Artificial Intelligence, machine learning and clinical data mining

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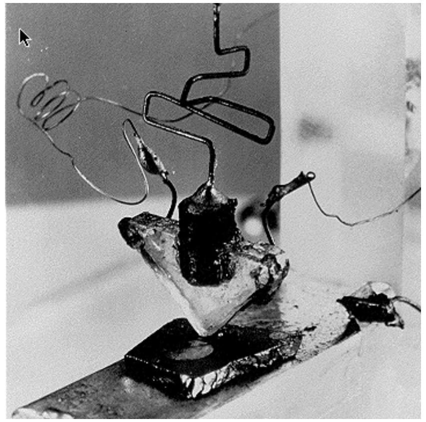
KU LEUVEN

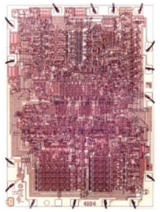
STADIUS
Center for Dynamical Systems, Signal Processing and Data Analytics

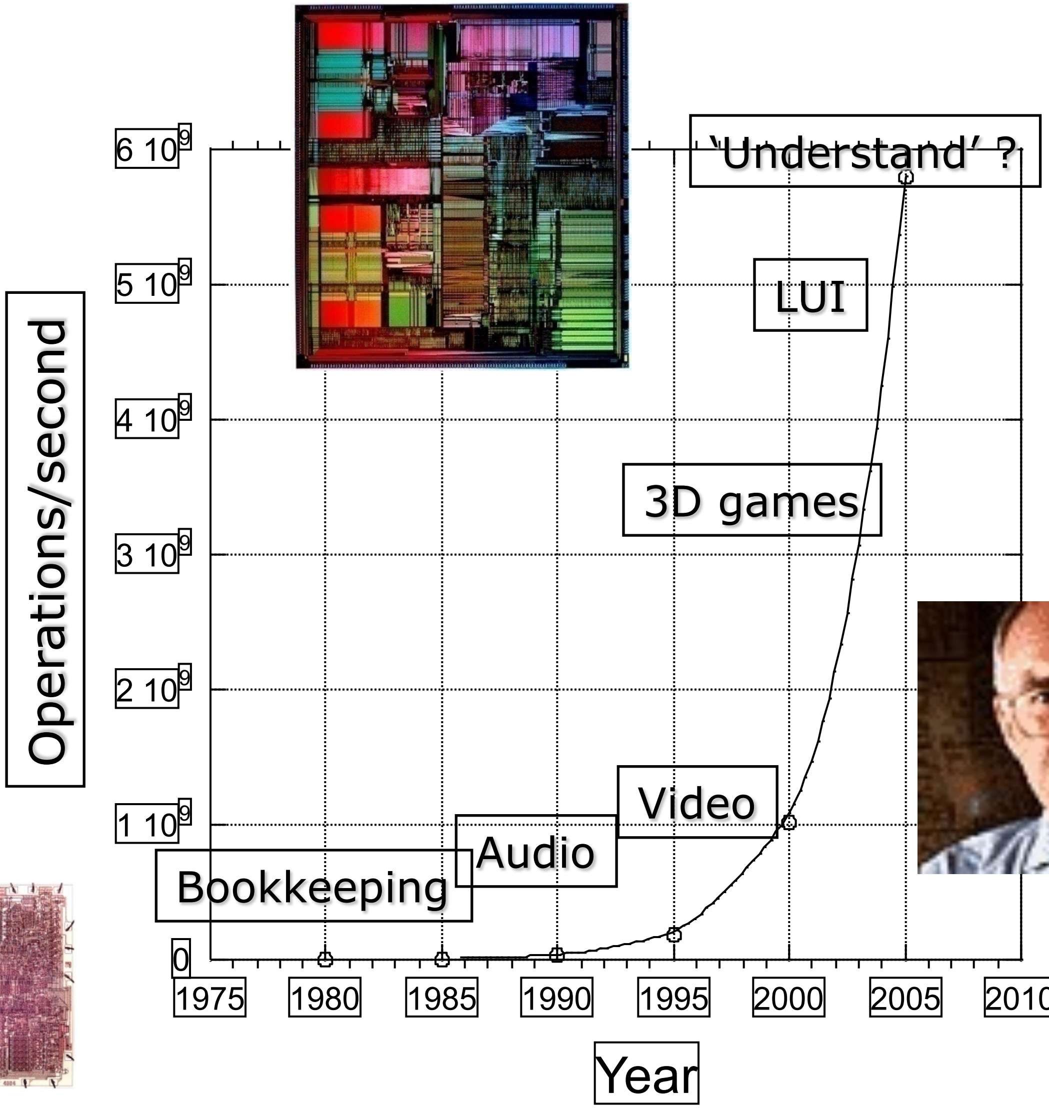
Outline

- AI: Why now ?
- Some clinical examples
- Future opportunities

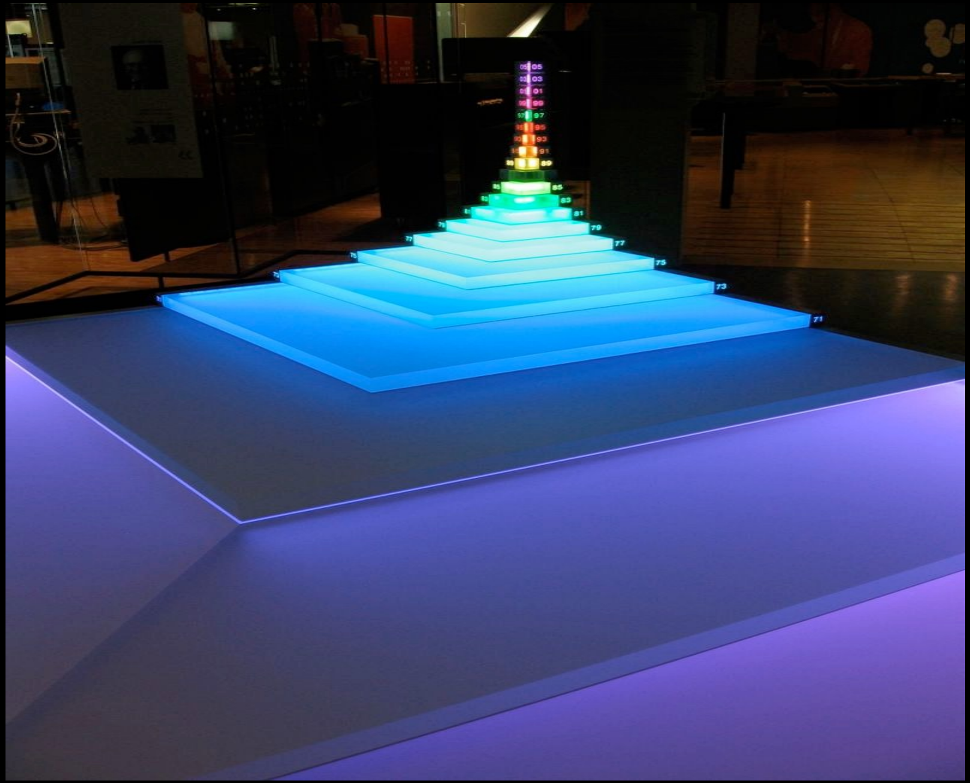
Technology and Engineering Design:
The third industrial revolution (1945…)





