Nieuwe wegen voor de wetenschap

Bart De Moor

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

1. Wat is
    1. Wetenschap ?
    2. Technologie ?
    3. Engineering ?

1. Analyseren en ontwerpen in de zeven ingenieurssferen
    1. Materie
    2. Energie
    3. Informatie
    4. Duurzaamheid
    5. Sociale netwerken
    6. Cultuur
    7. Leven

Wat is wetenschap ?

- De wereld beschrijven en begrijpen

- Verhalen, mythes, verifieerbare feiten

- Religie en wetenschap

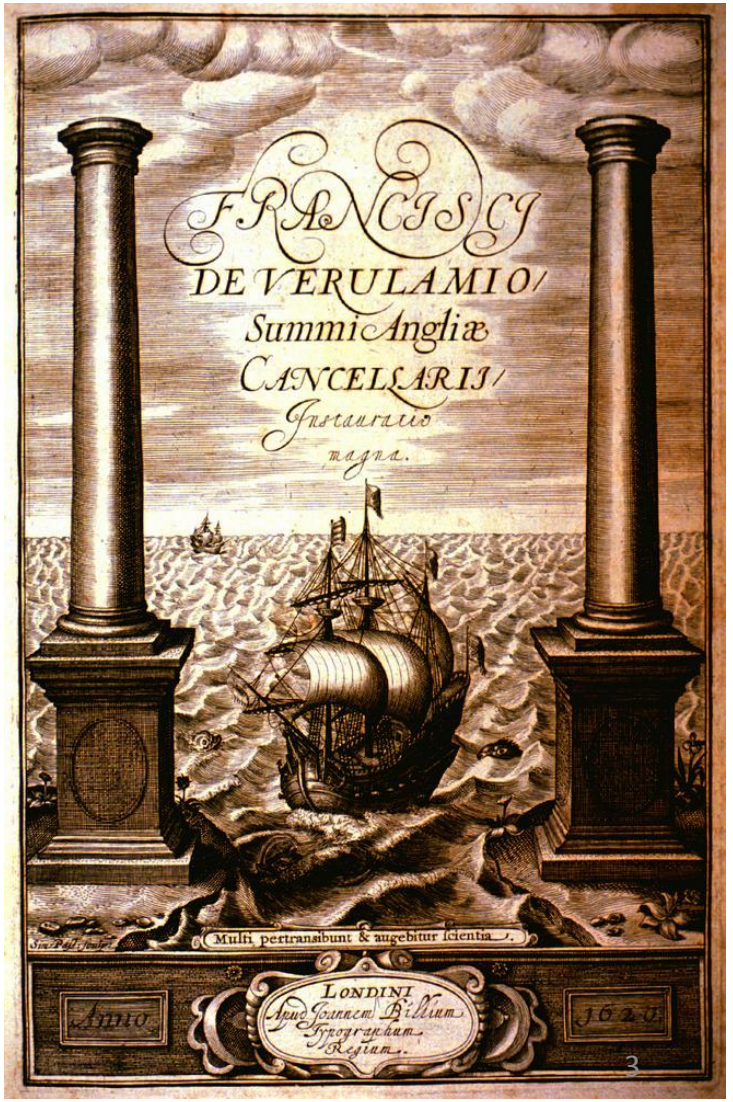
    - De Schepper buiten de Schepping

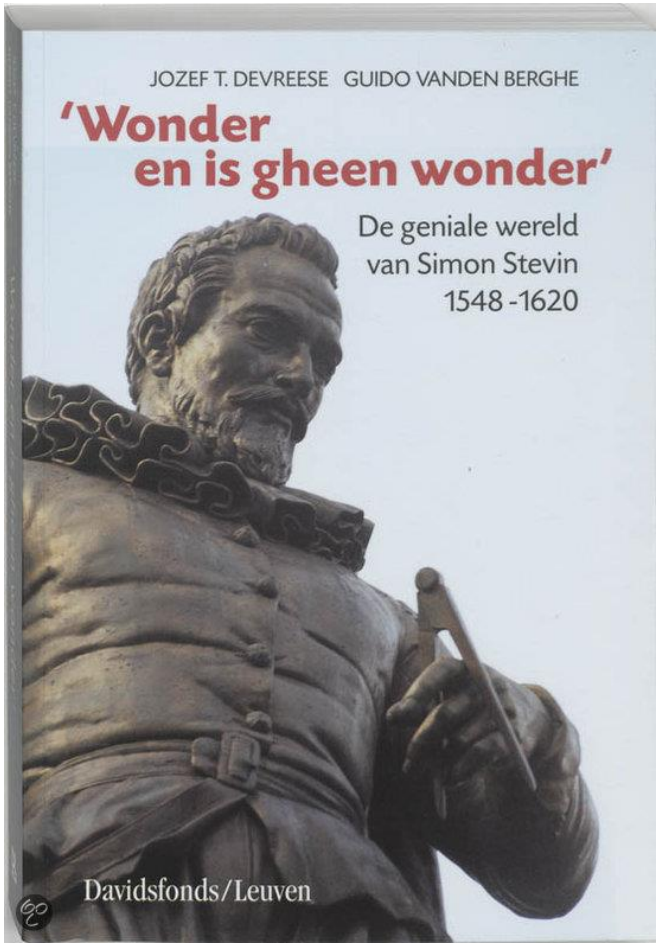
    - *Galileo Galilei en de Kerk*

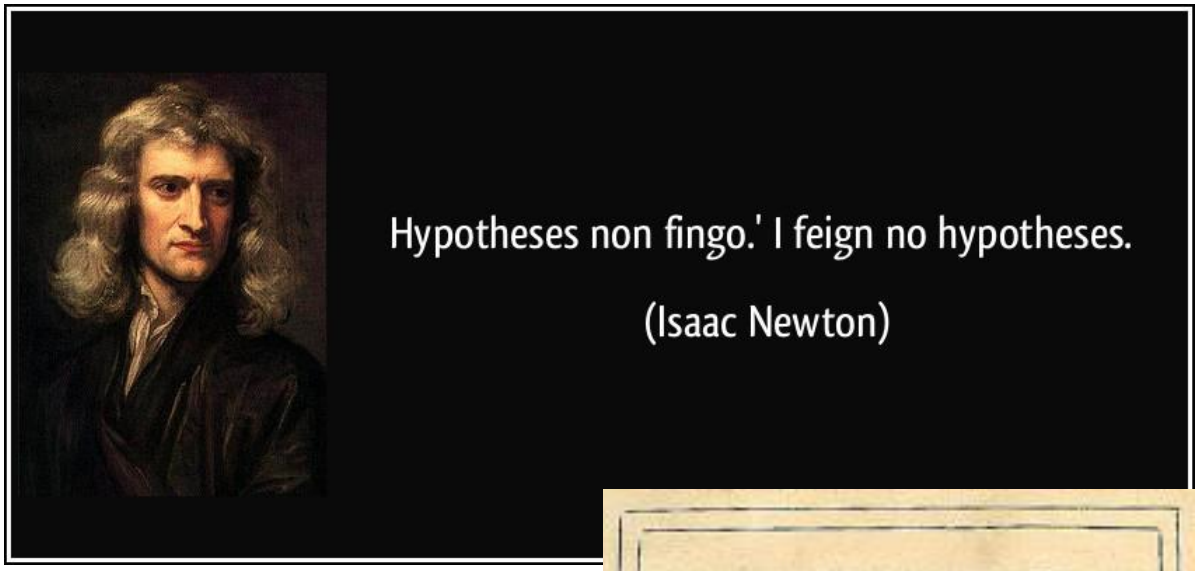
    - *Napoleon: Où est Dieu dans votre système ?*
      Laplace: Dieu ?
      Je n'ai pas besoin de cette hypothèse !

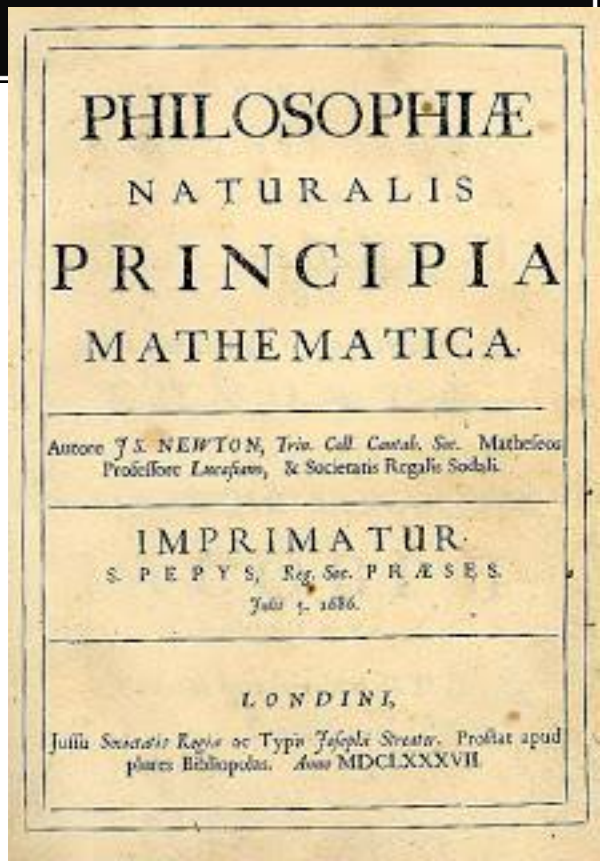
- Descartes: 'Je pense donc je suis' 'Cogito ergo sum'

- Francis Bacon (1561 – 1626)
    - De experimentale methode
    - Vooruitgangsdenken
    - Nec plus ultra; The limit is the sky !

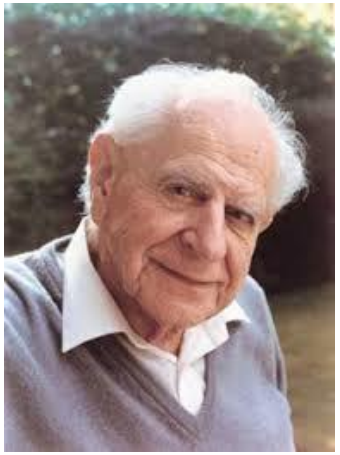



JOZEF T. DEVREESE GUIDO VANDEN BERGHE
'Wonder en is gheen wonder'
De geniale wereld van Simon Stevin 1548 -1620
Davidsfonds/Leuven


Hypotheses non fingo.' I feign no hypotheses.
(Isaac Newton)


PHILOSOPHIÆ
NATURALIS
PRINCIPIA
MATHEMATICA
Autore J.S. NEWTON, Trin. Coll. Cantab. Soc. Matheseos Professore Lucasiano, & Societatis Regalis Sodali.
IMPRIMATUR
S. PEPYS, Reg. Soc. PRÆSES.
Julii 5. 1686.
LONDINI,
Jussu Societatis Regiæ ac Typis Josephi Streater. Prostat apud plures Bibliopolas. Anno MDCLXXXVII.

Wat is wetenschappelijk ?



Karl Popper's Demarcatie-criterium

Een theorie is wetenschappelijk wanneer ze haar eigen zwakheden expliciteert

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)

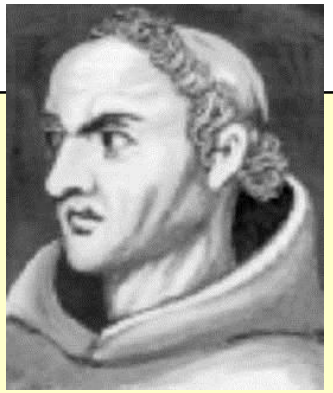
Geen enkele wetenschappelijke theorie is gegarandeerd voor altijd juist.

Een wetenschappelijke theorie 'verbiedt' meer dan wat ze verklaart. Een wetenschappelijke theorie laat toe om te voorspellen wat zal gebeuren, maar nog veel meer, wat niet zal gebeuren.

Niet wetenschappelijk:

- Elke godsdienst
- Ideologieen zoals Marxisme, Liberalisme, Socialisme, ….

Wetenschappelijke modellen reduceren de werkelijkheid



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

‘Reality is just another model’ ?

J’ai cherche la vie, je n’ai trouve que la science

Wat is technologie ?

- Technologie = techne logos
= de ‘kunst’ om te weten hoe je iets moet maken

-Technologie = de trans-biologische evolutie bovenop de natuurlijke biologische evolutie

Wat is ‘engineering’ ?

Engineering = technologie ontwerpen (=‘design’) en gebruiken om ‘problemen’ op te lossen

Wikipedia:

Engineering *(from Latin ingenium, meaning "cleverness" and ingeniare, meaning "to contrive, devise") is the application of scientific, economic, social, and practical knowledge in order to invent, design, build, maintain, and improve structures, machines, devices, systems, materials and processes.*
The discipline of engineering is extremely broad, and encompasses a range of more specialized fields of engineering, each with a more specific emphasis on particular areas of applied science, technology and types of application.

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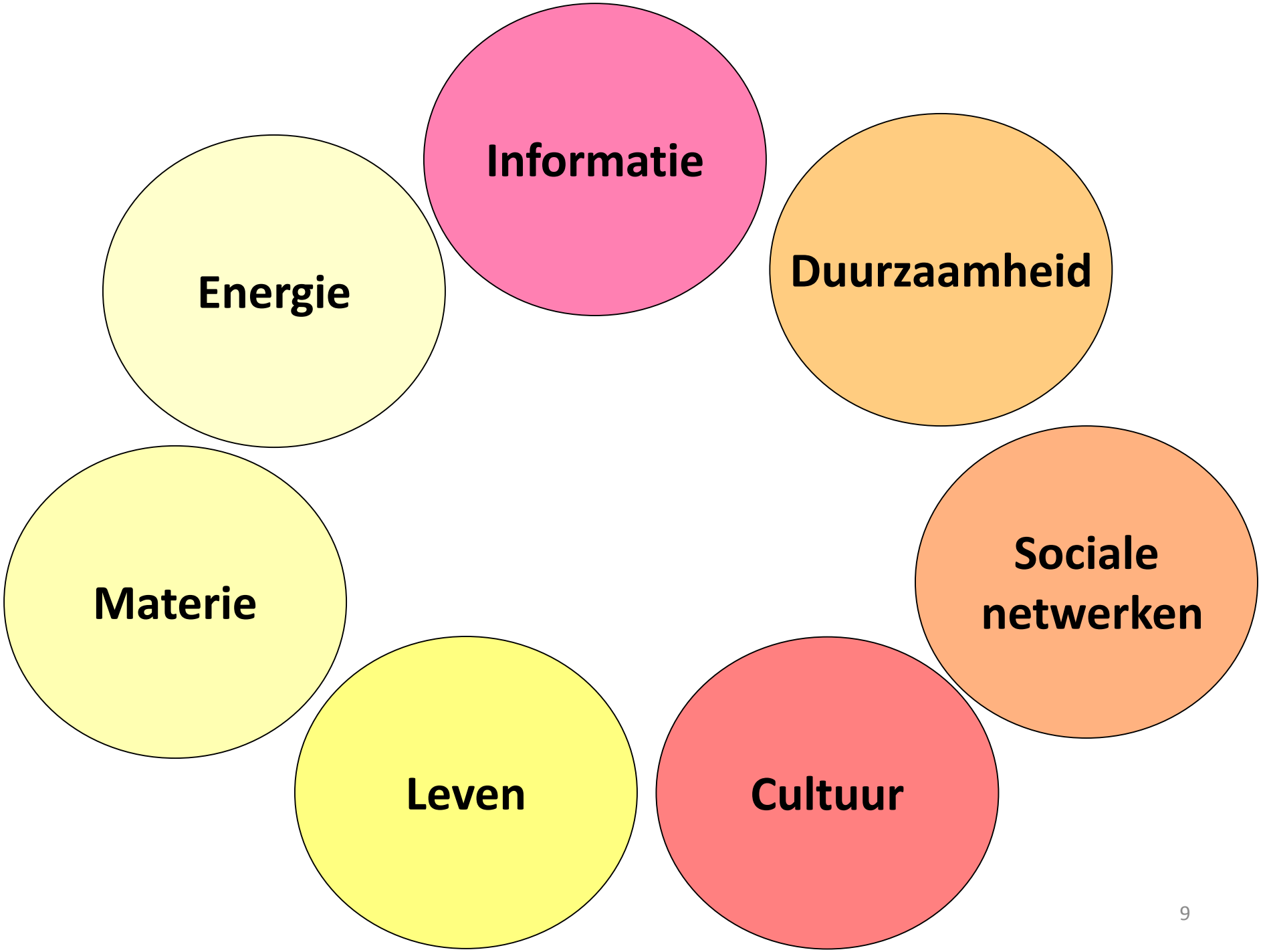
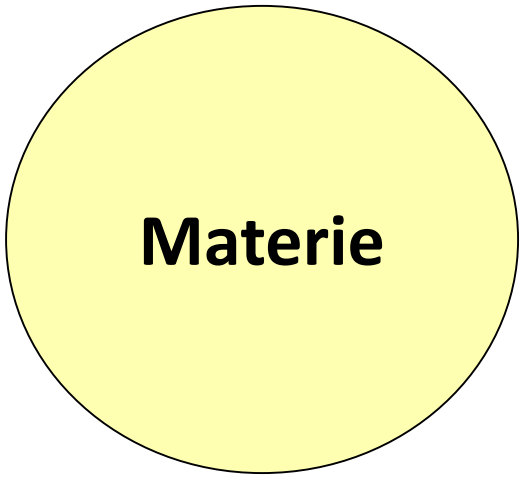

Informatie
Energie
Duurzaamheid
Materie
Sociale netwerken
Leven
Cultuur


Materie

De wetenschap (analyse)

