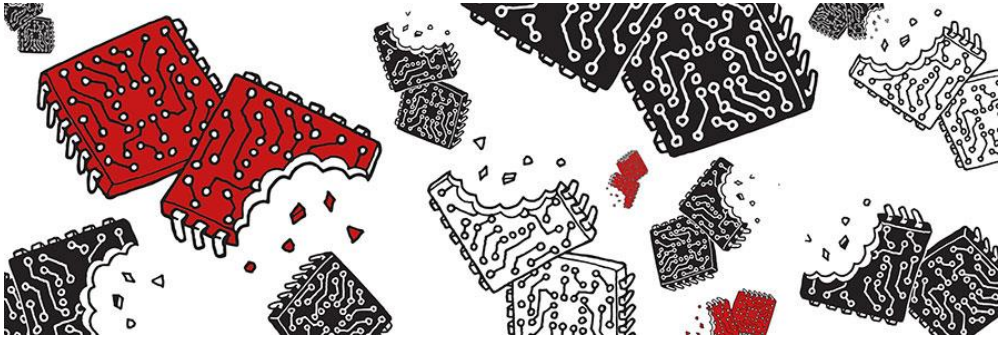


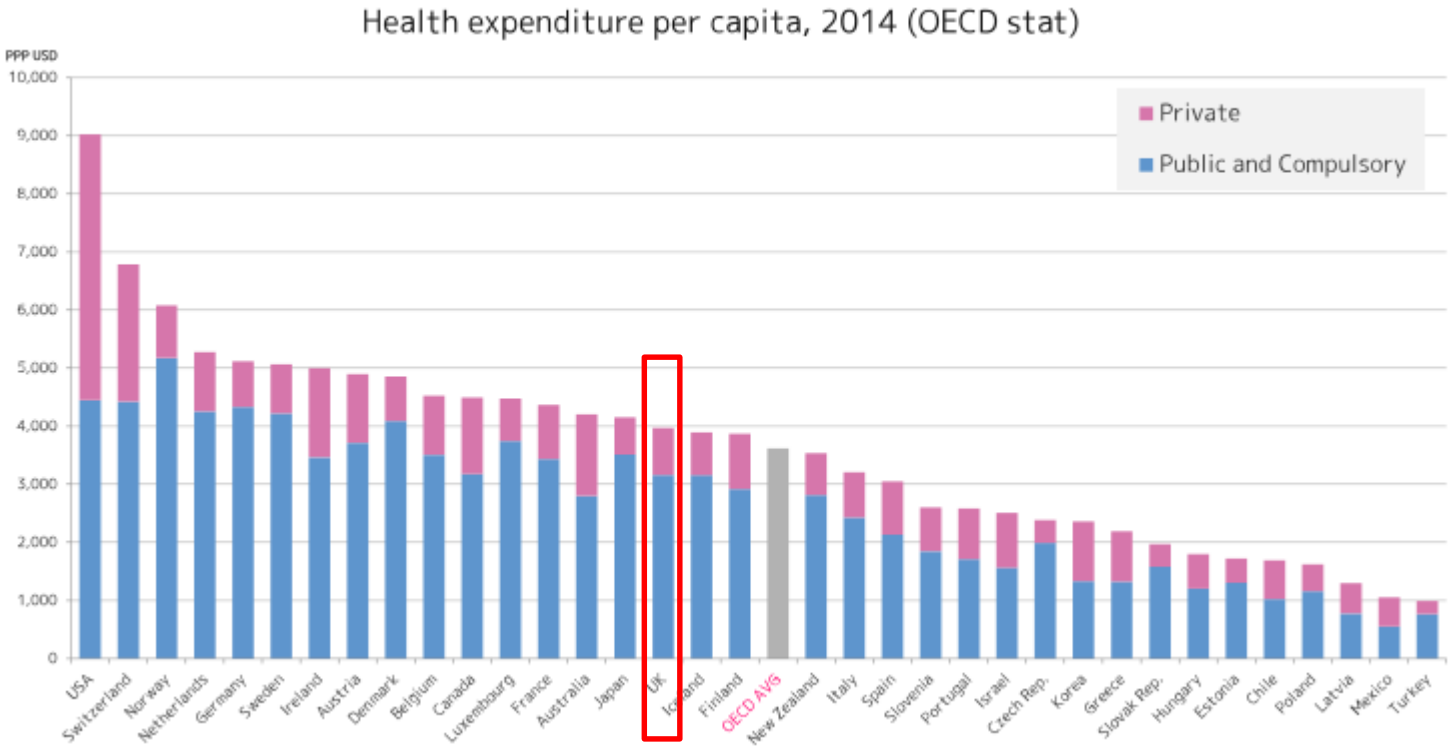
Data Bites

Deep health: Applications of deep learning in medical imaging

Dr Greg Slabaugh

18 Oct 2017

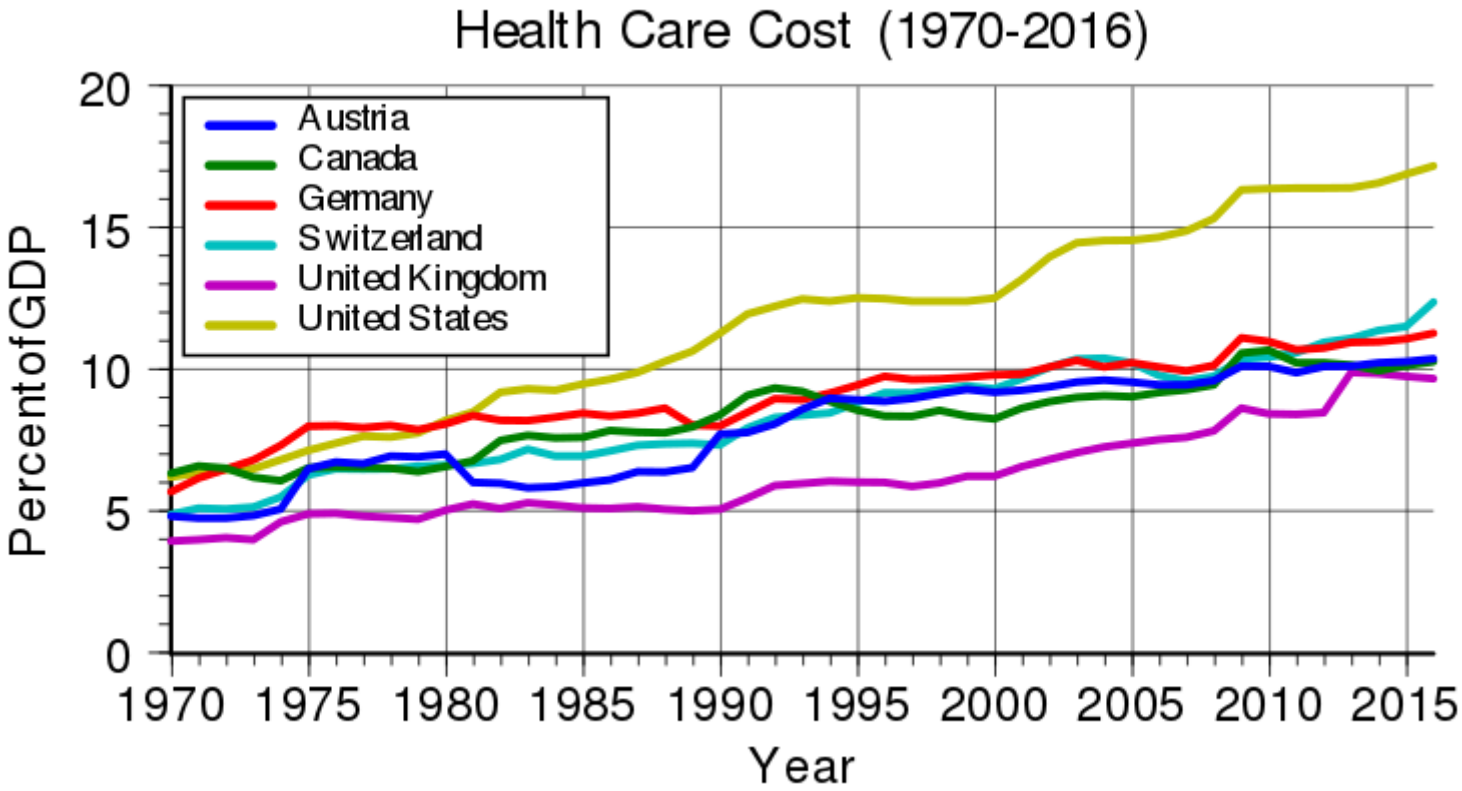
Healthcare



UK

https://en.wikipedia.org/wiki/List_of_countries_by_total_health_expenditure_per_capita

It's not getting any cheaper…

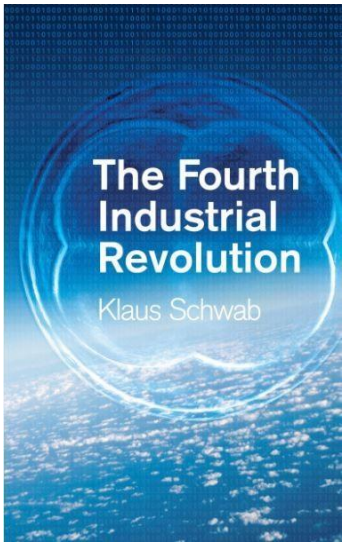


UK: ~£200B

https://en.wikipedia.org/wiki/List_of_countries_by_total_health_expenditure_per_capita

AI and the Fourth Industrial Revolution

"The last 10 years have been about building a world that is mobile-first. In the next 10 years, we will shift to a world that is AI-first." (Sundar Pichai, CEO of Google, October 2016)



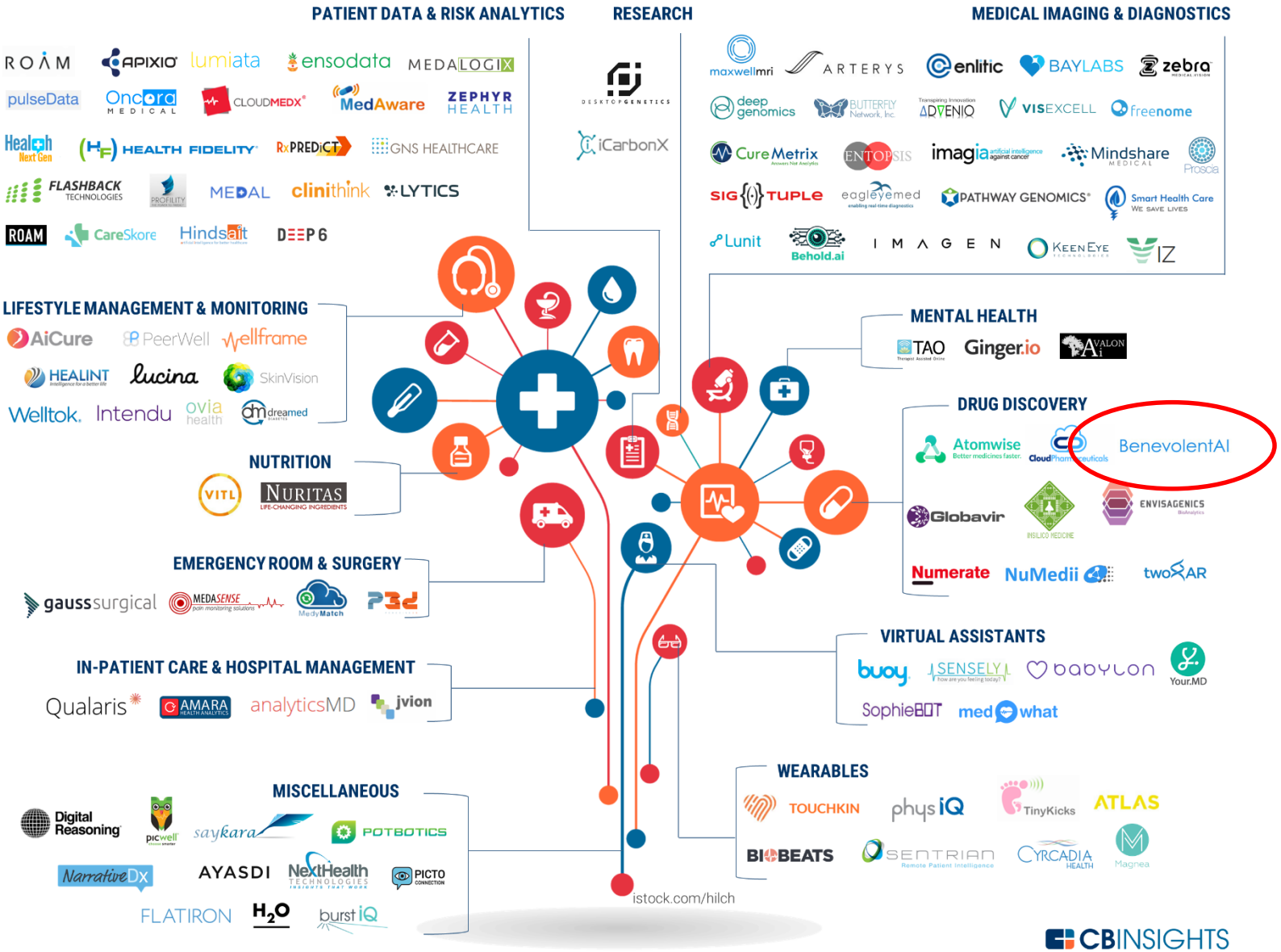
It is characterized by a range of new technologies that are fusing the physical, digital and biological worlds, impacting all disciplines, economies and industries, and even challenging ideas about what it means to be human.

Let’s disrupt healthcare with AI

Challenges

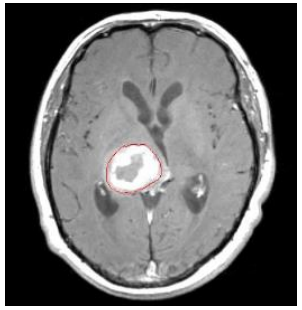
- **Access to data**
  - Ethics approval: IRB approval, Caldicott Guardian
  - Privacy
- IT infrastructure
- Large datasets
  - A single CT will contain hundreds, if not thousands of slices (images)
  - Data wrangling
- **Regulatory environment**
- **Risk adversion**

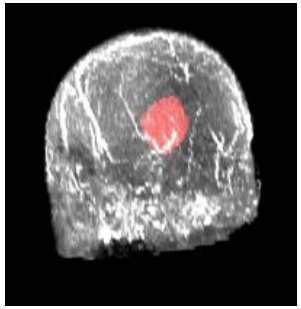
106 STARTUPS TRANSFORMING HEALTHCARE WITH AI



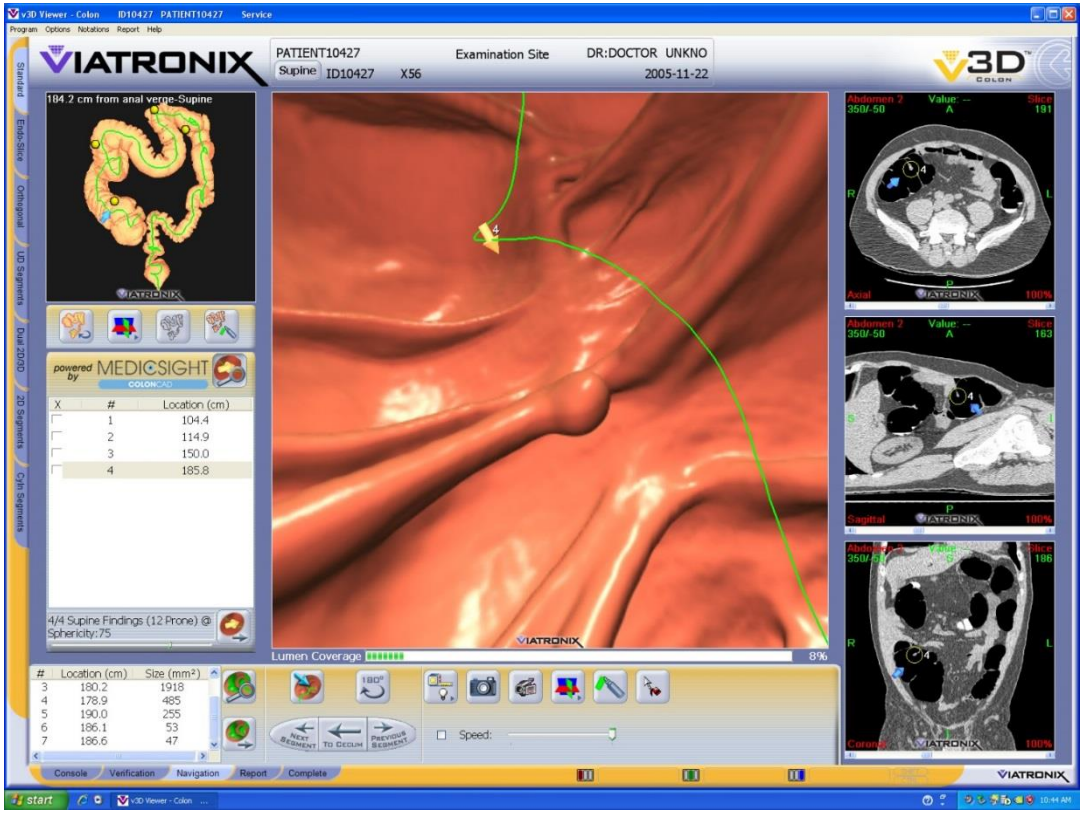
https://cbi-blog.s3.amazonaws.com/blog/wp-content/uploads/2017/01/healthcare_AI_map_2016_1.png

