

# Medical Image Analysis by Deep Learning

Mina Rezaei

# Data Management for Digital Health

## Summer 2017

# Deep Learning Theory & Applications

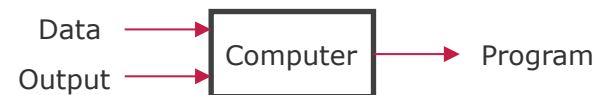
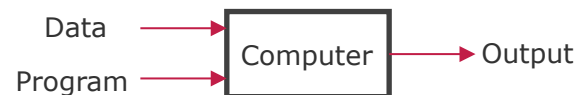
- Foundations
  - Deep Learning
  - Medical Image Analysis
  - Supervised Learning
- Application Examples
  - Medical Image Segmentation
  - Medical Image Registration
  - Computer-aided Diagnosis and disease quantification
  - Medical Image Synthetization



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# Traditional Programming vs Machine learning



## Some Applications

- Web search
- Computational biology
- Finance
- Robotics
- Information extraction
- Social networks
- Debugging
- *[Your favorite area]*

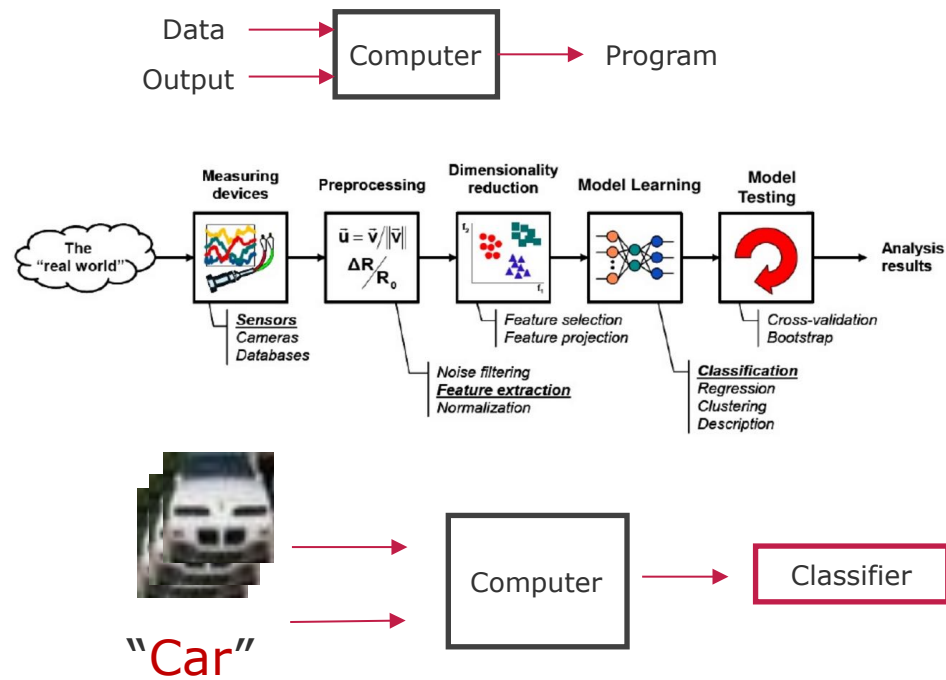
## Representation

- Decision trees
- Sets of rules / Logic programs
- Instances
- Graphical models (Bayes/Markov nets)
- Neural networks
- Support vector machines
- Model ensembles
- Etc.

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# Machine Learning



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## Key Idea Behind Neural Network

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- Learn features from data
- Use differentiable functions that produce feature efficiently
- “Deep” architectures: cascade of simpler non-linear modules
- End-to-end learning: no distinction between feature extractor and classifier

?

- What is the input-output mapping?
- How are parameters trained?
- How computational expensive is it?
- How well does it work?

