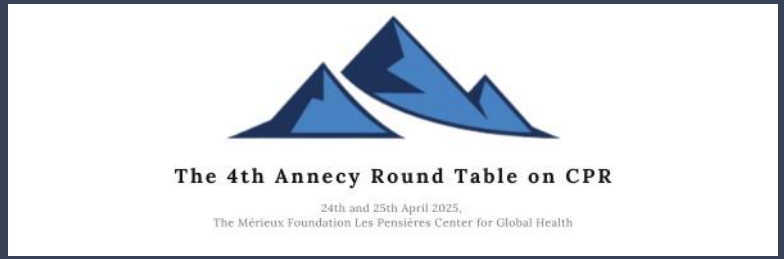
Digital Health in the 21th

Michel Dojat

Digital Health in the 21th



Michel Dojat
Deputy Scientific Director for Digital Biology and Digital Health

I declare relationships with the company Pixyl (pixyl.ai)

Warning …

I think if you work as a radiologist, you're like the coyote that's already over the edge of the cliff but hasn't yet looked down. People should stop training radiologists now. It's just completely obvious that within five years **deep learning** is going to do better than radiologists.

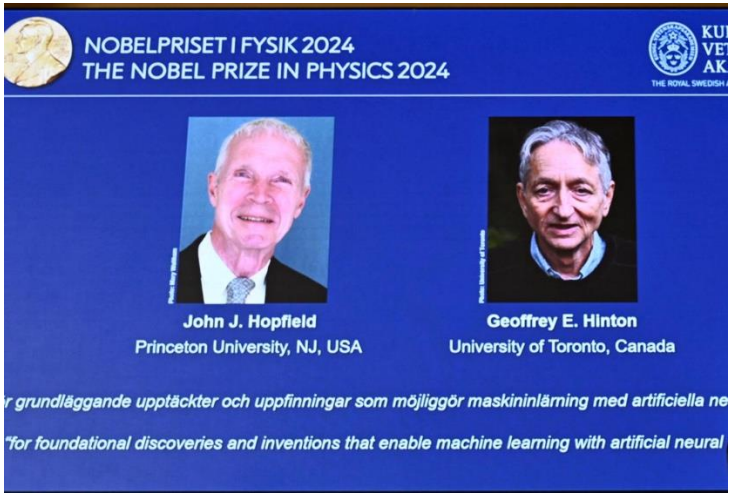
G. Hinton (2016)

Warning …

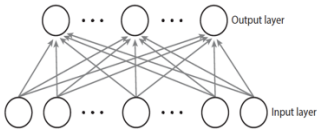
I think if you work as a radiologist, you're like the coyote that's already over the edge of the cliff but hasn't yet looked down. People should stop training radiologists now. It's just completely obvious that within five years **deep learning** is going to do better than radiologists.

G. Hinton (2016),

Turing Prize (2018), Nobel Prize in Physics (2024)



Artificial Neural Networks



ARTICLE 2017

doi:10.1038/nature24270

Mastering the game of Go without human knowledge

David Silver[1]*, Julian Schrittwieser[1]*, Karen Simonyan[1]*, Ioannis Antonoglou[1], Aja Huang[1], Arthur Guez[1], Thomas Hubert[1], Lucas Baker[1], Matthew Lai[1], Adrian Bolton[1], Yutian Chen[1], Timothy Lillicrap[1], Fan Hui[1], Laurent Sifre[1], George van den Driessche[1], Thore Graepel[1] & Demis Hassabis[1]

AlphaGO: approximately 4.6 million parameters*

Highly accurate protein structure prediction with AlphaFold

https://doi.org/10.1038/s41586-021-03819-2
Received: 11 May 2021
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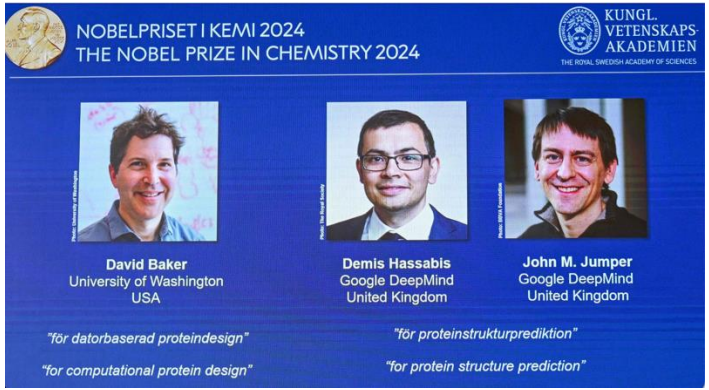
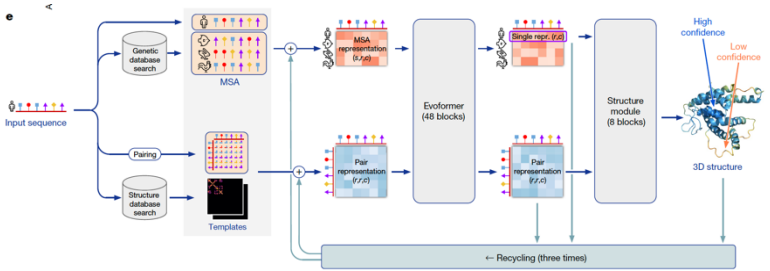
Open access
Check for updates

John Jumper[1,4]✉, Richard Evans[1,4], Alexander Pritzel[1,4], Tim Green[1,4], Michael Figurnov[1,4], Olaf Ronneberger[1,4], Kathryn Tunyasuvunakool[1,4], Russ Bates[1,4], Augustin Žídek[1,4], Anna Potapenko[1,4], Alex Bridgland[1,4], Clemens Meyer[1,4], Simon A. A. Kohl[1,4], Andrew J. Ballard[1,4], Andrew Cowie[1,4], Bernardino Romera-Paredes[1,4], Stanislav Nikolov[1,4], Rishub Jain[1,4], Jonas Adler[1], Trevor Back[1], Stig Petersen[1], David Reiman[1], Ellen Clancy[1], Michal Zielinski[1], Martin Steinegger[2,3], Michalina Pacholska[1], Tamas Berghammer[1], Sebastian Bodenstein[1], David Silver[1], Oriol Vinyals[1], Andrew W. Senior[1], Koray Kavukcuoglu[1], Pushmeet Kohli[1] & Demis Hassabis[1,4]✉





approximately tens of millions of parameters parameters*

Deep Neural Networks

*: from perplexityAI

To be in the race …

WASHINGTON — President **Donald Trump** on Tuesday talked up a joint venture investing up to **$500 billion** for infrastructure tied to artificial intelligence by a new partnership formed by OpenAI, Oracle and SoftBank. **January, 21t 2015**

Macron pledges to catch up with Trump with €109B AI investment

"We have to be in the race," the French president says.

Feb 10, 2025

AI ACTION SUMMIT

EU launches InvestAI initiative to mobilise €200 billion of investment in artificial intelligence

Feb 11, 2025

AI clusters

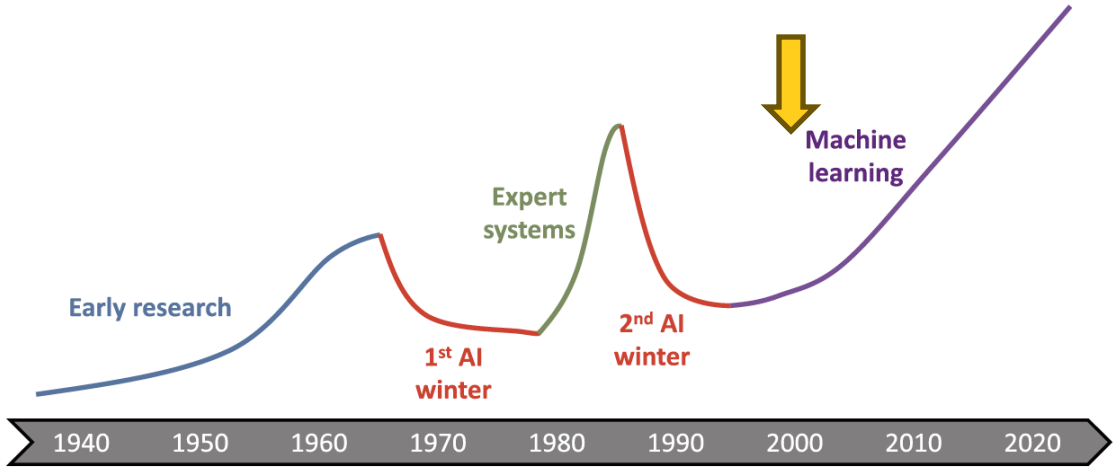
In 2022, the AI focus area with the most investment was medical and healthcare ($6.1 billion); followed by data management, processing, and cloud ($5.9 billion); and Fintech ($5.5 billion).

AI in Health
Macron wants us
to be the best

La Dépêche du midi
Feb 2025

With a digital health program

To surf the (new) wave …



Colliot 2023 Neuromethods 197 Springer

Two main streams in AI

Intelligent Agent: an entity that takes the best possible action in a situation

How to build such an artificial intelligent agent?

Machine Learning

- Bio-inspired
  - > Artificial life
  - > **Neural Networks**
- Classification (SVM,…)

Symbolic Processing

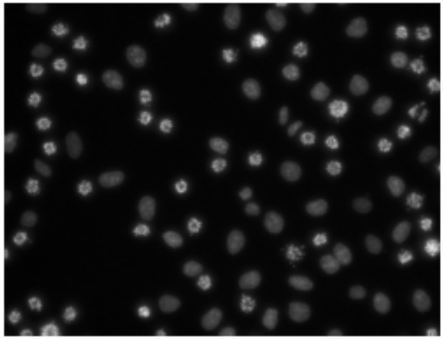
- Problem-solving
- Planning
- Logic
- Knowledge representation
  - Common knowledge
  - Meta-knowledge
  - Ontology
- Multi-agents
- Co-construction

Operations on vectors

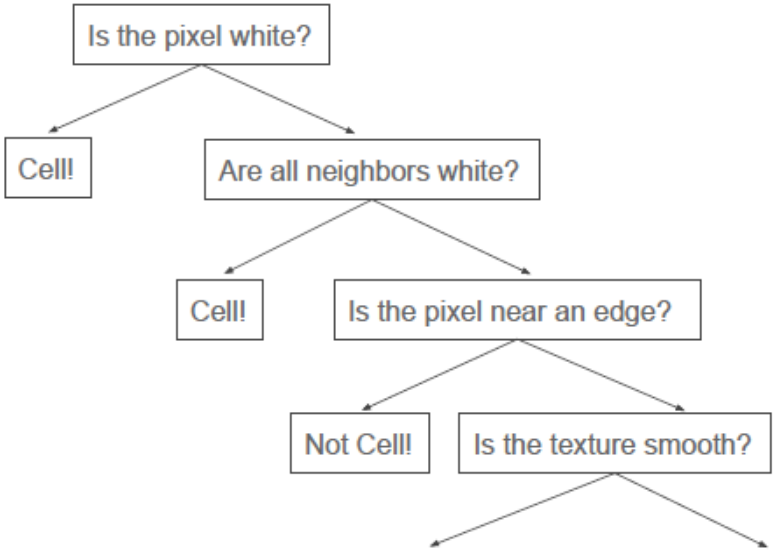
Symbols manipulation

Rule-based approach

Cells vs background segmentation

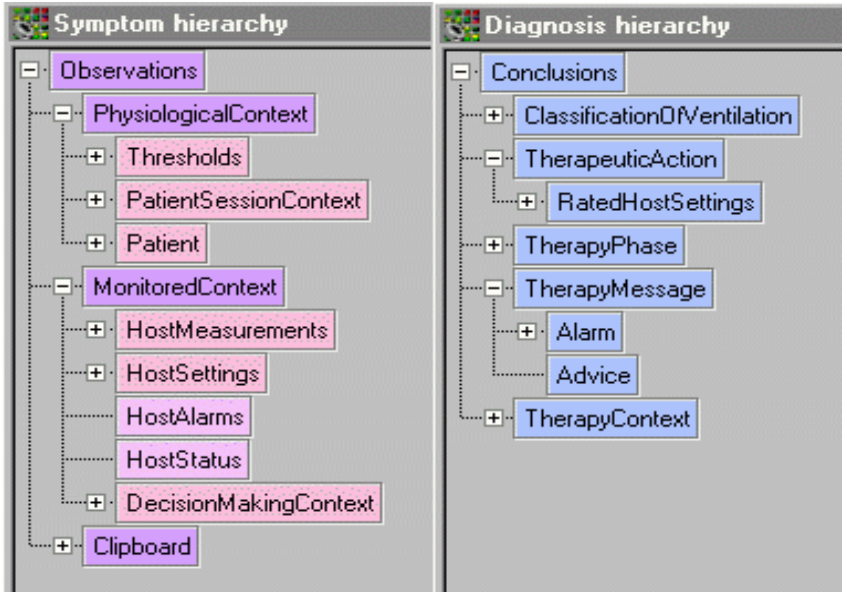


[Image: Gerlich Lab]

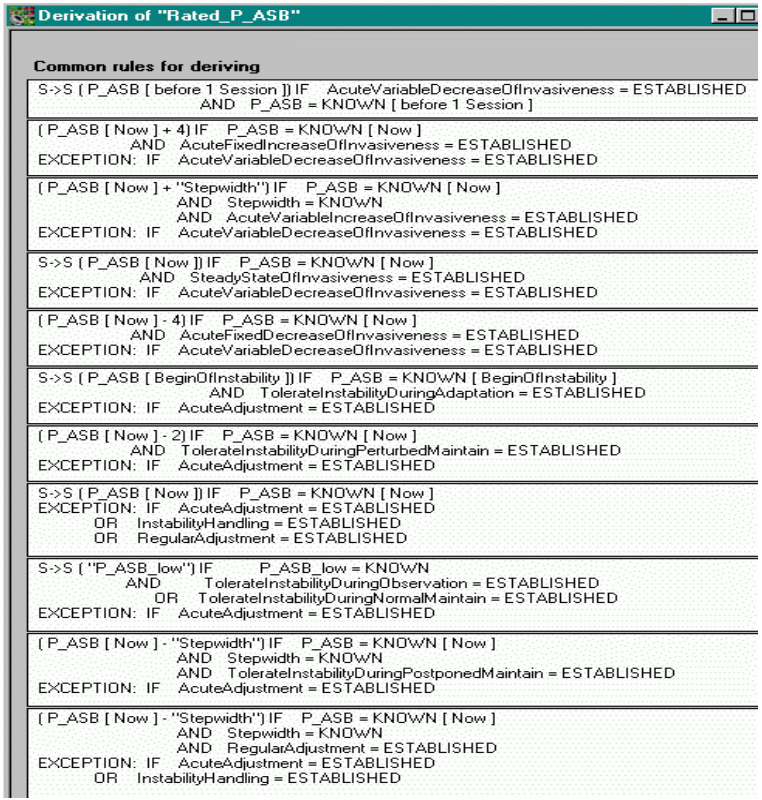


Courtesy A. Kreshuk

A knowledge base system for the Weaning



64 symptoms
50 diagnosis



Evita: Smartcare

Dojat et al. Am J Res Crit Care Med 96
Dojat et al. Am J Res Crit Care Med 00

Some limitations …

- Traditional rule-based systems have continue to perform in clinical tasks (adverse drug event …)

