ARAMIS LAB
BRAIN DATA SCIENCE

www.aramislab.fr

www.clinica.run

AI4Health School 2021

Practical session DL4MI

Deep learning for computer-aided diagnosis from images

Application to Alzheimer's disease

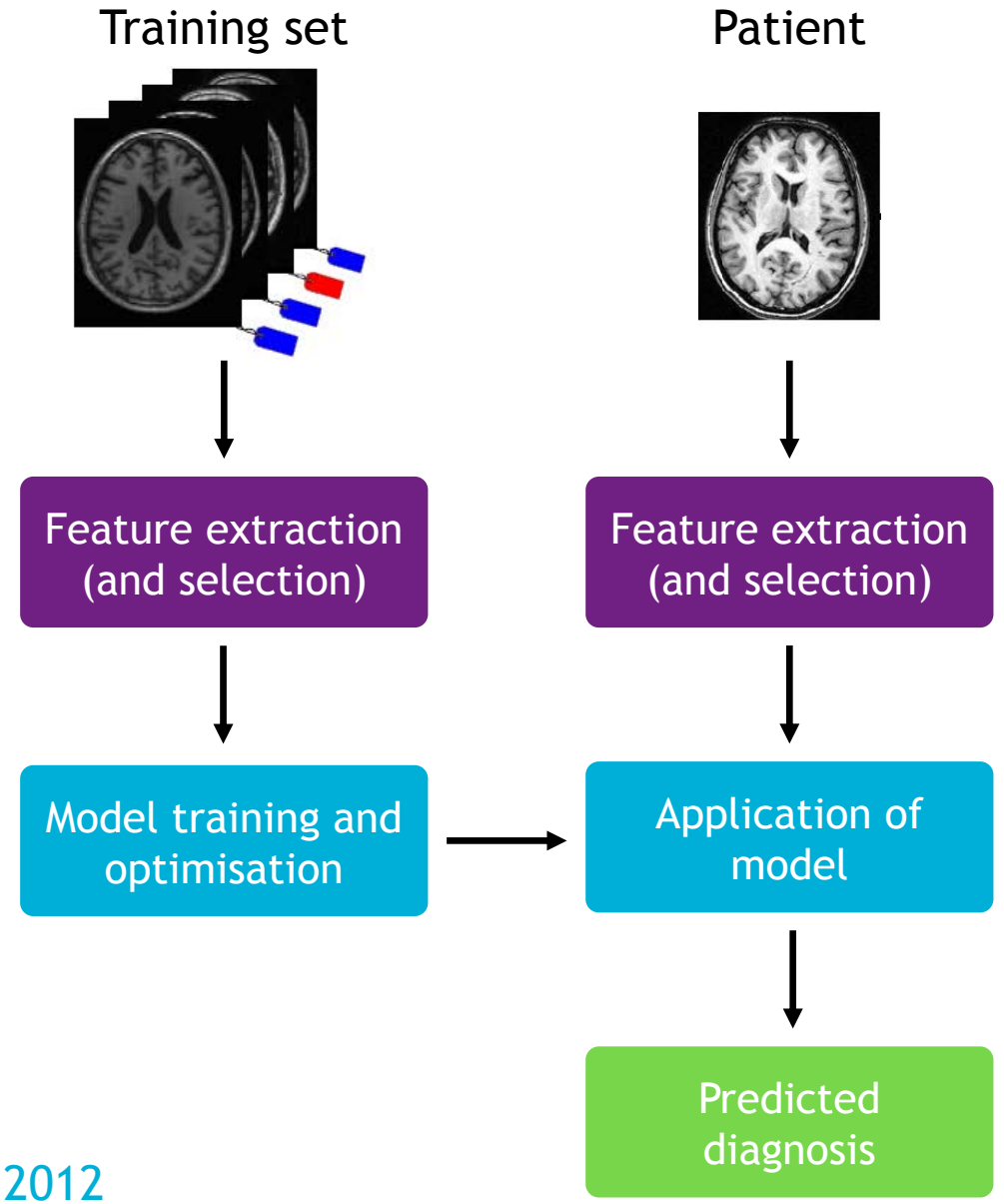
Ninon Burgos, with Simona Bottani, Mauricio Diaz Melo, Johann Faouzi and Elina Thibeau-Sutre

Aramis Lab, Paris Brain Institute, France

Clinical pattern recognition

Basic elements of a machine learning classification pipeline

- Training data set
- Feature extraction from raw data and dimensionality reduction
- Model training and optimisation
- Application to test data



Klöppel et al., NeuroImage, 2012

Clinical pattern recognition

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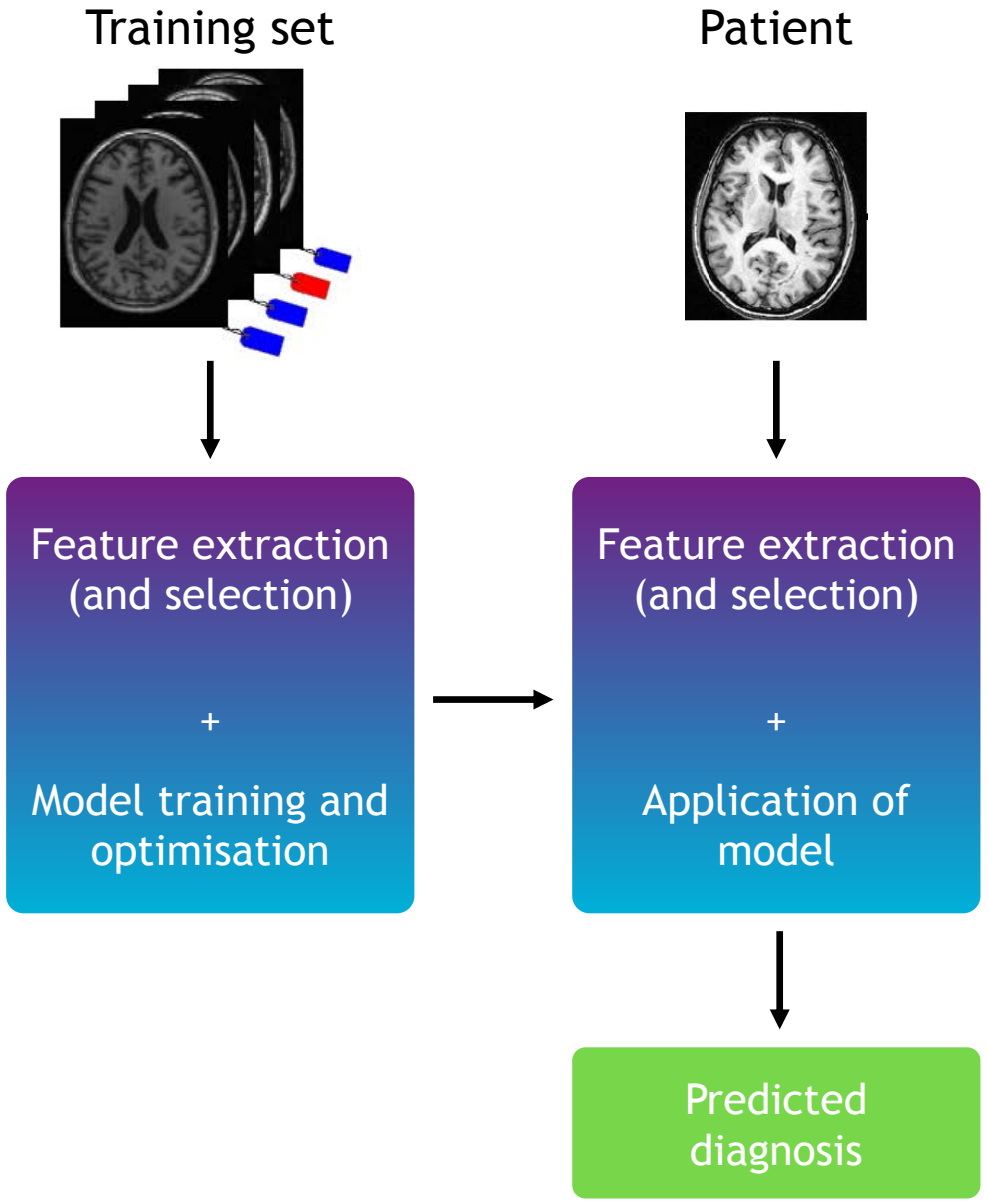
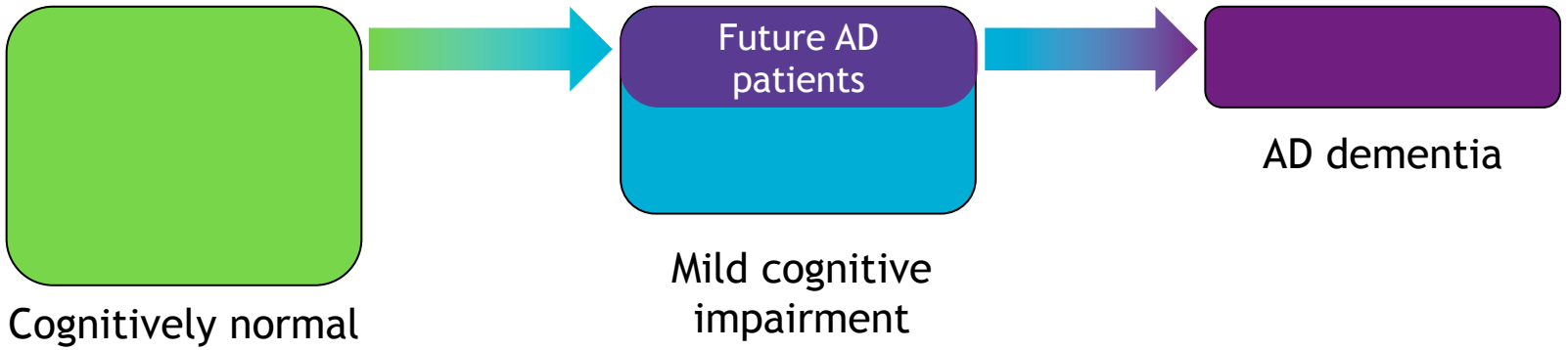


Use case: Alzheimer's disease (AD)

What is Alzheimer's disease?