Kepler

Newton

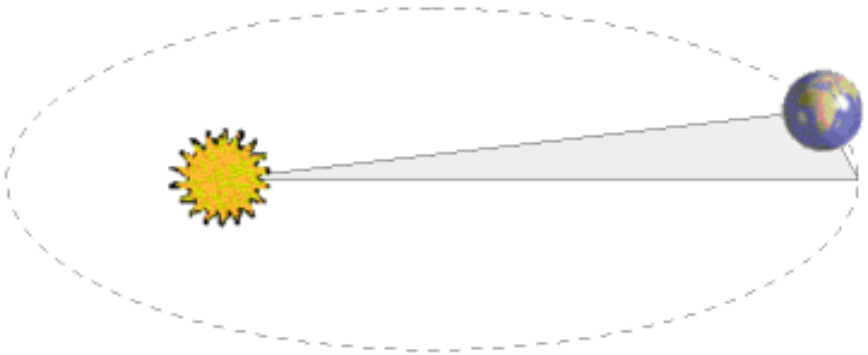
Wet 1: Orbit = ellips; Zon = brandpunt

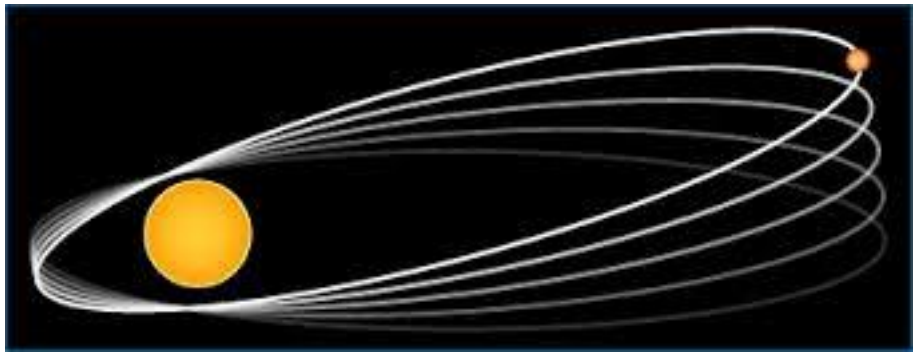
Wet 2: ‘Straal’ bestrijkt gelijke oppervlakken in gelijke tijdsintervallen

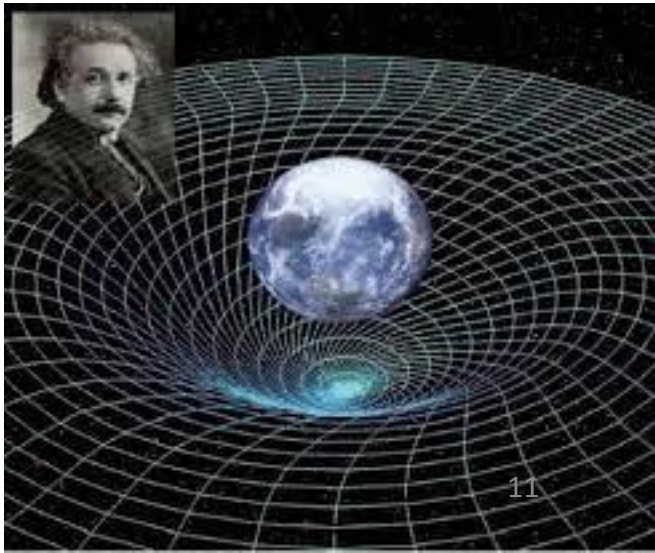
Wet 3: $$\frac{T_1^2}{T_2^2} = \frac{a_1^3}{a_2^3}$$

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

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







The unreasonable effectiveness of mathematics

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

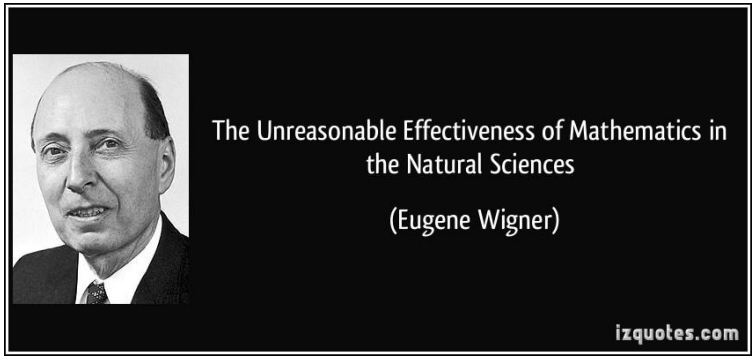
The Unreasonable Effectiveness of Mathematics in the Natural Sciences

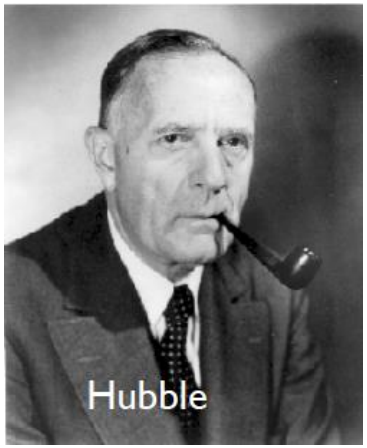
Richard Courant Lecture in Mathematical Sciences delivered at New York University, May 11, 1959

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."





EVOLUTION OF THE EXPANDING UNIVERSE

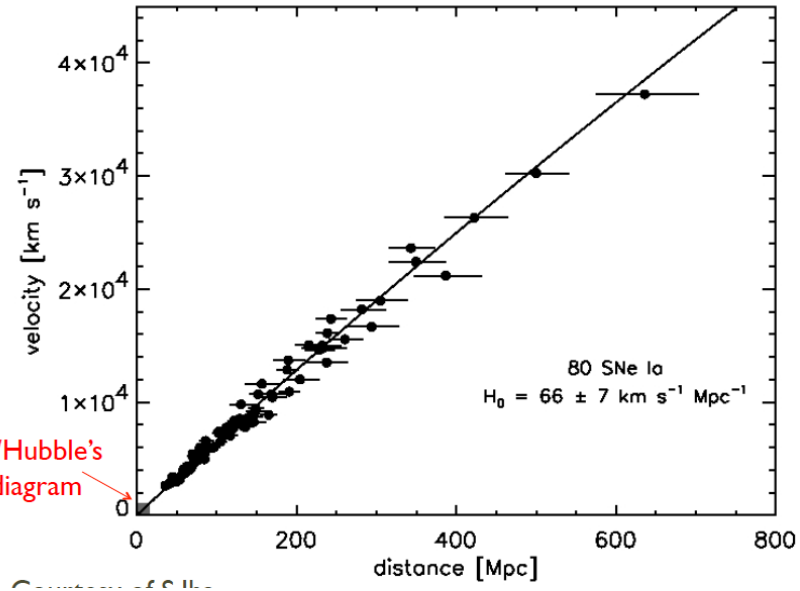
BY G. LEMAITRE

UNIVERSITY OF LOUVAIN

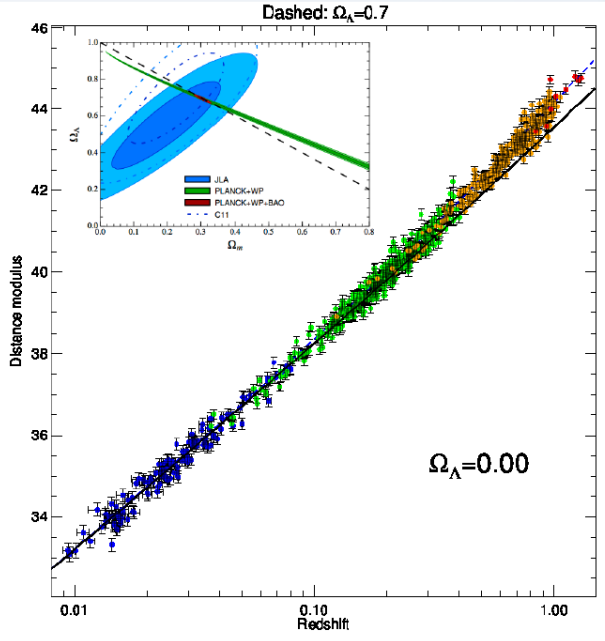
Read before the Academy, Monday, November 20, 1933

The problem of the universe is essentially an application of the law of gravitation to a region of extremely low density. The mean density of matter up to a distance of some ten millions of light years from us is of the order of 10^{-30} gr./cm.^{3}; if all the atoms of the stars were equally distributed through space there would be about one atom per cubic yard, or the total energy would be that of an equilibrium radiation at the temperature of liquid hydrogen. The theory of relativity points out the possibility of a modification of the law of gravitation under such extreme conditions. It suggests that, when we identify gravitational mass and energy, we have to introduce a constant. Everything happens as though the energy *in vacuo* would be different from zero. In order that absolute motion, i.e., motion relative to vacuum, may not be detected, we must associate a pressure $p = -\rho c^2$ to the density of energy ρc^2 of vacuum. This is essentially the meaning of the cosmical constant λ which corresponds to a negative density of vacuum ρ_0 according to

$$\rho_0 = \frac{\lambda c^2}{4\pi G} \cong 10^{-27} \text{ gr./cm.}^3 \qquad (1)$$



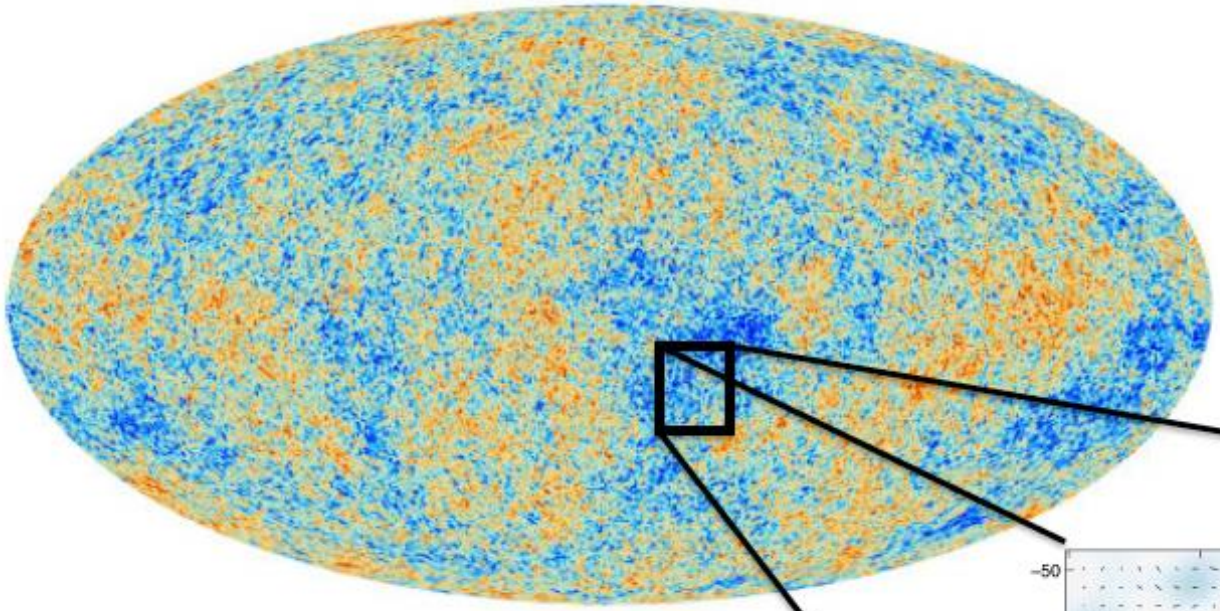
Lemaitre's/Hubble's original diagram

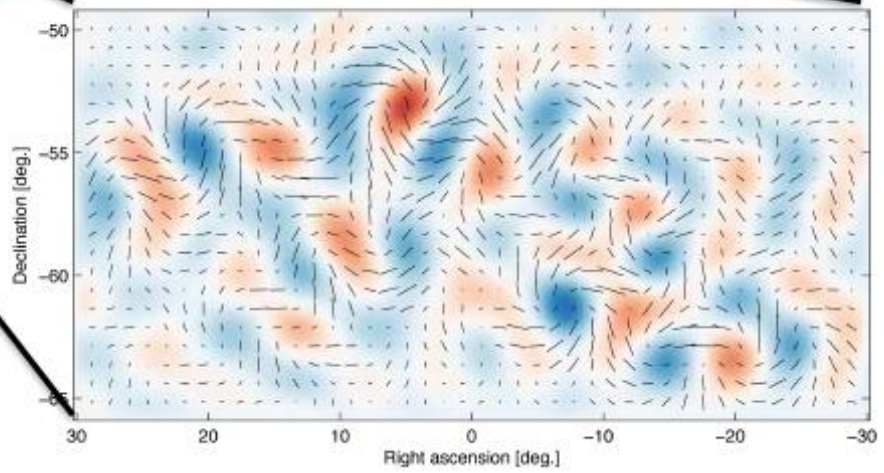


Kijken in het verleden

BICEP telescope, 2014

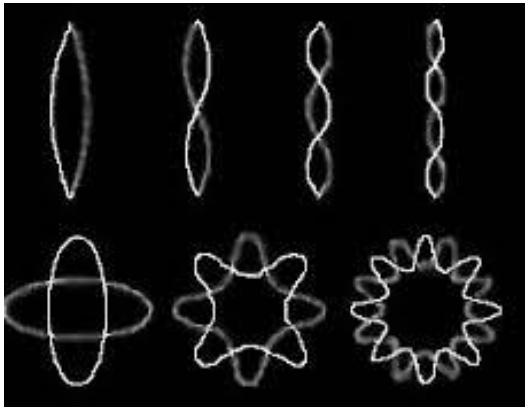
Temperature variations

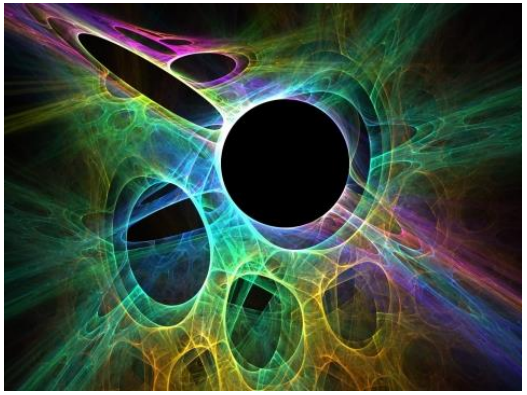


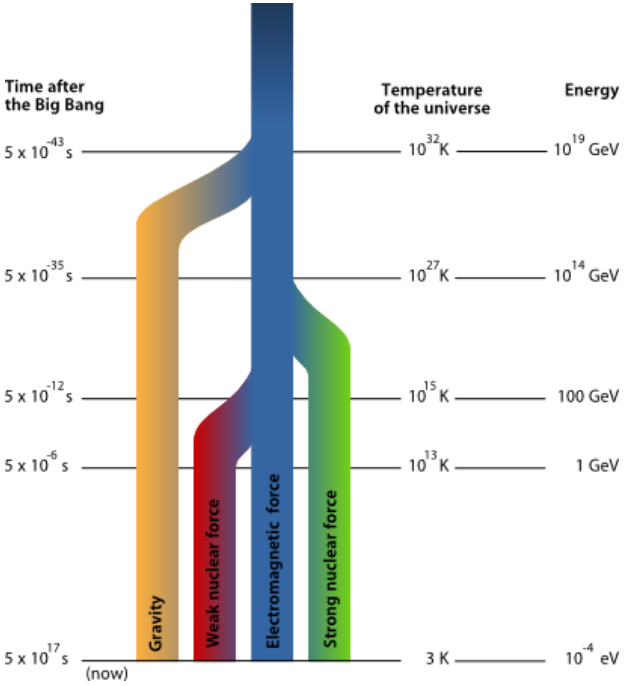


Polarization pattern

Kijken in de toekomst





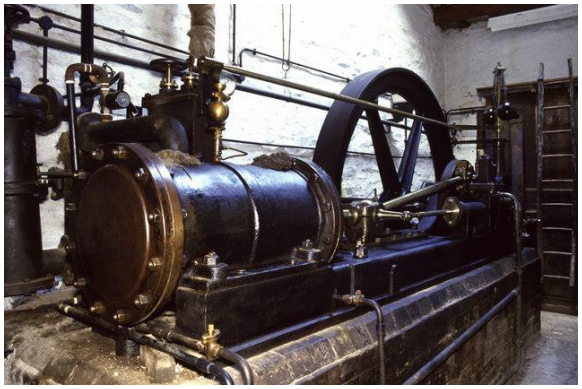


Hoe gravitatie en quantummechanica unificeren ?

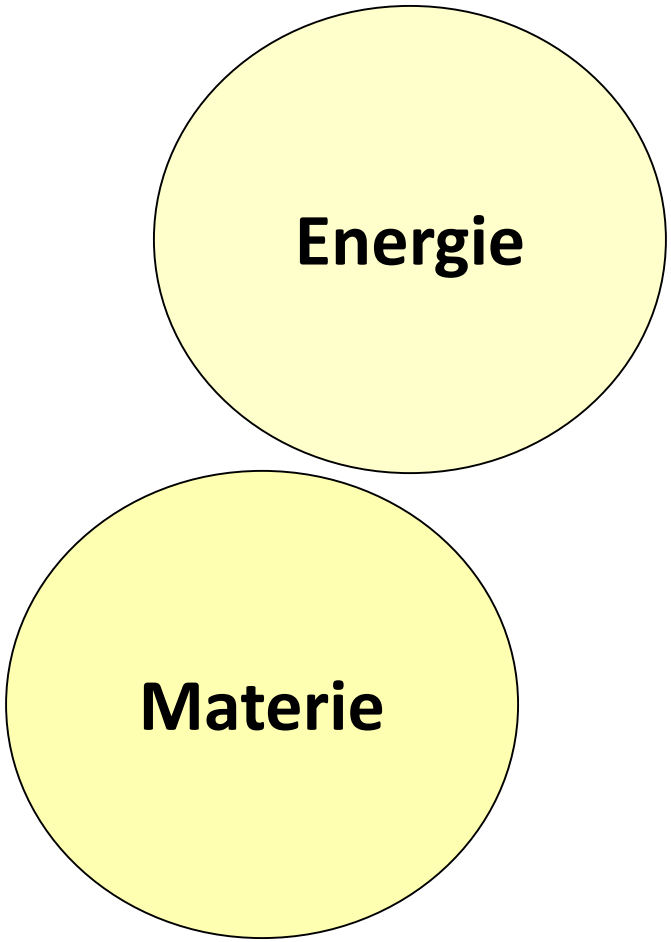
Zwarte gaten, string theorie, ….

