Clinical Decision Support

Bart De Moor

ESAT-STADIUS KU Leuven

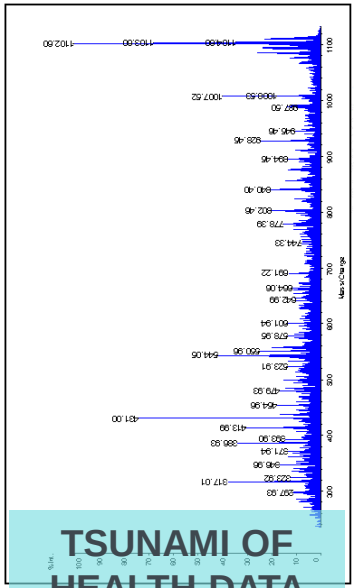
MISSION STATEMENT

To **support** healthcare professionals, patients and policy makers by providing a **health innovation accelerator** for research, development and deployment **of data driven decision support systems**

RATIONALE: HEALTHCARE IS CHANGING FAST…

INCREASING HEALTHCARE DEMANDS for QUALITY of LIFE

NEW EMERGING TRENDS demand for new ORGANISATION OF HEALTHCARE



TSUNAMI OF HEALTH DATA

Recent books (Dutch)

DIGITAL HEALTH CHALLENGES

REFUNDING MECHANISMS

BUDGET

DISRUPTED MARKET

ICT BASICS

OVERCONSUMPTION

CLINICAL VALIDATION

USER PROFILES

INTEROPERABILITY

BIOMARKERS

CUSTOMIZATION

MONITORING

IF WE CARE ABOUT THE FUTURE OF CARE…

- PATIENT HEALTH RECORD
- HEALTH DATA ANALYTICS
- TELEMEDICINE & -MONTORING
- WEARABLES & MHEALTH
- …OMICS (genomic, proteomics, metabolomics, interactomics,…)
- DECISION SUPPORT SYSTEMS

…TECHNOLOGY WILL BE KEY

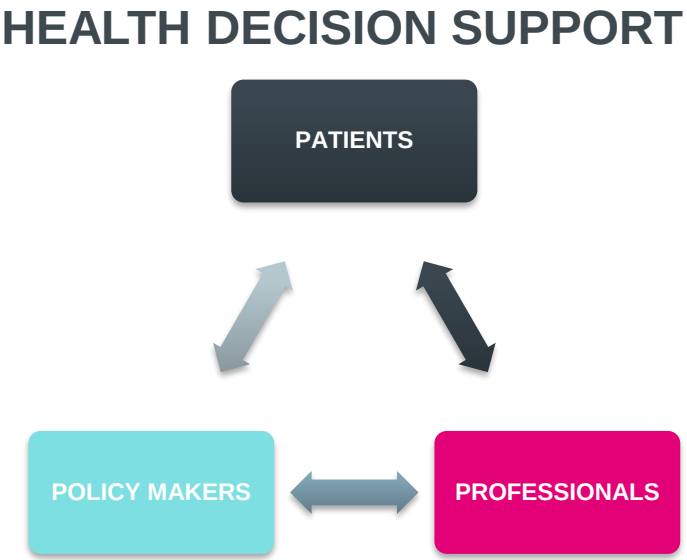
WHO IS IN DEMAND?

PATIENTS

POLICY MAKERS

PROFESSIONALS

HEALTH DECISION SUPPORT SYSTEMS



HDSS RESULT FROM TOP-NOTCH MEDICAL RESEARCH & DATA WELDED WITH INFORMATION TECHNOLOGY AND COMPUTER SCIENCE INTELLIGENCE

R & D ROAD MAP


Research Challenge I
Data Science Algorithms
Research Challenge 2:
Clinical Decision Support
Research Challenge 3:
Patient Decision Support
Research Challenge 4:
Policy Decision Support

R & D ROAD MAP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HEALTH CARE = TECHNOLOGY DRIVEN

Computer Tomography

Magnetic resonance

GS-FLX Roche
Applied Science 454

Sequencers

ACACATTAAATCTTATATGC
TAAAACTAGGTCTCGTTTTA
GGGATGTTTATAACCATCTT
TGAGATTATTGATGCATGGT
TATTGGTTAGAAAAAATATA
CGCTTGTTTTTCTTTCCTAG
GTTGATTGACTCATACATGT
GTTTCATTGAGGAAGGAAC
TTAACAAAACTGCACTTTTT
TCAACGTCACAGCTACTTTA
AAAGTGATCAAAGTATATCA
AGAAAGCTTAATATAAAGAC
ATTTGTTTCAAGGTTTCGTA
AGTGCACA
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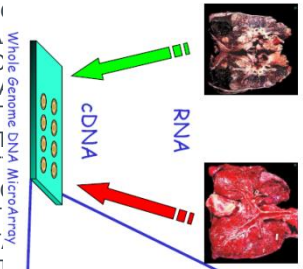
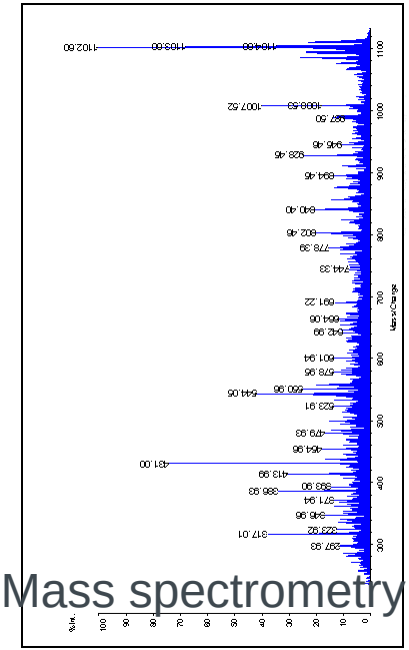
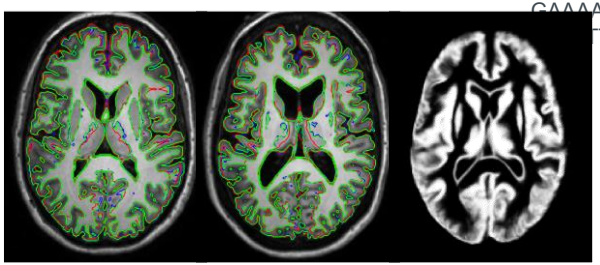
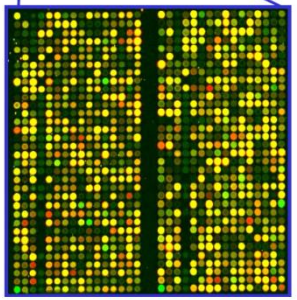
TTCC



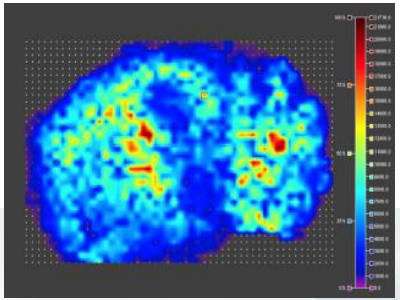


Mass spectrometry





Microarrays
(DNA chips)