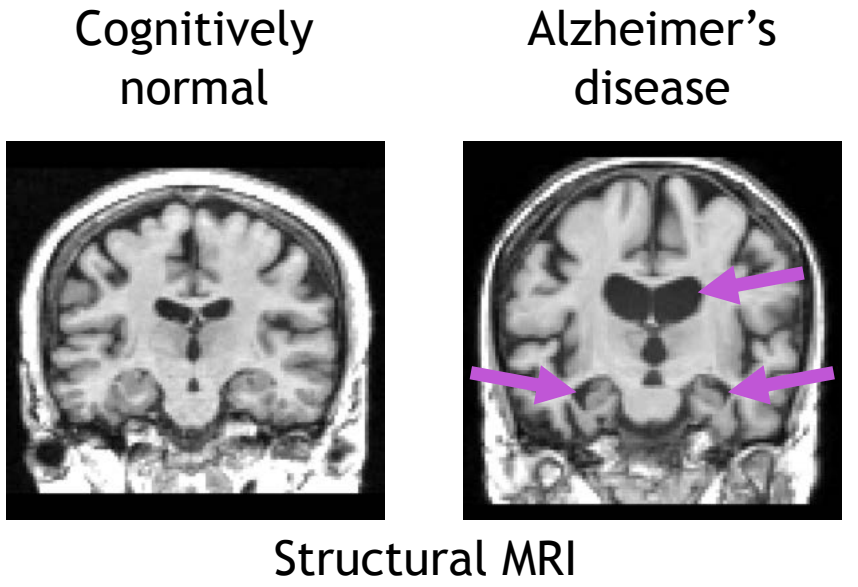
- Most common cause of dementia
- Disorder caused by abnormal brain changes
- Trigger decline in cognitive abilities, severe enough to impair daily life
- Affect behaviour, feelings and relationships
- Progressive disease



Use case: Alzheimer's disease (AD)

AD-related markers

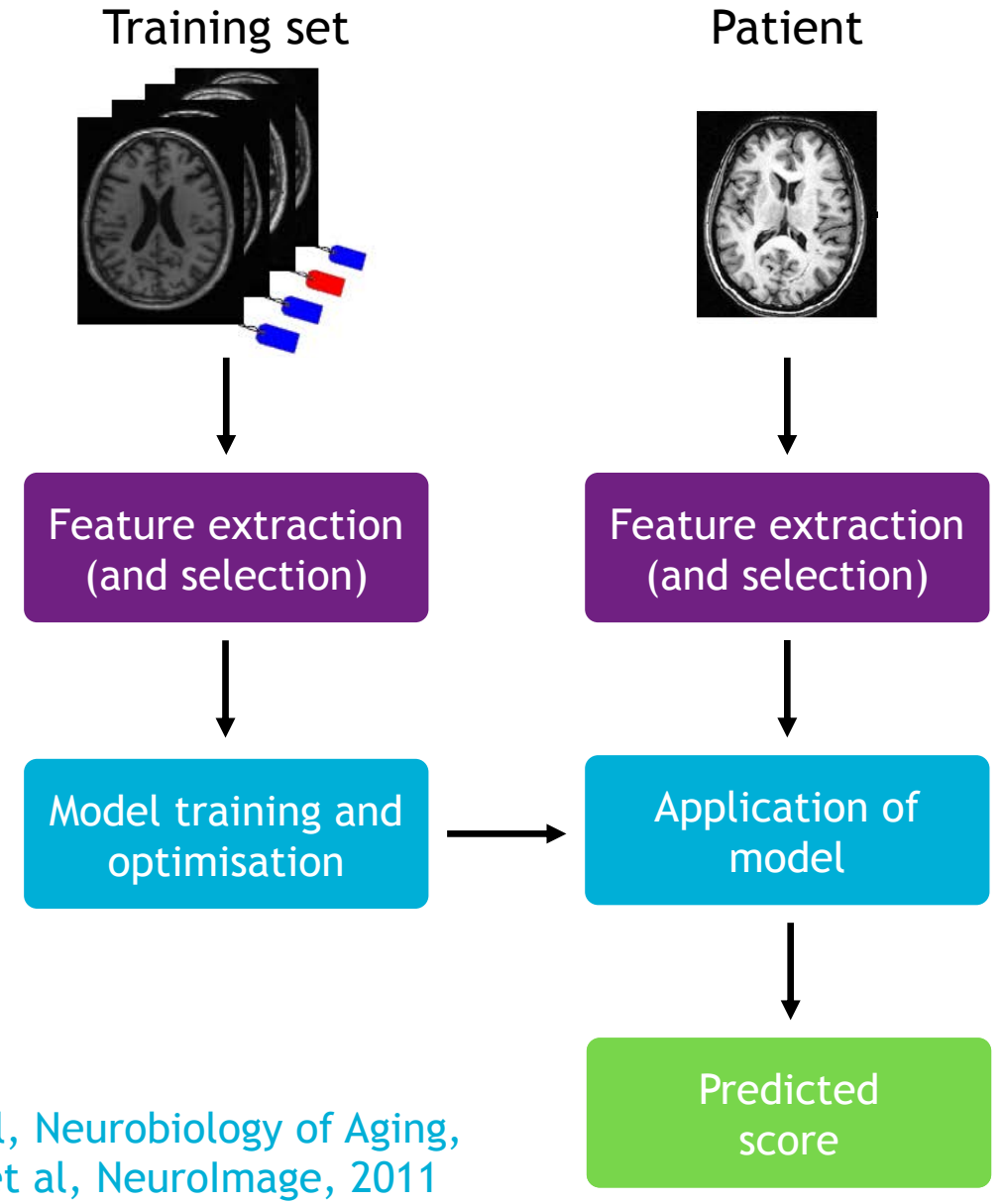
- **Clinical/cognitive tests**
  - Neuropsychological testing of cognitive functions (memory, language, etc.)
- **Structural MRI**
  - Atrophy
- **FDG PET**
  - Hypometabolism
- **CSF Aß42, CSF tau, amyloid PET, tau PET, diffusion MRI, etc.**



Clinical pattern recognition

Use case: Alzheimer's disease (AD)

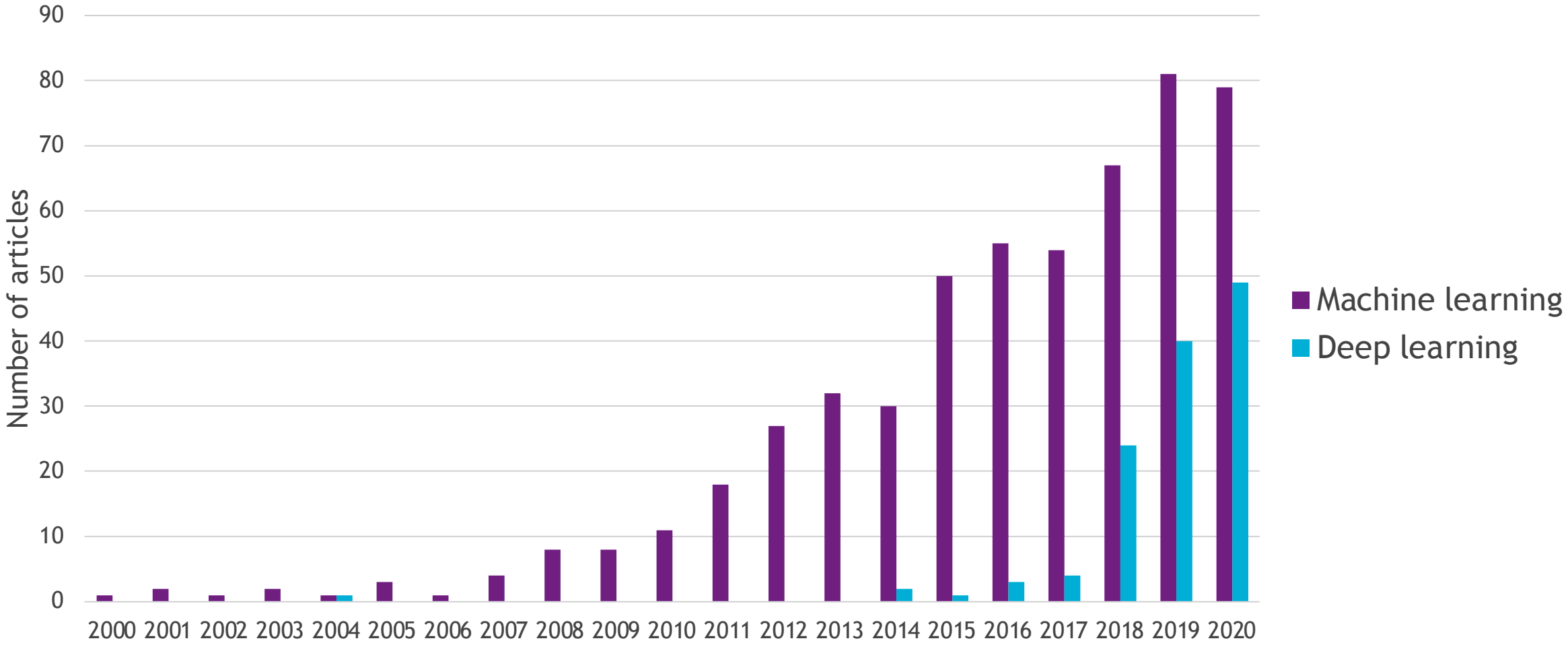
- **Classification**
  - Controls vs AD patients
  - Stable vs progressive mild cognitive impairment (MCI)
- **Regression**
  - Time of onset
  - Future clinical score



Klöppel et al., NeuroImage, 2008; Davatzikos et al, Neurobiology of Aging, 2008; Zhang et al, NeuroImage, 2011; Cuingnet et al, NeuroImage, 2011

