Computing Methods for Experimental Physics and Data Analysis

Data Analysis in Medical Physics

Lecture 8: DL applications on medical images: CNN for image categorization; CAE for image segmentation, and course summary

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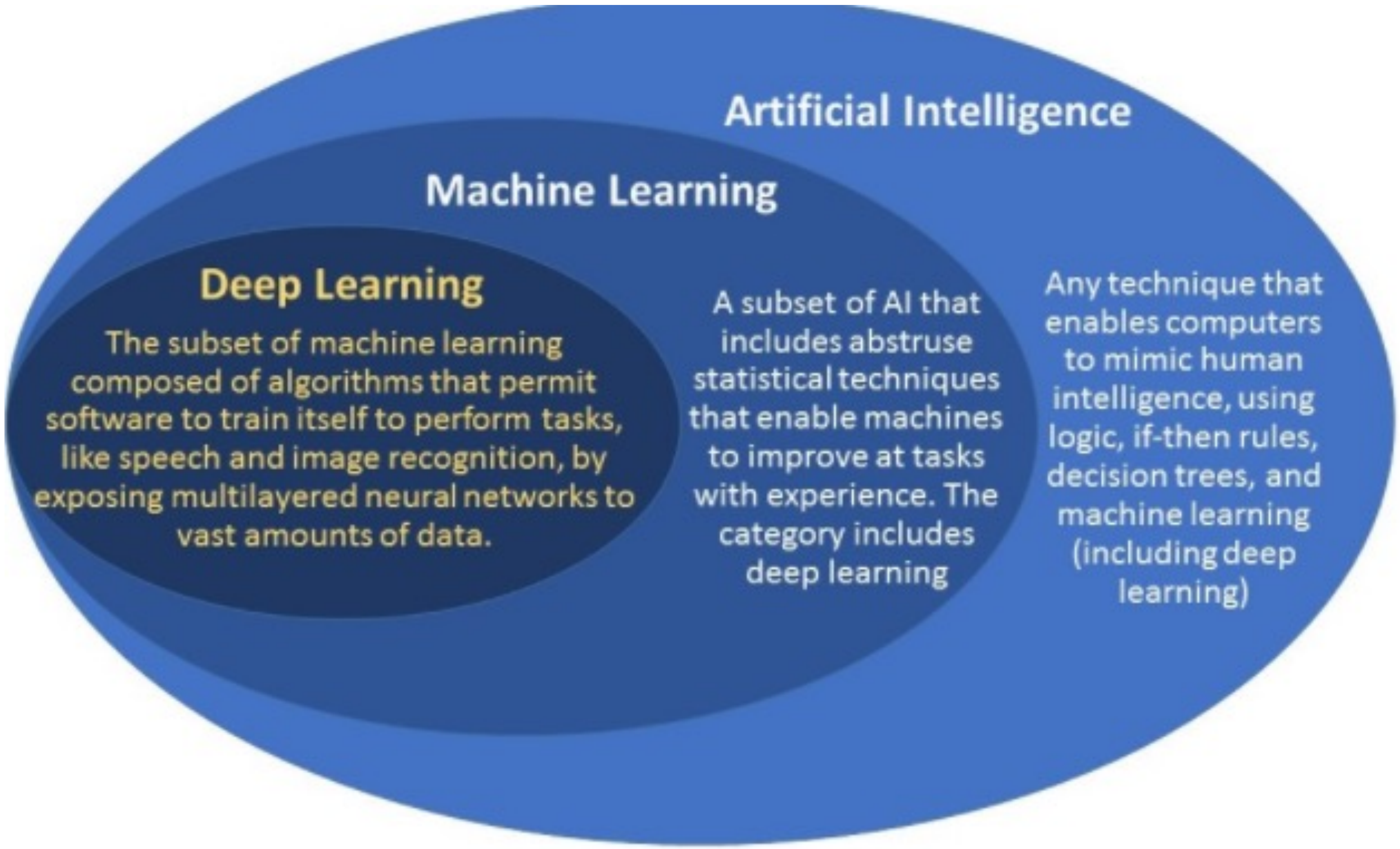
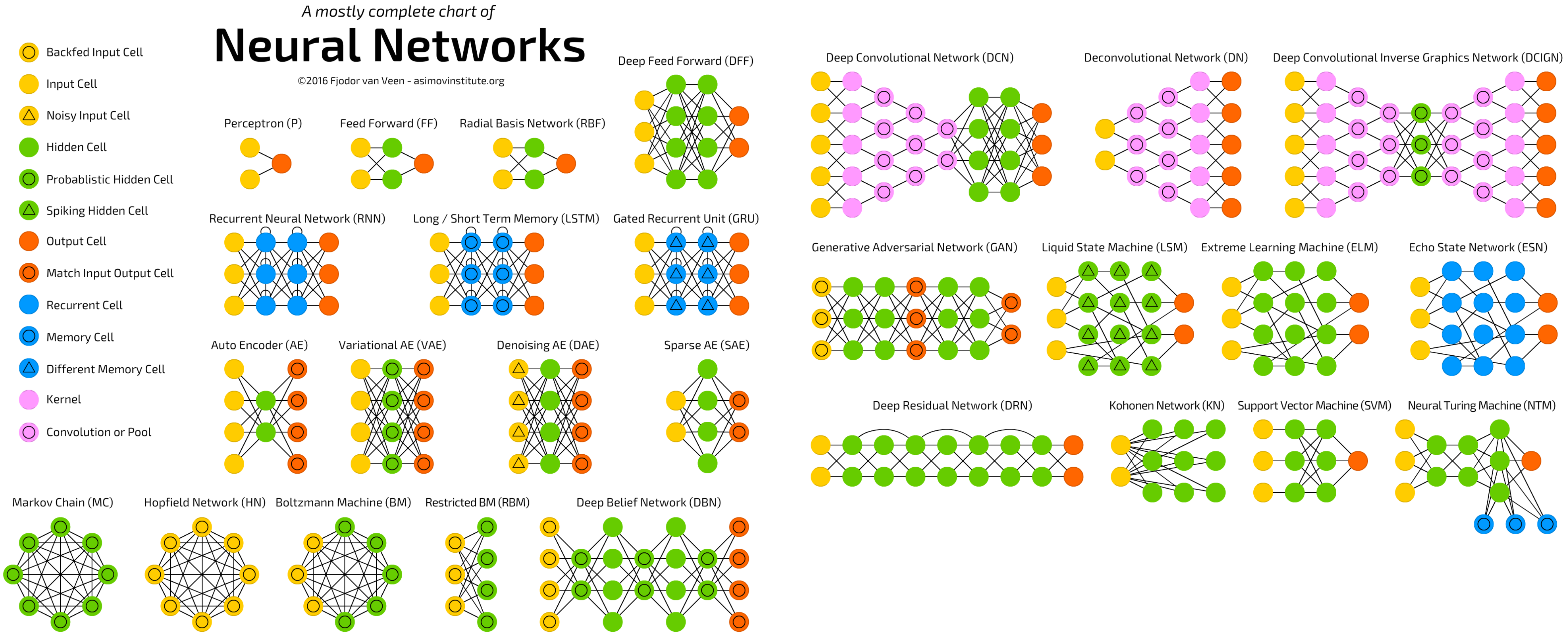
Artificial Intelligence, Machine Learning, Deep Learning



https://www.deeplearningitalia.com/una-panoramica-introduttiva-su-deep-learning-e-machine-learning/

Neural network Zoo

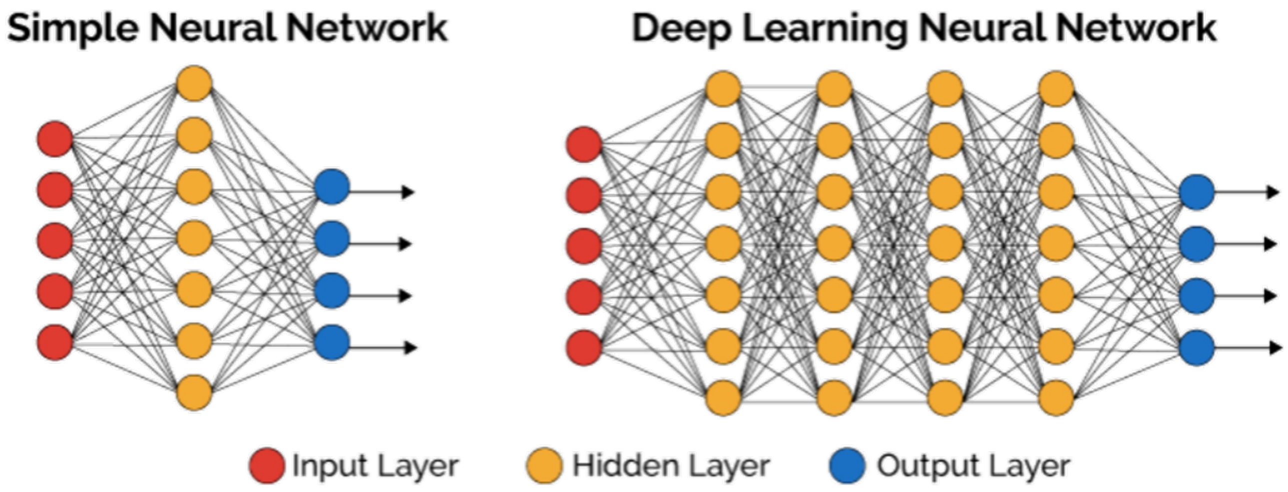


http://www.asimovinstitute.org/neural-network-zoo/

Deep Neural Networks

Deep Learning (DL) means using a neural network with several layers of nodes between input and output