My journey in healthcare and AI





Siemens Corporate Research

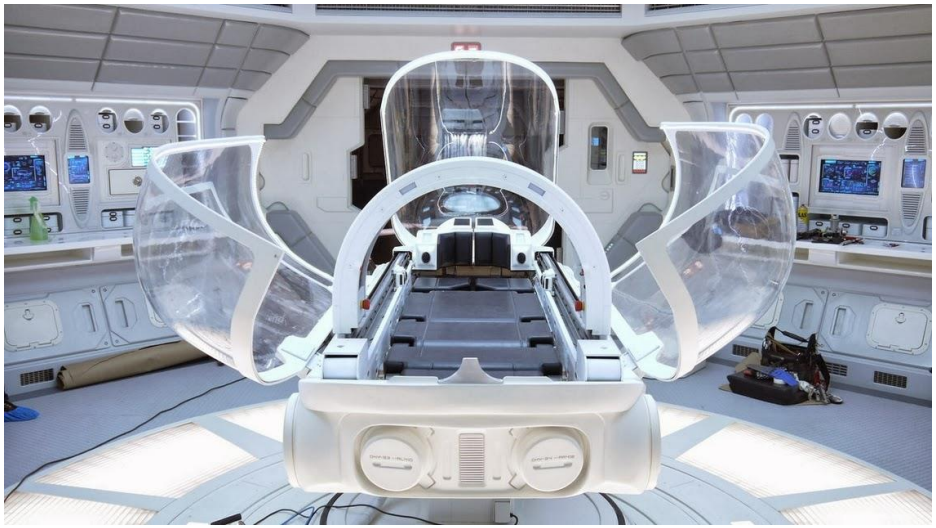


Medicsight

Strong vs weak AI

Strong AI

- Consciousness
- Ability to make judgements, plan, communicate, self-awareness

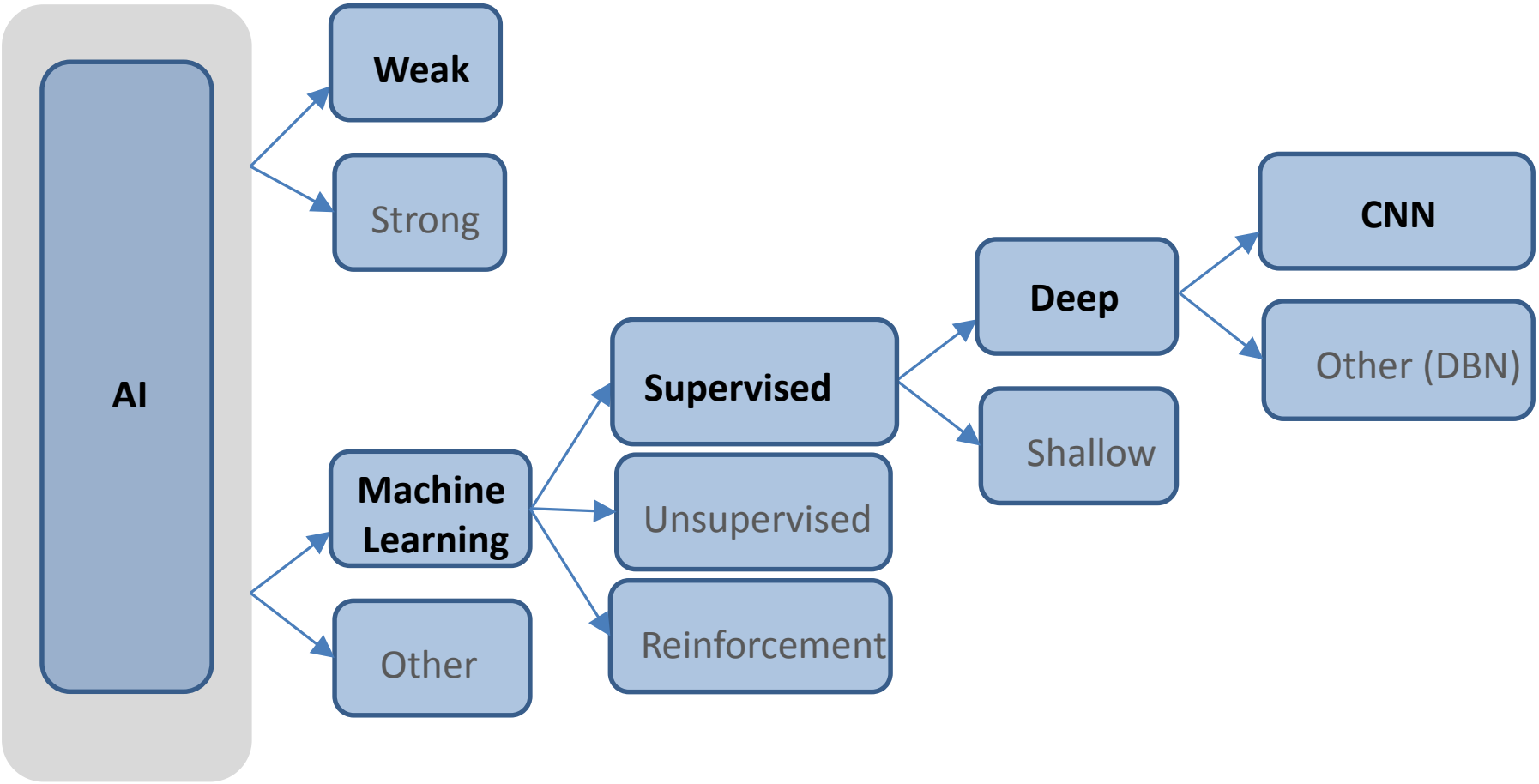


Weak AI

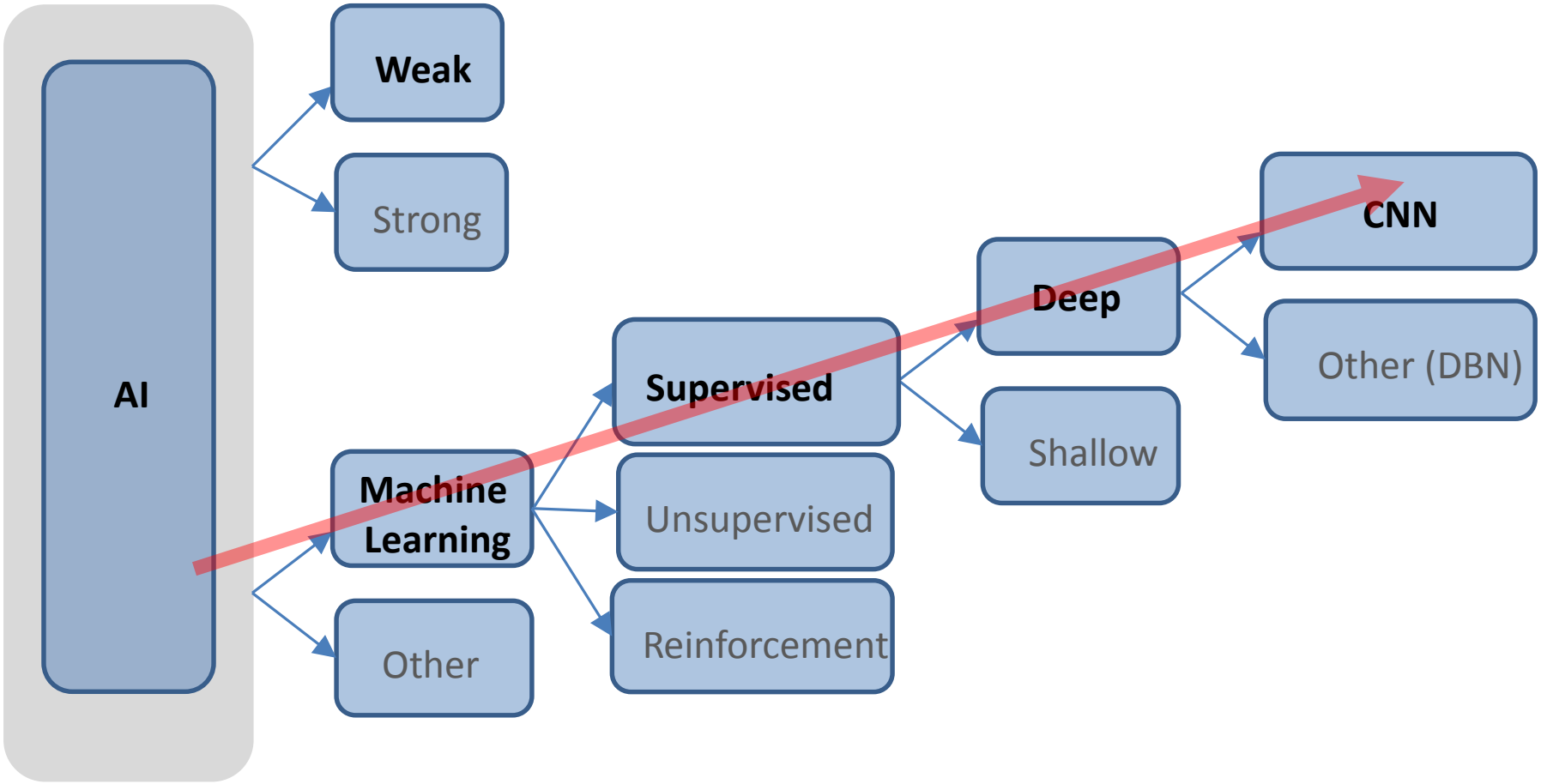
- Focuses on a specific task
- No self-awareness

AI… coming to (*or already in*) a device near you

The AI taxonomy (according to Greg)



The AI taxonomy (according to Greg)

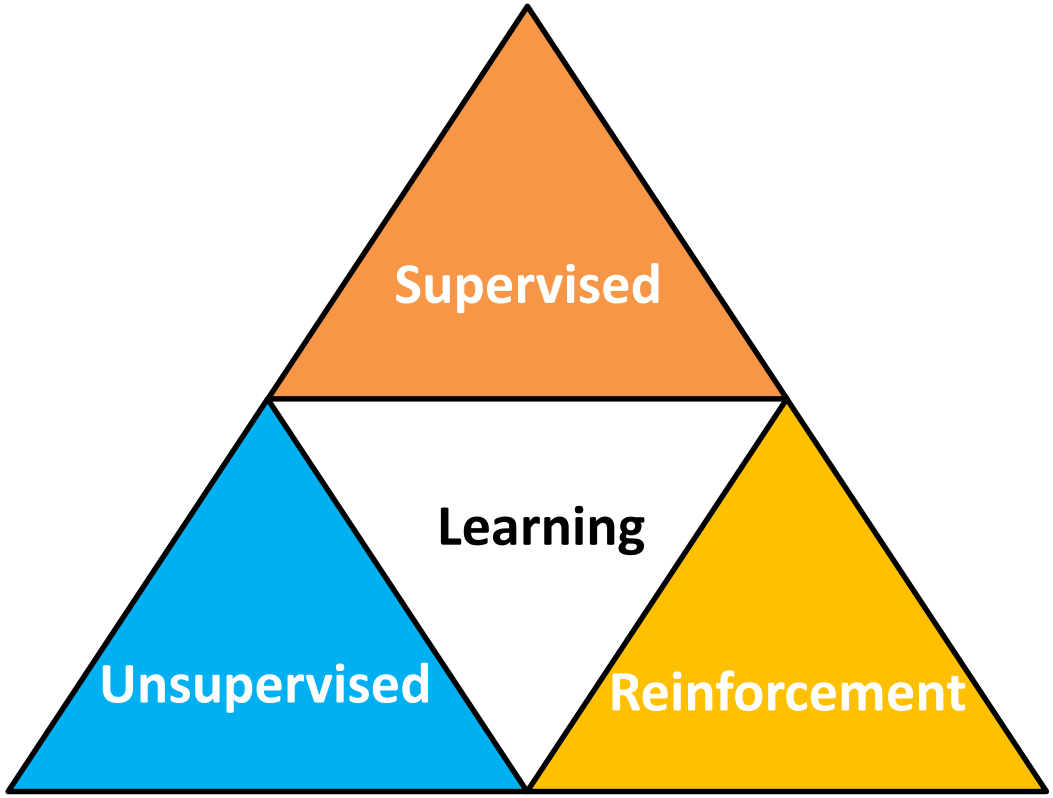


What is machine learning?

- **Machine learning** is a type of artificial intelligence (AI) that provides computers with the ability to learn without being explicitly programmed.

⇨ Learning from data

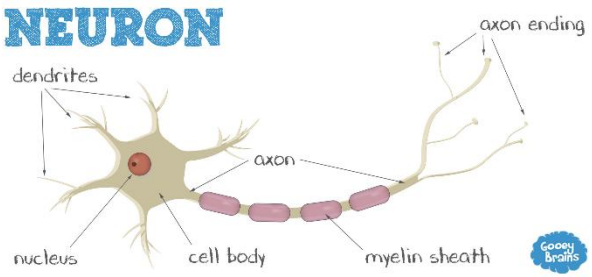
- Labelled data
- Learn a mapping between inputs and outputs
- Example: face detection

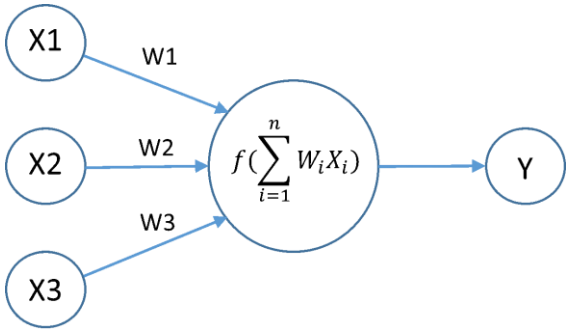


- No labels
- Computer groups similar data to discover hidden patterns
- Example: “People who bought X also bought Y”

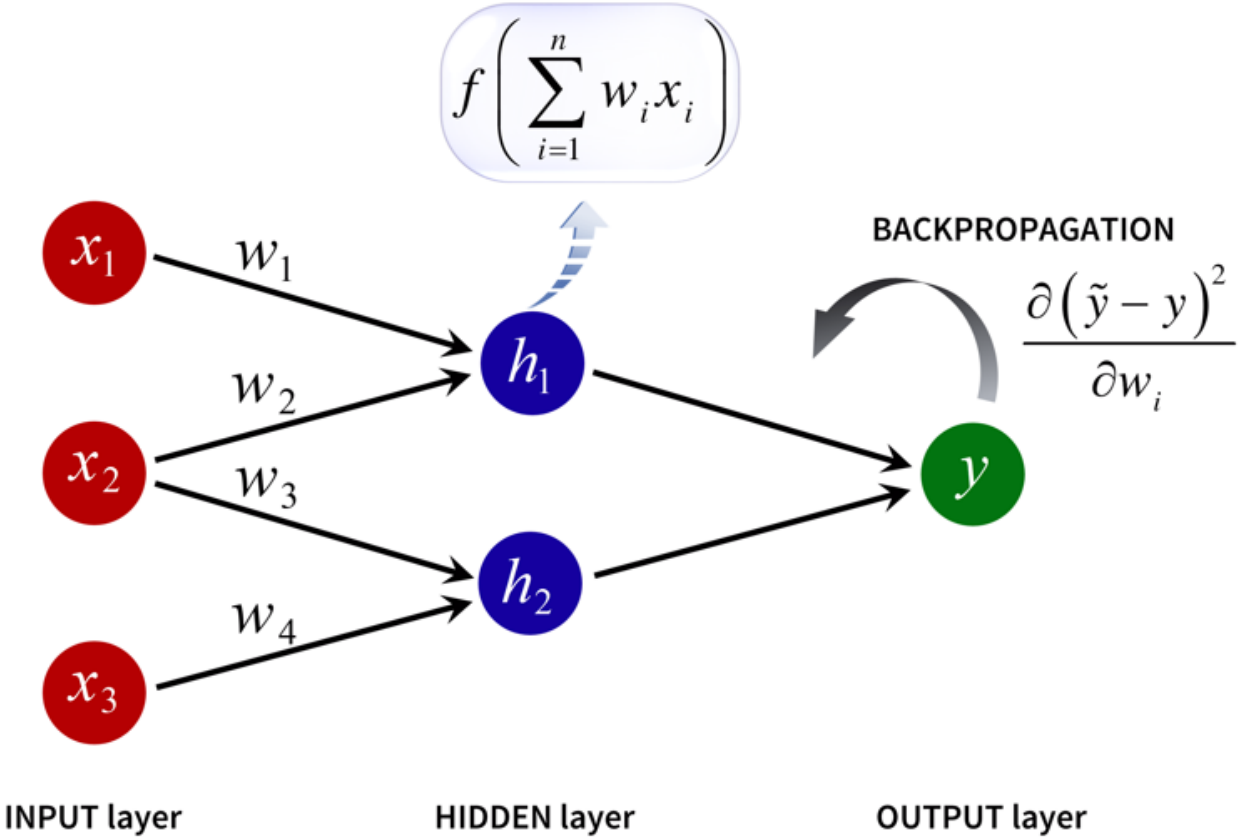
- Dynamic environment
- Computer gets feedback and learns to “win”
- Example: ML playing Atari 2600 games

Neural networks



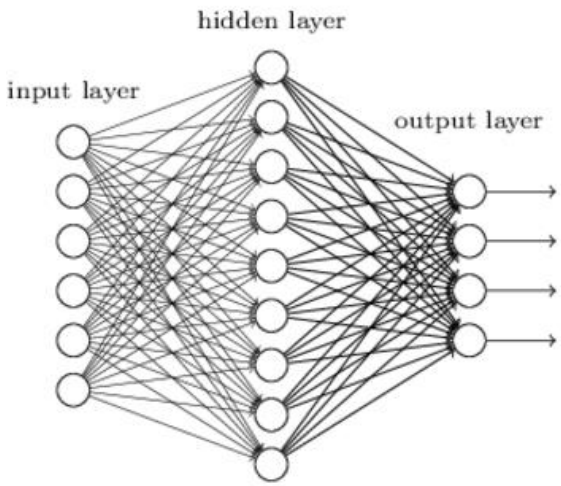


Learning

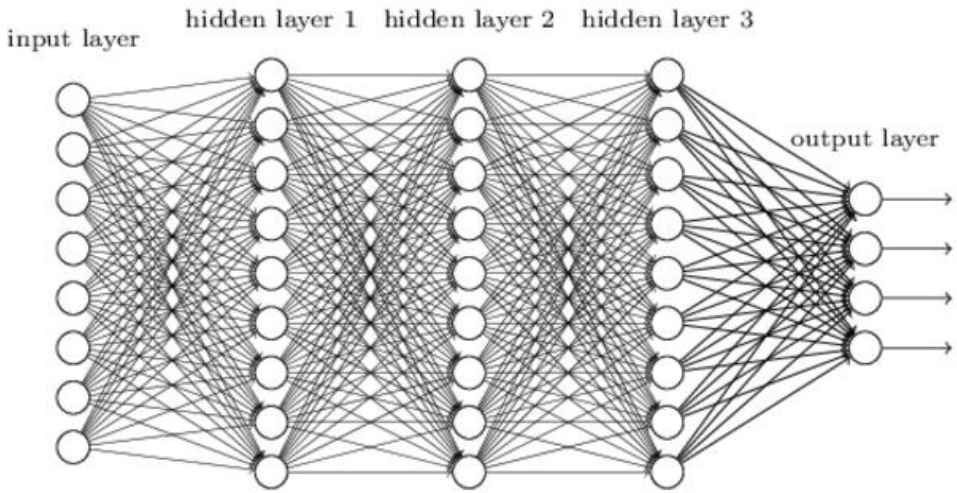

$f\left(\sum_{i=1}^{n} w_i x_i\right)$
BACKPROPAGATION
$\frac{\partial(\tilde{y}-y)^2}{\partial w_i}$
x_1
x_2
x_3
w_1
w_2
w_3
w_4
h_1
h_2
y
INPUT layer
HIDDEN layer
OUTPUT layer

