Artificial Intelligence for COVID-19 Outbreak Screening

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Artificial Intelligence (AI)
A subfield of computer science

- AI is any machine that simulates aspect of learning or any other feature of human intelligence (John McCarthy, 1956);
- AI is the theory and development of computer systems able to perform tasks normally requiring human intelligence;
- AI is any system able to pass the Turing test.

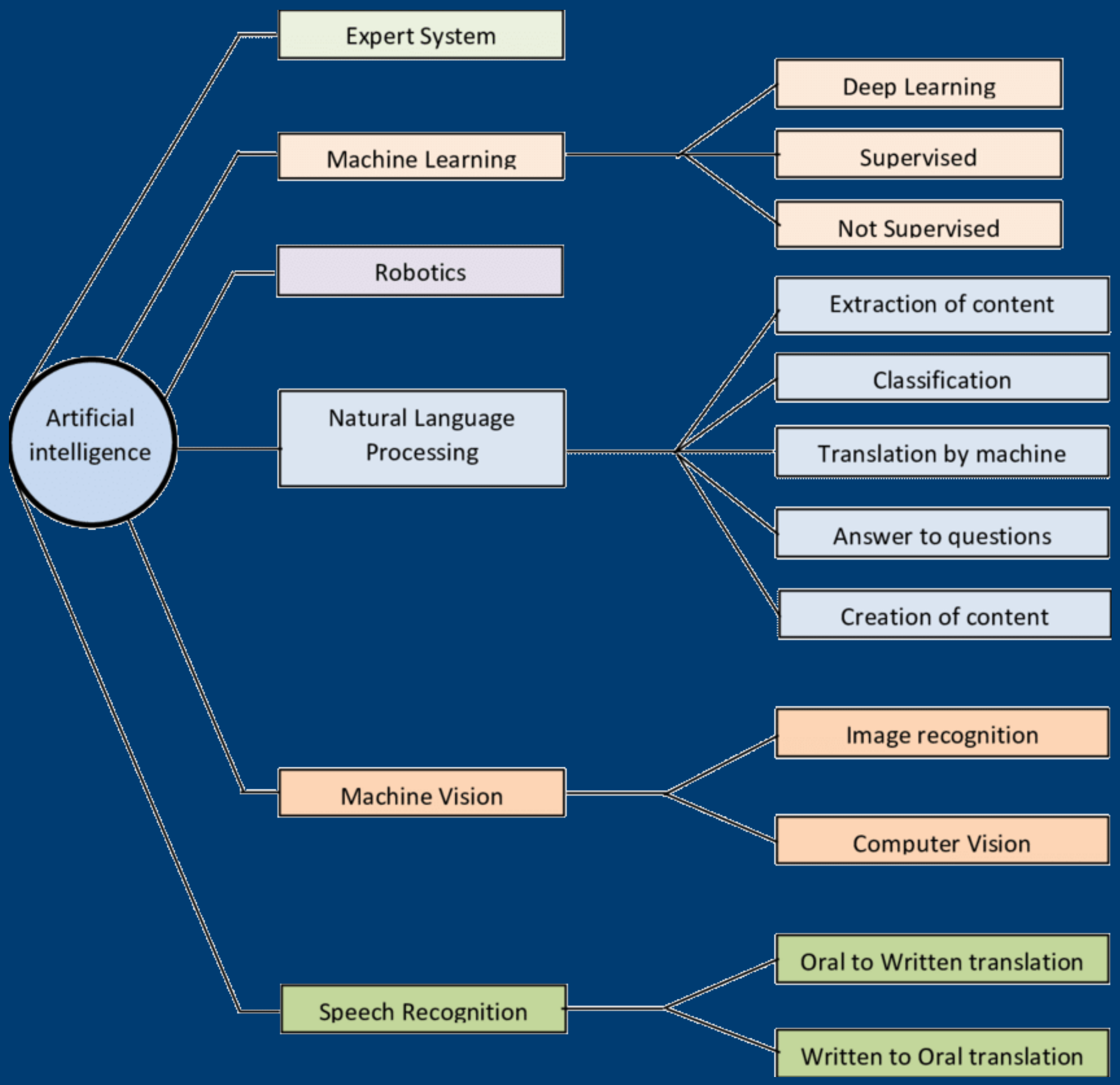
What is Machine Learning (ML)?

- Field of study that gives computers the ability to learn without being explicitly programmed. (Arthur Samuel);
- Study of algorithms that improve their performance P at some task T with experience E as we have well defined task <P,T,E>. (Tom Mitchell).

What is Deep Learning (DL) ?

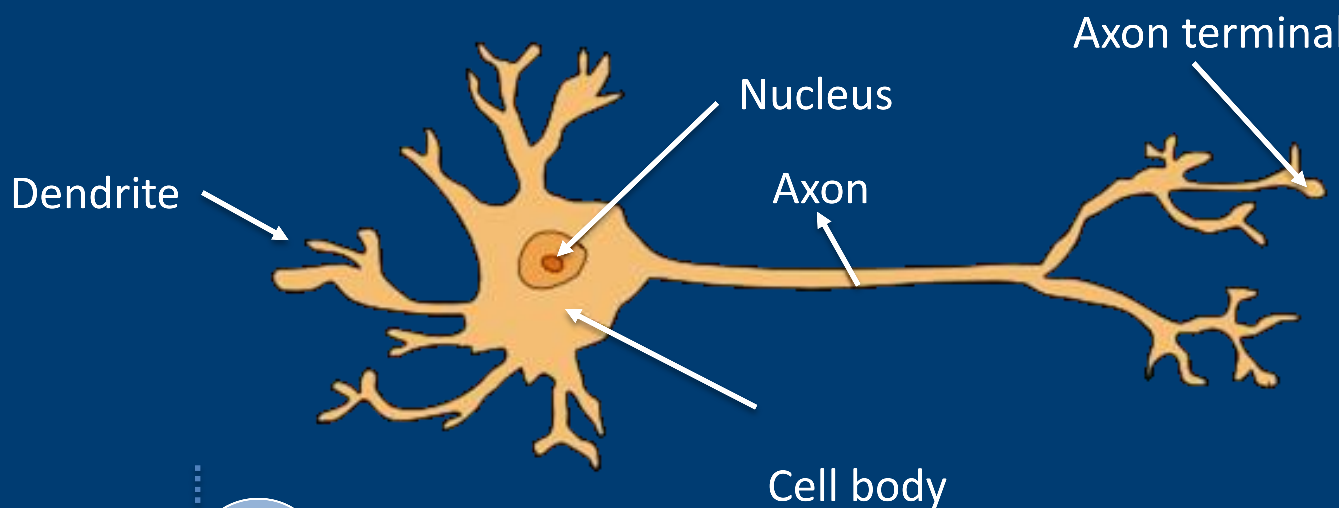
- DL methods are ML methods based on learning data representations. They are usually related to the training of neural networks with many layers (>100);
- Fast advances during the last decade, basically related to the Big Data boom and cheap GPU hardware;
- First developed as an applied then as a theoretical field.

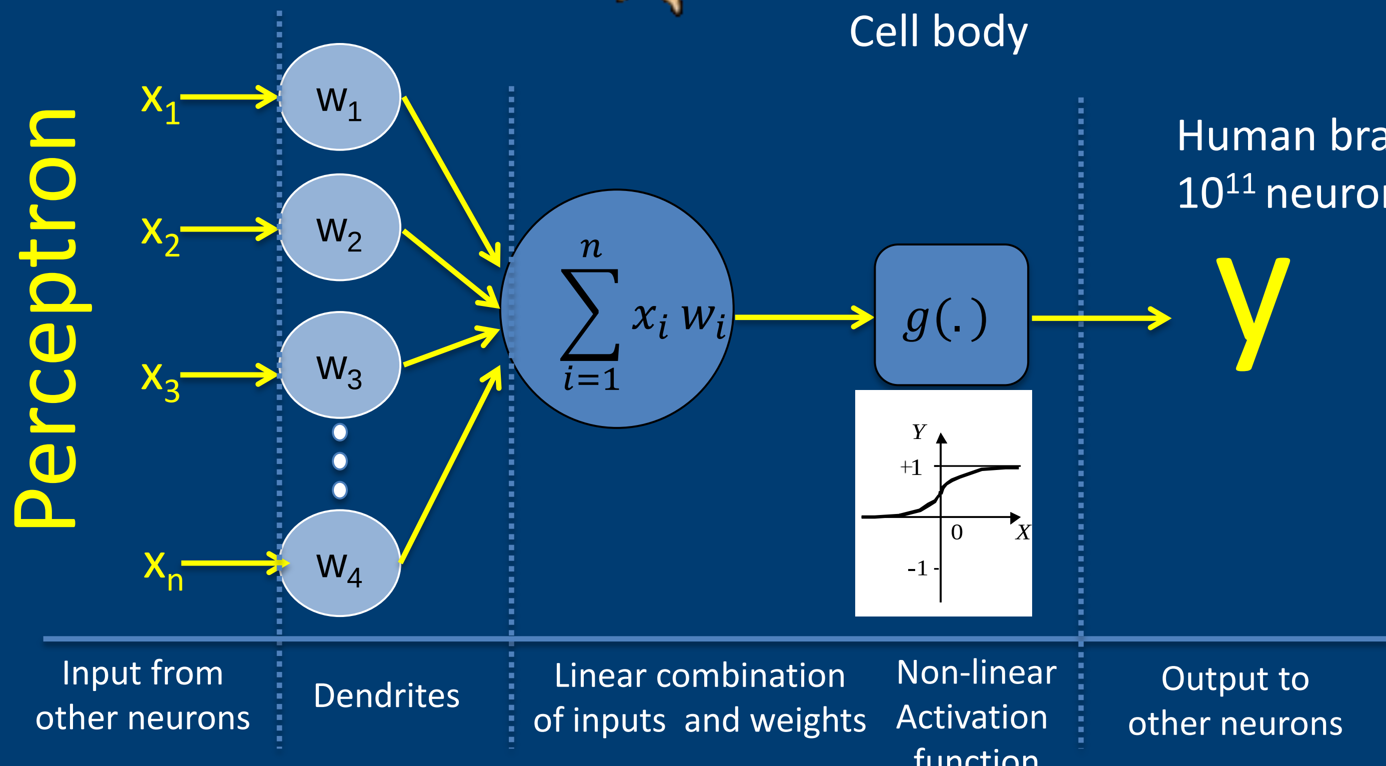
AI Subfields:



H. F. Atlam, R. J. Walters and G. B. Wills, "Intelligence of Things: Opportunities & Challenges," *2018 3rd Cloudification of the Internet of Things (CIoT)*, Paris, France, 2018, pp. 1-6, doi: 10.1109/CIOT.2018.8627114.

Mathematical model for a neuron

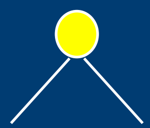
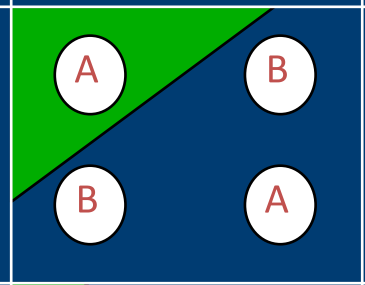
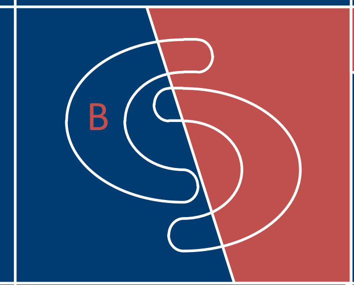
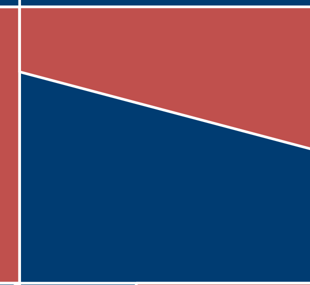
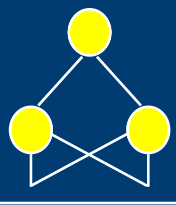
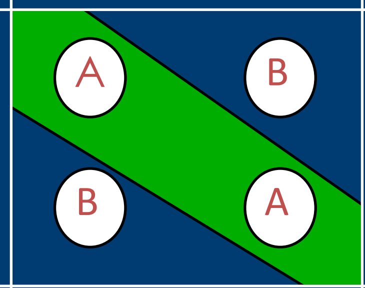
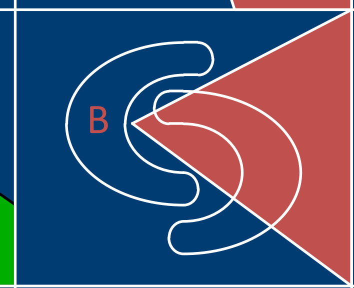
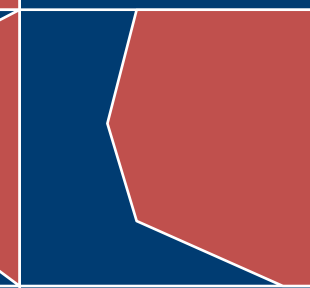
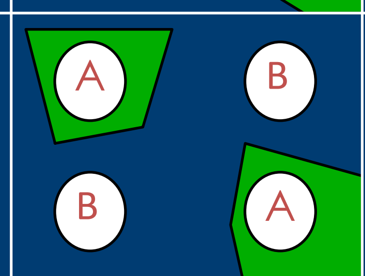
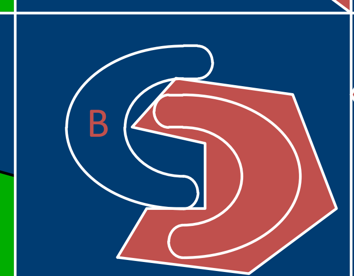
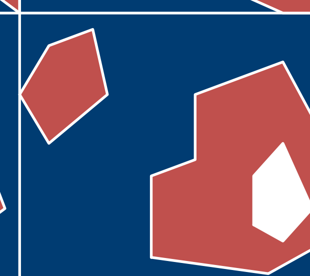




Human brain
10^{11} neurons = 100 billion

Rosenblatt, F. 1957. The Perceptron — a perceiving and recognizing automaton. Report 85–460–1, Cornell Aeronautical Laboratory.

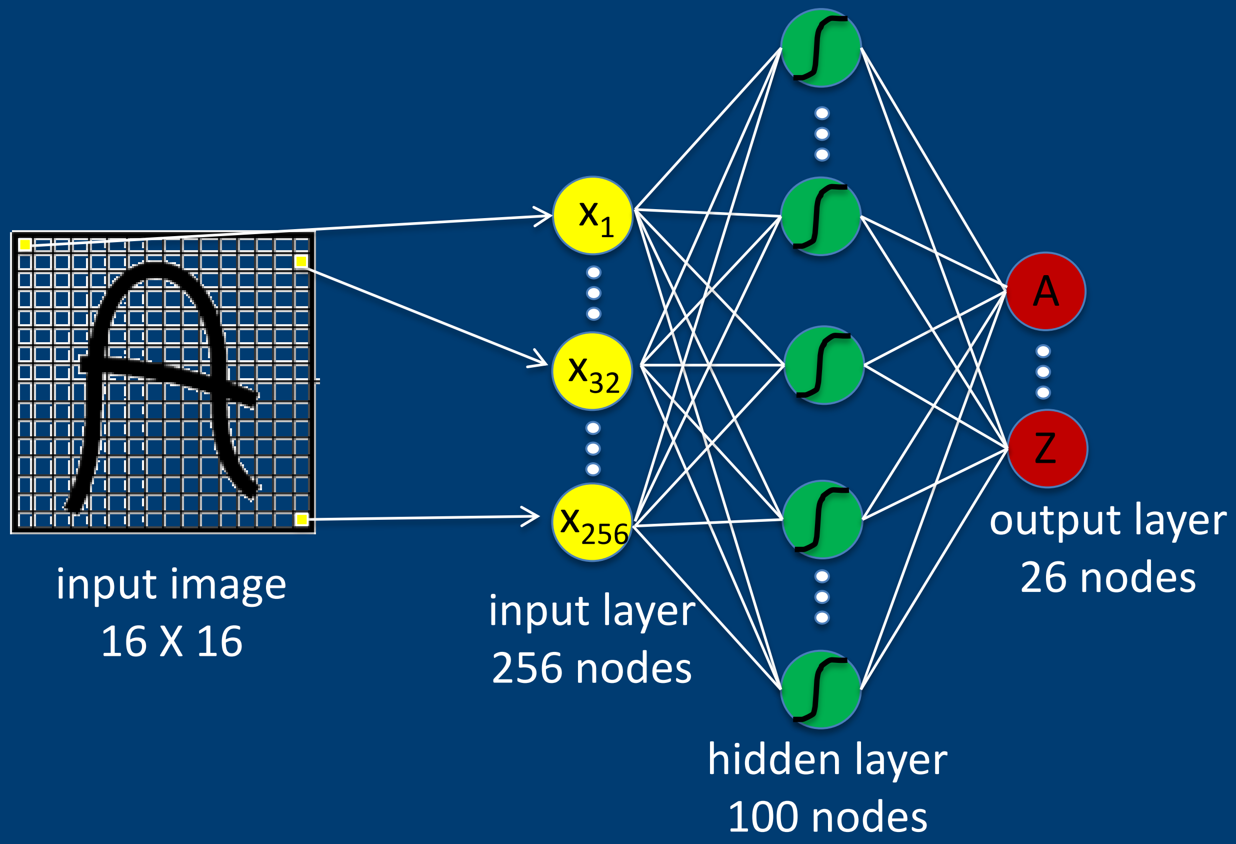
Behavior of multilayer neural networks

Structure	Types of Decision Regions	Exclusive-OR Problem	Classes with Meshed regions	Most General Region Shapes
Single-Layer 	Half Plane Bounded By Hyper plane			
Two-Layer 	Convex Open Or Closed Regions			
Three-Layer 	Arbitrary (Complexity Limited by No. of Nodes)			

Abin – Roozgard, “Convolutional Neural Networks”, lectures in Neural Networks.

