

Demystification of AI-driven medical image interpretation

Benoit GALLIX

Development and Validation of a Deep Learning Algorithm for Detection of Diabetic Retinopathy in Retinal Fundus Photographs

Varun Gulshan, PhD; Lily Peng, MD, PhD; Marc Coram, PhD; Martin C. Stumpe, PhD; Derek Wu, BS; Arunachalam Narayanaswamy, PhD; Subhashini Venugopalan, MS; Kasumi Widner, MS; Tom Madams, MEng; Jorge Cuadros, OD, PhD; Ramasamy Kim, OD, DNB; Rajiv Raman, MS, DNB; Philip C. Nelson, BS; Jessica L. Mega, MD, MPH; Dale R. Webster, PhD

Editorial by Wong and Bressler

- limits of the study
- need for further validation of the algorithm in different populations
- unresolved challenges



FDA permits marketing of artificial intelligence-based device to detect certain diabetes-related eye problems

FDA News Release

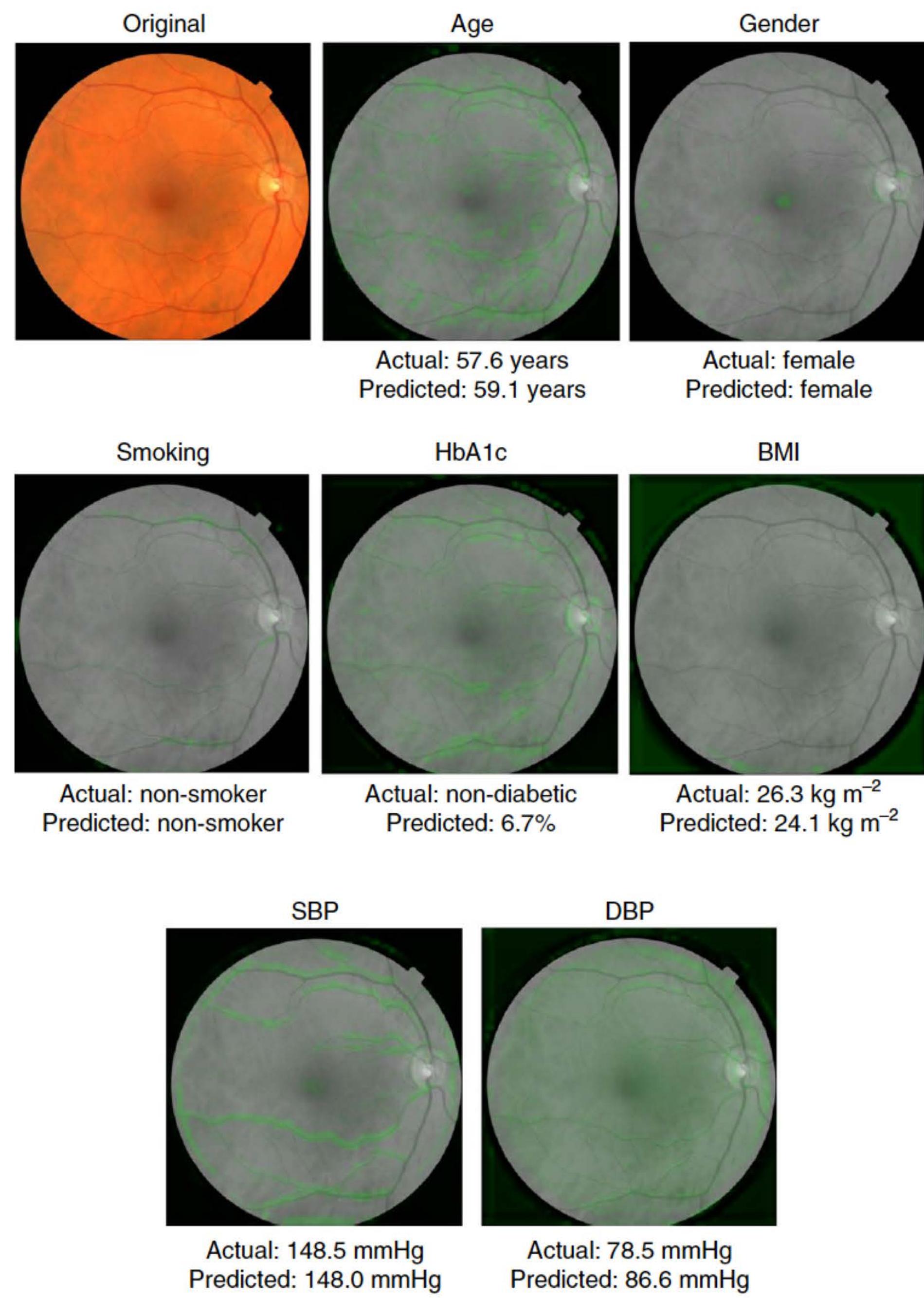
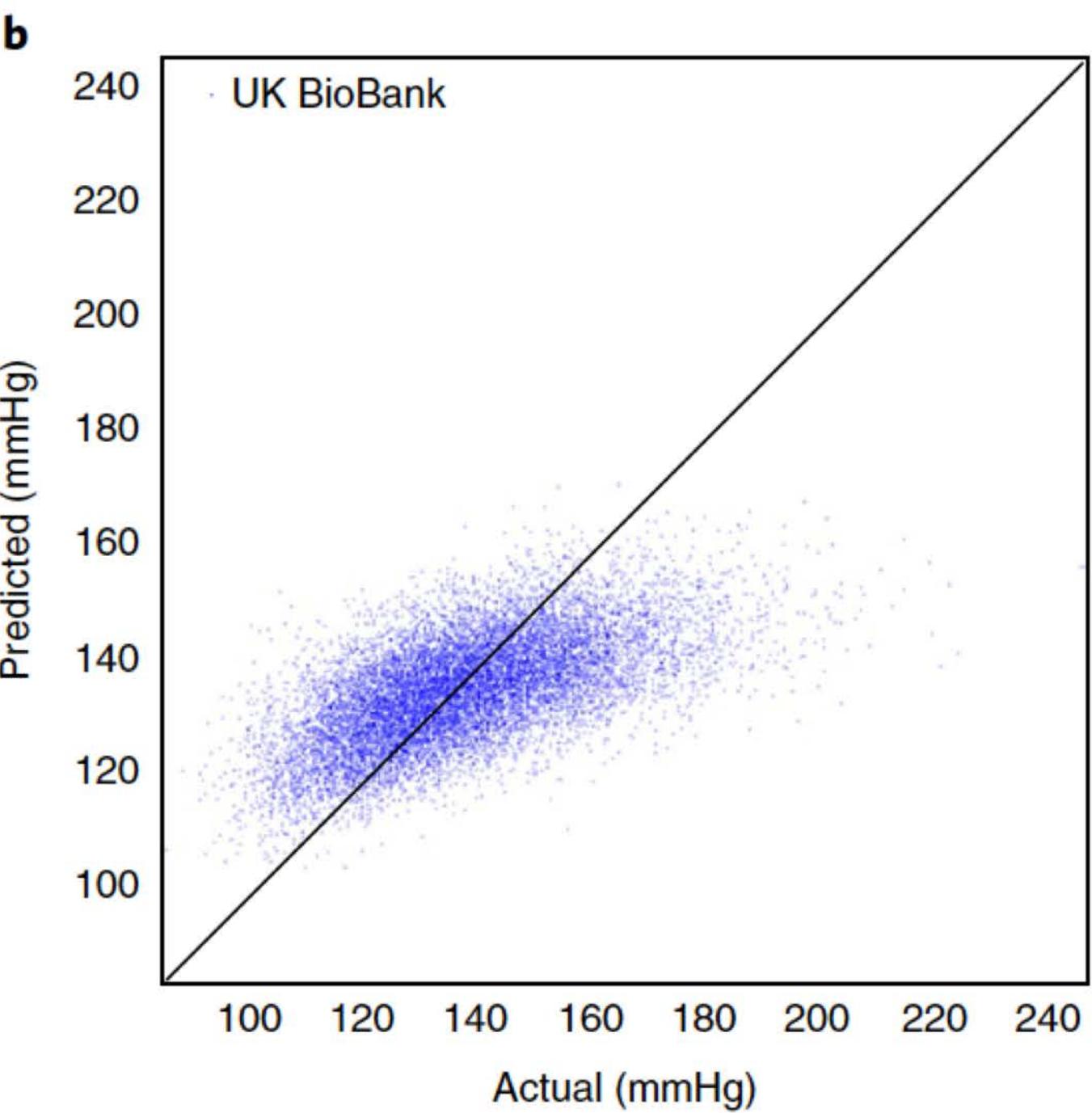
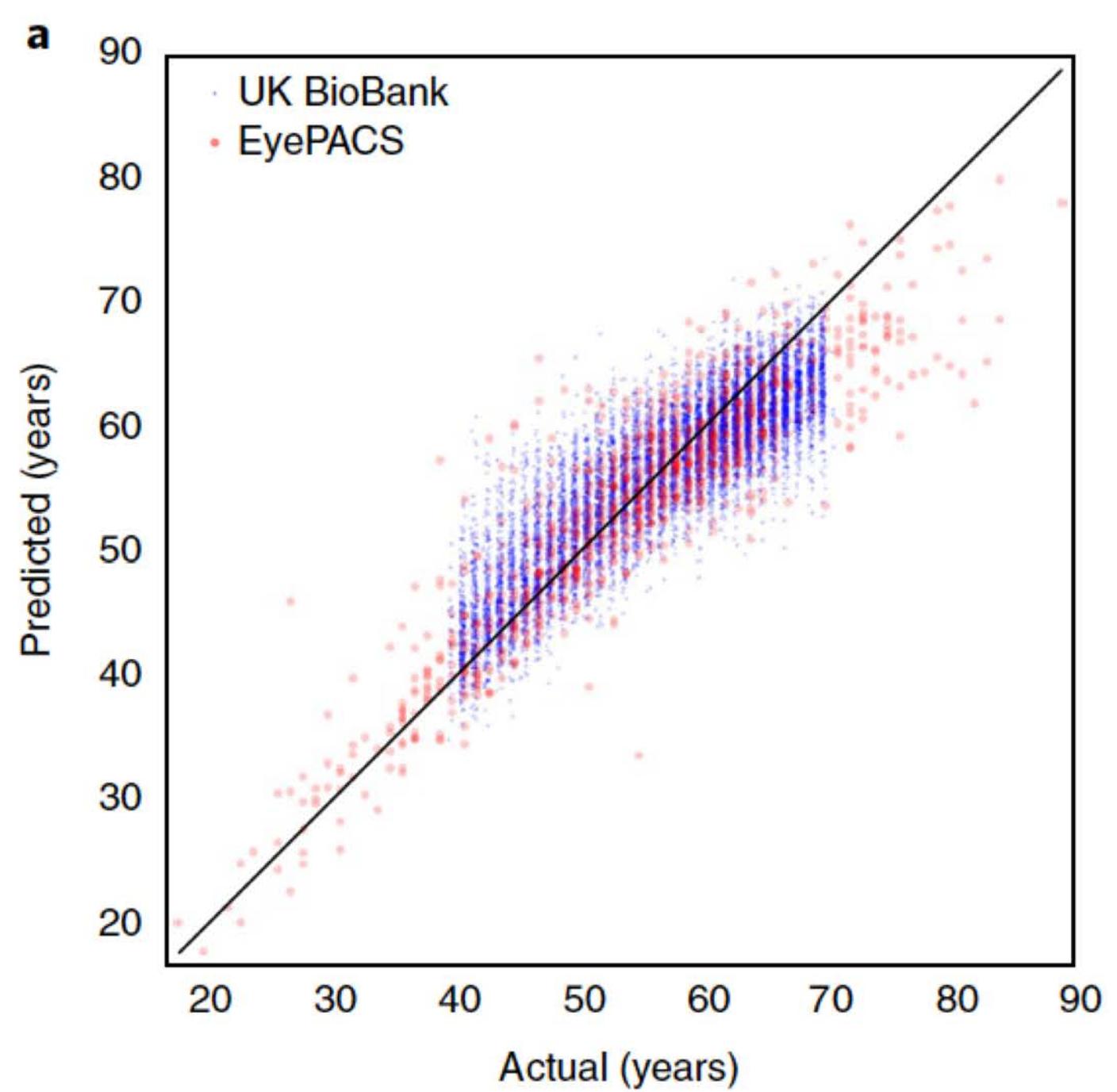
For Immediate Release



May, 2018

Prediction of cardiovascular risk factors from retinal fundus photographs via deep learning

Ryan Poplin^{1,4}, Avinash V. Varadarajan^{1,4}, Katy Blumer¹, Yun Liu¹, Michael V. McConnell^{2,3}, Greg S. Corrado¹, Lily Peng^{1,4*} and Dale R. Webster^{1,4}

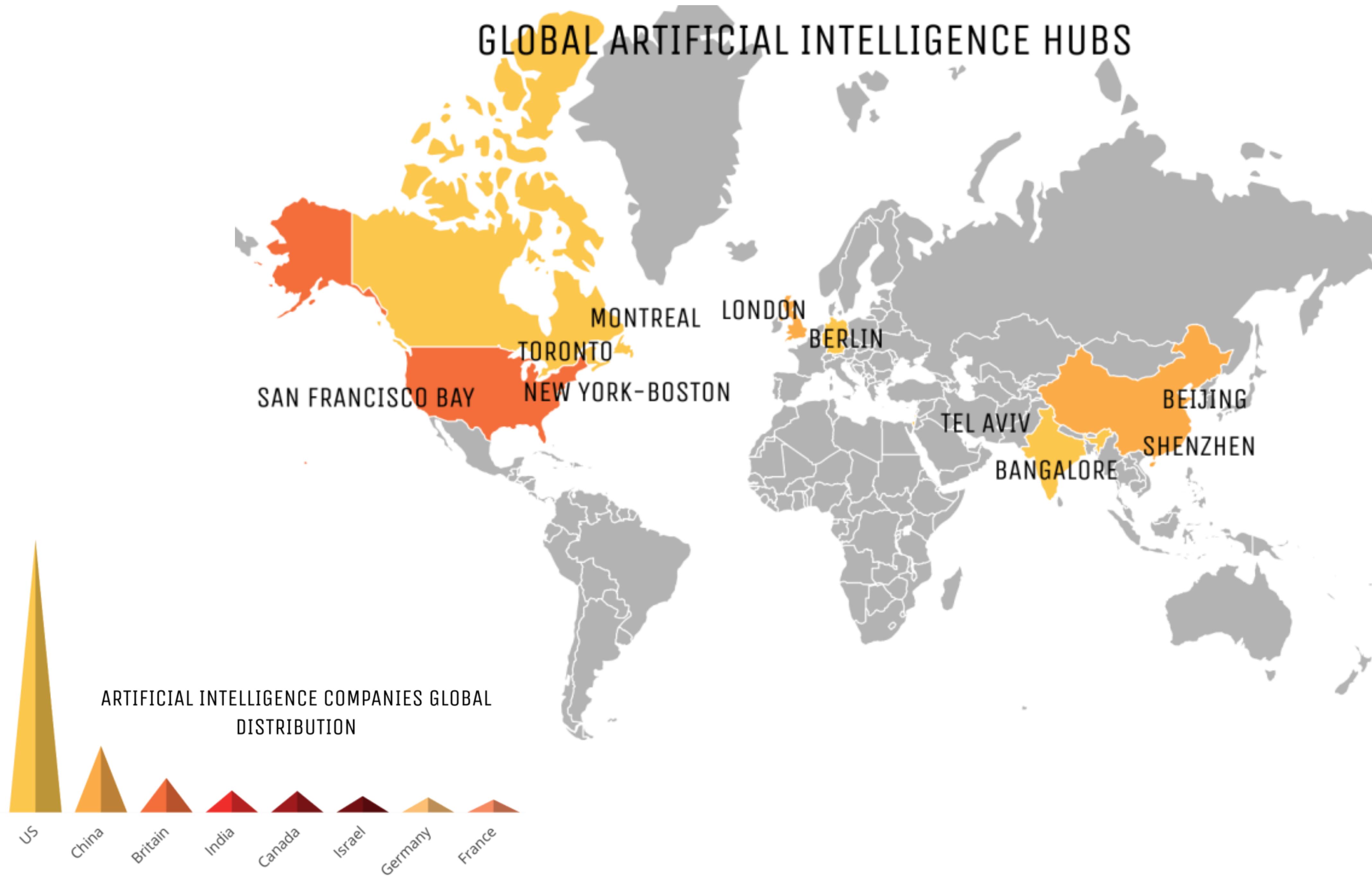


AlphaGo

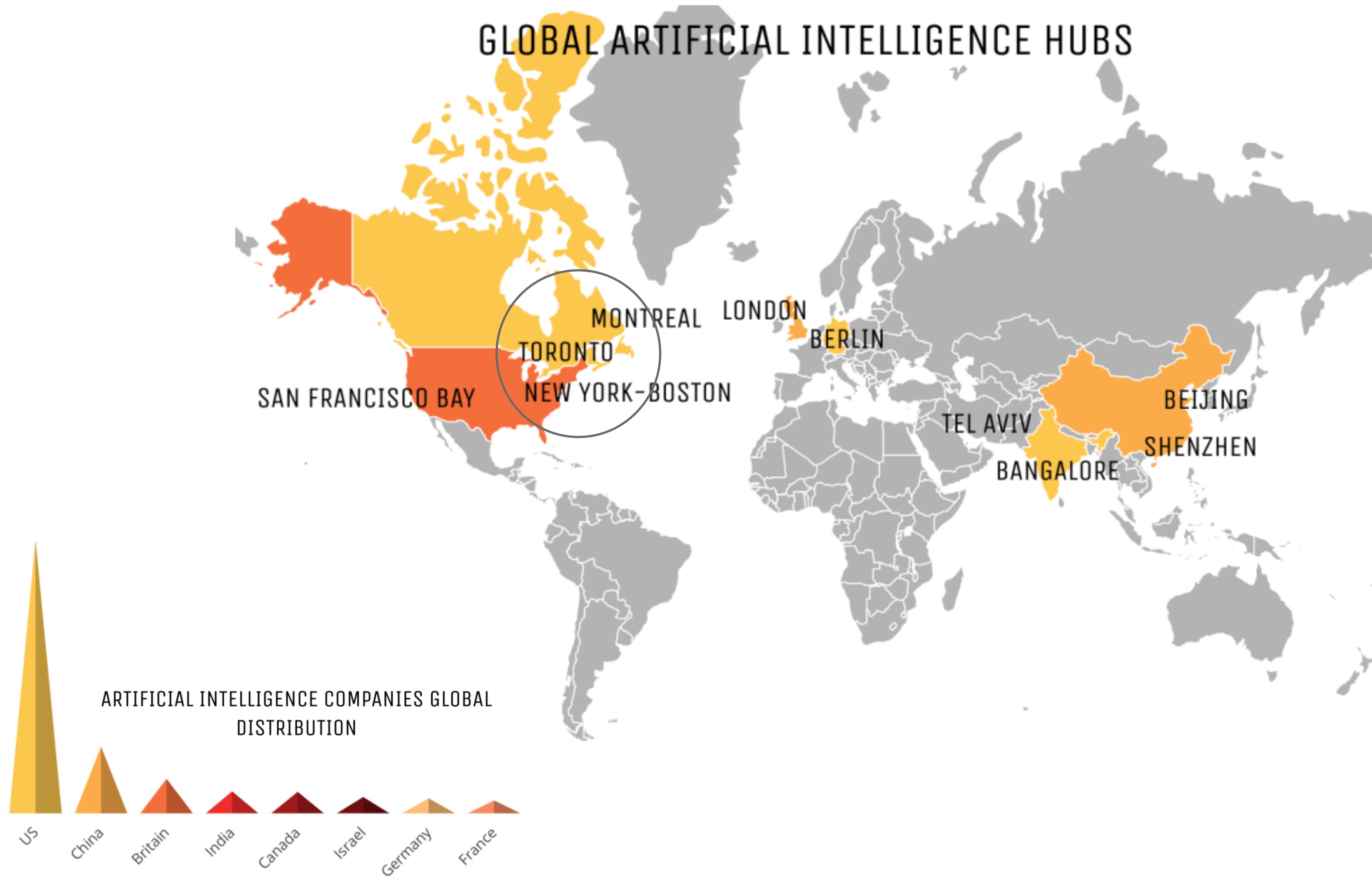


2017, May 27th

GLOBAL ARTIFICIAL INTELLIGENCE HUBS



GLOBAL ARTIFICIAL INTELLIGENCE HUBS



Turing Award Won by 3 Pioneers
in Artificial Intelligence
NYT Mar 27, 2019

2007

Yoshua Bengio

Stacked Auto-Encoders

2006

Geoffrey Hinton

Deep Belief Networks

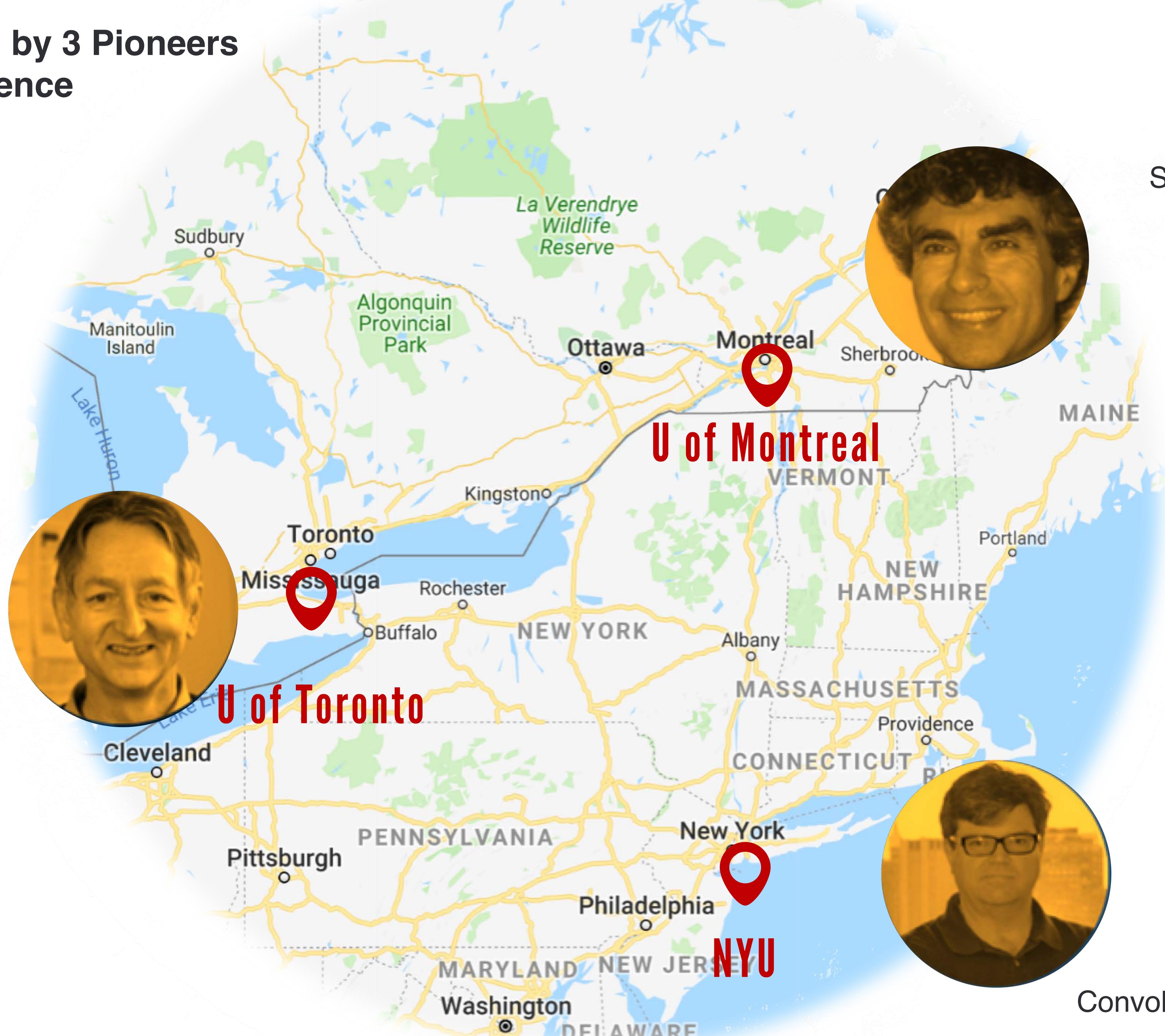


U of Toronto

1998

Yann LeCun

Second generation
Convolutional Neural Networks



Terminology Misuse

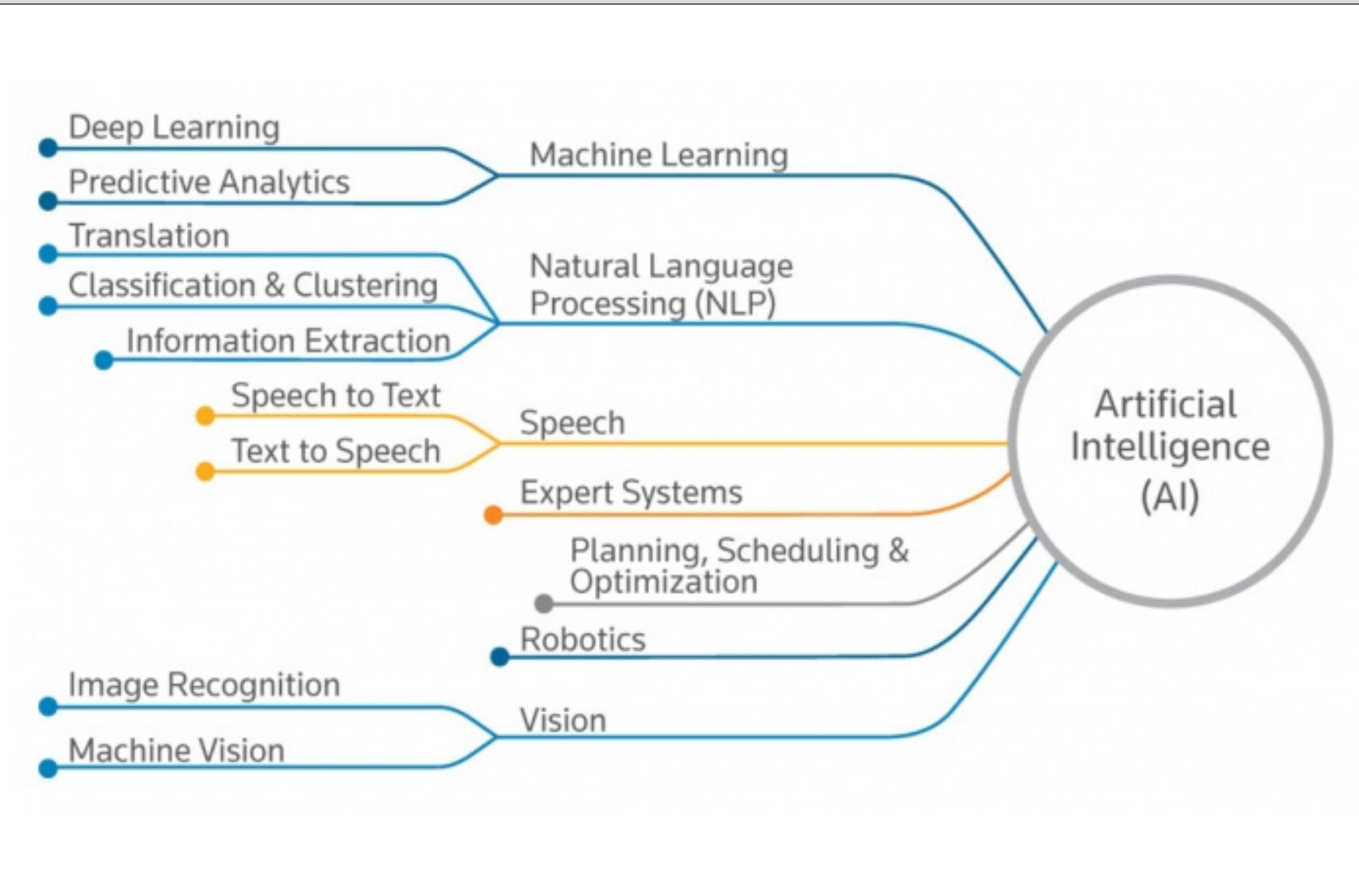
- * Deep Learning ≠ Artificial Intelligence
- * Deep Learning is the latest, most hyped set of machine learning techniques.

