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ICT and eHealth

New scientific challenges

IBBT

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Outline

-Trends

-Context

-Opportunities and challenges

-What to do ?

Trends

I. Exponential evolution in ICT, medical and bio-technology

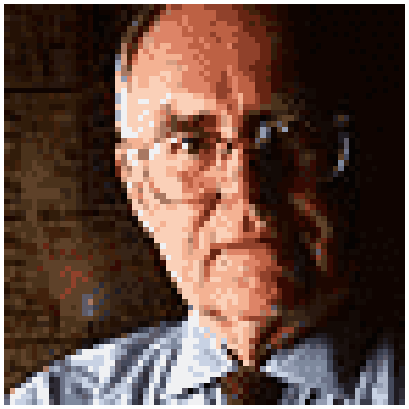
II. Tsunami of data

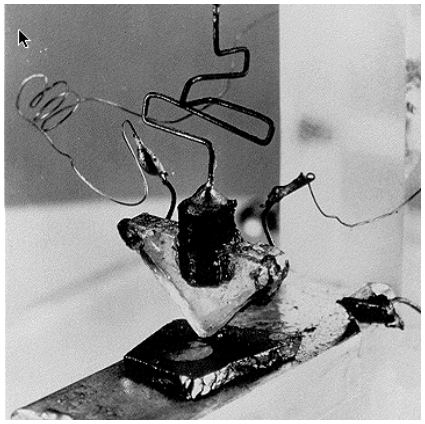
III. Inter-, cross-, and multi-disciplinarity

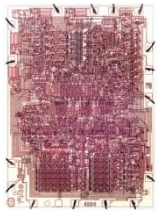
IV. Societal demands

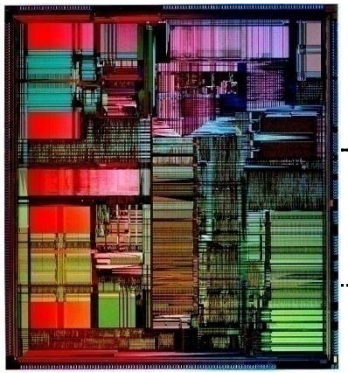
V. Translational gap

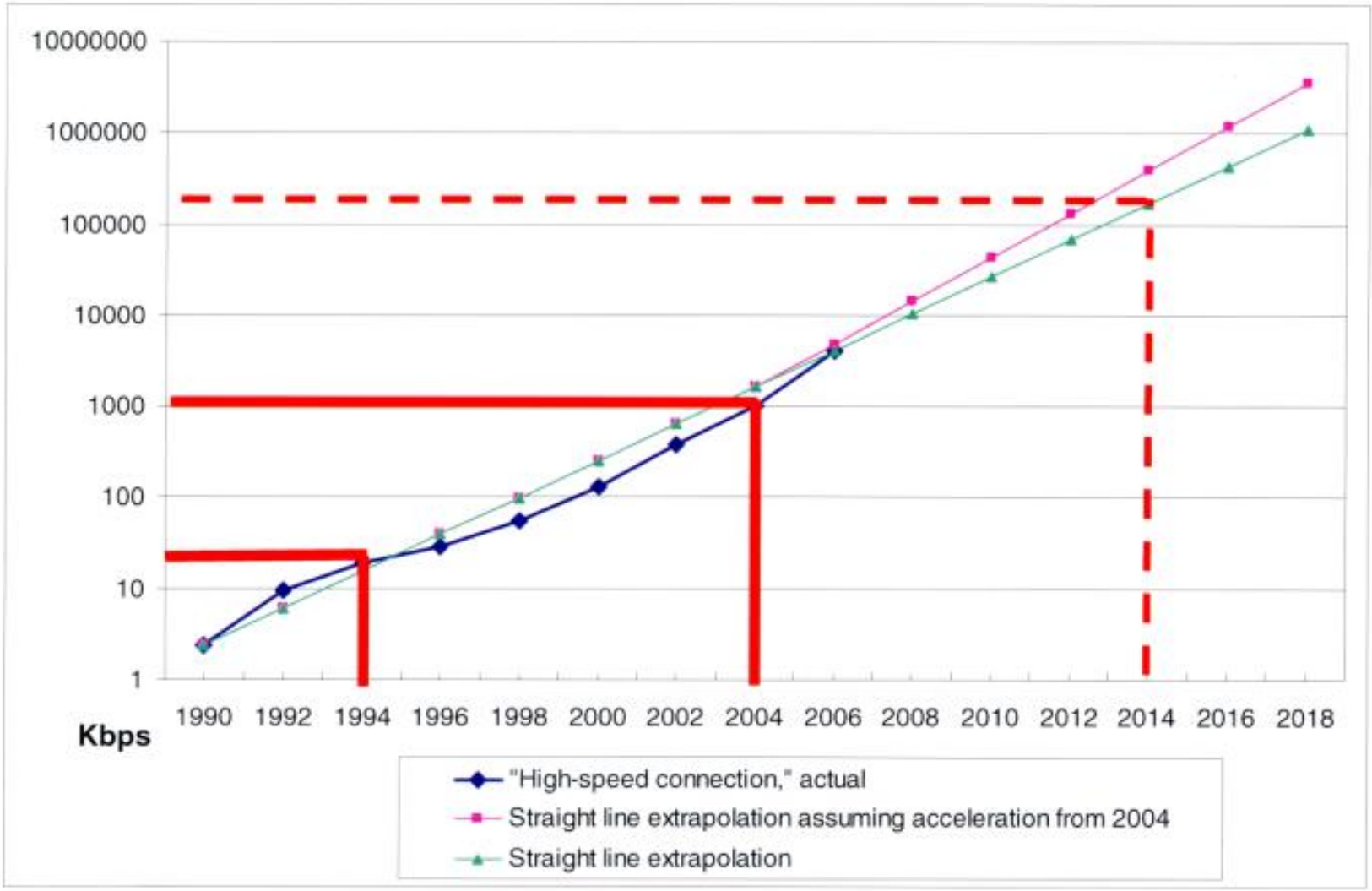
Gordon Moore’s law











Source: Heavy Reading report "FTTH Worldwide Market & Technology Forecast, 2006-2011"

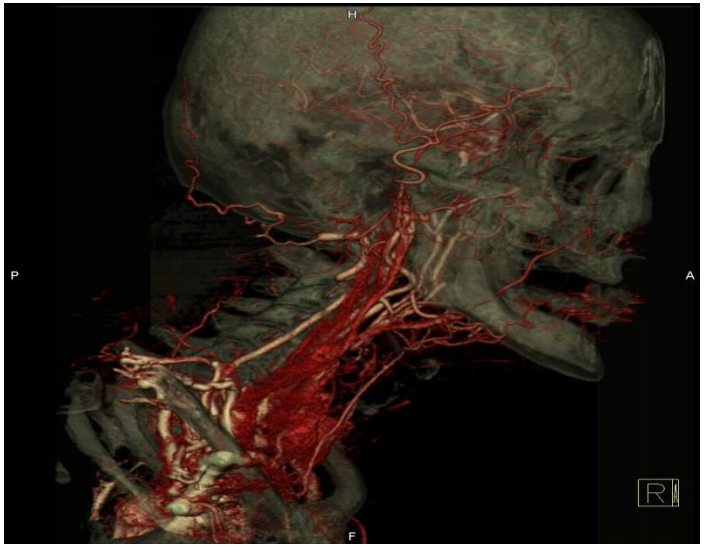
Tsunami of data

-New technologies generate more data

-Increased spatial and temporal resolution

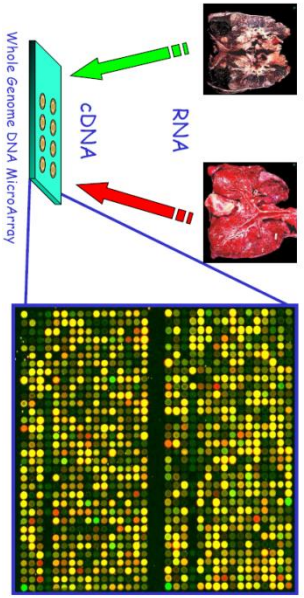
-More studies per patient, more datasets per study

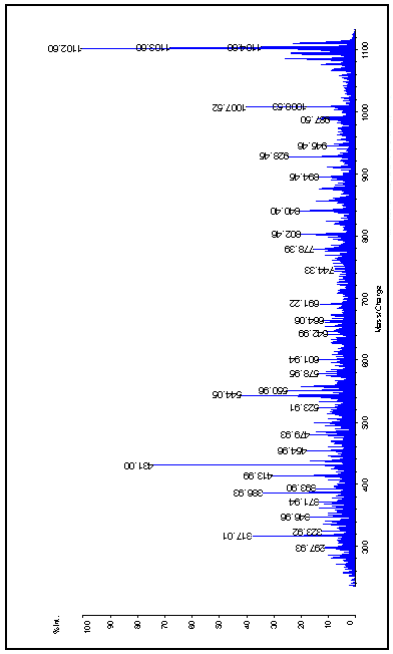
Virtual colonoscopy from CT images
with automatically detected polyps

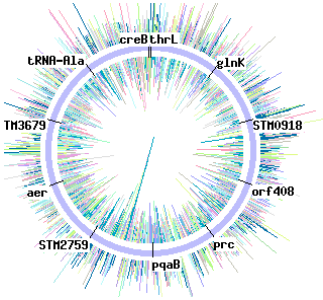


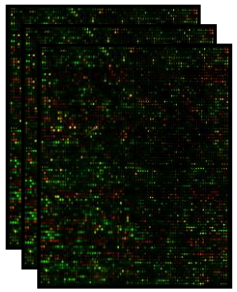
subtraction CT angiography

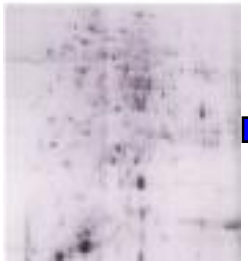
ACACATTAAATCTTATATGC
TAAAACTAGGTCTCGTTTTA
GGGATGTTTATAACCATCTT
TGAGATTATTGATGCATGGT
TATTGGTTAGAAAAAATATA
CGCTTGTTTTTCTTTCCTAG
GTTGATTGACTCATACATGT
GTTTCATTGAGGAAGGAAC
TTAACAAAACTGCACTTTTT
TCAACGTCACAGCTACTTTA
AAAGTGATCAAAGTATATCA
AGAAAGCTTAATATAAAGAC
ATTTGTTTCAAGGTTTCGTA
AGTGCACAATATCAAGAAG
ACAAAAATGACTAATTTTGT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

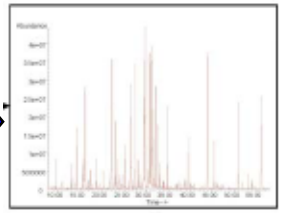


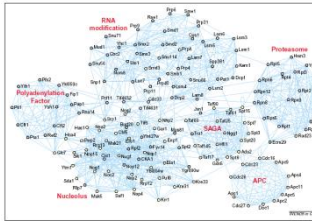












genome **transcriptome** **proteome** **metabolome** **interactome**

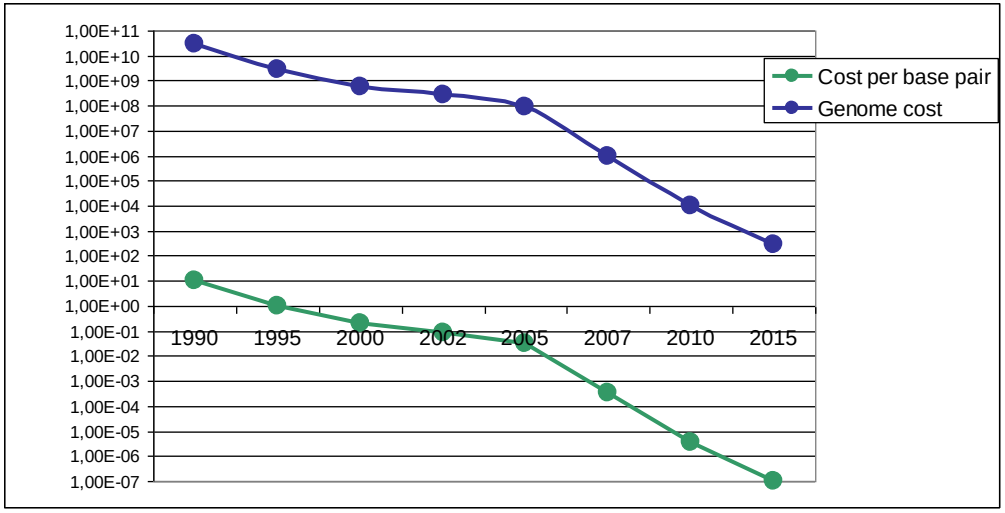
GS-FLX Roche
Applied Science 454

maf VIB
MicroArray Facility

Prometa

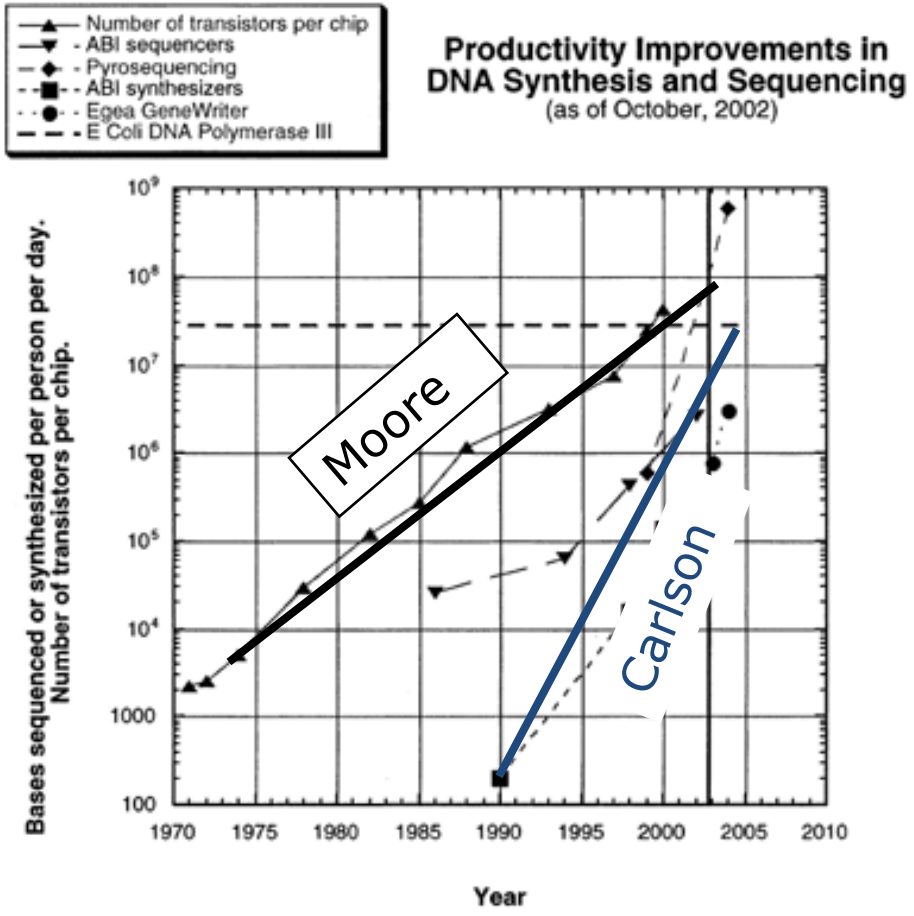
Making sense of the 1000 $ genome ?