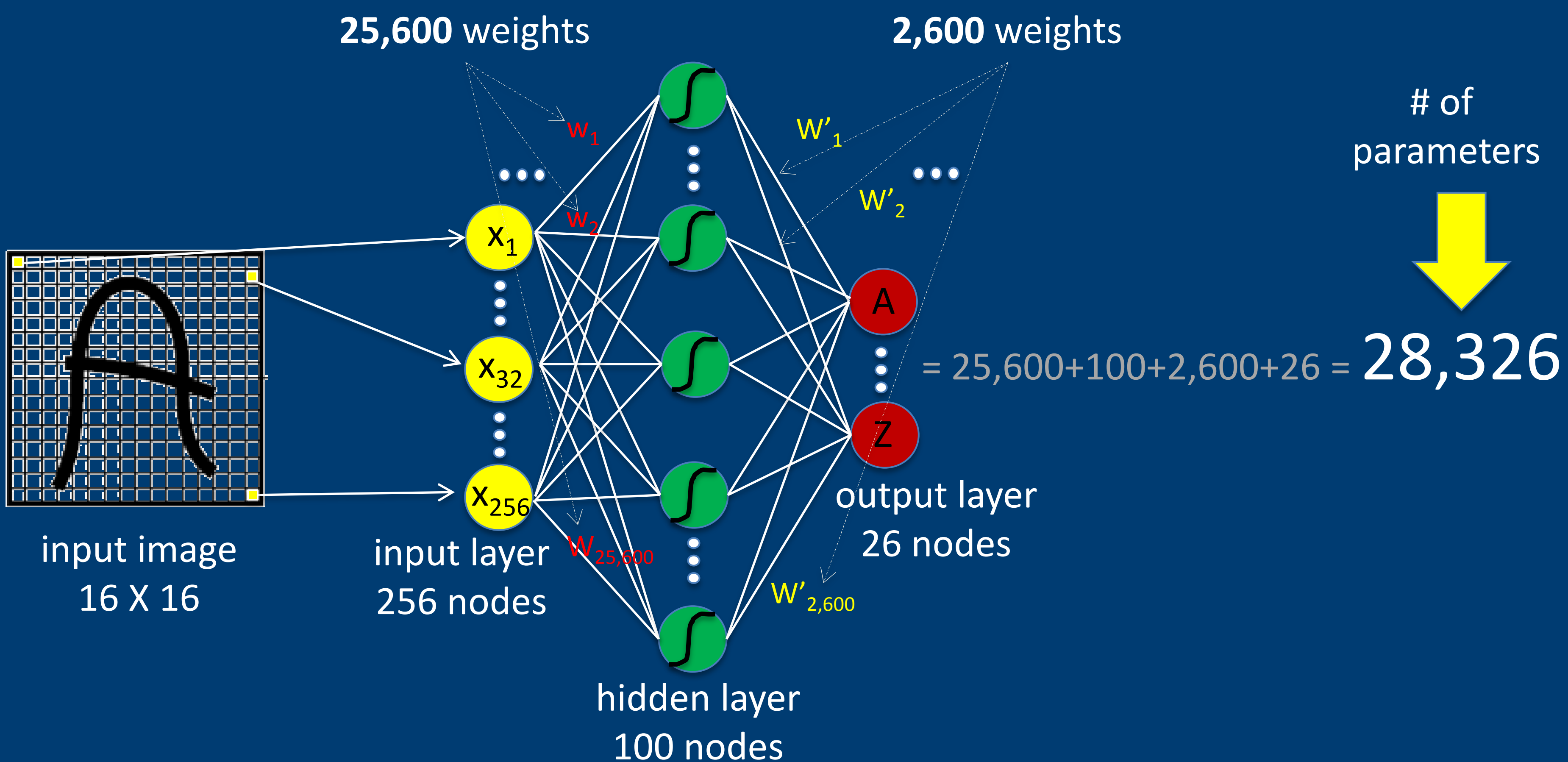
Multi-layer perceptron and image processing

- One or more hidden layers
- Sigmoid activations functions



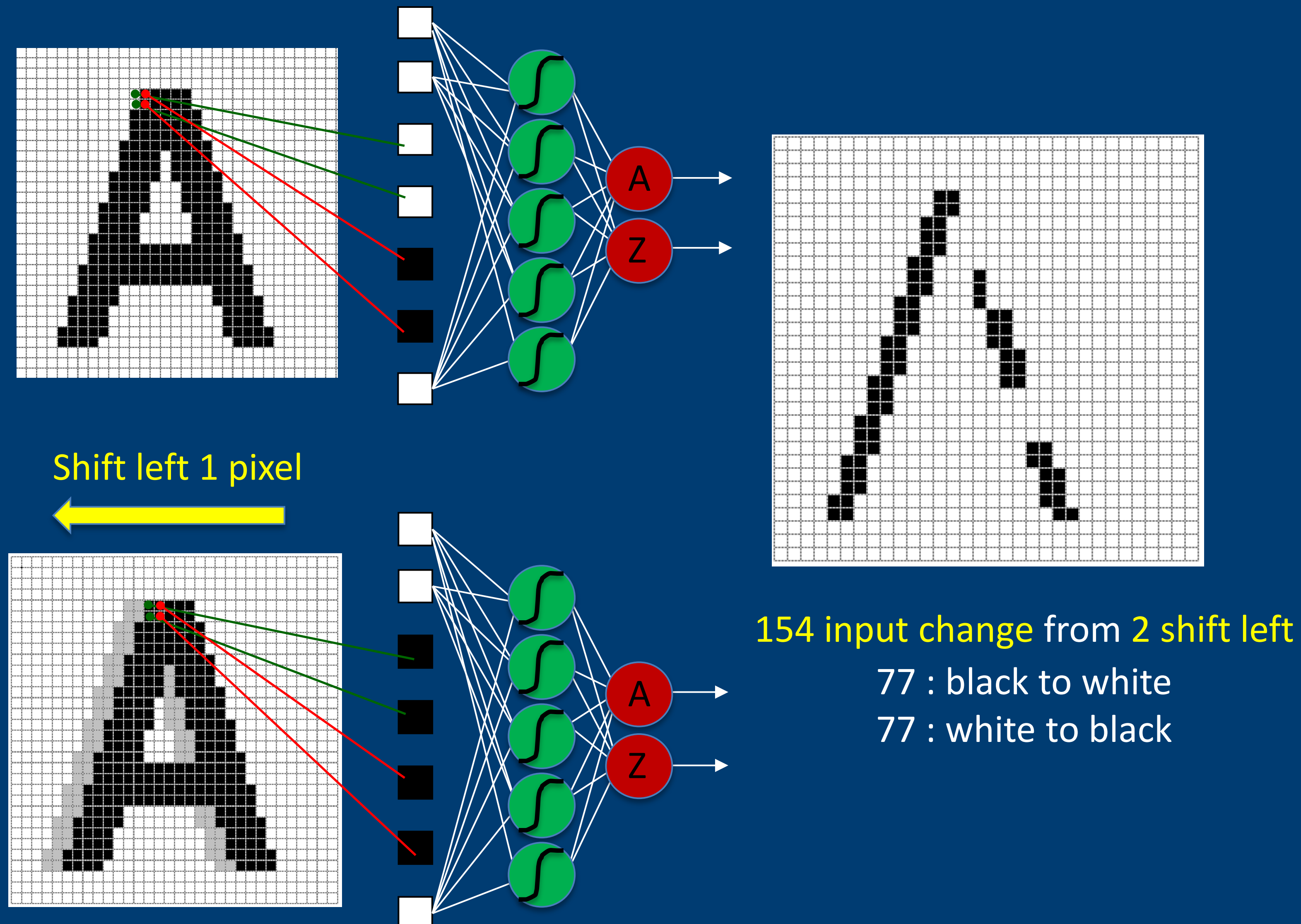
Drawbacks of previous neural networks

- The number of trainable parameters becomes extremely large



Drawbacks

- Little or no invariance to shifting, scaling, and other forms of distortion



Drawbacks

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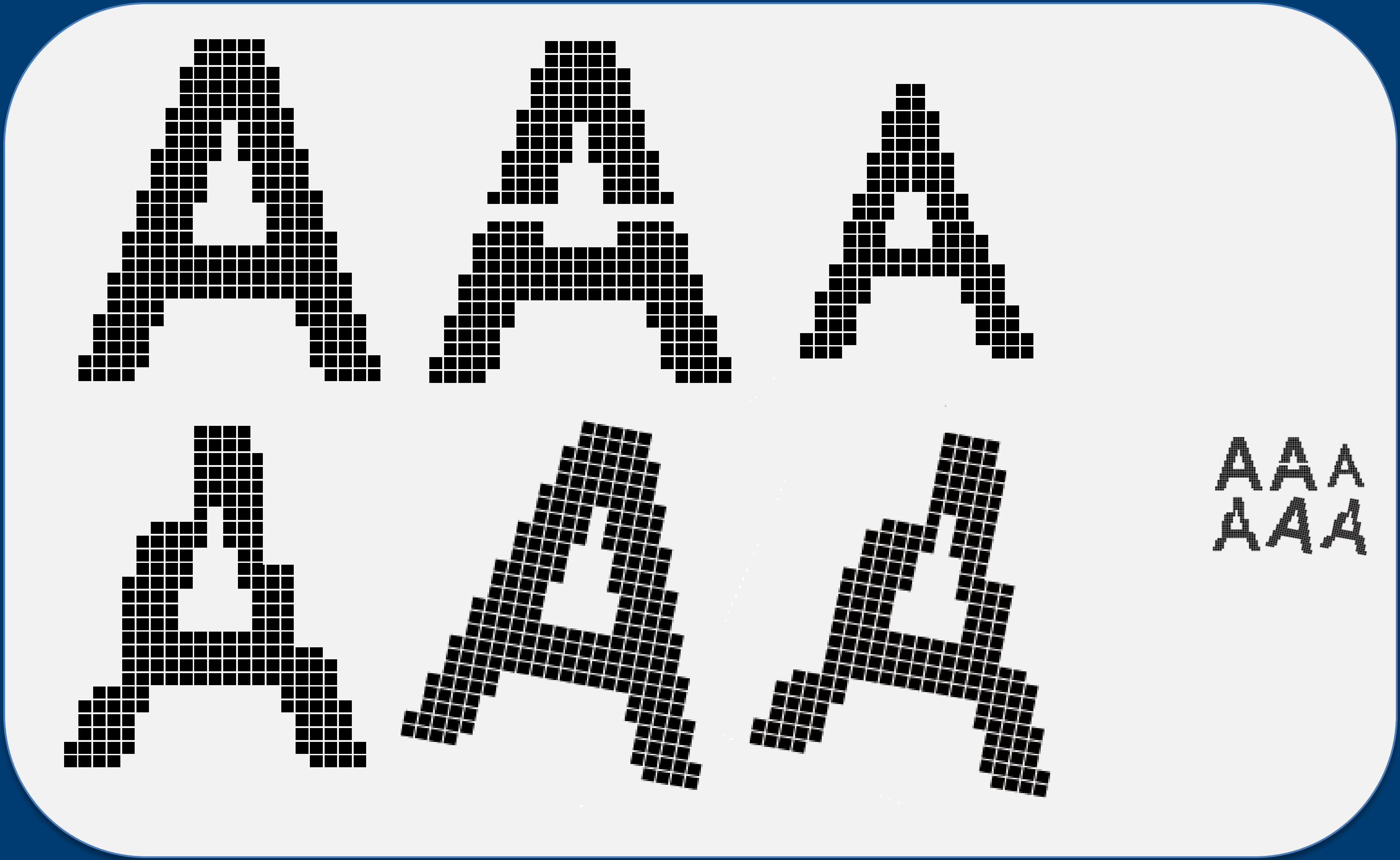
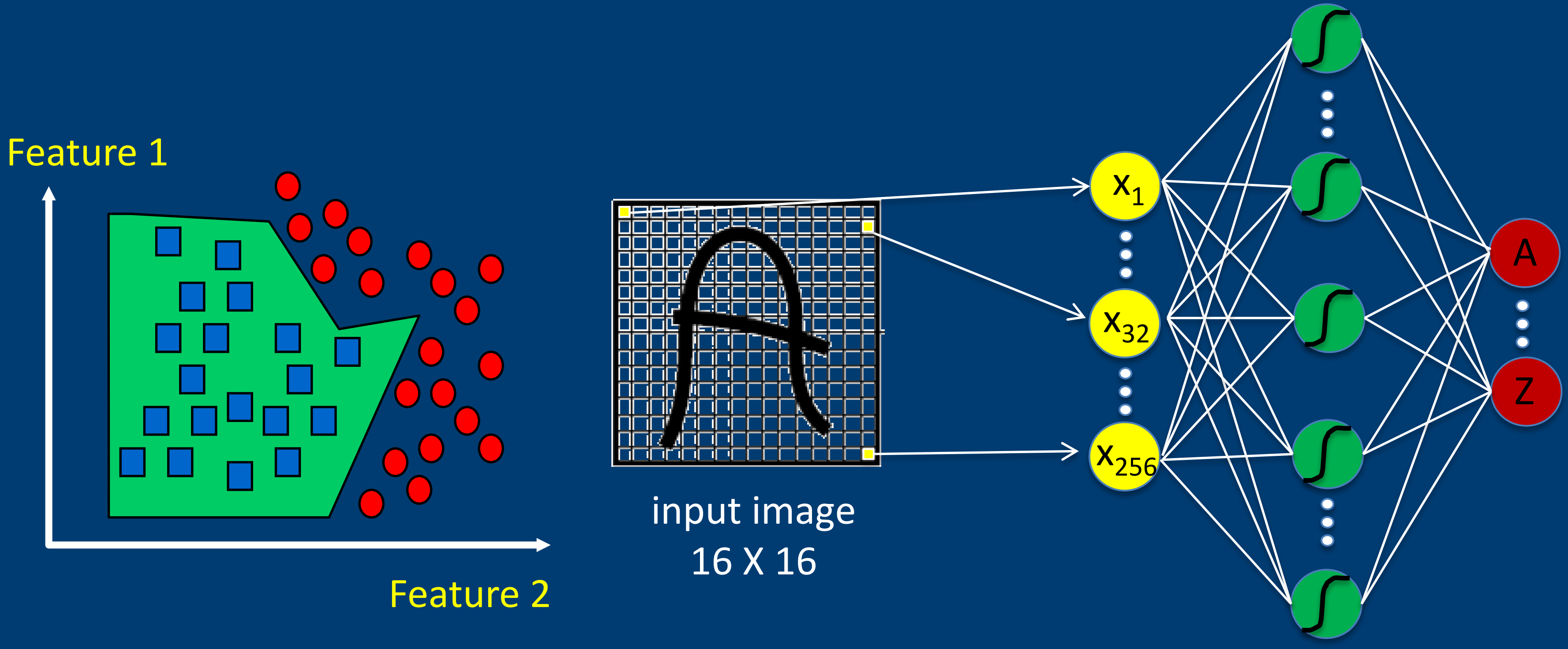


Drawbacks

- the topology of the input data is completely ignored, especially working with raw data

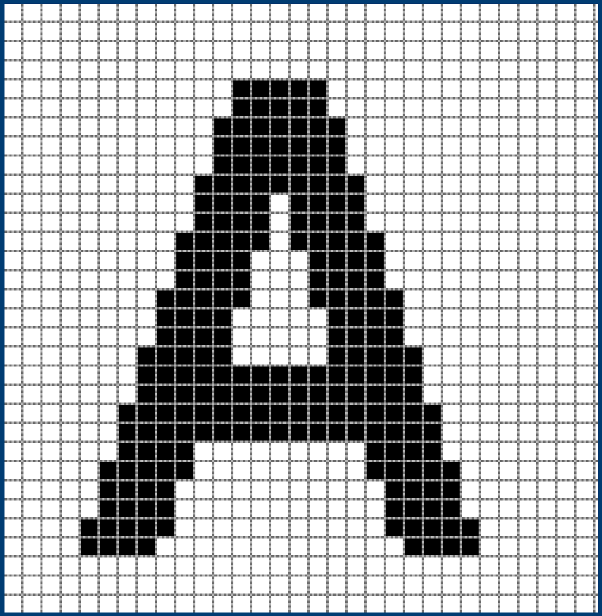


Drawbacks

- The increase in spatial resolution and levels intensity for each pixel results in an exponential increase in complexity.