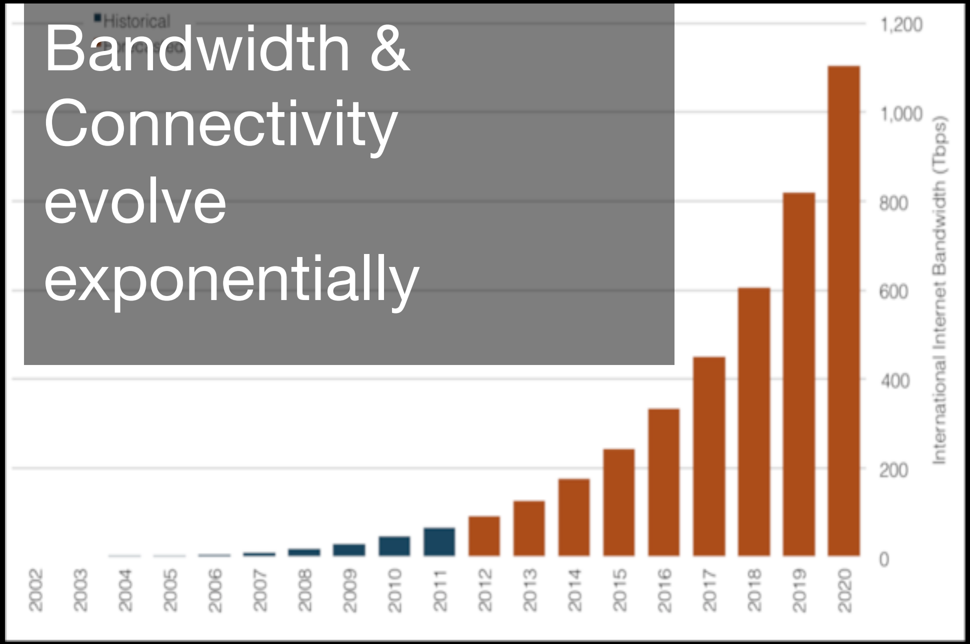


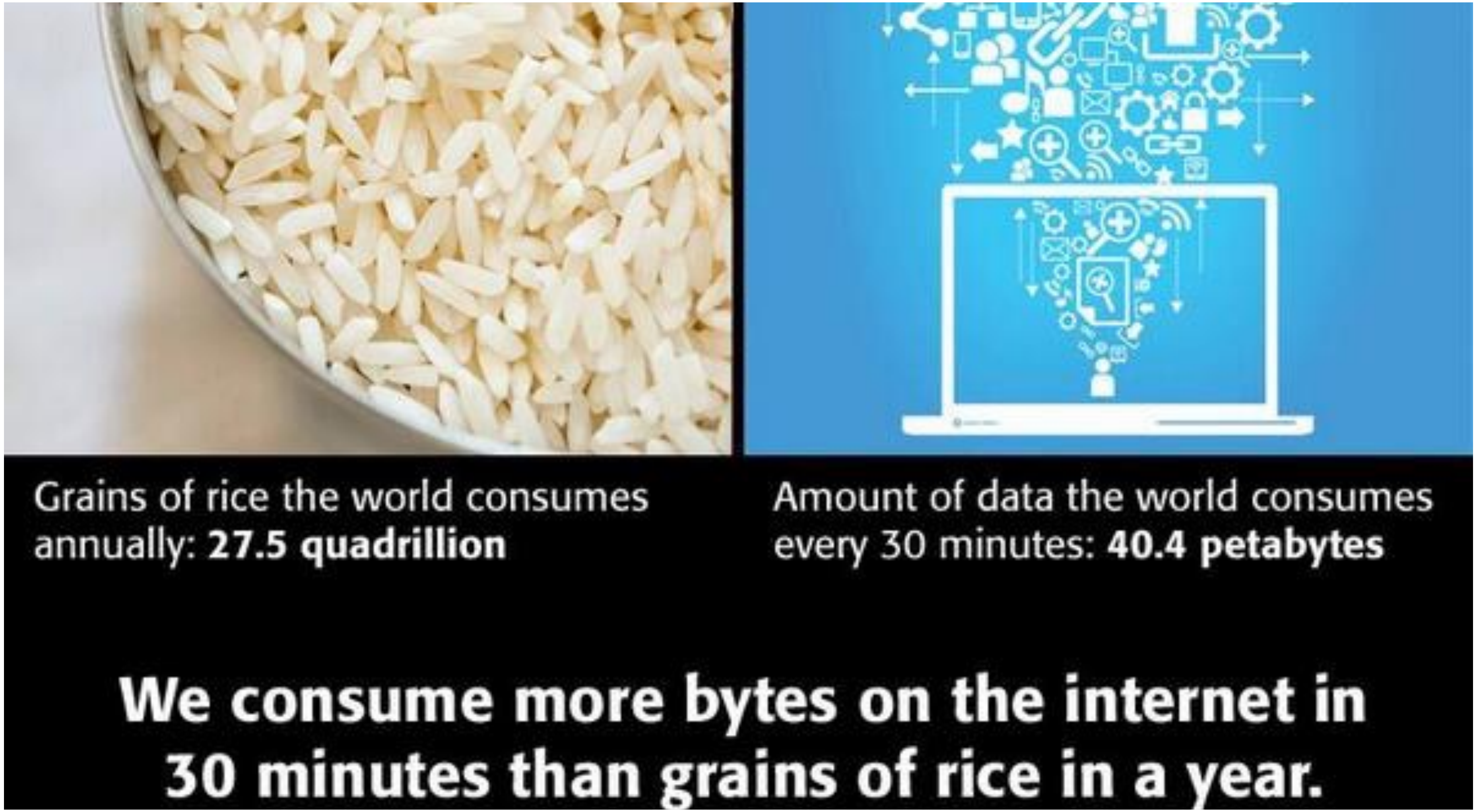
Computational power x 2 every 18 months



Moore's law:
computing power
doubles
every 18 months

Bandwidth &
Connectivity
evolve
exponentially





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

1 kB = 1 000
1 MB = 1 000 000
1 GB = 1 000 000 000
1 TB = 1 000 000 000 000
1 PB = 1 000 000 000 000 000

1 TB
= large university library
= 212 DVD discs
= 1430 CDs
= 3 year music CD quality


1
Data
2
Compute Infrastructure
3
Storage Infrastructure
4
Analytics
5
Visualization
6
Security & Privacy
Big Data

Data


UNSTRUCTURED
SEMI-STRUCTURED
STRUCTURED
VISUAL MEDIA
(Video scene detection, image understanding)
NETWORK SECURITY
(Intrusion detection, APTs, malware, virus attacks)
SENSOR DATA
(Intrusion detection, long term trends, weather)
SOCIAL NETWORKING
(Trend analysis, query processing)
RETAIL
(Sentiment analysis, behavior analysis)
FINANCIAL
(High-frequency trading)
LARGE SCALE SCIENCE
(High-energy physics, bioinformatics)
BATCH
NEAR REAL-TIME
REAL-TIME

The Fourth Paradigm

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

Evolution

From

I have a hypothesis

⇩

I need data to check it

⇨

To

I have data

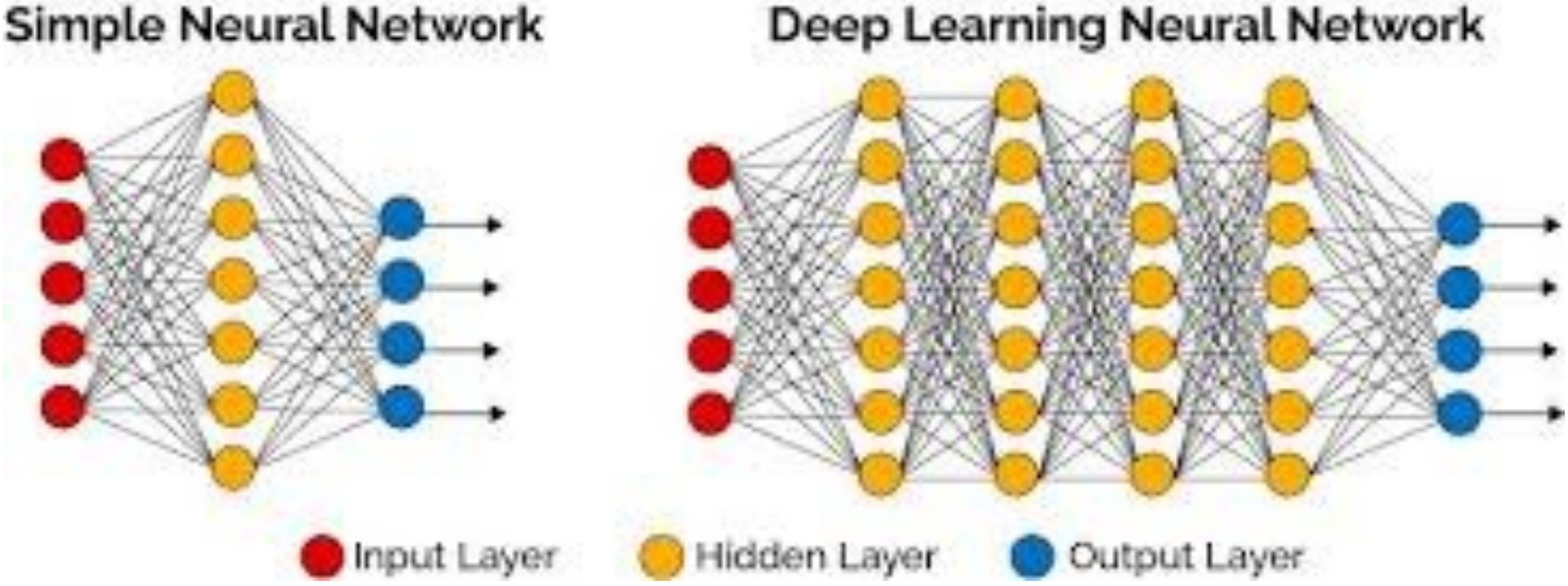
⇩

Which hypotheses can I check?

