Life goes live

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

The seven spheres of engineering

1. **Matter**
2. **Energy**
3. **Information**
4. **Sustainability**
5. **Social**
6. **Culture**
7. **Life**

Analysis and Design in the seven spheres

Utopia ? Design of living systems ?

What is science ?

- Describe and understand the world

- From myths/stories to verifiable facts

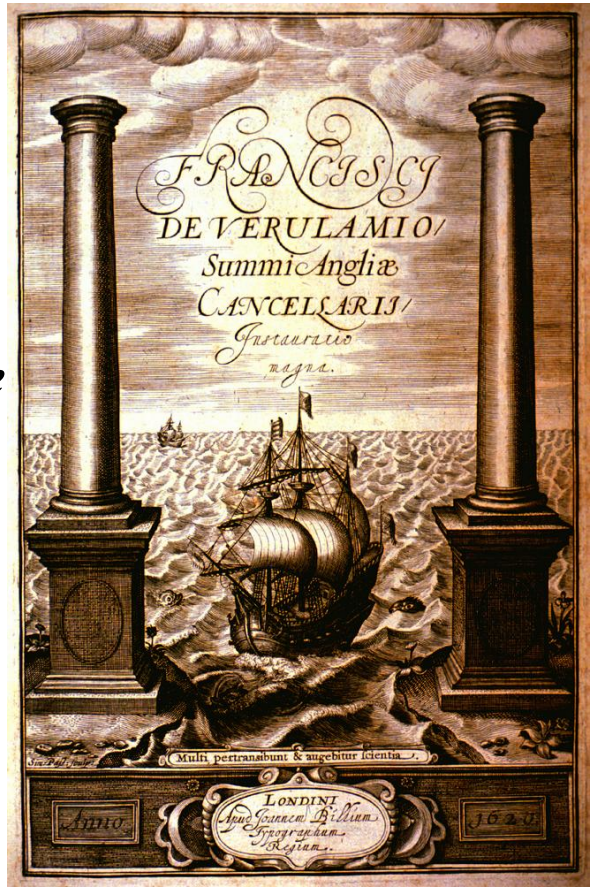
- Religion and science

  - The creator outside his creation
  - *Galilei and the church*
  - *Napoleon: Où est Dieu dans votre système ?*

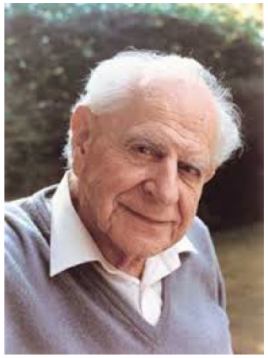
  Laplace: Dieu ? Je n'ai pas besoin de cette hypothèse

- 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”

An simple argument with the same explanatory power as a more complicated one, is to be preferred.

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* solutions to challenges and problems

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What is technology ? What is engineering ?

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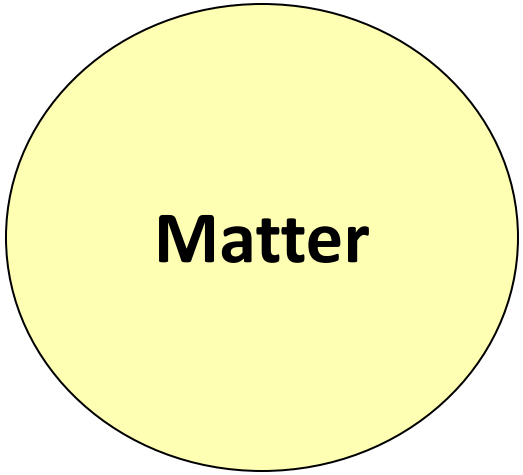
Analysis and Design in the seven spheres

Utopia ? Design of living systems ?


Matter

The science (analysis)

Kepler

Law 1: Orbit = ellips; Sun = focus

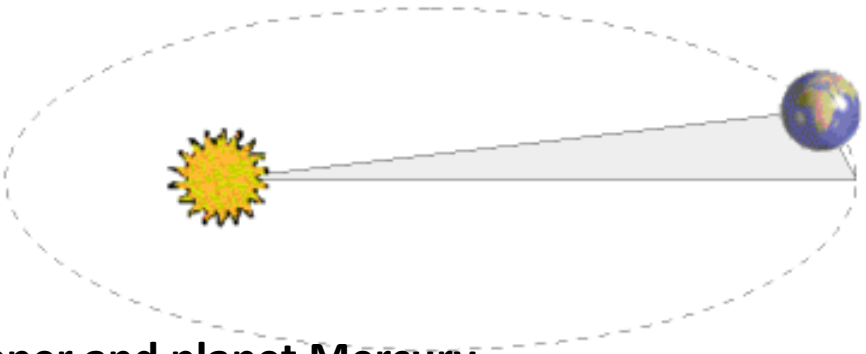
Law 2: 'Radial line' colors equal surfaces in equal time intervals

Newton

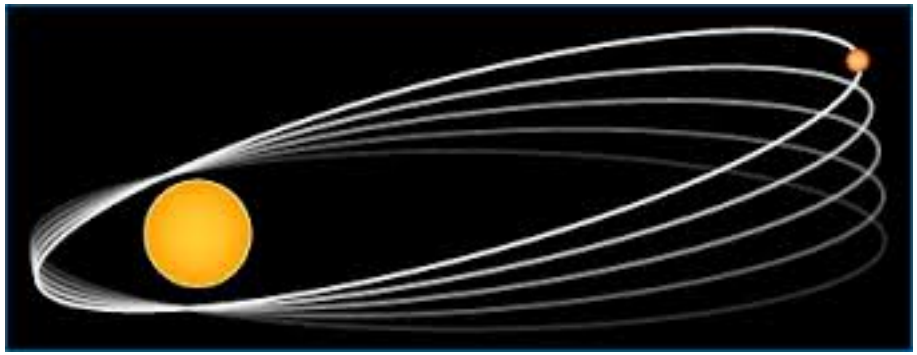
Law 3: $$\frac{T_1^2}{T_2^2} = \frac{a_1^3}{a_2^3}$$

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

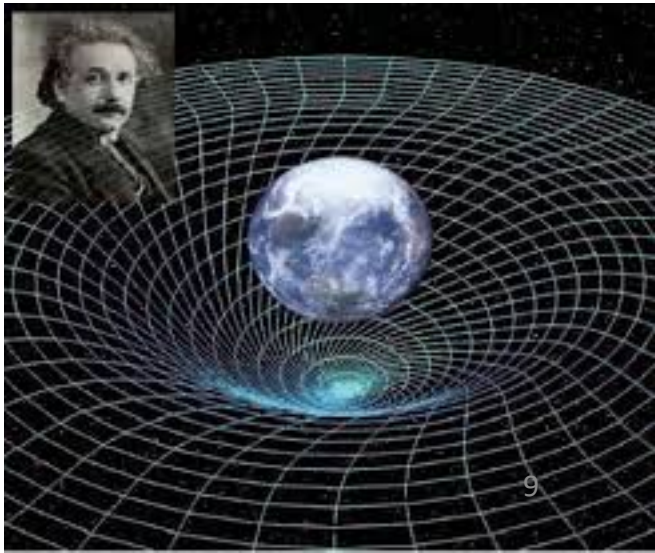
$$F = G\,\frac{m.M}{r^2}$$



Popper and planet Mercury



Einstein



The unreasonable effectiveness of mathematics

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

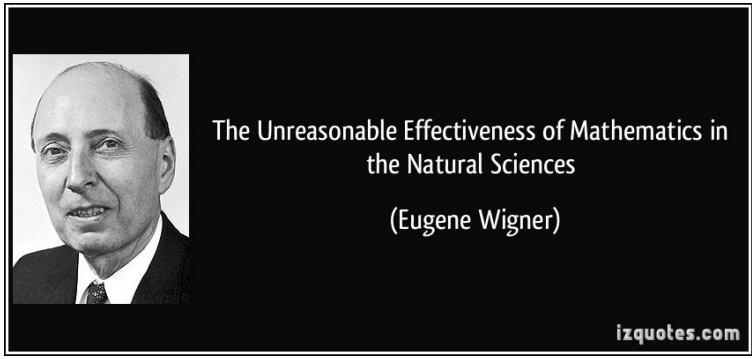
The Unreasonable Effectiveness of Mathematics in the Natural Sciences

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

EUGENE P. WIGNER
Princeton University

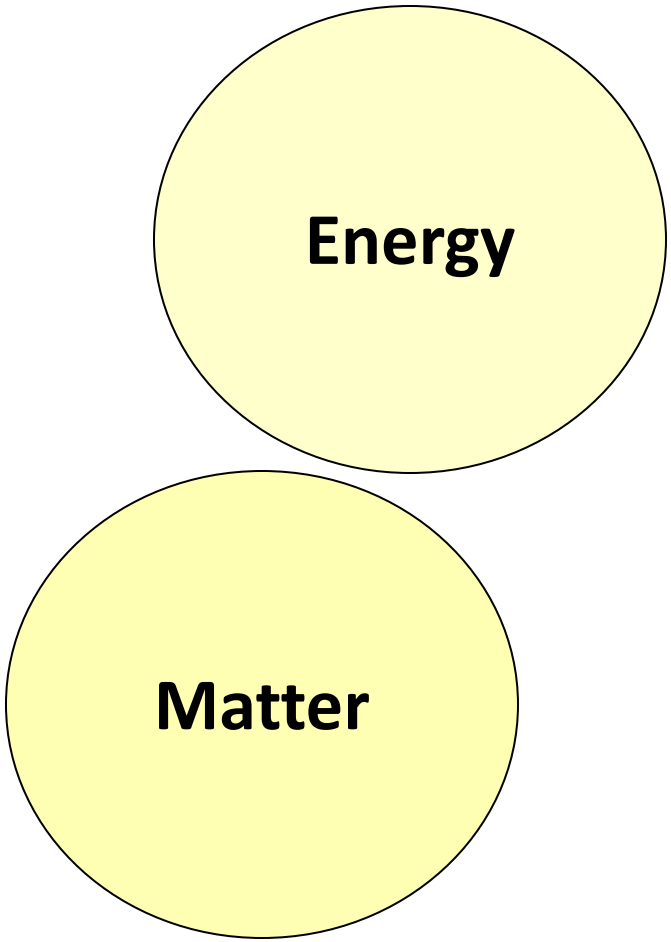
"and it is probable that there is some secret here which remains to be discovered." (*C. S. Peirce*)

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."

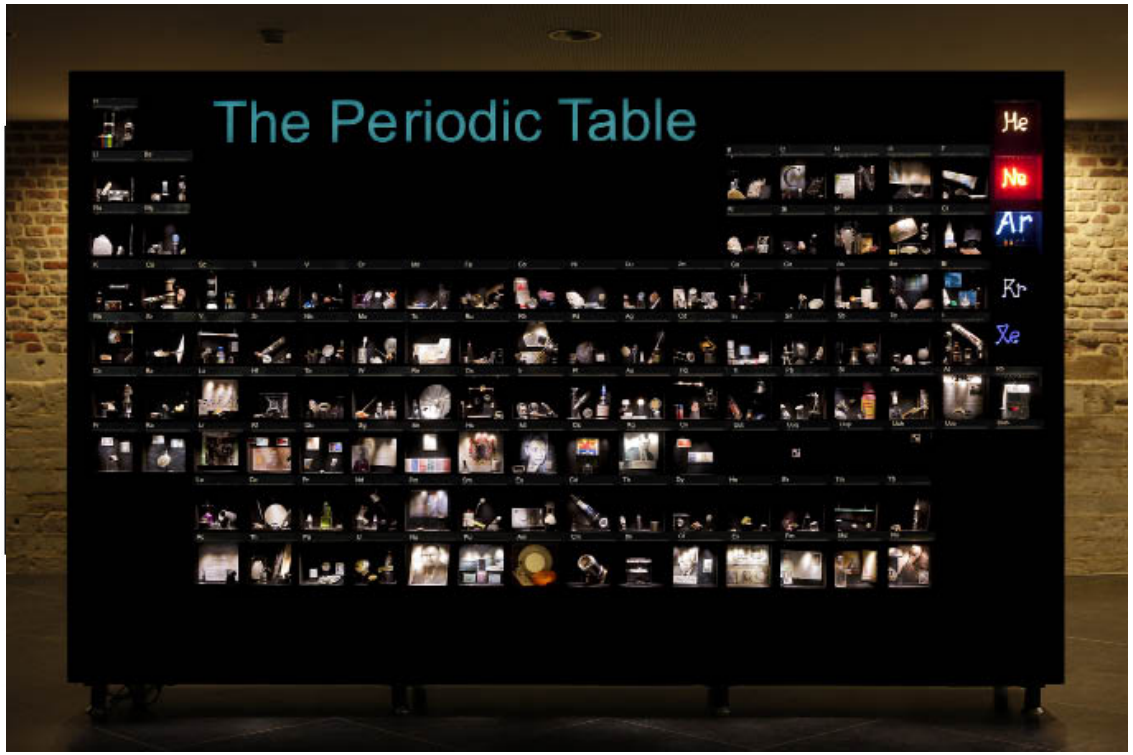


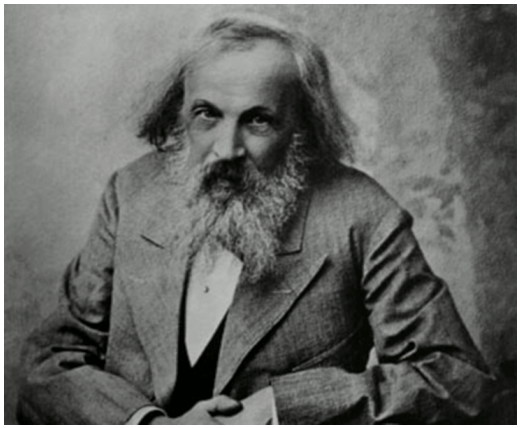
Technology and Engineering Design:
The first industrial revolution (1700…)

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


Energy
Matter

The science (analysis)



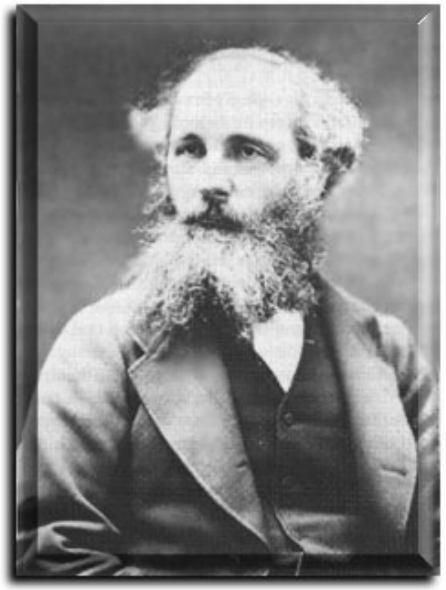


$$\nabla \cdot \mathbf{D} = \rho \qquad (1) \qquad \text{Gauss' Law}$$

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

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

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



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

-Mass production and consumption

-Electricity and oil as energy sources

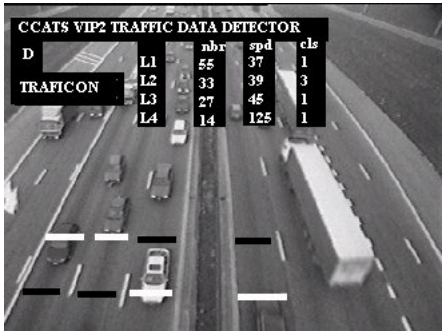
-Chemical industry develops

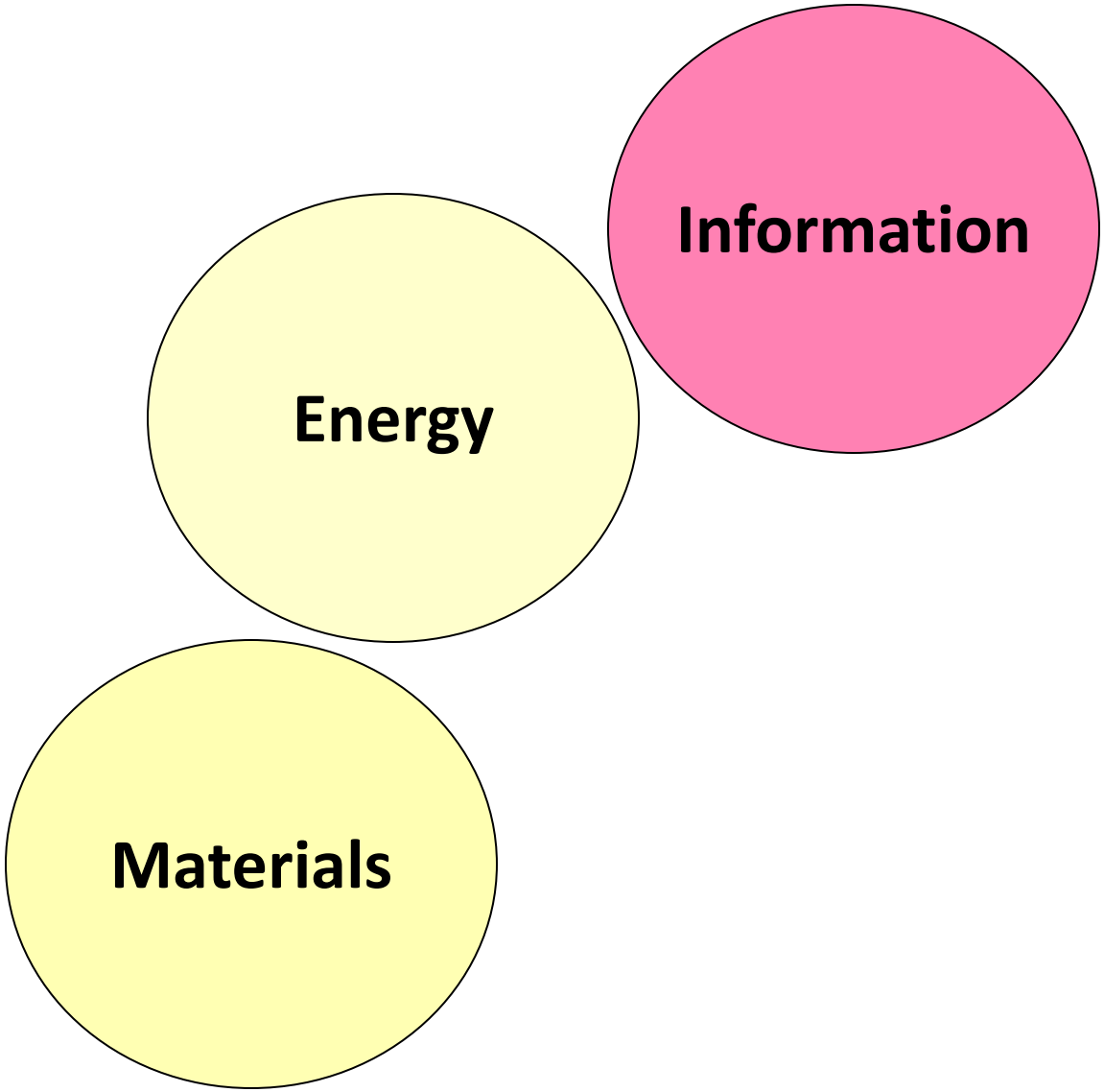
-Infrastructure for mobility: road networks