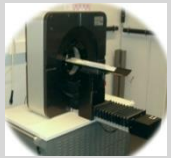
iMinds

Access to high end research infrastructure

Medical imaging

Small animal imaging

micro-MRI



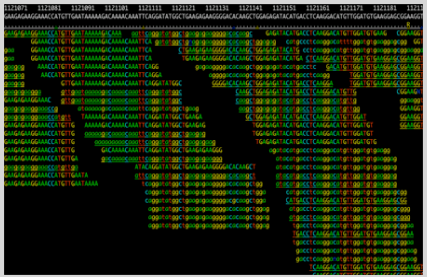
micro-PET

Hospital imaging

CT

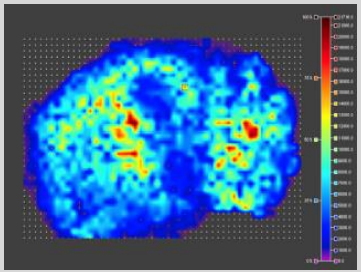
MR

KU Leuven Core Facilities



Genomics Core

Next Gen Sequencing GS FLX – HiSeq 2000 - PacBio



SyBioMa

Mass Spectrometry FT-ICR, LTQ, MALDI, QTof

Vlaams Supercomputer Centrum

ExaScience Lab
Intel Labs Europe
EXASCALE COMPUTING

nerf
Founded by
imec, K.U.Leuven and VIB

ACACATTAAATCTTATATGC
TAAAACTAGGTCTCGTTTTA
GGGATGTTTATAACCATCTT
TGAGATTATTGATGCATGGT
TATTGGTTAGAAAAAATATA
CGCTTGTTTTTCTTTCCTAG
GTTGATTGACTCATACATGT
GTTTCATTGAGGAAGGAAC
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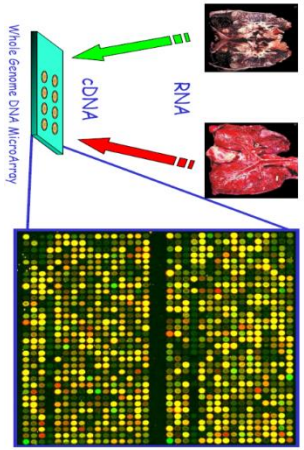
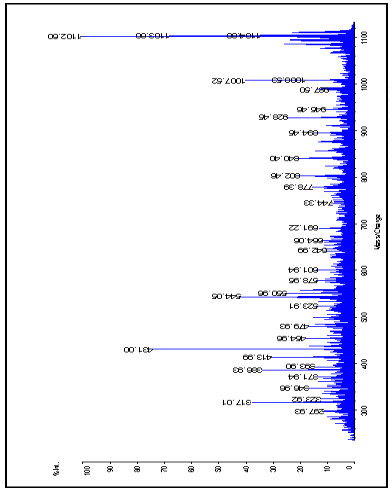
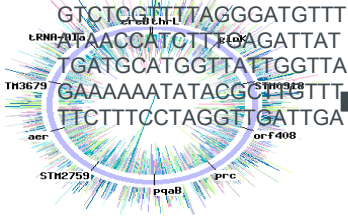
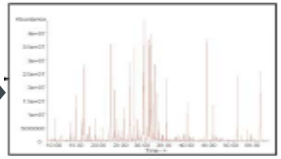
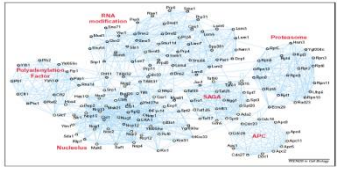










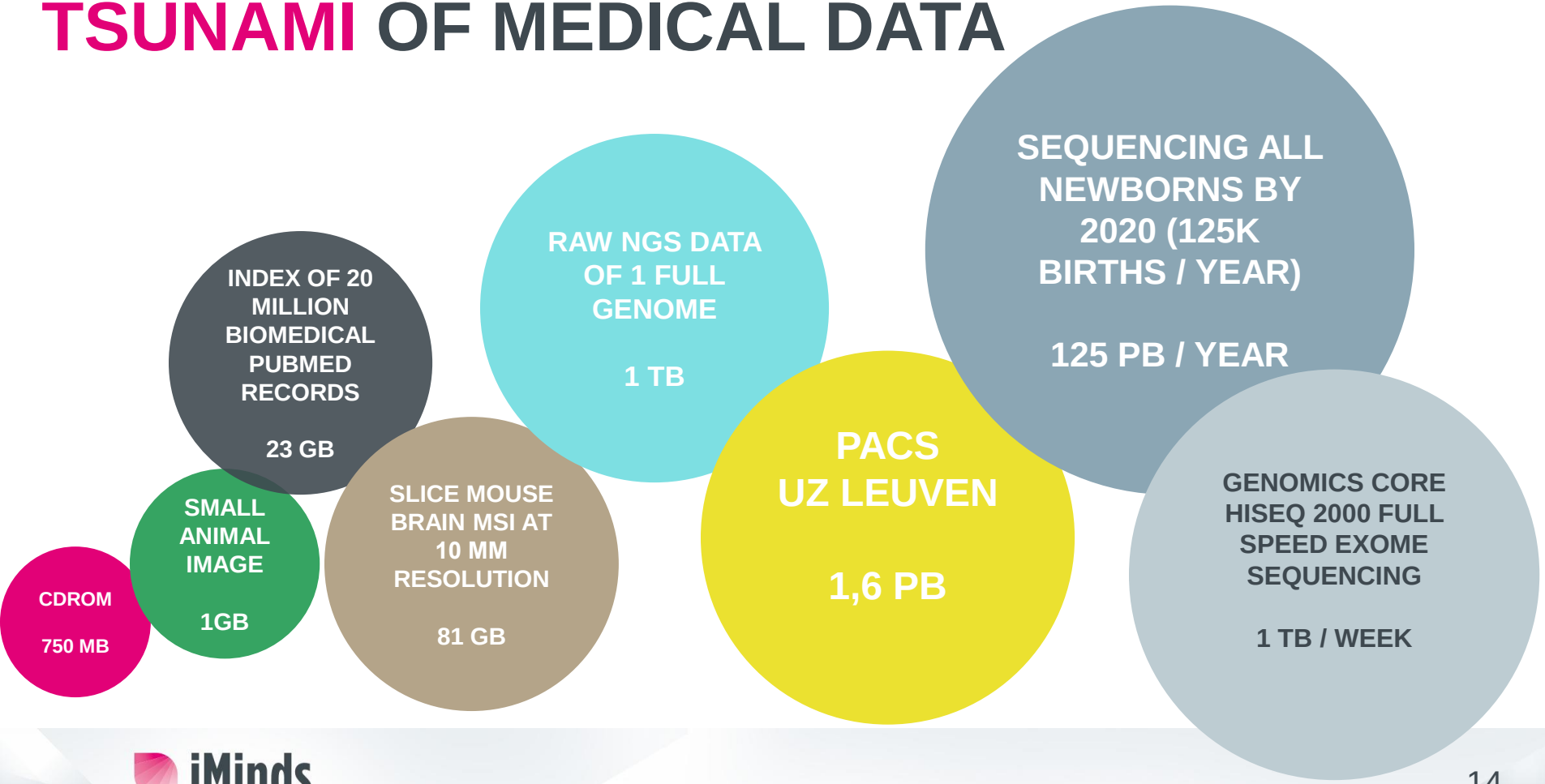
genome **transcriptome** **proteome** **metabolome** **interactome**