- Neural Networks for Supervised Training
  - Architecture
  - Loss function
- Unsupervised Training of Neural Networks
- Semi-supervised / multi-task / multi-modal
- Reinforcement Learning

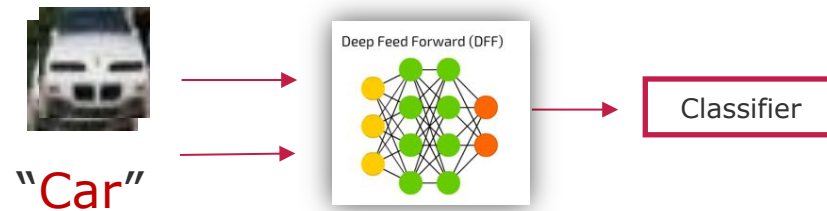
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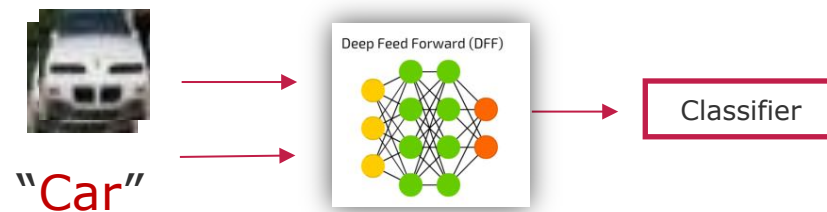
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## Artificial Neural Network (Deep Learning, Hierarchical learning)

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# Artificial Neural Network (Deep Learning, Hierarchical learning)



- Input Cell
- Output Cell
- Hidden Cell

Perceptron (P)



Feed Forward (FF)



Deep Feed Forward (DFF)



©2016 Fjodor van Veen - [asimovinstitute.org](http://asimovinstitute.org)

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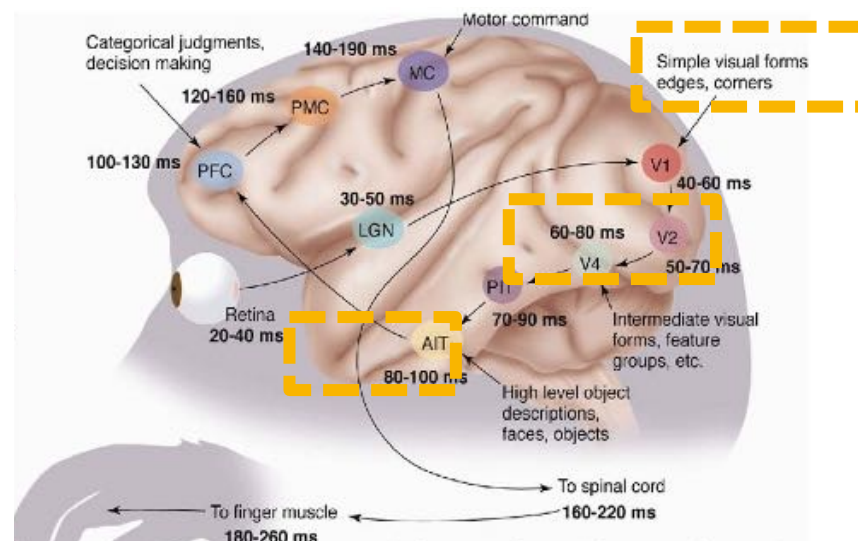
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## The Human Visual Cortex Consists of Hierarchies

The ventral (recognition) pathway in the visual cortex has multiple stage:

- Retina - LGN - V1 - V2 - V4 - PIT - AIT ..., lots of **intermediate representations**



[Gallant & Van Essen]