DL models are a family of parametric models which learn non-linear hierarchical representations



$$a_L(\mathbf{x};\mathbf{\Theta}) = h_L(h_{L-1}(\ldots(h_1(\mathbf{x},\boldsymbol{\theta}_1),\boldsymbol{\theta}_{L-1}),\boldsymbol{\theta}_L)$$

input

parameters of the network

non-linear activation function

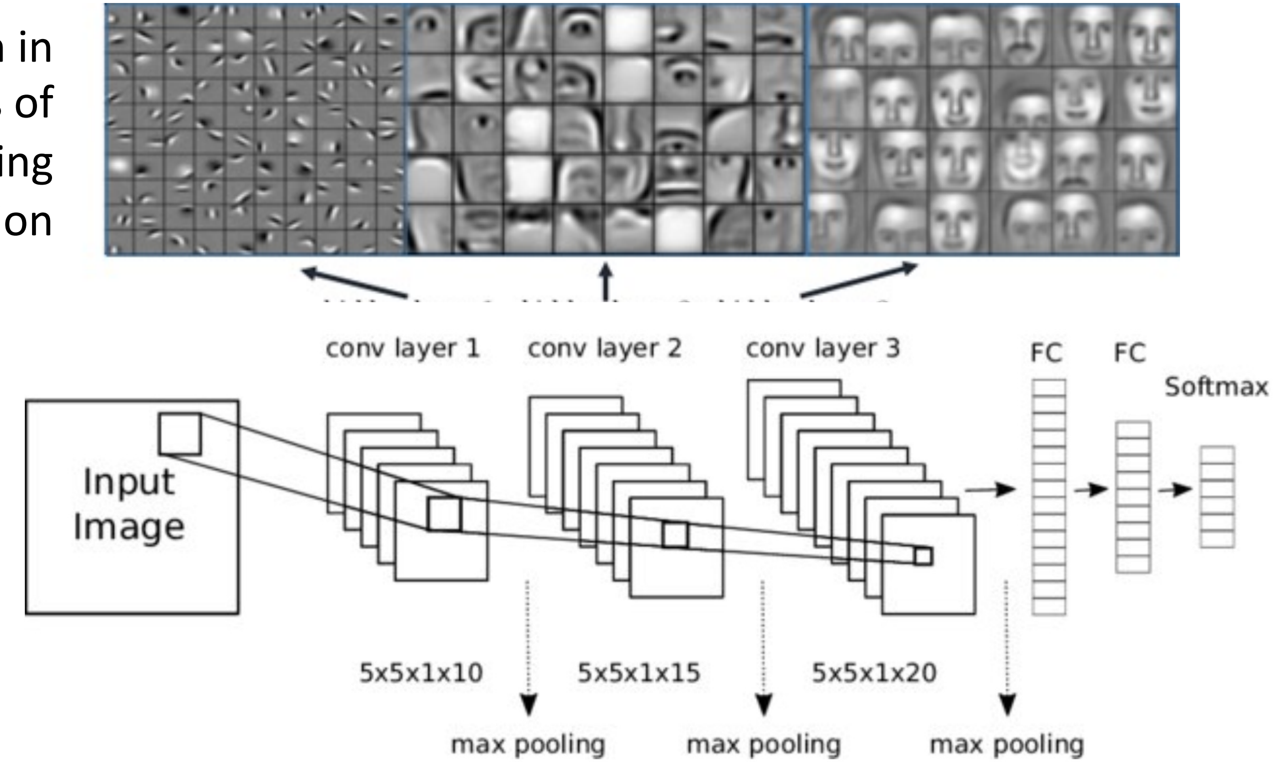
parameters of layer *L*

Deep Neural Networks

- Deep neural networks are generally better than other ML methods on images
- The series of layers between input and output compute relevant features automatically in a series of stages, just as our brains seem to do.

Deep neural networks learn in multiple levels of representation, corresponding to different levels of abstraction

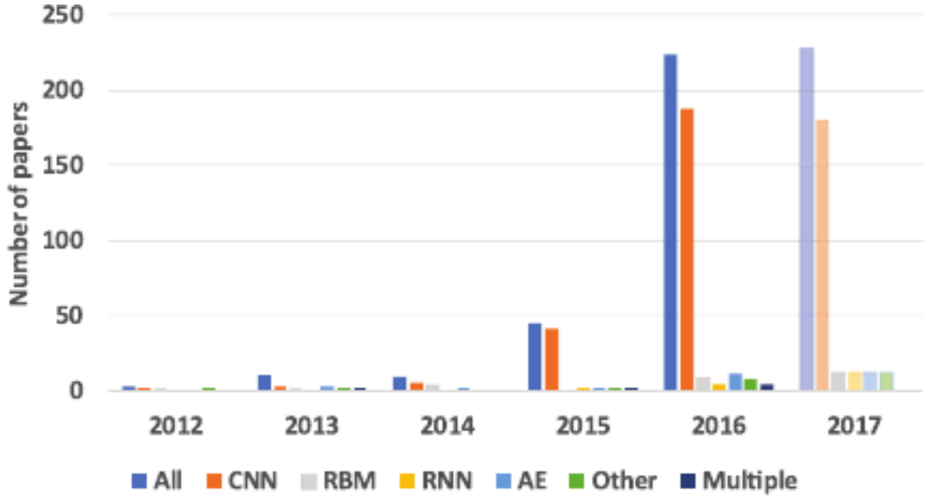
https://towardsdatascience.com

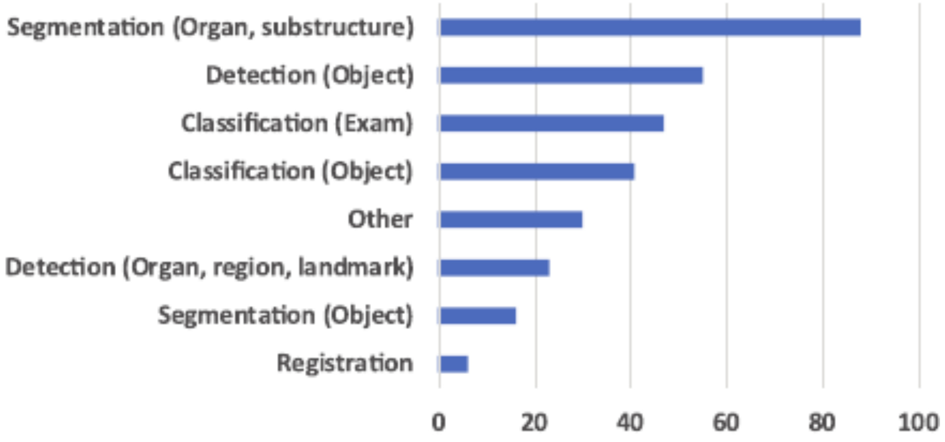


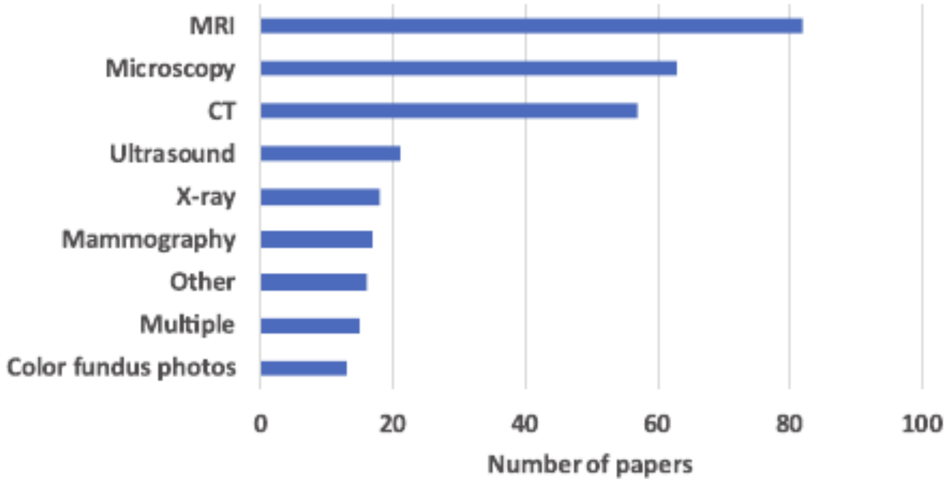
See demo code on L8_code/Lecture8_demo_train_CNN.m, Lecture8_demo_visualizing_CNN_layers.mlx

