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UNIVERSITÀ DEGLI STUDI DI BRESCIA

Realizing Trustworthy AI solutions for diagnosis and prognosis support

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Affiliations at University of Brescia

- Department of Medical and Surgical Specialties, Radiological Sciences, and Public Health (DSMC)
- [MediMint](https://medimint.unibs.it/): Medical Imaging and Multimodal Intelligence Laboratory
- [TRAIL](https://trail.unibs.it/) : Trustworthy AI Laboratory (multidepartmental)

Education

- 1997 MSc Electronics Engineering, University of Brescia
- 2001 PhD Information Engineering, University of Brescia
- 2019 Master in Management of Research, Innovation and Technology, Polytechnic of Milan

Main Courses taught at University of Brescia

- Image Data Analysis
- Law and Regulations for ICT
- Advanced Methods for Information Representation
- Artificial intelligence to aid medical diagnosis

Research interests

- Medical/Industrial image analysis
- Computer Vision/Graphics
- Machine/Deep Learning
- Signal/Image processing

Publications [\(Google Scholar page\)](https://scholar.google.it/citations?user=VQOouzYAAAAJ&hl=en)

Course Outline: AI systems in Health and Medicine

THE BASES: definitions, lexicon, taxonomy

THE WORKFLOW: the key steps of the AI pipeline

THE DATA CURATION: how to collect, prepare and feed data to AI systems

THE EXPERIMENTAL PHASES: how to lead or participate to the development and testing of new or existing AI-based solutions

THE DEPLOYMENT: ethical and regulatory aspects for reliable, explainable, trustworthy AI in health and medicine

The course in 5 pictures **The BASES**: definitions, lexicon, taxonomy

The course in 5 pictures **The WORKFLOW**: the key steps of the AI pipeline

The course in 5 pictures The DATA CURATION: how to collect, prepare and feed data

Ethical approval

Data selection

The course in 5 pictures **Participate**, The DEPLOYMENT: ethical and regulatory aspects for reliable,

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First: we need a shared language

<https://doi.org/10.3390/biomedinformatics2040049>

Artificial Intelligence vs Human intelligence

Performance

<https://doi.org/10.1038/s41568-018-0016-5>

Computer Vision vs Human Vision

A human expert easily classifies this image as an image of the right kidney.

Why is (**or was**) this task difficult for a computer?

Instead of shades of gray, a computer "sees" a matrix of numbers representing pixel brightness.

Computer vision typically involves computing the presence of **numerical patterns (features)** in this matrix, then applying **model-based** or **machine learning** algorithms to distinguish images on the basis of these features.

<https://doi.org/10.1148/rg.2017170077>

What is AI?

main definitions **Artificial Intelligence** (AI) *computer systems perform tasks that ordinarily require human intelligence.*

> **Machine Learning** (ML) *subfield of AI where algorithms can learn patterns from data, trough predetermined data features*

Representation Learning (RL) *a type of ML in which no feature engineering is used, but the algorithm learns on its own the best features to interpret data*

Deep Learning (DL) *a type of RL in which the algorithm learns a composition of features that reflect a hierarchy in the data interpretation structure.*

Foundation Models (FM) *large scale DL models trained on vast amount of data to serve as a base (foundation) of multiple applications*

Main definitions: The role of data and features in AI

- **Classic M**L depends on carefully designed features, requiring human expertise and complicated task-specific optimization.
- **DL systems** propose an end-to-end approach by learning simple features (such as signal intensity, edges, and textures) as components of more complex features such as shapes, lesions, or organs, therefore leveraging the compositional nature of images

Pattern (or feature) space

The pattern space dimensions are data channels/components or features extracted from data. Which features?

With **representation learning** the expectations is to learn good discriminative features for a given task in order to guarantee easy and accurate enough discriminations

Machine learning: kind of

Machine learning: kind of

Fitting data according to the kind of data/knowledge **Ensemble learning** Ensemble learning

Machine learning: methodological notes

Features describe the appearance of organs and points of interest in medical images. **Classifiers** integrate features to output a decision (eg. pixel-wise). **Shape extraction and regularization** recover a consistent shape despite classification noise. **Deep Learning** proposes an end-to-end approach where features are learned to maximize the classifier's performance. **Shape extraction** can become implicit (regularized pixel-wise info easy to obtain).

