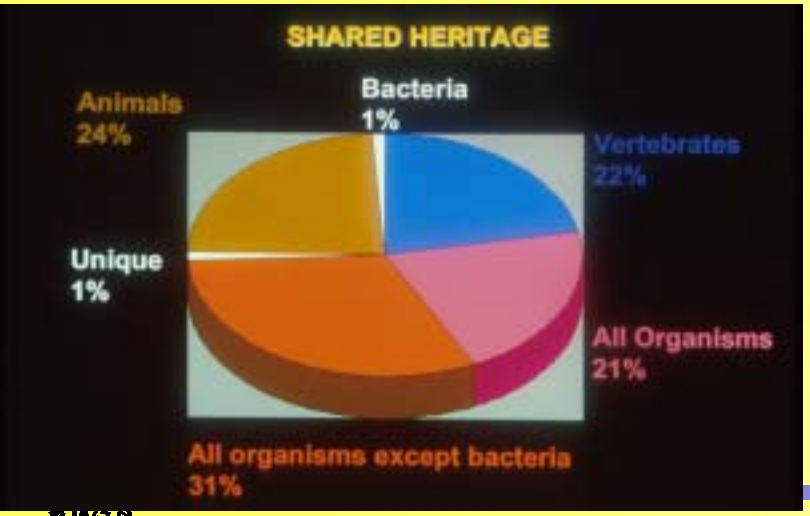
2002: Rat & Rice

2000

2002



1998



Sars genome, April 2003, 3 weeks !

Building blocks and mechanisms are the same for all living organisms !

‘Universality’ of the genetic code ….

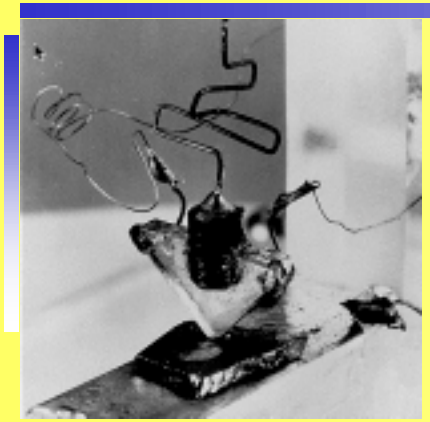
… Some genome numbers

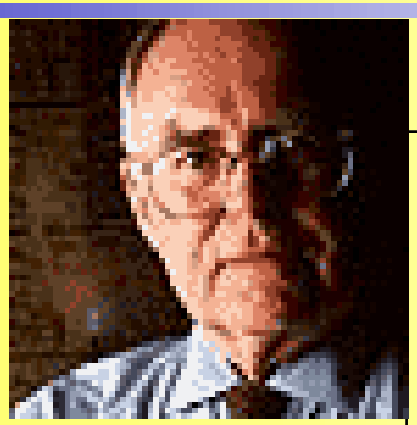
Group	Species	Genes	Genome (Mbase)
Phages	Bacteriophage MS2	4	0.003560
Viruses	HIV Type 2	9	0.009671
Bacteria	Haemophilus influenzae (1995)	1760	1.83
Archaea	Methanococcus jannaschii	1735	1.74
Fungi	Saccaromyces cerevisiae (yeast) (1996)	5800	12.1
Protoctista	Oxytricha similis	12000	600
Arthropoda	Drosophila melanogaster (fruit fly) (2000)	12000	165
Nematoda	Caenorhabdiis elegans (Round worm)(1998)	14000	100
Mollusca	Loligo Pealii	35000	2700
Plantae	Arabidopsis thaliana (Mustard cress)(2000)	25000	70-145
Chordata	Homo Sapiens	30000	3000

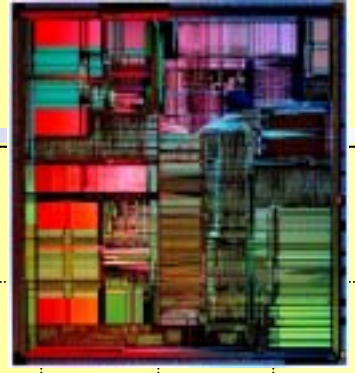
Estimated 265-350 genes are required for ‘life’.

Contents

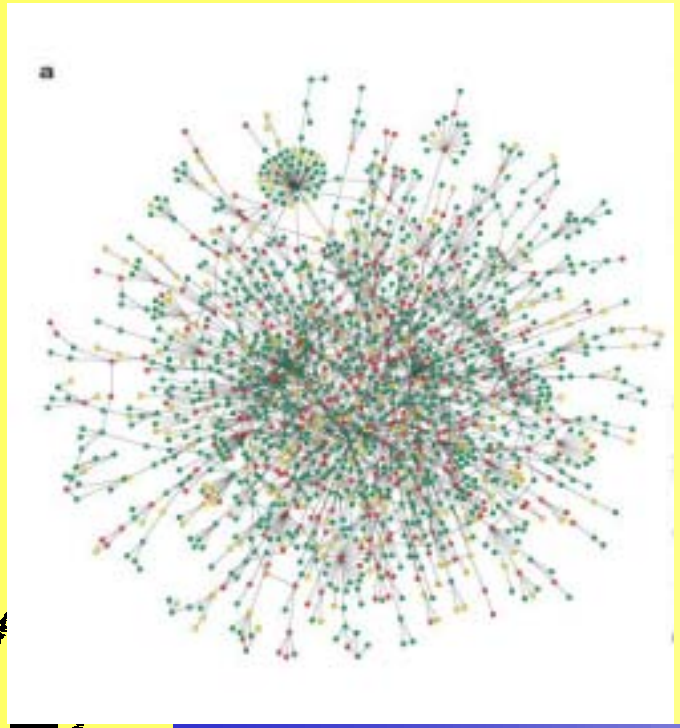
Moore's law

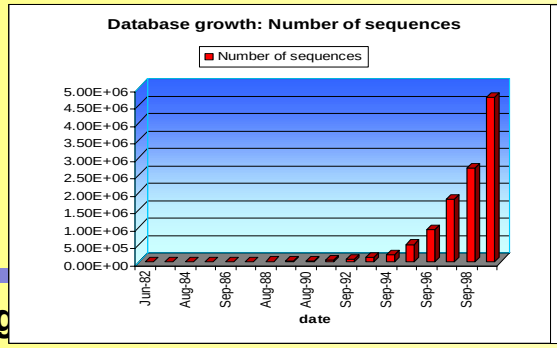


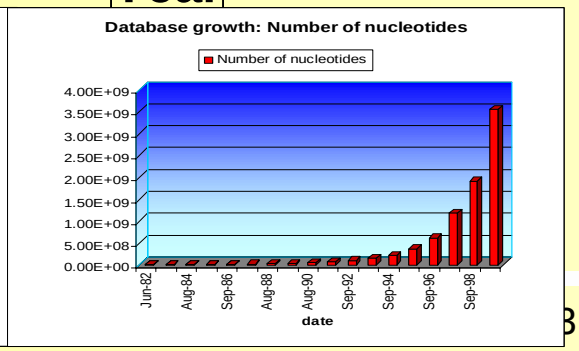




Small World







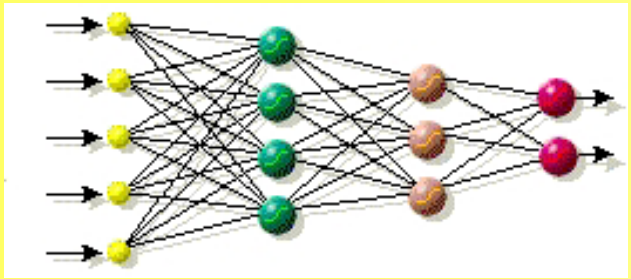
Mathematics and biology

1865: Mendel's Laws = statistics

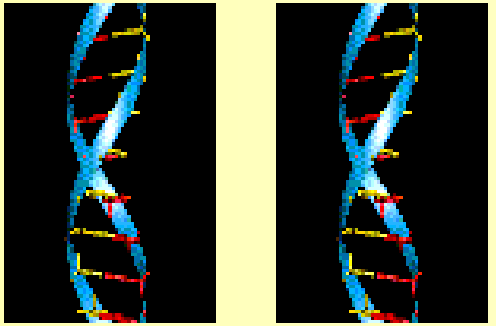
Shannon: 1940 PhD An algebra for theoretical genetics

1952: Turing The chemical basis of morphogenesis

1944: Schrö-dinger: What's life ?

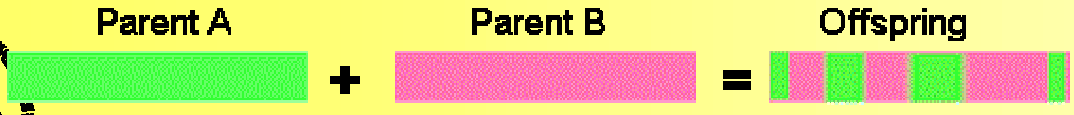


Neural networks !



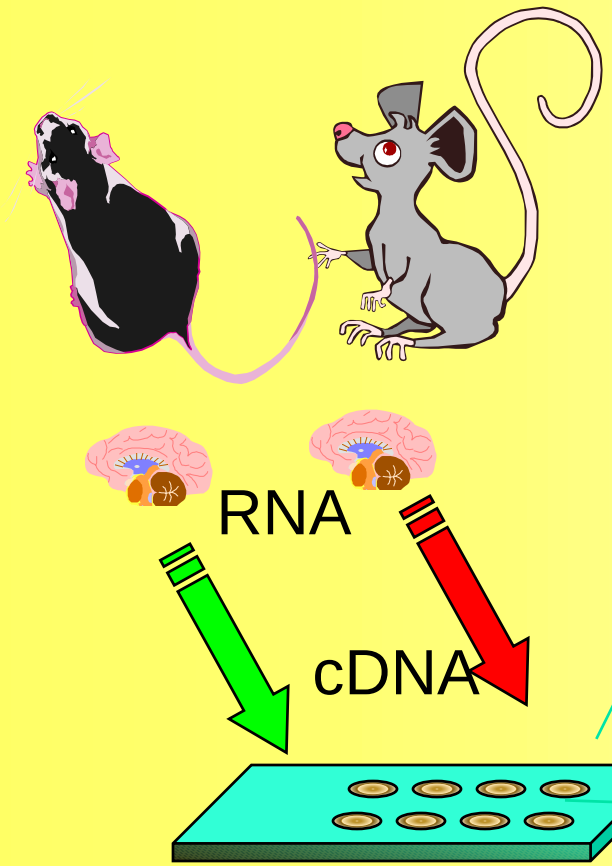
DNA computers

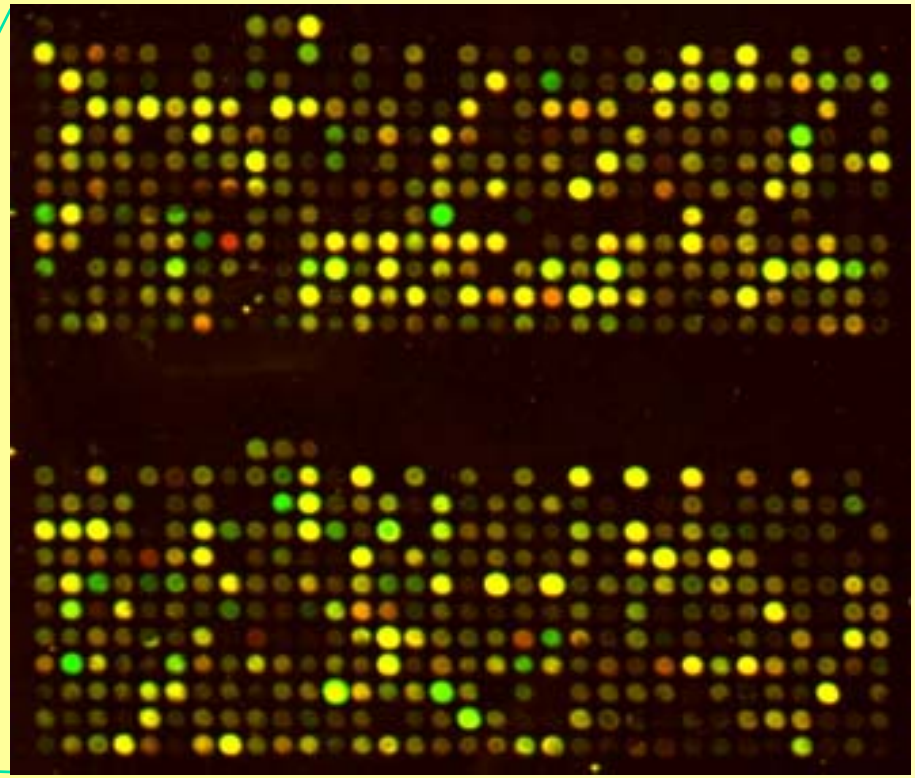
Genetic algorithms = optimization by 'survival of the fittest'



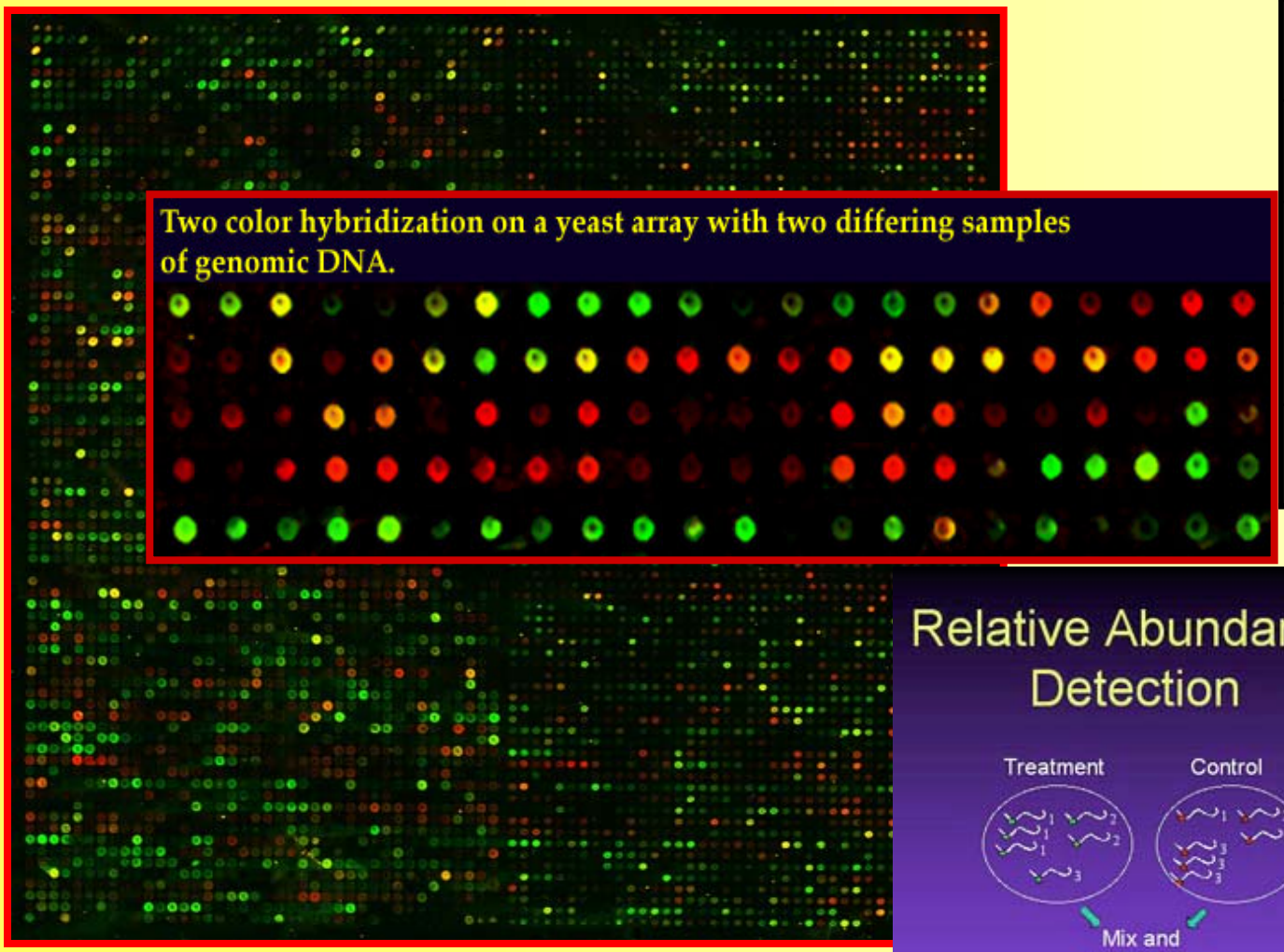
Contents

Differentially expressed genes

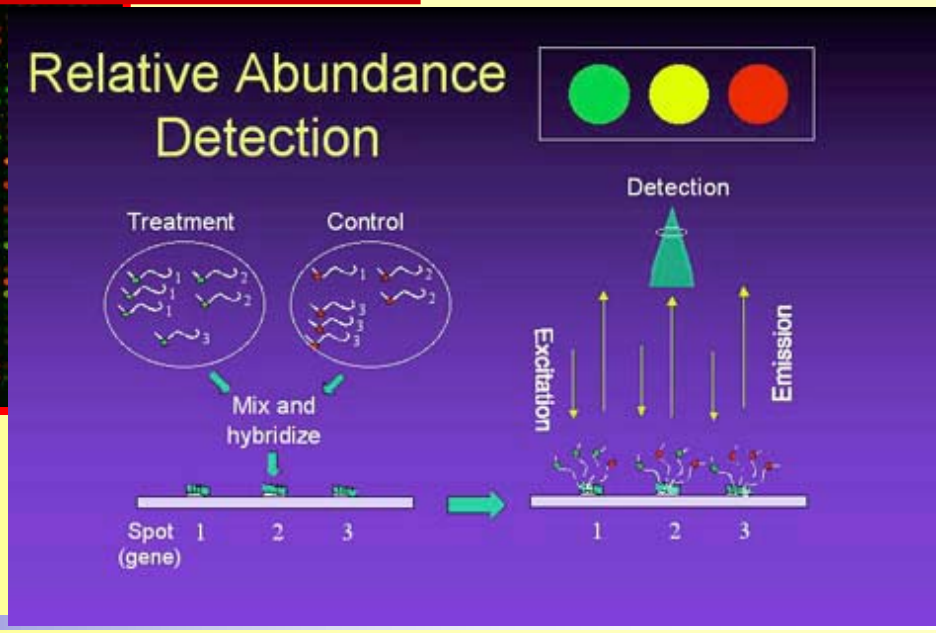




Technology: Microarrays / DNA-chips



	Test	Ref.
	High	Low
	Low	High
	High	High
	Low	Low



Contents

Bio-informatics

-High-throughput technology → lots of 'wet lab' data

-Computers → computing power

-Internet → Publicly accessible databases

-Applied mathematics, statistics, numerical algorithms, machine learning, data mining