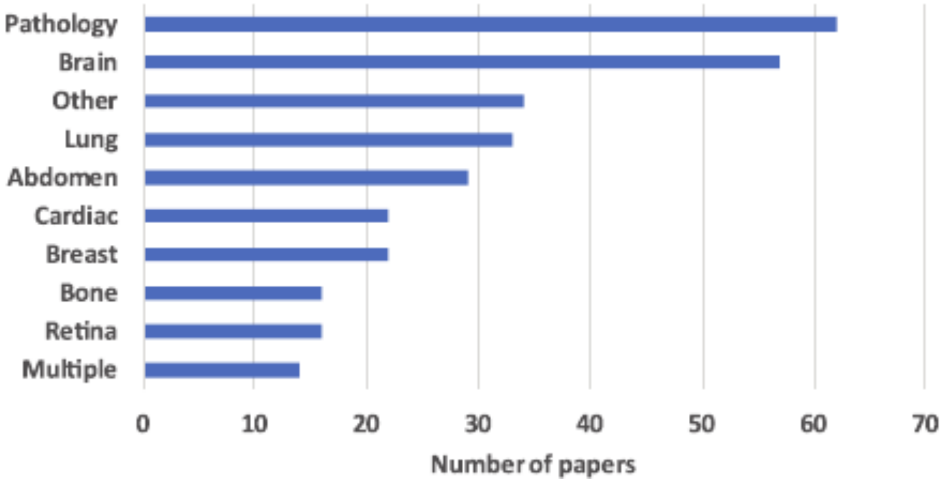
Deep Learning has become very popular in Medical Imaging

G. Litjens et al., A survey on in deep learning medical image analysis, Medical Image Analysis 42 (2017) 60–88









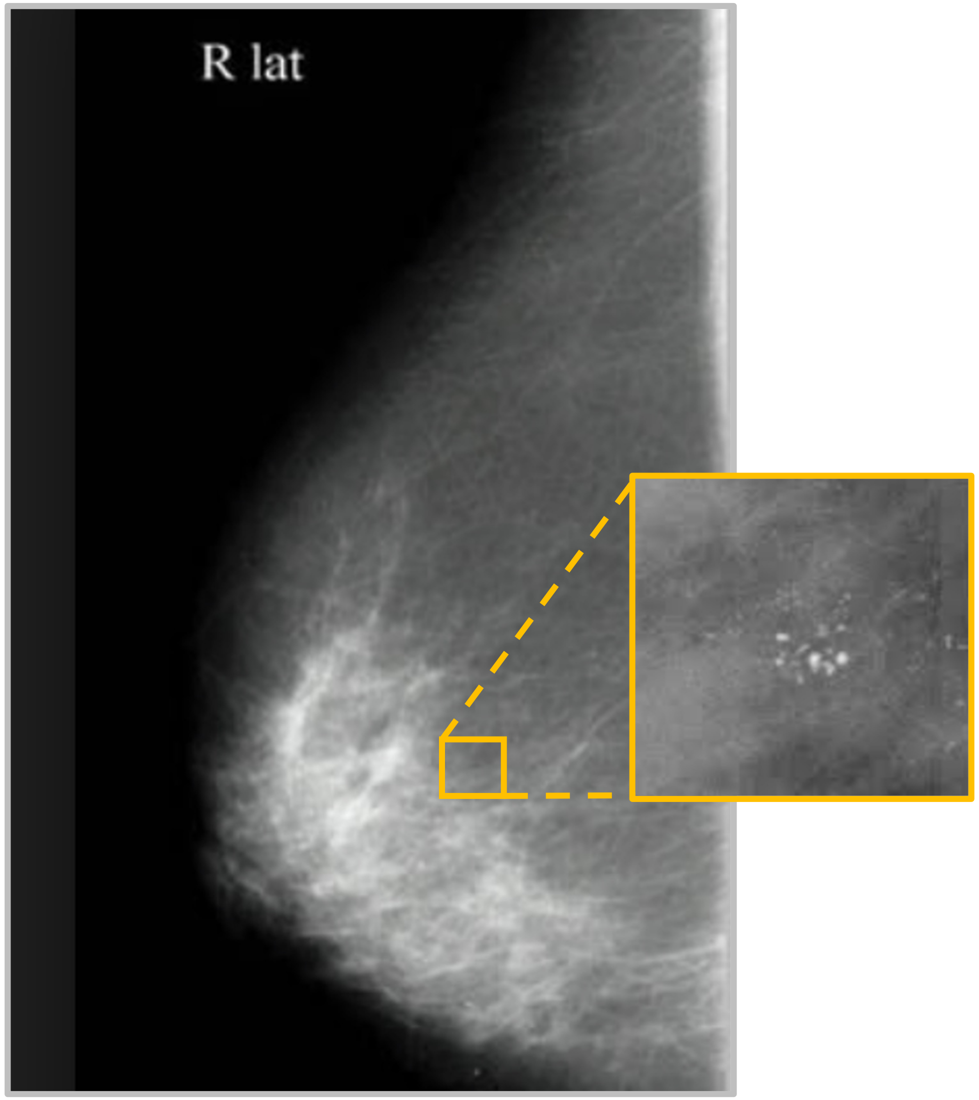
Breakdown of scientific papers by publication year, task addressed, imaging modality, and application area

CNN for image classification

CNN can be used for direct image classification:

- We can distinguish image portions of in mammograms containing either microcalcification clusters or normal tissue
- We can use a trained CNN to identify and localize regions suspected of containing a microcalcification clusters
- Thus we can build a:

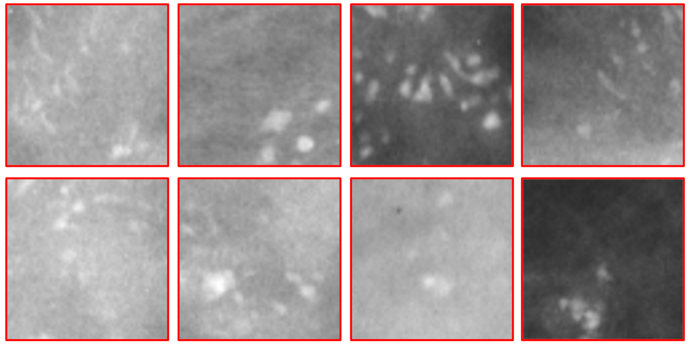
➔ Decision Support System (DSS) for microcalcification detection



