Live goes life
Synthetic biology

Bart De Moor

http://www.esat.kuleuven.be/stadius/
http://www.kuleuven.be/samenwerking/iminds/medicalit

1. What is science ? What are models ? What is technology ? What is engineering ?

1. The seven spheres of engineering
    1. Matter
    2. Energy
    3. Information
    4. Sustainability
    5. Social
    6. Culture
    7. Life

1. Analysis and Design in the seven spheres

1. Utopia ? Design of living systems ?

What is science ?

- Describe and understand the world

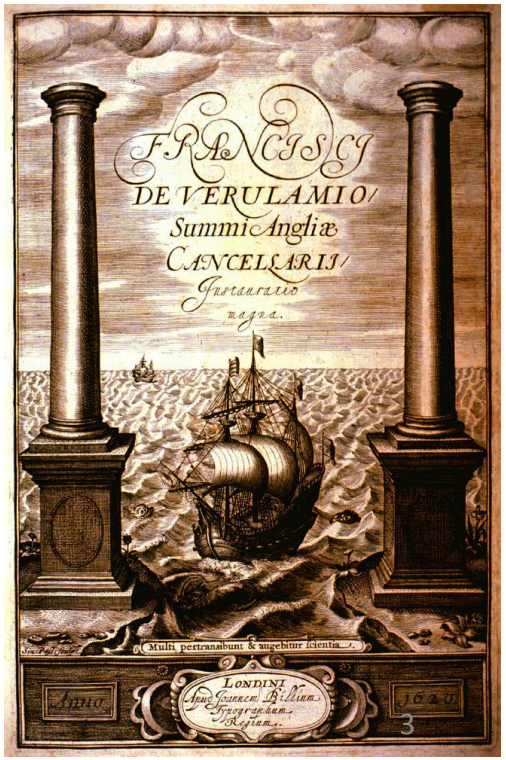
- From myths/stories to verifiable facts

- Religion and science

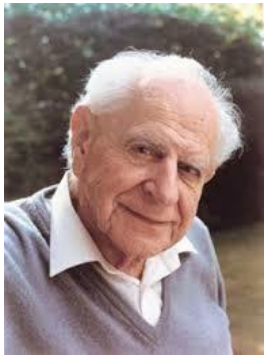
    - The creator outside his creation)
    - *Galilei and the church*
    - *Napoleon: Où est Dieu dans votre système ?*
      Laplace: Dieu ? Je n'ai pas besoin de cette hypothèse !

- Descartes: 'Je pense donc je suis' 'Cogito ergo sum'

- Francis Bacon (1561 – 1626)
    -Experimental method
    -Progress !
    -Nec plus ultra; The limit is the sky !



What is science ?



- Popper's Demarcation-criterion

A statement or a theory is scientific when it clarifies and establishes its own weaknesses

'Irrefutability is not a virtue of a theory, but a vice'
Karl Popper

No scientific theory is true for ever; A theory is scientific when it shows where it can be attacked

A scientific theory predicts, but forbids more than it will allow

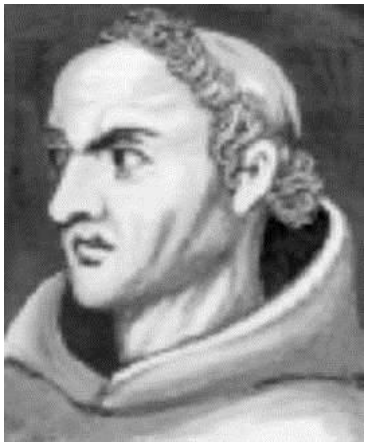
Not scientific:

- Any religion or 'belief'
- Marxism, Liberalism, Socialism, ….

What are models ?

William van Occam (1290-1349):
“Entia non sunt multiplicanda praeter necessitatem”
(Wezensbegrippen moeten niet onnodig vermeerderd worden)

Een eenvoudige verklaring van een fenomeen is te verkiezen boven een moeilijke



What is technology ?

- Technology = techne logos
= the discipline on know how to do something

-Technology = transbiological evolution on top of the natural biological evolution

What is engineering ?

Engineering = use technology to design technology and ‘solve’ ‘problems’

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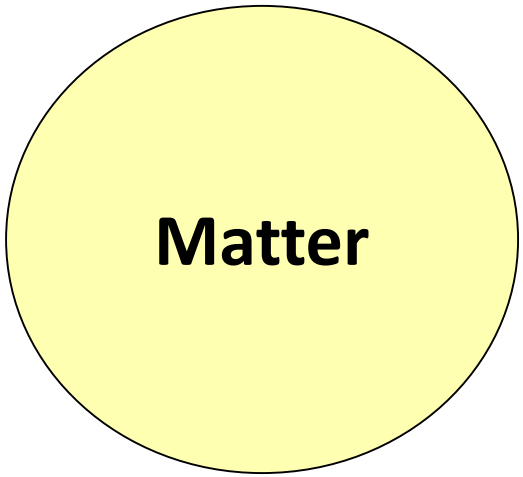
1. Analysis and Design in the seven spheres

1. Utopia ? Design of living systems ?


Matter

The science (analysis)

Kepler

Newton

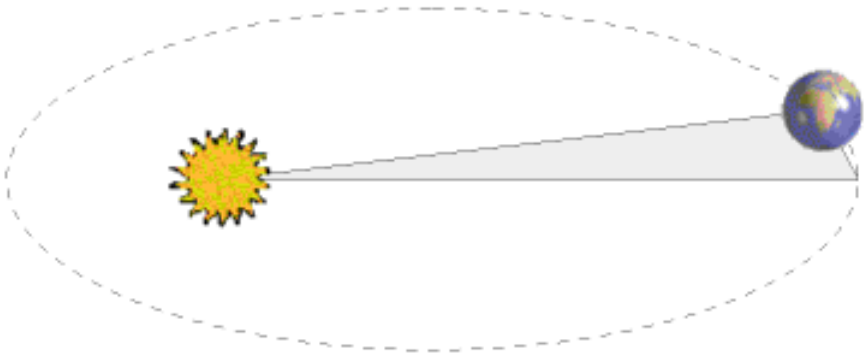
Law 1: Orbit = ellips; Sun = focus

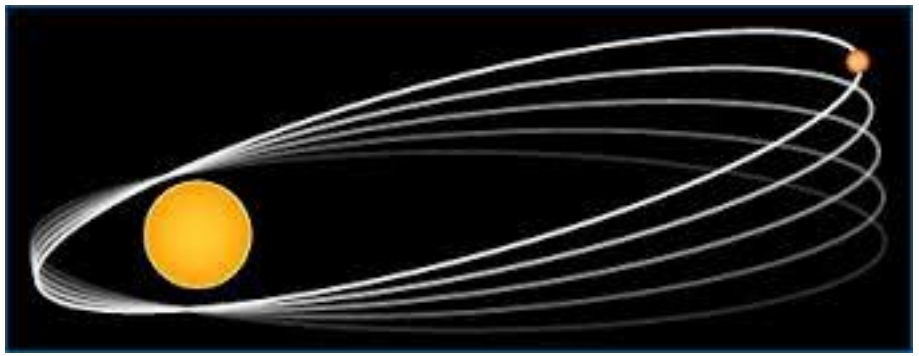
Law 2: 'Radial line' colors equal surfaces in equal time intervals

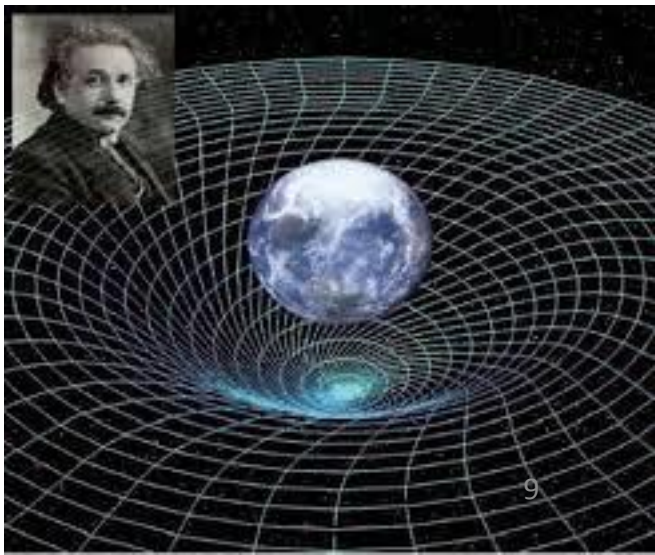
Law 3: $$\frac{T_1^2}{T_2^2} = \frac{a_1^3}{a_2^3}$$

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

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







The unreasonable effectiveness of mathematics

COMMUNICATIONS ON PURE AND APPLIED MATHEMATICS, VOL. XIII, 001–14 (1960)

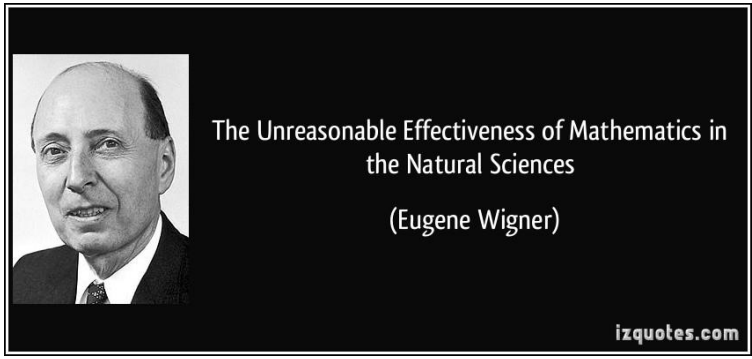
The Unreasonable Effectiveness of Mathematics in the Natural Sciences

Richard Courant Lecture in Mathematical Sciences delivered at New York University, May 11, 1959

EUGENE P. WIGNER
Princeton University

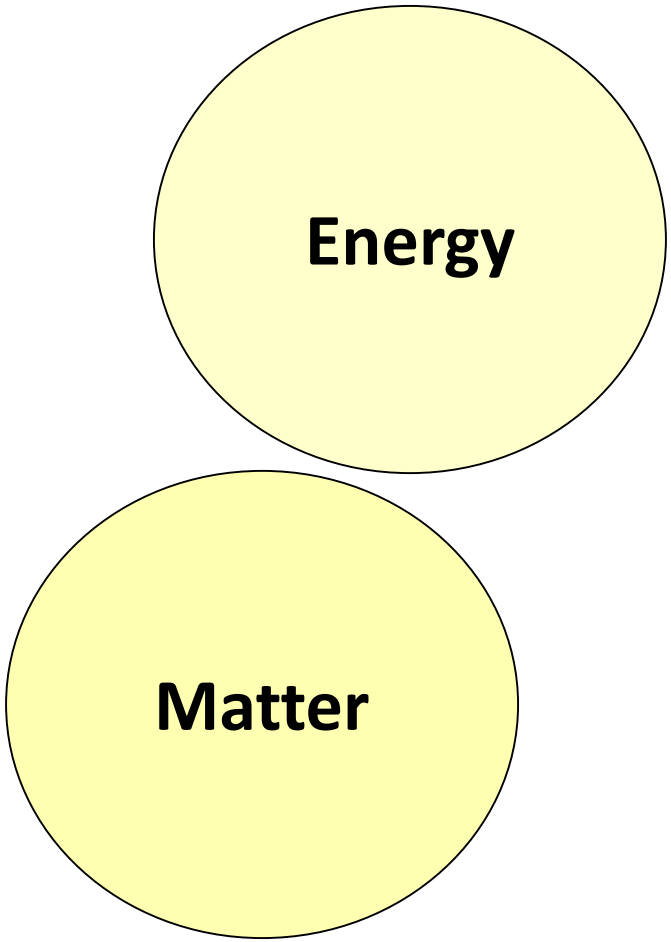
"and it is probable that there is some secret here which remains to be discovered." (*C. S. Peirce*)

There is a story about two friends, who were classmates in high school, talking about their jobs. One of them became a statistician and was working on population trends. He showed a reprint to his former classmate. The reprint started, as usual, with the Gaussian distribution and the statistician explained to his former classmate the meaning of the symbols for the actual population, for the average population, and so on. His classmate was a bit incredulous and was not quite sure whether the statistician was pulling his leg. "How can you know that?" was his query. "And what is this symbol here?" "Oh," said the statistician, "this is π." "What is that?" "The ratio of the circumference of the circle to its diameter." "Well, now you are pushing your joke too far," said the classmate, "surely the population has nothing to do with the circumference of the circle."

