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# IA pour l'imagerie médicale :

# de l'acquisition des images au pronostic

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### Deep learning for medical imaging



# Medical imaging





# X-ray computed tomography

















# Positron emission tomography





Radiotracer (molecule marked with a radioactive atom) The radioactive atom emits positrons which, when they meet electrons, create pairs of photons. Photon pairs are counted when they reach the detectors simultaneously.

# Positron emission tomography





Whole-body PET



Case courtesy of Dr Bruno Di Muzio (rID: 65743), Radiopaedia.org

## Magnetic resonance imaging





Protons in the body

Protons in the MRI scanner, aligned with the magnetic field

Protons subjected to the MRI magnetic field when a radio frequency pulse is applied

# Magnetic resonance imaging











Case courtesy of Dr Mostafa El-Feky (rID: 79193), Dr Pierre VIala (rID: 27366) and Dr Mohammad A. ElBeialy (rID: 52084), Radiopaedia.org



# Neural networks



#### Forward propagation in a neuron





Non-linear activation function

Inputs Weights Sum Non-Linearity Output



#### Forward propagation in a neuron





Inputs Weights Sum Non-Linearity Output



#### Importance of non-linear activation functions





Linear activation functions  $\rightarrow$  linear decisions

Non-linear activation functions  $\rightarrow$  arbitrarily complex decisions



#### **Simplified notation**





#### Multi output neural network with dense layers







 $z_i = w_{0,i}^{(1)} + \sum_{j=1}^{n} x_j w_{j,i}^{(1)}$ 

 $\hat{y}_i = h\left(w_{0,i}^{(2)} + \sum_{j=1}^{a_1} z_j w_{j,i}^{(2)}\right)$ 

Inputs Hidden Output





 $z_2 = w_{0,2}^{(1)} + \sum_{j=1}^m x_j w_{j,2}^{(1)} \mathbf{x}$ 

 $= w_{0,2}^{(1)} + x_1 w_{1,2}^{(1)} + x_2 w_{2,2}^{(1)} + x_m w_{m,2}^{(1)}$ 



#### **Simplified notation**





#### **Stacking layers**





Is this subject healthy?





#### Is this subject healthy?



Loss:  $l(f(x^{(i)}; W), y^{(i)})$ 

Predicted Actual



#### Is this subject healthy?





#### Loss optimisation

• Find the network weights that achieve the lowest loss



# **Training Neural Networks**

#### Gradient descent

#### Algorithm

- 1. Initialise weights randomly  $\sim \mathcal{N}(0, \sigma^2)$
- 2. Loop until convergence
  - a. Compute gradient  $\frac{\partial J(W)}{\partial W}$
  - b. Update weights  $W \leftarrow W \eta \frac{\partial J(W)}{\partial W}$
- 3. Return weights







#### **Computing gradients: backpropagation**



$$\frac{\partial J(W)}{\partial w_2} = \frac{\partial J(W)}{\partial \hat{y}} \times \frac{\partial \hat{y}}{\partial w_2}$$

$$\frac{\partial J(\boldsymbol{W})}{\partial w_1} = \frac{\partial J(\boldsymbol{W})}{\partial \hat{y}} \times \frac{\partial \hat{y}}{\partial w_1} = \frac{\partial J(\boldsymbol{W})}{\partial \hat{y}} \times \frac{\partial \hat{y}}{\partial z_1} \times \frac{\partial z_1}{\partial w_1}$$



Is this subject healthy?