-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

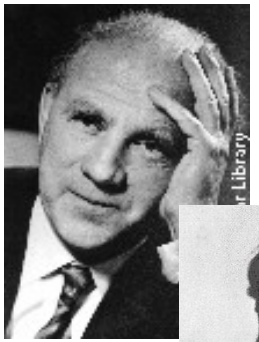
1910: Atom model Bohr

1930: Quantummechanics of Heisenberg, Schrödinger,..

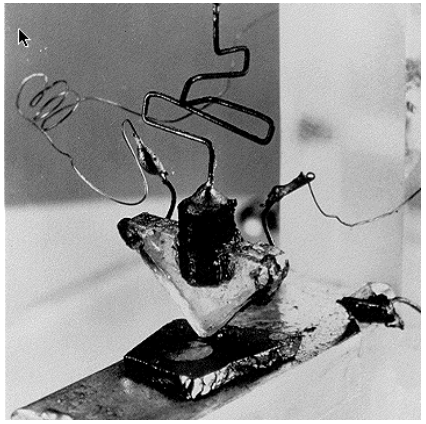
1940: Computer (principle) of Turing and von Neumann

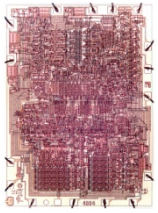
1948: Information theory of Shannon

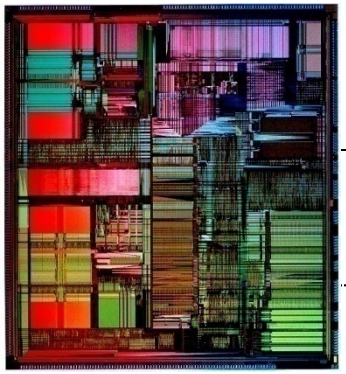
1950: Transistor of Shockley, Bardeen,…



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

The Fourth Paradigm: Data !

Paradigm	Time Ago	Method
First	A millenium	Empirical
Second	A few centuries	Theoretical
Third	A few decades	Computational
Fourth	Today	Data-driven

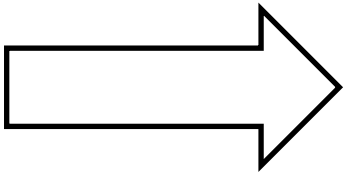
Evolution

From

I have a hypothesis

⇩

I need data to check it

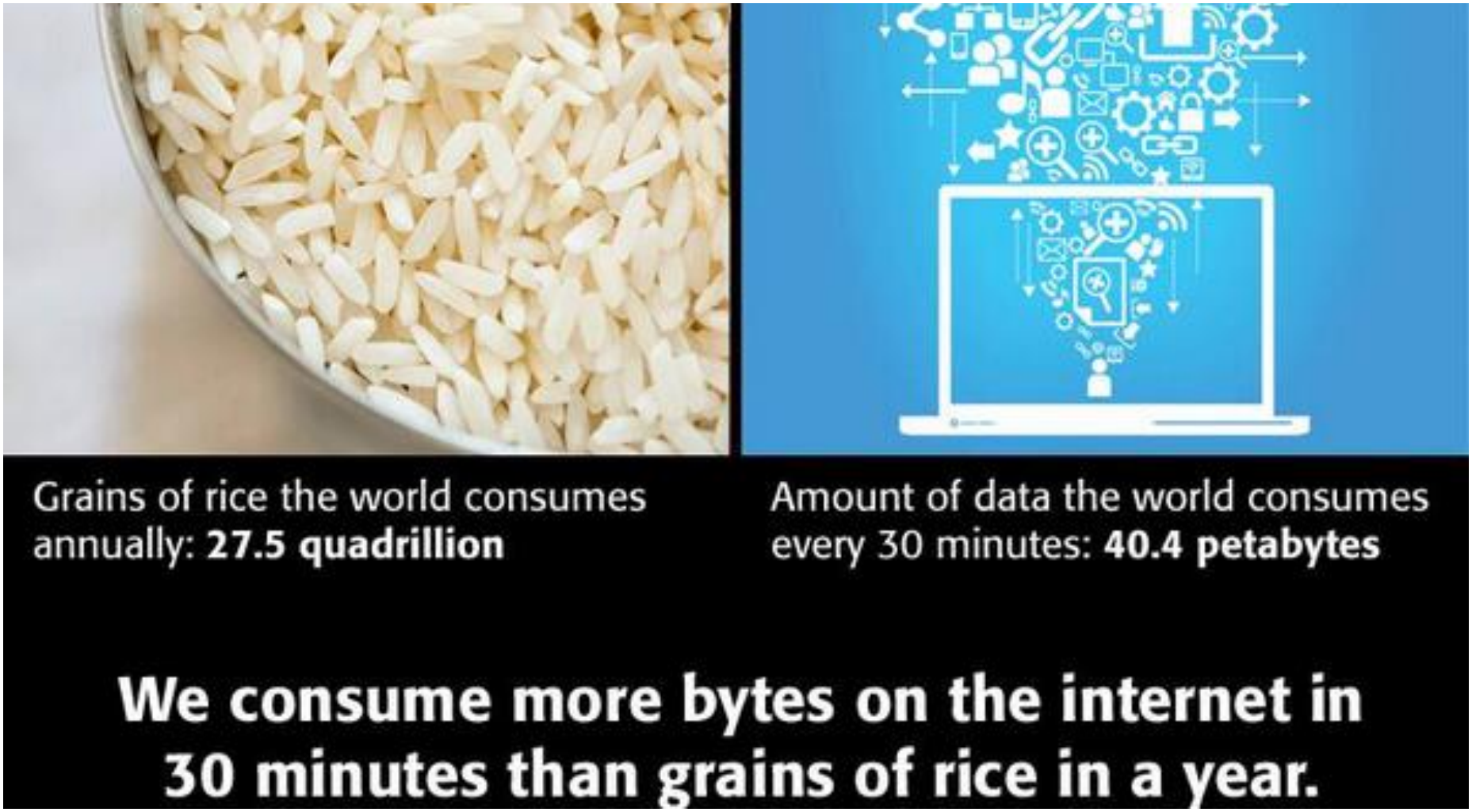


To

I have data

⇩

Which hypotheses can I check?

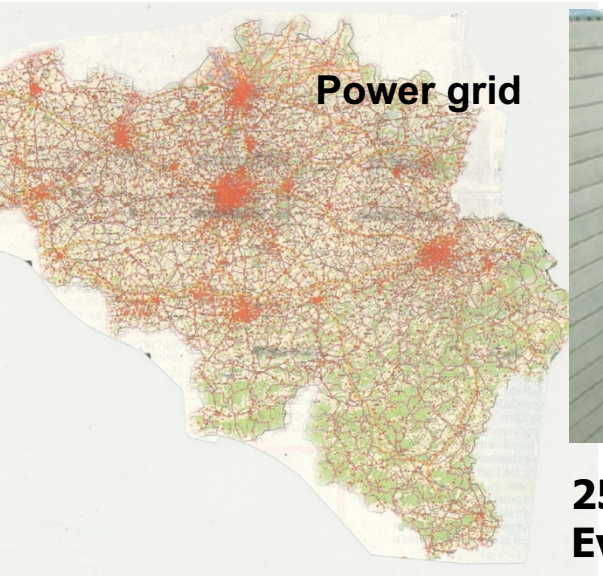


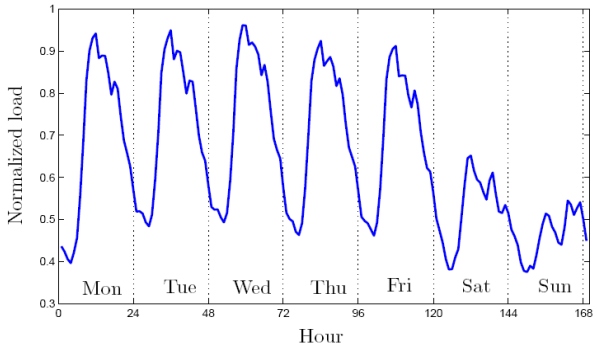
1 million = 1 000 000
1 billion = 1 000 000 000
1 trillion = 1 000 000 000 000
1 quadrillion =
1 000 000 000 000 000

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

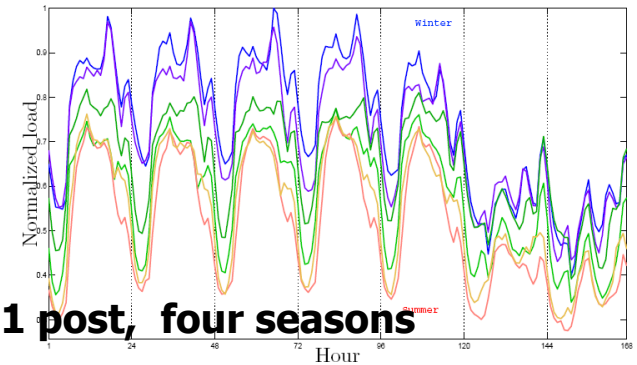
Belgian smart electricity grid DSS



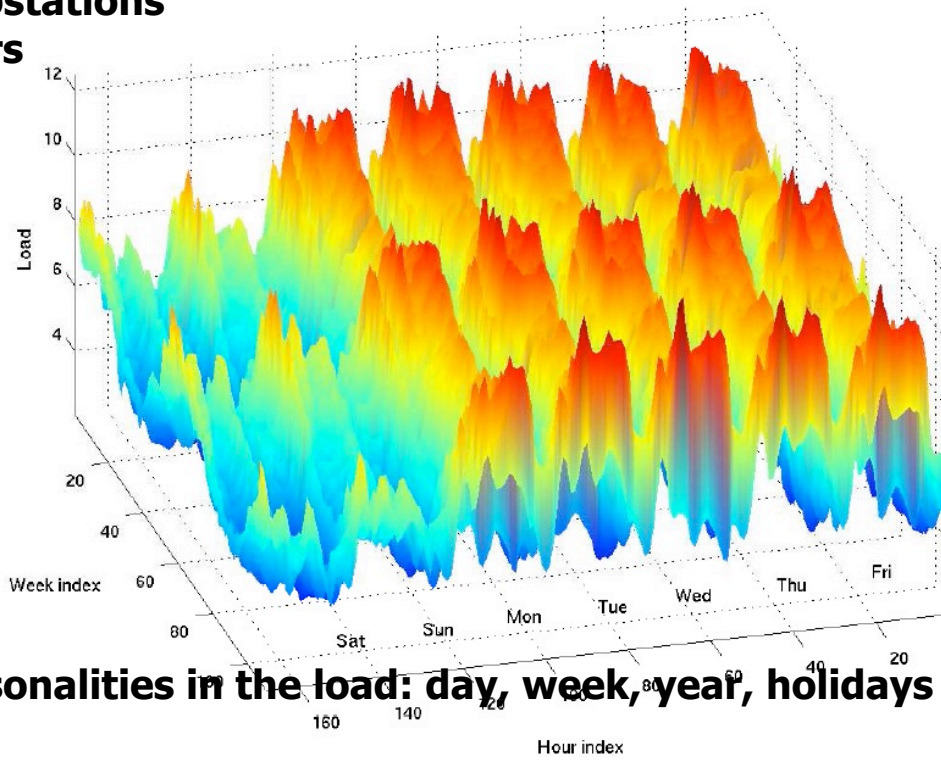


1 post, 1 week

250 transformer substations
Every 15 min, 5 years



1 post, four seasons



Seasonalities in the load: day, week, year, holidays

STADIUS
Center for Dynamical Systems, Signal Processing and Data Analytics

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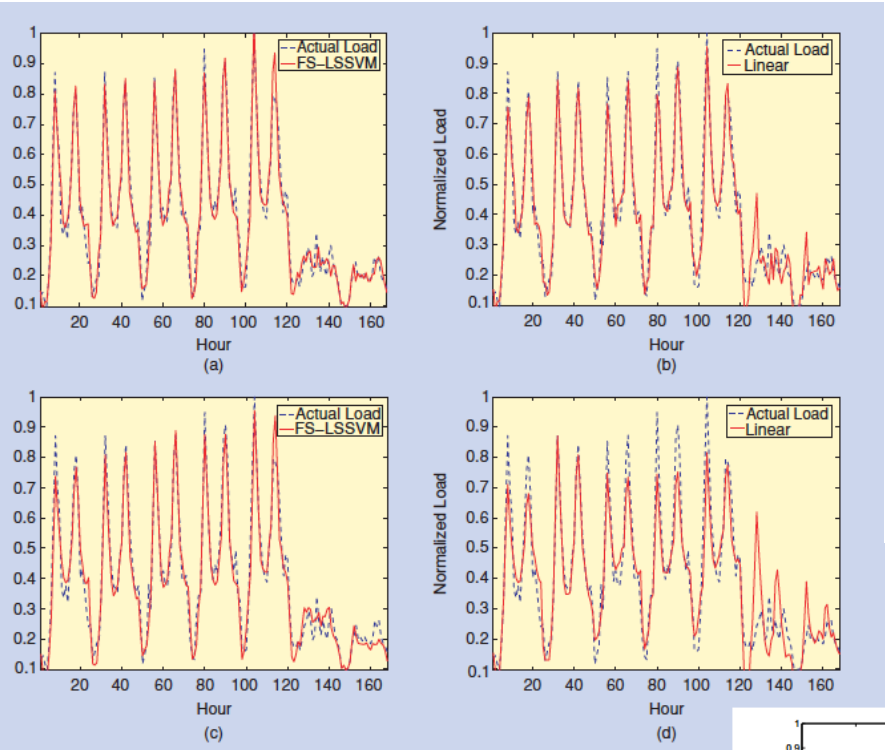
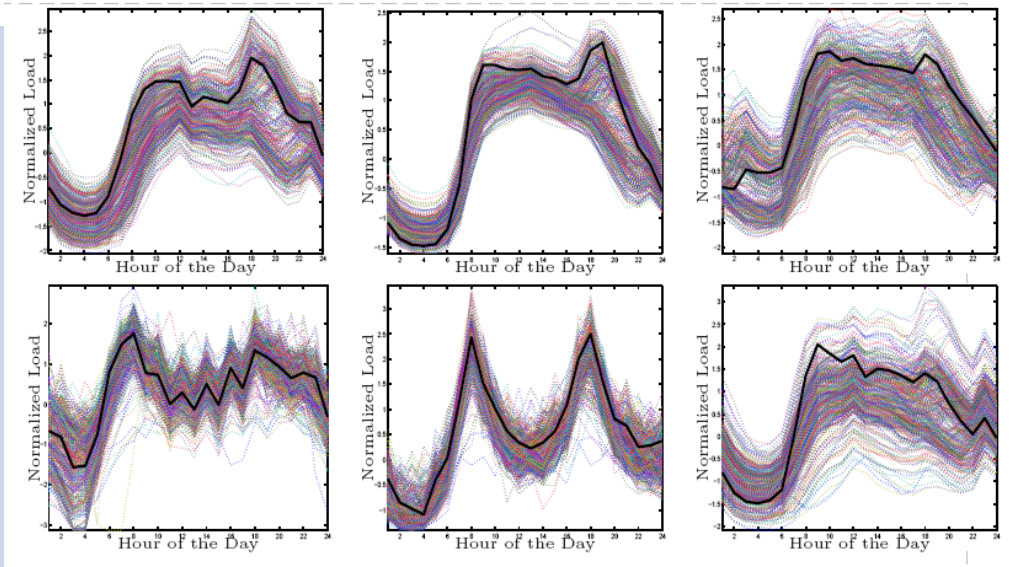
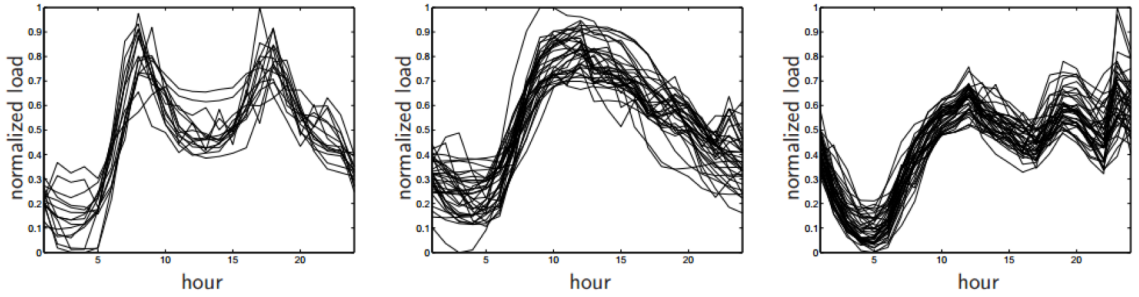




6 posts, 1 year
Seasonalities, calender holidays !