GS-FLX Roche
Applied Science 454

maf VIB
MicroArray Facility

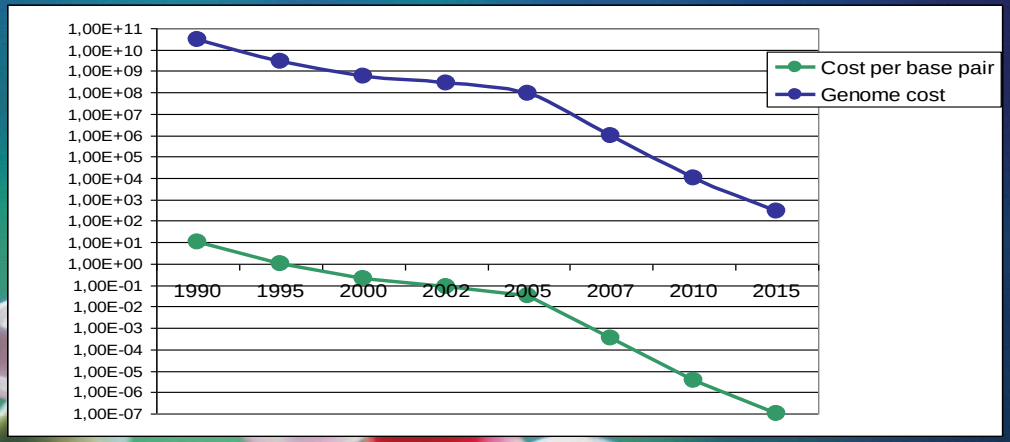
Prometa

TSUNAMI OF MEDICAL DATA



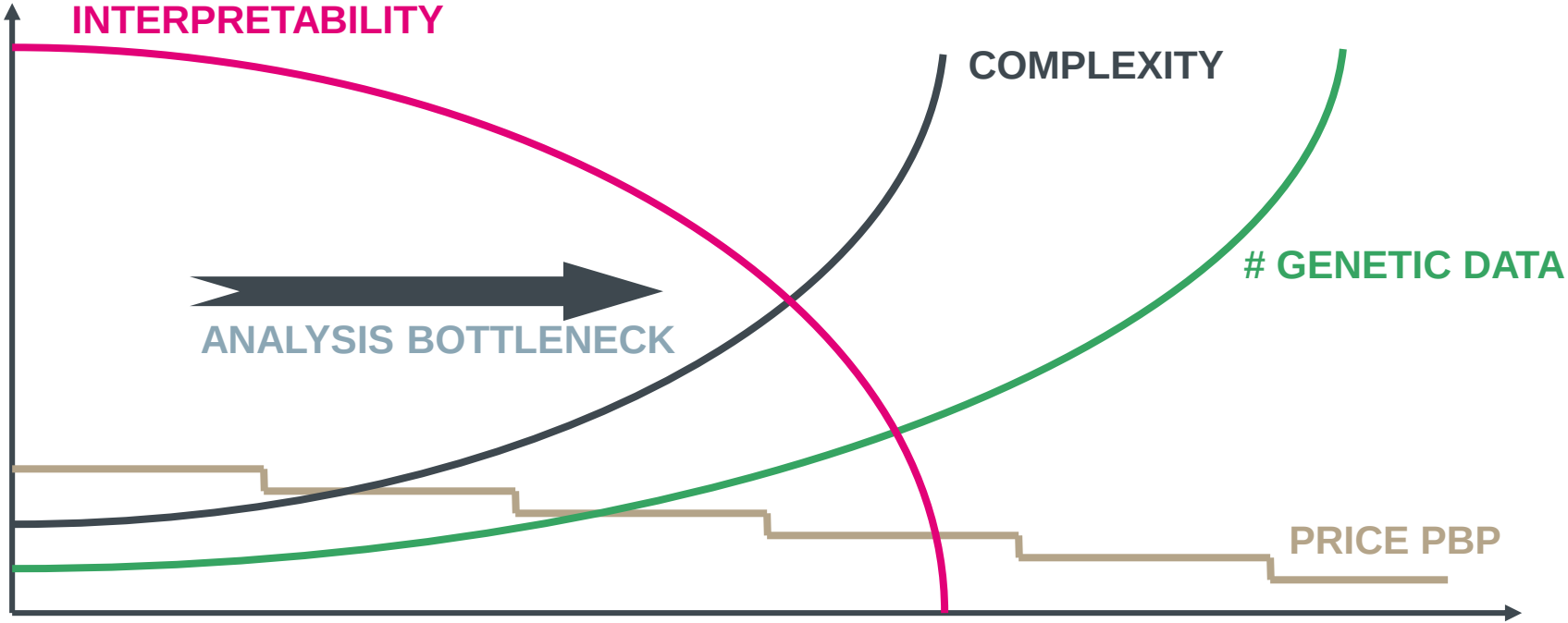
Genome data

- 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



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

INTERPRETABILITY OF GENOME DATA



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-data-science-will-do-more-for-medicine-than-all-biological-sciences-combined/

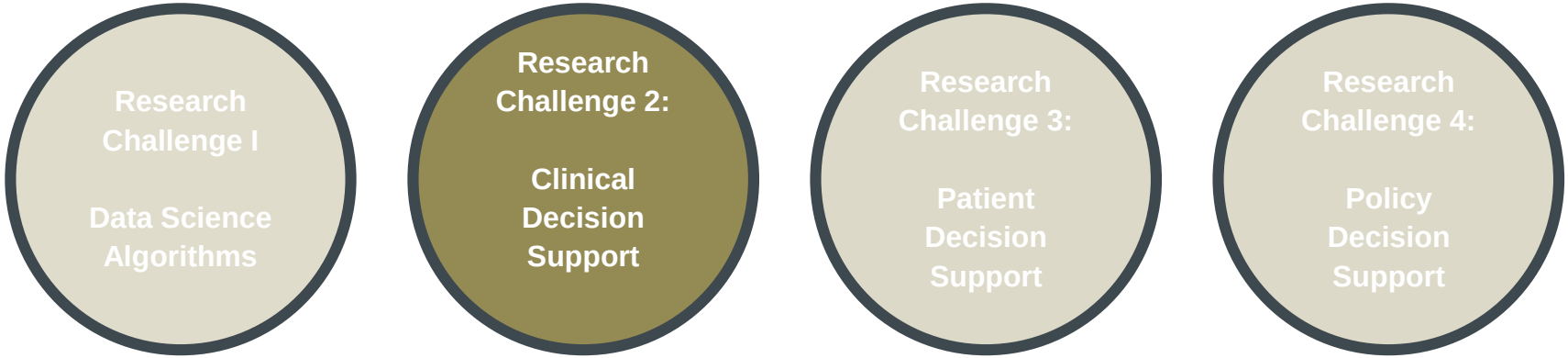
Generic data processing tasks

- Data preprocessing, denoising, normalization
- Clustering and classification; feature detection; profiling;
- Relevance detection, ranking
- Dynamic modelling, time series, longitudinal modelling
- Decorrelation, modelling, (Kalman) filtering
- Predictive analytics
- Vizualisation
- Heterogeneous data fusion
- Prediction, processing and monitoring

Numerical data science algorithms

- Mining
  - Regression, total least squares
  - Least squares support vector machines
  - Probabilistic algorithms (HMM, NN, Bayesian, Random Forests, Genetic algorithms, …)
  - Interactive data visualization
- Modelling
  - System identification, time series, longitudinal data modelling
  - Multilinear algebra, matrix & tensor decompositions
  - Blind source separation
  - nD signal and system theory
- Monitoring
  - control algorithms, automation
  - Signal processing, fault detection

R & D ROAD MAP


Research Challenge I
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Working with and for medical doctors