Shallow vs deep

"Non-deep" feedforward neural network



Deep neural network



Big data

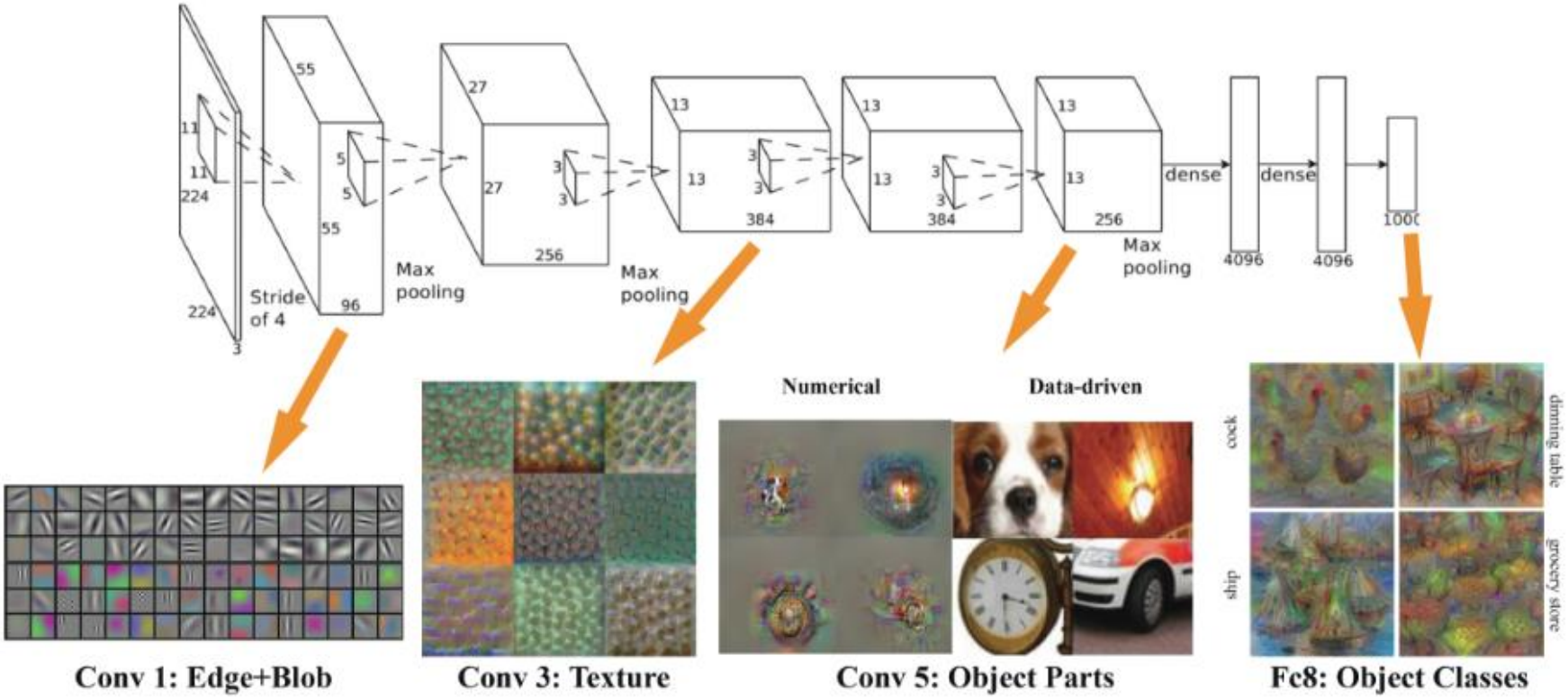
ImageNet

- A competition to classify images
- Running since 2010
- 1M+ images
- 1000 object categories

```
{0: 'tench, Tinca tinca',
 1: 'goldfish, Carassius auratus',
 2: 'great white shark, white shark,
 3: 'tiger shark, Galeocerdo cuvieri
 4: 'hammerhead, hammerhead shark',
 5: 'electric ray, crampfish, numbfi
 6: 'stingray',
 7: 'cock',
 8: 'hen',
 9: 'ostrich, Struthio camelus',
```

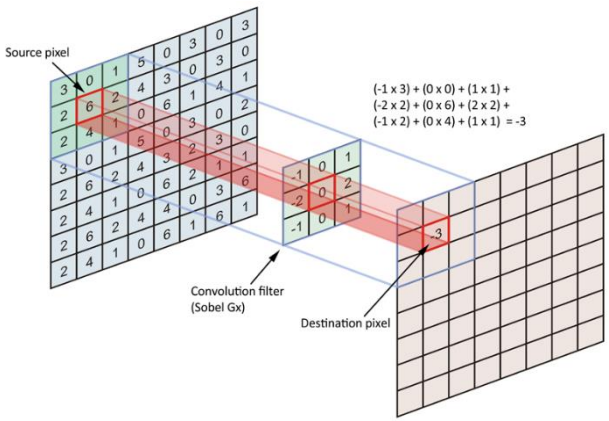
AlexNet (2012)

- AlexNet, a type of Convolutional Neural Network (CNN) won the ImageNet challenge by a large margin (15.4% error, compared to 26.2%). **This precipitated a swell of interest in Deep Learning techniques.**

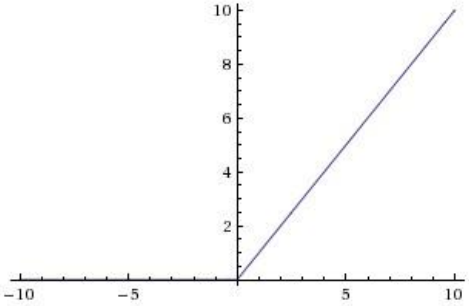


Key components

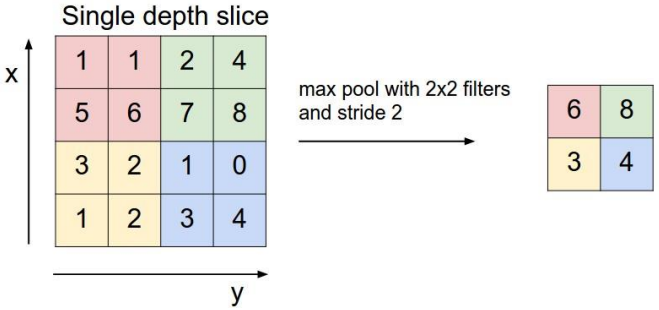
1. **Convolution**. This filters an image. The weights for the filter are learned.



2. **ReLU**. This applies a non-linear transformation to the data. This way, the CNN and find a non-linear mapping between the inputs and outputs.



3. **Pooling**. This combines adjacent pixels in a filtered output. This results in abstraction. The CNN learns more “high level” features (e.g. face, instead of edges).



Deep learning frameworks

Keras

MatConvNet

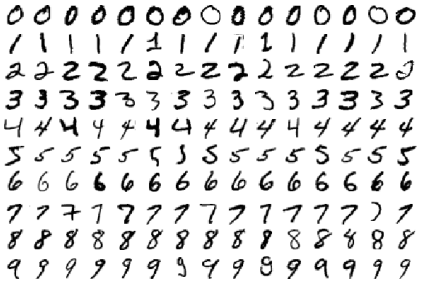
mxnet

TensorFlow

Caffe2

PYTORCH

Making it easy…



```
# Import libraries and modules
import numpy as np
np.random.seed(123)  # for reproducibility

from keras.models import Sequential
from keras.layers import Dense, Dropout, Activation, Flatten
from keras.layers import Convolution2D, MaxPooling2D
from keras.utils import np_utils
from keras.datasets import mnist

# Load pre-shuffled MNIST data into train and test sets
(X_train, y_train), (X_test, y_test) = mnist.load_data()

# Preprocess input data
X_train = X_train.reshape(X_train.shape[0], 1, 28, 28)
X_test = X_test.reshape(X_test.shape[0], 1, 28, 28)
X_train = X_train.astype('float32')
X_test = X_test.astype('float32')
X_train /= 255
X_test /= 255

# Preprocess class labels
Y_train = np_utils.to_categorical(y_train, 10)
Y_test = np_utils.to_categorical(y_test, 10)
```

```
# Define model architecture
model = Sequential()

model.add(Convolution2D(32, 3, 3, activation='relu',
input_shape=(1,28,28)))
model.add(Convolution2D(32, 3, 3, activation='relu'))
model.add(MaxPooling2D(pool_size=(2,2)))
model.add(Dropout(0.25))

model.add(Flatten())
model.add(Dense(128, activation='relu'))
model.add(Dropout(0.5))
model.add(Dense(10, activation='softmax'))

# Compile model
model.compile(loss='categorical_crossentropy',
optimizer='adam', metrics=['accuracy'])

# Fit model on training data
model.fit(X_train, Y_train, batch_size=32, nb_epoch=10,
verbose=1)

# Evaluate model on test data
score = model.evaluate(X_test, Y_test, verbose=0)
```

Why is deep learning so… *trendy*?

Recently there has been a surge of (research, commercial) interest in Deep Learning

1. Large datasets (e.g. ImageNet)

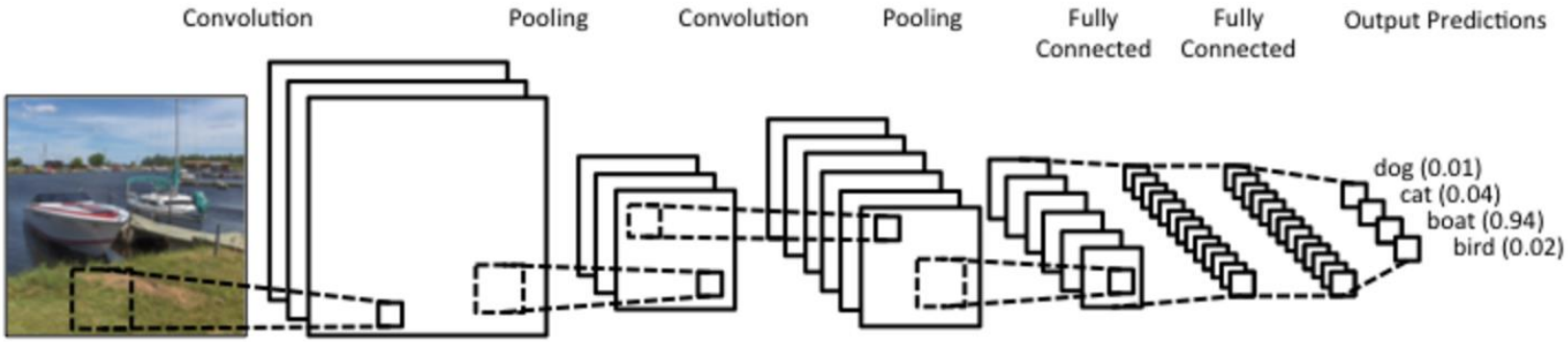
2. New algorithms and toolkits (e.g. TensorFlow, PyTorch, *MatConvNet*)

3. Graphics Processing Units (GPUs)

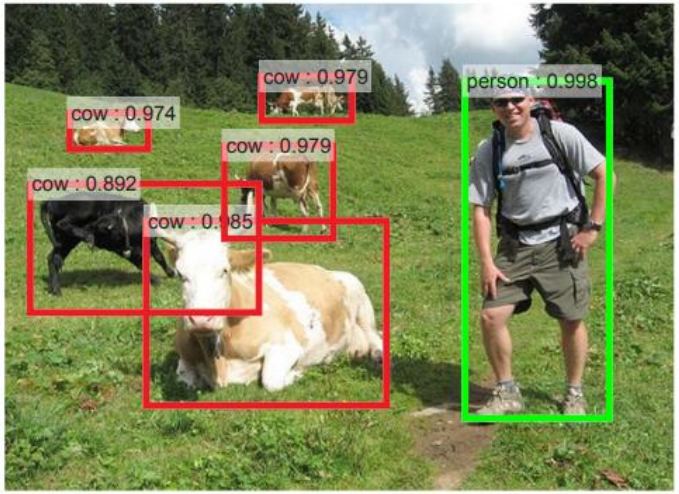
NVidia TitanX with 3584 cores

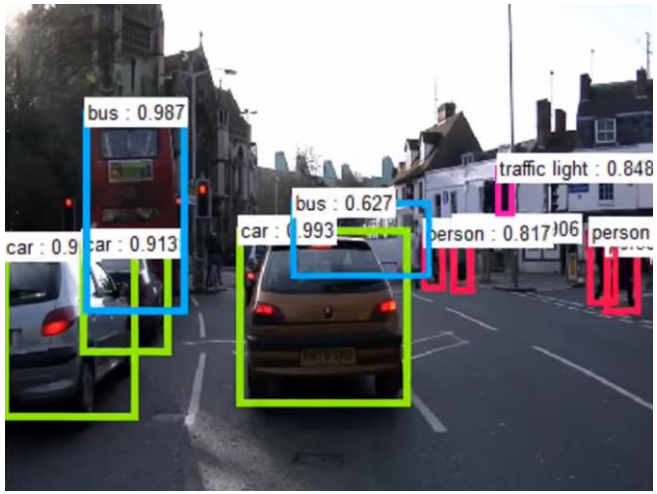
CNNs in computer vision

- Image classification (e.g. ImageNet)

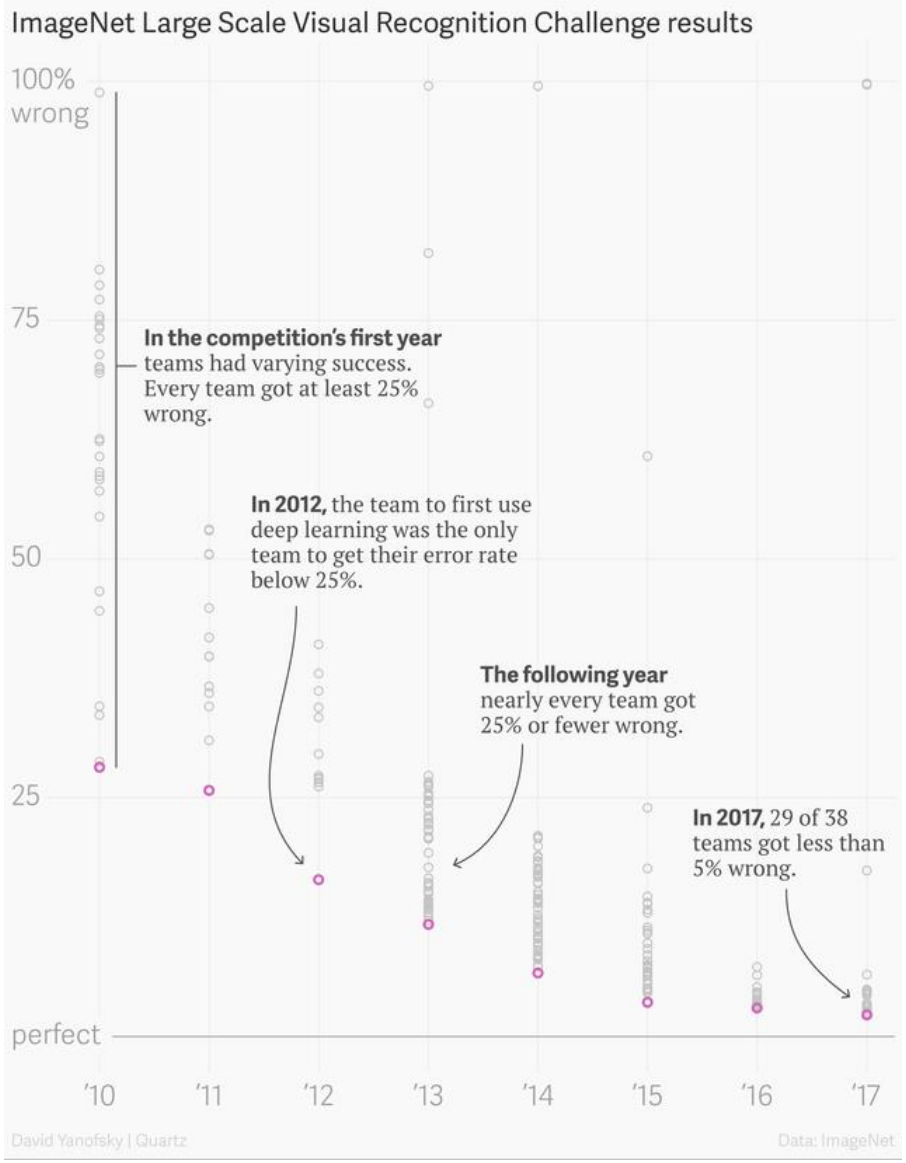


- Object detection





ImageNet



Current performance (2.25%) on ImageNet *exceeds* human ability in image classification.

2017: ImageNet is shutting down – problem solved?

https://qz.com/1034972/the-data-that-changed-the-direction-of-ai-research-and-possibly-the-world/

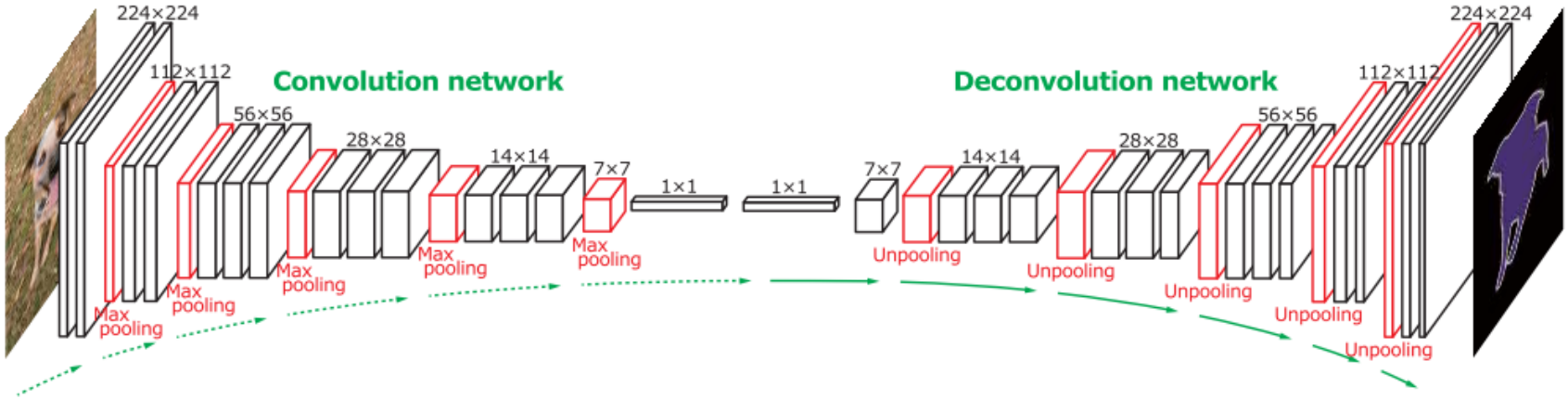
Segmentation

- Image segmentation partitions an image into regions (aka *segments*).