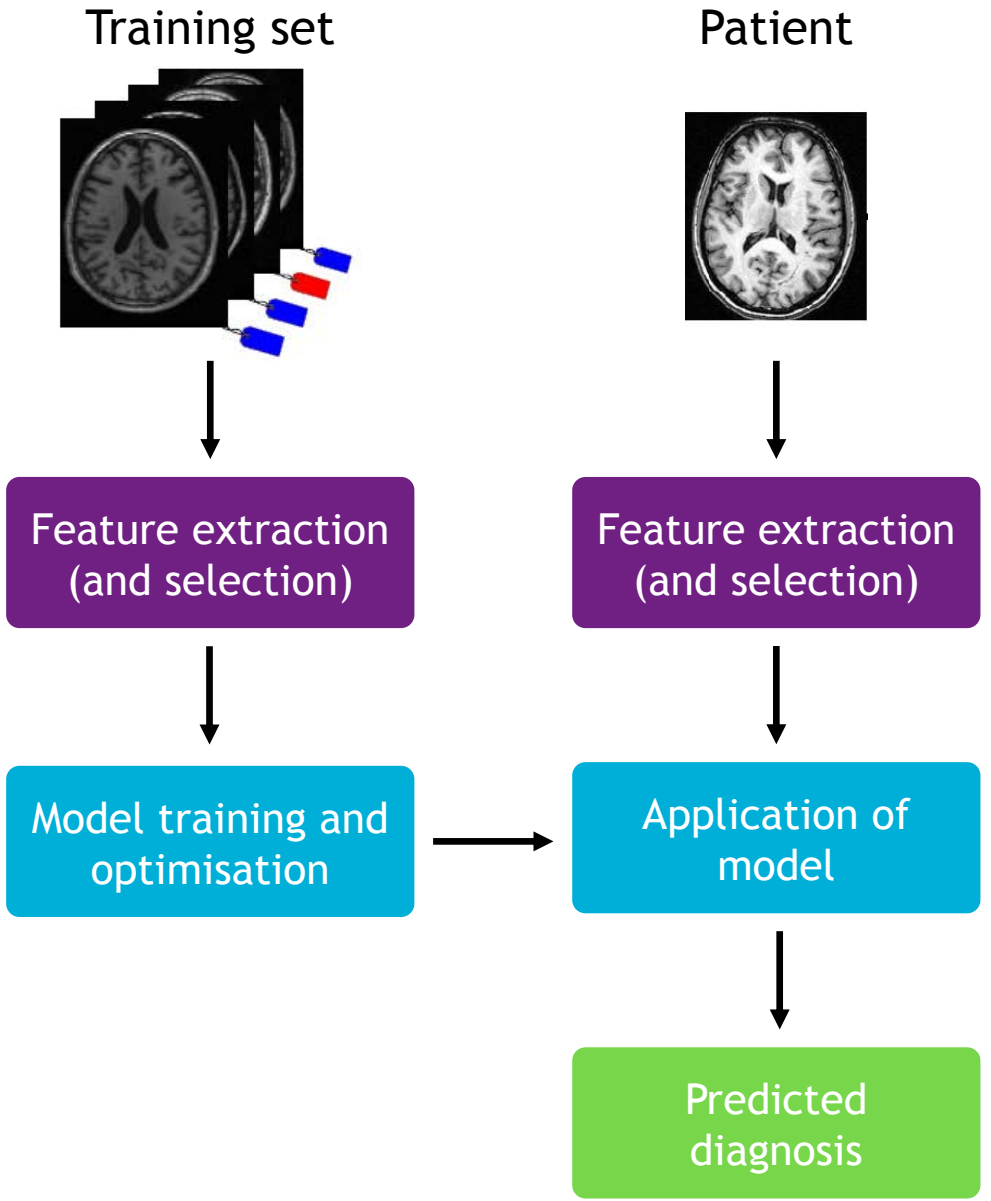
ML/DL for Alzheimer's diagnosis & prognosis

A very active field of research



DL for Alzheimer's diagnosis & prognosis

- Publicly accessible data
- Data organisation
- Image pre-processing
- Network types
- Network building blocks



Publicly accessible data

Dementia

- Image and Data Archive (https://ida.loni.usc.edu)

- Open Access Series of Imaging Studies (www.oasis-brains.org)

Other conditions

- BraTS (http:/braintumorsegmentation.org)
- IXI (https://brain-development.org/ixi-dataset)
- etc.

Data organisation and curation


```
094_S_4089
...
├── Accelerated_SAG_IR-SPGR
├── AV45_Coreg,_Avg,_Standardized_Image_and_Voxel_Size
...
├── Average_DC
├── Axial_DTI
├── Axial_FLAIR
├── Axial_T2_Star
├── Calibration_Scan
├── Coreg,_Avg,_Standardized_Image_and_Voxel_Size
...
├── Eddy_current_corrected_image
├── EPI_current_corrected_image
├── Fractional_Ansio.
├── HarP_135_final_release_2015
├── HHP_6_DOF_AC-PC_registered_MPRAGE
├── MT1__GradWarp__N3m
├── Sag_IR-SPGR
│   ├── 2011-06-29_14_37_16.0
│   ├── 2011-10-18_12_15_56.0
│   │   └── S125692
│   │       ├── ADNI_094_S_4089_MR_Sag_IR-SPGR__br_raw_20111019095510271_80_S125692_I261478.dcm
│   │       ├── ADNI_094_S_4089_MR_Sag_IR-SPGR__br_raw_20111019095512256_62_S125692_I261478.dcm
│   │       ├── ...
│   ├── 2011-12-14_15_53_24.0
│   ├── 2012-08-15_14_00_36.0
│   └── 2013-09-25_14_14_23.0
├── Sag_IR-SPGR_REPEAT
├── Spatially_Normalized,_Masked_and_N3_corrected_T1_image
└── T2-weighted_trace
```

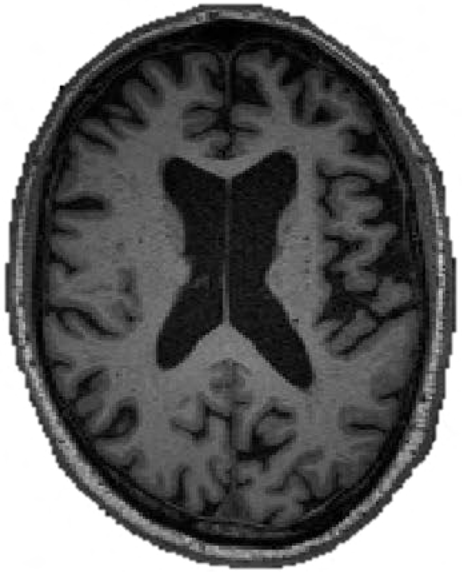
```
sub-ADNI094S4089
├── ses-M00
│   ├── anat
│   │   └── sub-ADNI094S4089_ses-M00_T1w.nii.gz
│   └── dwi
│       ├── sub-ADNI094S4089_ses-M00_acq-axial_dwi.bval
│       ├── sub-ADNI094S4089_ses-M00_acq-axial_dwi.bvec
│       └── sub-ADNI094S4089_ses-M00_acq-axial_dwi.nii.gz
│   ├── pet
│   │   ├── sub-ADNI094S4089_ses-M00_task-rest_acq-av45_pet.nii.gz
│   │   └── sub-ADNI094S4089_ses-M00_task-rest_acq-fdg_pet.nii.gz
│   └── sub-ADNI094S4089_ses-M00_scans.tsv
├── ses-M03
├── ses-M12
└── ses-M24
```

BIDS
BRAIN IMAGING DATA STRUCTURE

http://bids.neuroimaging.io
Gorgolewski et al., Nature Scientific Data, 2016

Image preprocessing

Original T1-weighted MR image



Correction of intensity inhomogeneities + affine registration to template

Non-rigid registration to template + skull stripping

Grey matter segmentation

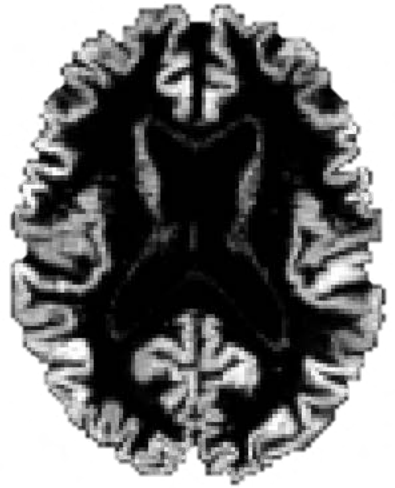


Image preprocessing

Statistical Parametric Mapping (SPM)

- www.fil.ion.ucl.ac.uk/spm
- **Modalities:** Structural and functional MRI, PET, SPECT, EEG, MEG
- **Features:** preprocessing, modelling, statistical inference, voxel-based morphometry, connectivity analysis

Frackowiak, Friston, Frith, Dolan, and Mazziotta, editors. Human Brain Function. Academic Press USA, 1997

FreeSurfer

- https://surfer.nmr.mgh.harvard.edu
- **Modalities:** Structural, functional, diffusion MRI
- **Features:** skullstripping, registration, cortical surface reconstruction, segmentation, longitudinal processing, fMRI analysis, tractography

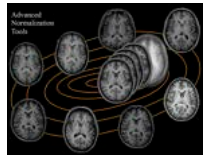
Fischl, NeuroImage, 2012

FMRIB Software Library (FSL)

- https://fsl.fmrib.ox.ac.uk
- **Modalities:** Structural, functional, diffusion MRI
- **Features:** brain extraction, segmentation, registration, tractography, longitudinal analysis, statistical analysis

Jenkinson et al., NeuroImage, 2012

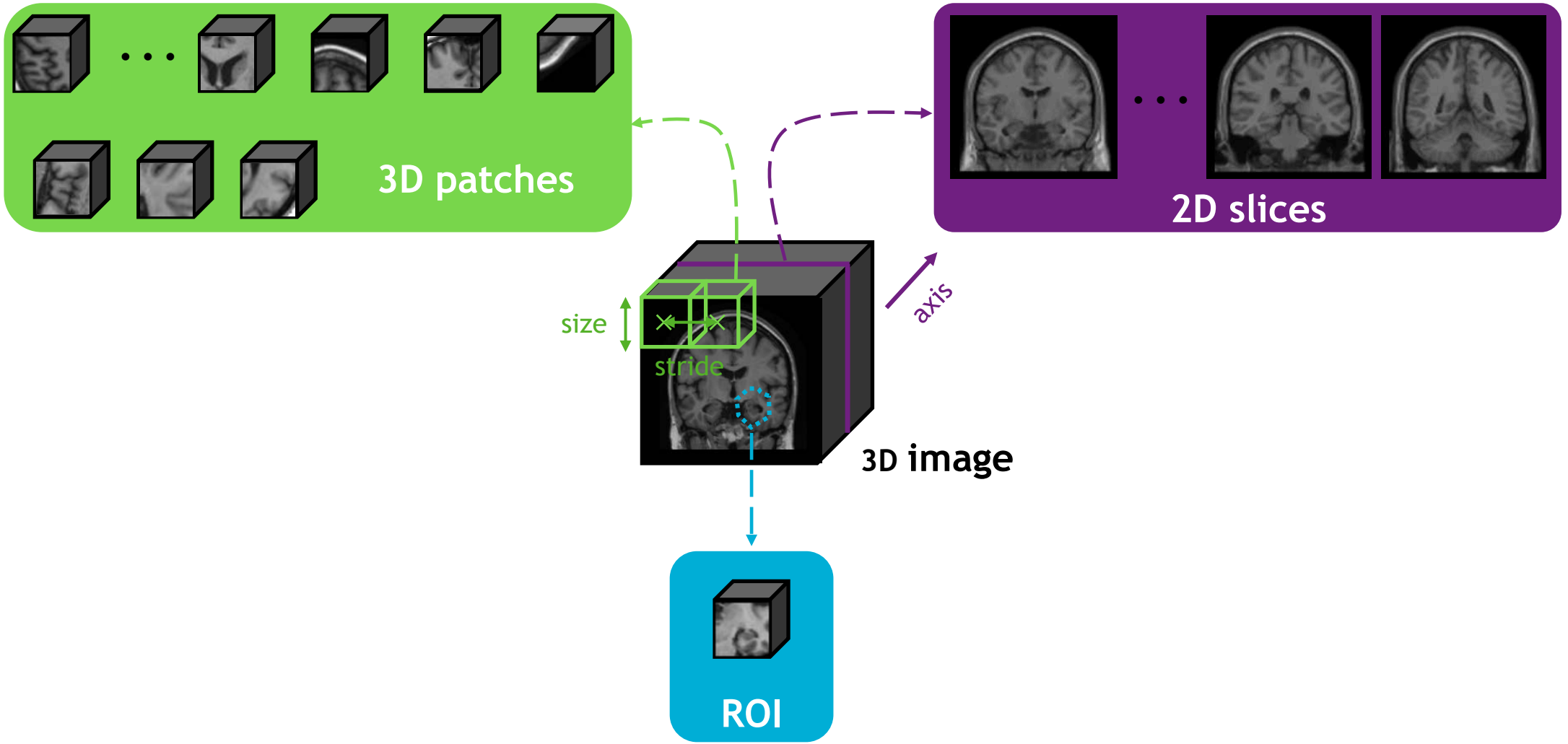
Advanced Normalization Tools (ANTs)