- 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

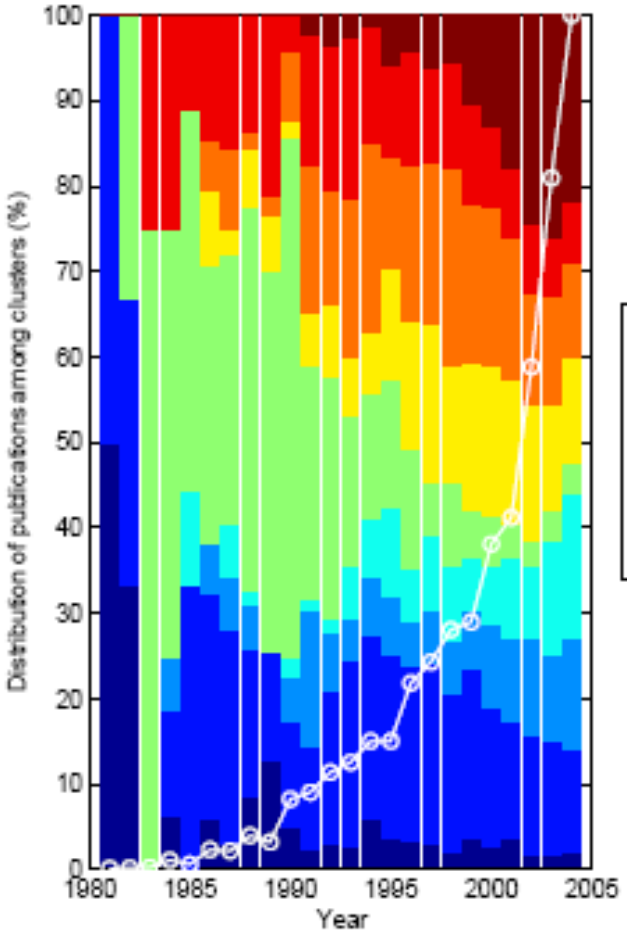


Year	Cost per base pair	Genome cost
1990	10	3E+10
1995	1	3.000.000.000
2000	0.2	600.000.000
2002	0.09	270.000.000
2005	0.03	90.000.000
2007	0.000333333	1.000.000
2010	3.33333E-06	10000
2015	0.0000001	300

Moore versus Carlson



Text mining



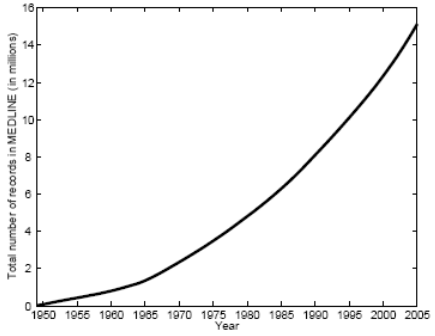
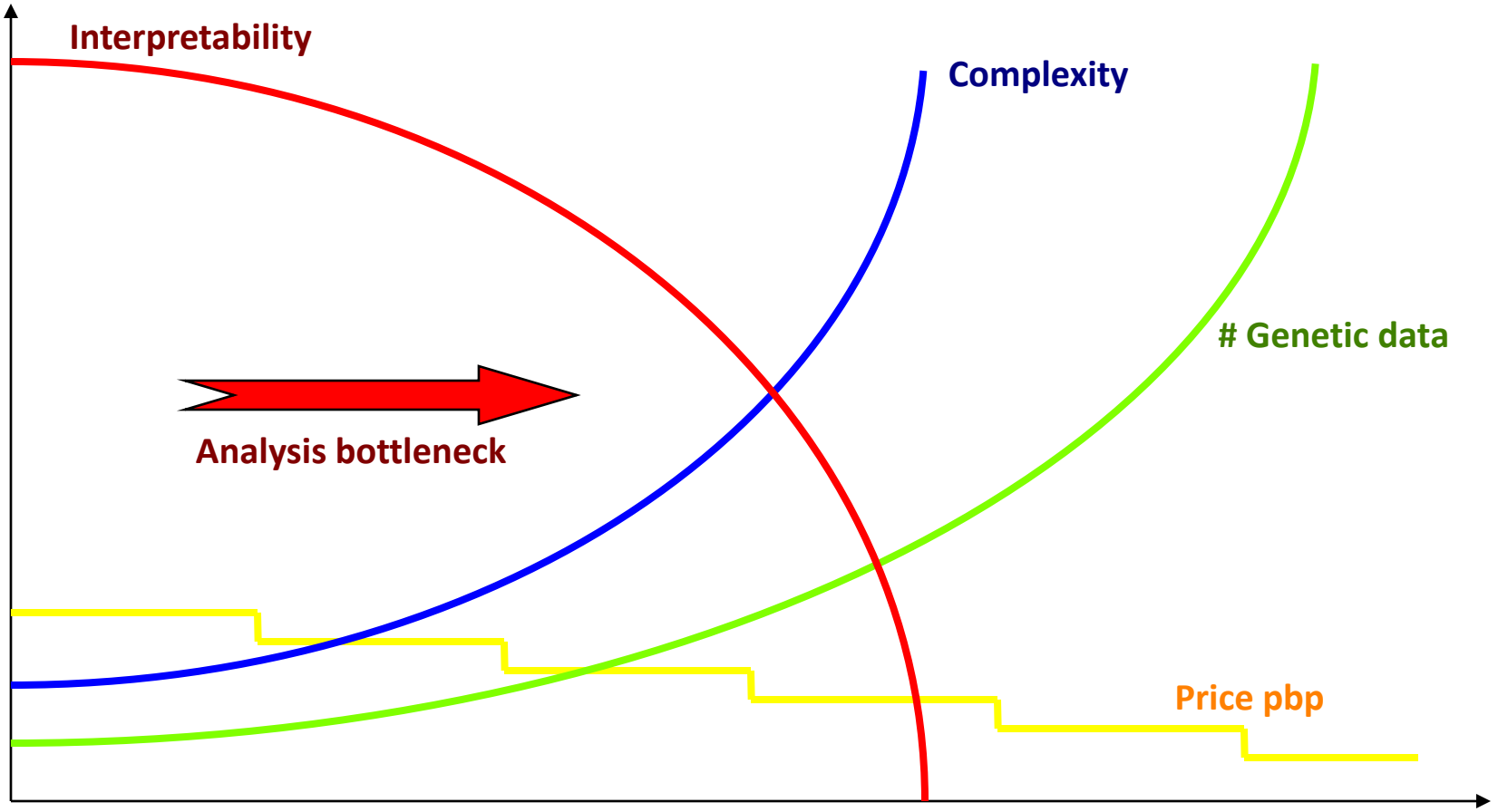


Figure 1.2: Growth of MEDLINE, the U.S. National Library of Medicine (NLM) premier bibliographic database covering the fields of medicine, nursing, dentistry, veterinary medicine, the health care system and preclinical sciences. The total number of scientific publications (in millions) is indicated for each year. Today, MEDLINE contains approximately 15 million unique records about journal articles in life sciences. This figure was constructed using data published by NLM [161].

By 2010, 1/3 of all world data bases will consist of biomedical data

Analysis bottlenecks



Outline

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Obama

But in order to lead in the global economy and to ensure that our businesses can grow and innovate, and our families can thrive, we're also going to have to address the shortcomings of our health care system.

The Recovery Act will support the long overdue step of ***computerizing America's medical records***, to reduce the duplication, waste and errors that cost billions of dollars and thousands of lives. But it's important to note, ***these records also hold the potential of offering patients the chance to be more active participants in the prevention and treatment of their diseases***. We must maintain patient control over these records and respect their privacy. At the same time, we have the opportunity to offer billions and ***billions of anonymous data points to medical researchers who may find in this information evidence that can help us better understand disease***.

History also teaches us the greatest advances in medicine have come from scientific breakthroughs, whether the discovery of antibiotics, or improved public health practices, vaccines for smallpox and polio and many other infectious diseases, antiretroviral drugs that can return AIDS patients to productive lives,
pills that can control certain types of blood cancers, so many others.

Because of recent progress –- ***not just in biology, genetics and medicine, but also in physics, chemistry, computer science, and engineering –- we have the potential to make enormous progress against diseases in the coming decades***. And that's why my administration is committed to increasing funding for the National Institutes of Health, including $6 billion to support cancer research -- part of a sustained, multi-year plan to double cancer research in our country. (Applause.)

http://www.whitehouse.gov/blog/09/04/27/The-Necessity-of-Science/

Need for investments

-RIZIV: 23 bio euro / year

-Cumulative R&D funding Flanders (FWO, IWT, IBBT, VIB, IMEC,…)
human health: 150 mio euro/year

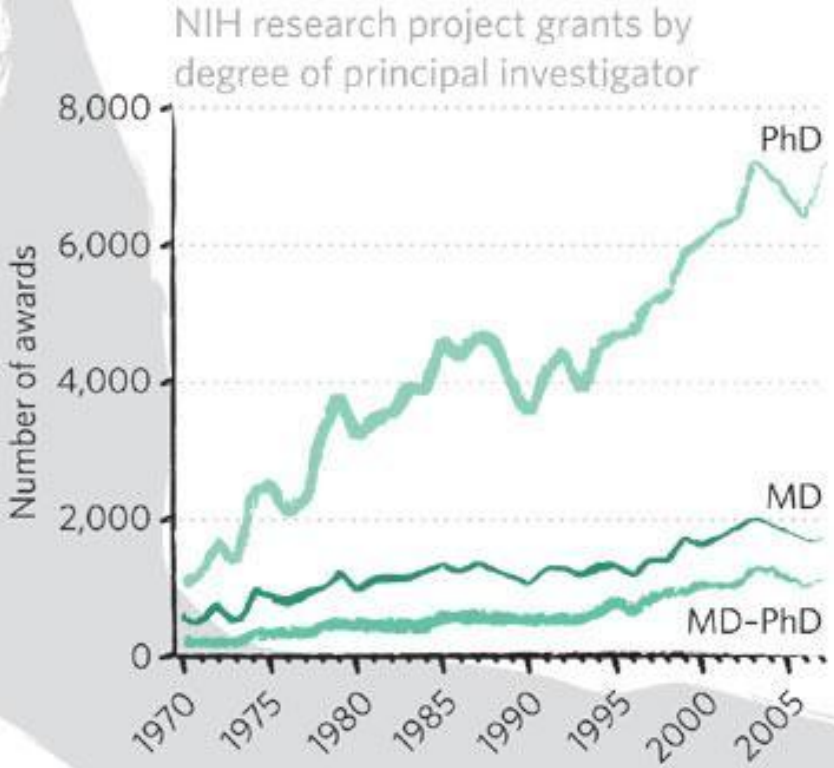
- Need for new funding federal / communities / regions on
Innovation in Health Care

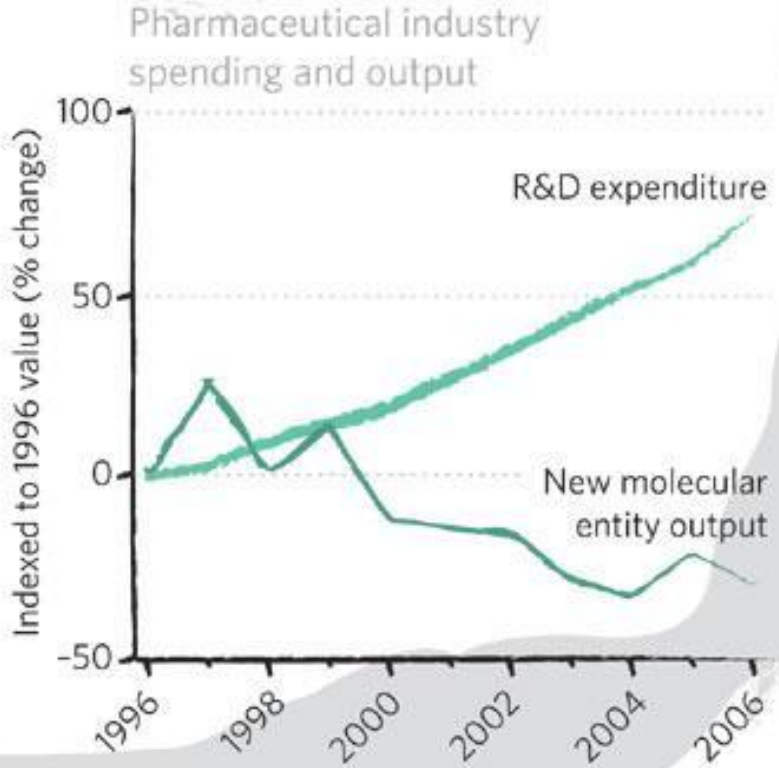
-FOD Volksgezondheid: 16 a 17 mio euro / year for IT Hospitals

