

KU LEUVEN



E-medicine

Impact van ICT op de gezondheidszorg

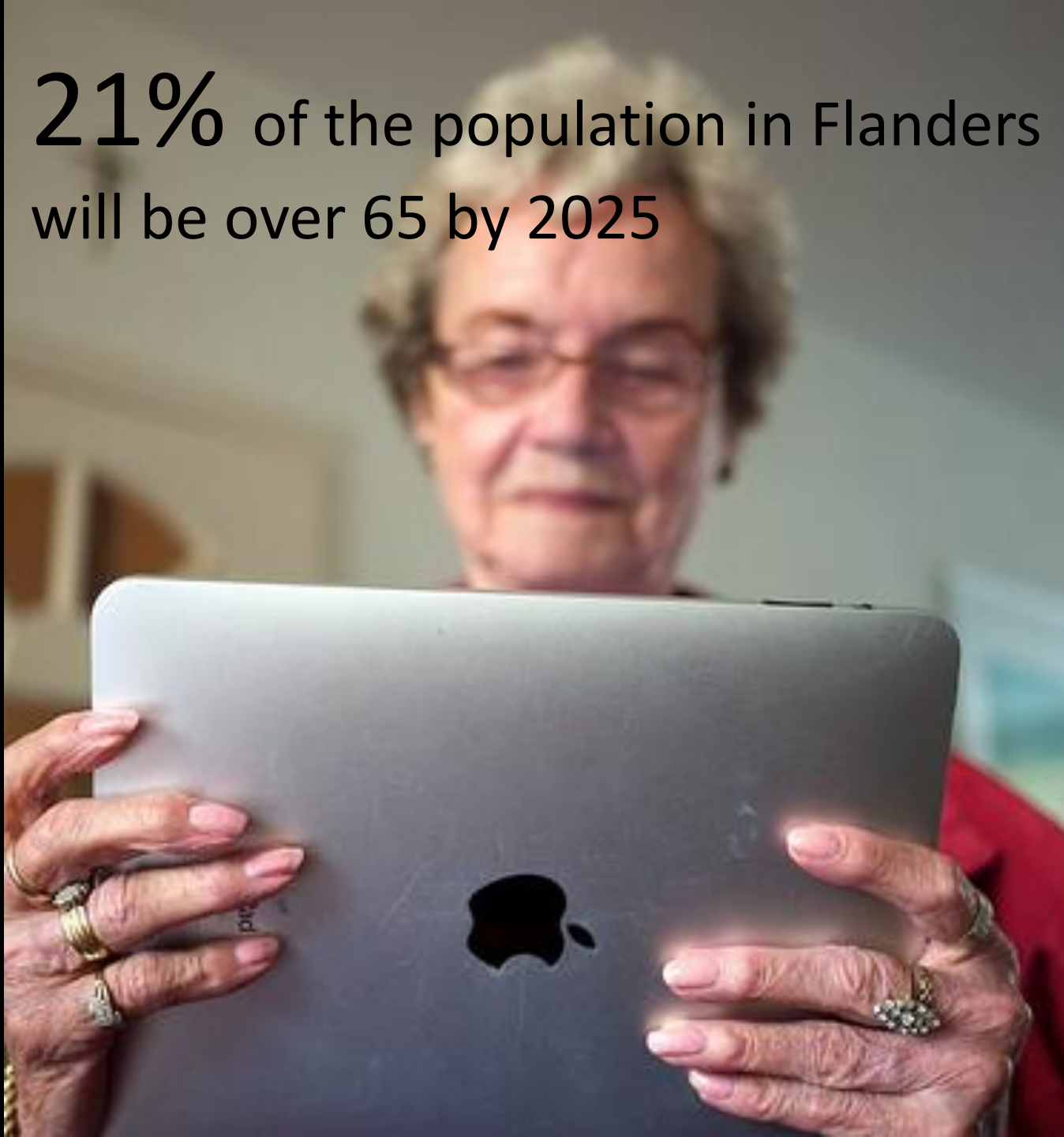
9 oktober 2012
Kulak

Bart De Moor

Outline

- Trends: societal & technological
- Decision support analytics for Professionals, Patients & Policy Makers
- iMinds – KU Leuven Future Health Department: who & what
- Track record & examples

21% of the population in Flanders
will be over 65 by 2025



Safari File Edit View History Bookmarks Window Help
kiesBeter.nl - Zorgverleners

http://www.kiesbeter.nl/zorgverleners/ Google

Apple Yahoo! Google Maps YouTube Wikipedia News (330) Popular


kiesBeter.nl
wijst u de weg in de zorg

Hoog contrast Sitemap Contact Help Zoeken:

Home Actueel Medische informatie Patiënteninformatie **Zorgverleners** Zorgverzekeringen

Home > Zorgverleners


Aandoening



Zoek bij welke zorgverlener u terecht kunt met deze aandoening.

[Aandoening >](#)


Kwaliteit



Kiezen voor kwaliteit? Bekijk hoe uw ziekenhuis, zorginstelling of zorgorganisatie scoort.

[Kwaliteit >](#)

Wachttijden



In welk ziekenhuis bent u het snelst aan de beurt?

[Wachttijden >](#)

Snel zoeken

Zorgverlener

Zoek op plaats of postcode

of

Zoek op naam

[Zoek zorgverlener](#)

Over zorgverleners

Onafhankelijke informatie over zorgverleners en zorginstellingen.

[Lees verder >](#)

[f](#) [t](#) [in](#) [H](#)


Meer over

- ▶ Info over zorgverleners
- ▶ Info over zorginstellingen
- ▶ Inspectierapporten
- ▶ Klachten over zorgverleners

Zie ook

- ▶ Lijst met zorgverleners met een beroepsverbod
- ▶ Instellingen en zorgverleners met een maatregel, bijvoorbeeld verscherpt toezicht

Uitgelicht




Online hulp bij psychische klachten

Op internet zijn voor verschillende psychische klachten verschillende sites waar u hulp kunt krijgen.

[Lees Verder >](#)

Speciale site



Voor jou

Kieswijzer voor mensen met een verstandelijke beperking. Zoek jij naar werk, een plek om te wonen of een hobby?.

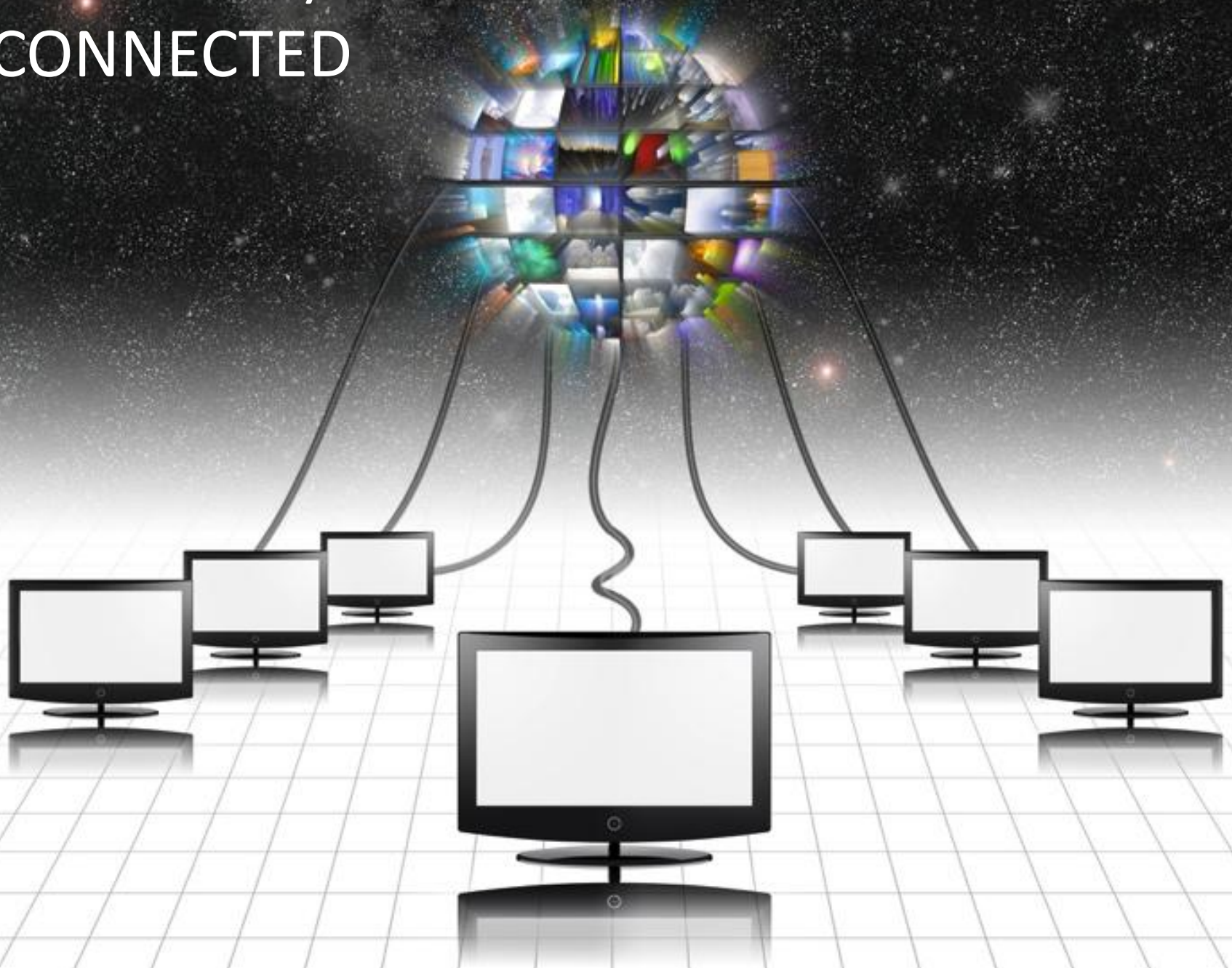
[Lees Verder >](#)

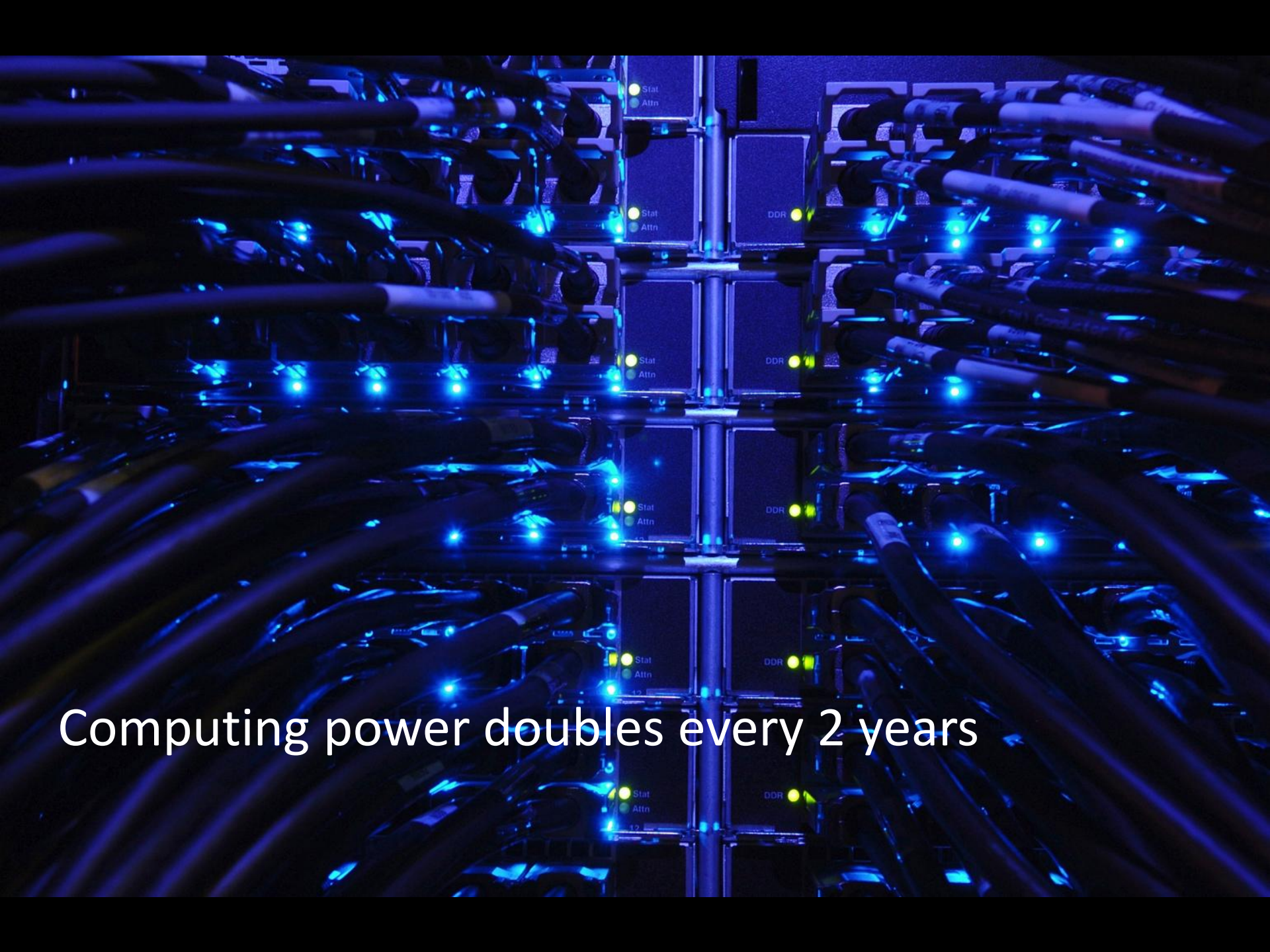
Colofon Bronnen Privacy & disclaimer [RSS](#) Toegankelijkheid