- http://stnava.github.io/ANTs
- **Modalities:** Structural, functional, diffusion MRI, PET
- **Features:** bias field correction, registration, segmentation, cortical thickness estimation

Avants et al., Frontiers in Neuroinformatics, 2014

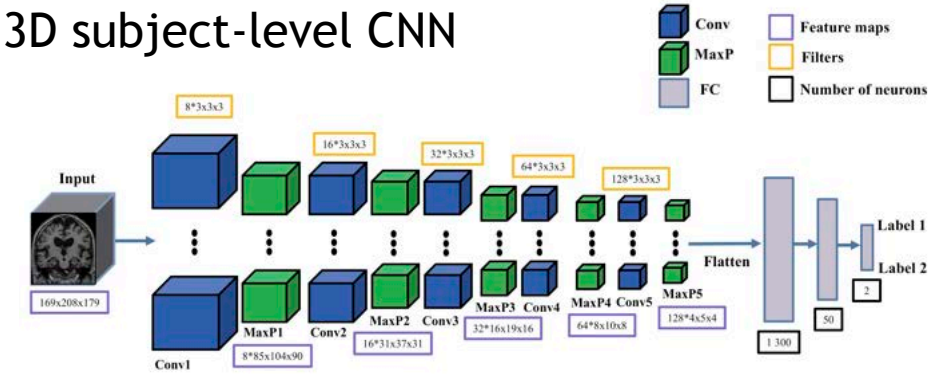
Image preprocessing



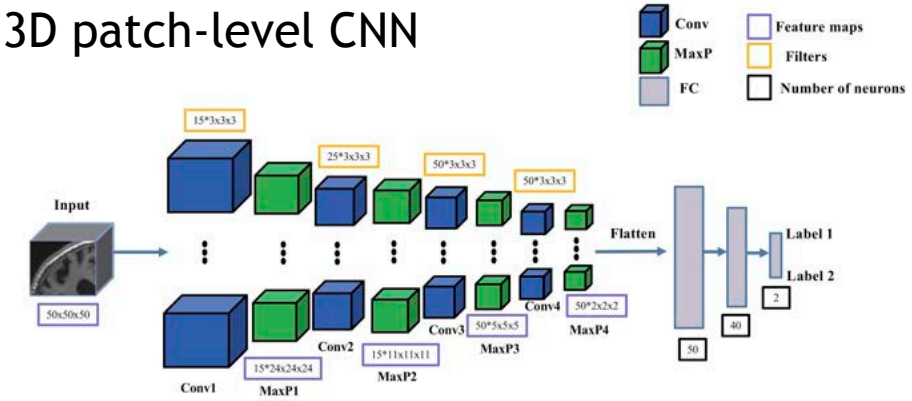
Classifiers

Convolutional neural networks

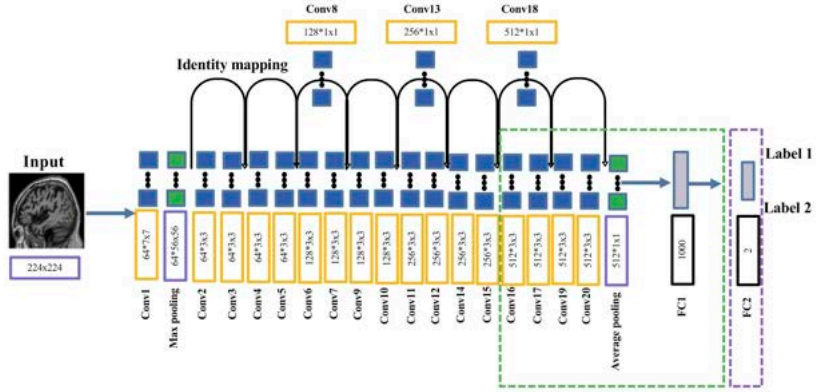
3D subject-level CNN



3D patch-level CNN

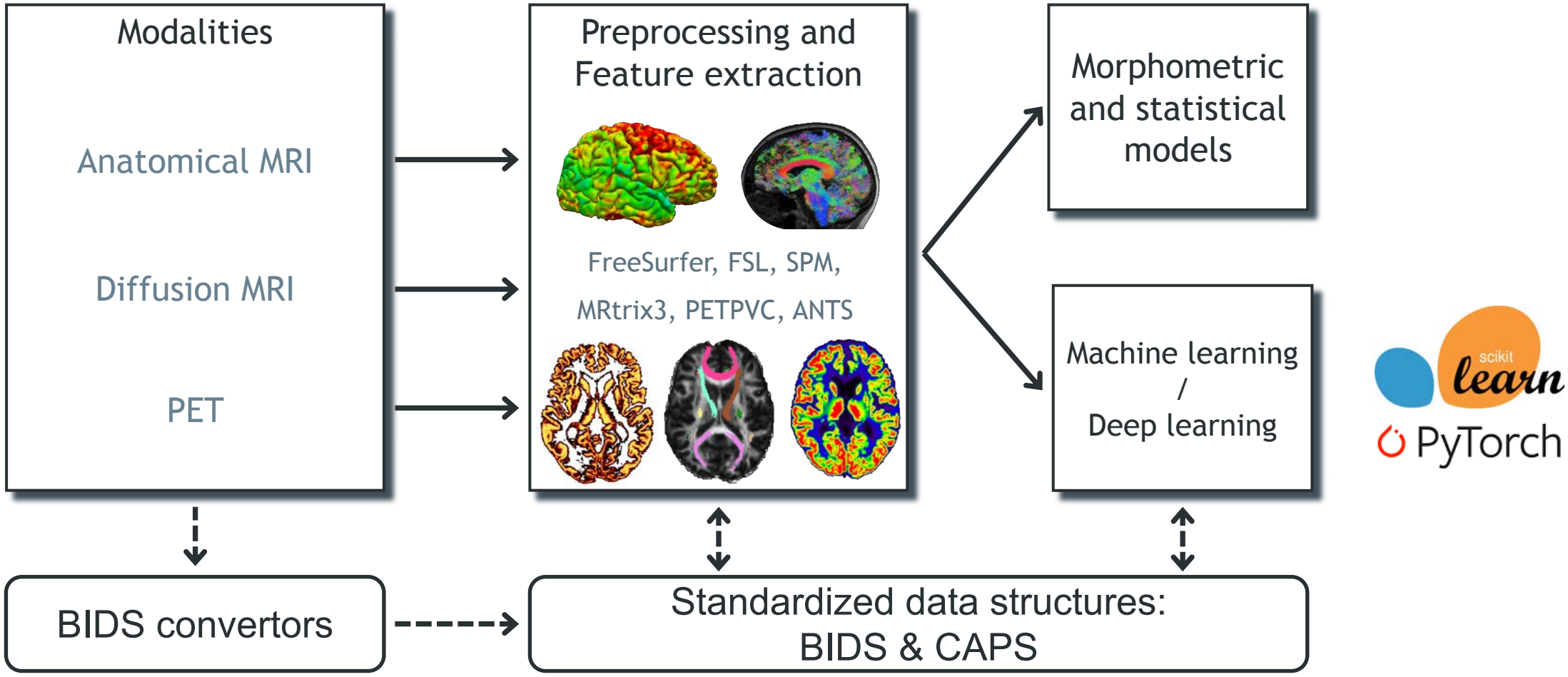


2D slice-level CNN



Wen, Thibeau-Sutre et al., Medical Image Analysis, 2020

Software platform for clinical neuroimaging studies



ClinicaDL

Clinica + PyTorch =

ClinicaDL

Prepare your imaging data

- `clinicadl preprocessing` - Preprocessing pipelines
  - `t1-linear` - Linear processing of T1w MR images: affine registration to the MNI standard space
  - `t1-extensive` - 'Extensive' processing of T1w MR images: non linear registration to the MNI standard space
- `clinicadl quality_check` - Quality control of preprocessed data: use a pretrained network [Fonov et al., 2018] to classify adequately registered images.
- `clinicadl extract` - Prepare input data for deep learning with PyTorch
- `clinicadl quality_check` - Evaluate registration quality

Train & test your classifier

- `clinicadl train` - Train with your data and create a model
- `clinicadl classify` - Classify one image or a list of images with your previously trained model