Rationales for eHealth

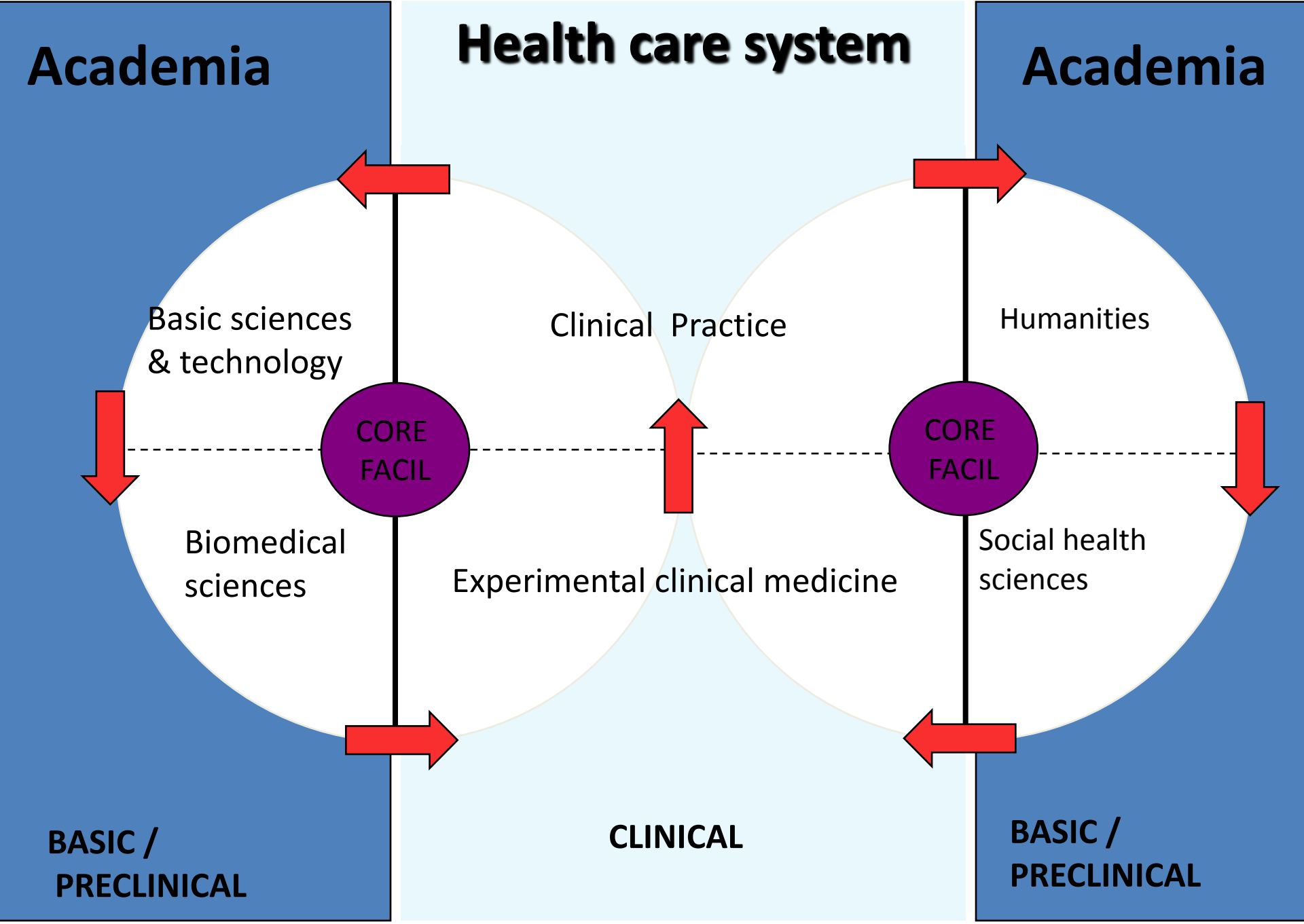
- **Improve quality performance of health decision/diagnosis systems**
  - Support individual medical doctor
    - Avoid/decrease number of medicial errors
    - Web portal for Evidence Based Medicine
      - Organised access to literature
      - Examples: UK, Norway, Sweden, Finland
  - Information sharing among doctors
    - avoid/monitor patient (s)hopping behavior
    - Global Medical File per patient
    - Interoperability
- **Deal with 'empowerment of the patient': Patient-centric health care**
  - Medical care in 4P: personalized, preventive, predictive, participatory
  - Increasing trend for 'customized''personalized' medicine
  - Improve transparancy and consistency
  - Deal/cope with 'professional' (chronical) patients (heart, diabetes, cancer,…)
  - Improve patient mobility
- **Cost effectiveness of the health care system**
  - Ageing population:
    - EU 2050: 65+ → +70%; 80+ → +180%
    - Vl. 2012: 60+ → 25 % of Vl.
  - Monitor overconsumption
  - Improve transparancy
  - Detect abnormalities in diagnosis/therapy/…
- **Cope with tsunami of available information and data (clinical, population, ….)**

THE TRANSLATION GAP





Source: NIH; CMR International & IMS Health


Academia
Health care system
Academia
Basic sciences & technology
Clinical Practice
Humanities
CORE FACIL
CORE FACIL
Biomedical sciences
Experimental clinical medicine
Social health sciences
BASIC / PRECLINICAL
CLINICAL
BASIC / PRECLINICAL

Outline

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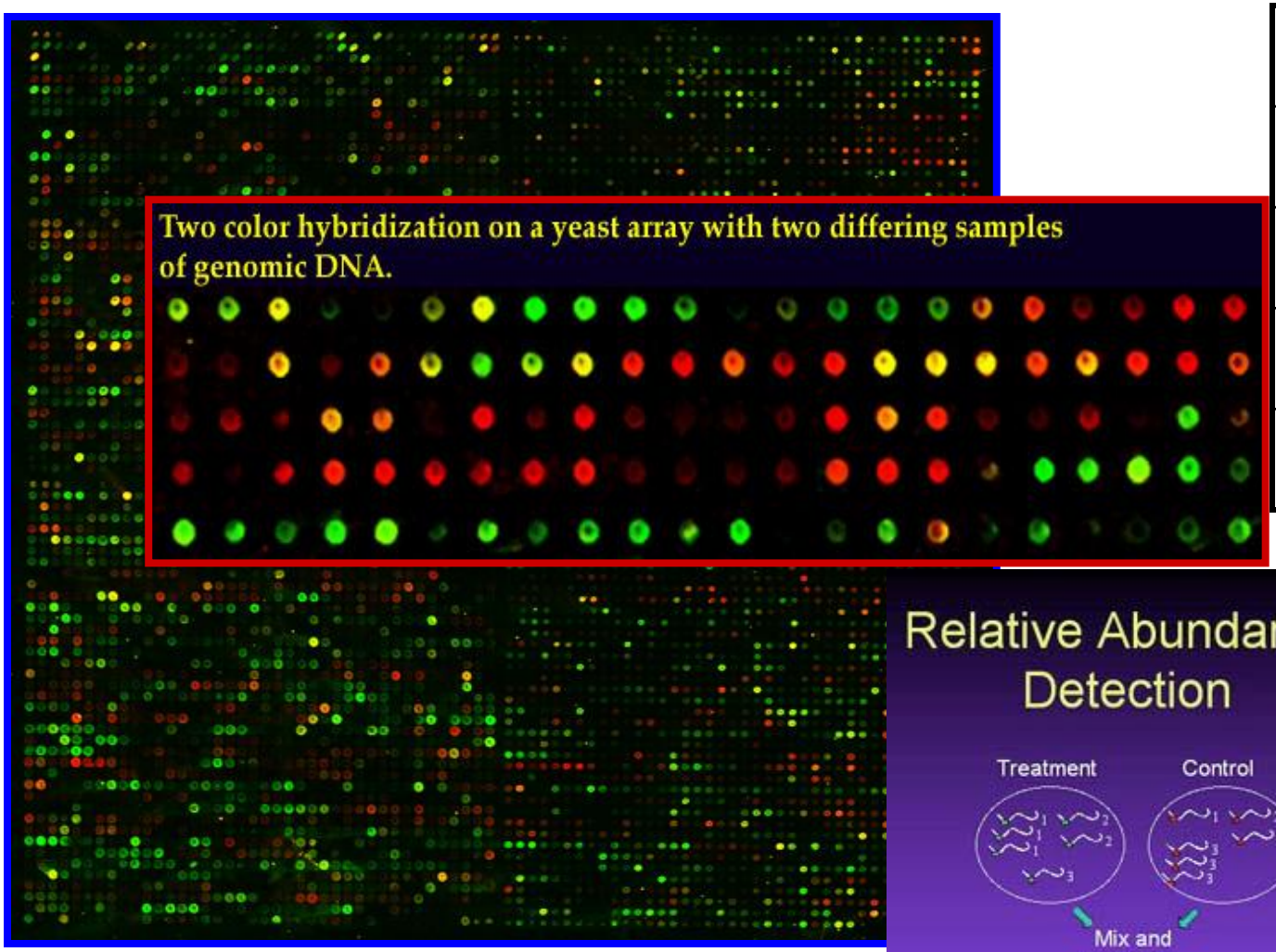
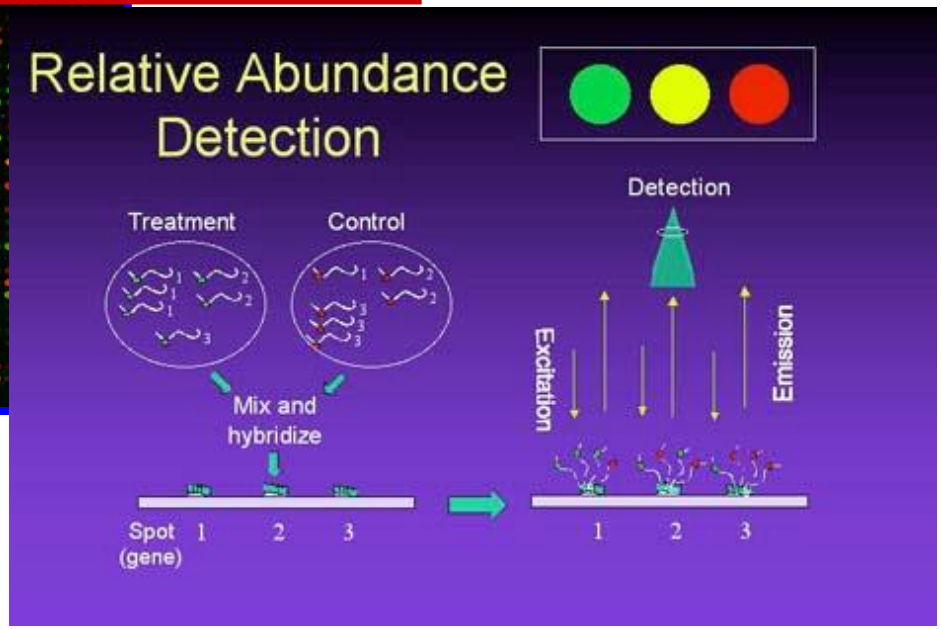
Examples and cases

- Diagnosis via DNA-chips
- Gene prioritization via multiple sources
- International Ovarian Tumor Analysis

Microarrays – DNA-chips



	Test	Ref.
	High	Low
	Low	High
	High	High
	Low	Low



Algorithm

- Abu Ja'far Muhammad ibn Musa al-Khwarizmi was born in Uzbekistan around 800 A.D

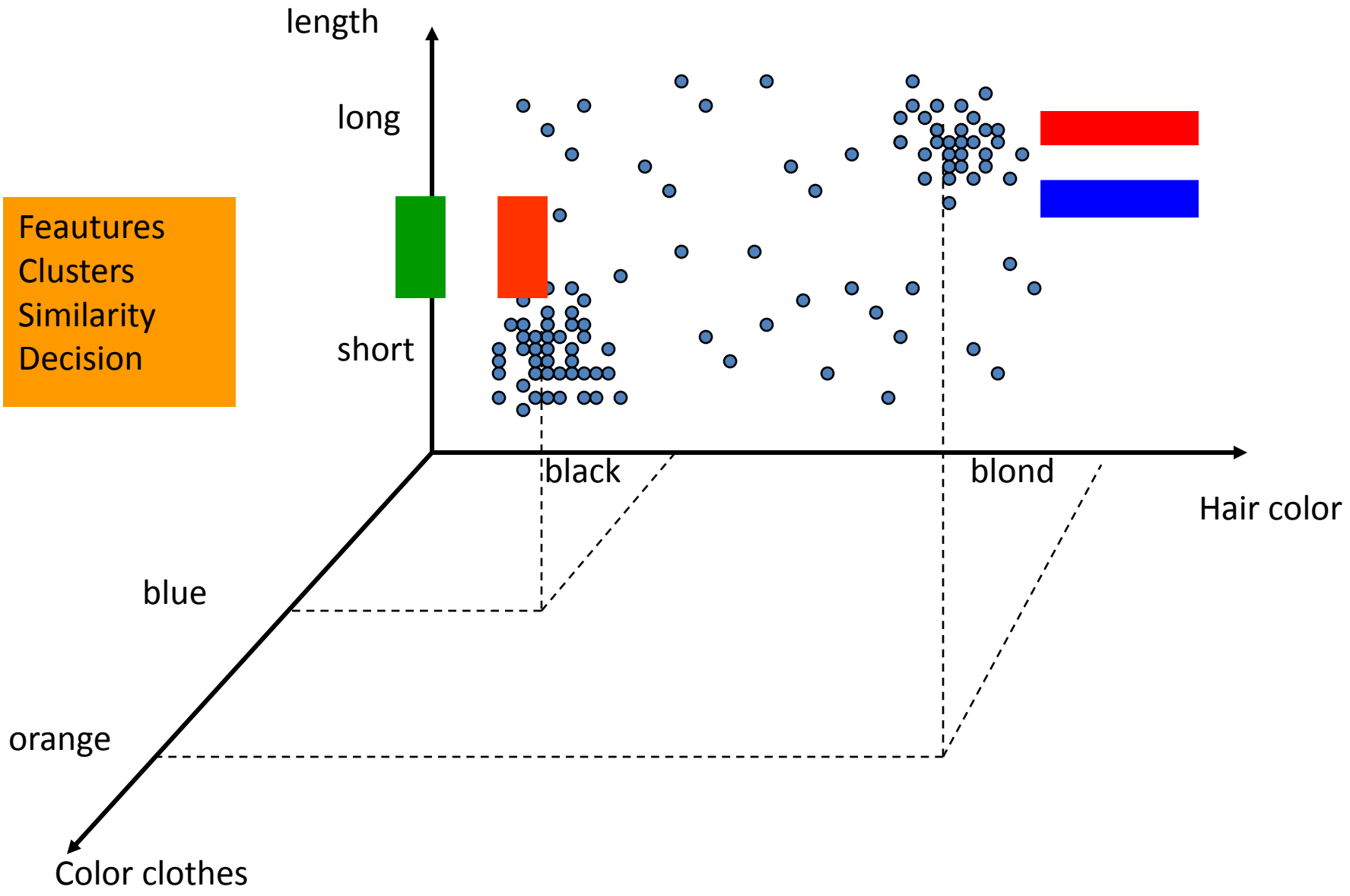
- His name persists in the word 'algorithm'.

