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

Information Technology

Bio-Technology

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Systems biology

Conclusions
Biology

1.000.000 cell types
100.000.000.000.000 cells

3.201.762.515 bp
Double helix of DNA

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

Guanine (G) – Cytosine (C)
Adenine (A) – Thimidine (T)

S&C: Challenges in 21st century, T.U.Delft, June 2004
Genetic (almost) universal code: codons

<table>
<thead>
<tr>
<th>Codon</th>
<th>Amino Acid</th>
<th>Codon</th>
<th>Amino Acid</th>
</tr>
</thead>
<tbody>
<tr>
<td>UUU</td>
<td>Phenylalanine</td>
<td>UCU</td>
<td>Serine</td>
</tr>
<tr>
<td>UUC</td>
<td></td>
<td>UCC</td>
<td></td>
</tr>
<tr>
<td>UUA</td>
<td></td>
<td>UCA</td>
<td></td>
</tr>
<tr>
<td>UUG</td>
<td></td>
<td>UCG</td>
<td></td>
</tr>
<tr>
<td>CUU</td>
<td>Leucine</td>
<td>CCU</td>
<td>Proline</td>
</tr>
<tr>
<td>CUC</td>
<td></td>
<td>CCC</td>
<td></td>
</tr>
<tr>
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<td>CCA</td>
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<td>CUG</td>
<td></td>
<td>CGA</td>
<td></td>
</tr>
<tr>
<td>AUU</td>
<td>Isoleucine</td>
<td>ACU</td>
<td>Asparagine</td>
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<tr>
<td>AUC</td>
<td></td>
<td>ACC</td>
<td></td>
</tr>
<tr>
<td>AUA</td>
<td></td>
<td>ACA</td>
<td></td>
</tr>
<tr>
<td>AUG</td>
<td>Methionine</td>
<td>GCU</td>
<td>Alanine</td>
</tr>
<tr>
<td>GUU</td>
<td>Valine</td>
<td>GCA</td>
<td></td>
</tr>
<tr>
<td>GUC</td>
<td></td>
<td>GCC</td>
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</tr>
<tr>
<td>GUA</td>
<td></td>
<td>GCG</td>
<td></td>
</tr>
<tr>
<td>AUG</td>
<td></td>
<td>GGU</td>
<td>Glutamic acid</td>
</tr>
<tr>
<td>GUG</td>
<td></td>
<td>GGA</td>
<td></td>
</tr>
<tr>
<td>GAG</td>
<td></td>
<td>GGG</td>
<td></td>
</tr>
</tbody>
</table>

- 20 amino acids
- 64 codons: Redundancy - robustness

Stop = UAA, UAG, UGA
Start = AUG

T in DNA
U in RNA
SNP: Single Nucleotide Polymorphism

11 million SNPs / 3 billion nucleotides

Monogenic diseases
- 1983: Huntington
- 1986: Muscular dystrophy
- 1989: Cystic-fibrosis
HGP: sequencing
The 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...

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

‘Universality’ of the genetic code ...
### Some genome numbers

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

Estimated 265-350 genes are required for ‘life’.
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Conclusions
Mathematics and biology

1865: Mendel’s Laws = statistics

1952: Turing The chemical basis of morphogenesis

1944: Schrödinger: What’s life?

1940: Shannon PhD An algebra for theoretical genetics

Genetic algorithms = optimization by ‘survival of the fittest’

Neural networks!

DNA computers

S&C: Challenges in 21st century, T.U.Delft, June 2004
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Differentially expressed genes

RNA → cDNA
Technology: Microarrays/ DNA-chips

Two color hybridization on a yeast array with two differing samples of genomic DNA.

<table>
<thead>
<tr>
<th>Test</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>Low</td>
</tr>
<tr>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td>Low</td>
<td>Low</td>
</tr>
</tbody>
</table>
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Conclusions
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

Find the pattern

Hidden 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**

<table>
<thead>
<tr>
<th>number of genes</th>
<th>% area ROC training</th>
<th>% area ROC prospective</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>15</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>10</td>
<td>1</td>
<td>99.29</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>98.57</td>
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<td>4</td>
<td>1</td>
<td>98.57</td>
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<td>3</td>
<td>1</td>
<td>97.50</td>
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<tr>
<td>2</td>
<td>98.32</td>
<td>98.21</td>
</tr>
<tr>
<td>1</td>
<td>93.60</td>
<td>71.07</td>
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</table>

**Relevance:**
Diagnostic kit
Bio-informatics

- High-throughput technology $\rightarrow$ lots of ‘wet lab’ data
- Computers $\rightarrow$ computing power
- Internet $\rightarrow$ 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
- 100,000s
- 3D-Folding / docking
- 'workhorse'

Exceptions exist: e.g. retrovirus (HIV)
Detecting regulatory elements
Junk DNA?