Intensive Care Unit

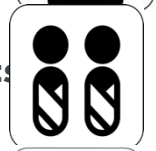

Radiology


Urology

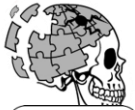

Cardiology


Pneumology


Orthopaedics


Neonatology


Dentistry

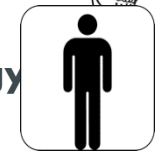

Forensics


Rehabilitation


Gynaecology

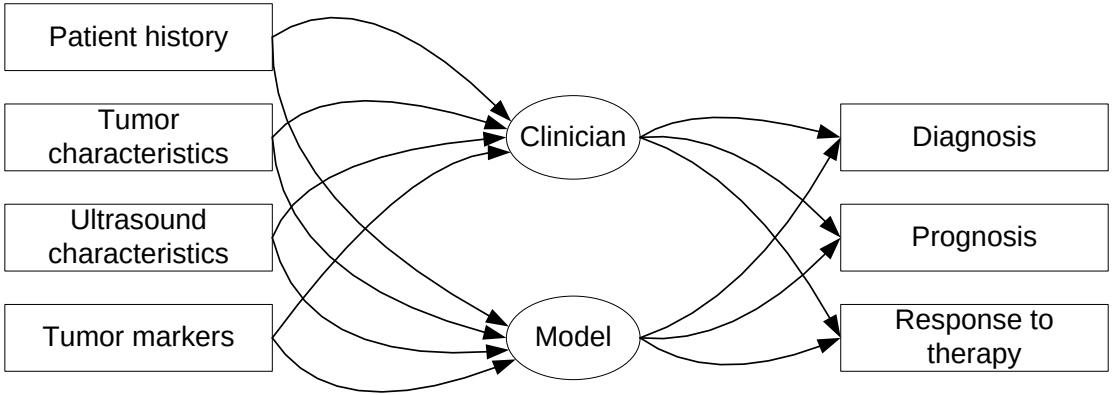

Radiotherapy


Neurology


Human Genetics

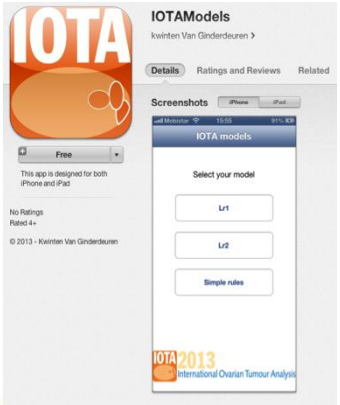

Oncology

Example: CDSS Ovarian Cancer



standardize ultrasonographic ovarian tumor analysis → models giving an indication of the probability of malignancy of an ovarian tumour based on 6 to 12 observed parameters

IOTA app to assess ovarian tumour malignancy: population based / standardized



IOTA 2013 International Ovarian Tumour Analysis

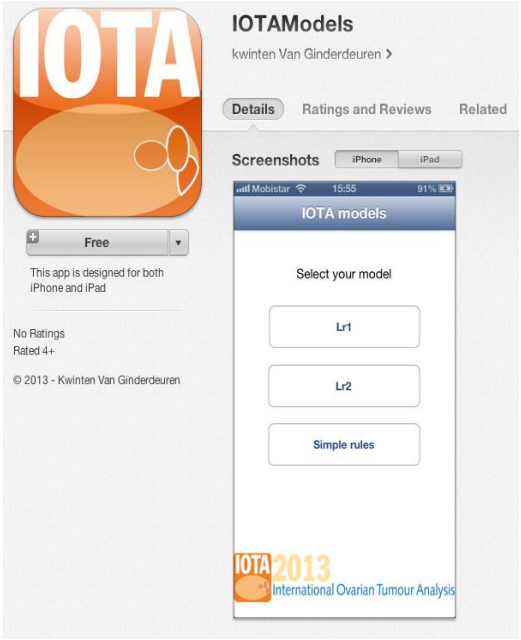
iMinds

General challenges & opportunities:

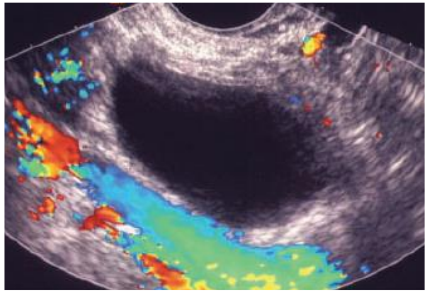
- Integration of various heterogeneous data sources
- Connect with Electronic Medical Records
- Need for population data

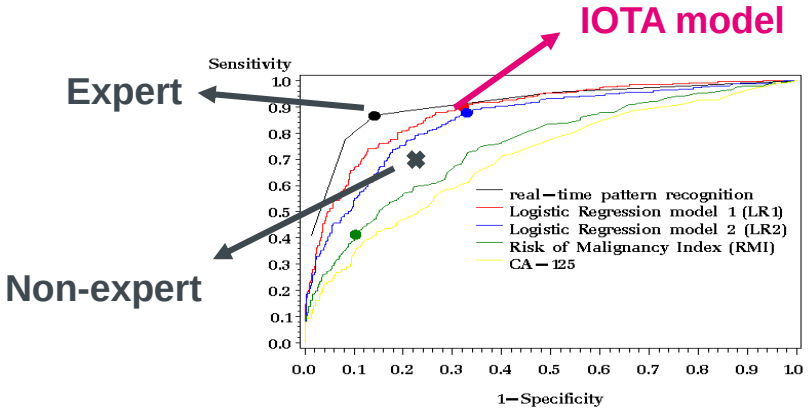
IOTA app available in iTunes app store and on http://homes.esat.kuleuven.be/~sistawww/biomed/iota/

PROFESSIONAL for clinicians



IOTA app to **assess ovarian tumour malignancy**: population based & standardized





IOTA app available in iTunes app store and on http://homes.esat.kuleuven.be/~sistawww/biomed/iota/

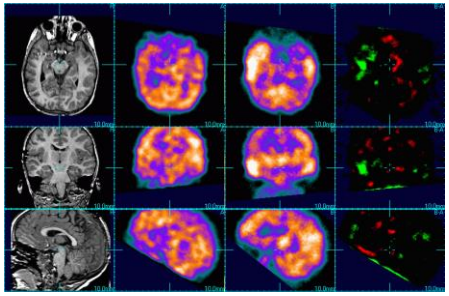
Example: Glycemia control in ICU

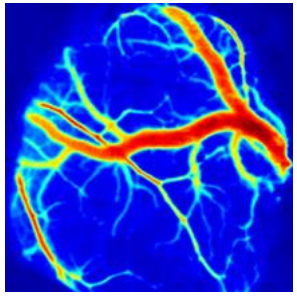
- 10 mio adult ICU patients / year (EU + US) (1-2 b$ market)
- ‘Tight Glycemic Control (TGC) in intensive care unit lowers mortality’
  - implement through LOGIC-Insulin: semi-automatic control system that advises nurse on insulin dosage and blood sampling interval aiming at TGC and avoiding hypoglycemia
- LOGIC-I randomized clinical trial (single-centre): compared with expert nurses, LOGIC-Insulin showed improved efficacy of TGC without increasing rate of hypoglycemia
- LOGIC-II randomized clinical trial (multi-centre): Start February 2014