- Essentially, segmentation is a grouping problem. Depending on the image, this can be difficult! Humans are adept at visual grouping!

Deep segmentation network

- Segmentation can be achieved using a CNN, by replacing fully connected layers with an expanding (deconvolutional) path



https://www.cv-foundation.org/openaccess/content_iccv_2015/papers/Noh_Learning_Deconvolution_Network_ICCV_2015_paper.pdf

Generative adversarial networks (GANs)

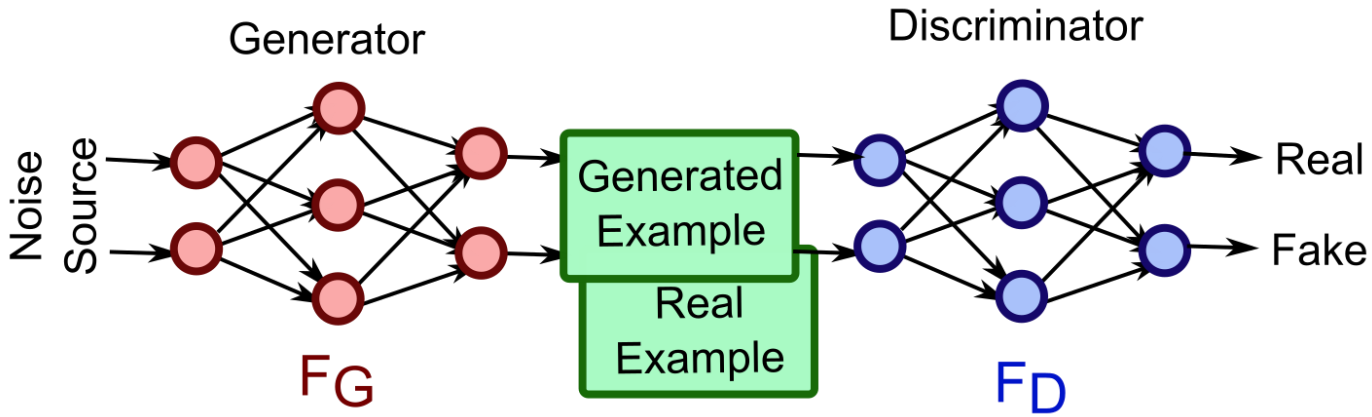
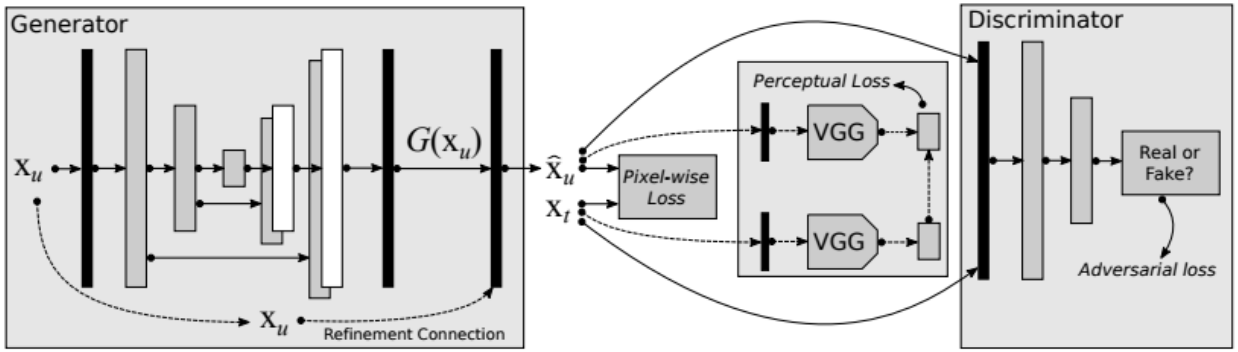


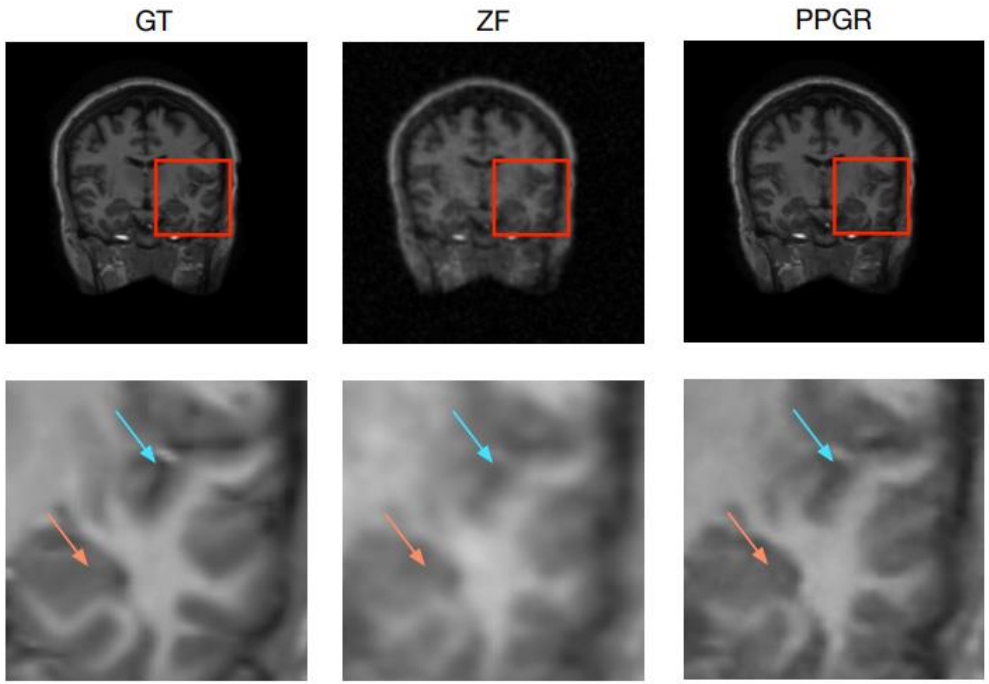
Image colourisation

Image-to-image networks

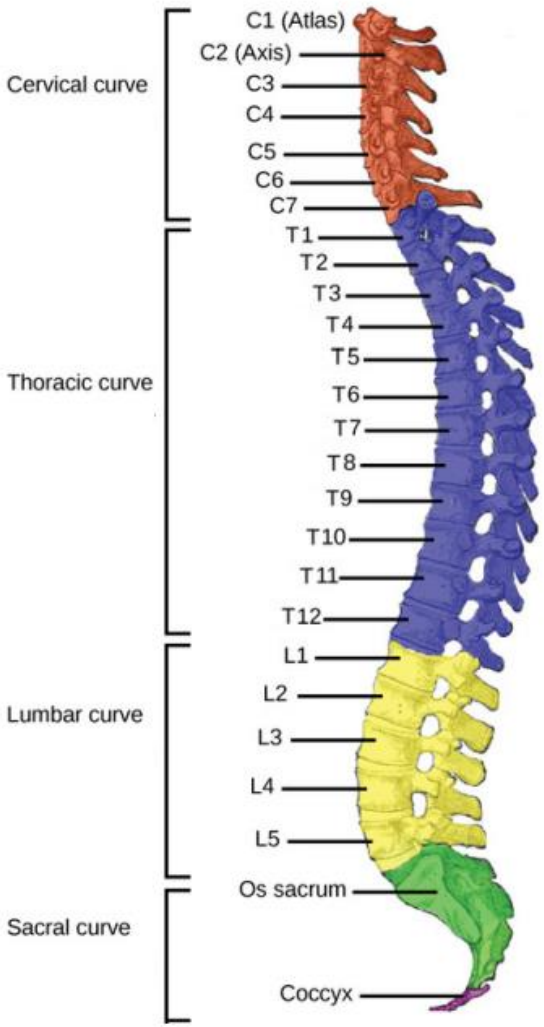
Generative adversarial networks (GANs)

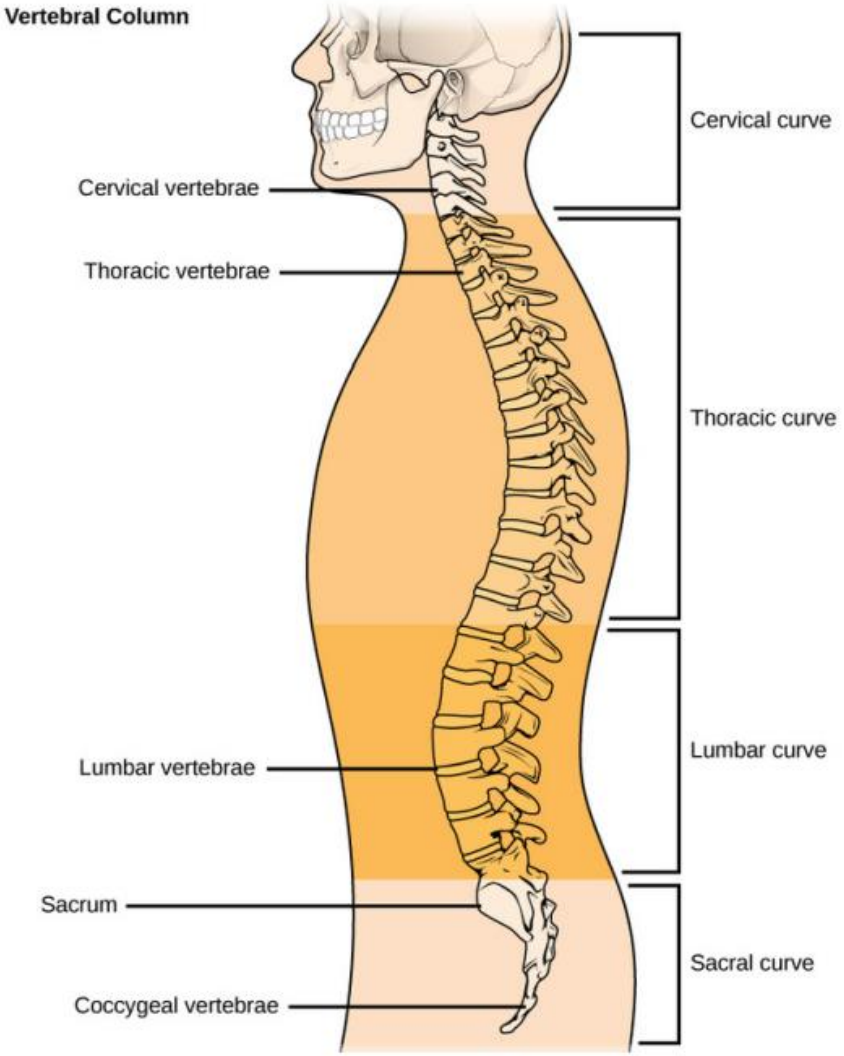
- Deep De-Aliasing of MRI





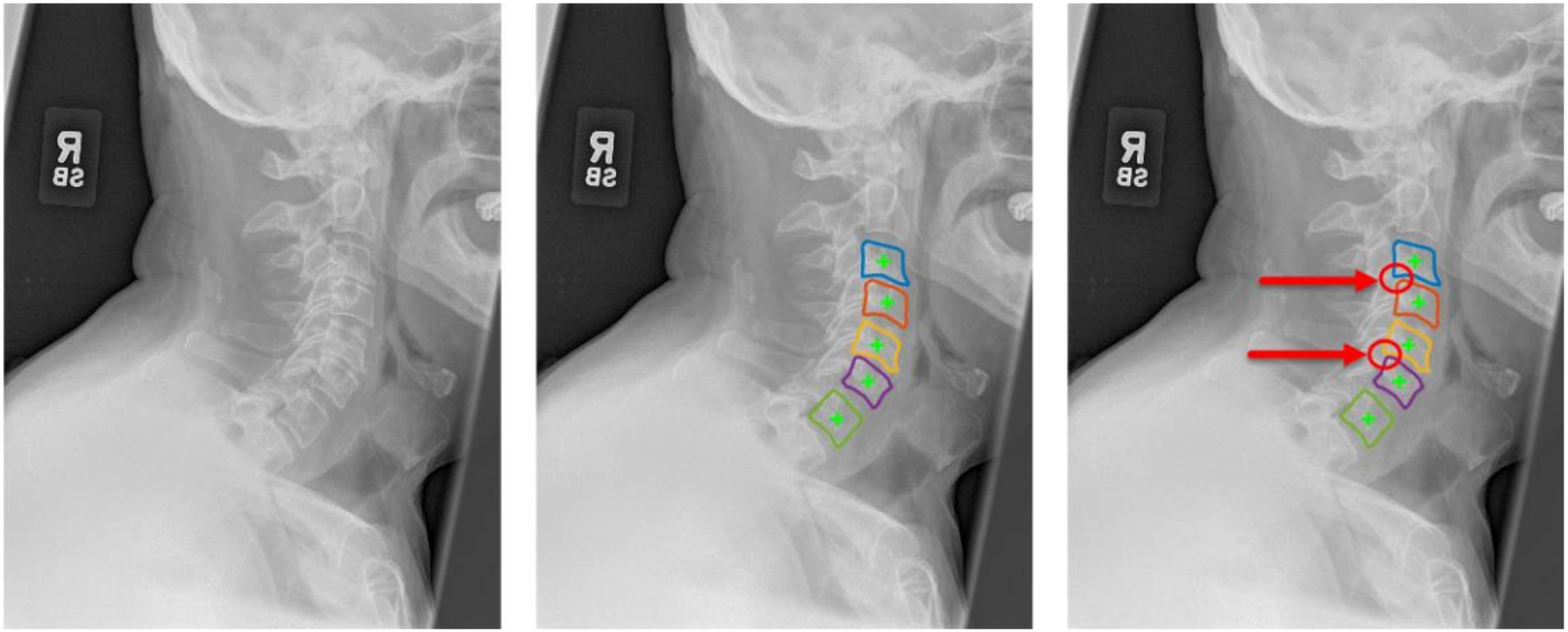
The spine


Cervical curve
Thoracic curve
Lumbar curve
Sacral curve
C1 (Atlas)
C2 (Axis)
C3
C4
C5
C6
C7
T1
T2
T3
T4
T5
T6
T7
T8
T9
T10
T11
T12
L1
L2
L3
L4
L5
Os sacrum
Coccyx


Vertebral Column
Cervical vertebrae
Thoracic vertebrae
Lumbar vertebrae
Sacrum
Coccygeal vertebrae
Cervical curve
Thoracic curve
Lumbar curve
Sacral curve

Clinical challenge

- Up to 20% of cervical spine injuries are missed or receive a delayed diagnosis
- Of these, up to 67% suffer neurological deterioriation
- Computer-aided detection may help
- This relies on accurate analysis of the x-ray image

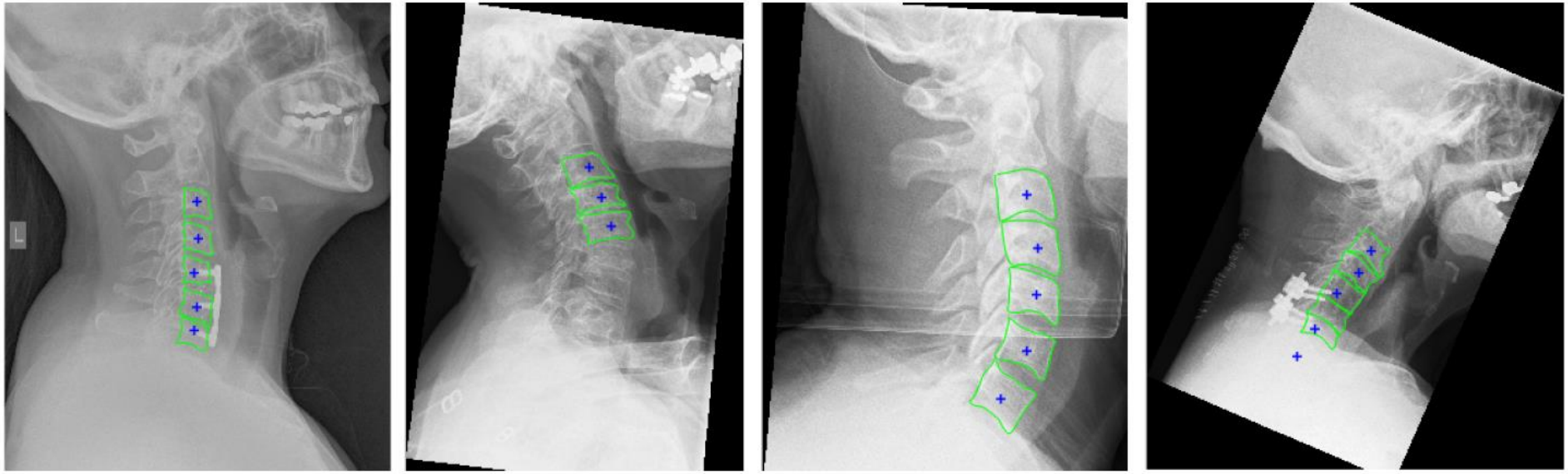


Data

- 336 X-ray images (ethically sourced) from the Royal Devon and Exeter Hospital
- 16 bit unsigned integer format (0 to 65,535)
- Patient ages: 17 to 96
- Different scanners (Philips, Agfa, Kodak, GE, Carestream)
- The data…“bites” (i.e., is *challenging*)
  - All patients had experienced trauma to the c-spine
  - Degenerative changes

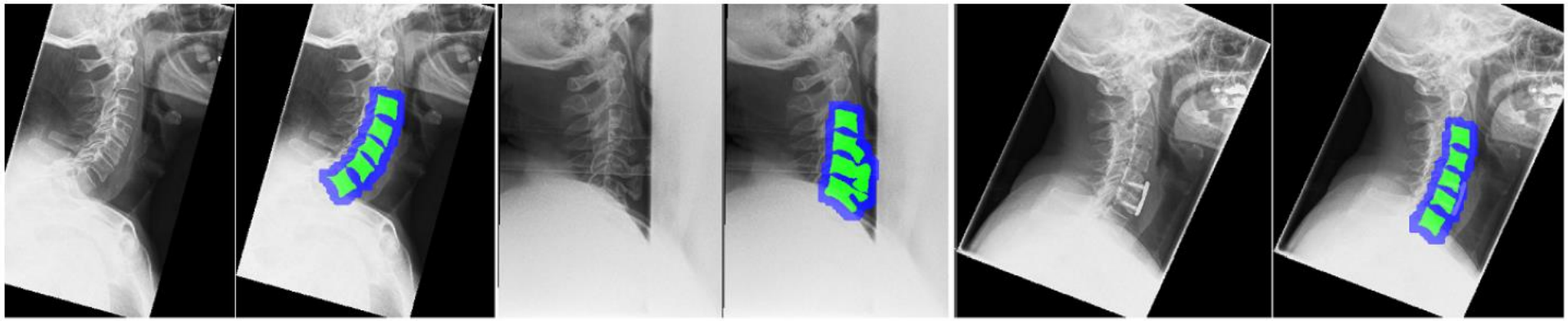
Ground truth

- C3 to C7 vertebrae have been outlined (segmented)
- Using a 20 point boundary representation (4 corners)
- For part of the data, multiple human annotations



CSpine localisation

- Given an X-ray image, where is the cervical spine?
- We approach this as a segmentation problem on coarse scale.
- We resize an X-ray image to 100x100, along with filled-in annotation.
- Goal: build a network to predict the cervical spine (blue) region, given an x-ray image of the cervical spine.