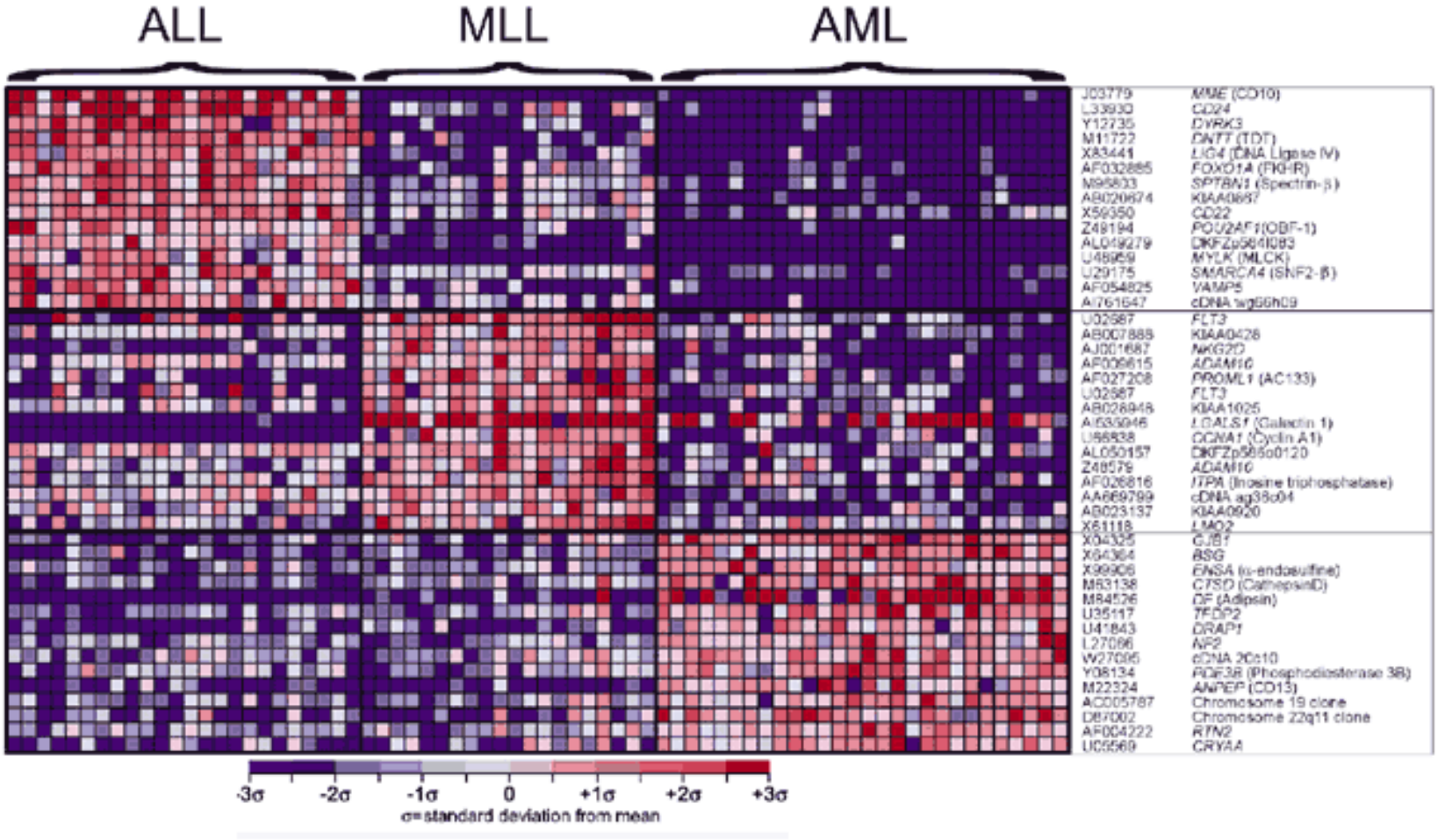
- Main work: “De kunst van het overbrengen en het wegstrepen”
“ Ilm aljabr wa'l muqabalah”, in which we recognize the root of the word “algebra”.

- al-Khwarizmi also enriched the Arabian number notation with the cipher zero.

- The calculus book by al-Khwarizmi lay hidden in the library of Bagdad before it was translated in Latin and found its way to Europe, where it was introduced by mathematicians such as Fibonacci (Sicily, 1200), Tartaglia (Venice, 1500), Cardano (Rome, 1500), Vieta (France, 1550), Descartes (France, 1625),
before it got its ultimate position in analytic geometry.

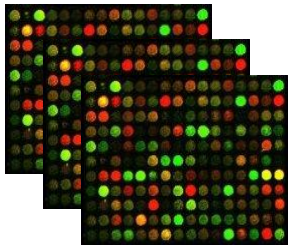
Clustering and classification algorithms



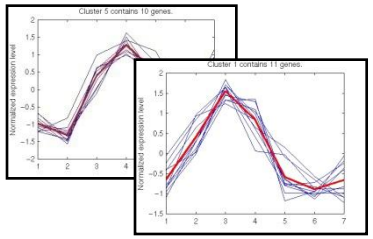

ALL
MLL
AML
J03779 MME (CD10)
L33930 CD24
Y12735 DYRK3
M11722 DNTT (TDT)
X83441 LIG4 (DNA Ligase IV)
AF032885 FOXO1A (FKHR)
M96803 SPTBN1 (Spectrin-β)
AB020674 KIAA0687
X59350 CD22
Z48194 POU2AF1(OBF-1)
AL049279 DKFZp564I083
U48959 MYLK (MLCK)
U29175 SMARCA4 (SNF2-β)
AF054825 VAMP5
AI761647 cDNA:wg66h09
U02687 FLT3
AB007885 KIAA0426
AJ001687 NKG2D
AF006615 ADAM10
AF027208 PROML1 (AC133)
U02687 FLT3
AB028948 KIAA1025
AI653946 LGALS1 (Galectin 1)
U66838 CCNA1 (Cyclin A1)
AL050157 DKFZp586o0120
Z48579 ADAM10
AF026816 ITPA (Inosine triphosphatase)
AA869799 cDNA:ag38c04
AB023137 KIAA0920
X61118 LMO2
X04325 GJB1
X64364 BSG
X99906 ENSA (α-endosulfine)
M63138 CTSD (CathepsinD)
M84526 DF (Adipsin)
U35117 TFDP2
U41843 DRAP1
L27096 AIF2
W27096 cDNA:20c10
Y08134 PDE3B (Phosphodiesterase 3B)
M22324 ANPEP (CD13)
AC005787 Chromosome 19 clone
D87002 Chromosome 22q11 clone
AF004222 RTN2
U05569 CRYAA
-3σ
-2σ
-1σ
0
+1σ
+2σ
+3σ
σ=standard deviation from mean

Heterogenous data source: gene prioritization

High-throughput genomics



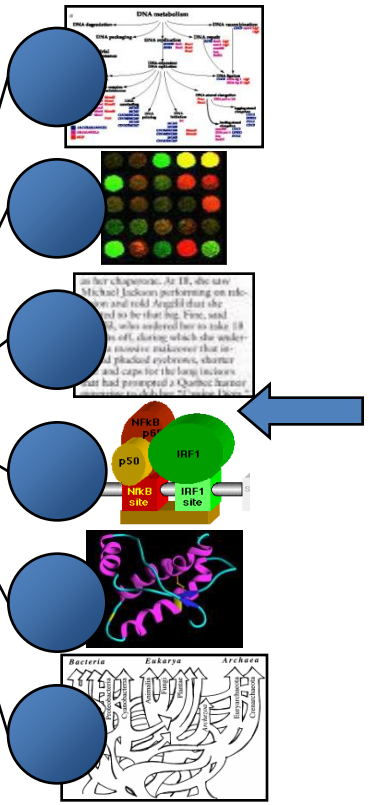
Data analysis



Candidate genes

Name	Ensembl
TTR	ENSG00000118271
PAH	ENSG00000171759
G6PC	ENSG00000131482
IGF1	ENSG00000017427
ALB	ENSG00000163631
CRP	00000132693
HABP2	00000148702
IF	00000138799
FST	00000134363
ARAF1	00000078061
HMGA2	G00000149948
C9	SG00000113600
PCBP2	ENSG00000111406
HOXB6	SG00000108511
RERE	ENSG00000142599
HOXA11	ENSG00000005073
CLIC1	ENSG00000096238
ERCC3	ENSG00000163161
ERCC3	ENSG00000163161
TLL2	ENSG00000095587
SYT4	ENSG00000132872
SYT4	ENSG00000132872
PIK4CB	ENSG00000143393
PKD2	ENSG00000118762
	ENSG00000081026
ANKRD3	ENSG00000183421
F13A1	ENSG00000124491
BPAG1	ENSG00000151914
KCNN3	ENSG00000143603
GRIN2A|GRIN2B	ENSG00000150086
SIM1	ENSG00000112246
	G00000174891
	SG00000089195
C14orf10	SG00000092020
STX8	NSG00000170310
	ENSG00000107671
MSH5	NSG00000096474
CRH	SG00000147571
MID1	G00000101871
	00000184508
	00000113460
TGFB3	ENSG0000
C10	EN
N	EN
PDG	ENSG
PD	1
NR	3
NFY	67
	98
	907
TN	106537
MMP3|MMP1	ENSG00000149968

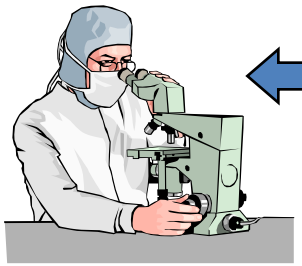
Information sources



Candidate prioritization

Rank	En	Ex	Ip	Ke	GO	Te Avg	Pval
1	TTR	G6PC	PAH	G6PC	IGF1	TTR	TTR
2	IGF1	TTR	IGF1	PAH	PAH	IGF1	PAH
3	CRP	ALB	TTR	RERE	G6PC	CRP	G6PC
4	HOXB6	HABP2	ALB	ERCC3	TTR	HOXB6	IGF1
5	ALB	PAH	HDC	ERCC3		ALB	ALB
6	NR4A2	IF	TLL2	ANKRD3		HMGA2	CRP
7	PAH		C1QR1	ARAF1	HDC	NR4A2	
8	HOXA11	IGF1	G6PC	PKD2	F13A1	PAH	IF
9	NFYA	CRP	HABP2	MTMR1	KCNN3	HOXA11	C13orf7	FST
10	C9	ARAF1	IF	HDC	CLIC1	NFYA	TTR	ARAF1

Validation



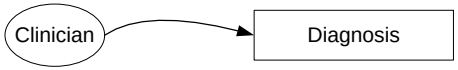
Aerts et al, Nature Biotechnology, 2006

International Ovariam Tumor Analysis Group (IOTA)

Making it easier to diagnose ovarian cancer

Motivation

- Clinicians have to make many decisions concerning the therapy of their patients e.g.:
  - Diagnosis



Motivation

- Clinicians have to make many decisions concerning the therapy of their patients e.g.:
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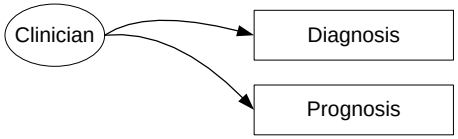
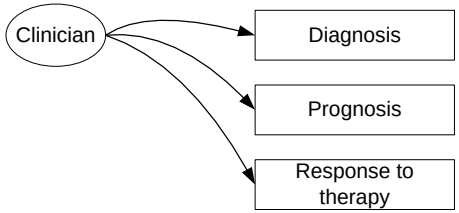
  - Prognosis



Motivation

- Clinicians have to make many decisions concerning the therapy of their patients e.g.:
  - Diagnosis
  - Prognosis
  - Therapy response

- Based on **expertise**
- But often the clinician has



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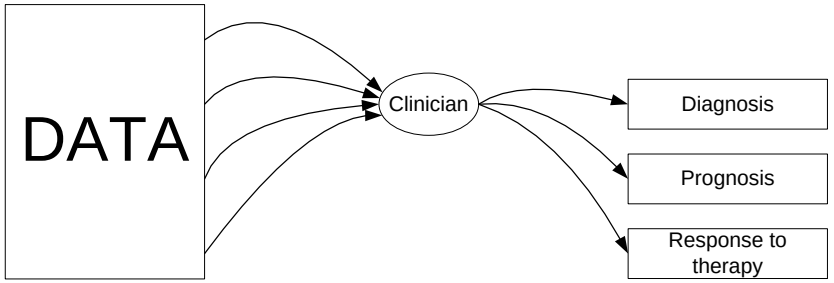
- Clinicians have to make many decisions concerning the therapy of their patients e.g.:
  - Diagnosis
  - Prognosis
  - Therapy response

- Based on **expertise**
- But often the clinician has
  - Patient Data



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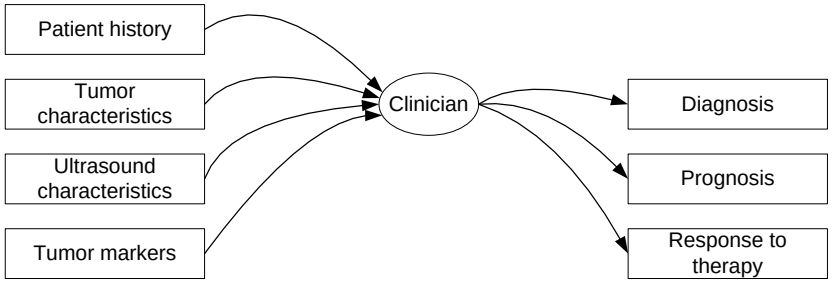
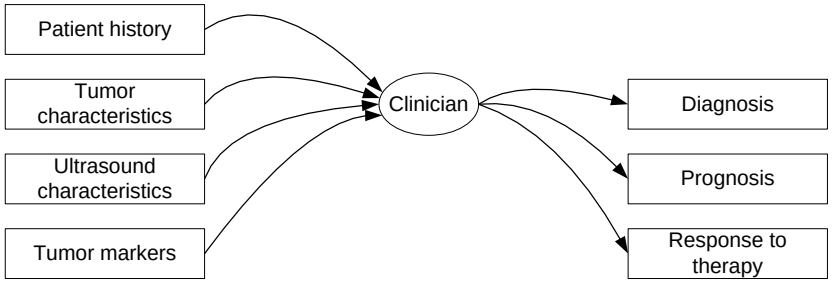
  - Prognosis
  - Therapy response
- Based on **expertise**
- But often the clinician has
  - Patient Data
    - Patient history
    - Tumor characteristics
    - Ultrasound characteristics
    - Tumor markers



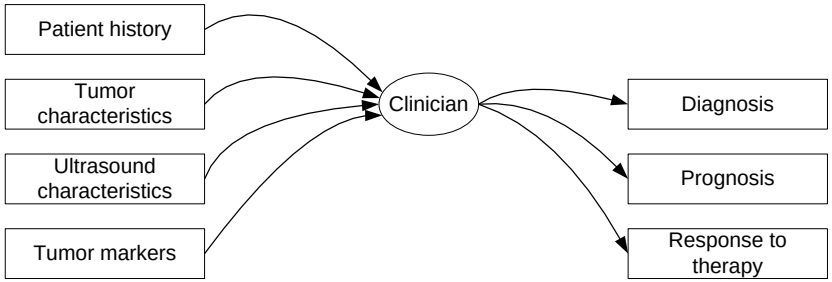
Motivation

- Not all these data types are relevant for every disease
- But for example for the diagnosis of ovarian masses <u>many data types</u> are suspected to be relevant



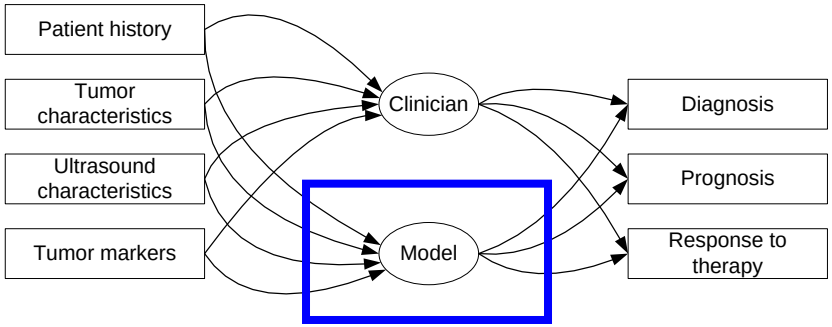
Motivation

- Solution:



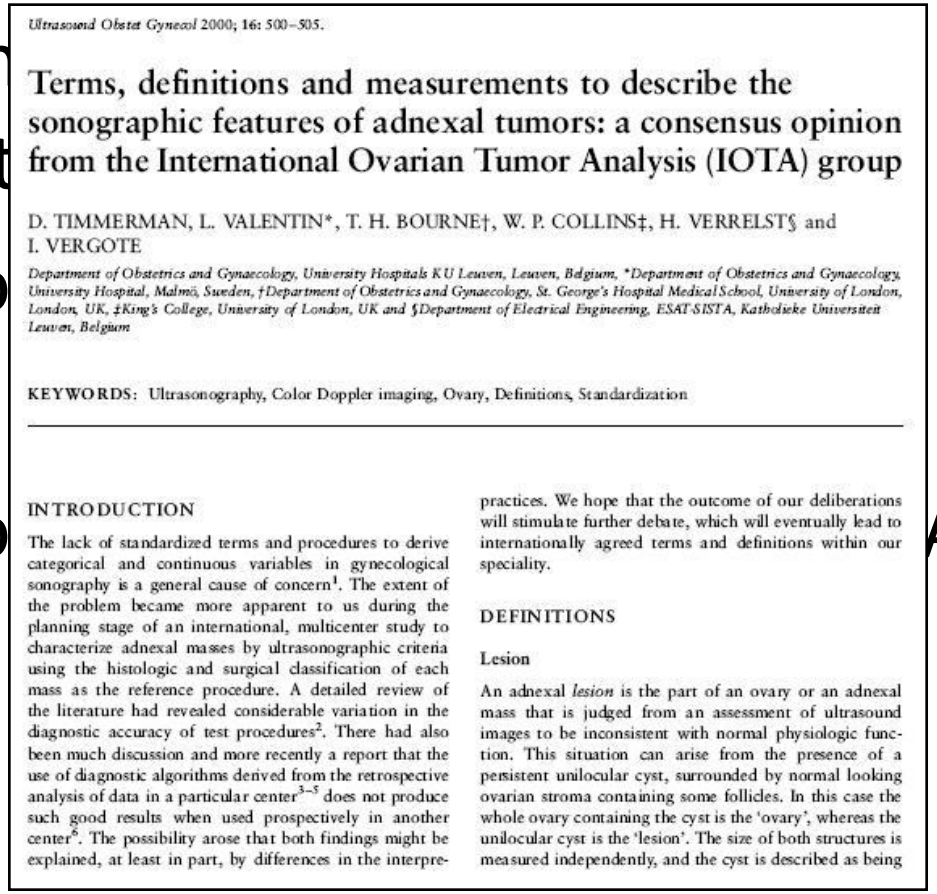
Motivation

- Solution:
  - Clinical decision support modeling
  - Building a mathematical model on the data
  - Use this model to predict patient outcome
    - Diagnosis
    - Prognosis
    - Therapy response



Standardization

- To make sure clinicians everywhere record the same data, they h
definitions of feat
- Standardization o
- Protocol for data
- European Panel o A features



Ultrasound Obstet Gynecol 2000; 16: 500–505.

Terms, definitions and measurements to describe the sonographic features of adnexal tumors: a consensus opinion from the International Ovarian Tumor Analysis (IOTA) group

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KEYWORDS: Ultrasonography, Color Doppler imaging, Ovary, Definitions, Standardization

INTRODUCTION

The lack of standardized terms and procedures to derive categorical and continuous variables in gynecological sonography is a general cause of concern[1]. The extent of the problem became more apparent to us during the planning stage of an international, multicenter study to characterize adnexal masses by ultrasonographic criteria using the histologic and surgical classification of each mass as the reference procedure. A detailed review of the literature had revealed considerable variation in the diagnostic accuracy of test procedures[2]. There had also been much discussion and more recently a report that the use of diagnostic algorithms derived from the retrospective analysis of data in a particular center[3–5] does not produce such good results when used prospectively in another center[6]. The possibility arose that both findings might be explained, at least in part, by differences in the interpre-practices. We hope that the outcome of our deliberations will stimulate further debate, which will eventually lead to internationally agreed terms and definitions within our speciality.

DEFINITIONS

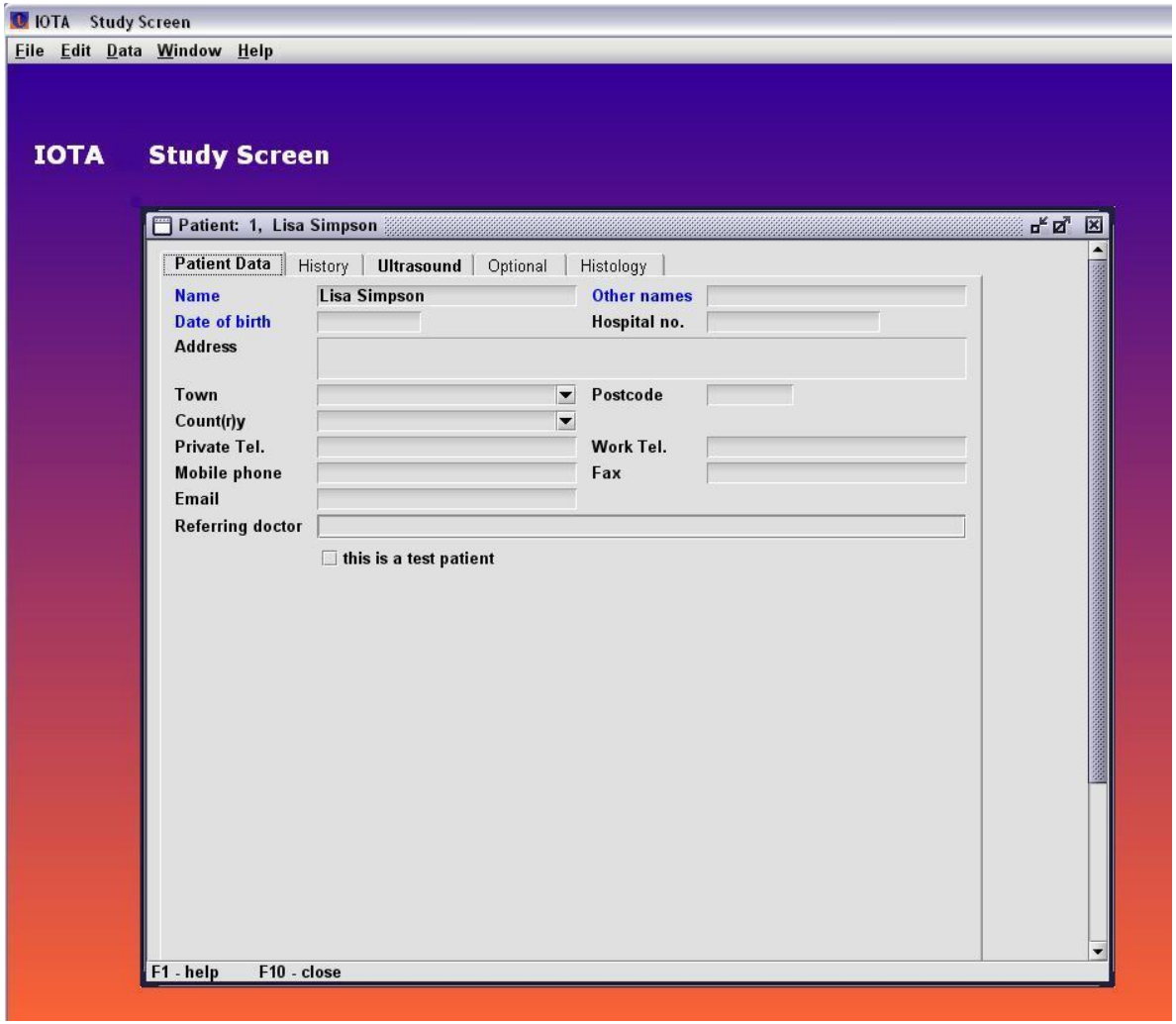
Lesion

An adnexal *lesion* is the part of an ovary or an adnexal mass that is judged from an assessment of ultrasound images to be inconsistent with normal physiologic function. This situation can arise from the presence of a persistent unilocular cyst, surrounded by normal looking ovarian stroma containing some follicles. In this case the whole ovary containing the cyst is the 'ovary', whereas the unilocular cyst is the 'lesion'. The size of both structures is measured independently, and the cyst is described as being

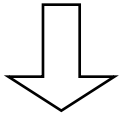
Clinical Data

- Data gathered by IOTA group
  - Standardized multi-centric collection of clinical data
  - AIM: diagnose ovarian cancer
  - > 60 variables collected, 32 selected relevant for prediction
- Data gathered in two phases:
  - Phase 1: 1066 patients in 9 European centers
  - Phase 2: 1938 patients in 12 new International centers

Data collection

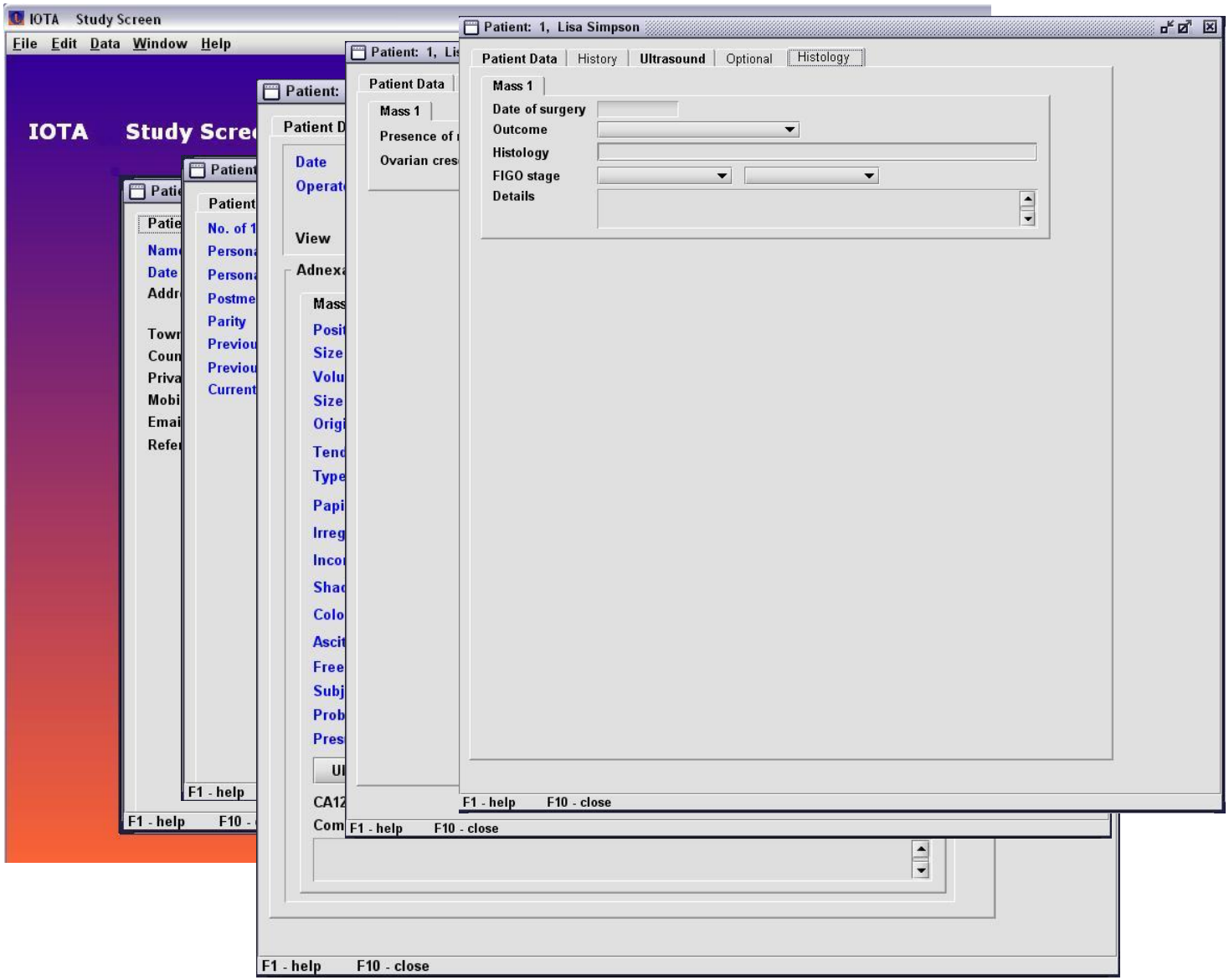


Privacy is ensured



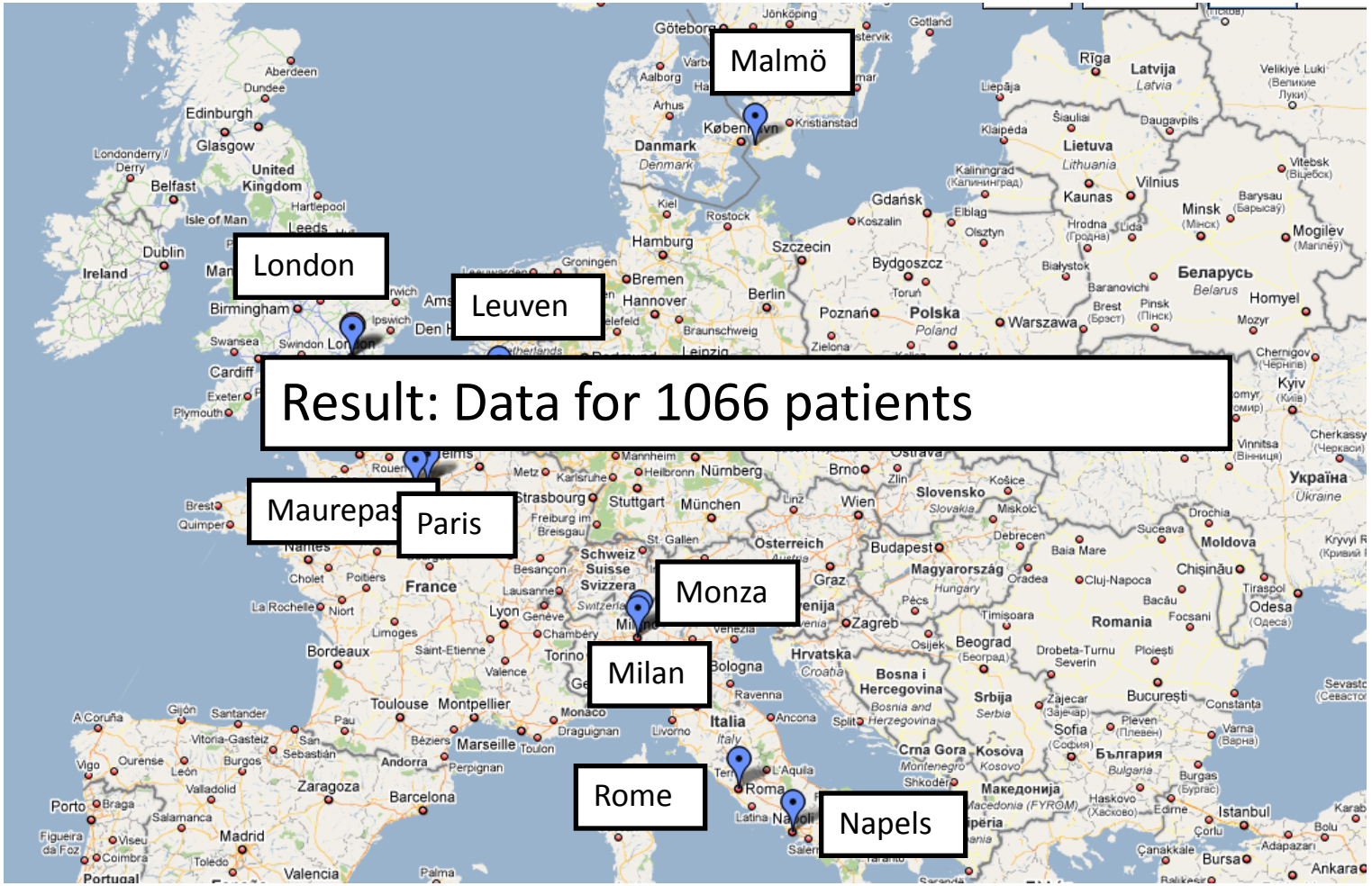
After input this data is anonymized and a unique code is given to each patient