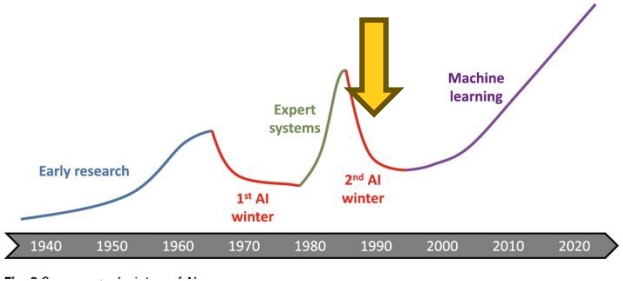
BUT:

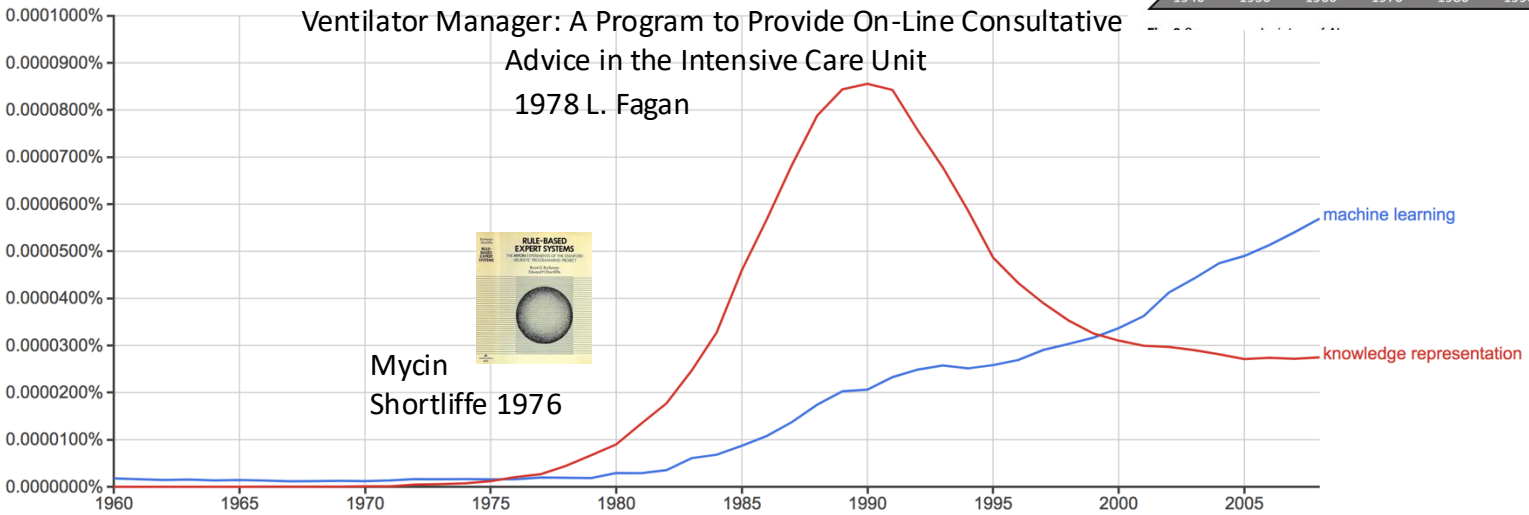
- Difficult to formalize expert's knowledge
- A lot of situations to represent

- Costly to develop and maintain

Trends …

Medical domain, a target application of AI



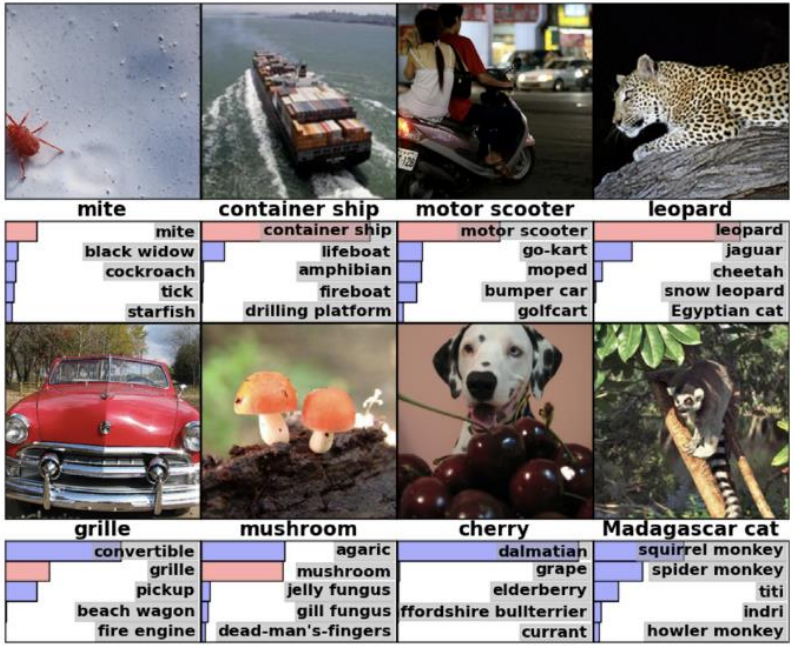


How did AI (DNN) take the power?

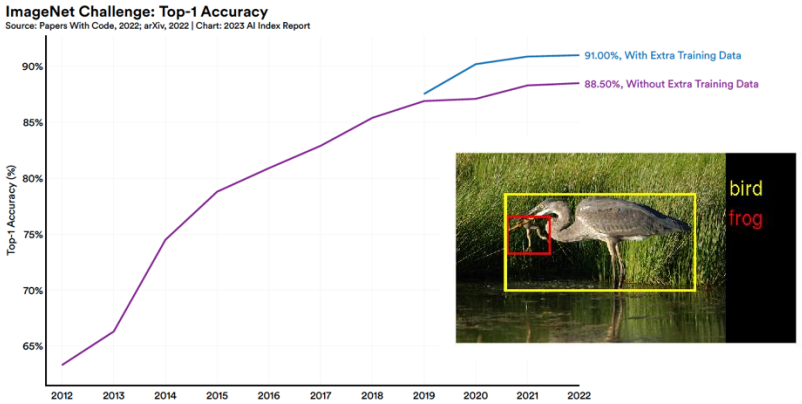
Back to the future …

Pioneered the deep learning revolution …

[Krizhevsky et al 2012]



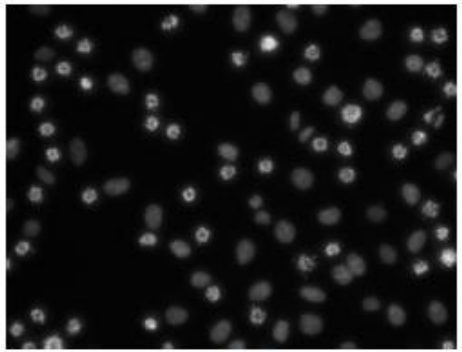
ImageNet 14 M images
20000 different object categories
2022 91% accuracy



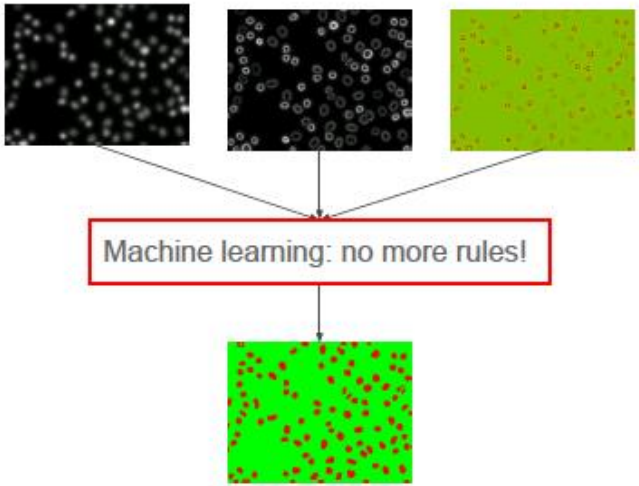
8 layers (5 convolutional + 3 fully connected), **60 Millions parameters**
1.2 M annotated images, 1000 classes => **reduced the top-5 error rate from ~26% to 15.3%**

ML approach: a new paradigm

Cells vs background segmentation



[Image: Gerlich Lab]



Automatic discovery of probabilistic regularities in the provided examples

Courtesy A. Kreshuk

ML approach: a new paradigm

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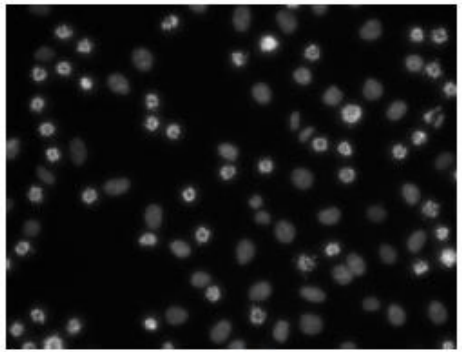

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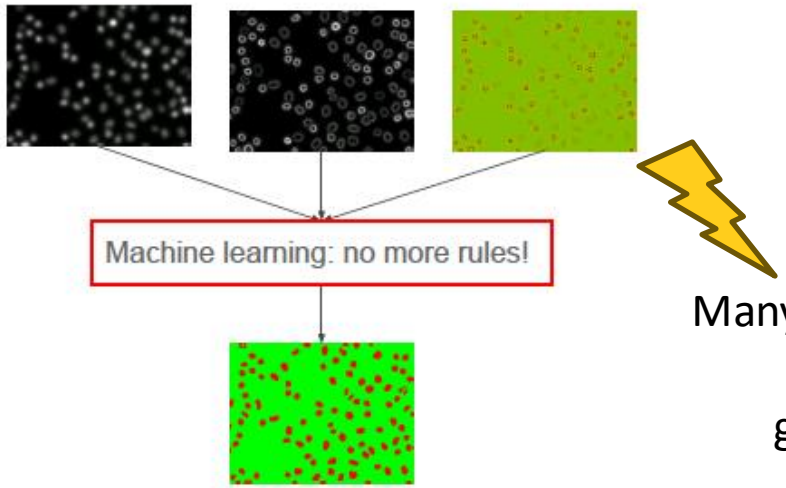


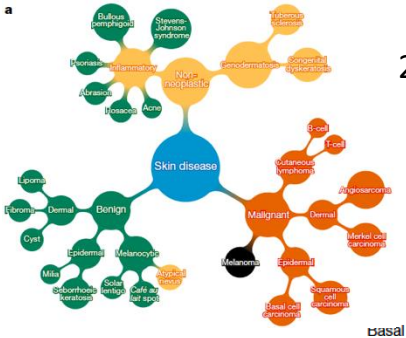
Many examples to be generic

Automatic discovery of probabilistic regularities in the provided examples

Courtesy A. Kreshuk

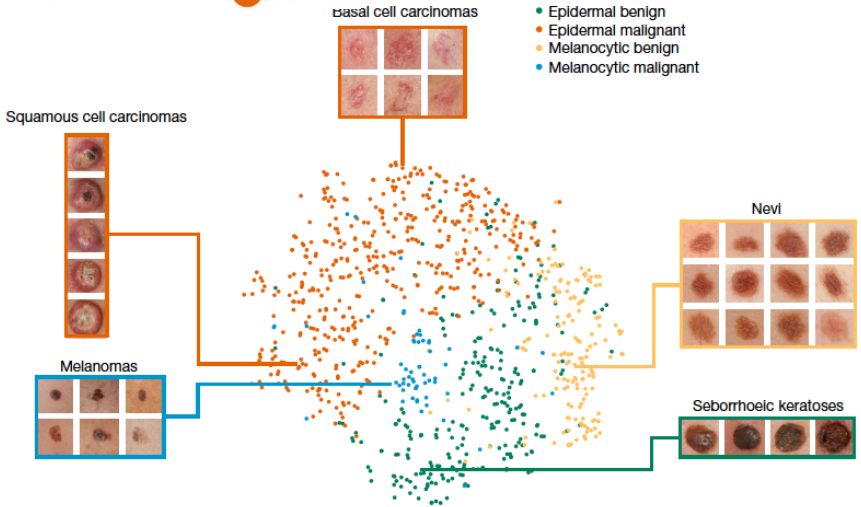
Skin cancer classification

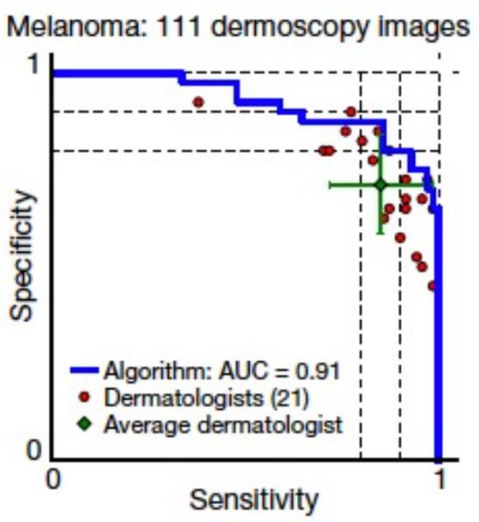
Esteva et al
Nature 2017



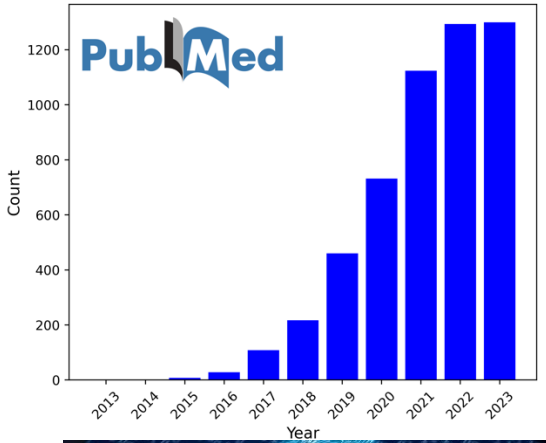
2032 diseases

127.463 biopsy images for training
1942 for validation
Inception v3
48 layers, 23 M parameters