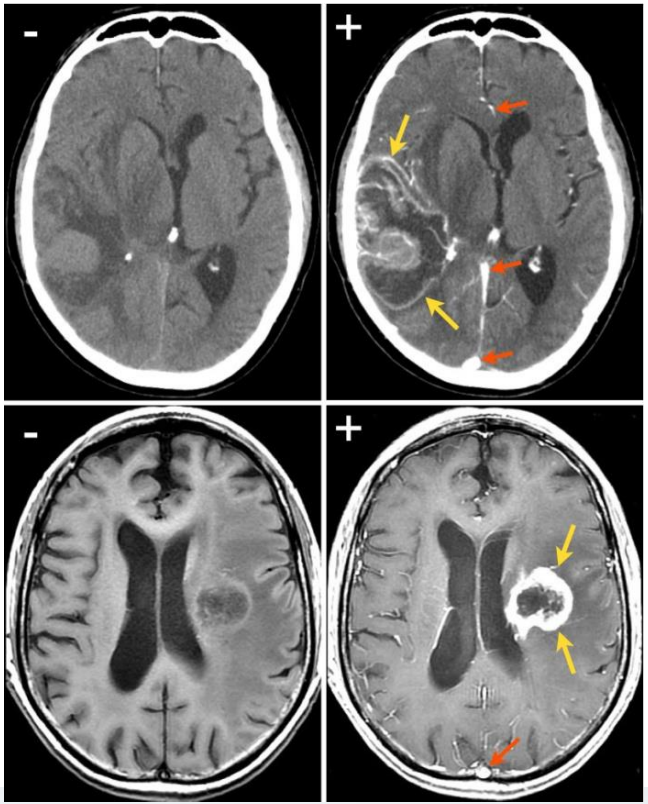
in collaboration with ICU UZ Leuven

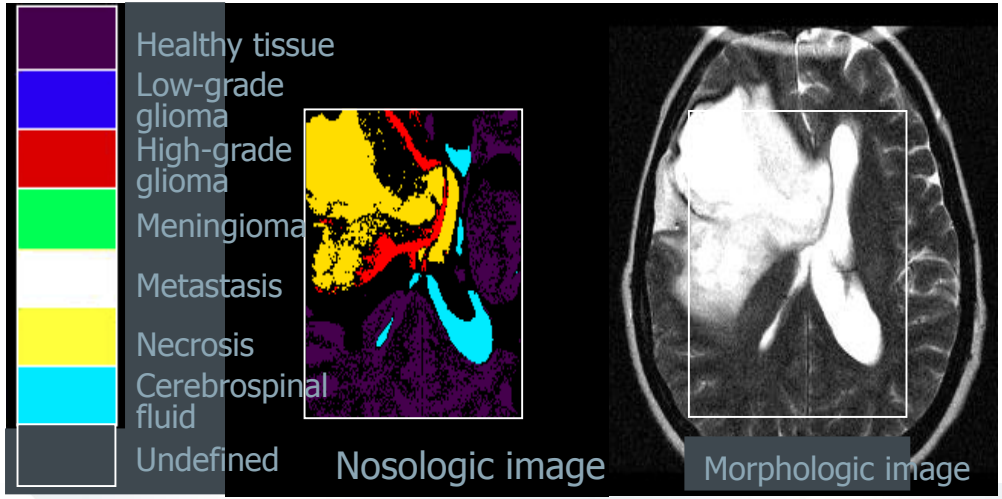
UZ LEUVEN

Medical imaging decision support

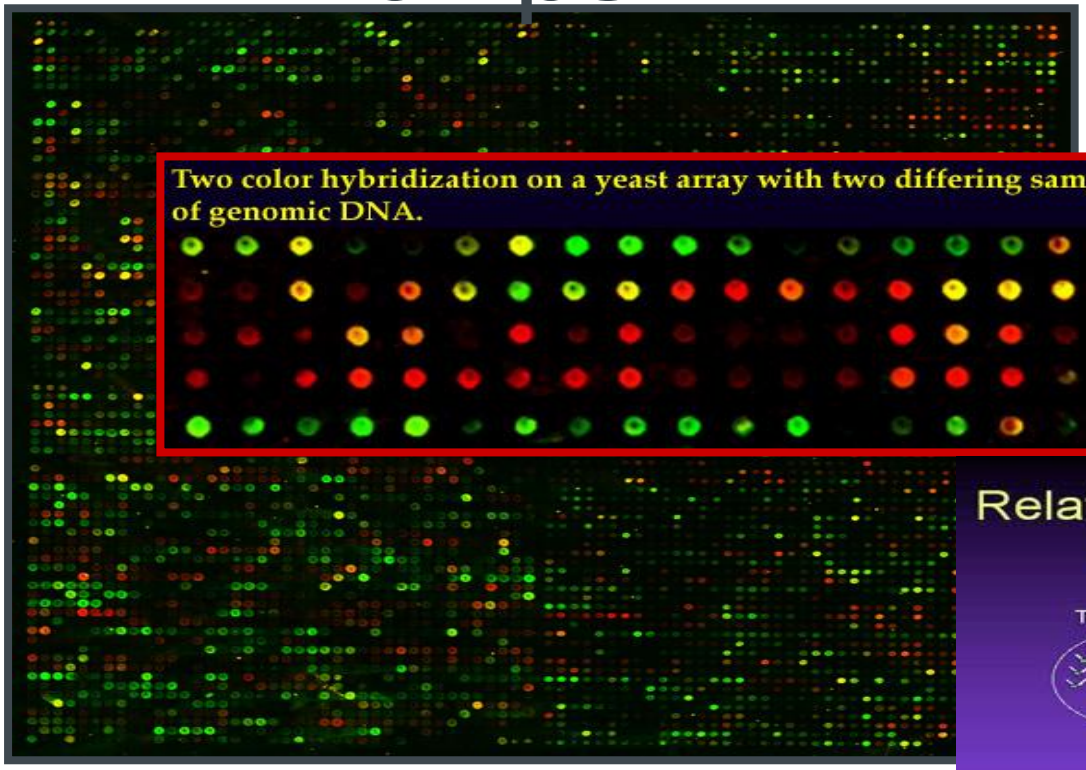




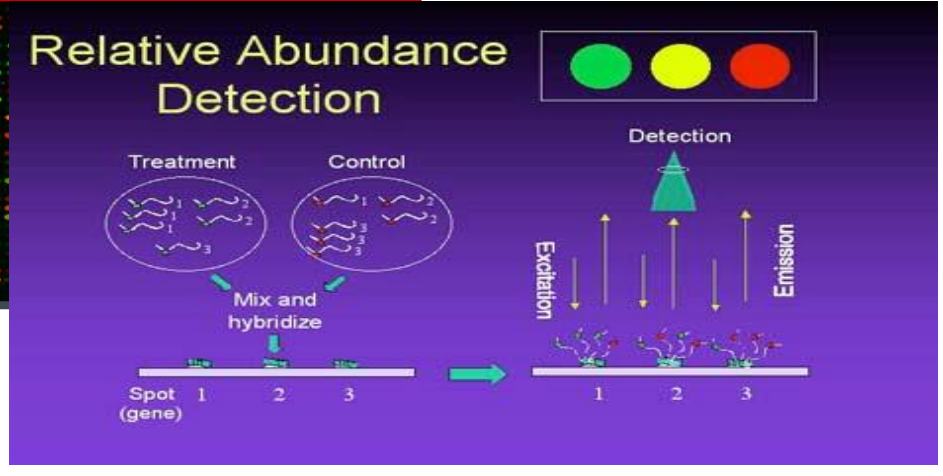




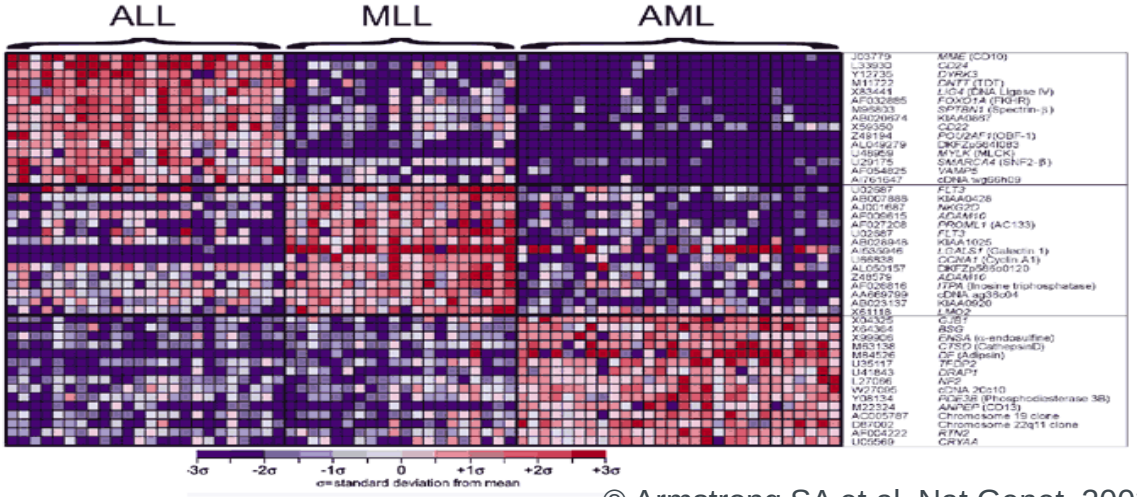
DNA-chips

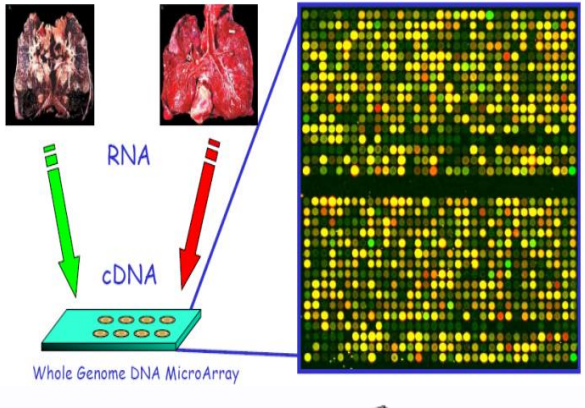


	Test	Ref.
	High	Low
	Low	High
	High	High
	Low	Low



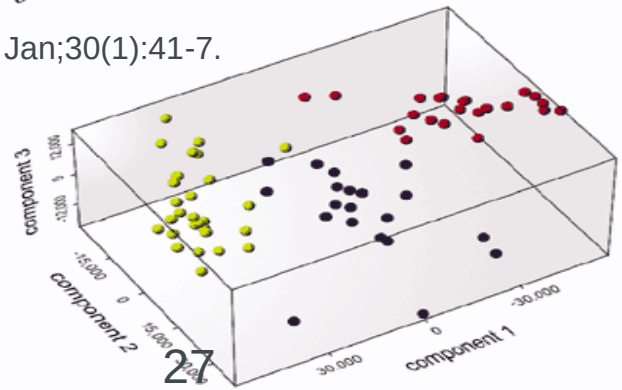
Example: Genomic markers for Leukemia





12 600 genes
72 patients

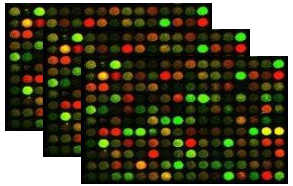
- 28 Acute Lymphoblastic Leukemia (ALL)
- 24 Acute Myeloid Leukemia (AML)
- 20 Mixed Linkage Leukemia (MLL)



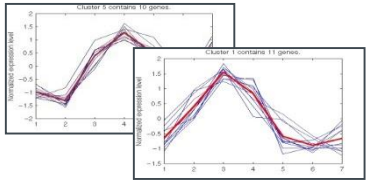

7

Example: Genomic Data Fusion

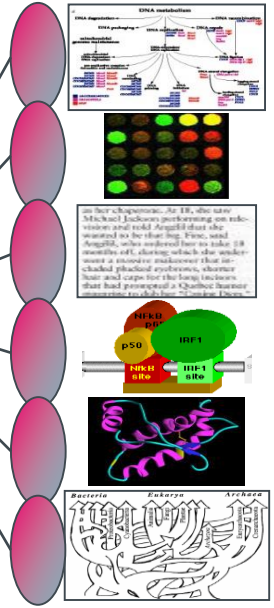
High-throughput genomics



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
PCBP2	ENSG00000111406
HOXB6	ENSG00000108511
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
	ENSG00000174891
	ENSG00000089195
C14orf10	ENSG00000092020
STX8	ENSG00000170310
	ENSG00000107671
MSH5	ENSG00000096474
CRH	ENSG00000147571
MID1	ENSG00000101871
	ENSG00000184508
	ENSG00000113460
TGFB3	ENSG00000119699
C1QR1	ENSG00000125810
NR4A2	ENSG00000153234
PDGFC	ENSG00000145431
PDGFC	ENSG00000145431
NR3C2	ENSG00000151623
NFYA	ENSG00000001167
	ENSG00000101898
C8orf4	ENSG00000176907