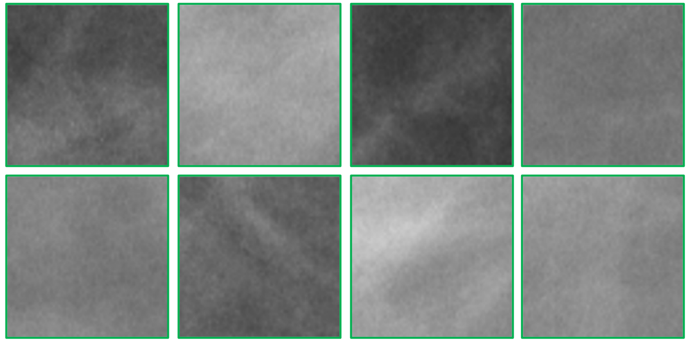
CNN for image classification

Input data

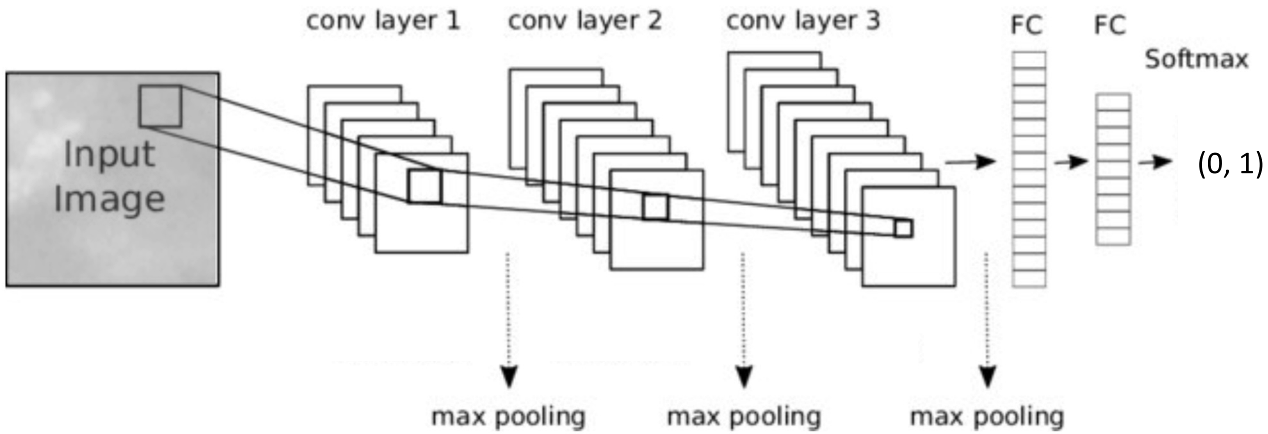
Label 1: images with microcalcifications



Label 0: images of normal tissue

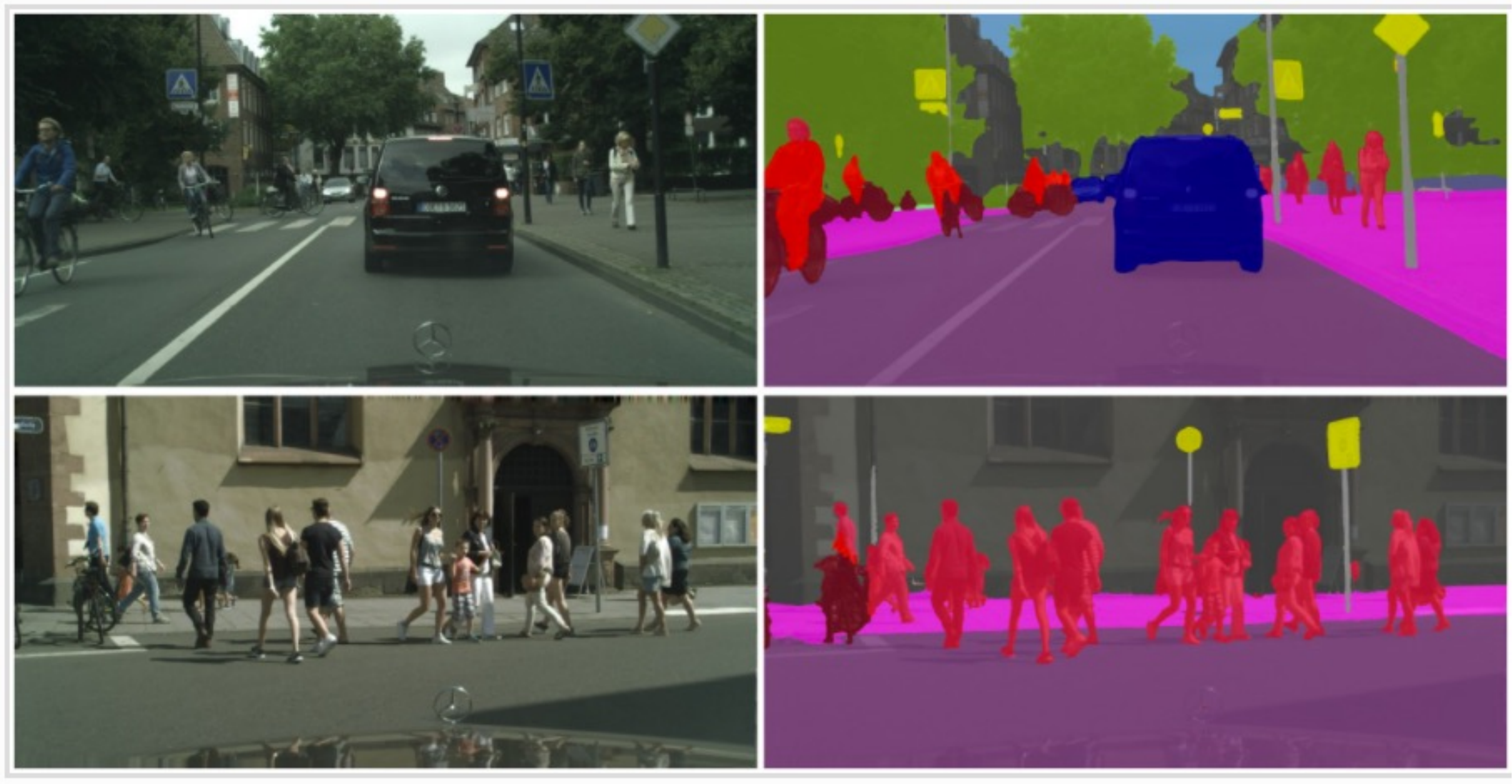


CNN classifier



See demo code: https://github.com/retico/cmepda_medphys/L8_code/
Lecture8_demo_train_CNN.mlx, Lecture8_demo_visualizing_CNN_layers.mlx
Data available on https://pandora.infn.it/public/cmepda/DATASETS/IMAGES/Mammography_micro
and on https://drive.google.com/drive/folders/1YqK7ZkM-P2IrqfD7Pj-SCmjz-GWd_1-Y

Semantic segmentation



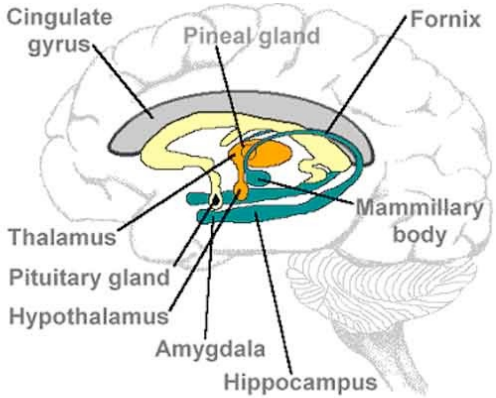
Semantic segmentation is the process of classifying each pixel belonging to a particular label.
It does not distinguish different instances of the same object.

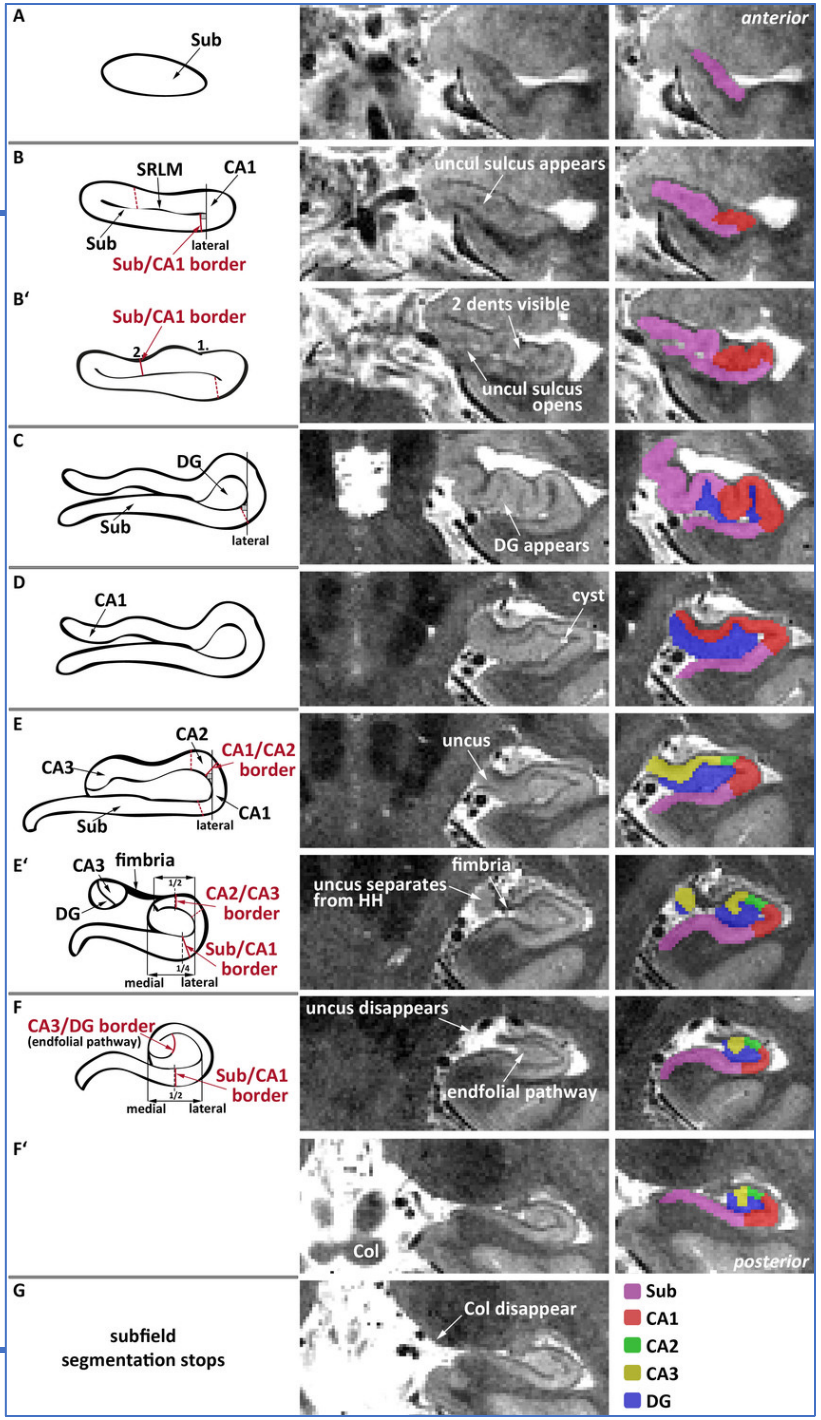
https://vladlen.info/publications/feature-space-optimization-for-semantic-video-segmentation/