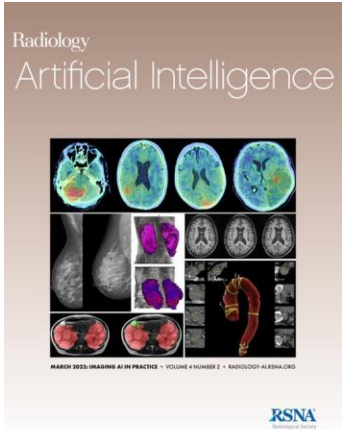


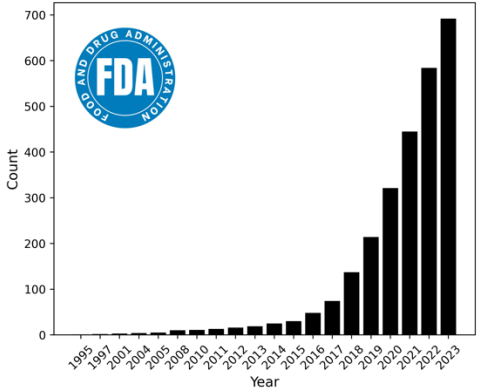


Automatic analysis of medical images: The winner takes all …



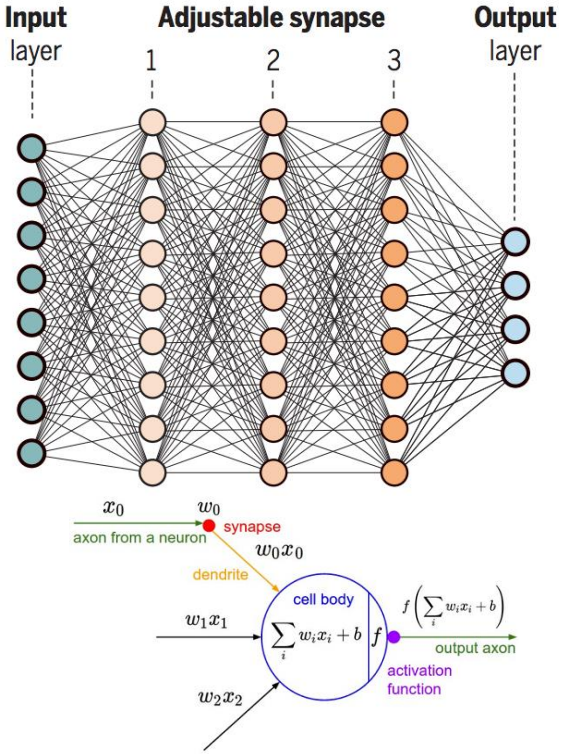
MIDL Paris 2024





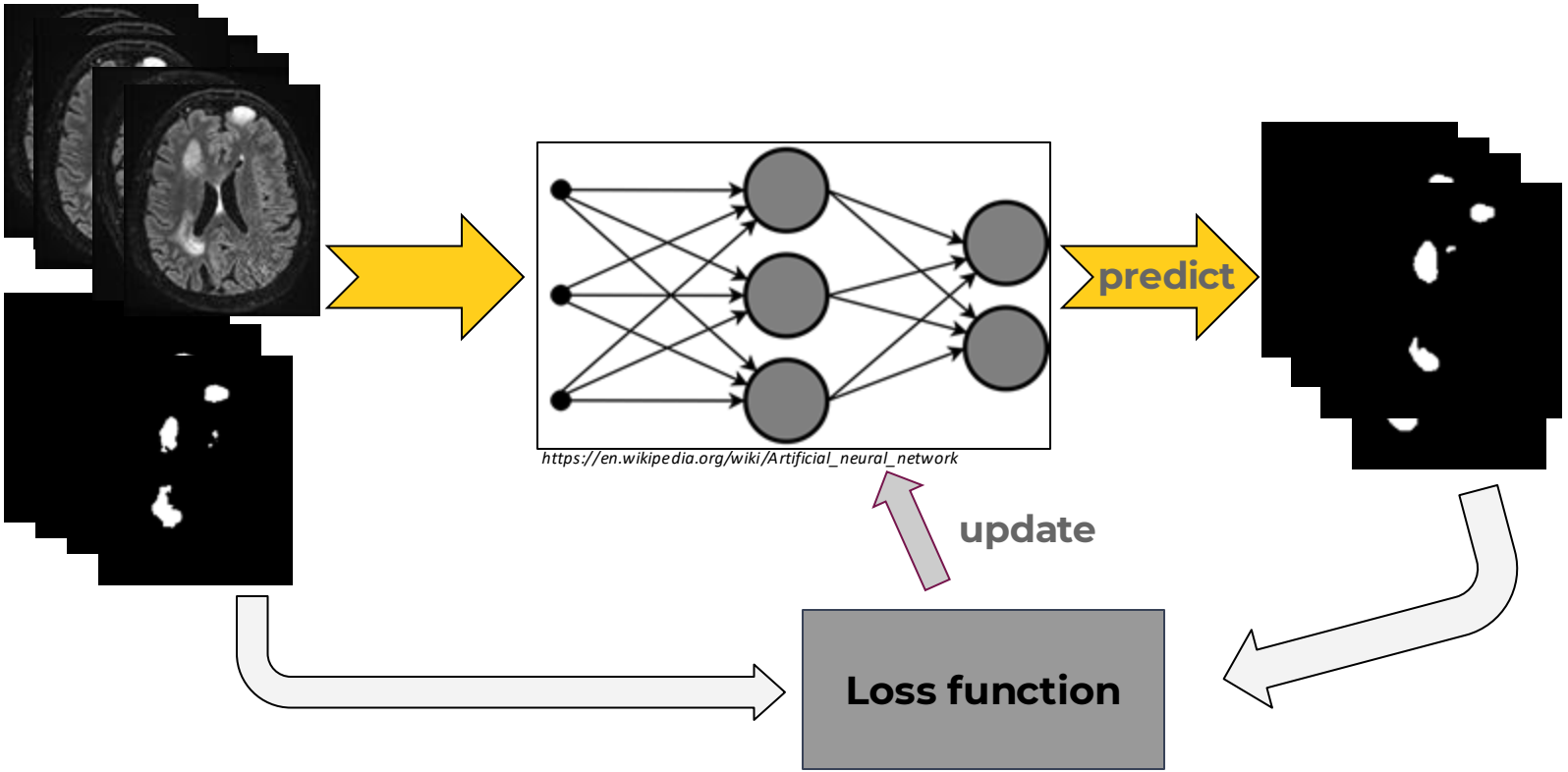
How does it works?

Ullman Science 2019



Artificial neurons (bio-inspired)

How does it works?



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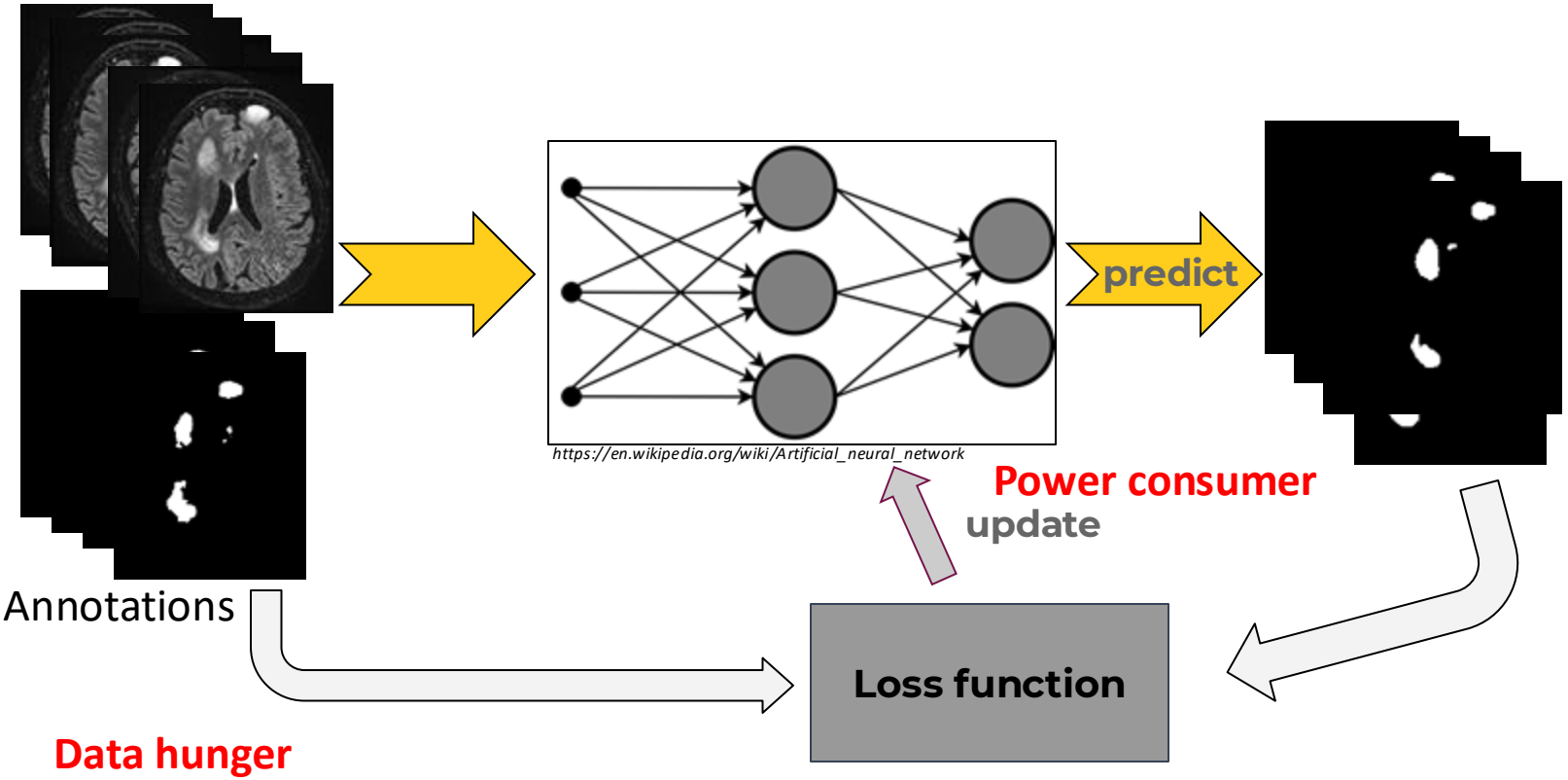
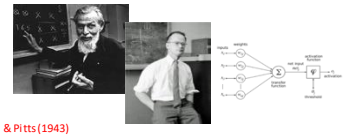


A brieve old bioinspired story: the pioneers

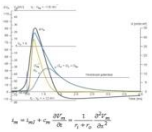
1940-1970

Donald Hebb (1949)
Neuropsychology
Learning=Synaptic modification



$$w_{ij} = \frac{1}{p}\sum_{k=1}^{p} x_i^k x_j^k,$$

McCulloch & Pitts (1943)
Neurology & Psychology
The first formal neuron



Hodgkin, A. L., & Huxley, A. F. (1952)
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Temporal dynamic in synapses modification

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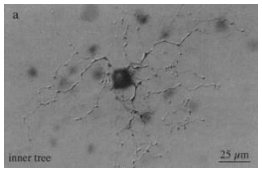
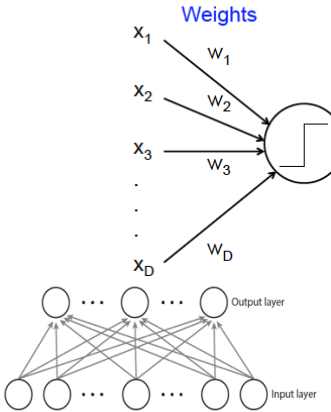
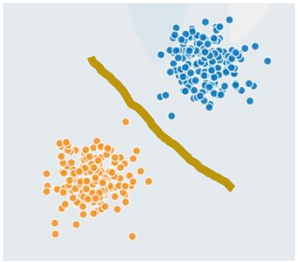


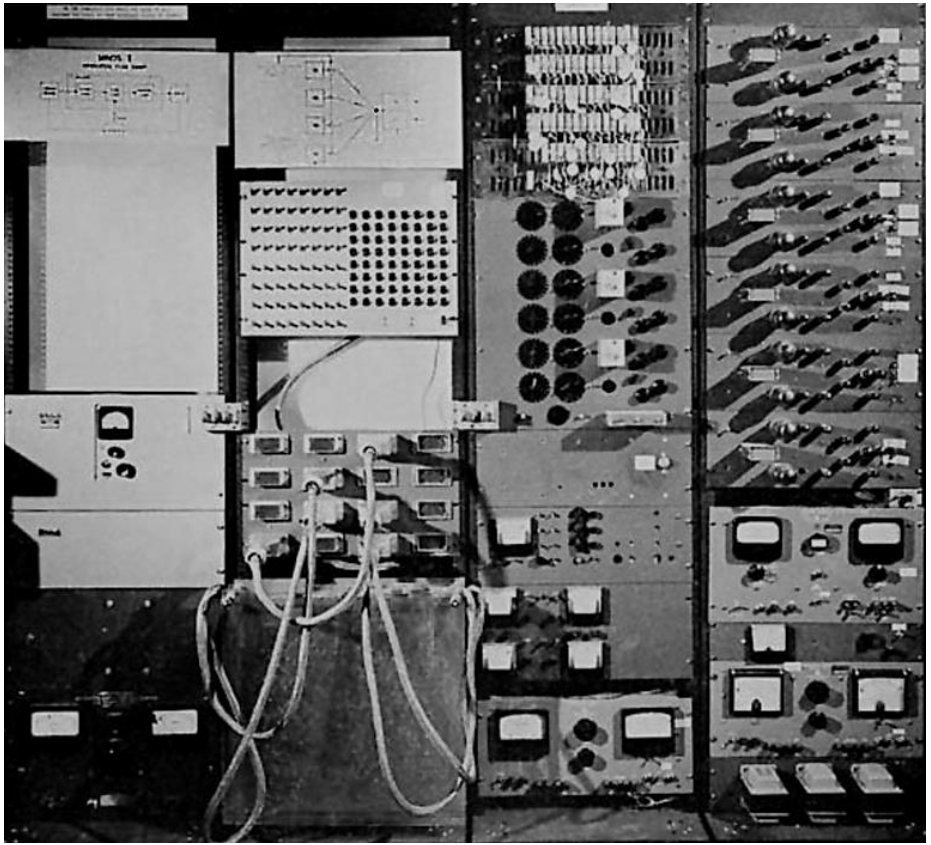




The pioneers …

Minos

1960
Stanford
Research
Institute



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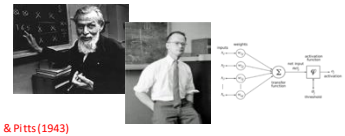

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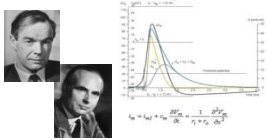

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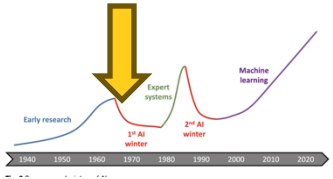
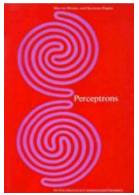
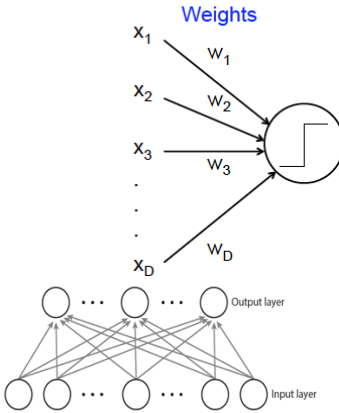
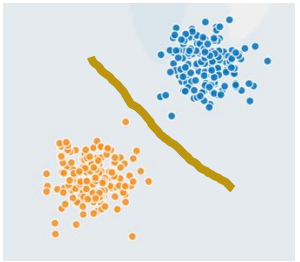




The fall of Perceptron





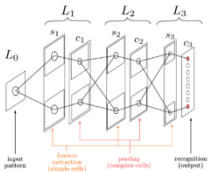
The new story …

1980-….