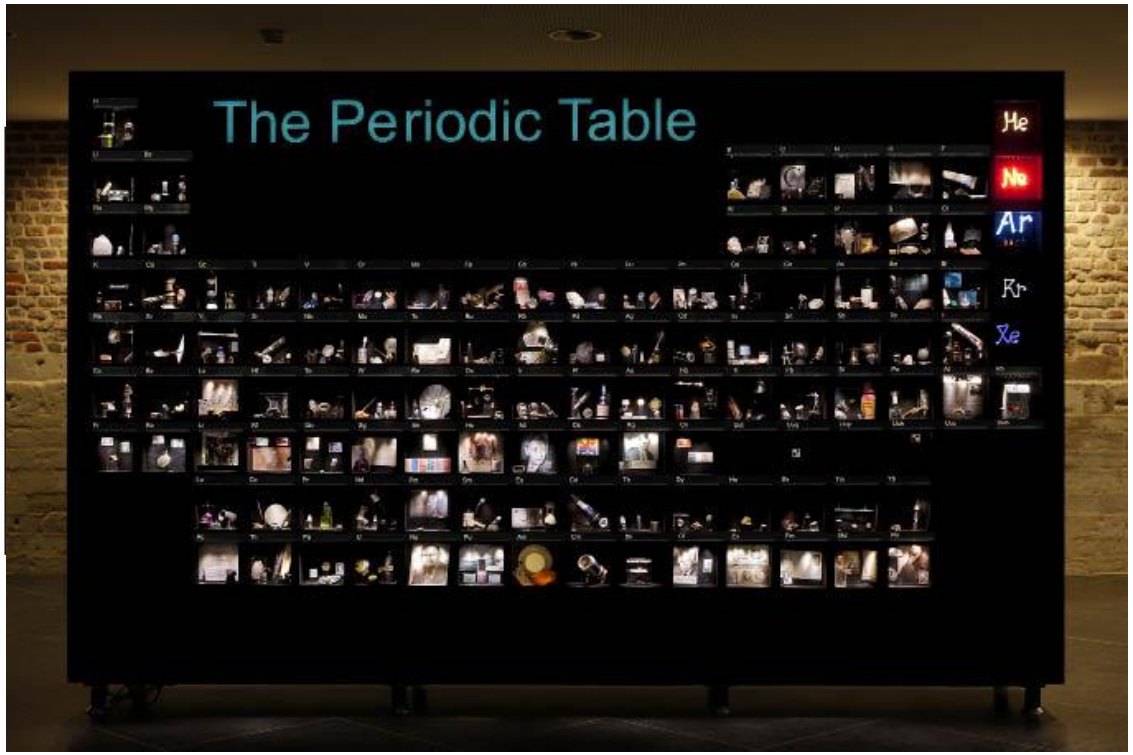


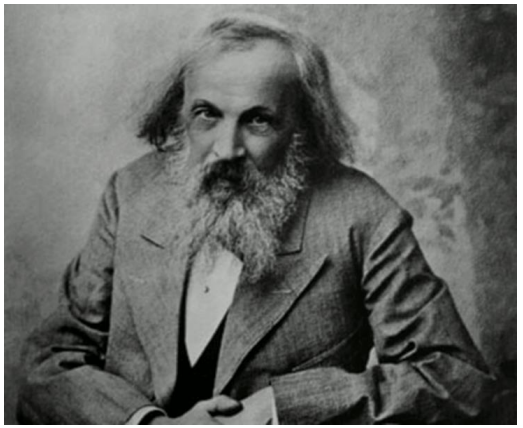
Technology and Engineering Design:
The first industrial revolution (1700…)

- Steam engine (Watt)
- Mechanisation of textile industries
- Infrastructure for mobility: rail roads
- Water and Coal as energy source
- *Transition of a feodal rural towards industrial society*
- *Socio-cultural evolution follows the economical-technical one (French revolution)*


Energy
Matter

The science (analysis)



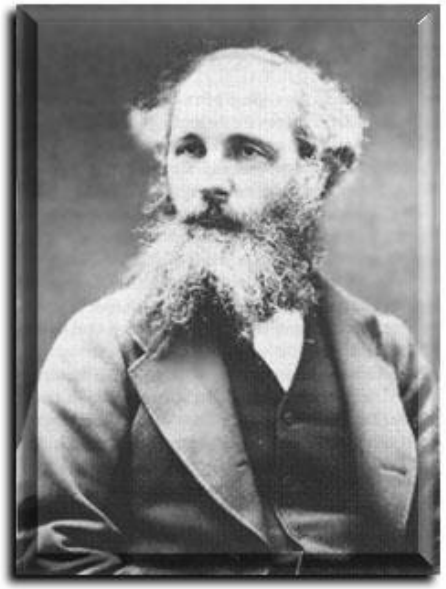


$$\nabla \cdot \mathbf{D} = \rho \qquad (1) \qquad \text{Gauss' Law}$$

$$\nabla \cdot \mathbf{B} = 0 \qquad (2) \qquad \text{Gauss' Law for magnetism}$$

$$\nabla \times \mathbf{E} = -\frac{\partial \mathbf{B}}{\partial t} \qquad (3) \qquad \text{Faraday's Law}$$

$$\nabla \times \mathbf{H} = \frac{\partial \mathbf{D}}{\partial t} + \mathbf{J} \qquad (4) \qquad \text{Ampère-Maxwell Law}$$



Technology & Engineering Design:
The second industrial revolution (1870…)

-Mass production and consumption

-Electricity and oil as energy sources

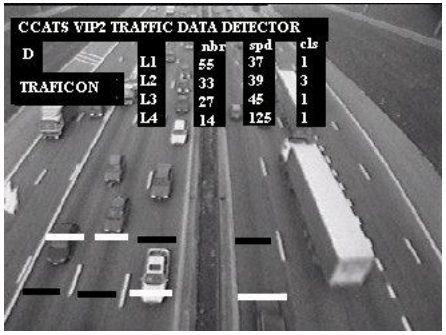
-Chemical industry develops

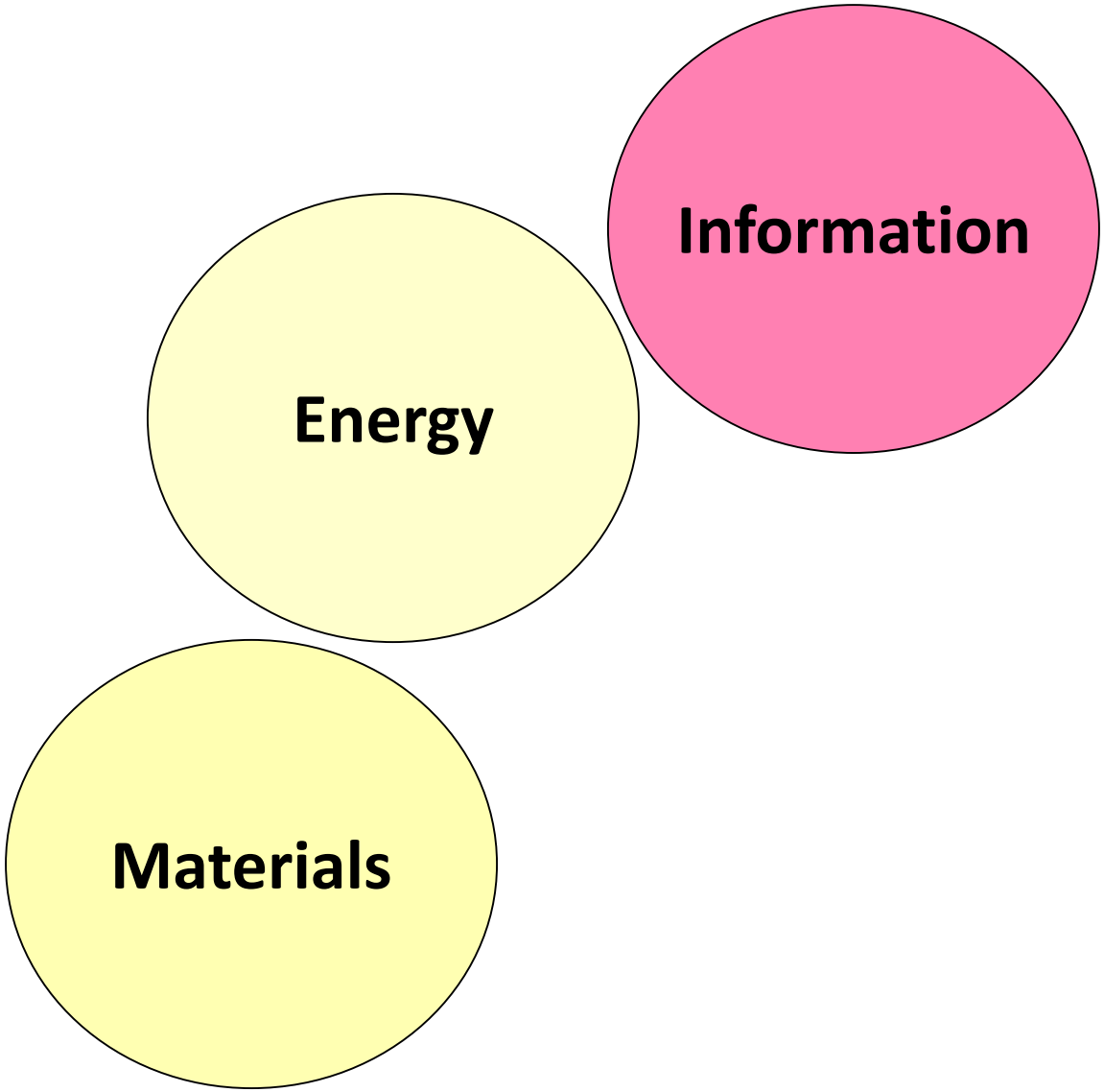
-Infrastructure for mobility: road network

-Telecommunication develops, radio, TV

-Labor and Capital (Marx) ; Unions ; Liberalism: Adam Smith

-Government as regulator and facilitator




Information
Energy
Materials

The science (analysis)

1880: Maxwell's laws (electro-magnetism)

1905: Quanta: Planck and Einstein

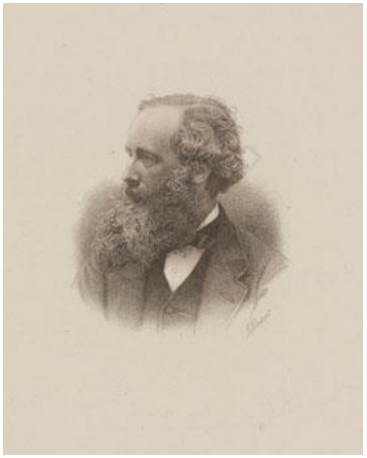
1910: Atom model Bohr

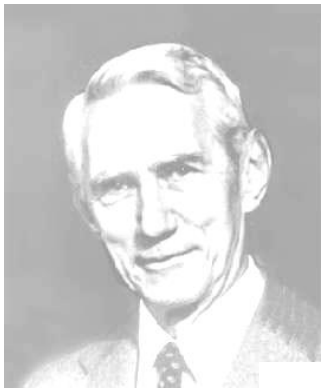
1930: Quantummechanics of Heisenberg, Schrödinger,…