Some cases / examples:

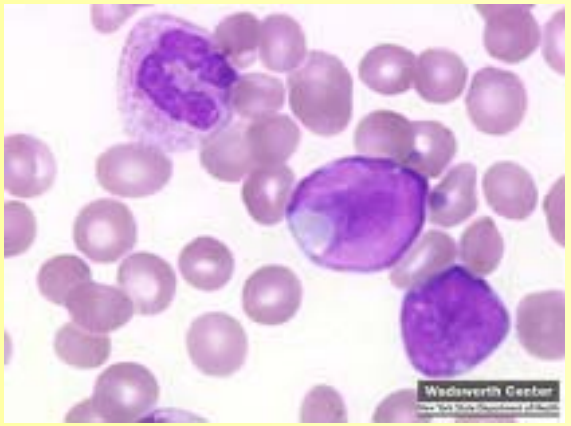
- Clinical bio-i: Classification of leukemia
- Gene regulation bio-i: Finding motifs in DNA sequences

Example: Classification of leukemia

12 600 genes

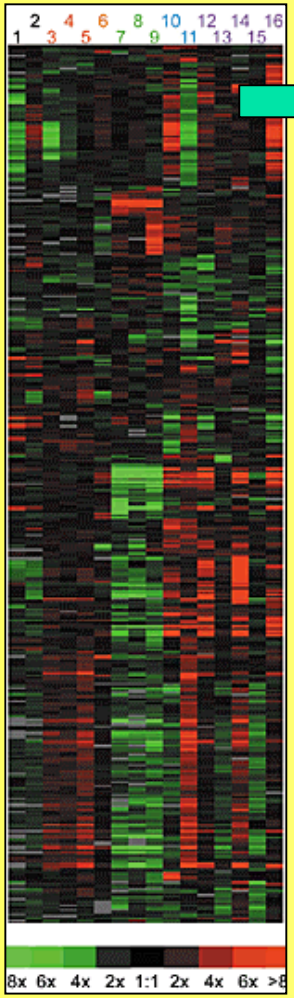
72 patients:

- 28 Acute Lymphoblastic Leukemia (ALL)
- 24 Acute Myeloid Leukemia (AML)
- 20 Mixed Linkage Leukemia (MLL)

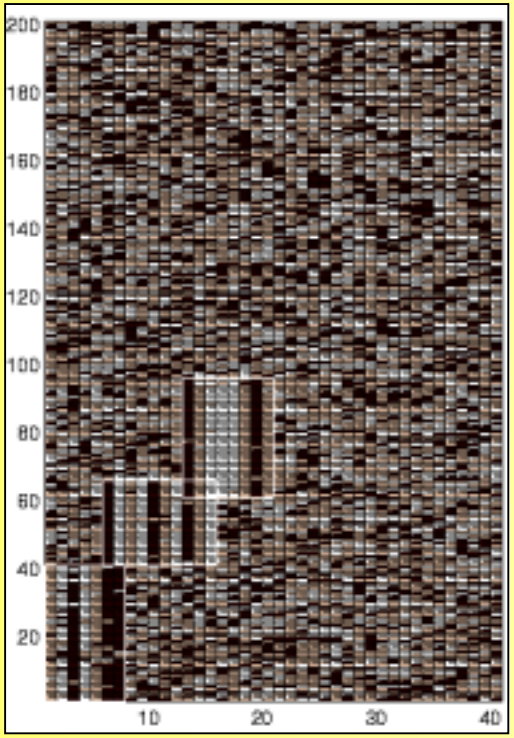


Pattern recognition algorithms

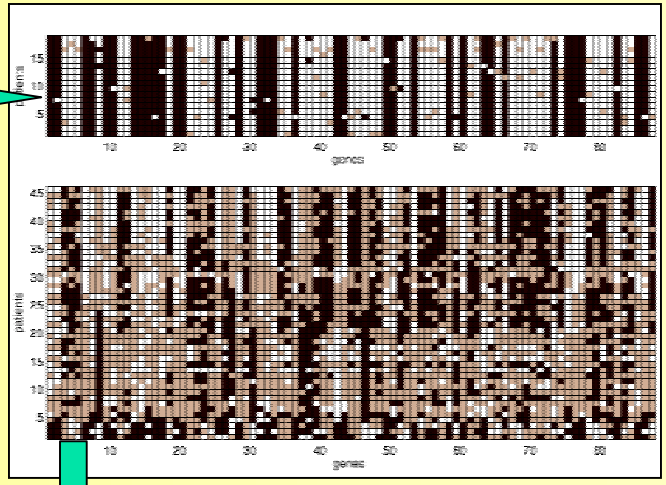
Data matrix



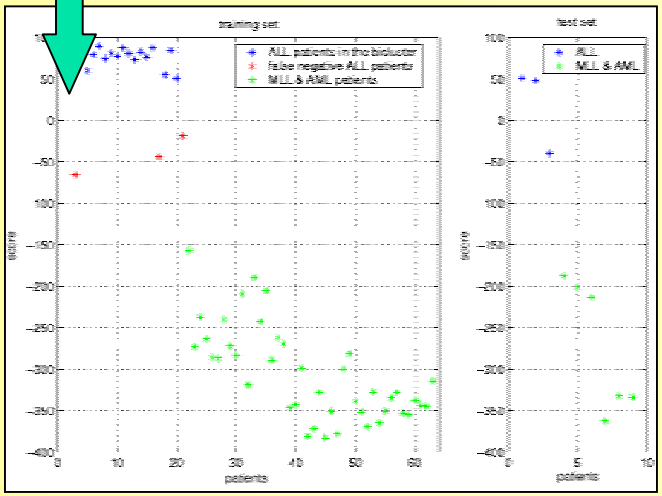
Hidden pattern



Find the pattern

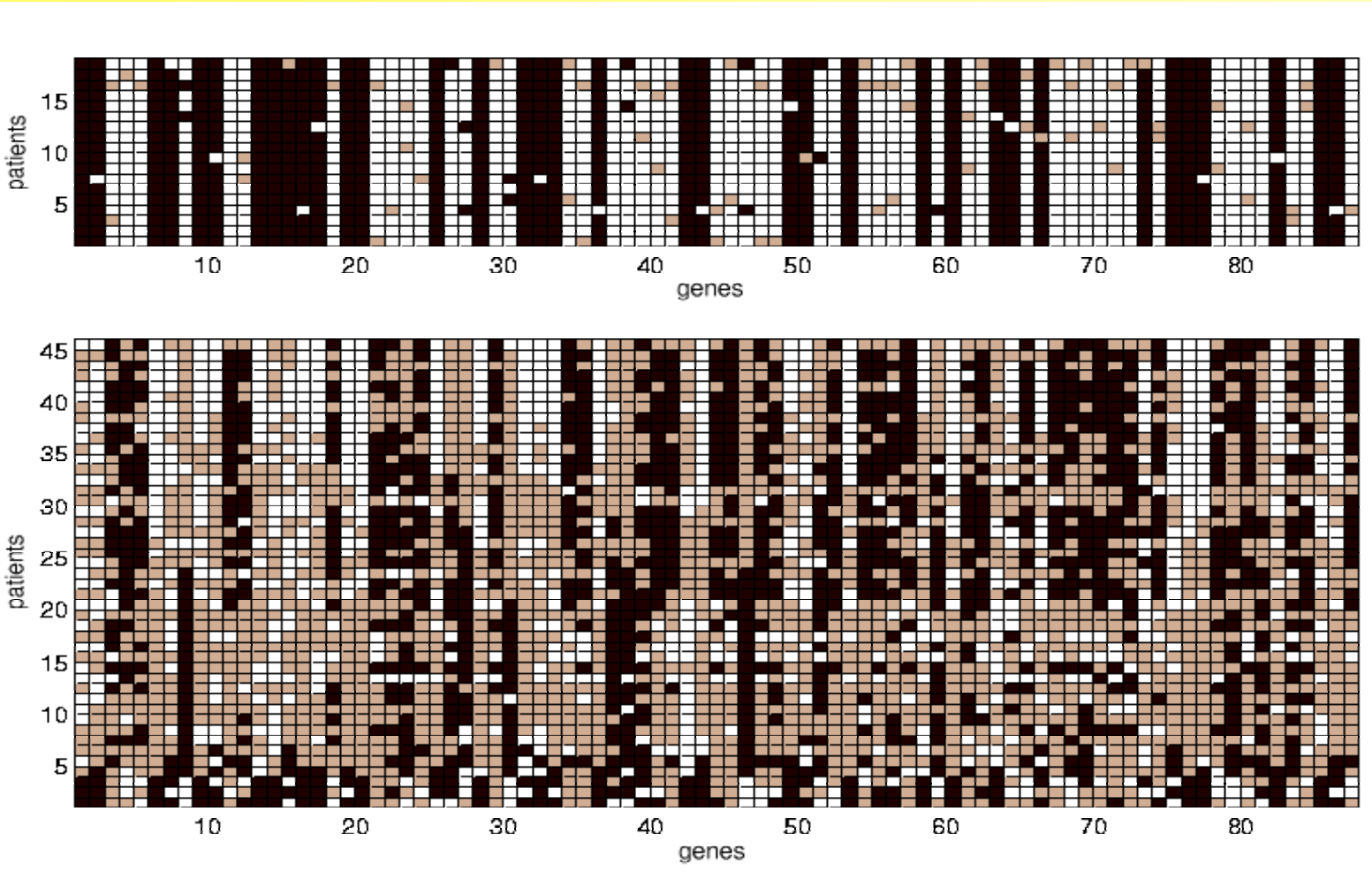


Pattern validation



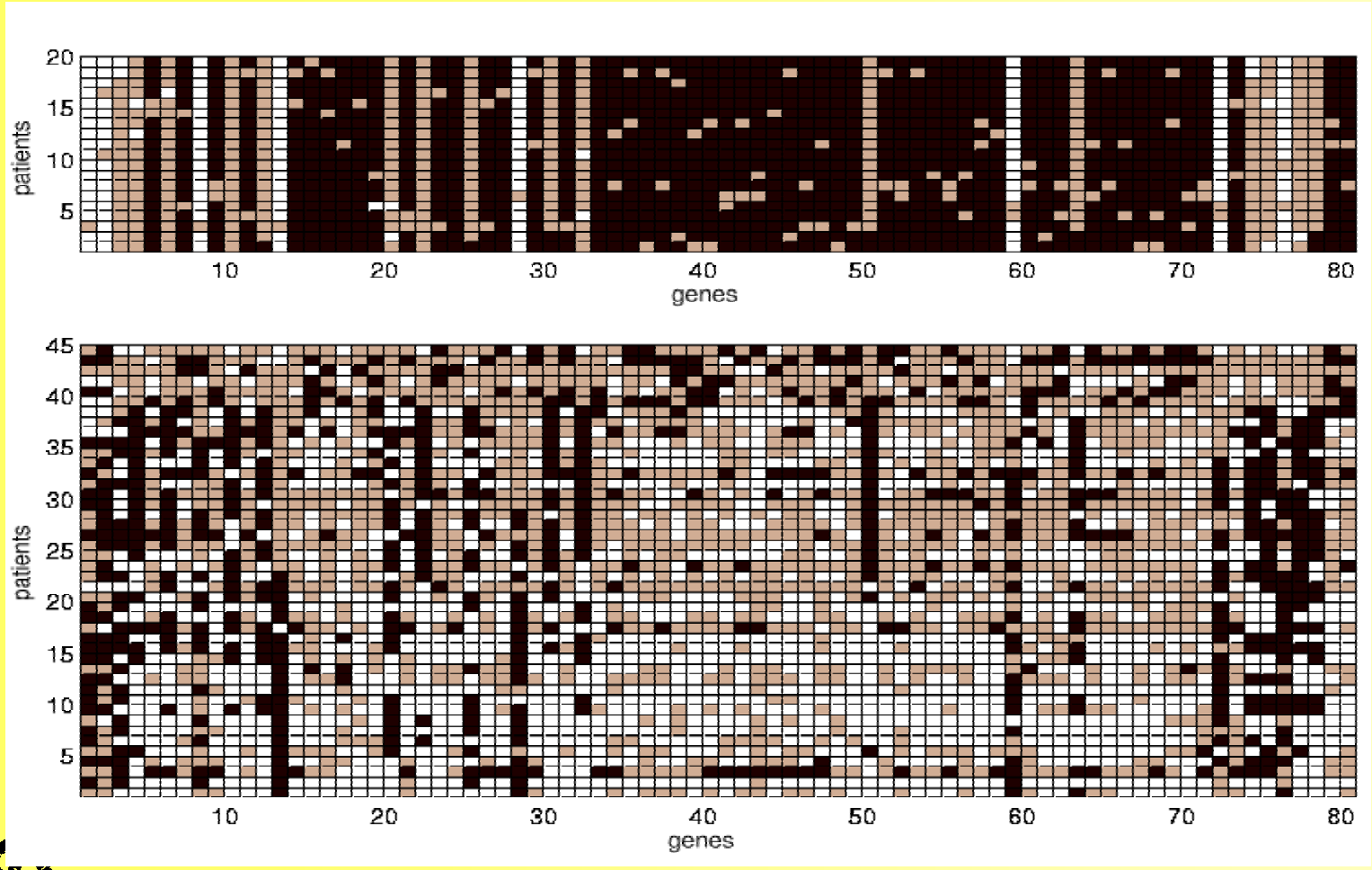
AML Pattern (=fingerprint)

18 AML patients (of 21) with 87 genes



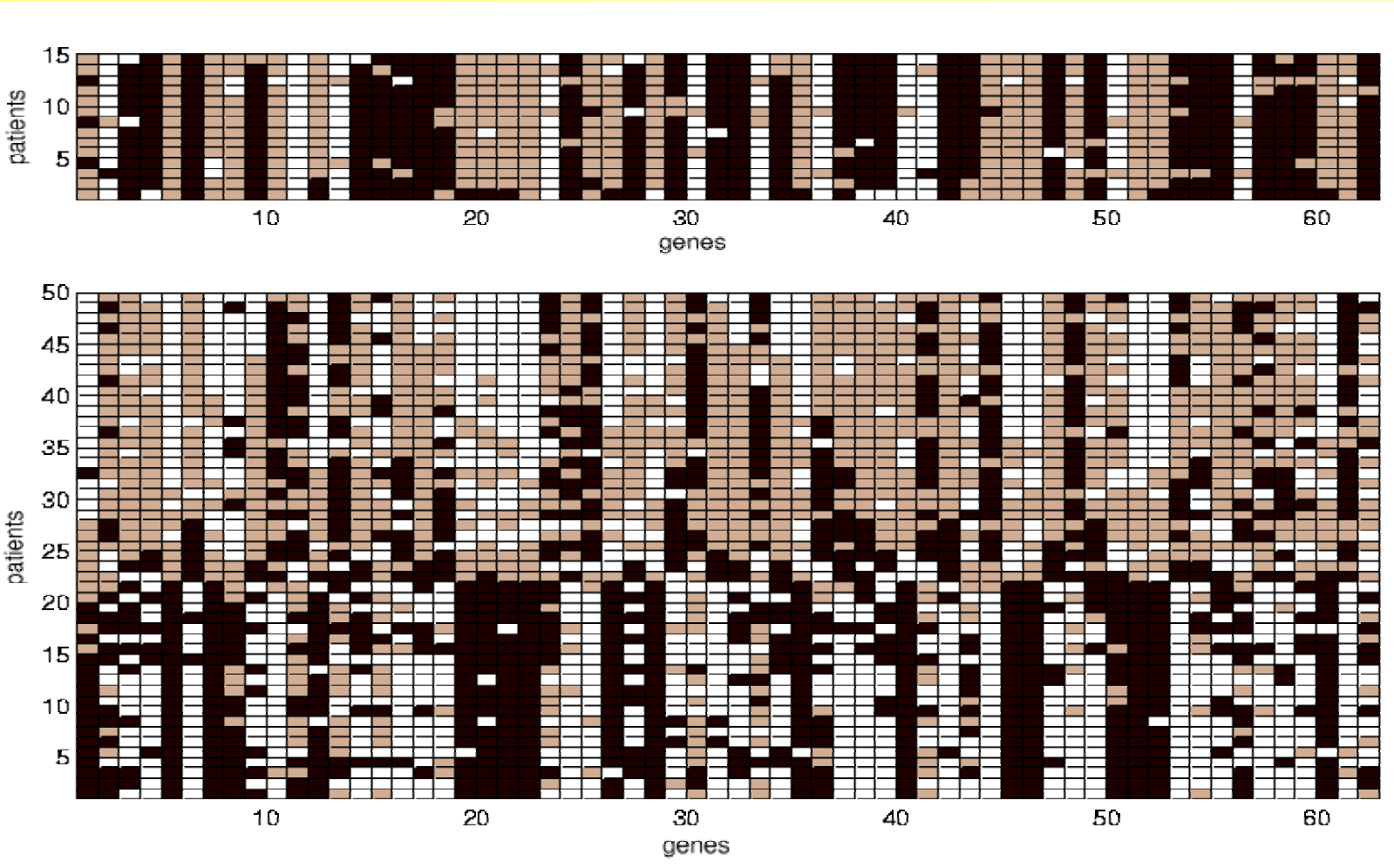
ALL pattern (=fingerprint)