Kunihiko Fukushima - Bio-inspired Computer Science

Fukushima, K. (1980). Neocognitron: A self-organizing neural network for a mechanism of pattern recognition unaffected by shift in position. *Bio Cyb 46-193-202*

Convolutional filter



Beyond the Perceptron: **the Multi-Layer Perceptron**

Deep Learning: the direct offspring of the Multi-Layer Perceptron

LeCun, Y., Bengio, Y., & Hinton, G. (2015). Deep learning. *Nature, 521*(7553), 436.

Turing Prize 2018

Yann LeCun
Computer Science

Geoffrey Hinton
Cognitive Psychology & Computer Science

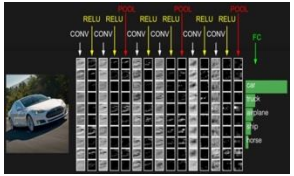
Yoshua Bengio Computer Science

Nobel Prize 2024

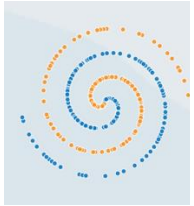
John Hopfiedld Life science
Mimics brain memories

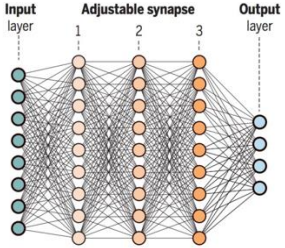
Machines & data

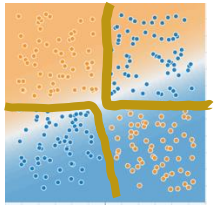
BackProp Algorithm

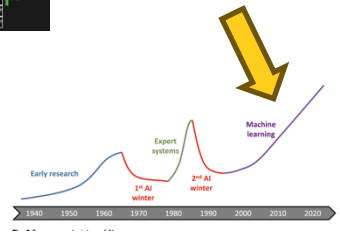


David Everett Rumelhart - Cognitive Psychology
Rumelhart, D. E., Hinton, G. E., & Williams, R. J. (1986). Learning representations by back-propagating errors. *Nature, 323*(6088), 533-536.









AI for Medical Imaging

Reconstruction

- Improve S/N, faster acquisition, finger printing

Analysis

- Classification, Segmentation, Anomalies detection, Triage, Signature

Generation

- Another modality synthesis, Report, Prediction

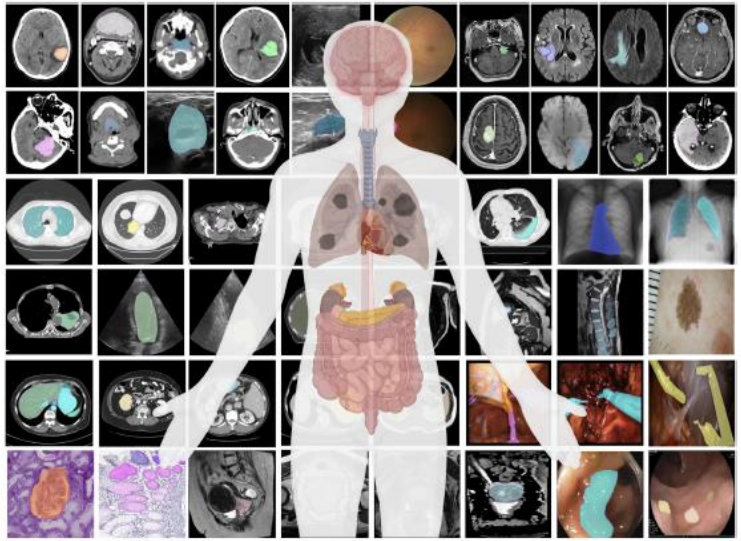
Fusion

- Time series, across modalities and subjects

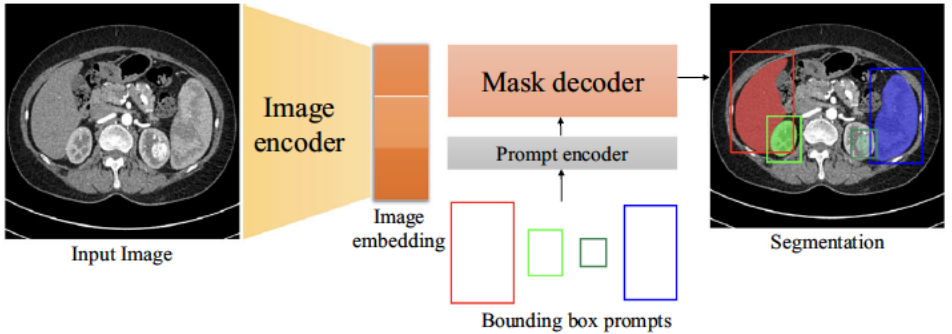
Repositories

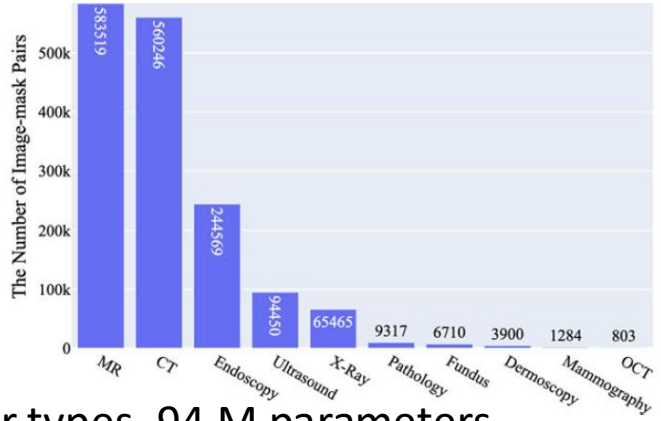
- Large databases: MJ Fox, Enigma, UK BioBank, Ofsep, …

A foundation model for medical image segmentation: MedSAM
(Segment Anything Model)



Ma et al Nat Comm 2024



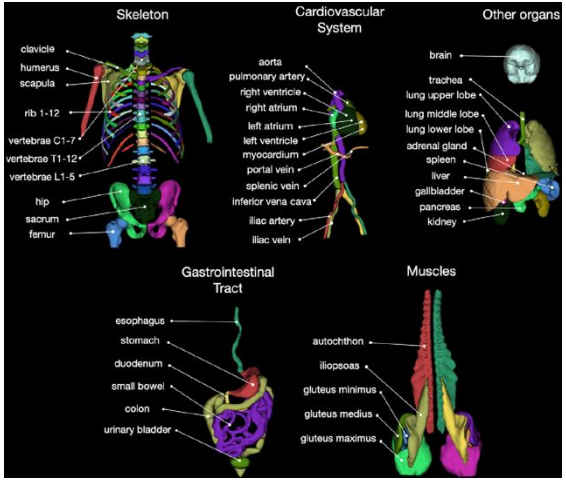


1.570.263 images, 10 imaging modalities, 30 cancer types, 94 M parameters

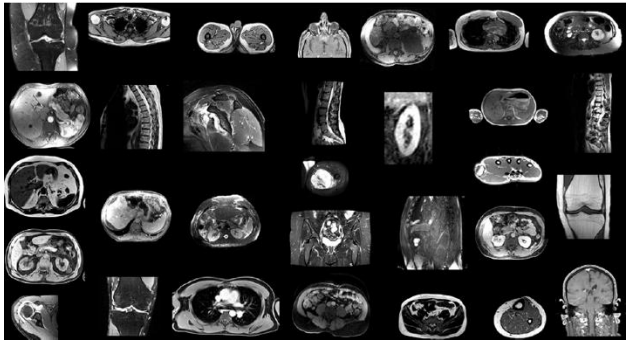
Total Segmentator

Wassserthal et al Radiology: AI 2024

12043 (CT), 104 structures, 27 organs, 59 bones, 10 muscles

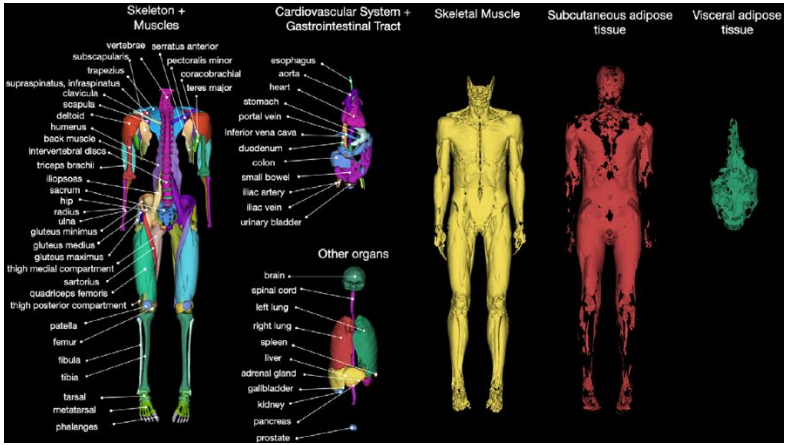


Total Segmentator MRI



D'Antonoli et al Radiology 2025

1143 (616 MRI, 527 CT), 80 structures



Main medical applications

Neurodegenerative diseases, aging
- support to diagnostic, prediction,…

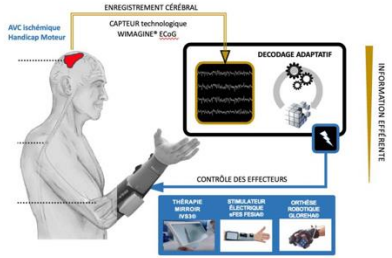
Oncology
-mechanisms, new treatment

Handicap, rehabilitation,
- neuroprothesis, BCI

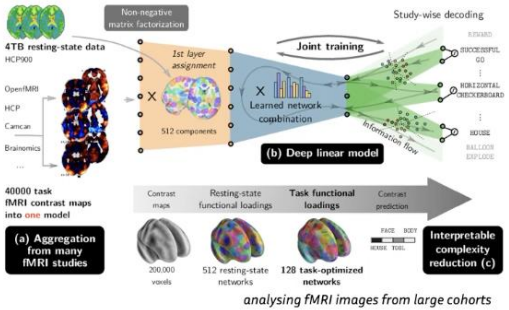
Pharmacology, drug resistance
-math. epidemiology

Public health
-clinical trials

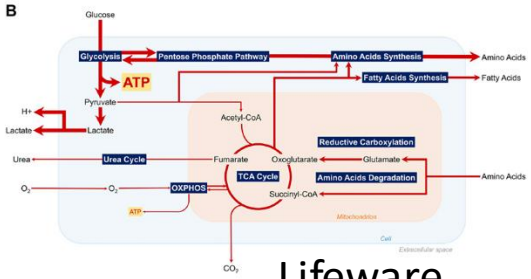
Medical robotics
-surgery, endoscopy



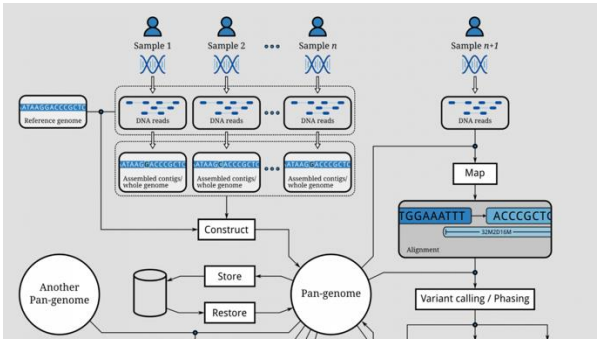
Mind



Aramis



Lifeware

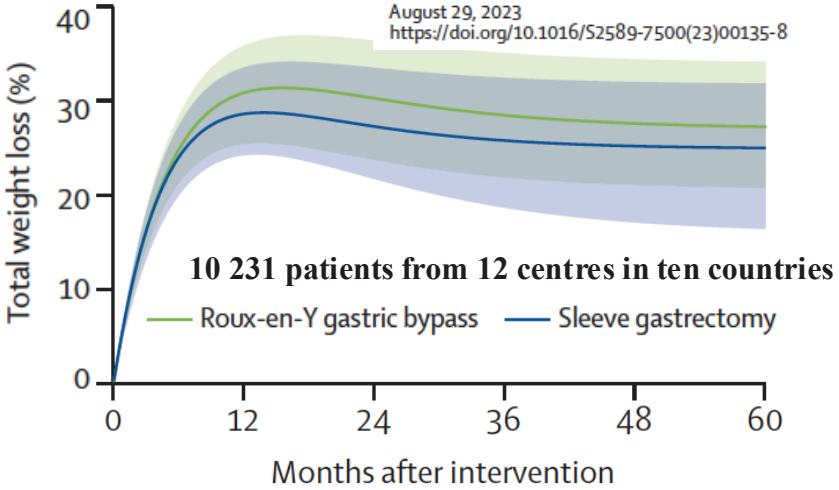


Genscale

Development and validation of an interpretable machine learning-based calculator for predicting 5-year weight trajectories after bariatric surgery: a multinational retrospective cohort SOPHIA study