1940: Computer (principle) of Turing and von Neumann

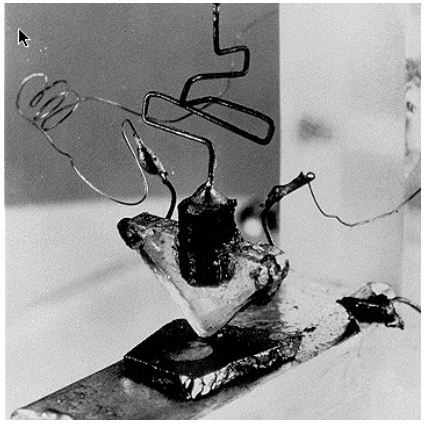
1948: Information theory of Shannon

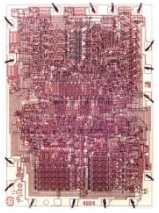
1950: Transistor of Shockley, Bardeen,…

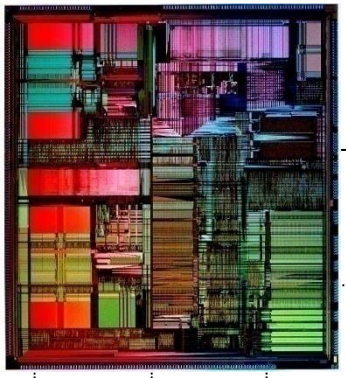


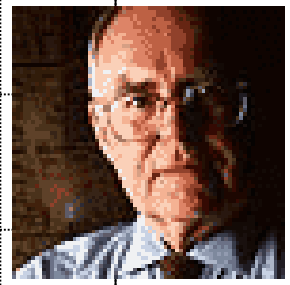


Technology and Engineering Design:
The third industrial revolution (1945…)





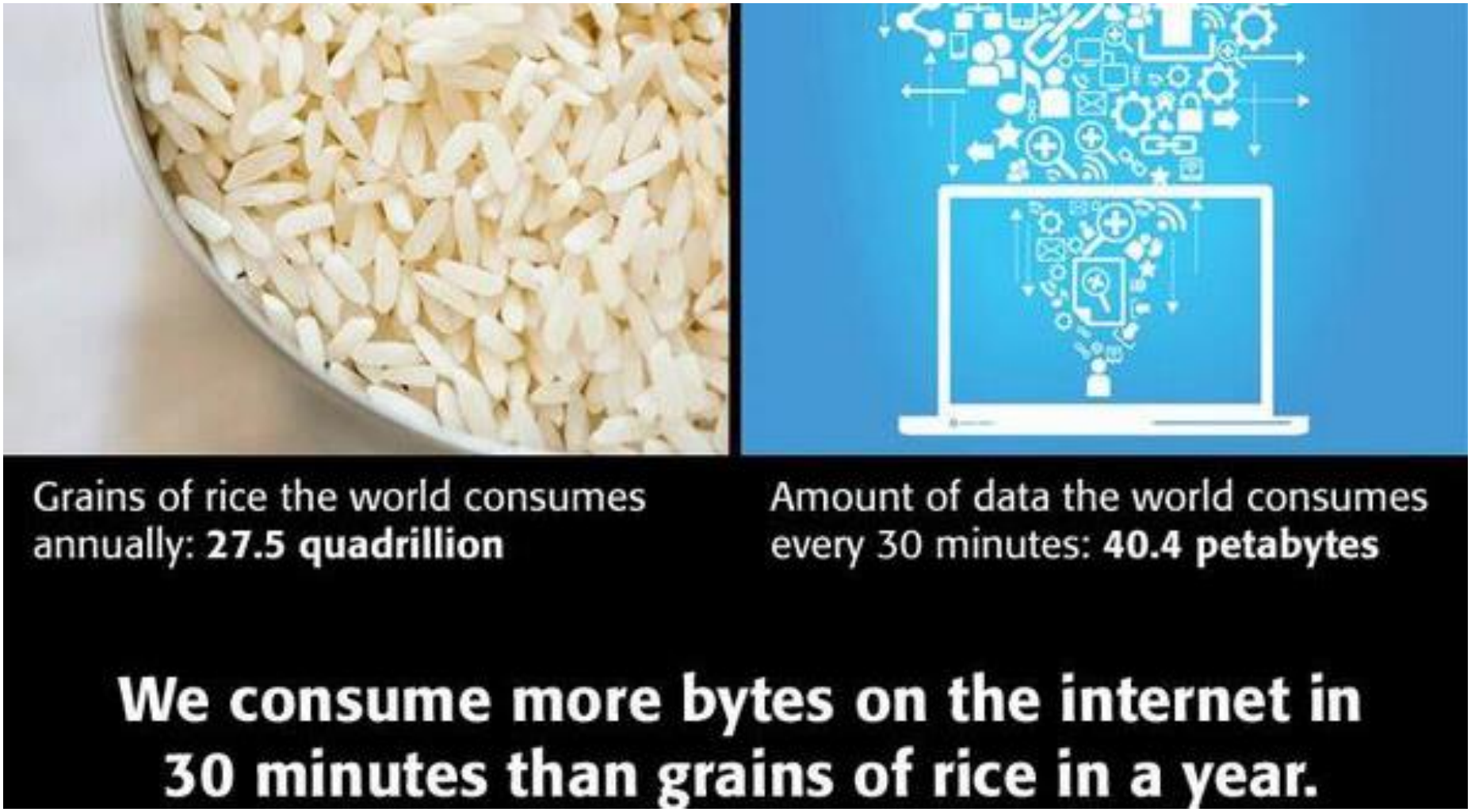




Computational power x 2 every 18 months

How is a chip designed ? Modular !

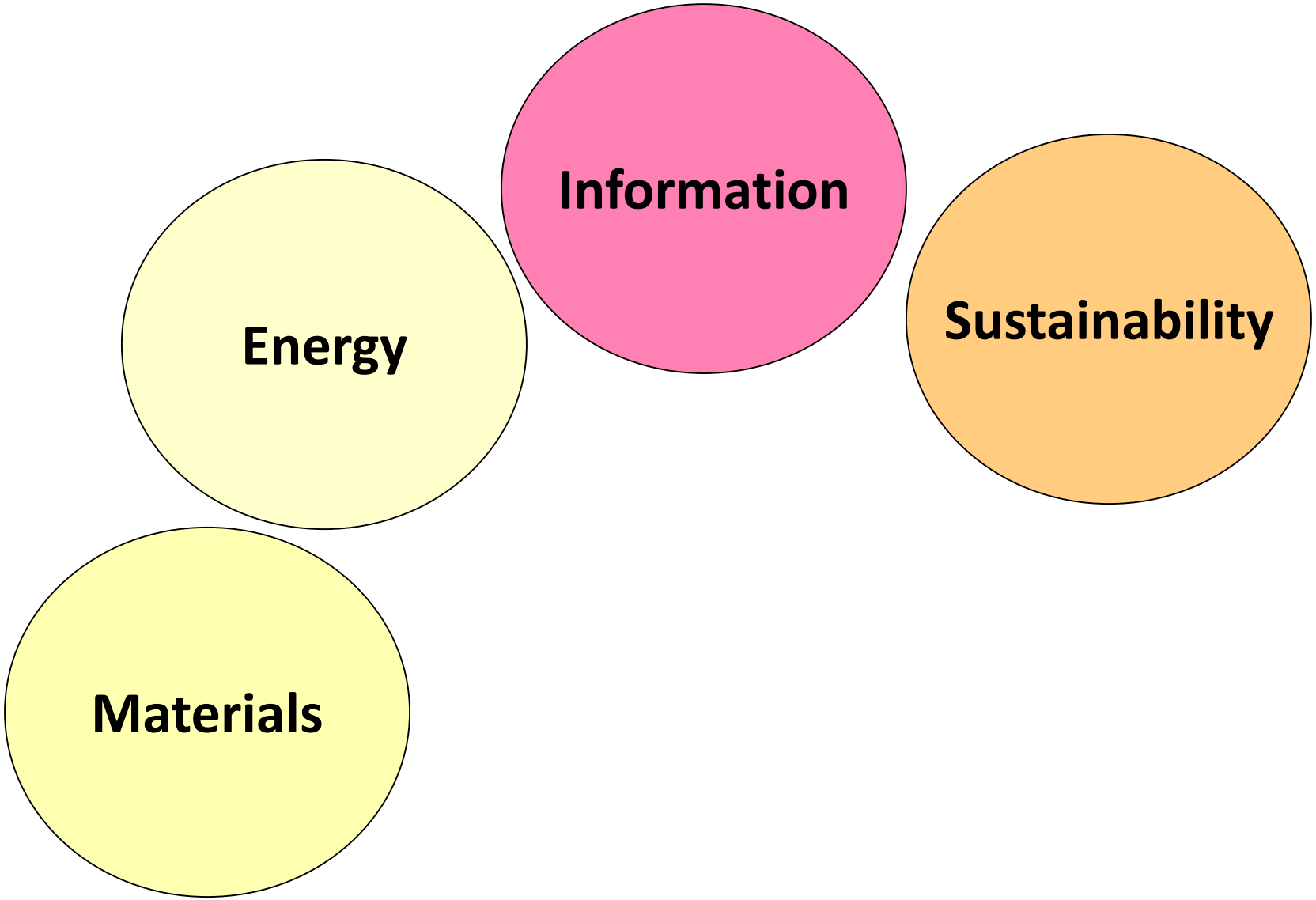
House	Chip
Living room	Memory
Kitchen	Clock
Bedroom	Control
Bath room	CPU
Garage	Communication
….	….
Utilities (water, electricity,…)	Utilities (power, communication….)
Bricks (clay)	Transistors (silicium)
…..	…..
Plan	Plan



1 million = 1 000 000
1 billion = 1 000 000 000
1 trillion = 1 000 000 000 000
1 quadrillion =
1 000 000 000 000 000

1 kB = 1 000
1 MB = 1 000 000
1 GB = 1 000 000 000
1 TB = 1 000 000 000 000
1 PB = 1 000 000 000 000 000

1 TB
= large university library
= 212 DVD discs
= 1430 CDs
= 3 year music in CD quality


Information
Energy
Sustainability
Materials

Sustainability

- Globalization

  Global Village Concept van CNN
  Internet
  Think globally, act locally (glocal)
  Netwerks of people and computers