Data collection

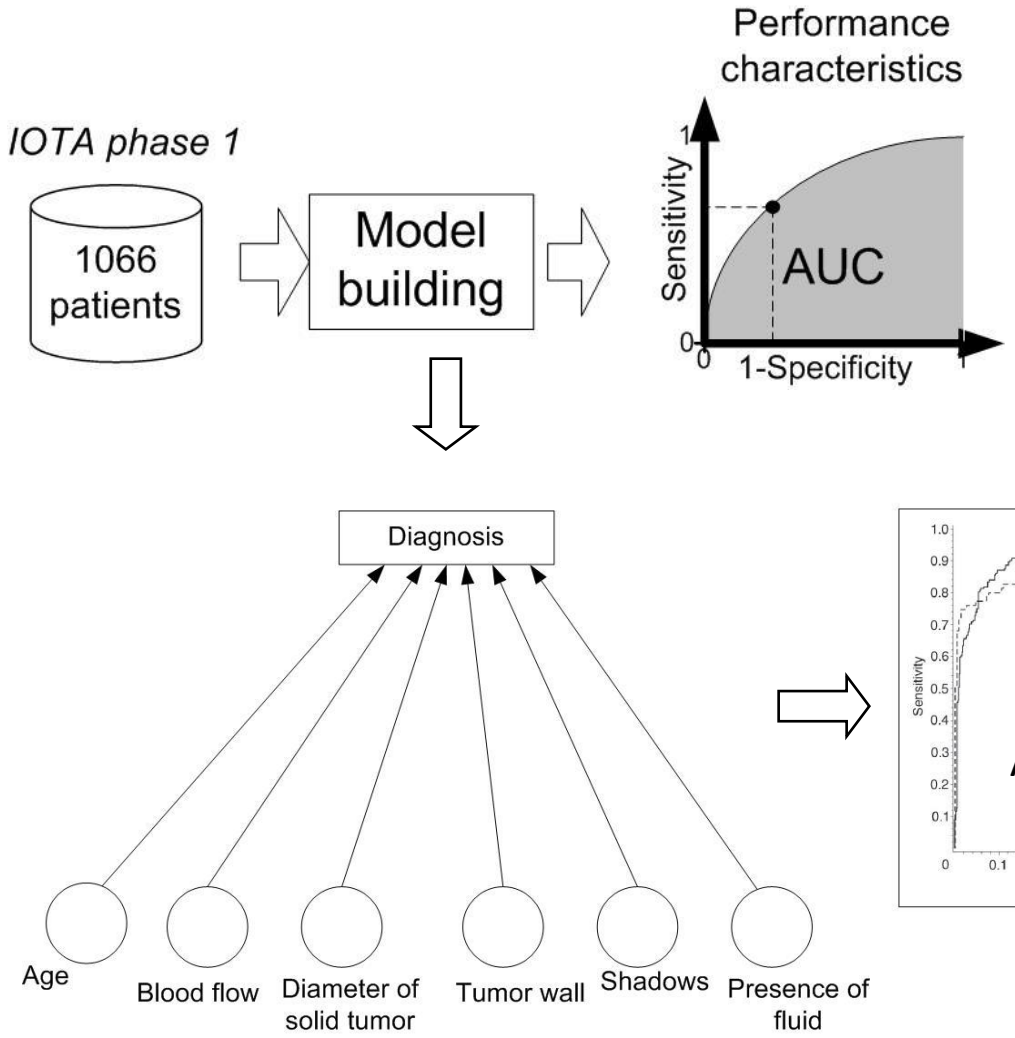


IOTA phase 1 centers

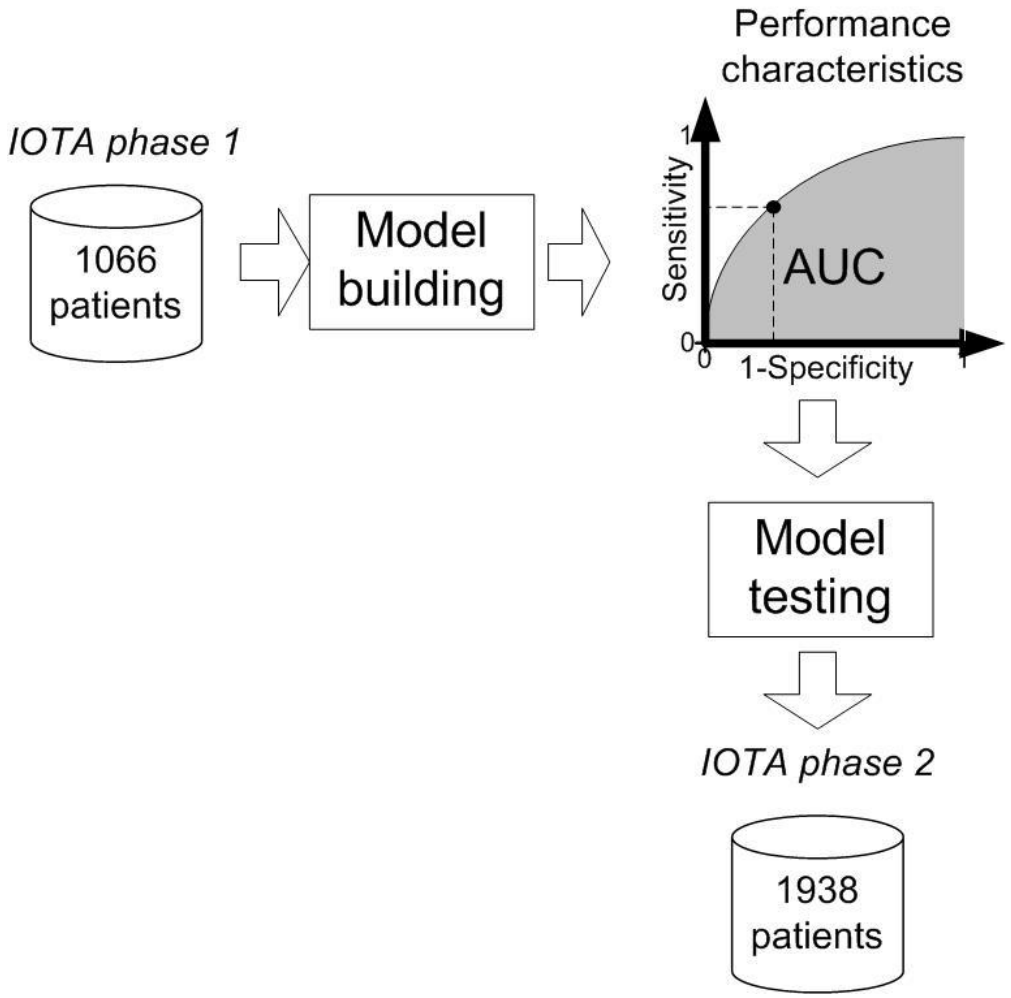
9 centers



Model building

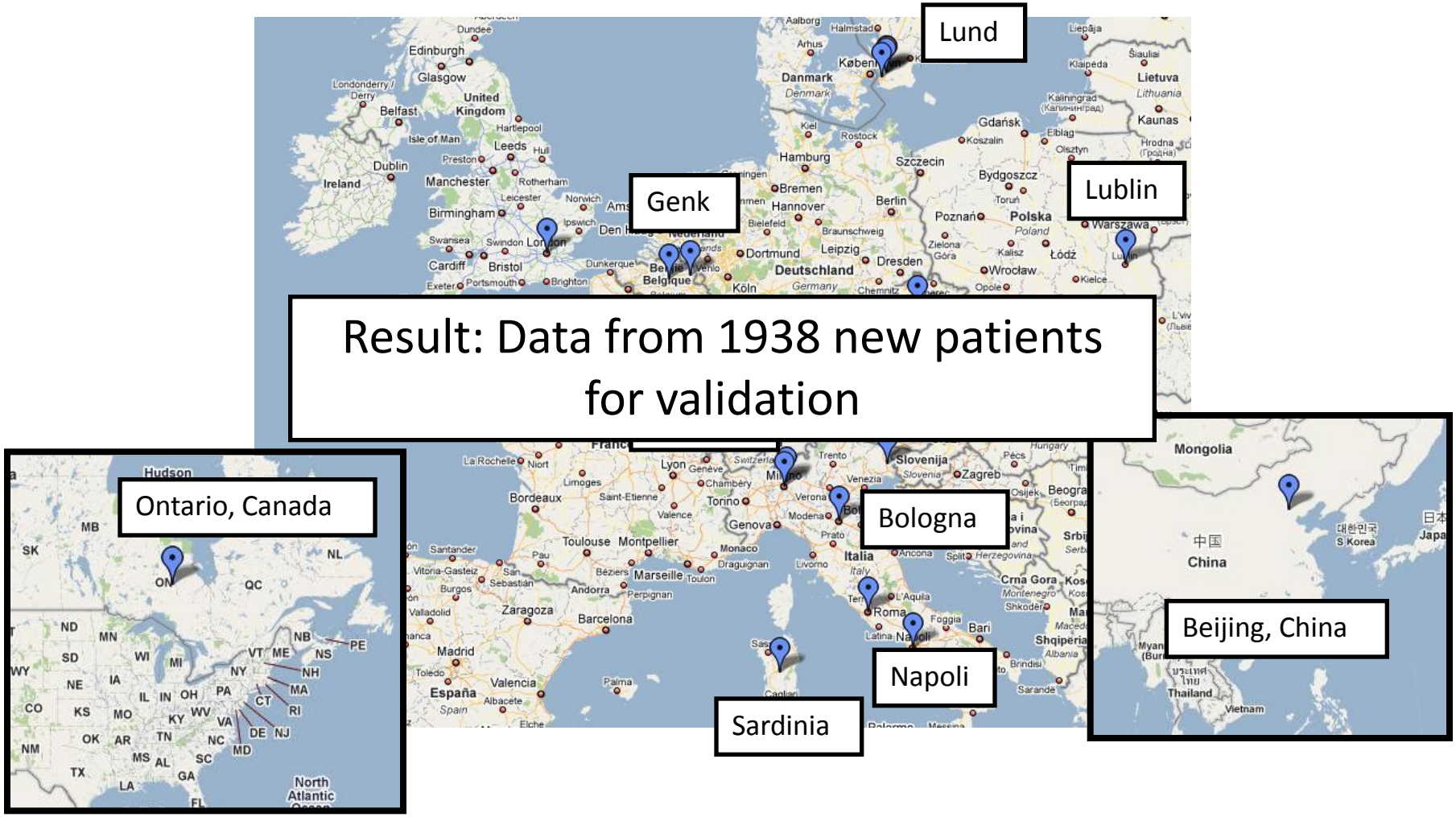


Validation of the model



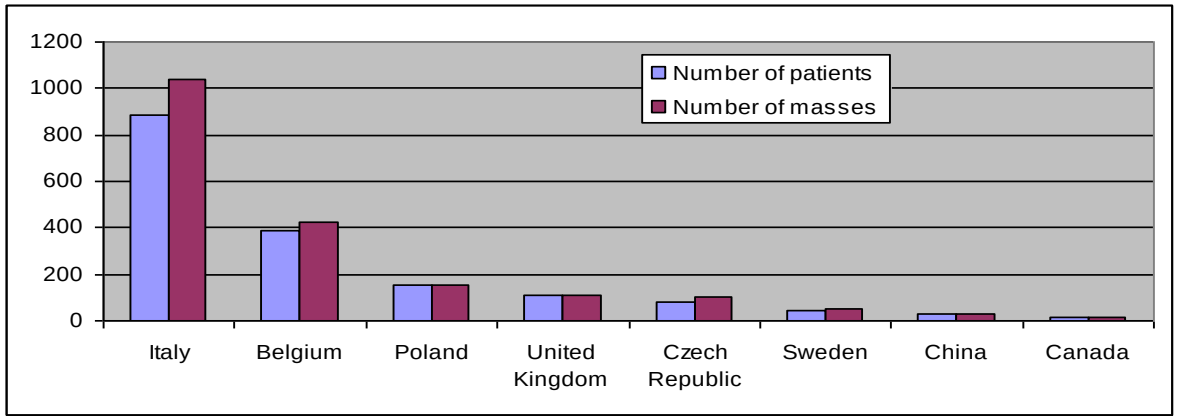
IOTA phase 2 centers

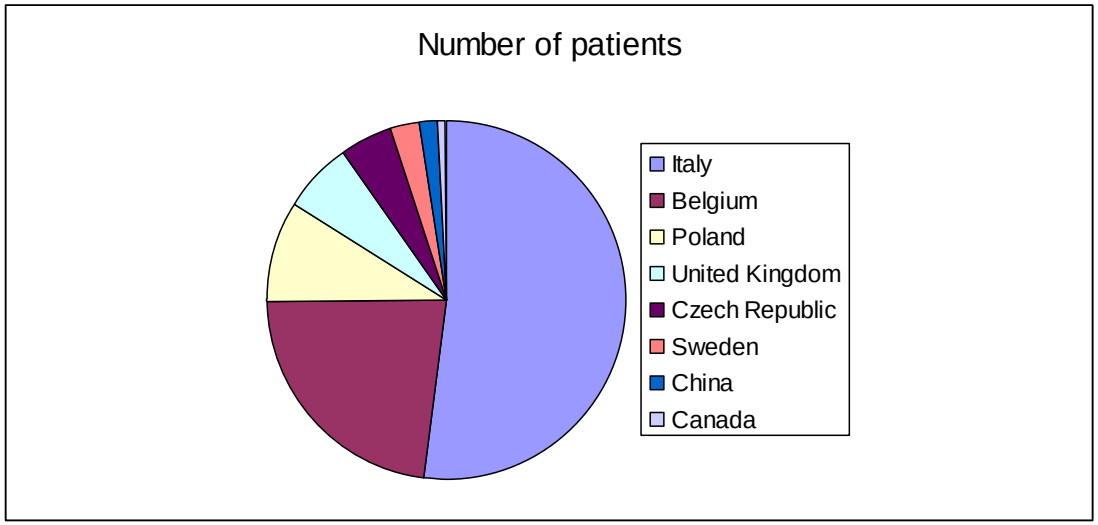
12 new centers



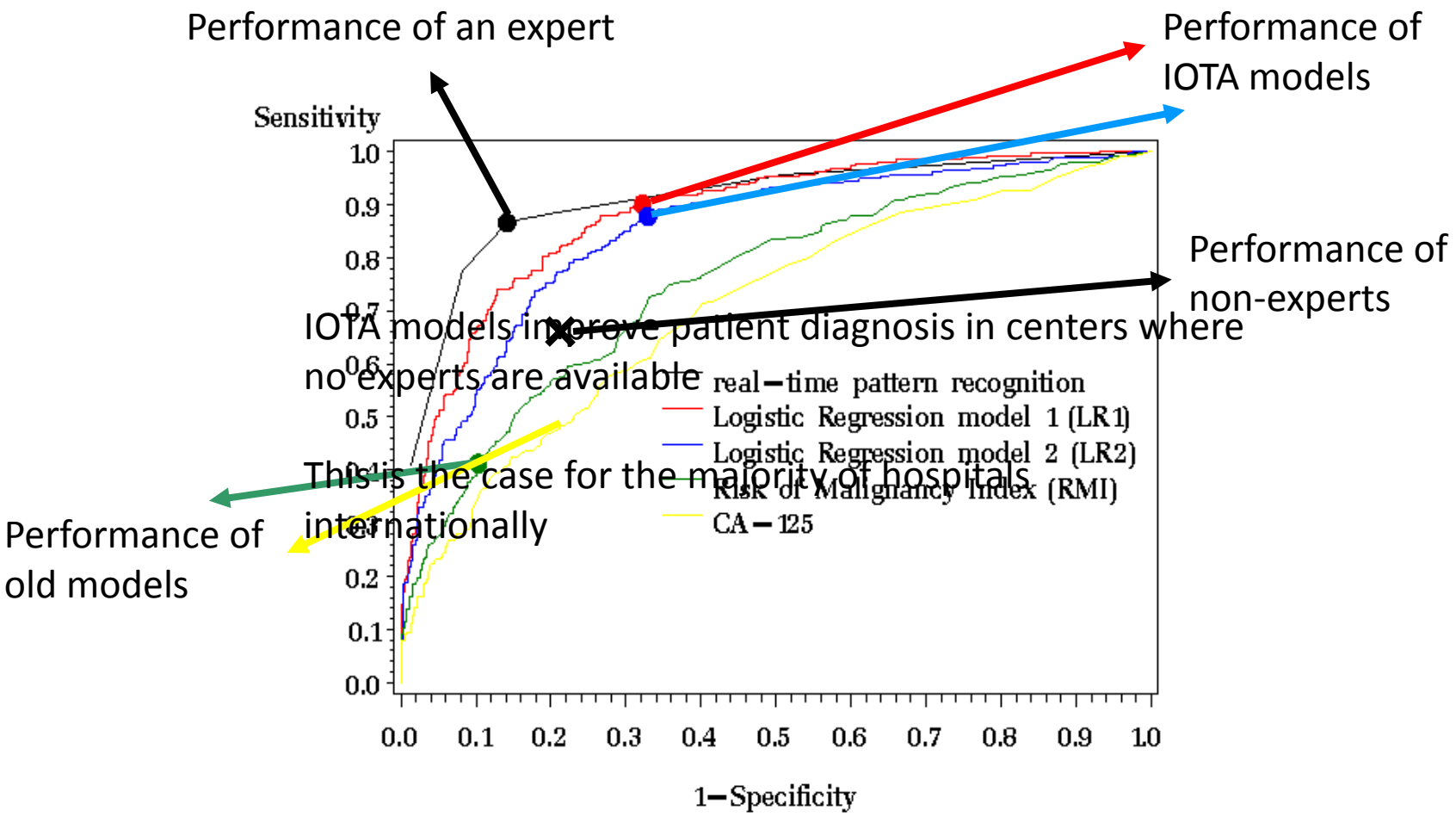
IOTA phase 2

numbers

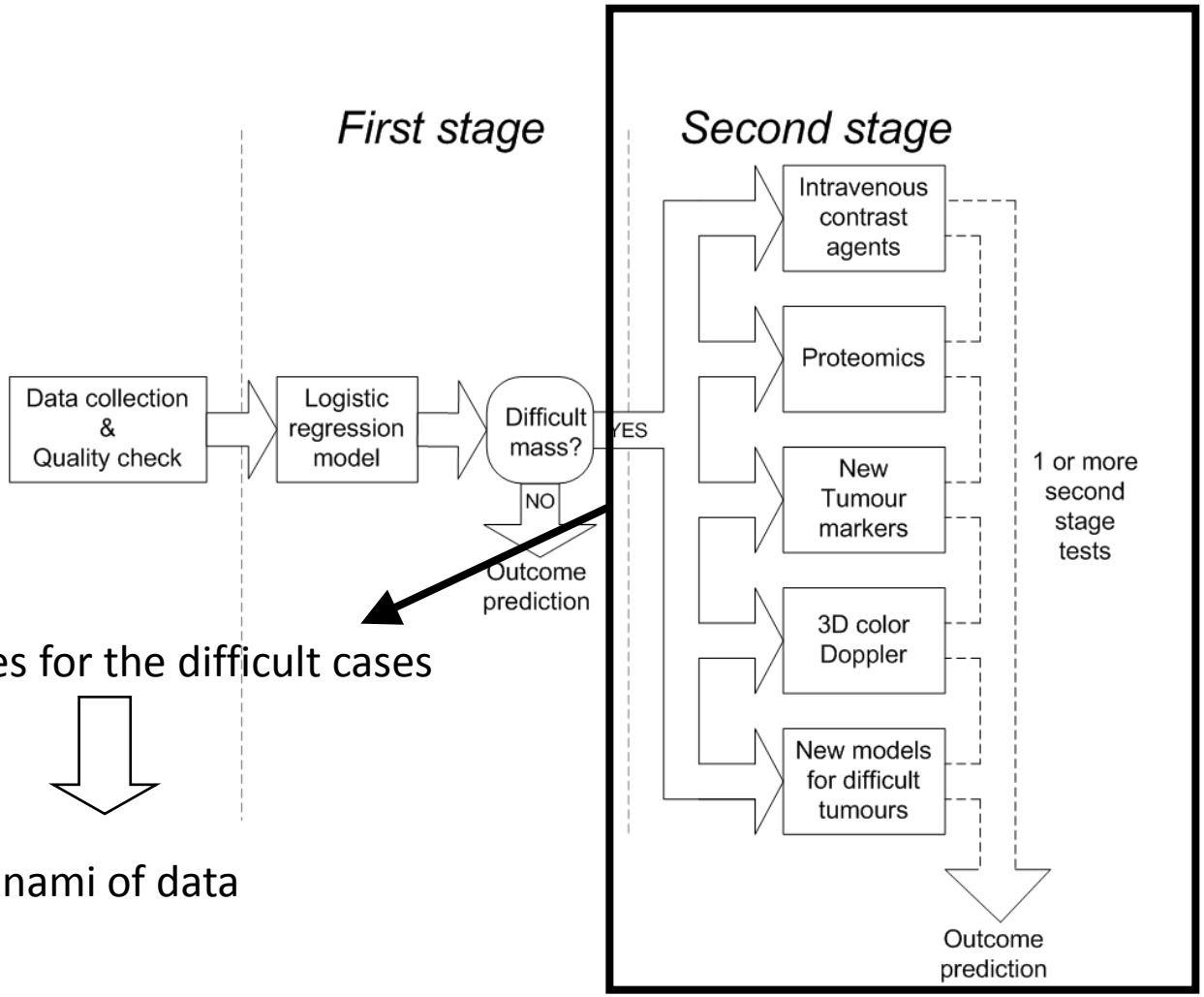




Performance comparison



Future of IOTA



New technologies for the difficult cases

Tsunami of data

Information security aspects

-Multilateral security for community-centric healthcare IT platforms

-System and software security of critical community (e-health) infrastructures