Wiskundige consistentie → 11 dimensies !

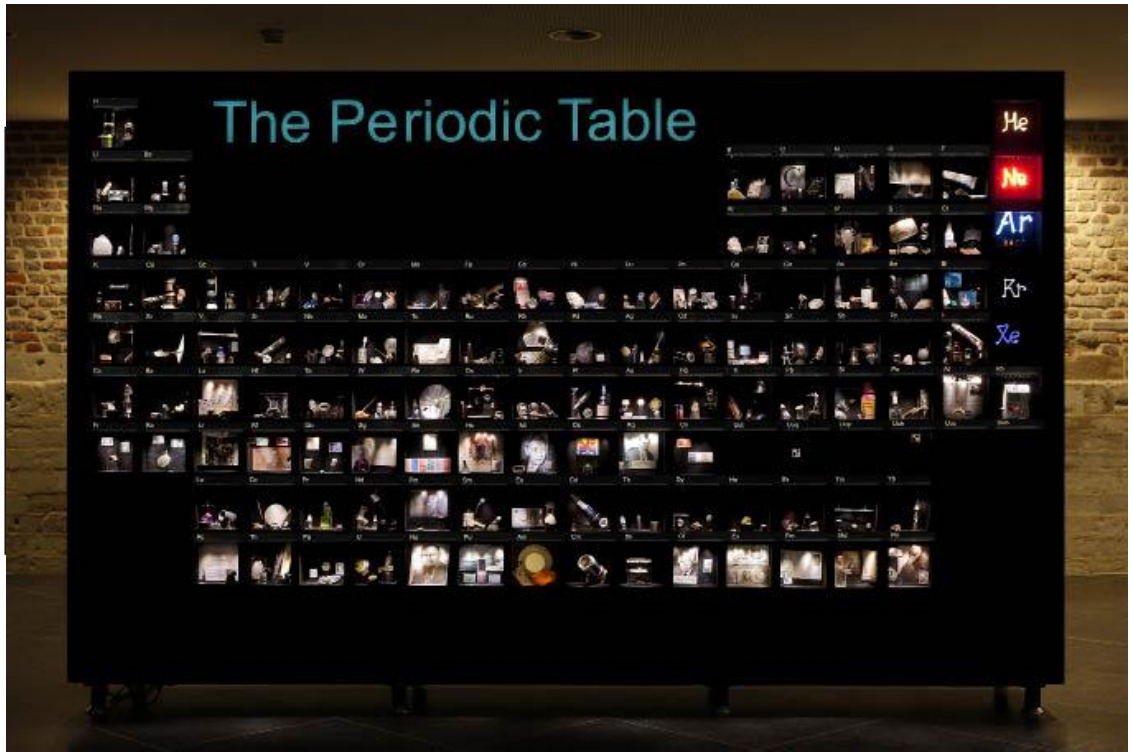
Technologie en ontwerpen: De eerste industriele revolutie (1700…)

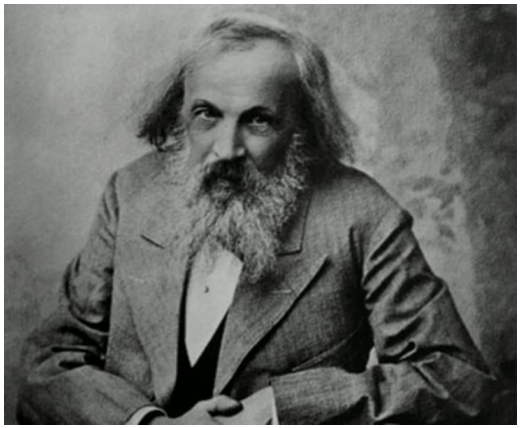


- Energie: Steenkool
- Stoom machine (Watt)
- Mechanisering van textielindustrie
- Wegen- en spoorwegnetwerken
- *Sociaal: Transitie van feodaal ruraal naar industriele samenleving*
- *Socio-culturele evolutie volgt de economisch-technische (Franse revolutie)*


Energie
Materie

De wetenschap (analyse)



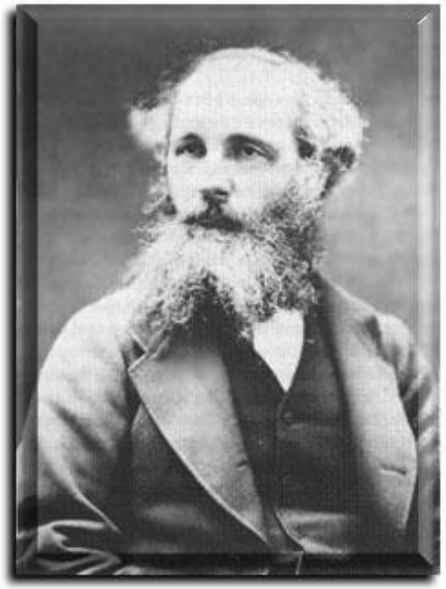


$$\nabla \cdot \mathbf{D} = \rho \qquad (1) \qquad \text{Gauss' Law}$$

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

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

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



Technologie en ontwerpen: De tweede industriele revolutie (1870…)

- Massa productie en –consumptie

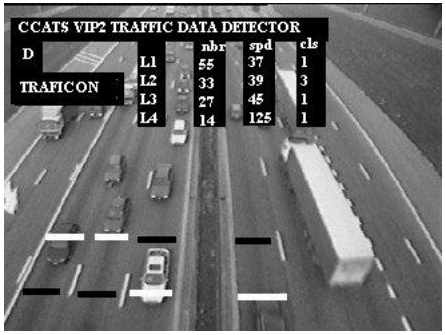
- Energie: Electriciteit en olie

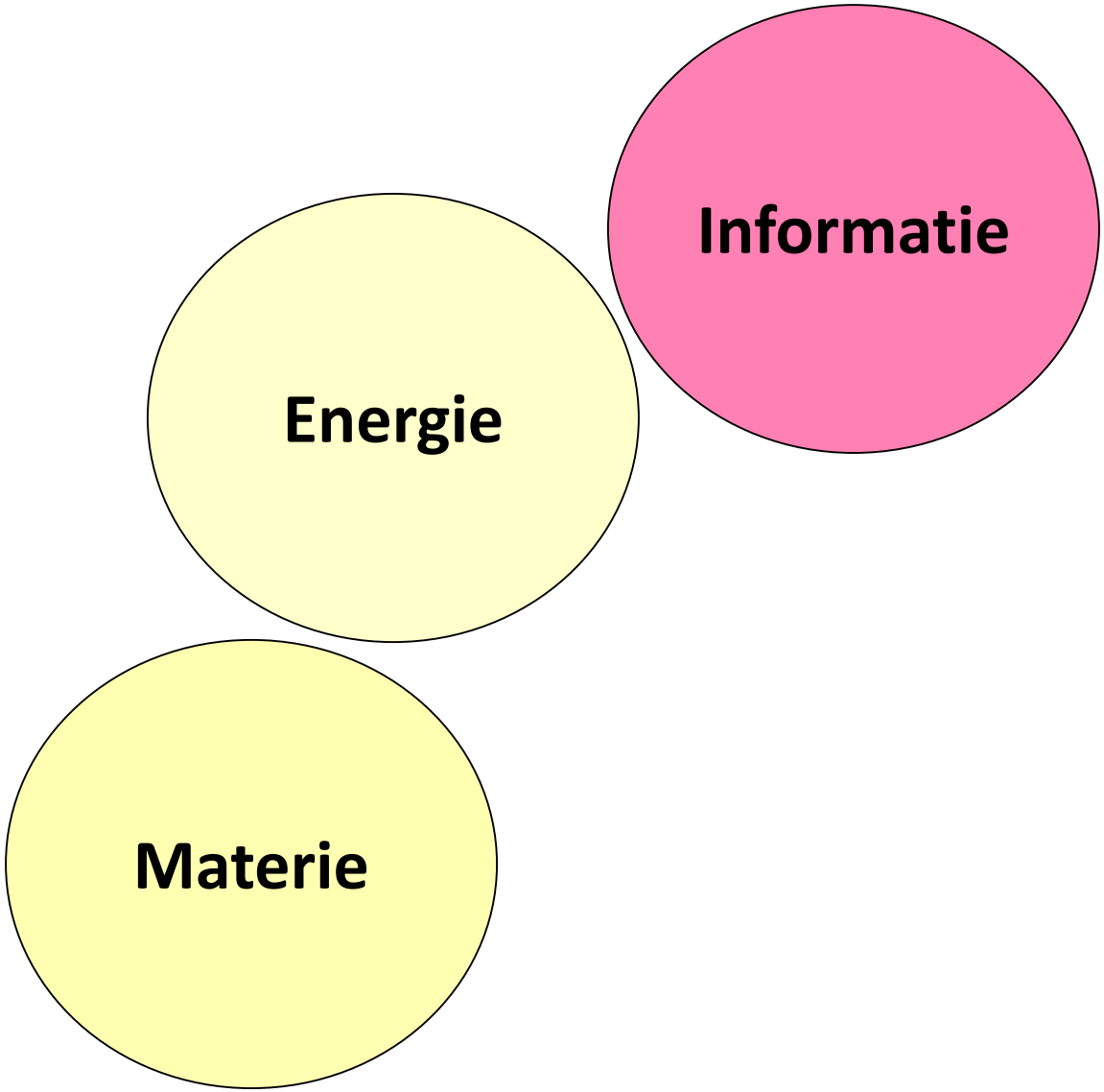
- Chemische industrie ontwikkelt zich

- Telecommunicatie: telegraaf, telefoon, radio, TV, …

- *Arbeid en Kapitaal (Marx) ; Vakbonden;*
  Liberalisme: De onzichtbare hand (Adam Smith)

- *Overheid als regulator maar ook facilitator*




Informatie
Energie
Materie

De wetenschap (analyse)

1880: Maxwell's wetten (electro-magnetisme)

1905: Quanta: Planck en Einstein

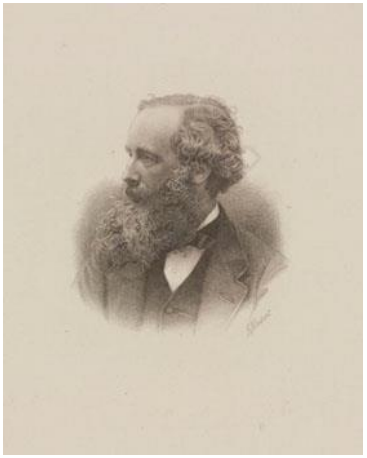
1910: Atoom model Bohr

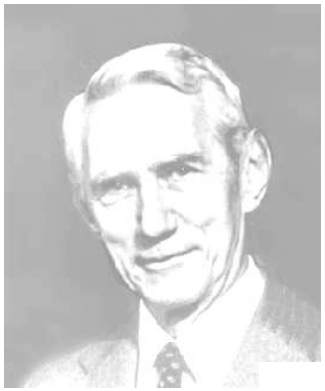
1930: Quantummechanica van Heisenberg, Schrödinger,…

1940: Computer-principe van Turing en von Neumann

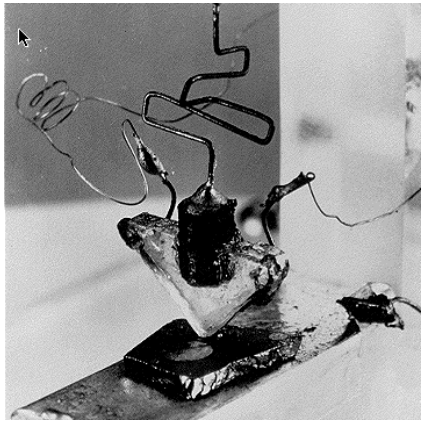
1948: Information theorie van Shannon

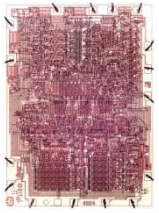
1950: Transistor

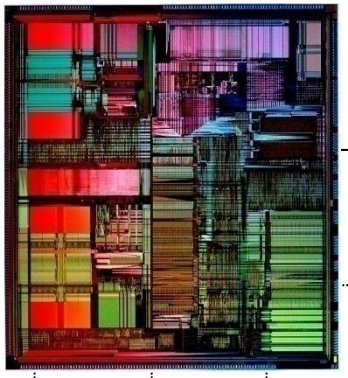


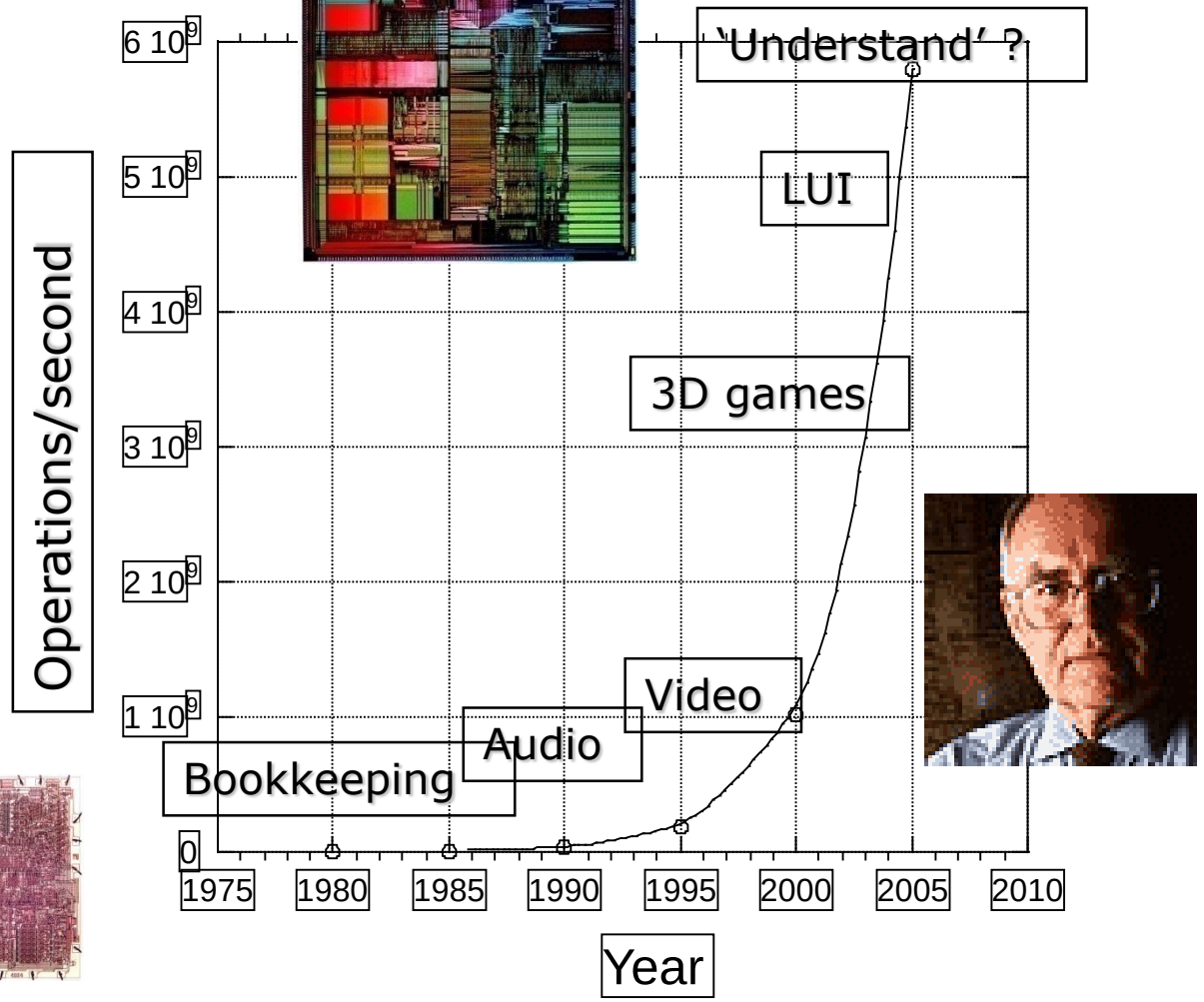


Technologie en ontwerp: Derde industriele revolutie (1945…)









Rekenkracht x 2 elke 18 maand

Ontwerp van een computer-chip: modulair !

Huis

Living
Keuken
Slaapkamer
Badkamer
Garage
….

water, electriciteit,…
Bakstenen (klei)
…..