Patrick Saux*, Pierre Bauvin*, Violeta Raverdy, Julien Teigny, Hélène Verkindt, Tomy Soumphonphakdy, Maxence Debert, Anne Jacobs, Daan Jacobs, Valerie Monpellier, Phong Ching Lee, Chin Hong Lim, Johanna C Andersson-Assarsson, Lena Carlsson, Per-Arne Svensson, Florence Galtier, Guelareh Dezfoulian, Mihaela Moldovanu, Severine Andrieux, Julien Couster, Marie Lepage, Erminia Lembo, Ornella Verrastro, Maud Robert, Paulina Salminen, Geltrude Mingrone, Ralph Peterli, Ricardo V Cohen, Carlos Zerrweck, David Nocca, Carel W Le Roux, Robert Caiazzo, Philippe Preux, François Pattou

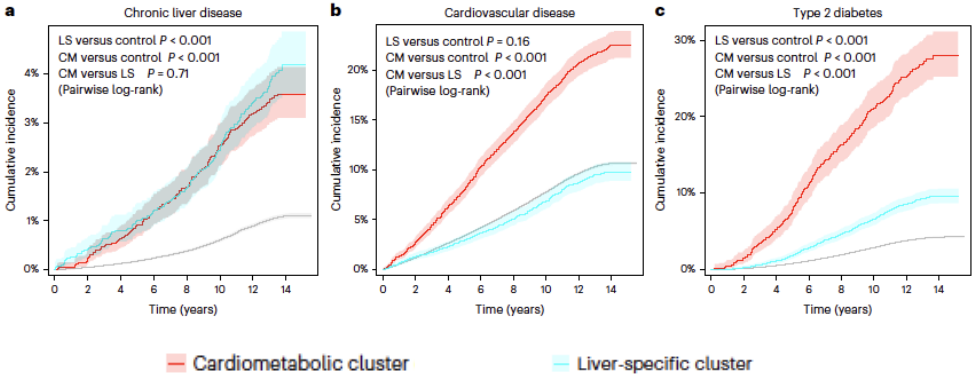
Lancet Digit Health 2023; 5: e692–702
Published Online
August 29, 2023
https://doi.org/10.1016/S2589-7500(23)00135-8



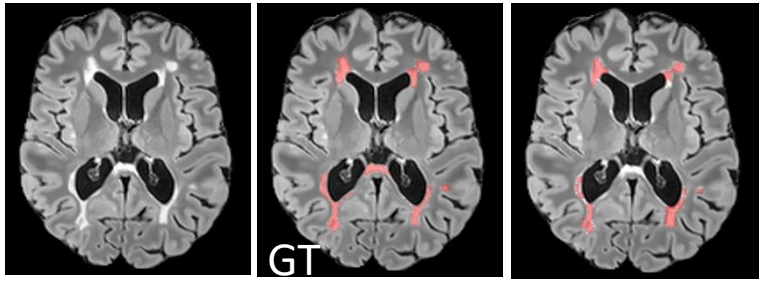
Data-driven cluster analysis identifies distinct types of metabolic dysfunction-associated steatotic liver disease

Accepted: 30 August 2024 nature medicine

1,389 individuals living with obesity



MS:Lesion load quantification



PIXYL

Pixyl.Neuro.BV
Longitudinal report

Patient Information

Name: **John Smith** | Sex: **M** | Born in: **1945** | ID: **2620**
Visit Date: **Jan 1, 2020**, Prior Visit Date: **Jan 1, 2015**

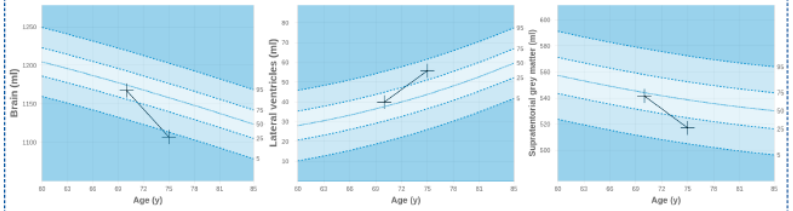
Quality Control

	Observations
Pass	-

THIS AUTOMATED REPORT DOES NOT REPLACE MEDICAL EXPERTISE.
PLEASE REFER TO THE RADIOLOGY REPORT.

Brain T1 volumetry and comparison with normative population values

	Prior visit	Current visit		
	Volume(ml)	Volume(ml)	Change(%)	Normal range(ml)
Brain	1167.37	1106.92	-5.18%	1113.29 - 1202.98
Supratentorial grey matter	541.59	517.07	-4.53%	504.91 - 572.4
Supratentorial white Matter	495.43	461.44	-6.86%	433.03 - 509.91
Cerebellum GM+WM	130.35	128.41	-1.49%	128.34 - 167.72
Left lateral ventricle	19.93	27.89	39.94%	13.02 - 32.26
Right lateral ventricle	19.96	27.87	39.63%	12.39 - 29.96



The normative distribution is calculated over 2700+ normal subjects. Volumes are normalized by the volume of the intracranial cavity when compared with the normative population of the same age. The curves displayed correspond to the 5th, 25th, 50th, 75th and 95th percentile for healthy subjects.

PIXYL

Pixyl.Neuro.MS
Longitudinal report

Patient Information

Name: **Jane Doe** | Sex: **F** | Born in: **1989** | ID: **2622**
Visit Date: **Oct 5, 2023**, Prior Visit Date: **Oct 6, 2022**

Quality Control

	Observations
Pass	-

THIS AUTOMATED REPORT DOES NOT REPLACE MEDICAL EXPERTISE.
PLEASE REFER TO THE RADIOLOGY REPORT.

Disease Activity

T2 FLAIR lesions			
New	7	Enlarging	2

Lesion Load

	Volume(ml)	Change(ml)	Lesion count *
Periventricular	9.87	0.61	≥ 1
Juxtacortical	2.27	0.47	≥ 1
Infratentorial	0.25	-0.09	≥ 1
Deep WM	0.95	0.1	≥ 1
Whole Brain	**13.34**	**1.09**	**≥ 9 ****

* The lesion count is based on the 2017 revision of the McDonald criteria.
** The Barkhof MRI criteria for MS diagnosis includes at least 9 lesions on T2-weighted images.

OxyTC: French national multicenter study

Intracranial pressure monitoring with and without brain tissue oxygen pressure monitoring for severe traumatic brain injury in France (OXY-TC): an open-label, randomised controlled superiority trial

The Lancet 2023; **22: 1005–14**

*Jean-François Payen, Yoann Launey, Russell Chabanne, Samuel Gay, Gilles Francony, Laurent Gergele, Emmanuel Vega, Ambroise Montcriol, David Couret, Vincent Cottenceau, Sebastien Pili-Floury, Clement Gakuba, Emmanuelle Hammad, Gerard Audibert, Julien Pottecher, Claire Dahyot-Fizelier, Lamine Abdennour, Tobias Gauss, Marion Richard, Antoine Vilotitch, Jean-Luc Bosson, Pierre Bouzat for the OXY-TC trial collaborators**

Summary

Background Optimisation of brain oxygenation might improve neurological outcome after traumatic brain injury. The OXY-TC trial explored the superiority of a strategy combining intracranial pressure and brain tissue oxygen pressure ($PbtO_2$) monitoring over a strategy of intracranial pressure monitoring only to reduce the proportion of patients with poor neurological outcome at 6 months.

Interpretation After severe non-penetrating traumatic brain injury, intracranial pressure and $PbtO_2$ monitoring did not reduce the proportion of patients with poor neurological outcome at 6 months. Technical failures related to intracerebral catheter and intracerebral haematoma were more frequent in the intracranial pressure and $PbtO_2$ group.

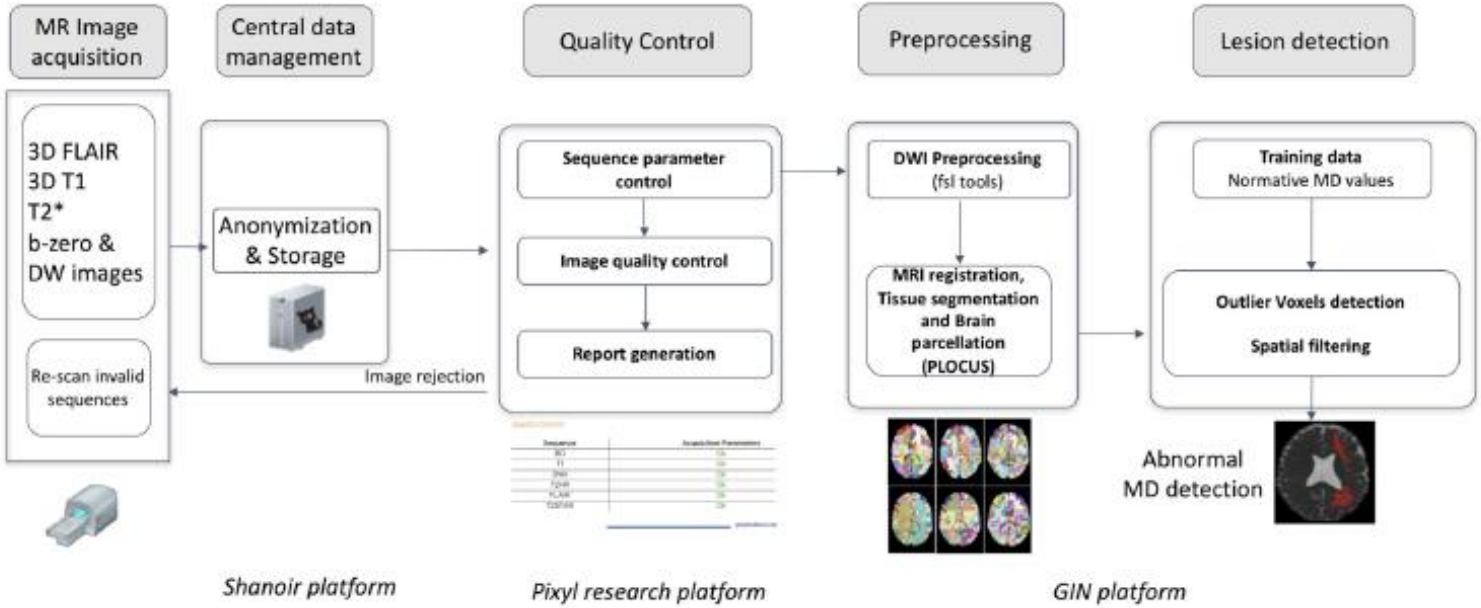
144 vs 147 patients

MRI study

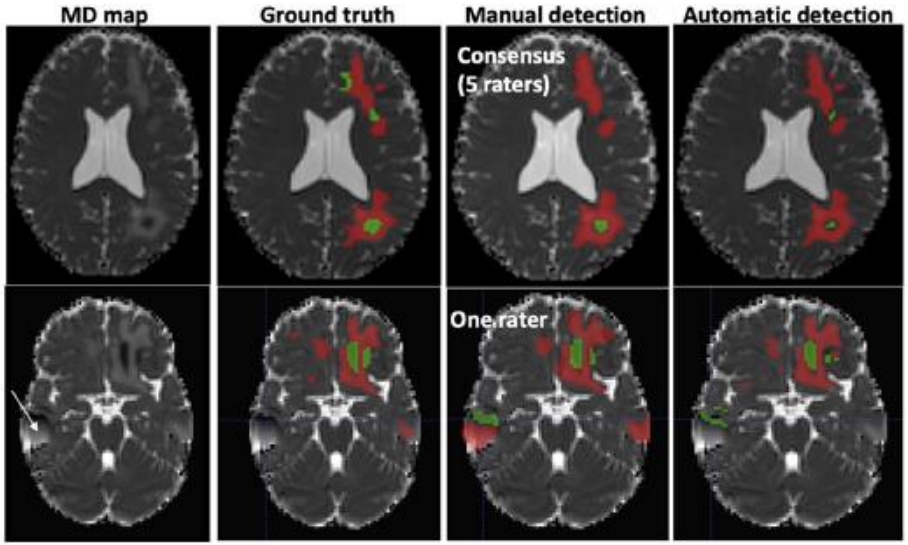
Goal: detection of abnormal mean diffusivity (MD) and fractional anisotropy (FA)

reduction MD cytotoxic edema, increase MD vasogenic edema

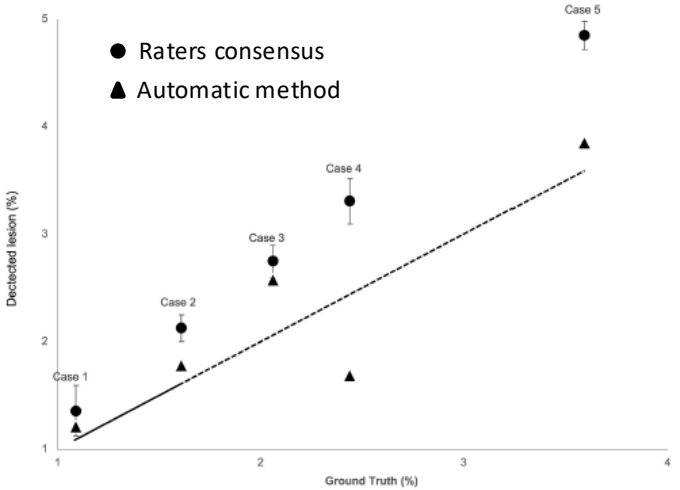
N=85, Gose 1-4, Diffusion Tensor Imaging, 23 centres