Medical image segmentation

- Image segmentation: the image is partitioned into its parts or regions (segments)
- Segmentation of tissues, organs, lesions or other **regions of interest (ROIs)** out of a medical image is often a useful step to extract meaningful information related to shape or texture of the object of interest

For example, in the study of Alzheimer’s Disease (AD), the hippocampus is one of the first regions of the brain to suffer damage; memory loss and disorientation are included among the early AD symptoms.



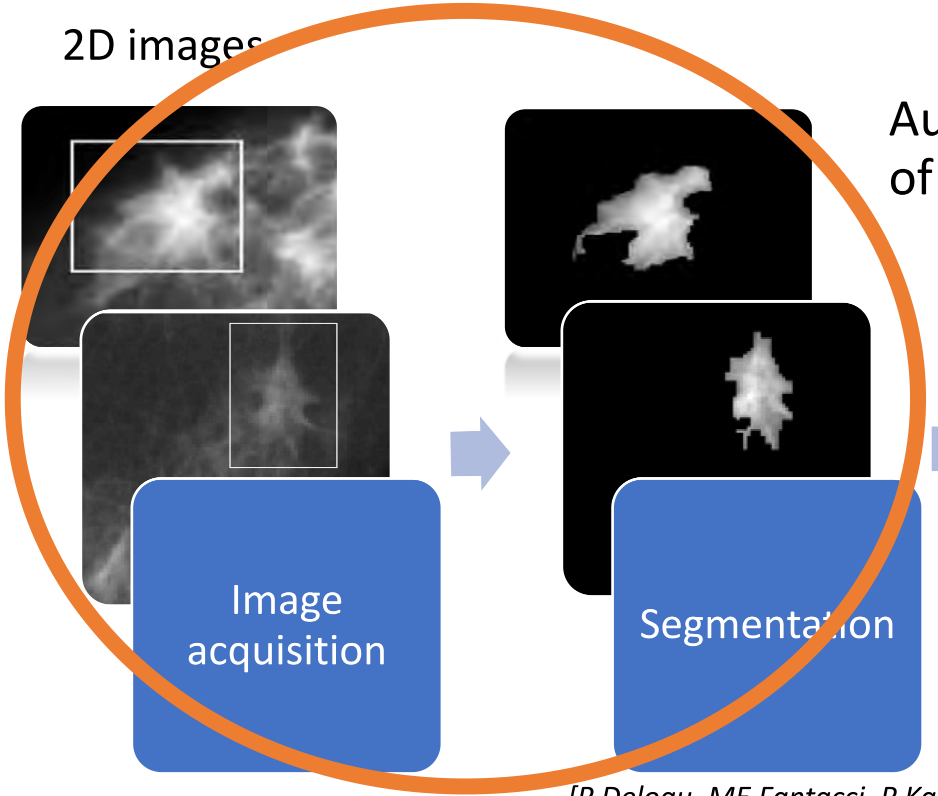


D. Berron et al., A protocol for manual segmentation of medial temporal lobe subregions in 7 Tesla MRI, NeuroImage: Clinical 15(C) 2017

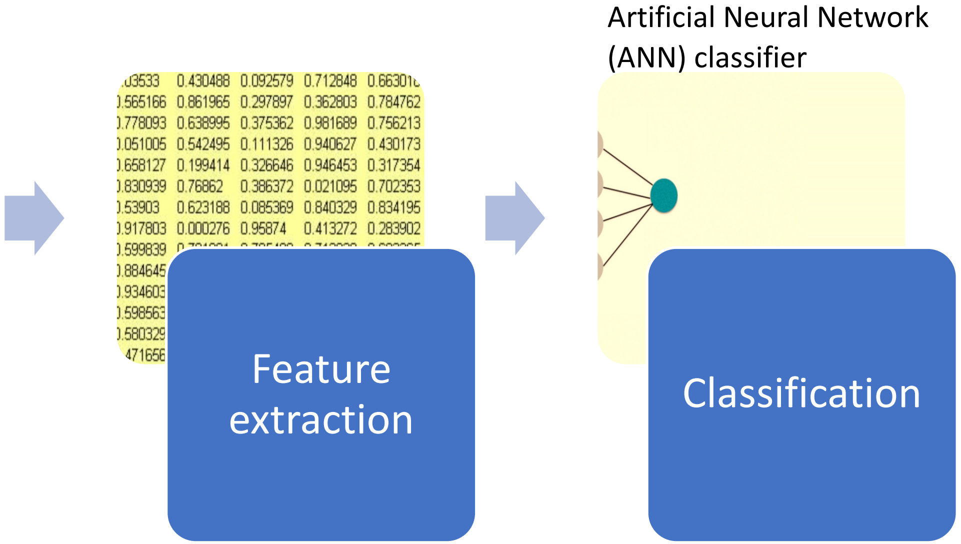
Typical image analysis pipeline for assisted diagnosis

Example: 1) Object segmentation; 2) Hand-crafted feature extraction; 3) Machine Learning classification

2D images



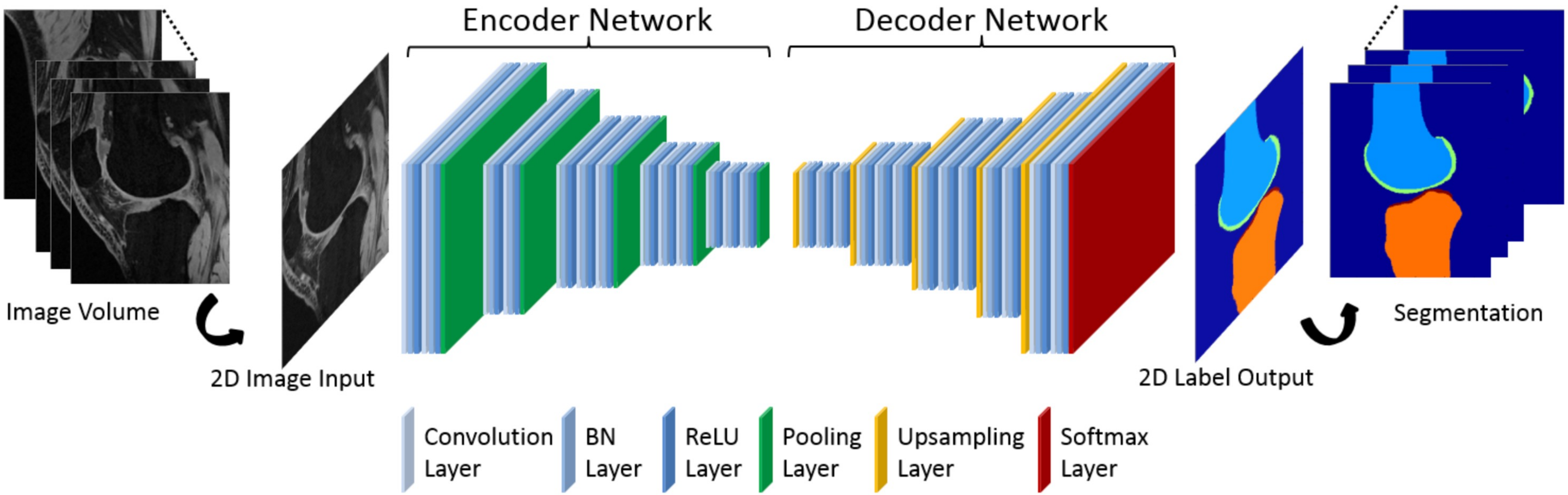
Automated classification (benign/malignant)
of mass lesions in mammograms