ML (learning from data to interpret new ones) vs Statistics (fitting to models to explain given data)

vice versa). For more insights [read at this link](https://towardsdatascience.com/the-actual-difference-between-statistics-and-machine-learning-64b49f07ea3) and [this other one](https://towardsdatascience.com/how-is-machine-learning-different-from-statistics-and-why-it-matters-5a8ed539976)

<https://www.turing.com/kb/introduction-to-statistics-for-machine-learning>

The *supervised* Machine Learning paradigm

https://odsc.com/blog/the-comprehensive-guide-to-model[validation-framework-what-is-a-robust-machine-learning-model/](https://odsc.com/blog/the-comprehensive-guide-to-model-validation-framework-what-is-a-robust-machine-learning-model/) <https://www.v7labs.com/blog/train-validation-test-set>

- Although neural networks were known and used for decades, in recent years three **key factors** have enabled the training of large neural networks:
	- **i. the possible availability of large quantities of labeled data**,
	- **ii. cost-effective inexpensive and powerful parallel computing hardware**,
	- **iii. improvements in training techniques and architectures**.
- Artificial neural networks **are inspired by biologic neuron activation** process and from what we know about the structure of the **visual cortex** (a).
- The artificial neuron (b) takes as an input a set of values representing features, each multiplied by a corresponding weight. The **weighted features are summed and passed through a non-linear activation function**. In this way, an artificial neuron can be viewed as producing an **activation** decision by weighing a set of evidence.

Artificial Neural Network Structure (layers > deep)

Number of parameters

WEIGHTS & BIAS \ parameters to be estimated for every neuron

https://www.youtube.com/watch?v=Tsvxx-GGlTg

- Although an individual artificial neuron is simple, neural network architectures called **multilayer perceptrons** (MLP) that consist of thousands of neurons can represent very complex nonlinear functions.
- These multilayer perceptrons are typically constructed by assembling multiple neurons to form **layers** and by stacking these layers connecting the output of one layer to the input of the following layer. This produces a **hierarchy of features** that are an increasingly complex composition of low-level input features, thereby modeling higher levels of abstractions in the data.
- **MLPs perform poorly on images** in which the object of interest tends to vary in shape, orientation, and position because they must encode redundant representations for the many feature arrangements that this results in.

- A neural network is **trained** by adjusting the parameters, which consist of the weights of each node. Modern neural networks contain millions of such parameters.
- Starting from a random initial configuration, the parameters are adjusted via an optimization algorithm called **gradient descent**, which attempts to find a set of parameters that performs well on a **training dataset**.

https://www.embedded.com/training-convolutional-neural-networks/

Learning process. Weights used by artificial neurons can be billions within a deep neural network. These parameters, are randomly initialized, are progressively adjusted via an optimization algorithm called *gradient descent*. When presenting a series of training samples to the network, a *loss function* measures quantitatively how far the prediction is to the target class or regression value. All parameters are then slightly updated in the direction that will favor minimization of the loss function.

with 3 hidden layers: each connection carries a weight. and each neuron an additional one.

Learning algorithm

- 1. Present a batch of training samples to the network to evaluate a prediction based on its current configuration.
- Evaluate the loss function by comparing the output prediction with the $2.$ target values or classes.
- 3. Compute the gradient of the loss function with respect to every parameter of the model.
- Update the weights of the model. $4.$
- Repeat steps 1 to 4 until the loss function reaches a minimum. 5.

<https://doi.org/10.1148/rg.2017170077>

Convolutional Neural Networks

 4×4

LearnOpenCV.com

 6×6

$3 \times 1 + 1 \times 1 + 2 \times 1 + 0 \times 0 + 5 \times 0 + 7 \times 0 + 1 \times -1 + 8 \times -1 + 2 \times -1 = -5$

Image Filtering Using Convolution in OpenCV

- For processing images, a deep learning architecture known as the *convolutional neural network* (CNN) has become dominant (from 2012 CNNs of increasing complexity kept winning popular image classification competitions even exceeding human performance).
- **CNNs introduces some robustness to image variations** by passing each feature detector over every part of the image in a **convolution operation**. Each feature detector is limited to detecting local features in its immediate input, which is acceptable for natural images.
- Since a feature may occur anywhere in the image, the filters' weights are shared across all the image positions. Thus, image features can be modeled with fewer parameters (shared kernel weights for all spatial positions), increasing model efficiency.