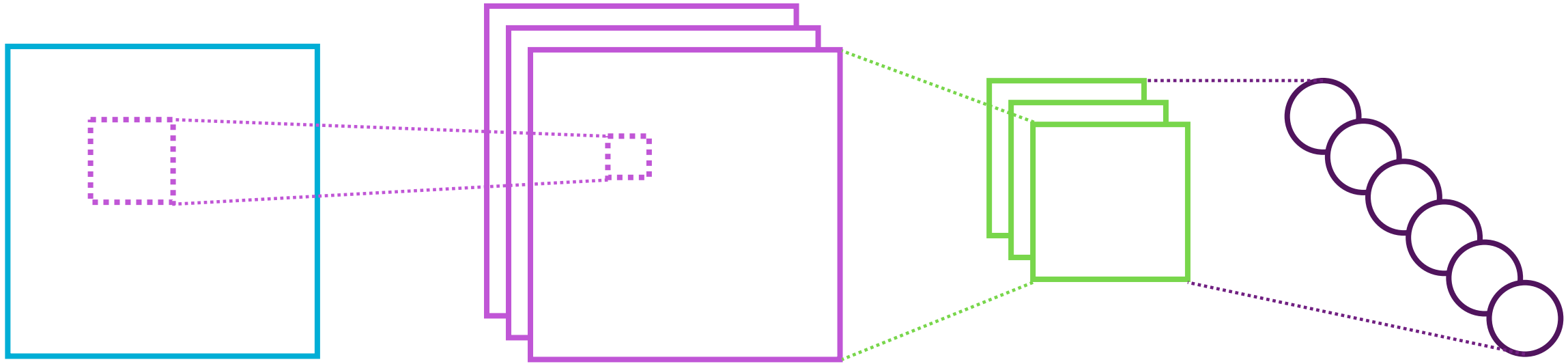
Utilitaries

- `clinicadl generate` - Generate synthetic data for functional tests
- `clinicadl tsvtool` - Handle TSV files for metadata processing and data splits

https://github.com/aramis-lab/AD-DL

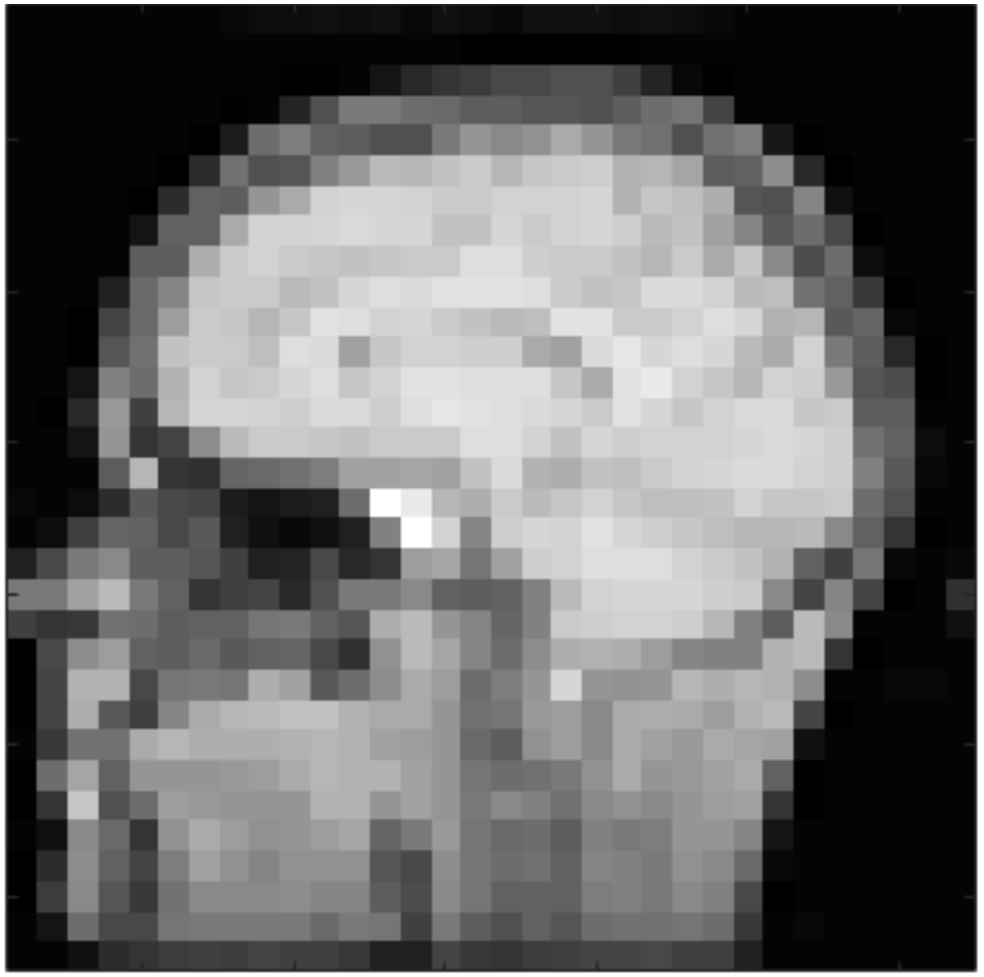
Convolutional neural networks

CNNs for classification



Using an image as input of a neural network

Image = matrix of numbers



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1	0	0	1	0	0	0	1	1	1	1	1	0	0	0	-1	-2	-1	-1	-1	-1	0	1	1	1	1	0	0	0	1	0	0
1	1	1	1	1	1	1	1	1	-1	-2	0	7	16	20	24	29	30	32	33	25	14	3	-1	0	1	1	1	1	1	1	1
1	1	1	1	1	1	1	-1	0	14	33	50	49	44	42	38	38	35	34	33	37	45	47	27	1	0	1	1	1	1	1	1
1	1	1	0	1	1	-1	11	45	51	39	37	33	33	49	61	57	60	70	61	49	46	33	46	51	9	-1	1	1	1	1	1
1	1	1	1	1	-1	18	46	33	34	53	63	77	74	79	84	74	82	83	85	73	74	68	37	40	58	16	-1	1	1	1	1
1	1	1	1	-1	18	40	37	61	70	87	89	88	87	83	83	87	86	86	88	73	81	78	72	35	33	54	6	0	1	1	1
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1	1	-2	28	42	64	83	81	75	82	93	91	87	88	84	79	77	78	93	94	83	83	87	92	88	73	74	36	41	2	1	1
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1	0	7	52	44	73	87	82	83	88	91	81	87	94	94	91	92	91	81	69	93	96	86	81	75	86	85	63	35	31	-1	1
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13	29	49	57	37	38	35	26	12	14	29	16	20	64	68	48	67	85	86	92	92	91	87	83	80	73	40	26	48	3	1	3
50	50	66	77	50	39	21	25	27	15	33	50	50	57	39	37	39	53	76	87	89	89	88	85	84	56	28	55	27	-1	0	19
26	20	23	46	44	38	40	39	47	50	40	35	72	77	62	54	41	52	83	85	86	86	85	75	52	37	76	57	1	0	1	6
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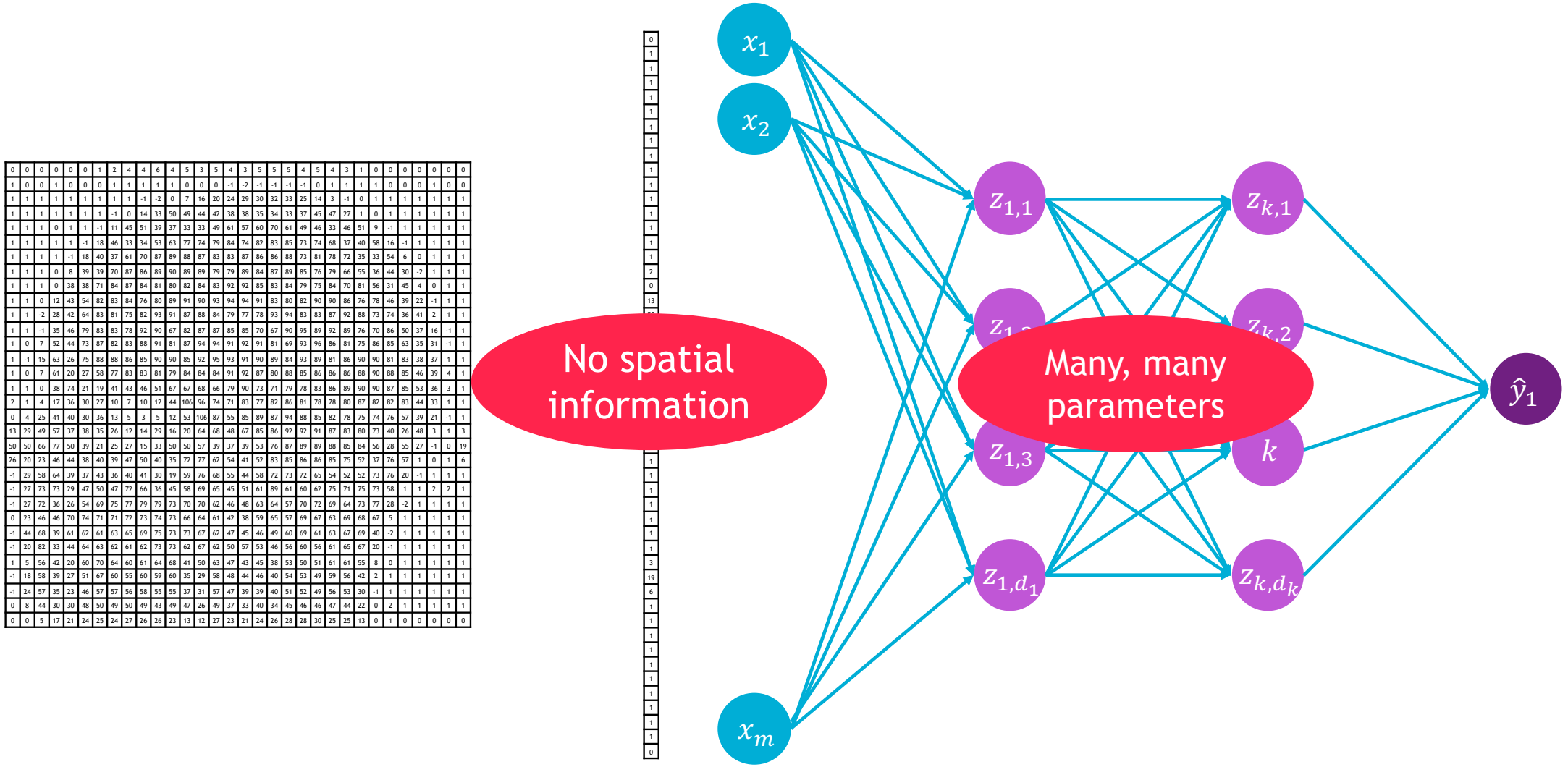
1	5	56	42	20	60	70	64	60	61	64	68	41	50	63	47	43	45	38	53	50	51	61	61	55	8	0	1	1	1	1	1
-1	18	58	39	27	51	67	60	55	60	59	60	35	29	58	48	44	46	40	54	53	49	59	56	42	2	1	1	1	1	1	1
-1	24	57	35	23	46	57	57	56	58	55	55	37	31	57	47	39	39	40	51	52	49	56	53	30	-1	1	1	1	1	1	1
0	8	44	30	30	48	50	49	50	49	43	49	47	26	49	37	33	40	34	45	46	46	47	44	22	0	2	1	1	1	1	1
0	0	5	17	21	24	25	24	27	26	26	23	13	12	27	23	21	24	26	28	28	30	25	25	13	0	1	0	0	0	0	0