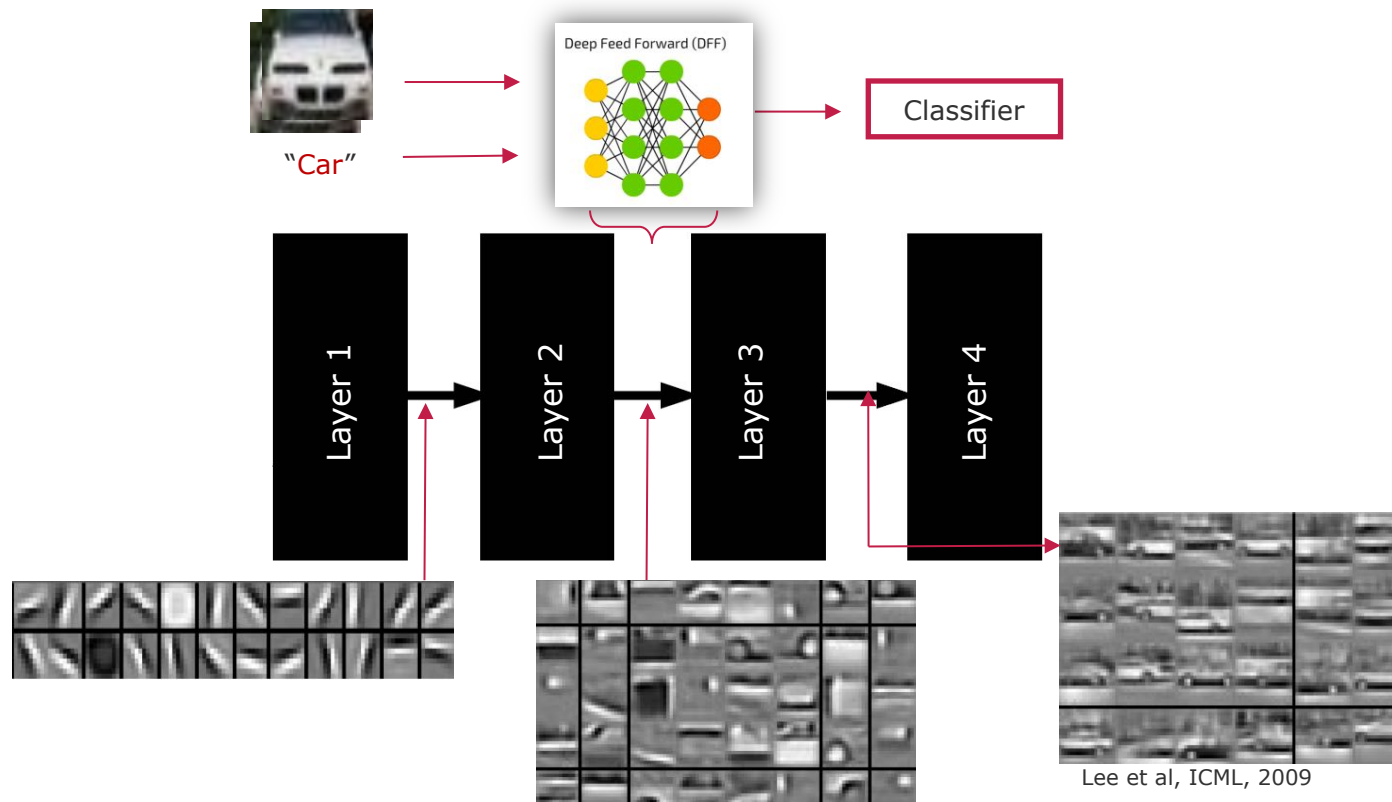
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