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

Introns contain
- Lots of DNA function unknown
- Centromeres
- Telomeres
- Regulators
  - Promoters, 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

### Transition Matrix

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>C</th>
<th>G</th>
<th>T</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>0.0643</td>
<td>0.8268</td>
<td>0.0659</td>
<td>0.0430</td>
</tr>
<tr>
<td>C</td>
<td>0.0598</td>
<td>0.0484</td>
<td>0.8515</td>
<td>0.0403</td>
</tr>
<tr>
<td>G</td>
<td>0.1602</td>
<td>0.3407</td>
<td>0.1736</td>
<td>0.3255</td>
</tr>
<tr>
<td>T</td>
<td>0.1507</td>
<td>0.1608</td>
<td>0.3654</td>
<td>0.3231</td>
</tr>
</tbody>
</table>

### Example Sequences

- ACGCGGTGTCCGTTGGACGTA
- ACGGTTACCGGACGTTGGT
- ACCTGCGTTGTACCTGTAACG
- ACGGAGTTTGCAGCCAGGGACG
- ACGCCGCTGACGTACGGTCGTG
- AGACCGTTCGGCGCGGCAGC
- ACGGGCTTGCCGCGCTGGACG
- AAGACGTTTGCTTCGCTGC
- ACCCGTTTCGAGCTGCTTC
- ACGTGACTCGTGAGTGCAGG
- ACCTGACTGCGTGGAGTACG
- ATACGGCGTCGGCGGGCGG
- ACGTACCGTACACGGCAAGA
- ACCTCGTGTTCAGAGCTC
- ACCTCGACCGGCGTGATCG
- ACGGCGGTGACGTCGCGTACG
- ACGTTGCGACGCGCCCGCC
- ACGGAACGGACGGCAACG
- ACGGCCGTCTCGGCGCGC

### Diagram

![DNA Markov Model Diagram](image-url)

- The diagram illustrates the transition probabilities between nucleotides over various positions.
- Colors represent different percentages, with red indicating higher percentages and green indicating lower percentages.
- The sequence positions are labeled along the x-axis, and the percentages are shown along the y-axis.
Statistical model of a motif

Motif 2: TyTTTCCA\textsuperscript{w}C

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>0.0979</td>
<td>0.0096</td>
<td>0.0096</td>
<td>0.0096</td>
<td>0.2747</td>
<td>0.0096</td>
<td>0.0096</td>
<td>0.0049</td>
<td>0.4514</td>
<td>0.0096</td>
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<tr>
<td>C</td>
<td>0.0049</td>
<td>0.4467</td>
<td>0.2700</td>
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<td>0.0049</td>
<td>0.9768</td>
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<td>0.0049</td>
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<tr>
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<td>0.0041</td>
<td>0.0041</td>
<td>0.0041</td>
<td>0.0041</td>
<td>0.0041</td>
<td>0.0041</td>
<td>0.0041</td>
<td>0.0041</td>
<td>0.0041</td>
</tr>
<tr>
<td>T</td>
<td>0.0931</td>
<td>0.5396</td>
<td>0.7164</td>
<td>0.9615</td>
<td>0.7164</td>
<td>0.0094</td>
<td>0.0094</td>
<td>0.1662</td>
<td>0.5396</td>
<td>0.3629</td>
</tr>
</tbody>
</table>

Scores
- Information Content: 1.1882
- LogLikelihood: 0.8687
- Consensus Score: 1.3043

Alignment:

<table>
<thead>
<tr>
<th>Name</th>
<th>Position</th>
<th>Site</th>
<th>Prob.</th>
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<tr>
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<td>TTTTACCAAC</td>
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<tr>
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<td>512</td>
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<tr>
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<tr>
<td></td>
<td>513</td>
<td>TCCTACCATC</td>
<td>0.9465</td>
</tr>
<tr>
<td>Seq 7</td>
<td>206</td>
<td>TCTTTCTTTT</td>
<td>0.9509</td>
</tr>
<tr>
<td>Seq 8</td>
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<td>ATTTTTCCAAT</td>
<td>0.5764</td>
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<tr>
<td>Seq 9</td>
<td>229</td>
<td>TCCTTTCCAAC</td>
<td>0.9808</td>
</tr>
</tbody>
</table>