19 ALL patienten (of 25) with 80 genes

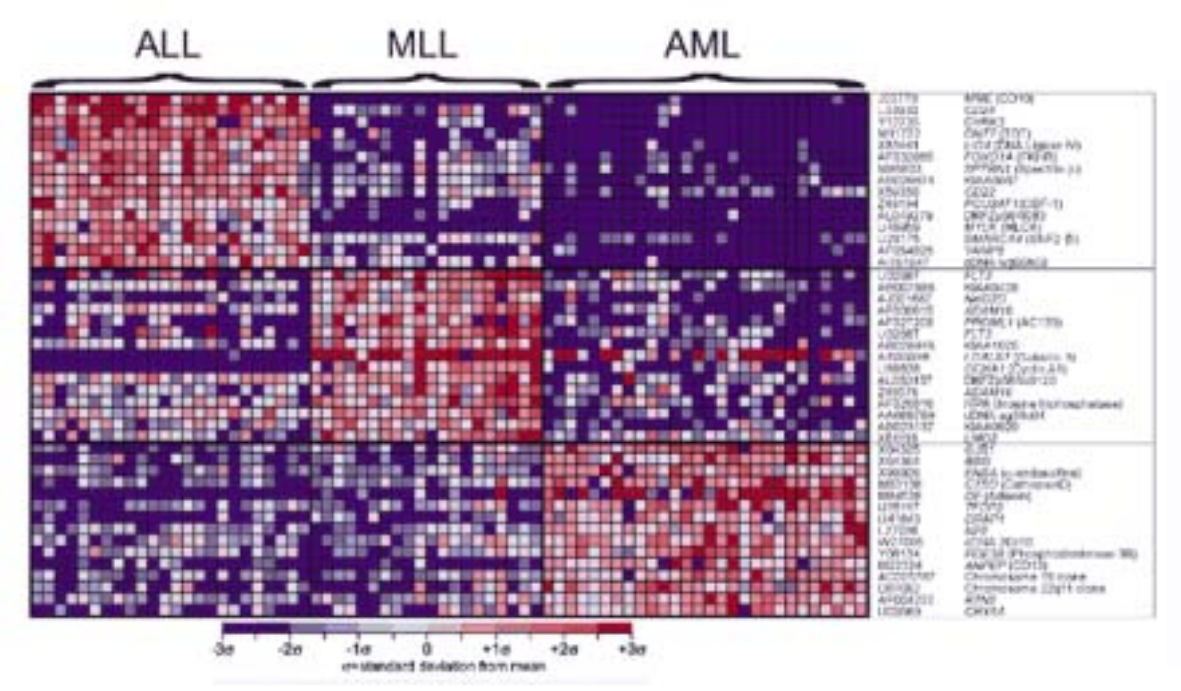


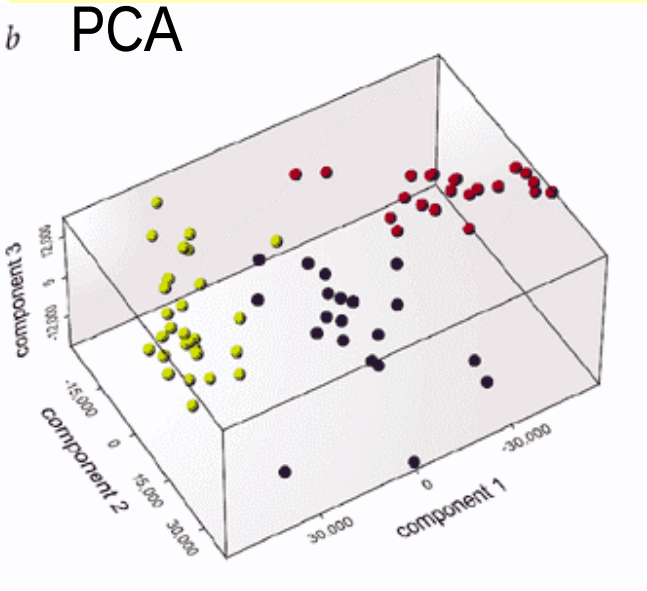
MLL pattern (=fingerprint)

14 MLL patienten (of 17) with 62 genes



ALL / AML / MLL dataset





12 600 genes

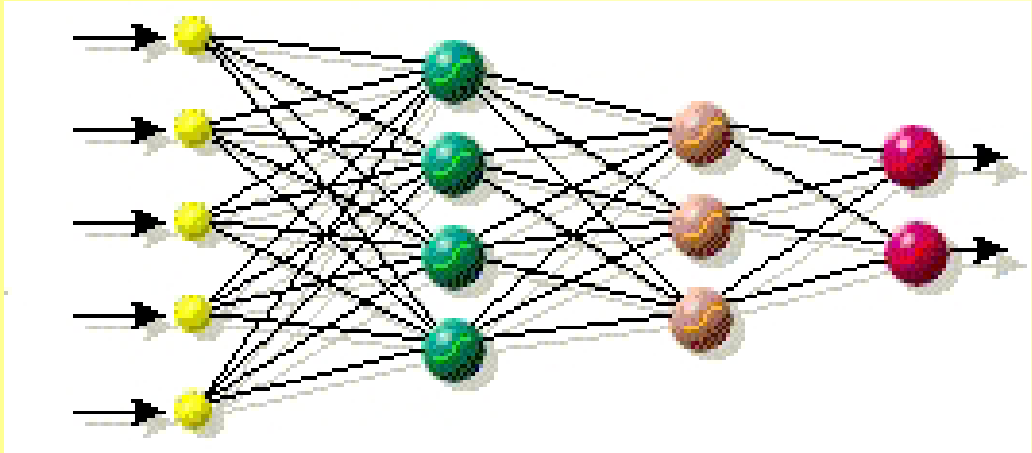
72 patients:

- 28 Acute Lymphoblastic Leukemia (ALL)
- 24 Acute Myeloid Leukemia (AML)
- 20 Mixed Linkage Leukemia (MLL)

3 patients for each class used as test set

How many genes needed for diagnosis ?

Neural net



number of genes	% area ROC training	% area ROC prospective
20	1	1
15	1	1
10	1	99.29
5	1	98.57
4	1	98.57
3	1	97.50
2	98.32	98.21
1	93.60	71.07

Relevance:
Diagnostic kit

Bio-informatics

-High-throughput technology → lots of 'wet lab' data

-Computers → computing power

-Internet → Publicly accessible databases

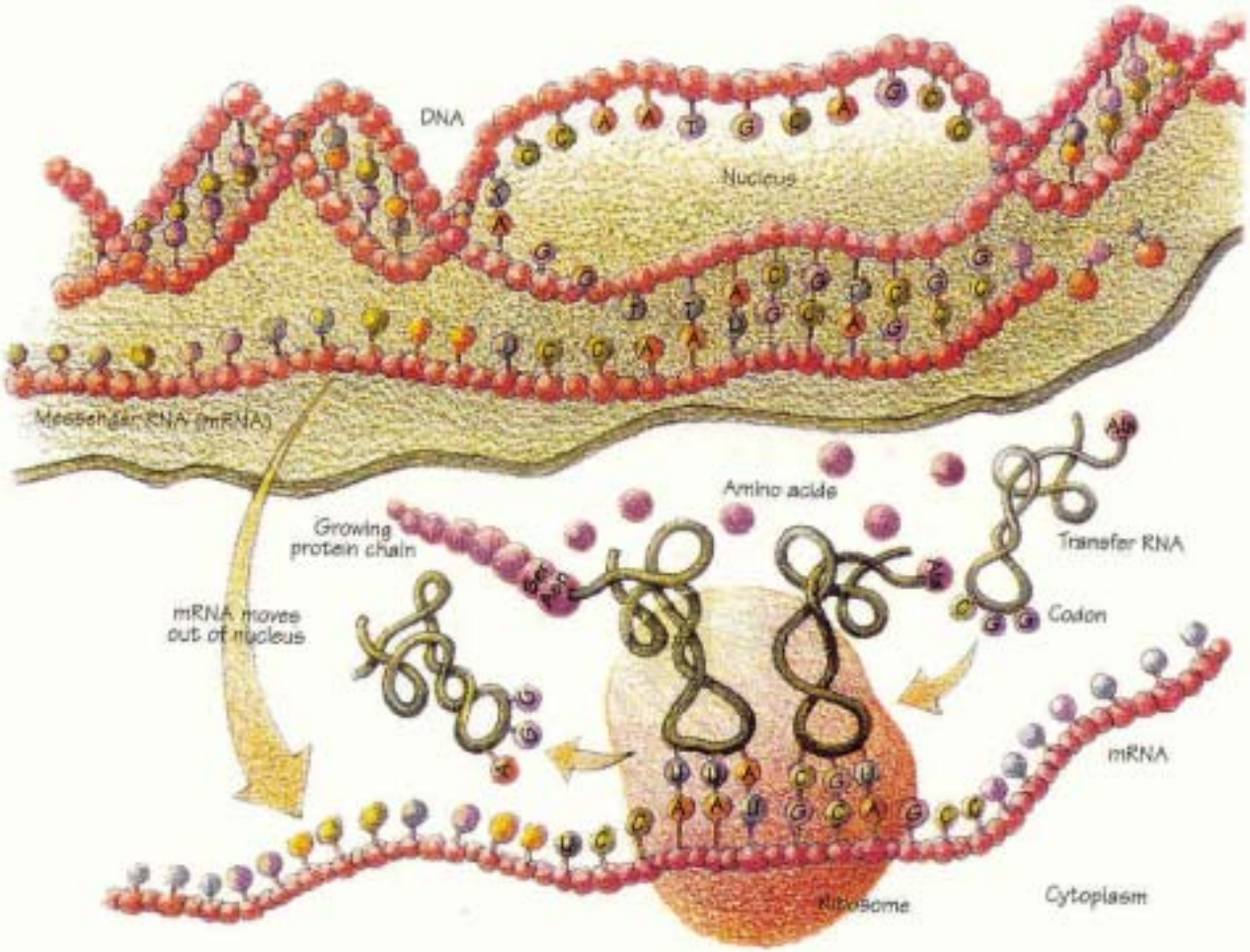
-Applied mathematics, statistics, numerical algorithms, machine learning, data mining

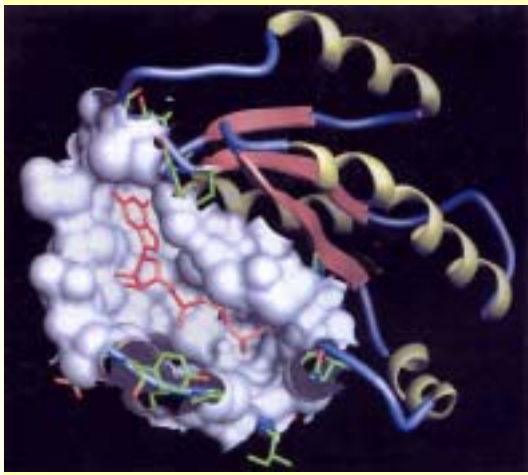
Some cases / examples:

- Clinical bio-i: Classification of leukemia
- Gene regulation bio-i: Finding motifs in DNA sequences

Central dogma (Crick, 1958)

DNA – mRNA – codon – amino-acid - protein

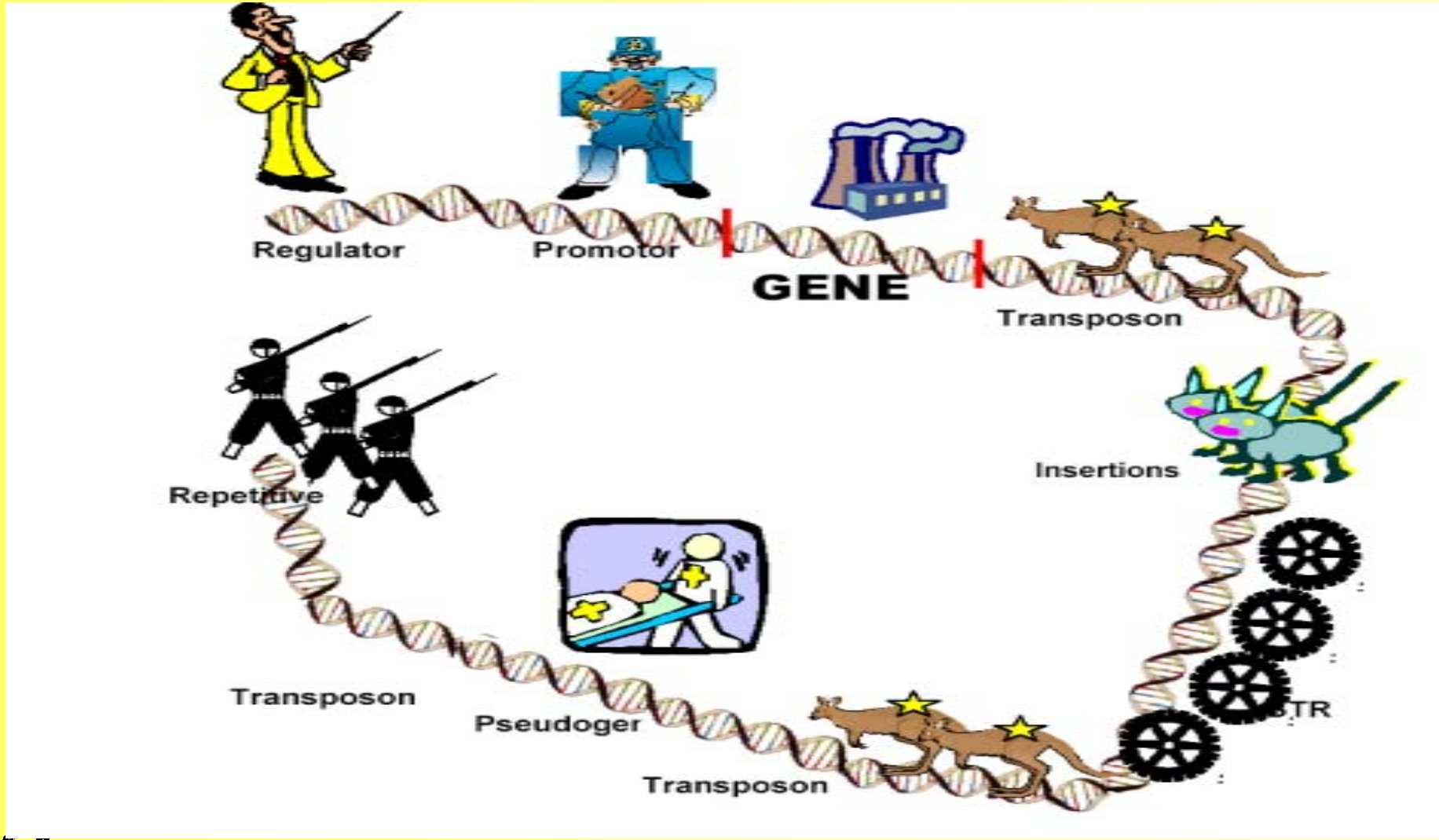




Protein:
-linear polymer
-100000s
-3D-Folding / docking
-'workhorse'

Exceptions exist: e.g. retrovirus (HIV)

Detecting regulatory elements



Junk DNA ?

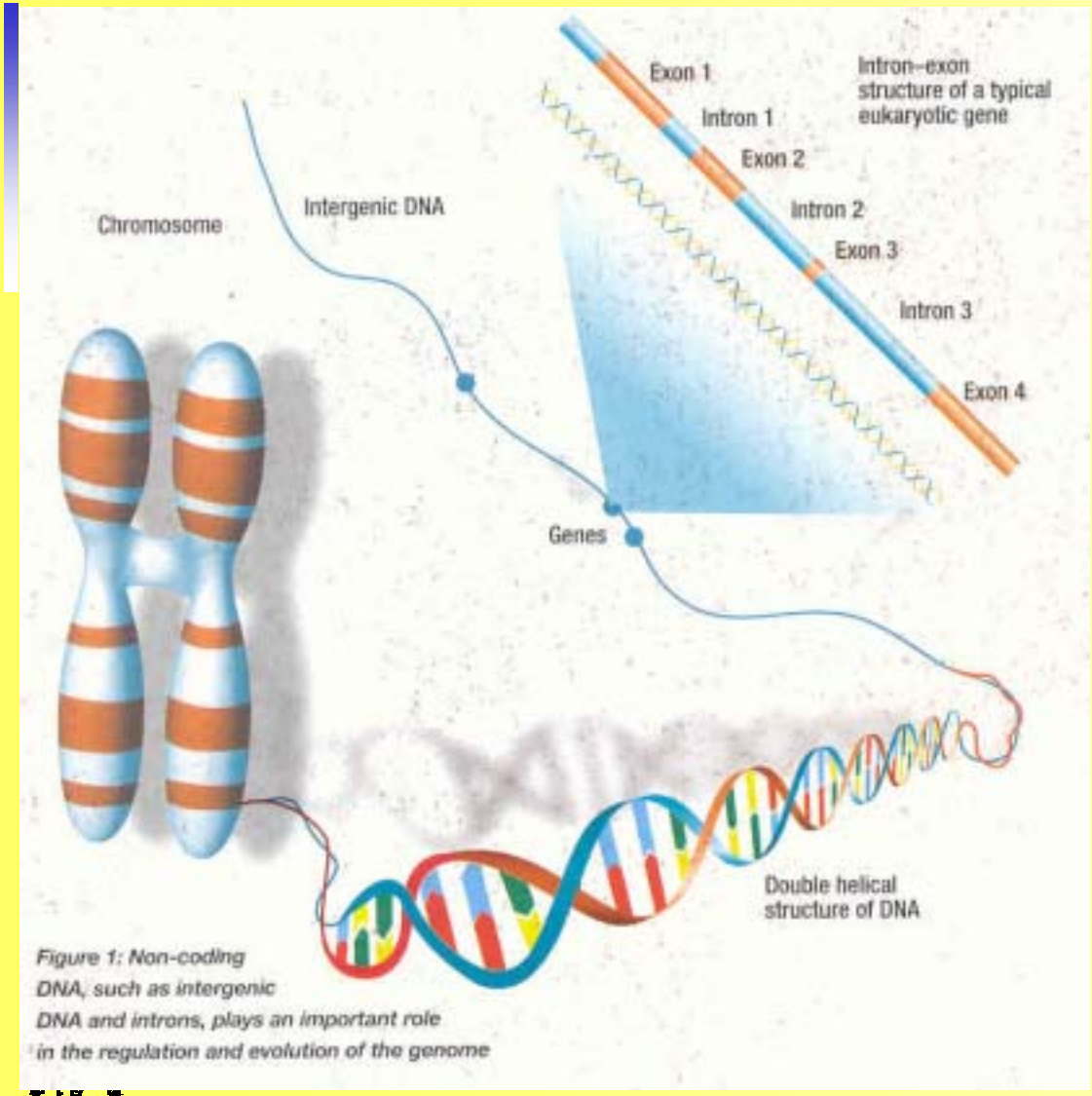


Figure 1: Non-coding DNA, such as intergenic DNA and introns, plays an important role in the regulation and evolution of the genome