Feedback

Patients want to make their own health care choices

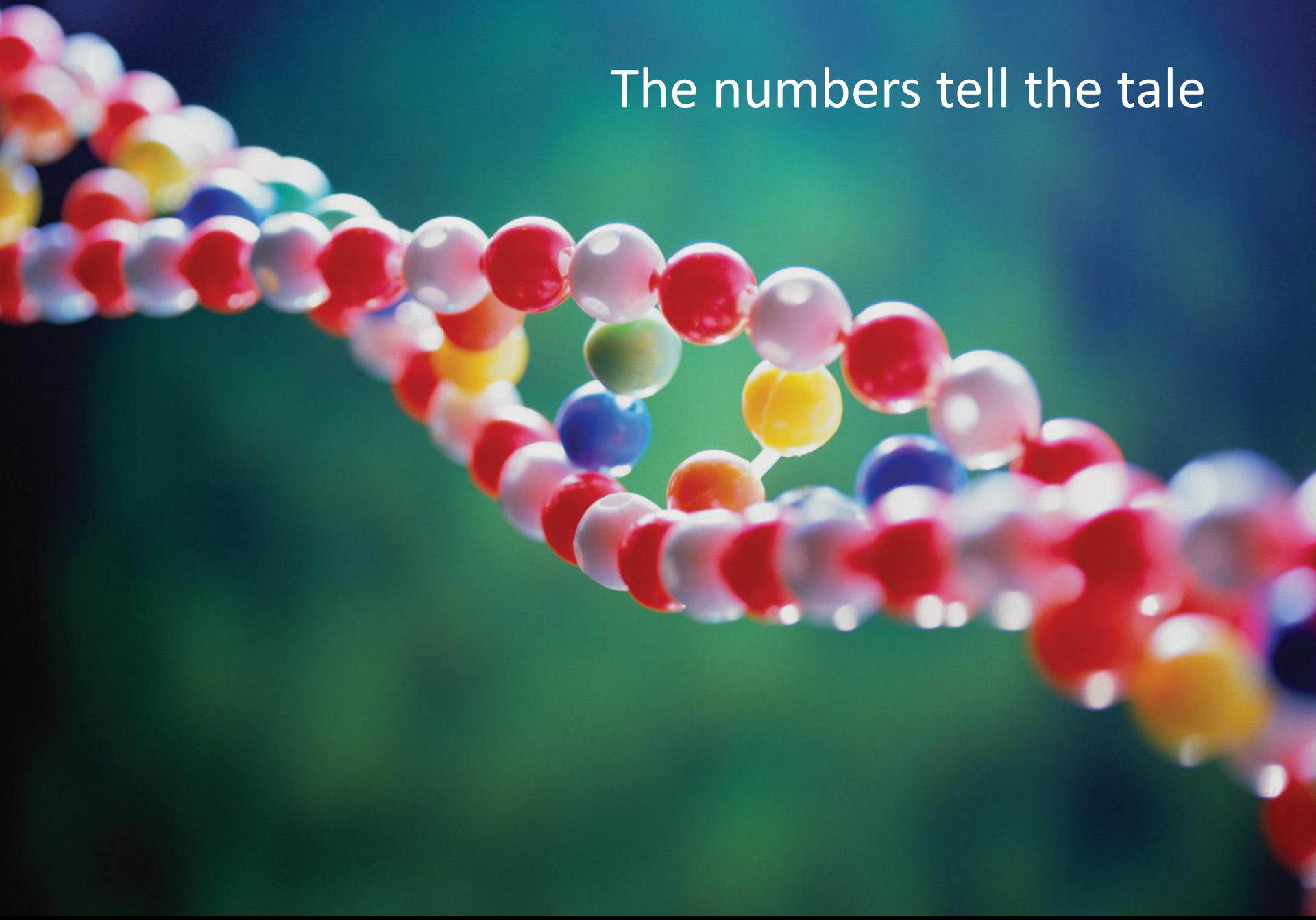
We are always
CONNECTED



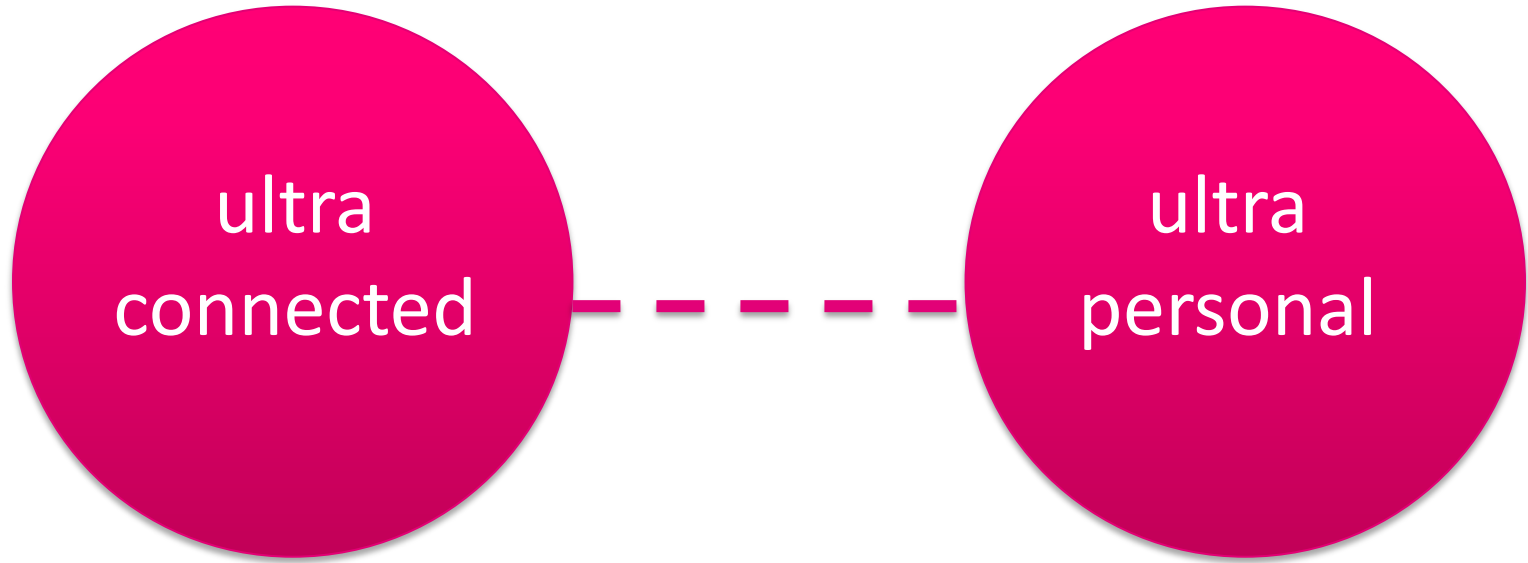


Computing power doubles every 2 years

The numbers tell the tale



The Future of Health Care



tap into the **whole** of
medical knowledge

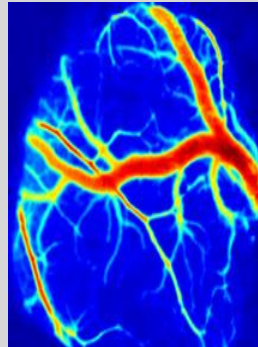
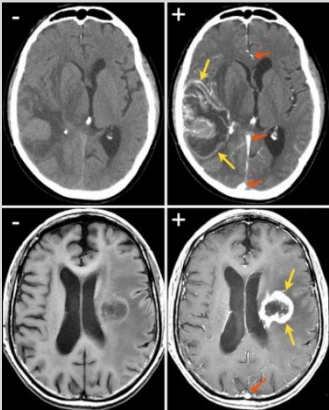
to find the perfect
solution for **you**

DATA

Decision Support Analytics

Professional (Clinical)

- interpretation of wide range of data
- demand-driven, user-centred, with future vision



Patient

Policy

Decision Support Analytics

Prof.

Patient



- 'online' telemonitoring



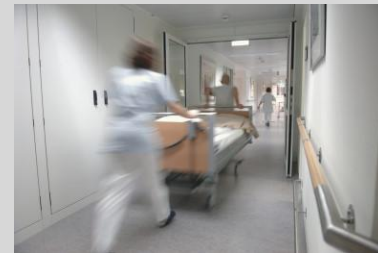
- 'patient empowerment':
e.g. disease management
for patients with chronic
diseases using new media

Policy

- data mining to identify best practices, monitor overconsumption, improve transparency ...



- hospital logistics





SISTA

Future Health Department decision support analytics



PSI

data



information



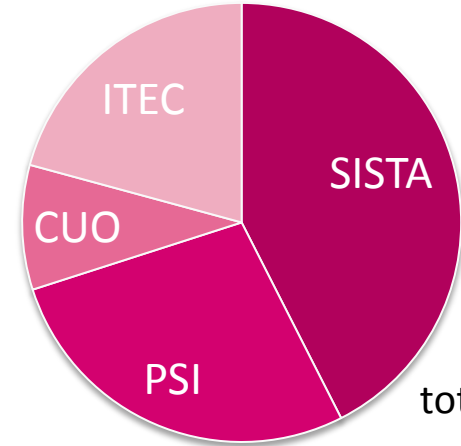
CUO



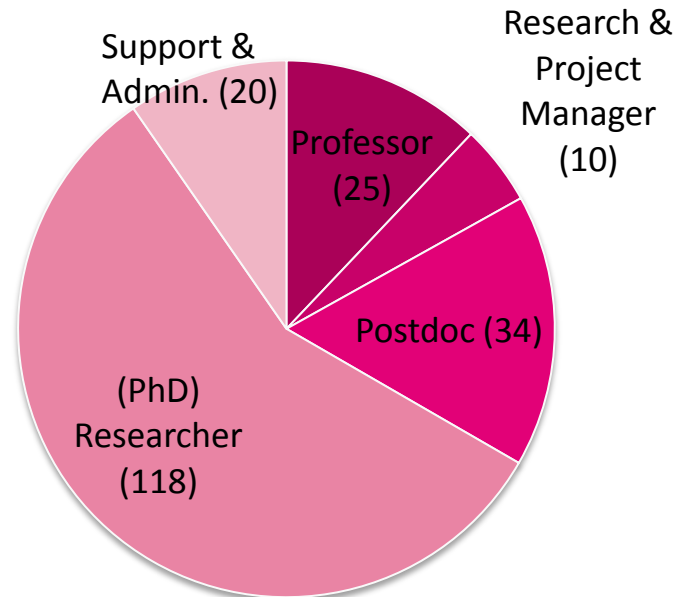
user



Interdisciplinary Research on Technology, Education & Communication



total = 207





- bioinformatics & machine learning
- biomedical data processing
- (audio) digital signal processing
- Fac. Engineering - Dept. ESAT



- medical image computing
- computer vision
- Fac. Engineering - Dept. ESAT
- located in UZ Leuven



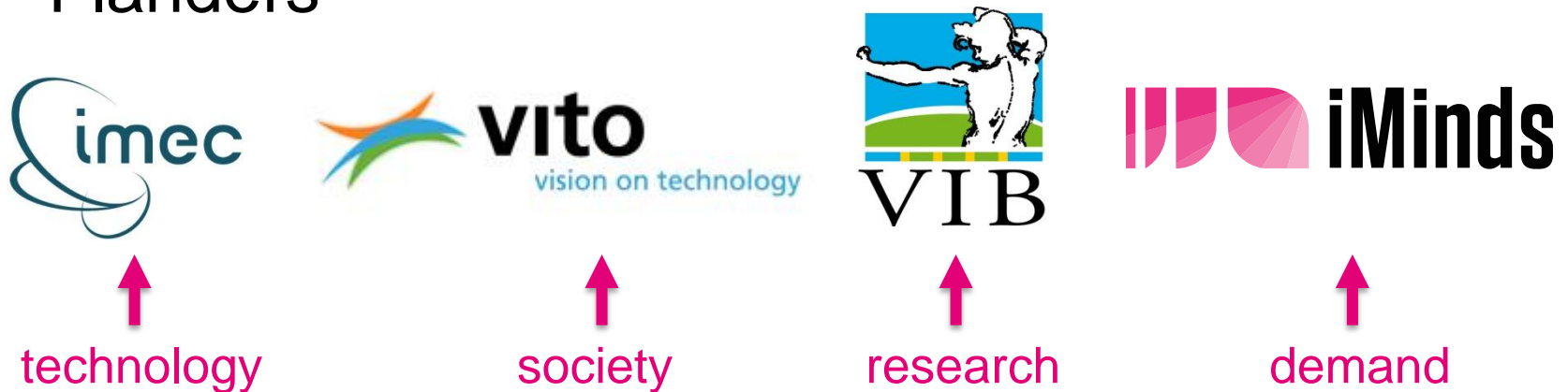
- user experience research
- Fac. Social Sciences



- bioinformatics & computer science
- education
- linguistics
- statistics
- KU Leuven campus Kortrijk

Positioning of iMinds

- 1 out of 4 strategic research centers (SOC) in Flanders



- Virtual: expertise of university research groups
- Link between research and industry
 - Innovative **ICT** services and applications in close collaboration with government and industry

5 iMinds research departments

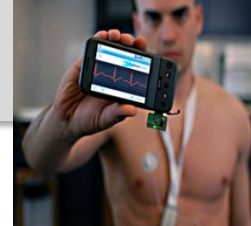
Future Internet



Security



Future Health

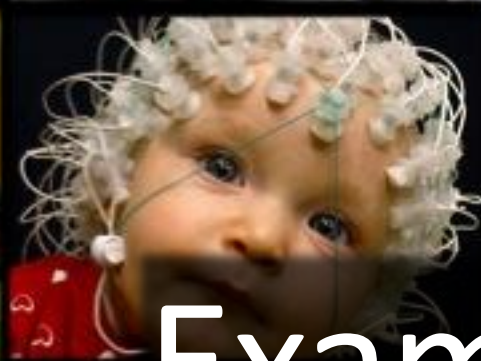


Digital Society

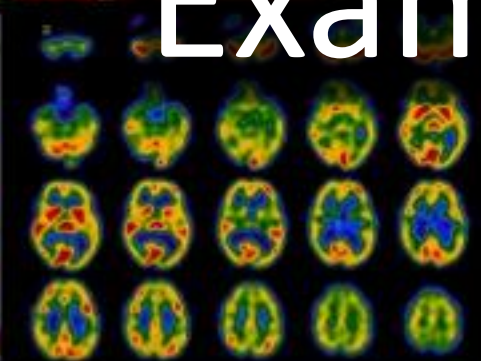
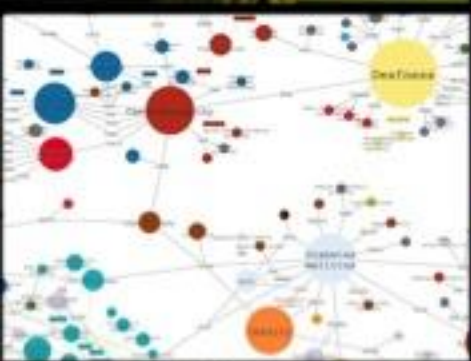