Networks

Fig. 3.5 (a) Legends (b) FCN (c) DeConvNet (d) UNet.

CSpine localisation

- We implemented three segmentation networks (FCN, DeConvNet, and UNet)
- Networks had between 1 and 6 million parameters to be learned.
- Training:

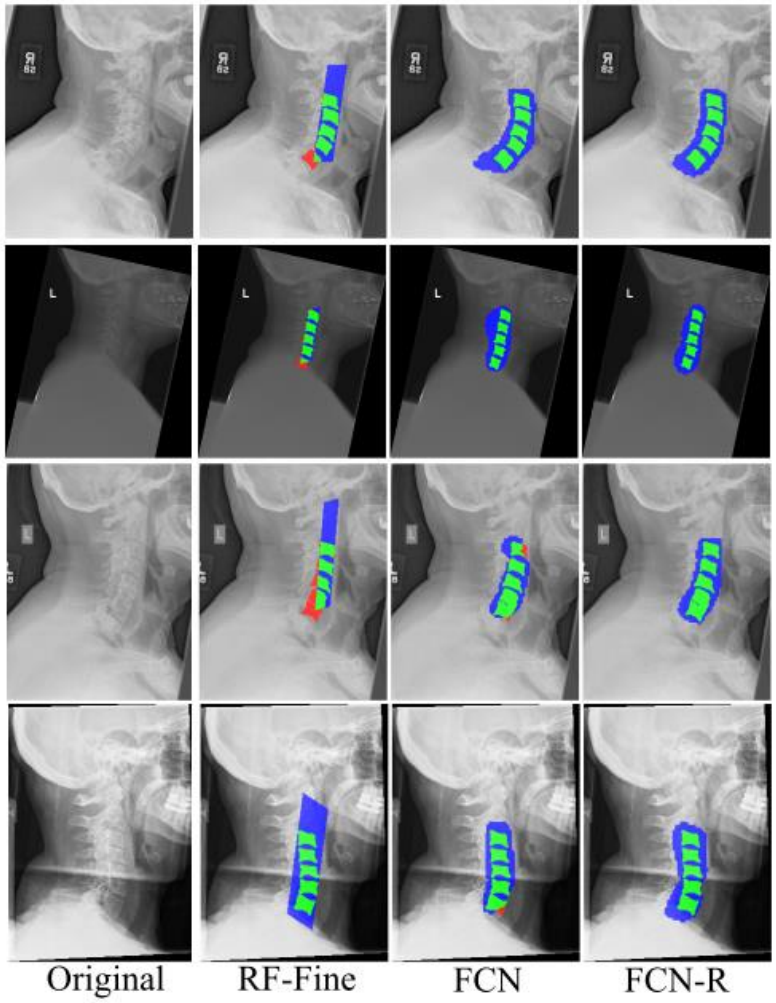
$$\hat{\boldsymbol{W}}_o = \arg\min_{\boldsymbol{W}} \sum_{n=1}^{N} L_t(\{x^{(n)}, y^{(n)}\}; \boldsymbol{W})$$

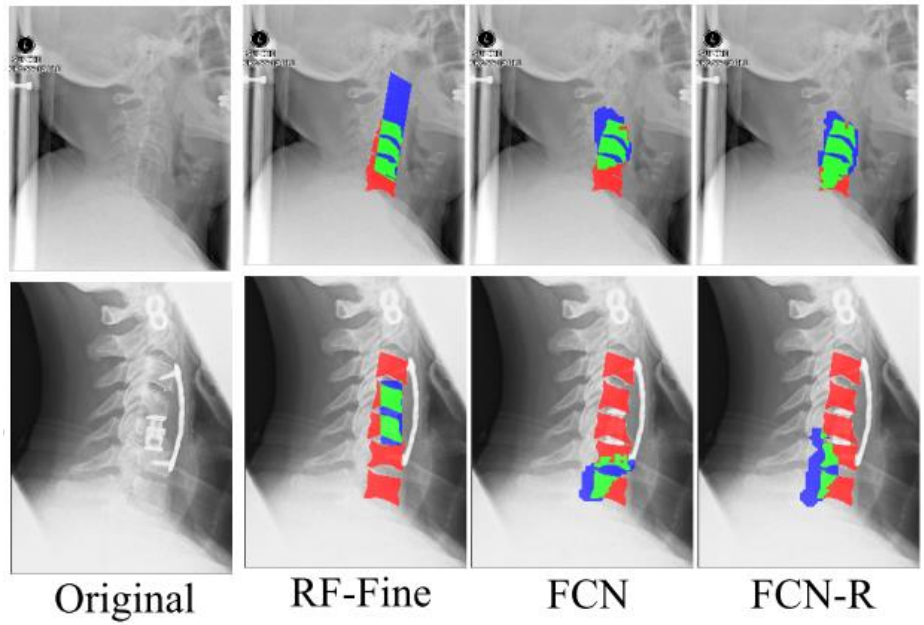
- Since the CSpine region should be a single connected component, we introduce a novel region-aware term to penalise more than one predicted region

$$\hat{\boldsymbol{W}} = \arg\min_{\boldsymbol{W}} \sum_{n=1}^{N} L_t(\{x^{(n)}, y^{(n)}\}; \boldsymbol{W}) + L_r(\{x^{(n)}, y^{(n)}\}; \boldsymbol{W})$$

- Training takes 30 hours using a dual NVidia Quadro M4000 workstation.

Localisation results

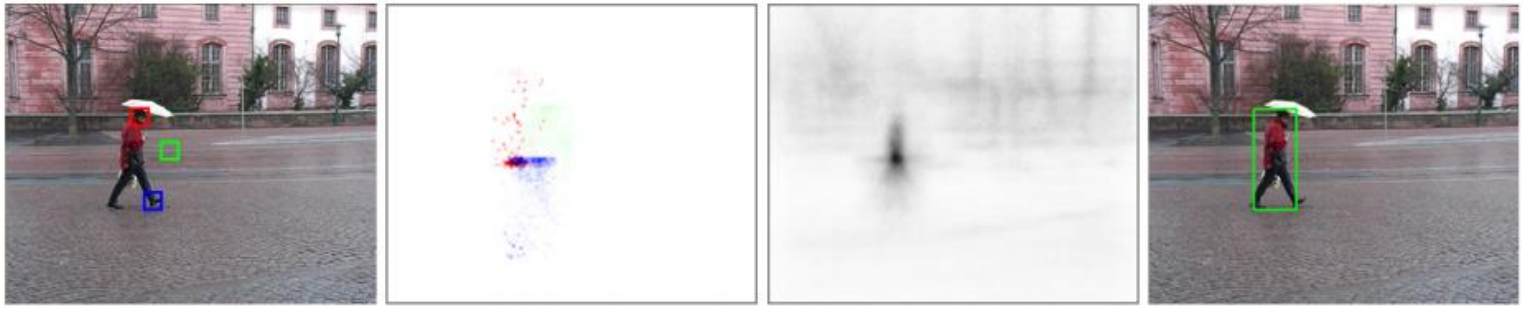




~96% pixel accuracy across dataset

Keypoint (landmark) detection

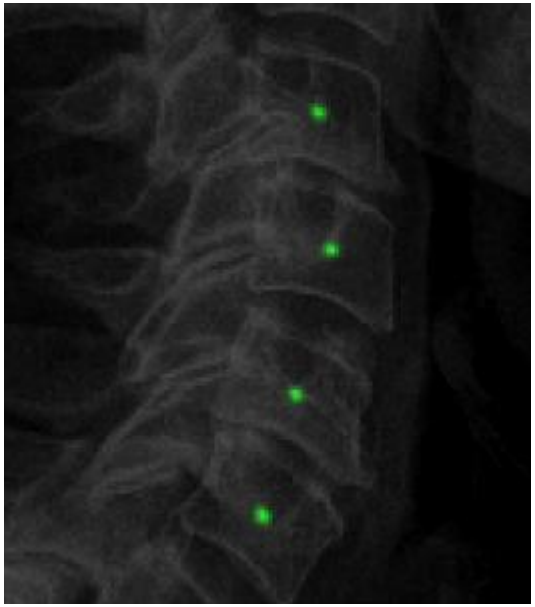
- Classic problem in computer vision: identify key points in an image.
- For example, pedestrian detection (Hough forest)
- Each patch classified as a pedestrian “votes” for the centre
- Output can be interpreted as a probability distribution



http://ieeexplore.ieee.org/document/5740927/

Probabilistic spatial regression

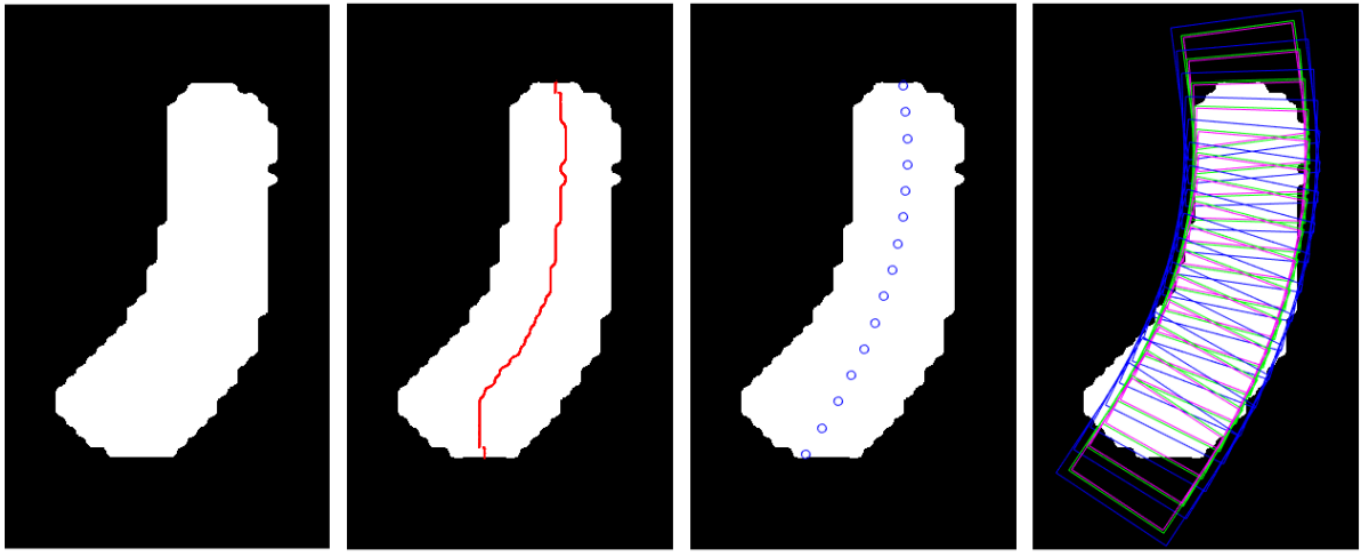
- Inspired by Hough forest, we recast the keypoint detection problem as a regression problem.
- Objective: regress a probability distribution over the image space to identify key points (such as the vertebral centre or corners)
- Essentially, this converts an image into a probability distribution



Ground truth has interobserver variation:
Can model centre as a 2D Gaussian

Forming patches

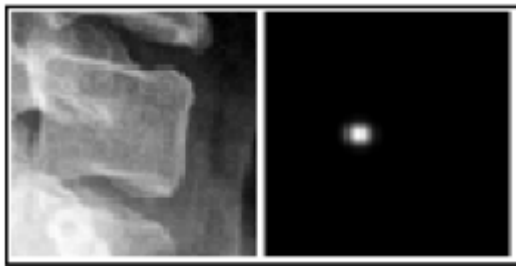
- From the localisation, we know roughly where the cervical spine is located
- We form patches along the length of the cervical spine



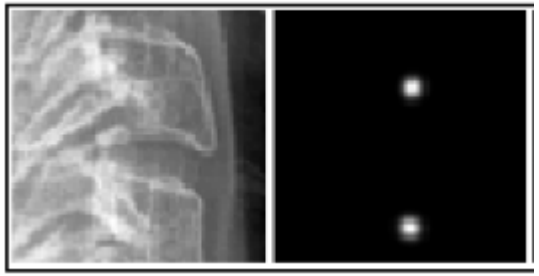
Probabilistic spatial regression: training

- For each patch, we regress a continuous function over the 2D image
- Various loss functions (squared difference, Bhattacharyya distance, etc.)

$$L(\{x, P_{GT}\}; \boldsymbol{W}) = \frac{1}{2|\Omega_p|} \sum_{i \in \Omega_p} \sum_{j=1}^{2} w_i (\hat{y}_i^j - P_{GT_{i,channel=j}})^2$$