Convolutional Neural Networks

Original image at 512 x 512 pixels

- CNNs were inspired by **early findings on biological vision** by Hubel & Wiesel in 1962 and from an early artificial NN called Neocognitron by Fukushima in 1979.
- In CNNs, **multiple different convolutional filters are learned for each layer**, yielding many different feature maps, each highlighting where different characteristics of the input image or of the previous hidden layer have been detected.
- In a CNN, the deeper the layer of representation, the coarser the characterization of the feature's spatial position (due to downsampling/pooling); thus, kernels in these deeper layers consider features over increasingly larger spatial scales.

Typical examples of feature maps extracted with different kernels

Internal feature map representation of 32 x 32 pixels

Convolutional Neural Networks

Pooling Pooling

The **final classification** task relies on a rich set of hidden features that represent a large receptive field and integrate multiscale information in a meaningful way.

Stacking multiple convolutional and max pooling layers allows the model to learn a hierarchy of feature representations.

- Neurons close to the input image are activated by the presence of edges and corners formed by a few pixels.
- Neurons located deeper in the network are activated by combinations of edges and corners that represent characteristic parts of organs and eventually whole organs.
- At each successive level of representation, neurons gain a larger receptive field in the input image.

CNNs for segmentation (coding+decoding)

- If **pixel-level outputs** are desired, we have to **upsample** the features again
	- e.g. to obtain semantic level maps, typically pixel-wise semantic classification (or segmentation, or contouring)
- Why we need downsampling (coding) first and then upsampling (decoding)?
	- Downsampling provides strong features with large receptive field (quick information aggregation with limited number of network parameters)
	- Upsampling yields output at the same resolution as input
	- Usually skip connections are used, like in ResNet, but longer, as we will see in U-Nets
		- Skip connections allow maintaining high level of accuracy related e.g. to object boundaries

CNNs for segmentation (coding+decoding)

Multiregion segmentation of bladder cancer structures in MRI with progressive dilated convolutional networks, J.Dolz et al., Medical Physics, 2018 <https://doi.org/10.1002/mp.13240>

The AI "epochs" categorization

 -1000

JAMA | Special Communication | AI IN MEDICINE

Three Epochs of Artificial Intelligence in Health Care

Jan 2024Michael D. Howell, MD, MPH; Greg S. Corrado, PhD; Karen B. DeSalvo, MD, MPH, MSc

JAMA. 2024;331(3):242-244. doi:10.1001/jama.2023.25057

Single task VS Foundation (generative) AI

Single Task DL Models

Typical technology *Convolutional Neural Networks*

(are a kind of Deep Neural Network)

Foundation Models

Typical technology *Transformers* (are a kind of Deep Neural Network)

The "big-mix" of AI 2.0 AI in medicine

Countless combinations among

- **Algorithms**
- **Tasks**
- **Applications** are possible.

The need of a sound partnership between **technical** (computer scientists, information engineers, data scientists) and **clinical** specialties (physicians, medical technologists, biologists, physicists,…) is evident.

Litjens, G. et al. J Am Coll Cardiol Img. 2019;12(8):1549-65.

Interpretation tasks

Classification: liver metastases

Semantic segmentation

Liver metastases \Box No metastasis

Object detection

Instance segmentation

\Box Metastasis 1 \Box Metastasis 2 \Box Metastasis 3

Metastasis 4

Interpretation tasks: diagnostic imaging

• Classification

allows to associate a "class" (output) to a given data (input). If the choice is among 2 classes we say *binary* classification, otherwise we say *multiclass*

• Detection

allows to localize a given object or a plurality of them by means of bounding boxes and to associate a class label to each of them.

• Segmentation (semantic)

allows to label every pixel in an image as to belonging to one of the available classes. Is a pixel-wise classification. Semantic segmentation can also be contour-aware (in this case we can say *contouring*)

• Segmentation (instance)

like semantic segmentation with the possibility to differenciate different instances of the same object (in this case it is necessarily contour-aware).