Future Media





Examples



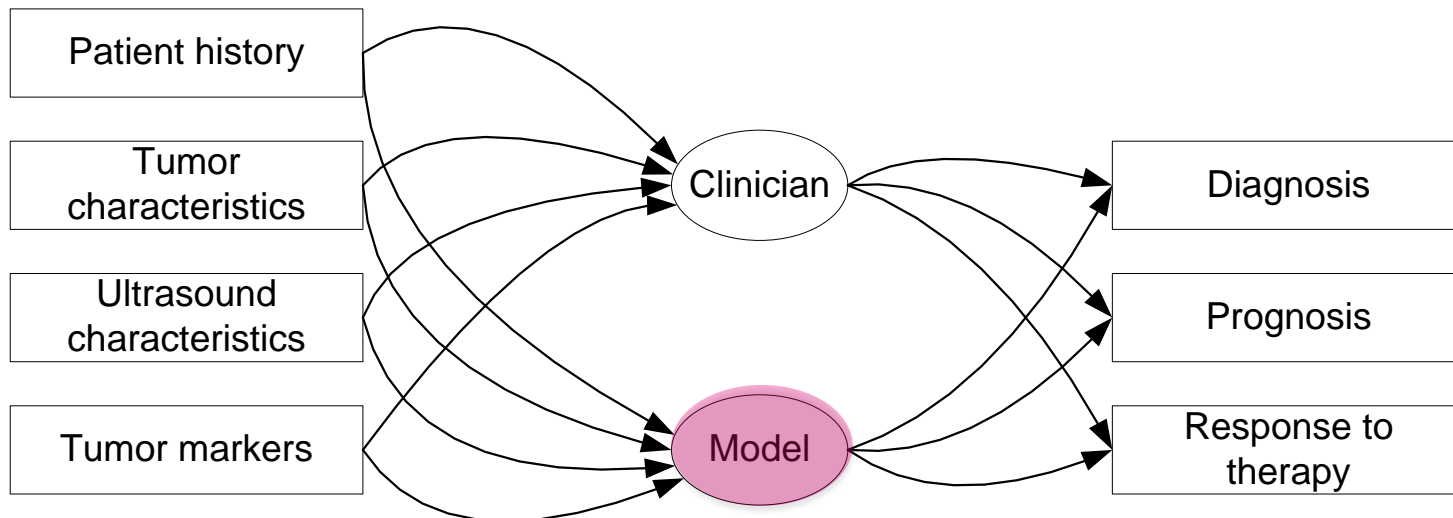
R

Clinical Decision Support

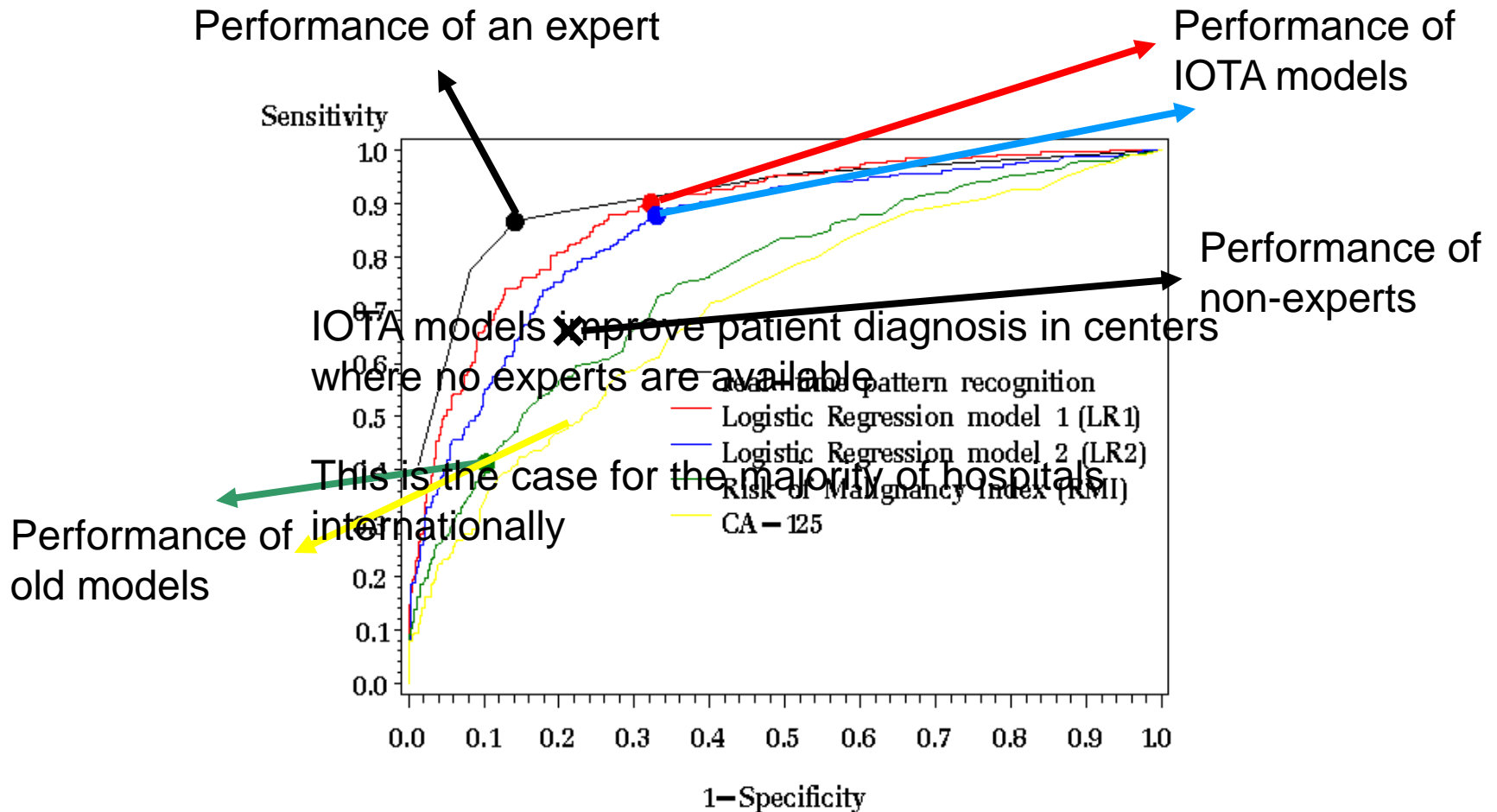
- IOTA: International Ovarian Tumor Analysis Group
- IETA: International Endometrial Tumor Analysis Group
- Genetic fingerprints to distinguish leukemia subtypes
- Biomarker panel for determining endometriosis status
- Interpretable clinical decision support
- Mass Spectral Imaging
- Tumor Classification via MRS

IOTA - International Ovarian Tumor Analysis Group

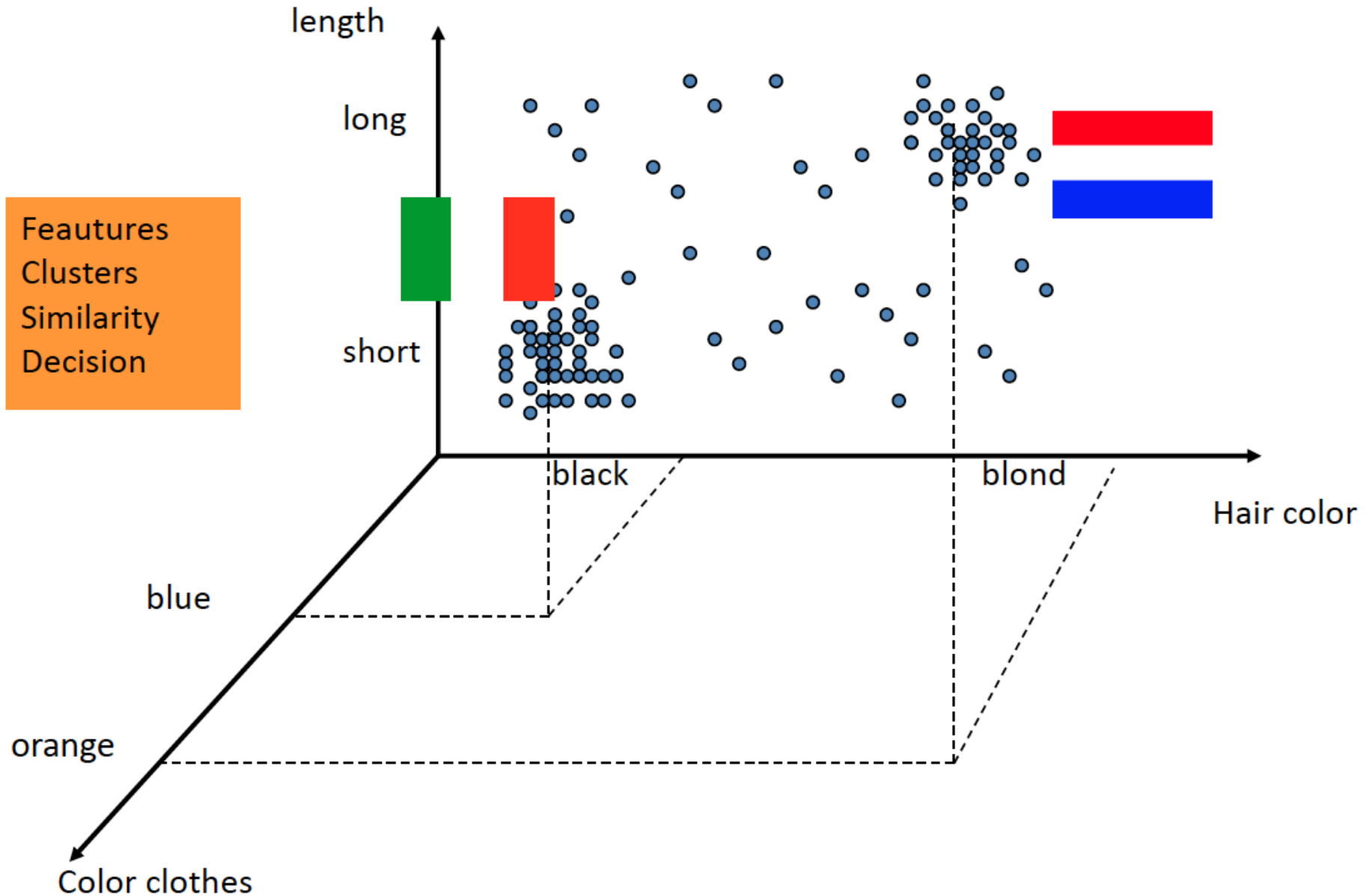
- goal = making it easier to diagnose ovarian cancer
 - help clinicians take decisions on diagnosis, prognosis and therapy response
 - make use of patient data and population information (patient biobank & database, literature ...)



IOTA - International Ovarian Tumor Analysis Group

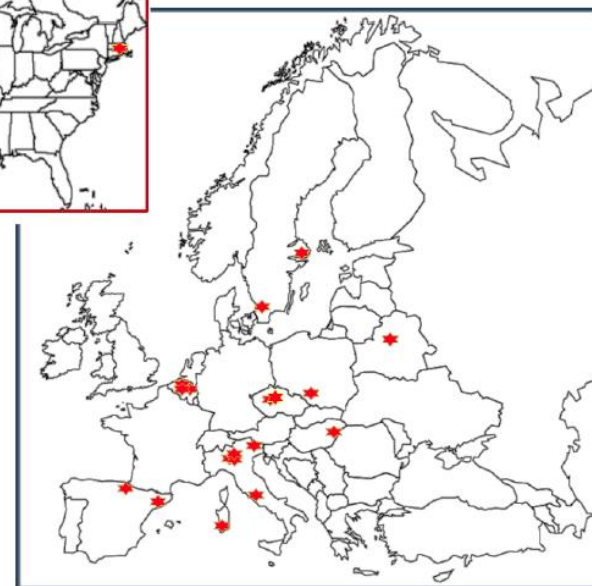


Method: Clustering & Classification



IETA: International Endometrial Tumor Analysis Group

- international group of gynaecologic ultrasonographers
 - 18 centres, currently 1484 patient samples
- defined standard for ultrasonographic endometrial tumor analysis



IETA: International Endometrial Tumor Analysis Group

- Data collection through Clinical Data Miner
 - Electronic Data Capture software
 - Modular: adaptable to computing infrastructures & new study settings
 - in collaboration with D.Timmerman (UZ Leuven) and IETA group

Enter patient Update patient [Login](#) [Help](#)

Patient ID:

<http://cdm.esat.kuleuven.be>

Day of scan Patient history Bleeding pattern Medical history Lifest & Constit Ultrasound **Unenhanced** Validation Sonohyst or Fluid Ovaries Outcome

Intracavitary fluid maximal diameter: mm

Is the amount of intracavitary fluid sufficient for optimal evaluation of the cavity? (For IETA #4, always click "no") no yes (click "Save page and go to next")

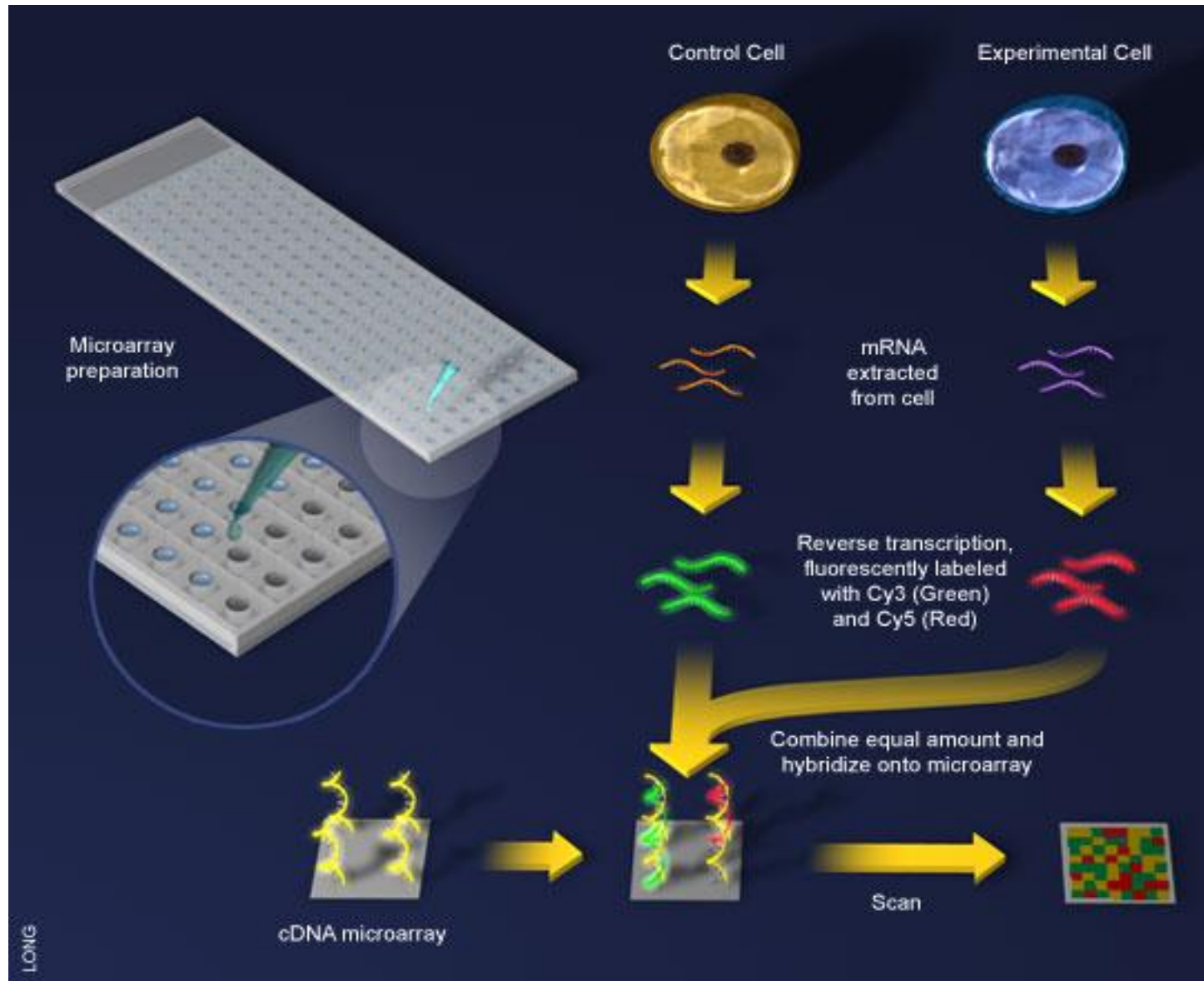
Is the thickness of the endometrium measurable? measurable not measurable but visible not visible