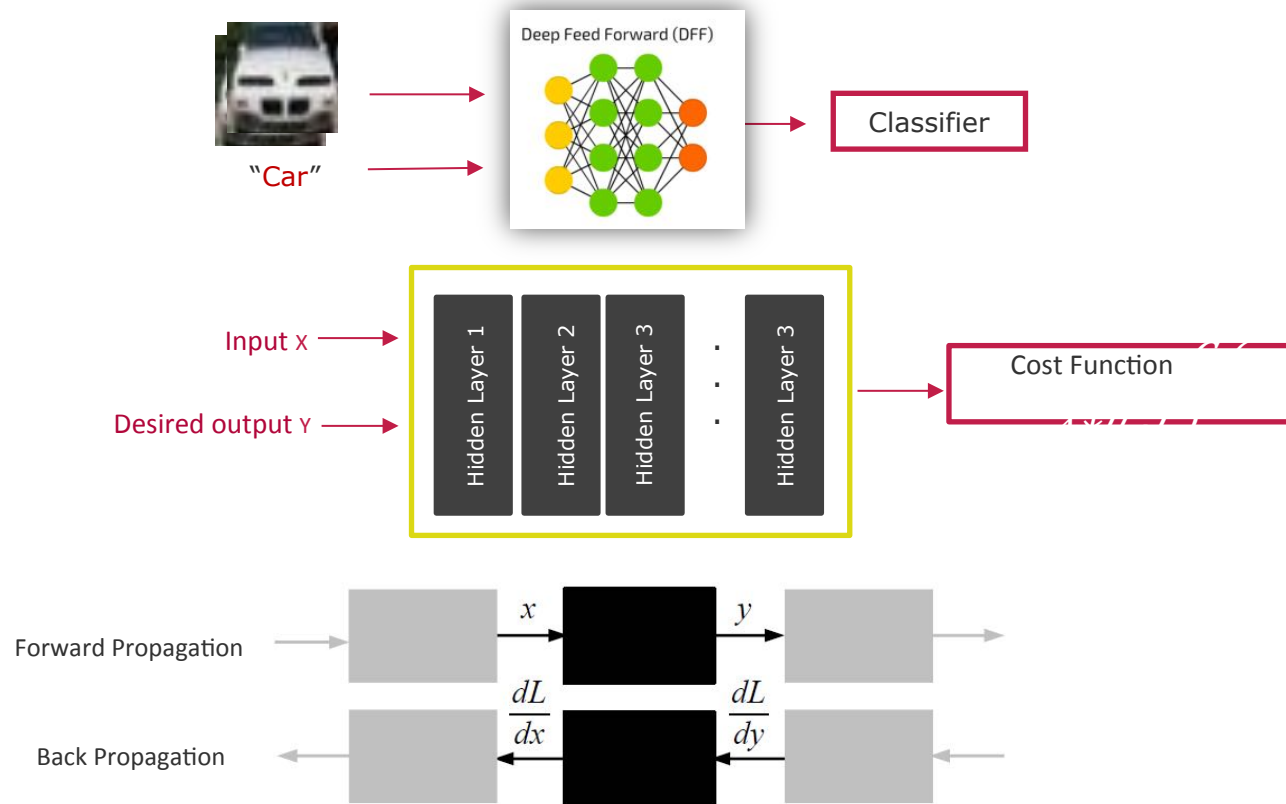
# Hierarchical Learning