# Convolutional neural networks

Using an image as input of a neural network of the science of the

#### Image = matrix of numbers



0	0	0	0	0	0	1	2	4	4	6	4	5	3	5	4	3	5	5	5	4	5	4	3	1	0	0	0	0	0	0	0
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
1	1	1	0	8	39	39	70	87	86	89	90	89	89	79	79	89	84	87	89	85	76	79	66	55	36	44	30	-2	1	1	1
1	1	1	0	38	38	71	84	87	84	81	80	82	84	83	92	92	85	83	84	79	75	84	70	81	56	31	45	4	0	1	1
1	1	0	12	43	54	82	83	84	76	80	89	91	90	93	94	94	91	83	80	82	90	90	86	76	78	46	39	22	-1	1	1
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
1	1	-1	35	46	79	83	83	78	92	90	67	82	87	87	85	85	70	67	90	95	89	92	89	76	70	86	50	37	16	-1	1
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
1	-1	15	63	26	75	88	88	86	85	90	90	85	92	95	93	91	90	89	84	93	89	81	86	90	90	81	83	38	37	1	1
1	0	7	61	20	27	58	77	83	83	81	79	84	84	84	91	92	87	80	88	85	86	86	86	88	90	88	85	46	39	4	1
1	1	0	38	74	21	19	41	43	46	51	67	67	68	66	79	90	73	71	79	78	83	86	89	90	90	87	85	53	36	3	1
2	1	4	17	36	30	27	10	7	10	12	44	106	96	74	71	83	77	82	86	81	78	78	80	87	82	82	83	44	33	1	1
0	4	25	41	40	30	36	13	5	3	5	12	53	106	87	55	85	89	87	94	88	85	82	78	75	74	76	57	39	21	-1	1
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
-1	29	58	64	39	37	43	36	40	41	30	19	59	76	68	55	44	58	72	73	72	65	54	52	52	73	76	20	-1	1	1	1
-1	27	73	73	29	47	50	47	72	66	36	45	58	69	65	45	51	61	89	61	60	62	75	71	75	73	58	1	1	2	2	1
-1	27	72	36	26	54	69	75	77	79	79	73	70	70	62	46	48	63	64	57	70	72	69	64	73	77	28	-2	1	1	1	1
0	23	46	46	70	74	71	71	72	73	74	73	66	64	61	42	38	59	65	57	69	67	63	69	68	67	5	1	1	1	1	1
-1	44	68	39	61	62	61	63	65	69	75	73	73	67	62	47	45	46	49	60	69	61	63	67	69	40	-2	1	1	1	1	1
-1	20	82	33	44	64	63	62	61	62	73	73	62	67	62	50	57	53	46	56	60	56	61	65	67	20	-1	1	1	1	1	1
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

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#### Fully connected neural network



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Using an image as input of a neural network ARAMIS LAB 29

#### Using spatial features



Idea: connect patches of input to neurons in hidden layer

#### Using spatial features



• Slide patch window across input image

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- Weight pixels inside the patch
- Apply weighted summation
- $\rightarrow$  Convolution

#### The convolution operation

- Slide the filter over the input image
- Element-wise multiply
- Add the outputs





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Image

Filter

#### The convolution operation

- Slide the filter over the input image
- Element-wise multiply
- Add the outputs

 $1 \times 1 + 1 \times 0 + 1 \times 1$  $+ 0 \times 0 + 1 \times 1 + 1 \times 0$  $+ 0 \times 1 + 0 \times 0 + 1 \times 1$ = 4





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Image

Filter

Feature map

#### The convolution operation

- Slide the filter over the input image
- Element-wise multiply
- Add the outputs

 $1 \times 1 + 1 \times 0 + 0 \times 1$  $+ 1 \times 0 + 1 \times 1 + 1 \times 0$  $+ 0 \times 1 + 1 \times 0 + 1 \times 1$ = 3

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Filter

Feature map

#### The convolution operation

- Slide the filter over the input image
- Element-wise multiply
- Add the outputs

 $1 \times 1 + 1 \times 0 + 1 \times 1$  $+ 1 \times 0 + 1 \times 1 + 0 \times 0$  $+ 1 \times 1 + 0 \times 0 + 0 \times 1$ = 4









Feature map



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#### **Different filters = different feature maps**