1 month predictions
depending
on day, season
and weather prediction



Electricity load: 245 substations in Belgian grid (1/2 train, 1/2 validation)
$x_i \in \mathbb{R}^{43.824}$: spectral clustering on **high dimensional data** (5 years)

3 of 7 detected clusters:
- *1: Residential profile: morning and evening peaks*
- *2: Business profile: peaked around noon*
- *3: Industrial profile: increasing morning, oscillating afternoon and evening*

Customer profiling:
Residential, business, industrial

Sport Analytics Decision Support Systems

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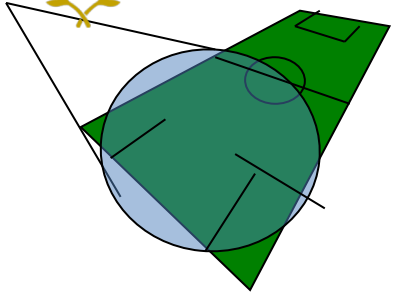
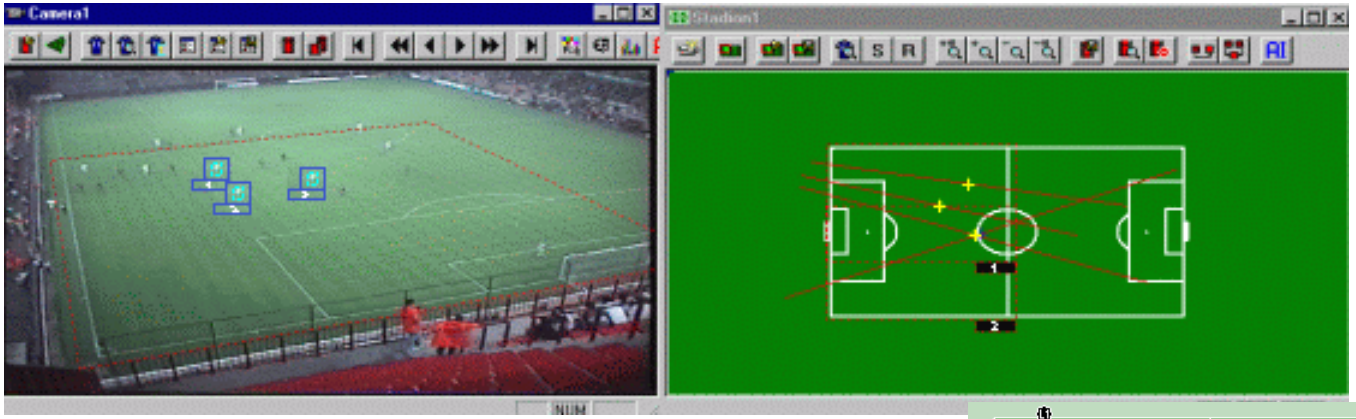
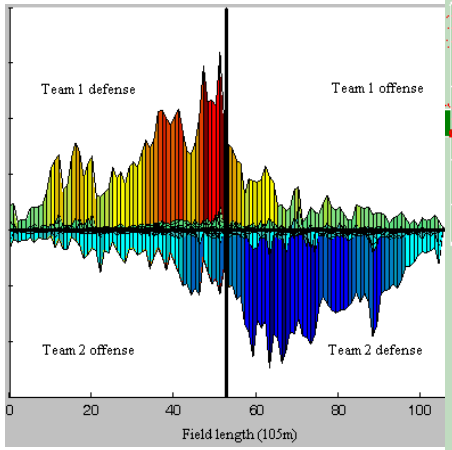
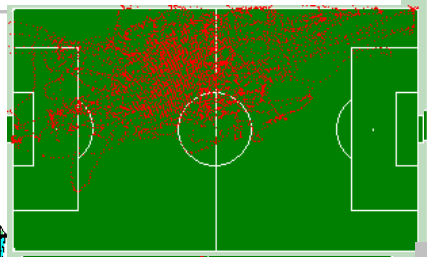
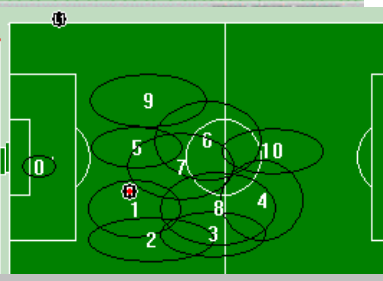


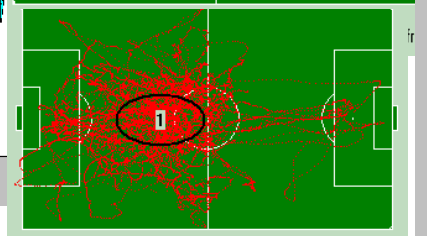


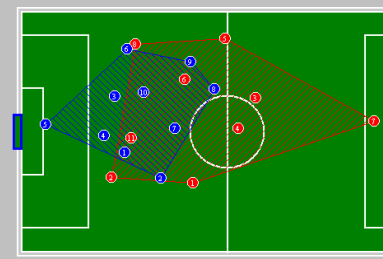
Time	Team	Action	Player	Position
0:00:00	1	Kick Off	9	(50,30)
0:00:01	1	Has Ball	10	(49,29)
0:00:04	1	Has Ball	8	(45,31)
...	...	...	...	...
0:12:25	1	Ball Out	6	(0,57)
0:12:46	2	Corner	3	(0,60)
0:12:47	2	Has Ball	4	(4,29)
0:12:49	2	Goal	4	(0,29)
0:13:38	1	Kick Off	10	(50,30)
...	...	...	...	...

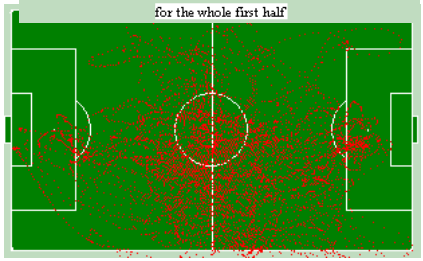


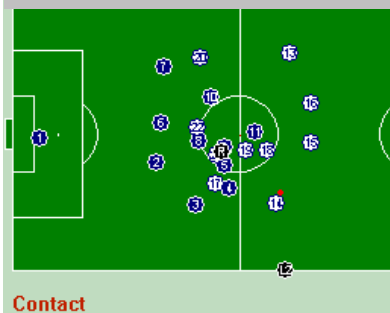


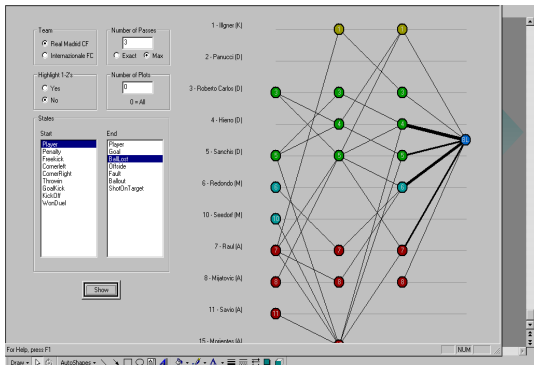


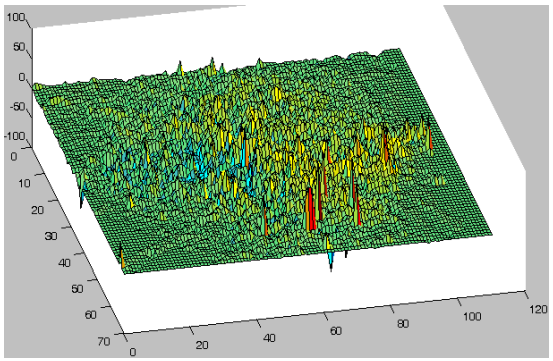


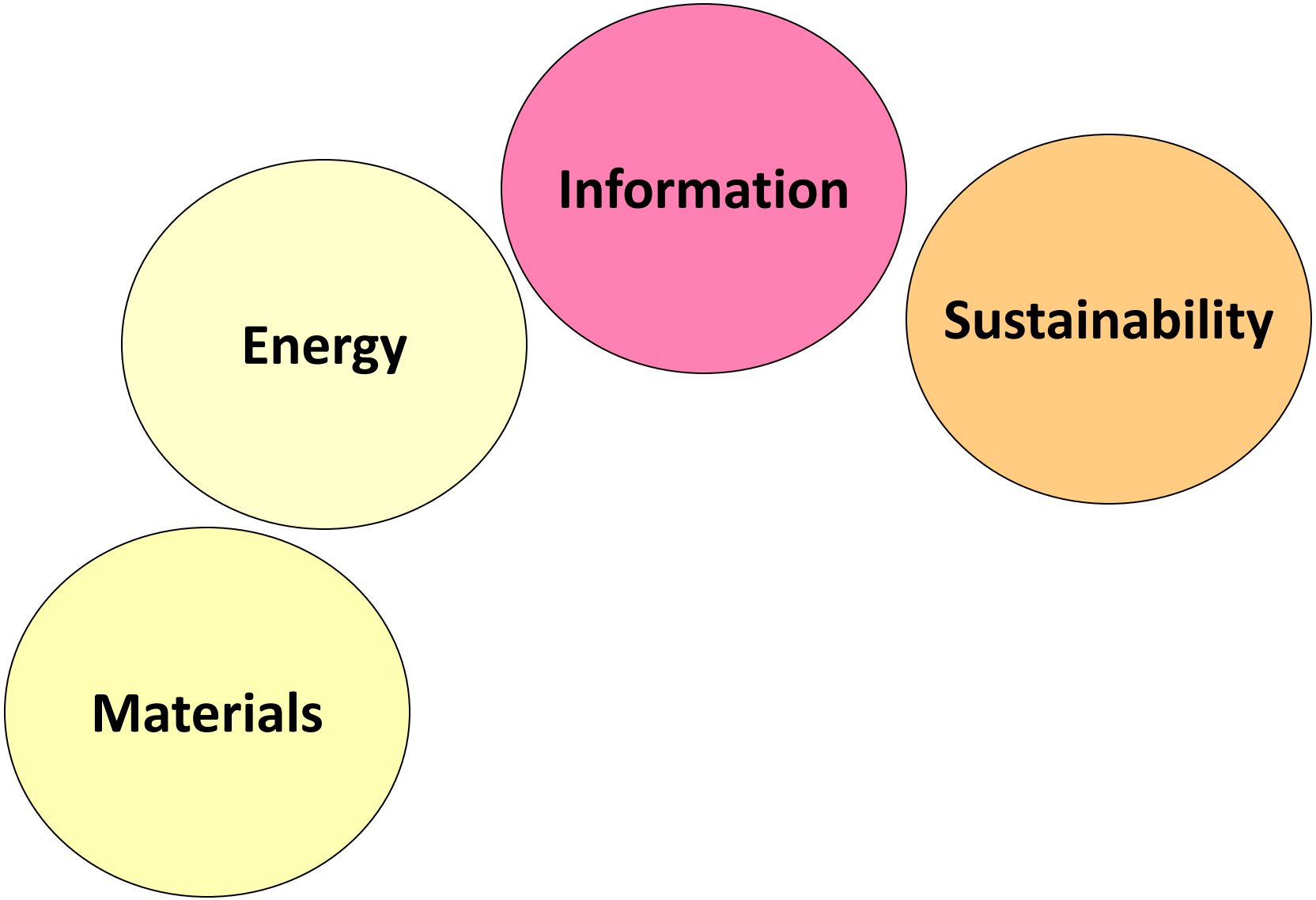











Information
Energy
Sustainability
Materials

Sustainability

- Globalization

CNN's *Global Village*
Internet
Think globally, act locally (glocal)
Netwerks of people and computers

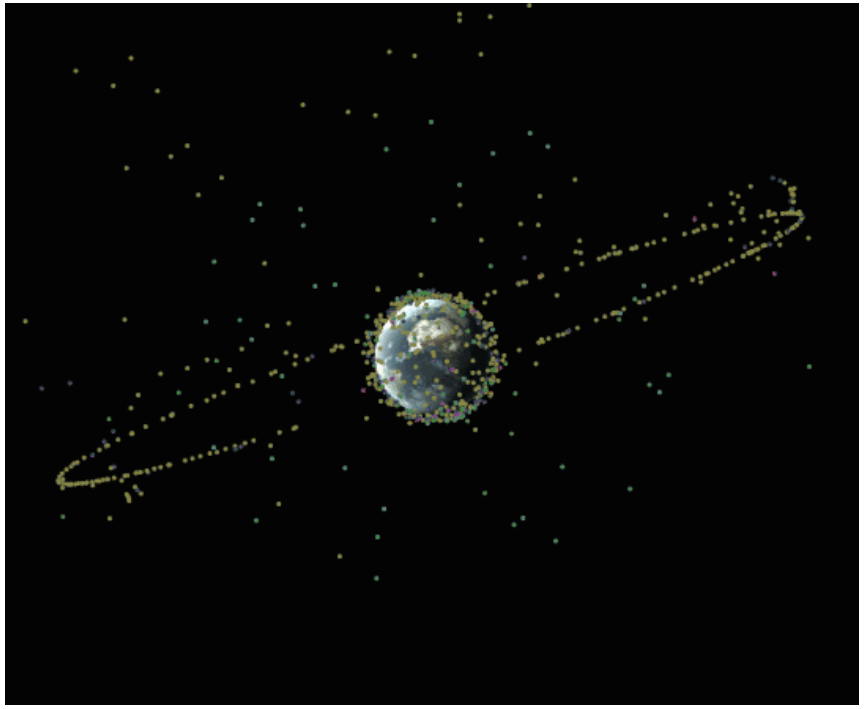
- Standardization, uniformisation, protocolization