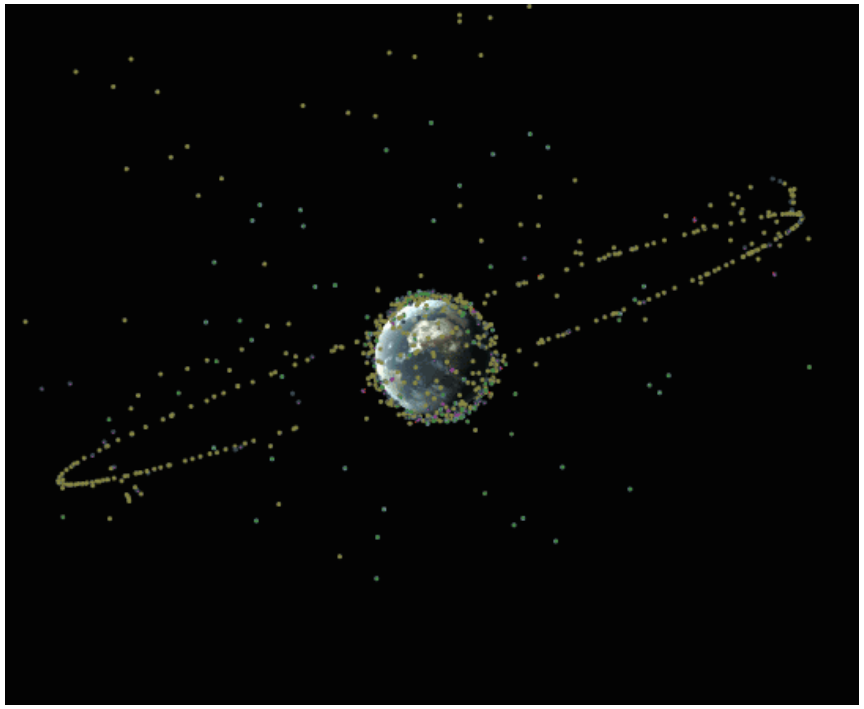
- Standardization, uniformization, protocollization

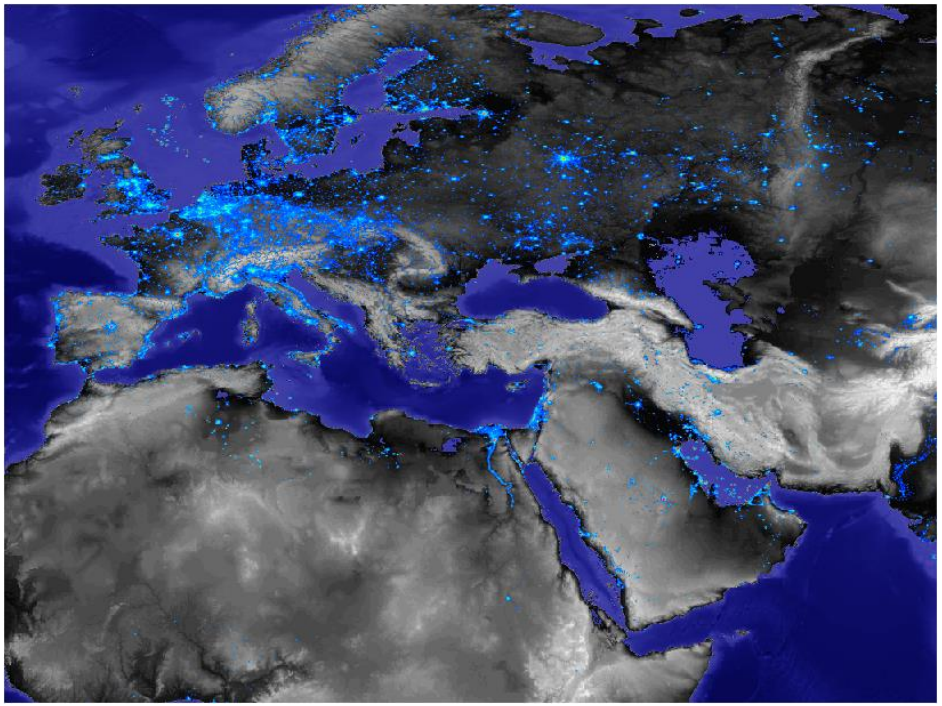
- Sustainable society

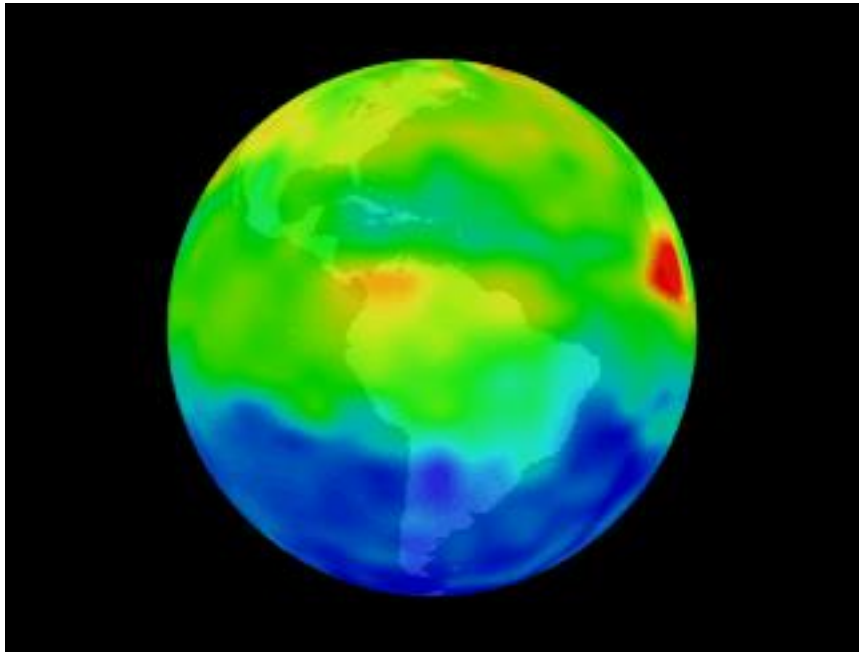
  Traditionally: Finite demands and infinite supplies
  Now: Infinite demands but finite supplies

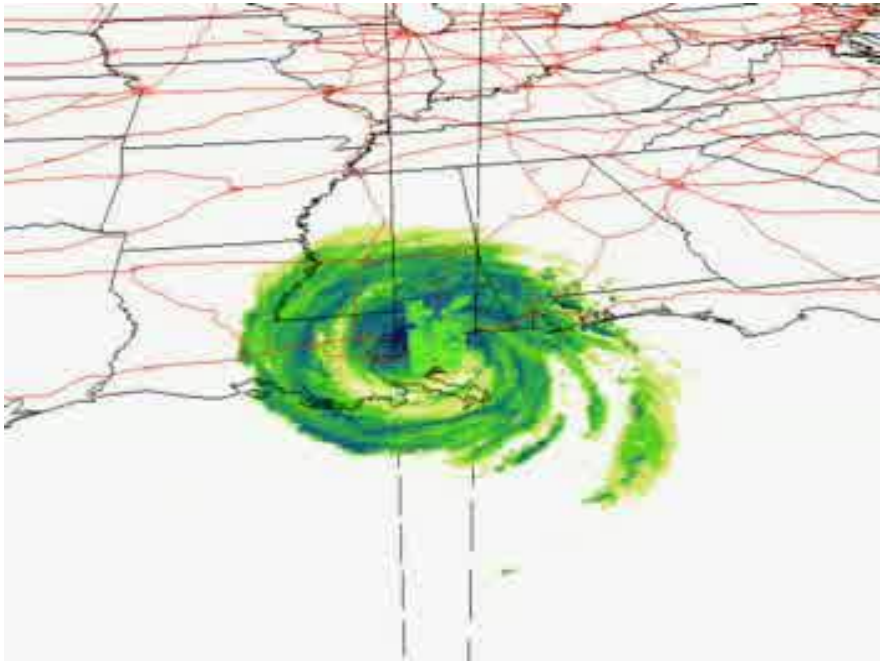
  We did not inherit the world from our ancestres, but have borrowed it from our children (Antoine de Saint-Exupery)

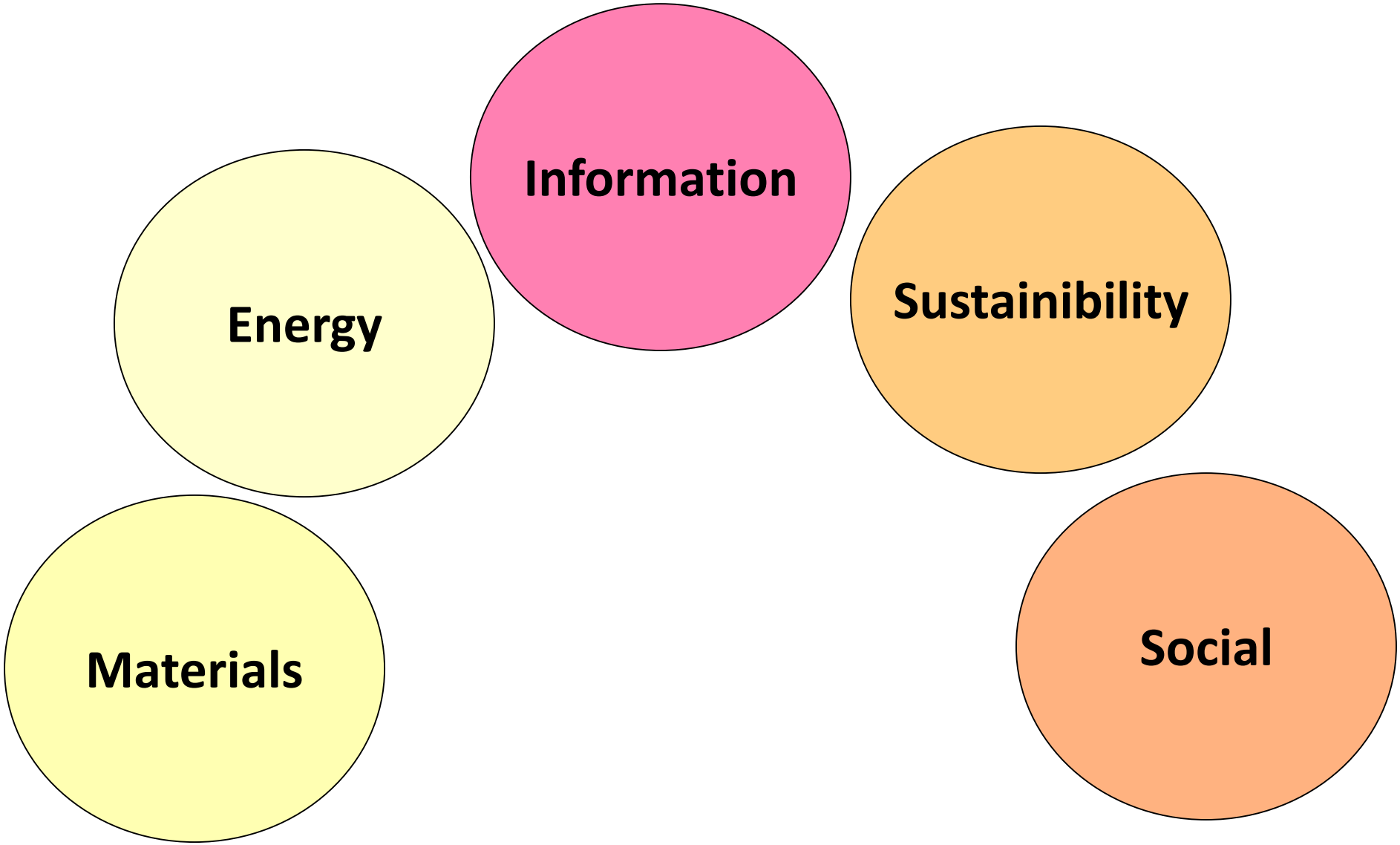
- *Cleantech, renewable energy, global warming, ….*