Original image





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Vertical edge detection

Horizontal edge detection

# **Convolutional neural networks**



#### **CNNs for classification**




#### **Convolutional layer**





## Spatial arrangement of output volume



#### Layer Dimensions:

h×w×d
h & w = spatial dimensions
d = number of filters



### Introducing non-linearity

#### Rectified linear unit (ReLU)





Black: negative values - White: positive values



#### Pooling

• Reduce dimensionality while preserving spatial invariance

Input feature map



Max pooling with 2×2 filter and stride 2

Pooled feature map





#### 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)





MIT Introduction to Deep Learning (introtodeeplearning.com)



# **Deep Learning for** Image Synthesis & Segmentation







#### **CNNs for many applications**





#### **CNNs for image generation**





#### Encoder





#### **Training autoencoders**



$$\mathcal{L}(x,\hat{x}) = \|x - \hat{x}\|^2$$

## **Autoencoders**





## **Autoencoders**







#### Generating images from scratch













#### Image translation







MRI

СТ





Isola et al., Image-to-Image Translation with Conditional Adversarial Networks, CVPR 2017











#### Image translation from paired or unpaired data

Paired data

Unpaired data



#### Wolterink et al., SASHIMI, 2017





#### Isola et al., Image-to-Image Translation with Conditional Adversarial Networks, CVPR 2017



#### Image translation with cycle GANs



Zhu et al., Unpaired Image-to-Image Translation using Cycle-Consistent Adversarial Networks, ICCV 2017



#### Structure of the discriminator





#### Structure of the generator:

encoder-decoder





#### Structure of the generator:

• U-Net





Ronneberger et al., MICCAI, 2015 (61570 citations on 10/05/2023)





#### **Convolutional Networks for Biomedical Image Segmentation**



Ronneberger et al., MICCAI, 2015 (61570 citations on 10/05/2023)

# Summary



#### **Neural Networks**

• Perceptron = structural building block





#### **CNNs**

- Convolutions for feature extraction
- Convolution  $\rightarrow$  nonlinearity  $\rightarrow$  pooling
- Stacking layers •

#### Applications

- Classification •
- Segmentation
- Synthesis •



# Summary







# Deep Learning for Medical Imaging

## Deep learning for medical imaging



prediction disease t 0 processing data From



## Deep learning for medical imaging



prediction disease t 0 processing data From





#### **Historical techniques**

Analytical reconstruction





Final images

#### Iterative reconstruction



#### Deep learning



#### Arndt et al., Fortschr Röntgenstr, 2021


## Image reconstruction by domain-transform manifold learning





#### Image reconstruction by domain-transform manifold learning



Zhu et al., Nature, 2018



## Image reconstruction by domain-transform manifold learning





#### Image denoising using a cGAN

Generator: turns a noisy image into a noise-free image







#### Image denoising using a cGAN



Original noisy MRI



#### **Denoised MRI**

Ran et al., Medical Image Analysis, 2019



#### Image denoising using a cGAN



Full dose CT

Low dose CT

Low dose CT after denoising

Yang et al., IEEE Transactions on Medical Imaging, 2018



# Example of 2D brain MRI



Zhao et al., Magnetic Resonance Imaging, 2019



#### Image super-resolution, a self-supervised approach



Zhao et al., Magnetic Resonance Imaging, 2019



#### Image super-resolution, a self-supervised approach



#### Quantitative results

Dice score (overlap between manual and automatic segmentations)

Thickness	Interpolation	SMORE	HR (0.9 mm)
1.205 mm	0.969	0.9696	0.9699
1.928 mm	0.9665	0.9690	
3.0125 mm	0.9602	0.9675	
3.856 mm	0.9524	0.9632	
4.82 mm	0.9408	0.9607	

Zhao et al., Magnetic Resonance Imaging, 2019

# Deep learning for medical imaging



prediction disease t 0 processing data From





#### Segmentation with a sliding-window CNN



Zhang et al., NeuroImage, 2015



#### Segmentation with a CNN



Input images (T1w, T2w, FA)

Manual segmentations (CSF, GM, WM)

CNN segmentations (CSF, GM, WM)