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# Neural Network for Supervised Learning

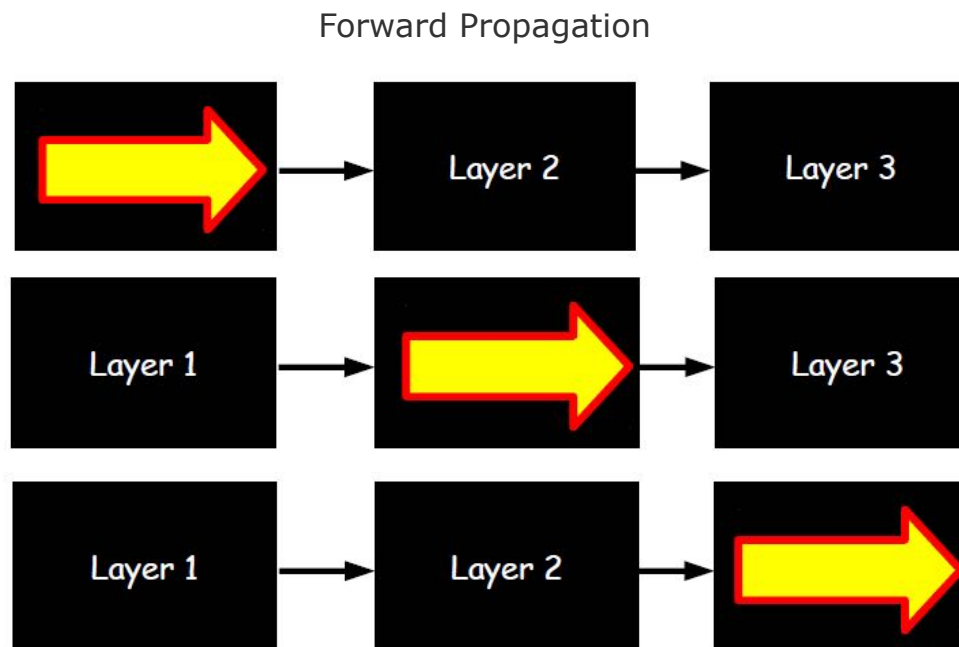


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## Neural Net Training (I)

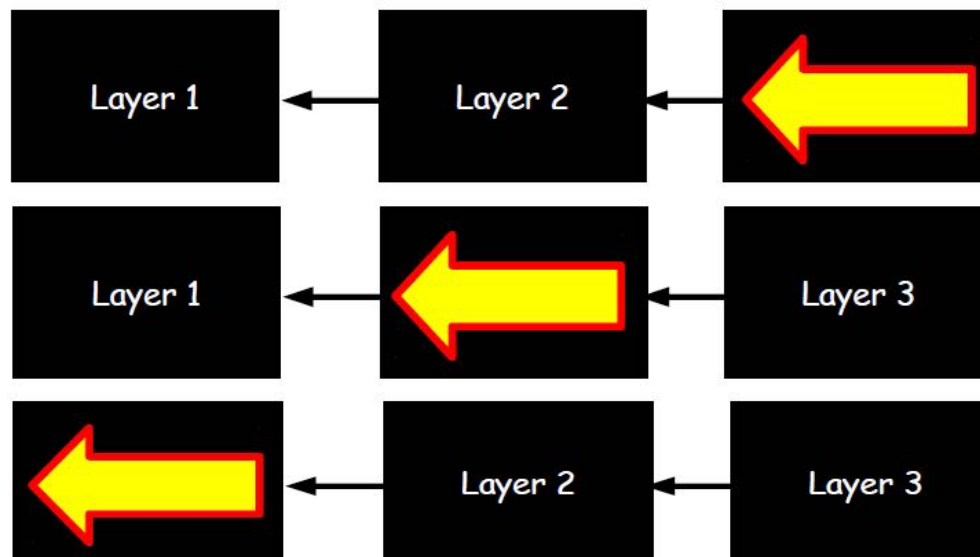
- Compute (Cost function) loss on small set of input



## Neural Net Training (II)

- Compute gradient w.r.t. parameters
- Use gradient to **update parameters**

Backward Propagation



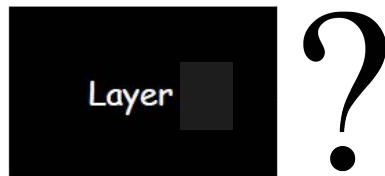
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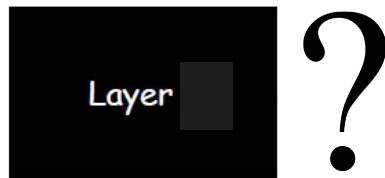
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## Layer Internals

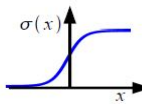
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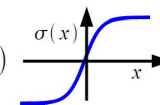
## Layer Internals Activation Function



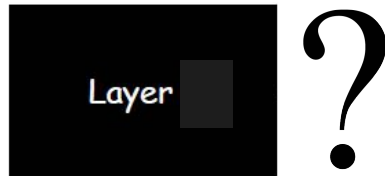
a)   $h_{j+1} = \sigma(W_{j+1}^T h_j + b_{j+1})$