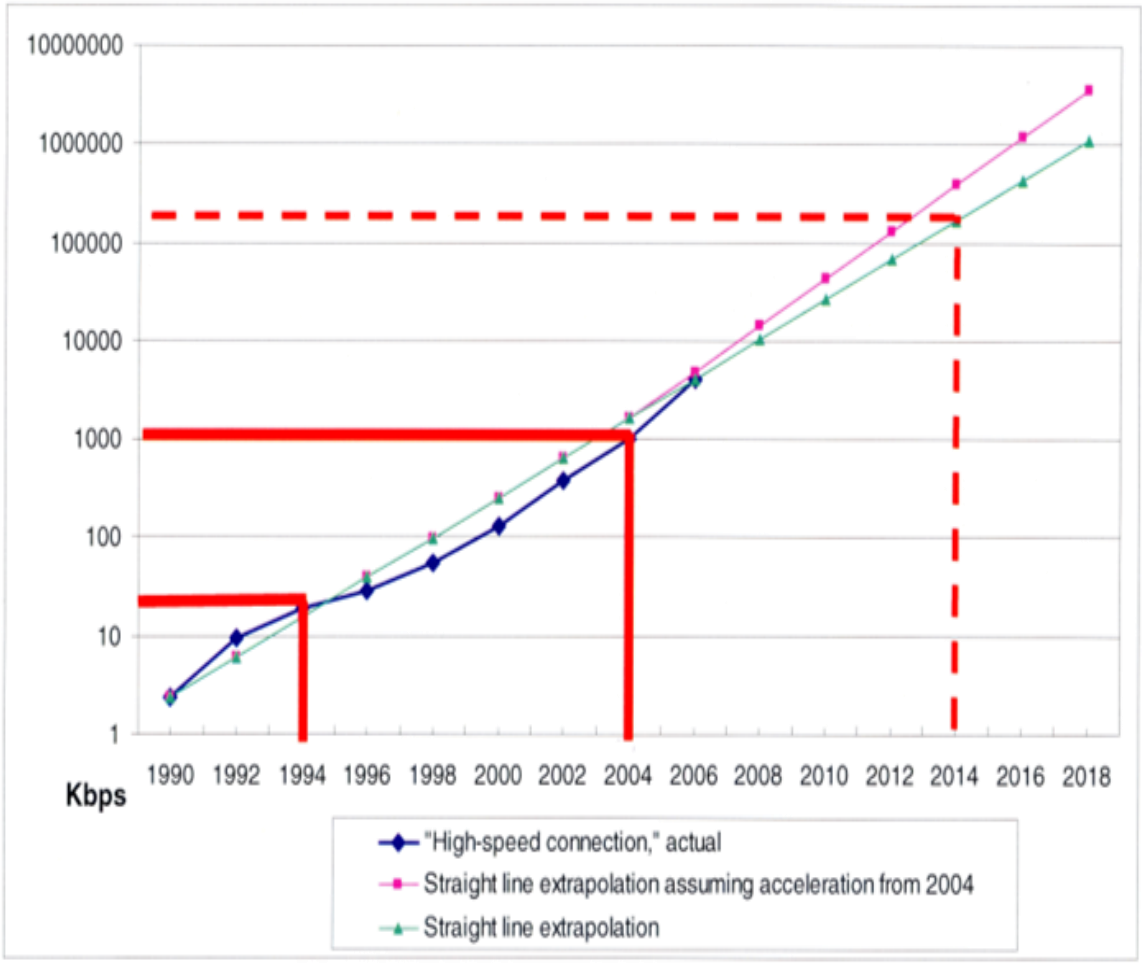







Information
Energy
Sustainibility
Materials
Social

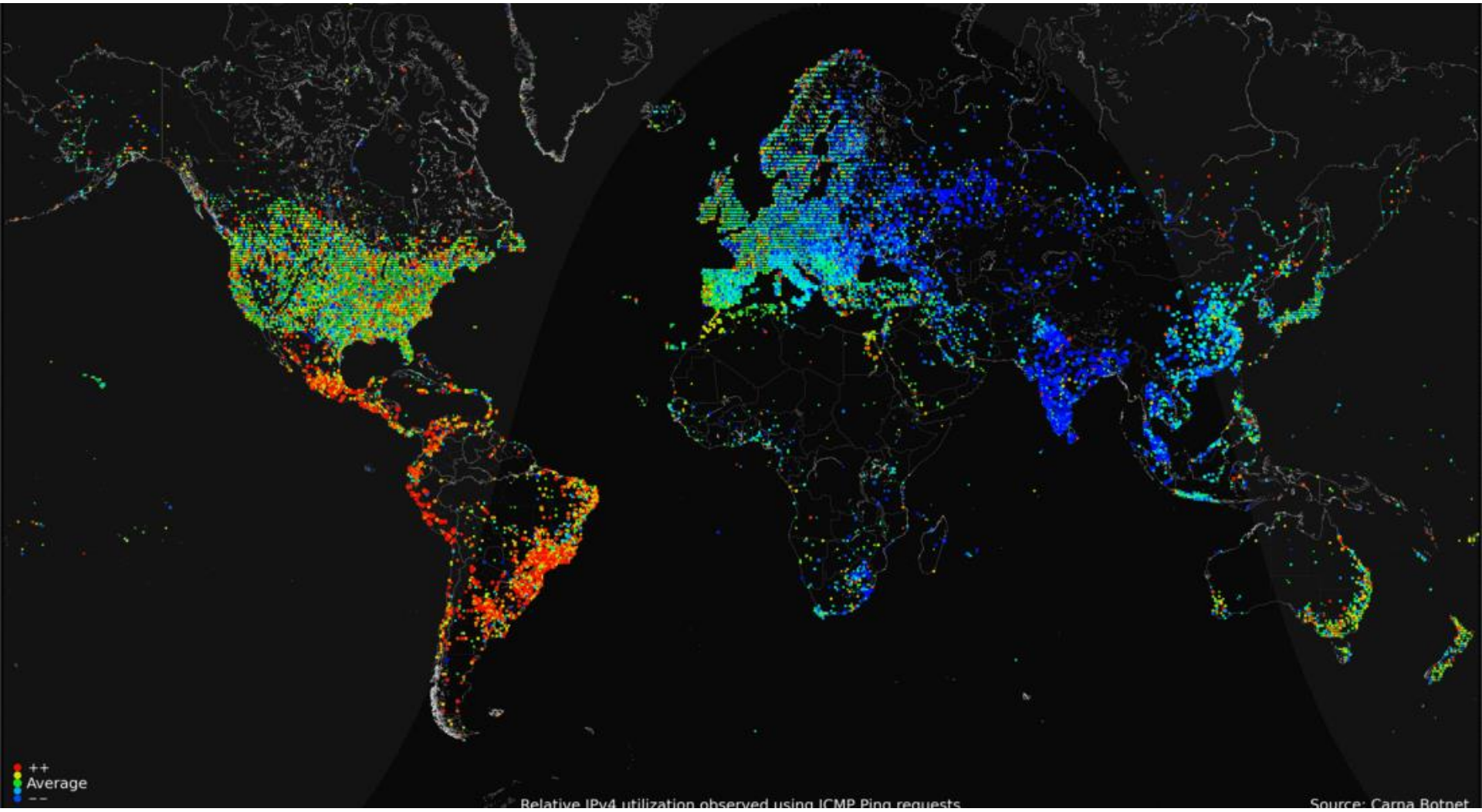
Connectivity



We are always CONNECTED

and FAST!

www: max 19 clicks !



Information

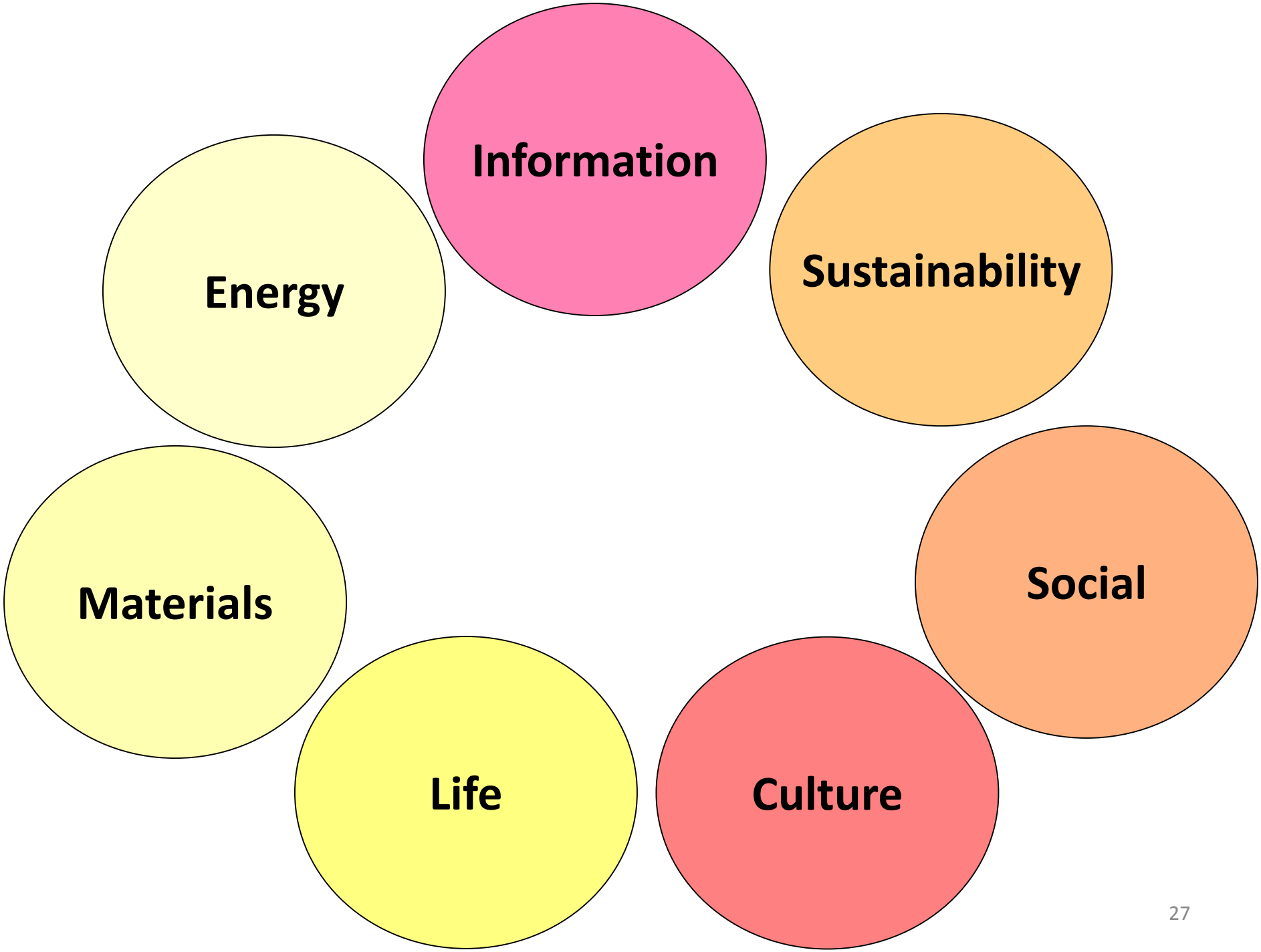
Energy

Sustainability

Materials

Social

Culture


Information
Energy
Sustainability
Materials
Social
Life
Culture

The science

1865: Mendel: Laws of inheritance from statistical inference

1944: Avery/MacLeod/McCarty: DNA = heriditary material

1953: Watson/Crick: DNA double helix

1965: Restriction enzymes: DNA ‘scissors’