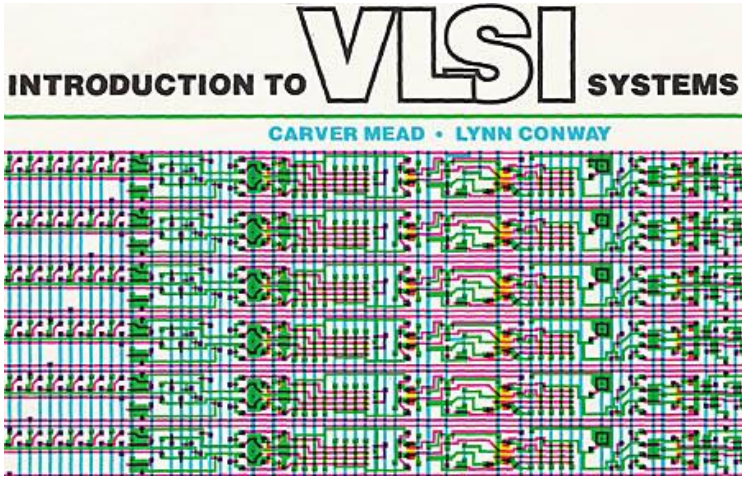
Plan

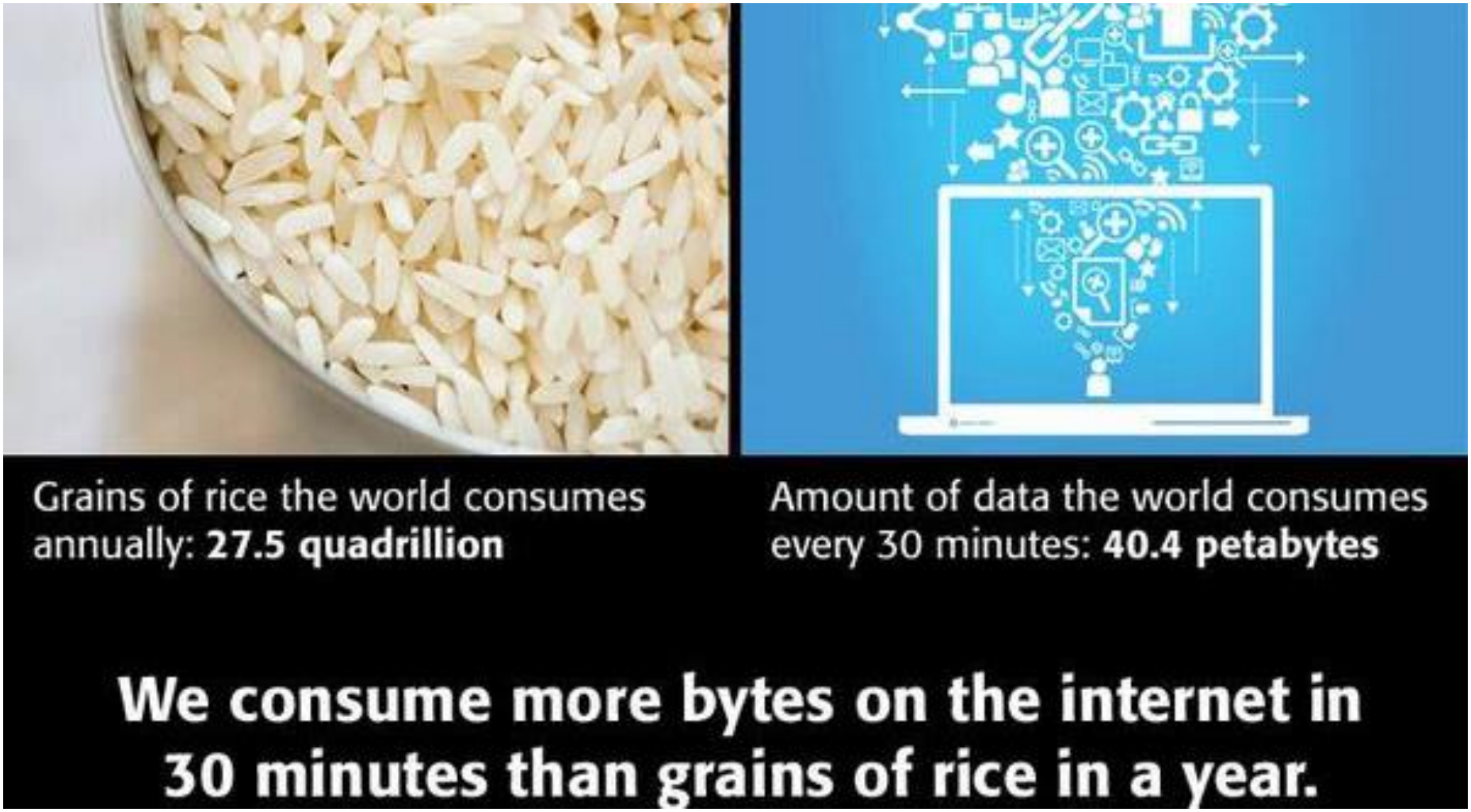
Chip

Geheugen
Klok
Controle eenheid
Rekeneenheid
Communicatie
….

Energie, communicatie,…
Transistors (silicium)
…..

Plan

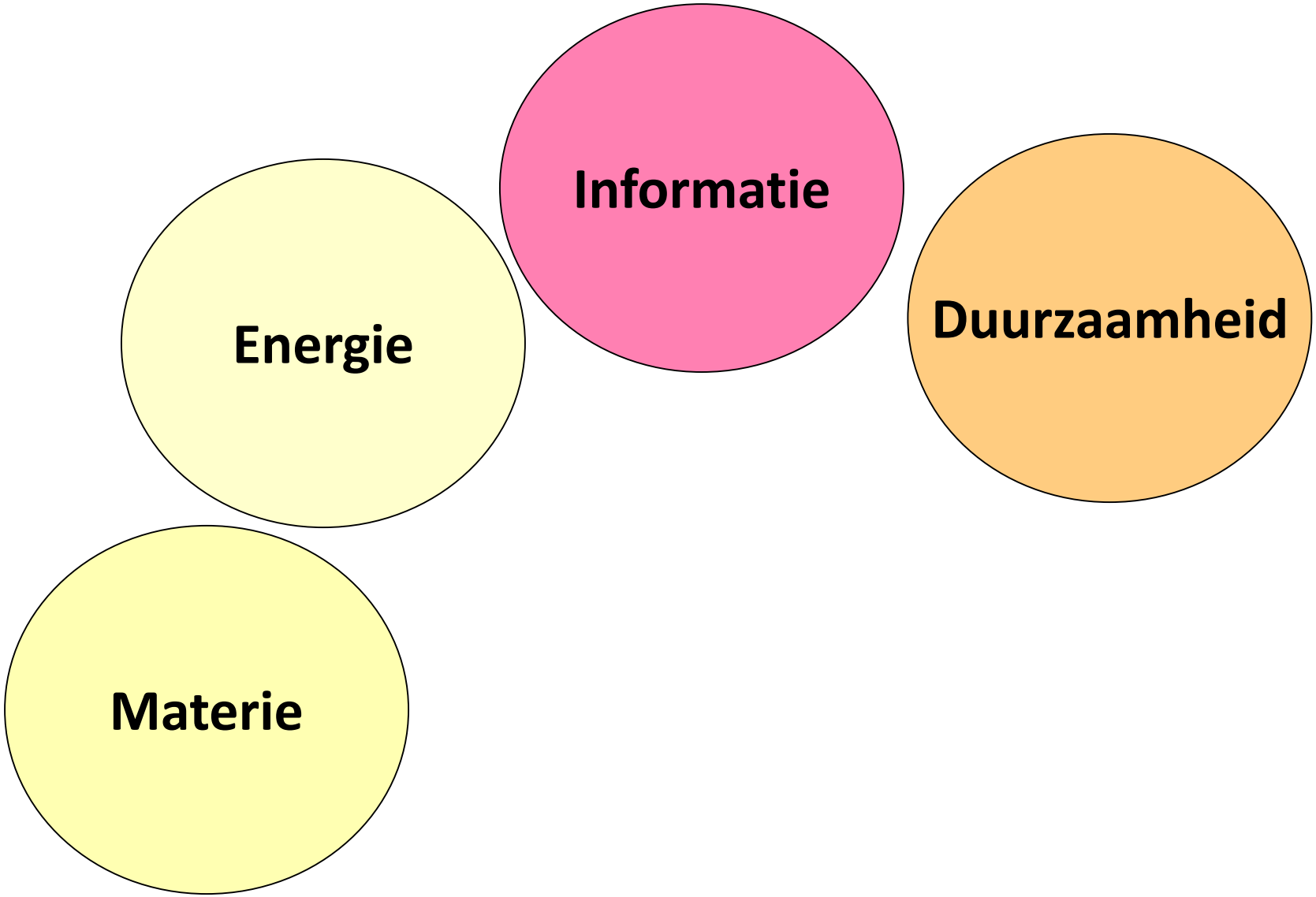




1 million = 1 000 000
1 billion = 1 000 000 000
1 trillion = 1 000 000 000 000
1 quadrillion =
1 000 000 000 000 000

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


Informatie
Energie
Duurzaamheid
Materie

Duurzaamheid

- Globalizering

  Global Village Concept van CNN
  Internet
  Think globally, act locally (glocal)
  Netwerken van mensen en computers

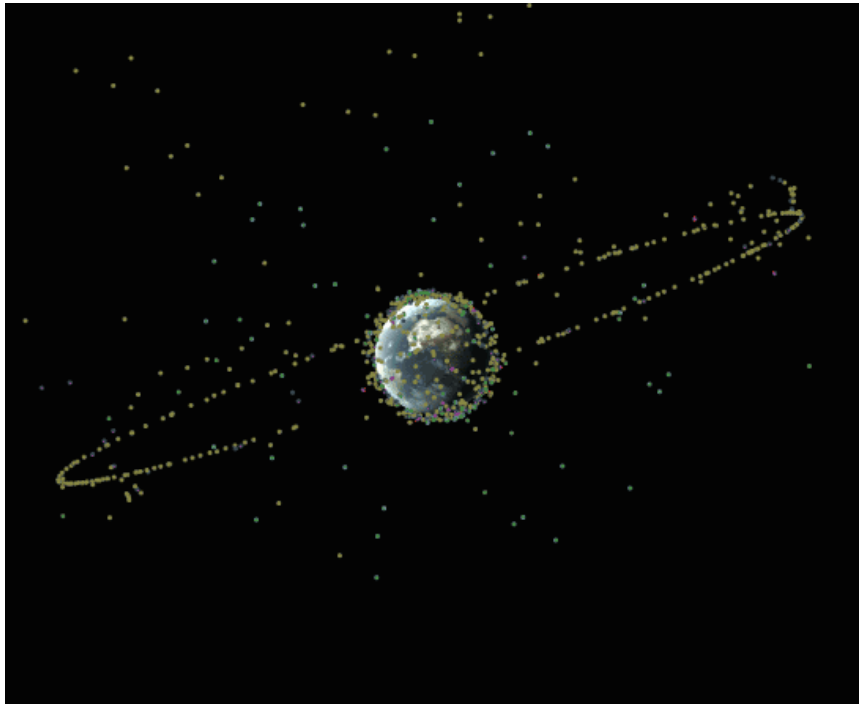
- Standardizatie, uniformizering, protocols

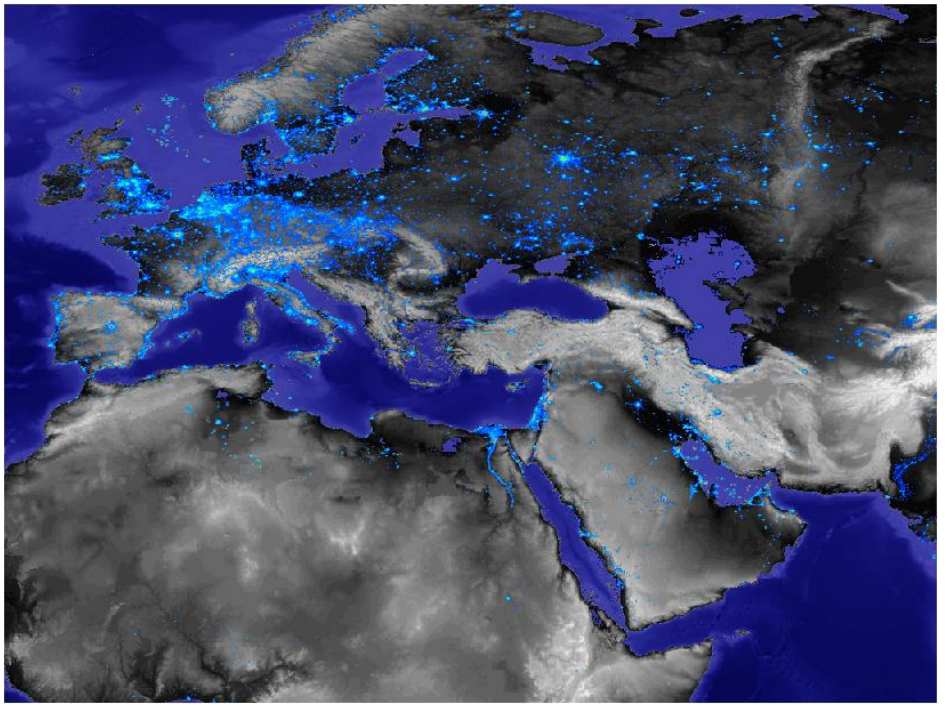
- Duurzame samenleving

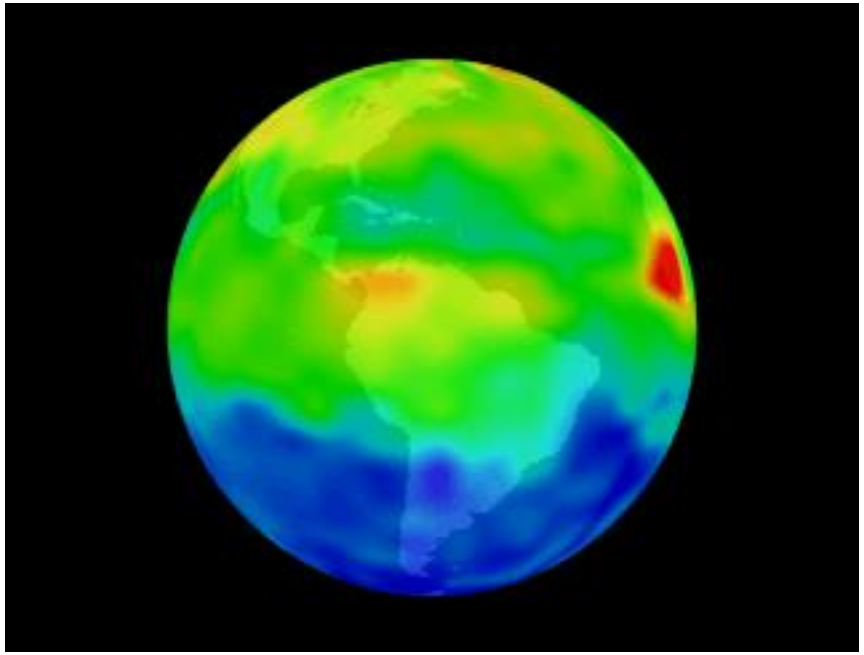
  Traditioneel: Eindige behoefte, oneindig aanbod
  Vandaag: Oneindige behoefte, eindig aanbod

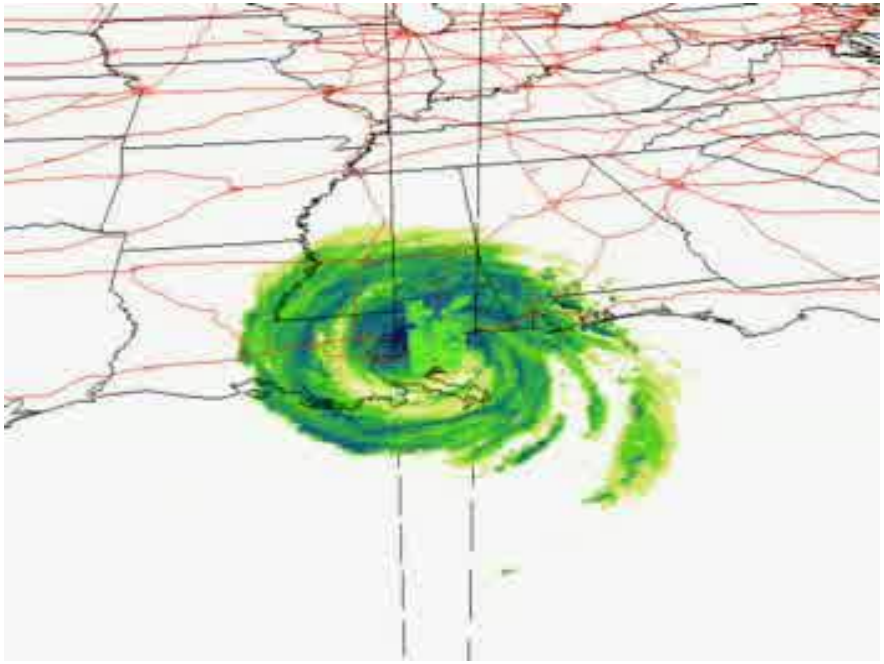
  We did not inherit the world from our ancestres, but have borrowed it from our children (Antoine de Saint-Exupery)