Thickness of the endometrium: mm

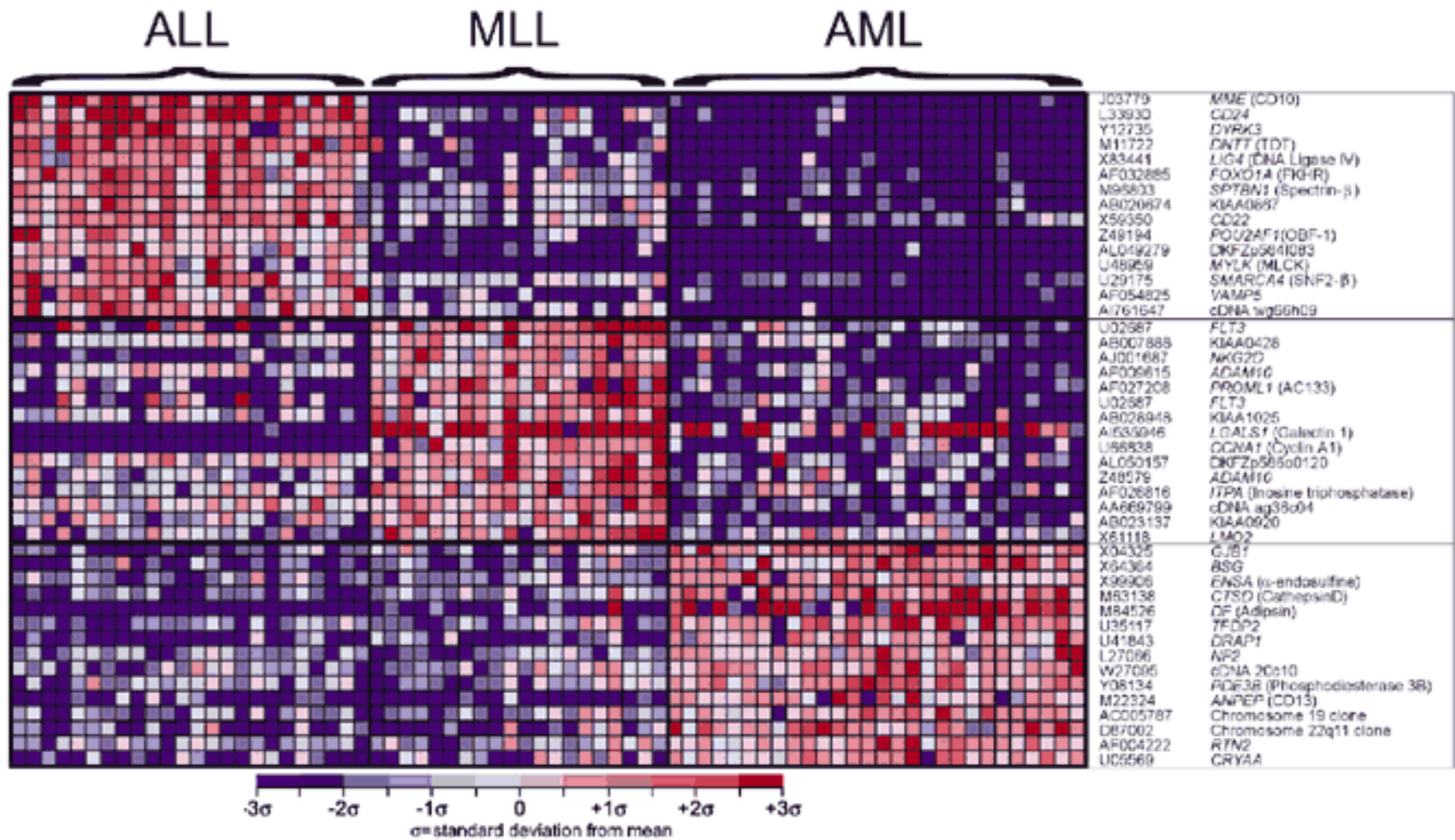
Endometrial echogenicity and pattern uniform non-uniform

Endometrial midline: linear non linear irregular not defined

Genetic fingerprint analysis: microarray

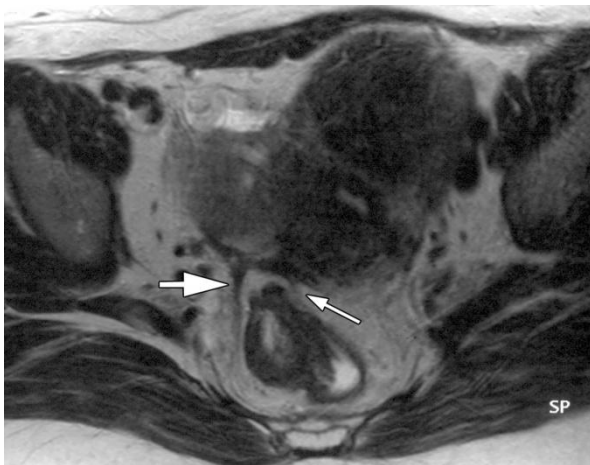


Leukemia subtype genetic fingerprints



Biomarker panel for determining endometriosis status

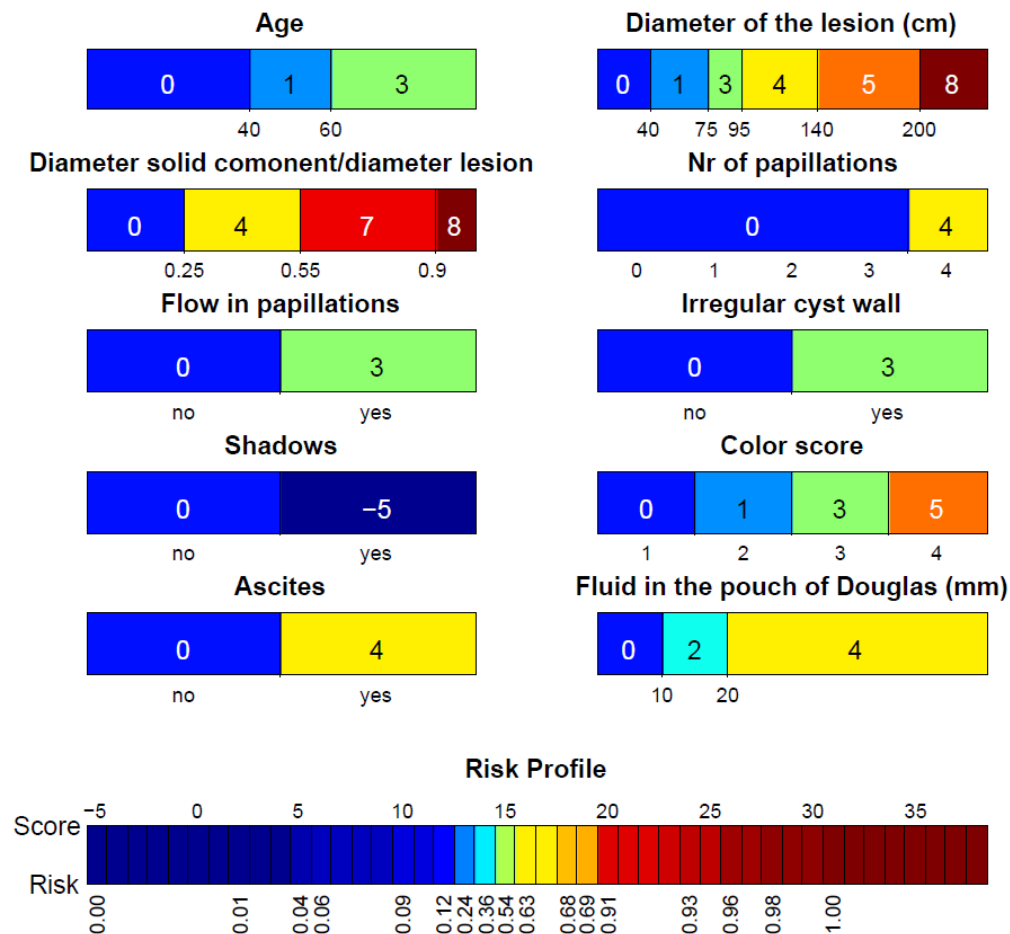
- Build predictor using **panel of biomarkers** (blood proteins) instead of single biomarker
- Capture **multivariate** relations between biomarkers by modeling
- Result: Panel of plasma biomarkers can **predict** endometriosis with high sensitivity in patients with ultrasound negative endometriosis



Collaboration with Leuven University Fertility Centre,
Department of Obstetrics and Gynaecology,
University Hospital Gasthuisberg (Prof. Thomas
D'Hooghe)

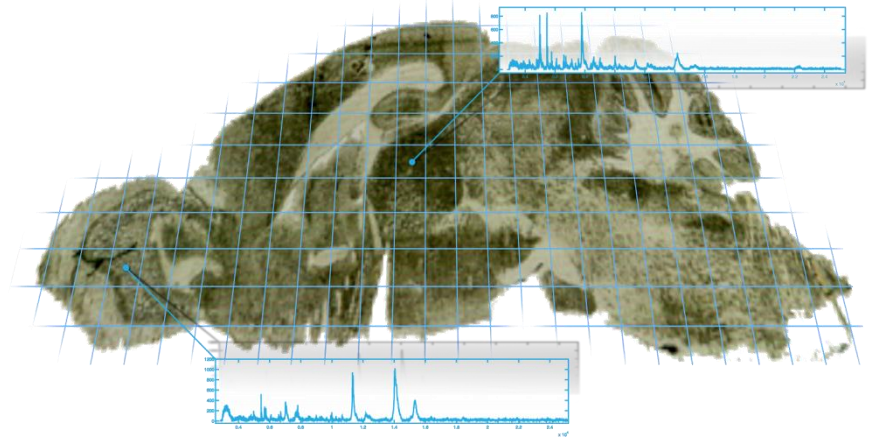
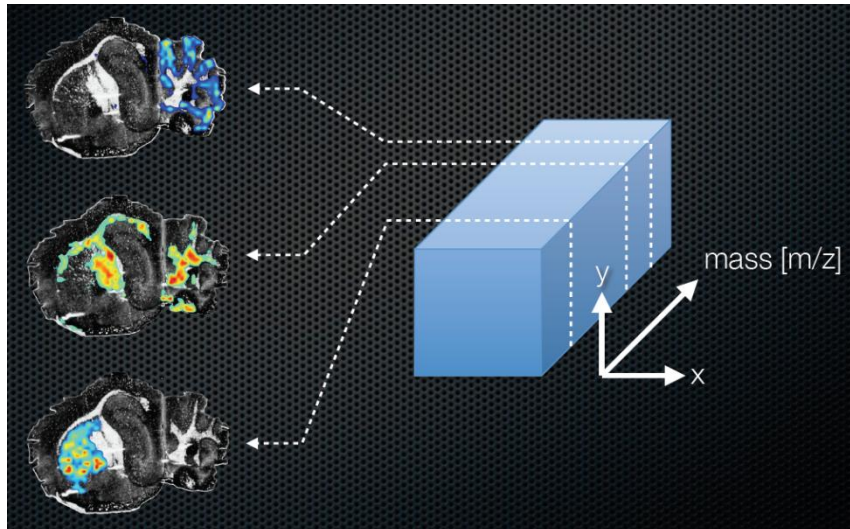
Interpretable prediction models

- interval coded score index for clinical decision support
- classification: diagnosis of ovarian cancer



Mass Spectral Imaging

- combines proteomic and metabolomic information with spatial distribution
 - localize biomarkers in tissue, and use these for clinical decision support
 - identify biological components that play a role in & unravel mechanisms underlying disease



Tumor classification via MRS

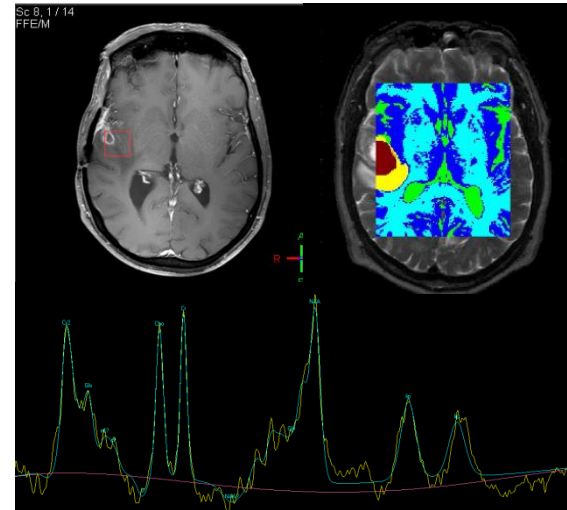


Nuclear magnetic resonance imaging (NMR):

- “water images”
- concentraion of protons → anatomical details

Magnetic resonance spectroscopic imaging:

- Quantitative metabolite maps



Key challenges:

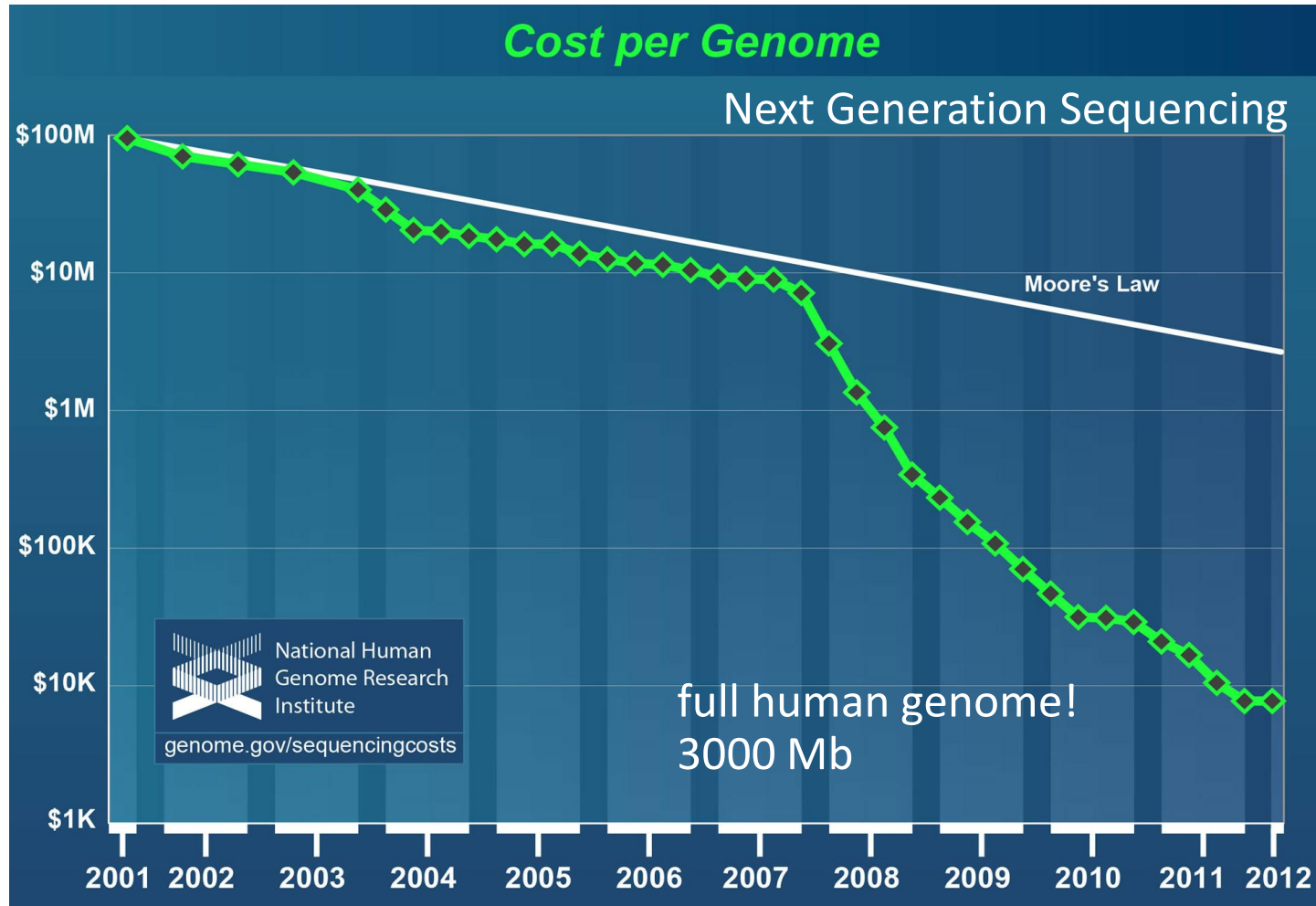
- Accurate and fast quantitaion
- Artifact removal
- Automated classification

Clinical genomics



- Towards personal genomics
- Clinical genetic diagnostics pipelines:
 - Cartagenia
 - Annotate-It
 - NGS logistics
 - Visual analytics
- Disease gene prioritization: Endeavour, Merkator, PINTA, Beegle & CHDWiki
- Preventive genomics

Towards personal genomics



→ how will this change health care and medicine?