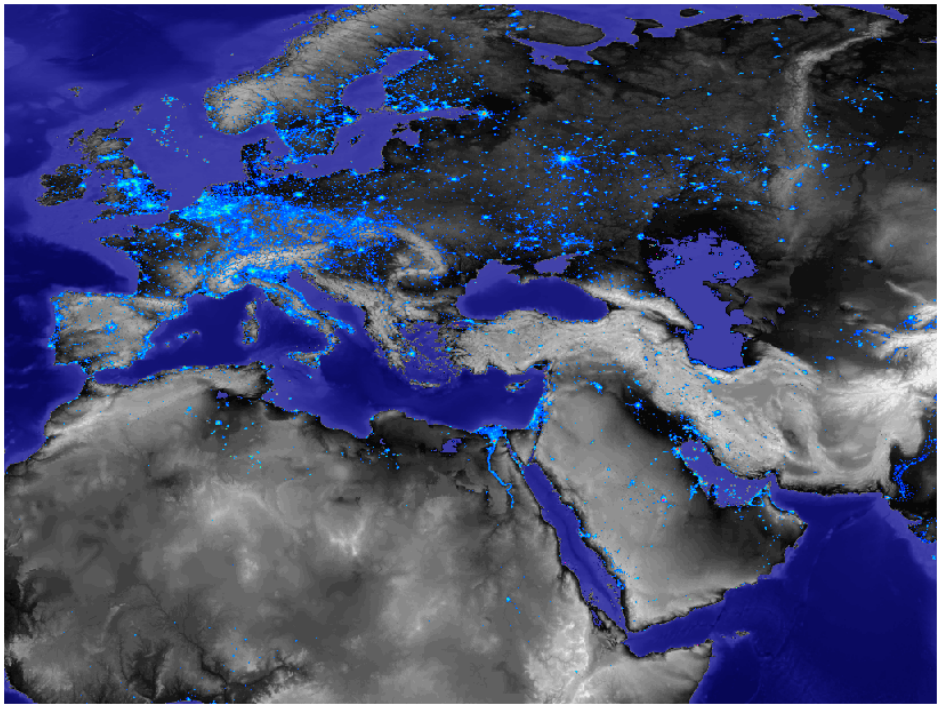
- Sustainable society

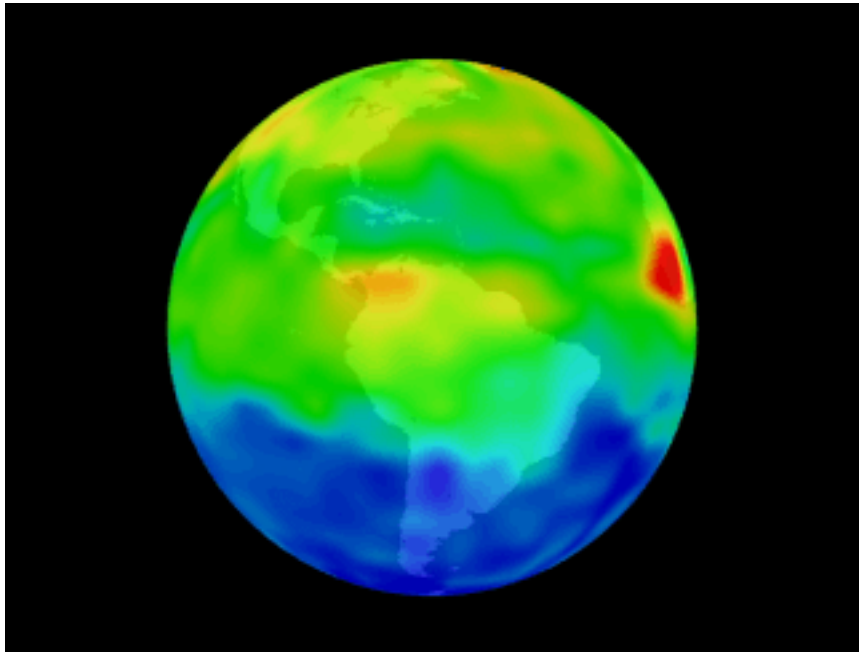
Traditionally: Finite demands and infinite supplies
Now: Infinite demands but finite supplies

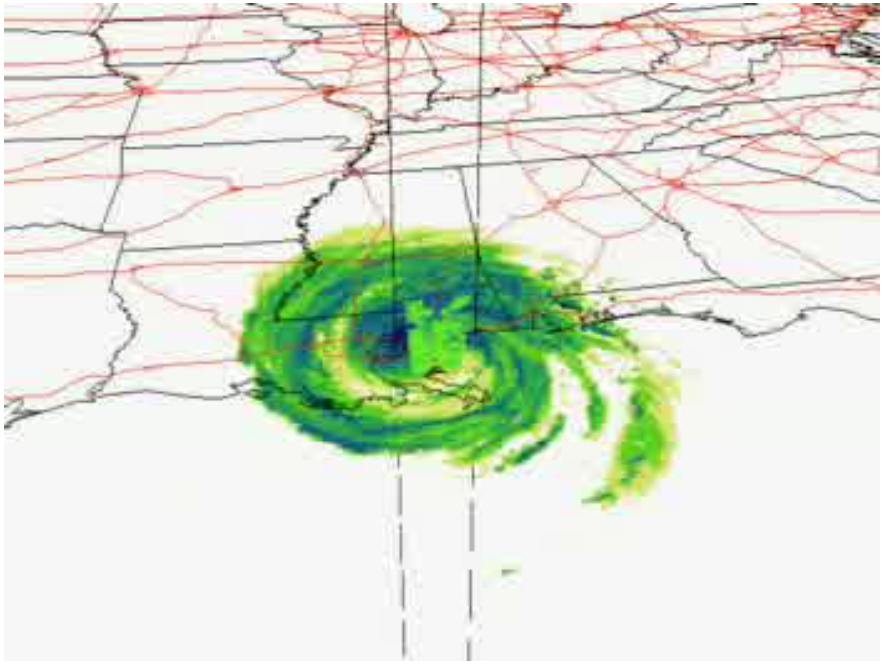
We did not inherit the world from our ancestres, but have borrowed it from our children (Antoine de Saint-Exupery)

- Clean-tech, renewable energy, global warming, ….



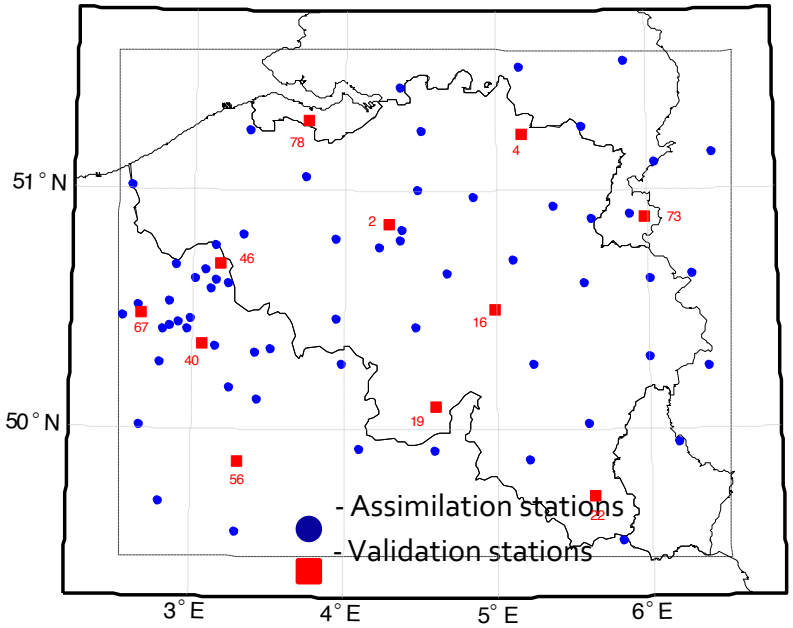




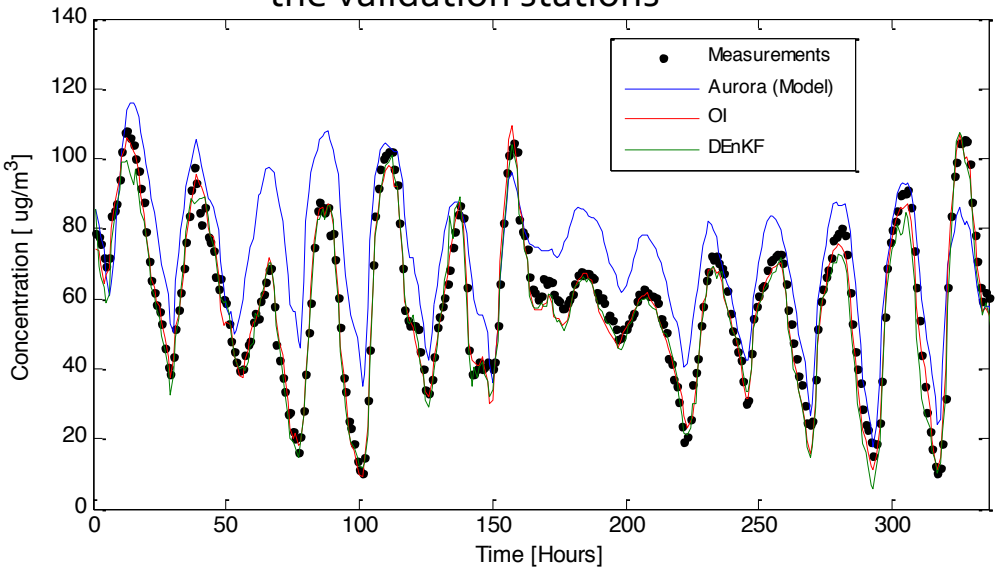


Flanders O3/fine particle DSS

O_3 air-quality stations

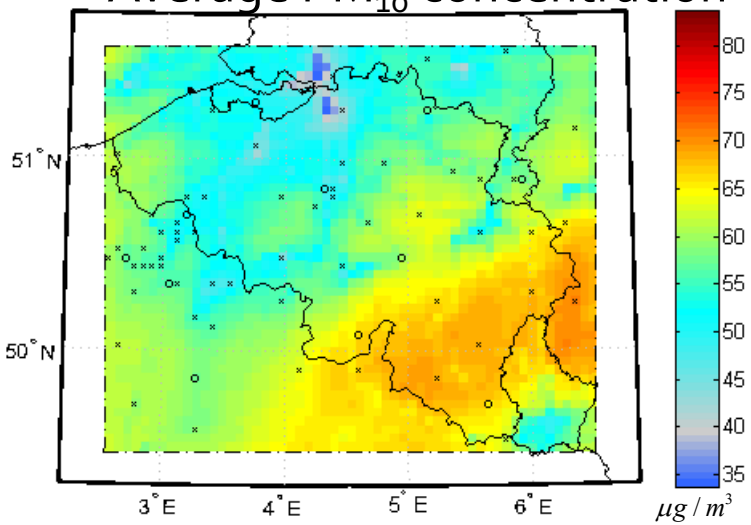


Average of the O_3 concentration over the validation stations

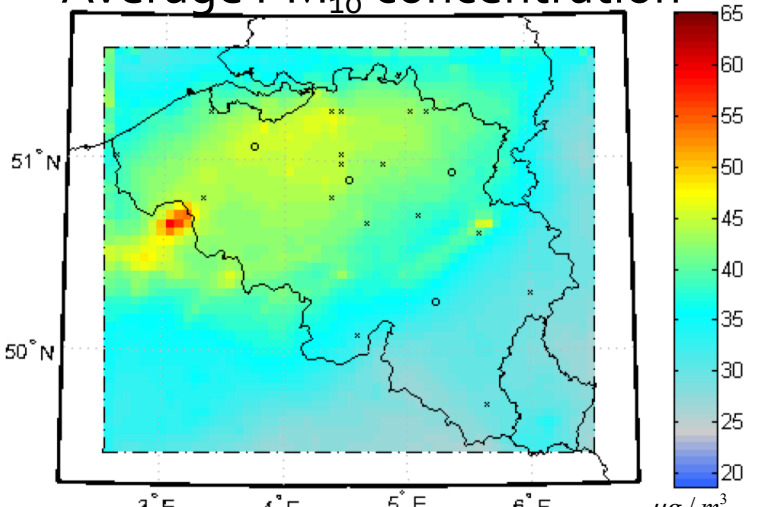


Starting date: May 28th, 2005 at midnight

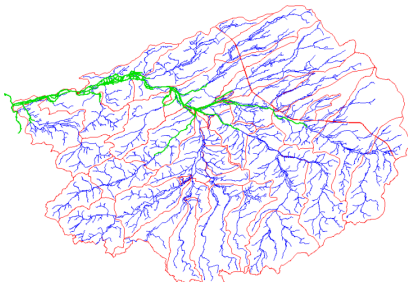
Average PM_{10} concentration

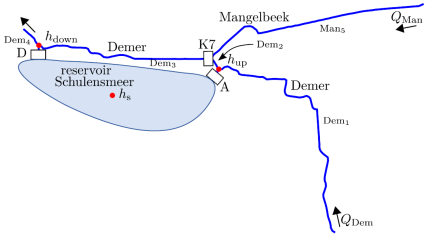


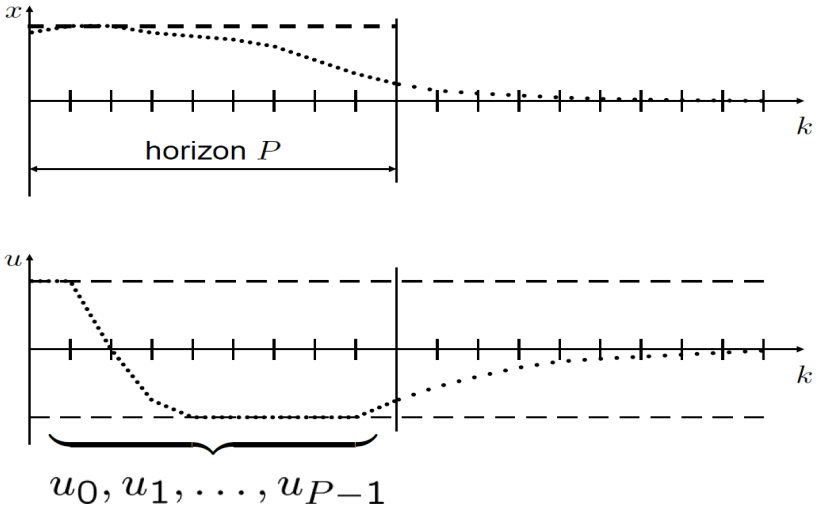
Average PM_{10} concentration



Demer Flood Regulation DSS







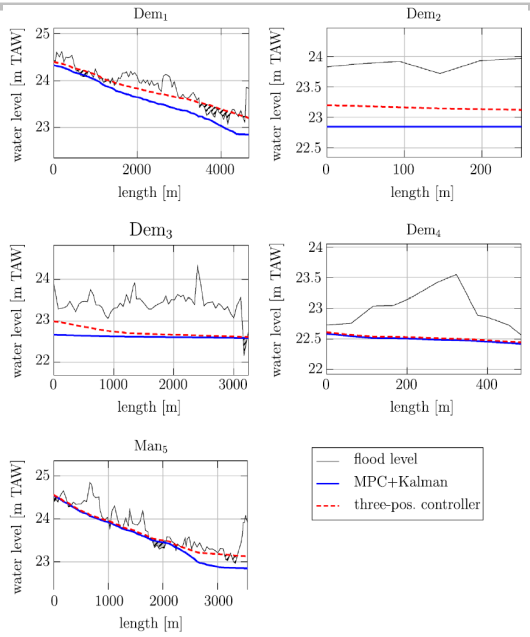
STADIUS
Center for Dynamical Systems, Signal Processing and Data Analytics

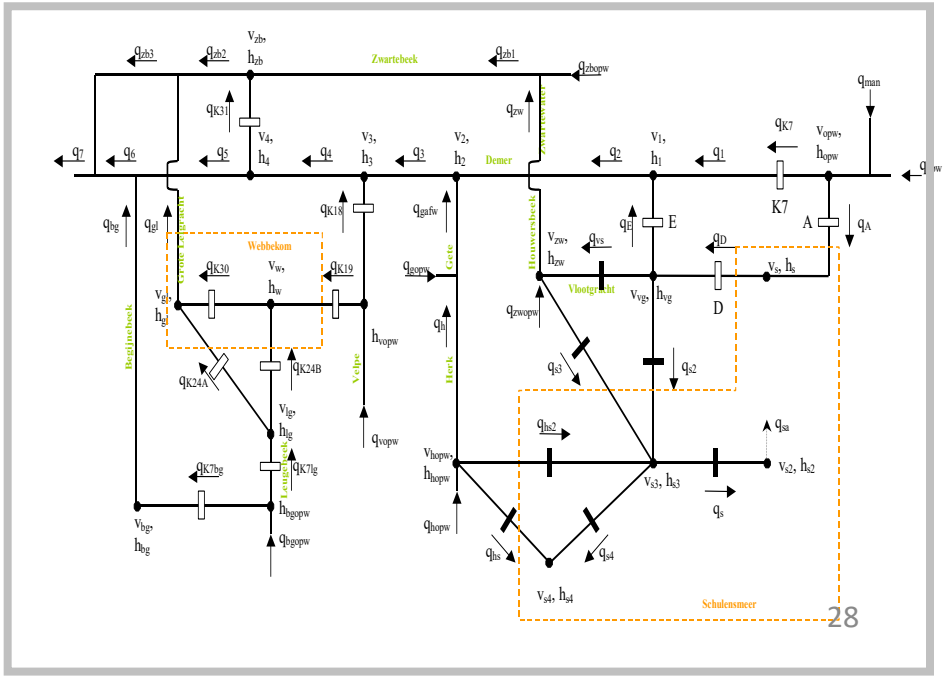
IMDC
International Marine & Dredging Consultants