3 % of human genome: genes
97 % non-coding

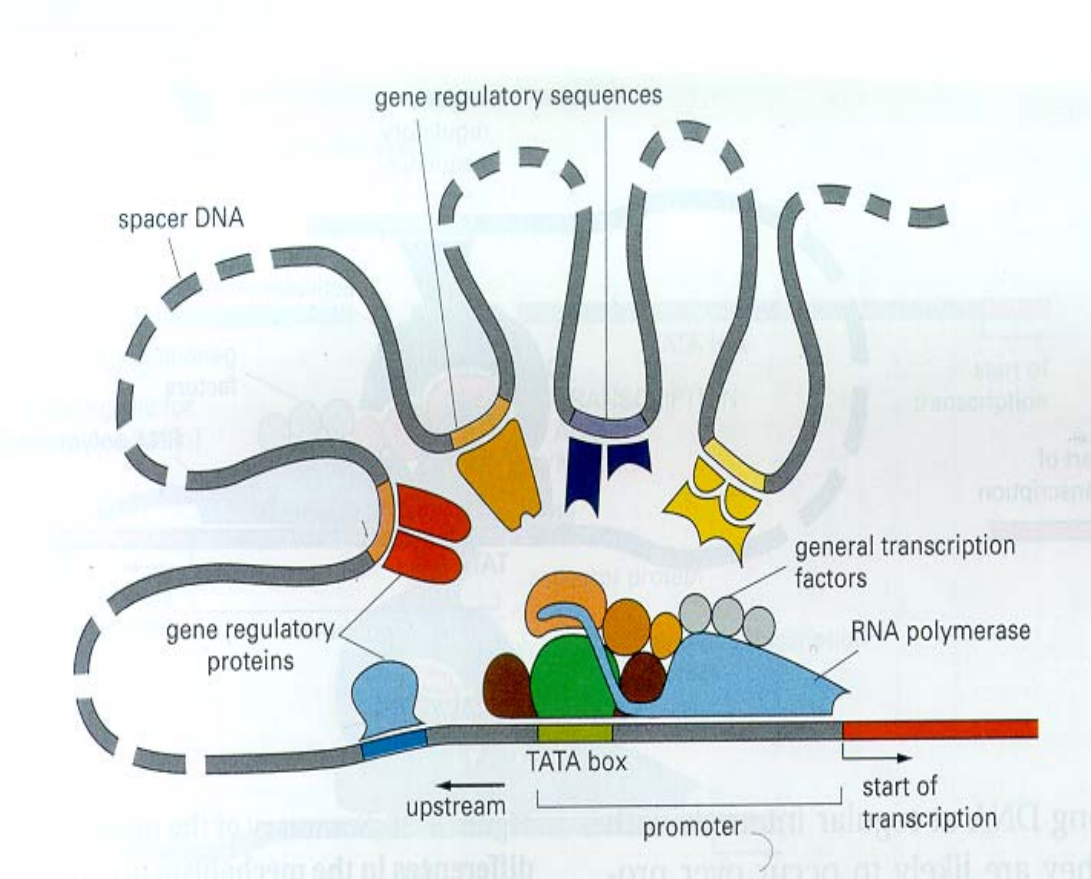
Introns contain
-Lots of DNA function unknown
-Centromeres
-Telomeres
-Regulators
-Promotors, enhancers
-Suppressors

During transcription, introns are removed (splicing)

Regulatory elements

-Many intermediate signals co-determine gene activity

-Regulatory elements determine when and how much a gene is active

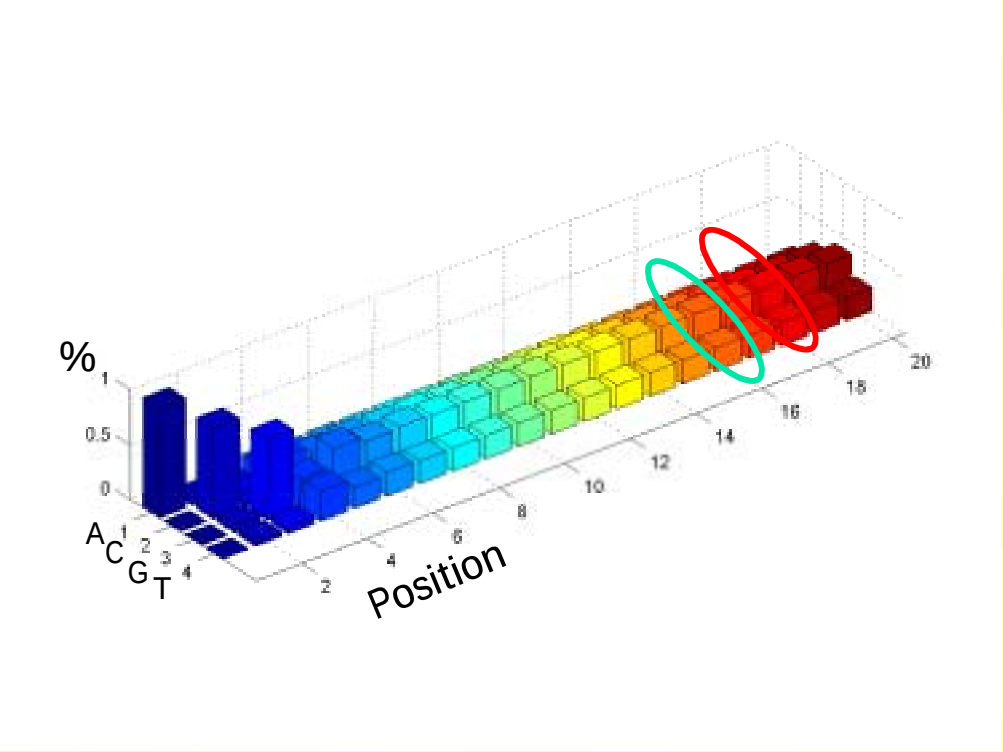


DNA Markov model

	A	C	G	T
A	*0.0643*	*0.8268*	*0.0659*	*0.0430*
C	*0.0598*	*0.0484*	*0.8515*	*0.0403*
G	*0.1602*	*0.3407*	*0.1736*	*0.3255*
T	*0.1507*	*0.1608*	*0.3654*	*0.3231*

$$\begin{pmatrix} 0.1188 \\ 0.2788 \\ 0.3905 \\ 0.2119 \end{pmatrix}^{T} \cdot \begin{pmatrix} 0.0643 & 0.8268 & 0.0659 & 0.0430 \\ 0.0598 & 0.0484 & 0.8515 & 0.0403 \\ 0.1602 & 0.3407 & 0.1736 & 0.3255 \\ 0.1507 & 0.1608 & 0.3654 & 0.3231 \end{pmatrix} = \begin{pmatrix} 0.1188 \\ 0.2788 \\ 0.3905 \\ 0.2119 \end{pmatrix}$$

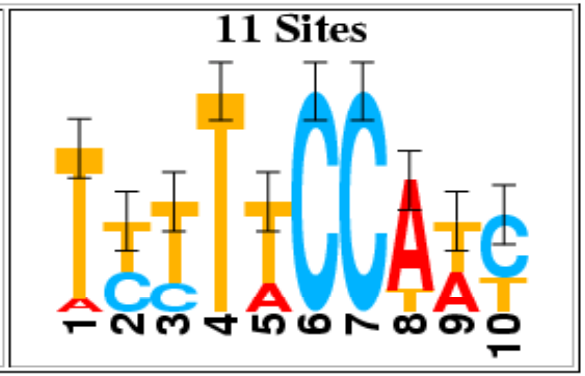
ACGCGGTGTGCGTTTGACGA
ACGGTTACGCGACGTTTGGT
ACGTGCGGTGTACGTGTACG
ACGGAGTTTGCGGGACGCGT
ACGCGCGTGACGTACGCGTG
AGACGCGTGCGCGCGGACGC
ACGGGCGTGCGCGCGGTGCG
AACGCGTTTGTGTTCGCTGC
ACCGCGTTTGACGTCGCTTC
ACGTGACGCGTAGTTCGACG
ACGTGACACGGACGTACGCG
ACCGTACTCGCGTTGACACG
ATACGGCGCGGCGCGCGCGG
ACGTACGCGTACACGCGGGA
ACGCGCGTGTTTACGACGTG
ACGTCGCACGCGTCGGTGTG
ACGGCGGTCGGTACACGTCG
ACGTTGCGACGTGCGTGCTG
ACGGAACGACGACGCGACGC
ACGGCGTGTTCGCGGTGCGG



Statistical model of a motif

Motif 2: TyTTTCCAwC

	1	2	3	4	5	6	7	8	9	10
A	0.0979	0.0096	0.0096	0.0096	0.2747	0.0096	0.0096	0.8049	0.4514	0.0096
C	0.0049	0.4467	0.2700	0.0049	0.0049	0.9769	0.9769	0.0049	0.0049	0.6235
G	0.0041	0.0041	0.0041	0.0041	0.0041	0.0041	0.0041	0.0041	0.0041	0.0041
T	0.8931	0.5396	0.7164	0.9815	0.7164	0.0094	0.0094	0.1862	0.5396	0.3629



Scores

Information Content	1.1892
LogLikelihood	65.1569
Consensus Score	1.3043

Alignment:

Name	Position	Site	Prob.
Seq 1	268	TTTTTCCAAT	0.8517
Seq 2	283	TTTTACCAAC	0.9887
	635	TTCTTCCAAT	0.7876
Seq 4	512	TTTTTCCATT	0.9053
Seq 5	442	TTTTTCCAAC	0.9980
	200	TCTTTCCTTC	0.9183
Seq 6	349	TCTTACCATC	0.9994
	513	TCCTACCATC	0.9465
Seq 7	286	TCTTTCCTTC	0.9509
Seq 8	346	ATTTTCCATT	0.5764
Seq 9	229	TCCTTCCAAC	0.9806

How to find motifs ?

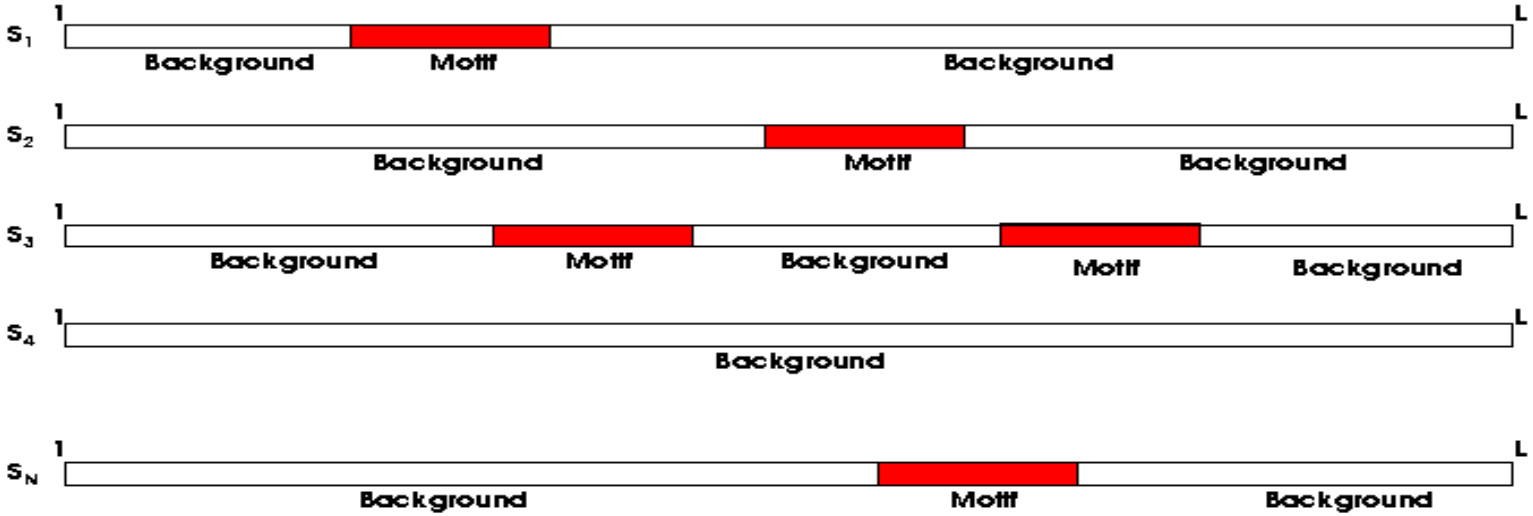
W.r.t. DNA background, look for 'overrepresented' patterns

-by analysing 'similarity' in DNA conserved regions between species;

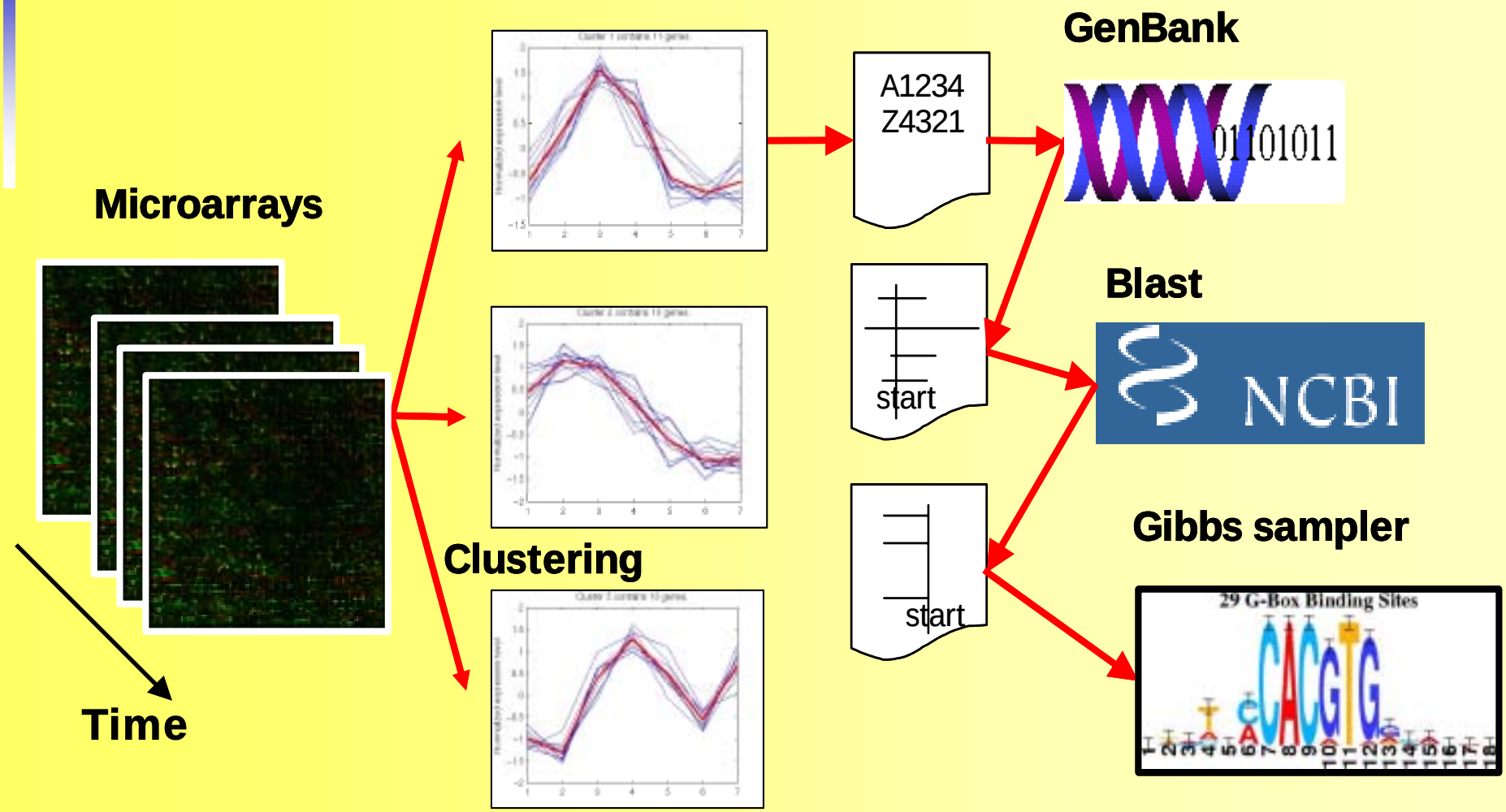
-'upstream' of co-expressed genes in one species;