Black and white patterns: $2^{32*32} = 2^{1024}$

Gray scale patterns : $256^{32*32} = 256^{1024}$

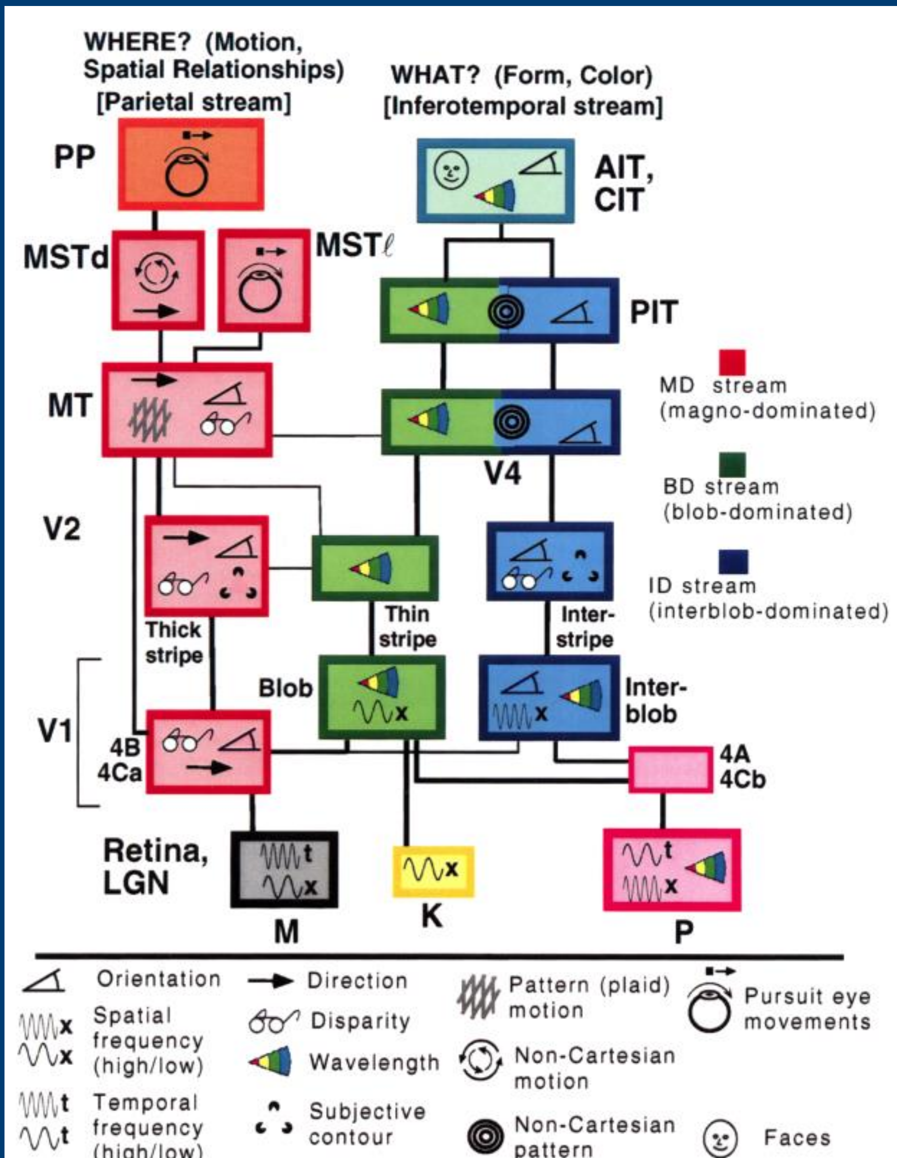


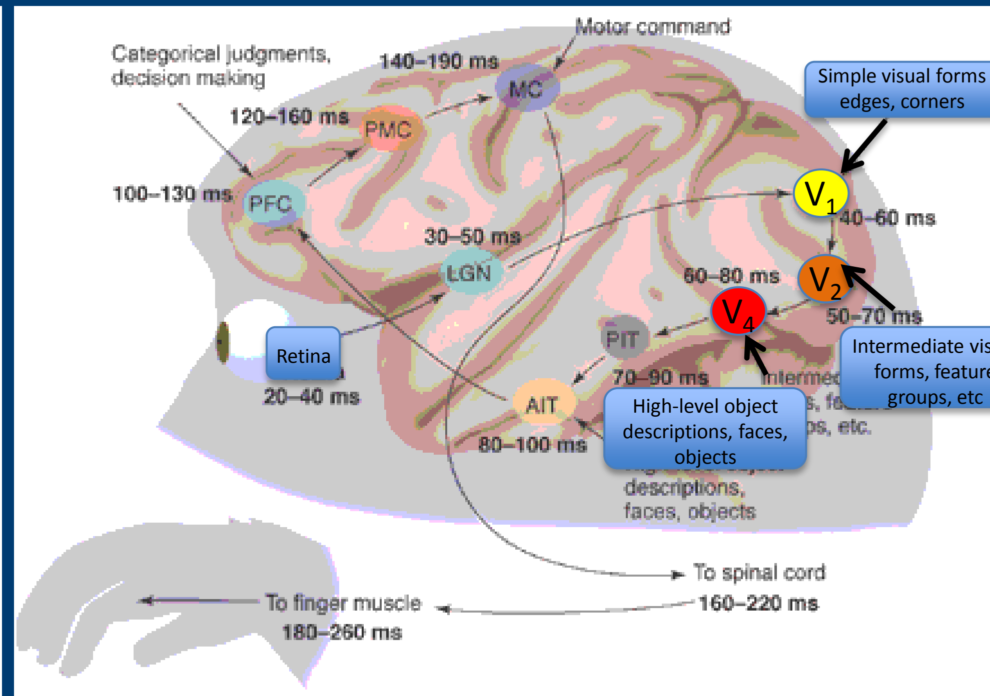
32 X 32 input image

Convolution Neural Networks (CNN)

- CNN are neurobiologically motivated by the findings of locally sensitive and orientation-selective nerve cells in the visual cortex;
- A network structure that implicitly extracts relevant features;
- CNN are a special kind of multi-layer neural networks.

The mammalian visual cortex is hierarchical





Thorpe SJ, Fabre-Thorpe M (2001) Seeking categories in the brain. Science 291:260–263. doi:10.1126/science.1058249

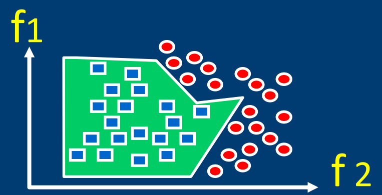
Van Essen DC, Gallant JL (1994) Neural Mechanisms of Form and Motion Processing in the Primate Visual System. Neuron 1-10. doi: 10.1016/0896-6273(94)90455-3

Convolution Neural Networks (CNN)

- CNN is a feed-forward network that can extract topological properties from an image;
- Like almost every other neural networks they are trained with a version of the backpropagation algorithm;
- Convolutional Neural Networks are designed to recognize visual patterns directly from pixel images with minimal preprocessing;
- They can recognize patterns with extreme variability (such as handwritten characters).

Classification vs. CNN

- Classification

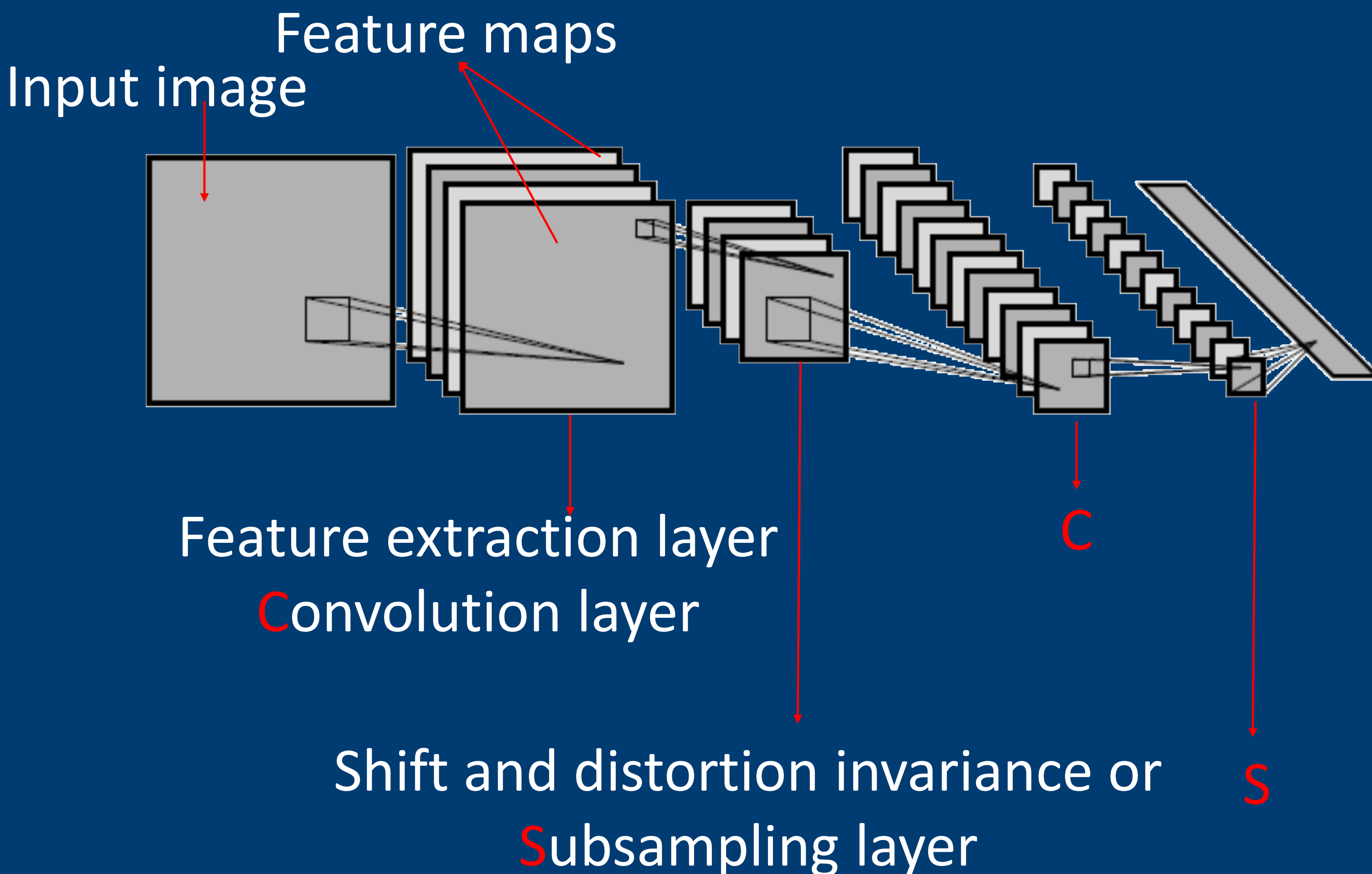


Input → Pre-processing for feature extraction → $f_1 \ldots f_n$ → Classification → output

- Convolutional Neural Networks

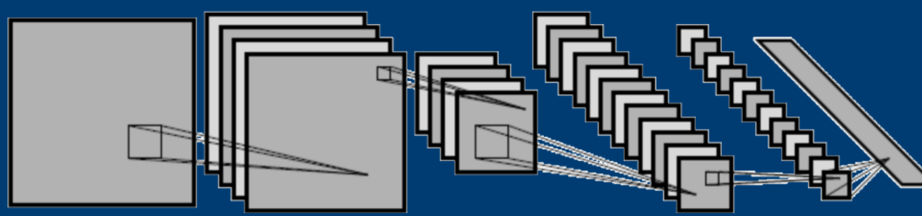
Input → Feature extraction → Shift distortion invariance → Classification → output