Understanding
the structure of
genomes

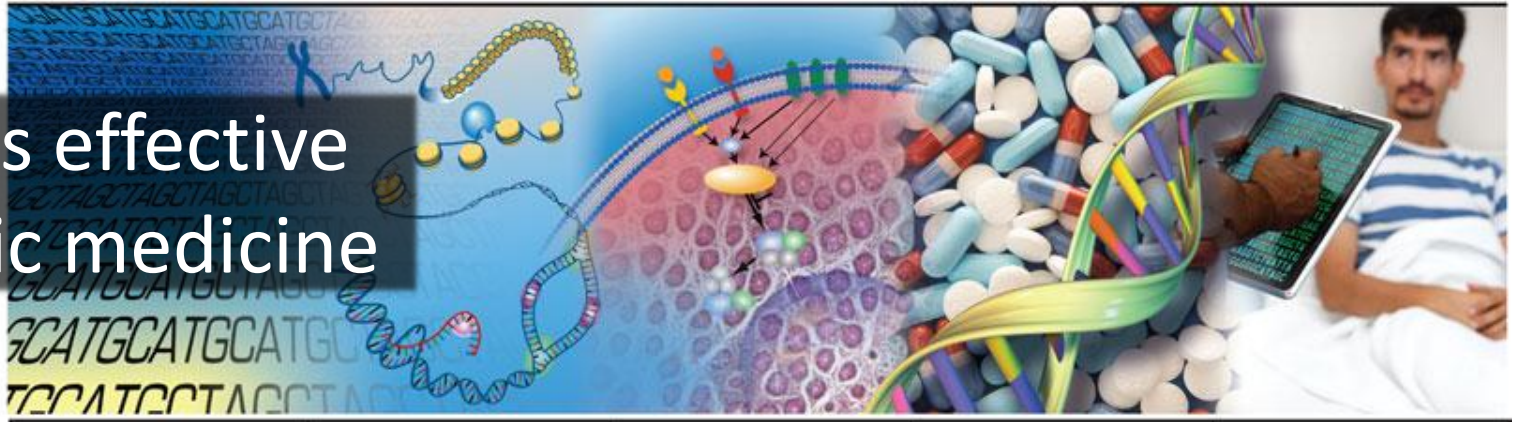
Understanding
the biology of
genomes

Understanding
the biology of
disease

Advancing
the science of
medicine

Improving the
effectiveness of
healthcare

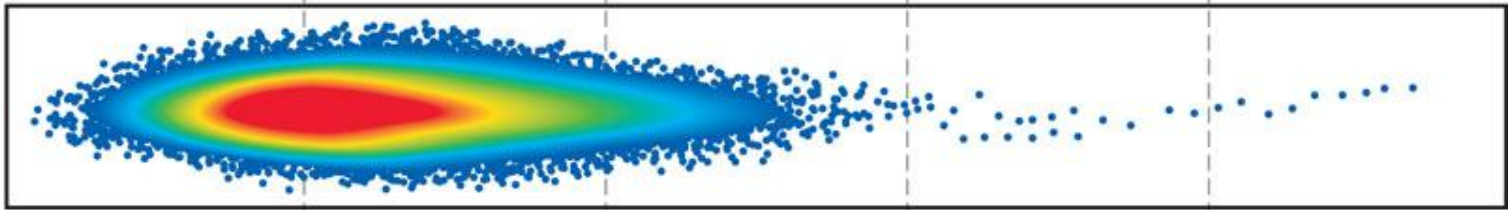
Towards effective genomic medicine



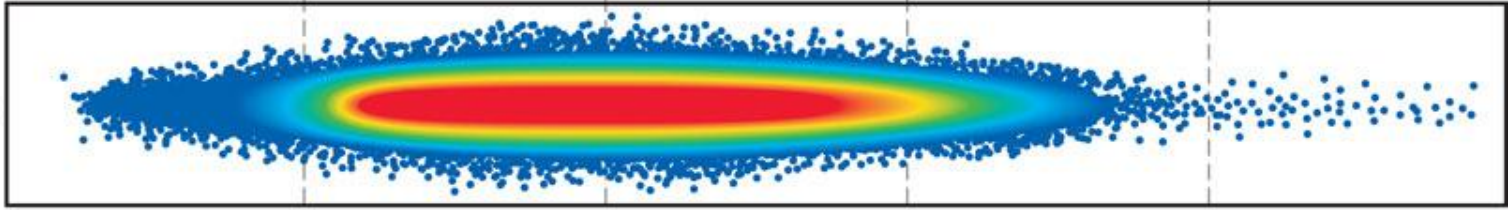
1990–2003
Human Genome Project



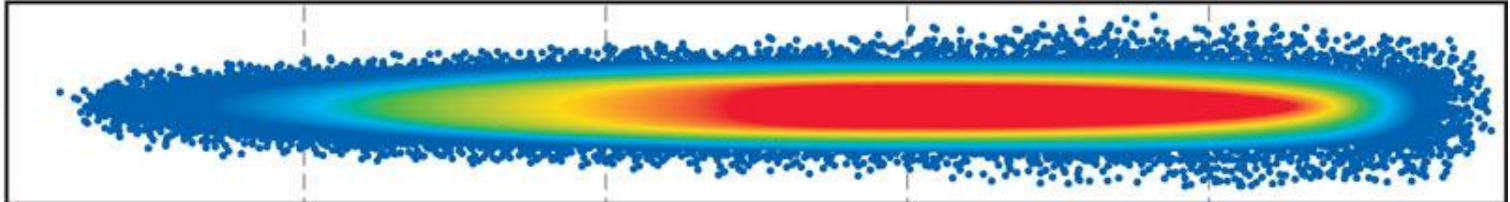
2004–2010



2011–2020



Beyond 2020





Personal Genomics

3.10⁹ base pairs:
where's the needle?

- rare genetic disorders
- personalized medicine
- pharmacogenomics
- preventive genomics

Genomics Community @ UZ + KU Leuven

- **Genomics Core**
 - GS FLX + HiSeq 2000
 - Hercules grant for PacBio RS based on single molecule, real-time (SMRT™) technology
 - <http://www.uzleuven.be/genomicscore>
- **SymBioSys KU Leuven Centre for Computational Systems Biology**
 - Research teams
 - ESAT-SCD-SISTA: bioinformatics (Yves Moreau, Jan Aerts, Bart De Moor)
 - CME – Molecular Pathogenesis of Leukemia Lab (Jan Cools)
 - Vesalius Research Center (Diether Lambrechts)
 - CME – Lab Computational Biology (Stein Aerts)
 - CME – Lab of Reproductive Genomics (Thierry Voet)
 - CME – Lab for cytogenetics and genome research (Joris Vermeesch)
 - AVALOK: computing cluster for patient files @ UZ Leuven
 - <http://www.kuleuven.be/symbiosys/>

Clinical genomics pipelines

clinician → extract relevant information in a timely manner!



BENCH = web-based software and database platform for interpretation of genomic variation in **routine diagnostics**

- array-CGH
- Next Gen Seq



NGS-Logistics: pipeline to handle genomic data distributed over various genetic centres

Annotate-it!

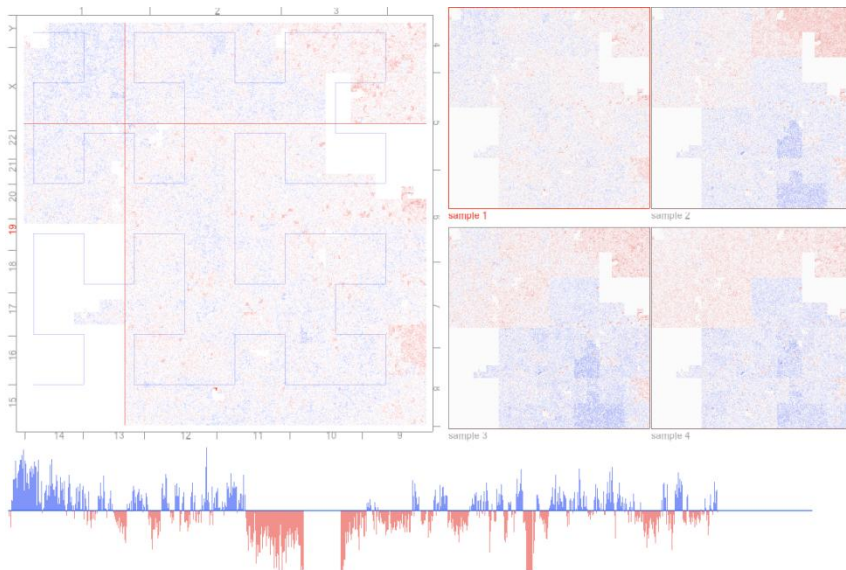
- Next Gen Seq data
- Annotation and interpretation of SNPs
- Data sharing / Collaboration
- Integrating phenotypic information (through Endeavour)
- Keeping annotation information up to date
- Helping non-bioinformaticians do Next Gen Seq data analysis
- collaboration UZ Leuven: Nicolaides Baraitser Syndrome

Clinical genomics: visual analytics

For **structural variation** beyond insertions, deletions and duplications

Meander

- tool to **find** small structural variations in raw data
- input data = Next Gen Seq data
- user = bioinformatician

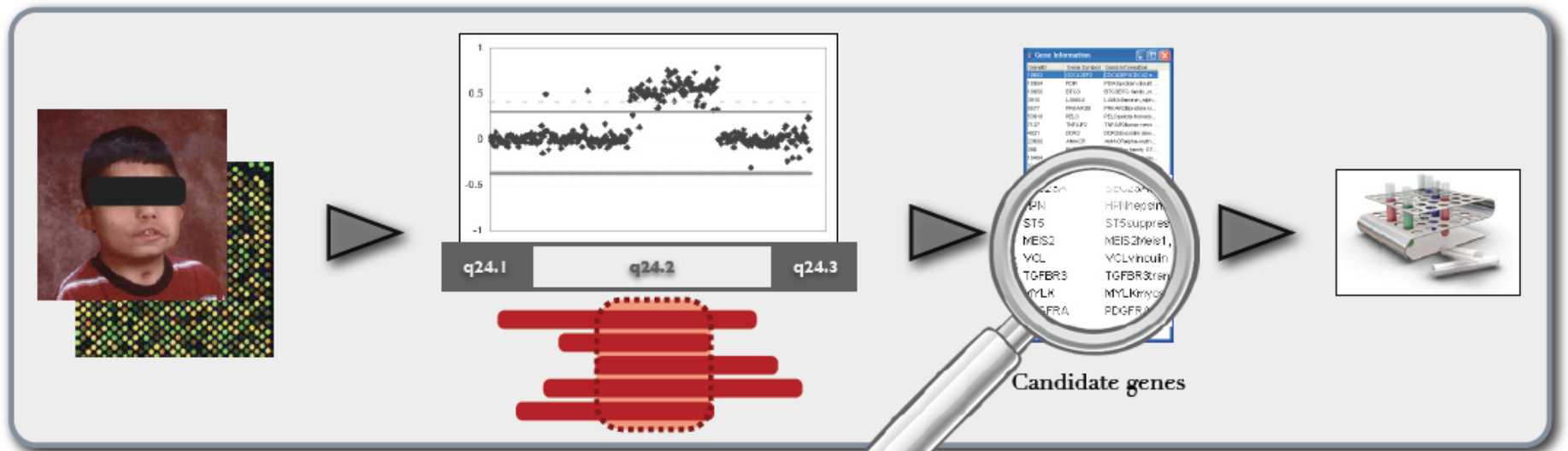


- tool to **study the effect** of structural variation on **human phenotype**
- input = list of structural variations
- user = clinical geneticist or biologist

mouseData.gvf: Overview



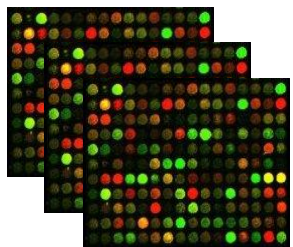
Disease gene discovery: gene prioritization



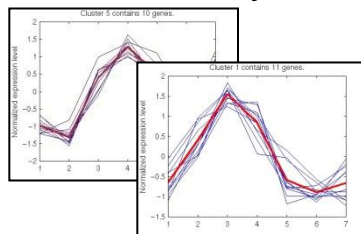
Which genes are the most promising candidates?

Endeavour & Merktor: gene prioritization by data fusion

High-throughput
genomics

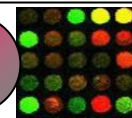
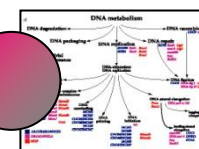


Data analysis

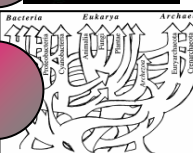
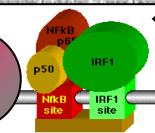


Candidate genes

Information sources



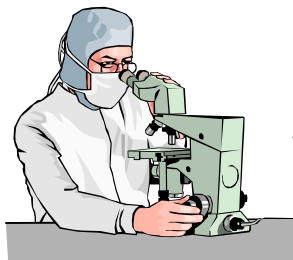
"The chaparral... the 11, who are Michael Jackson performing on television and right around that time... and to be that big. Fine, said... who ordered her to take 18... in a red, during which the under-... a movie producer that... al physical exercises, charmer and cars for the long hours... can had possessed a Charles..."