Artificial intelligence (AI)

Machine learning

Representation learning

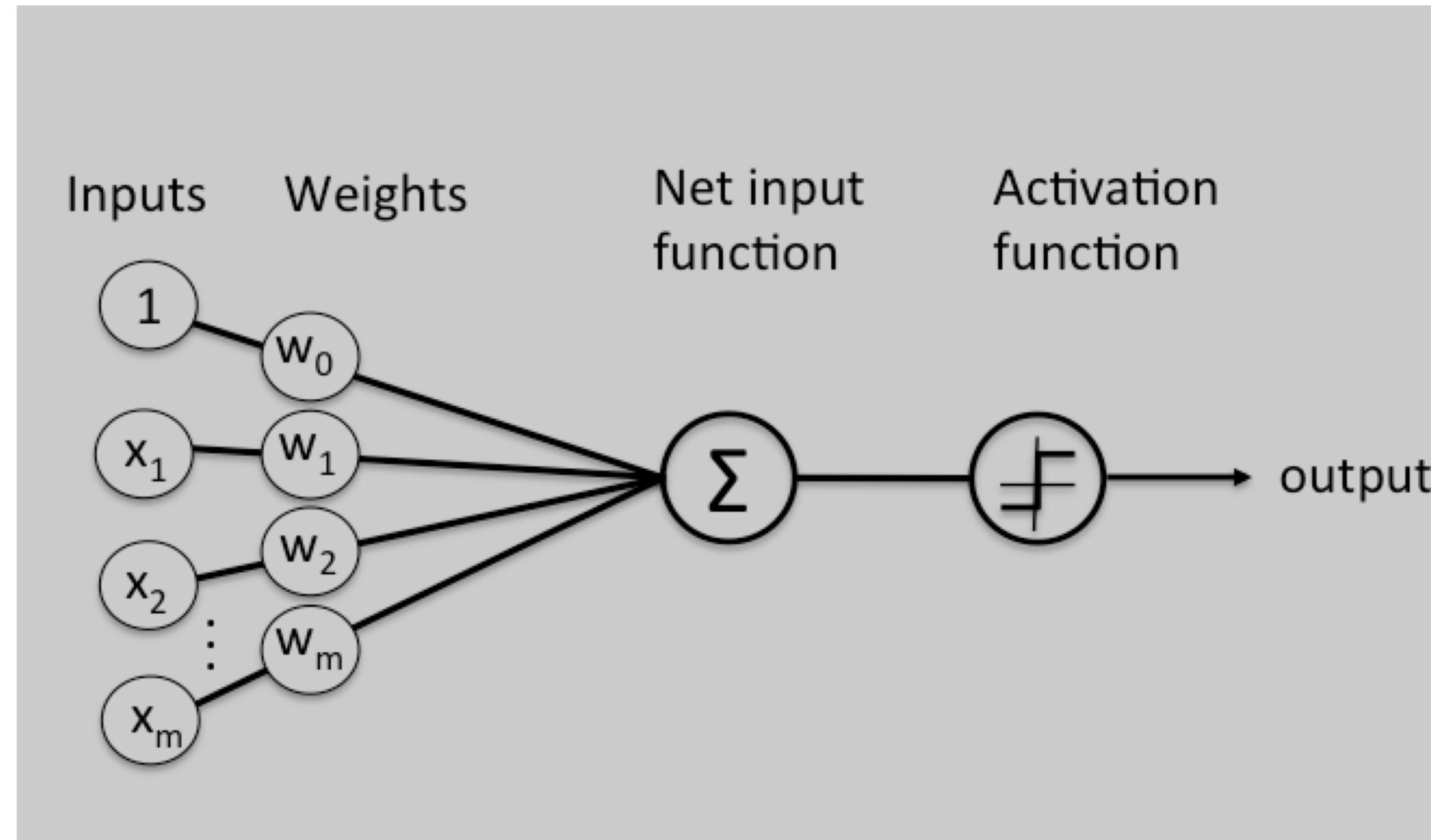
Deep learning



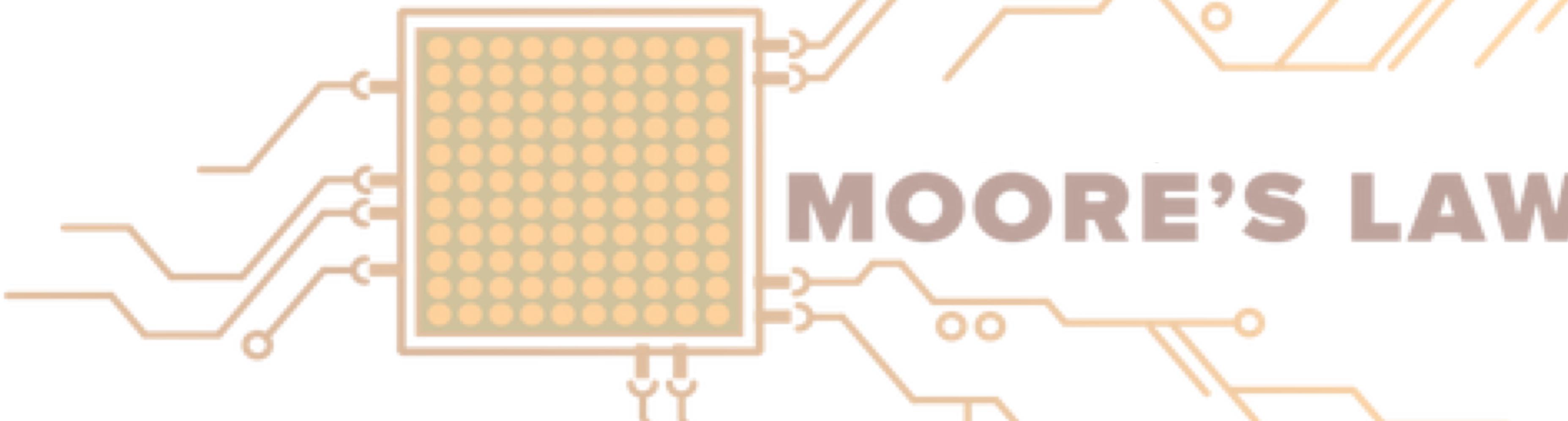
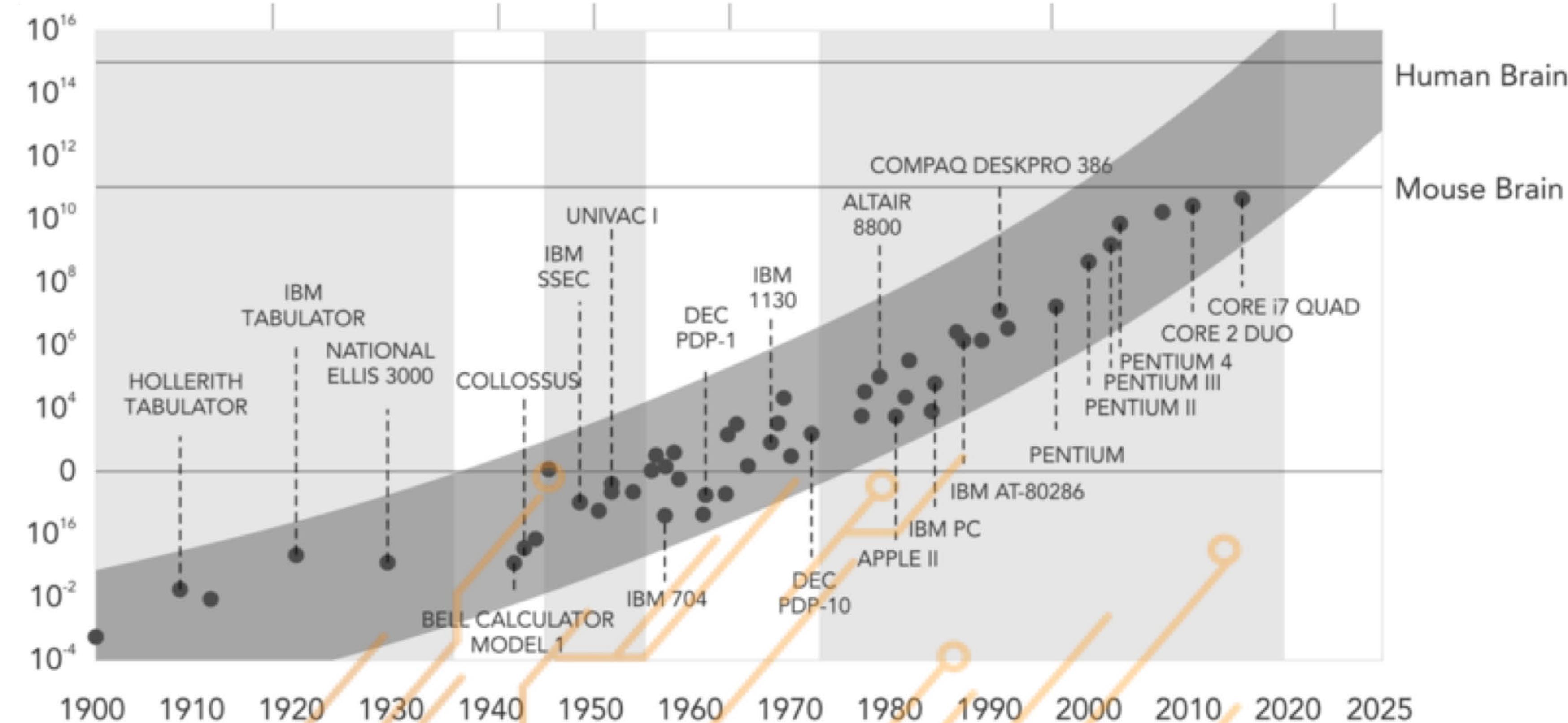
First Artificial Neural Network



Franck Rosenblatt's Perceptron, 1957



A simple simulated neuron with adaptive “synaptic weights”



Data Explosion

Exabytes (billions of GB)

50000

40000

30000

20000

10000

0

2006

2007

2008

2009

2010

2011

2012

2013

2014

2015

2016

2017

2018

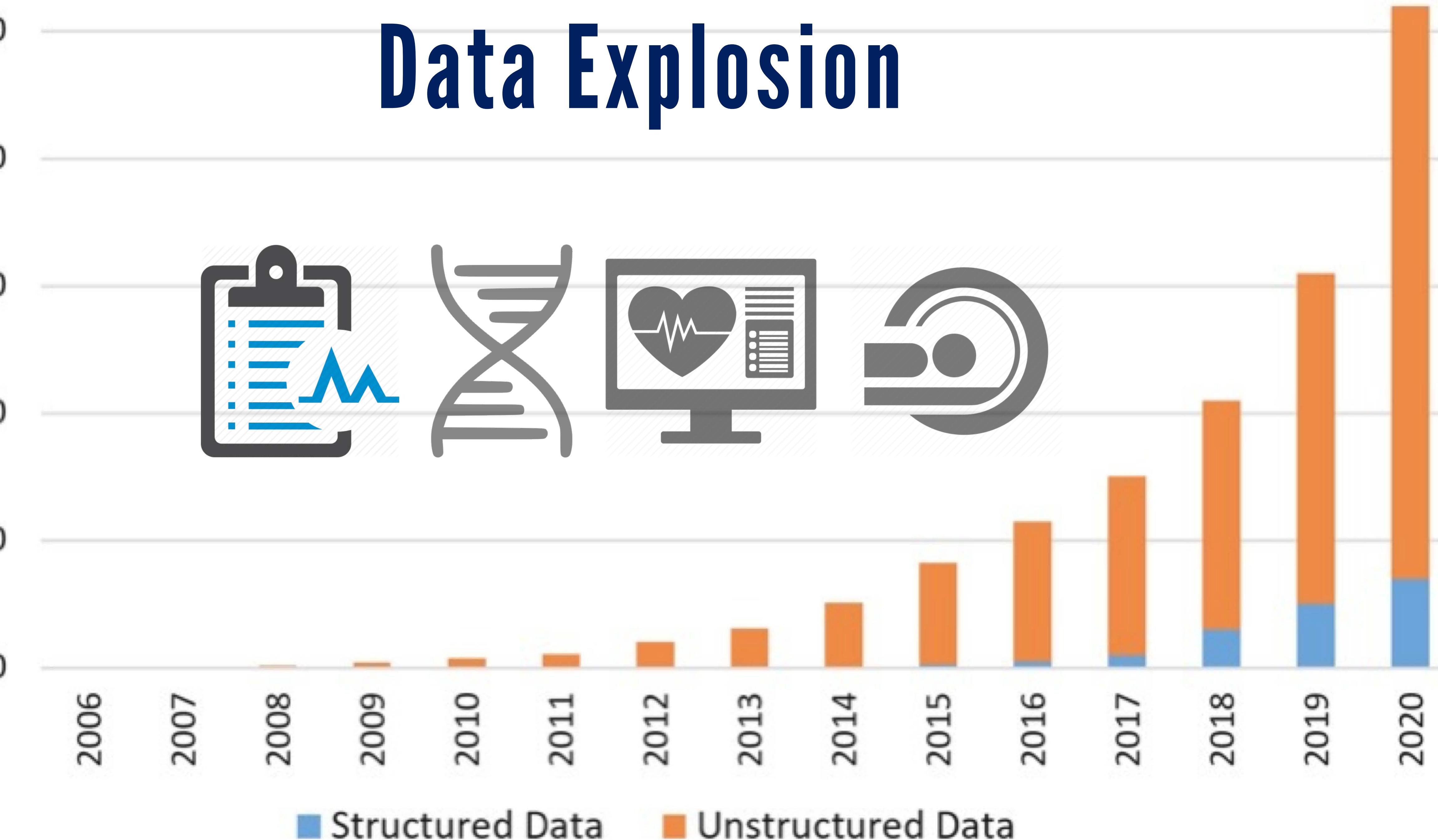
2019

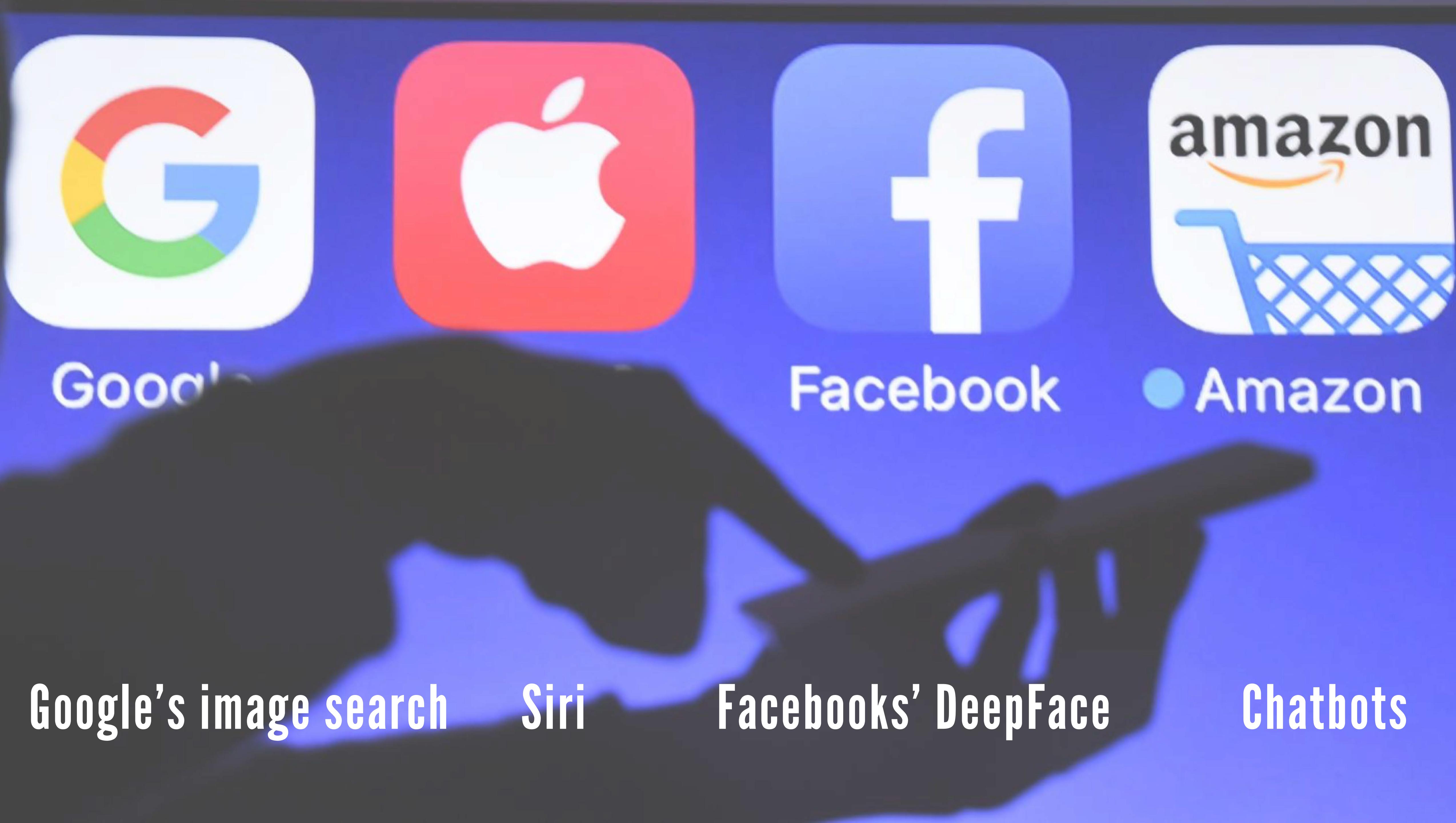
2020



■ Structured Data

■ Unstructured Data





Google's image search

Siri

Facebook's DeepFace

Chatbots

Tech investors think some actors will be ‘obsolete’ in five years

“

“There's no reason a human should be
anymore reading medical images”

Vinod Khosla



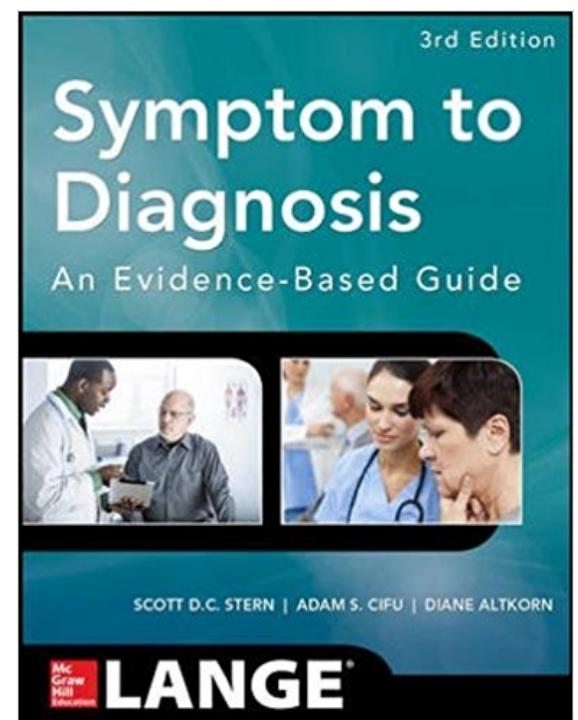
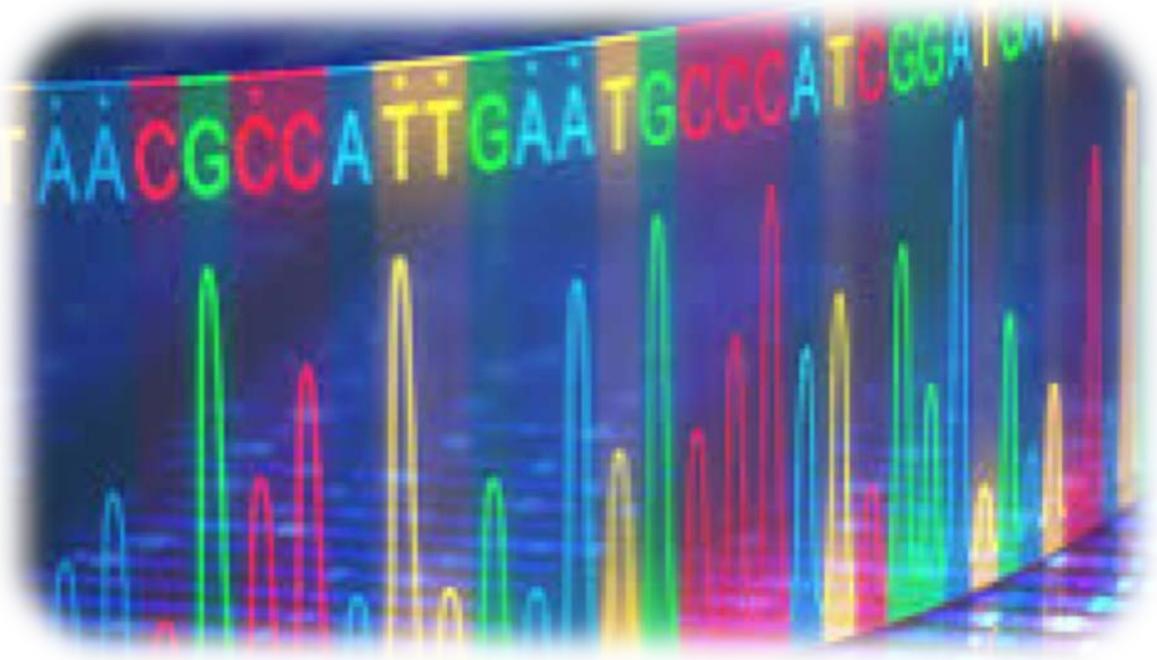
“

“AI won’t make jobs disappear, but will
certainly make many tasks disappear”

Healthcare Sector

Rich in complex data and process

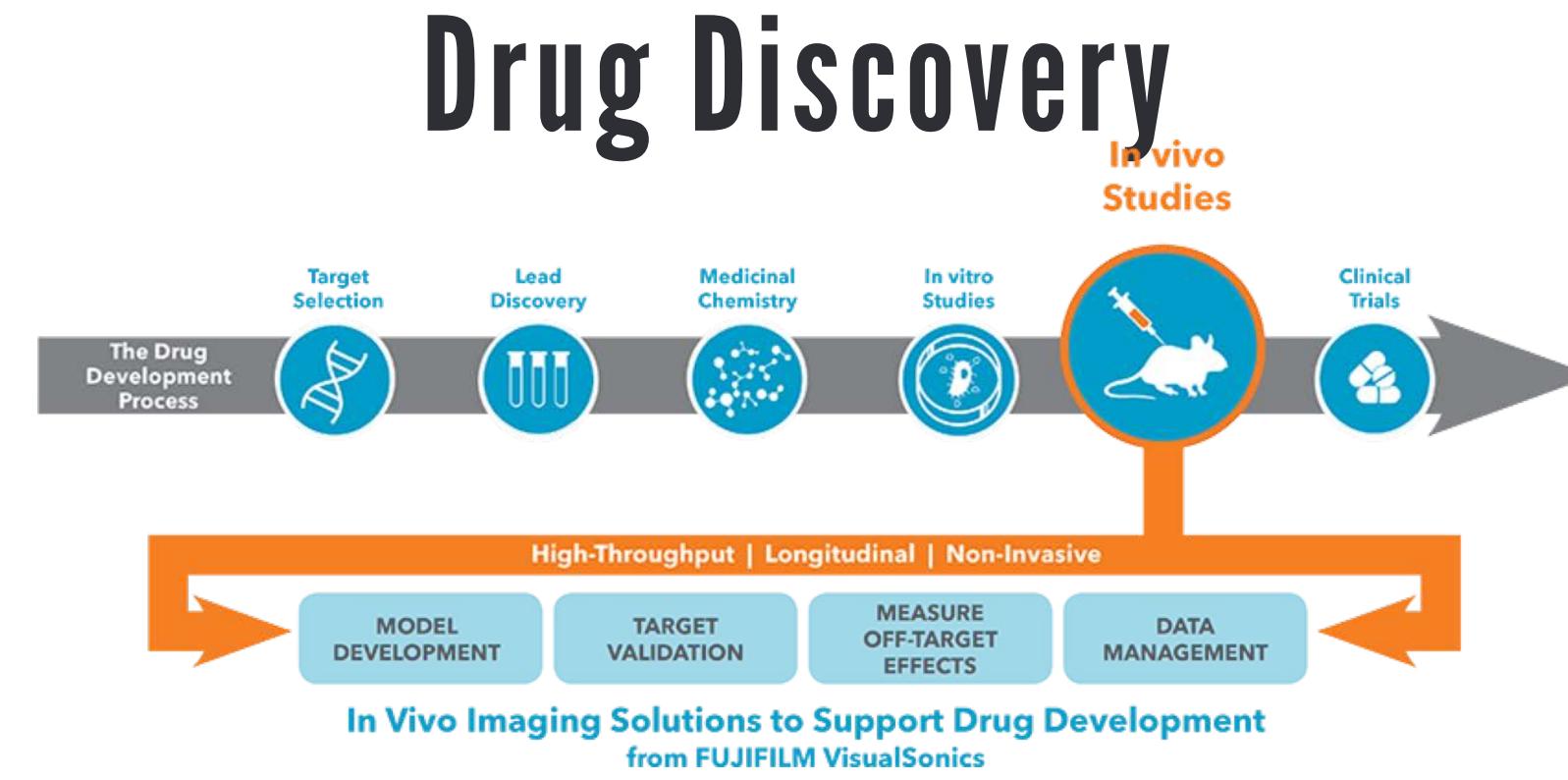
DNA and RNA sequencing



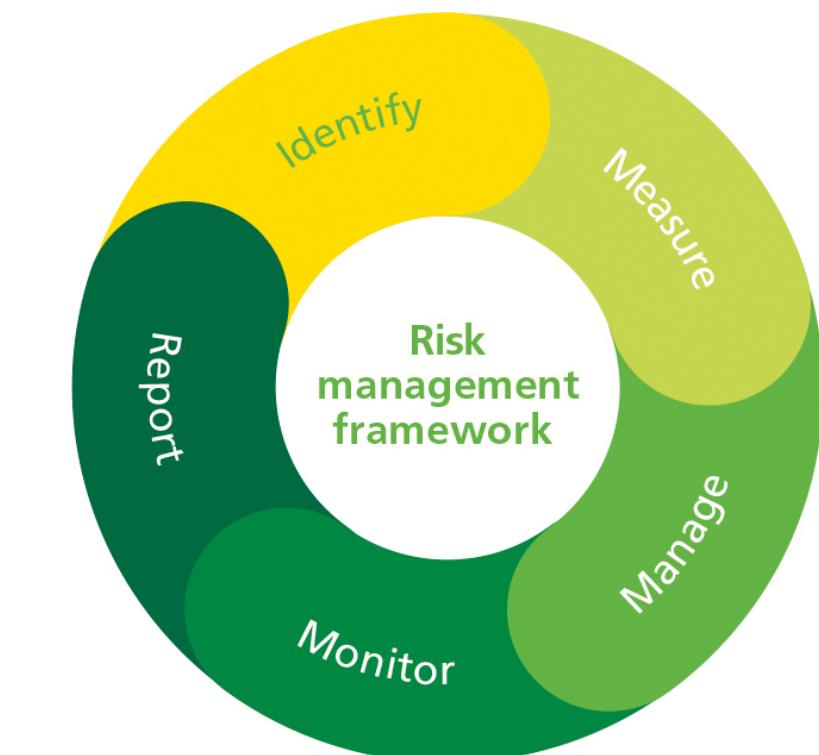
Medical Diagnosis



Hospital Management



Monitoring



Risk Management

Imaging Data

Radiology

Radiotherapy

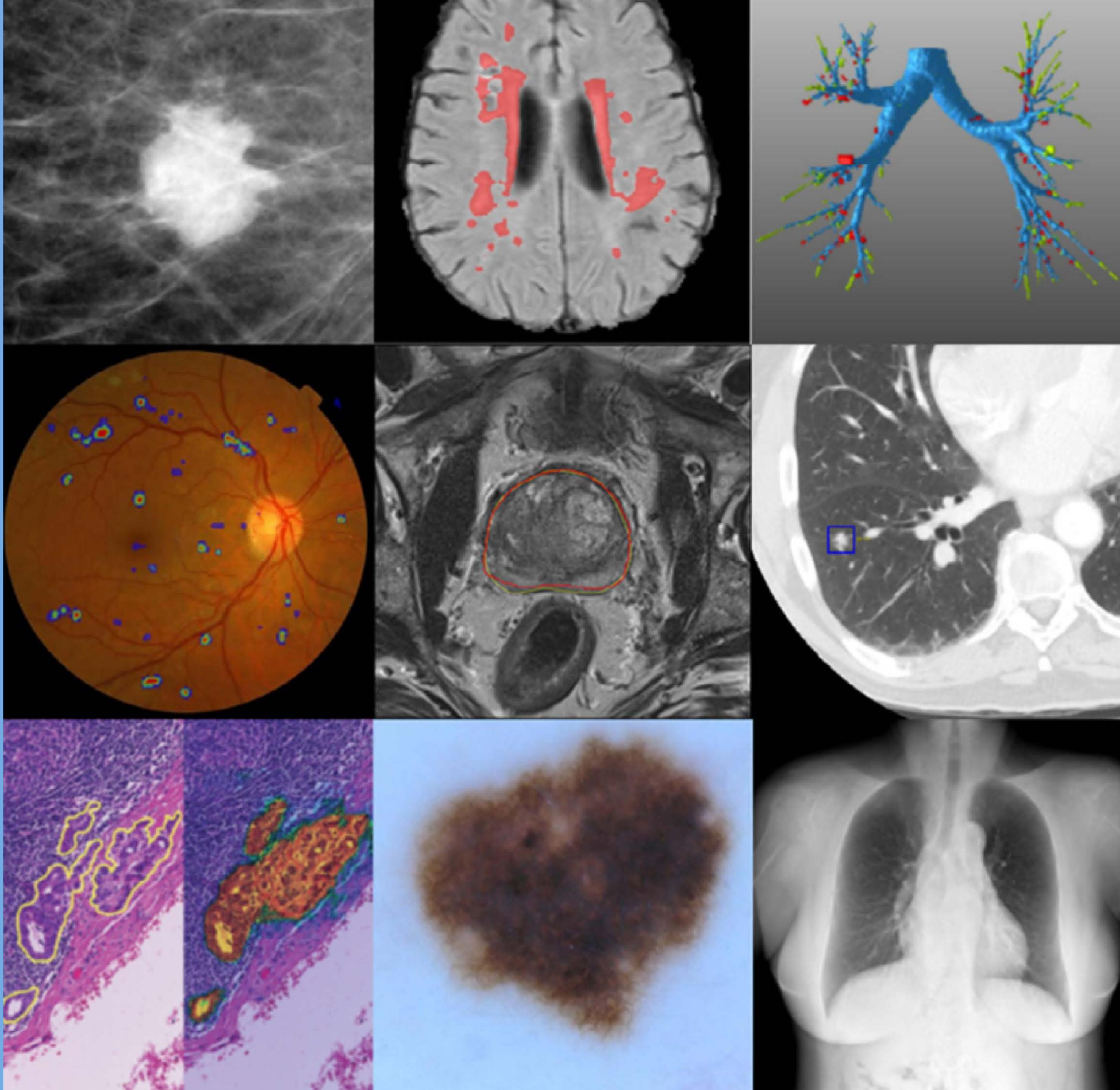
Imaged Guided Therapy

Pathology

Dermatology

Ophthalmology

Endoscopy



1990s-Present

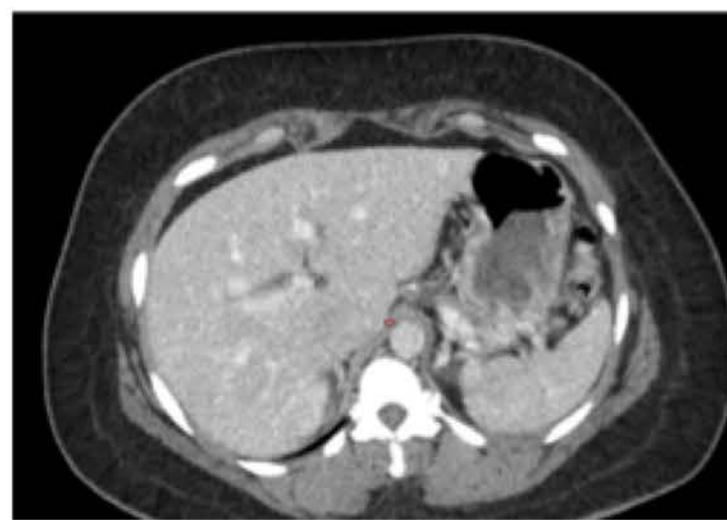
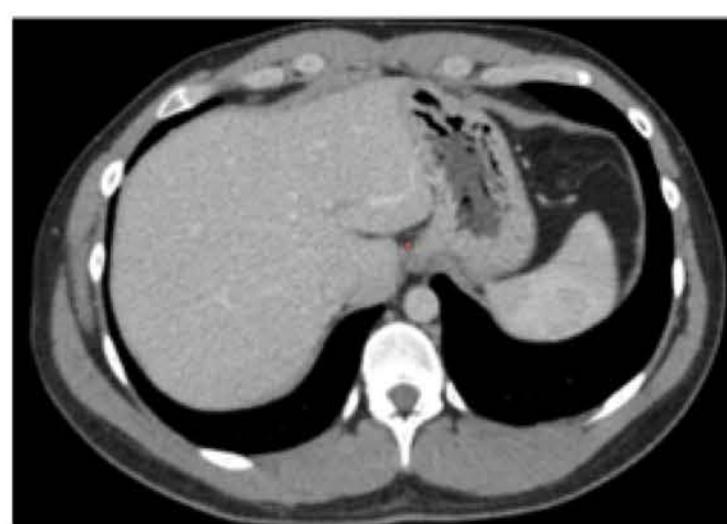
Atlas-based analysis

A statistical/probabilistic approach

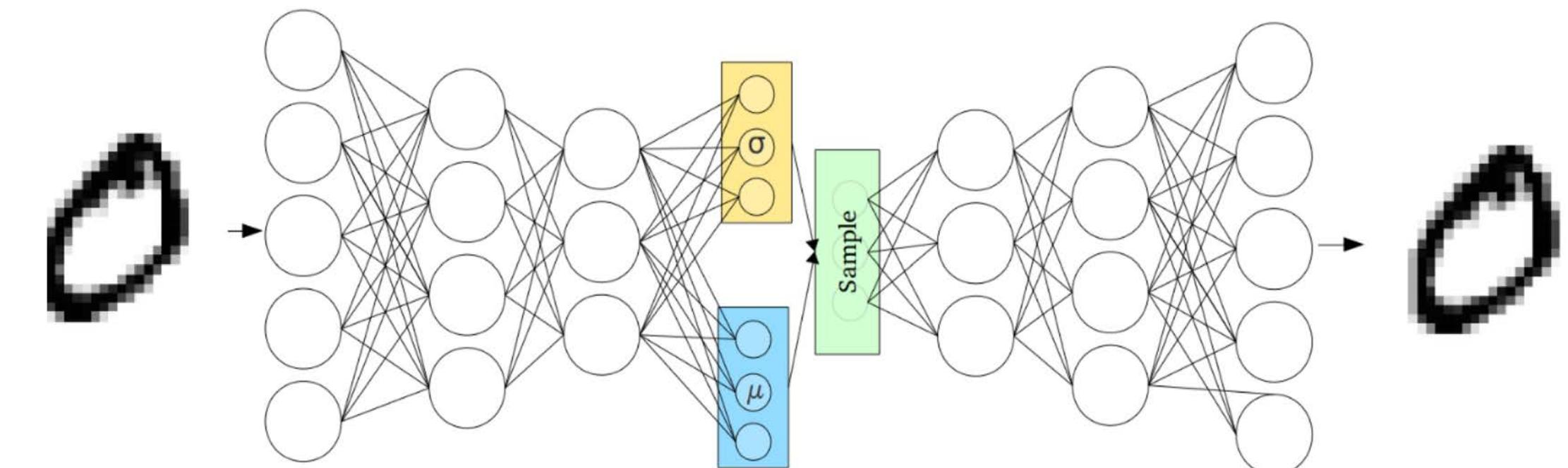
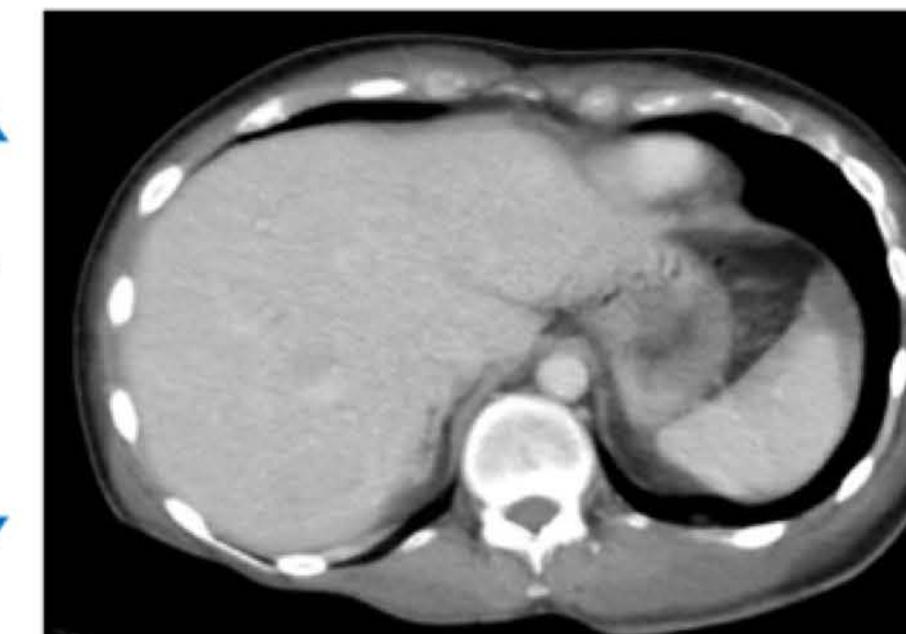
Individual healthy livers