Identifying regulatory sequences

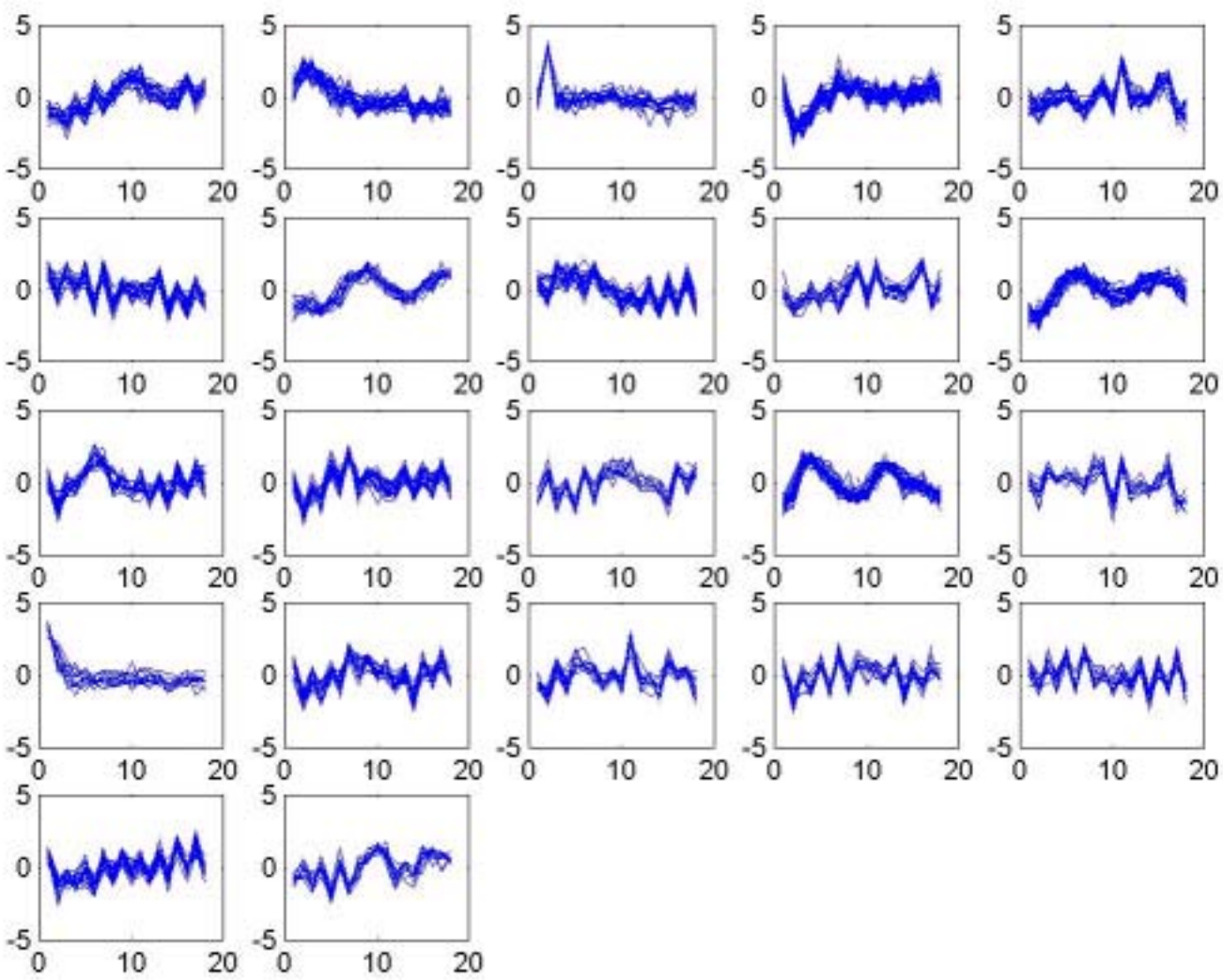
- Cluster genes from microarray expression data to build clusters of coexpressed genes
- Coexpressed genes may share regulatory mechanisms
- Most regulatory sequences are found in the upstream region of the genes (up to 2kb in *A. thaliana*)
- Motifs that are statistically overrepresented in the upstream regions are candidate regulatory sequences



Clustering then motif finding



Clusters: ‘Guilt by association’



Zooming in on one cluster

Results: BioDemo_270369

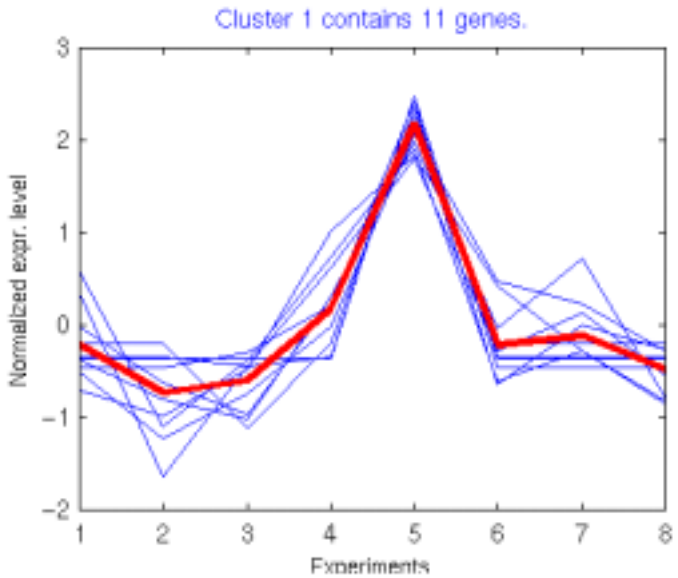
Input Parameters:

- Required probability of genes belonging to cluster: 0.95
- Minimal number of genes in cluster: 3
- Total number of genes in data set: 138

Results:

- Number of clusters: 12
- Number of genes not in a cluster: 68

Cluster 1



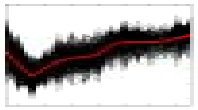
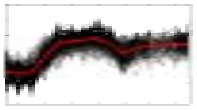
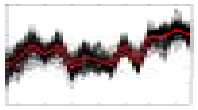
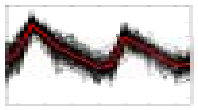
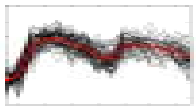
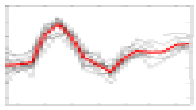
Accession Number	Gene Name
X99793	AWI31
L40031	CCOAMT
X67816	ELI3
X91957	GER2
AJ000470	GPX2
J04537	HMG1
AC001645	JIP
AF001168	LECRK
n.a.	MEKKK
U09958	NIT2
M34107	PR3AIII

Fetch Sequences

Similarity measure
-Euclidean distance
-Euclidean angle

Relevancy of measure?
- Biologically ?
- Dynamics (e.g. distance between time responses)?

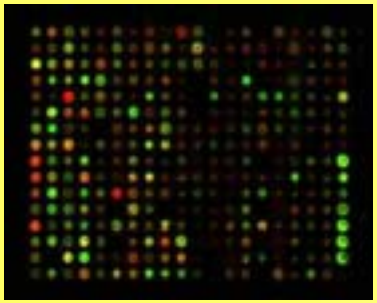
Results

Cluster number	Graphical representation of cluster	Number of ORFs	MIPS functional category (top-level)	ORFs within functional category	P-value ($-\log_{10}$)
1		426	energy transport facilitation	47 40	10 5
3		196	cell growth, cell division and DNA synthesis	48	5
4		149	protein synthesis cellular organisation	71 107	50 19
5		159	cell rescue, defense, cell death and ageing	20	4
6		171	cell growth, cell division and DNA synthesis	76	24
9		78	cell growth, cell division and DNA synthesis	23	4
37		11	metabolism	9	6

Arabidopsis Thaliana

Cluster	Consensus motif	Runs	PlantCARE	Description
1 [11 seq.]	TAArTAAGTCAC ATTCAAATTT CTTCTTCGATCT	7/10 8/10 5/10	TGAGTCA CGTCA ATACAAAT TTCGACC	Tissue specific GCN4-motif MeJA-responsive element element assoc. to GCN4-motif elicitor responsive element
2 [6 seq.]	TTGACyCGy mACGTCACCT	5/10 7/10	TGACG (T)TGAC(C) CGTCA ACGT	MeJa responsive element elicitor responsive element MeJA responsive element Abcissic acid response element
3 [5 seq.]	wATATATATmTT TCTwCnTC ATAAATAkGCnT	5/10 9/10 7/10	TATATA TCTCCCT -	TATA-box like element TCCC-motif,light response elem. -
4 [5 seq.]	yTGACCGTCCsA CACGTGG GCCTymTT AGAATCAAT	9/10 5/10 8/10 6/10	CCGTCC CCGTCC TGACG CGTCA CACGTG ACGT - -	meristem specific activation of H4 gene A-box, light or elicitor responsive element MeJA responsive element MeJA responsive element G-box light responsive element Abcissic acid response element - -

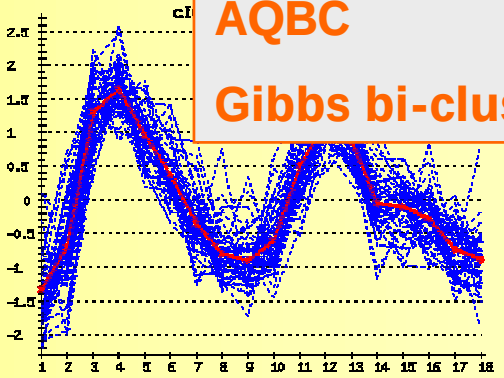
INCLUSive: online analysis of µ-array data



MARAN

Pre-processing

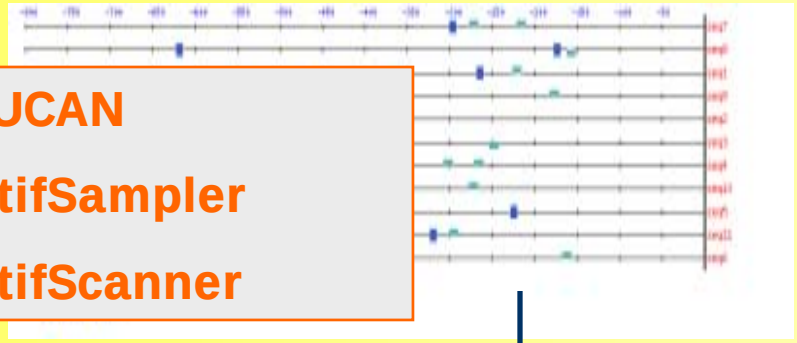
Clustering



AQBC

Gibbs bi-clustering

Sequence Analysis



TOUCAN

MotifSampler

MotifScanner

Functional Annotation

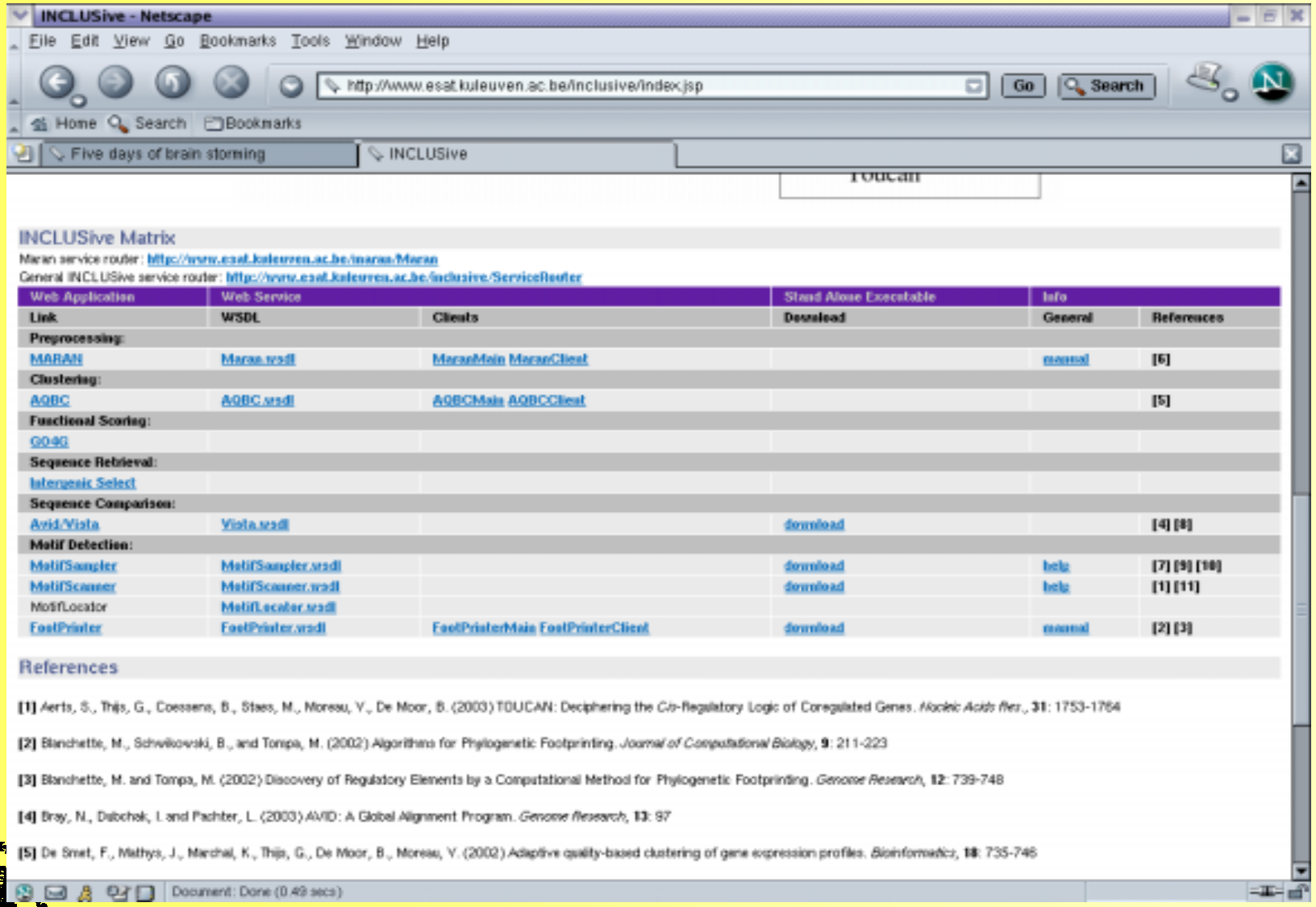
- Gene Ontology
- Text mining
- OMIM
- LocusLink

TXTGate

Go4G

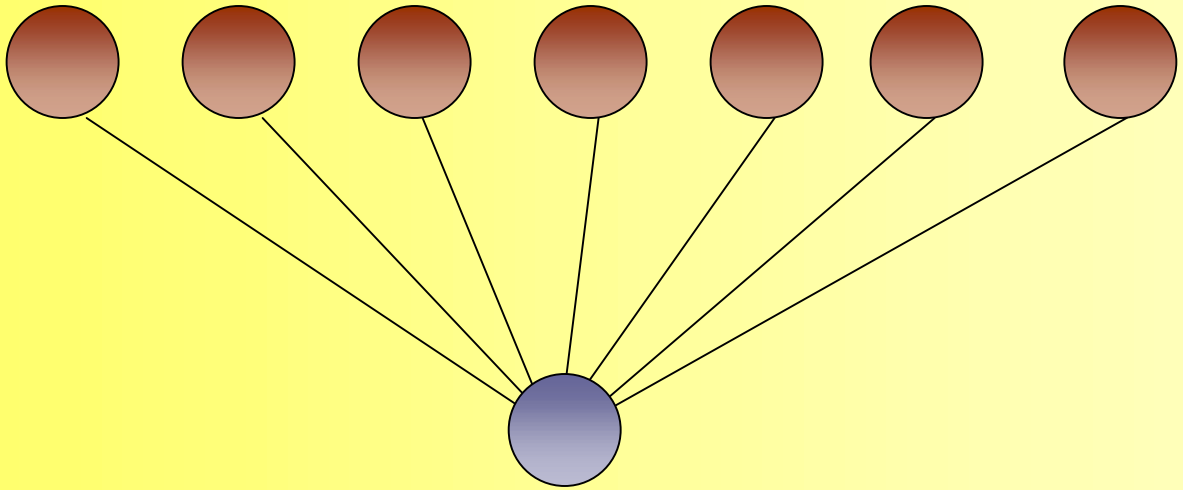
http://www.esat.kuleuven.ac.be/inclusive/

INCLUSive – web portal

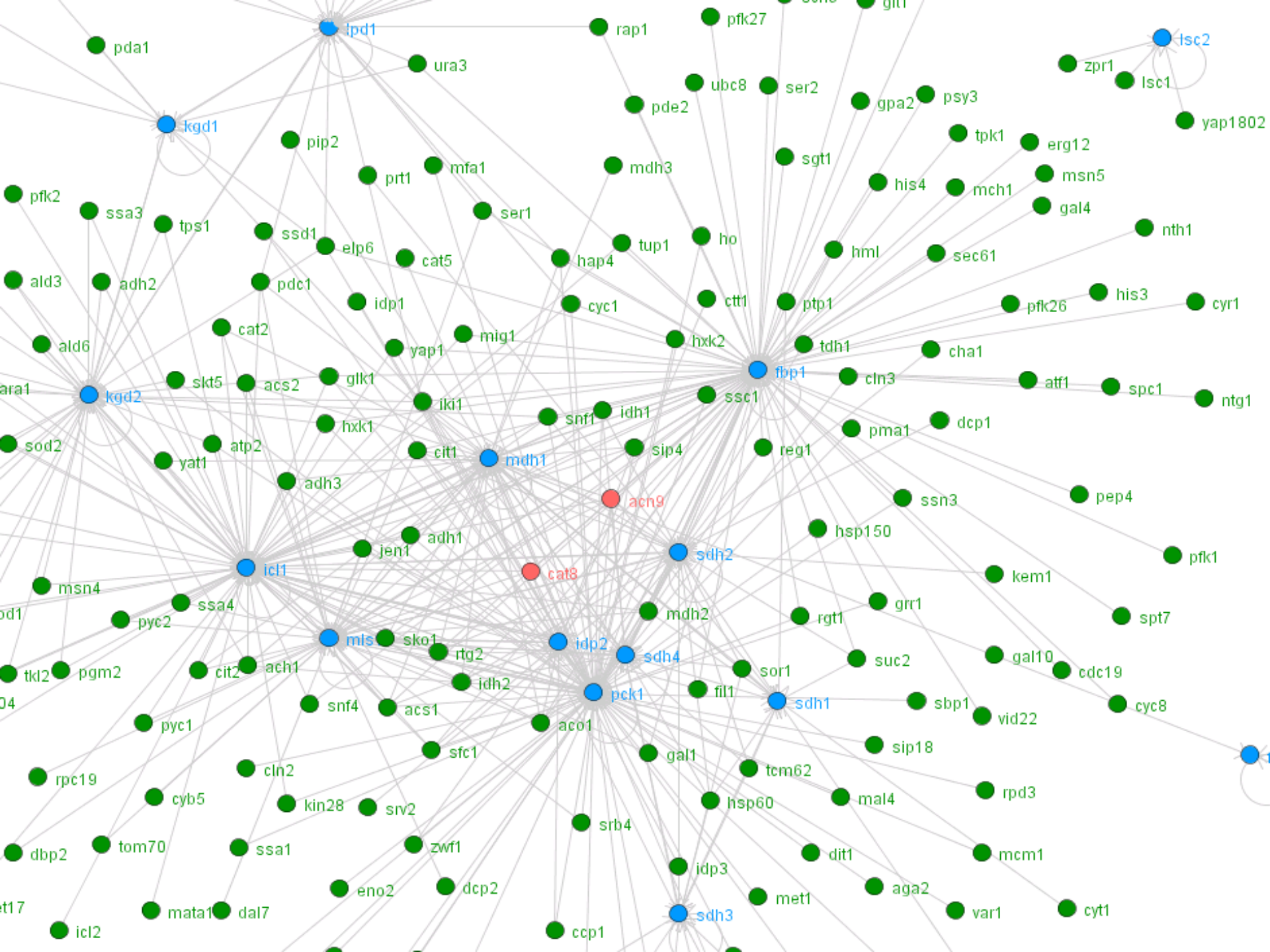


Endeavour: data & algorithm integration

Gene expression | Anatomical expression | Literature | Biological process | Gene regulation | Protein domains | Evolutionary conservation | ...