IPCOS

COFELY FABRICOM
GDF SUEZ

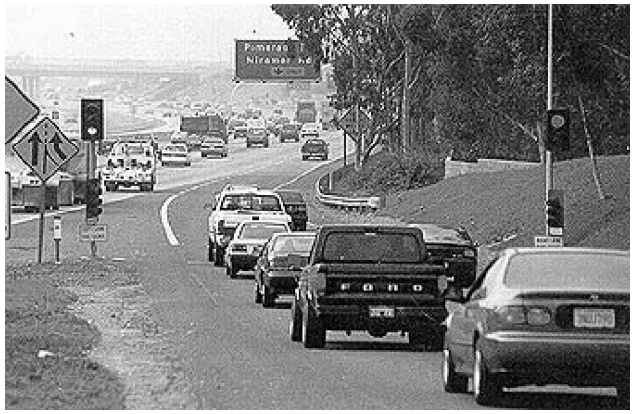
anteagroup





Traffic & Mobility DSS: control

Speed harmonisation

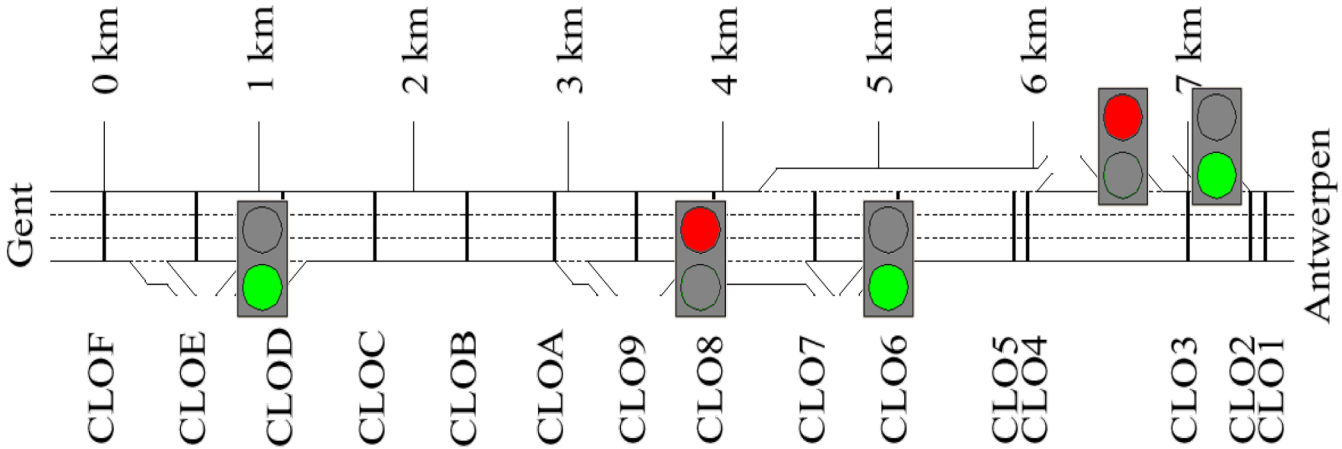


Ramp metering

DRIP

Vlaams Verkeerscentrum

Vlaamse overheid



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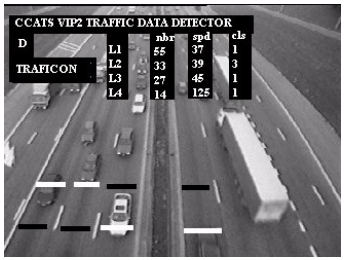
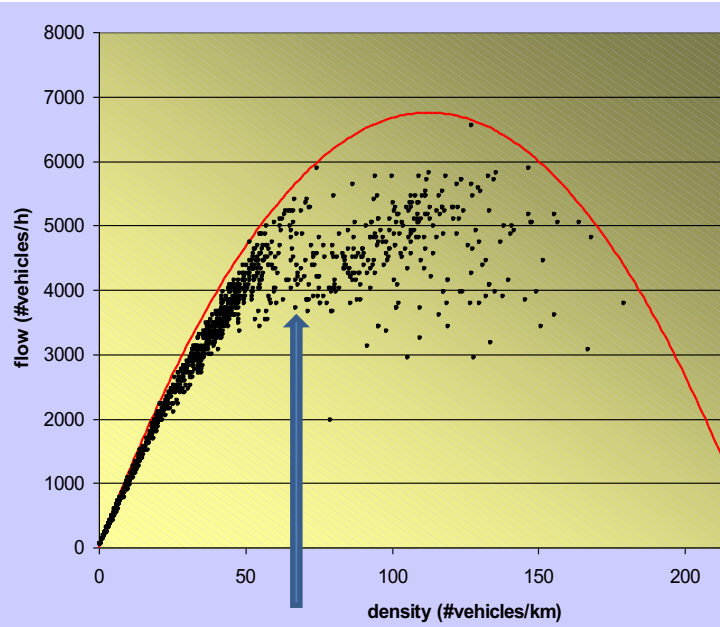
TRANSPORT & MOBILITY LEUVEN

Traffic & Mobility DSS

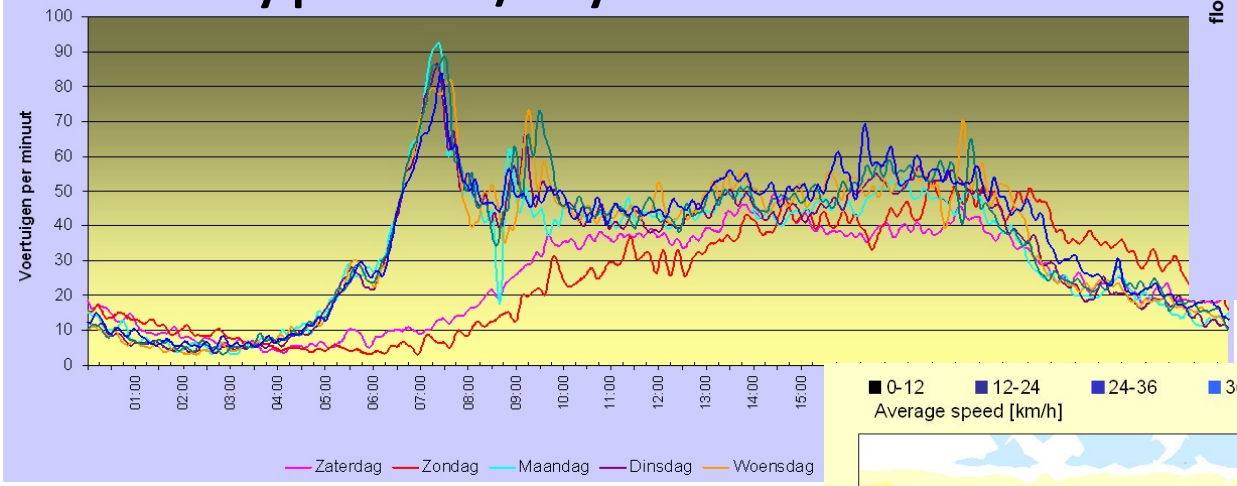
Detector technology: inductive loops, Gatso-meters, camera's