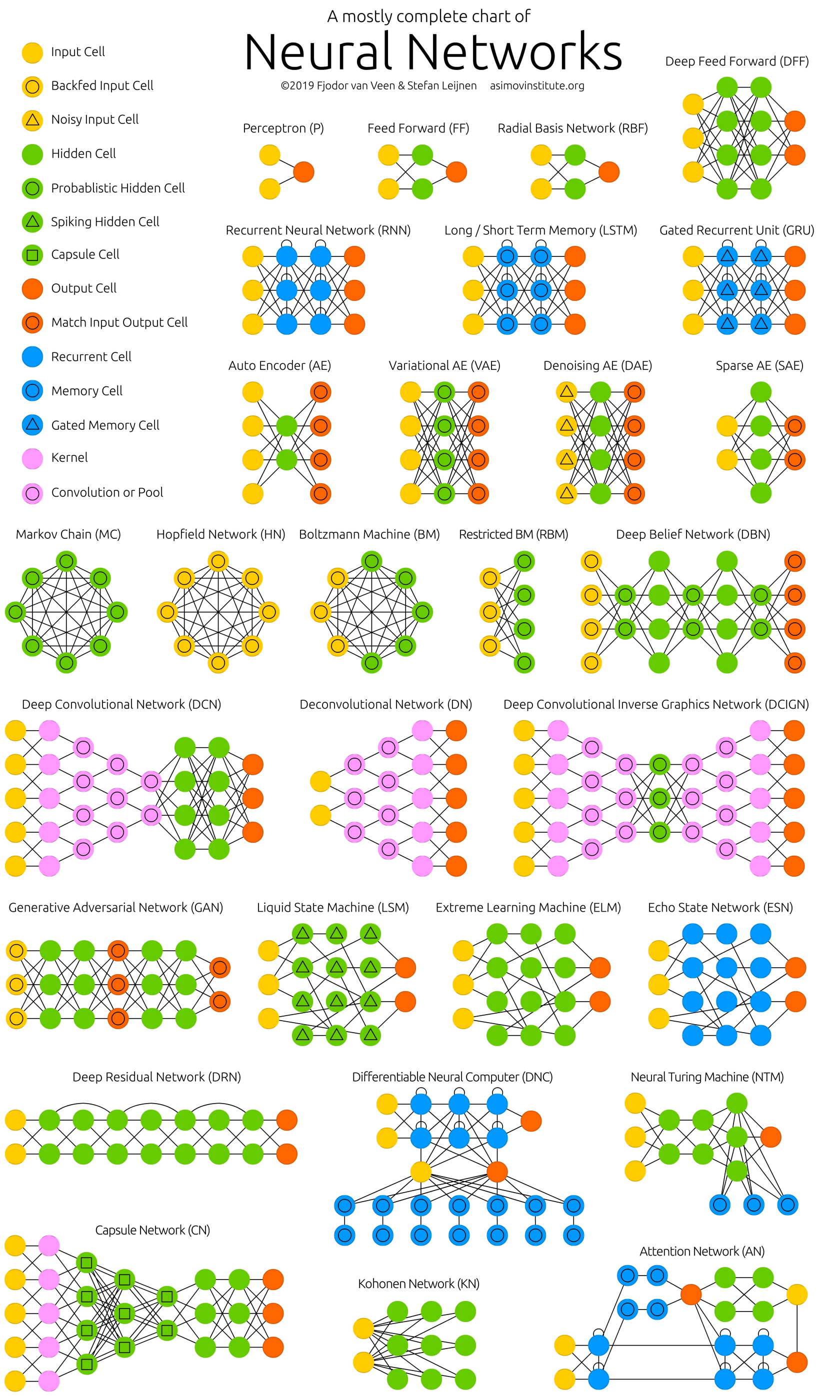
⇨ Data first!

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



Universal approximation


A mostly complete chart of
Neural Networks
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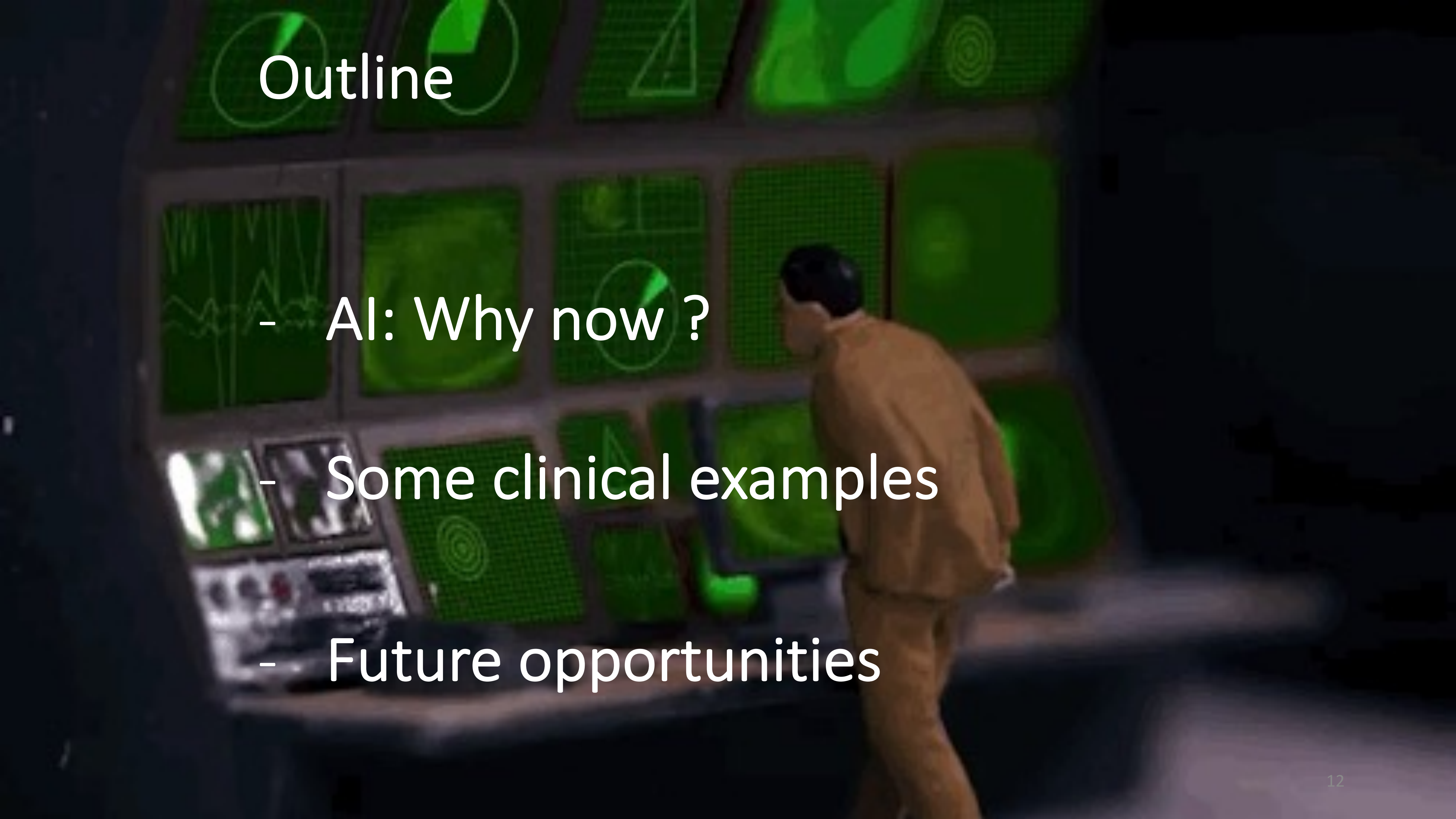
asimovinstitute.org
Input Cell
Backfed Input Cell
Noisy Input Cell
Hidden Cell
Probablistic Hidden Cell
Spiking Hidden Cell
Capsule Cell
Output Cell
Match Input Output Cell
Recurrent Cell
Memory Cell
Gated Memory Cell
Kernel
Convolution or Pool
Perceptron (P)
Feed Forward (FF)
Radial Basis Network (RBF)
Deep Feed Forward (DFF)
Recurrent Neural Network (RNN)
Long / Short Term Memory (LSTM)
Gated Recurrent Unit (GRU)
Auto Encoder (AE)
Variational AE (VAE)
Denoising AE (DAE)
Sparse AE (SAE)
Markov Chain (MC)
Hopfield Network (HN)
Boltzmann Machine (BM)
Restricted BM (RBM)
Deep Belief Network (DBN)
Deep Convolutional Network (DCN)
Deconvolutional Network (DN)
Deep Convolutional Inverse Graphics Network (DCIGN)
Generative Adversarial Network (GAN)
Liquid State Machine (LSM)
Extreme Learning Machine (ELM)
Echo State Network (ESN)
Deep Residual Network (DRN)
Differentiable Neural Computer (DNC)
Neural Turing Machine (NTM)
Capsule Network (CN)
Kohonen Network (KN)
Attention Network (AN)