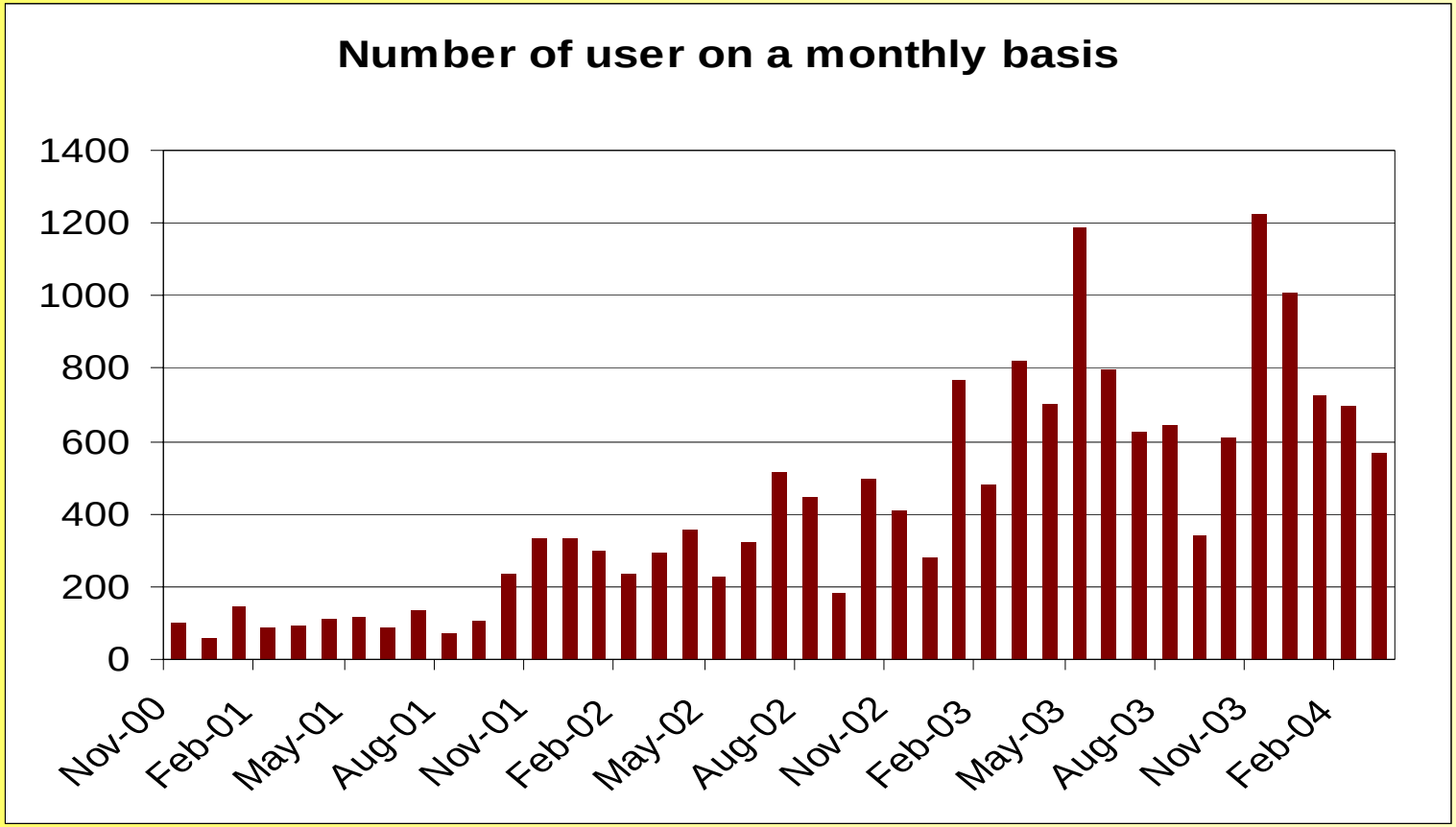


Pathology


lpd1
pda1
ura3
rap1
pfk27
lsc2
zpr1
lsc1
yap1802
kgd1
pip2
ubc8
ser2
pde2
gpa2
psy3
tpk1
erg12
msn5
gal4
nth1
pfk2
ssa3
tps1
prt1
mfa1
mdh3
sgt1
his4
mch1
ser1
ssd1
elp6
cat5
tup1
ho
hml
sec61
ald3
adh2
pdc1
hap4
idp1
cyc1
ctt1
ptp1
pfk26
his3
cyr1
cat2
ald6
yap1
mig1
hxk2
tdh1
cha1
fbp1
cln3
atf1
spc1
ntg1
kgd2
skt5
acs2
glk1
iki1
ssc1
snf1
idh1
pma1
dcp1
sod2
hxk1
atp2
cit1
mdh1
sip4
reg1
yat1
adh3
acn9
ssn3
pep4
adh1
hsp150
jen1
sdh2
pfk1
icl1
cat8
kem1
msn4
ssa4
mdh2
rgt1
grr1
spt7
pyc2
mls1
sko1
idp2
sdh4
suc2
gal10
cdc19
tkl2
pgm2
cit2
ach1
rtg2
idh2
sor1
pck1
fil1
sdh1
sbp1
vid22
cyc8
snf4
acs1
aco1
pyc1
sip18
sfc1
gal1
tcm62
cln2
rpc19
rpd3
cyb5
kin28
srv2
hsp60
mal4
srb4
dbp2
tom70
ssa1
zwf1
dit1
mcm1
idp3
eno2
dcp2
aga2
met1
mata1
dal7
sdh3
var1
cyt1
icl2
ccp1

Software statistics: example

Motif sampler



http://www.esat.kuleuven.ac.be/~dna/BioI/Software.html

Contents

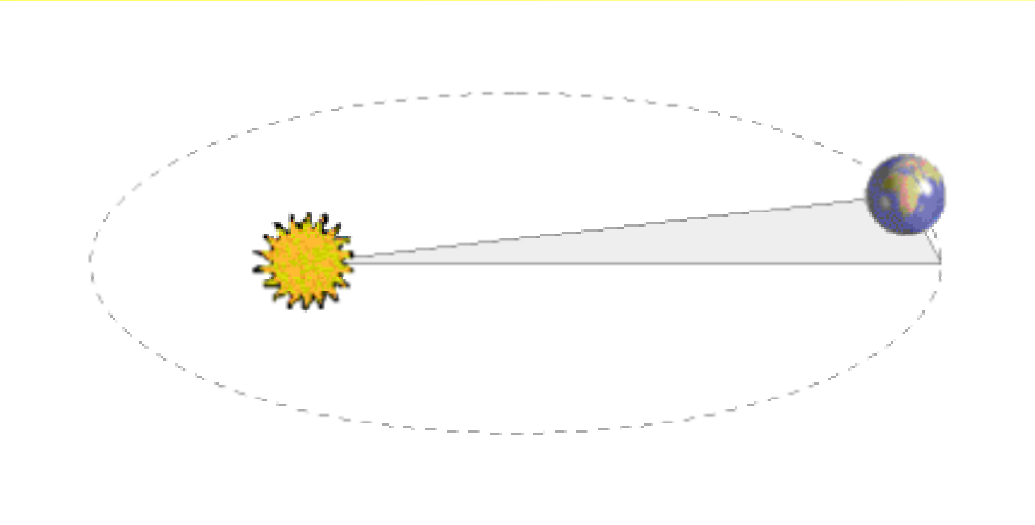
From Kepler to Newton

Kepler's laws:

Law 1: Orbit is ellips with Sun in focus

Law 2: Joing line sweeps out equal areas in equal time

Law 3: $\frac{T_1^2}{T_2^2} = \frac{a_1^3}{a_2^3}$

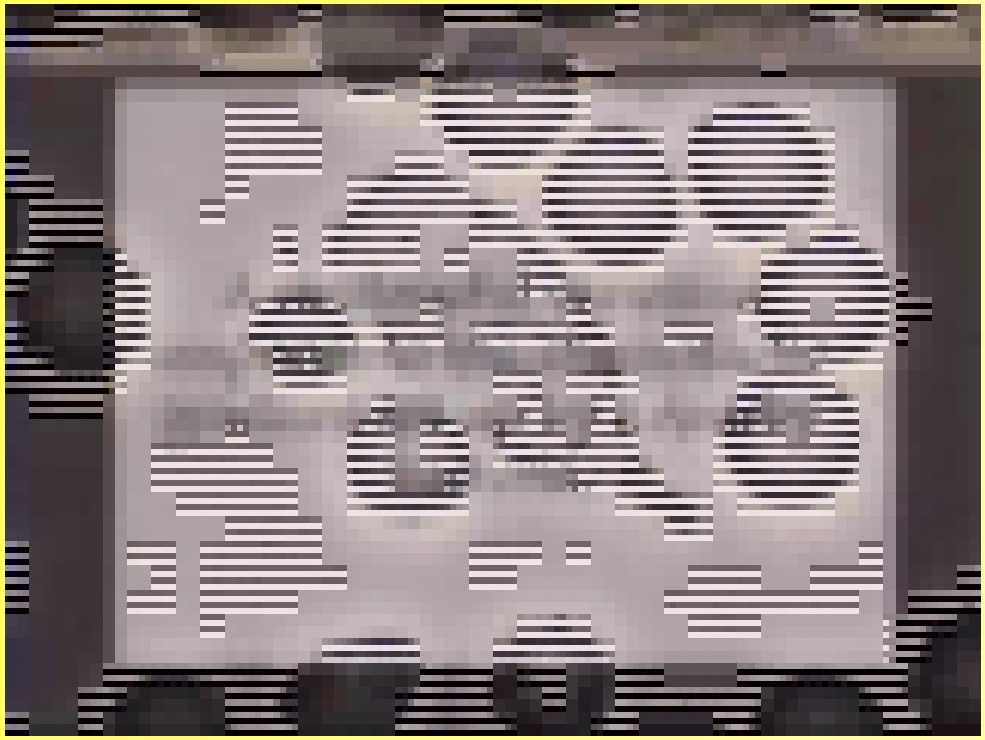


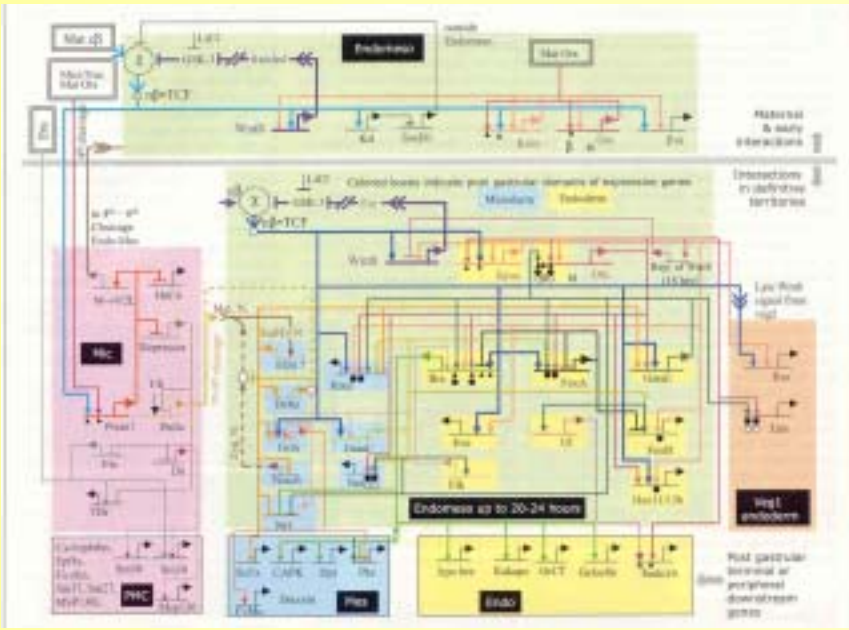
From conic sections to centripetal forces and states

$$\mathbf{F} = m.\mathbf{a}$$

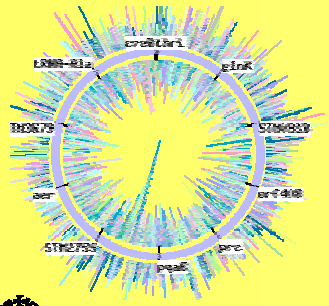
$$F = G\,\frac{m.M}{r^2}$$

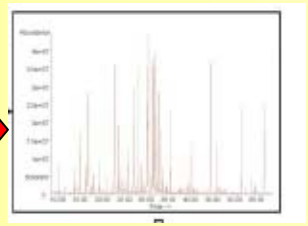
Example: Systems biology: Chemotaxis





‘high throughput ‘data





genome transcriptome proteome metabolome interactome

Frankenstein or the modern Prometheus ?

Venter Cooks Up a Synthetic Genome in Record Time

Elizabeth Pennisi , *Science*

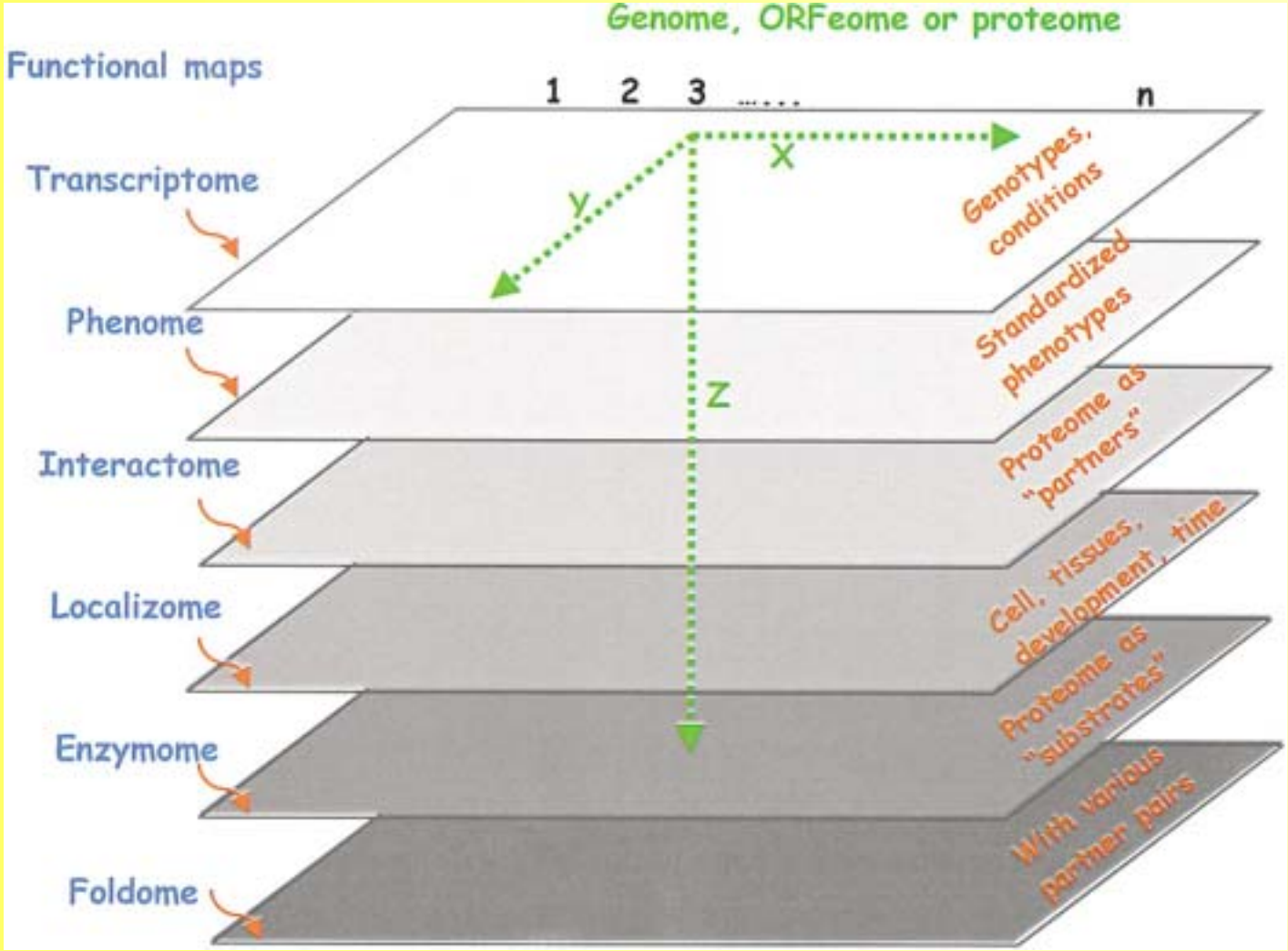
When the U.S. Department of Energy (DOE) announced last week that sequencing maverick J. Craig Venter had taken just 2 weeks to build a viral genome from scratch, Secretary of Energy Spencer Abraham called the work "nothing short of amazing." He predicted that it could lead to the creation of microbes tailored to deal with pollution or excess carbon dioxide or even to meet future fuel needs. But the $3 million DOE project drew ho-hum reviews from some scientists. "I didn't think it was a big deal," says Ian Molineux, a molecular biologist at the University of Texas, Austin. And Richard Ebright, a molecular biologist at Rutgers University in Piscataway, New Jersey, agrees: "This is strictly a limited incremental advance over current technologies."