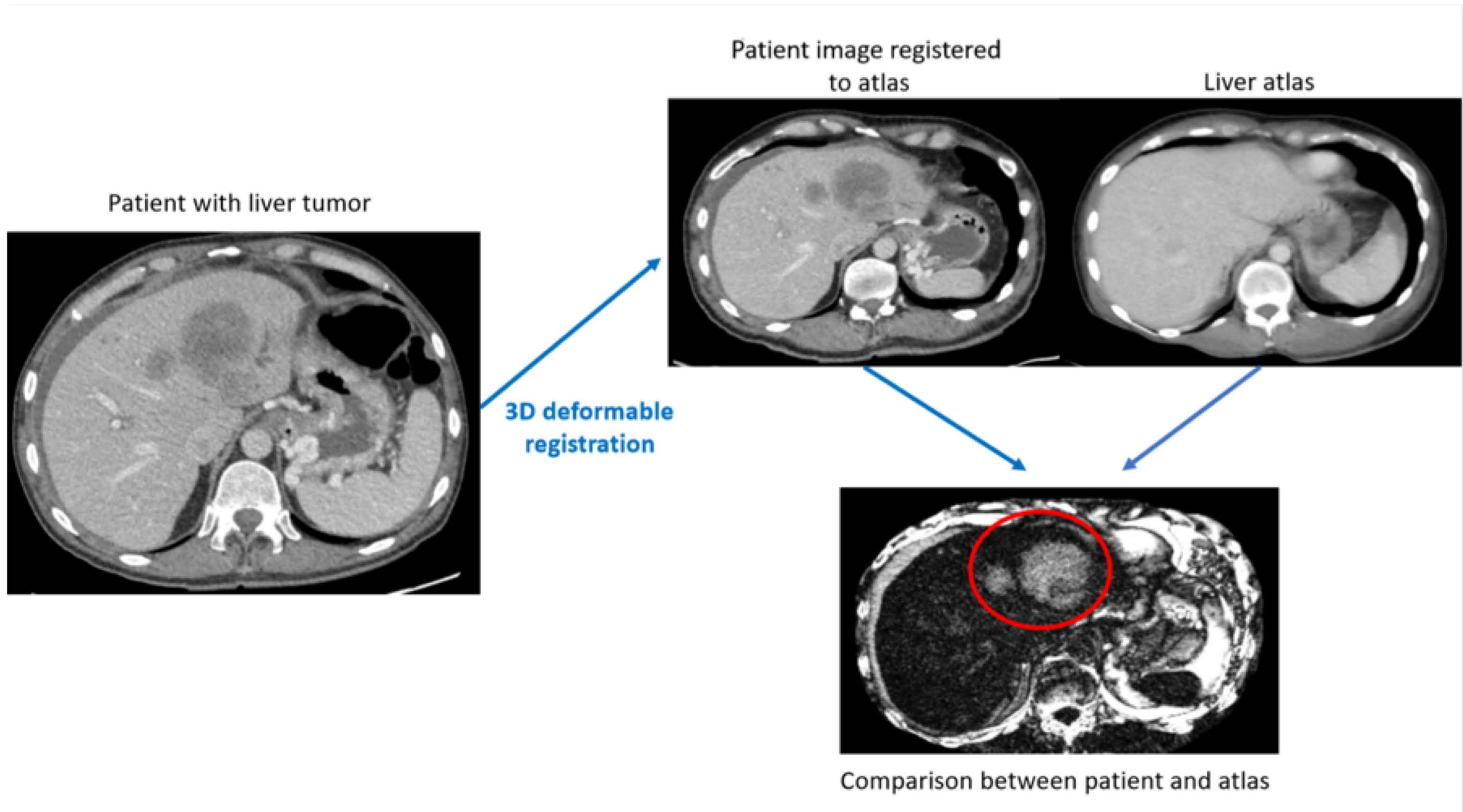
3D deformable registration



Liver atlas



Atlas-based analysis

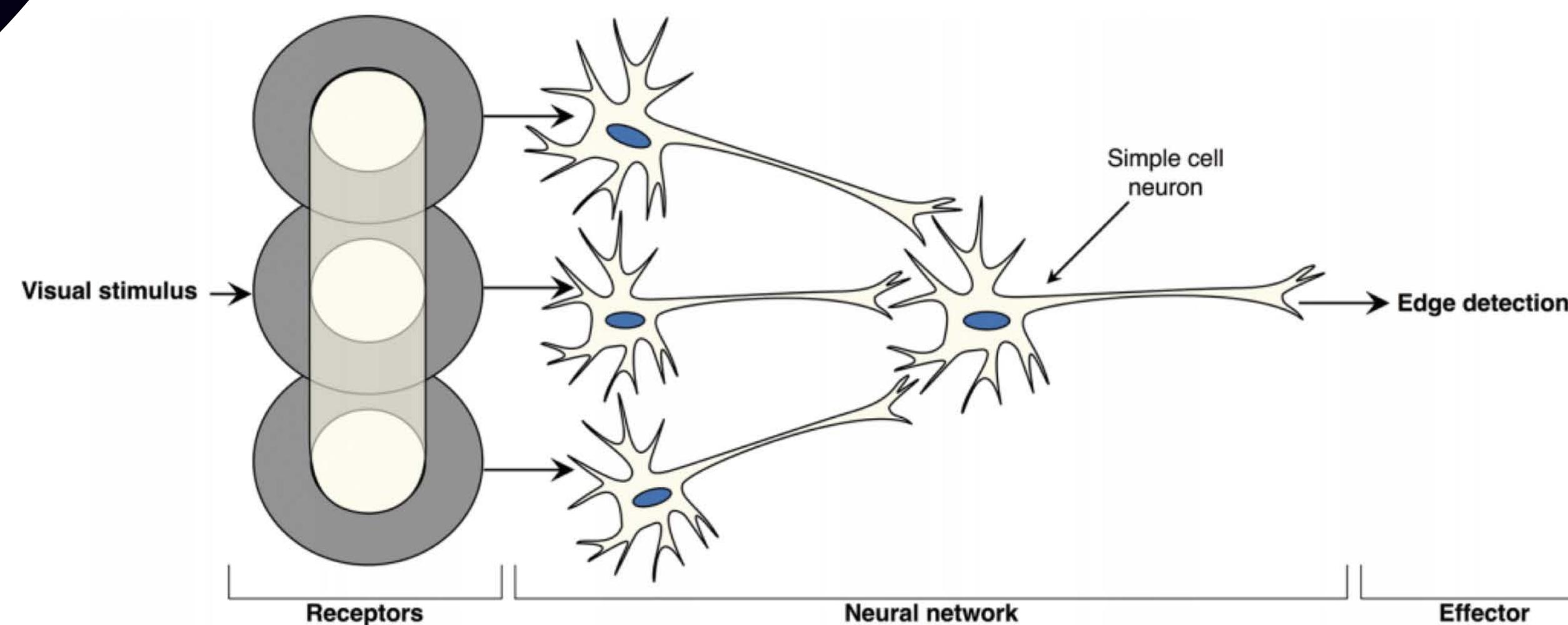




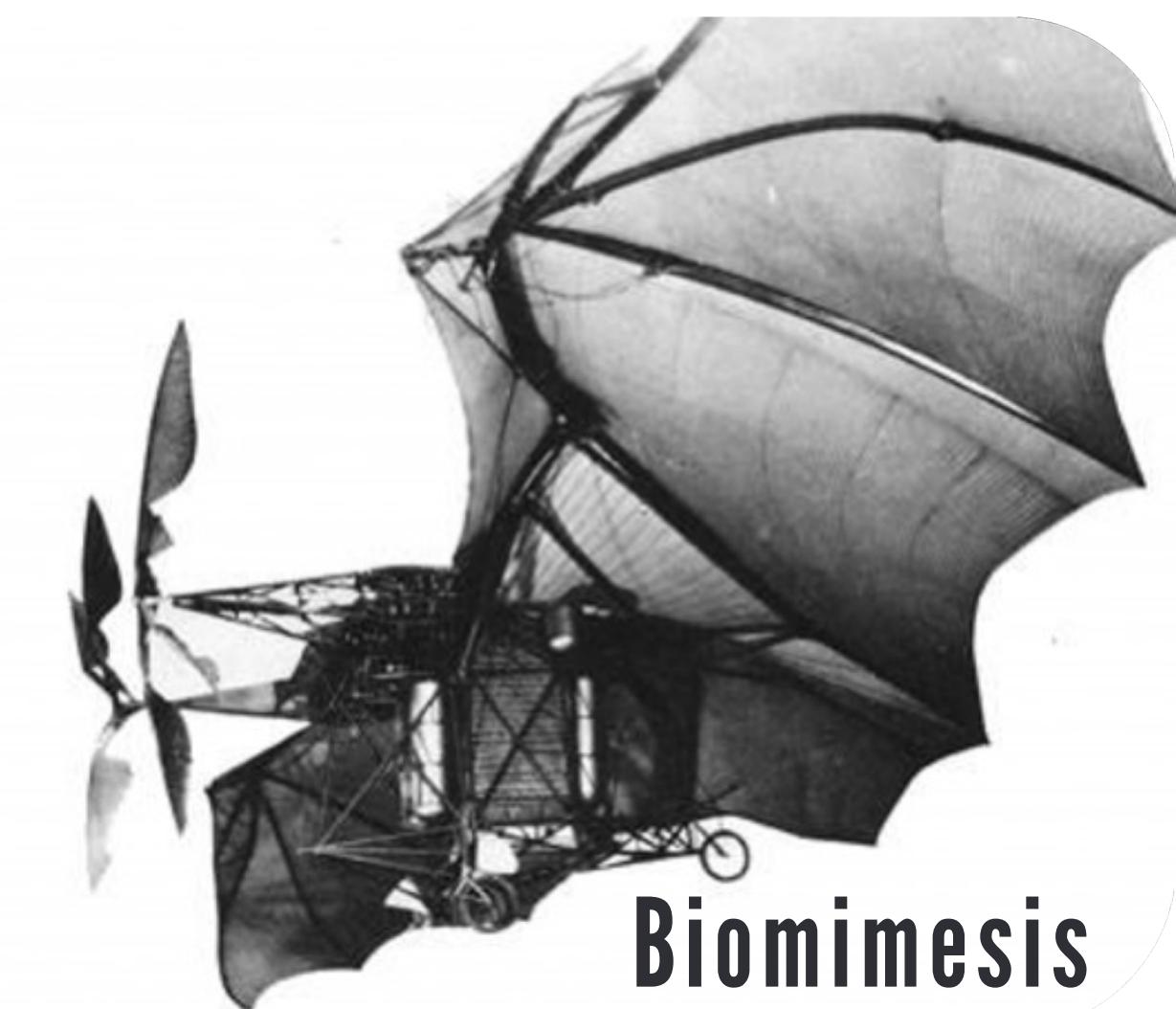
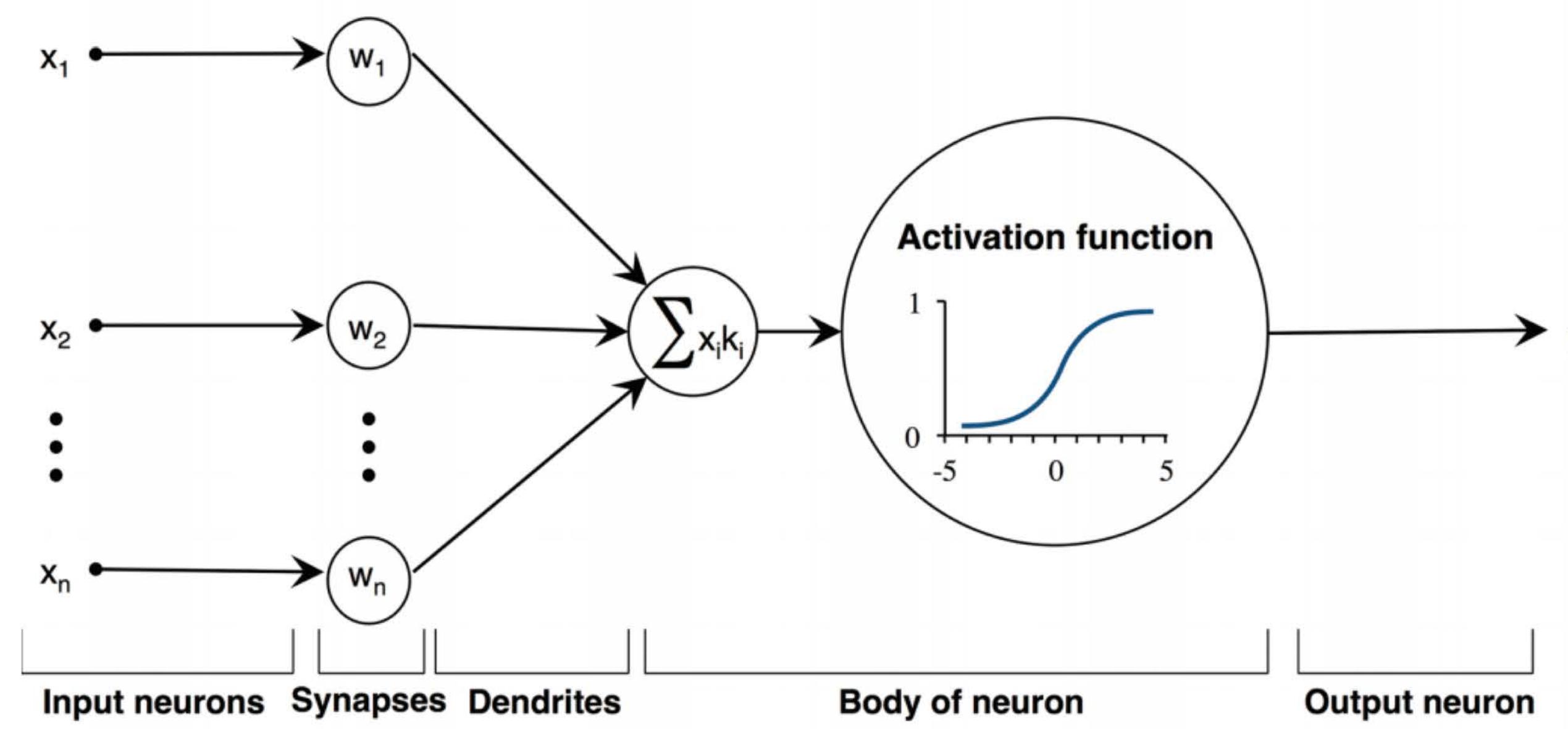
2010s-Present

Deep-Learning

A model free / Data driven method



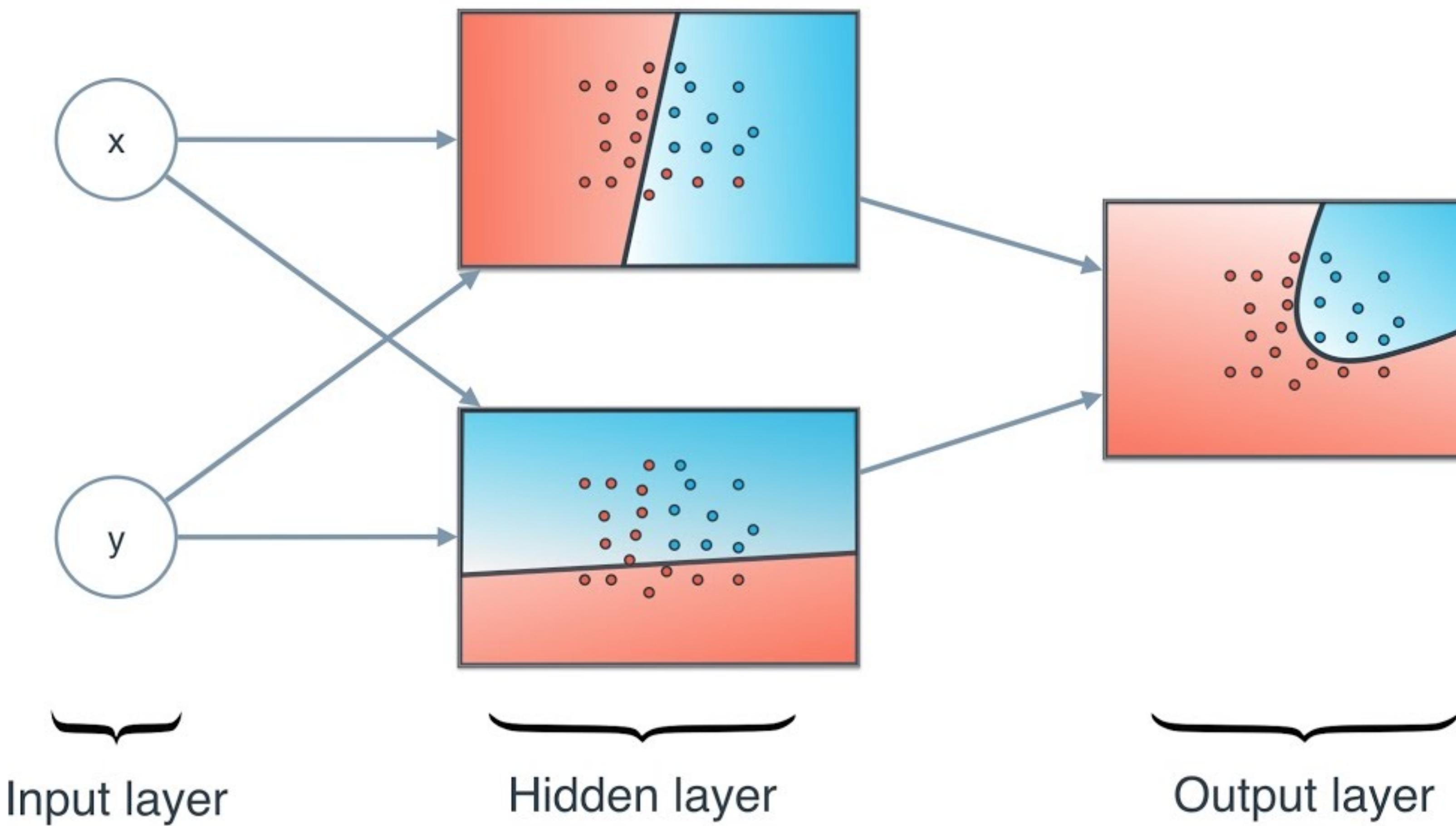
a.