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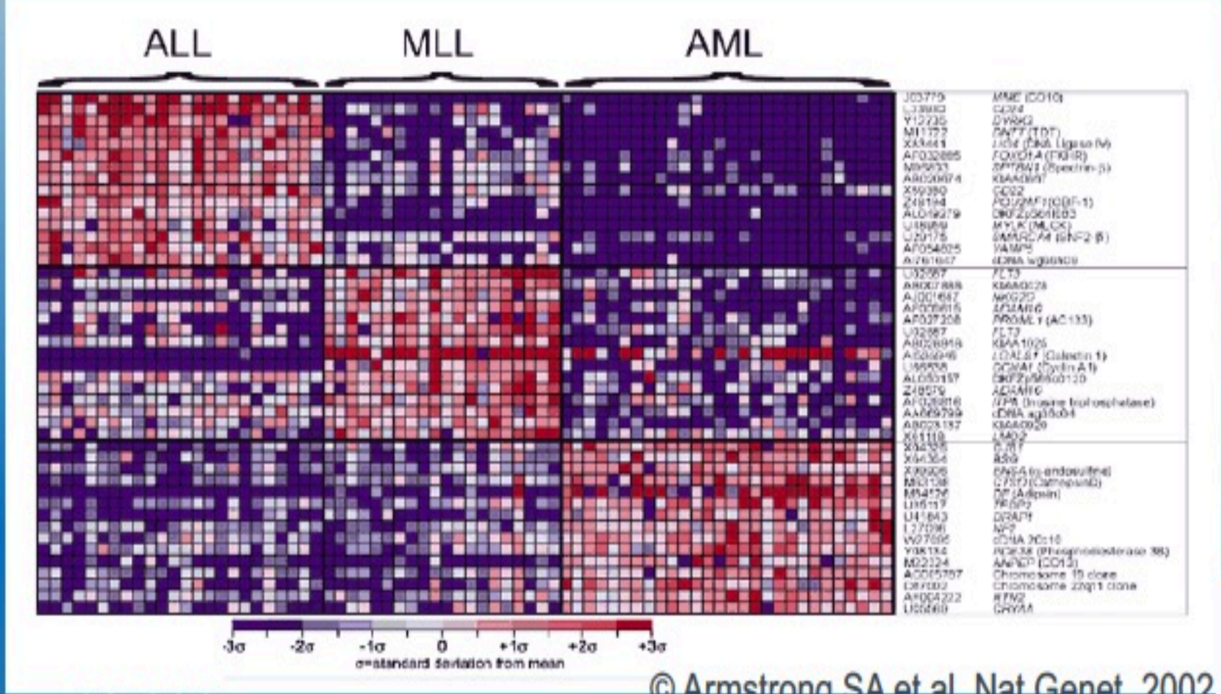
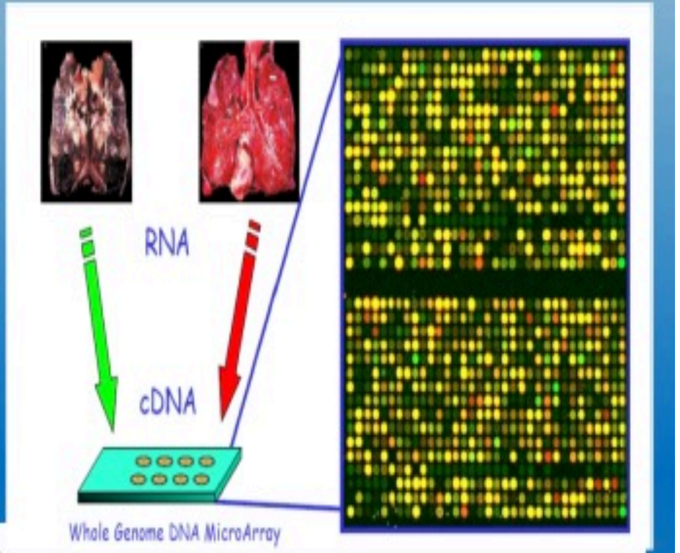
Dr. Algorithm is coming

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

– Vinod Khosla, Khosla Ventures

Example: Genomic markers for Leukemia



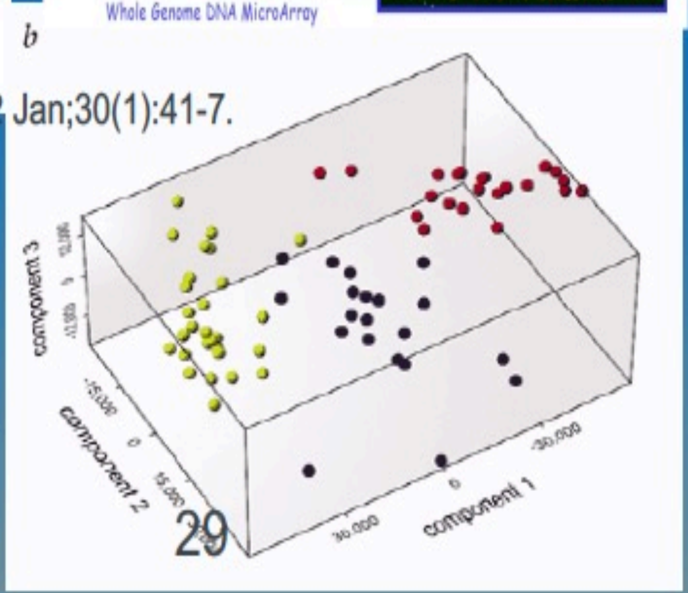


© Armstrong SA et al. Nat Genet. 2002 Jan;30(1):41-7.

12 600 genes

72 patients

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



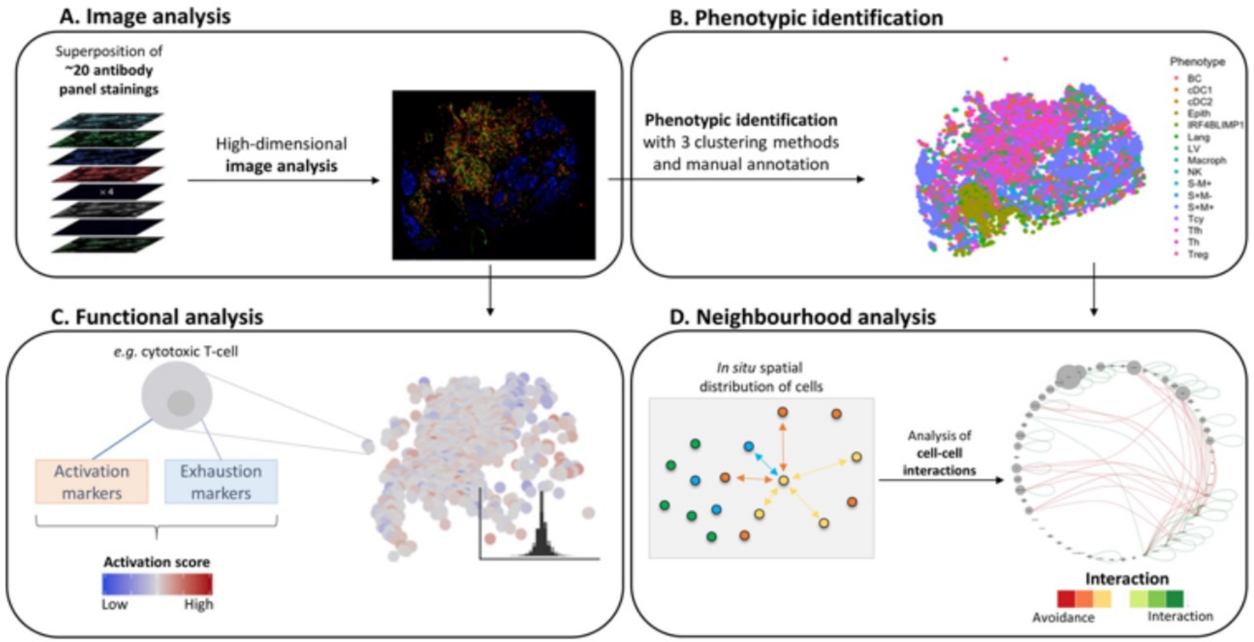
Multiple Iterative Labeling by Antibody Neodeposition **(MILAN)** method for multiplexed IHC analysis – **KOTK**

Problem: morphology-based methods that only allow the simultaneous assessment of 1-2 proteins in a single tissue slide

Aim: the generation of a reference set of 2500 highly characterized tissue samples across 9 cancer types.
the investigation of integrated tissue-based parameters (markers expression, cell types, spatial distribution, neighbourhood analysis) in order to identify two types of promising predictors of response to immunotherapy

Deliverables: A reference database for multiplex analysis of 9 cancer types and their microenvironment allowing for more precise diagnostics and a better, evidence-based design of future clinical trial projects.
Deliverable 2: A set of discriminant parameters for response to immunotherapy prediction.
Deliverable 3: Machine learning algorithms with potential for implementation in the clinics.