-Enabling technologies for collaborative work in the e-health sector

-Policy negotiation, enforcement and compliance

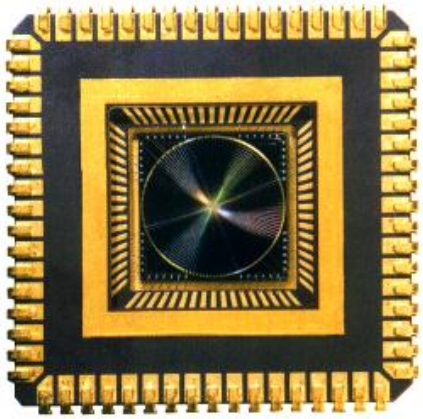
-Privacy preserving data-mining and statistical databases

-Body Area Networks (implanted devices, wearable devices,…) and Personal Area Networks

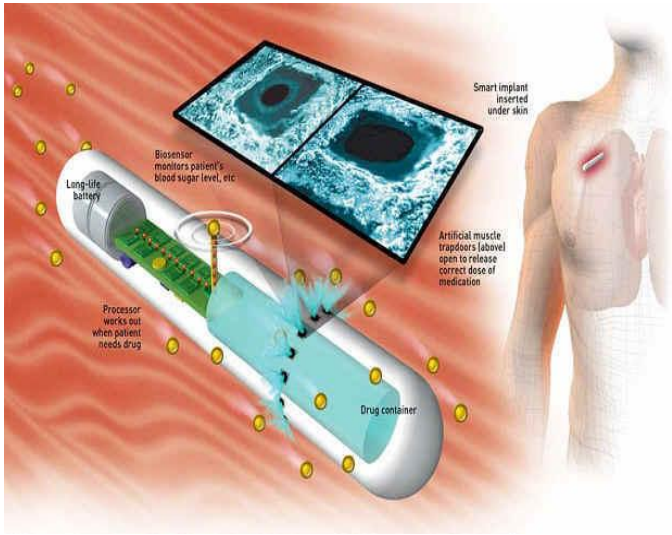
- E-government : identity management, delegation, controlled data exchange

You share, we care !

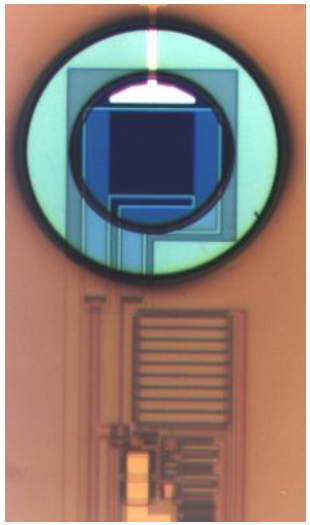
Nano-Sensoren en Actuatoren



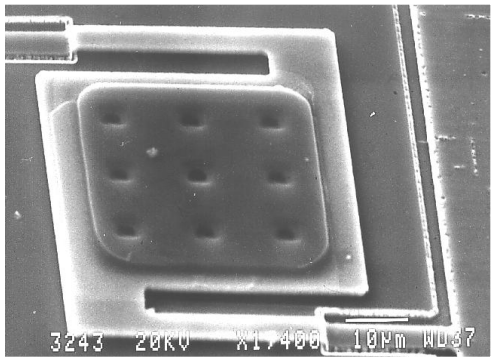
CMOS Imager



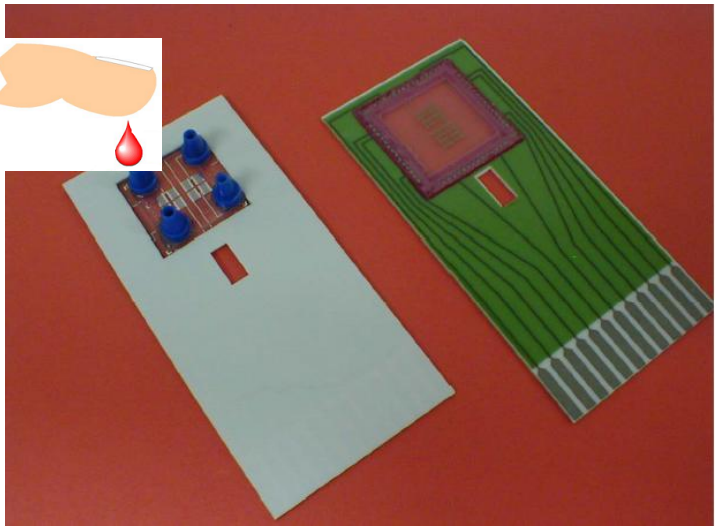
Smart Pill (Ohio State Univ)



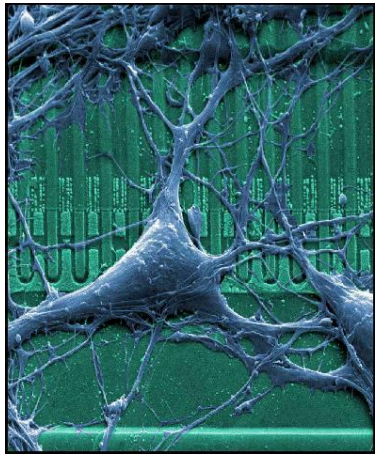
Blood gas sensor (IMEC)



IR Sensor (IMEC)