TM4SF13	ENSG00000106537
MMP3|MMP1	ENSG00000149968

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		HABP2
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

Endeavour: Aerts et al., Nature Biotechnology, 2006

Mutation prioritization

NOVEL GENETIC DISORDER

SEQUENCING

MUTATION PRIORITIZATION

PRIORITIZED VARIANTS

CONFIRMATORY EXPERIMENTS

DISCOVERY OF MUTATION CAUSING THE DISEASE

PERSONALIZED THERAPY

Proven record

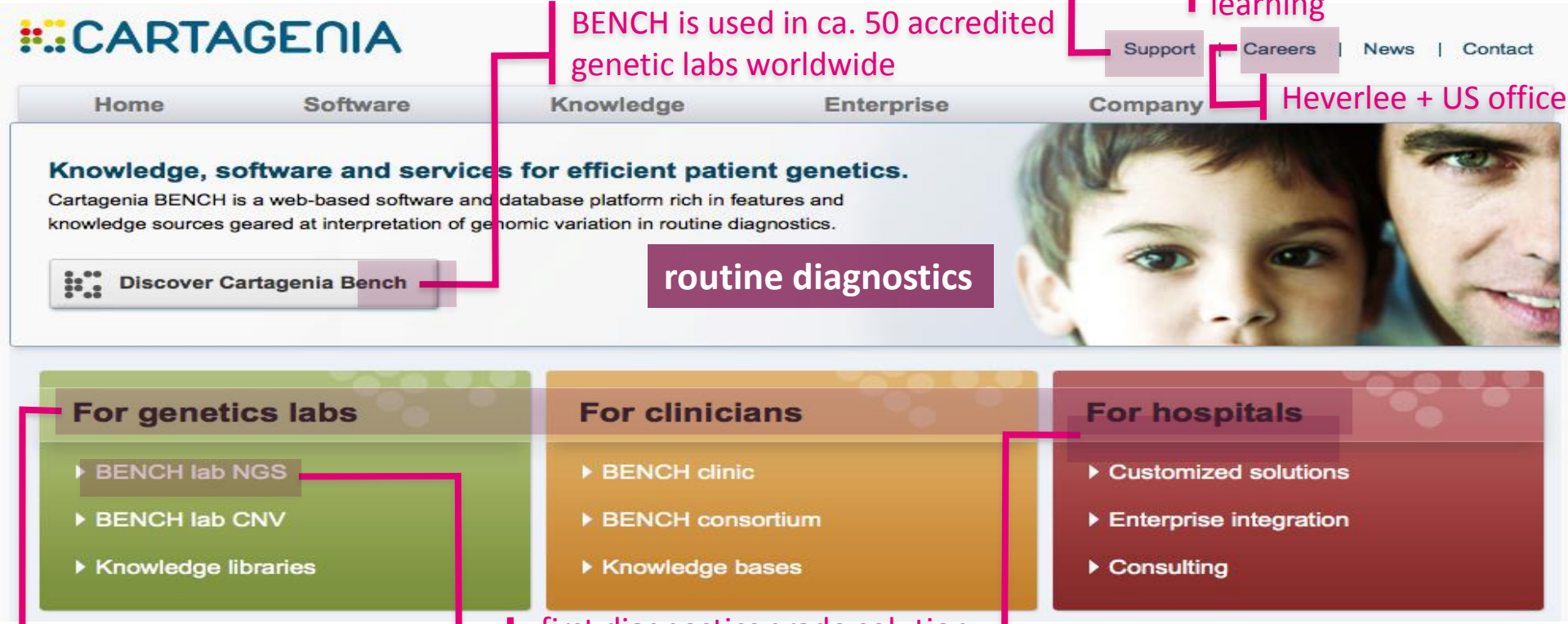
- Mining
  - Health and Clinical Decision Support systems/software
  - Clinical genomics:
  - Variant prioritization by genomic data fusion
  - Predicting in silico drug-target interaction
    - 10 000 compounds → 250 (preclinical) →5 (clinical) → (drug)
    - Mode of action; Side effect prediction; Drug repositioning;
    - Genome wide target ranking
- Predictive analytics in oncology
  - Cancer: Ovarian, breast, rectal, brain,…
  - Biomarkers
- Monitoring
  - Stress monitoring via EMG & HRV (Heart Rate Variability)
  - Neonatal brain monitoring
  - Glycemia control @ ICU
  - EEG-based epilepsy monitoring
  - Sleep monitoring
  - Event-Related potential analysis
- Signal Processing:
  - EEG: distributed SP, beamforming, probes SP, neuroimplants
  - Hearing Aids: binaural implants, wireless acousticnetworks
  - Wireless Body Area Networks
- Medical Image Processing