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

Microarrays → Clustering → GenBank → Blast → Gibbs sampler

Time
Clusters: ‘Guilt by association’
Zooming in on one cluster

Similarity measure
- Euclidean distance
- Euclidean angle

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

<table>
<thead>
<tr>
<th>Cluster number</th>
<th>Graphical representation of cluster</th>
<th>Number of ORFs</th>
<th>MIPS functional category (top-level)</th>
<th>ORFs within functional category</th>
<th>P-value (-log10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>426</td>
<td>energy transport facilitation</td>
<td>47</td>
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<td>3</td>
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<td>196</td>
<td>cell growth, cell division and DNA synthesis</td>
<td>48</td>
<td>5</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>149</td>
<td>protein synthesis cellular organisation</td>
<td>71</td>
<td>50</td>
</tr>
<tr>
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<td></td>
<td>159</td>
<td>cell rescue, defense, cell death and ageing</td>
<td>20</td>
<td>4</td>
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<tr>
<td>6</td>
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<td>cell growth, cell division and DNA synthesis</td>
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<tr>
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<td>cell growth, cell division and DNA synthesis</td>
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<tr>
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<td>metabolism</td>
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<td>6</td>
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## Arabidopsis Thaliana

<table>
<thead>
<tr>
<th>Cluster</th>
<th>Consensus motif</th>
<th>Runs</th>
<th>PlantCARE</th>
<th>Description</th>
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<tbody>
<tr>
<td>1 [ 11 seq.]</td>
<td>TAArTAAGTCAC ATTCAAATT TTCTTTCGATCT</td>
<td>7/10</td>
<td>TGAGTCA CGTCA ATACAAAT TTCCGACC</td>
<td>Tissue specific GCN4-motif MeJA-responsive element elicitor responsive element assoc. to GCN4-motif</td>
</tr>
<tr>
<td>2 [ 6 seq.]</td>
<td>TTGACyCGy mACGTCACCT</td>
<td>5/10</td>
<td>TGACG (T)TGAC(C) CGTCA ACGT</td>
<td>MeJa responsive element elicitor responsive element MeJA responsive element Abcissic acid response element</td>
</tr>
<tr>
<td>3 [ 5 seq.]</td>
<td>wATATATATmTT TCTwCnTC ATAAATTkGCnT</td>
<td>5/10</td>
<td>TATATA TCTCCCT</td>
<td>TATA-box like element TCCC-motif, light response element</td>
</tr>
<tr>
<td>4 [ 5 seq.]</td>
<td>yTGACCGTCCsA CACGTGG GCCTymTT AGAAATCAAT</td>
<td>9/10</td>
<td>CCGTCC CCGTCC TGACG CGTCA CACGTG ACGT</td>
<td>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</td>
</tr>
</tbody>
</table>
INCLUSive: online analysis of μ-array data

MARAN
Clustering
AQBC
Gibbs bi-clustering

Pre-processing

Sequence Analysis
TOUCAN
MotifSampler
MotifScanner

Functional Annotation
- Gene Ontology
- Text mining
- OMIM
- LocusLink

TXTGate
Go4G

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

S&C: Challenges in 21st century, T.U. Delft, June 2004
INCLUSive - web portal
Endeavour: data & algorithm integration

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

Pathology
Text mining: Txt-gate

- Gene modules over various expression data sets
- Reported two submodules of TCA cycle
- Two 'new' genes ACN9 & CAT8 in module 2

How?
- Medline
- Build huge document – gene matrices
- SVD-ize them
- Cluster
- Visualize
Software statistics: example

Motif sampler

Number of user on a monthly basis

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

S&C: Challenges in 21st century, T.U.Delft, June 2004
From Kepler to Newton

Kepler’s laws:

Law 1: Orbit is ellips with Sun in focus

Law 2: Joining 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

\[
F = m \cdot a
\]

\[
F = G \frac{m \cdot M}{r^2}
\]
Example: Systems biology: Chemotaxis

- genome
- transcriptome
- proteome
- metabolome
- interactome

‘high throughput ‘data
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


S&C: Challenges in 21st century, T.U. Delft, June 2004
Yeast protein-protein interactions