MRI study



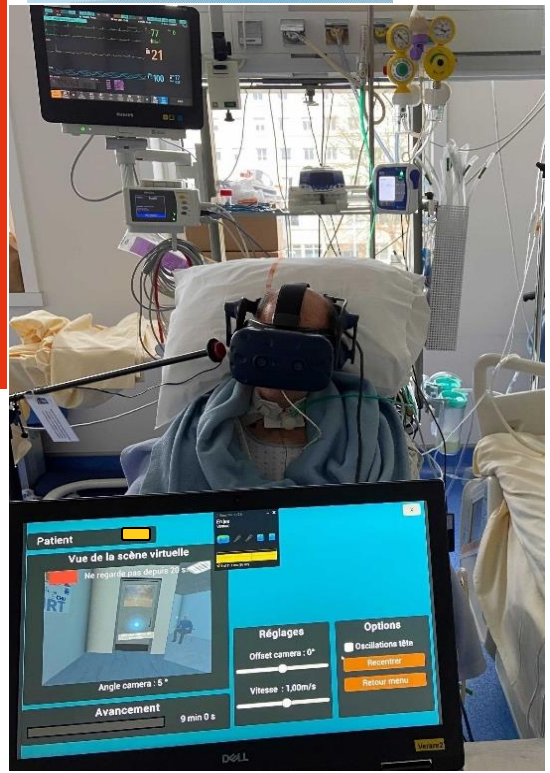
Mistral et al 2022 Front Neuro



Patients data: work in progress

Verare Project

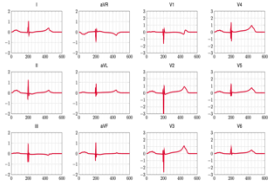
Inria
Mission Covid-19



65 patients included 2025

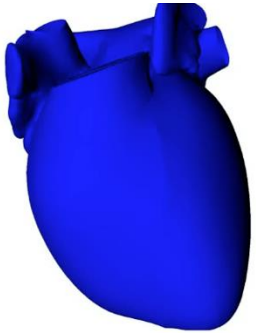
Seamless, courtesy A. Lecuyer

Digital Twin



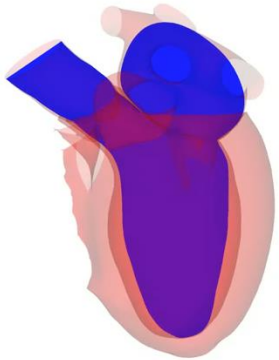
DATA

$P(k \mid D, F, O)$



$$\psi^{\cdot}(xi\ ,\ t\ ) = F(\psi(x, t),\ \{k\},\ u)$$

$$\tilde{D}(t) = O(\psi(x, t)$$



Prediction

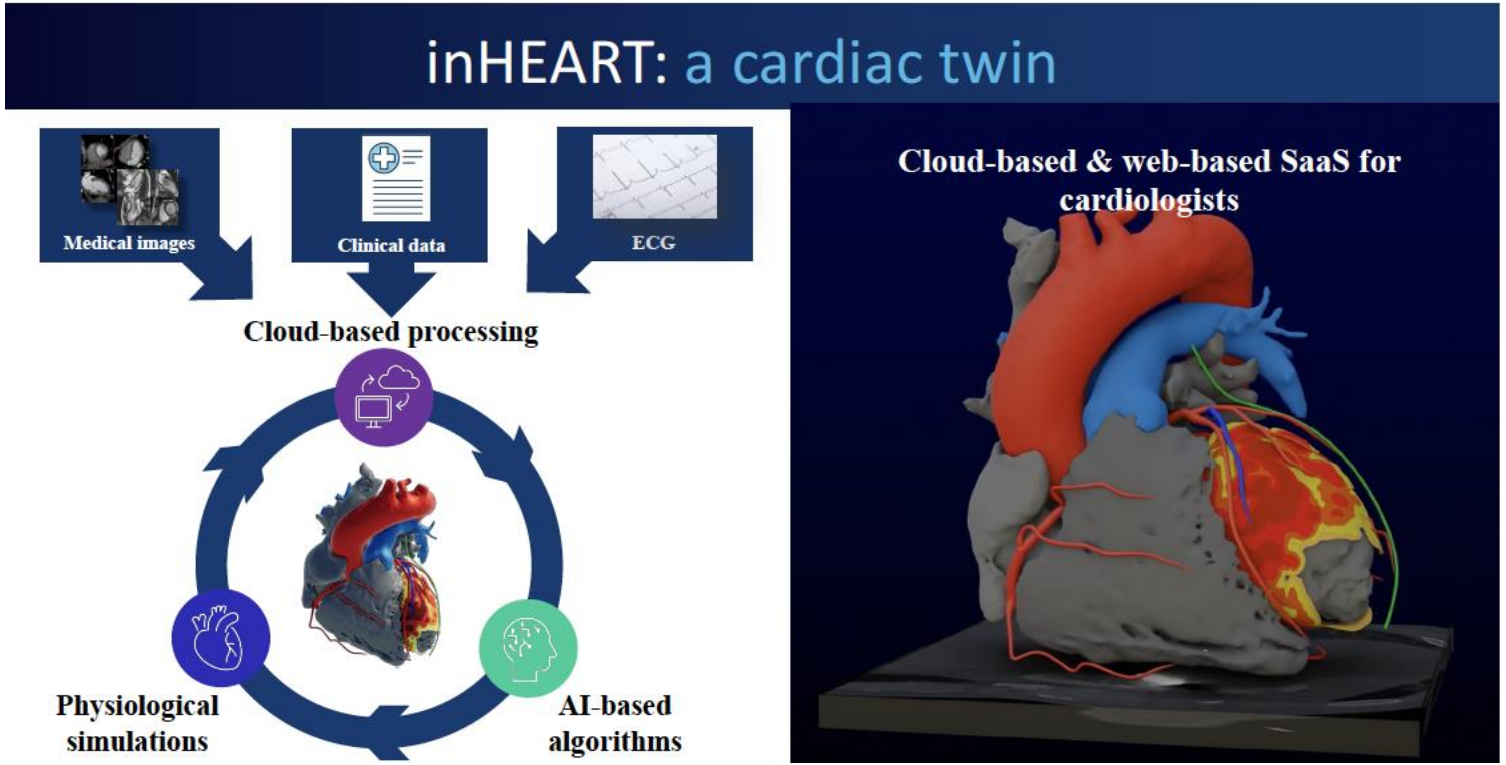
$P(\tilde{D} \mid k, F, O, u)$

Organ

Digital twin

Biomecanics of myocarde

Inspired by Wang et al *Natl Sci Rev*, 2024

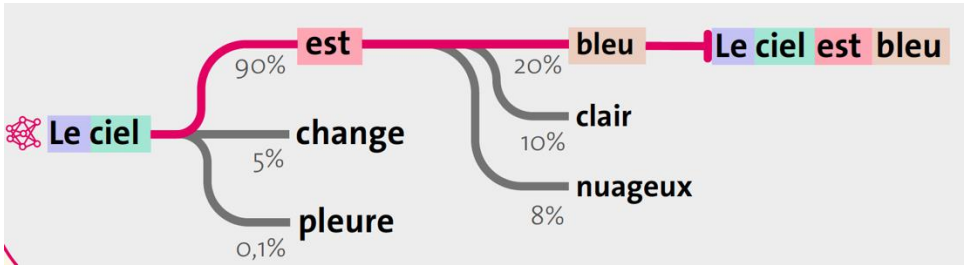


Courtesy N. Ayache

Text + Image + voice …

No grammatical rules !!!

Probability of words sequences based on a large corpus of text



	GPT-1	GPT-2	GPT-3	GPT-4
Date	2018	2019	2022	2023
Nb of parameters	117 M	1.5b	175b	?
Nb of layers	12	48	96	?
Context length	512	1024	20248	?
Dimensions	768	1600	12288	?

Text (LLM) + Image + voice …

For GP

- Analyse of medical files
- Writing of medical report
- Action coding
- Training
- Analyse of medical publications

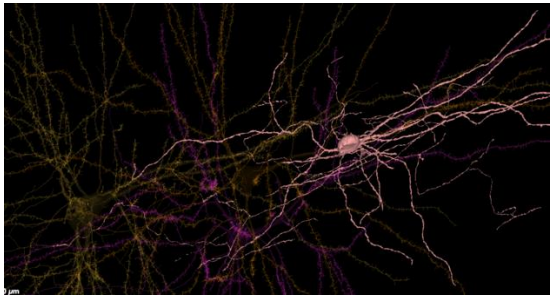
For Researchers

- Medical decision support
- Triage, cohort constitution
- Discovery of signatures
- Evolution prediction …

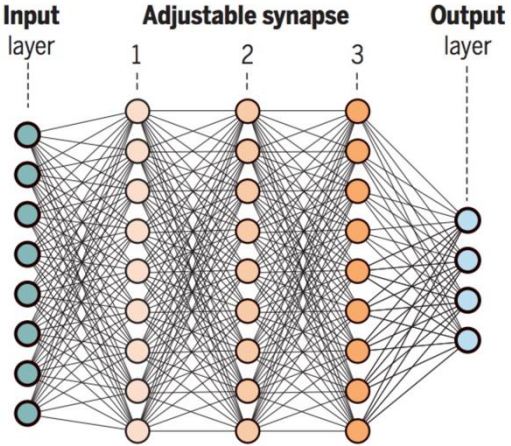
For Patients

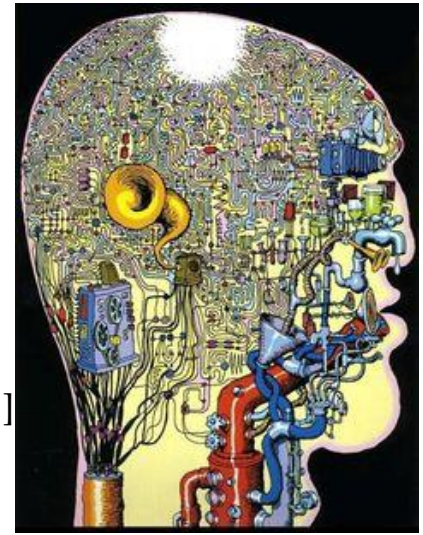
- Documentation
- Prevention
- Patient interview (chatbot)
- Follow-up chronic disease

The curse of the Black-Box



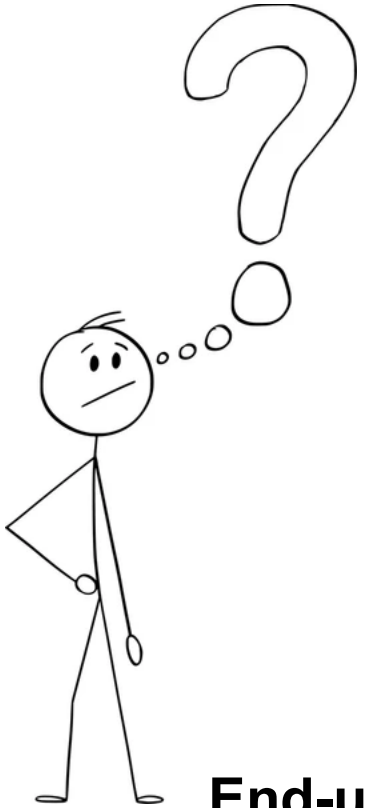
[Shapson-Coe et al. Science 384, 635 (2024)]



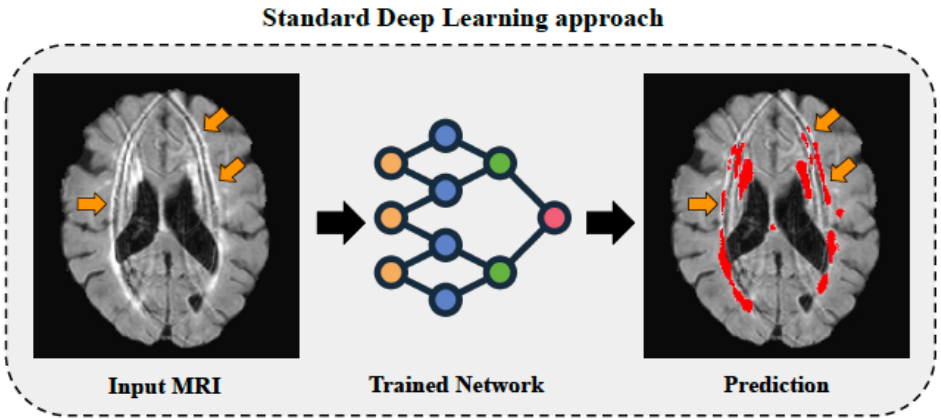


[Crumb, Says 1967 Num 1]

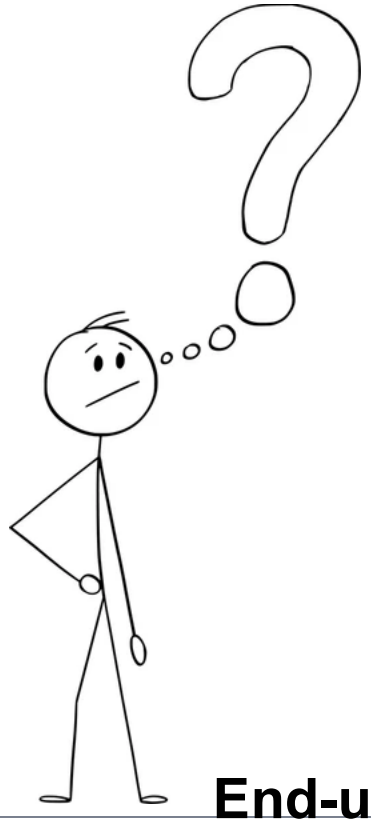
The curse of the Black-Box



End-user



The curse of the Black-Box



Explainability (XAI)
Interpretability
Understandability

For who?
About what?
At which level?
…

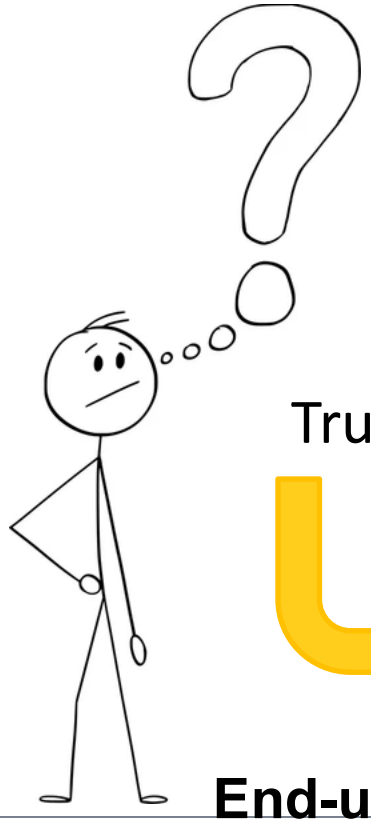
[Erasmus et al 2021 Philosophy & Technology]