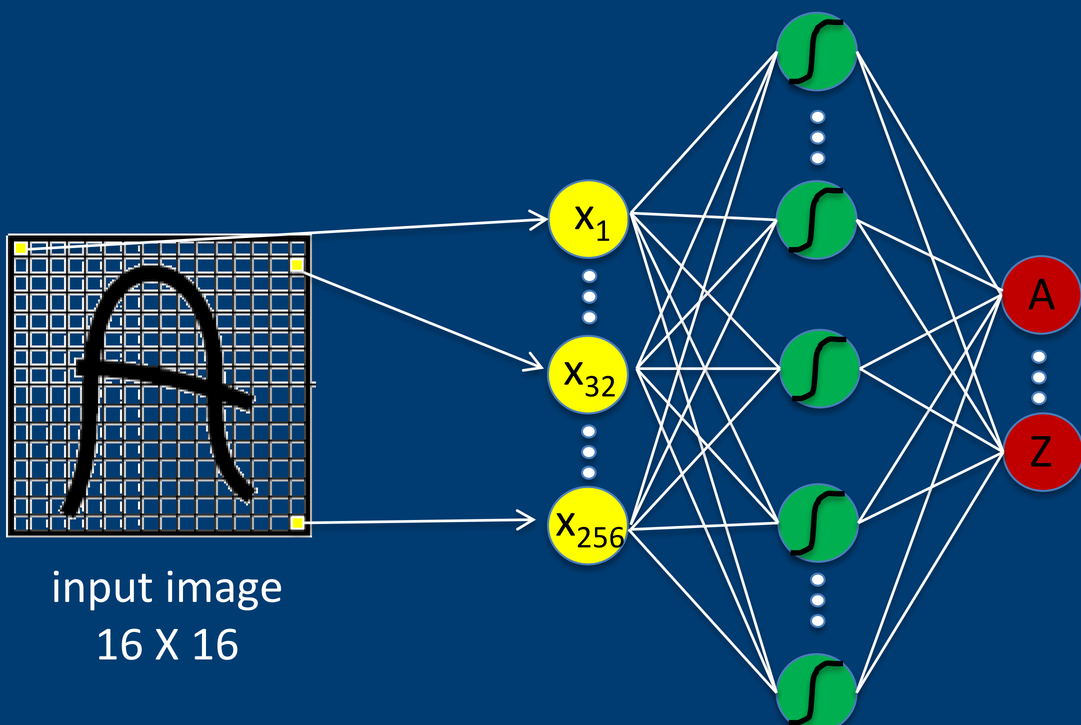
CNN's Architecture

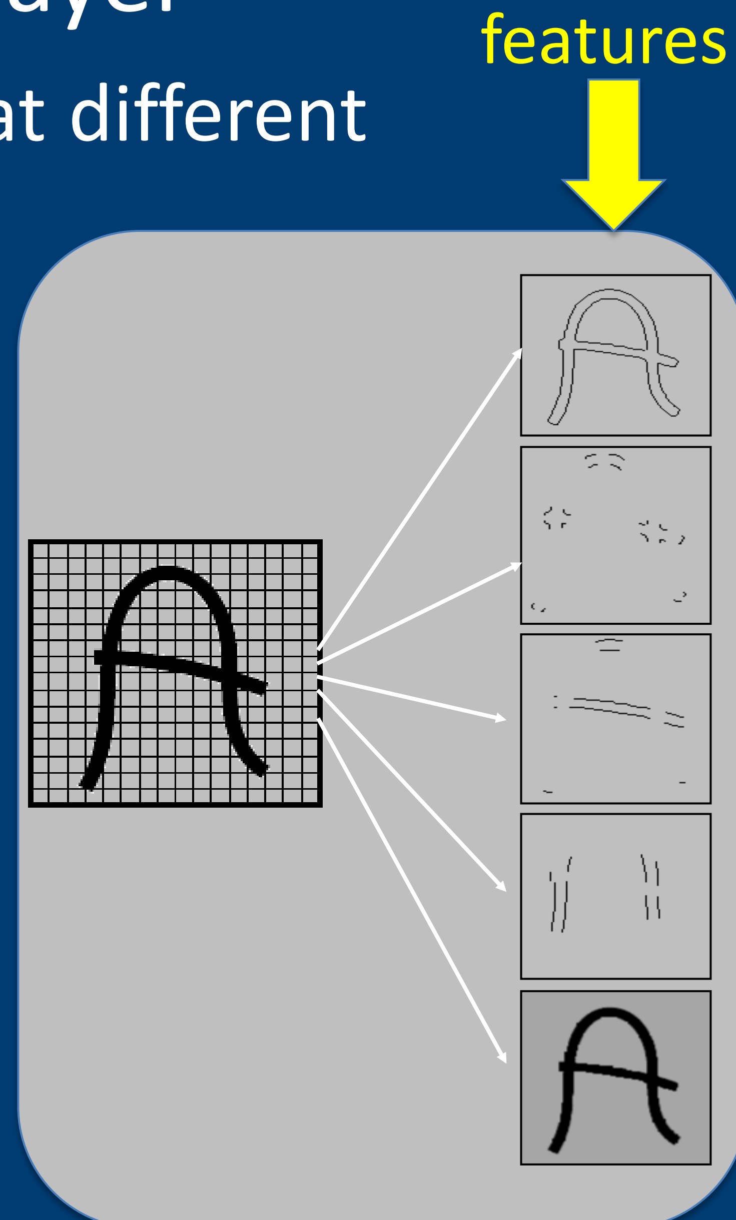


Feature extraction layer or Convolution layer

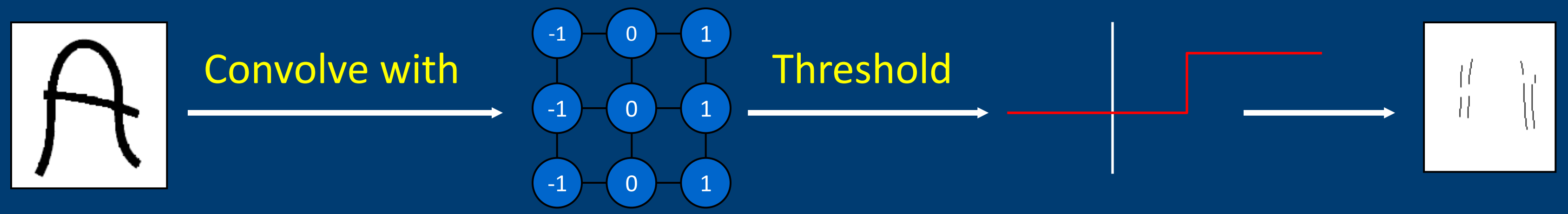
- It detects the same feature at different positions in the input image.

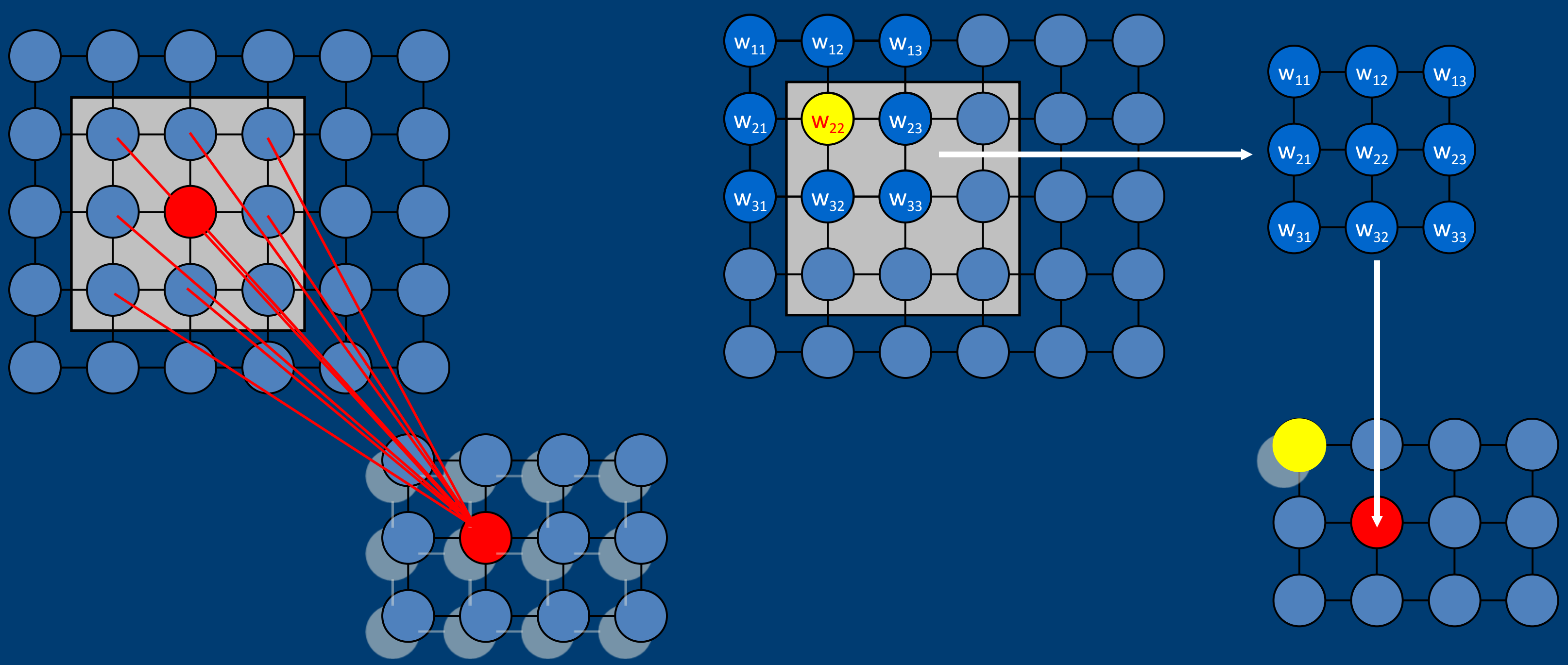






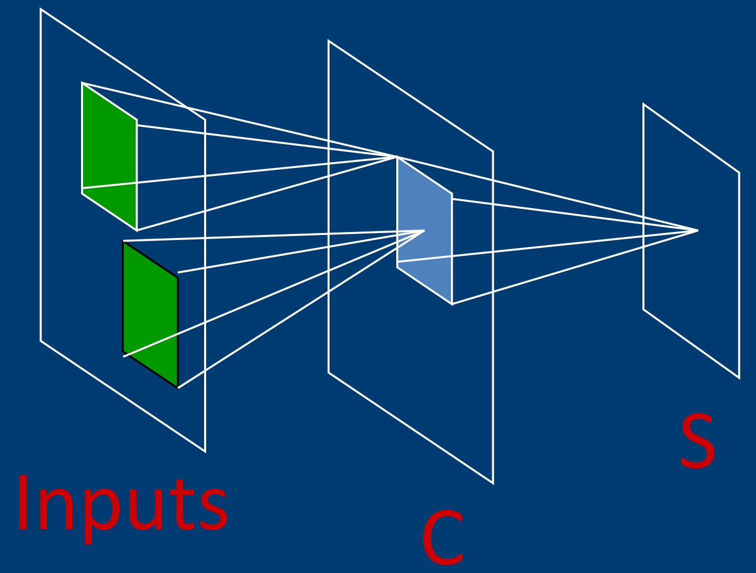
Feature extraction





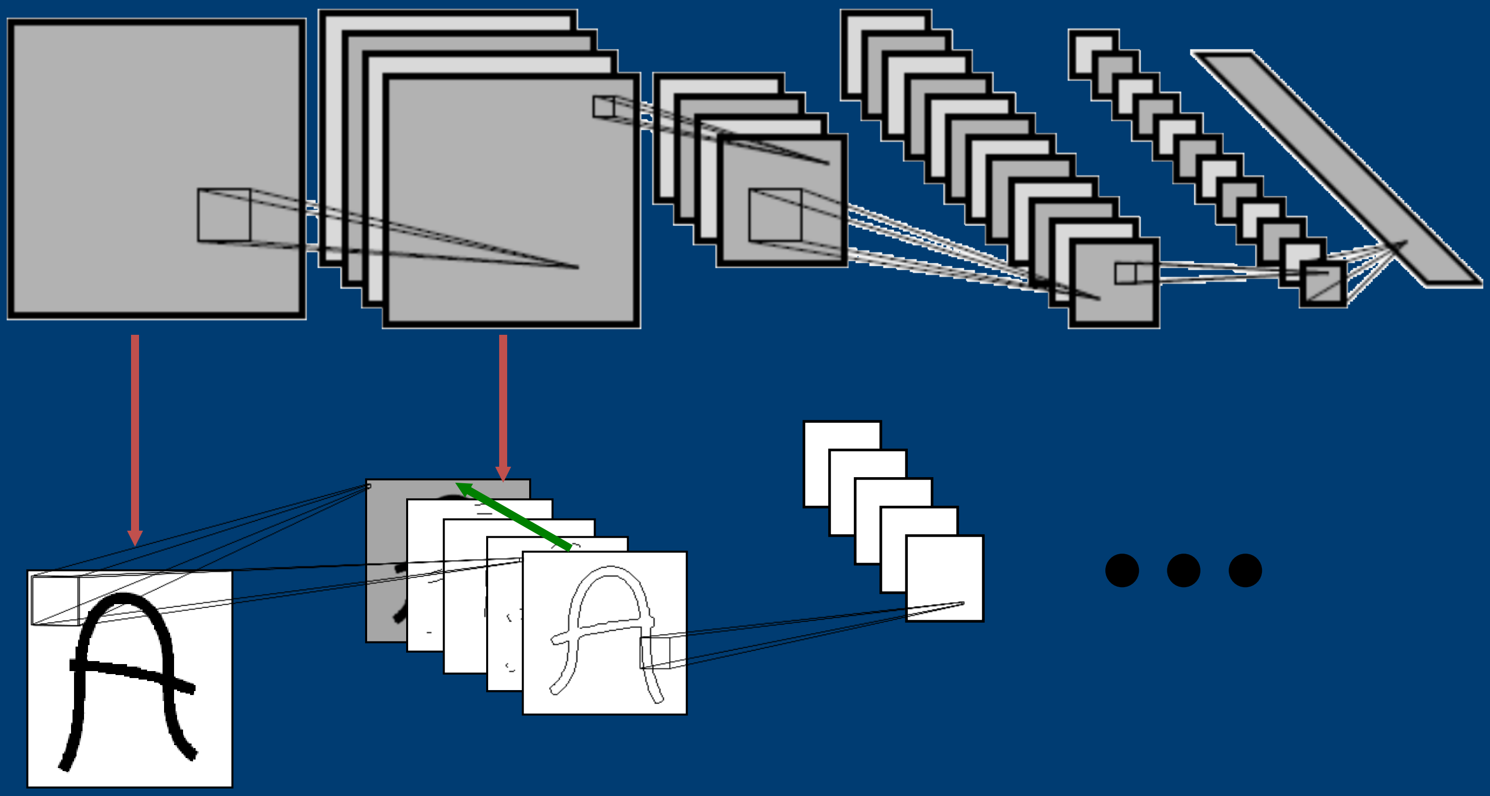
Feature extraction

- Shared weights: all neurons in a feature share the same weights;
- In this way all neurons detect the same feature at different positions in the input image;
- Reduce the number of free parameters.



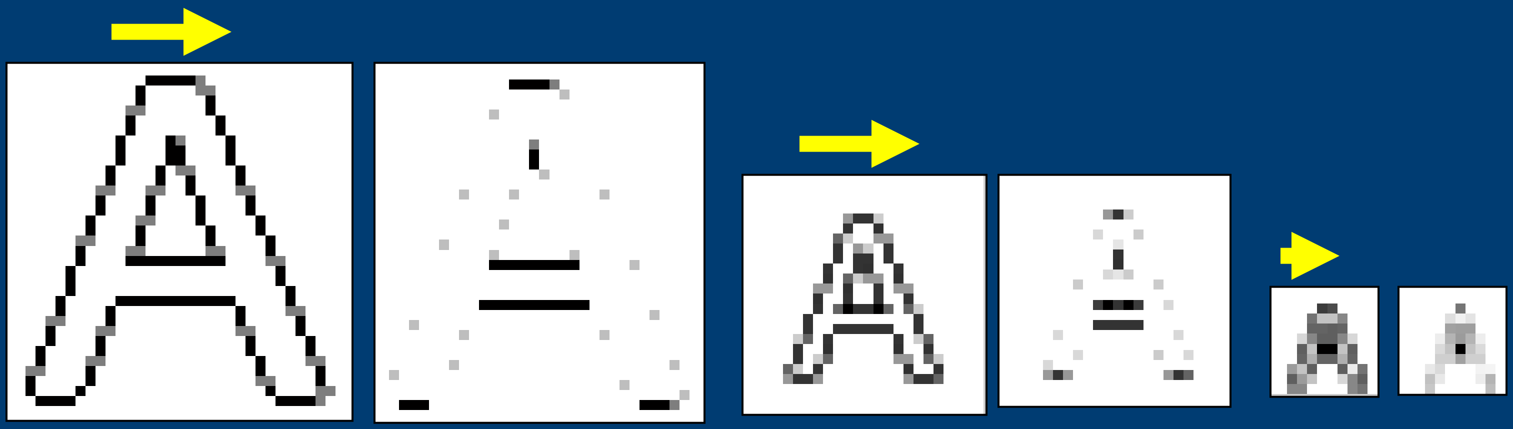
Feature extraction

- If a neuron in the feature map fires, this corresponds to a match with the template.