- 78% of proteins shown in giant component
- Protein-protein interactions
  - Red: lethal mutation
  - Orange: slow growth
  - Green: non-lethal
  - Yellow: 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*

\[ \frac{d}{dt} \text{Rum}1 = k_s - k_e' \text{Rum}1 - k_p' (\text{MPF}_a + \epsilon_p \text{SK}\cdot\text{mass}) \text{Rum}1 + (k_{pp} + k_{pp'}PP) \text{Rum}1P - k_p' \text{MPF}\cdot\text{Rum}1 + k_{rr'} \text{CR} + k_{2c}\cdot\text{CR} \]

\[ \frac{d}{dt} \text{Rum}1P = k_p' (\text{MPF}_a + \epsilon_p \text{SK}\cdot\text{mass}) \cdot \text{Rum}1 - (k_{pp} + k_{pp'}PP) \cdot \text{Rum}1P - (k_o + k_{o'}) \cdot \text{Rum}1P - k_p' \text{MPF}\cdot\text{Rum}1P + k_{rr'} \text{CRP} + k_{2c}\cdot\text{CRP} \]

\[ \frac{d}{dt} \text{CR} = k_p' \text{MPF}\cdot\text{Rum}1 - k_{rr'} \text{CR} - k_{2c}\cdot\text{CR} - k_{o'} \text{CR} - k_{o'} (\text{MPF}_a + \epsilon_p \text{SK}\cdot\text{mass}) \]

\[ \frac{d}{dt} \text{CRP} = k_p' (\text{MPF}_a + \epsilon_p \text{SK}\cdot\text{mass}) \cdot \text{CR} - (k_{pp} + k_{pp'}PP) \cdot \text{CRP} + k_p' \text{MPF}\cdot\text{Rum}1P \]

\[ \frac{d}{dt} \text{MPF} = k_s' \text{mass} - k_{2c} \text{MPF} - k_{\text{preMPF}} \text{MPF} + k_{\text{preMPF}} \text{preMPF} - k_p' \text{MPF}\cdot\text{Rum}1 \]

\[ \frac{d}{dt} \text{preMPF} = k_{\text{preMPF}} \text{MPF} - k_{2c} \cdot \text{preMPF} - k_{2c} \cdot \text{preMPF} \]

\[ \frac{d}{dt} \text{Ste9} = (k_{\text{Ste9R}} + k_{\text{Ste9PP}}) \cdot \frac{1 - \text{Ste9}}{1 - \text{Ste9} + (\text{MPF}_a + \epsilon_p \text{SK}\cdot\text{mass})} \]  

\[ \frac{d}{dt} \text{Mik1} = (k_s + k_{\text{Mik1R}} + k_{\text{Mik1PP}}) \cdot \frac{1 - \text{Mik1}}{1 - \text{Mik1} + (\text{MPF}_a + \epsilon_p \text{SK}\cdot\text{mass})} \]  

\[ \frac{d}{dt} \text{Wee1} = (k_{\text{Wee1R}} + k_{\text{Wee1PP}}) \cdot \frac{1 - \text{Wee1}}{1 - \text{Wee1} + (\text{MPF}_a + \epsilon_p \text{SK}\cdot\text{mass})} \]  

\[ \frac{d}{dt} \text{Slp1} = k_{\text{Slp1a}}' (\text{MPF}_a - \text{Slp1}) - k_{\text{Slp1a}} \text{Slp1} \]  

\[ \frac{d}{dt} \text{Pl} = k_{\text{Pl}} (\text{PP} - \text{Pl}) - k_{\text{Pl}} \text{Pl} \]  

\[ \frac{d}{dt} \text{mass} = \mu \cdot \text{mass}, \quad \frac{d}{dt} \text{R}_{\text{DNA}} = \frac{K}{1 + Y} \]  


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Biology

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‘Enlightenment’: Split up sciences

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.”

‘Renaissance’: Merge sciences
Nano-Sensoren en Actuatoren

- CMOS Imager
- Smart Pill (Ohio State Univ)
- Blood gas sensor (IMEC)
- IR Sensor (IMEC)
- NeuronSensor (KNS)
- Prostate cancer diagnosis (IMEC)

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Human++ programma IMEC

Transducer Nodes
- EEG
- Hearing
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- Blood pressure
- Implants

Personal Assistant

- Vision positioning
- Glucose
- DNA protein
- Cellular
- POTS

WLAN

www Network

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This is the (very near) future...

‘Customized’ medicine

Massive automated genetic screening of 1000s of assays
GMOs

- Herbicide tolerant
- Resistant against insects, virusses,…
- Larger yield
- Better color, taste,…
- Caffeine free
What to read and study (the specialist)?
What to read and study?

- Het ABC van het DNA
- Adam en Eva
- De komende vijftig jaar
- De code van het leven
- De zeven dochters van Eva
- Een monnik en twee erwten
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**S&C: Challenges in 21st century, T.U.Delft, June 2004**
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