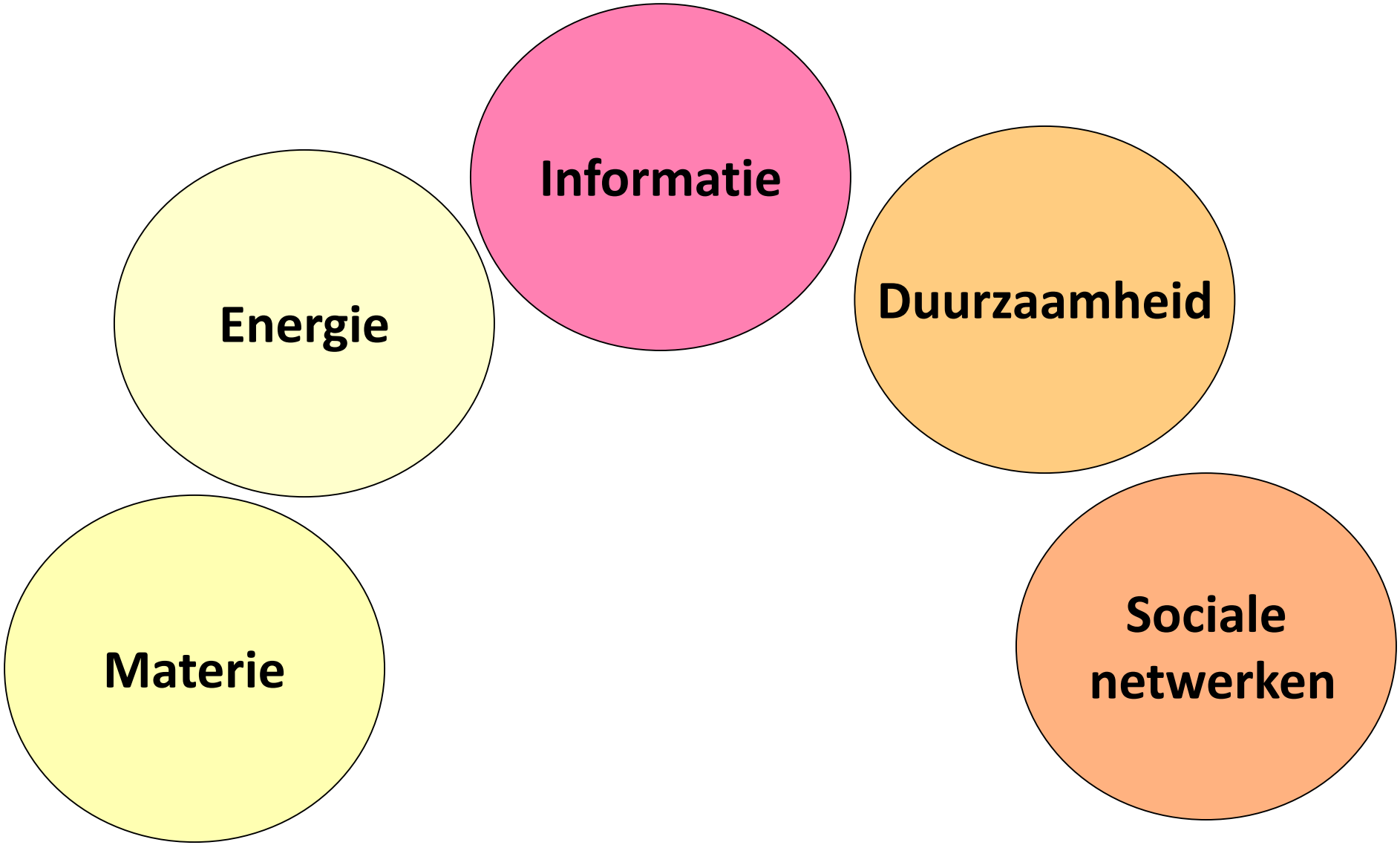
- *Cleantech, hernieuwbare energie, klimaat-opwarming,….*



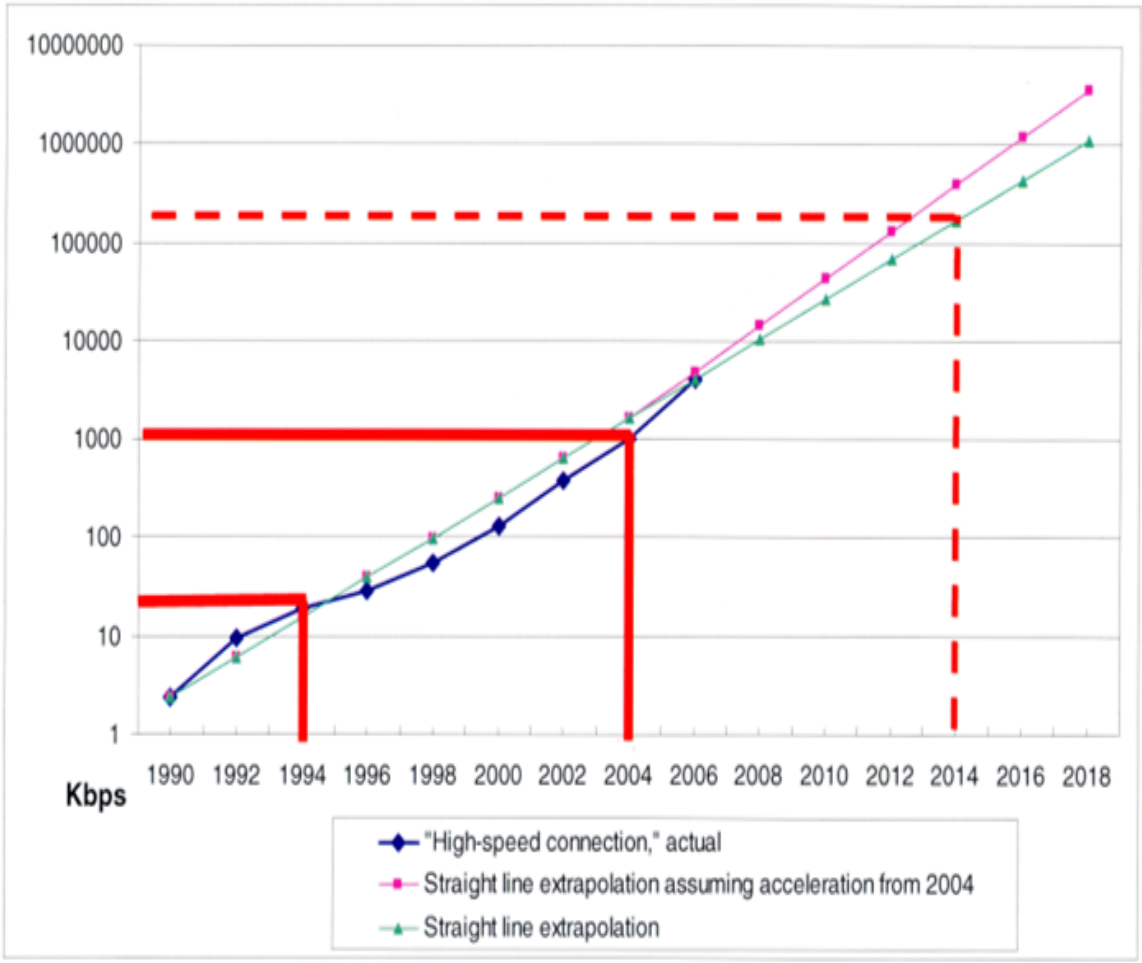







Informatie
Energie
Duurzaamheid
Materie
Sociale netwerken

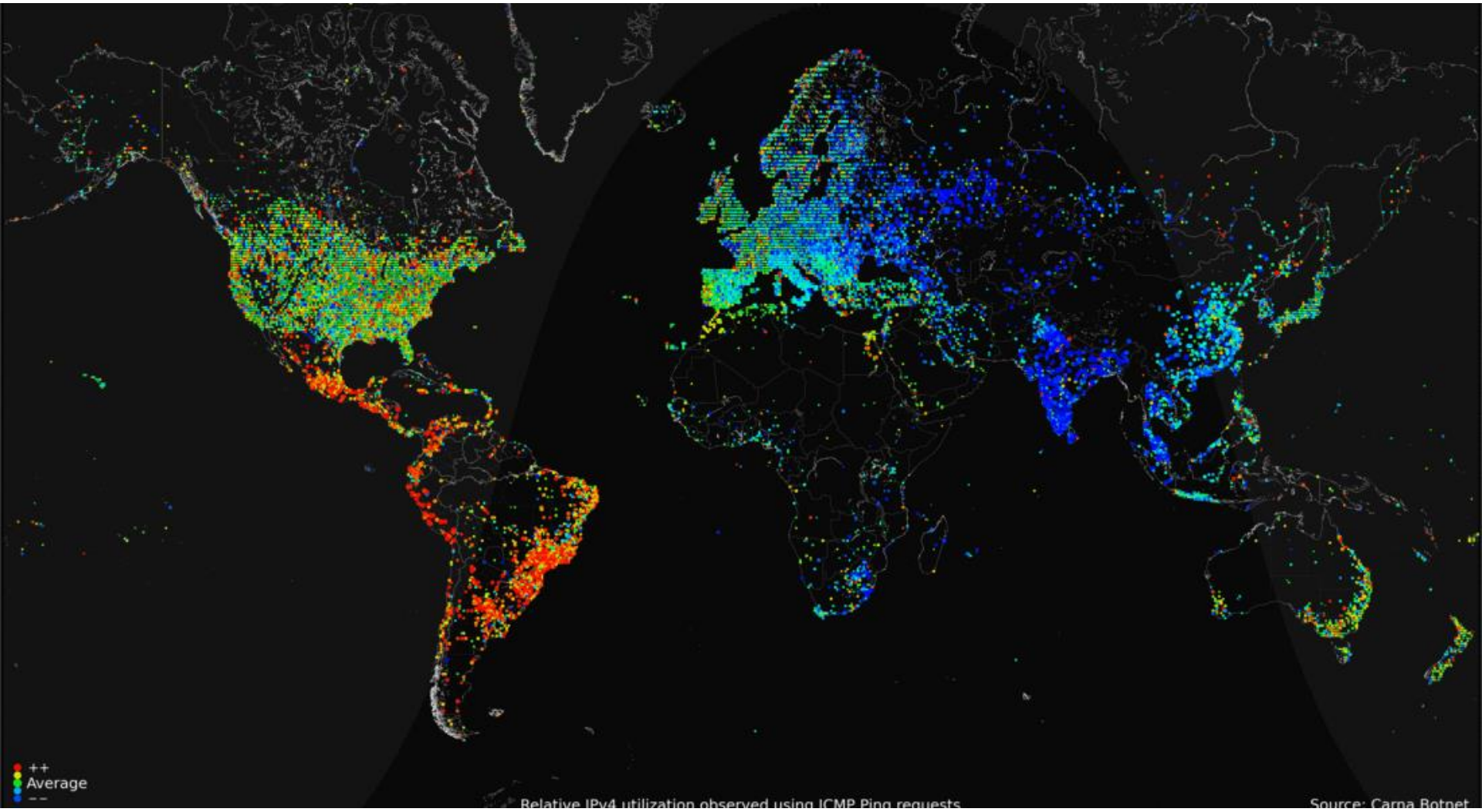
Connectivity



We are always CONNECTED

and FAST!

www: max 19 clicks !



Informatie

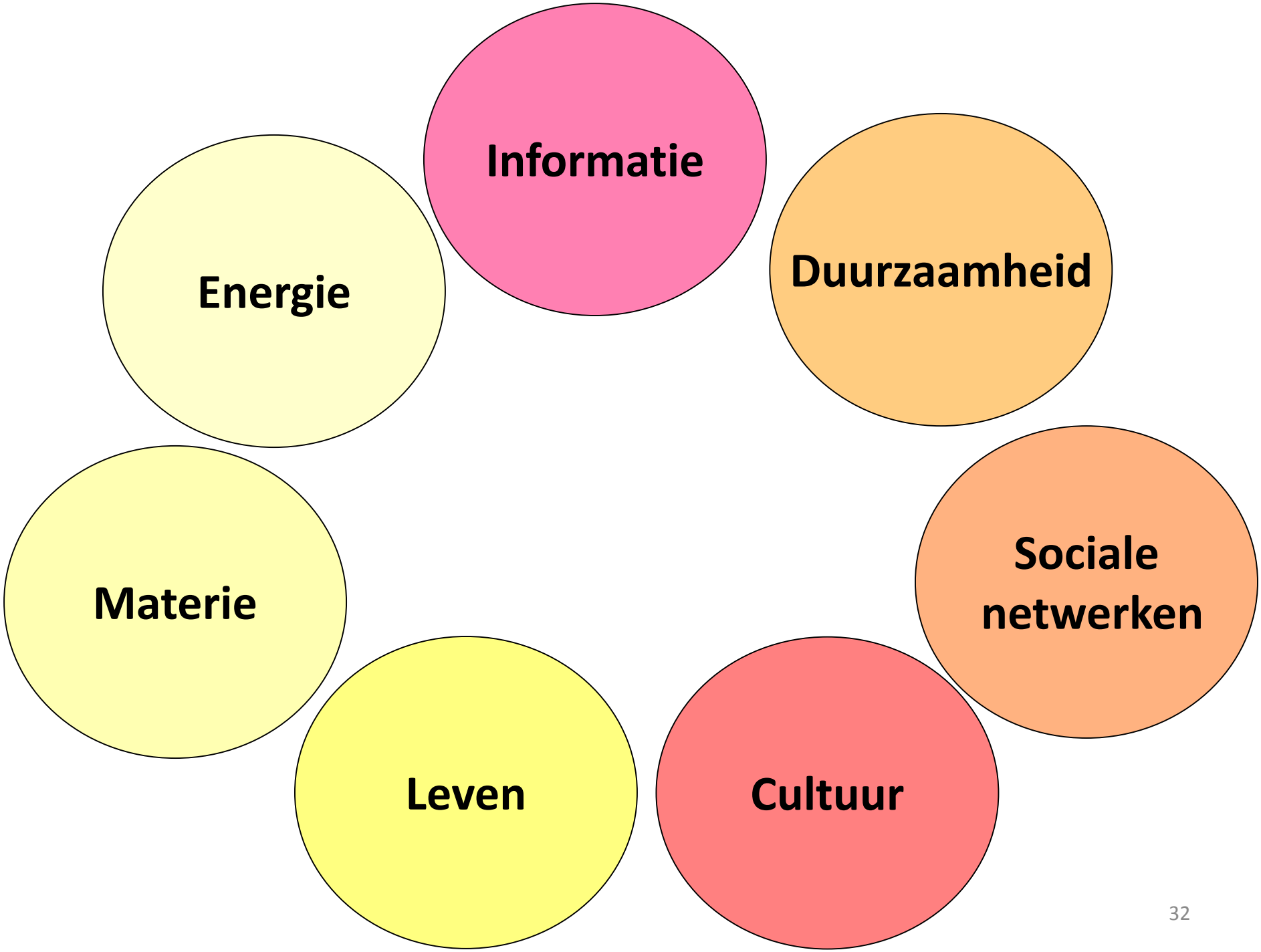
Energie

Duurzaamheid

Materie

Sociale netwerken

Cultuur


Informatie
Energie
Duurzaamheid
Materie
Sociale netwerken
Leven
Cultuur

De wetenschap

1865: Mendel: Erfelijkheidswetten

1944: Avery/MacLeod/McCarty: DNA = drager erfelijk materiaal

1953: Watson/Crick: DNA dubbele helix

1965: Restriction enzymes: DNA ‘scharen’

1966: Nirenberg/Khorana/Holley: Genetische code ontrafeld

1972: Cohen/Boyer: Recombinant DNA, transfer van gene naar bacteria

1977: Sanger/Maxam/Gilbert: DNA sequenceer methodes

1982: Insuline door transgene bacteria

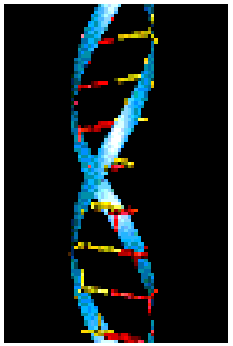
1985: Polymerase Chain Reaction (PCR)

1991: Eerste transgeen dier: Herman de stier

1994: Genetisch Gemodificeerde Tomaten

1997: Eerste gekloond dier: Dolly

2001: Menselijk Genoom Project



Tsunami van data door technologische vooruitgang

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
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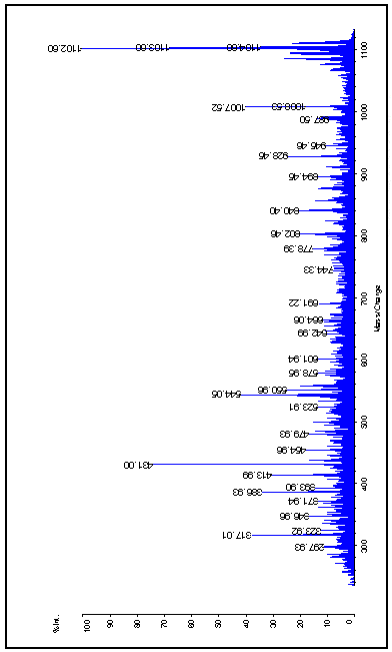
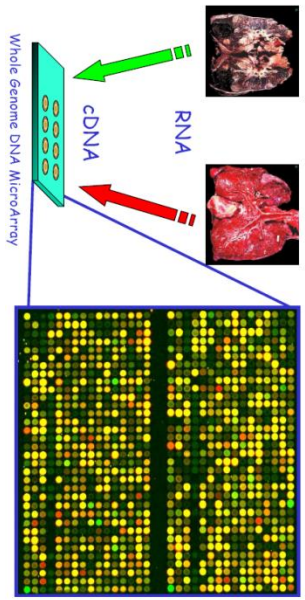
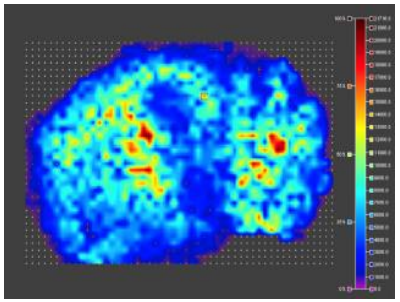


Magnetic resonance

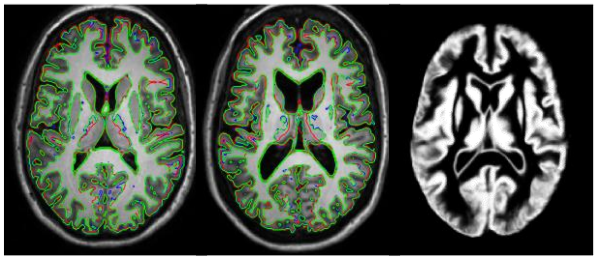
maf VIB
MicroArray Facility

Microarrays
(DNA chips)