[P Delogu, ME Fantacci, P Kasae, A Retico, Computers in Biology and Medicine 37 (2007) 1479 – 1491]

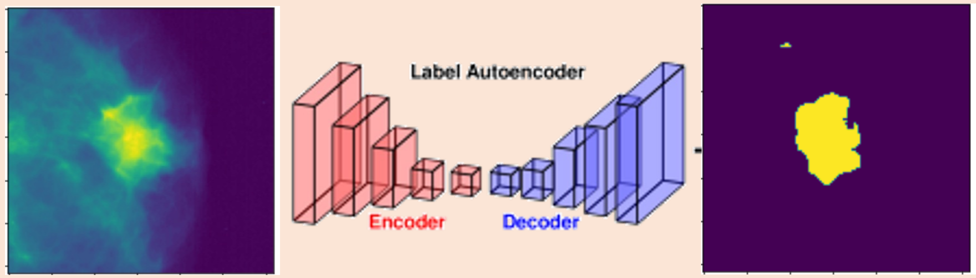
See demo code (L5_code/mass_segmentation): mass_segment.m
Data available on https://pandora.infn.it/public/cmepda/DATASETS
and on https://drive.google.com/drive/folders/1YqK7ZkM-P2IrqfD7Pj-SCmjz-GWd_1-Y

Convolutional Auto-Encoders for image segmentation



Liu et al, Deep Convolutional Auto-Encoder and 3D Deformable Approach for Tissue Segmentation in Magnetic Resonance Imaging, Proc. Intl. Soc. Mag. Reson. Med. 25, 2017

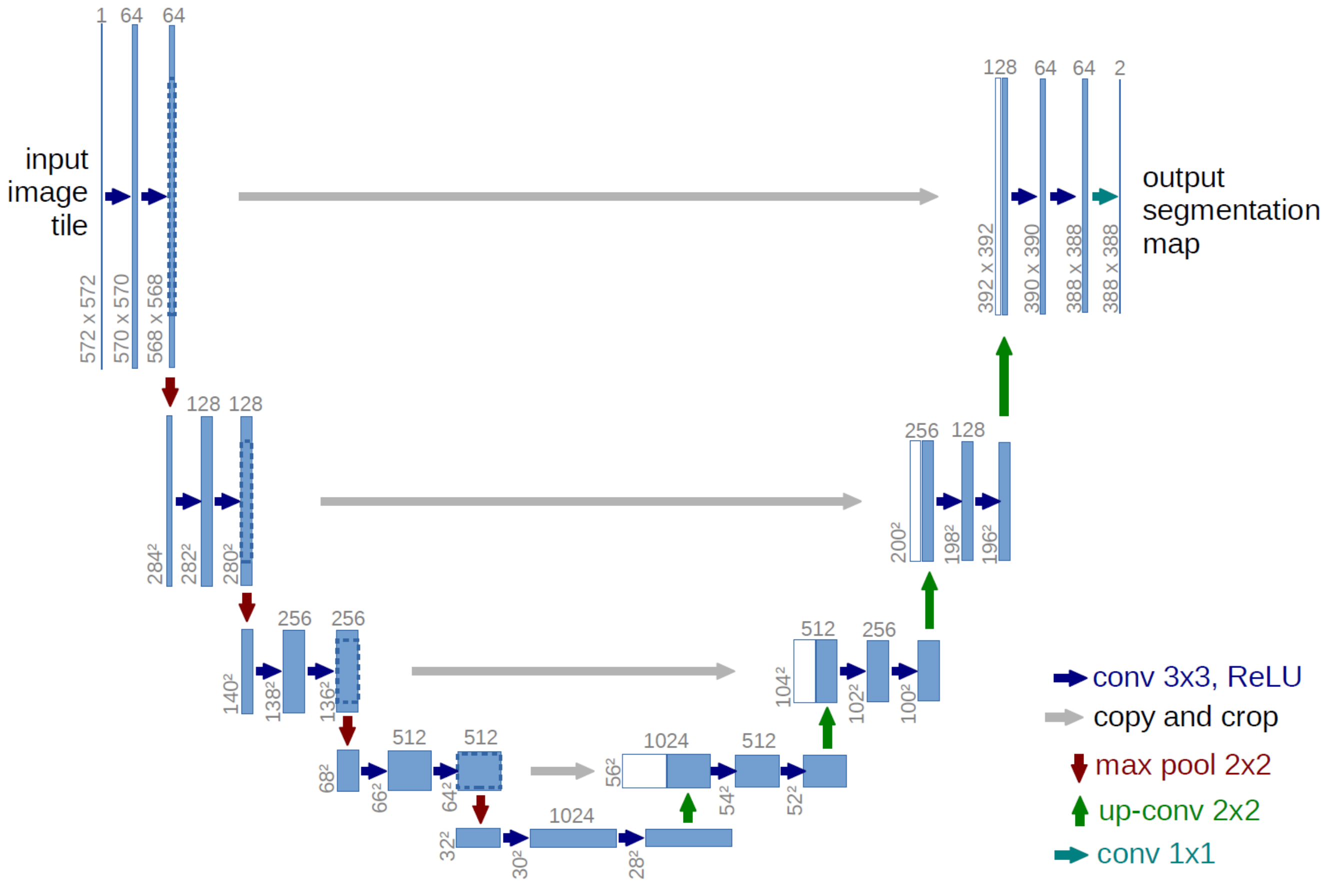
See L8_code/ Lecture8_demo_CAE_semantic_segmentation.ipynb on https://github.com/retico/cmepda_medphys/



U-net

U-Net: Convolutional Networks for Biomedical Image Segmentation
Olaf Ronneberger, Philipp Fischer, Thomas Brox
Medical Image Computing and Computer-Assisted Intervention (MICCAI), Springer, LNCS, Vol.9351: 234--241, 2015, available at arXiv:1505.04597

Winner of [ISBI Challenge: Segmentation of neuronal structures in EM stacks]



https://lmb.informatik.uni-freiburg.de/people/ronneber/u-net/

3D nnUNet by Fabian Isensee
https://github.com/MIC-DKFZ/nnUNet

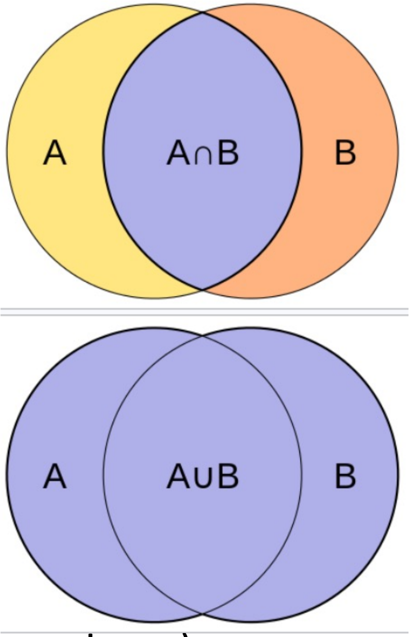
Challenges in data collection

- Precise object localization is hard to annotate
- Annotating every pixel is extremely time consuming
- Common solution is to define a segmentation mask:
  - annotate relevant objects (foreground)
  - mark rest as “other” (background)

Segmentation similarity measures

- **Jaccard similarity coefficient: Intersection over Union**

$$J(A,B) = \frac{|A \cap B|}{|A \cup B|} \qquad 0 \le J(A,B) \le 1.$$



- **Sørensen-Dice similarity coefficient**

$$DSC = \frac{2|X \cap Y|}{|X| + |Y|}$$

where $|X|$ and $|Y|$ are the cardinalities of the two sets (i.e. the number of elements in each set).
The Sørensen index equals twice the number of elements common to both sets divided by the sum of the number of elements in each set.
When applied to boolean data, using the definition of true positive (TP), false positive (FP), and false negative (FN), it can be written as

$$DSC = \frac{2TP}{2TP + FP + FN}.$$

It is different from Jaccard index which only counts true positives once in both the numerator and denominator.