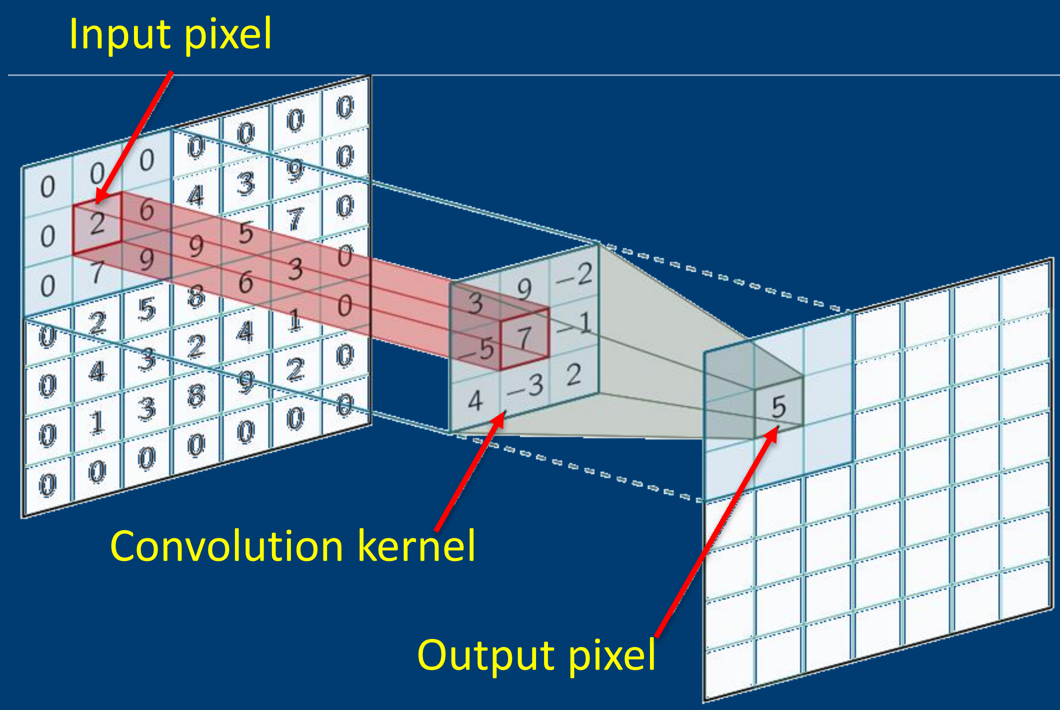
Subsampling layer (pooling)

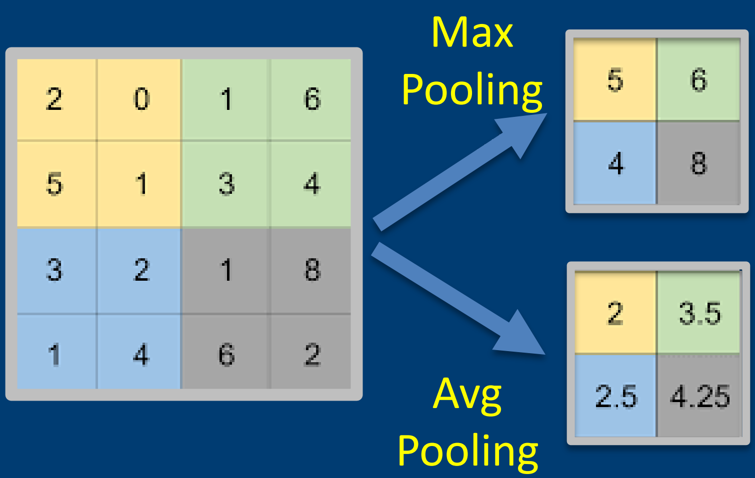
- the subsampling layers reduce the spatial resolution of each feature map
- By reducing the spatial resolution of the feature map, a certain degree of shift and distortion invariance is achieved.



Convolutional Neural Networks

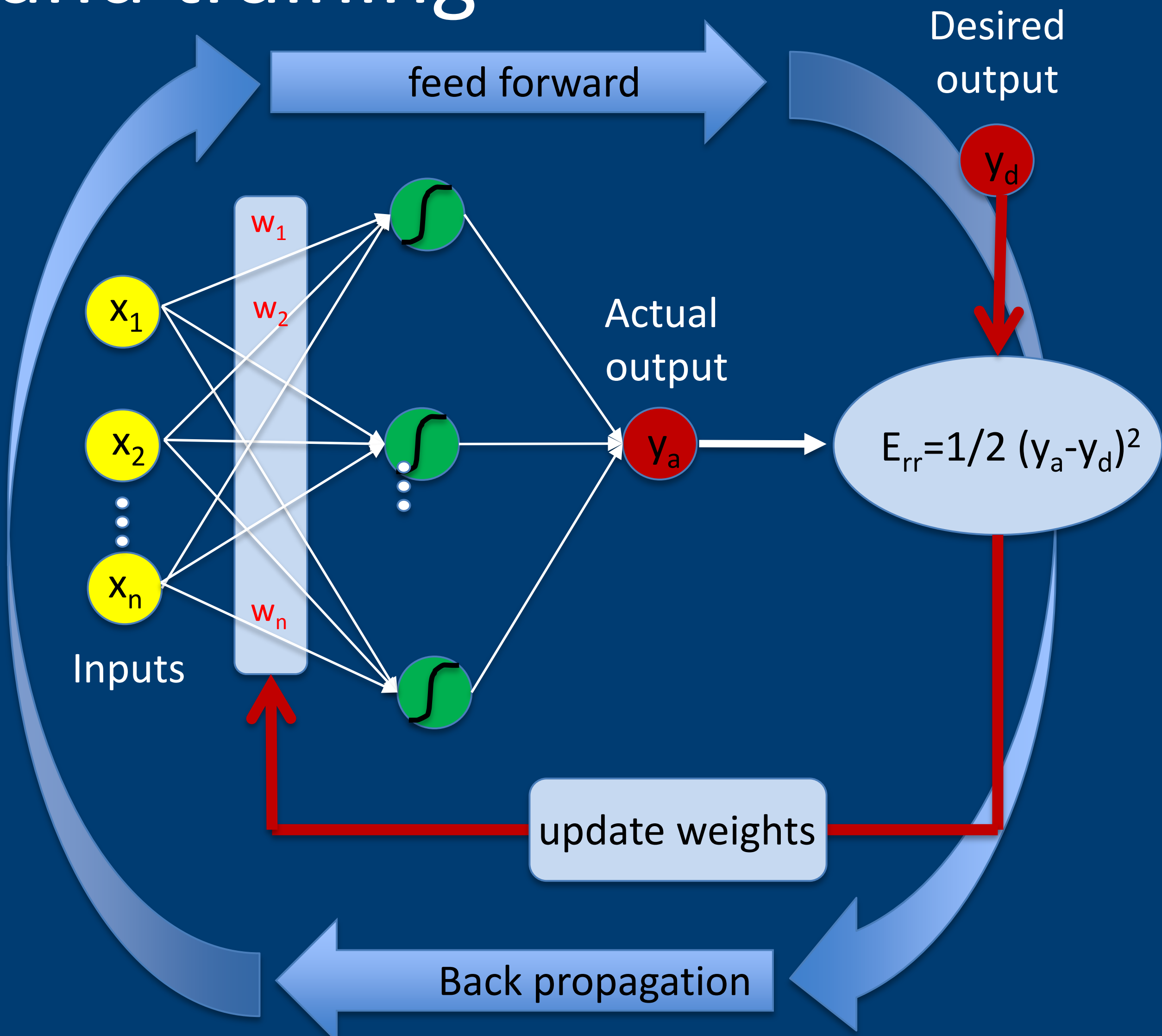
- Weight sharing (convolution) + Subsampling (pooling)
  - Reduce the # of parameters
  - Translational invariance





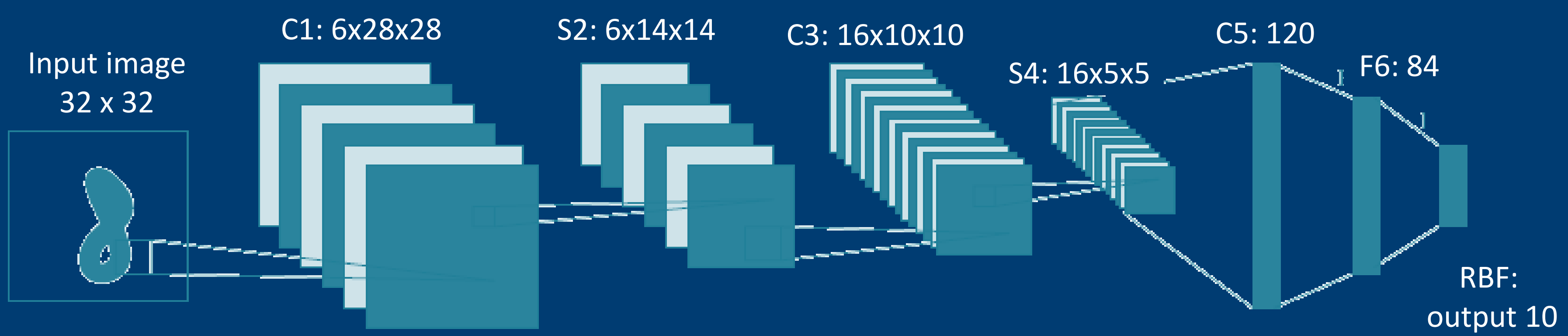
Backpropagation algorithm and training

1. Input is modeled using real randomly selected weights;
2. Calculate the output for every neuron from the input layer, to the hidden layers, to the output layer;
3. Calculate the error in the output E_{rr}
4. Travel back from the output layer to the hidden layer to adjust the weights such that the error is decreased;
5. Keep repeating the process until the desired output is achieved.



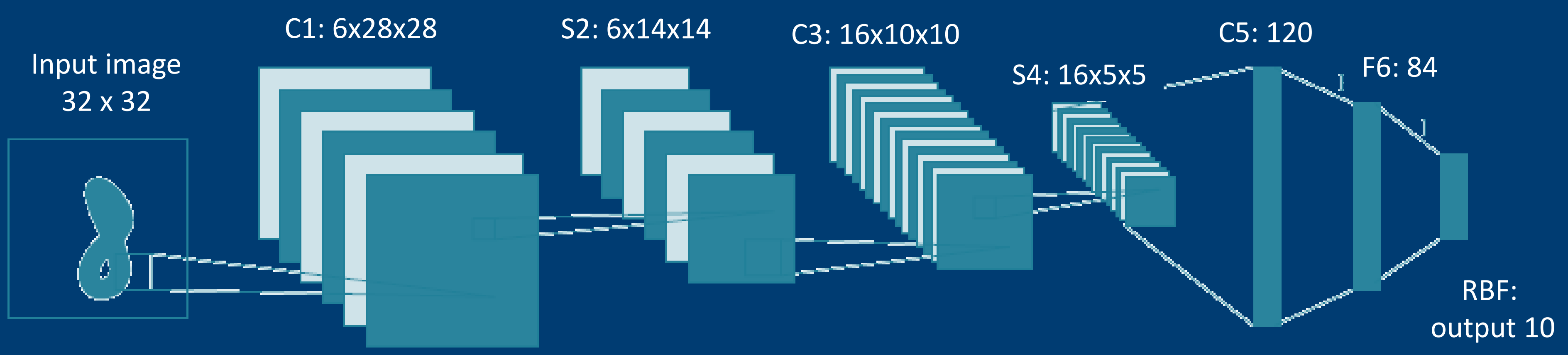
Example: LeNet5

- LeNet 5 Archtecture
  - raw image of 32 × 32 pixels as input
  - C1,C3,C5 : Convolutional layer.
    - 5 × 5 Convolution matrix.
  - S2 , S4 : Subsampling layer.
    - Subsampling by factor 2.
  - F6:Fully connected layer (sigmoid activation function).

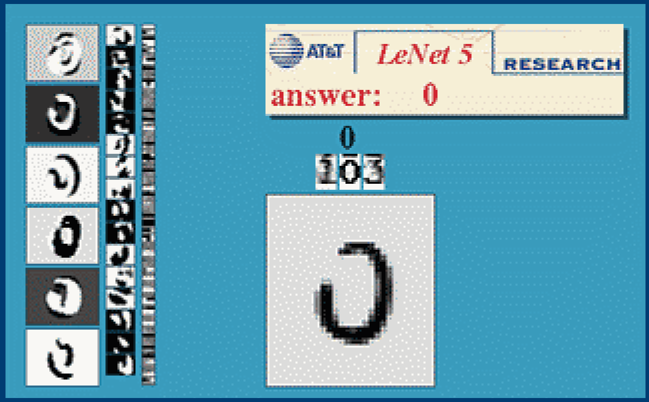


LeCun, Y.; Boser, B.; Denker, J. S.; Henderson, D.; Howard, R. E.; Hubbard, W. & Jackel, L. D. (1989). Backpropagation applied to handwritten zip code recognition. Neural Computation, 1(4):541-551.

Example: LeNet5



- ~187,000 connections.
- ~14,000 trainable weight.

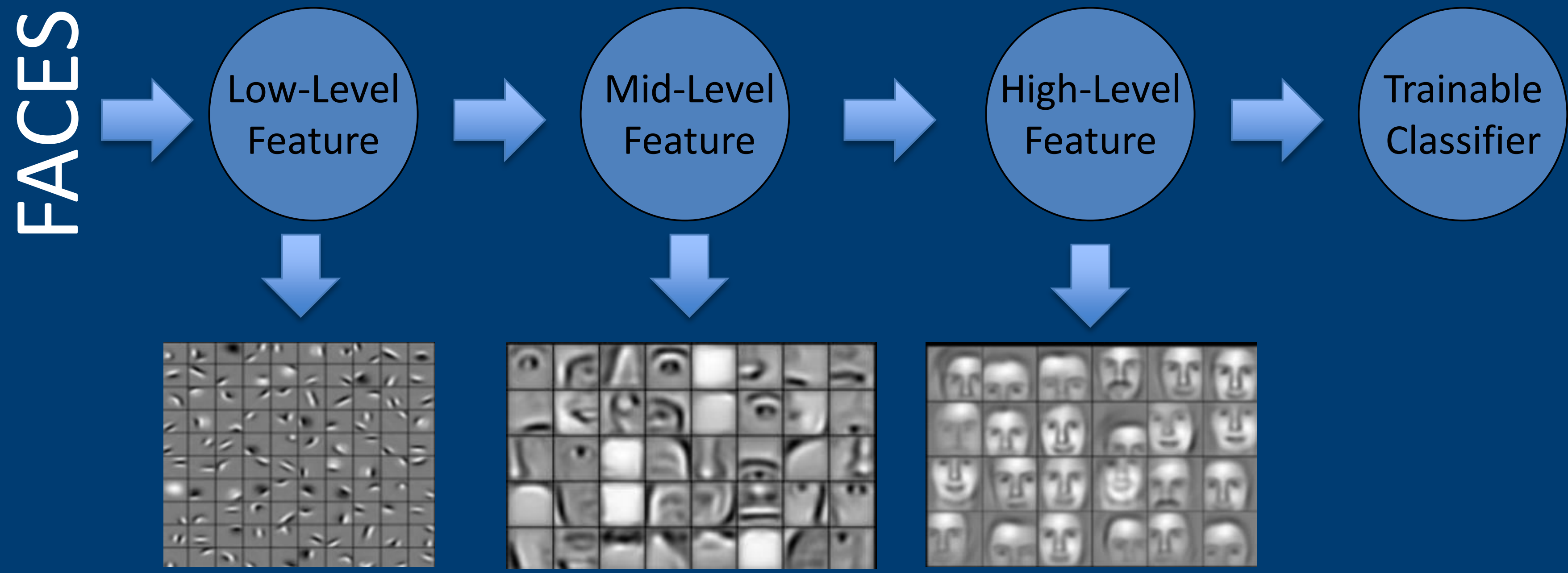


http://yann.lecun.com/exdb/lenet

Example: LeNet5

Deep Learning = Learning Hierarchical Representations

- It´s deep if it has more than one layer of non-linear feature transformation.