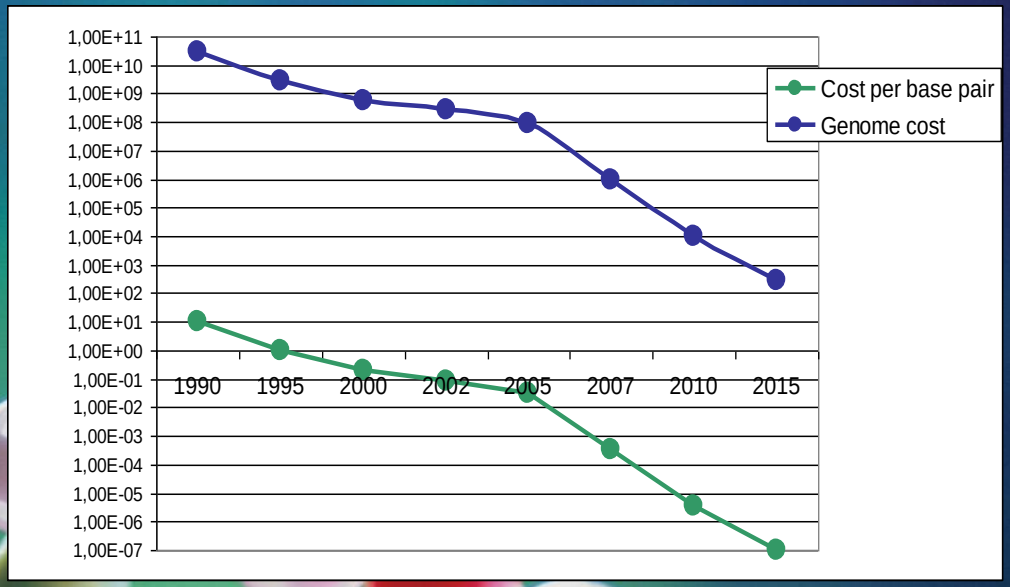




Mass spectrometry

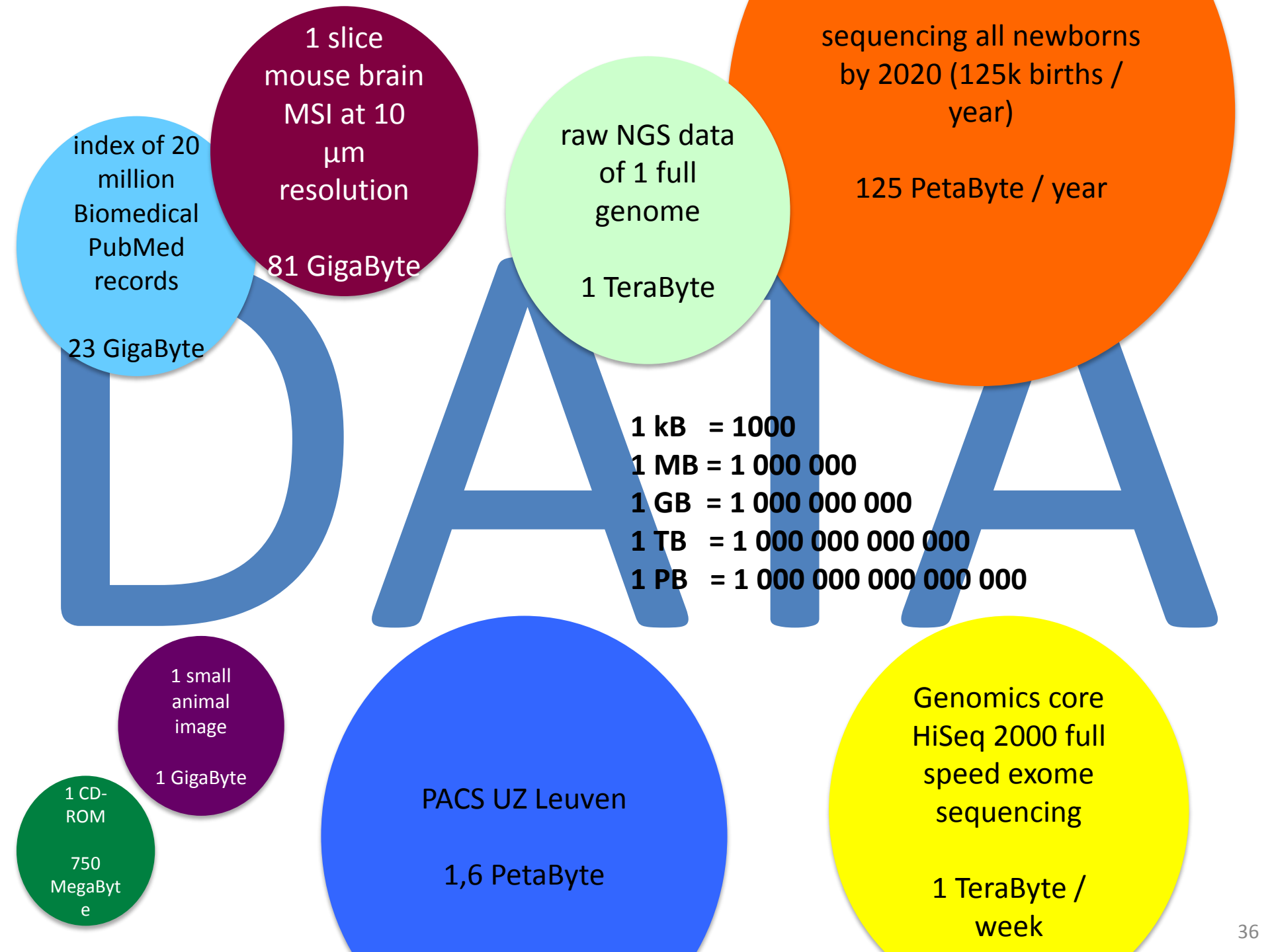


Genome data



- 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.

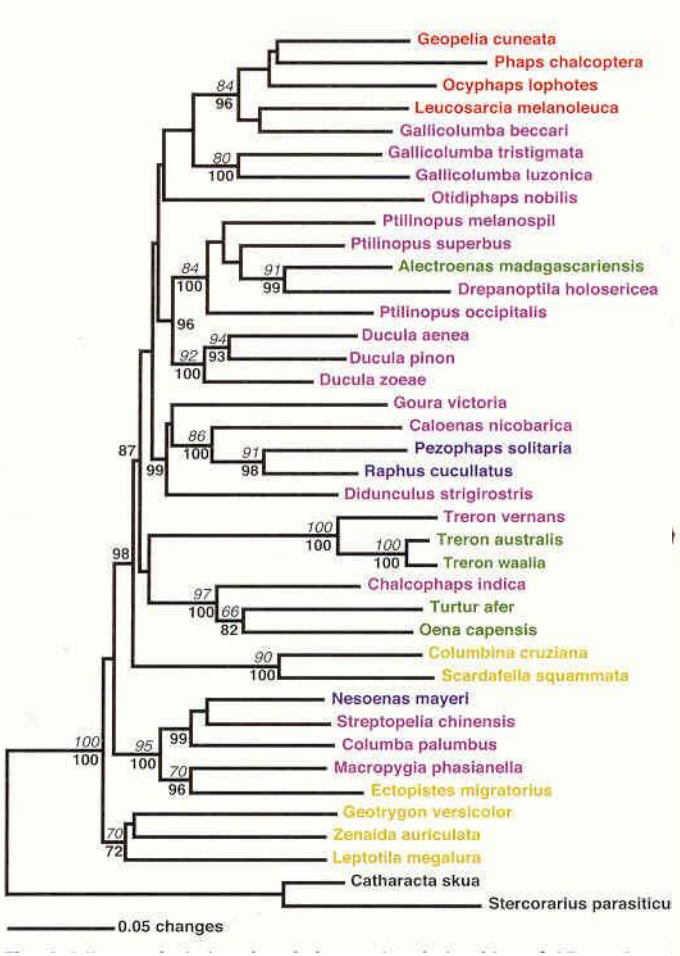
Why might it be reasonable to doubt the effectiveness of mathematics in biology? Observed properties of living systems are determined by a combination of

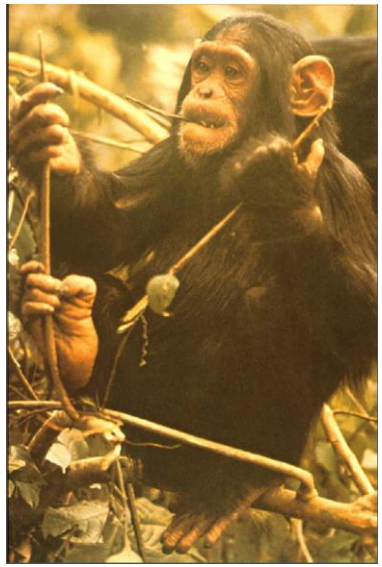
- The laws of physics and chemistry
- The mechanism of evolution
- Historical accident

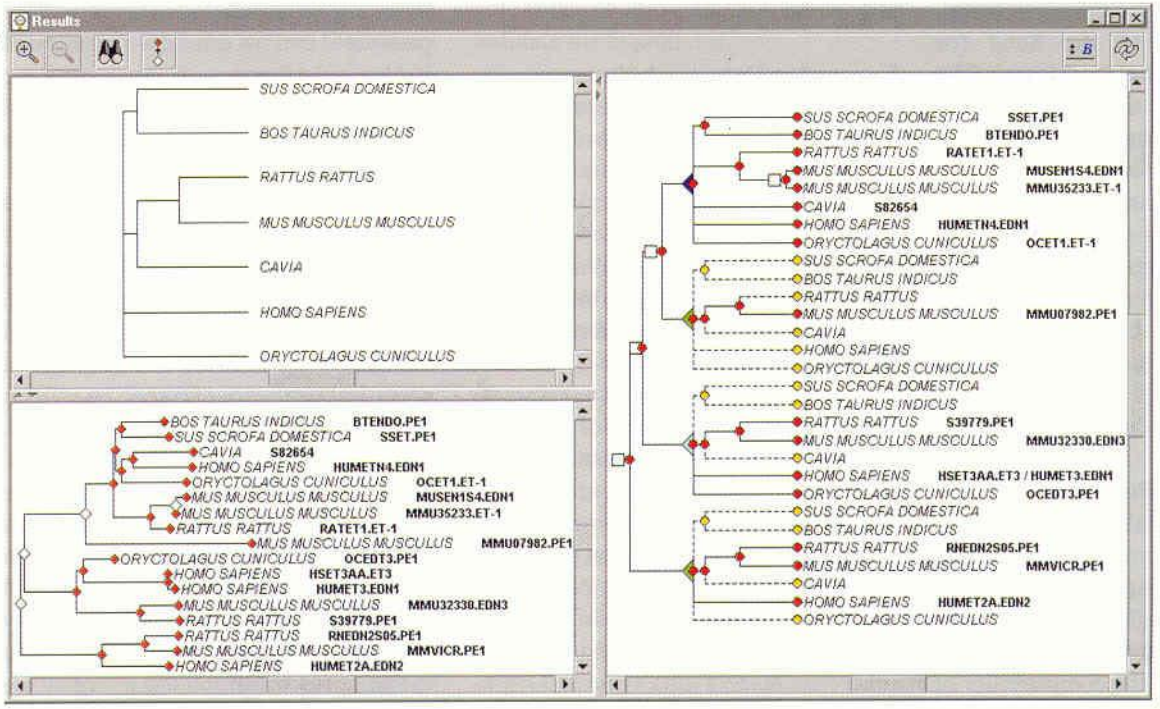
It is difficult to sort out their effects, and a creative tension among them pervades our investigations. Many of the laws of physics describe the natural world—including living systems—by specifying relations between initial and fi-

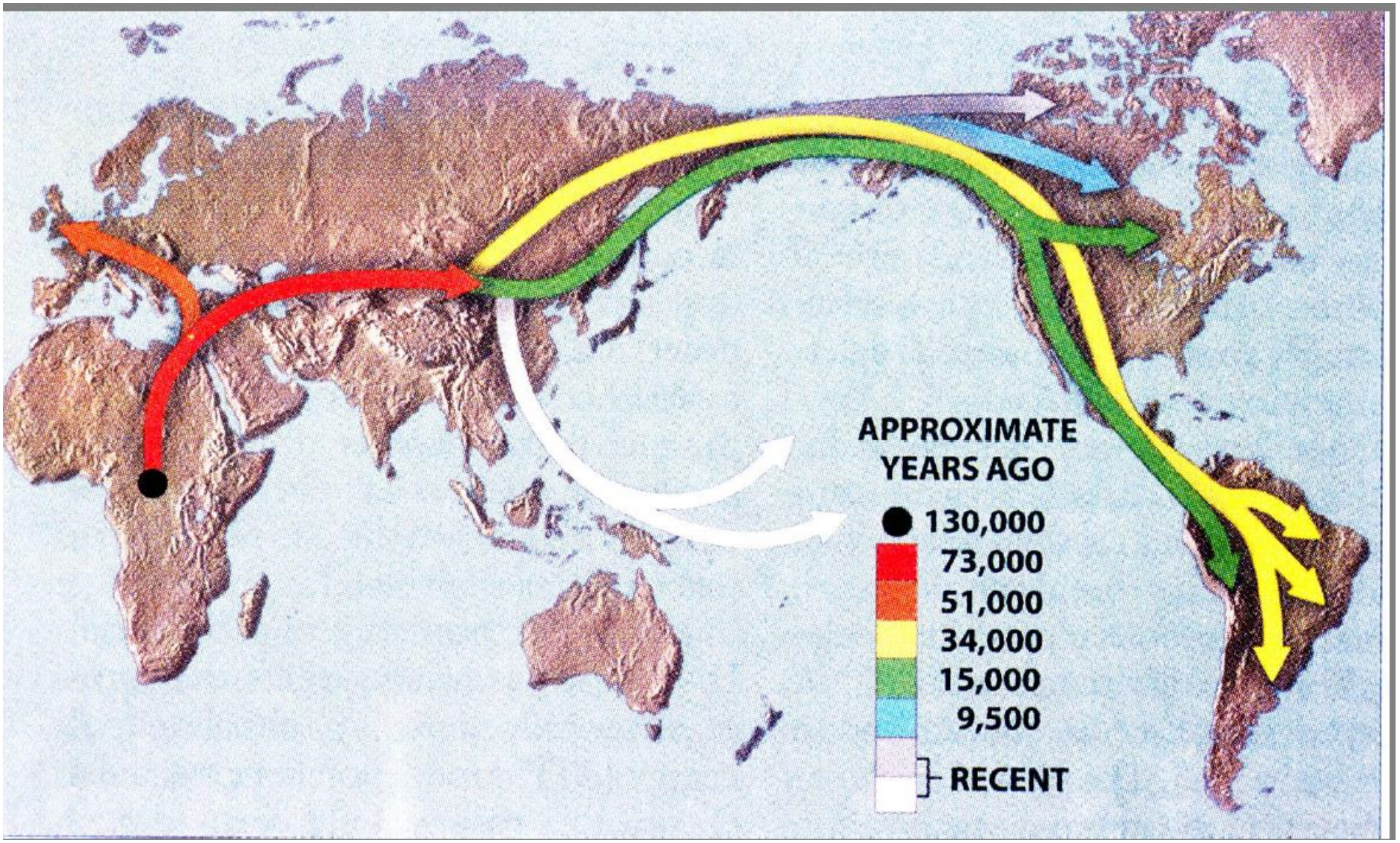
*Based on a talk delivered at the final symposium of the program, "Biomolecular Function and Evolution in the Context of the Genome Project," at The Isaac Newton Institute for the Mathematical Sciences, Cambridge, U.K., 20 Dec. 1998.

Biology = information processing = mathematics

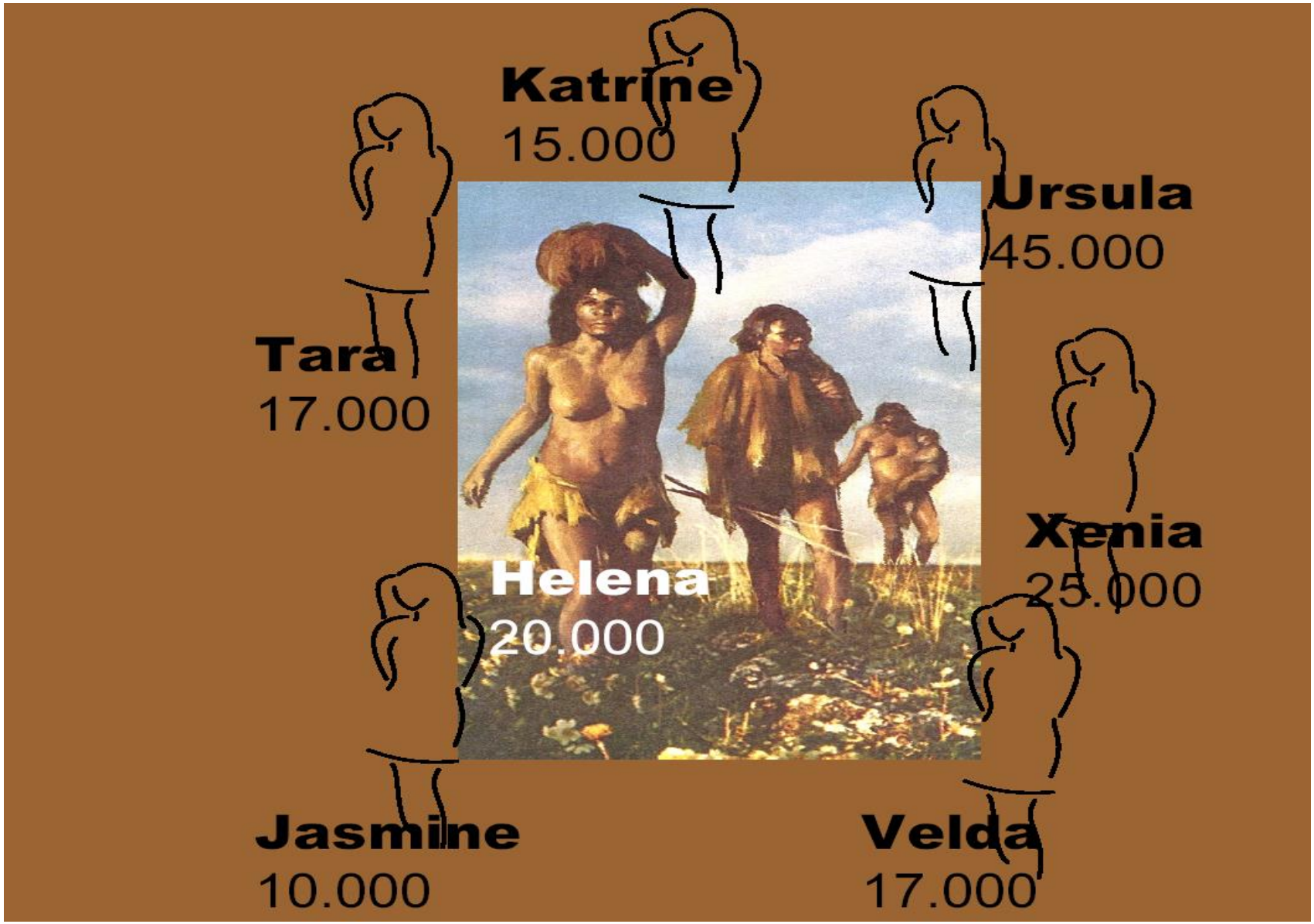

Geopelia cuneata
Phaps chalcoptera
Ocyphaps lophotes
Leucosarcia melanoleuca
Gallicolumba beccari
Gallicolumba tristigmata
Gallicolumba luzonica
Otidiphaps nobilis
Ptilinopus melanospil
Ptilinopus superbus
Alectroenas madagascariensis
Drepanoptila holosericea
Ptilinopus occipitalis
Ducula aenea
Ducula pinon
Ducula zoeae
Goura victoria
Caloenas nicobarica
Pezophaps solitaria
Raphus cucullatus
Didunculus strigirostris
Treron vernans
Treron australis
Treron waalia
Chalcophaps indica
Turtur afer
Oena capensis
Columbina cruziana
Scardafella squammata
Nesoenas mayeri
Streptopelia chinensis
Columba palumbus
Macropygia phasianella
Ectopistes migratorius
Geotrygon versicolor
Zenaida auriculata
Leptotila megalura
Catharacta skua
Stercorarius parasiticu
0.05 changes