Project partners: Frederik De Smet, Francesca Bosisio, Oliver Bechter, Birgit Wynand, Christophe Dooms, Thomas Tousseyn, Giuseppe Floris, Hans Wildiers, Ines Nevelsteen, Raf Sciot, Paul Clement, Steven De Vleeschouwer, Tania Roskams, Chris Verslype, Frederik Nevens, Sabine Tejpar, Xavier Sagaert, Evelyne Lerut, Benoit Beuselinck, Bart De Moor, Daan Dierickx, Ann Smeets, Eric Verbeken, Esther Hauben



Direct detection and identification of neuro-oncology markers in brain tumours (TBM project)

Problem: The discrimination between tumour and normal, healthy tissue is of critical importance to achieve optimal surgical results and an improved prognosis, in any type of oncological surgery but in particular in brain tumour surgery

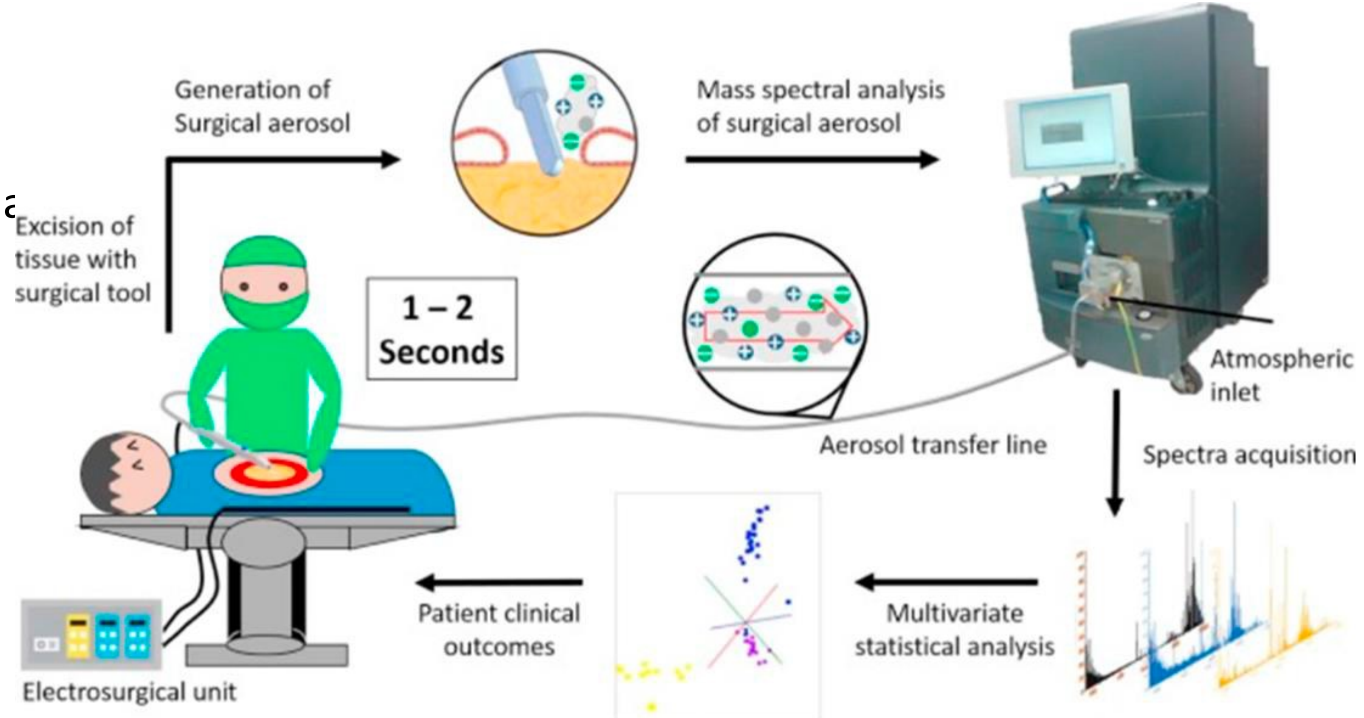
Aim: Use Mass Spectrometry Imaging (MSI) data and REIMS (surgical iKnife) to assess tumour delineation

Build a database containing typical profiles of healthy and brain tumour tissue

Identify principal components for the differentiation between healthy brain and brain tumour tissue

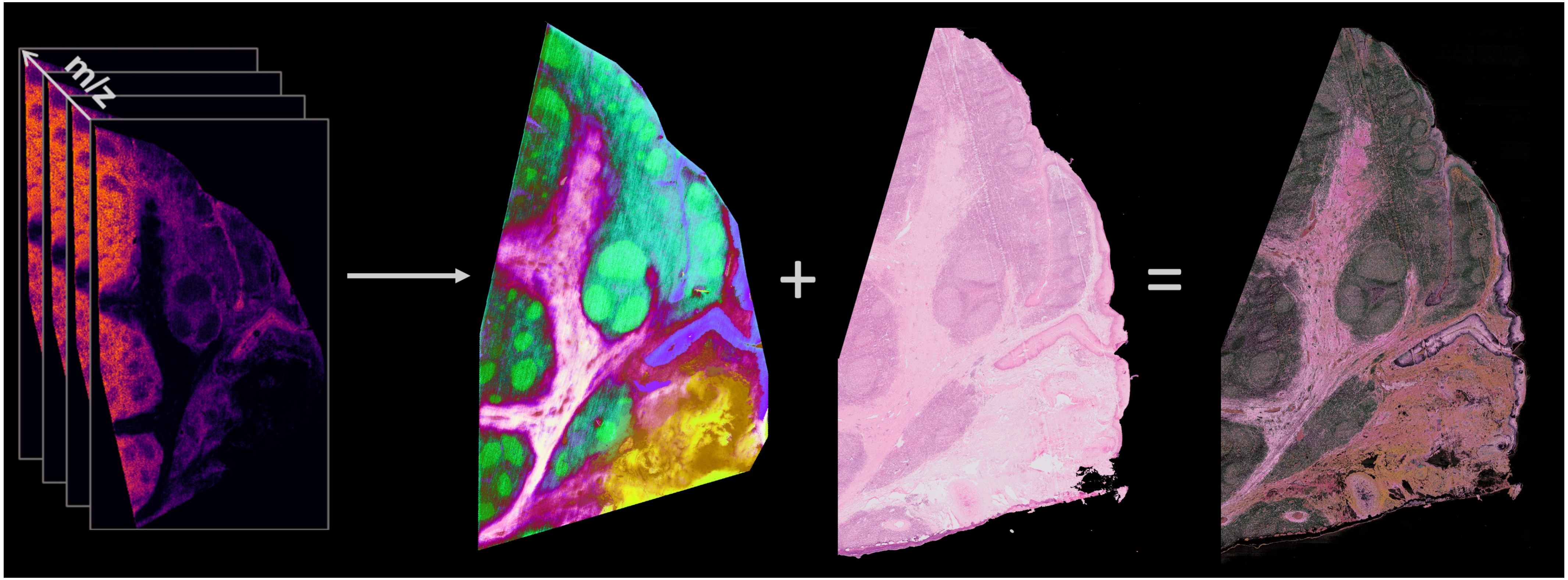
Build pattern recognition program

Deliverables: software system connected to database tha warns the neurosurgeon when approaching normal or benign tissue such that neurosurgeon knows better where tumour boundaries are located



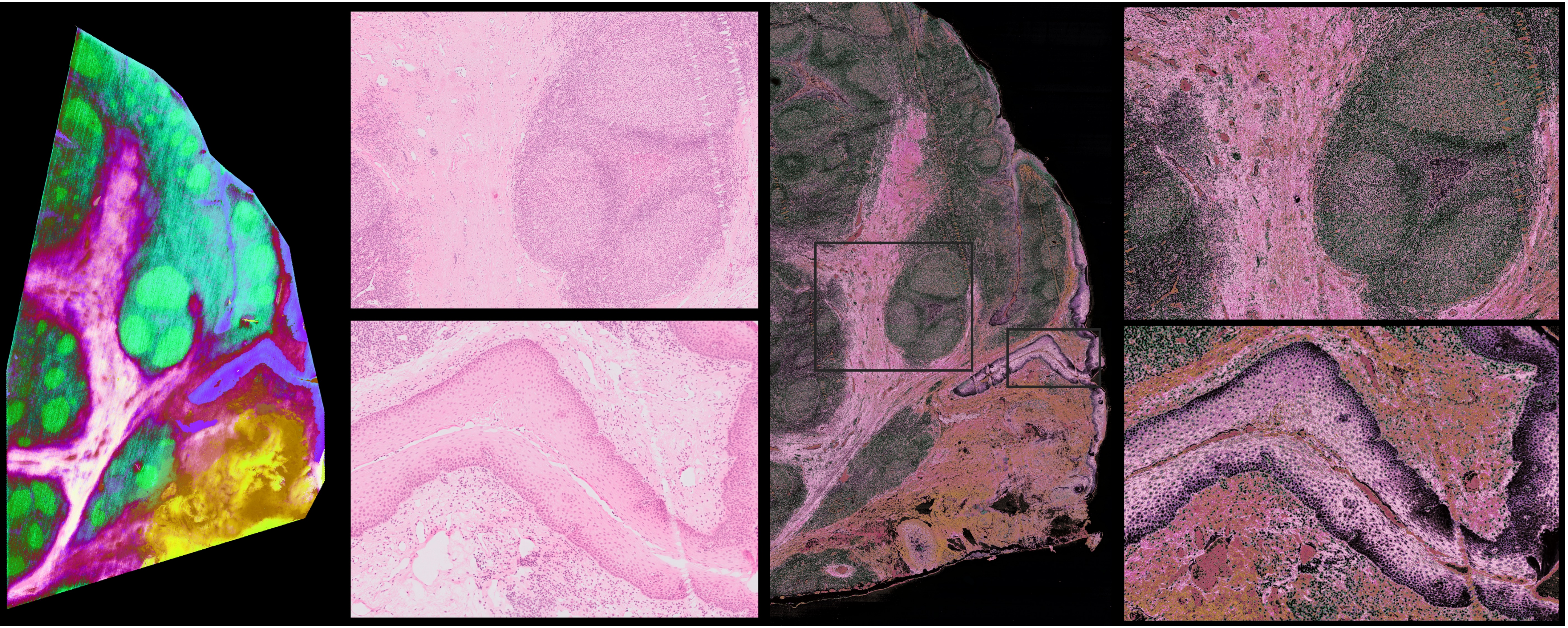
Partners: prof. De Vleeschouwer, prof. De Moor, prof. Cuypers, prof. Sciot, prof. De Smet