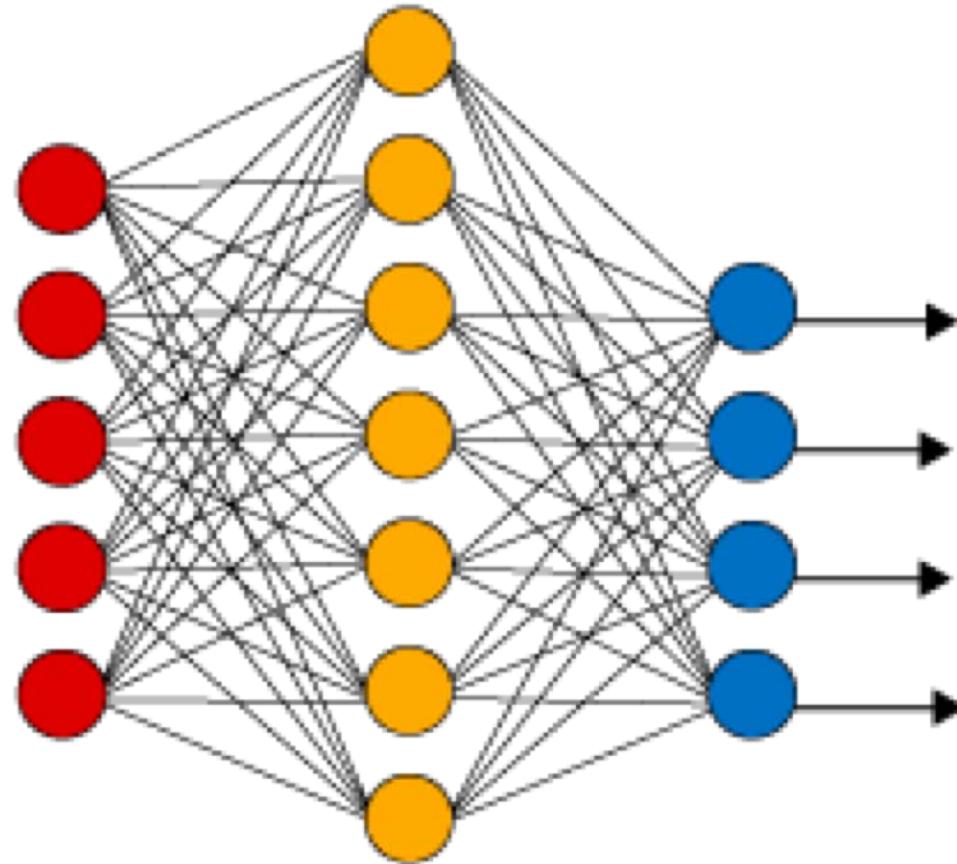
2010s-Present

Deep-Learning
A model free / Data driven method

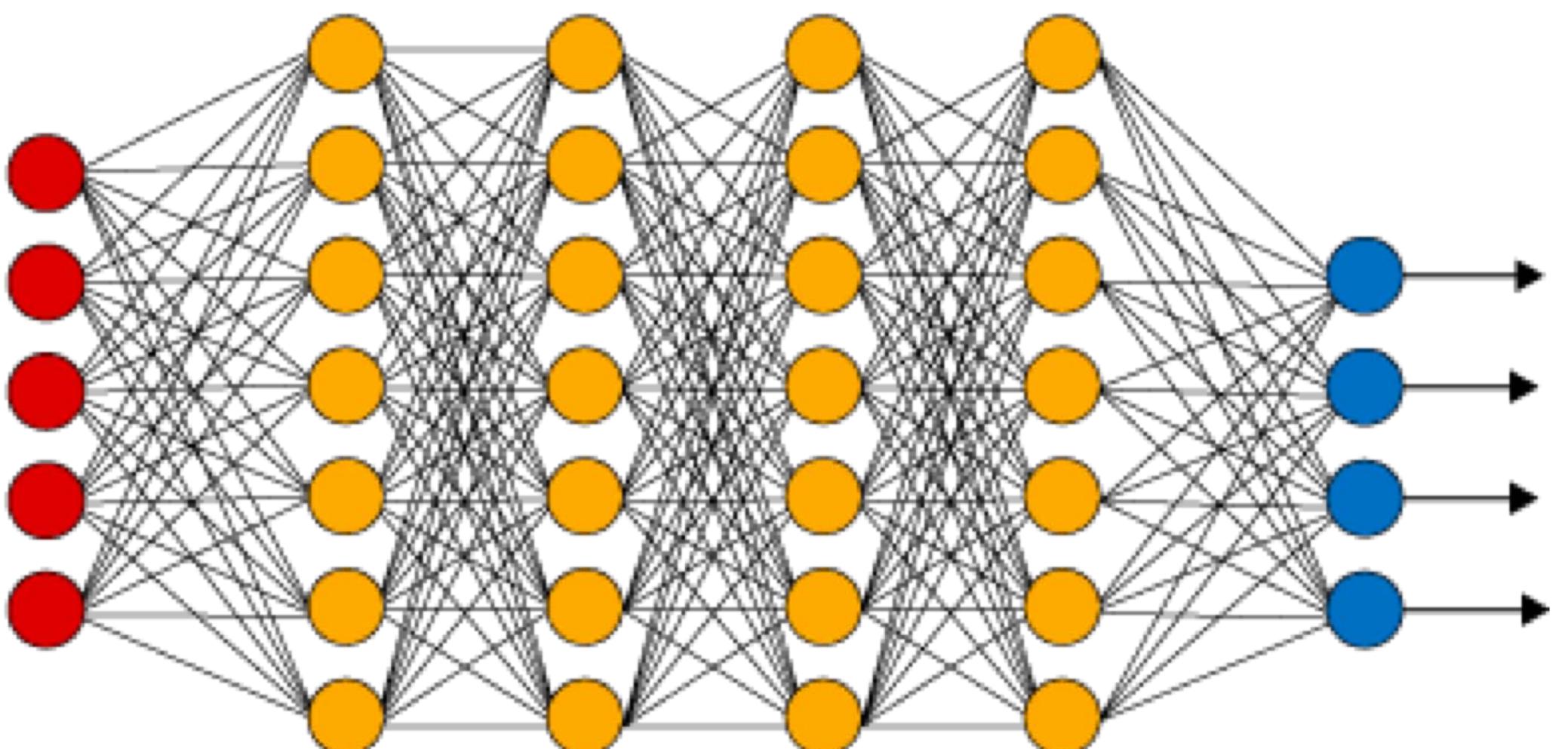
Neural Network



Simple Neural Network



Deep Learning Neural Network

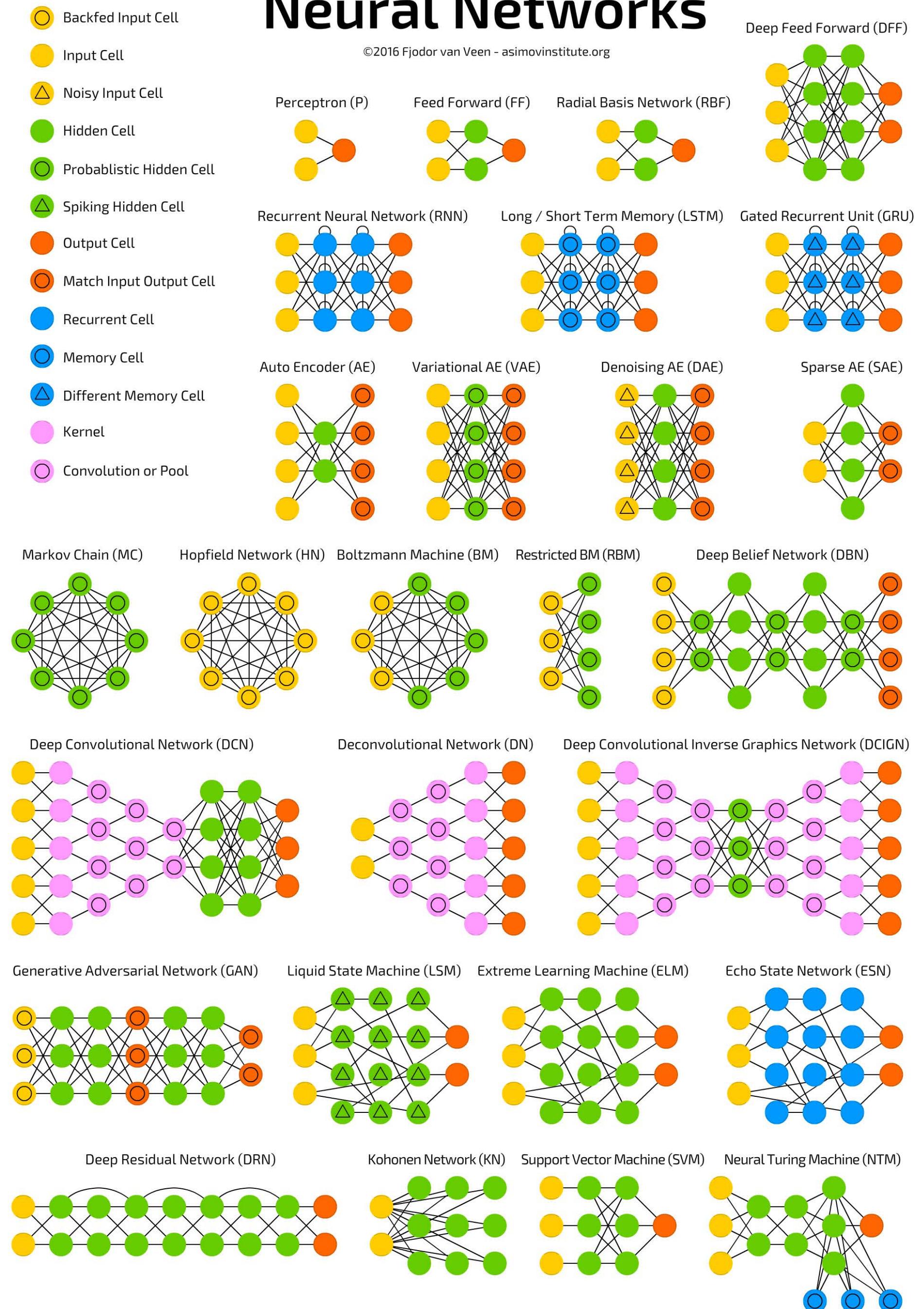


A mostly complete chart of

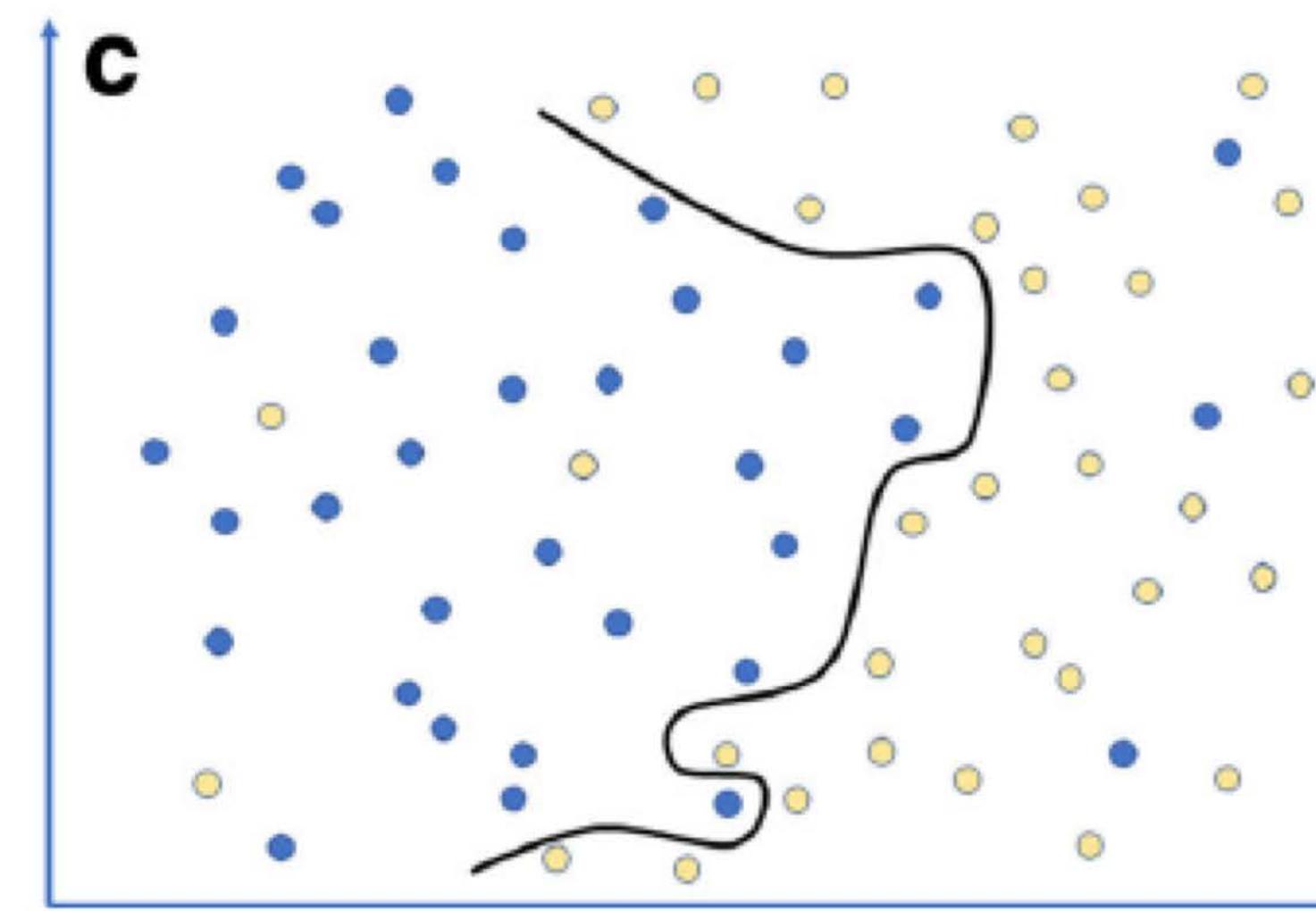
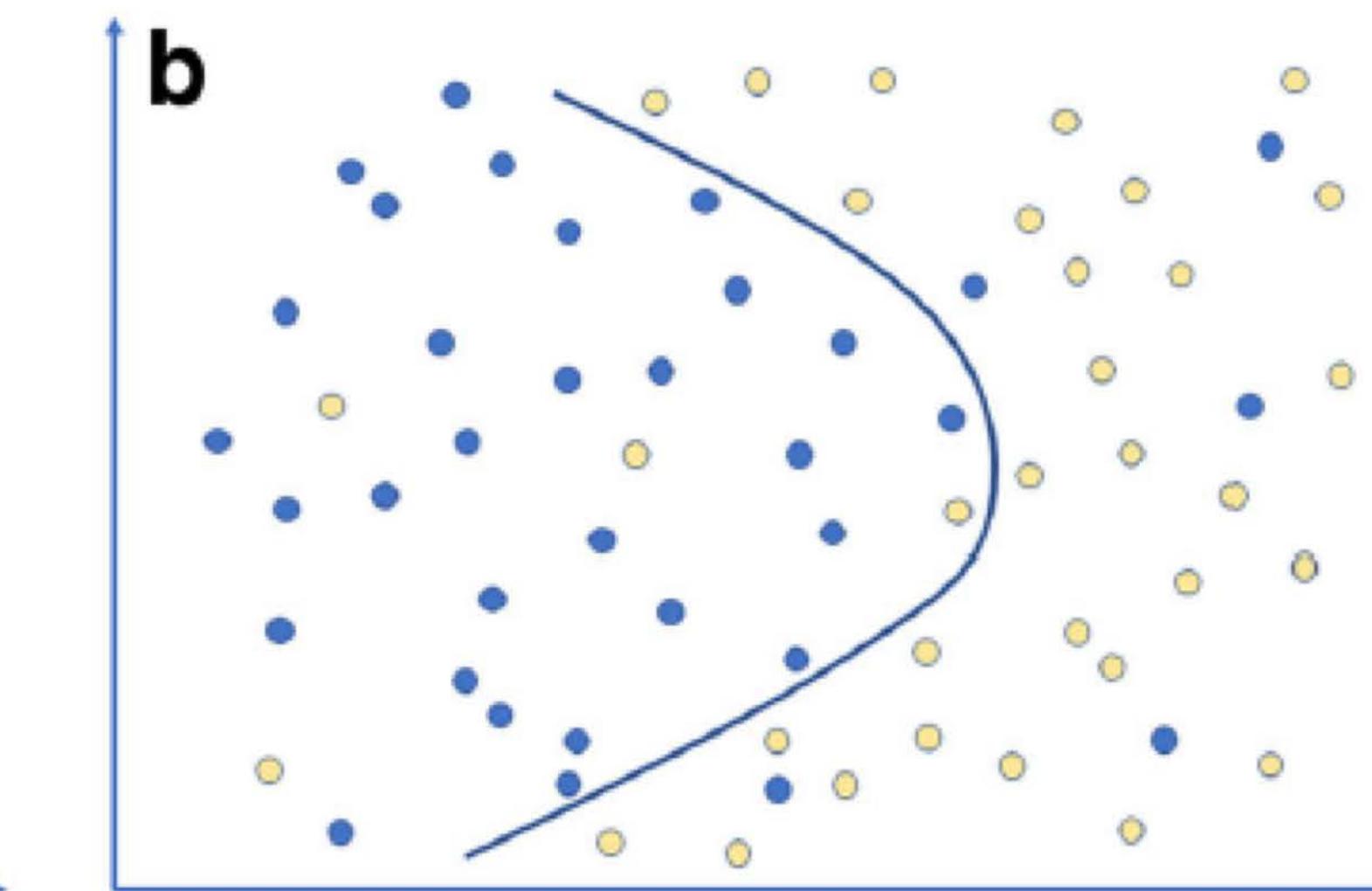
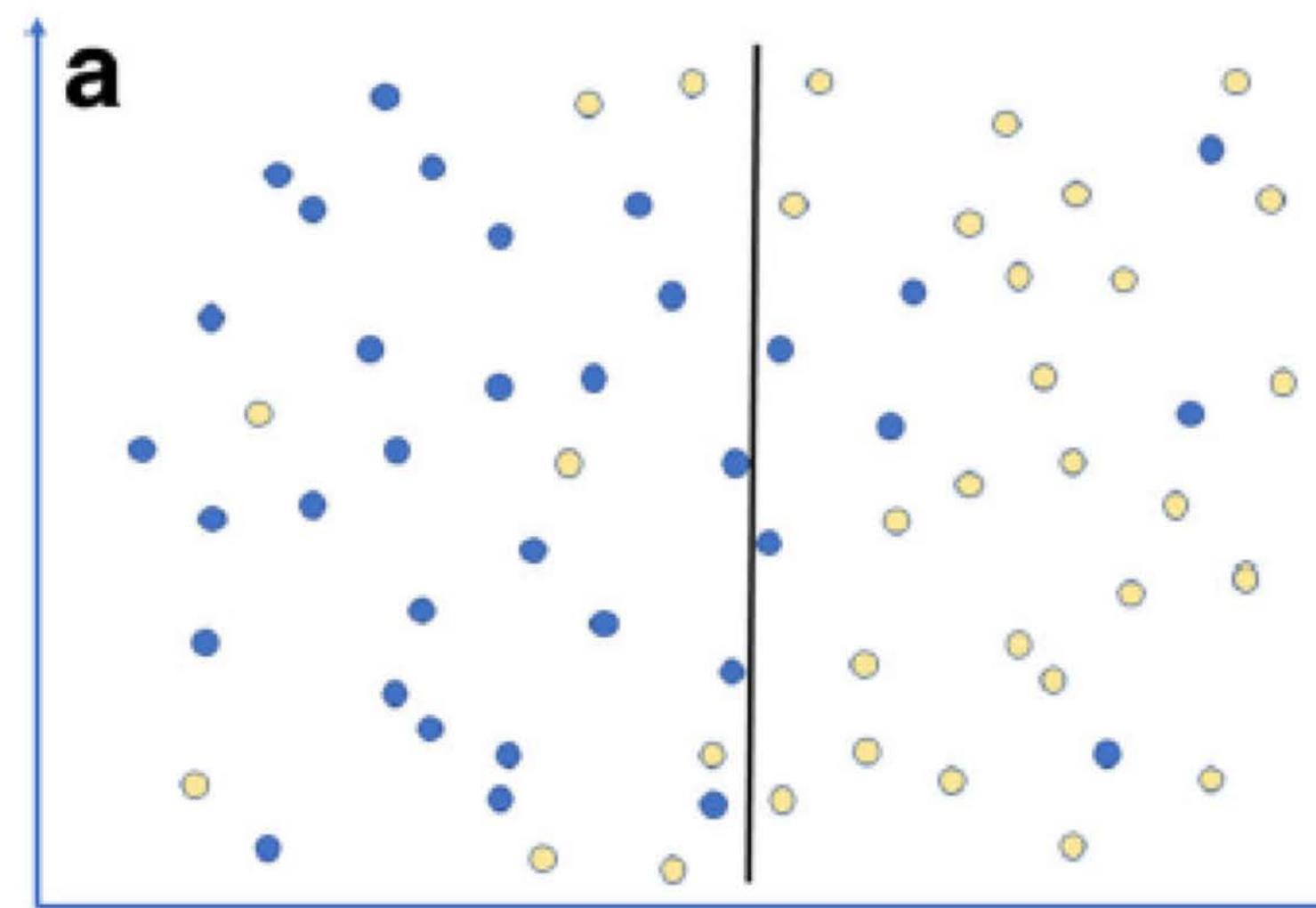
Neural Networks

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Deep Feed Forward (DFF)

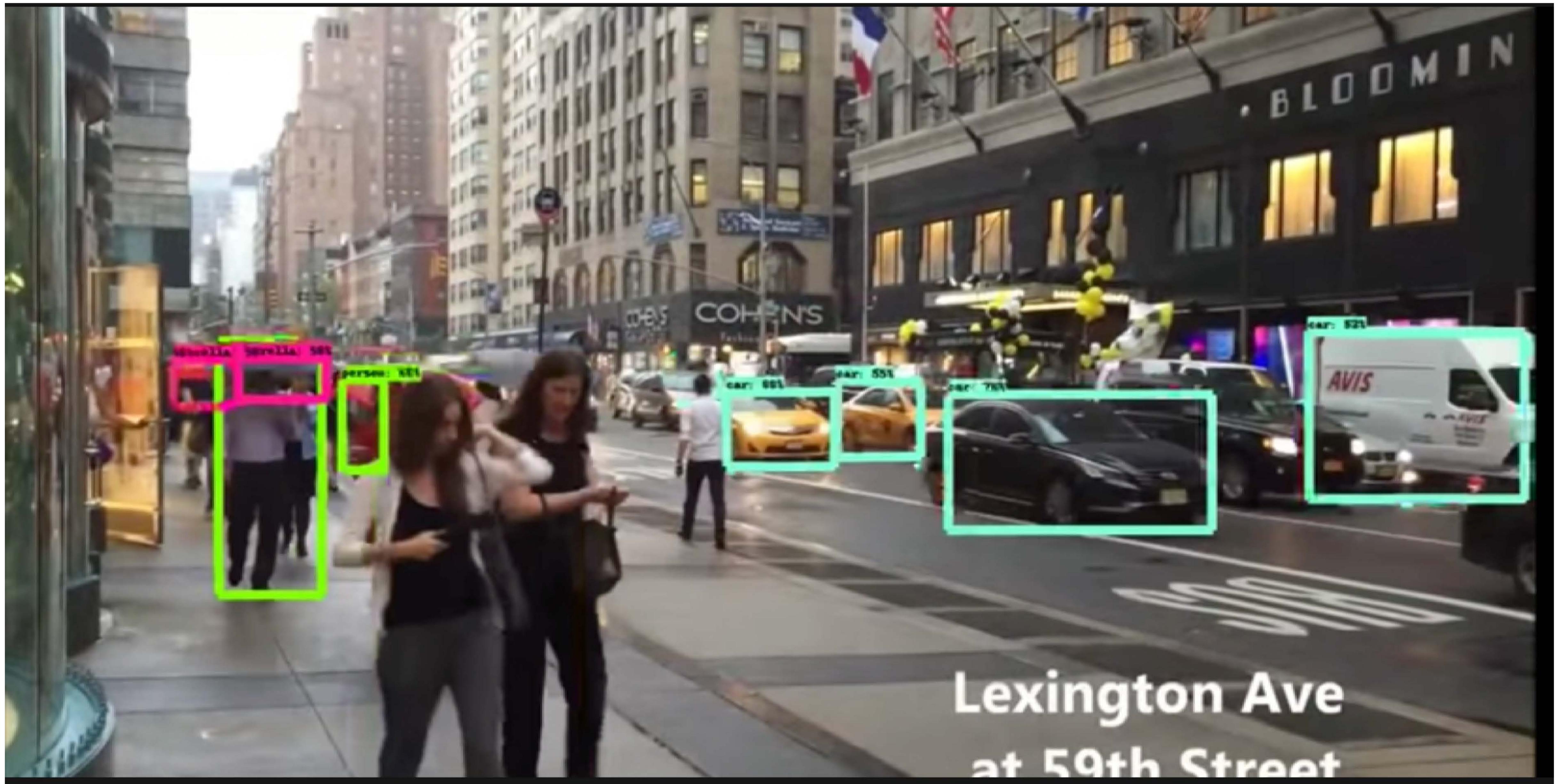


Overfitting

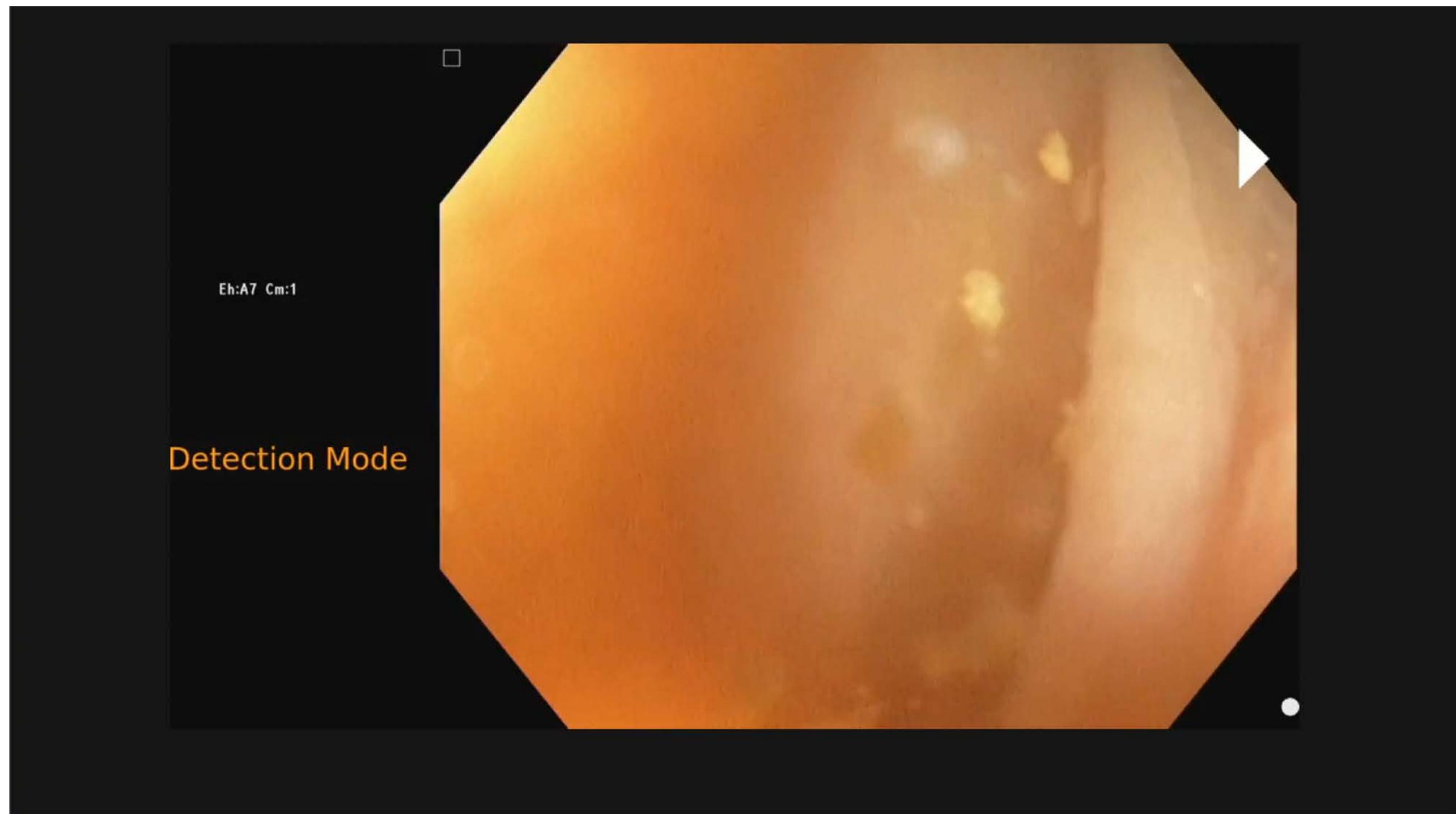


Deep-Learning

- Deep learning arose to take advantage of the large amounts of digital data
- It performs classification without the need of feature engineering done by humans
- Its power lies in that it can automatically discover and learn discriminatory features, in order to perform classification better than other algorithms or even humans.

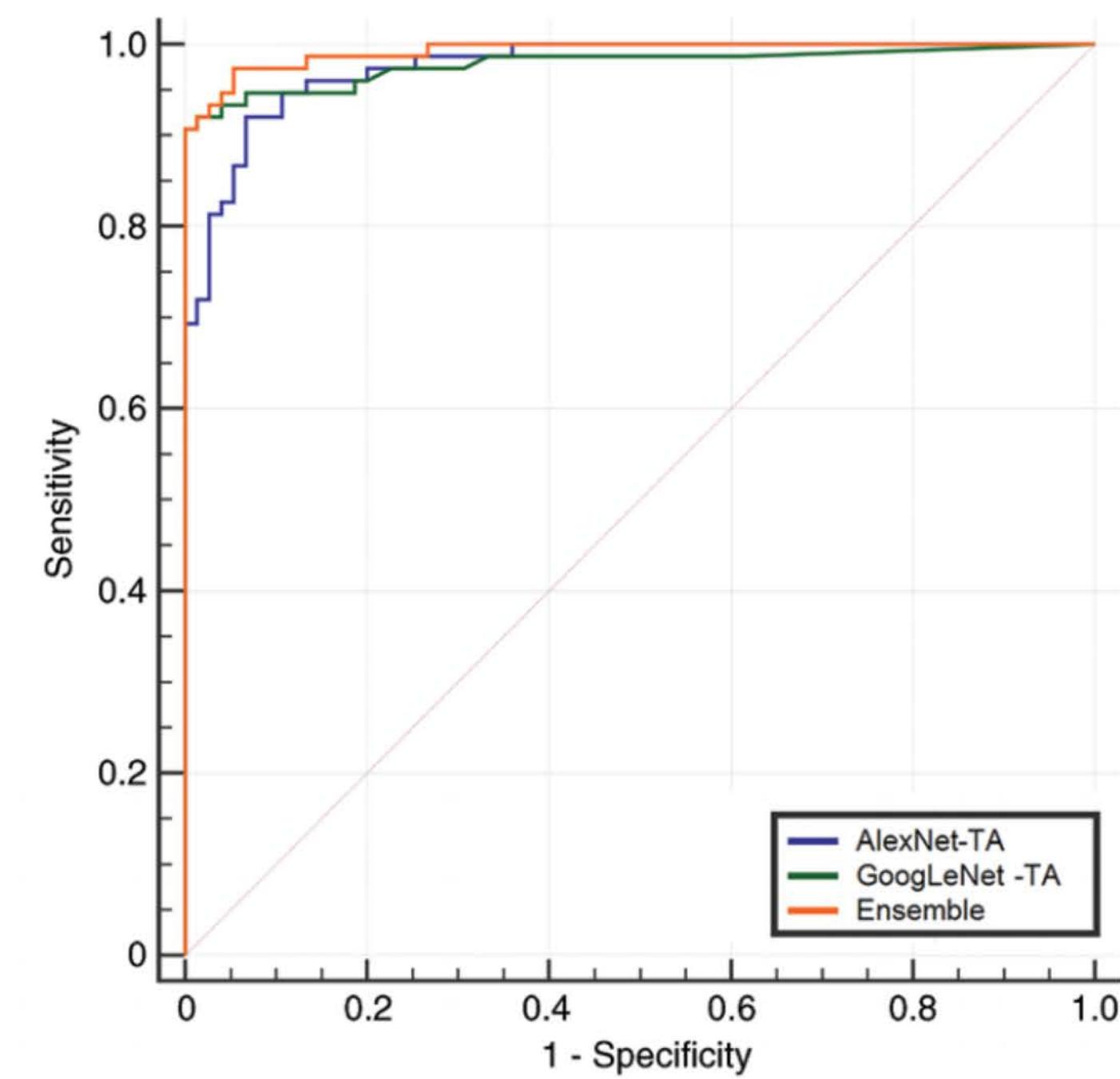
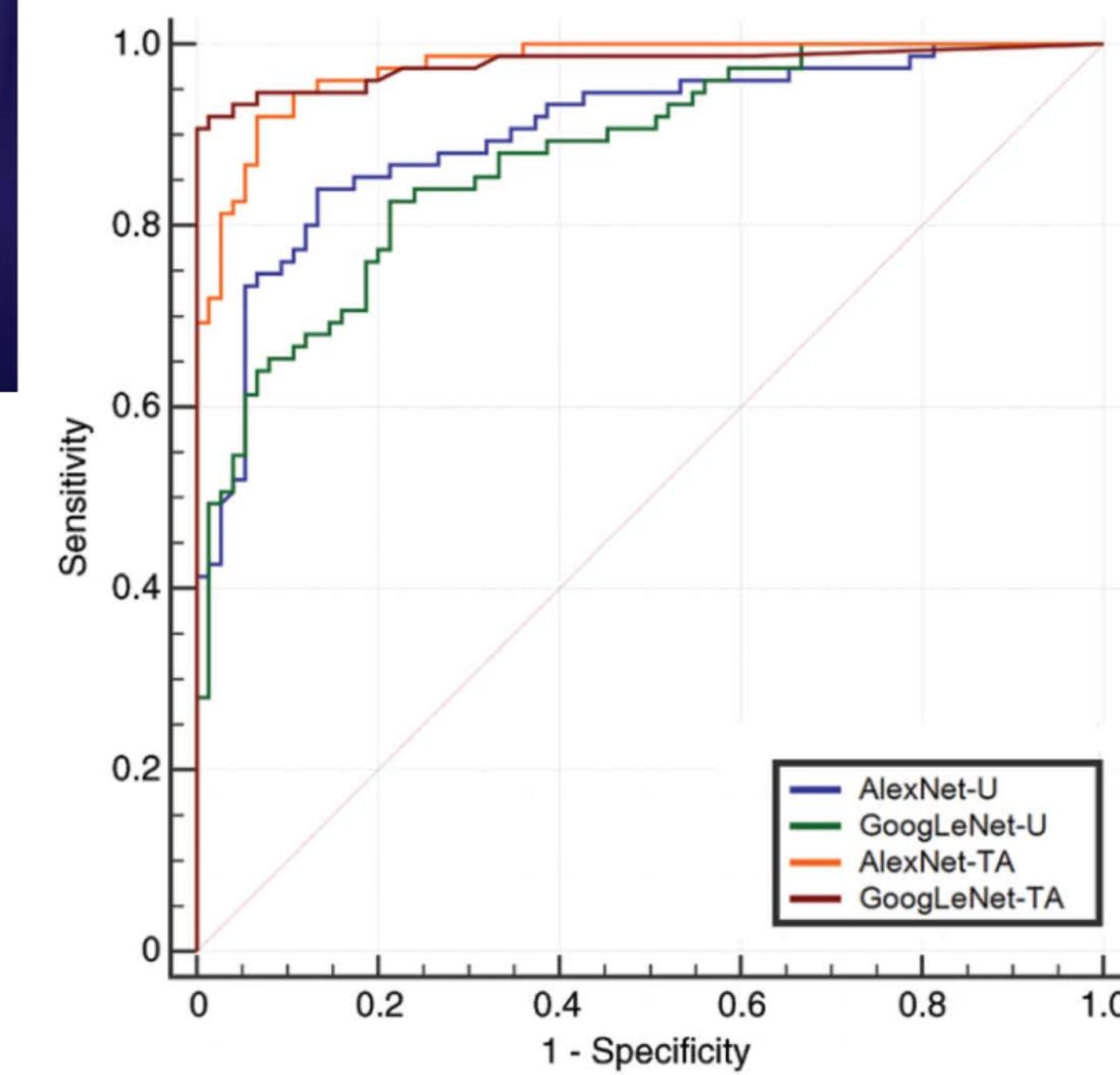
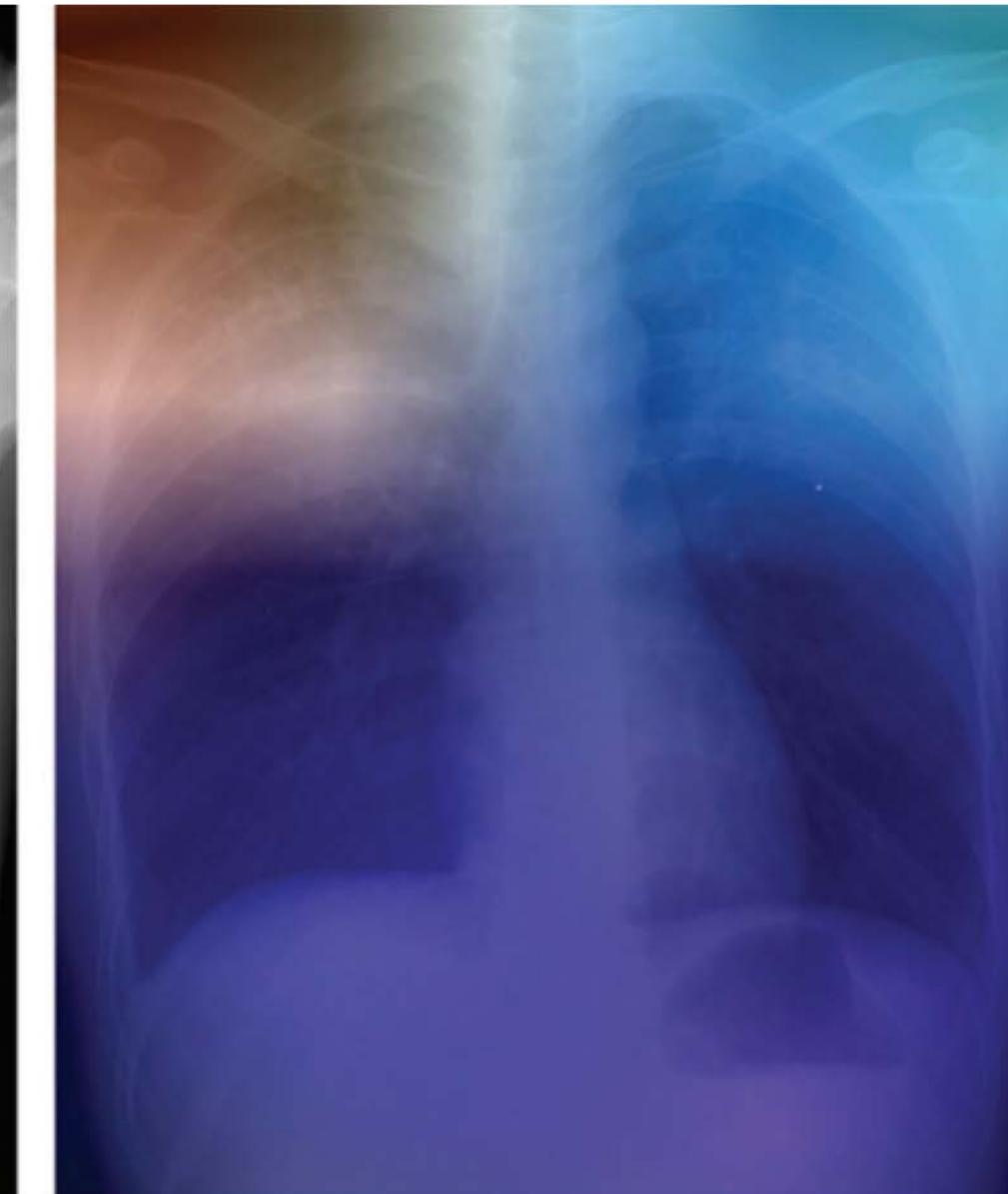


Lexington Ave at 59th Street

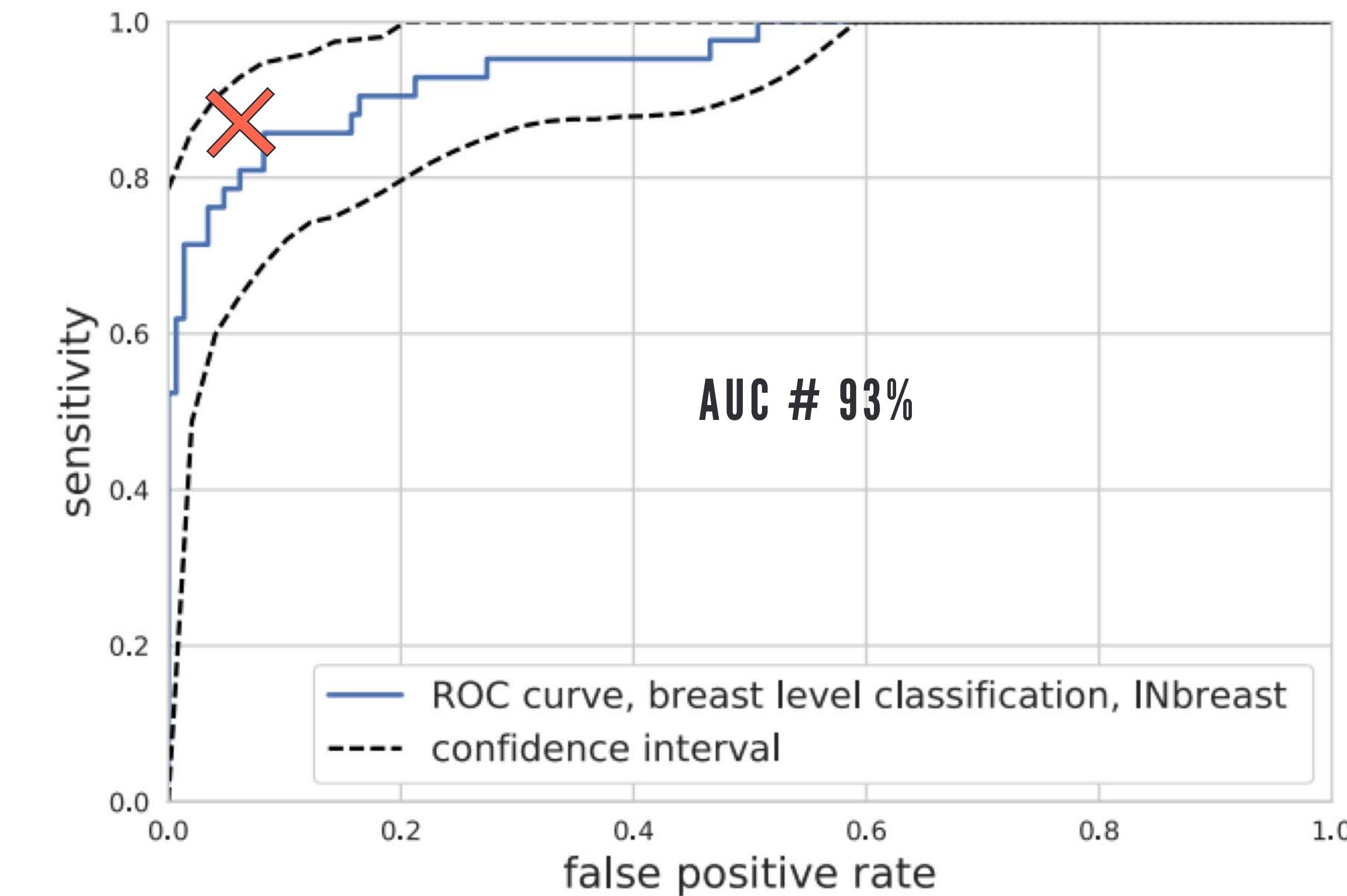
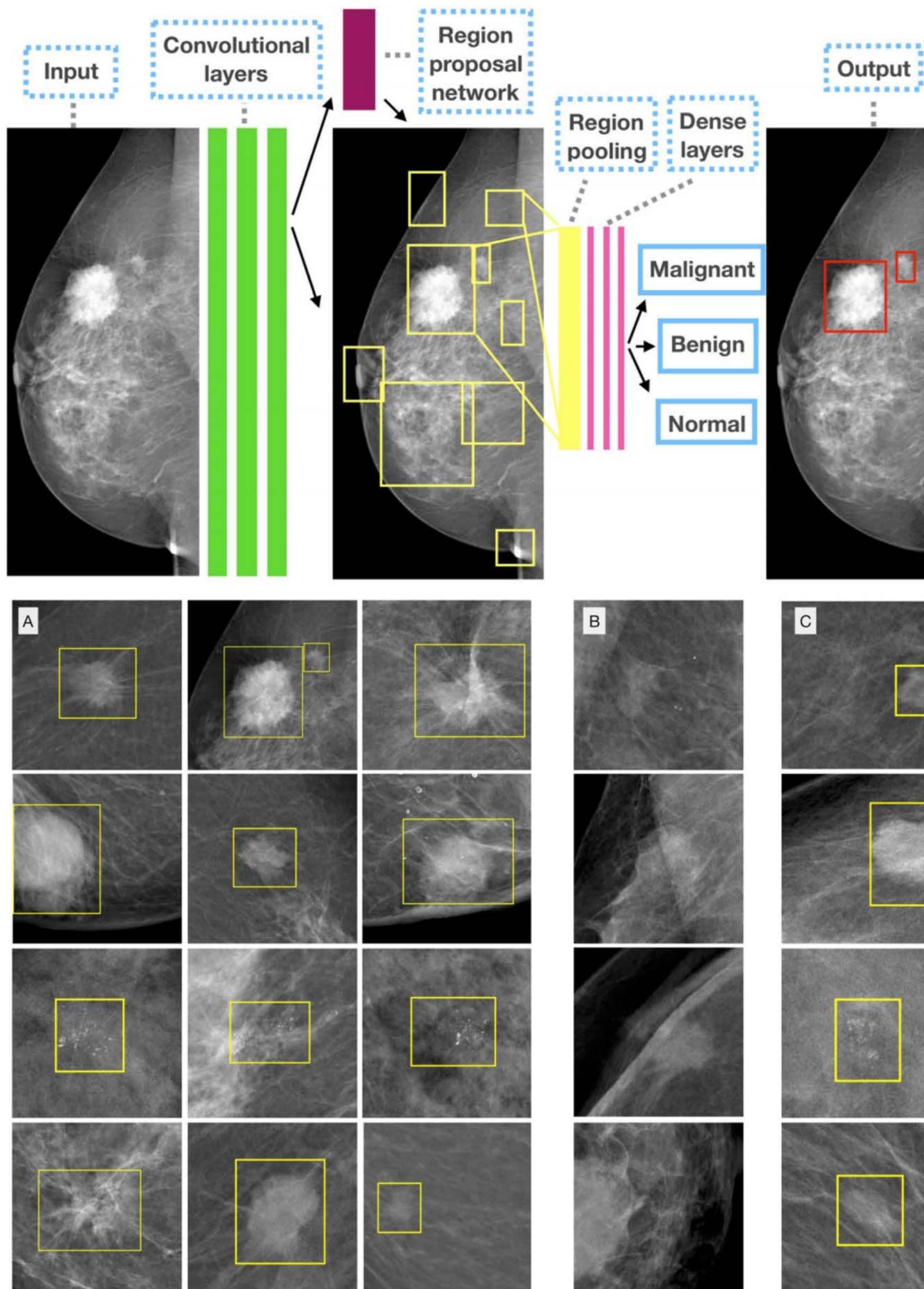


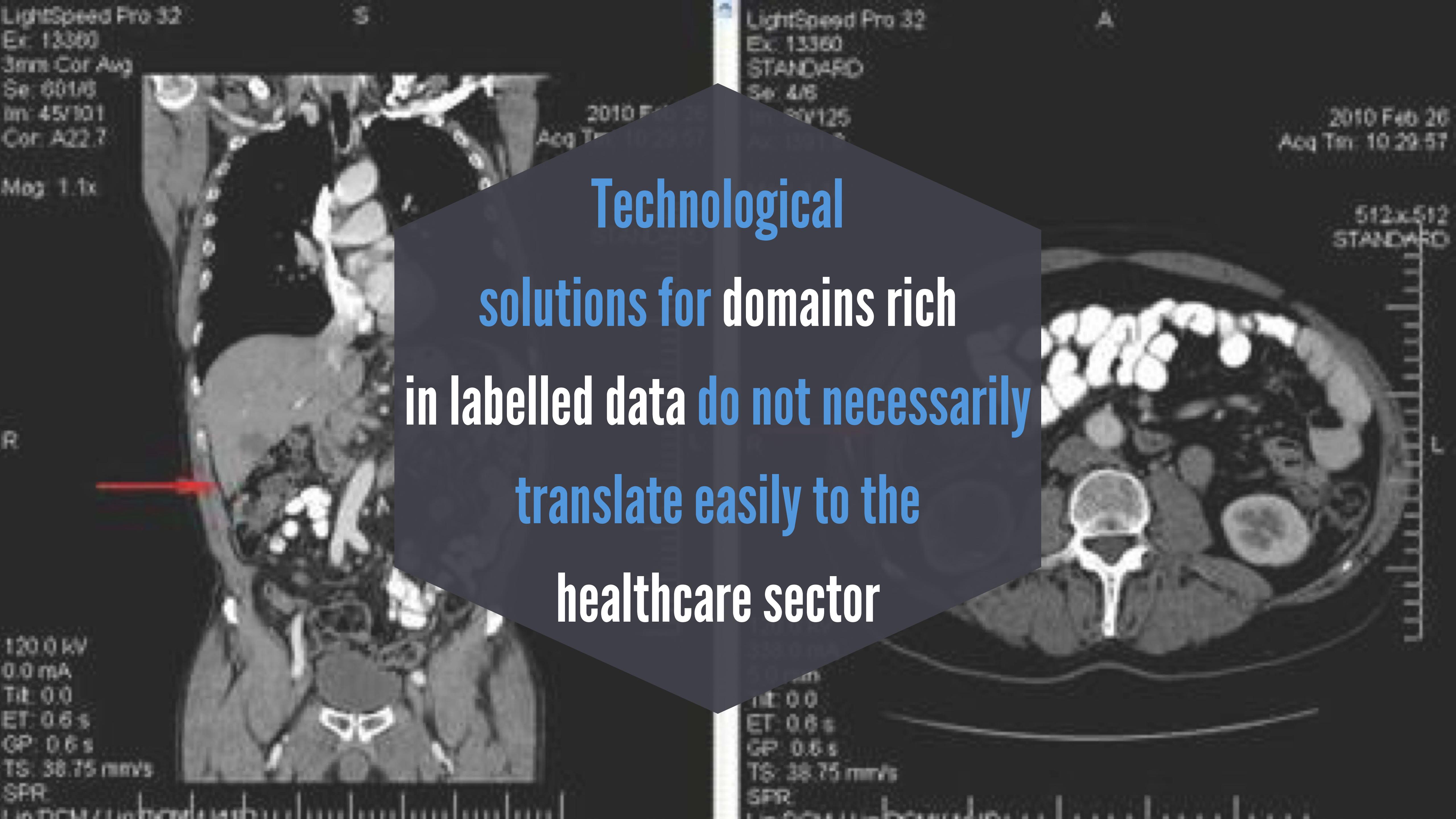
Deep Learning at Chest Radiography

Automated Classification of Pulmonary Tuberculosis by Using Convolutional Neural Networks.