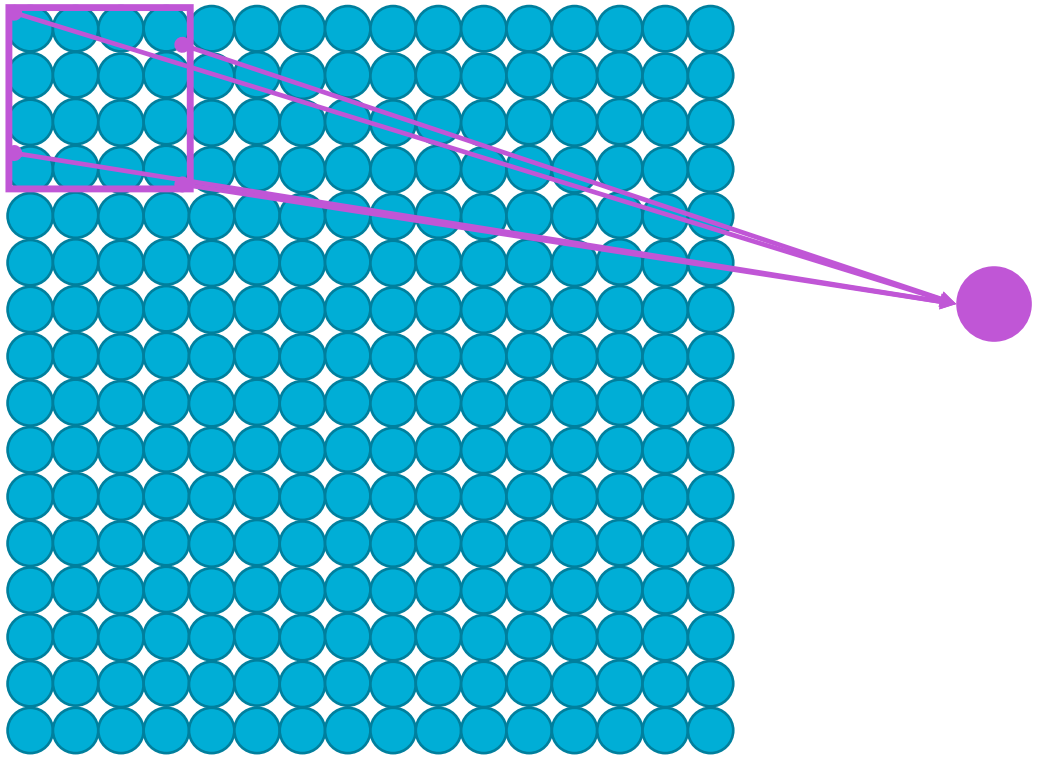
Using an image as input of a neural network

Fully connected neural network



Using an image as input of a neural network

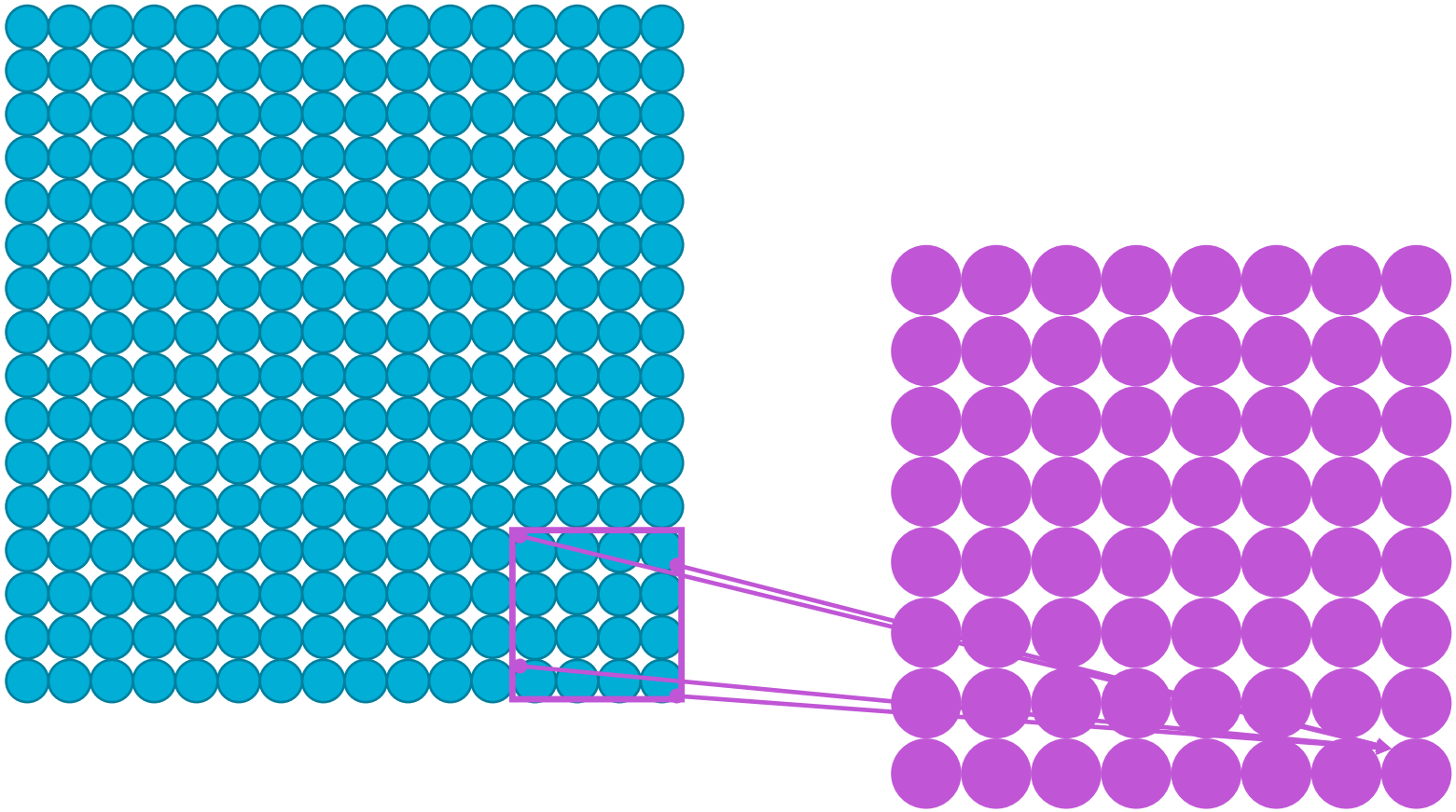
Using spatial features



Idea: connect patches of input to neurons in hidden layer

Using an image as input of a neural network

Using spatial features



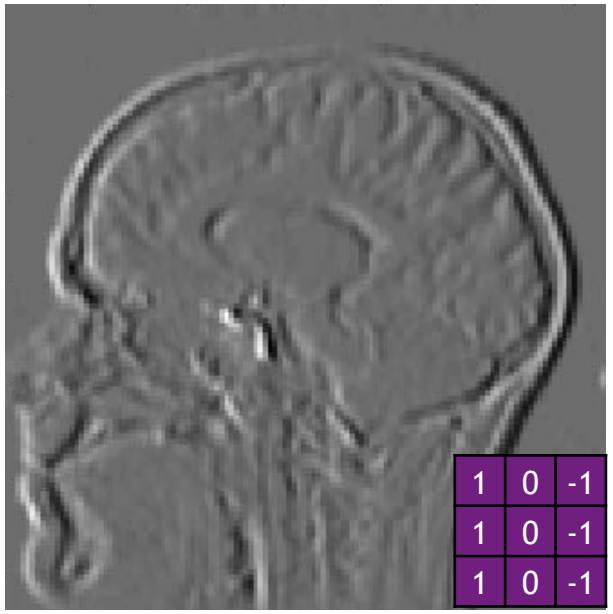
- Slide patch window across input image
- Weight pixels inside the patch
- Apply weighted summation

→ Convolution

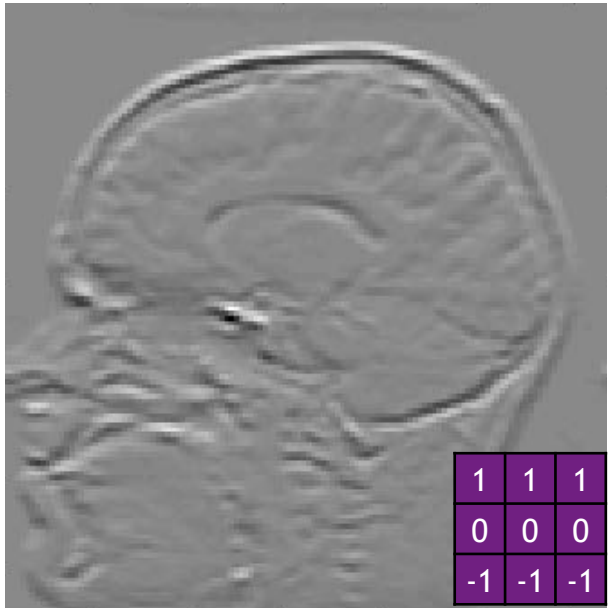
Using an image as input of a neural network