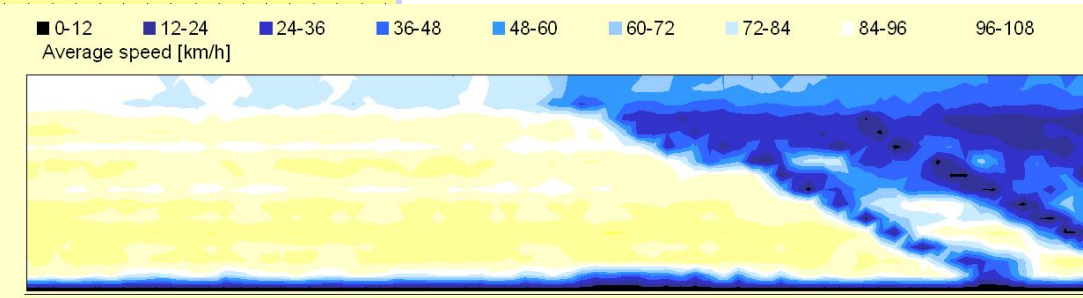
Density – Flow

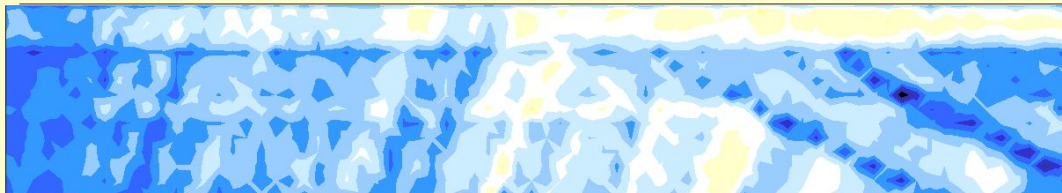


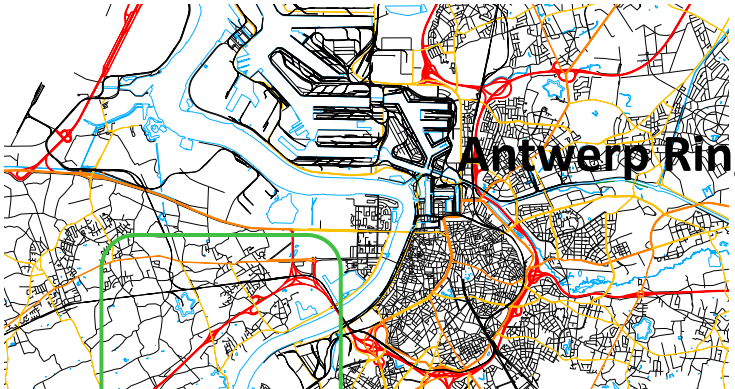
Density per hour / day of the week

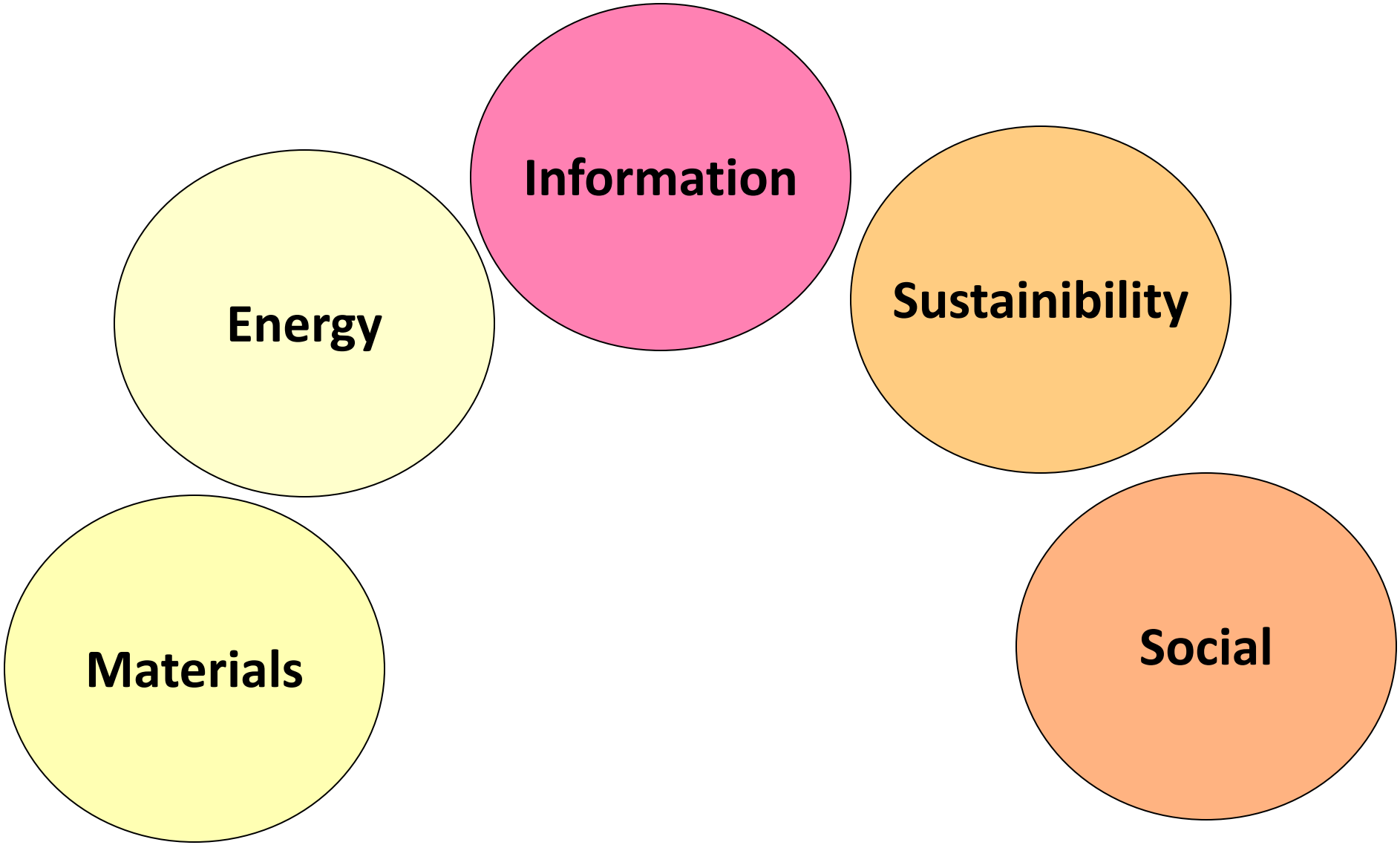


Traffic jam prediction

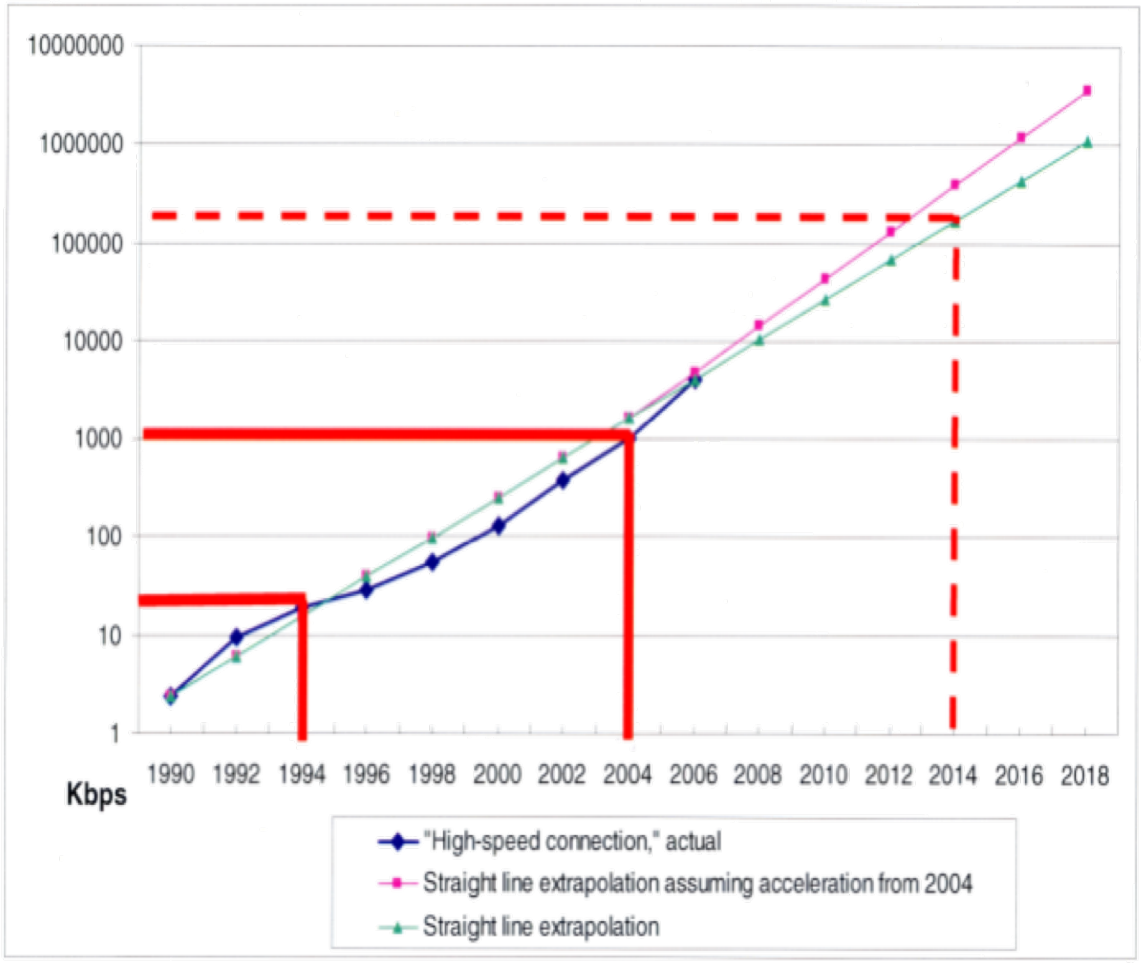




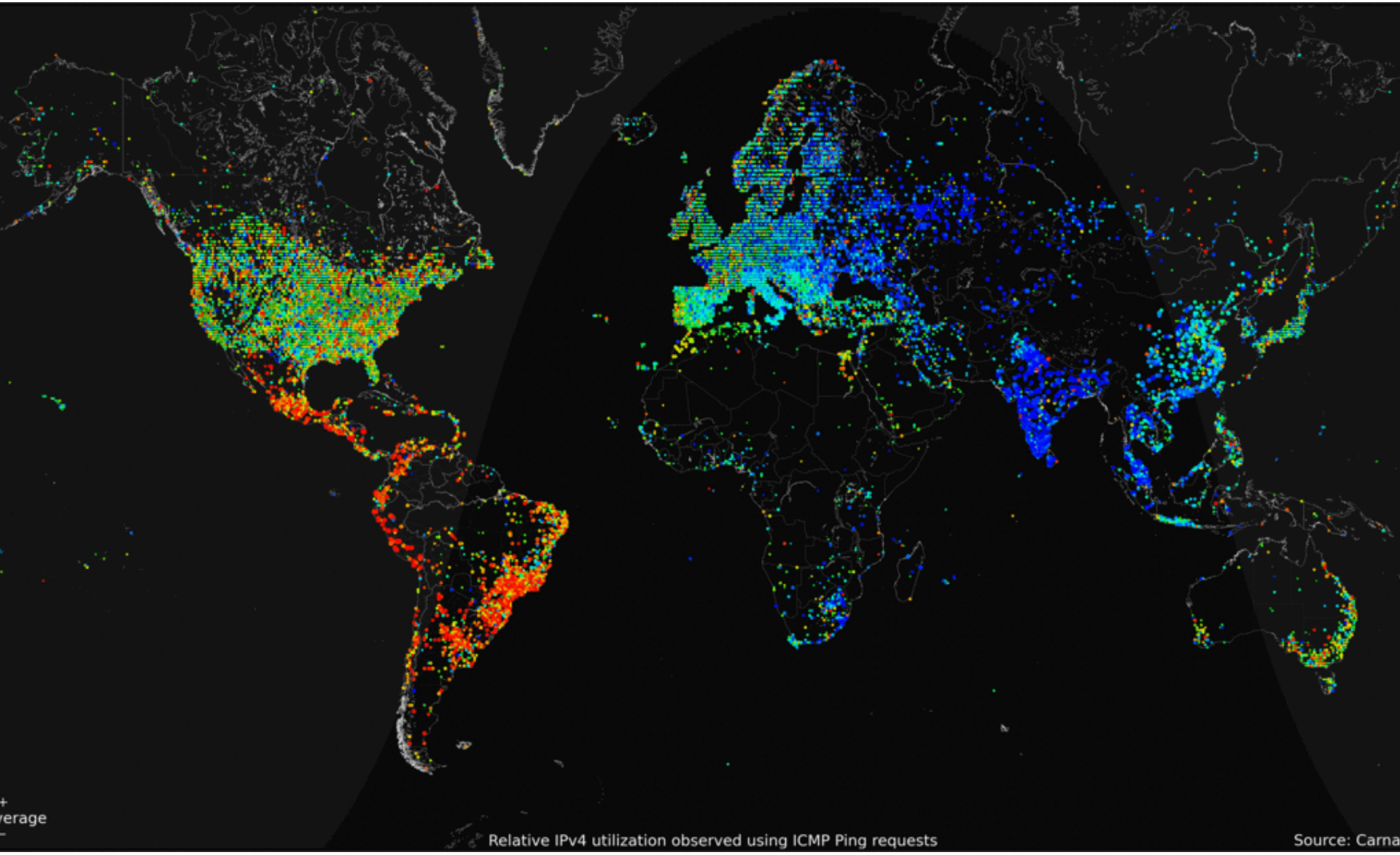



Information
Energy
Sustainibility
Materials
Social

Connectivity



We are always CONNECTED and FAST!


+
verage
-
Relative IPv4 utilization observed using ICMP Ping requests
Source: Carna

Information

Energy

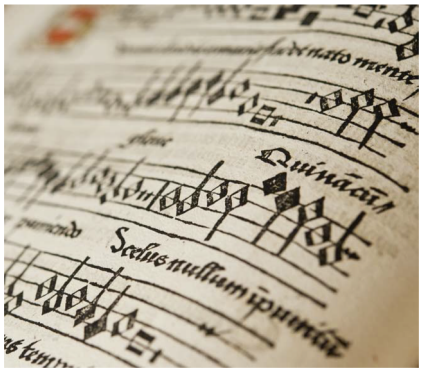
Sustainability

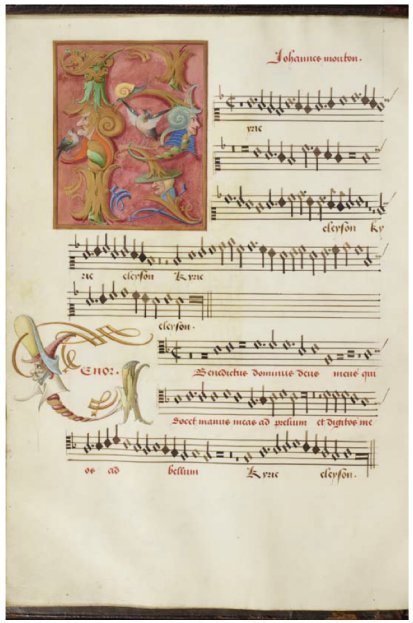
Materials

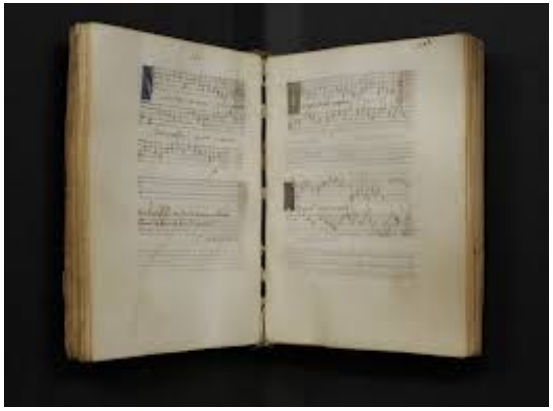
Social

Culture

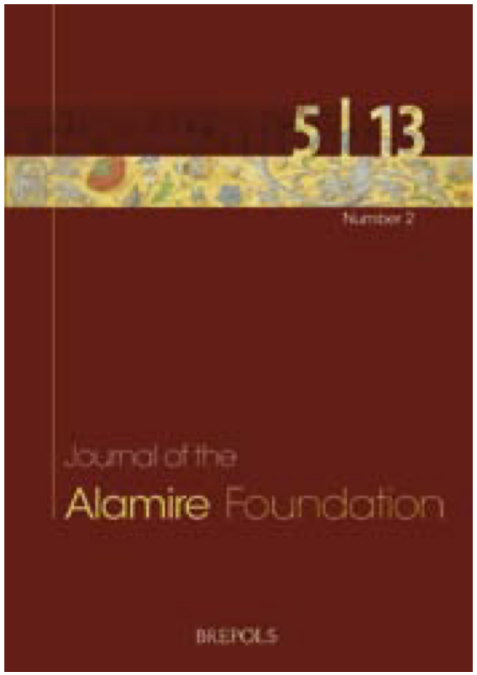
Digital Heritage





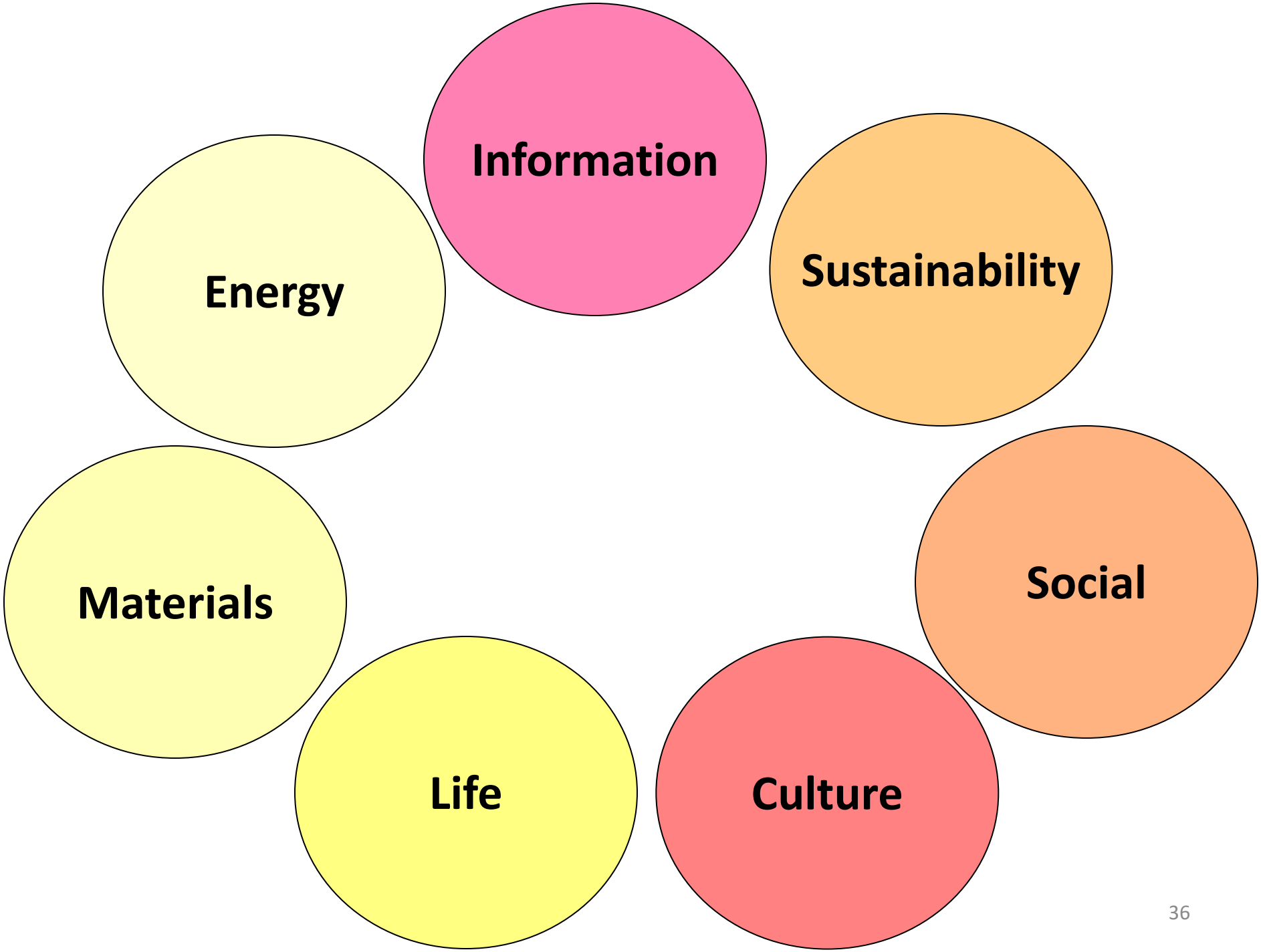


Leuven Chansonnier
1472

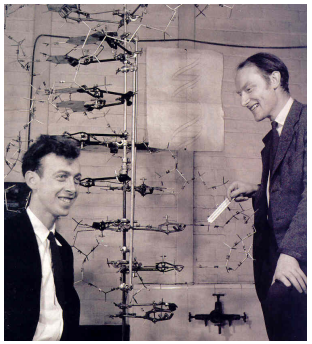


Alamire Journal

Digital Lab
(a.o. Vaticano)


Information
Energy
Sustainability
Materials
Social
Life
Culture

The science

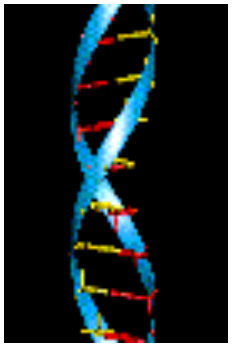


1865: Mendel: Laws of inheritance from statistical infer

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

1953: Watson/Crick: DNA double helix

1965: Restriction enzymes: DNA ‘scissors’



1966: Nirenberg/Khorana/Holley: Determine genetic code

1972: Cohen/Boyer: Recombinant DNA

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

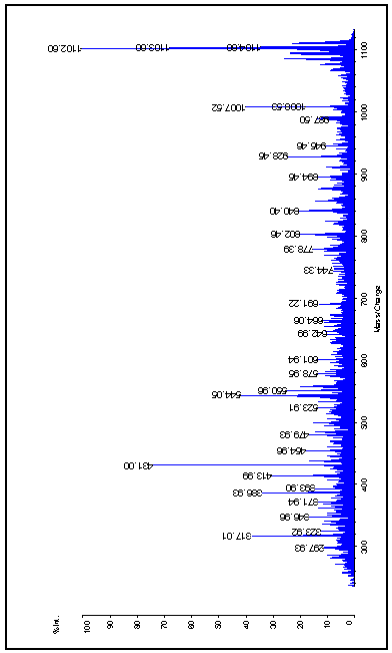
Tsunami of data from progress in technology

Computer Tomography

GS-FLX Roche
Applied Science 454

Sequencers

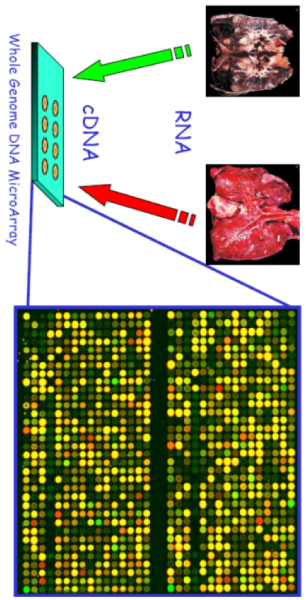
ACACATTAAATCTTATATGC
TAAAACTAGGTCTCGTTTTA
GGGATGTTTATAACCATCTT
TGAGATTATTGATGCATGGT
TATTGGTTAGAAAAAATATA
CGCTTGTTTTTCTTTCCTAG
GTTGATTGACTCATACATGT
GTTTCATTGAGGAAGGAAC
TTAACAAAACTGCACTTTTT
TCAACGTCACAGCTACTTTA
AAAGTGATCAAAGTATATCA
AGAAAGCTTAATATAAAGAC
ATTTGTTTCAAGGTTTCGTA
AGTGCACAATATCAAGAAG
ACAAAAATGACTAATTTTGT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

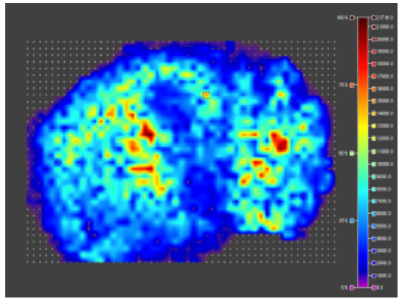


Magnetic resonance

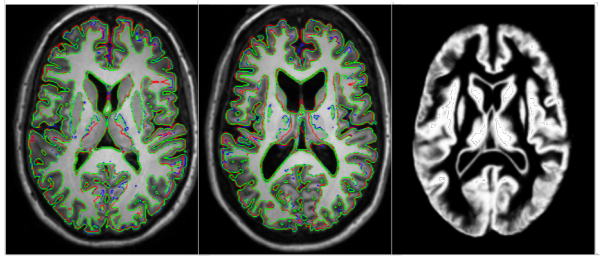
maf VIB
MicroArray Facility

Microarrays
(DNA chips)