$\sigma(x) = \frac{1}{1 + e^{-x}}$  

b)   $h_{j+1} = \sigma(W_{j+1}^T h_j + b_{j+1})$

$\sigma(x) = \tanh(x)$  

## Layer Internals Activation Function





A black rectangular box with an arrow labeled  $h_j$  entering from the left and an arrow labeled  $h_{j+1}$  exiting to the right.

$$h_{j+1} = \sigma(W_{j+1}^T h_j + b_{j+1})$$
$$W_j \in \mathbb{R}^{M \times N}, b_j \in \mathbb{R}^N$$
$$h_j \in \mathbb{R}^M, h_{j+1} \in \mathbb{R}^N$$



## Probabilistic Interpretation

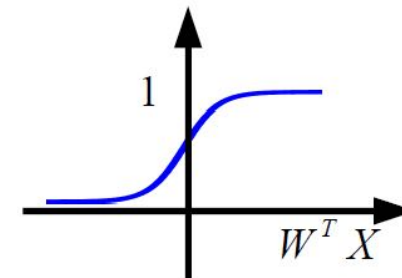
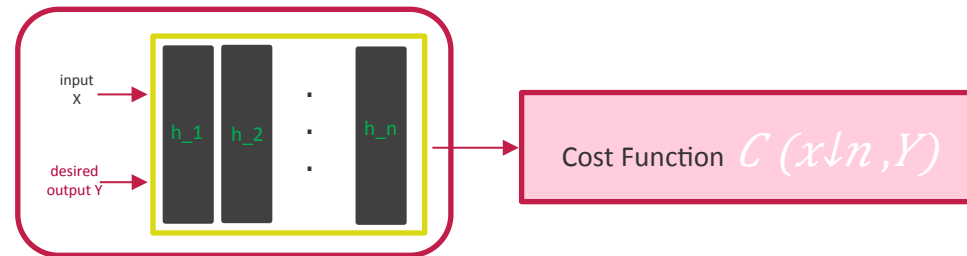
Input:  $X \in \mathbb{R}^D$

Binary label:  $y$

Parameters:  $W \in \mathbb{R}^D$

Output prediction:  $p(y=1|X) = \frac{1}{1 + e^{-W^T X}}$

Loss:  $L = -\log(p(y|X))$



# Support Vector Machine

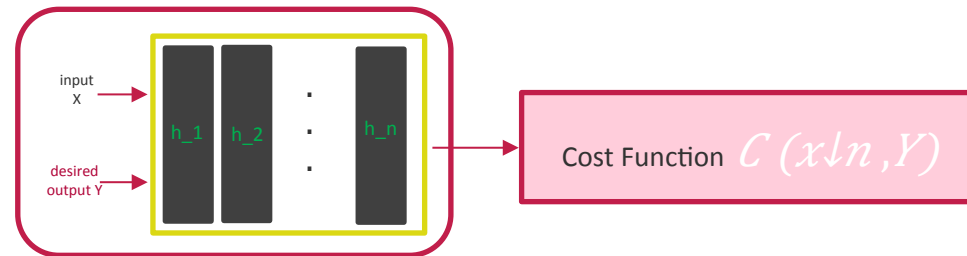
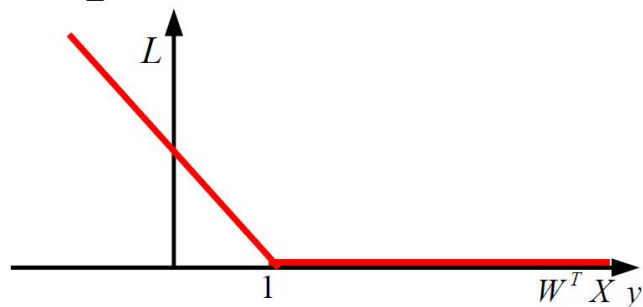
Input:  $X \in \mathbb{R}^D$