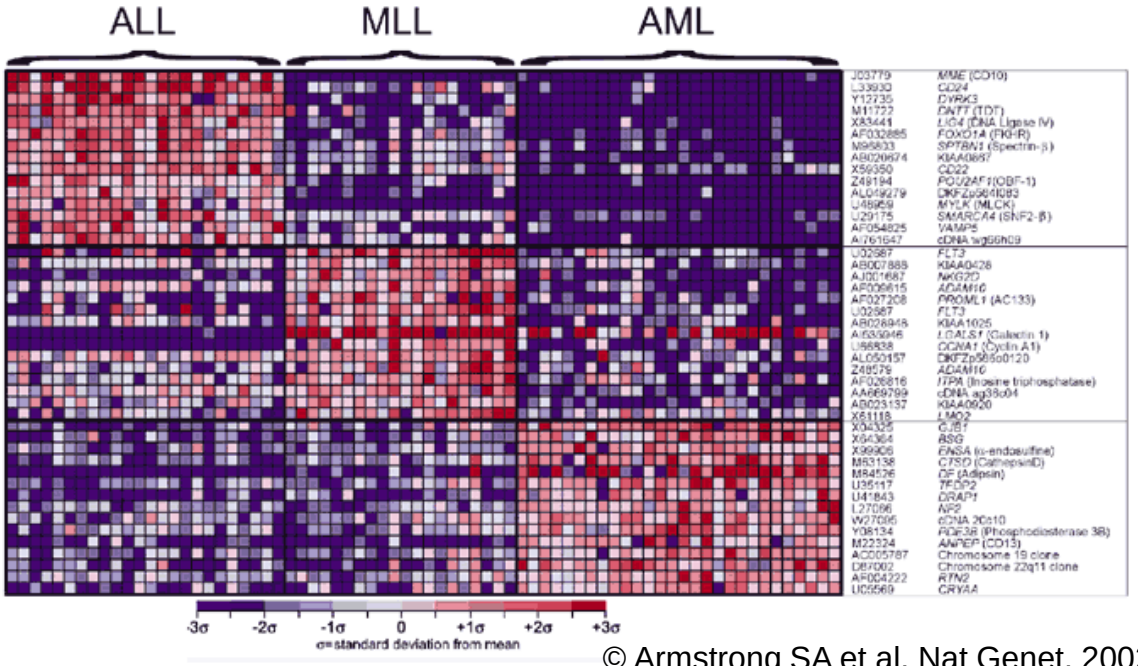

Results
SUS SCROFA DOMESTICA
BOS TAURUS INDICUS
RATTUS RATTUS
MUS MUSCULUS MUSCULUS
CAVIA
HOMO SAPIENS
ORYCTOLAGUS CUNICULUS
SUS SCROFA DOMESTICA SSET.PE1
BOS TAURUS INDICUS BTENDO.PE1
RATTUS RATTUS RATET1.ET-1
MUS MUSCULUS MUSCULUS MUSEN1S4.EDN1
MUS MUSCULUS MUSCULUS MMU35233.ET-1
CAVIA S82654
HOMO SAPIENS HUMETN4.EDN1
ORYCTOLAGUS CUNICULUS OCET1.ET-1
MUS MUSCULUS MUSCULUS MMU07982.PE1
MUS MUSCULUS MUSCULUS MMU32330.EDN3
HOMO SAPIENS HSET3AA.ET3 / HUMET3.EDN1
ORYCTOLAGUS CUNICULUS OCEDT3.PE1
RATTUS RATTUS S39779.PE1
RATTUS RATTUS RNEDN2S05.PE1
MUS MUSCULUS MUSCULUS MMVICR.PE1
HOMO SAPIENS HUMET2A.EDN2

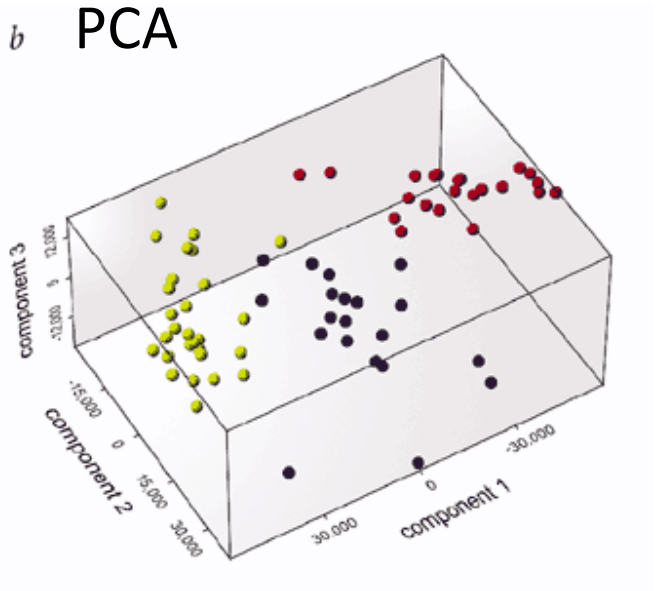

APPROXIMATE
YEARS AGO
130,000
73,000
51,000
34,000
15,000
9,500
RECENT

Mitochondral DNA: Europa's moeders



Diagnose van leukemie gebaseerd op genetische biomarkers





© Armstrong SA et al. Nat Genet. 2002 Jan;30(1):41-7.

12 600 genes

72 patienten

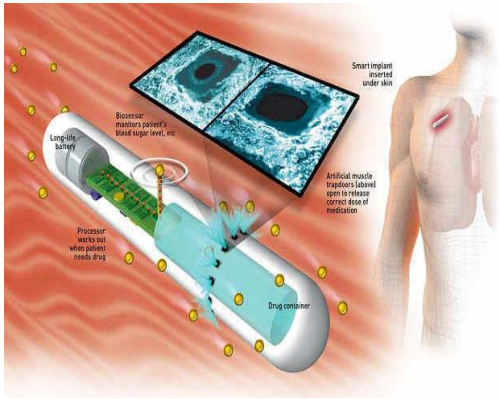
- 28 Acute Lymphoblastic Leukemia (ALL)
- 24 Acute Myeloid Leukemia (AML)
- 20 Mixed Linkage Leukemia (MLL)

Transdisciplinaire ingenieursontwerpen

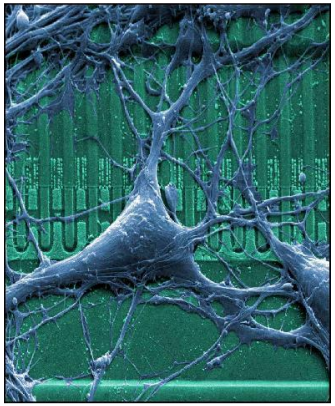
Materials, energy, IT

Ubiquitous computing

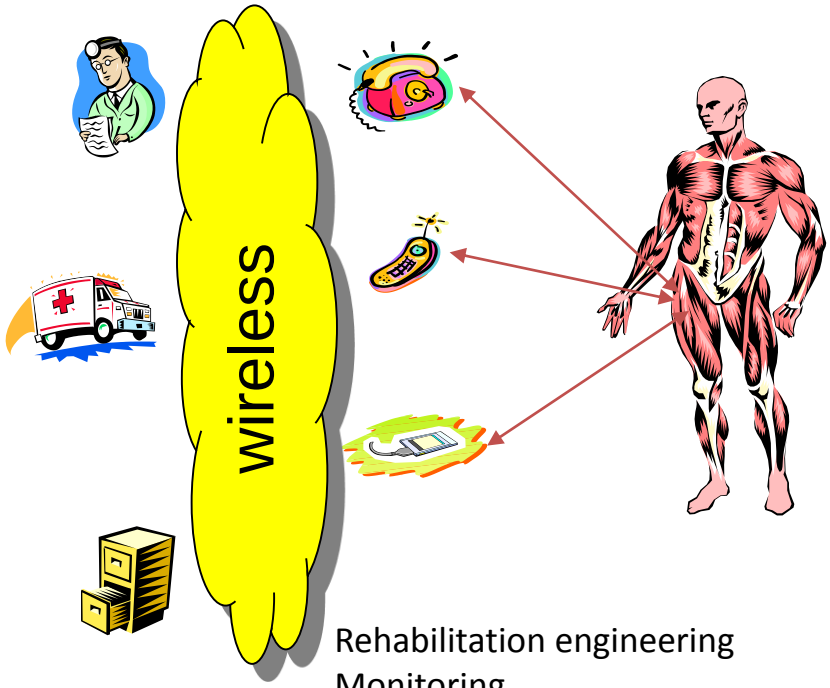
Ambient intelligence



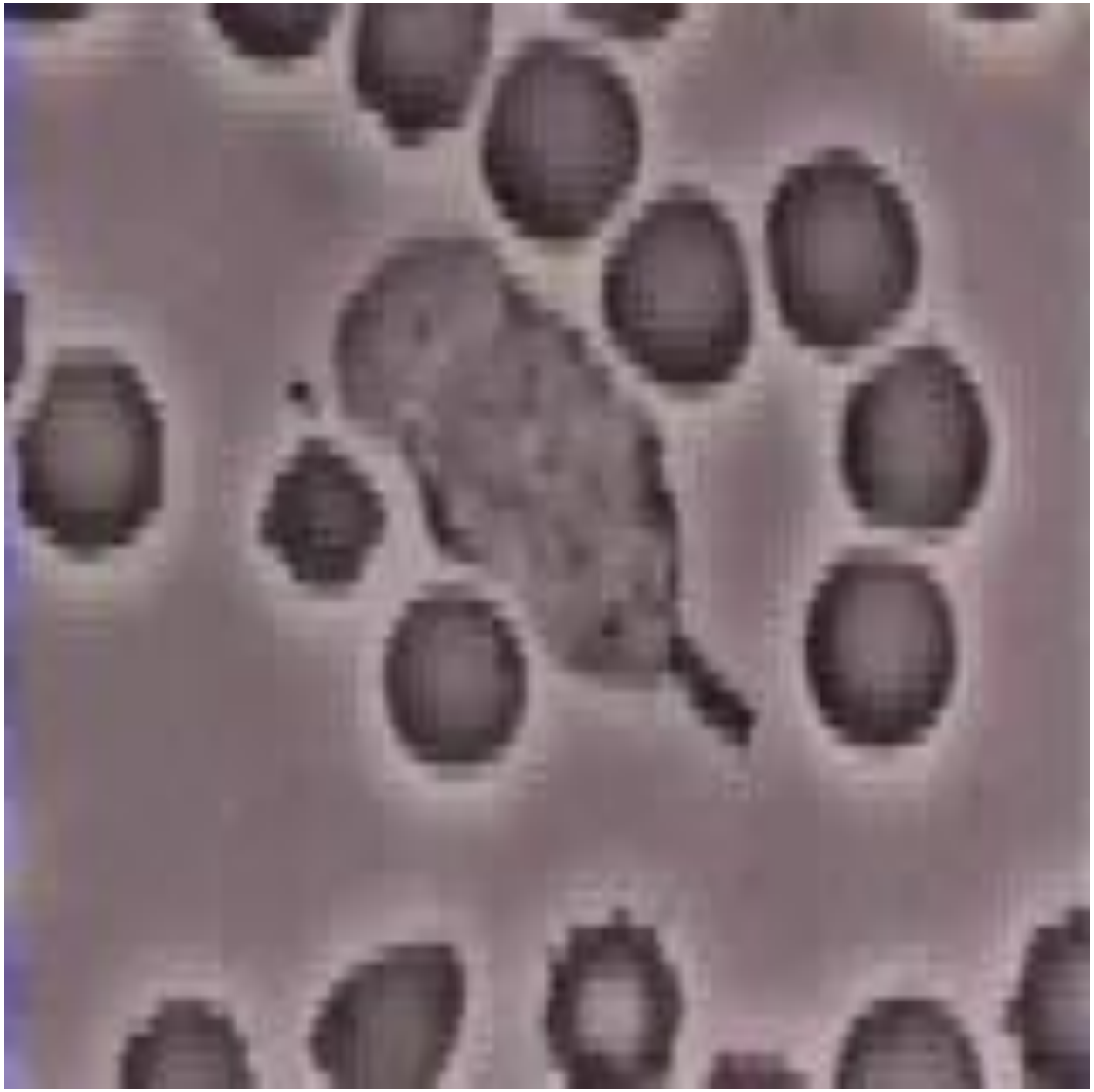
Embedded intelligence
Smart pills



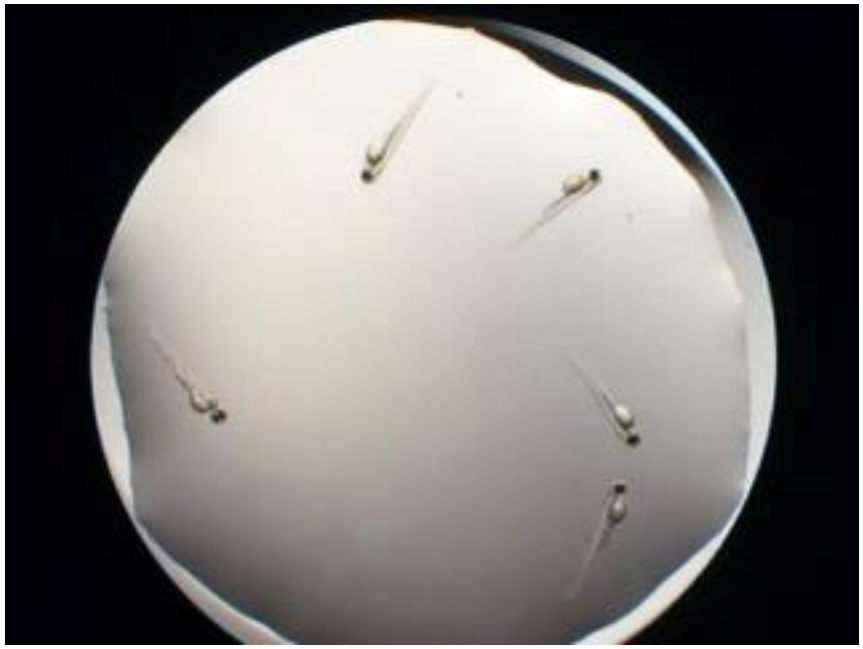
Neuron on chip

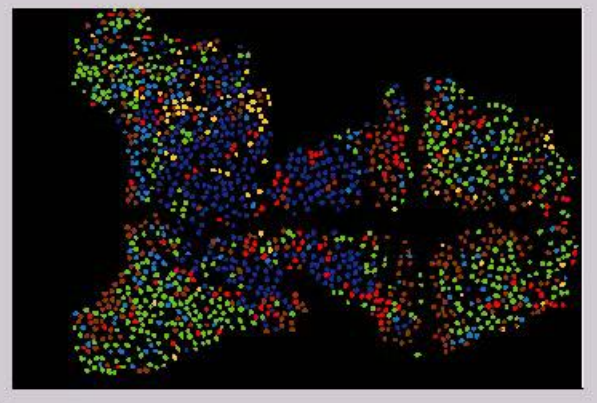


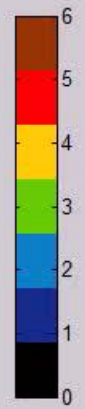
Rehabilitation engineering
Monitoring
Sensors: EEG, glucose,blood, DNA, …
Add-ons: vision, hearing, implants, …