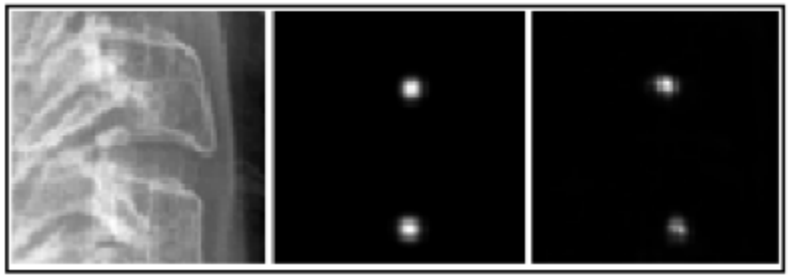
Input patch GT



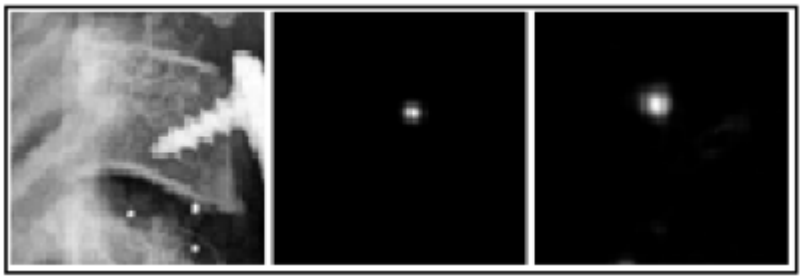
Input patch GT

Probabilistic spatial regression: testing

- Patches are put into the network, which predicts a probability map

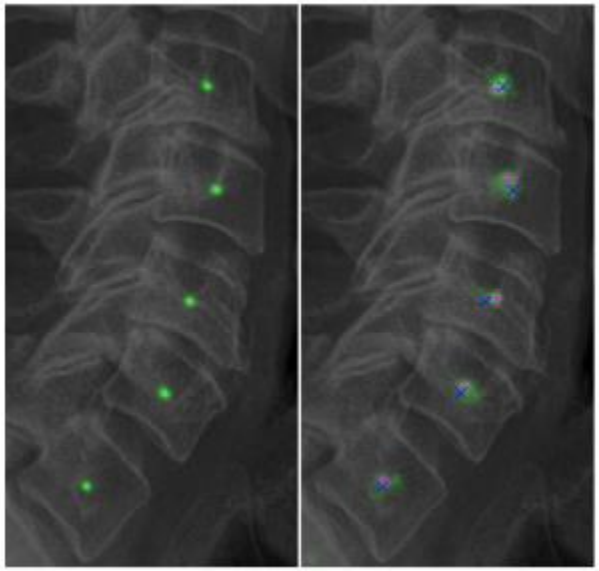


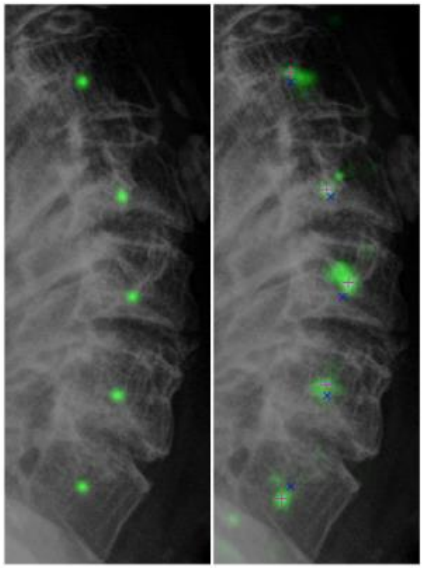
Input patch GT Prediction

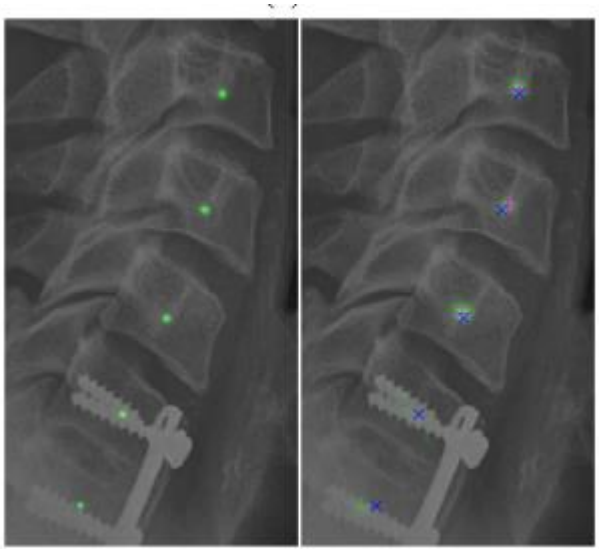


Input patch GT Prediction

- Accumulate over all patches and detect peaks x GT, + detection

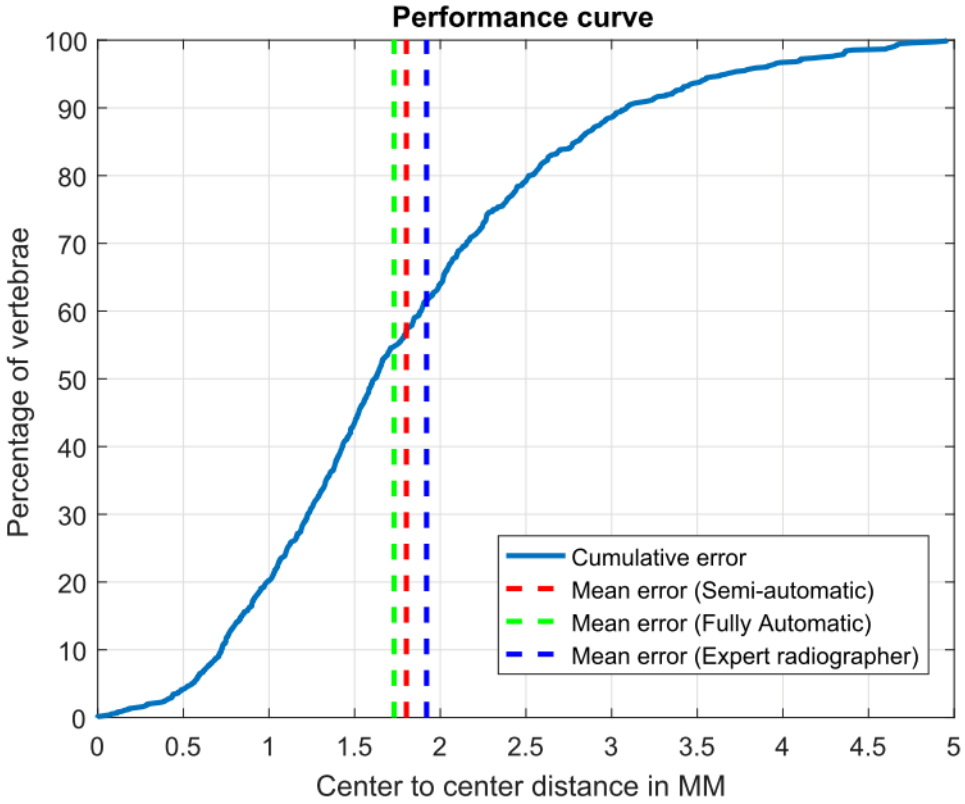




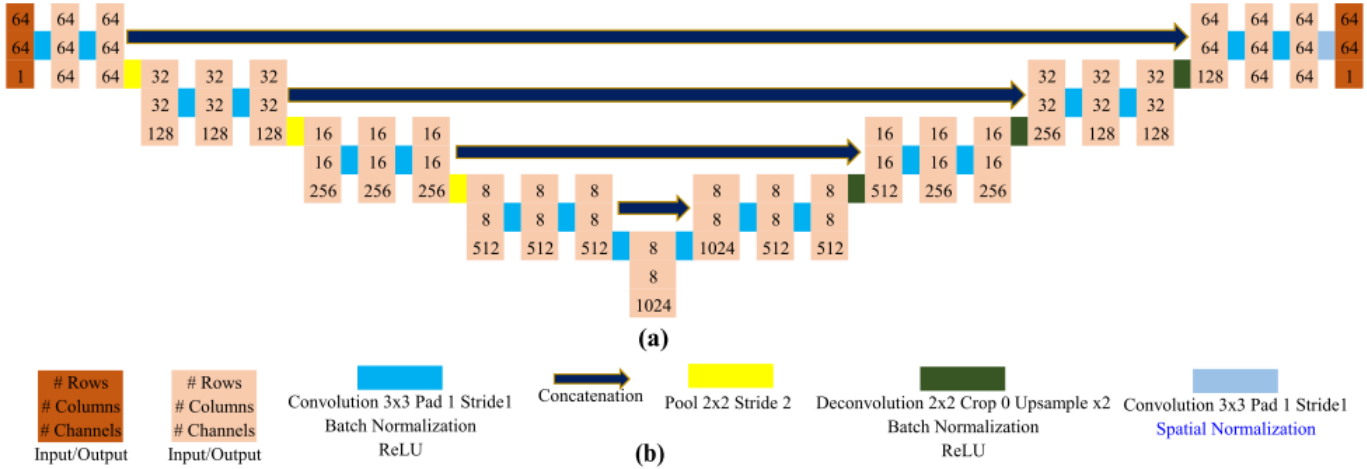


Quantitative results

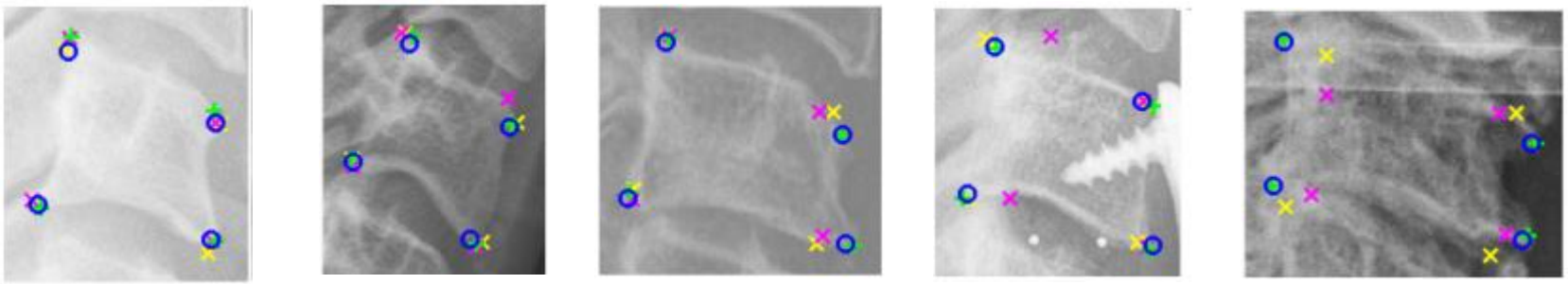
Test patch creation	Fully automatic		
True positive rate (TPR)	93.10%		
False discovery rate (FDR)	9.40%		
	Median	Mean	Std
Distance error (mm)	1.54	1.72	0.99



Corner detection



- Spatial probability produced using a spatial normalisation layer at the end of the network.
- Results: 1.54 mm accuracy (average), 0.99 (median), 38% improved



Blue: predicted, green: ground truth, yellow: Hough forest, pink: Harris corner

Boundary detection

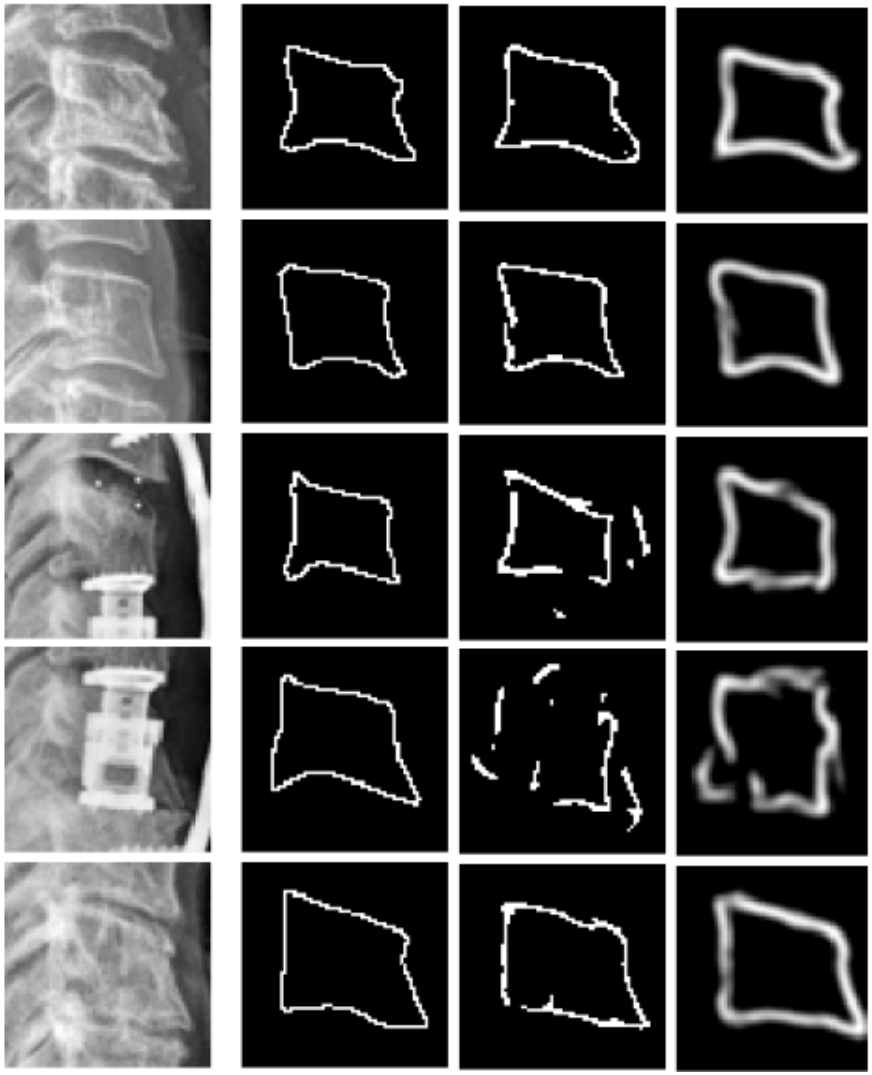


Image GT Seg PSR

Boundary detection – full CSpine

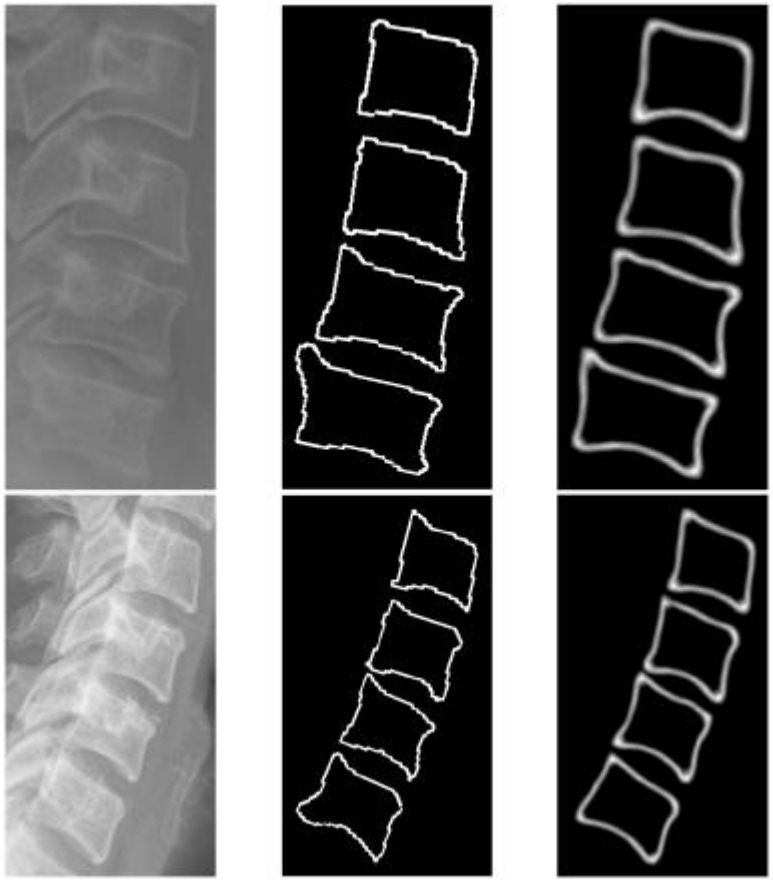


Image GT PSR

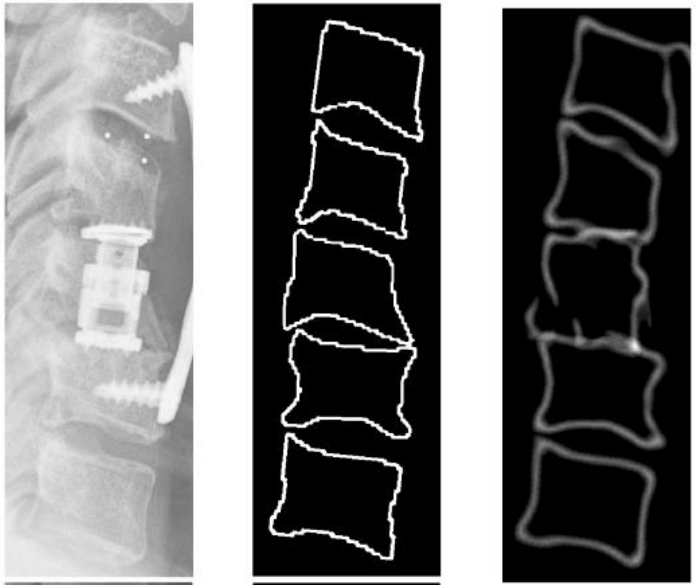
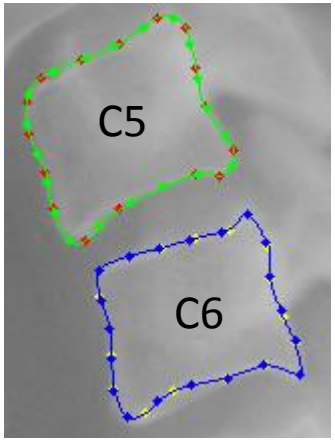
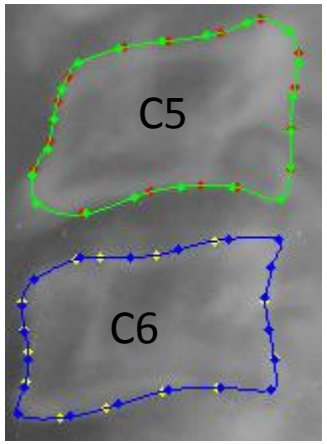


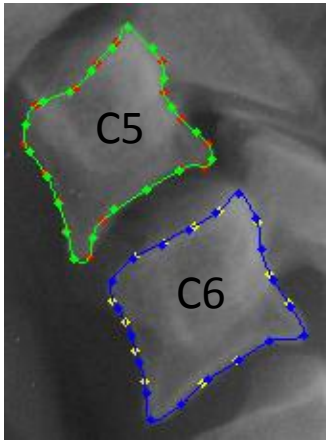
Image GT PSR

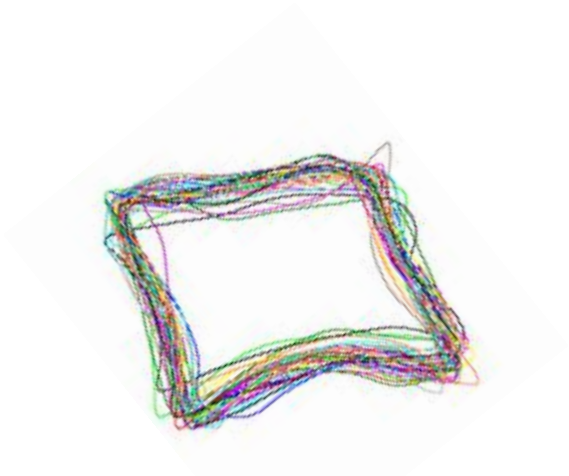
Shape

- The boundary of a segment provides a *shape.*
- We can collect and align a large number of shapes and do interesting things, such as
  - Population statistics: mean, median, etc.
  - Principal component analysis (PCA) to study variation in the data
  - (others)





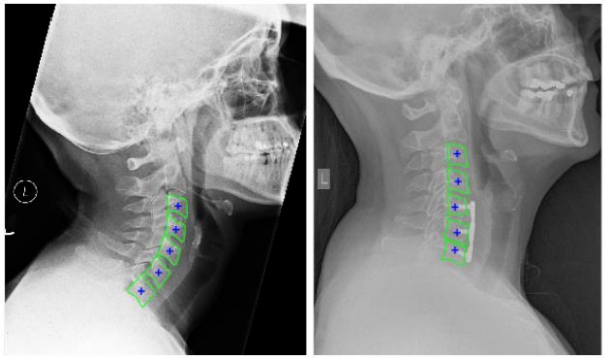




Registered (aligned)
C4 vertebra shapes

Deep vertebral body segmentation

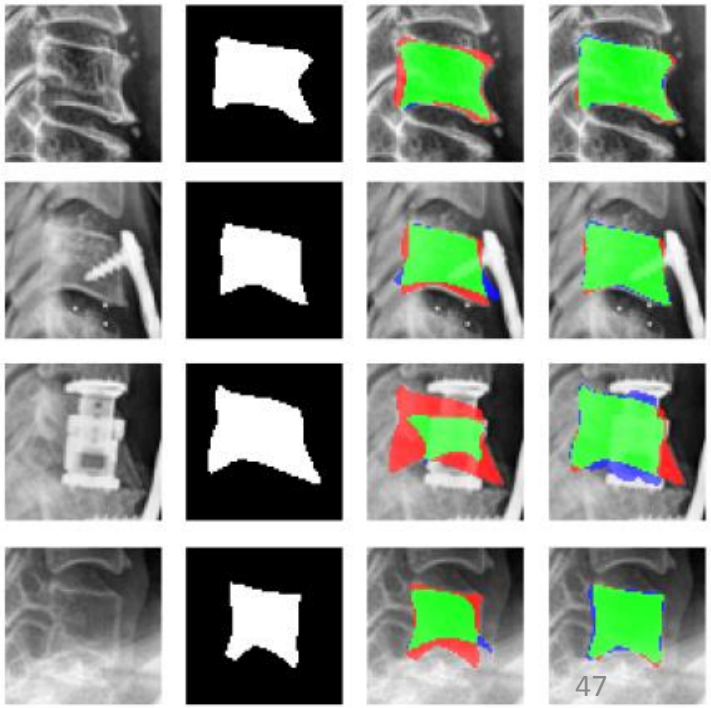
- Objective: perform a precise segmentation of vertebral bodies in x-ray images given a collection of manually segmented images.