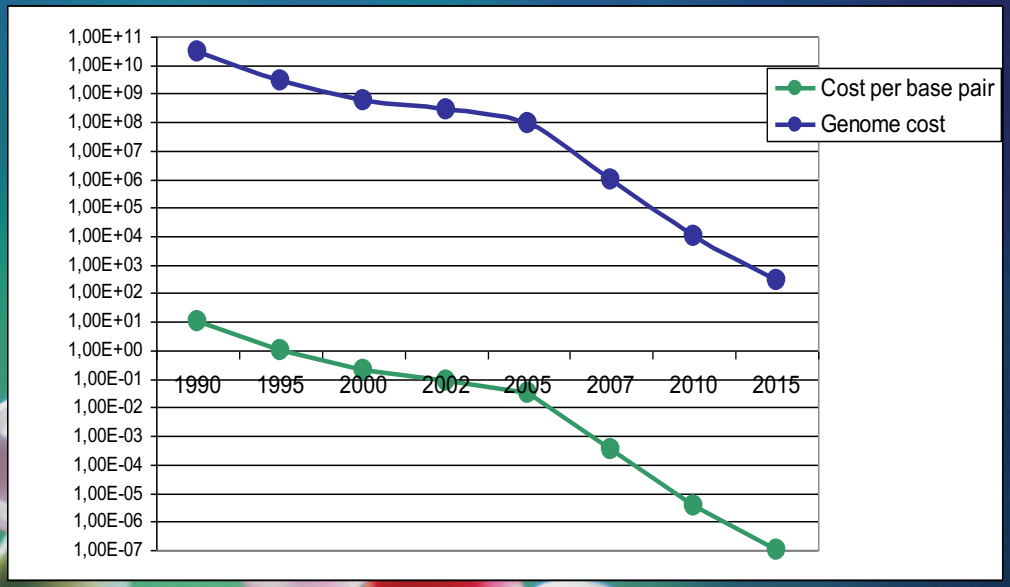




Mass spectrometry



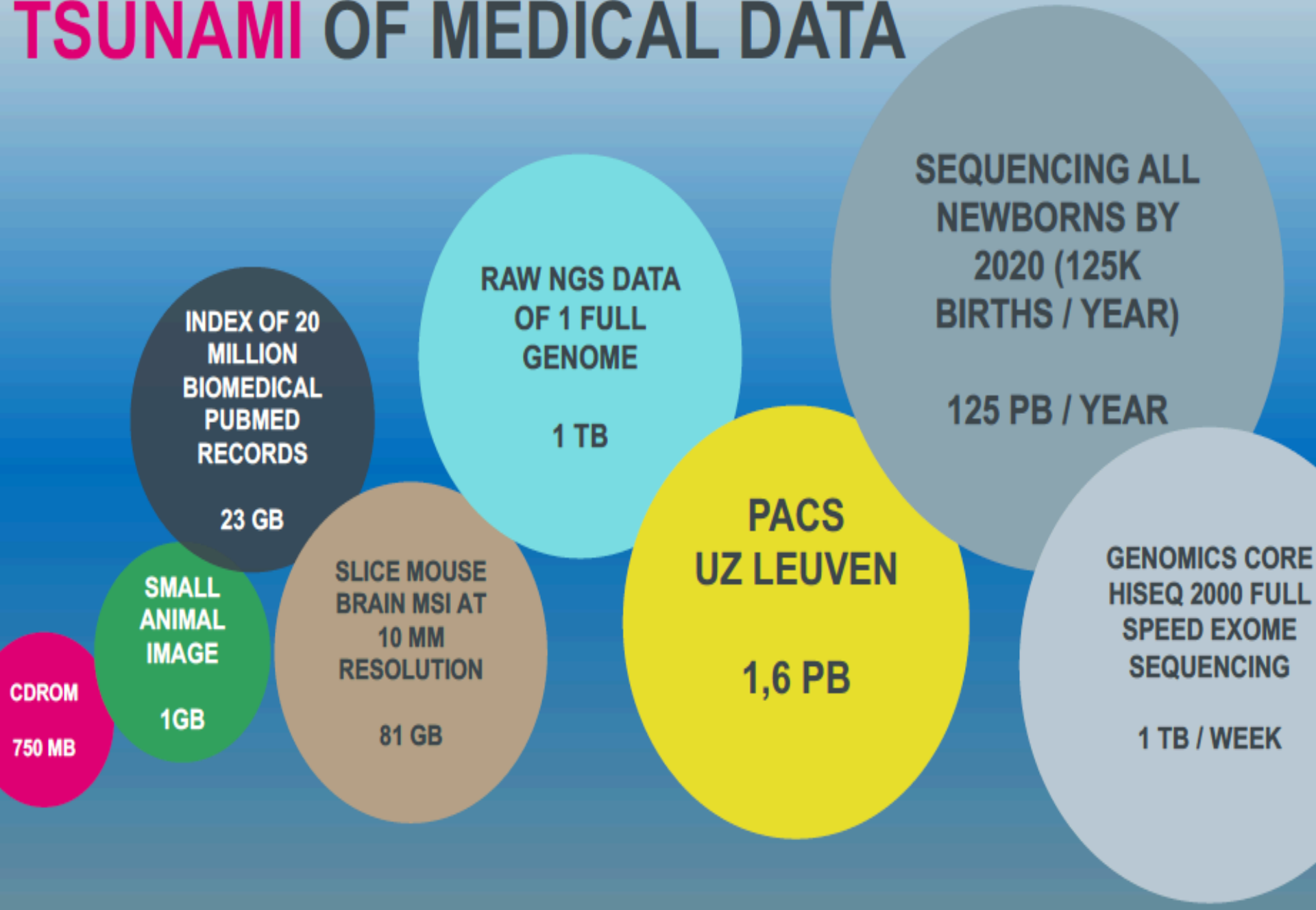
Genome data



- 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

TSUNAMI OF MEDICAL DATA



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

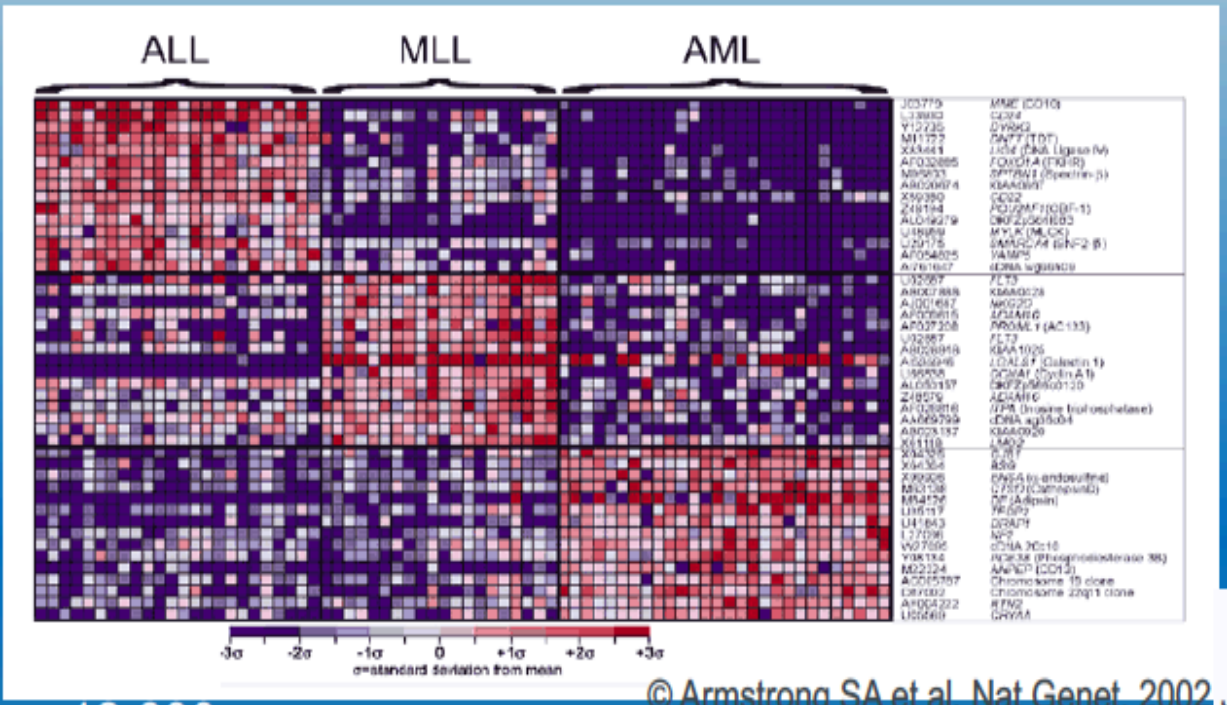
Dr. Algorithm is coming

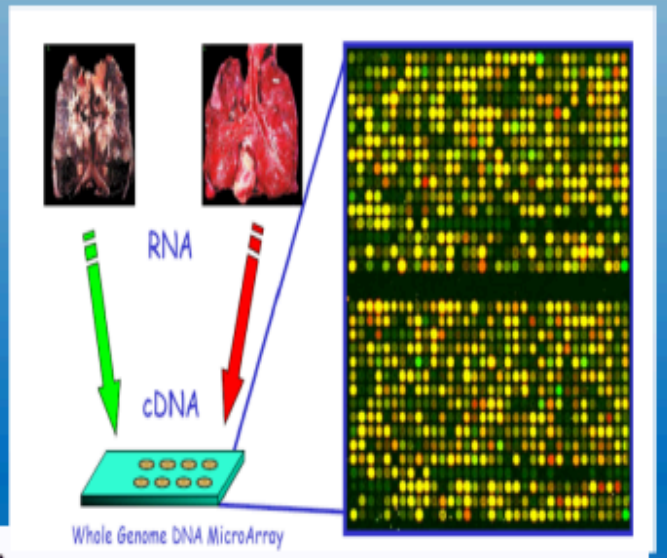
"In the next 10 years, data science and software will do more for medicine than all the biological sciences together."

– Vinod Khosla, Khosla Ventures

http://techcrunch.com/2013/09/11/vinod-khosla-in-the-next-10-years-dat
science-will-do-more-for-medicine-than-all-biological-sciences-combine

Example: Genomic markers for Leukemia



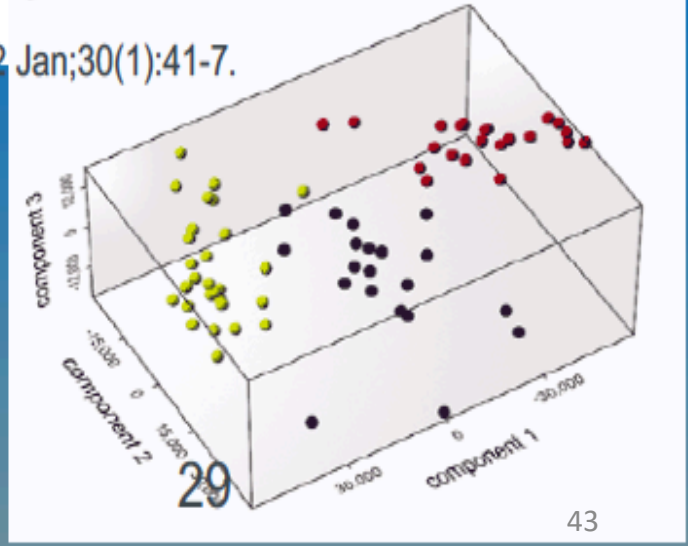


© Armstrong SA et al. Nat Genet. 2002 Jan;30(1):41-7.

12 600 genes

72 patients

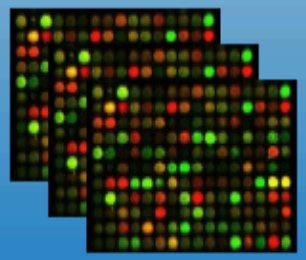
- 28 Acute Lymphoblastic Leukemia (ALL)
- 24 Acute Myeloid Leukemia (AML)
- 20 Mixed Linkage Leukemia (MLL)



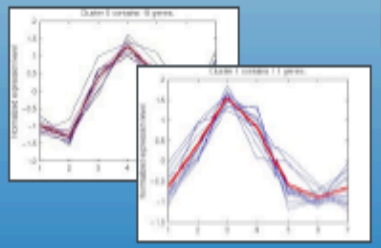
29

Example: Genomic Data Fusion

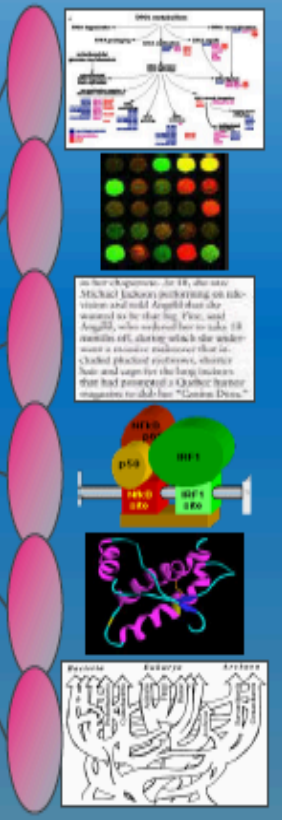
High-throughput genomics



Data analysis



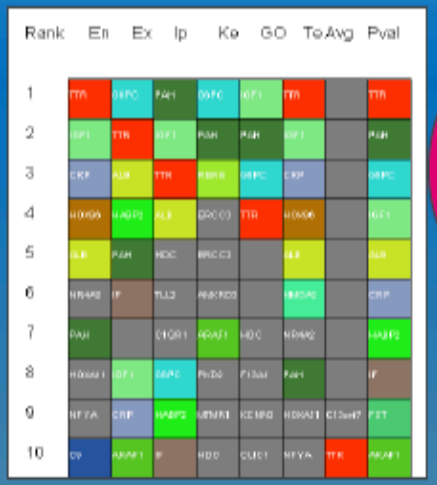
Information sources



Candidate genes

Name	Ensembl
TTR	ENSG00000118271
PAH	ENSG00000171759
G6PC	ENSG00000131482
IGF1	ENSG00000017427
ALB	ENSG00000163631
CRP	ENSG00000132693
HABP2	ENSG00000148702
IF	ENSG00000138799
FST	ENSG00000134363
ARAF1	ENSG00000078061
HMGA2	ENSG00000149948
C9	ENSG00000113600
PCBP3	ENSG00000111405
HOXB6	ENSG00000108511
RERE	ENSG00000142599
HOXA11	ENSG00000005073
CLIC1	ENSG00000213238
ERCC3	ENSG00000163161
ERCC3	ENSG00000163161
TLL2	ENSG00000095587
SYT4	ENSG00000132272
SYT4	ENSG00000132672
PIK4CB	ENSG00000143393
PKD2	ENSG00000118762
	ENSG00000081026
ANKRD3	ENSG00000183421
F13A1	ENSG00000124491
BPAG1	ENSG00000161814
KCNN3	ENSG00000143603
GRIN2A|GRIN2B	ENSG00000160098
SIM1	ENSG00000112246
	ENSG00000174891
	ENSG00000088305
C14orf10	ENSG00000092020
STX5	ENSG00000170310
	ENSG00000107671
MSH5	ENSG00000095474
CRH	ENSG00000147571
MID1	ENSG00000101871
	ENSG00000184508
	ENSG00000113460
TGFB3	ENSG00000119699
C1QR1	ENSG00000125810
NR4A2	ENSG00000153234
PDGFC	ENSG00000145431
PDGFC	ENSG00000145431
NR3C2	ENSG00000151623
NFYA	ENSG00000001167
	ENSG00000101898
C8orf4	ENSG00000175807
TM4SF13	ENSG00000108537
MMP3|MMP1	ENSG00000149968

Candidate prioritization



Validation

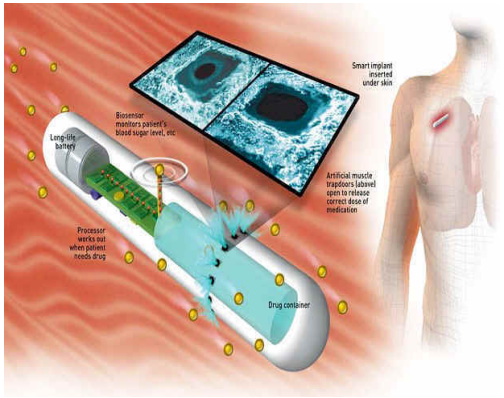
Endeavour: Aerts et al., Nature Biotechnology, 2006