Different filters = different feature maps

Original image



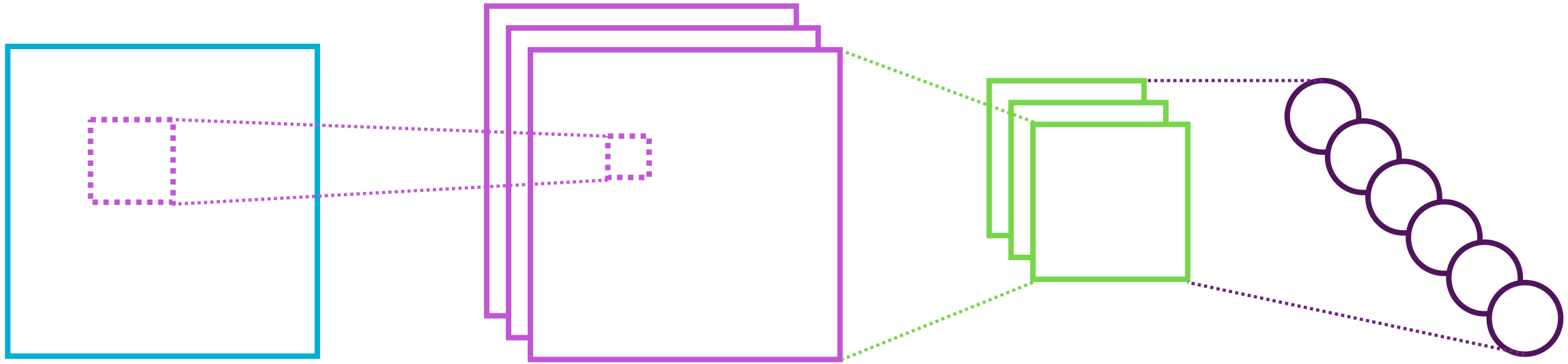
Vertical edge detection



Horizontal edge detection

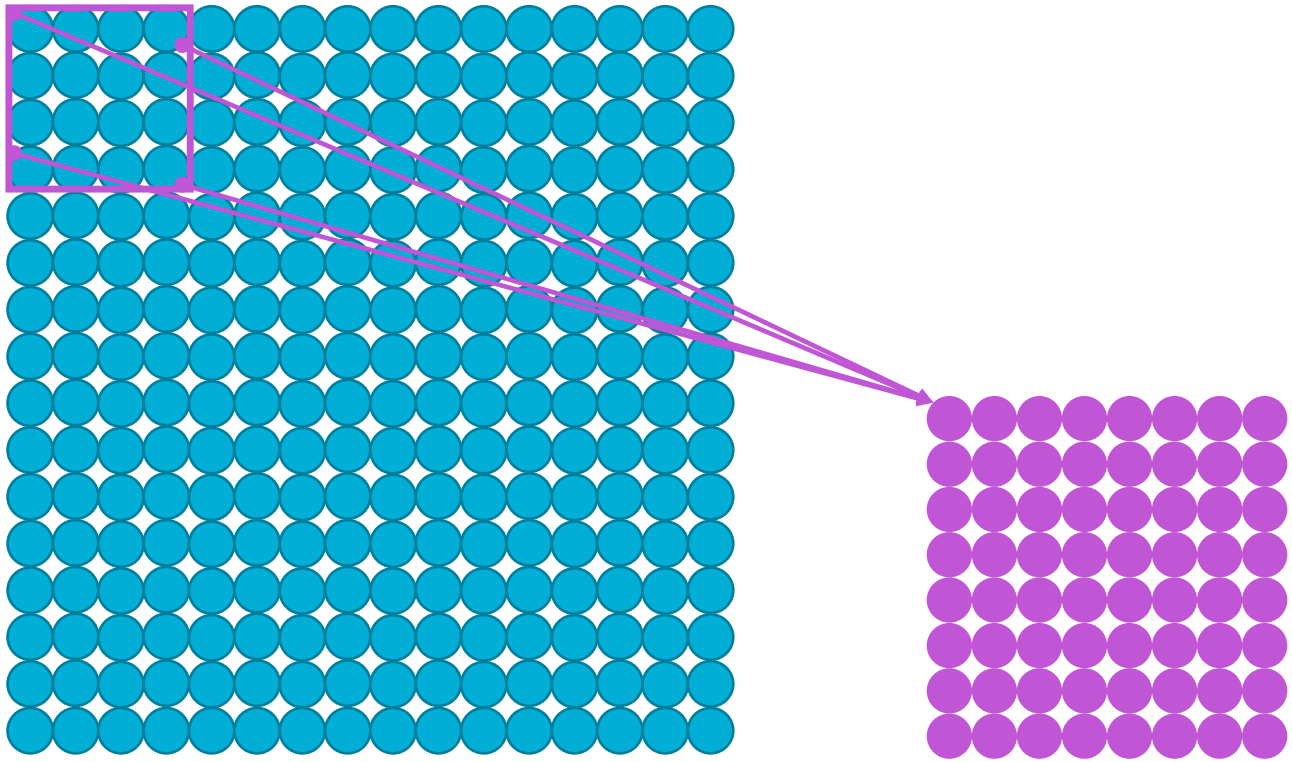
Convolutional neural networks

CNNs for classification



Convolutional neural networks

Convolutional layer



Neuron (p, q) in hidden layer
Filter size 4×4
Weights $w_{i,j}$

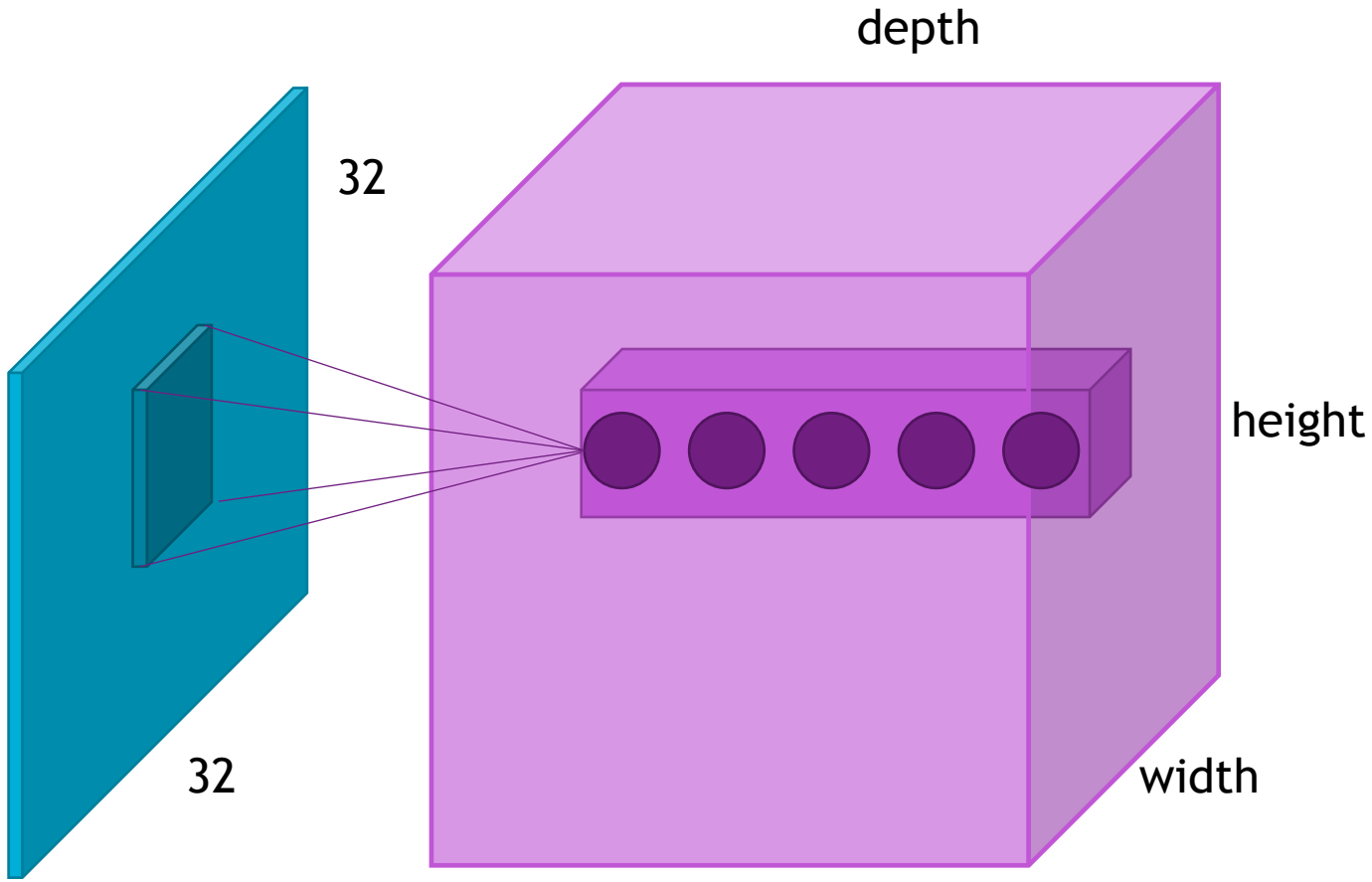
$$h\left(\sum_{i=1}^{4}\sum_{j=1}^{4} w_{i,j} x_{i+p,j+q} + b\right)$$

For a neuron in hidden layer:

- Take inputs from patch
- Compute weighted sum
- Apply bias
- Activate with non-linear function

Convolutional neural networks

Spatial arrangement of output volume



Layer Dimensions:

$h \times w \times d$

h & w = spatial dimensions

d = number of filters

Stride:

Filter step size

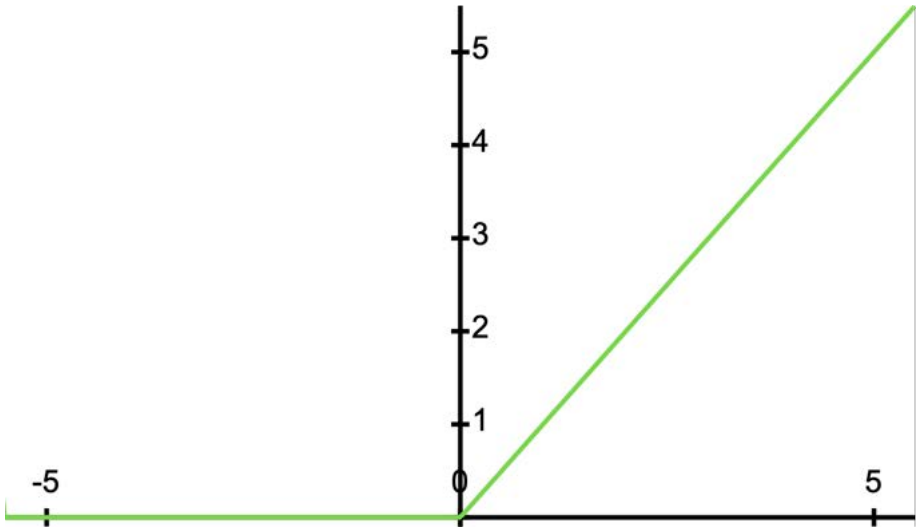
Receptive Field:

Locations in input image that a node is connected to

Convolutional neural networks

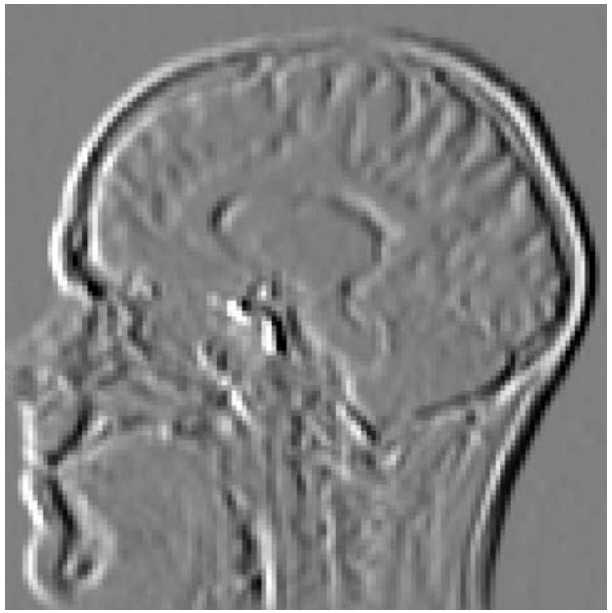
Introducing non-linearity

Rectified linear unit (ReLU)



$$h(z) = \max(0, z)$$

Input feature map



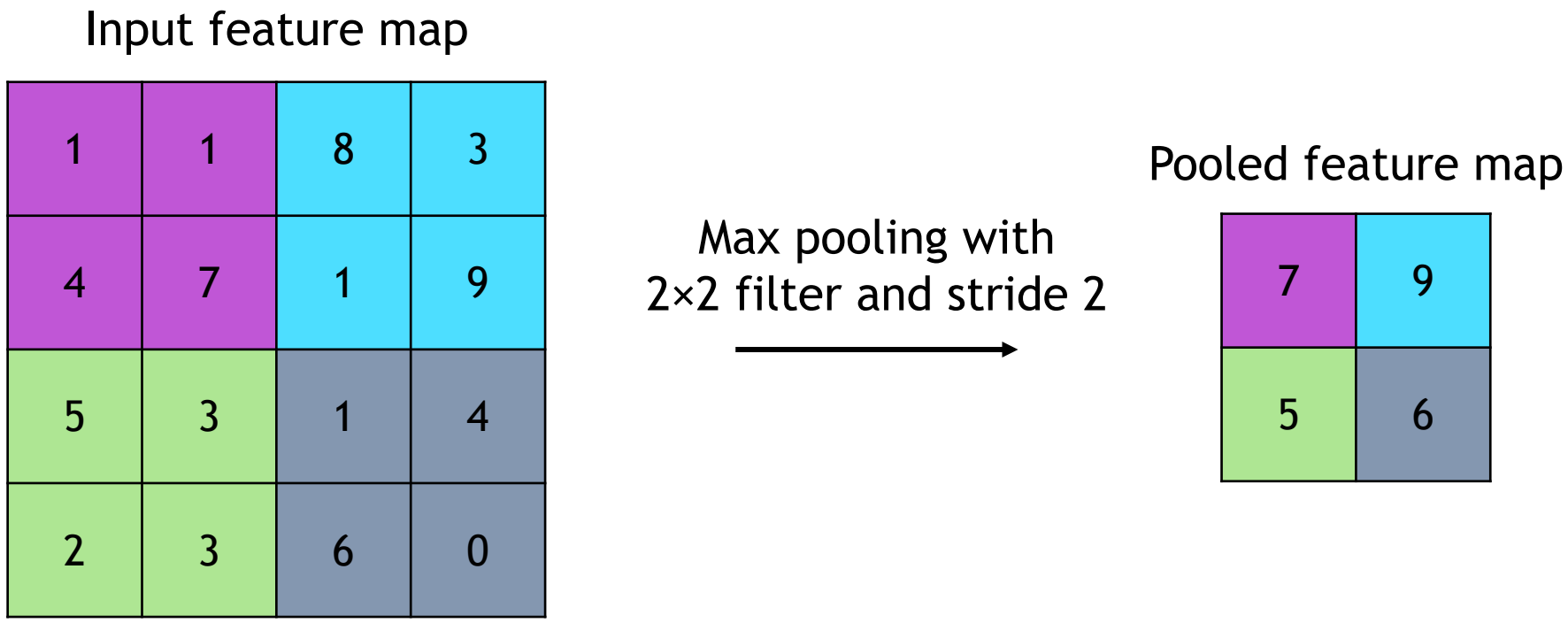
Rectified feature map

ReLU

Black: negative values - White: positive values

Pooling

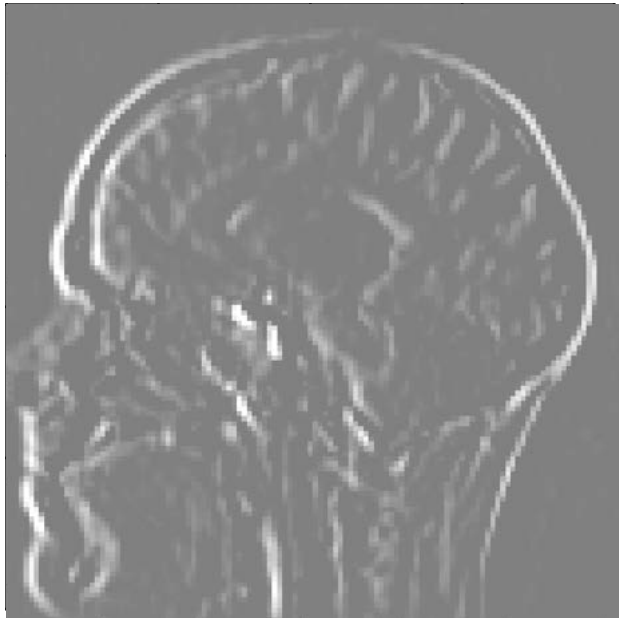
- **Reduce dimensionality while preserving spatial invariance**



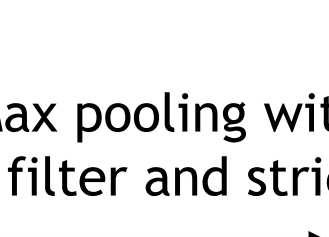
Pooling

- **Reduce dimensionality while preserving spatial invariance**

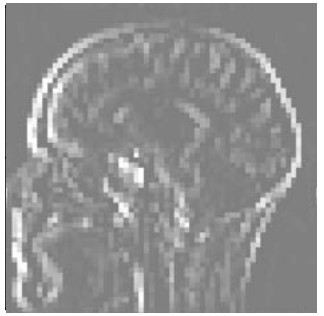
Input feature map



Max pooling with
2×2 filter and stride 2

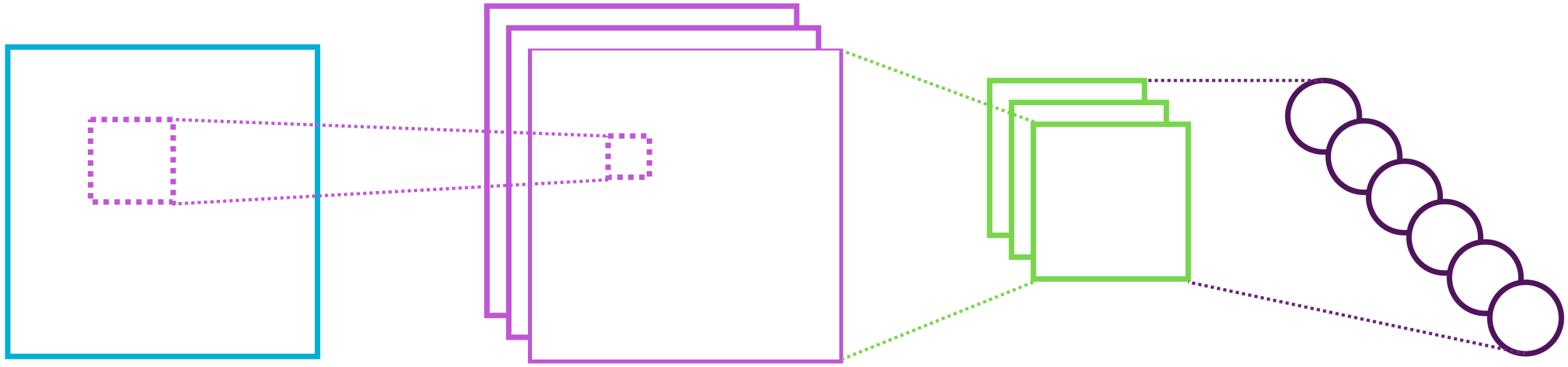


Pooled feature map



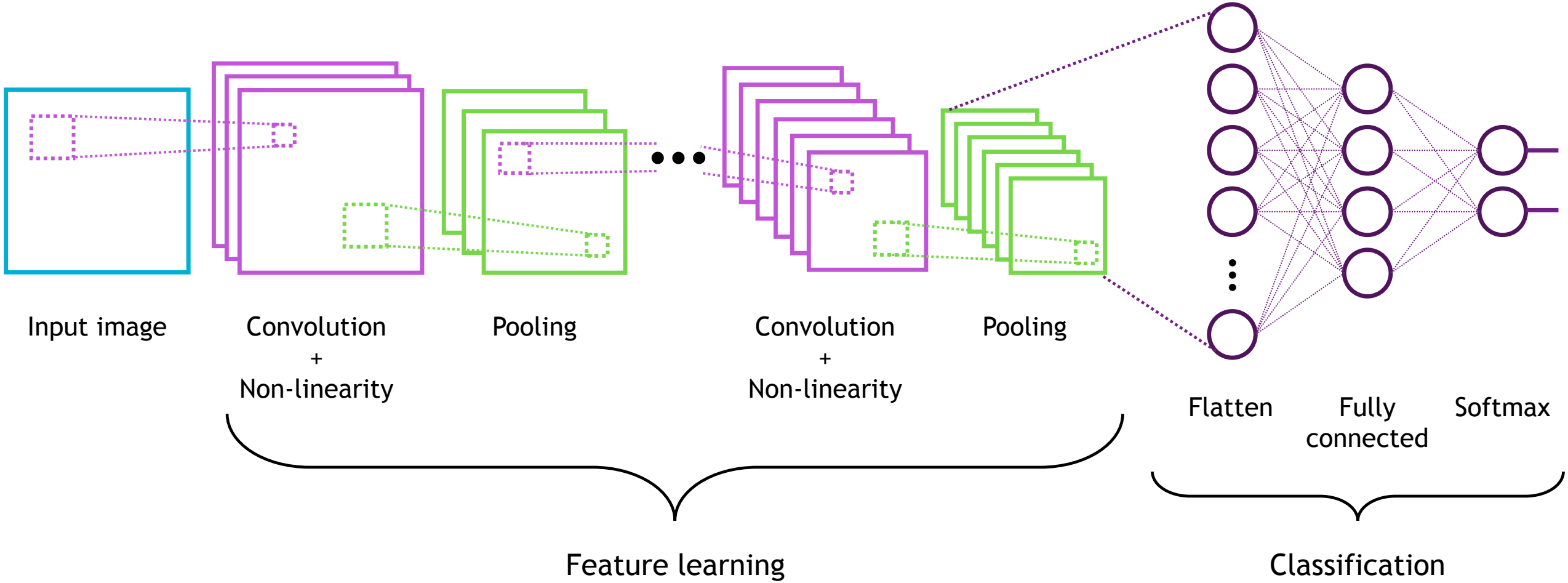
Convolutional neural networks

CNNs for classification



Convolutional neural networks

CNNs for classification



MIT Introduction to Deep Learning (introtodeeplearning.com)

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www.aramislab.fr

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AI4Health School 2021

Practical session DL4MI

Deep learning for computer-aided diagnosis from images

Application to Alzheimer's disease

https://aramislab.paris.inria.fr/workshops/DL4MI