- We implemented a deep segmentation approaches.

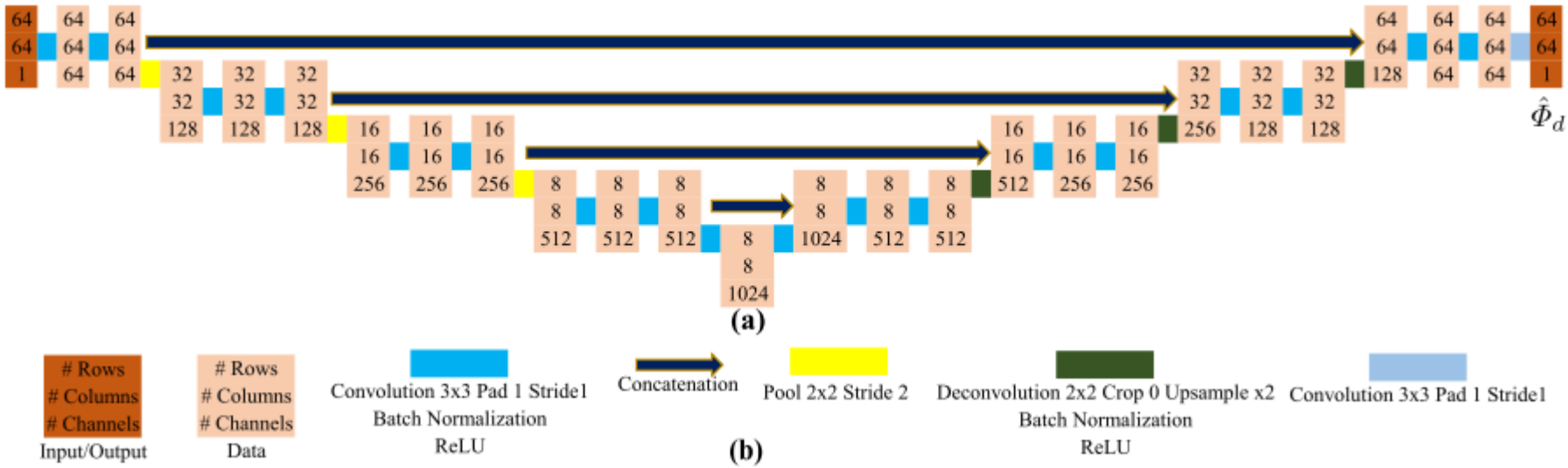
- For training, we introduce a novel shape aware term that penalises differences between the ground truth shape and the predicted shape.

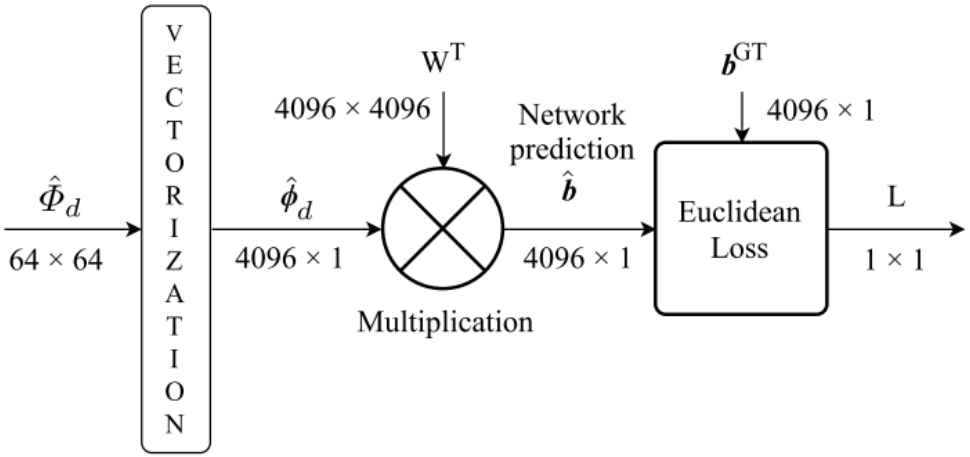
$$\hat{\boldsymbol{W}} = \arg\min_{\boldsymbol{W}} \sum_{n=1}^{N} L_t(\{x^{(n)}, y^{(n)}\}; \boldsymbol{W}) + L_s(\{x^{(n)}, y^{(n)}\}; \boldsymbol{W})$$



- Results show 35% improvement over non-deep learning methods.

Shape regression network





Results

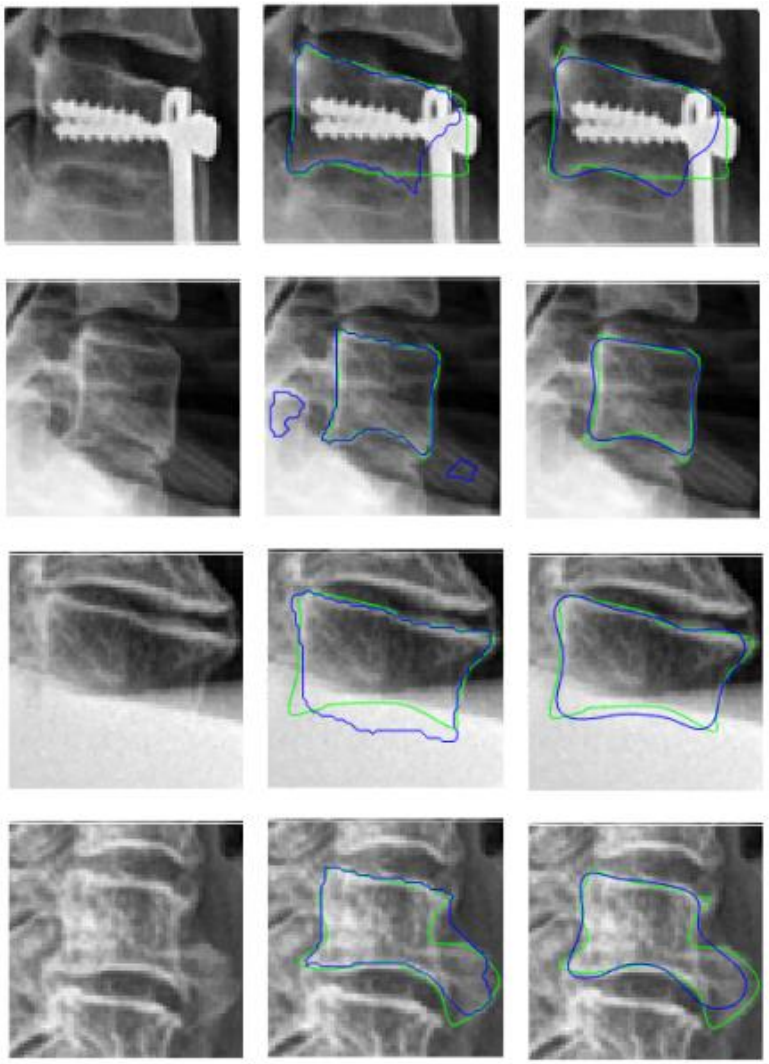
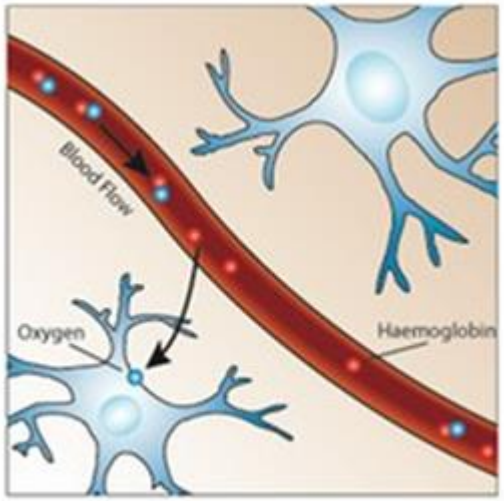


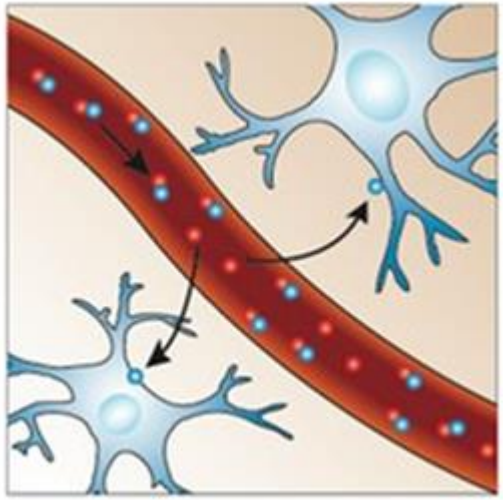
Image UNet Our method

functional MRI (fMRI)

- Functional Magnetic Resonance Imaging (fMRI) provides opportunity to observe neural activity in brain.
  - Active brain regions need nutrients, thus drawing these from oxygen-enriched blood
- fMRI can differentiate between oxygen-rich and deoxygenated blood.
- Applications
  - Understanding cognition
  - Identification of brain function altered by brain disorders



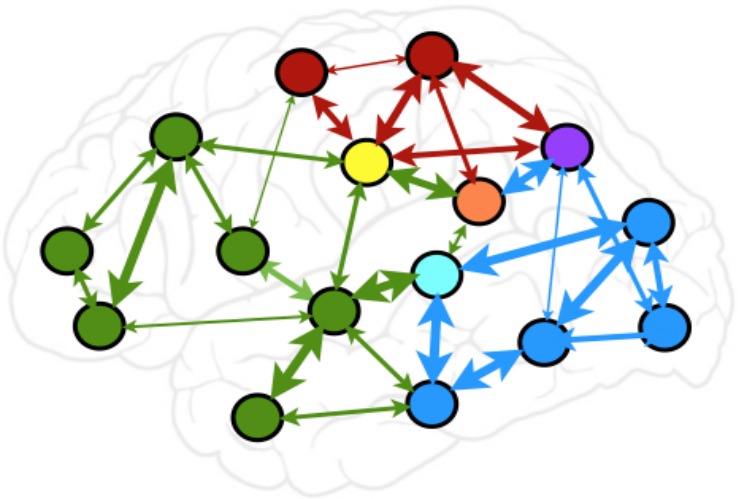
Resting

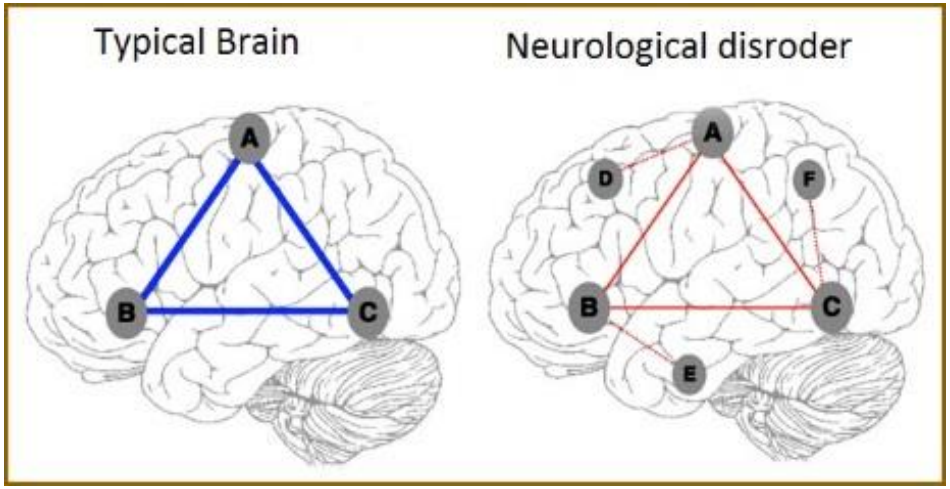


Activated

The brain as a network

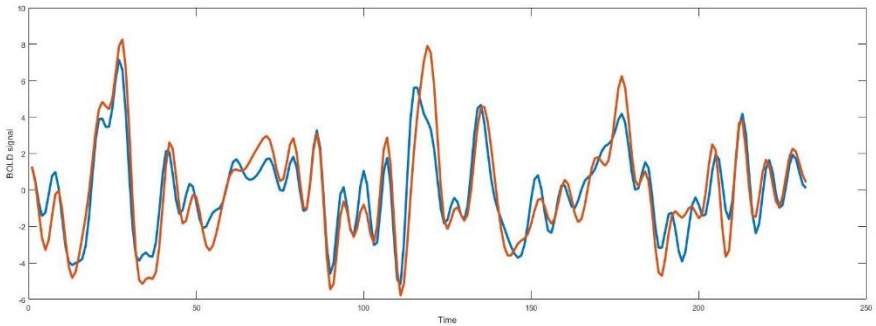
- Brain – a complex network controlling all body functions
- Studies have revealed that the functional connectivity of brain networks are altered in a particular neurological disorders



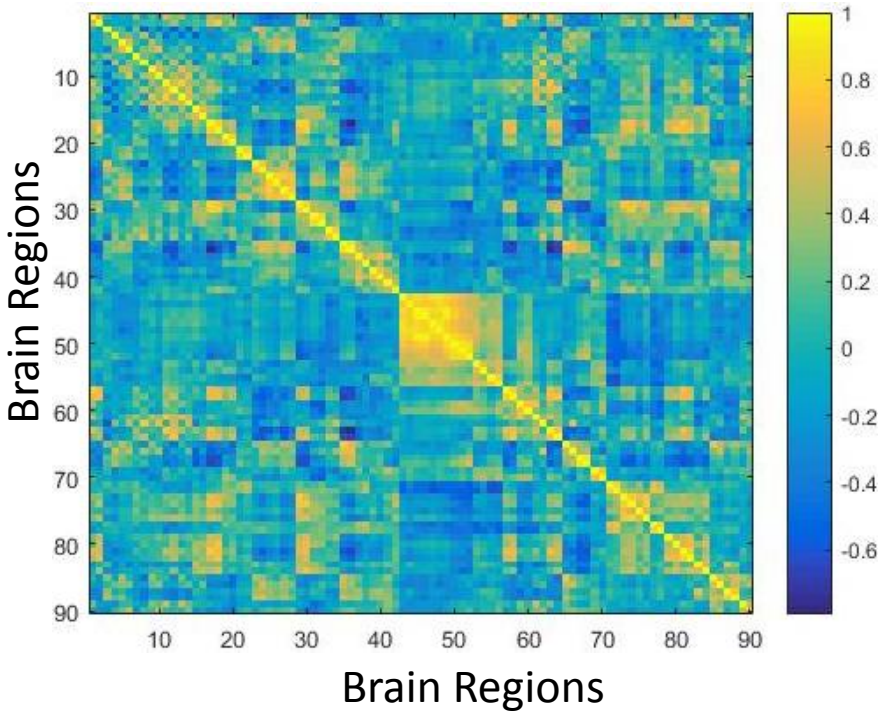


Functional connectivity

AAL template



Functionally connected regions



Attention Deficit Hyperactive Disorder (ADHD)

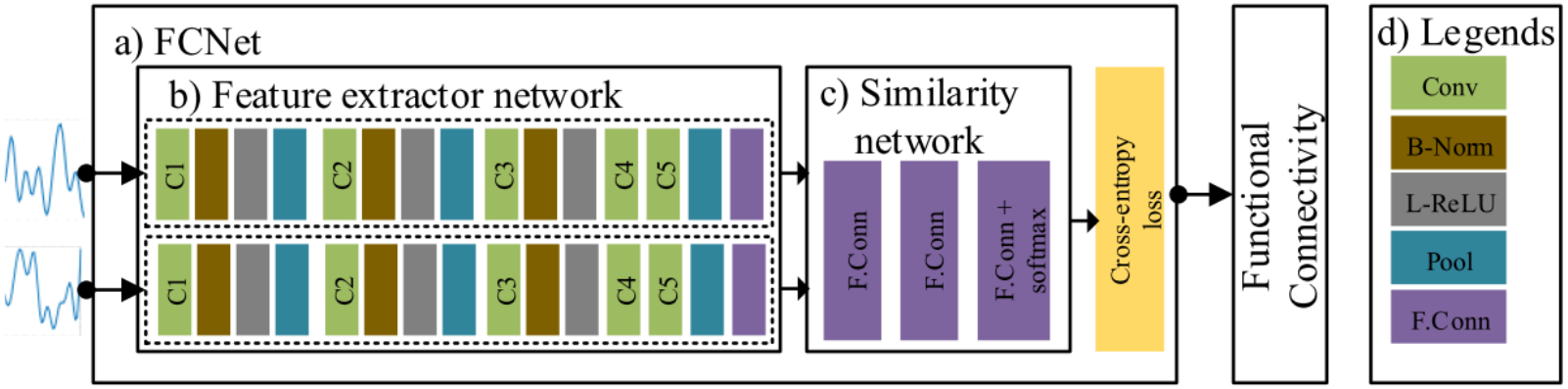
- One of the most common childhood disorder
- 3-5% children affected
- Underlying mechanism not clearly understood
- No single diagnostic test
- Diagnostics typically based upon symptoms observed for months

ADHD-200

- Resting state fMRI
- Multiple institutions
  - NYU
  - NeuroImage
  - Peking University
- Brains parcelleated into 90 regions, each with a time series signal