DL vs. traditional ML approaches

- Deep Neural Networks are competing with traditional handcrafted feature extraction + ML approaches to Medical Image Analysis, fostering a more

  $\longrightarrow$ ***data driven decision making***

  - **Pros:**
    - No prior selection of problem-related features => no loss of information
  - **Cons:**
    - **Larger annotated** data samples are necessary
    - **Deep Neural Networks are black boxes: which image features are relevant for discrimination?**

Data augmentation (flip, rotate, scale images to augment data sets)

Model interpretability, explainable AI

Reproducibility in Medical Imaging Analysis studies

- Different analysis pipelines with the same purpose may rely both on different principles and on different algorithm implementations
- Extensive tests should be performed to assess the **reliability** of the features/measures they produce, before the output of SW packages for the analysis of medical data is used to infer results in the field of clinical research
- To estimate the precision of a SW package, a reference “gold standard” is necessary
- In most cases “gold standard” measures on large samples are not available, nevertheless, we can evaluate:
  - the robustness of a SW pipeline (**intra-method agreement**)
  - the reproducibility of the same measure across different SW pipelines (**inter-method agreement**)

- **The lack of intra-method and inter-method agreement can produce inconsistent results in medical imaging studies**

The *gold standard (ground truth)* problem

- Expert radiologists :
  - They quite often do not agree with each other on the presence of lesions or on the lesion relevance
  - Their manual segmentations will not be highly reproducible in inter- and intra-reader analyses

- The most common strategy to create a gold standard is to form a panel of experts to jointly find a solution in doubtful cases

- Problems when performing algorithm training and validation:
  - the algorithm performance may drastically change according to the gold standard

- A possible alternative approach is to rely on **synthetic datasets…**

MATLAB and Python

- MATLAB provides a flexible, two-way integration with other programming languages, allowing you to reuse legacy code
- Since the MATLAB release R2014, you can access Python functionality from MATLAB (you call Python functions and objects directly from MATLAB)
- To call Python modules in MATLAB, you must have a supported version of the reference implementation (CPython) installed on your system: https://it.mathworks.com/support/requirements/python-compatibility.html

Install Supported Python Implementation

- MATLAB supports versions 2.7, 3.6, 3.7 and 3.8.
- MATLAB selects the version of Python based on your system path.
- To call a Python function, type py. in front of the module name and function name.
- Pass MATLAB data as arguments to Python function.
- MATLAB converts the data into types that best represent the data to the Python language.

https://it.mathworks.com/help/matlab/call-python-libraries.html

```
>> pyenv                          % to determine which version MATLAB is using
>> pyenv('Version','/usr/bin/python3’)     % Change default environment of Python interpreter
>> py.help('len’)                 % To call a Python function, type py. in front of the function name.
>> L=py.os.listdir(".");
```

How to call Python from MATLAB

Configure Your System to Use Python

- **Python Support**
- To call Python® modules in MATLAB®, you must have a supported version of the reference implementation (CPython) installed on your system. Install a distribution, such as those found at https://www.python.org/downloads/. MATLAB does not support CPython versions installed from the Microsoft® store. For supported version information, see Versions of Python Compatible with MATLAB Products by Release. If you are on a Linux® or Mac platform, you already have Python installed. If you are on Windows®, you need to install a distribution, if you have not already done so. For more information, see Install Supported Python Implementation.
- To verify that Python is installed on your system, open the Python interpreter from your system prompt and call Python functions.
- By default, MATLAB selects the version of Python based on your system path. To view the system path in MATLAB, use the getenv('path') command. To determine which version MATLAB is using, call the pyenv function.

```
pe = pyenv; pe.Version

ans = "3.8"
```

- The value set by pyenv is persistent across MATLAB sessions. If you have multiple supported versions, use pyenv to display the version currently used by MATLAB. MATLAB automatically selects and loads a Python version when you type a Python statement. For example, to call *funcname*, type:

```
py.funcname
```

See https://github.com/retico/cmepda_medphys/L8_code/ matlab_python /How_to_call_Python_from_MATLAB.mlx

Python and MATLAB

https://it.mathworks.com/help/matlab/matlab_external/install-the-matlab-engine-for-python.html

Get Started with MATLAB Engine API for Python

R2019b

The MATLAB® Engine API for Python® provides a Python package named `matlab` that enables you to call MATLAB functions from Python. You install the package once, and then you can call the engine in your current or future Python sessions. For help on installing or starting the engine, refer to:

- Install MATLAB Engine API for Python
- Start and Stop MATLAB Engine for Python

The `matlab` package contains the following:

- The MATLAB Engine API for Python
- A set of MATLAB array classes in Python (see MATLAB Arrays as Python Variables)

The engine provides functions to call MATLAB, and the array classes provide functions to create MATLAB arrays as Python objects. You can create an engine and call MATLAB functions with `matlab.engine`. You can create MATLAB arrays in Python by calling constructors of an array type (for example, `matlab.double` to create an array of doubles). MATLAB arrays can be input arguments to MATLAB functions called with the engine.

```
>>>  import matlab.engine
>>> eng = matlab.engine.start_matlab()
…
>>> eng.quit()
```

How to call MATLAB from Python

Install MATLAB Engine API for Python

- To start the MATLAB® engine within a Python® session, you first must install the engine API as a Python package.

Verify Your Configuration

- Before you install, verify your Python and MATLAB configurations.
- Check that your system has a supported version of Python and MATLAB R2014b or later. For more information, see Versions of Python Compatible with MATLAB Products by Release.

Install Engine API

- You can install the MATLAB Engine API for Python using the pip command or a Python setup script setup.py.
- **Install Using pip**
- Starting with MATLAB R2022b, you can use the pip command to install the API. Choose one of the following procedures and execute from the system prompt.
- To install from the MATLAB folder, on Windows® type:

  cd "*matlabroot*\extern\engines\python" python -m pip install .

- Install the engine API from https://pypi.org/project/matlabengine with the command:

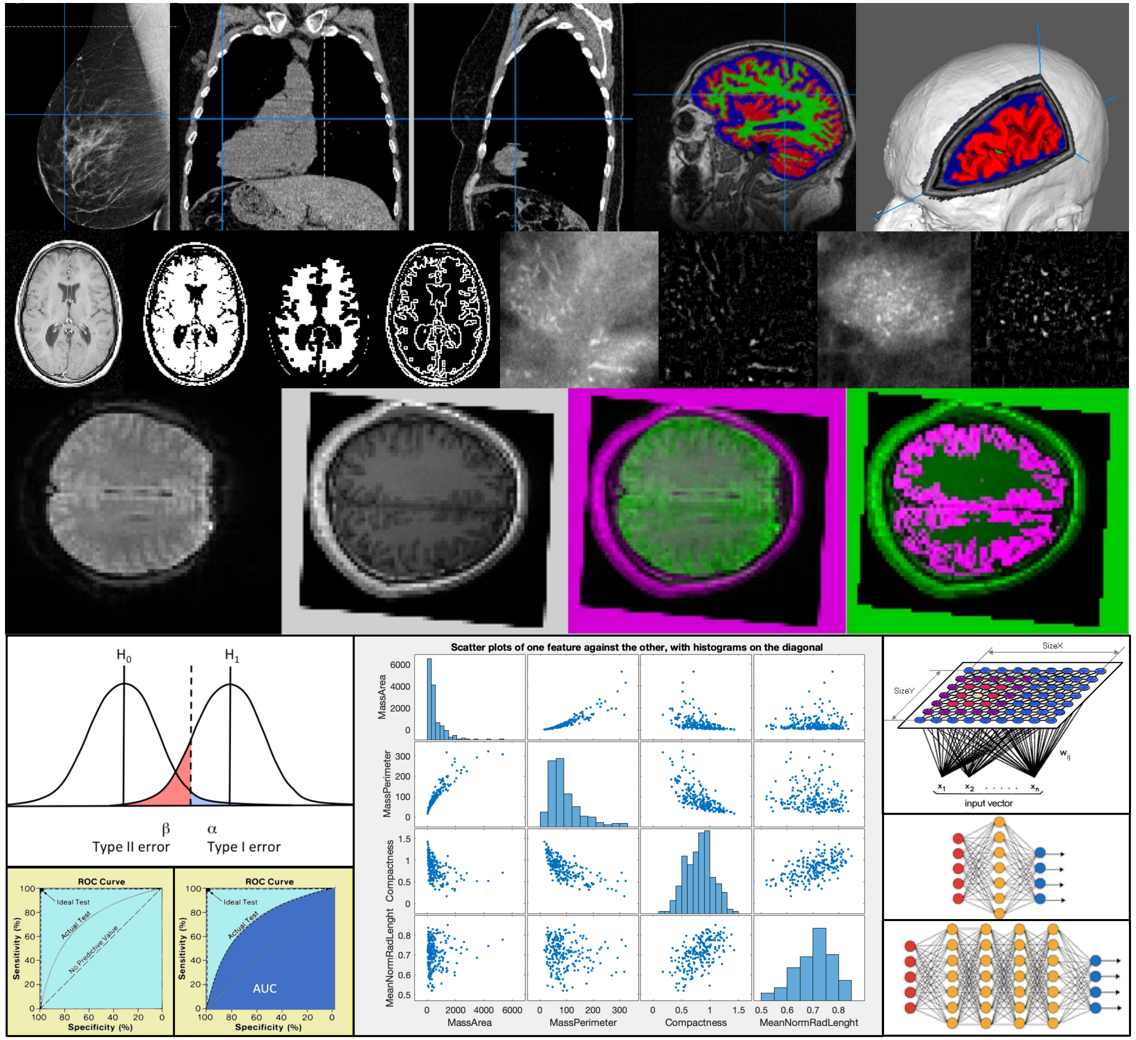
  python -m pip install matlabengine

See https://github.com/retico/cmepda_medphys/L8_code/ matlab_python /How_to_call_MATLAB_from_Python.ipynb

Summary of the course module

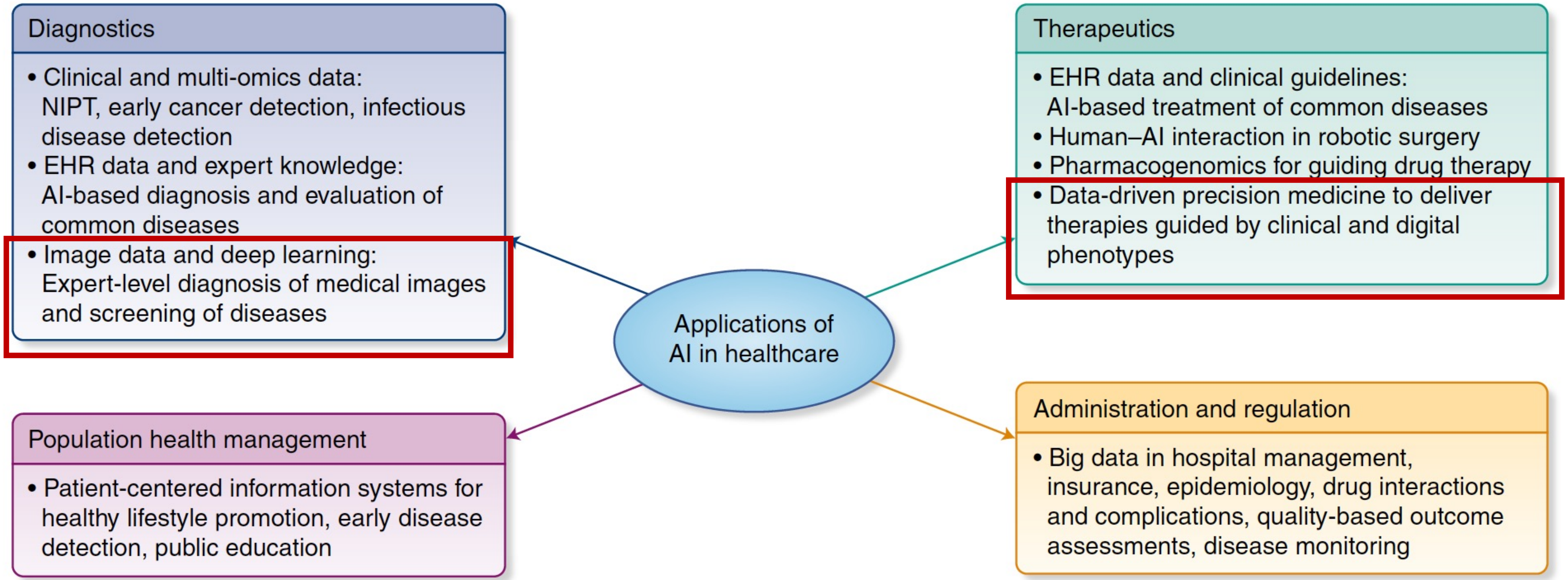
Medical data processing, feature extraction, feature/image classification:

- ✓ Handling standard-format medical data (DICOM), data anonymization, visualization
- ✓ Image filtering
- ✓ Deriving features form images, image segmentation, image coregistration
- ✓ Data quality control, outlier removal, dimensionality reduction
- ✓ Data exploration and analysis, supervised and unsupervised machine learning techniques
- ✓ Performance evaluation: metrics and cross-validation strategies
- ✓ Machine-learning and deep-learning tools for segmentation and classification



Artificial Intelligence applications in healthcare

*J He et al., The practical implementation of artificial intelligence technologies in medicine, Nature Medicine **25**, 30–36 (2019)*



Legend: HER, Electronic Health Records; NIPT, noninvasive prenatal test

For an overview of INFN activities in this field have a look at the Artificial Intelligence in Medicine (AIM) project, https://www.pi.infn.it/aim/

Concluding remarks

- Medical diagnostic imaging daily produces to an incredible amount of digital information
  - ➢ not fully exploited neither for diagnosis nor for research!

- Clinicians need to be supported by reliable, effective and easy-to-use tools for diagnosing and monitoring a wide range of disease conditions

- Large Consortia are sharing multimodal and multicenter data in different medical fields

- The Medical Imaging community still lacks:
  - automated data quality pipelines
  - data harmonization strategies both for longitudinal and multicenter studies
  - new computational approaches to process and to mine multimodal data (imaging, genetics, clinical, demographic, etc.)
  - **Reliable, validated and explainable** expert systems to support diagnosis and follow up of patients

References, sources and useful links

- References-Books

  - Y. LeCun, B. Boser, J. S. Denker, D. Henderson, R. E. Howard, W. Hubbard and L. D. Jackel: Backpropagation Applied to Handwritten Zip Code Recognition, Neural Computation, 1(4):541-551, Winter 1989
  - S. Haykin, Neural Networks: A Comprehensive Foundation, Prentice-Hall
  - I. Goodfellow, Y. Bengio, A. Courville. Deep Learning, The MIT Press
  - A. Géron, Hands-On Machine Learning with Scikit-Learn and TensorFlow, O'Reilly
  - Python Data Science Handbook by Jake VanderPlas https://colab.research.google.com/github/jakevdp/PythonDataScienceHandbook/blob/master/notebooks/Index.ipynb

- Sources

  - https://www.deeplearningitalia.com/una-panoramica-introduttiva-su-deep-learning-e-machine-learning/
  - http://www.asimovinstitute.org/neural-network-zoo/
  - https://towardsdatascience.com
  - https://it.mathworks.com/help/matlab/matlab-engine-for-python.html

References, sources and useful links

Papers

- Liu et al, Deep Convolutional Auto-Encoder and 3D Deformable Approach for Tissue Segmentation in Magnetic Resonance Imaging, Proc. Intl. Soc. Mag. Reson. Med. 25, 2017
- Vijay Badrinarayanan et. al 2017 "SegNet: A Deep Convolutional Encoder-Decoder Architecture for Image Segmentation" https://arxiv.org/abs/1511.00561
- U-Net: Convolutional Networks for Biomedical Image Segmentation   Olaf Ronneberger, Philipp Fischer, Thomas Brox, Medical Image Computing and Computer-Assisted Intervention (MICCAI), Springer, LNCS, Vol.9351: 234--241, 2015, available at arXiv:1505.04597

Blogs

- https://towardsdatascience.com/master-the-coco-dataset-for-semantic-image-segmentation-part-1-of-2-732712631047
- https://neptune.ai/blog/image-segmentation-in-2020

Datasets

- https://archive.ics.uci.edu/ml/datasets/Image+Segmentation
- https://cocodataset.org/#home
- https://groups.csail.mit.edu/vision/datasets/ADE20K/
- https://www2.eecs.berkeley.edu/Research/Projects/CS/vision/grouping/fg/
- https://medium.com/playment/top-10-open-image-datasets-for-machine-learning-research-93ab9c18bed1

Repos

- https://github.com/Xanthor-Aditya/
- https://lmb.informatik.uni-freiburg.de/people/ronneber/u-net/