The skeptics focus on how hard it will be to go beyond the initial step, while Venter, head of the Institute for Biological Energy Alternatives (IBEA) in Rockville, Maryland, and former president of Celera Genomics, and his backers are proud to have gotten this far. All are in agreement, however, that the experiment demonstrated speed in converting raw ingredients into a functioning virus.

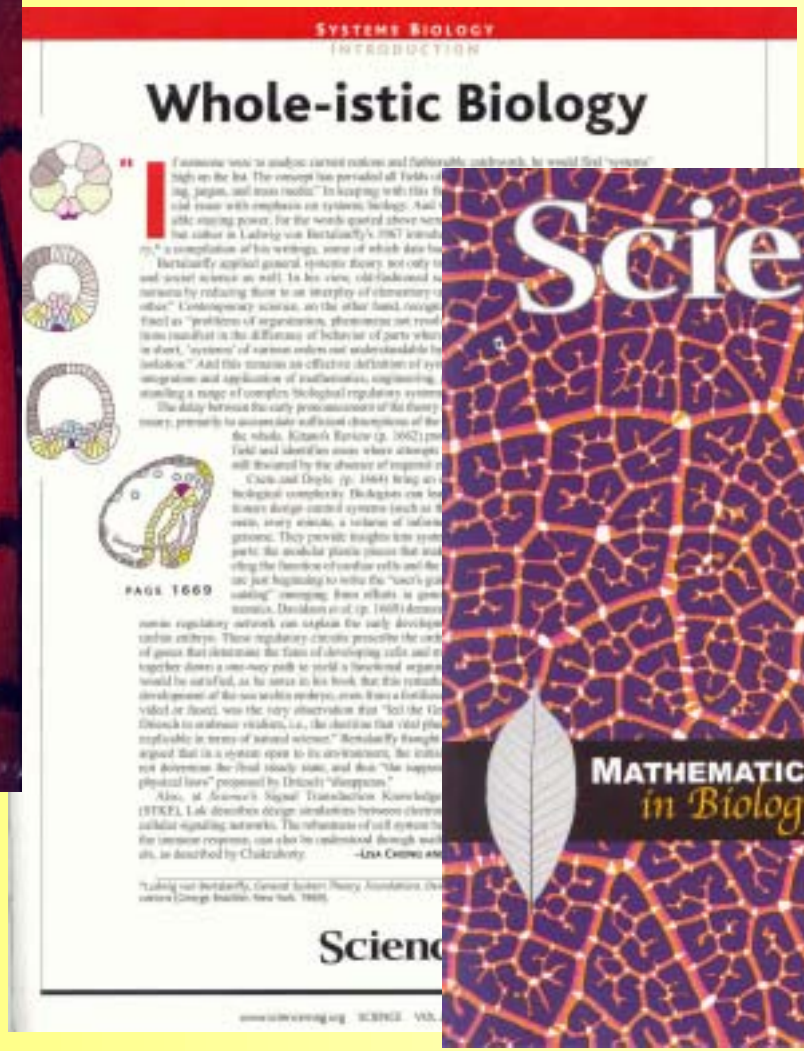
The genome synthesized by the Venter-led group belongs to a bacterial virus, called a phage; when it was tested in a lifelike situation, Venter reported, it infected and killed bacteria just as natural phages would.

Because his team stitched together the phage's DNA in just a few weeks instead of years, molecular virologist Eckard Wimmer of the State University of New York, Stony Brook, called the effort "a very smart piece of work."

Omics' world

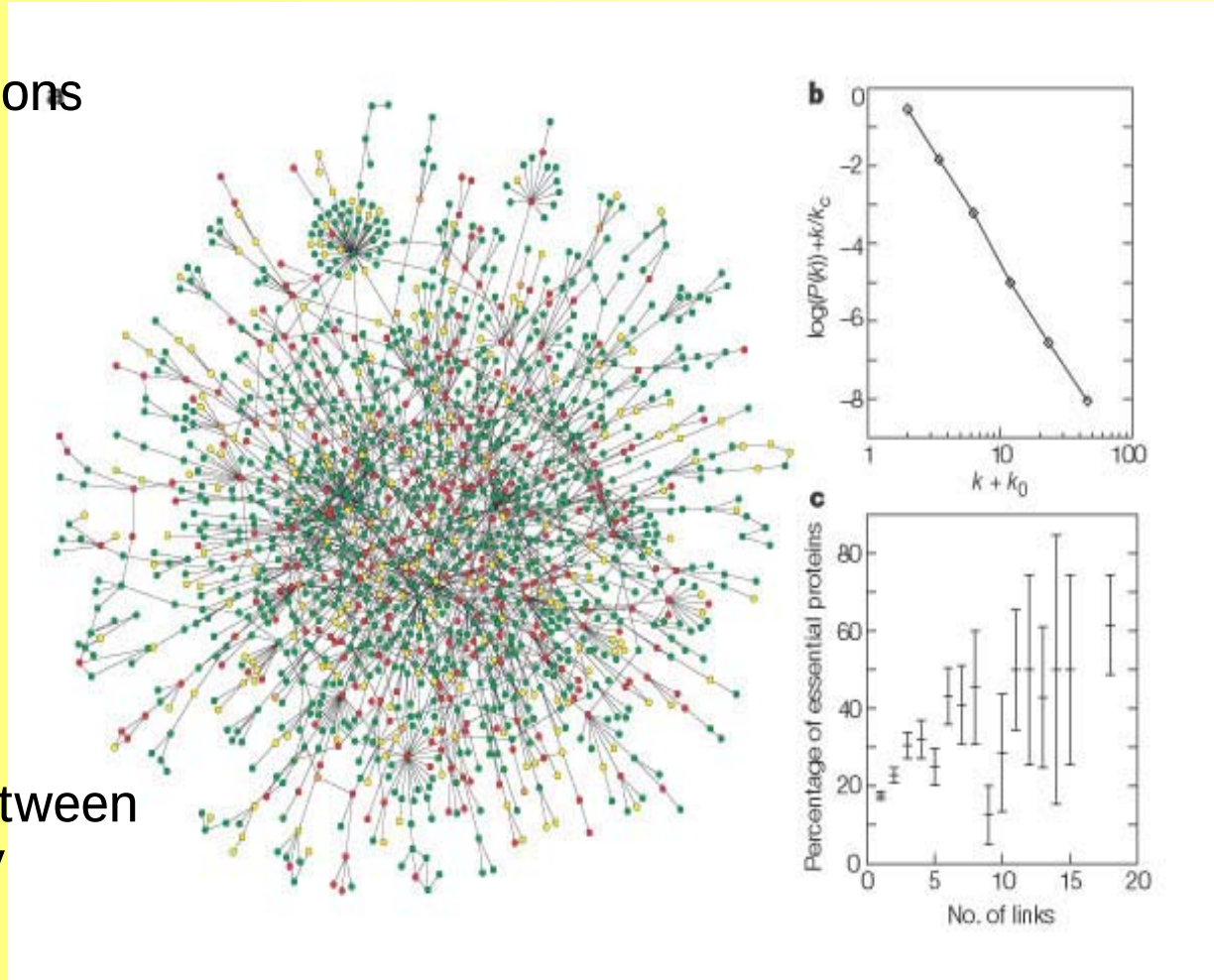


Systems biology / Whole-istic / Integration



Yeast protein-protein interactions

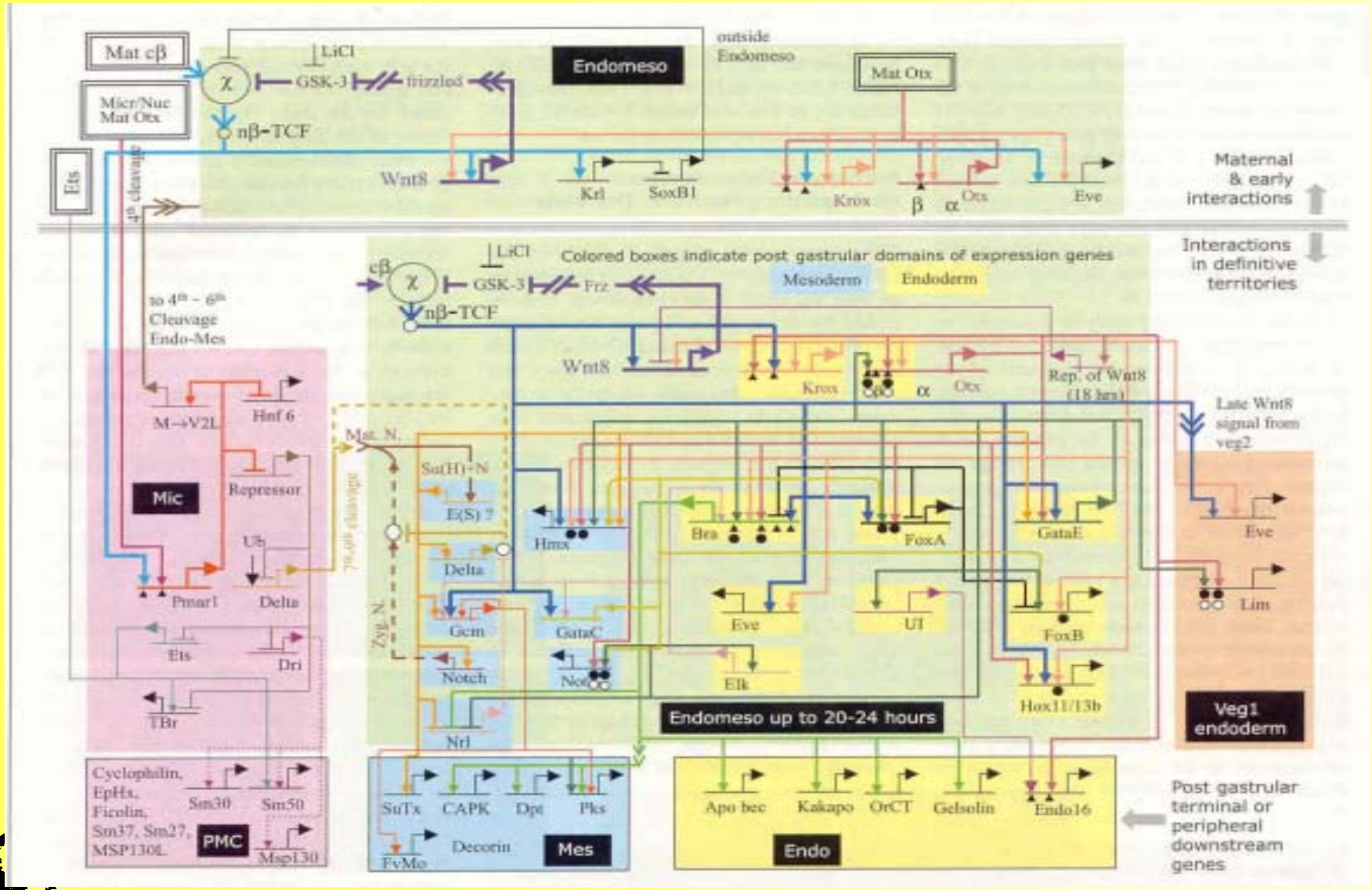
- 78% of proteins shown in giant component
- Protein-protein interactions



- : lethal mutation
- : slow growth
- : non-lethal
- : unknown

- Connectivity $P(k)$
- Fragility: Correlation between connectivity and lethality

Unravelling genetic networks....



ODE model of cell cycle

Table 1. A mathematical model of the proposed mechanism (Fig. 1) for the fission yeast cell cycle

Differential equations*

$$\frac{d}{dt}Rum1 = k_S - k'_6 \cdot Rum1 - k_P \cdot (MPF_a + \varepsilon_P \cdot SK \cdot mass) \cdot Rum1 + (k'_{PP} + k_{PP} \cdot PP) \cdot Rum1P - k_J \cdot MPF \cdot Rum1 + k_{JR} \cdot CR + k_{2c} \cdot CR$$

$$\frac{d}{dt}Rum1P = k_P \cdot (MPF_a + \varepsilon_P \cdot SK \cdot mass) \cdot Rum1 - (k'_{PP} + k_{PP} \cdot PP) \cdot Rum1P - (k'_6 + k_6) \cdot Rum1P - k_J \cdot MPF \cdot Rum1P + k_{JR} \cdot CRP + k_{2c} \cdot CRP$$

$$\frac{d}{dt}CR = k_J \cdot MPF \cdot Rum1 - k_{JR} \cdot CR - k_{2c} \cdot CR - k'_6 \cdot CR - k_P \cdot (MPF_a + \varepsilon_P \cdot SK \cdot mass$$

$$\frac{d}{dt}CRP = k_P \cdot (MPF_a + \varepsilon_P \cdot SK \cdot mass) \cdot CR - (k'_{PP} + k_{PP} \cdot PP) \cdot CRP + k_J \cdot MPF \cdot Rum1$$

$$\frac{d}{dt}MPF = k_1 \cdot mass - k_2 \cdot MPF - k_{Wee} \cdot MPF + k_{C25} \cdot preMPF - k_J \cdot MPF \cdot (Rum1$$

$$\frac{d}{dt}preMPF = k_{Wee} \cdot MPF - k_{C25} \cdot preMPF - k_2 \cdot preMPF$$

$$\frac{d}{dt}Ste9 = (k'_{Ste9R} + k_{Ste9R} \cdot PP) \cdot \frac{1 - Ste9}{J_{Ste9R} + 1 - Ste9} - k_{Ste9} \cdot (MPF_a + SK \cdot mass) \cdot$$

$$\frac{d}{dt}Mik1 = (k_S + k'_{MR} + k_{MR} \cdot PP) \cdot \frac{1 - Mik1}{J_{MikR} + 1 - Mik1} - k_M \cdot MPF_a \cdot \frac{Mik1}{J_{Mik} + Mik1}$$

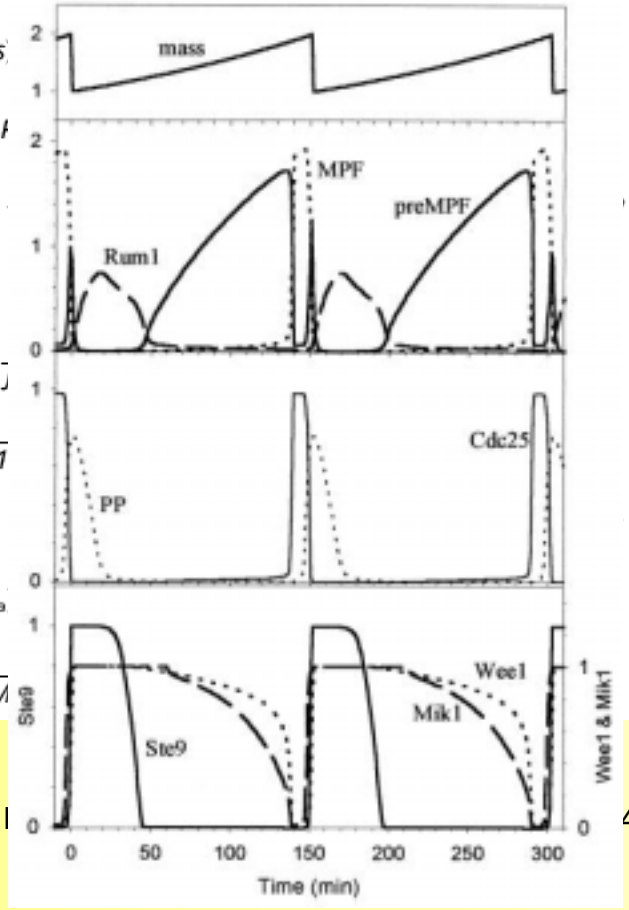
$$\frac{d}{dt}Wee1 = (k'_{WR} + k_{WR} \cdot PP) \cdot \frac{1 - Wee1}{J_{WeeR} + 1 - Wee1} - k_W \cdot MPF_a \cdot \frac{Wee1}{J_{Wee} + Wee1}$$

$$k_{25R} \cdot PP) \cdot \frac{Cdc25}{J_{25R} + Cdc25}$$

$$\frac{d}{dt}Slp1 = k_{as} \cdot MPF_a - k_{ad} \cdot Slp1, \quad \frac{d}{dt}Slp1_a = (k'_{aa} + k_{aa} \cdot MPF_a) \cdot (Slp1 - Slp1_a$$

$$k_{iR} \cdot PI - k_4 \cdot Inh$$

$$\frac{d}{dt}PI = k_I \cdot Inh \cdot PP - k_{iR} \cdot PI - k_4 \cdot PI, \quad \frac{d}{dt}mass = \mu \cdot mass, \quad \frac{d}{dt}R_{DNA} = \frac{K}{1 + Y \cdot M}$$



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Contents

Innovation through multidisciplinarity

‘Enlightment’: Split up sciences

20th Century

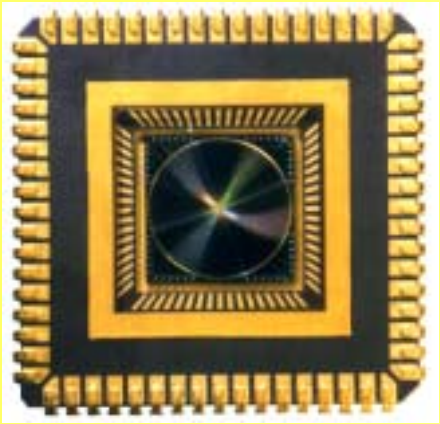
Dr. Eric Lander

“For me as a scientist in the world of genomics, watching this amazing convergence of biology, medicine, computer science and technology, is tremendously exciting.”