End-user

The curse of the Black-Box

~~Explainability (XAI)~~
~~Interpretability~~
~~Understandability~~

For who?
About what?
At which level?
…



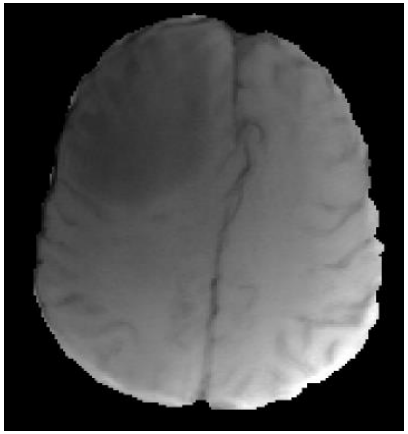
Trusted AI

G. Hinton [In response to how do we trust systems?] ***You should regulate them based on how they perform***.

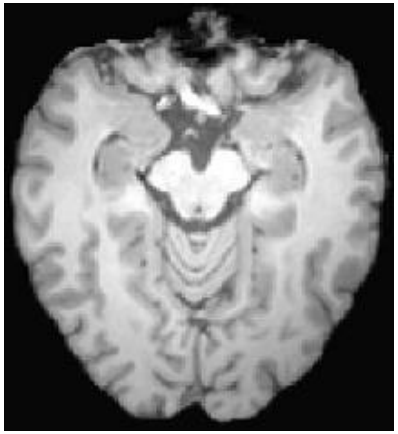
Uncertainty Quantification in NN decision

End-user

DLL trained for Gioblastoma detection on T1w

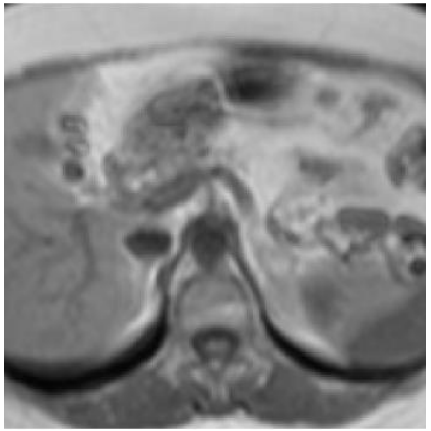


Artefacted T1w



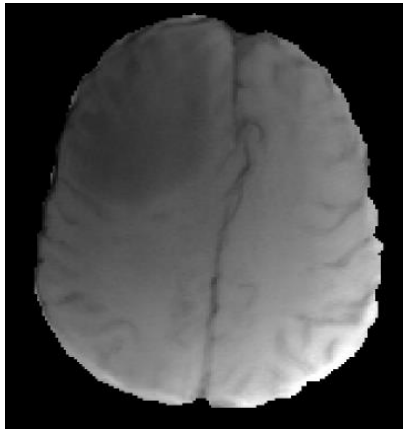
Healthy subject

FLAIR

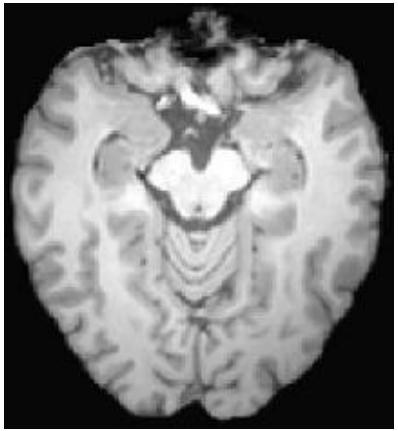


Abdominal T1w

Know-it-all

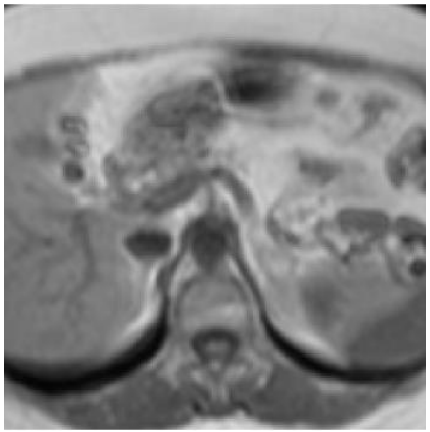


Artefacted T1w

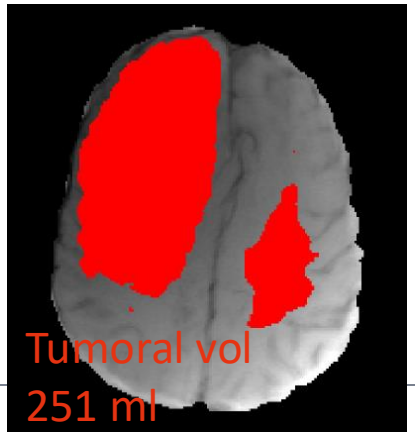


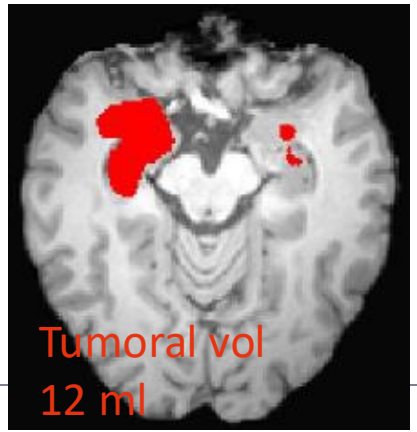
Healthy subject

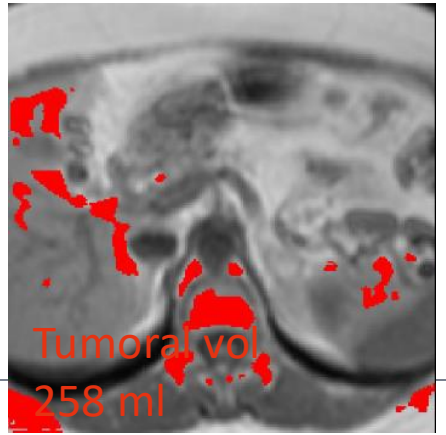
FLAIR



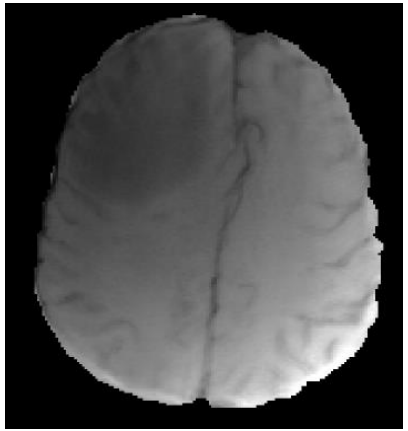
Abdominal T1w



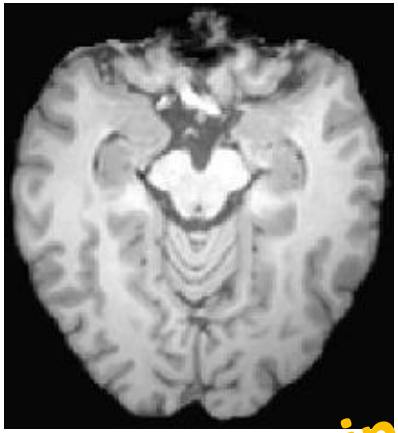




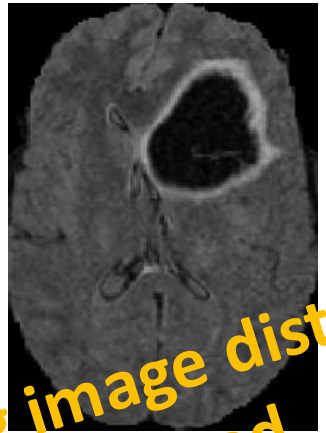
Know-it-all



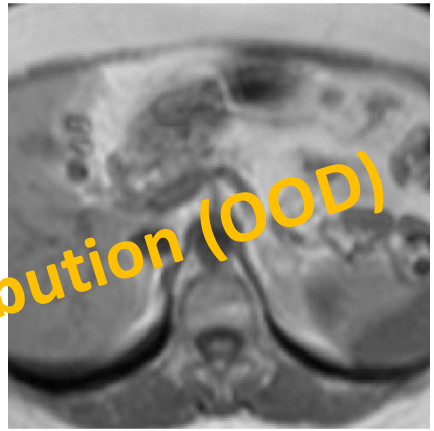
Artefacted T1w



Healthy subject

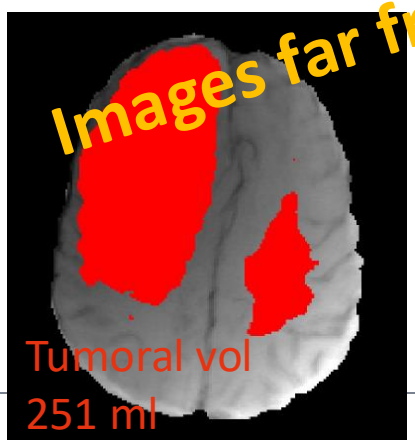


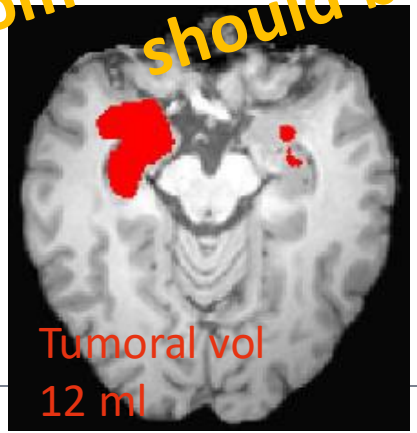
FLAIR

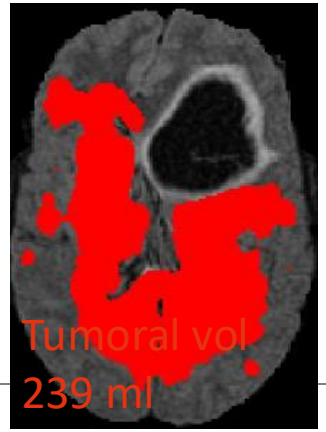


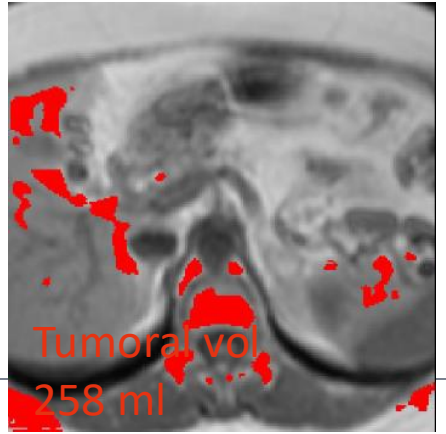
Abdominal T1w

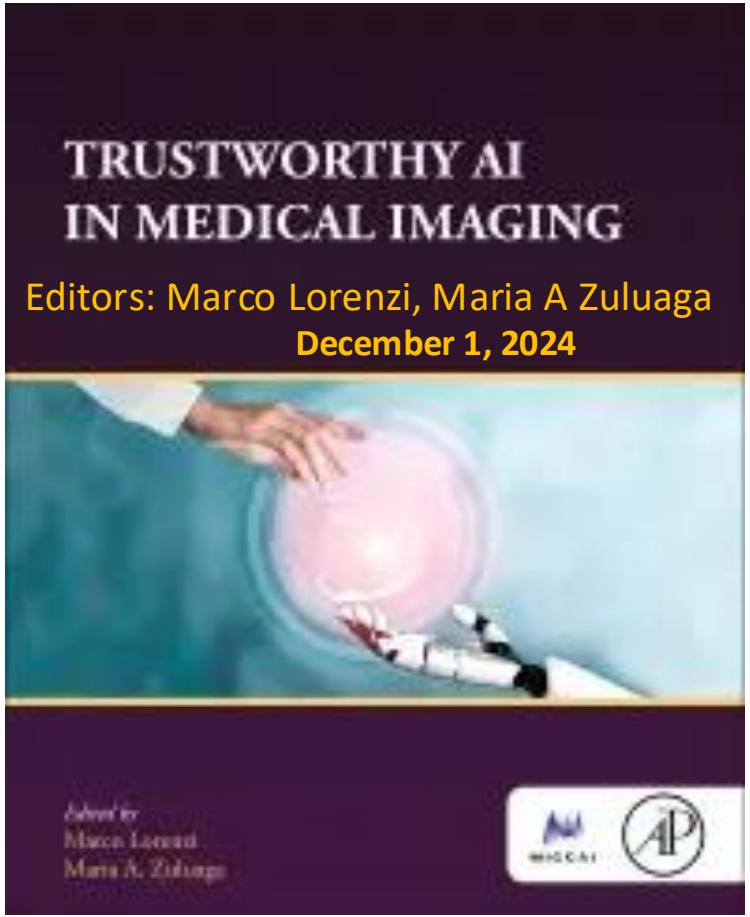
Images far from the training image distribution (OOD) should be detected











Section 1 – Robustness

Section 2 - Validation, Transparency and Reproducibility

Section 3 – Bias and Fairness

Section 4 - Explainability, Interpretability and Causality

Section 5 - Privacy-preserving ML

Section 6 - Collaborative Learning

Section 7 - Beyond the Technical Aspects

AI for Medical Imaging

- **Pros**:
  - Excellent performances
  - Automatic feature learning
  - Knowledge emergence
  - On the shelves tools
  - Discharge Expert
  - Automatic Quantification

- **Cons**:
  - Importance of Image Quality
  - Annotation
  - Data hungry
  - Computational cost
  - Black box / trustability
  - Specific to one problem
  - Adversarial attack
  - Catastrophic forgetting
  - Ethic, social and law
  - Needs for specific tools &infra

Challenges

Rajpurkar et al 2022 Nat Med

Clinical use

Specific tools & infrastructures

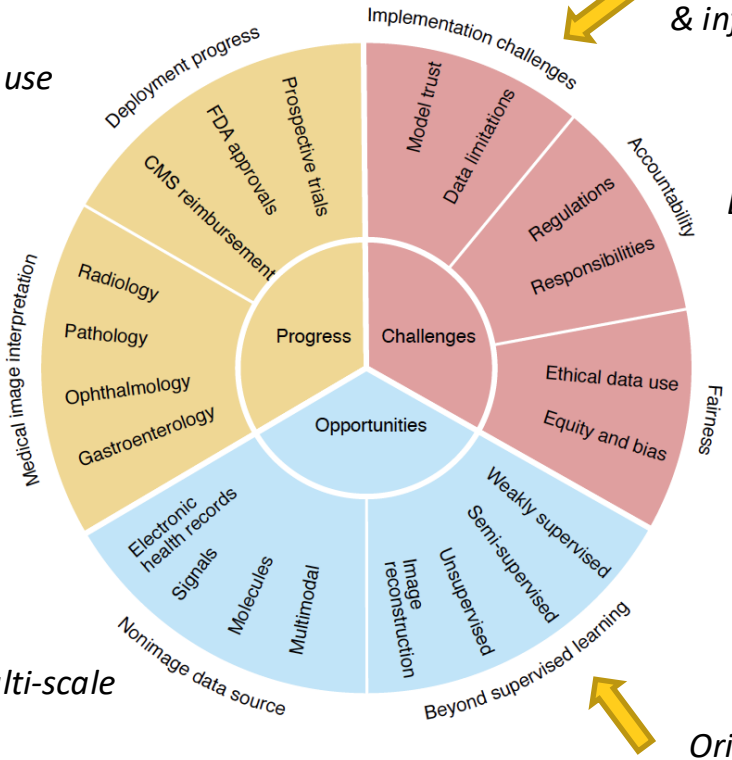
Legal / Societal

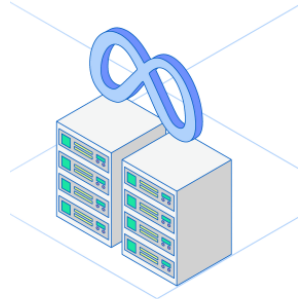
Ethical

Applications

Multi-modal/Multi-scale

Original ML techniques





Meta used **22 million liters of water** training its LLaMA-3 open source AI model

Frugality: Small is beautiful

GPT-4, ≈ 10 GWh for training,
≈ 6000 x energy a European per year

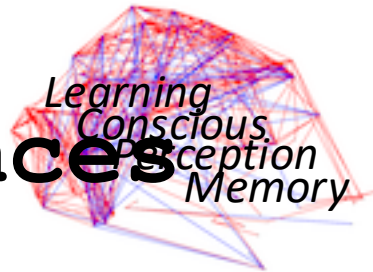
Intelligent Agent: an entity that takes the best possible action in a situation

How to build an artificial intelligent agent?