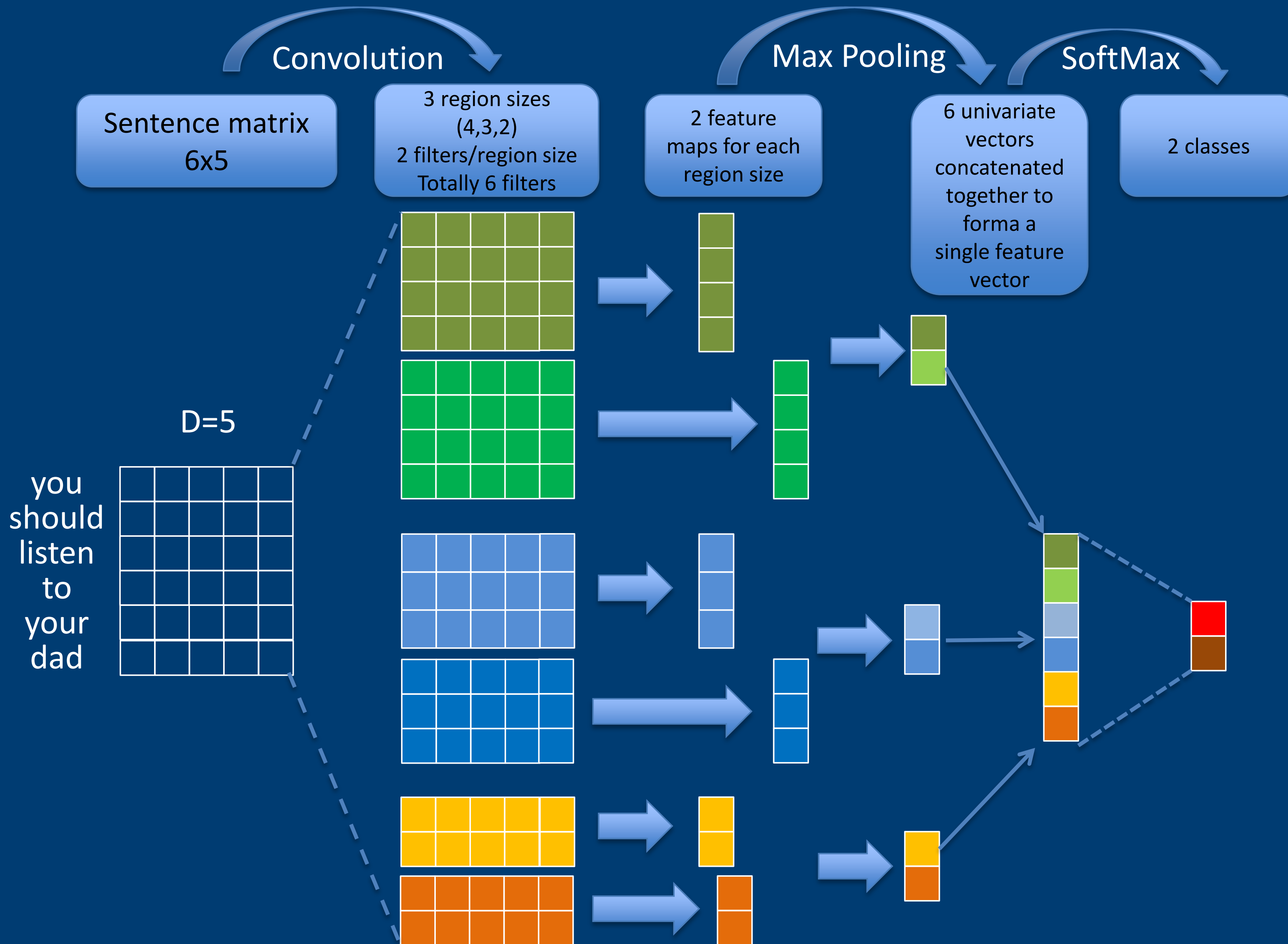
Patterns of local contrast

Face features

Faces

- Image recognition: pixel-> edge -> part -> object
- Text: char -> word -> word group -> clause -> sentence -> story
- Speech: sample -> spectral band -> sound -> …-> phone -> phoneme -> word ->

Deep Learning based NLP



AI in Healthcare

- AI is a powerful tool and a partner
  - Man + Machine = enhanced human capabilities (AMA, 2018)
- AI can help human
  - Unlock the power of big data and gain insight into patients;
  - Support evidence-based decision making, improving quality, safety, and efficiency;
  - Coordinate care and foster communication;
  - Improve patient experience and outcomes;
  - Deliver value and reduce costs;
  - Improve health system performance & optimization.

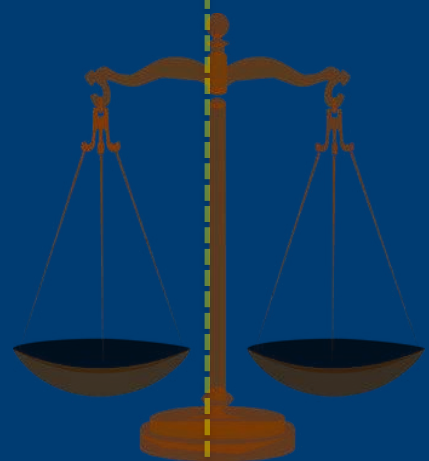
Human-machine Partnership in Healthcare

Man ⟷ Machine

AI-powered automation

Improving effectiveness

- Quality
  - Experience
  - Outcomes
- Safety
  - Ways to ensure
  - Patient safety
- Efficiency
  - Usability
  - Productivity
- Access to care
- Controlling costs



AI-powered automation

- Machine learning
  - Supervised learning
  - Unsupervised learning
  - Reinforcement learning
- Natural language processing
  - Statistical vs. rule-based NLP
- AI voice technology
  - Clinical voice documentation
  - Voice nursing assistants
- Medical robotics

Supervised Learning

- Most AI successes in healthcare are achieved through supervised learning;
- Identifying the underlying structure/patterns of data and trying to map input variables into discrete categories;
- Data-driven clinical decision support:
  - Diagnostic analysis using medical imaging (e.g., CT-scan, X-rays, MRI procedures);
  - Making medical diagnosis based on the symptoms;
  - Designing and selecting treatments based on biomarkers or other attributes;
  - Identifying at-risk groups based on health-related factors and social determinants.

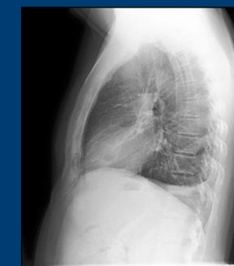
Supervised Learning: Classification problem

Identifying different types of diseases

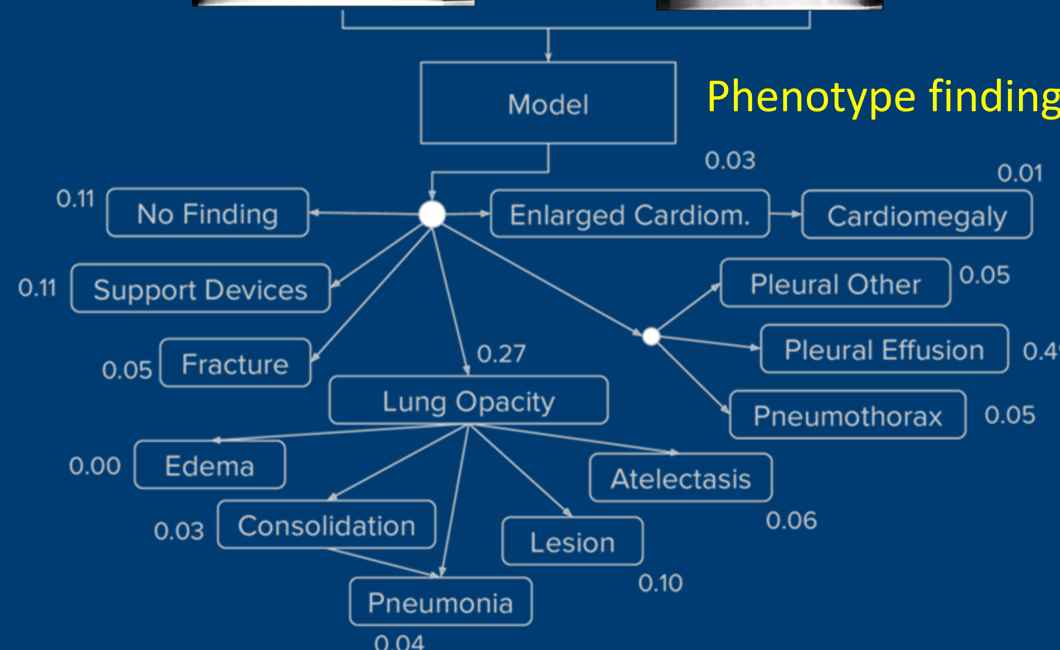
CheXpert: A large dataset of chest X-rays and competition for automated chest x-ray interpretation (Launched in 2019 by Stanford university)

Rank	Date	Model	AUC	Num Rads Below Curve
1	Sep 01, 2019	Hierarchical-Learning-V1 (ensemble) *Vingroup Big Data Institute* https://arxiv.org/abs/1911.06475	0.930	2.6
2	Oct 15, 2019	Conditional-Training-LSR *ensemble*	0.929	2.6
3	Dec 04, 2019	Hierarchical-Learning-V4 (ensemble) *Vingroup Big Data Institute* https://arxiv.org/abs/1911.06475	0.929	2.6
4	Oct 10, 2019	YWW(ensemble) *JF&NNU* https://github.com/jfhealthcare/Chexpert	0.929	2.8
5	Oct 17, 2019	Conditional-Training-LSR-V1 *ensemble*	0.929	2.6

224,316 chest radiographs of 65,240 patients



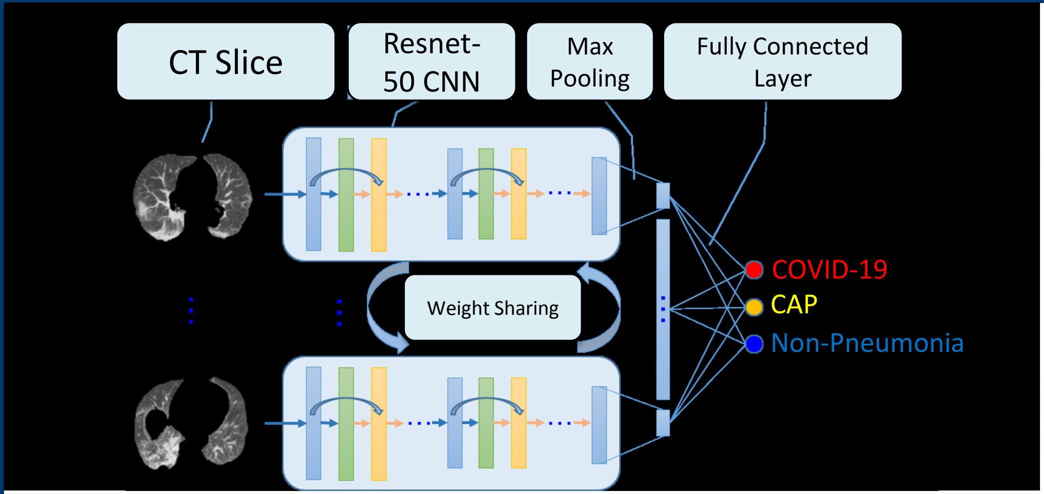
Phenotype findings

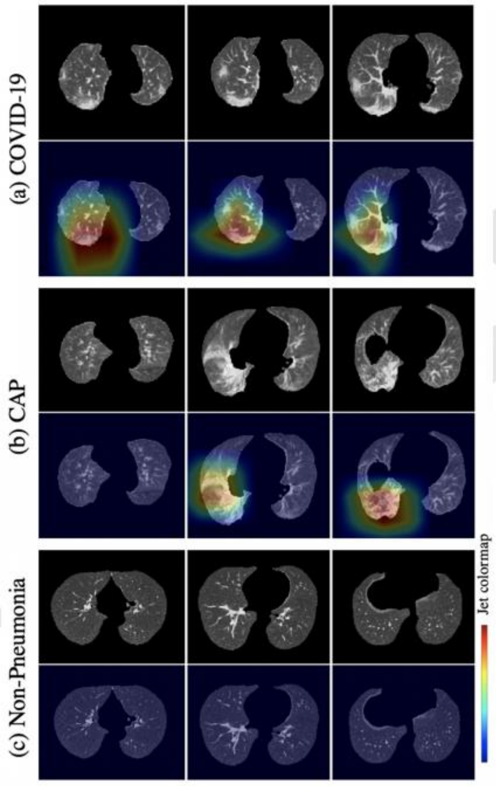


https://stanfordmlgroup.github.io/competitions/chexpert/

AI to distinguish COVID in CT Exams

- To extract visual features from chest CT exams for the detection of: COVID-19, Community acquired pneumonia (CAP) and other non-pneumonia;
- 4,356 CT Exams, based on Resnet50, training set 90%, test 10%





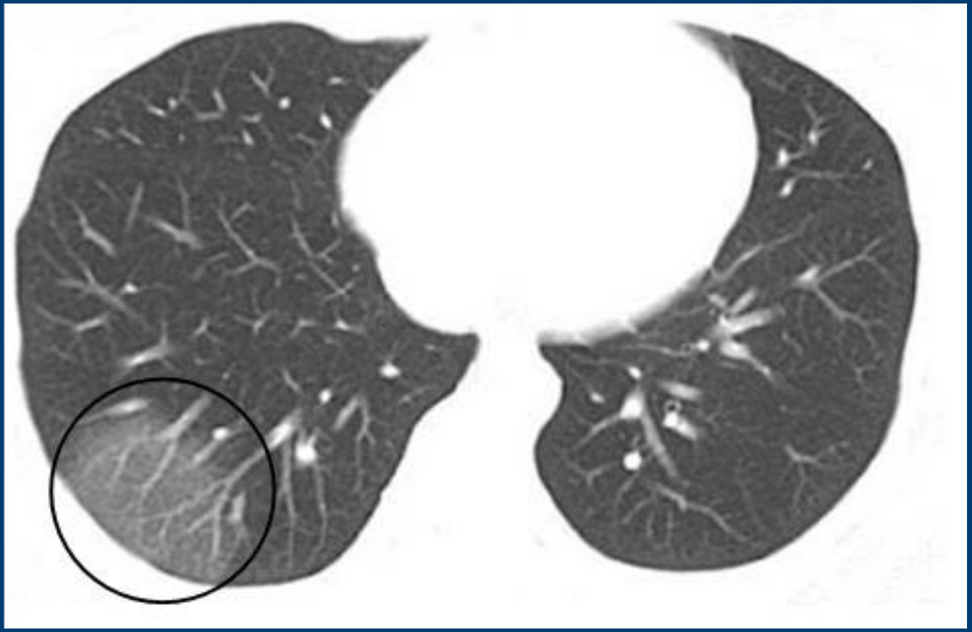
	Sensitivity %	Specificity %	AUC	P-value
COVID-19	90 (114 of 127) [83, 94]	96 (294 of 307) [93, 98]	0.96 [0.94, 0.99]	<0.001
CAP	87 (152 of 175) [81, 91]	92 (239 of 259) [88, 95]	0.95 [0.93, 0.97]	<0.001
Non-Pneumonia	94 (124 of 132) [88, 97]	96 (291 of 302) [94, 98]	0.98 [0.97, 0.99]	<0.001

Lin Li at al. Artificial Intelligence Distinguishes COVID-19 from Community Acquired Pneumonia on Chest CT. Radiology, 2020 https://doi.org/10.1148/radiol.2020200905

AI to distinguish COVID in Chest X-Ray Exams

Chest X-Ray

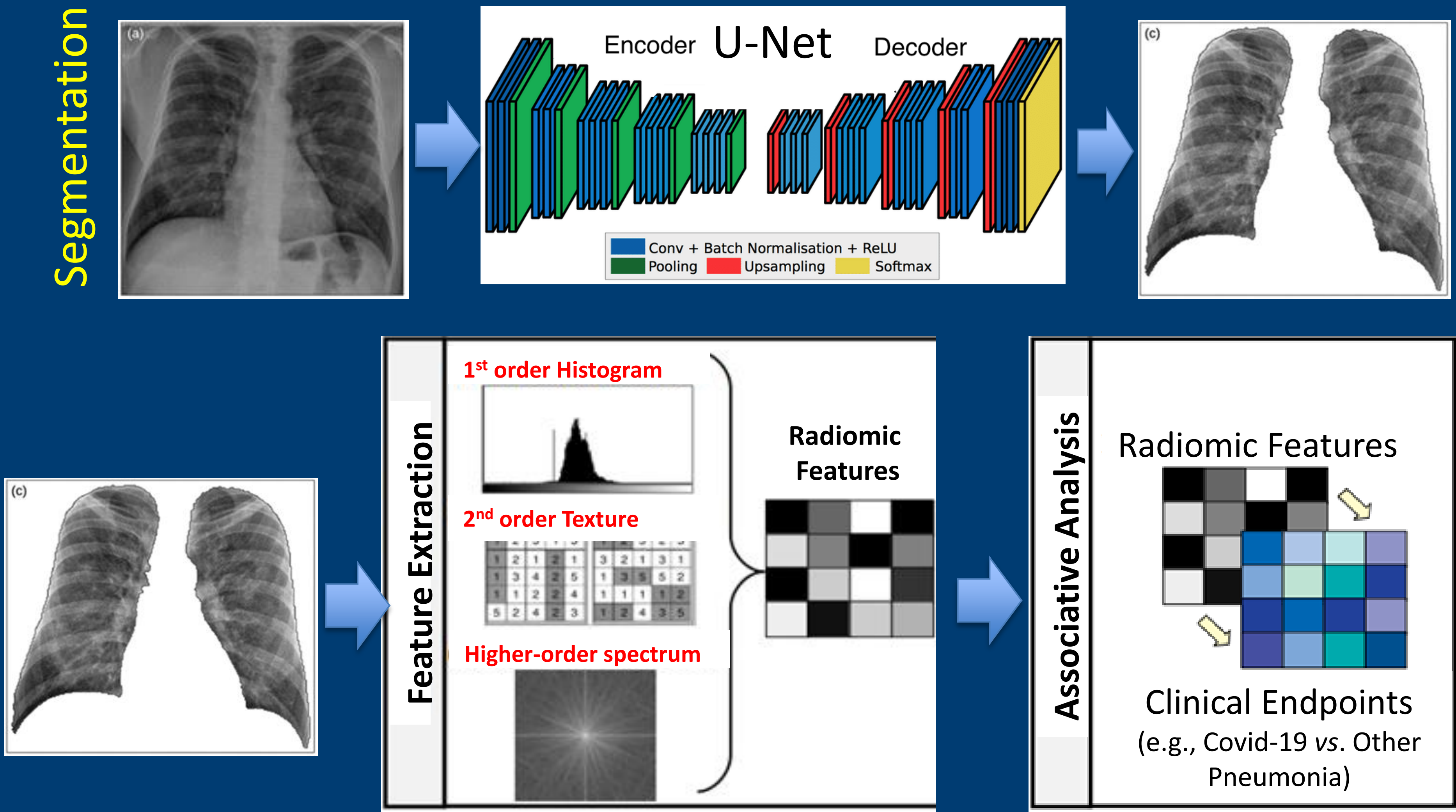
Chest CT



Chest CT is the gold standard image modality for detect COVID-19

Motivation: Chest CT is not available in some health centers in comparison with X-Ray, especially in low income countries.