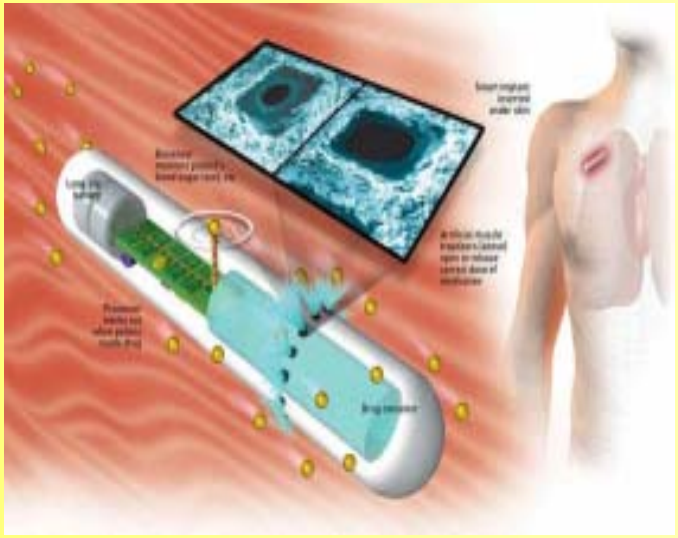
21th Century

‘Renaissance’: Merge sciences

Nano-Sensoren en Actuatoren

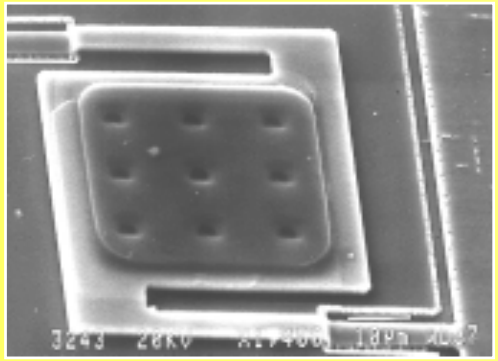


CMOS Imager

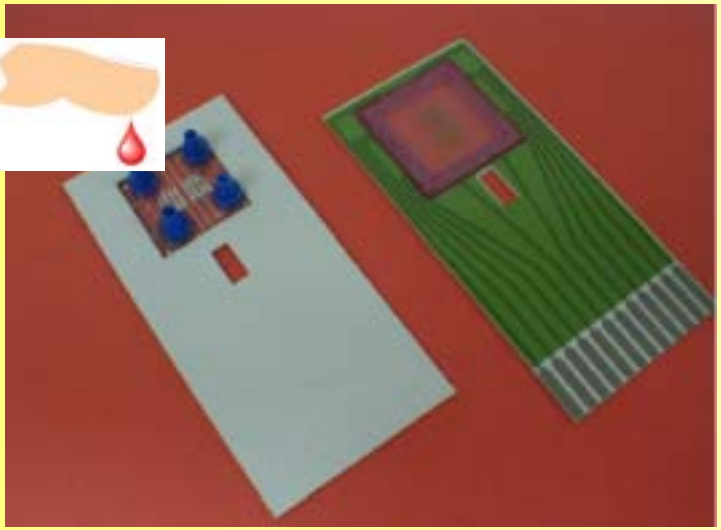


Smart Pill (Ohio State Univ)

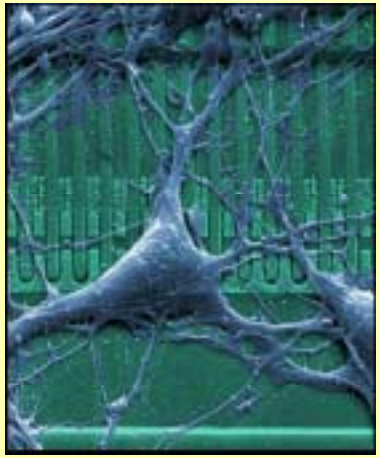
Blood gas sensor (IMEC)



IR Sensor (IMEC)

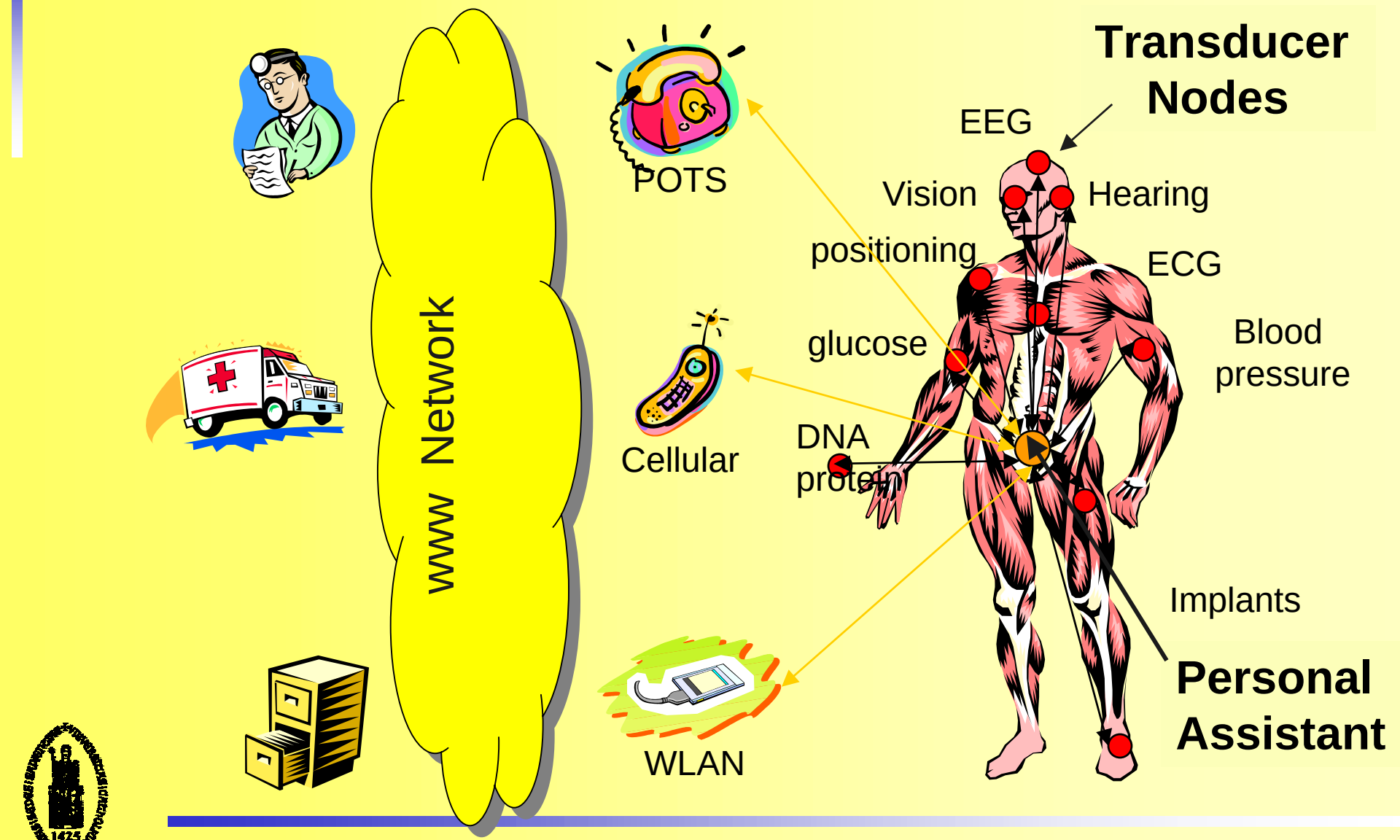


Prostate cancer diagnosis (IMEC)

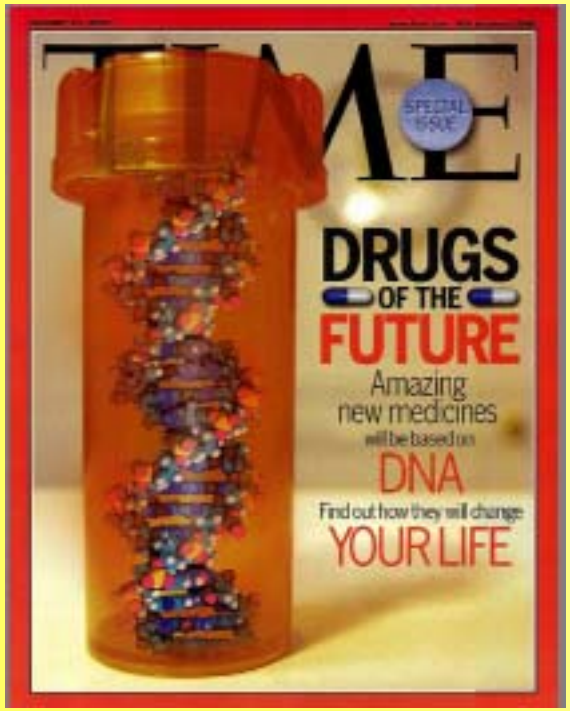


NeuronSensor (KNS)

Human++ programma IMEC



This is the (very near) future…



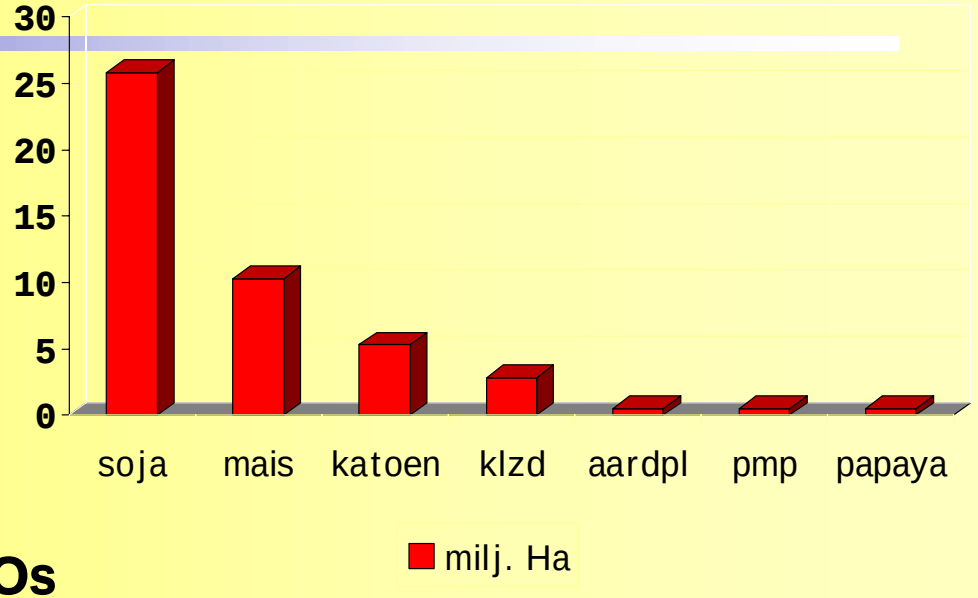
'Customized' medicine

Massive automated genetic screening of 1000s of assays

GMOs

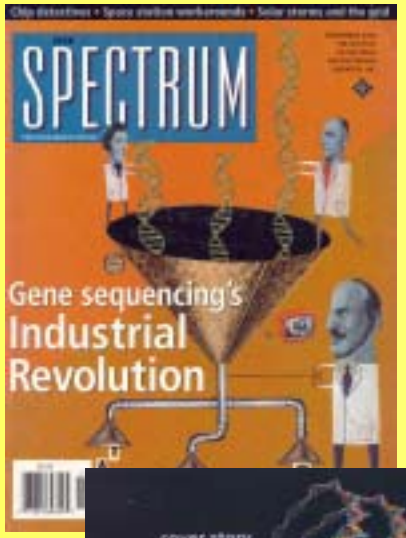

Landbouwafdeling BASF surft mee op tweede biotechnologiegolf

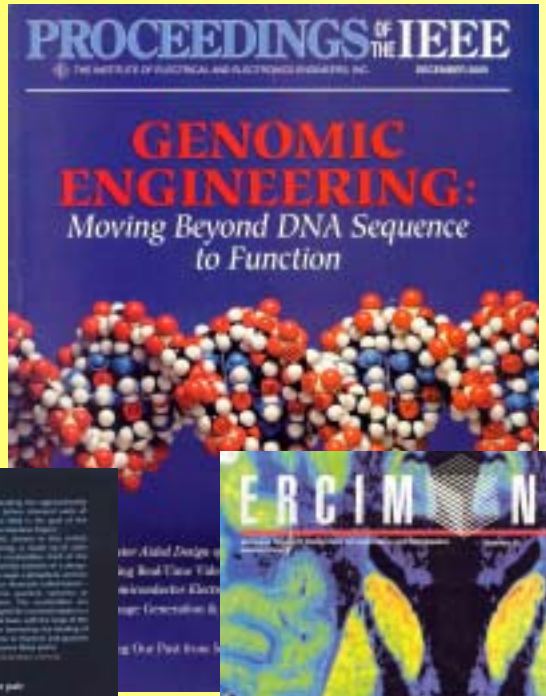
De nieuwste KUSTKRANT

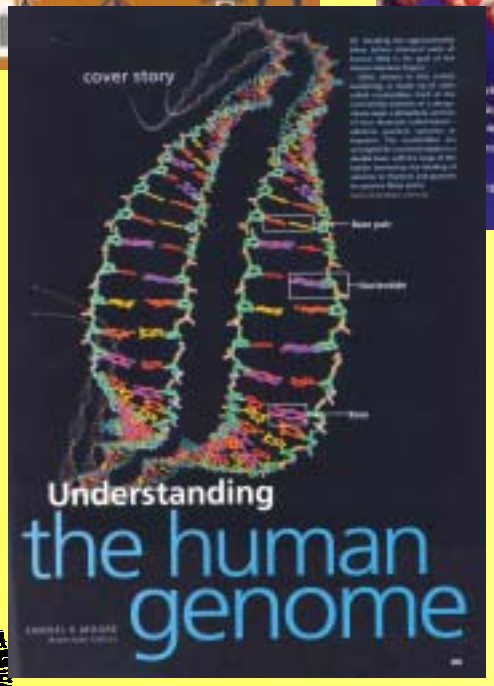


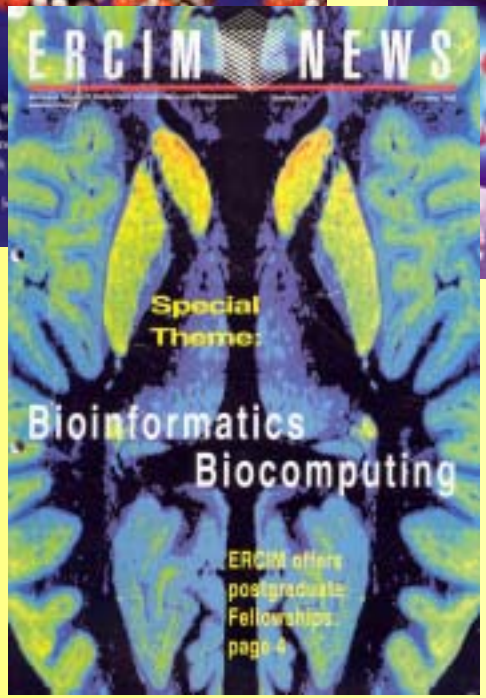
GMOs
-herbicide tolerant
-Resistent against insects, virusses,...
-Larger yield
-Better color, taste,...
Caffeine free

What to read and study (the specialist) ?

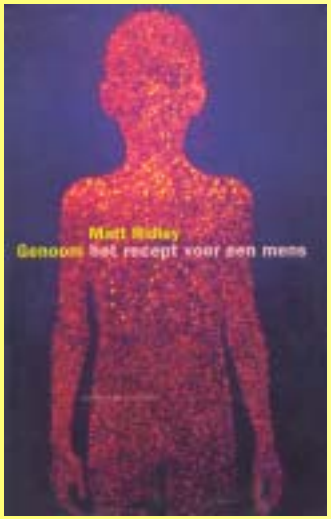








What to read and study ?



Relation Impact Factor – Research Domain

1996	1997	1998	1999	2000	2001	2002
2.698	2.257	2.257	2.401	2.15	29.6	7.323
1.402	2.257	2.257	2.196	2.081	13.251	7.323
1.402	1.545	1.545	2.196	1.873	13.251	7.051
1.402	1.402	1.368	2.196	1.851	6.668	4.615
1.368	1.402	1.178	2.106	1.566	6.373	4.615
0.874	1.402	0.816	2.106	1.203	3.688	3.561
0.856	1.402	0.816	1.643	1.182	3.437	3.456
0.816	1.017	0.773	1.643	1.182	3.421	2.986
0.816	0.874	0.773	1.475	1.182	2.81	2.986
0.816	0.856	0.773	1.405	1.096	2.81	2.986
0.816	0.773	0.742	0.877	0.996	2.81	2.784
0.773	0.773	0.739	0.877	0.866	2.81	2.387
0.773	0.773	0.588	0.877	0.845	2.43	2.387
0.739	0.773	0.482	0.729	0.805	2.43	2.387
0.508	0.773	0.412	0.729	0.685	2.332	2.313
0.508	0.773	0.412	0.729	0.685	1.479	2.222
0.482	0.741	0.286	0.702	0.685	1.466	2.211
0.482	0.739		0.663	0.675	1.453	2.095
0.482	0.739		0.658	0.654	1.449	1.806
0.482	0.508		0.597	0.595	1.431	1.806
0.466	0.508		0.597	0.595	1.268	1.806
0.448	0.482		0.405	0.531	1.268	1.806
0.286	0.444		0.295	0.5	1.222	1.717
	0.392		0.209	0.491	0.97	1.553
	0.392		0.209	0.491	0.838	1.553
	0.25			0.455	0.838	1.441
	0.084			0.367	0.756	1.404
	0.042			0.339	0.627	1.274
				0.305	0.533	1.203
				0.275	0.514	1.203
					0.488	1.159
					0.488	1.159
					0.488	1.144
					0.488	1.144
					0.484	0.861
					0.484	0.681
					0.468	0.62
					0.438	0.62
					0.415	0.458
					0.398	0.417
						0.415
						0.317
						0.282
						0.282
						0.176

SP [0.8]

QIT [3.5]

S&C [0.86]

Bio-i [5.6]

Biomed [2.3]

…and finally…

The Human Genome Project has catalyzed striking paradigm changes in biology - *biology is an information science*. […] Systems biology will play a central role in the 21st century; there is a need for global (high throughput) tools of genomics, proteomics, and cell biology to decipher biological information; and *computer science and applied math* will play a commanding role in converting *biological information into knowledge*.

Leroy Hood, Institute for Systems Biology, Seattle, WA, 2002