Candidate prioritization

Rank	En	Ex	Ip	Ke	GO	Te	Avg	Pval
1	TTR	G6PC	PAH	G6PC	IGF1	TTR		
2	IGF1	TTR	IGF1	PAH	PAH	IGF1		
3	CRP	ALB	TTR	RERE	G6PC	CRP		G6PC
4	HOXB6	HABP2	ALB	ERCC3	TTR	HOXB6		IGF1
5	ALB	PAH	HDC	ERCC3		ALB		
6	NR4A2	IF	TLL2	ANKRD3	HMG2	CRP		
7	PAH		C10R1	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

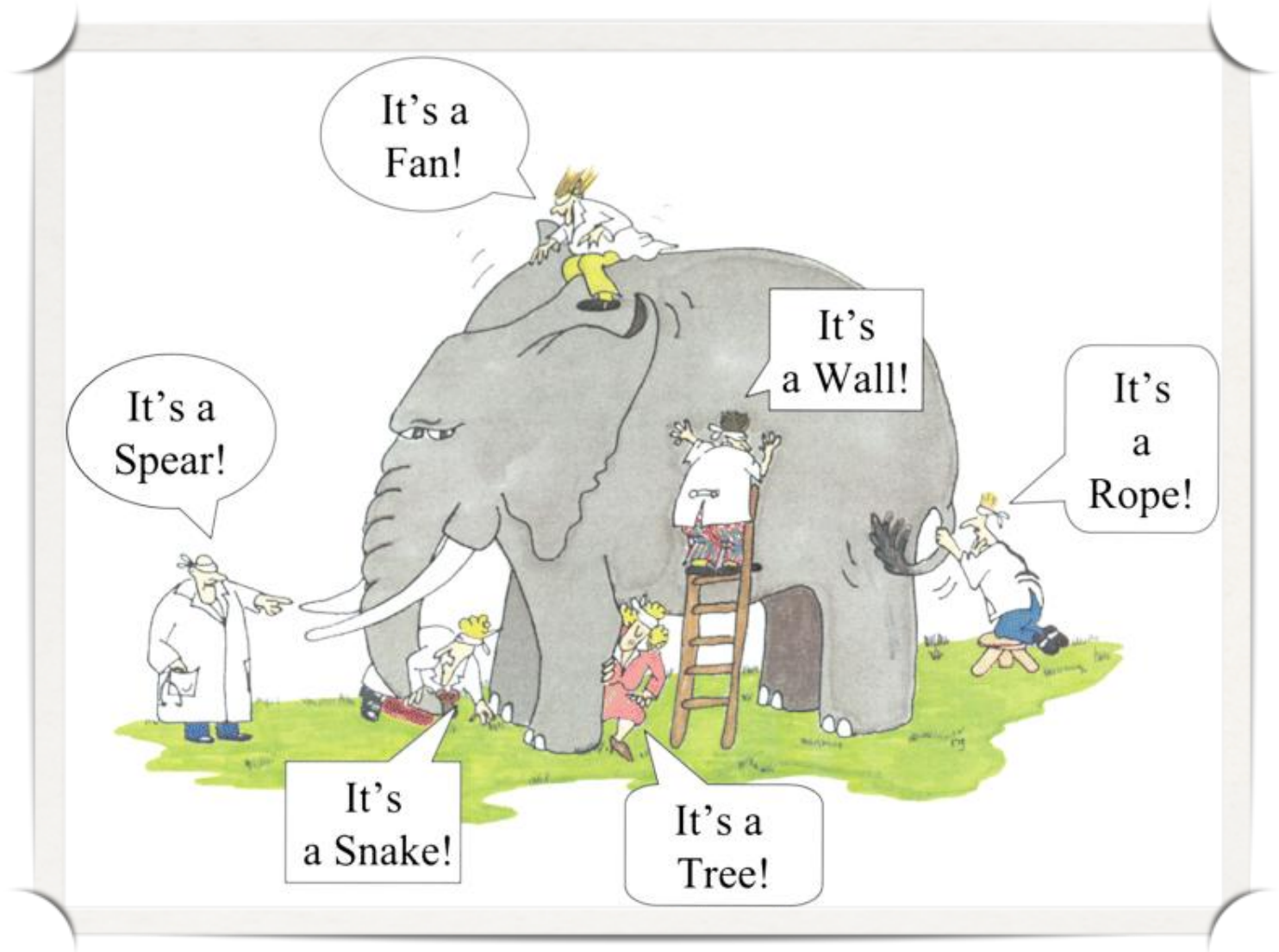


Name	Ensembl
TTR	ENSG00000118271
PAH	ENSG00000171759
G6PC	ENSG00000131482
IGF1	ENSG0000017427
ALB	ENSG00000163631
CRP	ENSG00000132693
HABP2	ENSG00000148702
IF	ENSG00000138799
FST	ENSG00000134363
ARAF1	ENSG00000078061
HMG2	ENSG00000149948
C9	ENSG00000113600
PCBP2	ENSG00000111406
HOXB6	ENSG00000108511
RERE	ENSG00000142599
HOXA11	ENSG00000005073
CLIC1	ENSG00000096238
ERCC3	ENSG00000163161
ERCC3	ENSG00000163161
TLL2	ENSG00000095587
SYT4	ENSG00000132872
SYT4	ENSG00000132872
PIK4CB	ENSG00000143393
PKD2	ENSG00000118762
PKD2	ENSG00000081026
ANKRD3	ENSG00000183421
F13A1	ENSG00000124491
BPAG1	ENSG00000151914
KCNN3	ENSG00000143603
GRIN2A GRIN2B	ENSG00000150086
SIM1	ENSG00000112246
	ENSG00000174891
	ENSG00000099195
C14orf10	ENSG00000202020
STX8	ENSG00000170310
	ENSG00000107671
MSH5	ENSG00000096474
CRH	ENSG00000147571
MID1	ENSG00000101871
	ENSG00000184508
	ENSG00000113460
TGFB3	ENSG00000113460
C10orf10	ENSG00000202020
PDGFRA	ENSG00000107671
NFYA	ENSG00000107671
NFYA	ENSG00000107671
	ENSG00000107671
	ENSG00000107671
	ENSG00000107671
MMP3 MMP1	ENSG00000149968
	ENSG00000149968

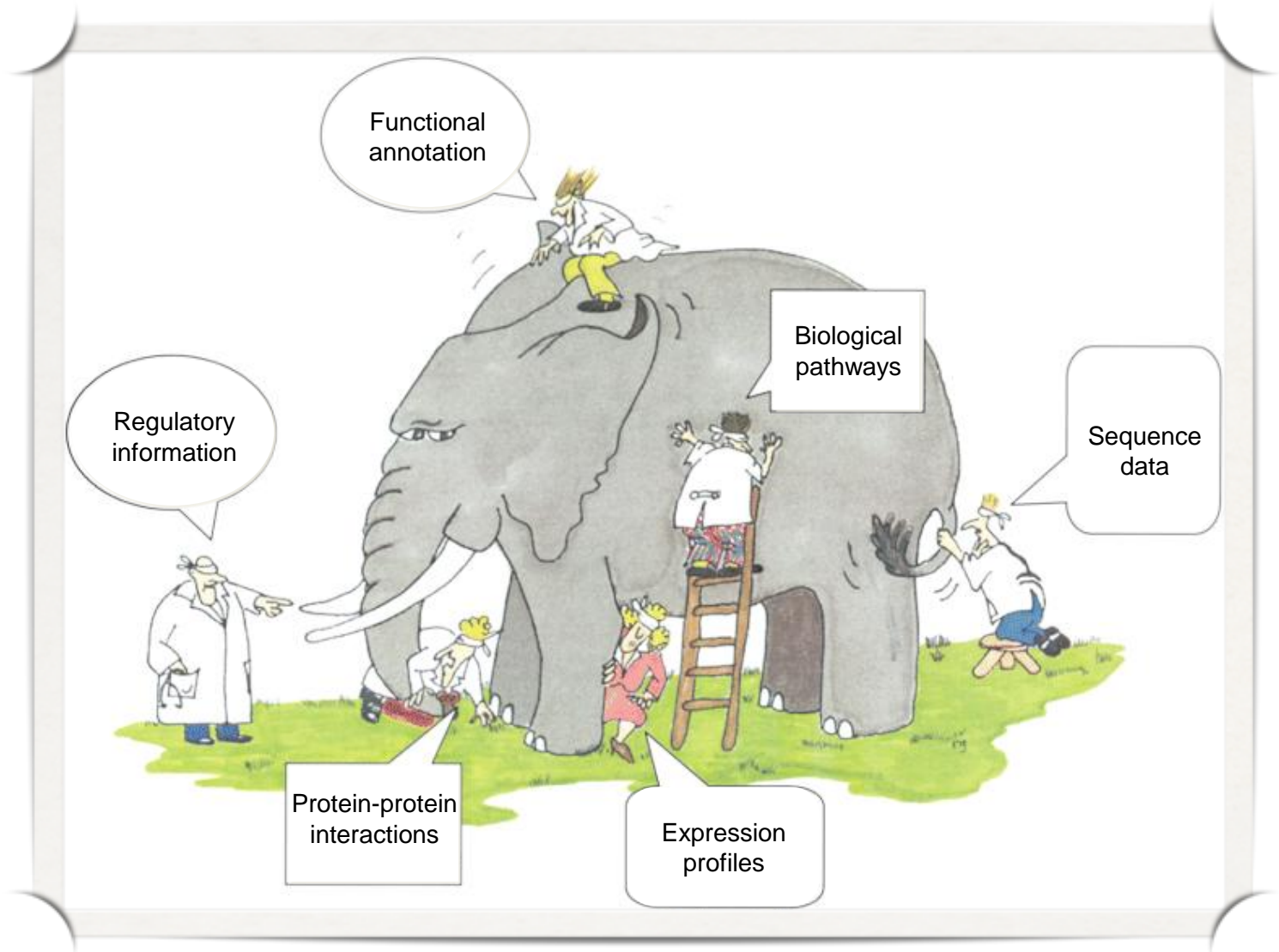
Aerts et al., Nature Biotechnology, 2006

www.esat.kuleuven.be/endeavour

Data fusion



Data fusion



Beegle: Biomedical Text Mining

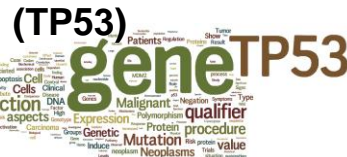
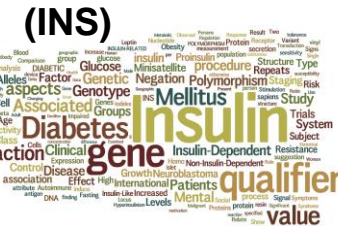
(Cancer)



Endeavour builds on known disease genes – what to do when these are not known?

→ create list of relevant genes through biomedical text mining

Beegle



huge knowledge base!
1/3 of all world databases consists of biomedical data

(Cancer Identified Genes)

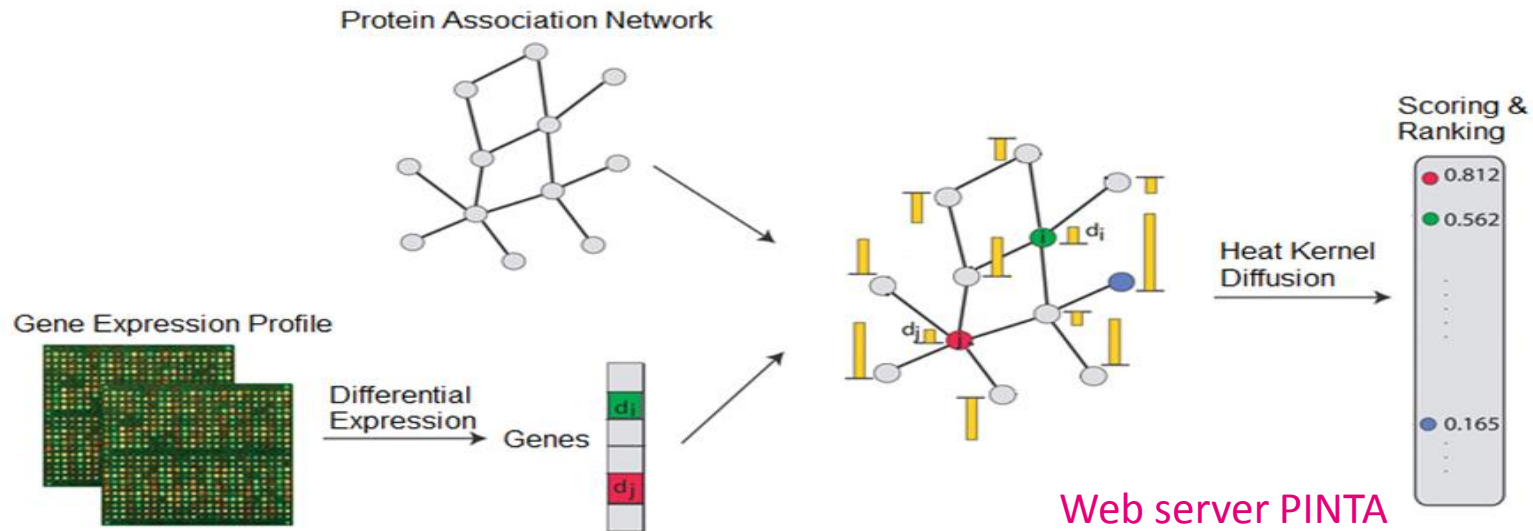
- CCND1
- EGFR
- TNFSF10
- BRCA1
- BCL2
- ERBB2
- BIRC5
- TP53

Match query profile against gene profiles



PINTA: gene prioritization by network analysis

Endeavour builds on known disease genes – what to do when these are not known?
→ diffusion of differential expression values over a functional network to identify the most promising genes



Web server PINTA

Nitsch *et al.*, **Nucleic Acids Research** (2011); Nitsch *et al.*, **BMC Bioinformatics** (2010); Nitsch *et al.*, **PLoS ONE** (2009).

<http://www.esat.kuleuven.be/pinta/>



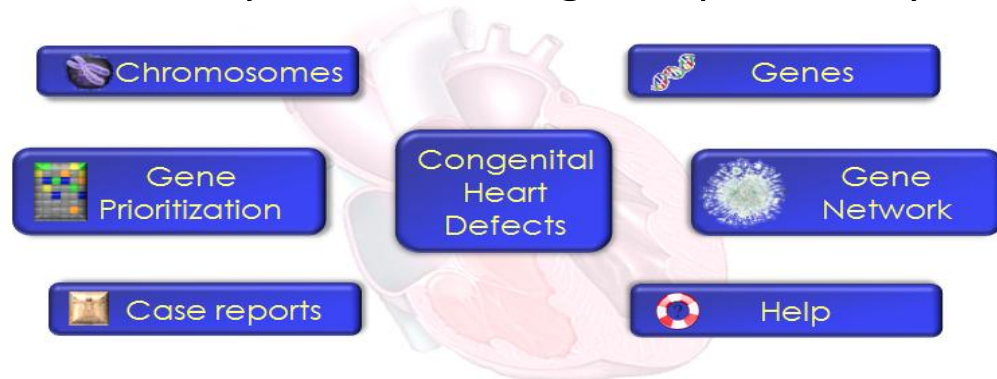
- Both genome-wide and candidate gene prioritization
- 5 organisms
- Graphical view of strongest contributing interacting genes

Collaborative disease portals: CHDWiki

→ integrate the daily practice of molecular biologists, geneticists, and clinicians with databases and tools (e.g. Endeavour gene prioritization)

CHDWiki = portal for congenital heart defects (CHD)

- community repository of current knowledge on the genetic basis of CHDs
- collaborative environment for the study of candidate genes potentially implicated in CHDs



Barriot R et al., Collaboratively charting the gene-to-phenotype network of human congenital heart defects. *Genome Med.* 2010 Mar 1;2(3):16

homes.esat.kuleuven.be/~bioiuser/chdwiki/

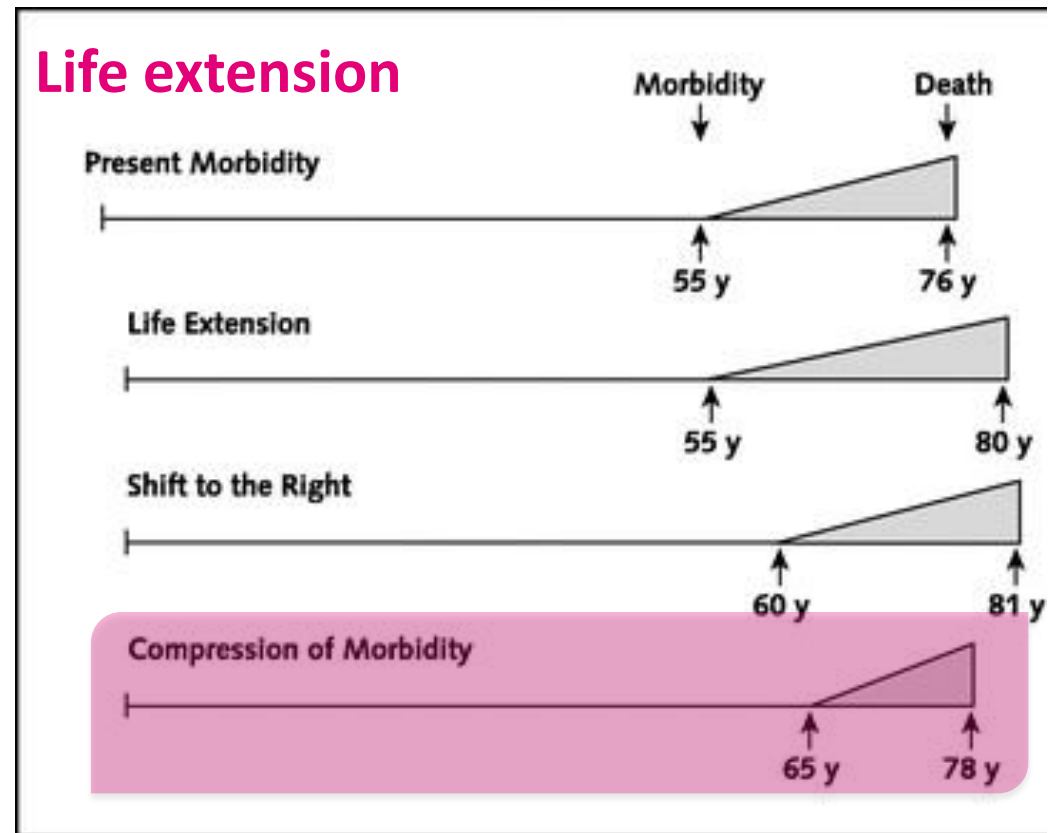
in collaboration with Centre for Human Genetics UZ Leuven (K. Devriendt) & Institute for Medical Genetics and Human Genetics at Charité, Berlin (P. Robinson)

Preventive genomics: extension of healthy life

Can genomic data be used to extend healthy life?