Transdisciplinary engineering design

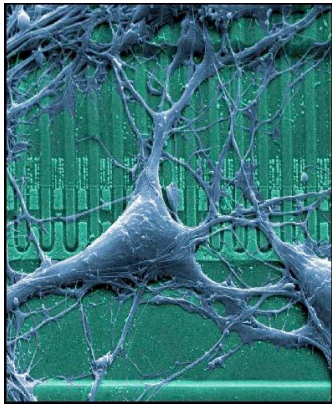
Materials, energy, IT

Ubiquitous computing

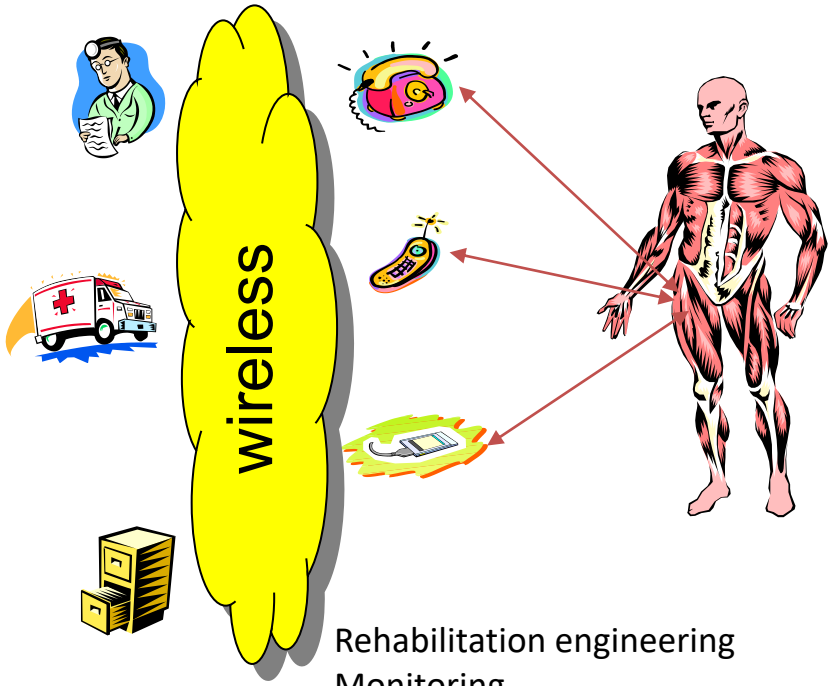
Ambient intelligence



Embedded intelligence
Smart pills

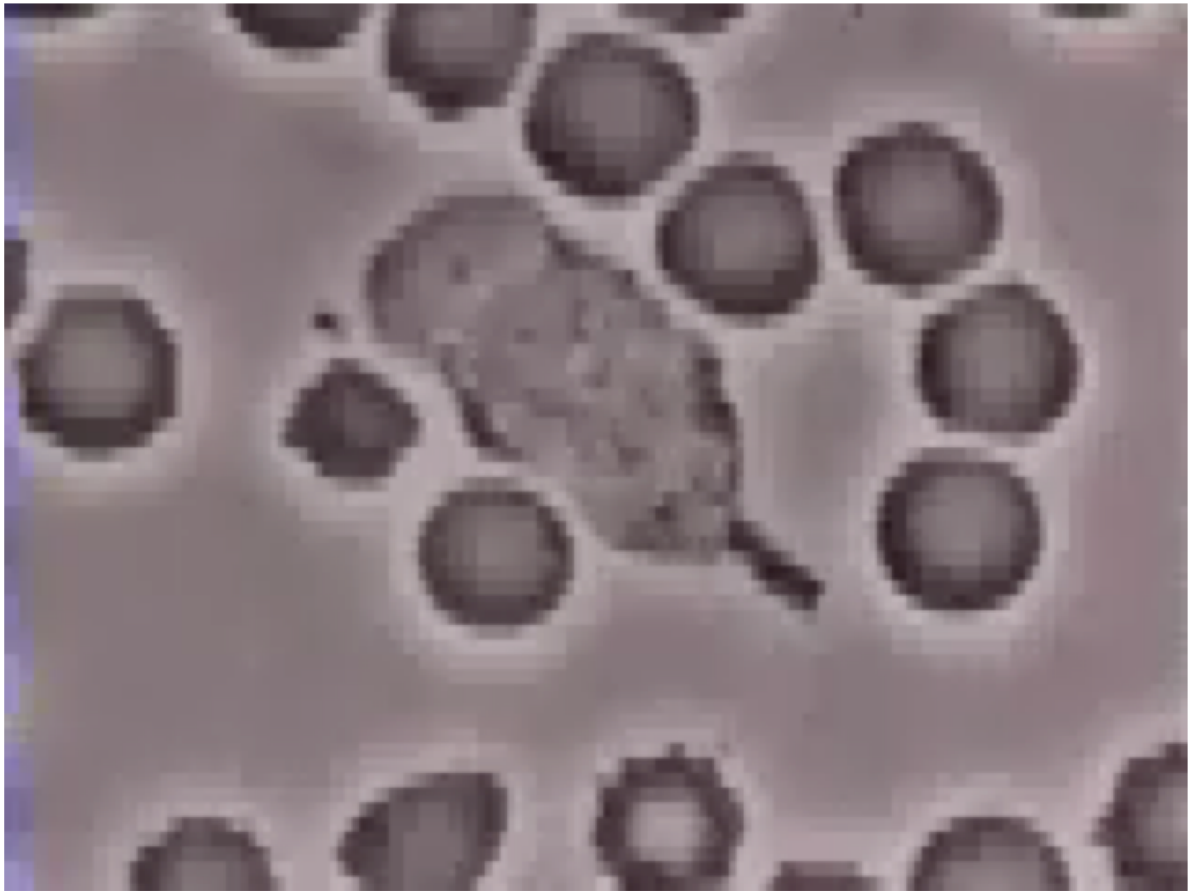


Neuron on chip



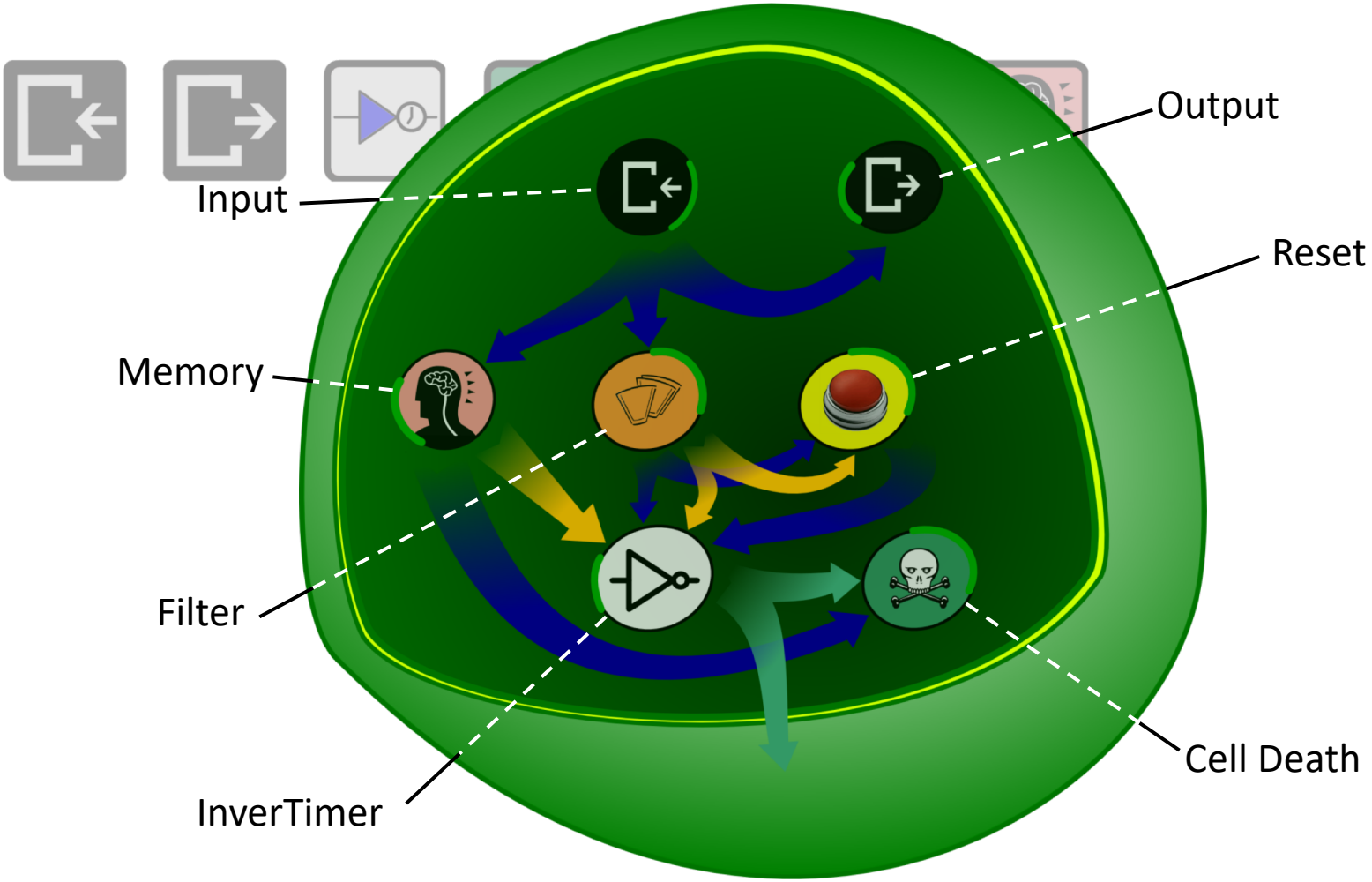
Rehabilitation engineering
Monitoring
Sensors: EEG, glucose,blood, DNA, …
Add-ons: vision, hearing, implants, …

Neutrophil



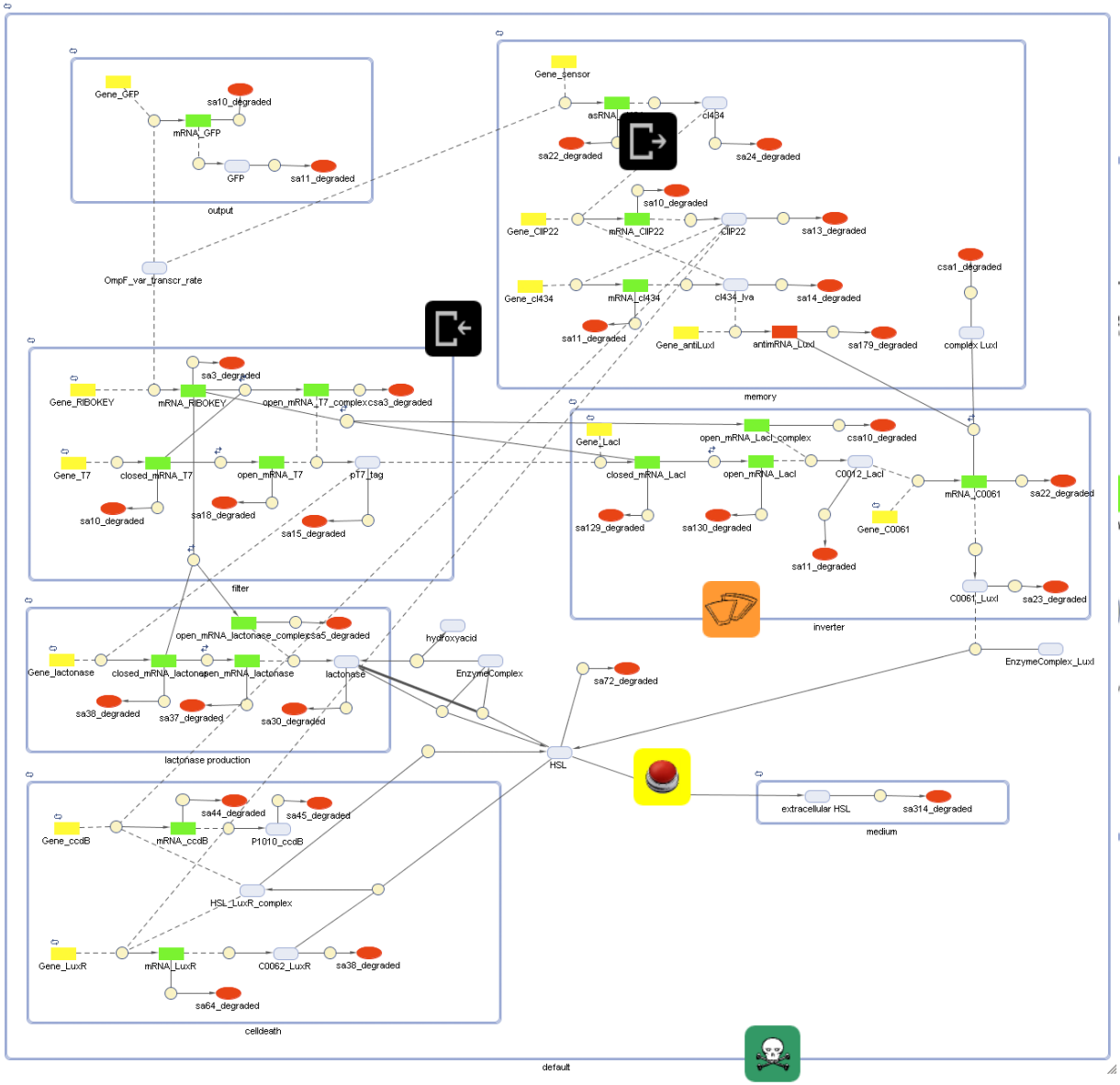
Chemotaxis = Tracking control problem with sensors, decisions, actuators

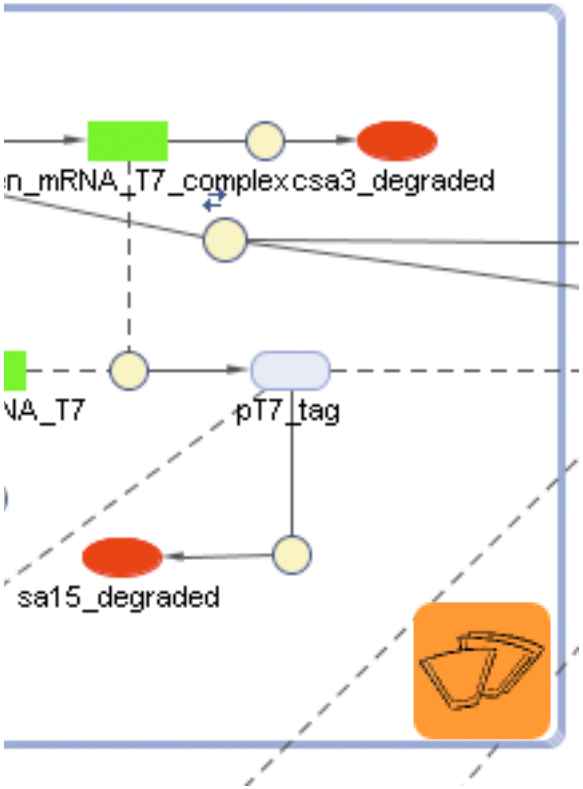
Synthetic biology: design new functional life
Bacterium detecting cancer cells



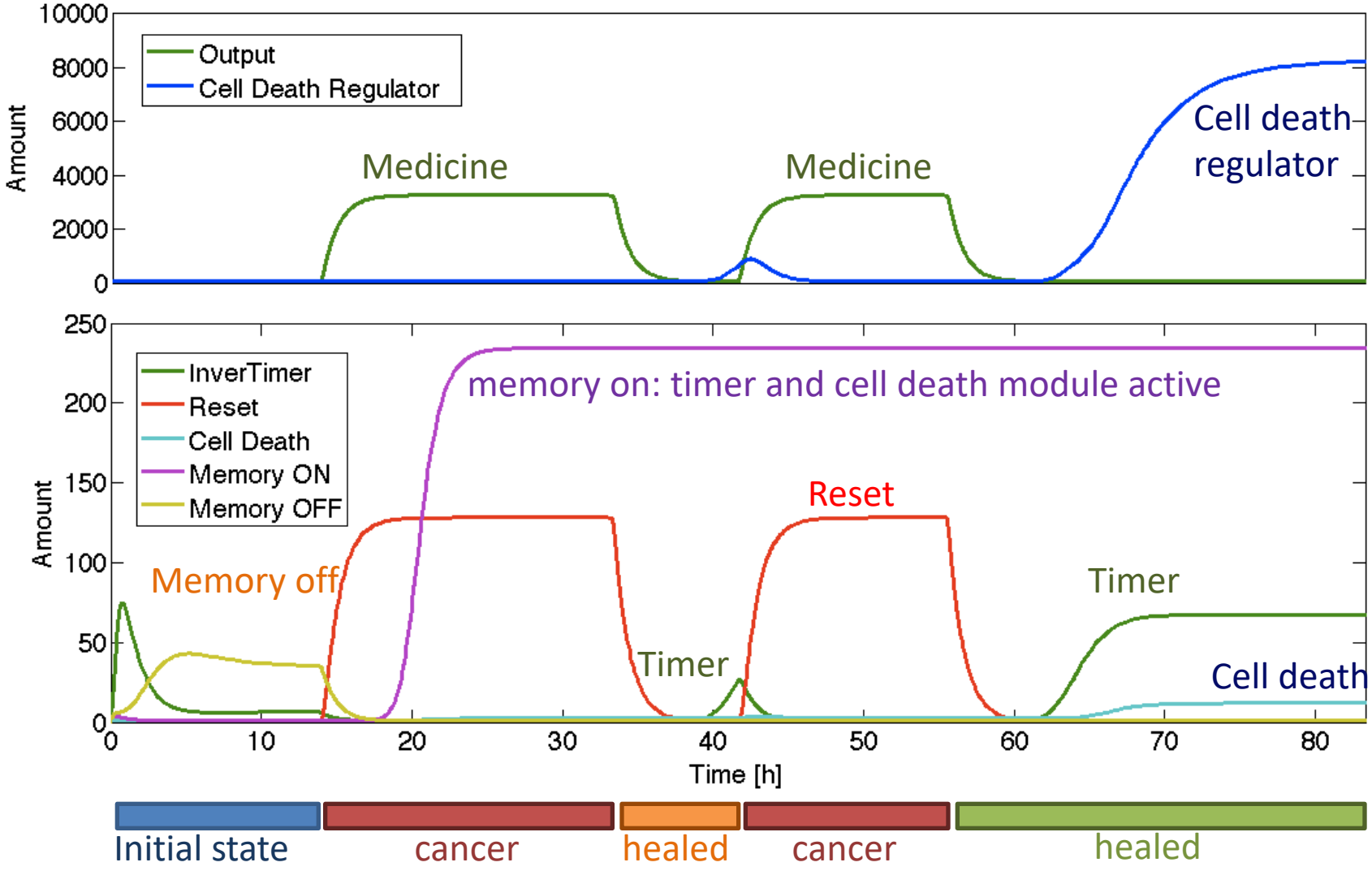
http://2013.igem.org/Team:KU_Leuven

in silico model Dr. Coli





Dr. Coli does the job !



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

The seven spheres of engineering

1. **Matter**
2. **Energy**
3. **Information**
4. **Sustainability**
5. **Social**
6. **Culture**
7. **Life**

Analysis and Design in the seven spheres

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,….)**

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