Detecting and classifying lesions in mammograms with Deep Learning





LightSpeed Pro 32
Ex: 12360
3mm Cor Avg
Se: 601/6
Im: 45/101
Cor A22.7
Mag: 1.1x

LightSpeed Pro 32
Ex: 13360
STANDARD
Se: 4/6
Im: 125
Cor T10-11
Aq T10-11
Mag: 1.1x

2010 F46 26
Aug Ten: 10.29.57
512x512
STANDARD

R L

120.0 kV
0.0 mA
TIL: 0.0
ET: 0.6 s
GP: 0.6 s
TS: 38.75 mm/s
SPR:
Lip: 0.0 mm/s - 1.0 mm/s

S

Technological
solutions for domains rich
in labelled data do not necessarily
translate easily to the
healthcare sector

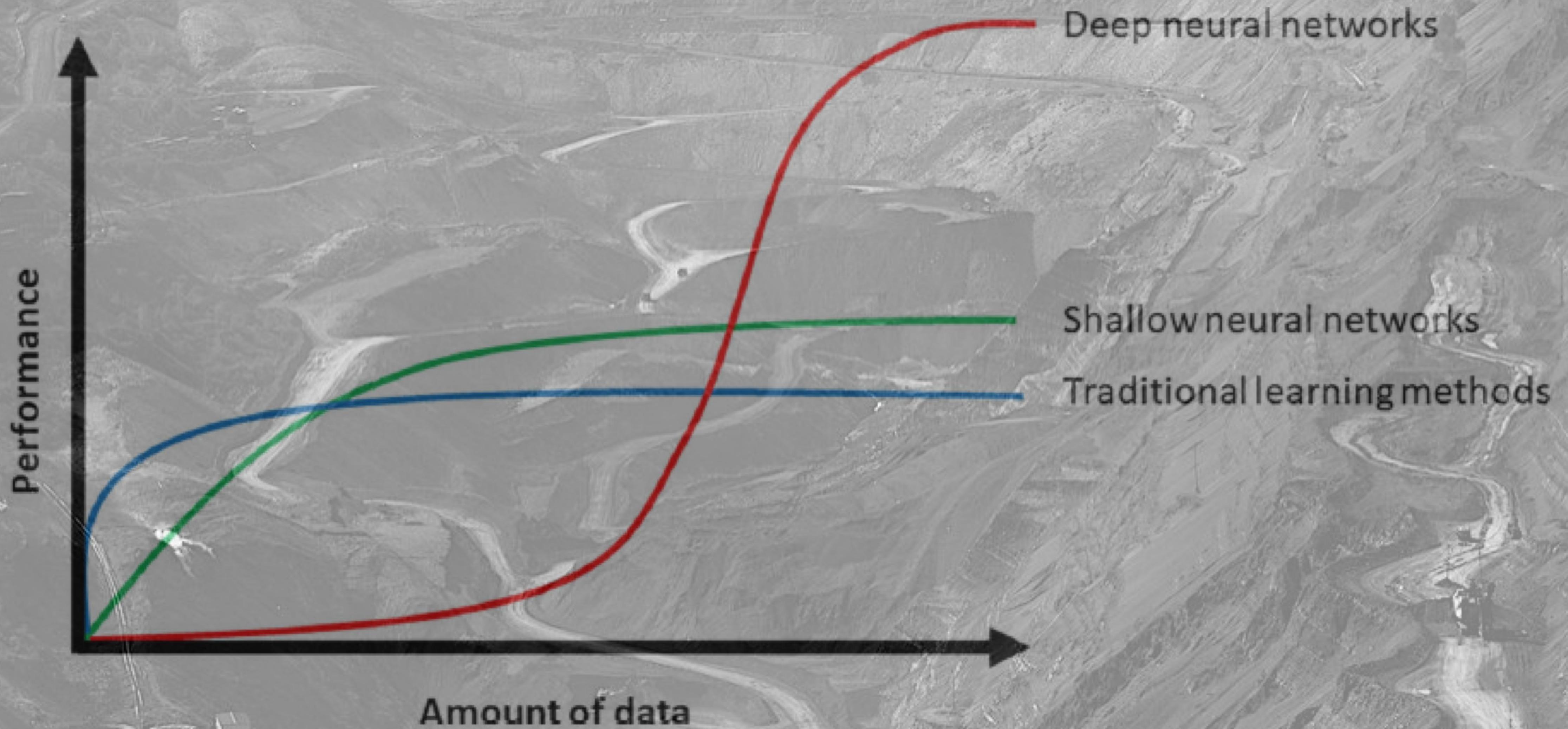
Limitation 1: inefficient use of data

Data delusion

The progress is driven far more by data availability than by improvement in algorithms

To train for a particular task, DL requires far more data points than a human would

“you really need data mines”



Limitation 2: lack of generalization

Once trained on a given task, deep networks are incredibly good at a very specific task. However, any such network can only perform that one task.

“specialization is for insects”

Limitation 3: lack of explainability

Neural networks are usually inscrutable to observers.

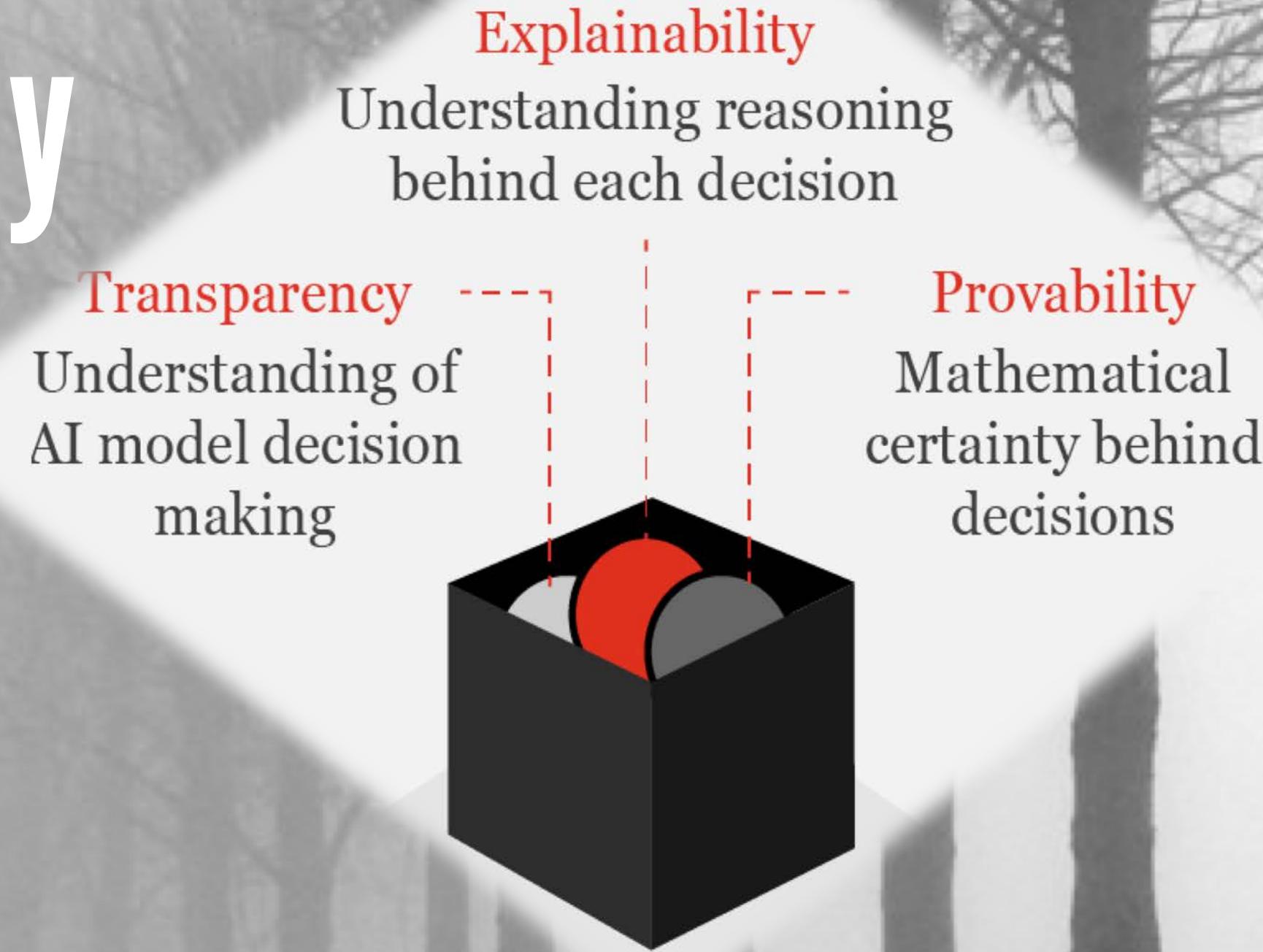
We know how they are constructed, and we know the data that goes in, but the reasons why certain conclusions are reached are usually unknown.

”It is generally infeasible to interpret DL features because their meaning depends on complex interactions with uninterpreted features in other layers”

Limitation 3: lack of explainability

Neural networks are usually inscrutable to observers.

“We know how they are constructed, and we know the data that goes in, but the reasons why certain conclusions are reached are usually unknown”



Limitation 4: lack of transferability

The results of the models depends mainly on the quality and representativeness of the data sets

“It’s a lot about Database”



Massachusetts
Institute of
Technology

NORMAN

World's first psychopath AI.

RORSCHACH TEST

WHAT DOES AI SEE?

We trained Norman on Reddit, and compared captions with standard image captioning neural network.

Here is what both AIs see on Rorschach's inkblot tests.

**CAPTIONS BY
NORMAN AI**



**CAPTIONS BY
STANDARD AI**



INKBLOT #8
Standard AI sees:
**“A PERSON IS HOLDING AN
UMBRELLA IN THE AIR.”**

RORSCHACH TEST

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**CAPTIONS BY
NORMAN AI**

INKBLOT #8
Norman sees:
**“MAN IS SHOT DEAD IN FRONT
OF HIS SCREAMING WIFE.”**



**CAPTIONS BY
STANDARD AI**

INKBLOT #8
Standard AI sees:
**“A PERSON IS HOLDING AN
UMBRELLA IN THE AIR.”**

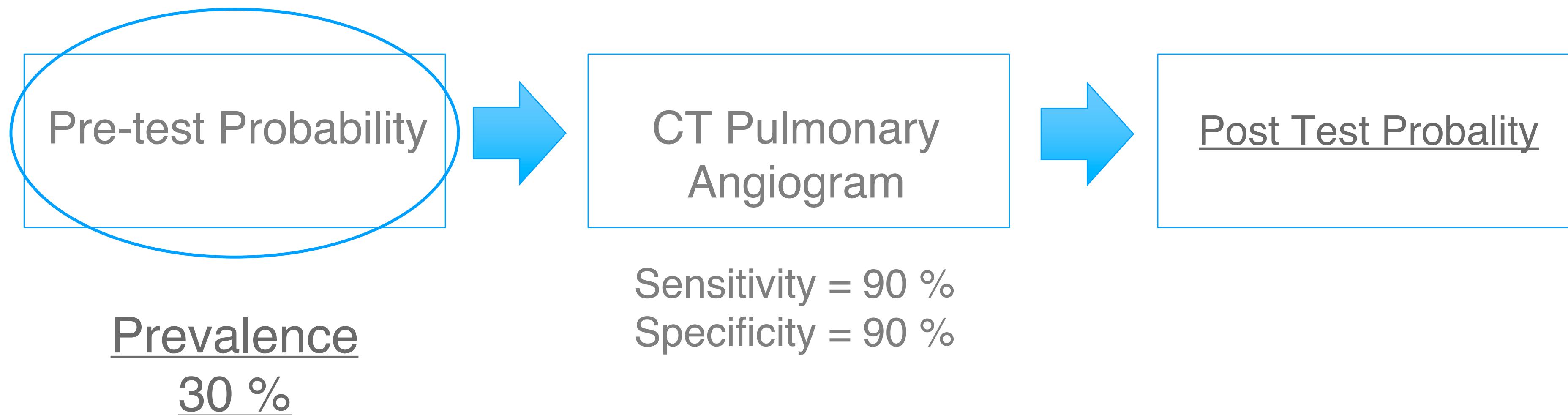


“

the principle of deep learning implies
that the tested data have the same
distributions as the trained data ”

“ the machine will have as much bias as there
is in the data that was used to train it ”

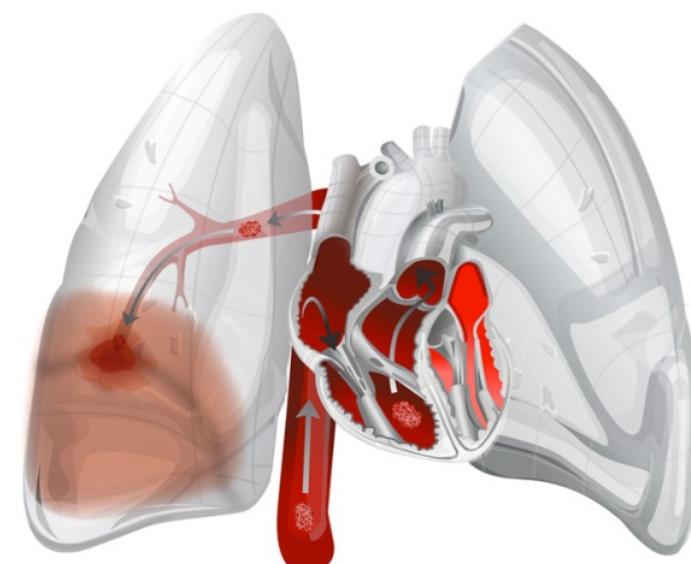
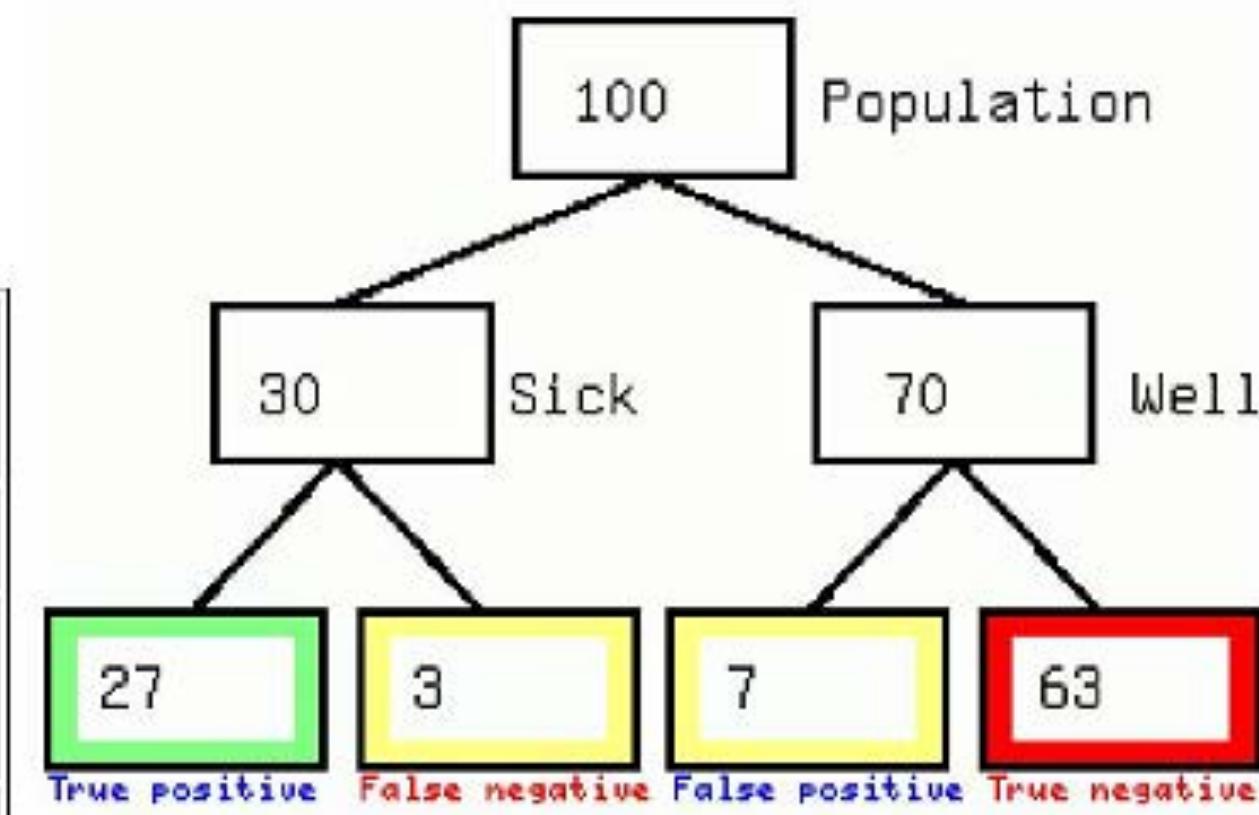
CT angiography for the Diagnostic of Pulmonary Embolism



- When prevalence decrease from 30% to 10%

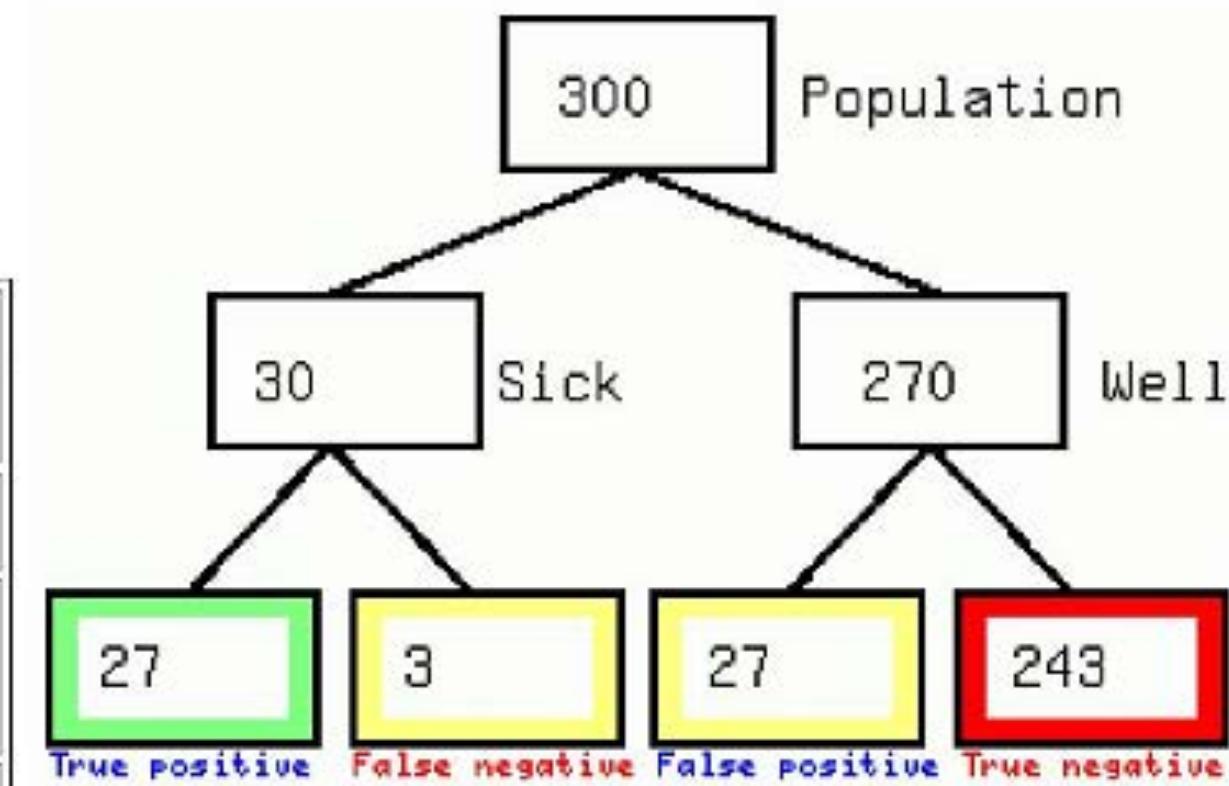
Numbers of patients with and without the disease who test positive and negative:

	Disease present	Disease absent	Total
Test positive	27	7	34
Test negative	3	63	66
Total	30	70	100



Numbers of patients with and without the disease who test positive and negative:

	Disease present	Disease absent	Total
Test positive	27	27	55
Test negative	3	243	245
Total	30	270	300



AI in Healthcare should be drive by Care Givers

- Invincible aura that AI has in popular perception
- A common mistake is to expect AI to find analyzable information in medical data even where none exists or for which there is no biological plausibility.
- Improperly designed AI experiments could misinform, mislead, or without critical analysis could result in patient harm.

Data-driven vs Hypothesis-driven

- The data-driven approach can be powerful and lead to novel insights
- Yet, it cannot replace the cognitive integration of complex information combining the semeiological analysis in a precise anatomical and physio-pathological context.
- These methodological approaches have been refined over centuries of scientific and medical thought, and they allow for solutions that are still inaccessible to AI.

Data-driven vs Hypothesis-driven

	PICO KEY STEP	PARTICULARITY OF AI IN RADIOLOGY
POPULATION	Describe the patient population. What are the most important patient characteristics and/or the problem type?	Describe the specific disease or condition and the methods tested
INTERVENTION	Describe the diagnostic test(s) being considered	Describe: <ul style="list-style-type: none">- Method of data acquisition- Process of data quality assurance- Method of building the image database
COMPARISON (CONTROL)	Describe the current “gold standard” test for that disease or condition	Comparison of AI to human performance (radiologist?)
OUTCOME	Determine a clinical outcome that will be used to evaluate the performance of the intervention	Determine how AI will be applied to screening, triage, staging Describe how the data set will be annotated for AI training

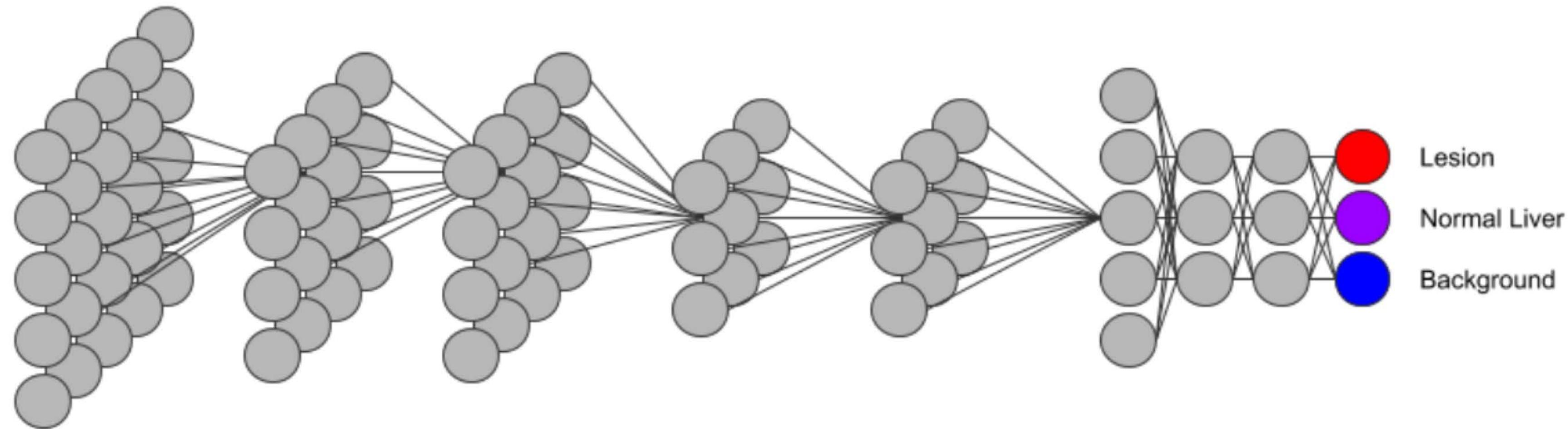
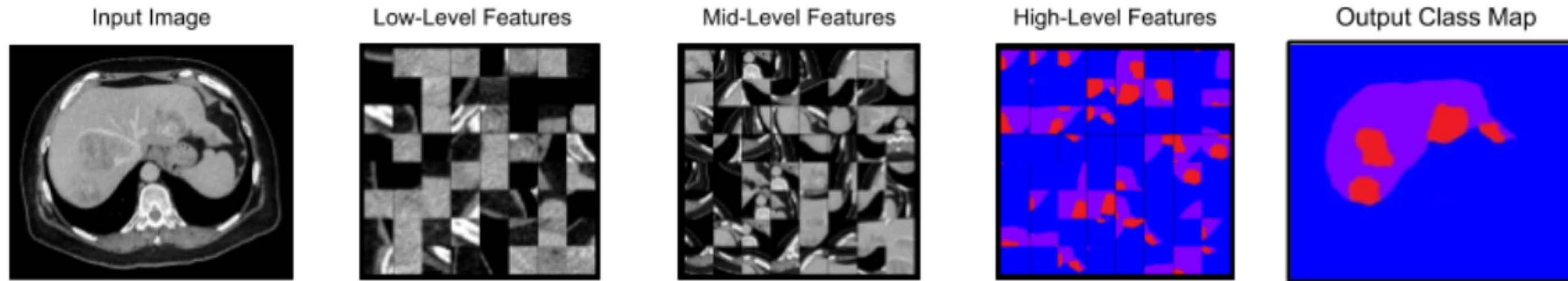
“Research hypotheses, whether AI-based or not, must be clinically relevant and answerable”

Savadjiev P, et al. European Radiology 2018

Rigorous translation pipelines is needed

1. Hypothesis generation
2. In silico replication to validate the predictive algorithm with data from other populations
3. Prototype intervention combining the predictive algorithm with information and decision support for health care teams and patients.
4. Feasibility and utility of the intervention in a pilot study in a health care setting.
5. Document efficacy under clinical trial conditions.
6. Document effectiveness when the AI application is deployed in practice.