1966: Nirenberg/Khorana/Holley: Determine genetic code

1972: Cohen/Boyer: Recombinant DNA, gene transfer in bacteria

1977: Sanger/Maxam/Gilbert: DNA sequencing methods

1982: Insuline by transgene bacteria

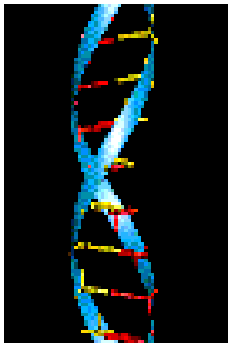
1985: Polymerase Chain Reaction (PCR)

1991: First transgene animal: Herman the bull

1994: GM tomatoes to market

1997: First cloned animal: Dolly

2001: Human Genome Completion announced



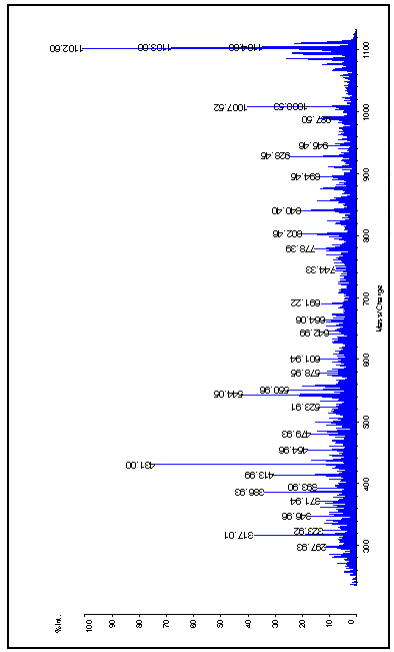
Tsunami of data from progress in technology

Computer Tomography

GS-FLX Roche
Applied Science 454

Sequencers

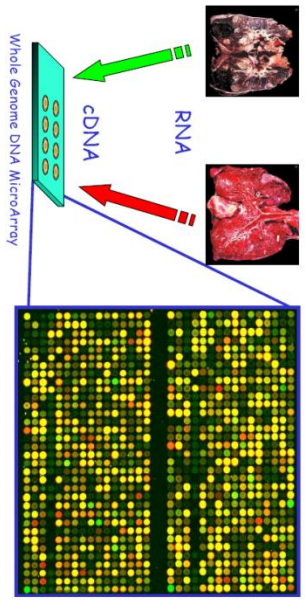
ACACATTAAATCTTATATGC
TAAAACTAGGTCTCGTTTTA
GGGATGTTTATAACCATCTT
TGAGATTATTGATGCATGGT
TATTGGTTAGAAAAAATATA
CGCTTGTTTTTCTTTCCTAG
GTTGATTGACTCATACATGT
GTTTCATTGAGGAAGGAAC
TTAACAAAACTGCACTTTTT
TCAACGTCACAGCTACTTTA
AAAGTGATCAAAGTATATCA
AGAAAGCTTAATATAAAGAC
ATTTGTTTCAAGGTTTCGTA
AGTGCACAATATCAAGAAG
ACAAAAATGACTAATTTTGT
TTTCAGGAAGCATATATATT
ACACGAACACAAATCTATTT
TTGTAATCAACACCGACCAT
GGTTCGATTACACACATTAA
ATCTTATATGCTAAAACTAG
GTCTCGTTTTAGGGATGTTT
ATAACCATCTTTGAGATTAT
TGATGCATGGTTATTGGTTA
GAAAAAATATACGCTTGTTT
TTCTTTCCTAGGTTGATTGA

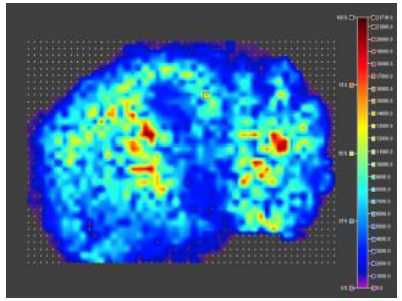


Magnetic resonance

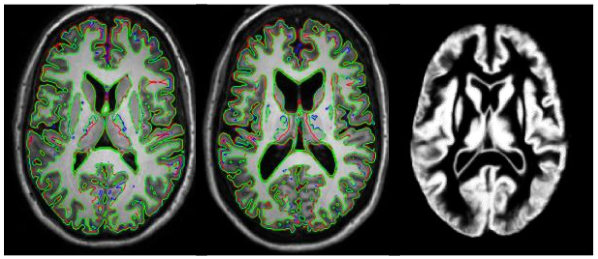
maf VIB
MicroArray Facility

Microarrays
(DNA chips)

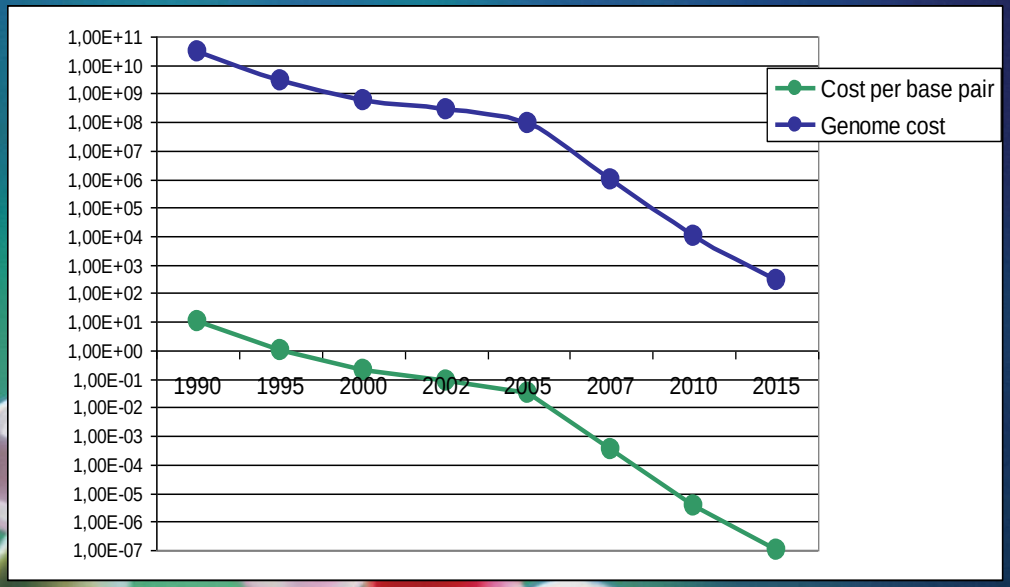




Mass spectrometry

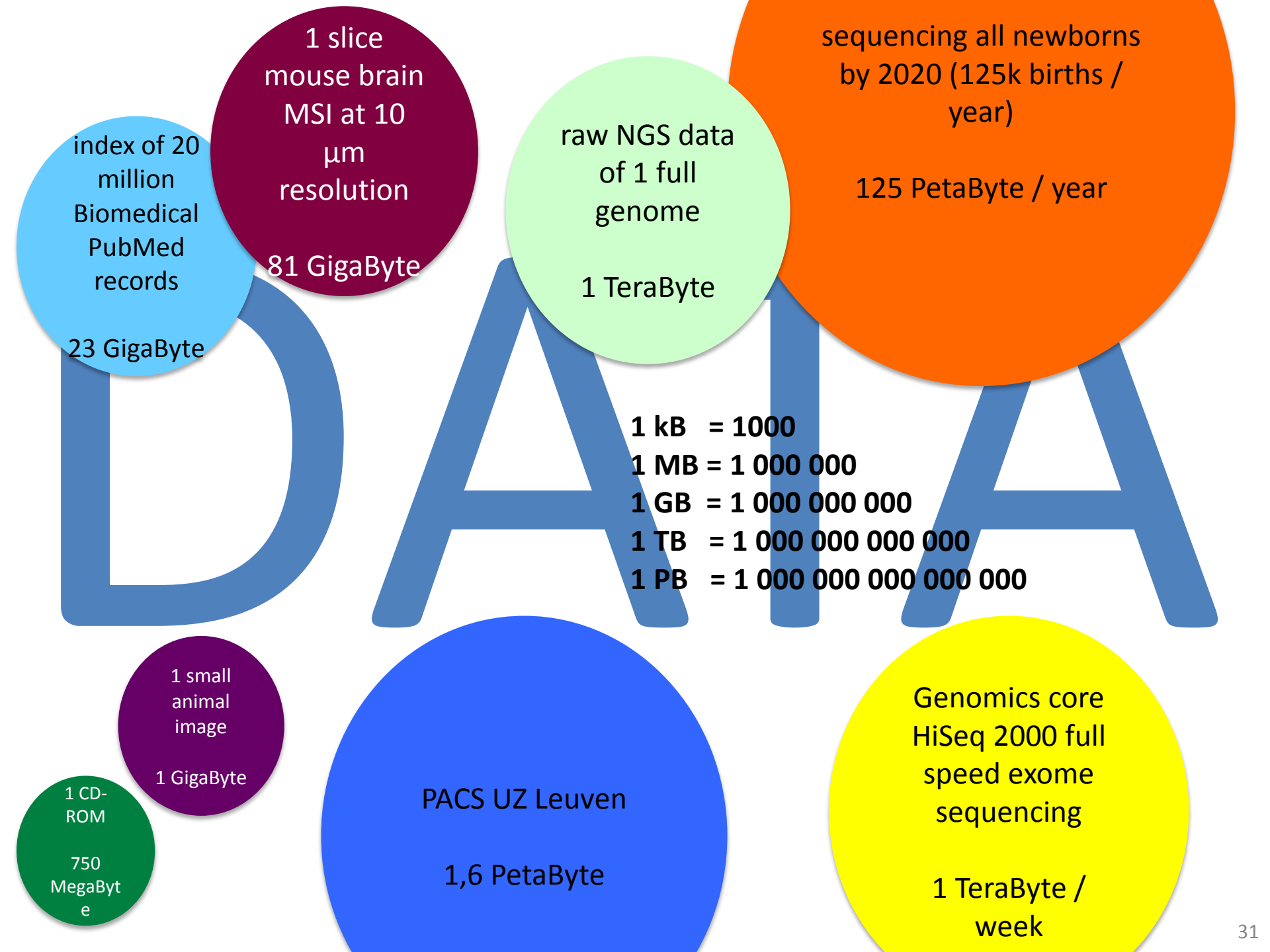


Genome data



- Human genome project
  - Initial draft: June 2000
  - Final draft: April 2003
  - 13 year project
  - $300 million value with 2002 technology
- Personal genome
  - June 1, 2007
  - Genome of James Watson, co-discoverer of DNA double helix, is sequenced
    - $1.000.000
    - Two months
- €1000-genome
  - Expected 2012-2020

YearΩ	Cost per base pair	Genome cost
1990	10	3E+10
1995	1	3.000.000.000
2000	0.2	600.000.000
2002	0.09	270.000.000
2005	0.03	90.000.000
2007	0.000333333	1.000.000
2010	3.33333E-06	10000
2015	0.0000001	300


1 slice mouse brain MSI at 10 µm resolution
81 GigaByte
index of 20 million Biomedical PubMed records
23 GigaByte
raw NGS data of 1 full genome
1 TeraByte
sequencing all newborns by 2020 (125k births / year)
125 PetaByte / year
DATA
1 kB = 1000
1 MB = 1 000 000
1 GB = 1 000 000 000
1 TB = 1 000 000 000 000
1 PB = 1 000 000 000 000 000
1 small animal image
1 GigaByte
1 CD-ROM
750 MegaByte
PACS UZ Leuven
1,6 PetaByte
Genomics core HiSeq 2000 full speed exome sequencing
1 TeraByte / week

ARTHUR M. LESK

The Unreasonable Effectiveness of Mathematics in Molecular Biology*

My title is an emulation of that of the well-known paper by E.P. Wigner, "The unreasonable effectiveness of mathematics in the natural sciences [1]." Of course the irony cuts in opposite ways in physics and molecular biology. In physics, mathematics is obviously effective—

many of the giants on whose shoulders physicists stand are mathematicians—and the surprise is Wigner's suggestion that this is unreasonable. In molecular biology, the proper role of mathematics is not obvious, and there is fear, far more credible than for physics, that it may be unreasonable to expect mathematics to be effective. Of course, many common *tools* of computational molecular biology—for instance, searching in databases for sequences similar to a probe sequence—are certainly based on mathematics and computer science. But whether our ultimate understanding of living processes will be expressed in the language of mathematics—in the way, for example, that concepts of symmetry underlie the statement of laws of physics—or in the traditional descriptive "anecdotal" language of biology, is still moot.