4 requirements:

- **Analytical validity:**
test reflects **genotype** of interest?
- **Clinical validity:**
test detects or predicts the **outcome** of interest?
- **Clinical utility:**
will the test significantly **improve** patient outcomes?
- **Ethical, Legal and Social Issues**



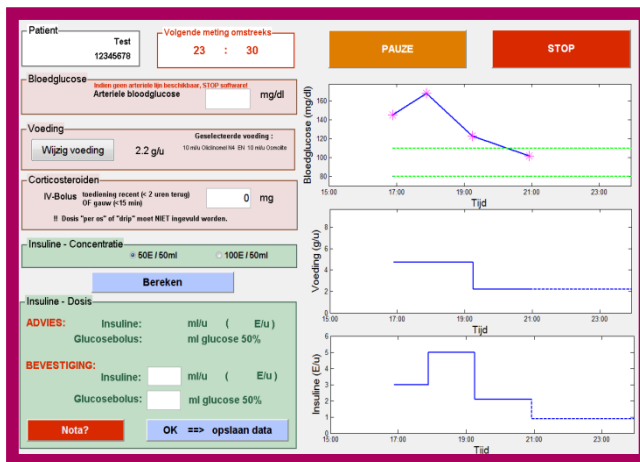
Data Mining, Control & Optimization



- Blood glucose control @ ICU
- Zebrafish neural circuits
- Text & Data Mining of health care records
- Hospital management: personnel rostering

Blood Glucose Control @ ICU

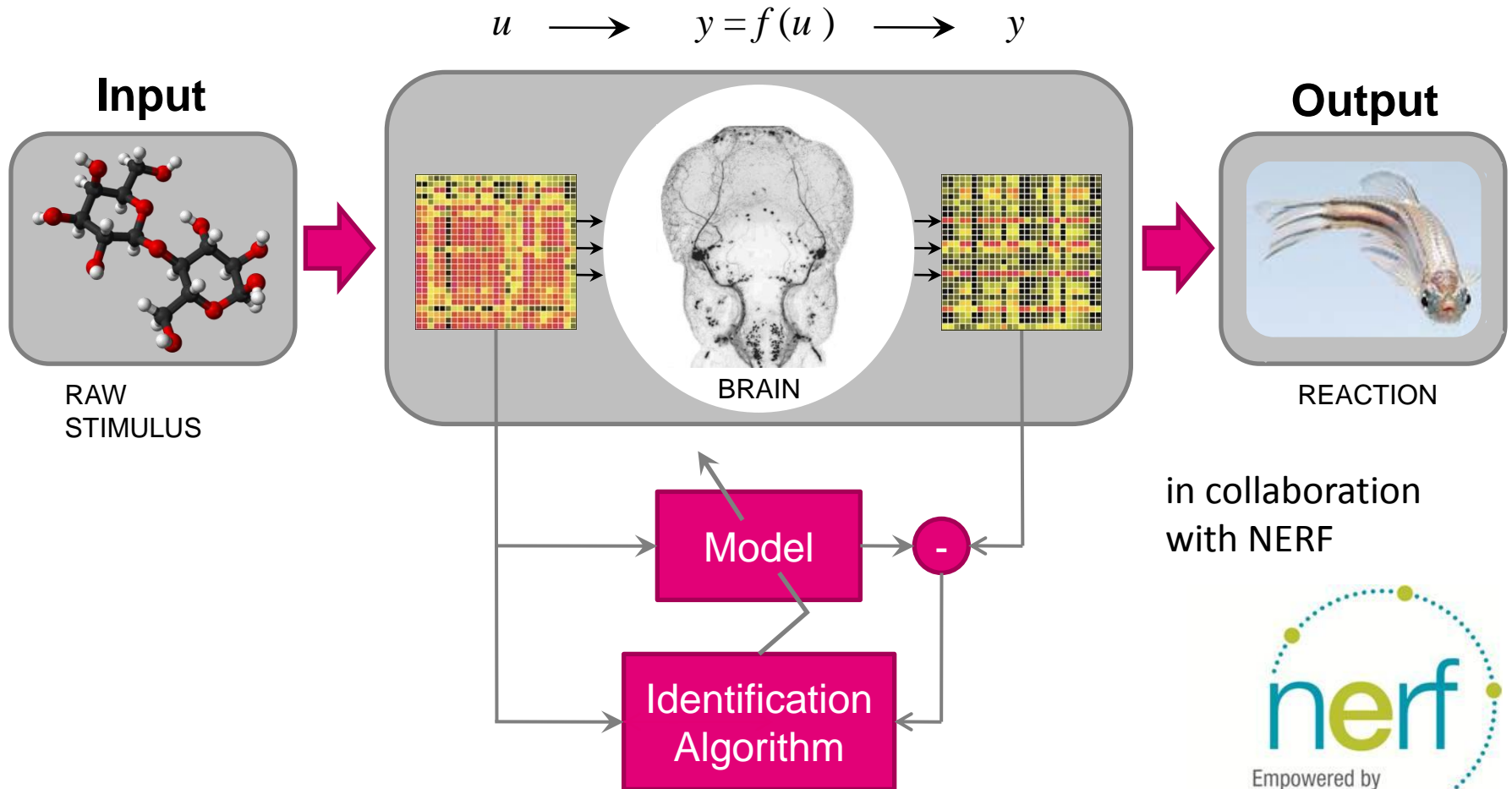
- Intensive Care Unit UZ Leuven studies: **Tight Glycemic Control (TGC) in intensive care unit lowers mortality**
- LOGIC-Insulin**: semi-automatic control system that advises nurse on insulin dosage and blood sampling interval aiming at TGC and avoiding hypoglycemia
- clinical trial: compared with expert nurses, **LOGIC-Insulin showed improved efficacy** of TGC without increasing rate of hypoglycemia



in collaboration
with ICU UZ
Leuven

Zebrafish Neural Circuits

- understand dynamical behaviour of neural circuits in Zebrafish through system identification



in collaboration
with NERF

Text & Data Mining of health care records

- Example: medical report annotation
 - use medical history to predict adverse drug effects
 - use information for patient selection in clinical trials



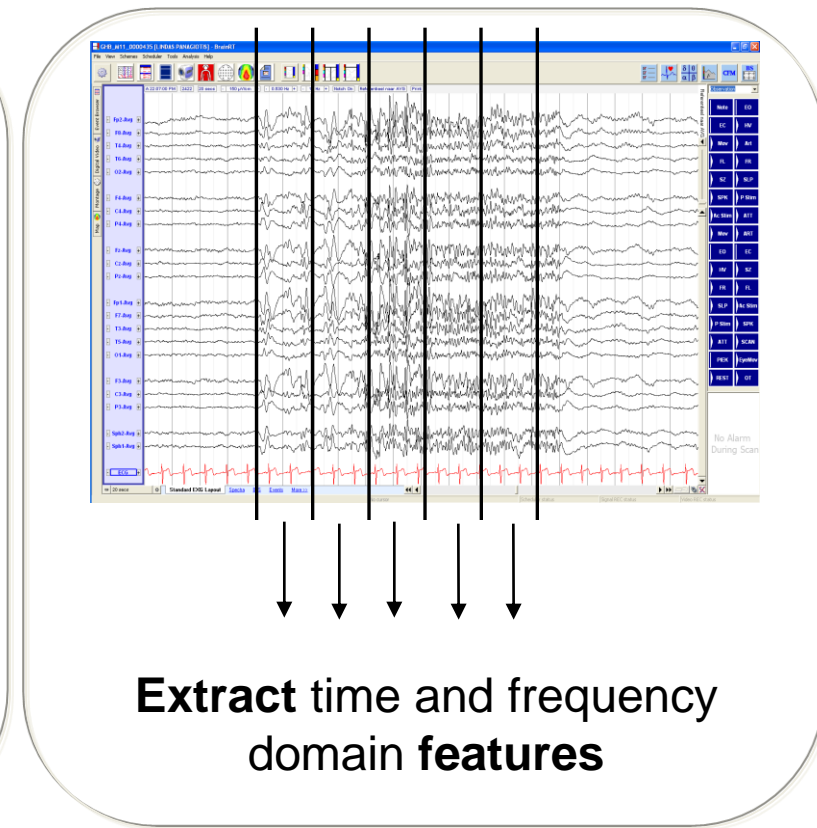
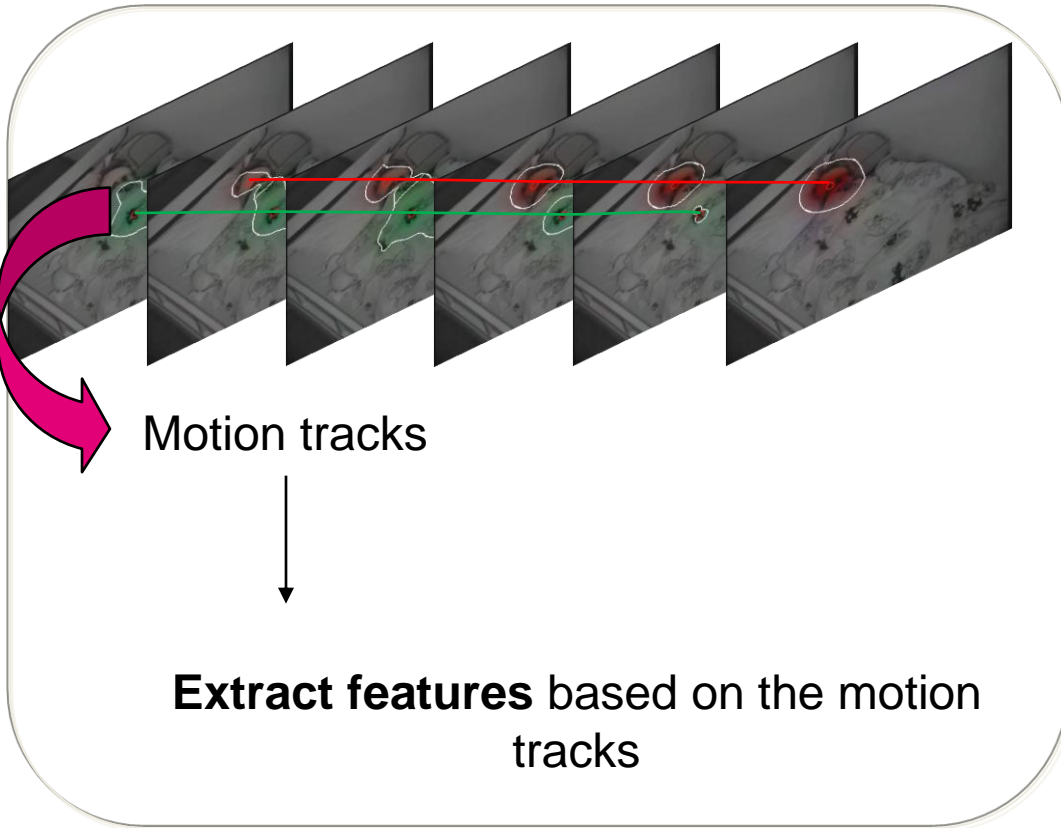
- Example: Data mining of health care system data
 - population-based mining
 - trend detection, clustering, outlier detection, prediction, longitudinal time series
 - collaboration with LCM

Biomedical & Digital Signal Processing

- Epilepsy detection
- Seizure localization



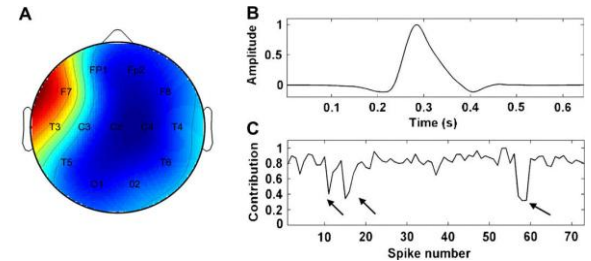
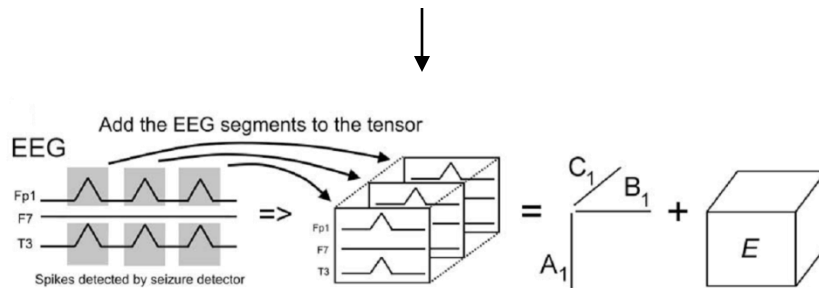
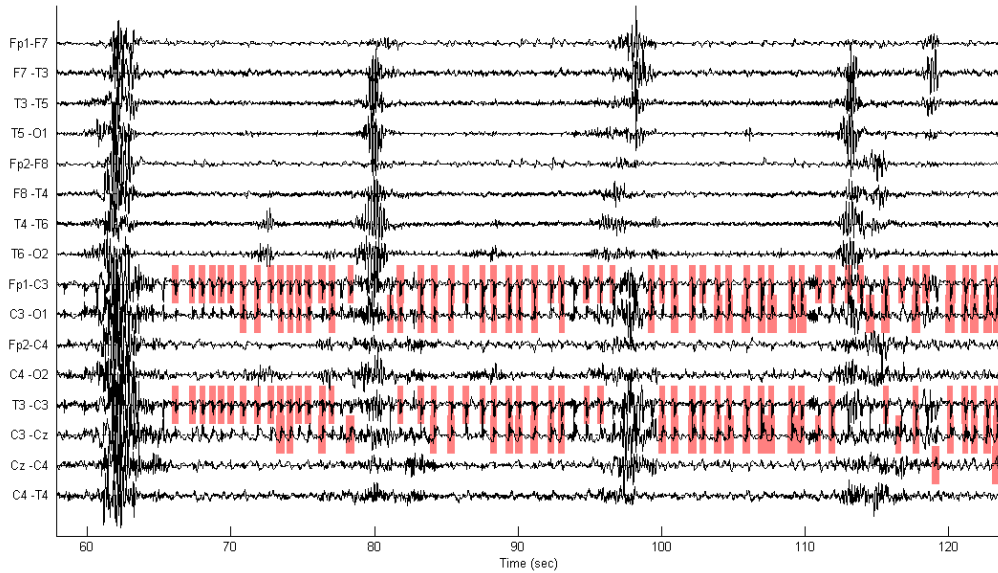
Epilepsy detection