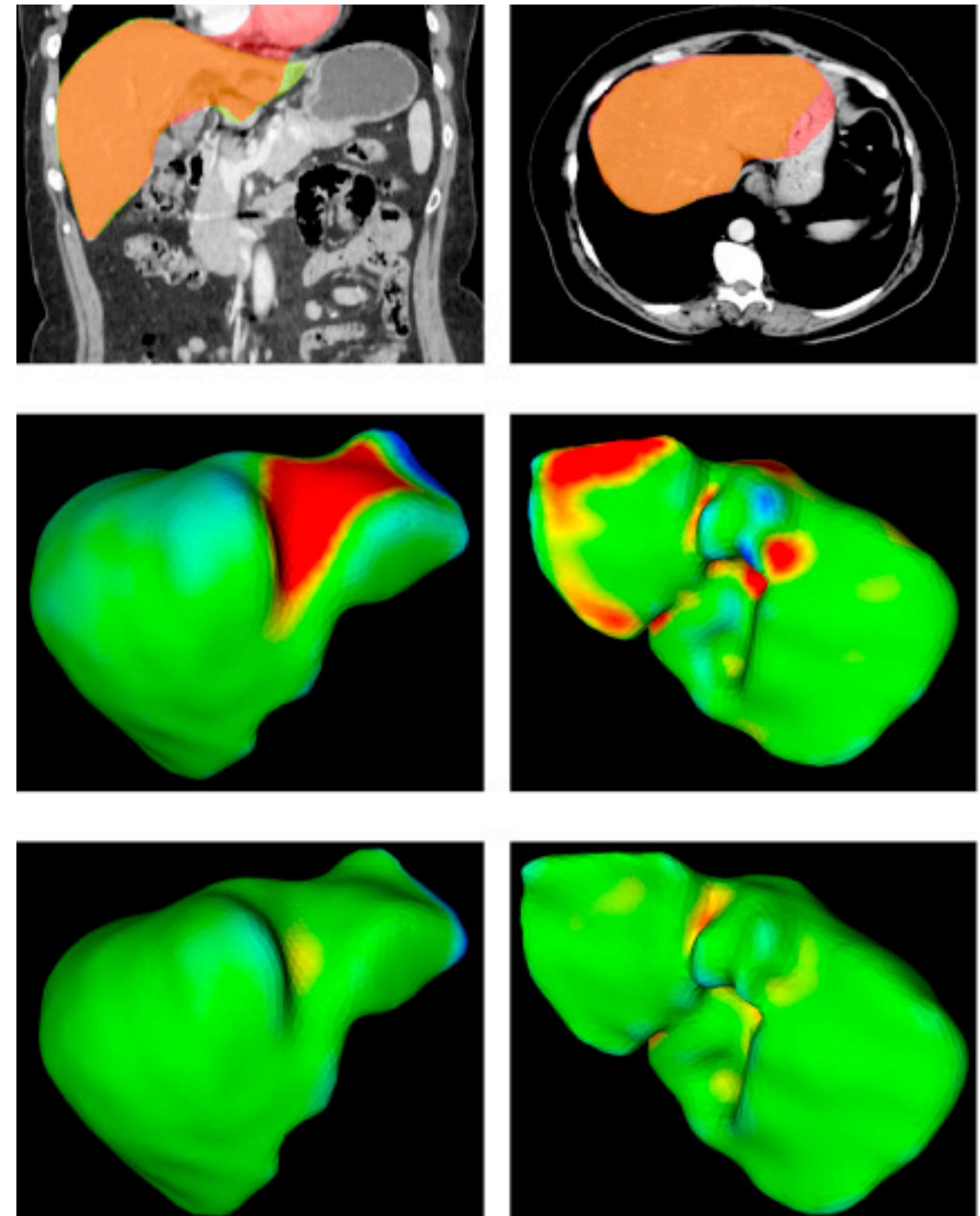
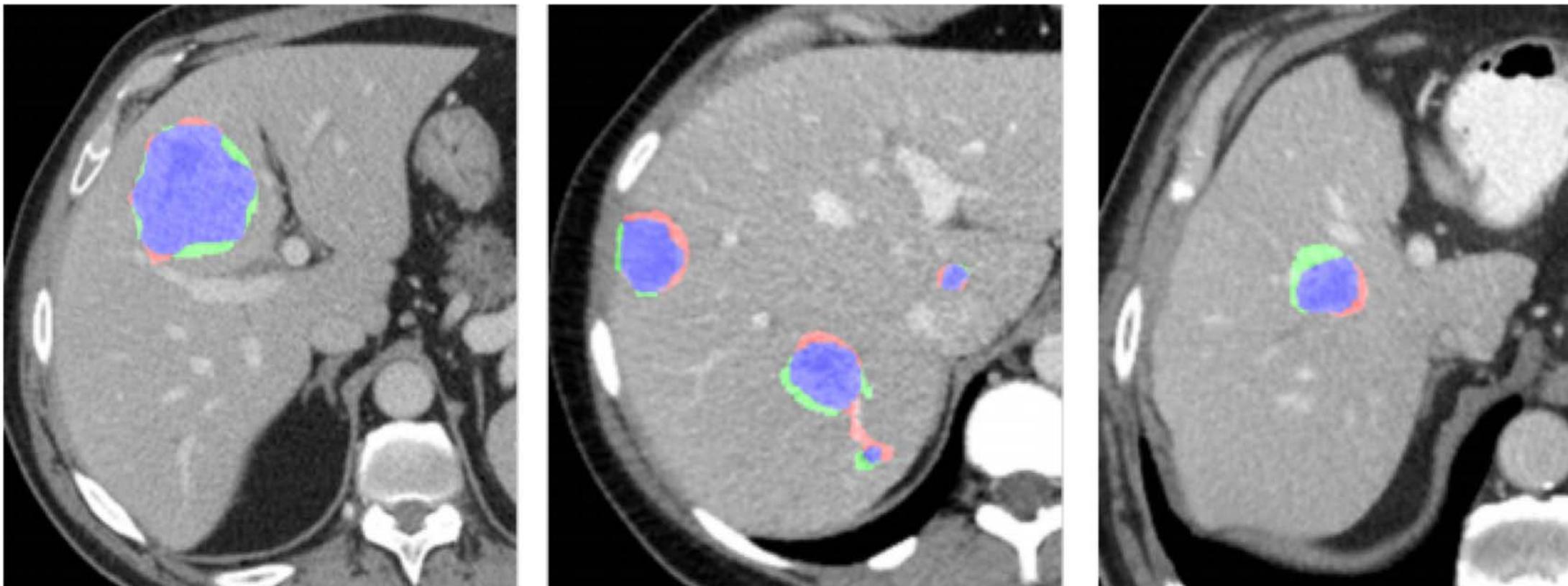
Application in Imaging



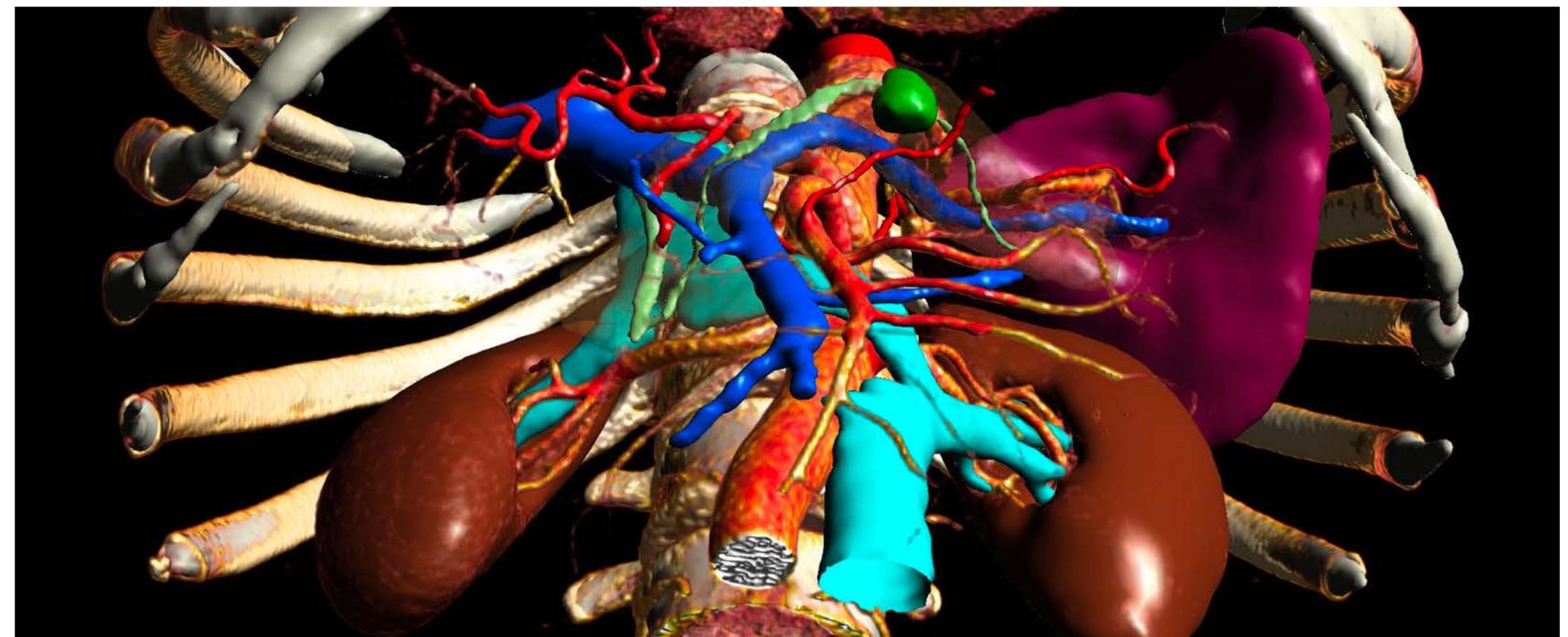
Data-driven/model-free approaches to automated knowledge discovery

Application in Imaging (narrow tasks)

- Detection
- Segmentation
- Registration



Real time movement adaptation

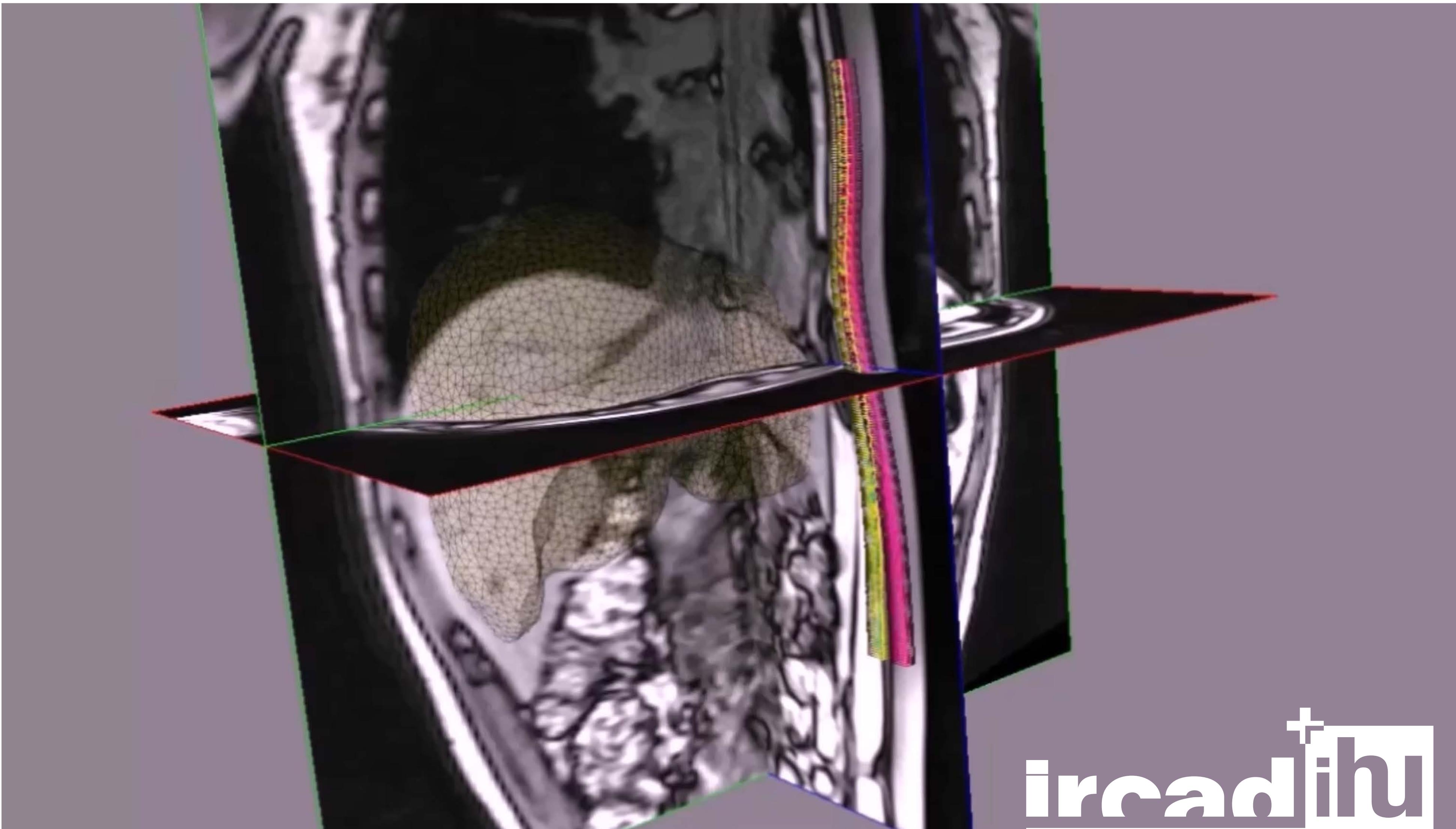


Real time movement adaptation



ircad⁺ihu

Real time movement adaptation



ircad⁺ihu

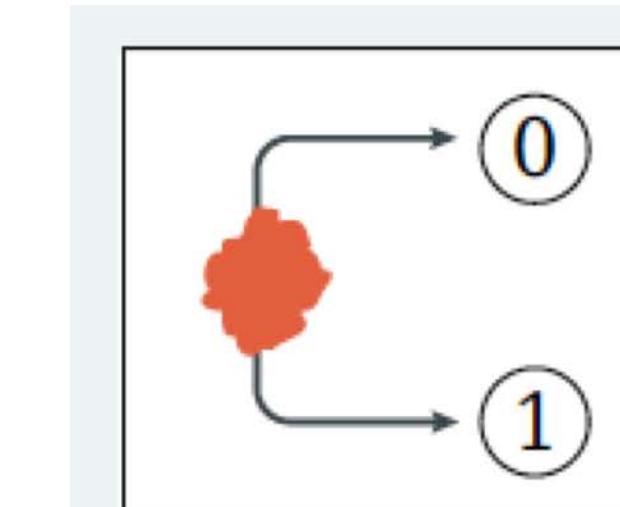
Application in Imaging (broader tasks)

Patient classification (diagnostic prediction, patient prognosis)

- **Separate Normal from not normal**
 - Definition of normal is very complex, depend of age, anatomical variant, presence of benign lesions
 - Normality should not be defined by radiologist reading but by the patient outcome for a specific disease

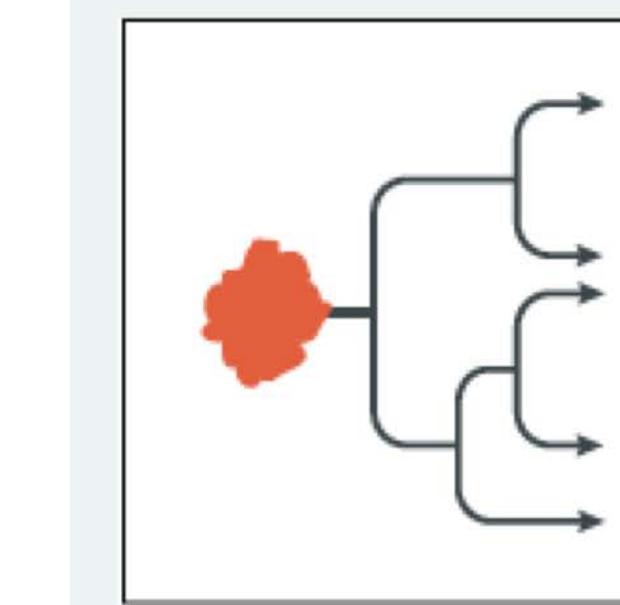
- **Classification of the disease**

- Disease phenotyping
- Patient stratification
- Prediction and prognosis (probability to respond to treatment)



Diagnosis

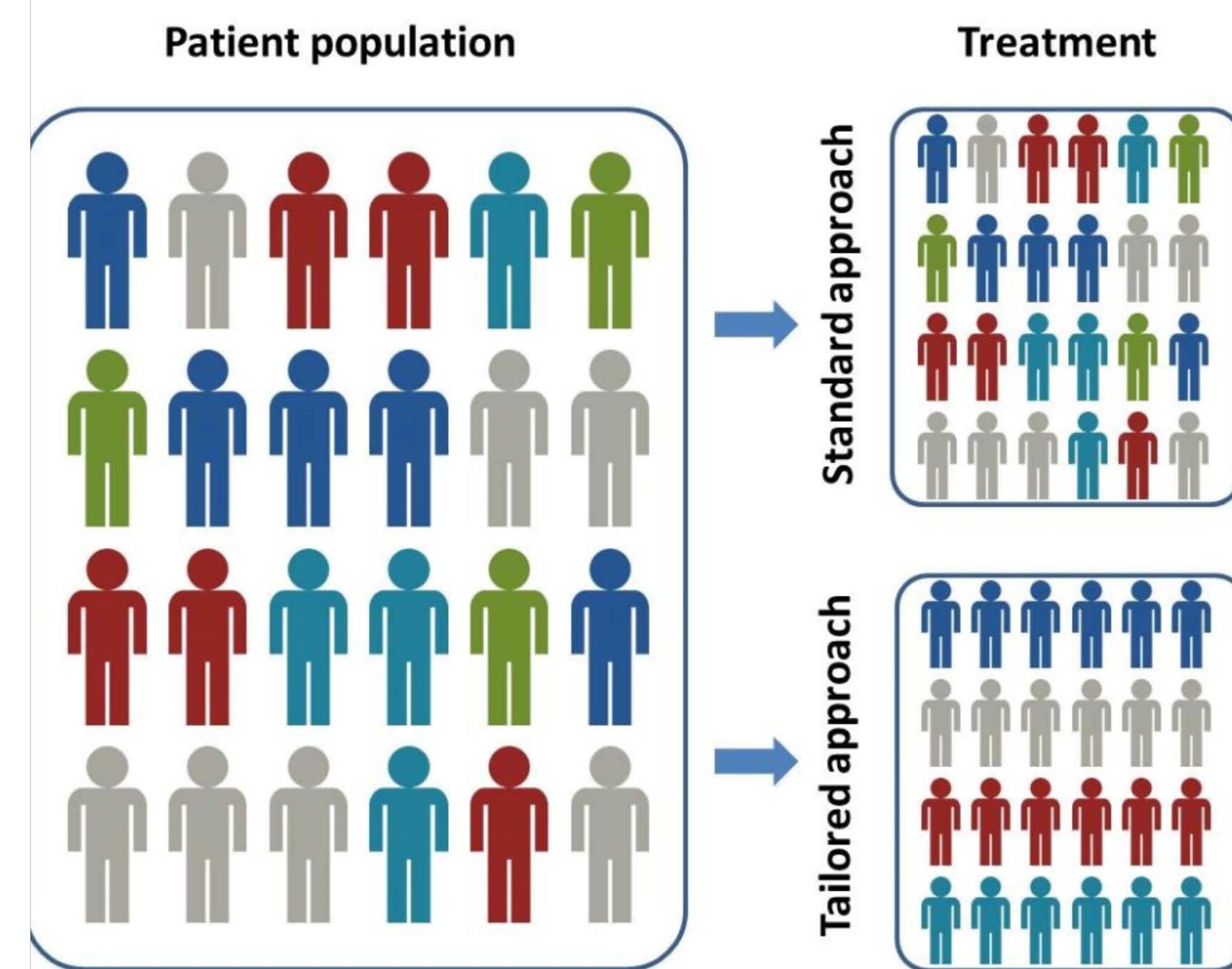
Evaluating and classifying abnormalities such as benign vs malignant



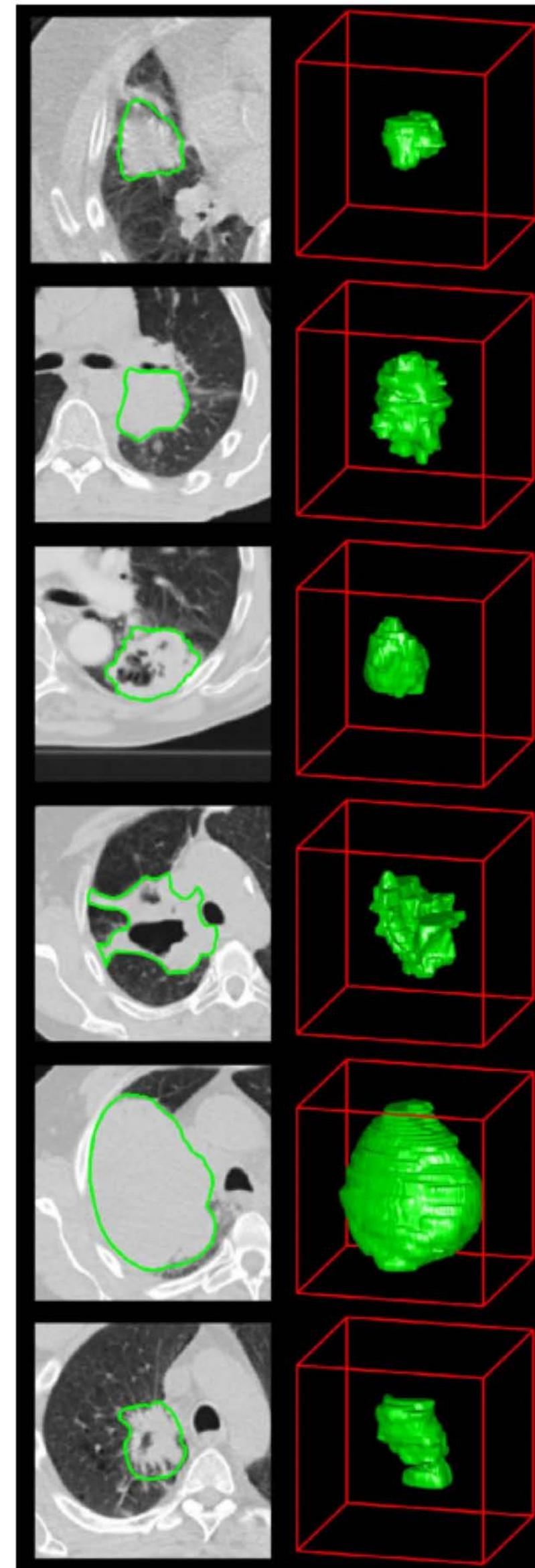
Staging

Classifying abnormalities into multiple predefined categories such as the TNM classification of malignant tumours

Prognostic & Predictive Biomarkers



Imaging Phenotype



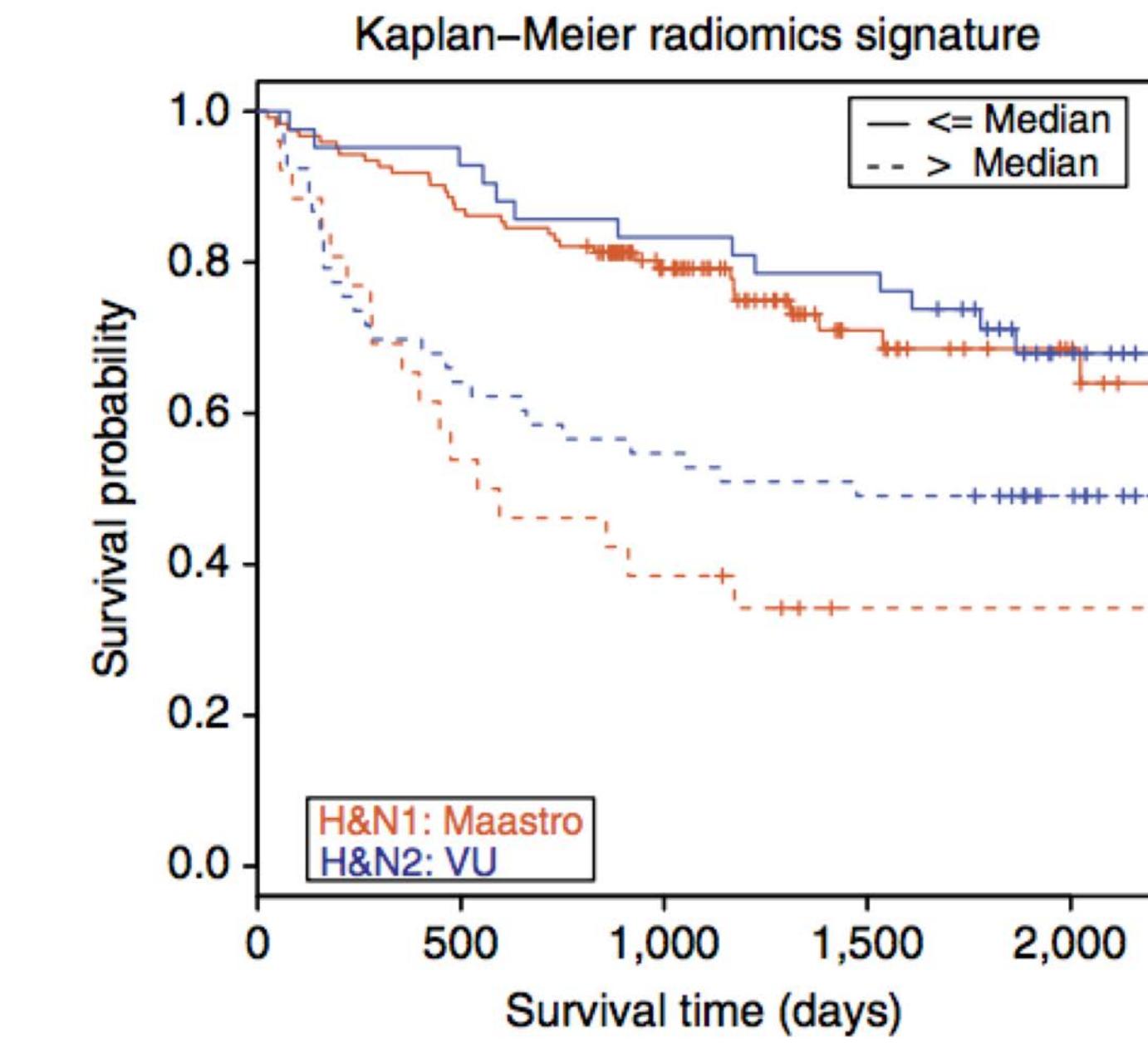
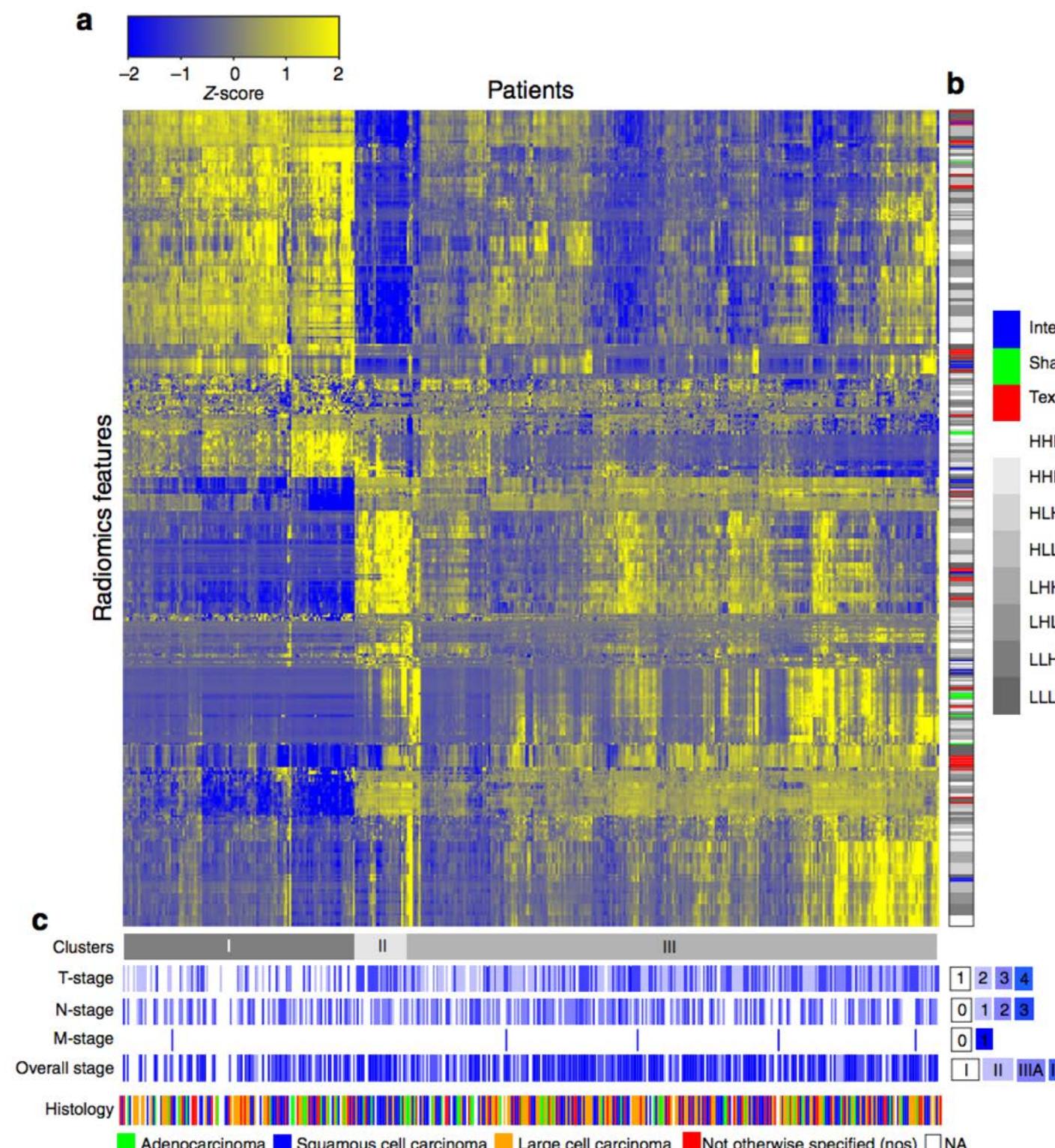
ARTICLE

Received 25 Nov 2013 | Accepted 29 Apr 2014 | Published 3 Jun 2014 | Updated 7 Aug 2014

DOI: 10.1038/ncomms5006

Decoding tumour phenotype by noninvasive imaging using a quantitative radiomics approach

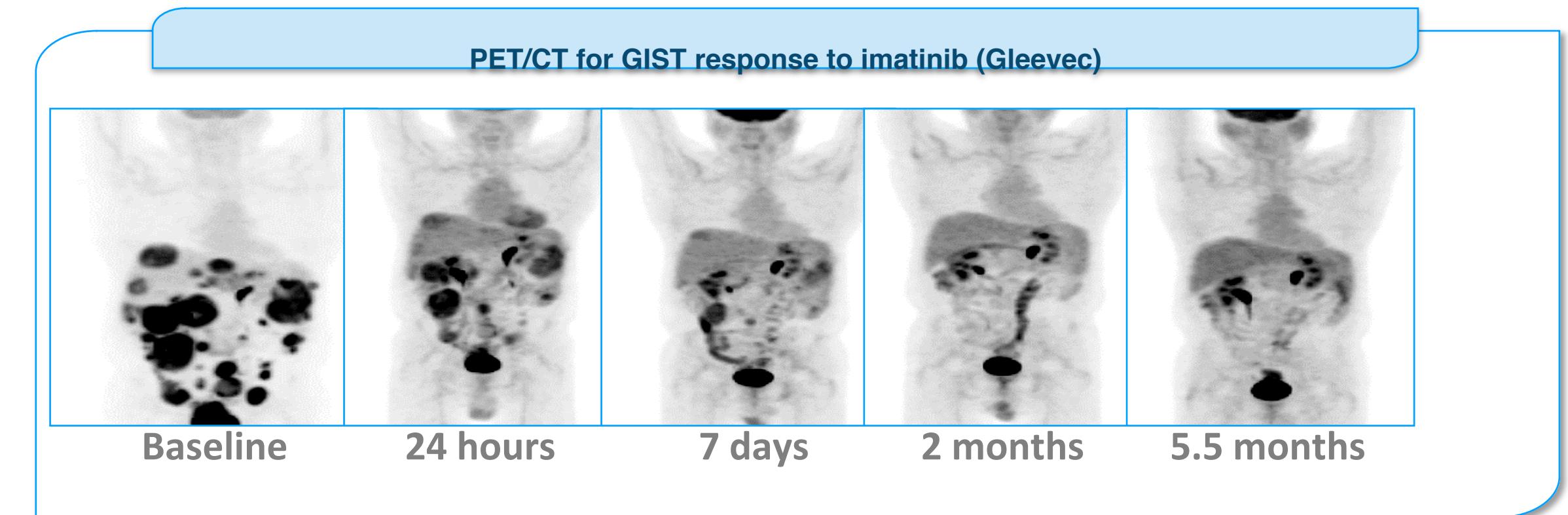
Hugo J.W.L. Aerts^{1,2,3,4,*}, Emmanuel Rios Velazquez^{1,2,*}, Ralph T.H. Leijenaar¹, Chintan Parmar^{1,2},



Two broad types of strategies to deriving an imaging biomarker

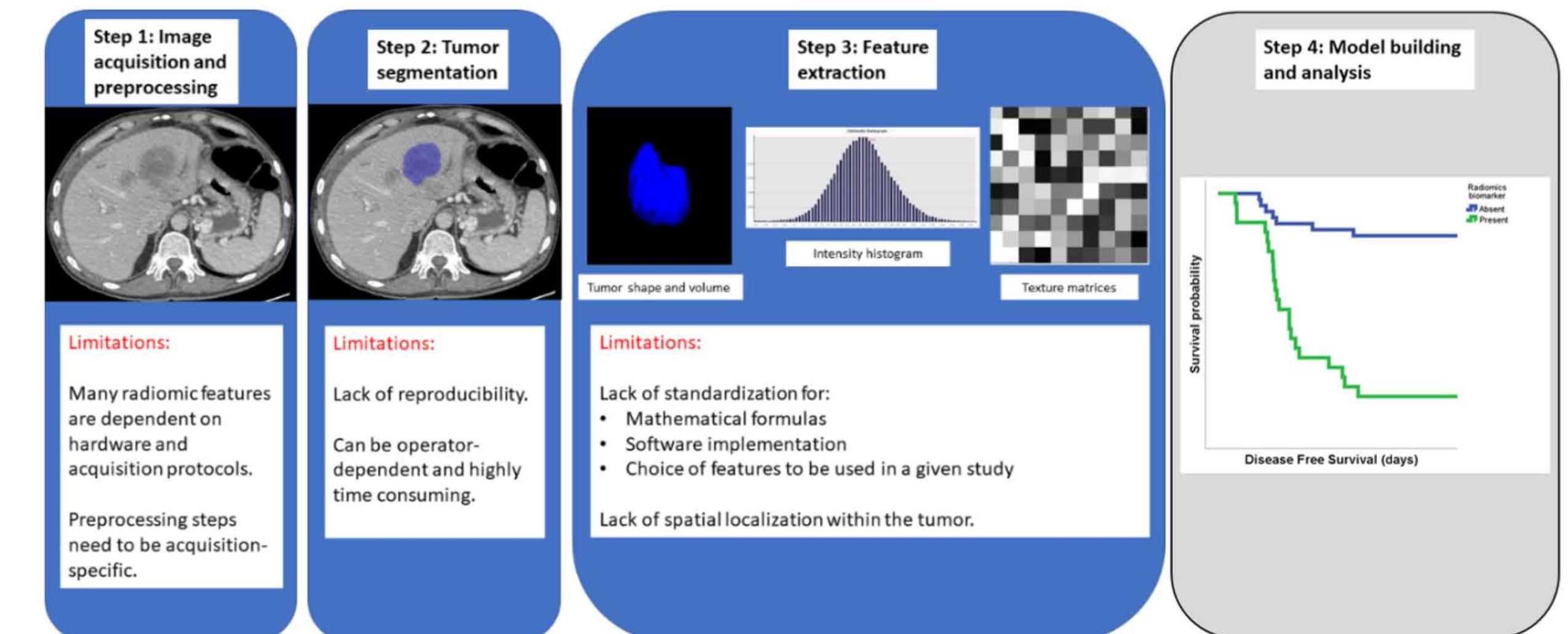
Defining the biomarker as a function of the physics of an underlying image acquisition designed to be specific to particular aspects of tumor biology