Interpretation tasks: non-image data sources

Interpretation tasks: non-image data sources

Deep Learning Classifier Process

https://doi. org/10.1371/journal.pone.0268880

Interpretation tasks: non-image data sources

<https://doi.org/10.1016/j.patcog.2020.107561>

Organ-based/pathology-driven tasks

Composite interpretation tasks: multi-network approach

AI-driven evaluation of the «Brixia score» for COVID-19 pneumonia severity assessment https://brixia.github.io

-
- **Score 1**: interstitial infiltrates
- **Score 2**: interstitial and alveolar infiltrates (interstitial predominance)
- **Score 3**: interstitial and alveolar infiltrates (alveolar predominance)

 $\overline{2}$

 $\overline{2}$

Foundation Models (FM)

Data source/sources AI 3.0 Text **Foundation Models** Images **Foundation Training Model GATHER DATA AT SCALE** Speech **TRAIN FOUNDATION MODEL ONE TIME** Structured **EVALUATE MODEL'S PERFORMANCE** nnn Data **Core**

Application driven tasks (not defined in advance)

(general)

task

FM: Large Language Models

Generalist/Generative tasks in medicine

Perspective

Foundation models for generalist medical artificial intelligence

Generalist/Generative tasks: based on LLMs

Free Text

<https://doi.org/10.1148/radiol.223312>

HISTORY: A 42-year-old female presents with shoulder pain. COMPARISON: None available. TECHNIQUE: A 3T MRI of the right shoulder was conducted, using a variety of sequences, including axial proton density with fat saturation, axial GRE, coronal proton density with fat saturation, coronal T2 with fat saturation, coronal T1, sagittal T2 with fat saturation, and sagittal T1. FINDINGS: The MRI reveals preserved articular cartilage and hematopoietic bone marrow. The acromioclavicular joint displays mild to moderate degenerative changes, with inferior joint capsule hypertrophy and enthesophytes causing mass effect on the underlying supraspinatus tendon. The coracoacromial ligament appears mildly thickened. Bone marrow edema is present within the clavicle, likely due to osteoarthritis, but may also be indicative of early distal clavicular osteolysis. A small amount of flui edema can be seen within the subacromial/subdeltoid bursa, which may suggest bursitis. No glenohumeral joint effusion is observed. Mild tendinopathy is present in the supraspinatus, infraspinatus, and subscapularis tendons The supraspinatus tendon also exhibits mild bursal-sided fraying. The teres minor tendon appears normal. The biceps tendon and anchor are intact. Evaluation of the labrum is limited due to lack of joint fluid. A tear of th superior labrum, posterosuperiorly, is identified. Incidentally noted are breast implants. IMPRESSION: Posterosuperior superior labral tear. Bone marrow edema in the clavicle, likely secondary to osteoarthritis but possibl to early changes of distal clavicular osteolysis. Mild tendinopathy in the supraspinatus, infraspinatus, and subscapularis tendons. Mild to moderate degenerative changes in the acromioclavicular joint.

Generative tasks: imaging (both A2.0 and A3.0 approaches)

Reconstruction (Brain MRI De-Aliasing)

De-noising (Cardiac CT)

(Brain MRI to CT)

Current frontiers: generative text-to-video

Impressive… but still "statistics" (no evidence of "meaning appropriation")

Prompt: A grandmother with neatly combed grey hair stands behind a colorful birthday cake with numerous

candles at a wood dining room table, expression is one of pure joy and happiness, with a happy glow in her eye. She leans forward and blows out the candles with a gentle puff, the cake has pink frosting and sprinkles and the candles cease to flicker, the grandmother wears a light blue blouse adorned with floral patterns, several happy friends and family sitting at the table can be seen celebrating, out of focus. The scene is beautifully captured, cinematic, showing a 3/4 view of the grandmother and the dining room. Warm color tones and soft lighting enhance the mood.

Prompt: Archeologists discover a generic plastic chair in the desert, excavating and dusting it with great care.

Parameter trends

https://hua-hua.org/large-

AI in medicine: current "directions"

Other higher complexity dimensions still to be fully explored, e.g.:

- **Multimodality** (what, where, when)
- **Preventive medicine** (patient timeline)
- **Affordable size Foundation Models**

Progress, challenges and opportunities for AI in health

- Progresses
	- Almost all medical specialties have been impacted by AI: not only diagnosis but also risk prediction and treatment
	- Not only experimental: growing market of deployed (FDA or CE certified) AI products
- Opportunities
	- Multimodal data fusion (not only images)
	- Not only supervised learning: many possible
"learning" paradigms (full data labeling can be too expensive/time consuming)
	- Not only human vs machine: collaborative approaches, human-in-the-loop
- Challenges
	- Implementation: data/label acquisition costs, dataset dimensions, data biases
	- Regulation: locked vs continual learning, accountability, explainability
	- Ethics: fairness, privacy, equity, do not harm