CARTAGENIA

- BENCH = web-based software and database platform for interpretation of genomic variation in routine diagnostics
- array-CGH + Next Gen Seq: first diagnostics grade solution for NGS data based diagnostics in the world
- SaaS go-to-market model
- Leuven + US office
- large customer base of diagnostic labs, private labs, academic institutes, and consortia in Europe, Northern America and Australia
- rare genetic disorders, extension towards cancer and prenatal

building on expertise in big data & machine learning

BENCH is used in ca. 50 accredited genetic labs worldwide



Heverlee + US office

tools for non-IT users

first diagnostics grade solution for Next Generation Sequencing data based diagnostics in the world

originating from research in rare genetic disorders in close collaboration with Centre Human Genetics UZ Leuven

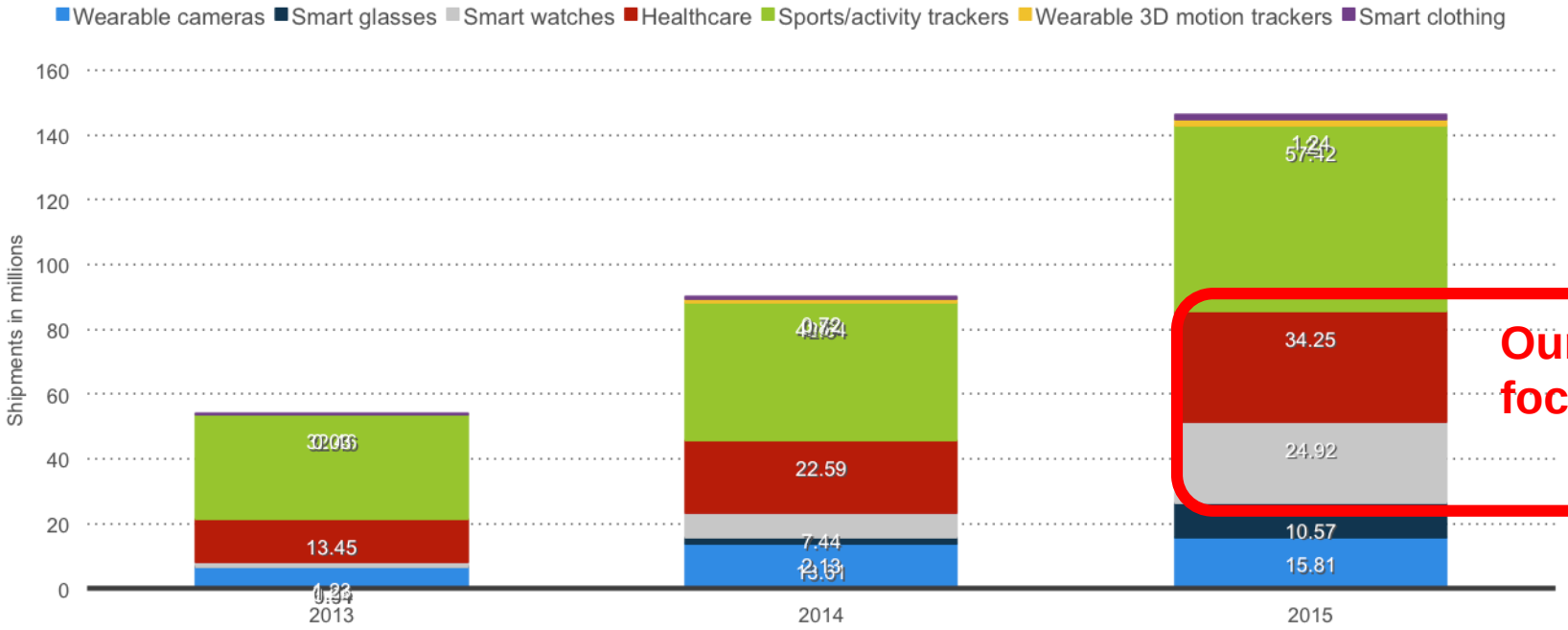
iMinds

R & D ROAD MAP


Research Challenge I
Data Science Algorithms
Research Challenge 2:
Clinical Decision Support
Research Challenge 3:
Patient Decision Support
Research Challenge 4:
Policy Decision Support

SERIOUS WEARABLES = SERIOUS BUSINESS

Worldwide shipments of wearable computing devices 2013-2015, by category



SERIOUS WEARABLES: 3 HURDLES

SERIOUS WEARABLES

Serious wearables = Wearables that are clinically relevant validated and tested, as part of a decision support system.

3 HURDLES FOR MARKET ADOPTION

1. Degree of clinical validation needed (class I, IIa,IIb or III)
2. How to bridge the second valley of death
3. Security and privacy aspects.

1

CLINICAL VALIDATION OF DEVICES & APPS

Device

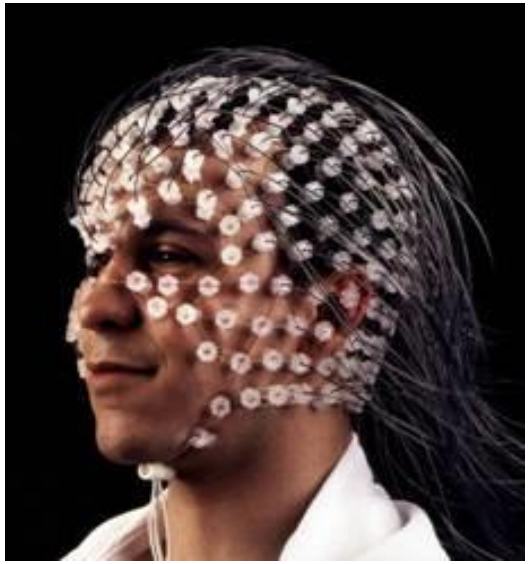
- Sensors
- Other hardware that measure and generate data

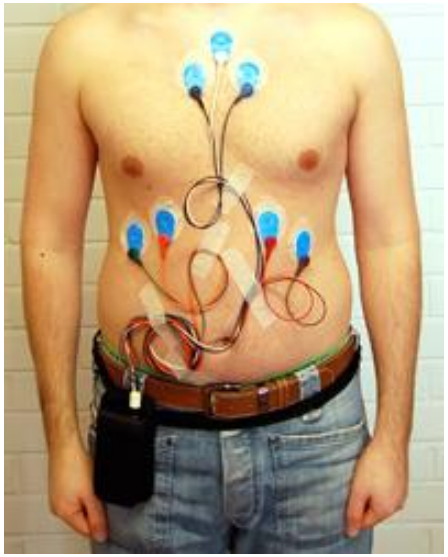
Apps/software

- Diagnose or support in diagnosis
- Sleep, stress, cardio…

Which class type of medical device: I, IIa or IIb (class III is mostly for implants such as defibrillators)?