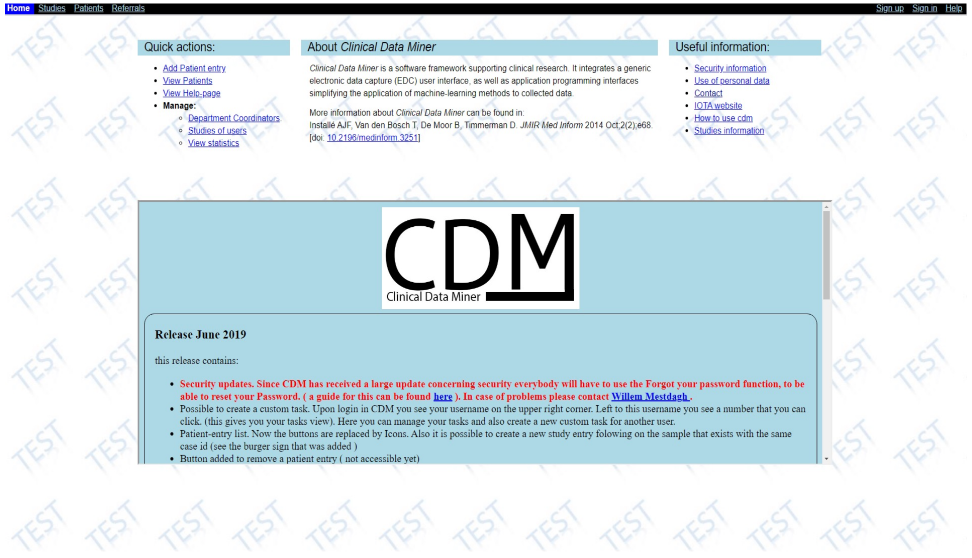
Example application: **Mass Spectrometry Imaging and H&E data fusion**



MSI dataset:
500 000 pixels x 8000 m/z
<u>30 Gb</u>

Example application: **Mass Spectrometry Imaging and H&E data fusion**





Collaboration:

- Prof. Timmerman Dirk (UZ-Leuven)
- Prof. De Moor Bart (ESAT / STADIUS)

Electronic Data Capture system for clinical studies

Cleaned Data

Integrated quality checks on data

Context of study items explanation made possible by the use of pictograms.

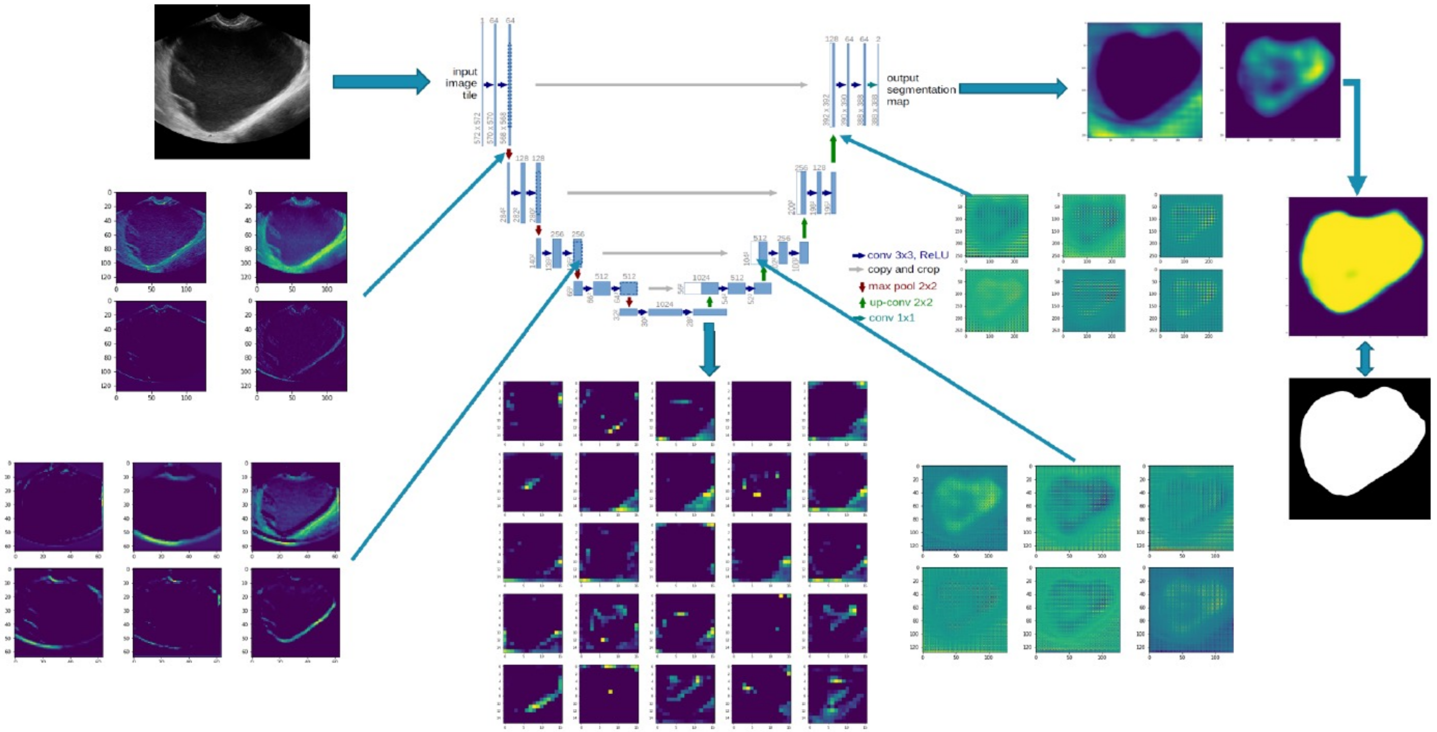
Cloud solution, international accessible

GDPR compliant

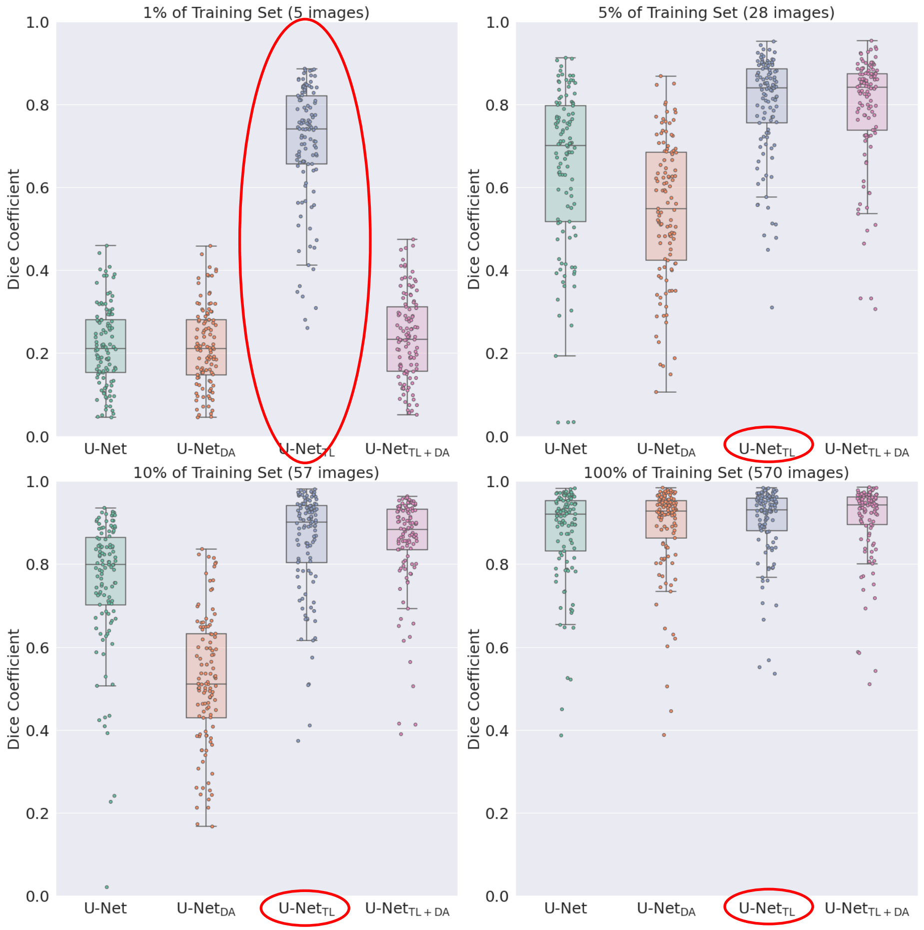
Capturing study data of:

- International Ovarian Tumor Analysis Studies (IOTA)
- International Endometrial Tumor Analysis Studies (IETA)
- International Deep Endometriosis Analysis (IDEA)

Studies	#samples	#centers
IOTA7	>6500	>50
IETA	>6000	28
IDEA	>300	11



Automated segmentation of ovarian ultrasound 2D images via modified U-net[1] convolutional neural network. The top left figure is an ovarian ultrasound image and the most right lower figure is the segmentation prediction from our learned model. The figure shows the intermediate layers' outputs from our model, in order to provide more intuition and interpretation in 'black box' deep learning model, which is very important in medical field.