Zhang et al., NeuroImage, 2015



#### Segmentation with a U-Net



#### Results on the ISBI cell tracking challenge



#### Segmentation results (IOU "intersection over union")

Name	PhC-U373	DIC-HeLa
IMCB-SG $(2014)$	0.2669	0.2935
KTH-SE (2014)	0.7953	0.4607
HOUS-US $(2014)$	0.5323	-
second-best 2015	0.83	0.46
u-net $(2015)$	0.9203	0.7756

Ronneberger et al., MICCAI, 2015 (61570 citations on 10/05/2023)



#### Segmentation with a U-Net

Adult cohort



Paediatric cohort



Han et al., NeuroImage, 2020



#### nnU-Net ('*no new net*')



#### Isensee et al., Nature Methods, 2021



### Segmentation with a sliding-window CNN



T1c sequence



Manual Segmentation



T1c sequence



Manual Segmentation



Pereira et al., IEEE TMI, 2016





#### Unsupervised anomaly segmentation in brain MR images



Baur et al., MICCAI Brainlesion Workshop, 2019



#### Unsupervised anomaly segmentation in brain MR images



Baur et al., MICCAI Brainlesion Workshop, 2019



#### Unsupervised anomaly segmentation in brain MR images



True Positives False Positives False Negatives

Baur et al., MICCAI Brainlesion Workshop, 2019

# Deep learning for medical imaging



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#### 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





#### Imaging in Alzheimer's disease

• Structural magnetic resonance imaging (MRI) to detect atrophy

Cognitively normal

Mild cognitive impairment

Alzheimer's disease



Disease progression





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## Classification of Alzheimer's disease using CNNs



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

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## **Classification of Alzheimer's disease using CNNs**



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

# **Disease recognition**







# Computer-aided diagnosis of dementia in a clinical data warehouse

Data set		Task	Classification strategy		
		-	CNN	SVM	
Clinical D	D vs NDNL	63.2	61.9	<ul> <li>D: dementia,</li> <li>NDNL: no dementia and no lesions,</li> <li>NDL: no dementia with lesions</li> </ul>	
	D vs NDL	67.5	64.6		
ADNI Alzheimer's Disease					

Balanced accuracy (%)

Balanced accuracy ~20 percent points lower than when training/testing on research data

Bottani et al., Under revision at Medical Image Analysis · hal-03656136



## Identification and subtyping of intracranial haemorrhage (ICH)



Ye et al., European Radiology, 2019

# Deep learning for medical imaging



prediction disease t 0 processing data From





# Deep learning for the diagnosis and prognosis of AD

- 'Diagnostic' classification task
  - Differentiate cognitively normal (CN) subjects from patients with AD: CN vs AD
  - Not clinically relevant but useful when developing algorithms
- 'Predictive' classification task
  - Different patients with mild cognitive impairment (MCI) that will stay stable (sMCI) from the ones that will progress to AD dementia (pMCI): sMCI vs pMCI
  - Clinically relevant but more difficult



## Classification of mild cognitive impairment using CNNs



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

# Generation of images that mimic disease progression

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Ravi et al., MICCAI, 2019



#### Generation of images that mimic disease progression



Neurodegeneration simulation of a 69-year old ADNI participant

Ravi et al., MICCAI, 2019

# Deep learning for medical imaging



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## Challenges that currently prevent bringing DL to the clinic

- DL usually requires a large amount of data, which can be hard to collect for some medical applications.
- Research cohort specificities may prevent the application of models trained on such data to clinical cohorts.
- Algorithms are often black boxes, with poor interpretability of the decision-making process.
- Validating models accurately is crucial as the algorithms can very easily overfit the training data.

# Deep learning for medical imaging







#### Further reading:

• Litjens et al., 2017. A survey on deep learning in medical image analysis. *Medical Image Analysis* 42, 60-88.

doi:10.1016/j.media.2017.07.005

- Burgos et al., 2020. Deep learning for brain disorders: from data processing to disease treatment.
   Briefings in Bioinformatics. doi:10.1093/bib/bbaa310
- Zhou, S.K., Greenspan, H. and Shen, D. eds., 2017. Deep learning for medical image analysis. Academic Press. <u>ISBN:9780128104088</u>