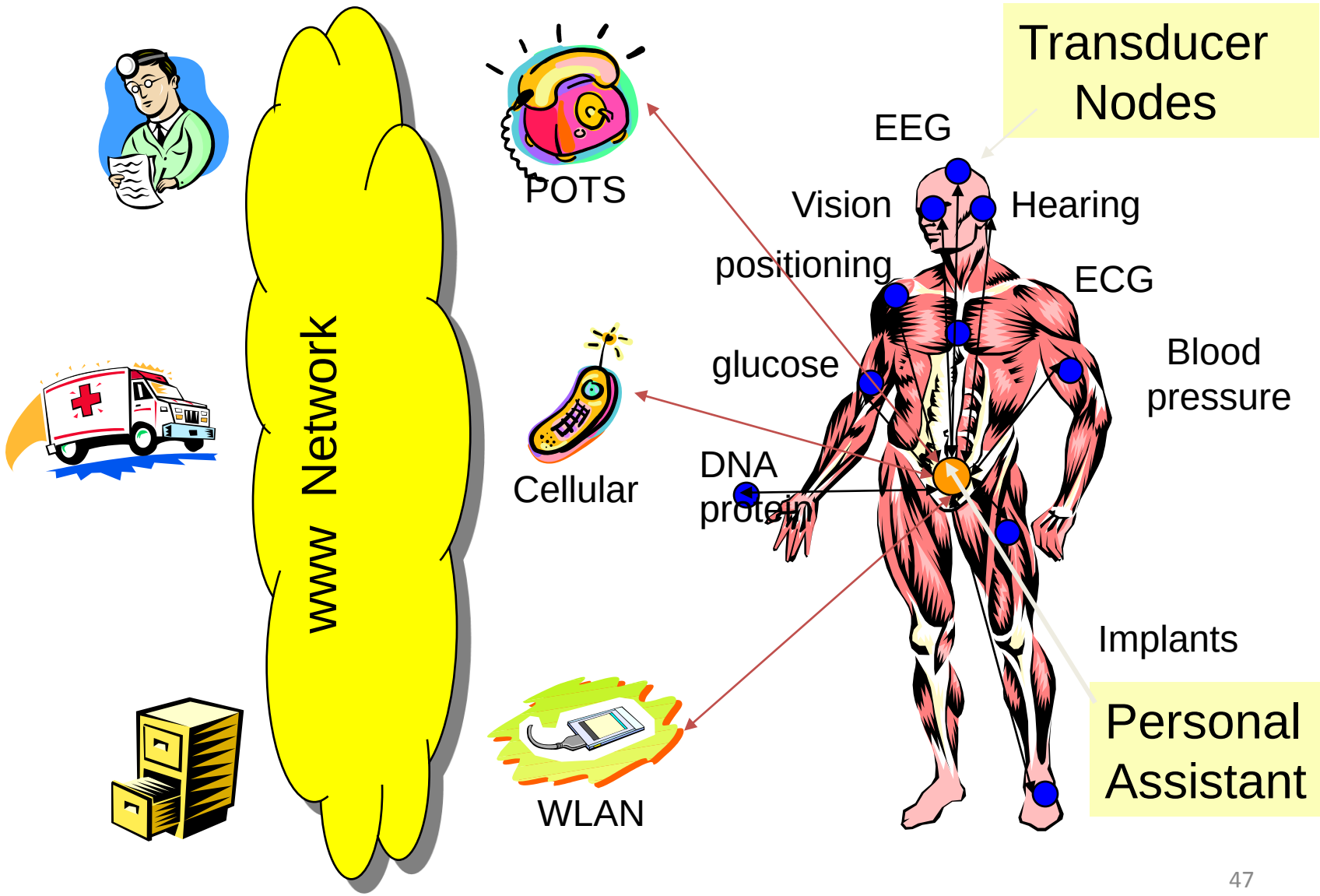


Prostate cancer diagnosis (IMEC)



NeuronSensor (KNS)

Human++ programma IMEC



KATHOLIEKE UNIVERSITEIT LEUVEN

Synthetic Biology

Dr. Coli

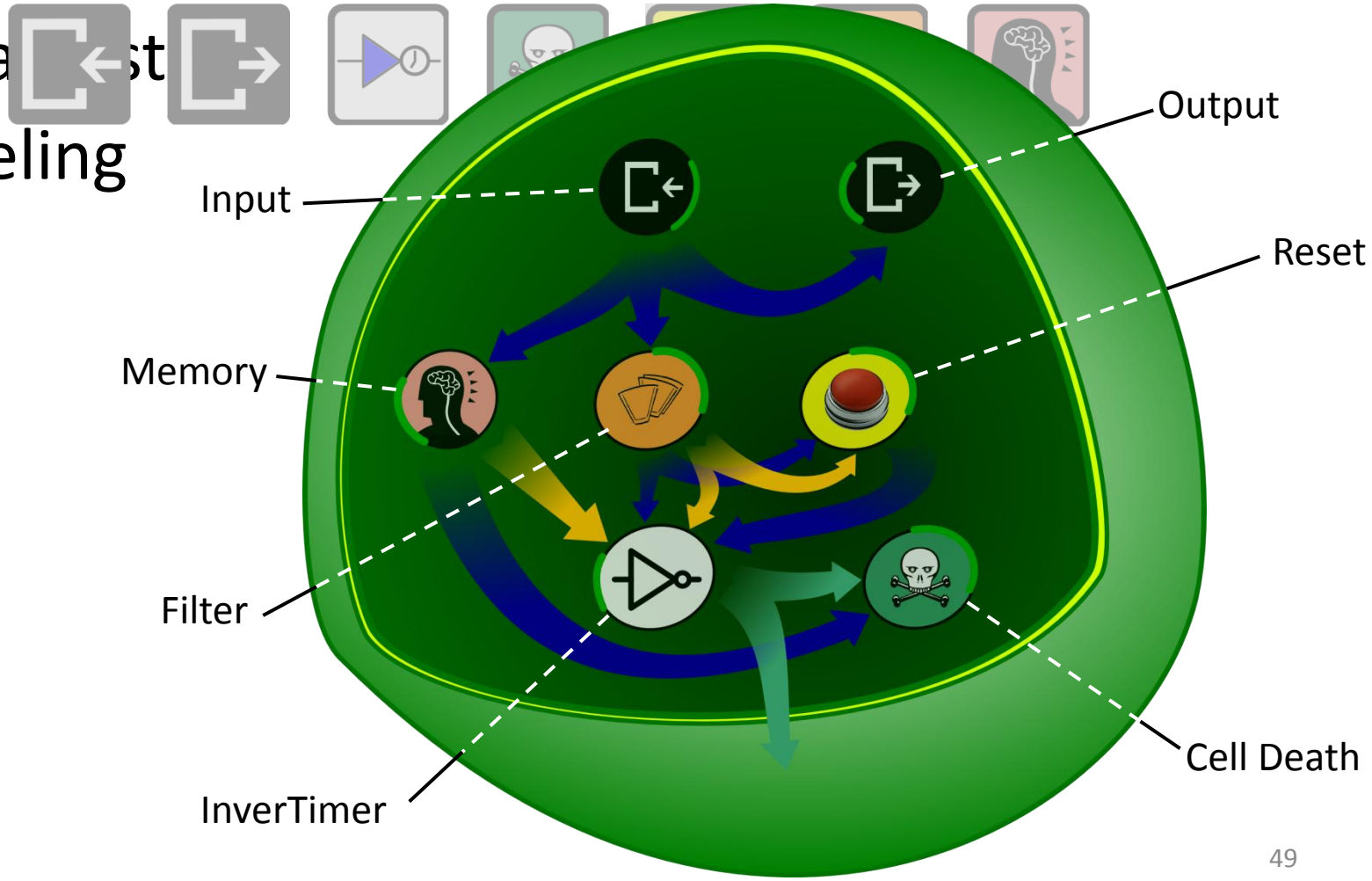
The bacterial drug delivery system

Leuven - BELGIUM

Multidisciplinary team

Overview

- 7 subsystems
- Global Reset
- Modeling



Outline

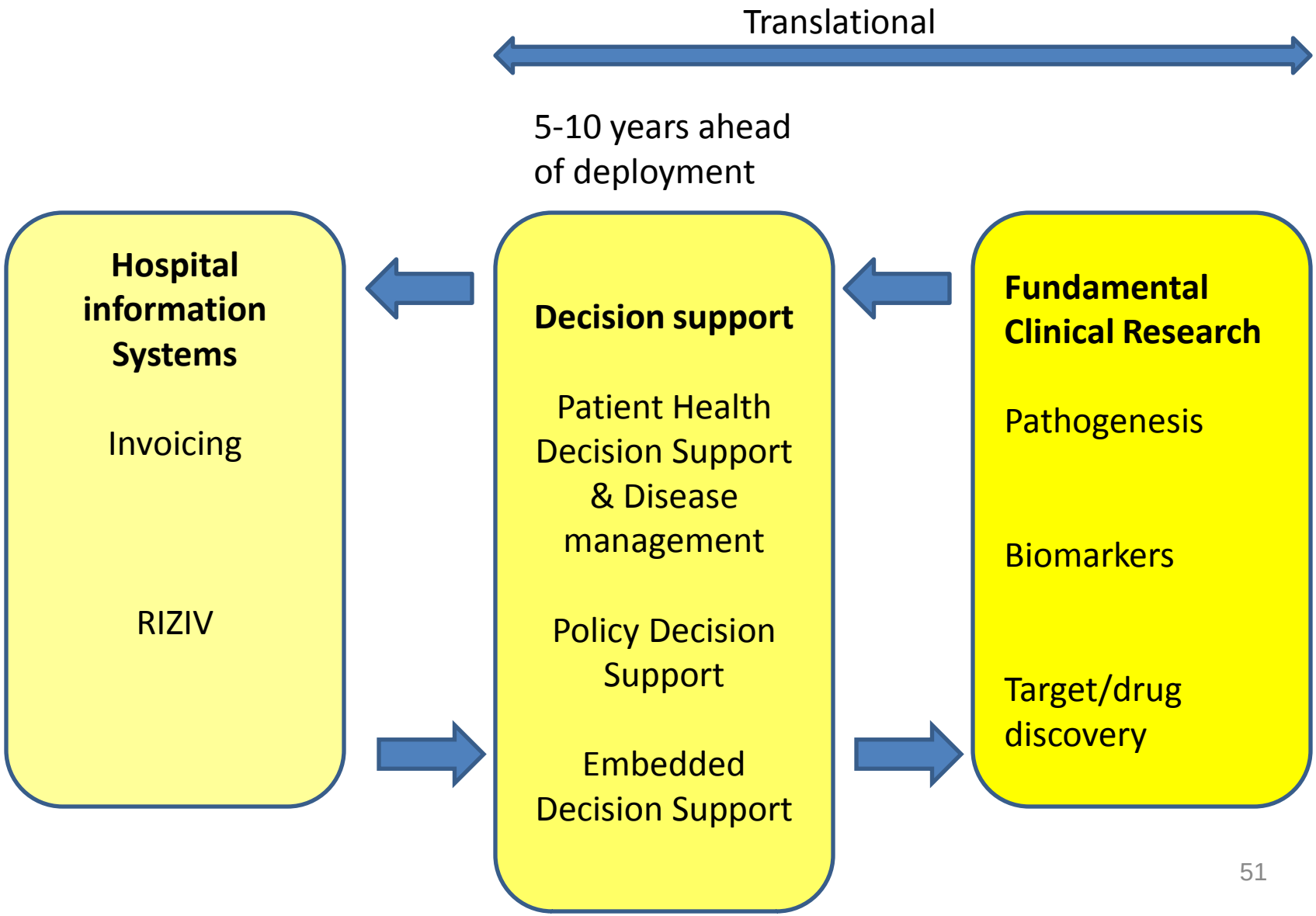
-Trends

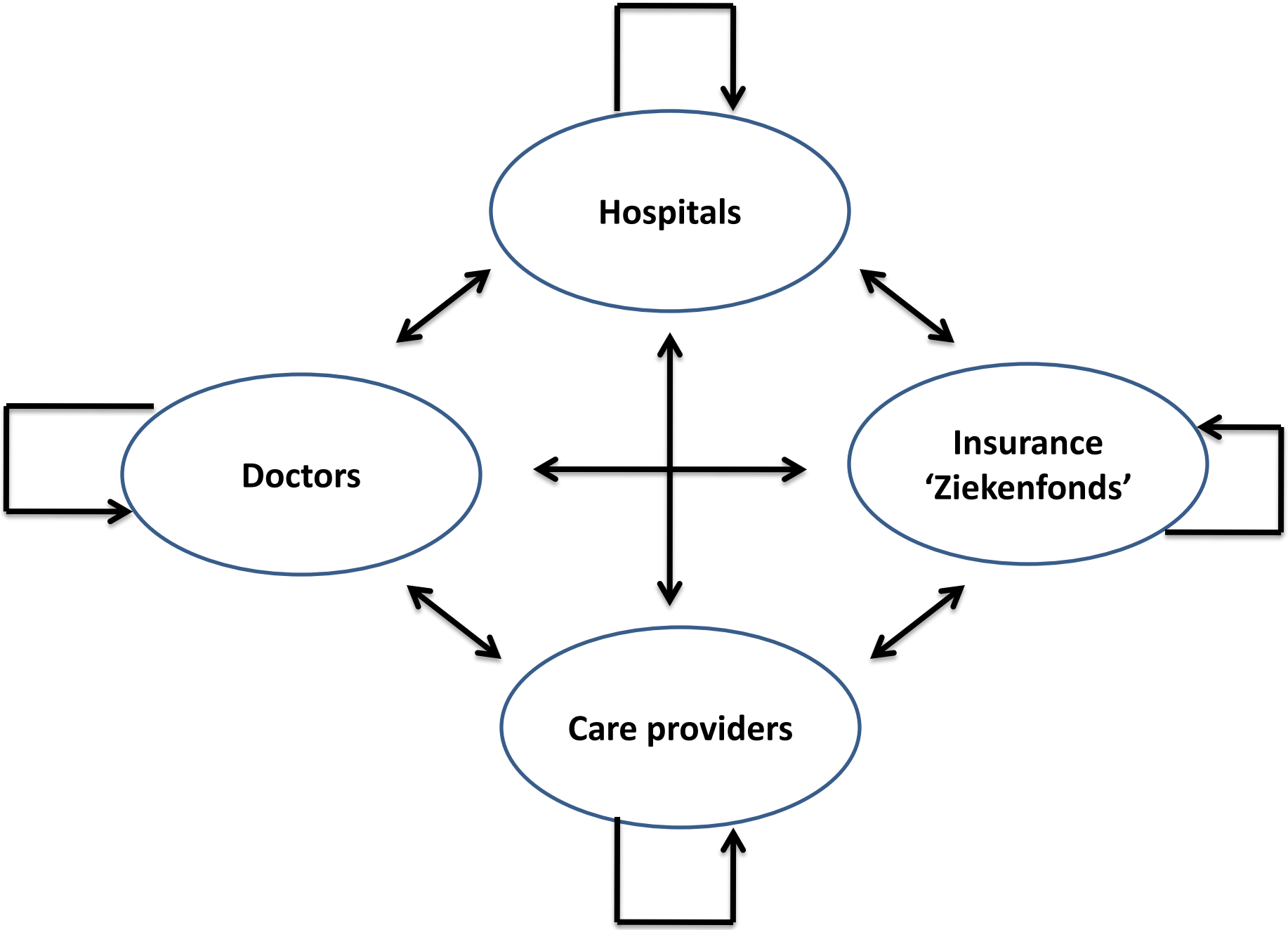
-Context

-Opportunities and challenges

-What to do ?

What to do ?


Translational
5-10 years ahead of deployment
Hospital information Systems
Invoicing
RIZIV
Decision support
Patient Health Decision Support & Disease management
Policy Decision Support
Embedded Decision Support
Fundamental Clinical Research
Pathogenesis
Biomarkers
Target/drug discovery


Hospitals
Doctors
Insurance
'Ziekenfonds'
Care providers