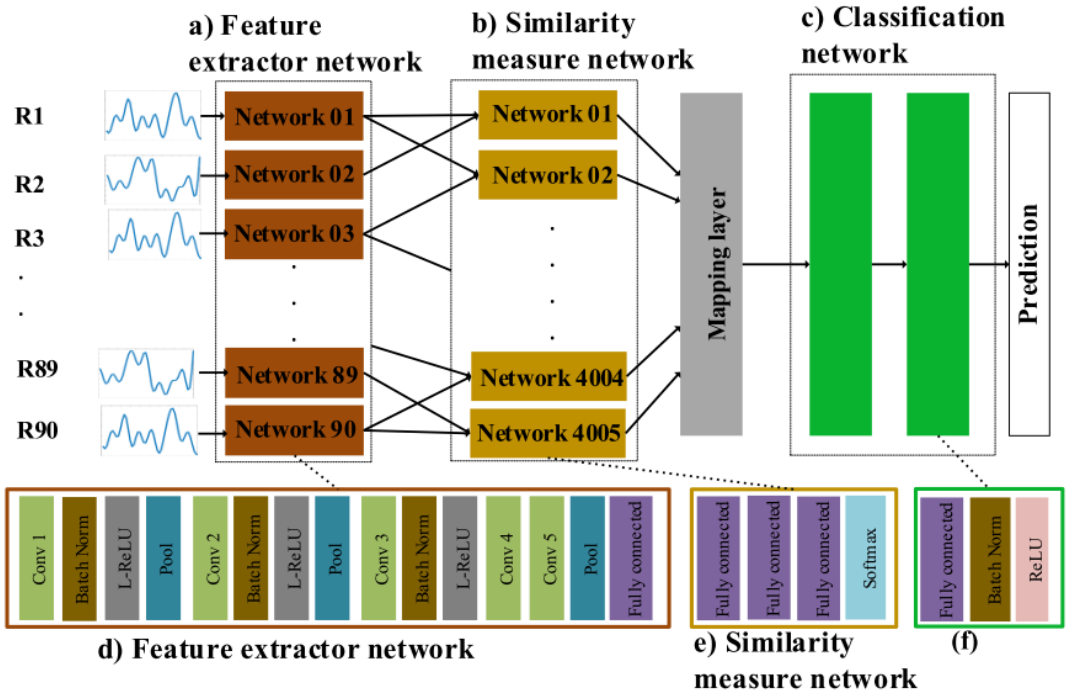
Deep functional connectivity

- We introduce FCNet, which is a convolutional neural network that measures functional connectivity
- FCNet has a Siamese architecture



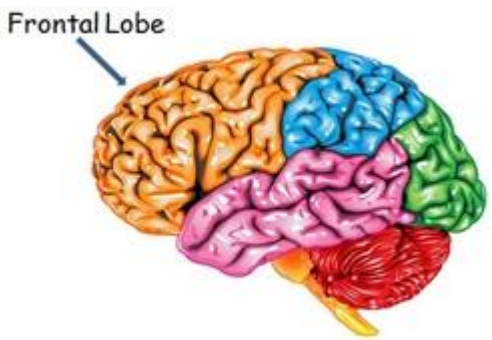
DeepFMRI

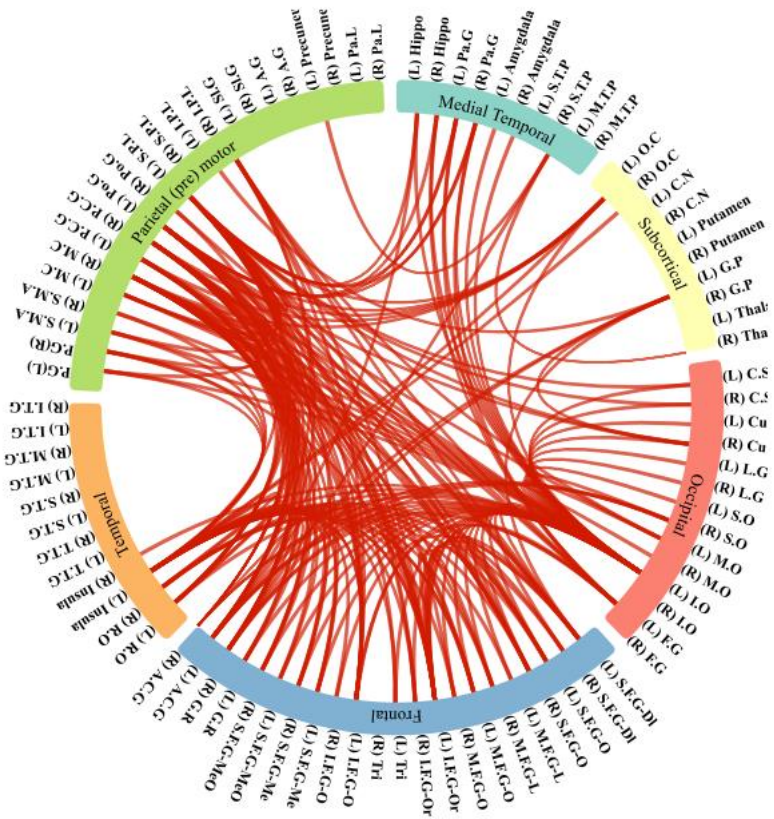
- We then put FCNet with shared weights into an architecture with a classification network, which makes predictions on the patient level from predicted functional connectivity



Results

	NI	Peking	NYU
Average accuracy [8]	56.9%	51.0%	35.1%
Highest accuracy [11]	–	58%	56%
Clustering method [1]	44%	58.8%	24.3%
Correlation	52.0%	52.9%	56.1%
FCNet [7]	60.0%	**62.7%**	58.5%
DeepFMRI	**67.9%**	**62.7%**	**73.1%**



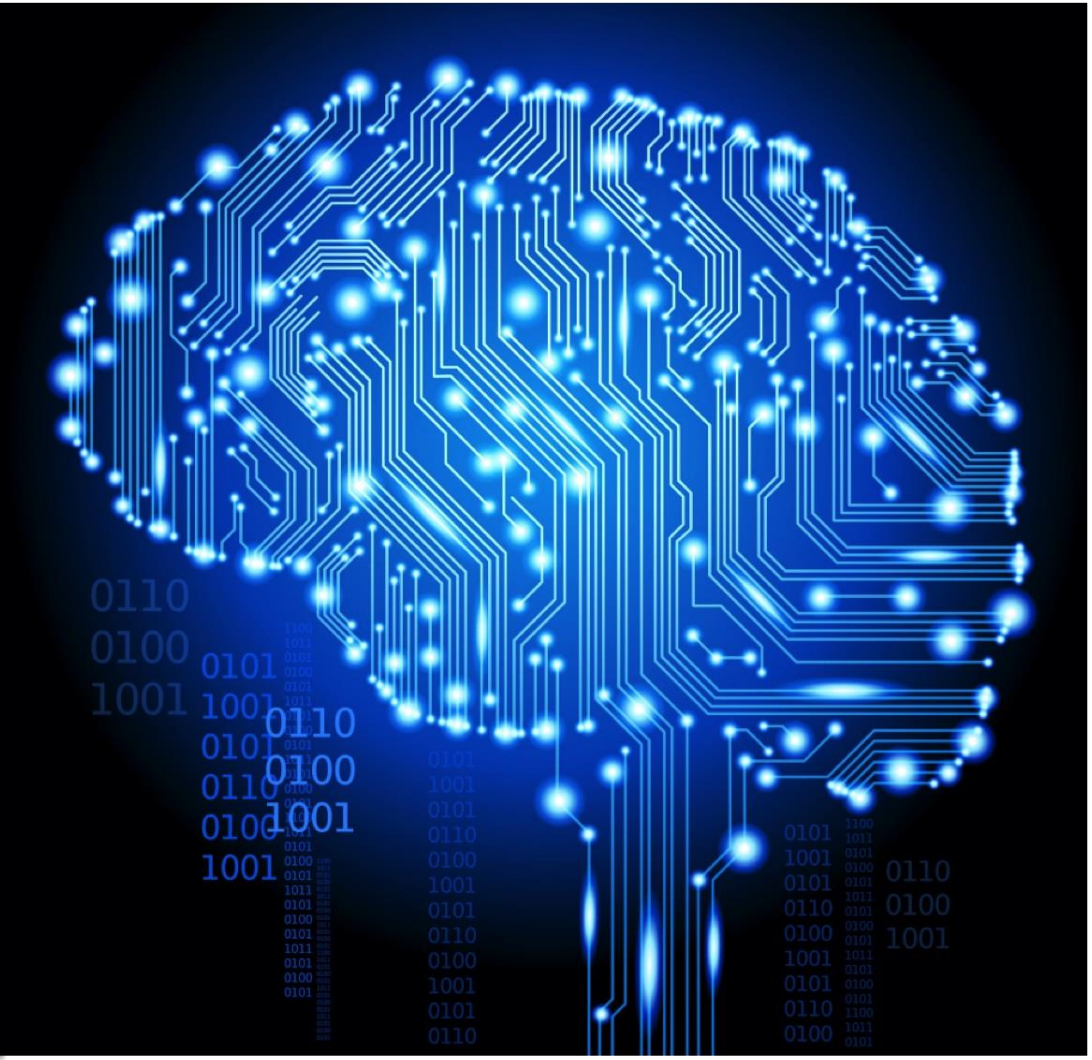


Top 200 differences visualised

- We have observed differences frontal lob functional connectivity is altered the most in this dataset.
- Frontal lobe controls important cognitive skills, including emotional expression, problem solving, memory, and behaviour

Deep learning

Hype, or hope?



Deep learning limitations

- Requires large datasets
- Methods described in this talk also require *labelled* data
- Algorithms are complex
  - Slow to train (but fast at test time)
  - Difficult to interpret results (Explainable AI)
  - Black-box
- Biologically inspired, but don’t capture the biological mechanisms of the brain
- Limited theoretical understanding
- Hyperparameters

Thanks

- City's Computer Vision Group: http://computervision.city.ac.uk/
- In particular,

Arif

Atif

NVIDIA ACCELERATED COMPUTING

GPU Grant Program

References

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2. https://www.weforum.org/pages/the-fourth-industrial-revolution-by-klaus-schwab/
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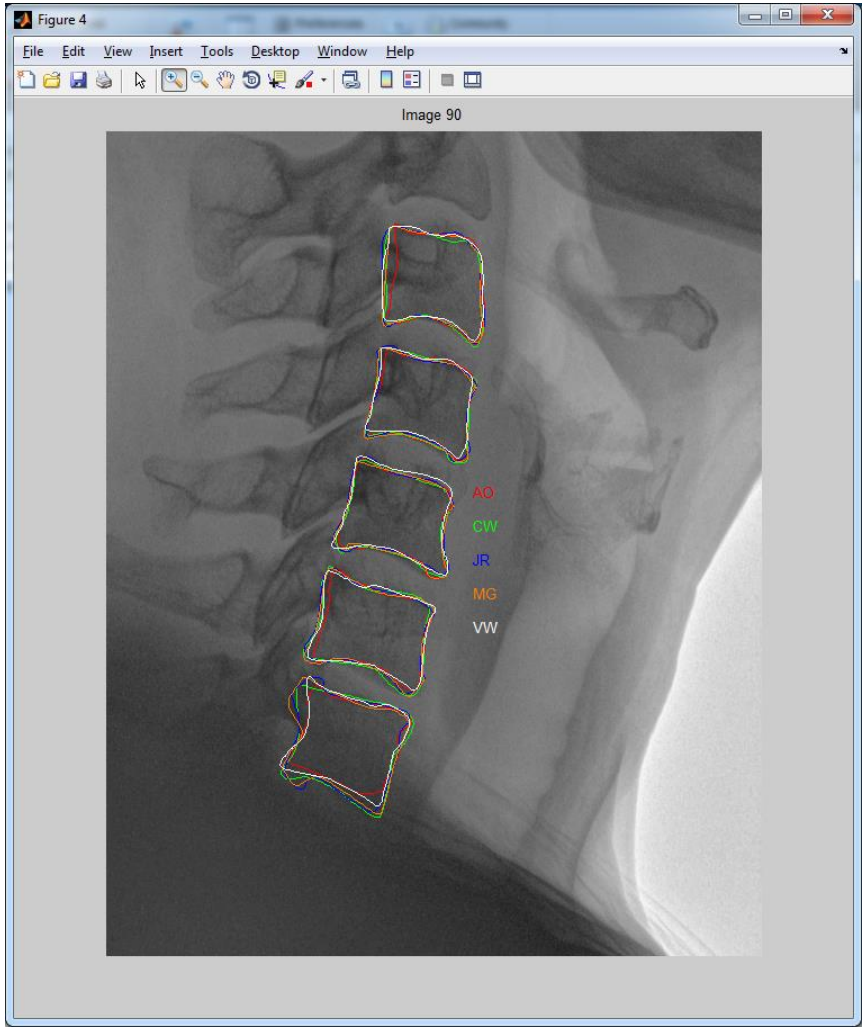
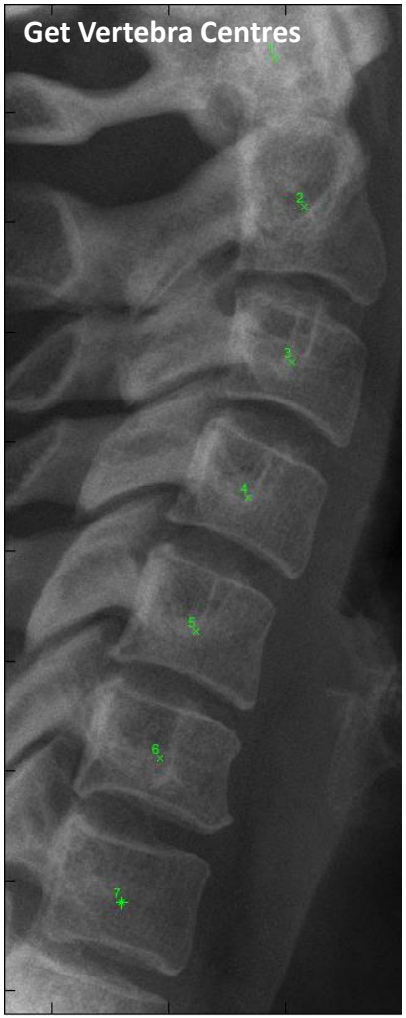
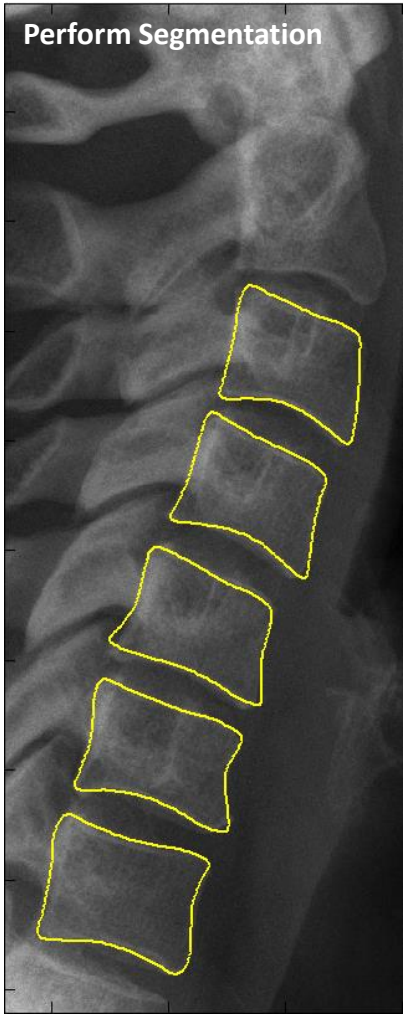
5. Deep Learning for Single-molecule Science, T Albrecht, G Slabaugh, E Alonso, S M M Al-Arif, *Nanotechnology*, IOP Science, 2017.
6. Shape-aware Deep Convolutional Neural Network for Vertebrae Segmentation, S M M R Al Arif, K Knapp, G Slabaugh, *MICCAI Workshop on Computational Methods & Clinical Applications in Musculoskeletal Imaging (MSKI)* 2017.
7. FCNet: A Convolutional Neural Network for Calculating Functional Connectivity from functional MRI, A Riaz, M Asad, S M M R Al Arif, E Alonso, D Dima, P Corr and G Slabaugh, *1st International Workshop on Connectomics in NeuroImaging (CNI), MICCAI* 2017.
8. Image-to-Image Translation with Conditional Adversarial Networks, Isola et al., CVPR 2017
9. Deep De-Aliasing for Fast Compressive Sensing MRI, Yu et al., 2017

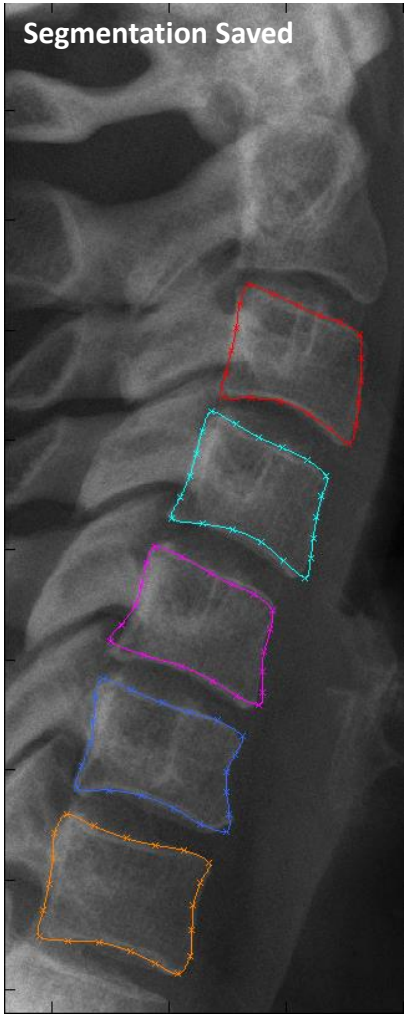
Interobserver error - segmentation

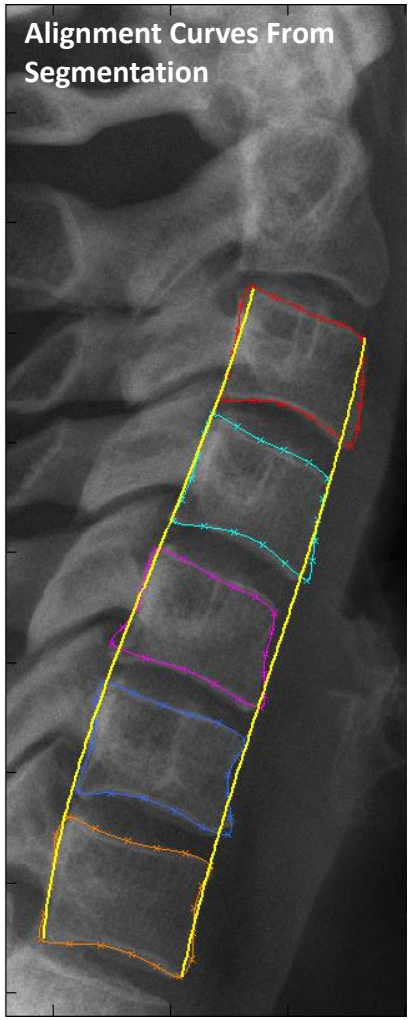


CSpine CAD


Get Vertebra Centres


Perform Segmentation


Segmentation Saved


Alignment Curves From Segmentation