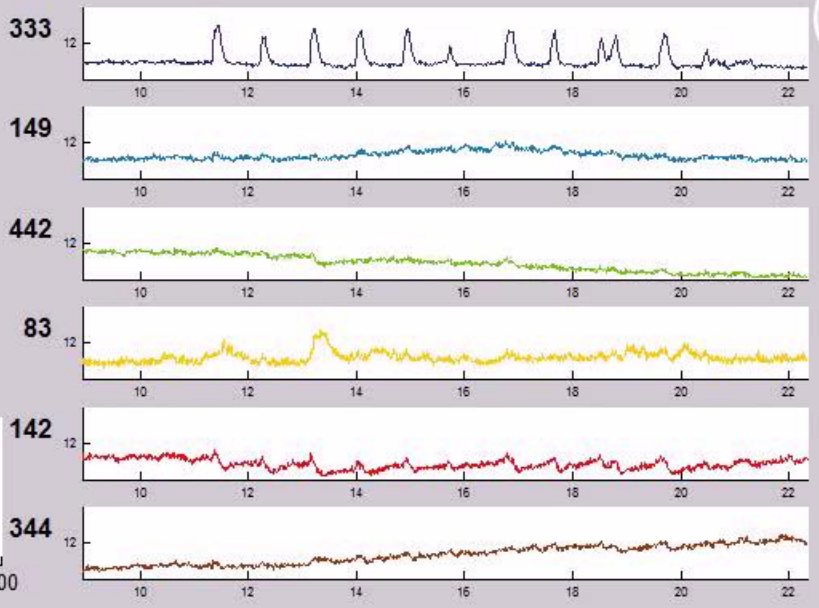


‘Chemotaxis’ verstaan






6
5
4
3
2
1
0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149
442
83
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12
10
12
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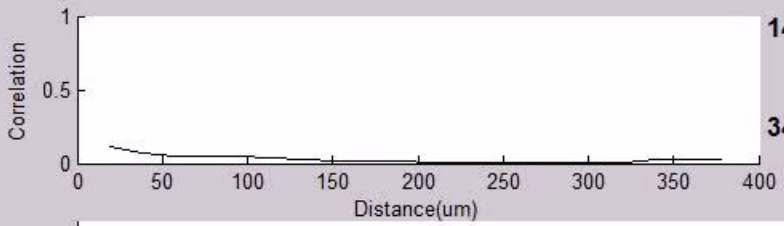
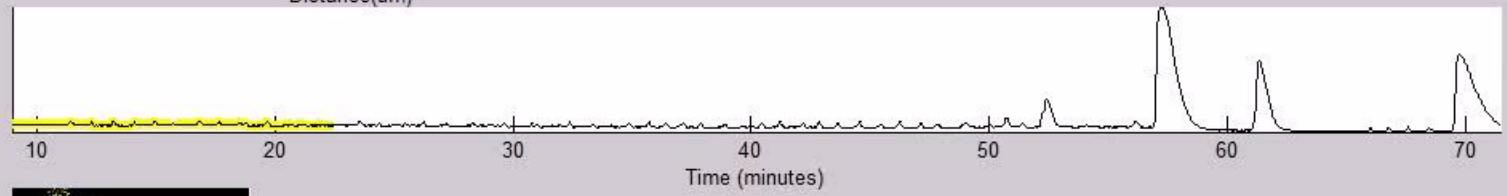
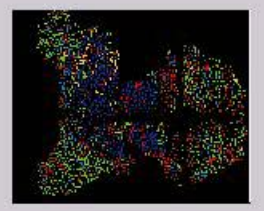
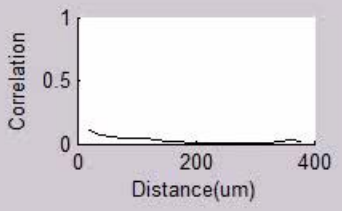
22

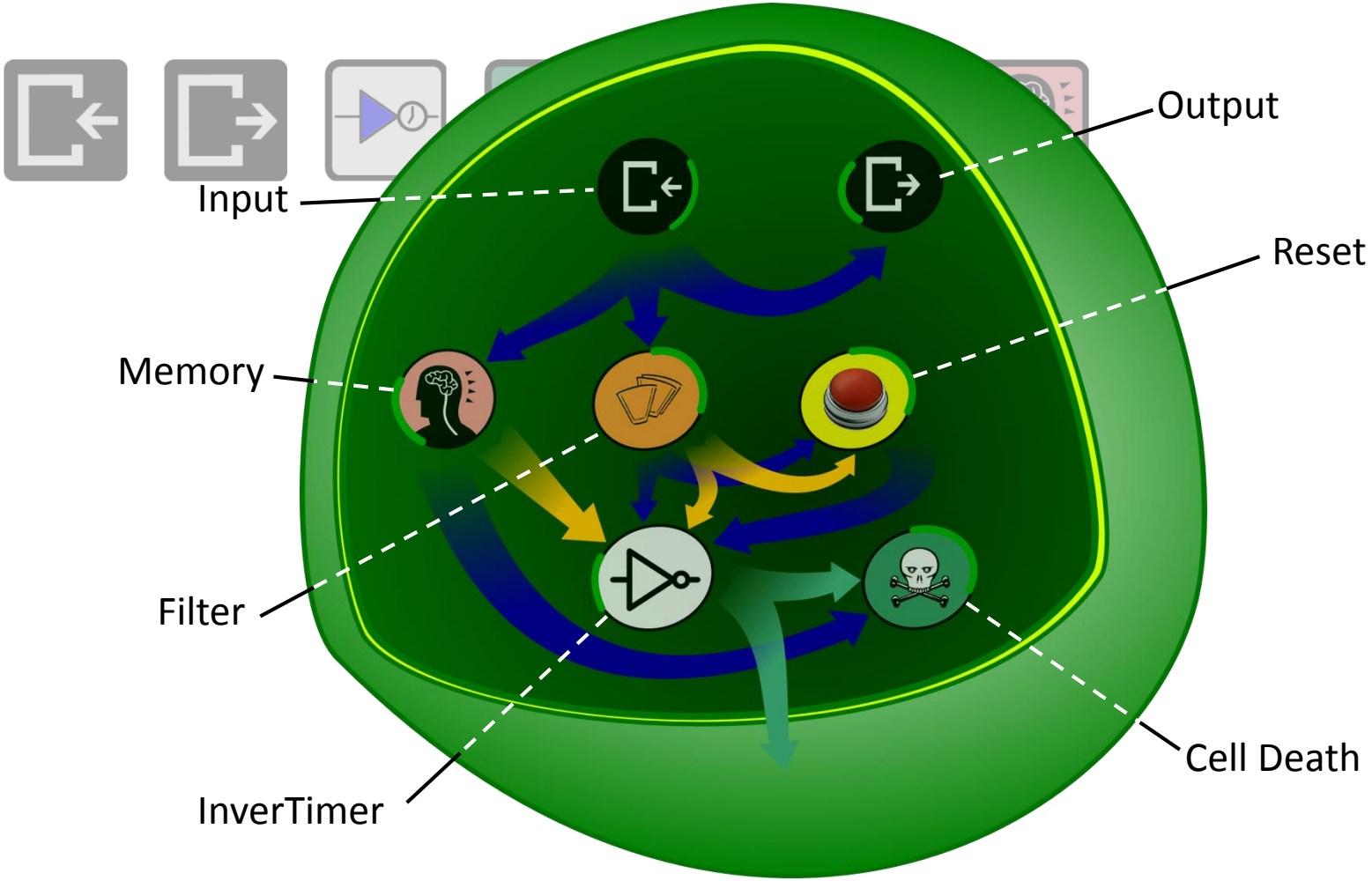

Correlation
1
0.5
0
0
50
100
150
200
250
300
350
400
Distance(um)


10
20
30
40
50
60
70
Time (minutes)



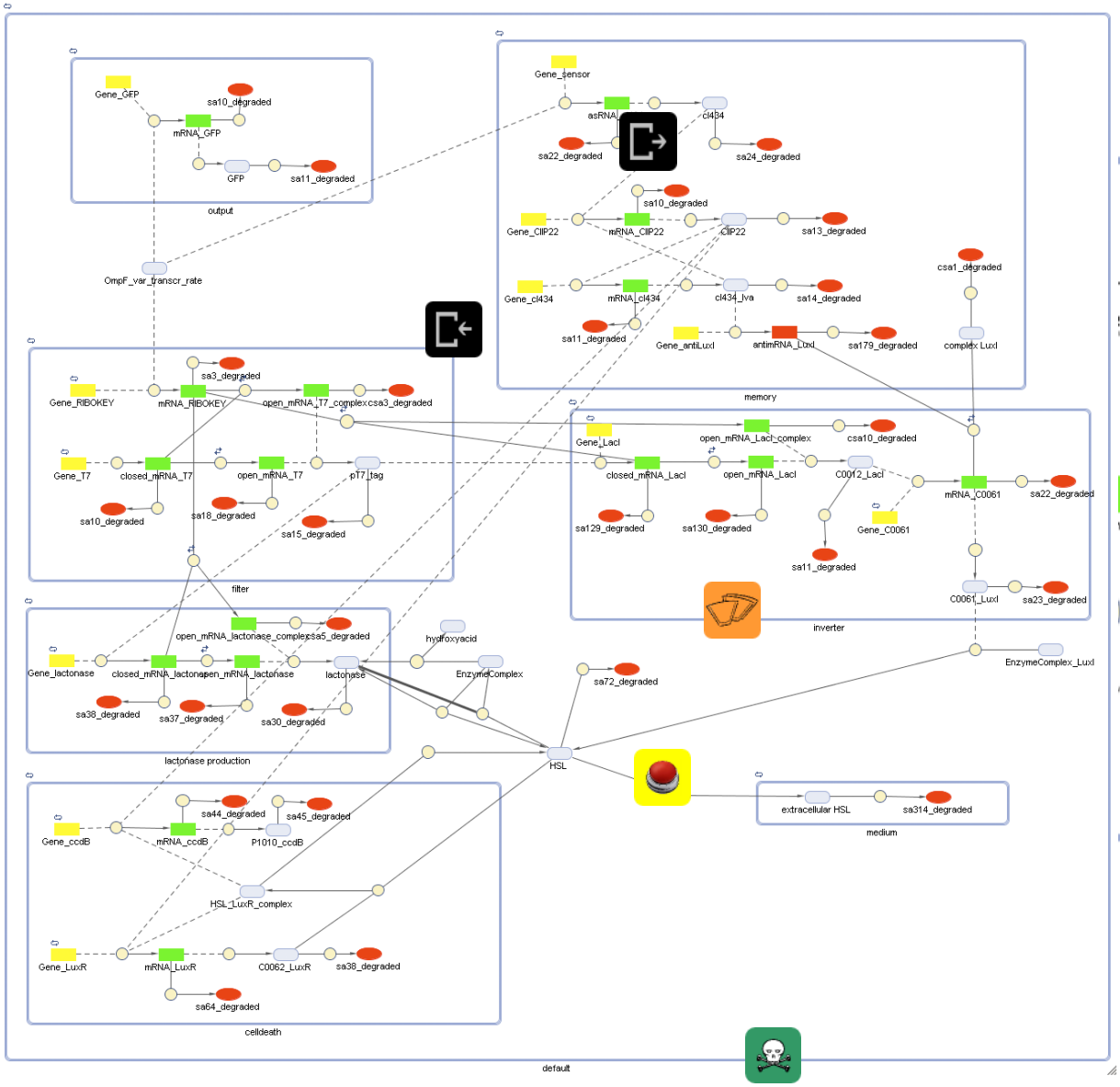

Correlation
1
0.5
0
0
200
400
Distance(um)

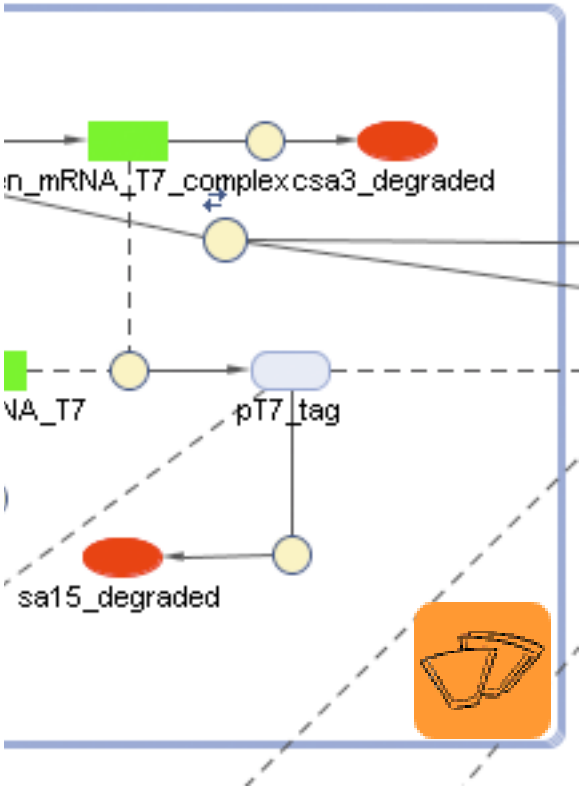
Synthetische biologie: Ontwerp een bacterie die kankercellen detecteert en vernietigt



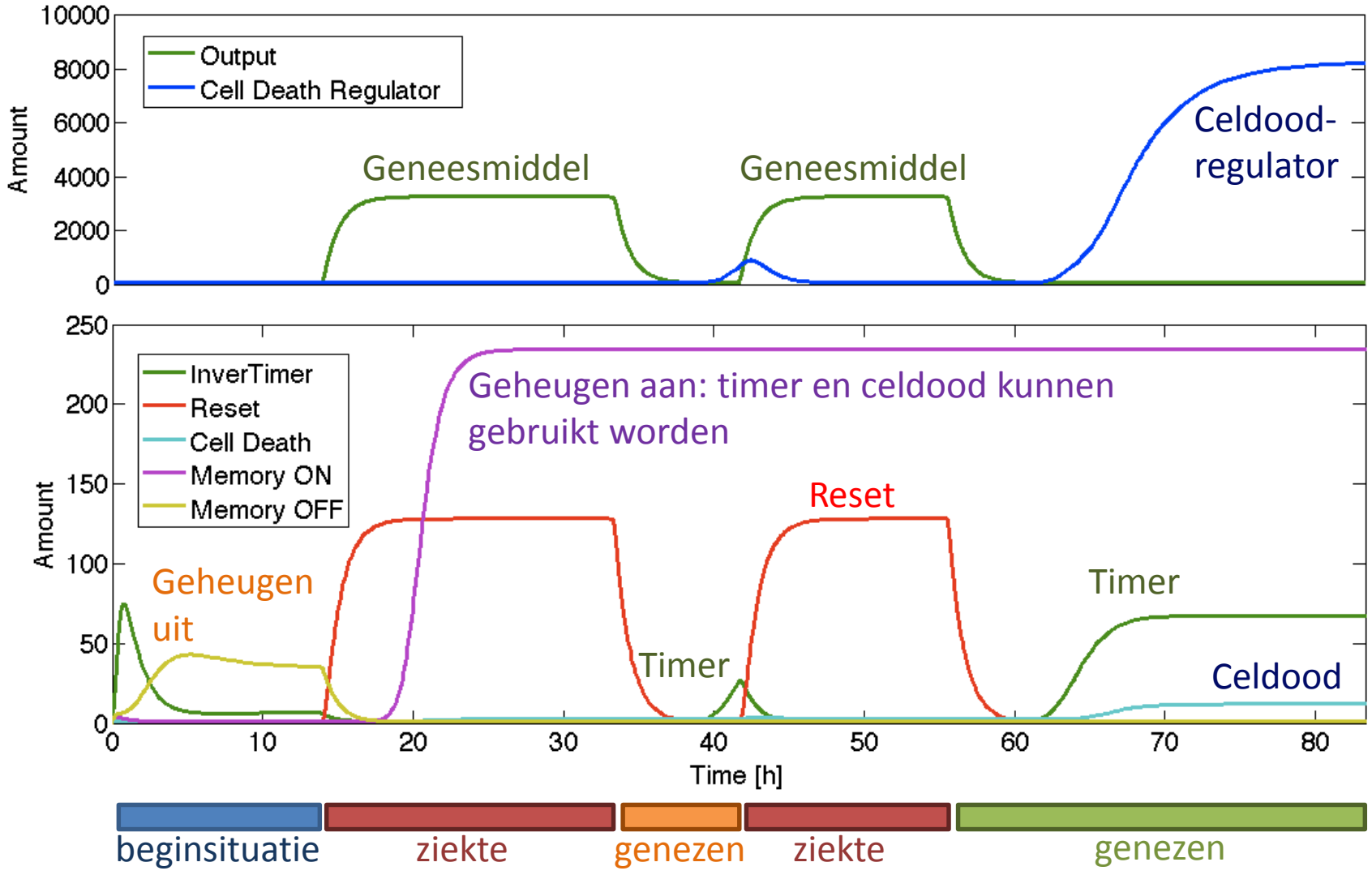
http://2013.igem.org/Team:KU_Leuven

in silico model Dr. Coli

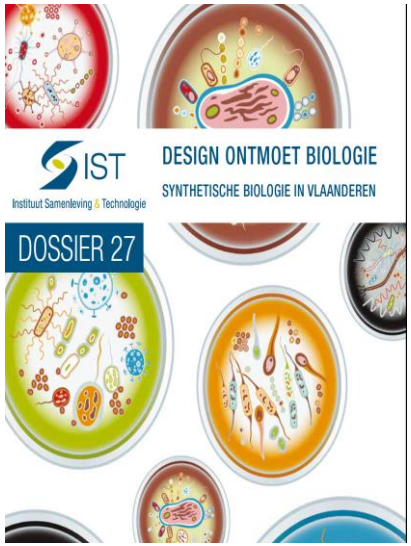




Dr. Coli doet zijn job !



Life goes live ?



- Design life ?
- Design bacteria voor energie, clean tech, menselijke therapie
- Design artificiele organen

- **Three deficits**
  - Legaal (de wet loopt achter)
  - Democratisch (zijn beleidsmensen voldoende geschoold ?)
  - Ethisch (not how but what !) (GGO, stamcellen, in vitro fertilisatie, ….)

CARTAGENIA

1. Wat is
    1. Wetenschap ?
    2. Technologie ?
    3. Engineering ?

1. Analyseren en ontwerpen in de zeven ingenieurssferen
    1. Materie
    2. Energie
    3. Informatie
    4. Duurzaamheid
    5. Sociale netwerken
    6. Cultuur
    7. Leven