Metabolic Imaging

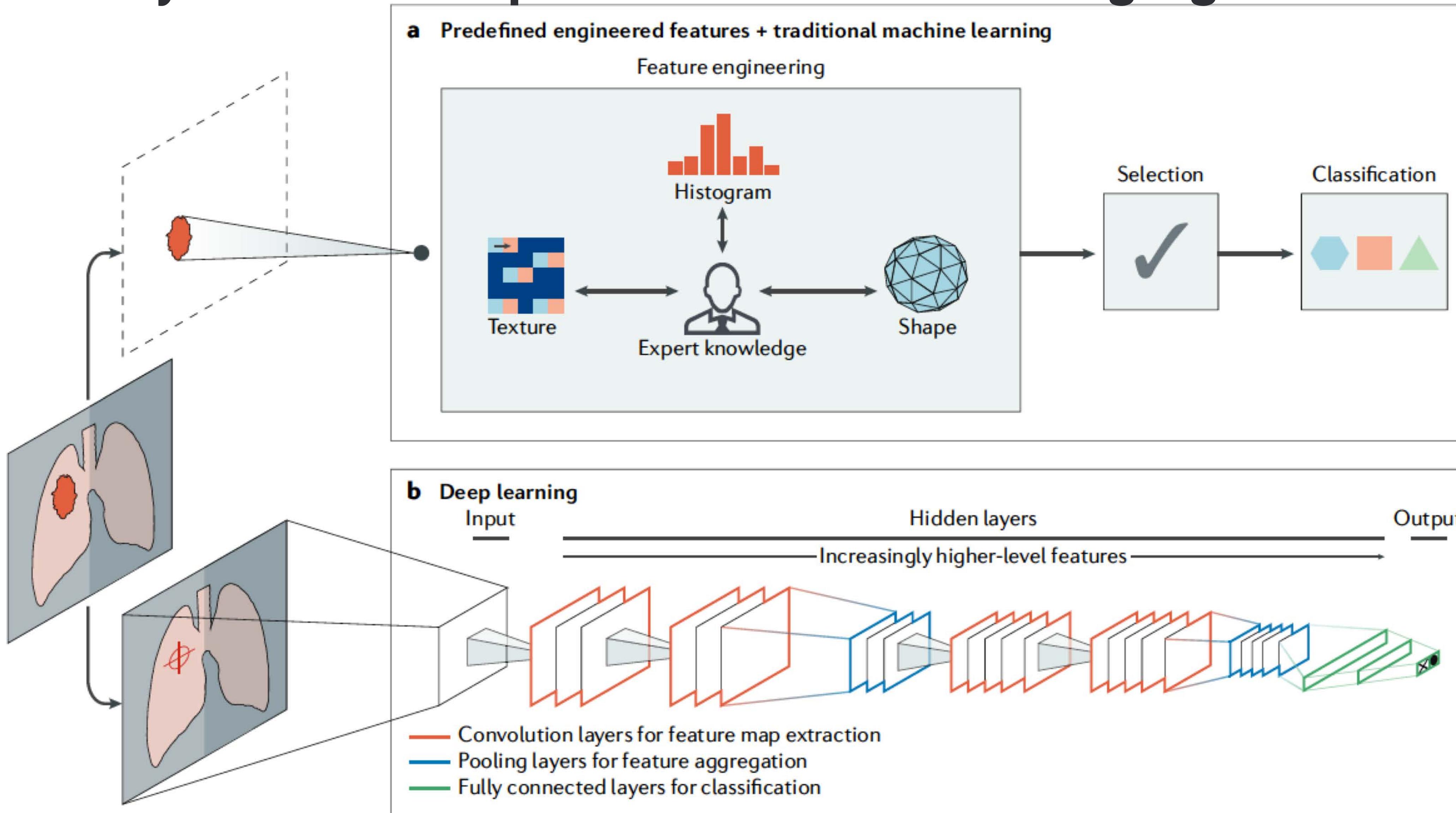


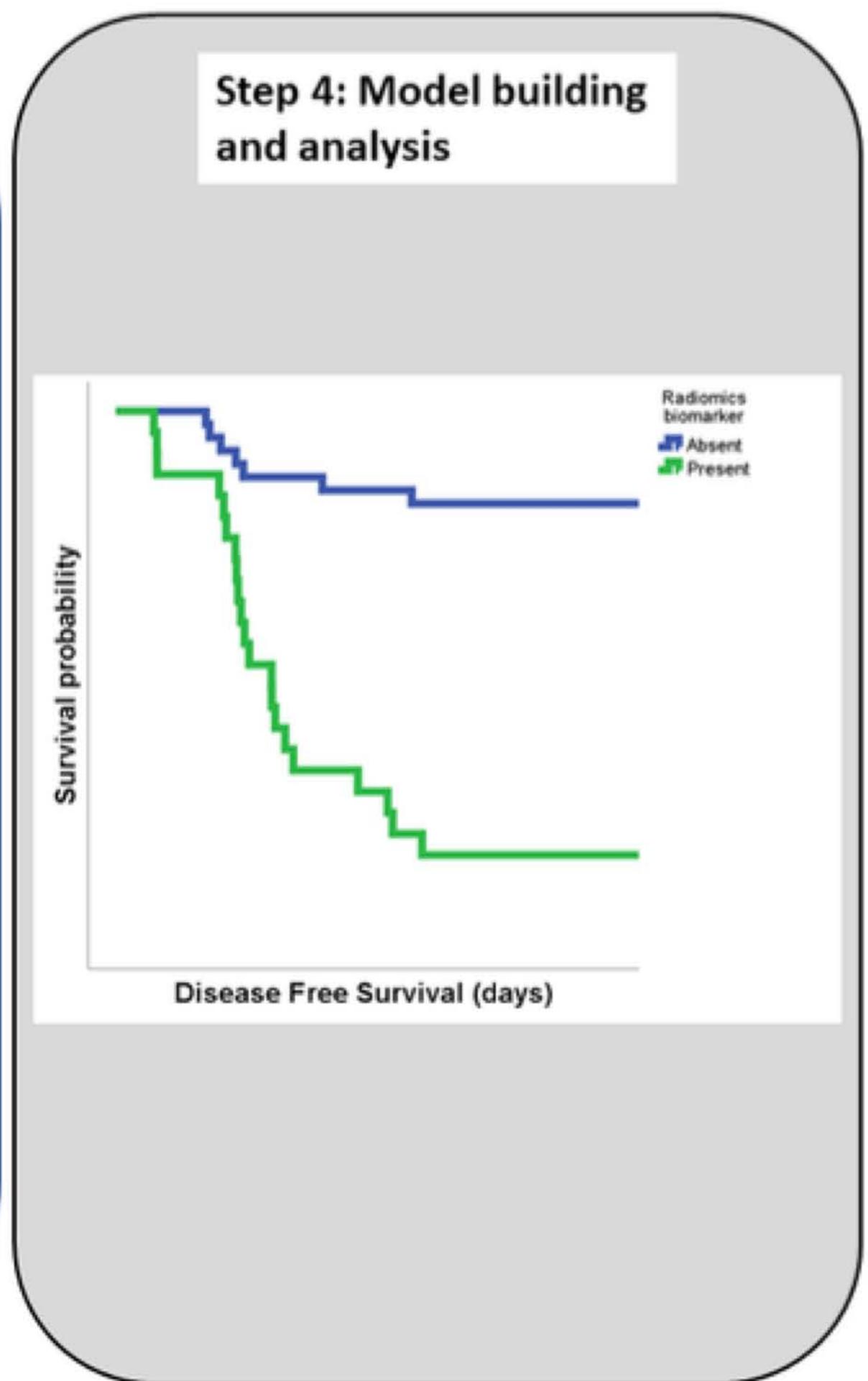
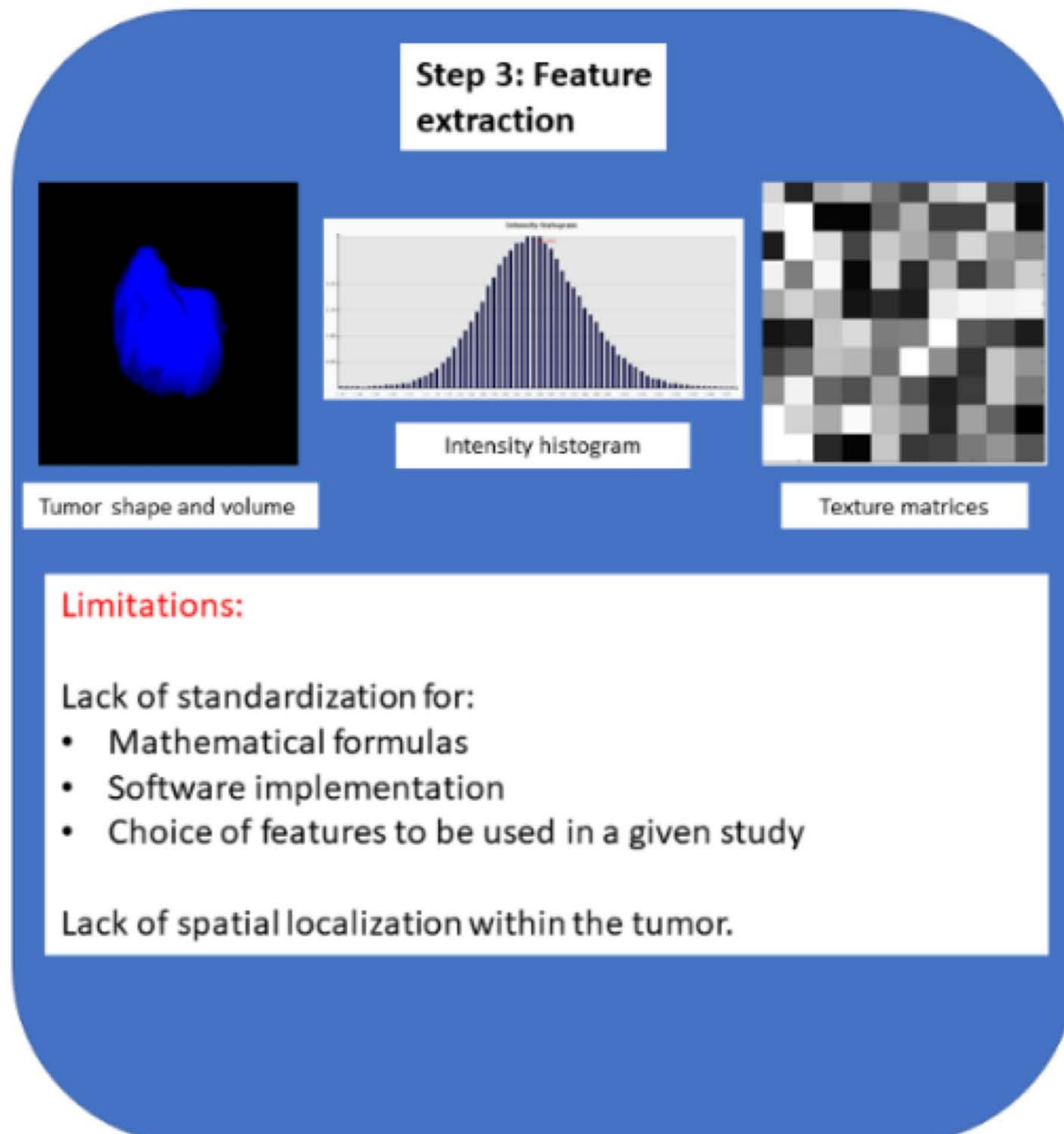
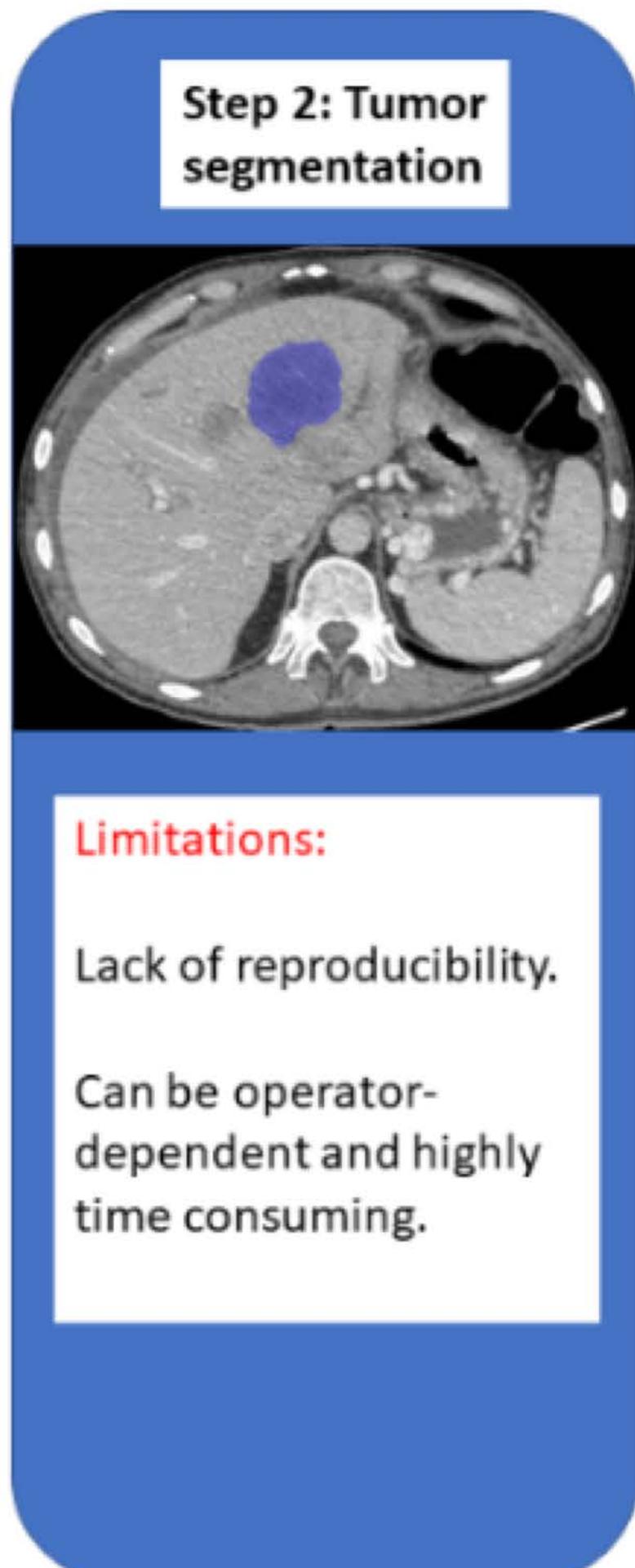
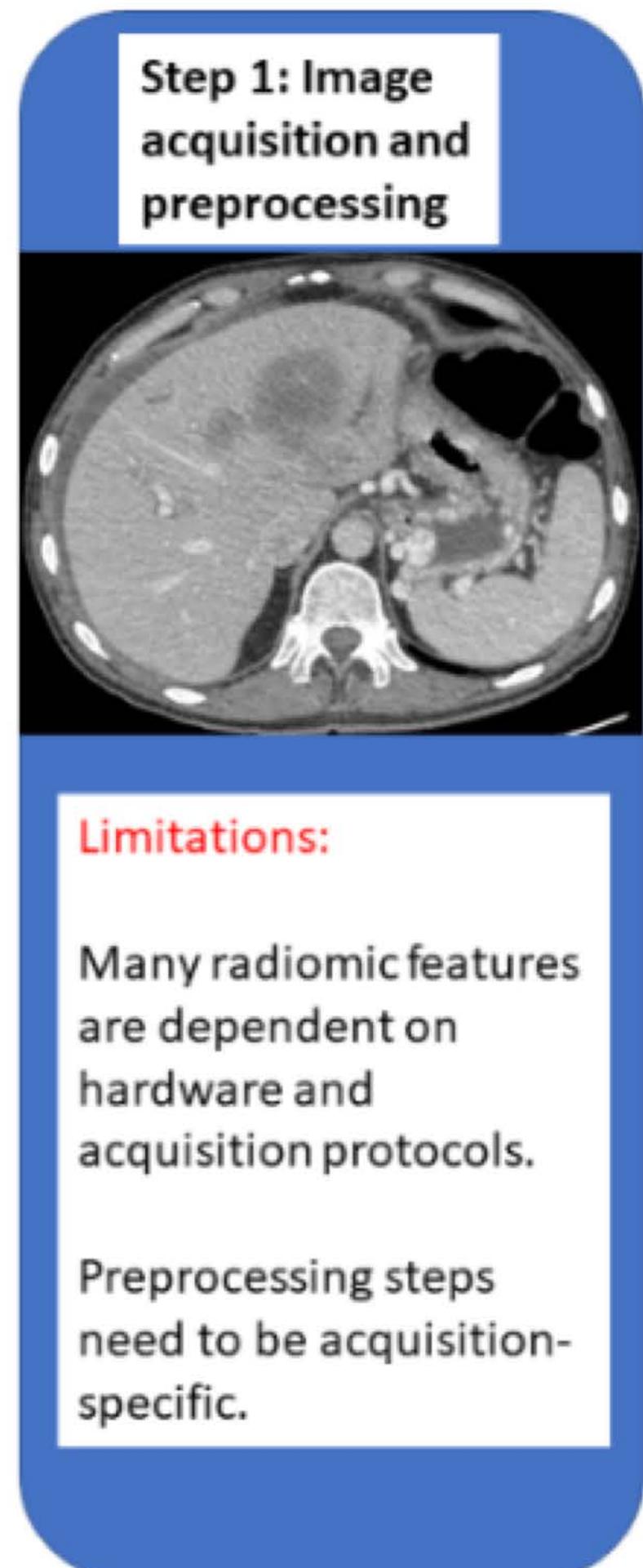
Using standard-of-care imaging techniques that are already in wide clinical use

Radiomics



2 pathways for tumor quantification with imaging

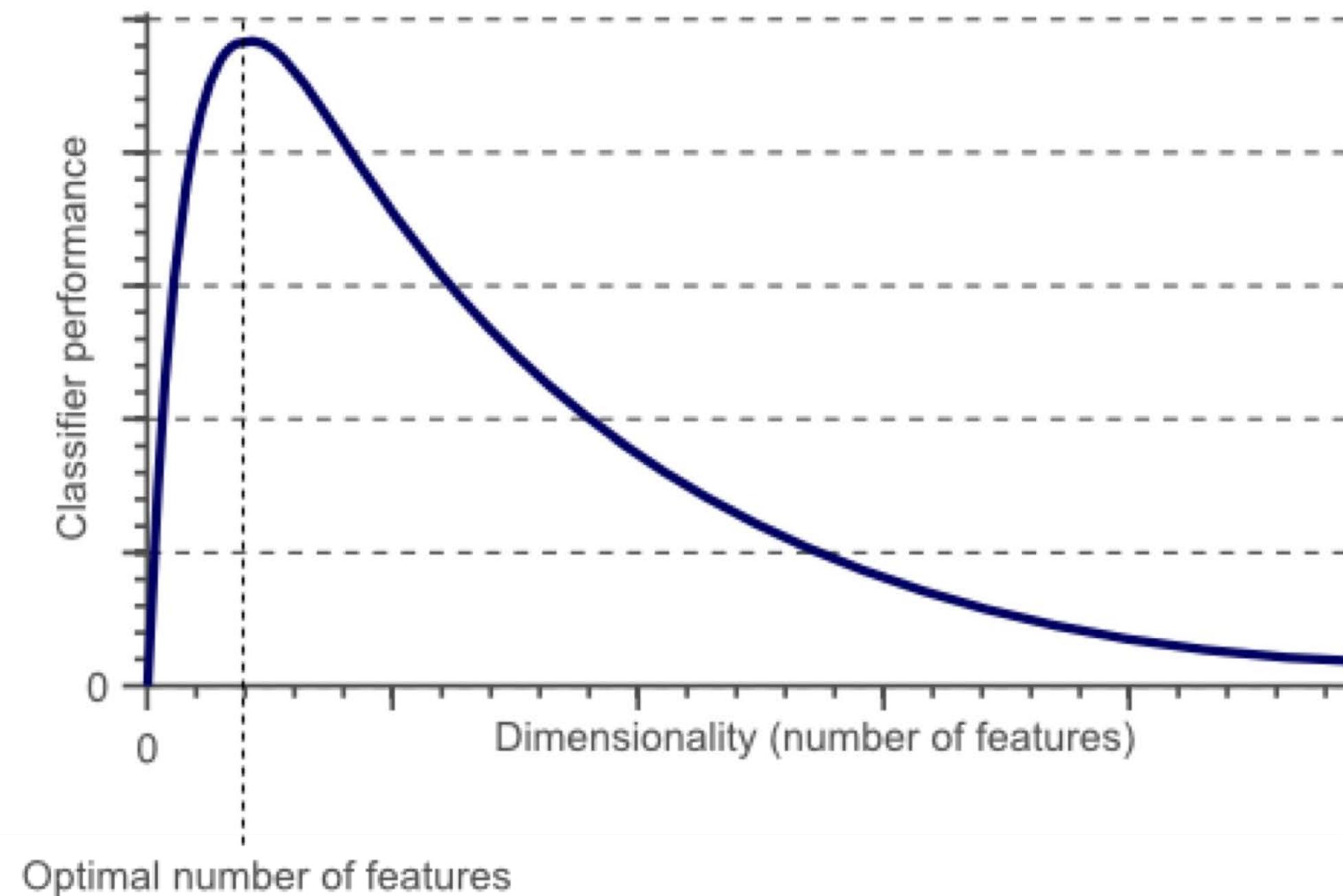




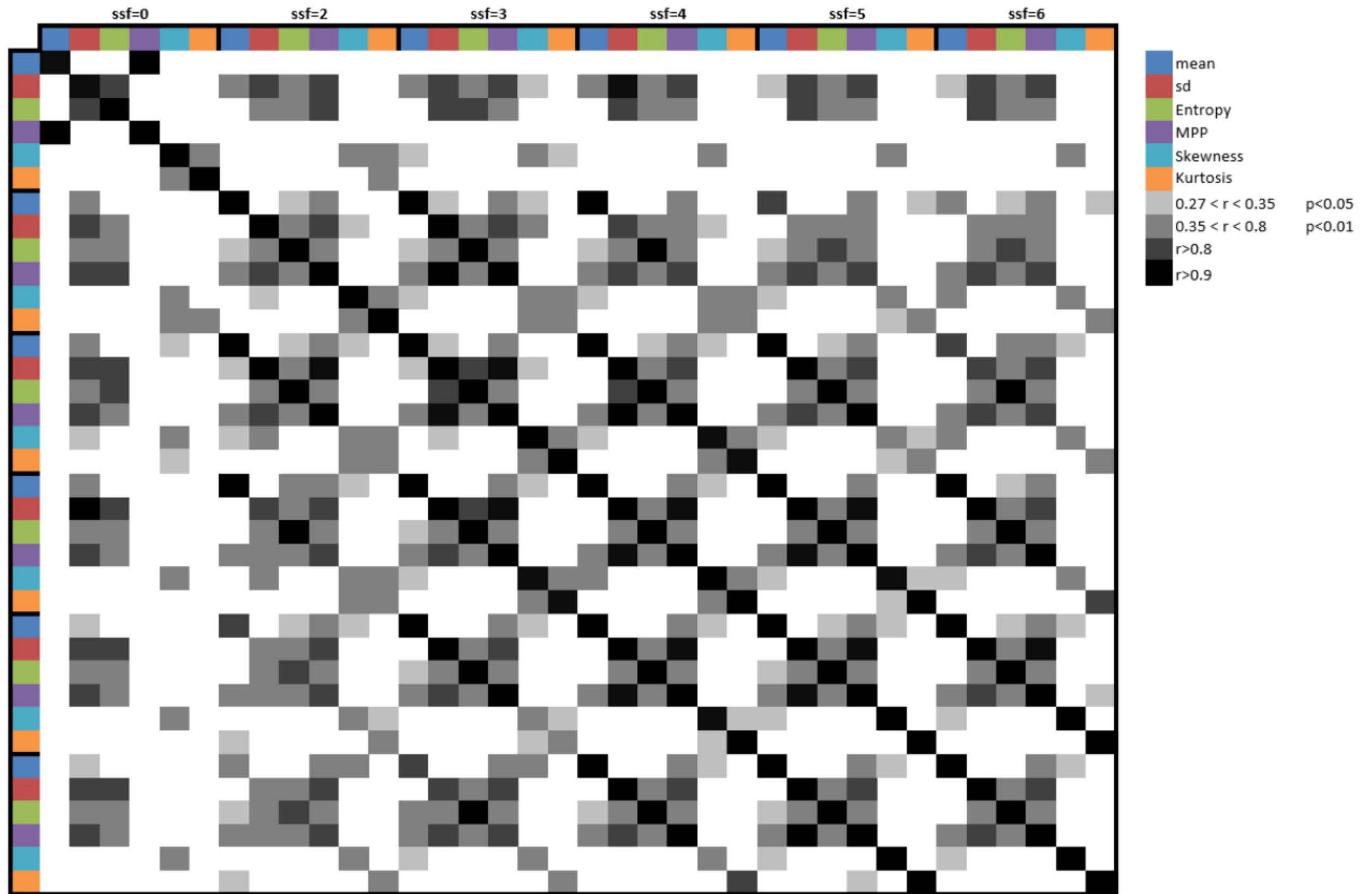
Typical features used in a radiomics workflow		Category		Examples																																		
86.4899979	25.6200008	4.55000019	86.4899979	1.13	4.8499999	-11.71	82.3700027	5.5999999	47.6199989	-0.70999998	5.23000002	-18.6599998	87.5699997	5.69000006	48	-0.79000002	3.16000009	-22.3999996	82.3399963	5.67000008	45.1699982	-0.50999999	1.90999997	-24.2700005	76.1399994	5.6500001	45.9399986	-0.09	1.5	-24.9599991	74.1800003	5.63000011	48.25	0.43000001	1.59000003	386.899994	97.4300003	5.
33.3199997	8.68000031	3.54999995	33.3199997	0.11	-0.14	3.6099999	22.1700001	4.42999983	17.8400002	-0.17	1.13999999	7.51000023	20.5599995	4.38000011	19.3199997	0.09	0.22	10.6300001	20.9500008	4.38000011	21.2700005	0.19	0.23	12.4200001	20.7299995	4.36000013	22.3700008	0.20999999	-0.01	13.0900002	20.0900002	4.34000015	22.3700008	0.16	-0.31	153.679993	56.6500015	
34.3600006	13.5799999	3.86999989	34.3600006	1.26999998	2.67000008	8.43999958	41.0200005	4.92999983	34.0600014	1.11000001	3.49000001	10.9499998	41.25	4.98999977	36.7099991	0.85000002	1.7200003	11.3299999	35.9399986	4.88000011	34.4799995	0.63999999	0.88999999	9.97999954	30.0900002	4.73999977	29.0599995	0.43000001	0.51999998	7.7899996	26.6399994	4.6500001	24.8799992	0.25	0.07	40.2400017	19.2299995	4.
113.449997	27.4899998	4.48999977	113.449997	-0.94	1.5	64.6500015	73.2399979	5.32000017	91.2699966	-0.33000001	-0.41999999	113.580002	70.5400009	5.28999996	121.580002	-0.17	-0.41	160.550003	20.2099991	5.2899996	202.050003	-0.44999999	-0.70999998	230.460007	83.6800003	5.38000011	230.460007	-0.36000001	-0.70999998	284.82999	73.82	5.						
28.5100002	9.60000038	3.55999994	28.510002	0.72	0.003	3.38000011	13.029997	27.3099995	4.53999996	26.2700005	1.08000004	3.0999999	17.590002	26.1200008	4.46999979	26.8500004	1.73000002	7.7899996	25.7099991	4.42000008	28.2199993	1.51999998	6.67000008	25.2399998	25.0099992	30.2999992	1.08000004	3.49000001	29.1599998	24.1599998	4.46000004	33.7099991	0.64999998	1.02999997	130.949997	38.75	4.	
56.0100001	6.602000000	6.602000000	6.602000000	0.001	1.07	-0.005	2.19998	8.91.2399979	4.1239	6.90004	14.70013	1.100004	6.000000000	7.123.00002	455.33.96	9.000002	42.60015	1.08.0004	3.3999999	45.7.996	45.119.000000	44.5.989	0.000003	7.00001	6.000000	453.7.13	2.000000	50.000000000	-0.43000001	194	447.25	7	492.130005	0.41999999	-0.83999997	2079.17993	596.409973	7.
35.2000001	1.3000002	1.600000000	1.600000000	0.000000000	1.34999997	-0.28.99999	0.000000000	3.565.9993	0.029999	4.4.0001	2.3700008	-0.30.0001	-0.000000000	6.28.996	31.659.98	6.1.00013	28.4.998	-0.38.99999	-0.000000000	7.15.001	30.600.6	5.5.00000	29.0000004	38999999	-9.0.0001	1.4.999	1.4.000000000	-0.97000003	12.1999998	22.7399998	4.30999994	24.2800007	-0.38	-0.89999998	119.400002	49.4399986	4.	
35.2000001	1.3000002	1.600000000	1.600000000	0.000000000	1.34999997	-0.28.99999	0.000000000	3.565.9993	0.029999	4.4.0001	2.3700008	-0.30.0001	-0.000000000	6.28.996	31.659.98	6.1.00013	28.4.998	-0.38.99999	-0.000000000	7.15.001	30.600.6	5.5.00000	29.0000004	38999999	-9.0.0001	1.4.999	1.4.000000000	-0.97000003	12.1999998	22.7399998	4.30999994	24.2800007	-0.38	-0.89999998	119.400002	49.4399986	4.	
1.670000000	6.670000008	3.18000007	18.3700008	1.63999999	7.36000013	-1.0299997	21.0599995	4.30999994	15.21	1.08000004	5.55999994	-1.72000003	20.0400009	4.34000015	15.0699997	0.36000001	1.41999996	-2.49000001	18.4899998	4.2699998	14.5600004	0.19	0.52999997	-3.19000006	16.6100006	4.17000008	13.5600004	0.23	-0.07	-3.52999997	14.6599998	4.05000019	40.25	0.47	-0.5	118.18	36.9799995	4.
37.19	8.47000027	3.51999998	37.75	0	1.02999997	3.03999996	24.7000008	4.57000017	21.7800007	0.23	0.41999999	4.13000011	24.6100006	4.57000017	22.6000004	0.31	-0.05	4.53999996	23.9200001	4.5	22.2199993	0.60000002	0.28999999	4.86999989	22.9899998	4.46000004	20.7099991	0.76999998	0.92000002	5.46999979	22.75	4.40999985	19.4099998	0.69999999	1.20000005	79.7200012	19.7399998	4.
27.5300007	15.1999998	4.01999998	27.5300007	0.56999999	-0.11	5.05000019	29.1399994	4.7100004	25.4799995	0.62	0.88999999	5.78000021	30.1800003	4.73000002	27.7299995	0.67000002	0.66000003	6.01999998	30.5200005	4.76000023	29.1800003	0.58999997	0.18000001	6.32999992	30.7000008	4.75	30.4799995	0.60000002	-0.15000001	7.05000019	30.6599998	4.73999977	31.1399994	0.61000001	-0.18000001	124.599998	39.5200005	5.
51.3300018	20.0599995	4.30999994	51.3300018	1.01999998	4	17.1000004	50.1199989	5.17000008	46.5499992	0.66000003	1.34000003	26.9200001	40.5900002	4.98999977	42.7999992	0.36000001	0.25	36.8199997	35.6800003	4.8499999	45.1100006	0.49000001	0.28999999	46.5200005	35.66999982	4.86000013	50.52999988	0.56999999	0.12	55.4599991	38.18999986	4.92000008	59.2900009	0.44999999	-0.23999999	285.769989	105.029999	5.
78.5899963	21.1900005	4.30000019	78.5899963	0.20999999	1.58000004	24.9300003	70.3199997	5.32999992	70.8300018	0.81	0.63999999	38.6800003	67.0299988	5.32000017	74.4400024	0.63	-0.02	52.5999985	57.9399986	5.23999977	73.9499969	0.28	-0.47999999	67.0299988	45.6300011	5.07999992	75.9199982	-0.01	-0.50999999	82.5199966	32.9900017	4.76999998	82.5199966	0.02	-0.16	291.869995	76.5	5.
51.6100006	12.7399998	3.8900001	51.6100006	-0.5	-0.04	8.56999969	36.75	4.82999992	31.3400002	-0.72000003	0.75999999	13.75	34.4000015	4.84000015	32.6800003	-0.52999997	-0.03	18.7600002	29.8799992	4.73000002	32.7700005	-0.20999999	-0.38	23.7000008	24.3899994	4.51999998	31.7299995	0.03	-0.81	28.6900005	21.0900002	4.36000013	32.0299988	-0.07	-0.88	214.759995	61.7799988	5.
22.2399998	8.88000011	3.51999998	22.2399998	0.75999999	0.73000002	10.6499996	21.9699993	4.4000001	21.4400005	0.73000002	1.32000005	13.079999	22.079999	4.38000011	22.9400005	0.83999997	1.05999994	14.5799999	21.8099995	4.34000015	23.4899998	0.79000002	0.56	15.3599997	20.2199993	4.30000019	22.2399998	0.68000001	0.08	15.5600004	17.7600002	4.19999981	21.0100002	0.46000001	-0.37	100.43	47.7900009	5.
101.510002	29.2999992	4.73000002	101.510002	0.18000001	0.68000001	30.8199997	93.3300018	5.71000004	87.0999985	0.81	0.5	44.0400009	83.3799973	5.65999985	87.9400024	0.64999998	0.23	55.5600014	77.5299988	5.61999989	89.0699997	0.25	-0.31999999	67.3099976	73.6999969	5.5999999	92.5800018	0.05	-0.36000001	79.6500015	67.4300003	5.5	93.6299973	0.19	-0.16	361.51001	102.980003	5.
67.099985	16.6000004	4.17000008	67.099985	-0.25	-0.62	10.3400002	37.5699997	4.96999979	33.8600006	0							2	-0.13	-0.34	21.8400002	47.1899986	5.15999985	46.1399994	-0.01	-0.28999999	262.529999	58.0499992	5.										
528.02002	176.309998	6.30999994	528.02002	0.56	0.5	196.100006	477.440002	6.96000004	461.399994	0.550000							3	-0.52999997	0.28999999	391.540009	429.220001	6.90999985	544.26001	-0.5	0	1367.48999	494.540009	6.										
50.069997	10.96	3.75999999	50.069997	0.28999999	0.63	2.53999996	32.4399986	4.7899996	25.2900009	-0							4	0.34999999	0	18.6900005	40.5299998	4.98000002	44.0099983	0.23999999	-0.51999998	230.770004	54.0200005	5.										