The potential of exploring transfer learning in medical field. After applying a pre-trained neural network (based on ImageNet[2] dataset) in our original model, the result shows a big potential that the required number of training data for deep learning model could be reduced with the help of utilizing transfer learning.

[1]Ronneberger, O., Fischer, P., & Brox, T. (2015, October). U-net: Convolutional networks for biomedical image segmentation. In International Conference on Medical image computing and computer-assisted intervention (pp. 234-241). Springer, Cham.

[2]Deng, Jia, et al. "Imagenet: A large-scale hierarchical image database." *2009 IEEE conference on computer vision and pattern recognition*. Ieee, 2009.

Forecasting kidney allograft function

Project cooperator: UZ Leuven

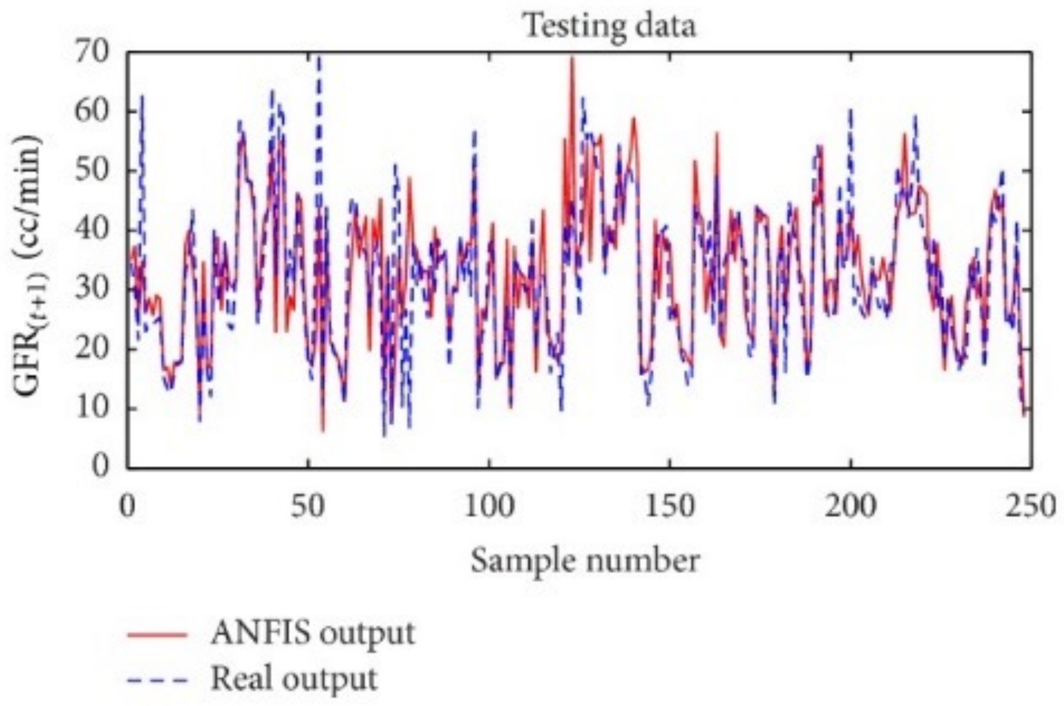
Time: 10/2018 – current (Ongoing)

Aim of Project: Forecast the kidney allograft function after kidney transplantation based on patients' sequential kidney function values

Impact: provide a renal allograft function forecasting model for clinicians to help guide indication for biopsies in transplant recipients in the early stage after kidney transplantation

Related research:

'Predicting Renal Failure Progression in Chronic Kidney Disease Using Integrated Intelligent Fuzzy Expert System' [1]



Comparison of the ANFIS prediction and real $GFR_{(t+1)}$ values for the test dataset at 6-month interval [1].

[1] Norouzi, Jamshid, et al. "Predicting renal failure progression in chronic kidney disease using integrated intelligent fuzzy expert system." *Computational and mathematical methods in medicine* 2016 (2016).

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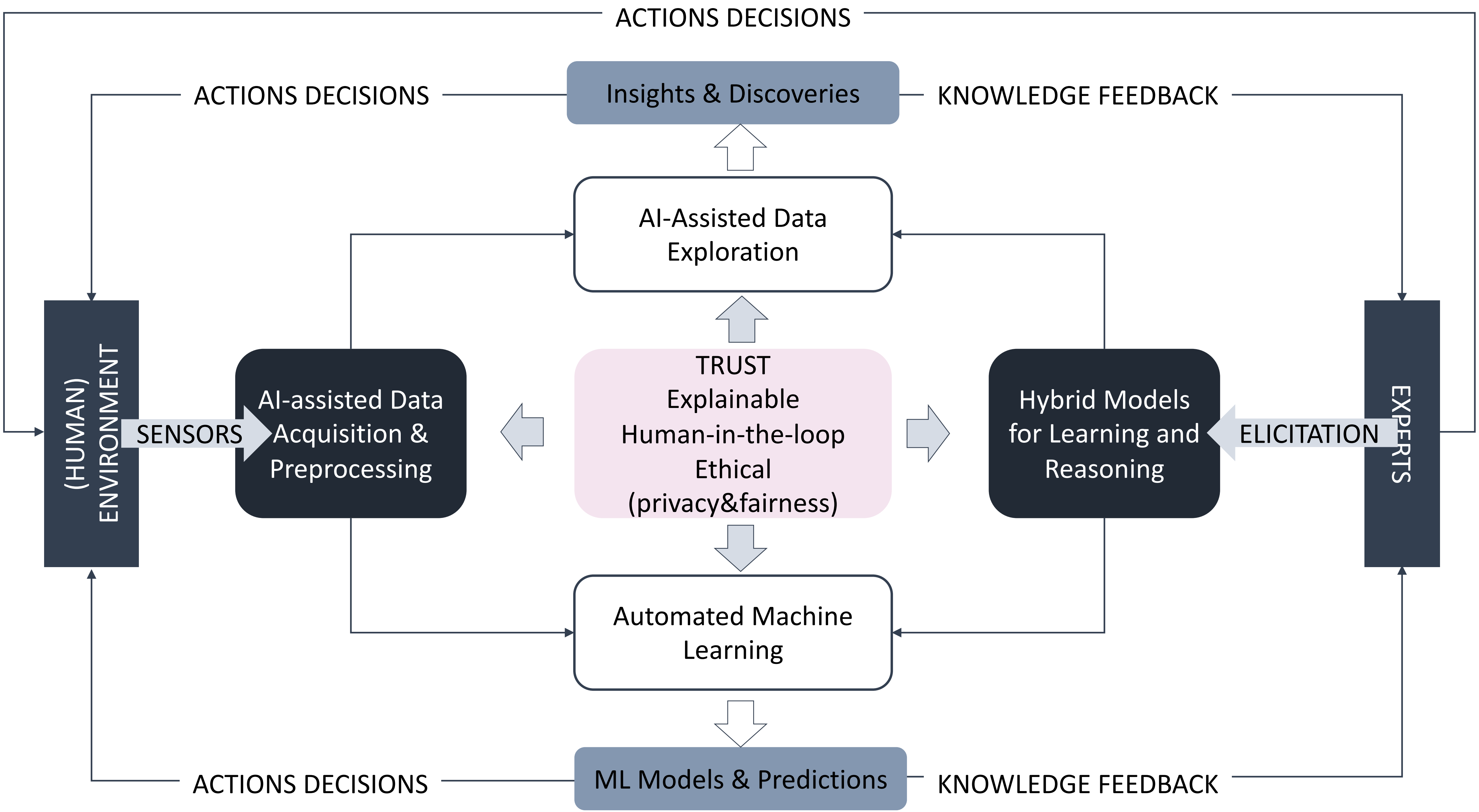
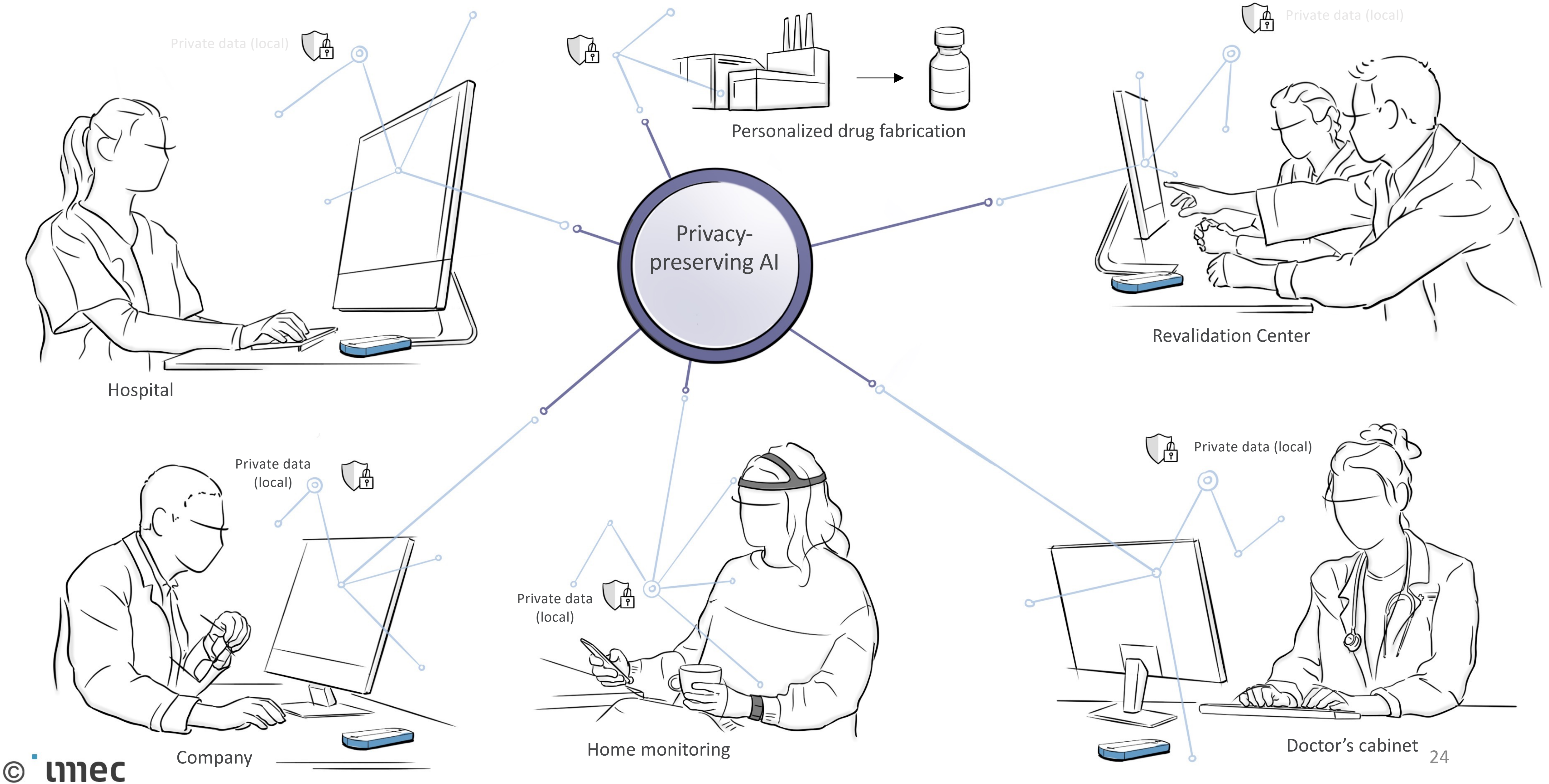