Video-EEG
monitoring

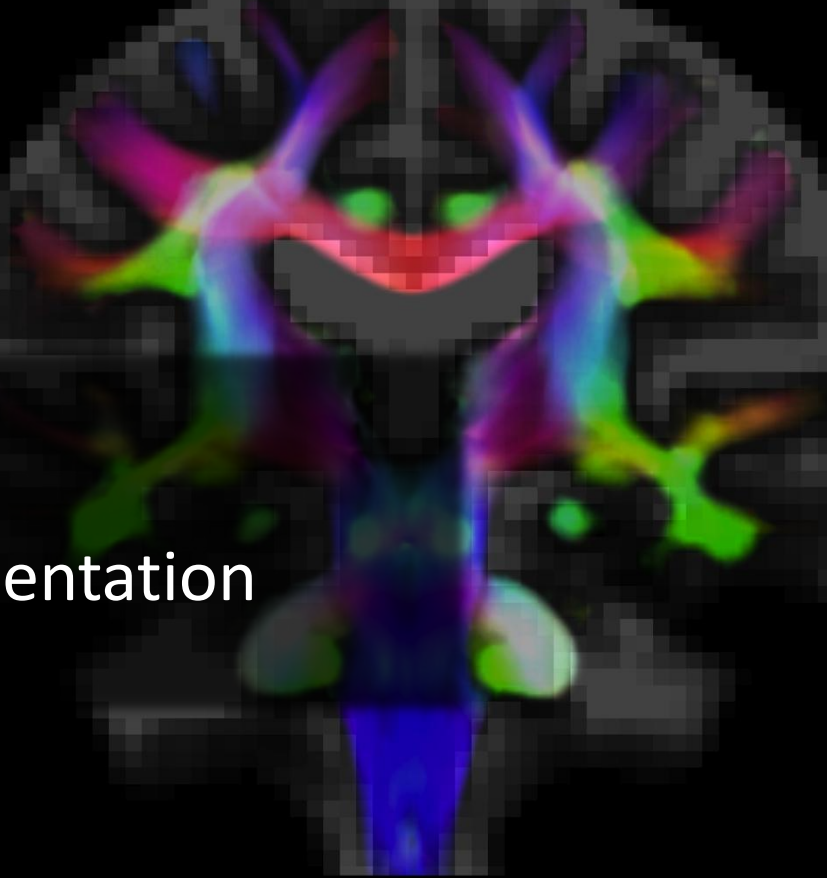
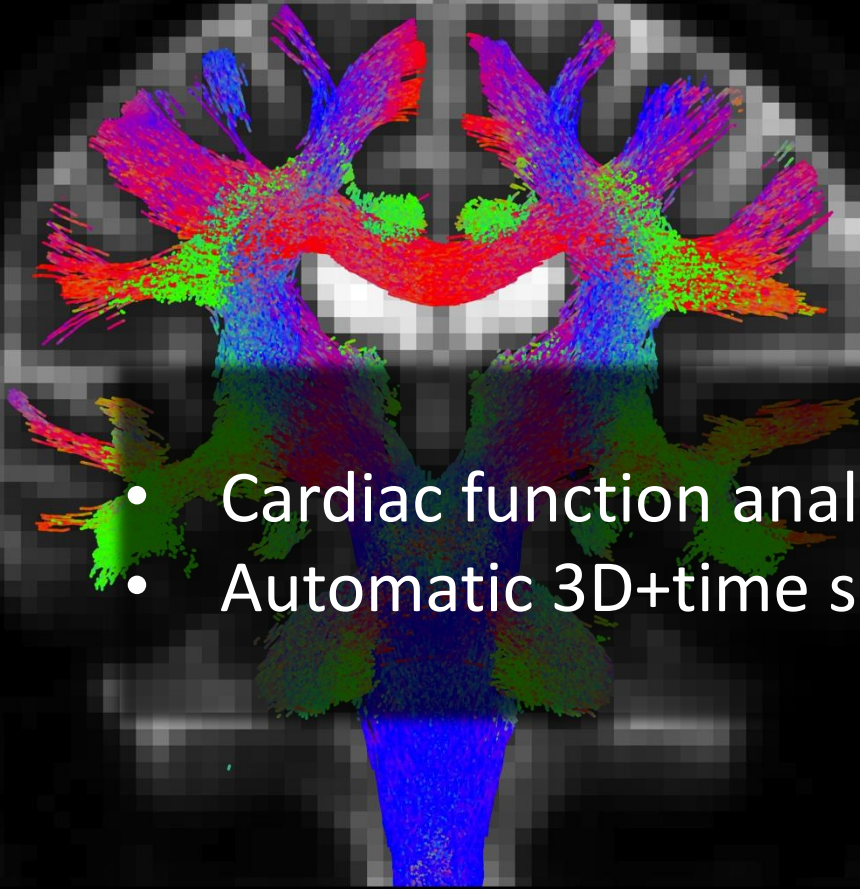
Discriminate between
normal and epileptic events

Seizure localization



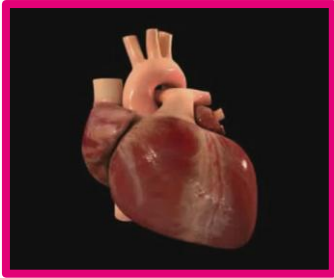
Parafac component
corresponding to seizure

Medical Image Computing



- Cardiac function analysis
- Automatic 3D+time segmentation

Cardiac function analysis



Heart = Four-chamber system

Supply body with oxygen and nutrients and remove metabolic waste products

Cardiovascular disease (CVD): Ischemia, arrhythmias, valvular heart disease, ...

→ 17 million = 30% of all worldwide deaths in 2008 due to CVD*

→ 100 deaths per day in Belgium**

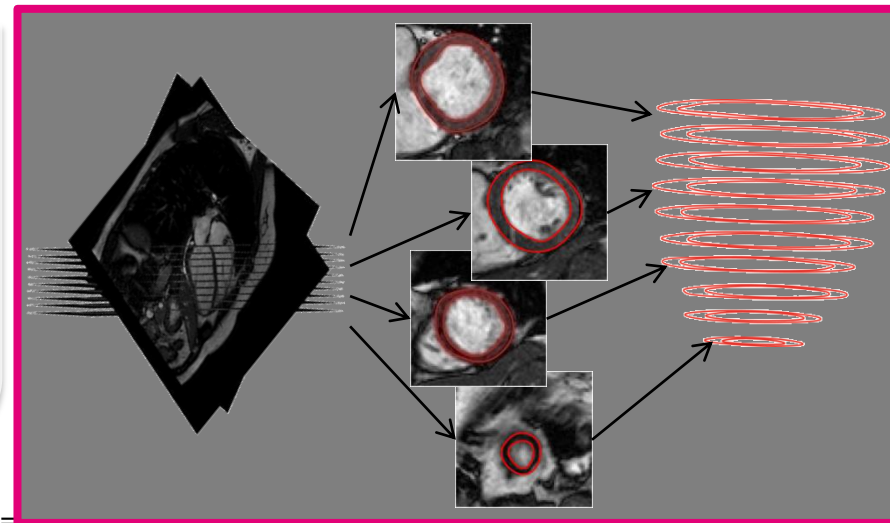
→ **Cardiac imaging** for non-invasive quantification of heart function



MR

Functional parameters:

- Myocardial thickening
 - Stroke volume
 - Ejection fraction
 - Wall strain
- Manual segmentation

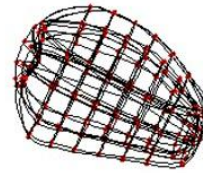
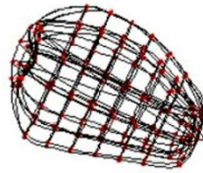
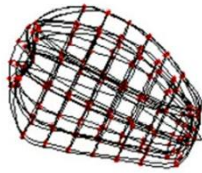
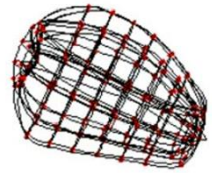


<http://www.youtube.com/watch?v=P5fR2pCzm3k&feature=>

*World health organization

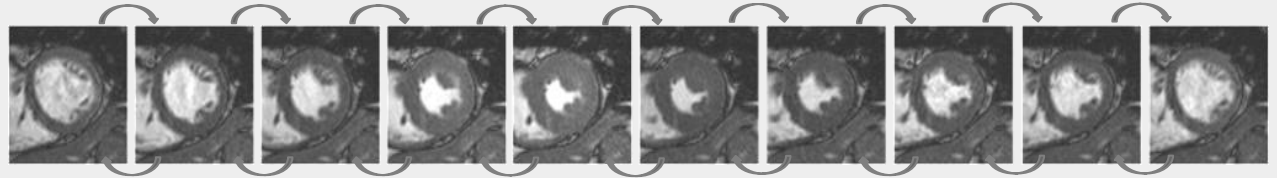
**Belgische cardiologische liga

Automatic 3D+time segmentation

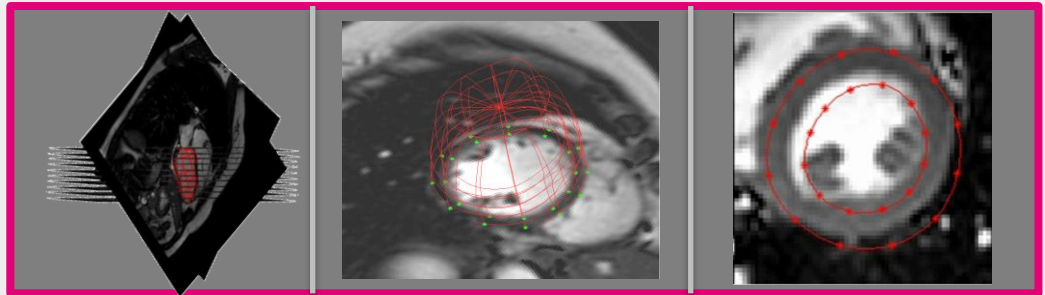


Statistical models
of shape and
intensity, learned
from training data

Information of all
timeframes and
slices **linked**
together



→ Results in **automatic,**
consistent, accurate
measurements of
cardiac function



User Experience Research



- ACCIO: Ambient aware provisioning of Continuous Care for Intra-mural Organizations
- Theraplay: video games for therapy

ACCIO: Ambient aware provisioning of Continuous Care for Intra-mural Organizations

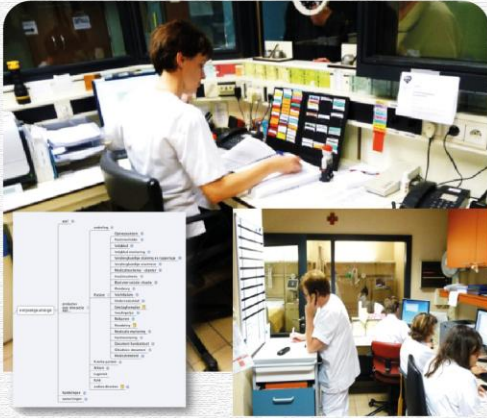
- Define scope, concepts & rules of a human-centred **ontology**
- Supports **continuous care** in multiple care settings
 - Residencies > Care
 - Hospitals > Cure
- **Modelling** relevant knowledge
- **User-centred design**
- Product ecology (tools, practices and attitudes)
- ER observation concept
- Guidelines for involving end-users in medical ontology creation



Ambient aware provisioning of continuous care for intra-mural organizations

ACCIO

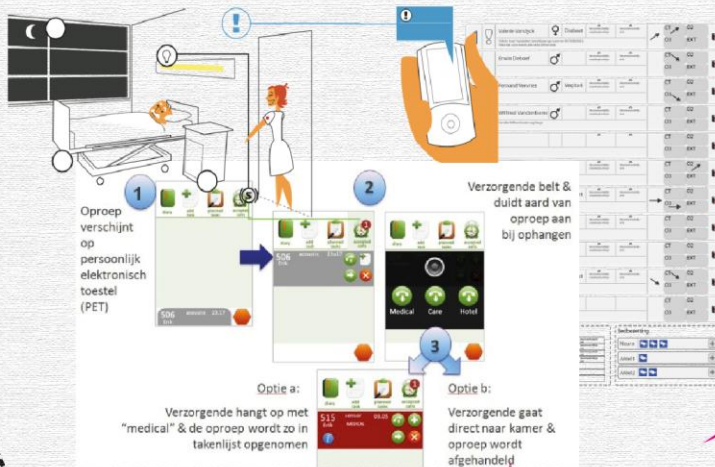
Context Mapping



Participatory Design



Prototyping



User Experience Evaluation



Theraplay



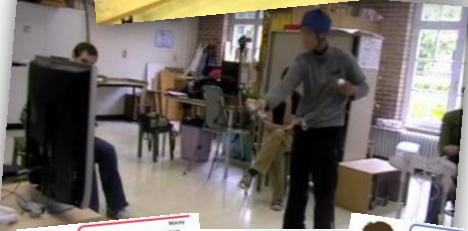
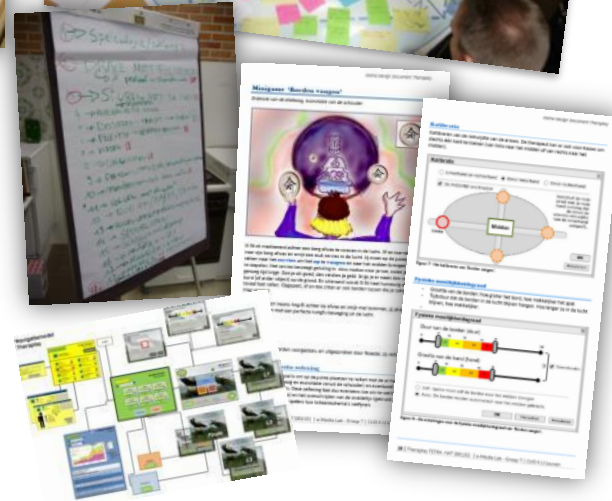
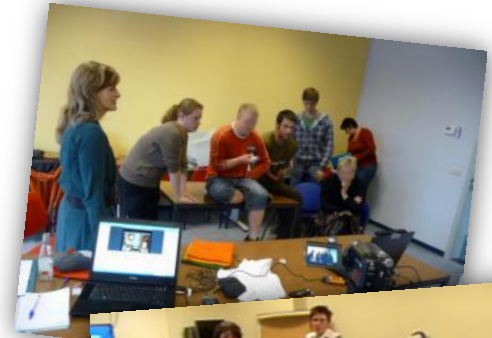
THERAPLAY



Analysis

Design

Evaluation



Kung Fu Kitchen



Track record

- ~ 250 publications & ~ 15 PhDs /year
- ~ € 5 million external financing /year
- 8 patents granted in 2008-2010



Cartagenia
data handling & mining
for clinical genetics



in silico
drug
discovery

icoMetrix
Quantifying Your Images

image quantification



social interest software

televic
education
(e-)learning solutions

 **medicim**
MEDICAL IMAGE COMPUTING

medical image
computing

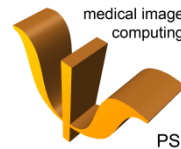
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vision soft- & hardware

Decision Support Analytics

for Professionals, Patients & Policy makers



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