AI to distinguish COVID in Chest X-Ray Exams

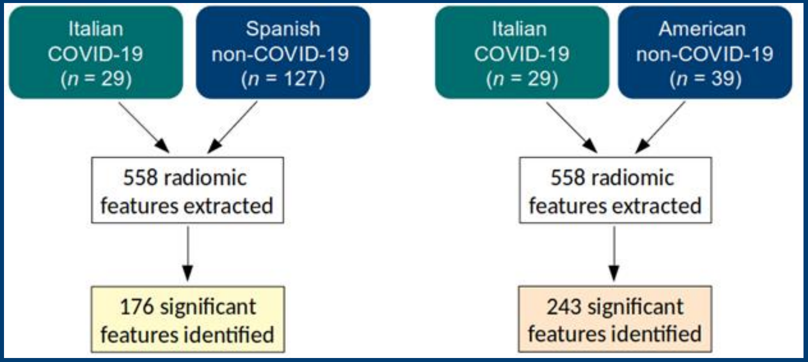


Ferreira Junior, JR et al. Radiographic biomarkers for COVID-19: A pilot radiomic study. Pre-print.

AI to distinguish COVID in Chest X-Ray Exams

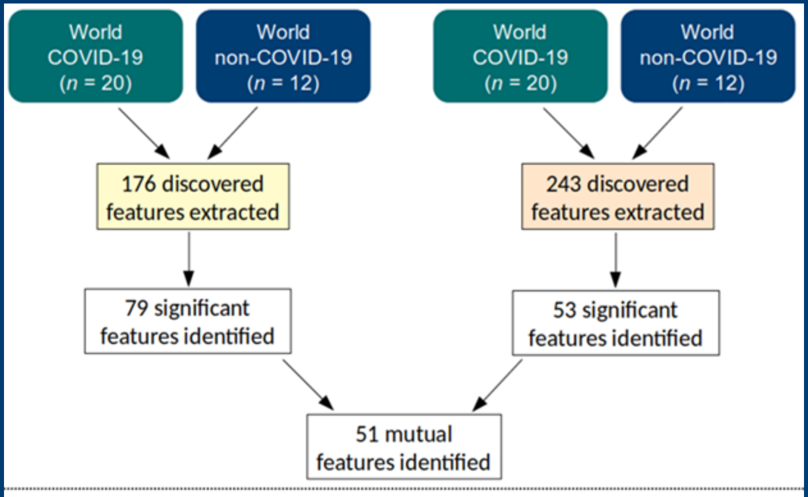
Discovery Datasets

- 29 patients with COVID-19 provided by the Italian Society of Medical and Interventional Radiology
- 127 cases of pneumonia non-related to COVID-19 from the Spanish chest XR cohort (PadChest dataset)
- 39 patients with pneumonia non-related to COVID-19 from the National Library of Medicine, National Institutes of Health (OpenI dataset)



Validation

- 32 patients from around the world. In this set, images and clinical data were initially collected from the literature by researchers of the University of Montreal
- Then it was completed with follow-up data (survival time, imaging and event dates) by us to perform the radiomic analysis
- From those 32 patients, 20 had the diagnosis confirmed for COVID-19 by RT-PCR, and 12 from a different etiology



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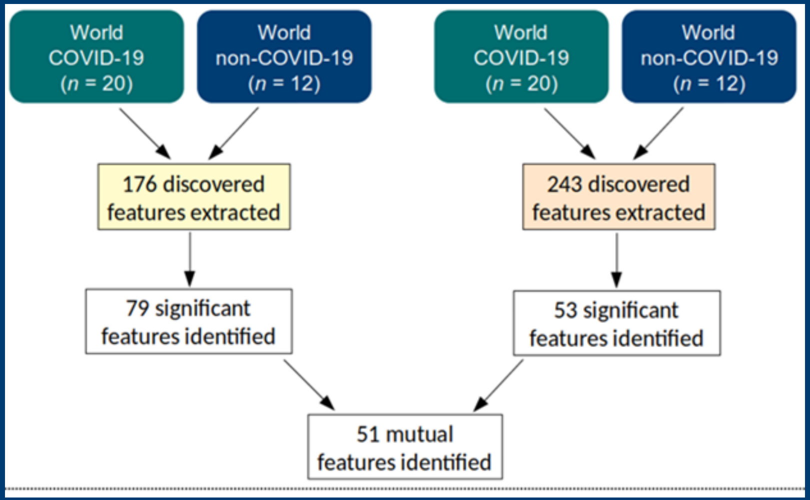
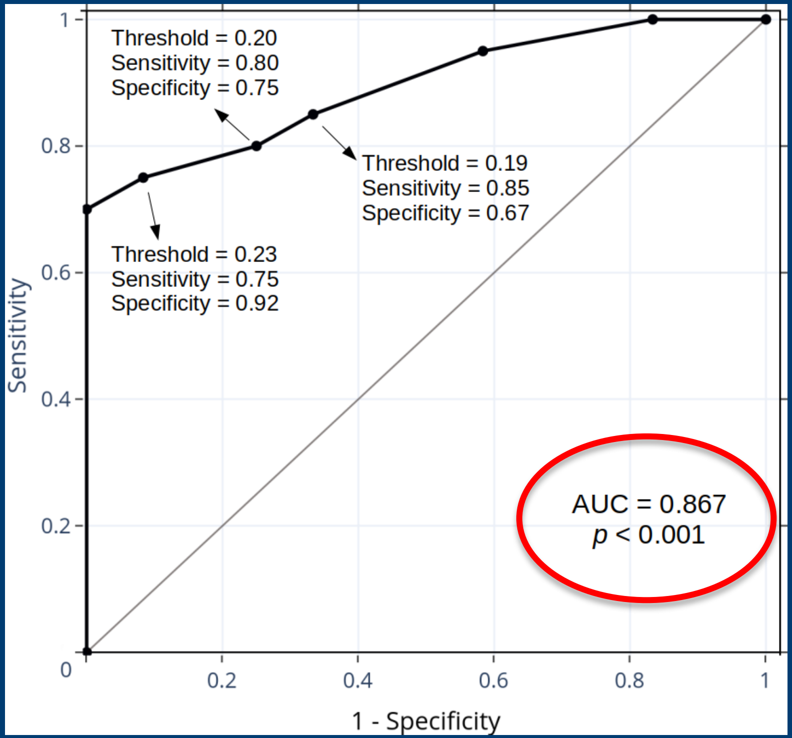
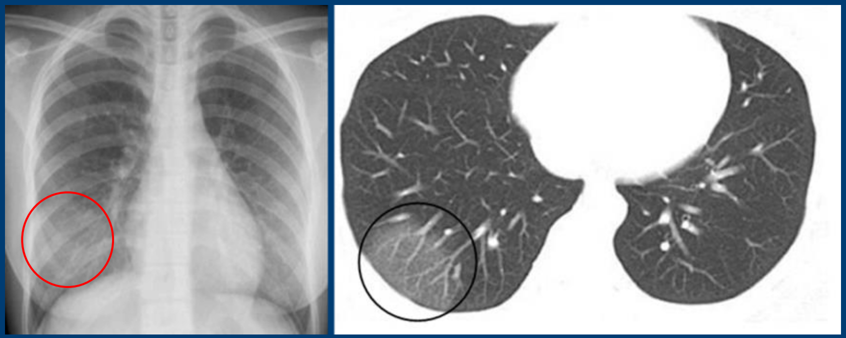
AI to distinguish COVID in Chest X-Ray Exams



Top features ROC curve





Ferreira Junior, JR et al. Radiographic biomarkers for COVID-19: A pilot radiomic study. Pre-print.

Summary of AI methods for COVID-19 diagnosis using radiology images

Ref.	DATA	AI Method	Performance
[6]	4,356 chest CT exams, 3,322 patients from 6 medical centers: 1,296 exams for COVID-19, 1,735 for CAP and 1,325 for non-pneumonia	A 3D convolutional ResNet-50 (COVnet)	AUC 0.96 for detecting COVID-19
[7]	970 CT volumes of 496 patients with confirmed COVID-19 and 1,385 negative cases	2D deep CNN	ACC 94.98% and AUC 97.91%
[8]	1,341 normal, 1,345 viral pneumonia, and 190 COVID-19 chest X-ray images	AlexNet [18], ResNet-18 [3], DenseNet-201 [19], SqueezeNet [20]	ACC 98.3%
[9]	5,941 Posterior-anterior chest radiography images across 4 classes (normal: 1,583, bacterial pneumonia: 2,786, non-COVID-19 viral pneumonia: 1,504, and COVID-19: 68)	Drop-weights based Bayesian CNNs	ACC of 89.92%
[10]	1,065 CT images (325 COVID-19 and 740 viral pneumonia)	Modified INCEPTION transfer-learning model	Sensitivity 0,67, Specificity 0.83, and ACC 79.3%
[11]	16,756 chest radiography images across 13,645 patient cases from two open access data repositories	A deep CNN, namely COVID-Net	ACC 92.4%
[12]	CT images of 1,136 training cases (723 positives for COVID-19) from 5 hospitals	A combination of 3D UNet++ and ResNet-50	Sensitivity 0.97 and specificity 0.922

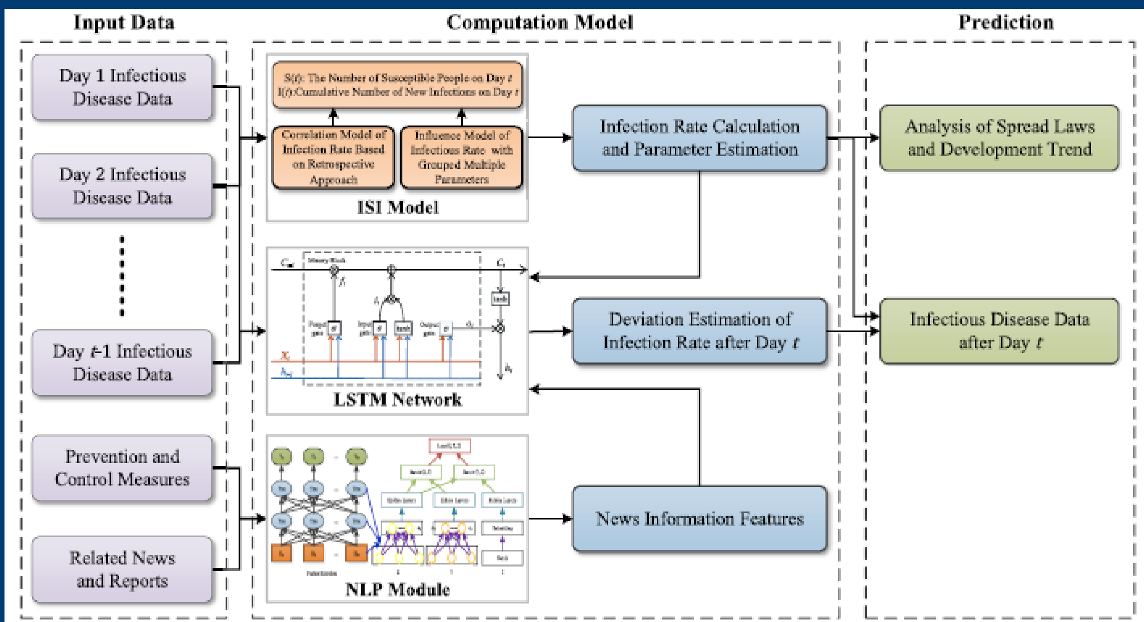
Supervised Learning : Regression problem

Predicting results within a continuous output

- Predicting inpatient mortality and long length of stay based on EHR Big Data
- Predicting the number of ER patients during a specific period, needed staff and beds based on past data
- Predicting patients' survival rates based on health conditions, age, and other characteristics

AI hybrid model to predict COVID-19

- Combination of Improve Susceptible–Infected (ISI) model, Natural Language Processing (NLP) module and the Long Short-Term Memory (LSTM) network are embedded to predict COVID-19



	ISI	ISI+LSTM+NLP	GT
Feb.19	45,260	44,970	45,027
Feb. 20	45,997	45,504	45,346
Feb. 21	46,628	45,872	45,660
Fed. 22	47,138	46,163	46,201
Feb. 23	47,532	46,265	46,607
Feb. 24	47,842	46,439	47,071
MAPE	1.62%	0.52%	----------

Zheng N., et al. Predicting COVID-19 using hybrid AI model. IEEE Trans Cybern. 2020 May 8. doi: 10.1109/TCYB.2020.2990162

Risk estimation for COVID from meta-analysis of symptoms and conditions

- Descriptive statistics of population groups from Singapore ILI study (H1N1, Seasonal Influenza, Influenza-) and Shanghai meta-analysis of patients with COVID-19 (30 retrospective obs. studies) (COVID-19 severe and non-severe)

Variable	A(H1N1/2009) (n=547)	Seasonal Influenza (n=193)	Influenza Negative (n=1943)	*P* Value
Age, y				
0-5	7.9	25.9	10.9	
6-18	41.5	15.5	14.9	
19-35	35.1	21.2	38.6	<.001
36-50	9.1	14.5	16.9	
≥51	6.4	22.8	18.7	
Male sex	57.4	60.6	54.7	.19
Fever	79.3	88.1	52.4	<.001
Cough	88.1	81.3	60.7	<.001
Sore throat	53.7	37.3	37.0	<.001
Rhinorrhea	49.9	53.9	37.0	<.001
Myalgia	20.3	15.0	14.6	.005
Headache	20.8	10.9	13.2	<.001
Dyspnea	0.5	6.7	2.1	<.001
Vomiting	1.1	2.6	1.7	.34
Diarrhea	0.7	0.0	1.9	.03

Prevalence of symptoms in *Pandemic(H1N1/2009)*, *Seasonal Influenza* and *Influenza Negative* groups. Reproduced from [1]