ACTIONS DECISIONS
ACTIONS DECISIONS
Insights & Discoveries
KNOWLEDGE FEEDBACK
AI-Assisted Data Exploration
(HUMAN) ENVIRONMENT
SENSORS
AI-assisted Data Acquisition & Preprocessing
TRUST
Explainable
Human-in-the-loop
Ethical
(privacy&fairness)
Hybrid Models for Learning and Reasoning
ELICITATION
EXPERTS
Automated Machine Learning
ACTIONS DECISIONS
ML Models & Predictions
KNOWLEDGE FEEDBACK

Data interaction on a need to know basis - privacy preserving machine learning



Flanders AI Impulse Program

Program Structure with 3 pillars, funded by the Flemish Government

Pillar	Yearly budget	
1 FLANDERS AI RESEARCH PROGRAM	12 Mio €	
2 FLANDERS AI IMPLEMENTATION PROGRAM	15 Mio €	Funding for R&D Projects Digital transformation trajectories in companies,...
3 FLANDERS AI SUPPORTING ACTIVITIES: ETHICS, EDUCATION AND TRAINING	5 Mio €	Knowledge Centre Data & Society Flanders AI Academy

Our consortium in Numbers

5	Universities
5	(Strategic) Research Centers
40	Research Teams
89	Professors
500	PhD students
100+	R&D projects with funding of Flemish government
200+	Companies in Collaborative funded R&D projects
18	“PhD interns” in companies in 2020
400+	Publications in peer-reviewed journals
40+	European Funded Projects

Challenge-Based Research with Demand-Driven Impact

CHALLENGE BASED RESEARCH

WITH DEMAND-DRIVEN IMPACT

AI-DRIVEN DATA SCIENCE | AI IN THE EDGE | MULTI-AGENT COLLABORATIVE AI | HUMAN-LIKE AI

PROOFS-OF-CONCEPTS (Demonstrators)

FOCUS DOMAINS and USE CASES

Management Flanders AI Research Program

Sabine Demey
Director Flanders AI Research Program
imec

AI-driven Data Science

KU LEUVEN

Prof. Bart De Moor
ESAT, KULeuven

Prof. Piet Demeester
IDLab, Ghent University-imec

UNIVERSITEIT GENT

Multi-agent Collaborative AI

Ann Nowé
Professor AI Lab, VUB

VUB VRIJE UNIVERSITEIT BRUSSEL

AI in the Edge

Mieke De Ketelaere
Program Director AI, imec

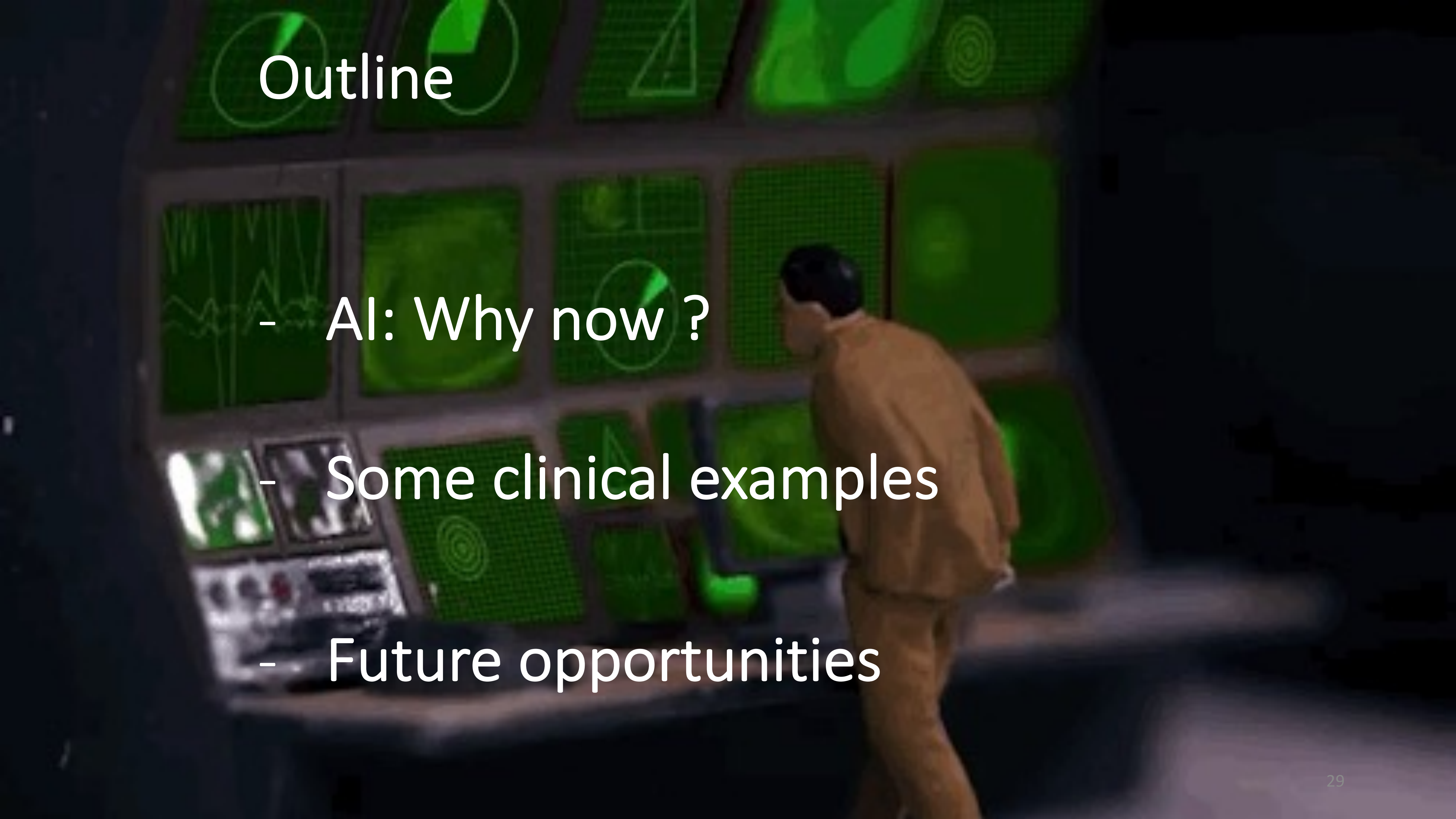
imec

CONFIDENTIAL

Human-Like AI

Prof. Steven Latré
IDLab, University of Antwerp - imec

Universiteit Antwerpen



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