Curse of dimensionality

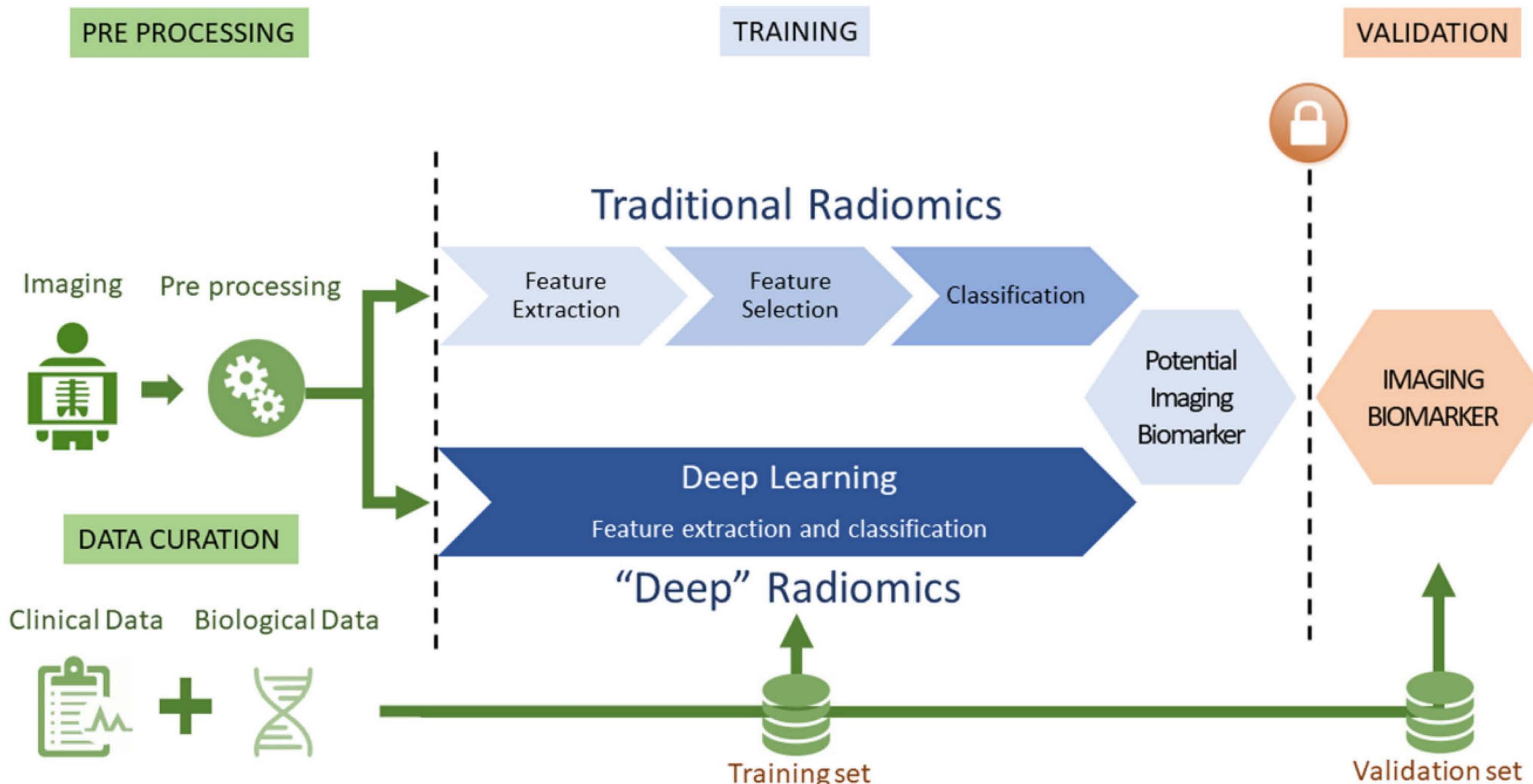
- The number of features generate is high
- As the numbers of features grows, the amount of data we need to generalize grows exponentially



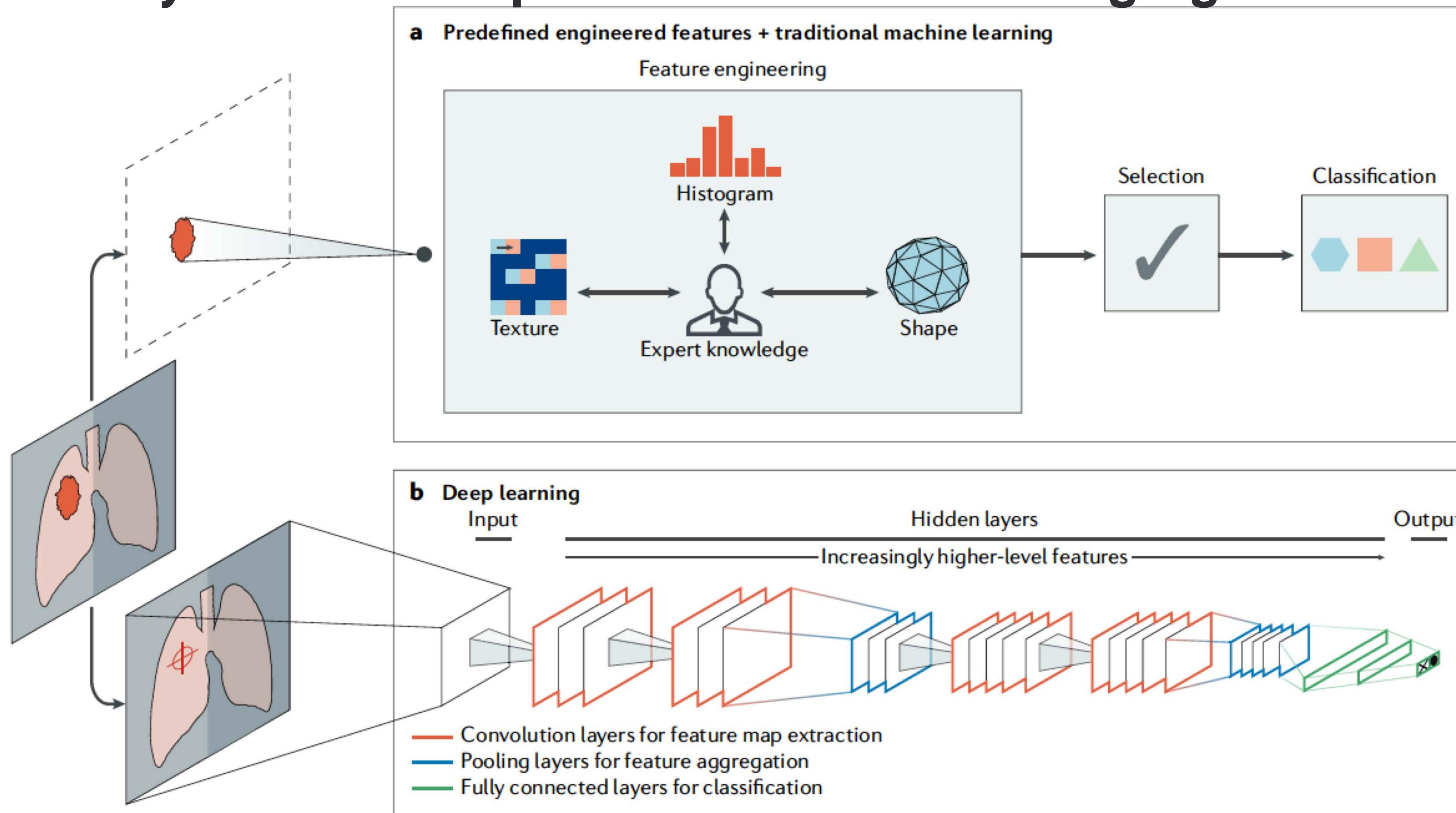
High level of correlation between features



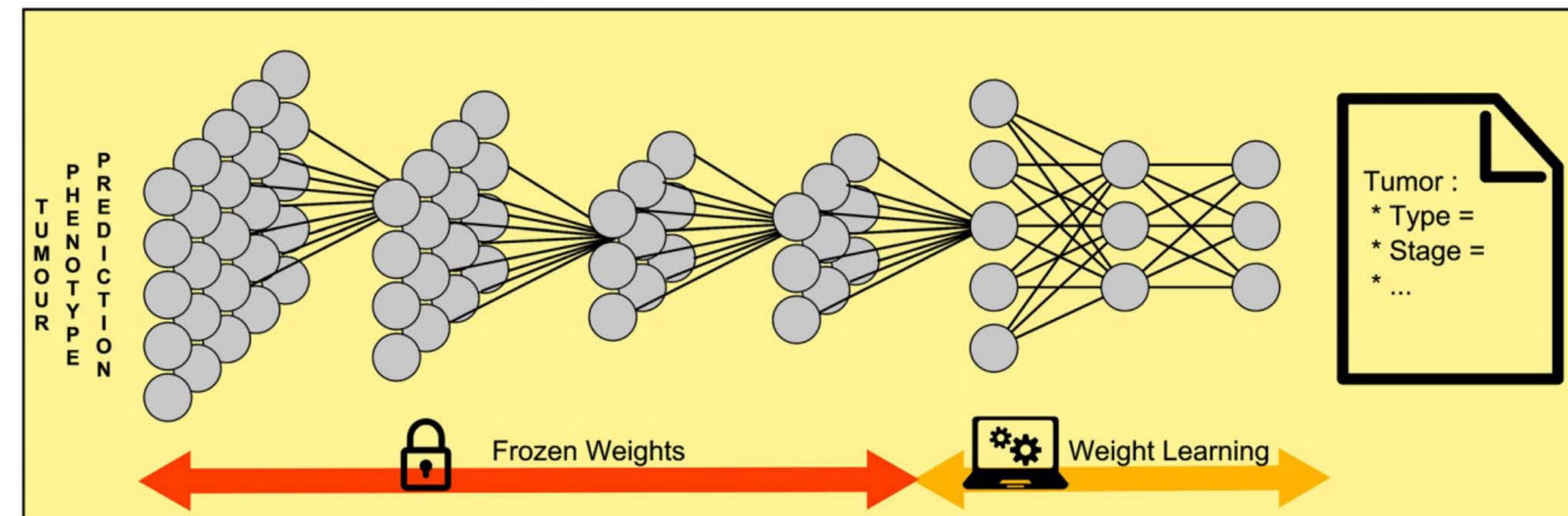
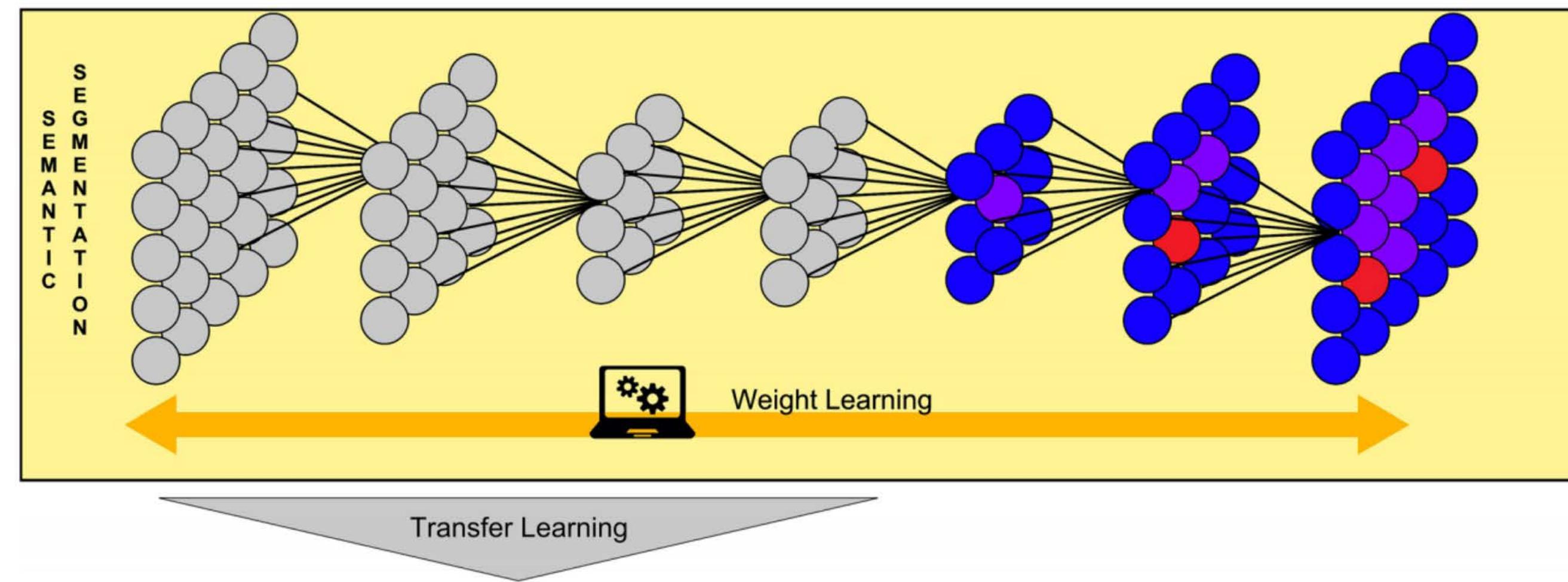
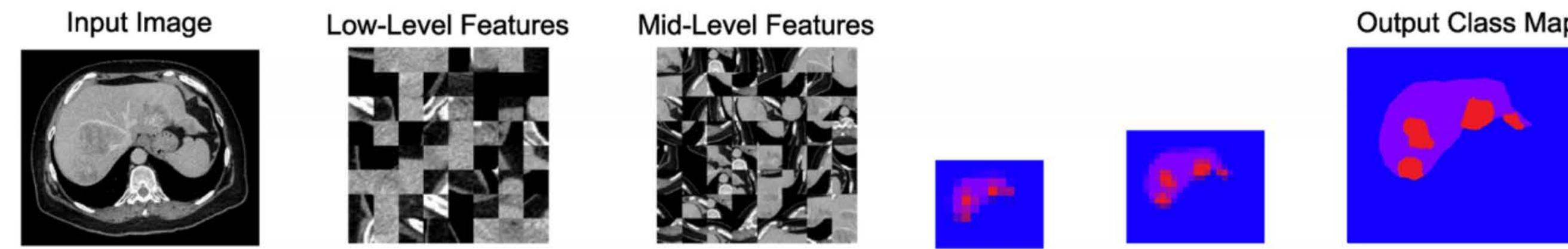
2 pathways for tumor quantification with imaging



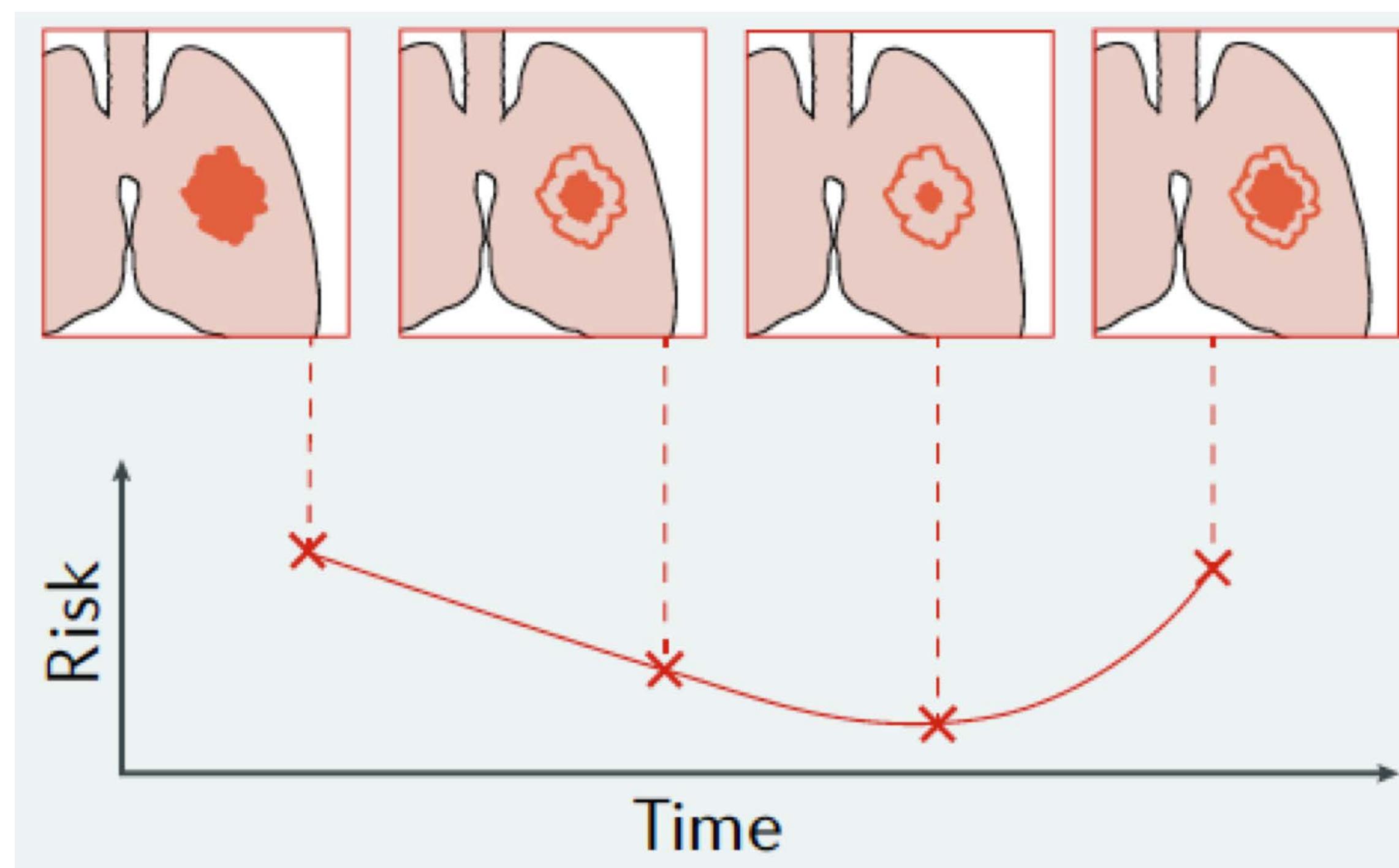
2 pathways for tumor quantification with imaging



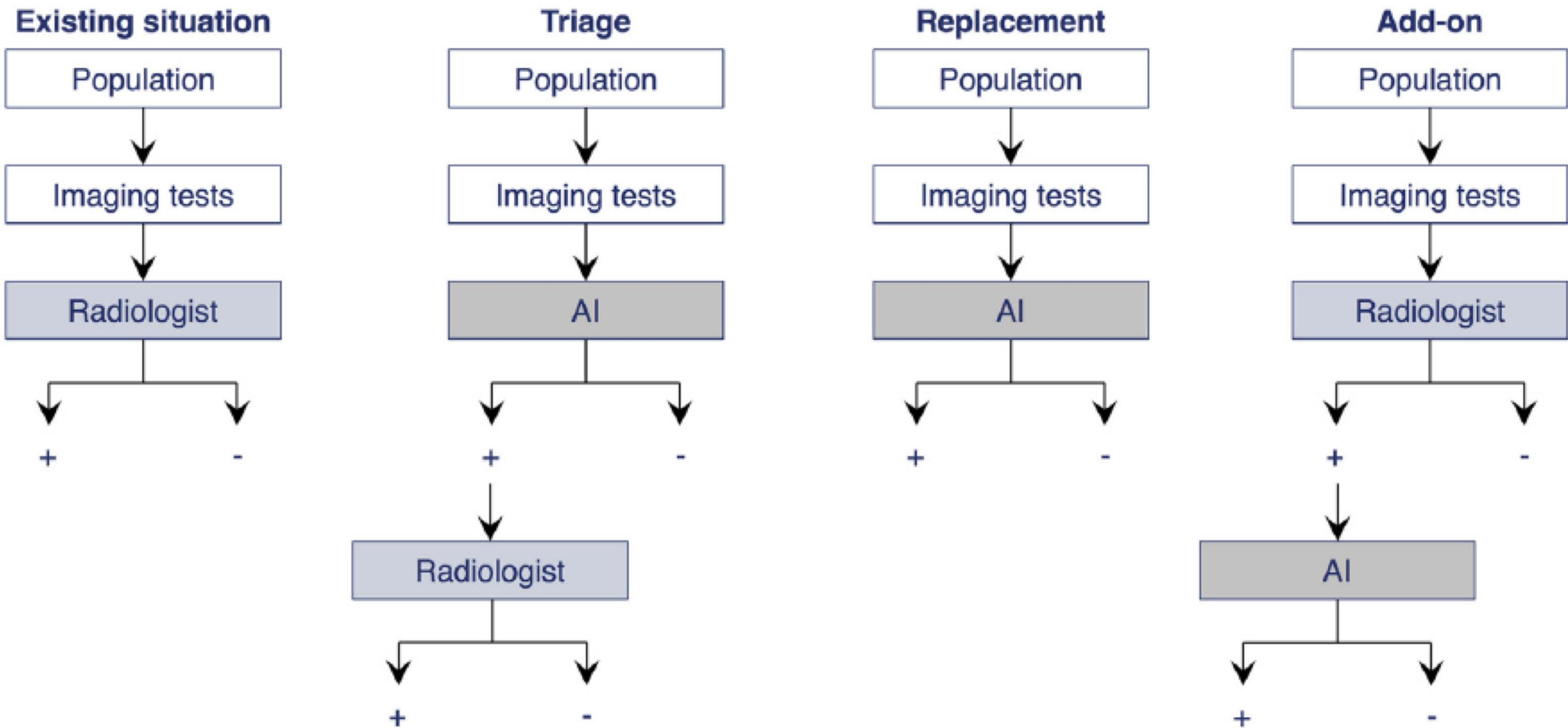
Tumor characterization using a two-step deep neural network analysis



Monitoring the disease



Canadian Association of Radiologists White Paper on Artificial Intelligence in Radiology



Factors that will drive the adoption of AI in Healthcare

the strengths of digital imaging over human interpretation

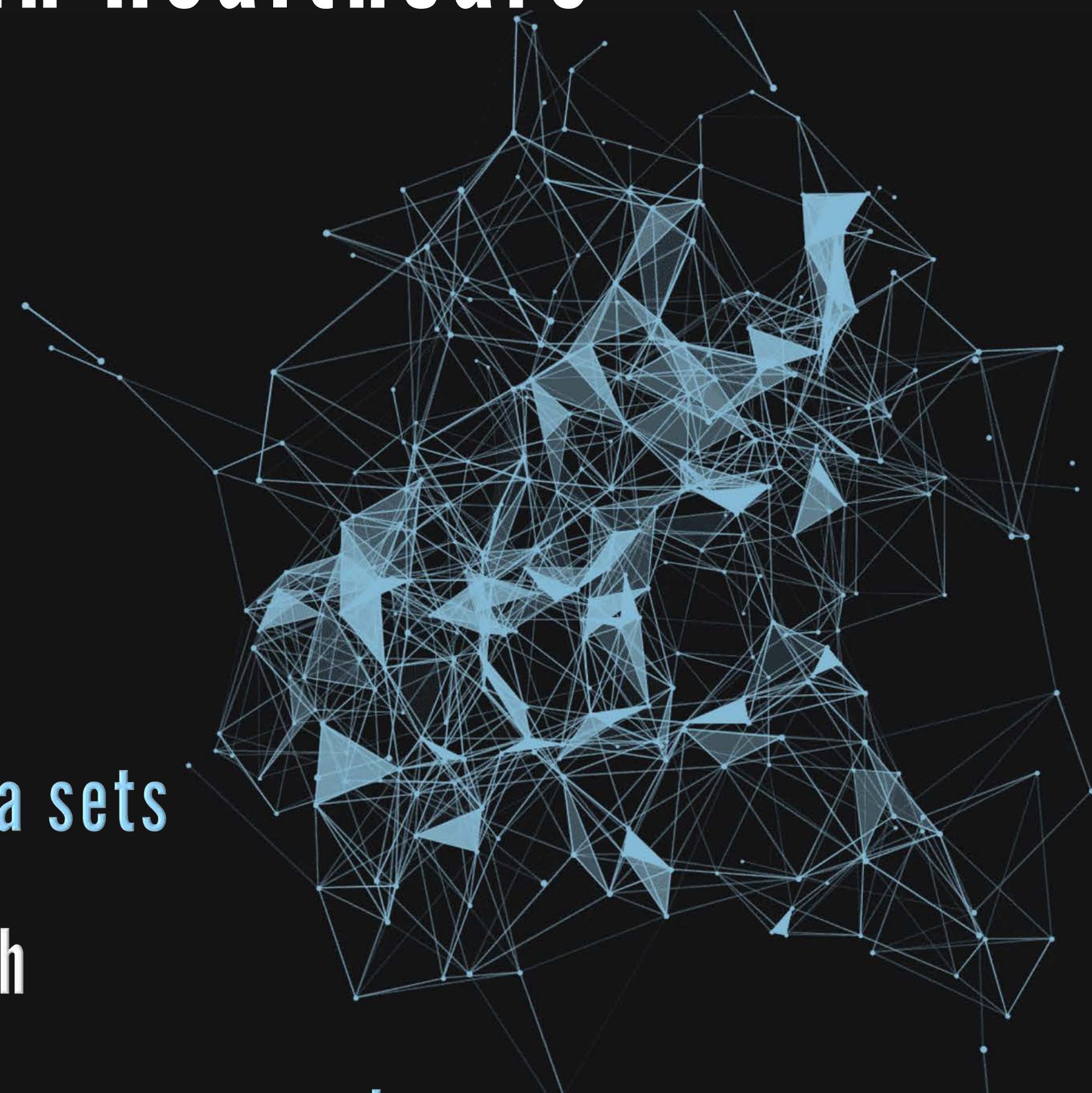
the digitization of health-related records and data sharing

the adaptability of deep learning to analysis of heterogeneous data sets

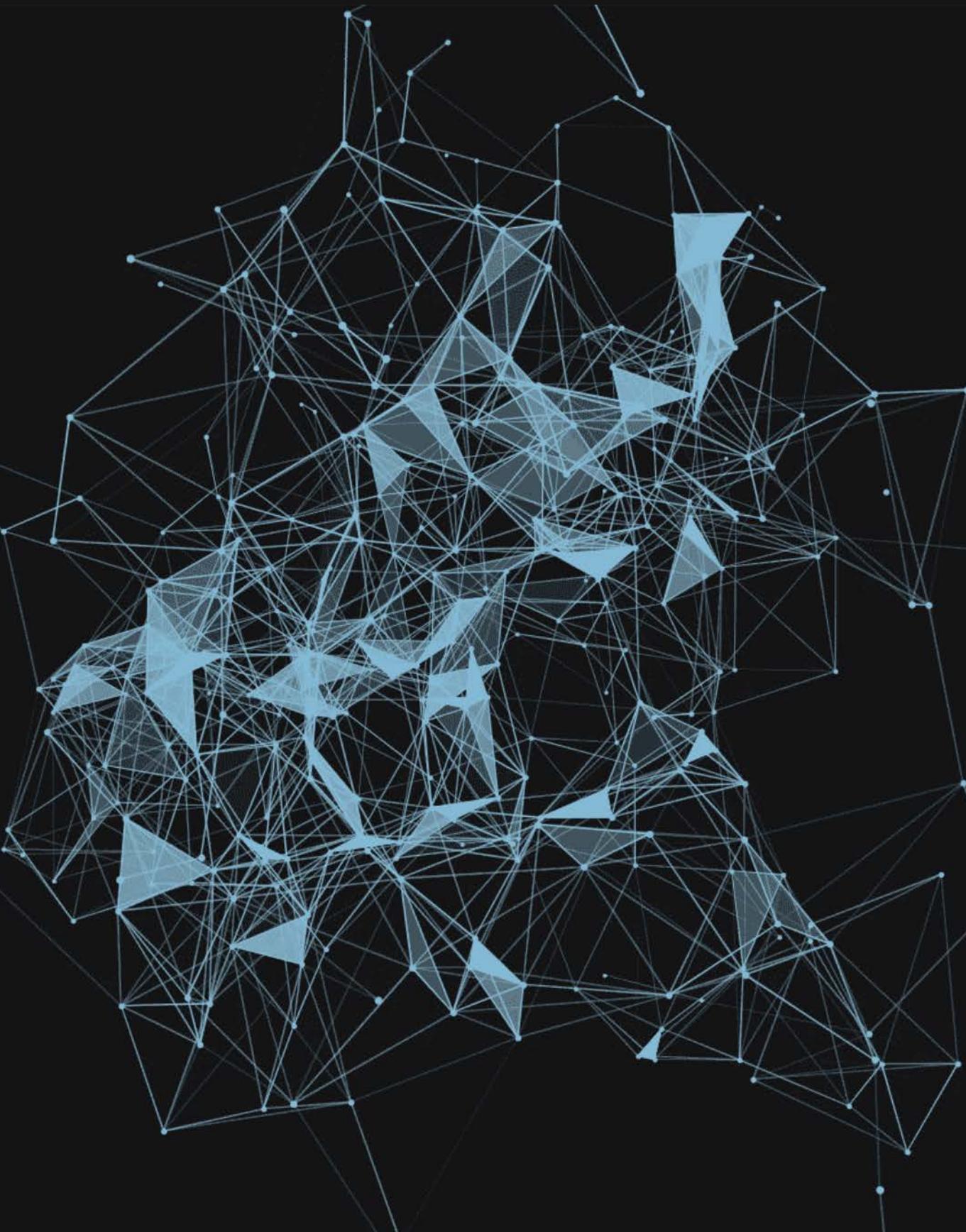
the capacity of deep learning for hypothesis generation in research

the promise of deep learning to streamline clinical workflows and empower patients

the rapid-diffusion open-source and proprietary deep learning programs



Questions



How to validate AI tools ?

Who controls AI and is ultimately responsible for its actions ?

How generalize AI across different

patient demographics?

geographic regions

healthcare system ?

How to insure privacy of the data and social acceptability ?

How to allow acceptance of AI applications in clinical practice ?

How access to quality and representative training data ?

How to maintain professional knowledge ?

Conclusion

AI and DL are entering the mainstream of clinical medicine.

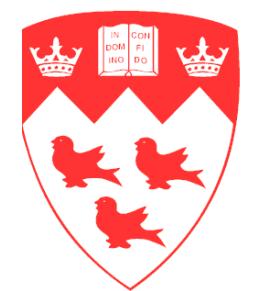
AI can augment human intelligence to improve decision making and operational processes.

Physicians need to actively engage to adapt their practice and to shape the technology.

“The good physician treats the disease; the great physician treats the patient who has the disease.”

William Osler





McGill

A r t i C

Artificial Intelligence for Care