Clinically validated wearables





R & D ROAD MAP


Research Challenge I
Data Science Algorithms
Research Challenge 2:
Clinical Decision Support
Research Challenge 3:
Patient Decision Support
Research Challenge 4:
Policy Decision Support

Policy mining

Collaboration modi

Direct contract research

Consortia: ICON, Cluster Policy, IWT, H2020, KIC Health

Service Catalogue Health Lab

Health House


INDUSTRIAL PARTNERS
reMYND
Janssen
PATHOMATION
BARCO
Visibly yours
MINDBYTES
YORBODY HEALTH & COACH
DELHAIZE GROUP
AML
CARTAGENIA
HistoGeneX
icoMetrix
Quantifying your Images
CORILUS
Path licon
health CONNECT
ICT EXPERTISE THAT CARES
Materialise
brandnewhealth
we change behaviour
REGIONAL & EUROPEAN NETWORKS
vka health community
we care for innovation
FlandersBio
BUILDING BIOTECH BRIDGES
ELAT
EINDHOVEN LEUVEN AACHEN TRIANGLE
dsp valley
designing smart products
anacura
ADVISING HEALTH DELIVERING OUTCOMES
Flanders Smart Hub
Microsoft
Innovation Center Vlaanderen
LEUVEN.INC
INNOVATION NETWORKING CIRCLE
UNIVERSITIES & STRATEGIC RESEARCH CENTRES FLANDERS
GOVERNMENT & HEALTHCARE STAKEHOLDERS
CEBAM
EBMPracticeNet
iMinds
imec
ExaScience Lab
Intel Labs Europe
EXASCALE COMPUTING
vito
vision on technology
e Health
isp wiv
WETENSCHAPPELIJK INSTITUUT VOLKSGEZONDHEID
INSTITUT SCIENTIFIQUE DE SANTÉ PUBLIQUE
TREF PUNT ZELF HULP
KU LEUVEN
GENOMICS CORE
UZ LEUVEN
VSC
Vlaams Supercomputer Centrum
Vlaams Agentschap Zorg & Gezondheid
Belgian Cancer Registry
domus medica
vitalink
gegevens delen, van vitaal belang
Flanders'Care
Event partner tot 2014
nerf
Founded by imec, K.U.Leuven and VIB
SyBioMa
LMTC
BioSCENTer
SCience, ENgineering & Technology
liet
LEUVEN ICT
KU LEUVEN
Vlaams Patiëntenplatform
IMA-AIM
CHRISTELIJKE MUTUALITEIT
Intego
UZ LEUVEN
iMinds

IMINDS HEALTH LAB: SERVICE CATALOGUE

EVIDENCE-BASED VALIDATION

- Assist in certification acquisition
- Assist in clinical trials for software/apps
- Process validation
- Device validation
- Validation of analytical methods

LIVING LAB USER RESEARCH

- Qualitative and quantitative surveys
- Community/panel management
- Construe user experience
- Co-creation sessions

INTEROPERABILITY

- Comply and test to health standards
- Define use cases
- Facilitate mini labs
- Project coordination
- Education

BUSINESS MODELLING

- Define business cases
- Analyse value network (user ⇔buyer ⇔ payer)
- Business development health support (for start-ups/spin-offs)

FUNCTIONAL HEALTH KNOWLEDGE

INFRASTRUCTURE

METHODOLOGY

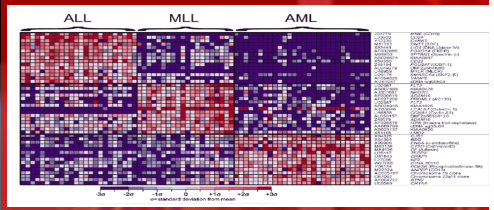
ACCESS TO & DISCLOSING OF DATA

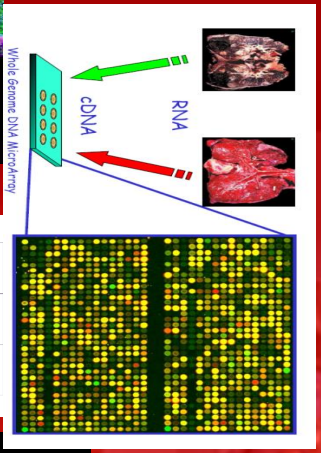

HOUSE


HEALTH
HOUSE

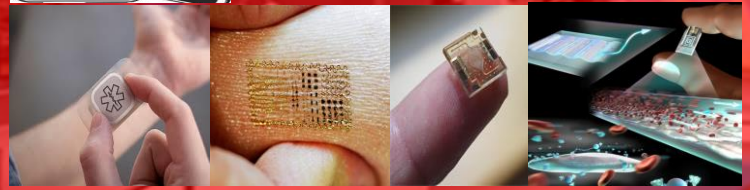
Robotics

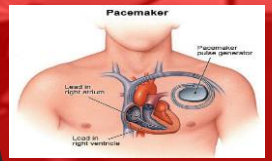
Omics big data

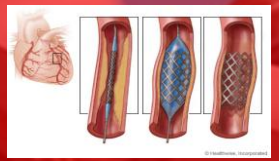




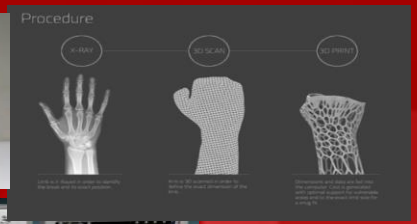
Wearables & Implants

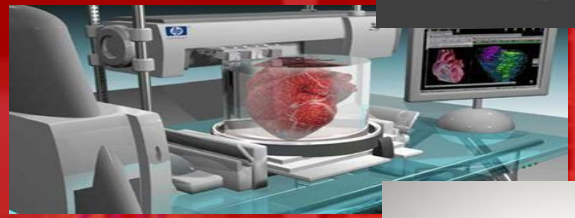




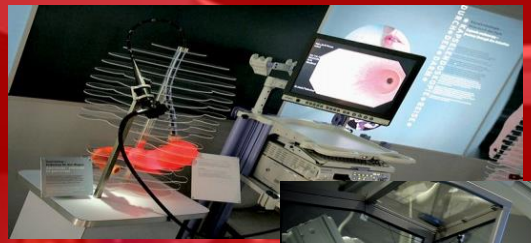


3D printing

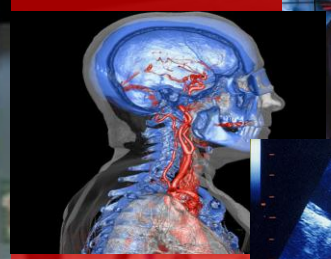


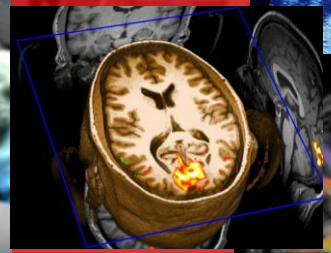


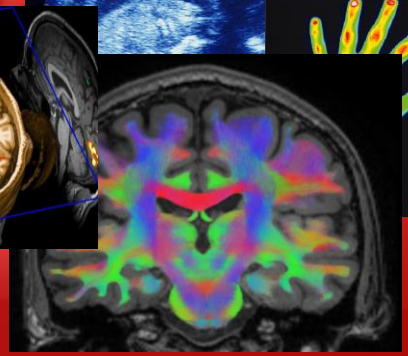
Computer assisted surgery



Visualization







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

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.)

Clinical Decision Support

Bart De Moor

ESAT-STADIUS KU Leuven