Why might it be reasonable to doubt the effectiveness of mathematics in biology? Observed properties of living systems are determined by a combination of

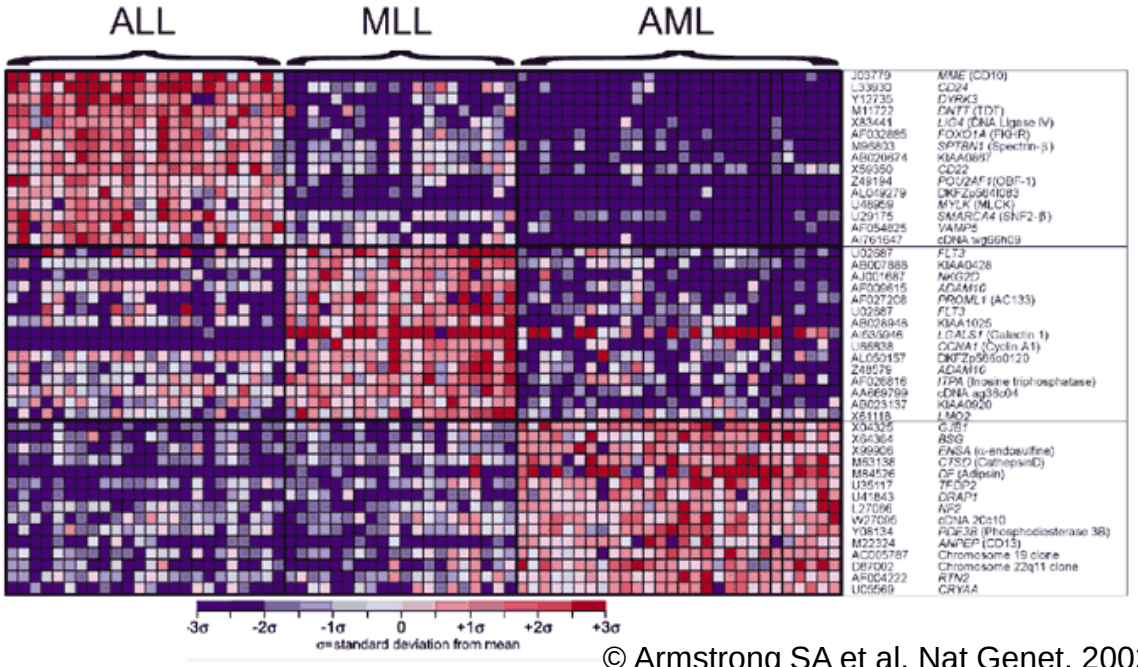
- The laws of physics and chemistry
- The mechanism of evolution
- Historical accident

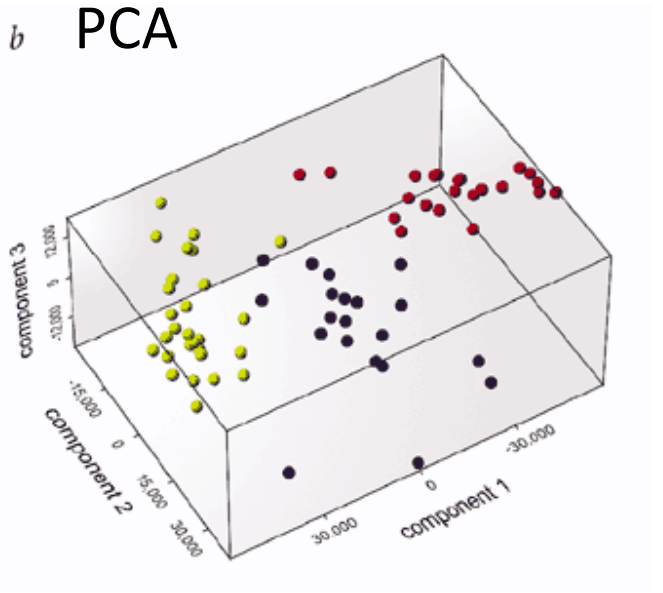
It is difficult to sort out their effects, and a creative tension among them pervades our investigations. Many of the laws of physics describe the natural world—including living systems—by specifying relations between initial and fi-

*Based on a talk delivered at the final symposium of the program, "Biomolecular Function and Evolution in the Context of the Genome Project," at The Isaac Newton Institute for the Mathematical Sciences, Cambridge, U.K., 20 Dec. 1998.

Biology = information processing = mathematics

Genetics based cancer diagnosis





12 600 genes

72 patients:

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

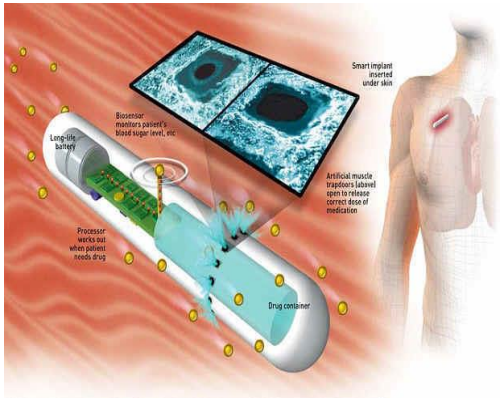
3 patients for each class used as test set