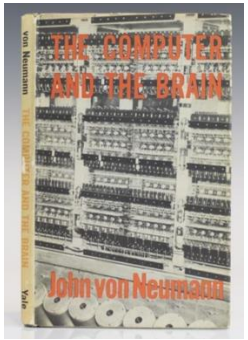
Test our models of natural intelligent agents?

Computer science

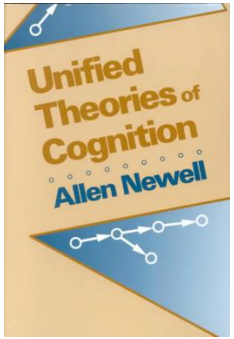
Neurosciences



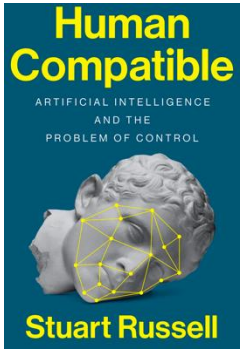
Computer & Brain



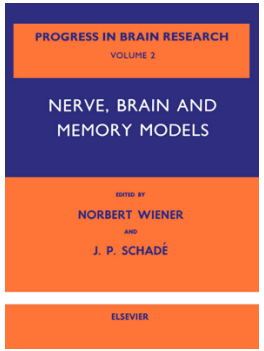
1958
Yale University Press, New Haven



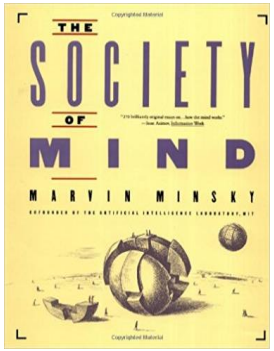
1982



2019



1963



1988

REVIEW

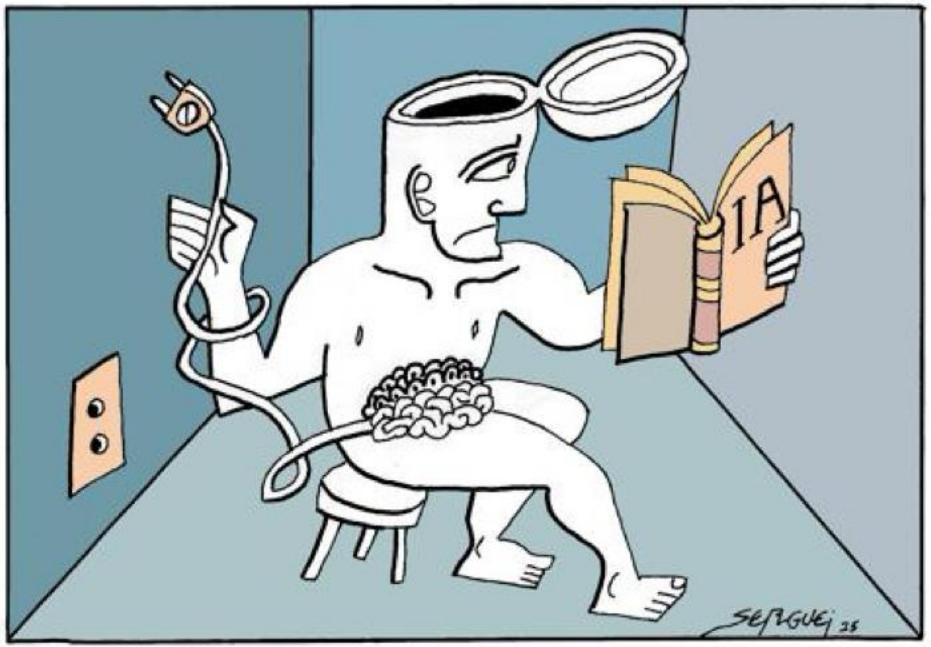
What is consciousness, and could machines have it?

Stanislas Dehaene,[1,2]* Hakwan Lau,[3,4]* Sid Kouider[5]

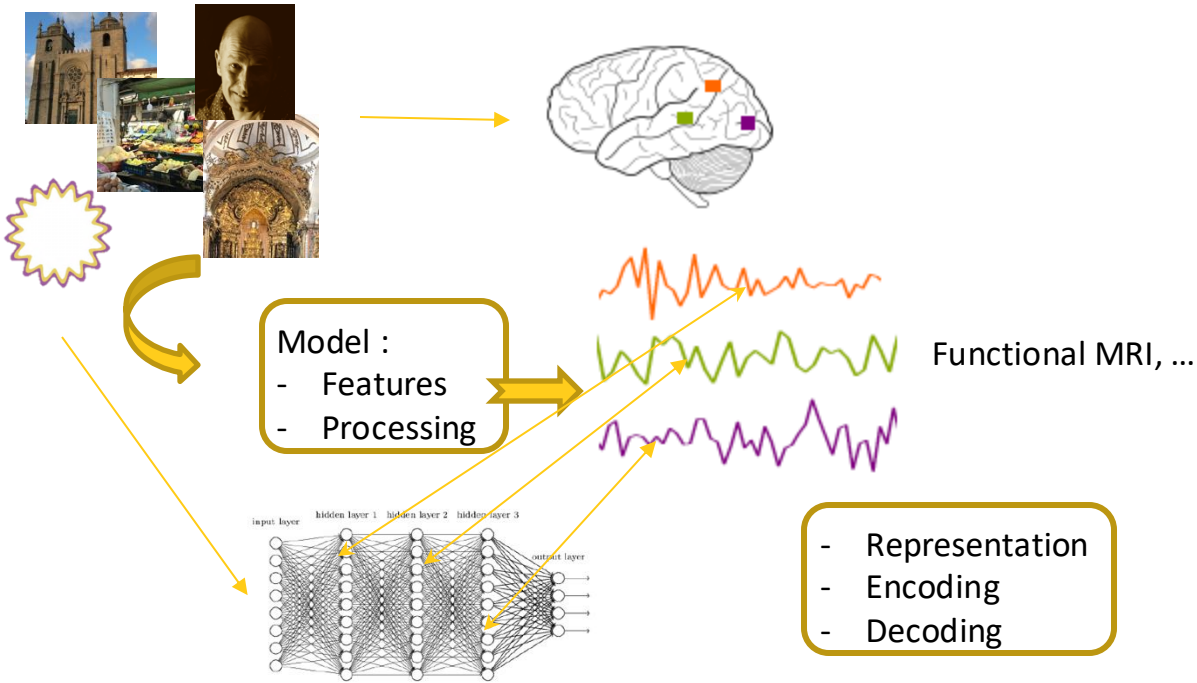
2017 Science

NN: a framework for modelling the computational brain?

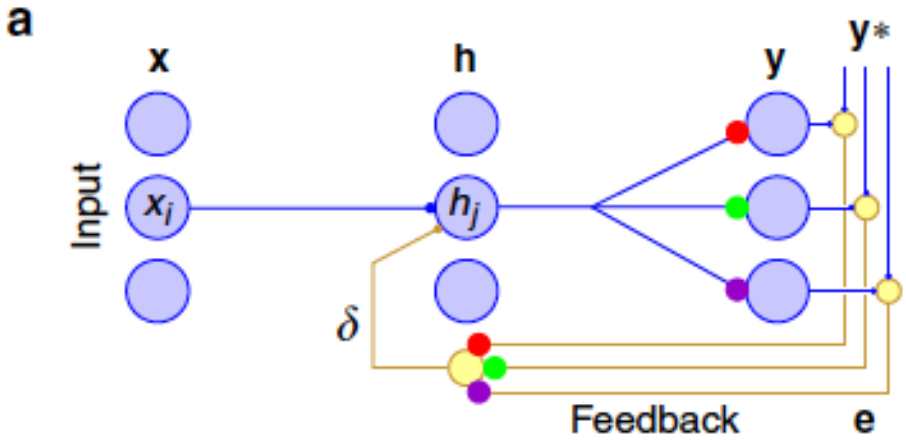
Instructions for use



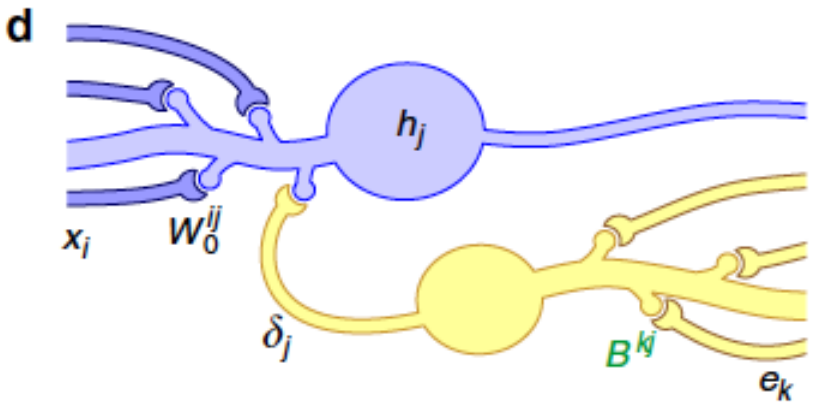
NN: a framework for modelling human vision?



Backprop: the weight transport problem



[Lillicrap et al Nat Com 2016]



Take home messages

- **NN: A disruptive technology in Health**
  - From bedside to the understanding of complex patho-physiological states

- **Several drawbacks**
  - Data hunger
  - Consummation
  - To be in the race

- **NN: Model to investigate brain functions**

To conclude

Human Cognitive Limitations

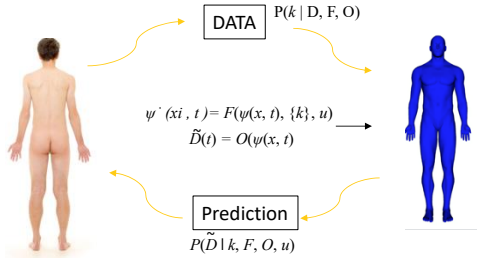
Broad, Consistent, Clinical Application of Physiological Principles Will Require Decision Support

Alan H. Morris 2017

« I counted **236** variable categories being considered by the intensive care unit clinicians » (wo various notes)

« Those experts should be aided by detailed **computer protocols** that embrace core **physiological constructs** and deliver personalized clinical instructions. »

Digital Twin



To conclude

Bernoulli_Lab

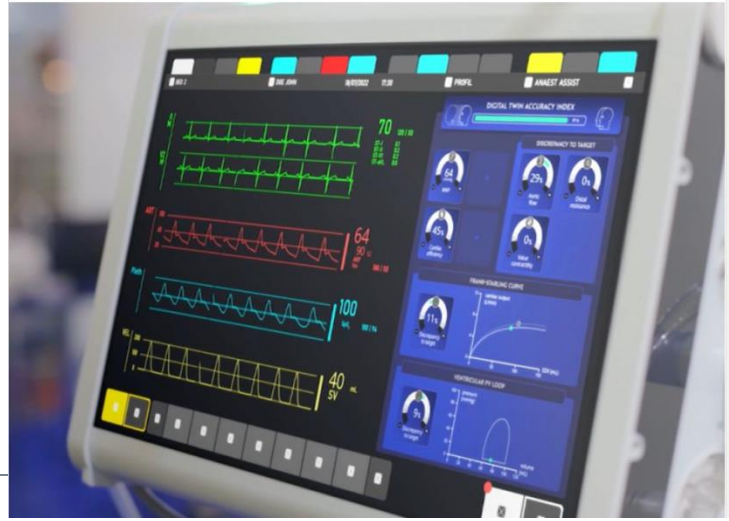
AP-HP – Inria joint laboratory Daniel Bernoulli

Dans le cadre d'une collaboration entre le département d'anesthésie-réanimation de l'hôpital Lariboisière **Greater Paris University Hospitals - AP-HP** et **Inria** (équipes **#COMMEDIA** et **#M3DISIM**), des outils de modélisation et simulation numérique sont développés afin de construire des jumeaux numériques permettant d'améliorer le monitorage, notamment cardiovasculaire, des patient·es sous anesthésie générale. La personne recrutée, pour une durée de 15 mois (prise de poste souhaitée en juin 2025), aura pour mission de développer des outils de simulation permettant ainsi la mise en oeuvre de jumeaux numériques des systèmes cardiovasculaire et cardiopulmonaire, et confrontera également les résultats de simulation aux données cliniques de manière à en évaluer le domaine de validité.

Pour plus de détails et postuler, voir **https://lnkd.in/eE53PWiz**

Céline Grandmont François Kimmig Alexandre Mebazaa Bernoulli Lab

Show translation



Thank you!

www.inria.fr

https://neurosciences.univ-grenoble-alpes.fr/fr/michel-dojat

Michel.Dojat@inria.fr