	Overall	Severity		
		Severe	Non-severe	P value
CFR, % (95%CI)	3.1 (1.9-4.2)	6.0 (4.6-7.3)	0.1 (0-0.2)	**<0.001**
Fever	79.1 (68.0-90.3)	88.4 (73.1-100.0)	81.4 (62.6-100.0)	0.552
Cough	58.0 (42.0-74.0)	71.1 (59.6-82.7)	65.7 (57.8-73.5)	0.449
Fatigue	29.3 (23.4-35.3)	60.3 (39.9-80.8)	44.2 (32.6-55.9)	0.181
Expectoration	11.5 (9.2-13.9)	37.6 (22.7-52.6)	28.0 (19.0-37.0)	0.281
Headache	6.0 (4.0-7.9)	11.3 (7.4-15.2)	13.5 (7.6-19.4)	0.542
Diarrhea	5.7 (3.9-7.5)	5.7 (3.1-8.4)	5.8 (3.3-8.3)	0.957
Myalgia	3.8 (2.4-5.2)	26.0 (11.1-40.9)	13.1 (8.4-17.8)	0.107
Shortness of breath	3.5 (2.2-4.9)	35.7 (17.8-53.7)	12.8 (4.7-20.9)	**0.023**
Sore throat/Pharyngalgia	3.2 (1.7-4.6)	7.8 (0-16.1)	9.7 (4.0-15.4)	0.706
Nausea or vomiting	2.0 (1.0-2.9)	5.9 (3.1-8.7)	5.7 (2.3-9.0)	0.928
Chill	1.1 (0.3-1.9)	26.0 (8.9-43.1)	10.9 (9.0-12.9)	0.087
Nasal congestion/Rhinorrhoea	1.1 (0.3-1.9)	2.8 (0.4-5.2)	5.1 (3.8-6.3)	0.097
Dyspnea	1.0 (0.3-1.7)	44.2 (7.8-80.6)	5.7 (0-10.7)	**0.042**
Anorexia	1.0 (0.4-1.7)	14.9 (8.3-21.5)	8.2 (2.4-13.9)	0.135
Dizziness	0.1 (0.0-0.5)	16.1 (3.5-28.8)	12.1 (5.0-19.2)	0.591
Any comorbidity, % (95% CI)	37.1 (28.1-46.1)	54.9 (37.2-72.6)	27.6 (19.4-35.8)	**0.006**
Specific comorbidity, % (95% CI)				
Hypertension	19.0 (13.2-24.9)	29.4 (24.8-34.1)	16.1 (11.5-20.7)	**<0.001**
Diabetes	8.2 (6.3-10.0)	17.2 (13.4-20.9)	5.8 (3.4-8.1)	**<0.001**
CVD	2.7 (1.4-4.1)	6.9 (3.9-9.8)	2.1 (1.4-2.9)	**0.002**
Cerebrovascular disease	1.0 (0.3-1.6)	3.0 (1.2-4.9)	0.9 (0.4-1.3)	**0.031**
COPD	0.6 (0.3-0.9)	4.1 (1.8-6.3)	0.7 (0.2-1.1)	**0.004**

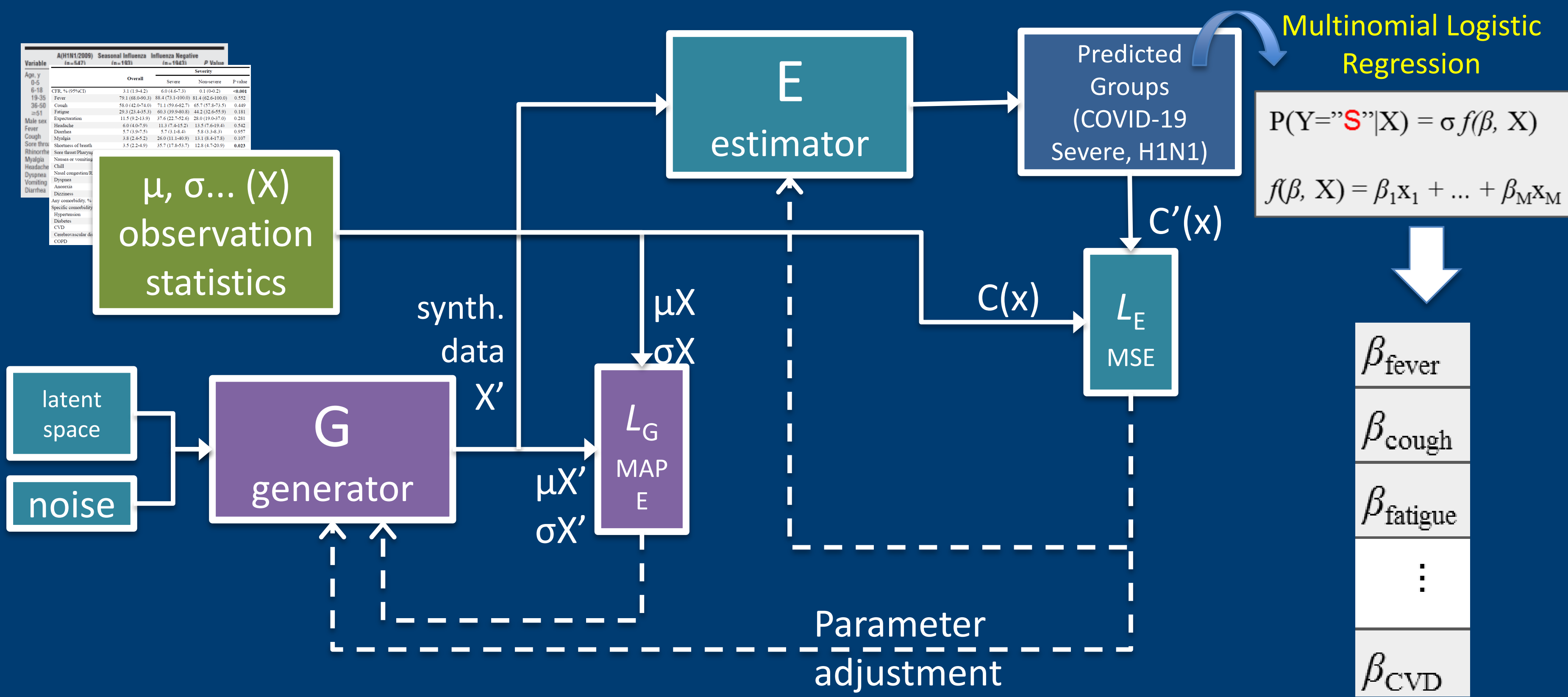
Fatality Rates and Prevalence of symptoms and conditions in *Severe* and *Non-severe* COVID patients. Excerpt from [2]

1. Tang J. et al. Differing Symptom Patterns in Early Pandemic vs Seasonal Influenza Infections. Arch Intern Med 170(10):861-867. 2010 May 24. doi:10.1001/archinternmed.2010.108

2. Ma C. et al. Incidence, clinical characteristics and prognostic factor of patients with COVID-19: a systematic review and meta-analysis. medRxiv preprint. 2020 March 20. doi:10.1101/2020.03.17.20037572

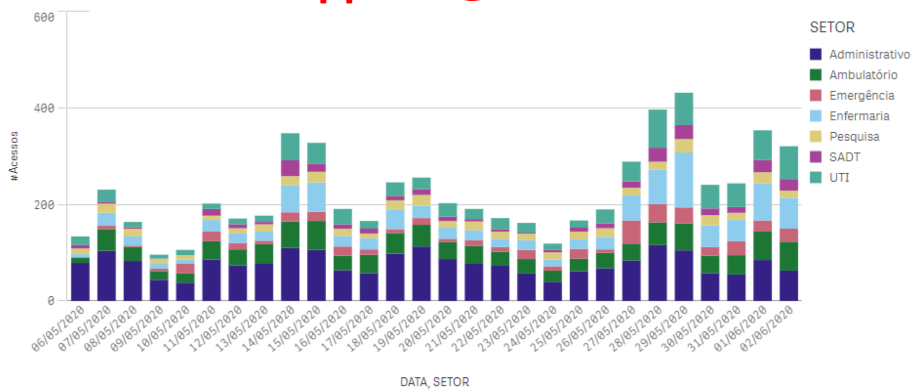
Risk estimation for COVID from meta-analysis of symptoms and conditions

- ReGEN: ReGenerative Estimator Neural Network
  - synthesizer + estimator neural network, inspired by GANs (Goodfellow et al 2014)



COVIDuc (COVID Under Control Score)

COVIDuc applied @ Heart Institute



#Acessos
6.298

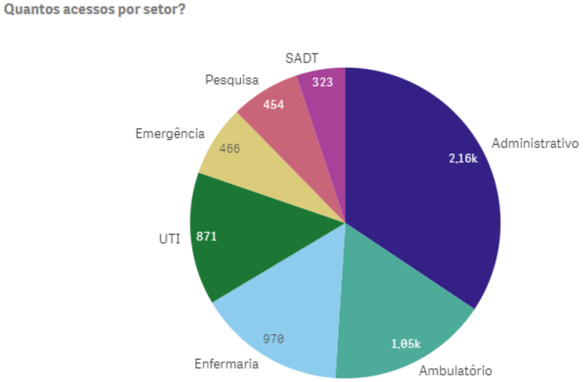
#Pessoas
1.436

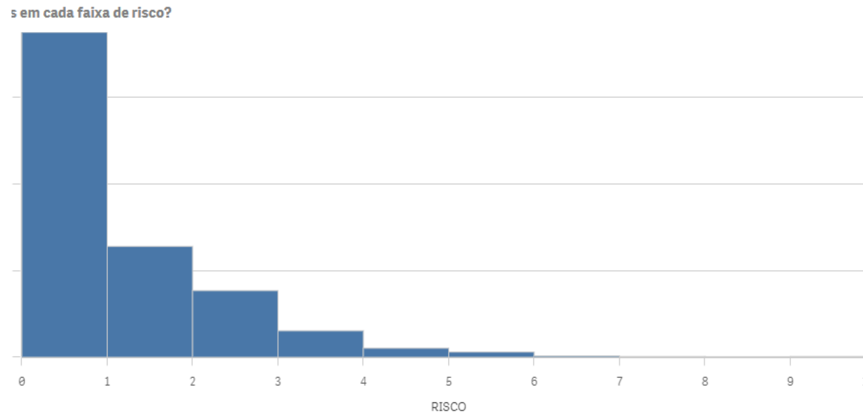
#Risco3+
281

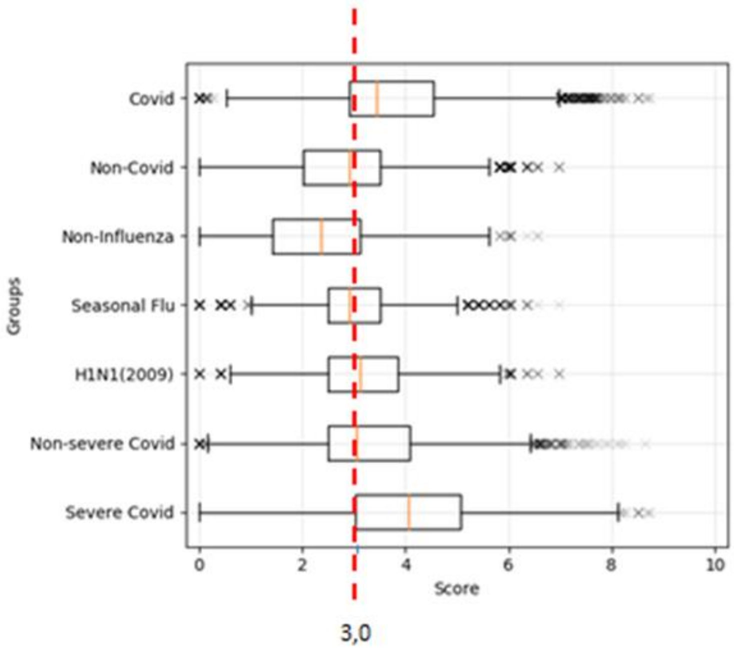
Méd. Acessos/Pessoa
4,39

RiscoMed
1,03

RiscoMax
9,53





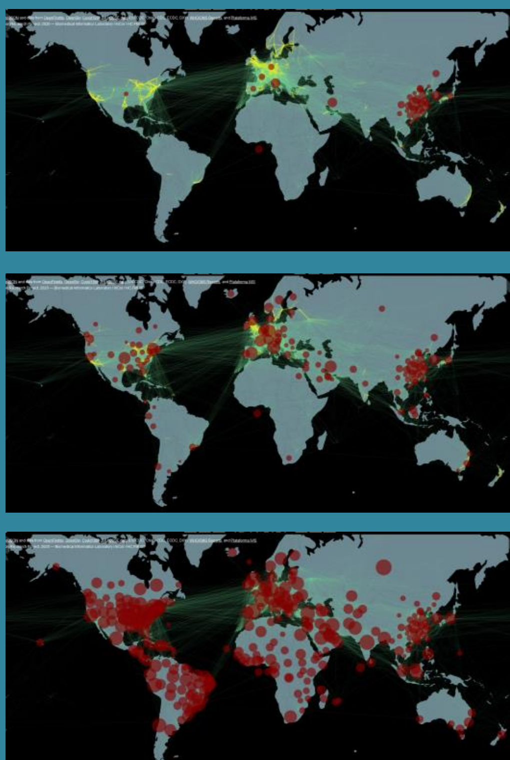


Risk if COVIDuc > 3,0 !

COVID time series propagation

- Number of cases in each city
- Augmented with flight map (STGCN)

JHU + WHO nCov2019
+ OpenFlights/OpenSky



Temporal neural network models

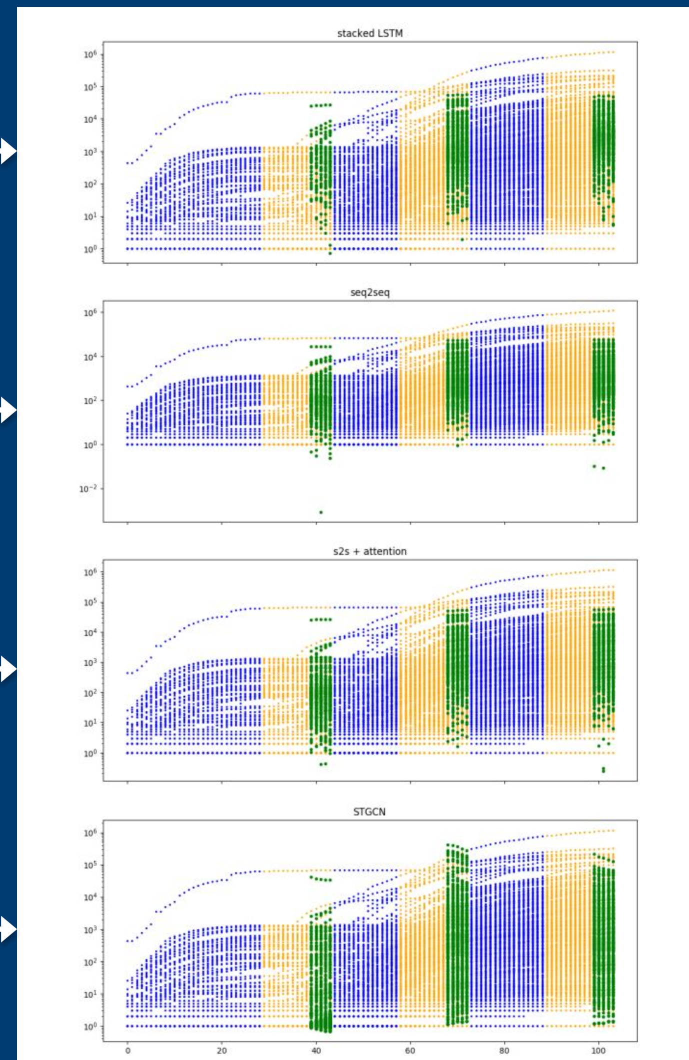
LSTM

Seq2Seq

Seq2Seq +Attention

STGCN

train | valid. | test



Benefits of AI for healthcare

- Deep learning has produced remarkable results for complex real-world problems that involve big data;
- It has the potential to provide data-driven, evidence-based clinical intelligence for advancing both biomedical research and service delivery;
- A new paradigm to derive insights on biological, diagnostic and therapeutic processes and behaviors from data;
- Accelerate the process of digesting and interpreting vast quantities of complex and diverse information.

Limitations of AI for healthcare

- AI is not an all-purpose solution
  - For tasks that require common-sense solutions or domain-specific expertise, and situations that are outside of the AI training dataset, it is less applicable.
- AI Weakness
  - AI identifies superficial features and patterns, but lacks the understanding of meanings and concepts;
  - Lacks common sense reasoning, general intelligence, and domain knowledge integration;
  - Needs big data, machine learning models are as good as the training data (biases, noises, errors often exist in real-world data);
  - Difficulty to generalize the findings beyond its training dataset.

Limitations of AI for COVID-19 outbreak screening

- AI technologies have penetrated into our daily lives with many successes, they have also contributed to helping humans in the extremely tough fight against COVID-19;

- AI Apps range from medical image diagnosis (Chest Rx & CT), virus transmission modelling and forecasting based on number of cases time series data, text mining and NLP;

- Although various studies have been published, we observe that there are still relatively limited applications and contributions of AI in this battle;

- This is partly due to the limited availability of annoteted data about COVID-19 and AI methods normally require large amounts of data for computational models to learn and acquire knowledge.

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Thank you!

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