Transdisciplinary engineering design

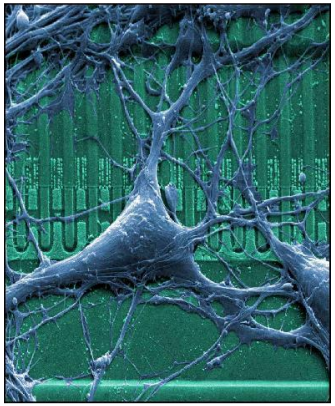
Materials, energy, IT

Ubiquitous computing

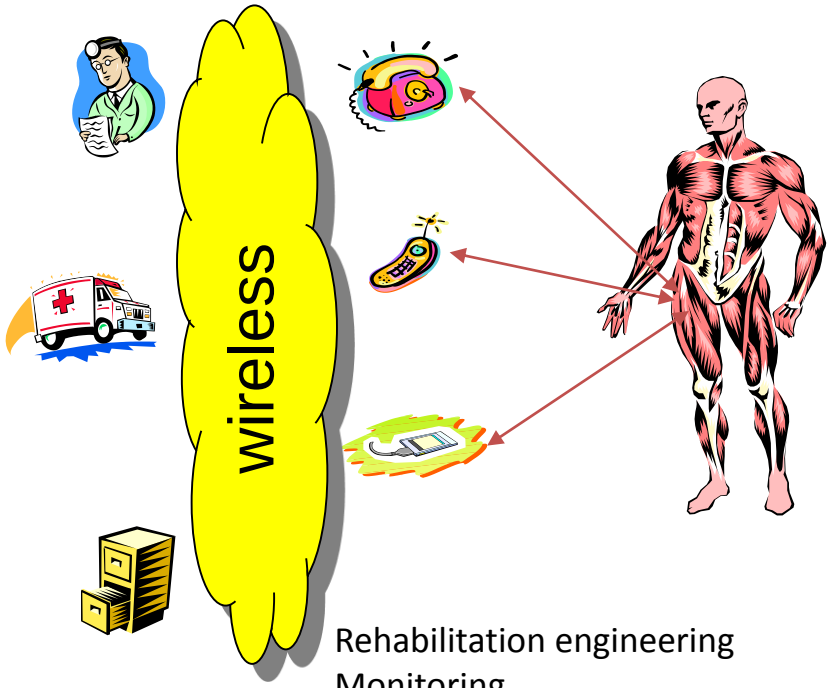
Ambient intelligence



Embedded intelligence
Smart pills

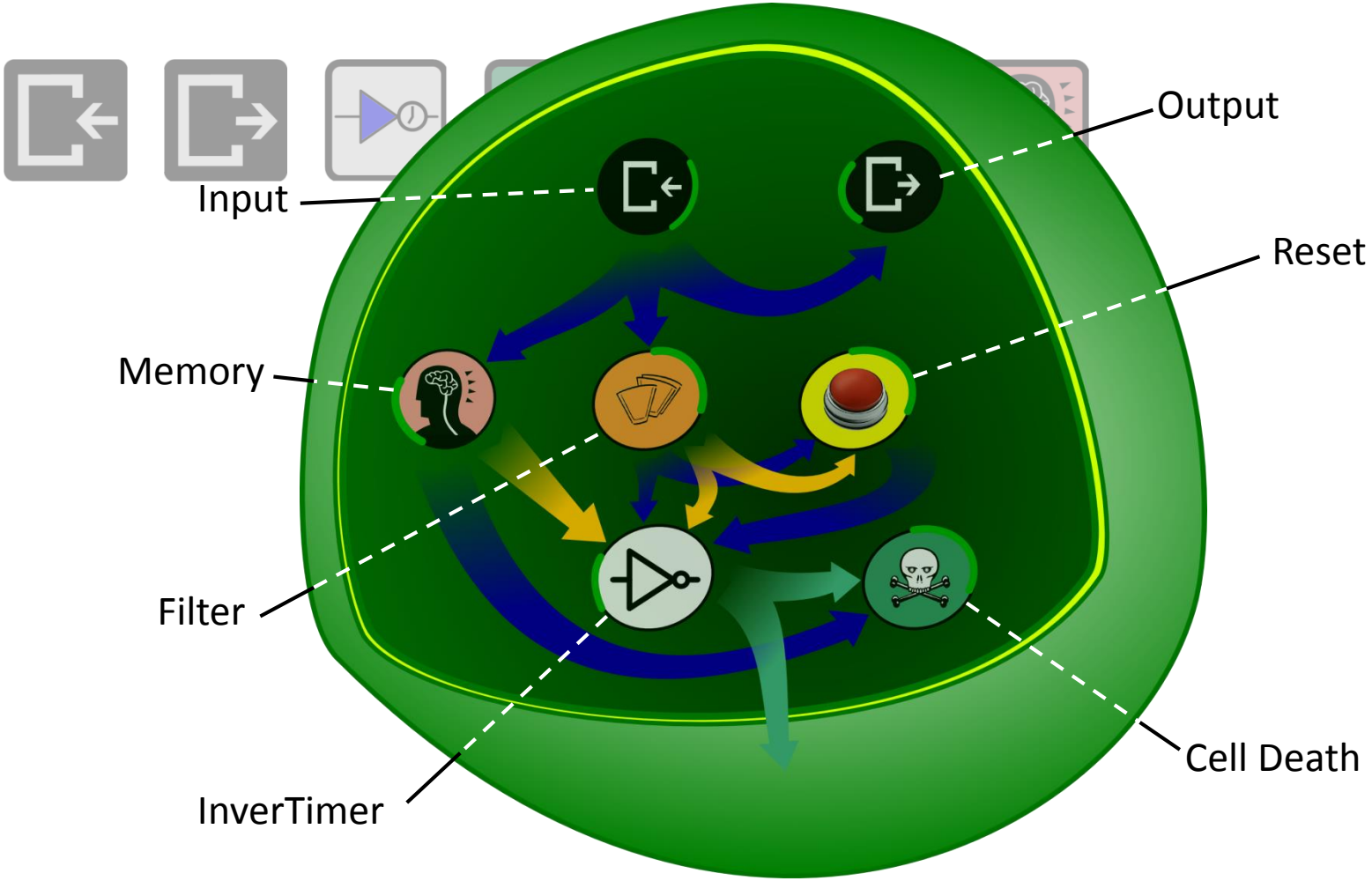


Neuron on chip



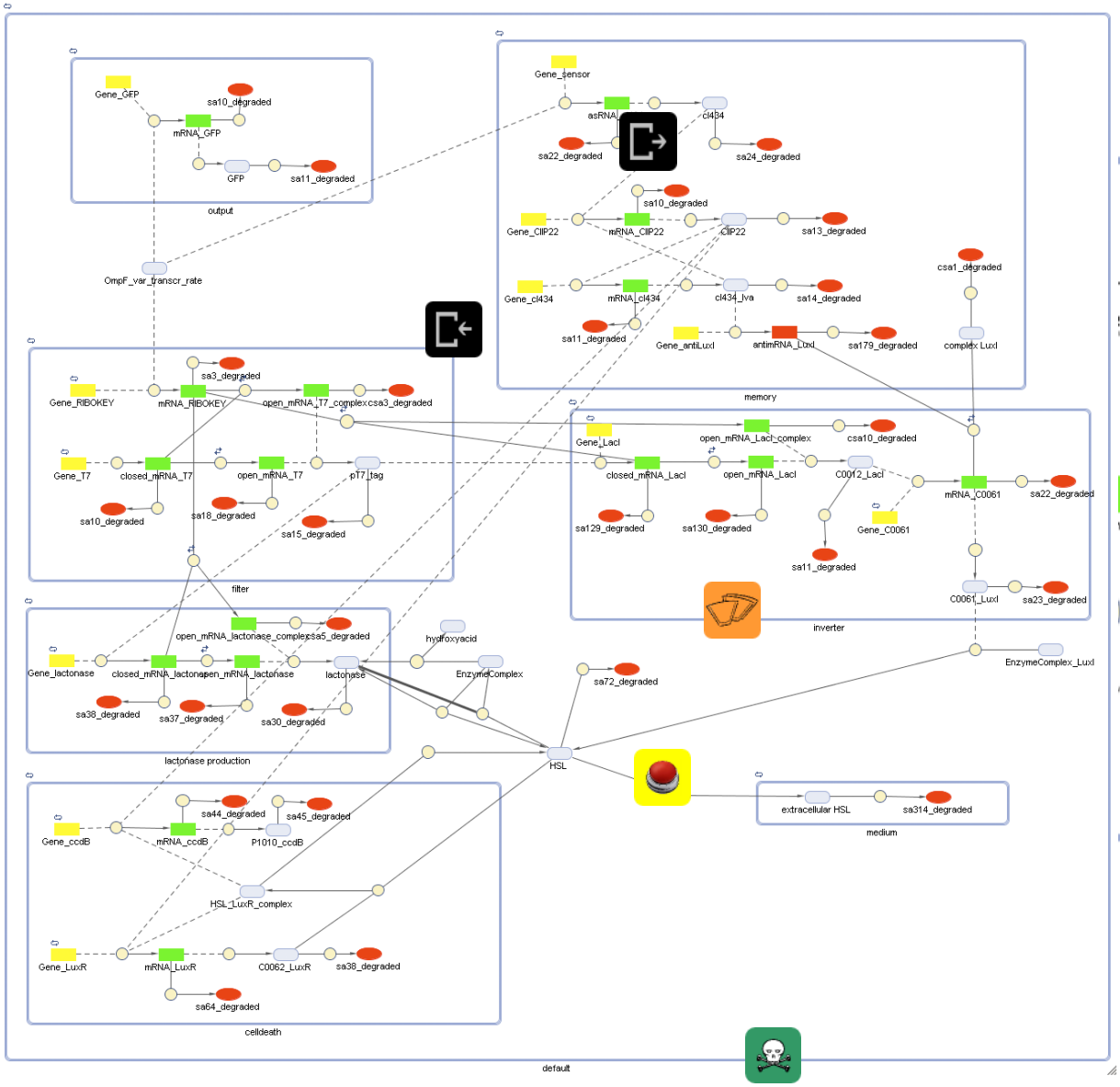
Rehabilitation engineering
Monitoring
Sensors: EEG, glucose,blood, DNA, …
Add-ons: vision, hearing, implants, …

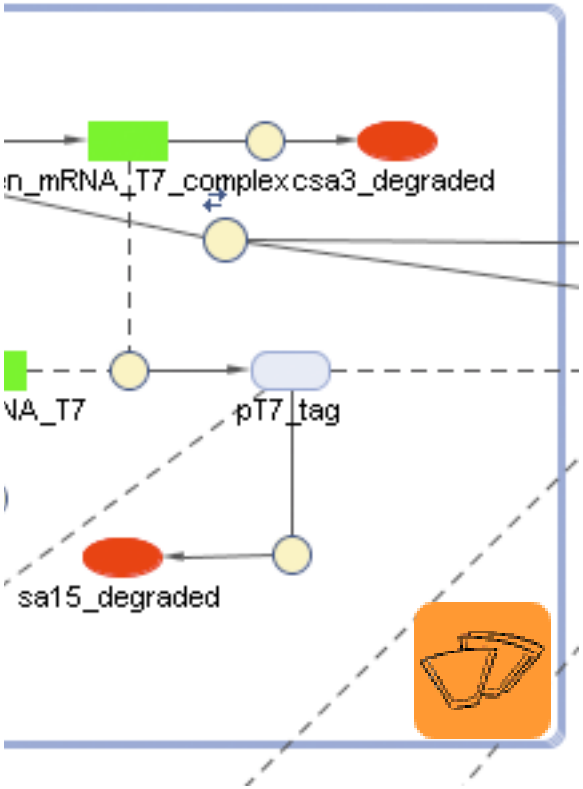
Synthetic biology: design new functional life
Bacterium detecting cancer cells



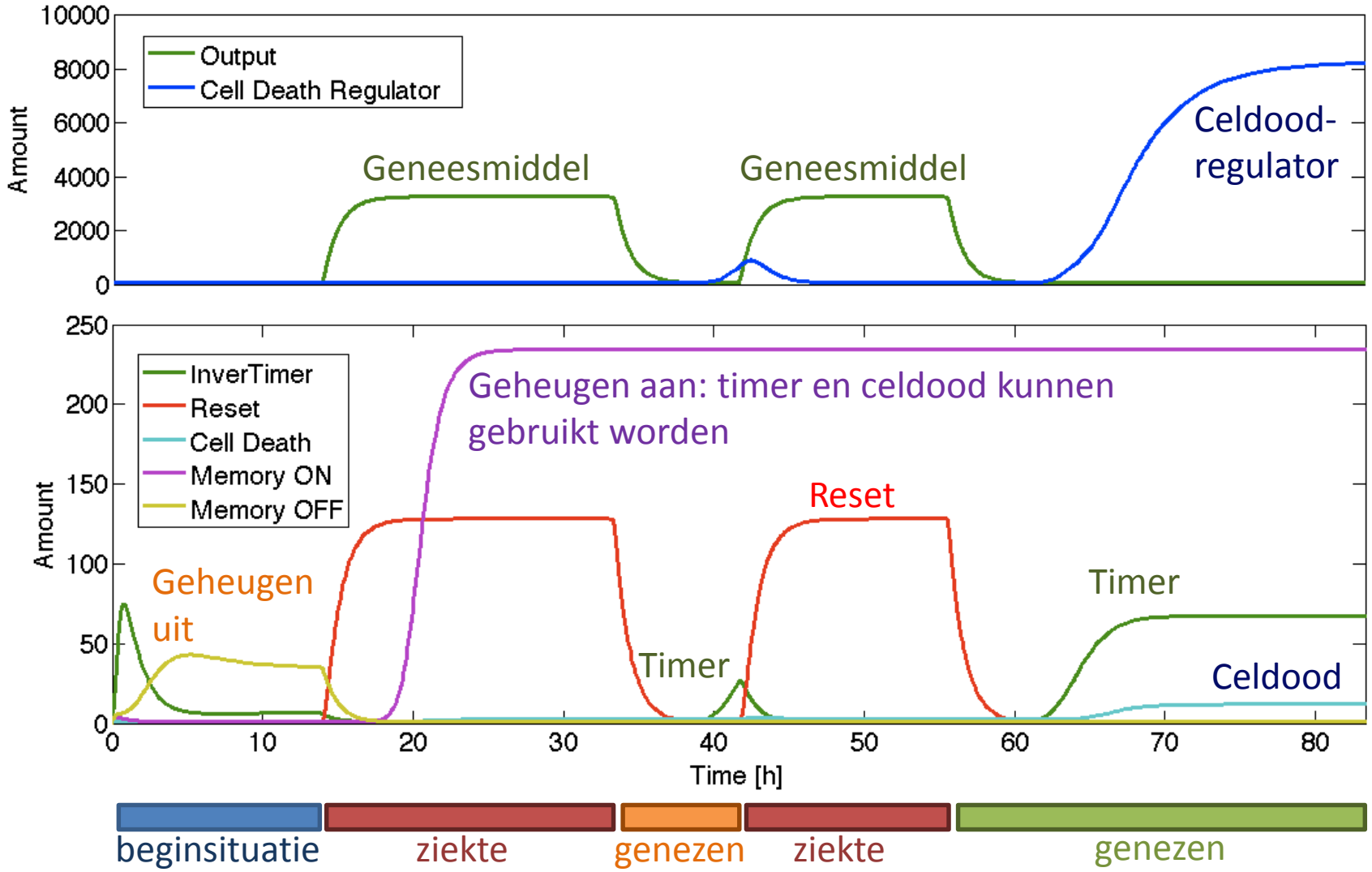
http://2013.igem.org/Team:KU_Leuven

in silico model Dr. Coli





Dr. Coli does the job !



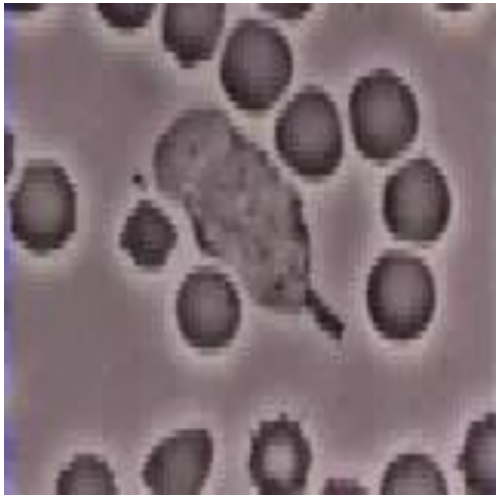
1. What is science ? What are models ? What is technology ? What is engineering ?

1. The seven spheres of engineering
    1. Matter
    2. Energy
    3. Information
    4. Sustainability
    5. Social
    6. Culture
    7. Life

1. Analysis and Design in the seven spheres

1. Utopia ? Design of living systems ?

Life goes live: Utopia ?



- Design life ?
- Bacteria for energy, clean tech, human therapy
- Design artificial organs ? Artifical limbs ?

- Utopia ? I don't think so !!

- Three deficits
  - -Legal (law lags behind !)
  - -Democratic (who decides ? Frankenstein ? Science sharing)
  - -Ethical (not how but what !) (genetics, stem cells, IVF,….)