Binary label:  $y$


Parameters:  $W \in \mathbb{R}^D$

Output prediction:  $W^T X$

Loss:  $L = \frac{1}{2} \|W\|^2 + \lambda \max[0, 1 - W^T X y]$



Hinge Loss

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# Logistic Regression

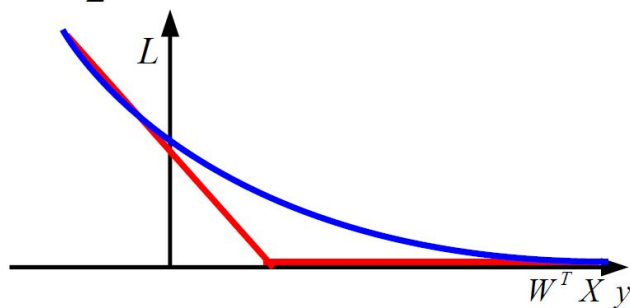
Input:  $X \in \mathbb{R}^D$

Binary label:  $y$


Parameters:  $W \in \mathbb{R}^D$

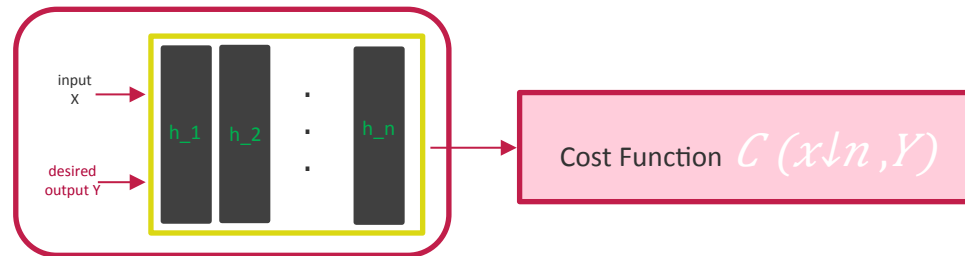
Output prediction:  $W^T X$

Loss:  $L = \frac{1}{2} \|W\|^2 + \lambda \log(1 + \exp(-W^T X y))$



Log Loss

Ranzato 



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## Example

Input :

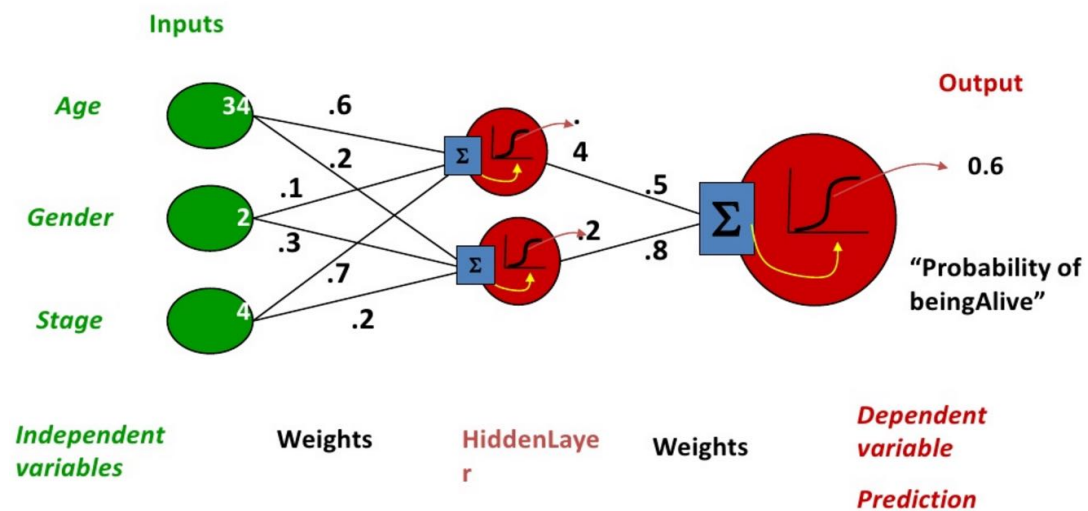
Age:34

Gender: female

Stage: IV

Output :

Probability of being alive?



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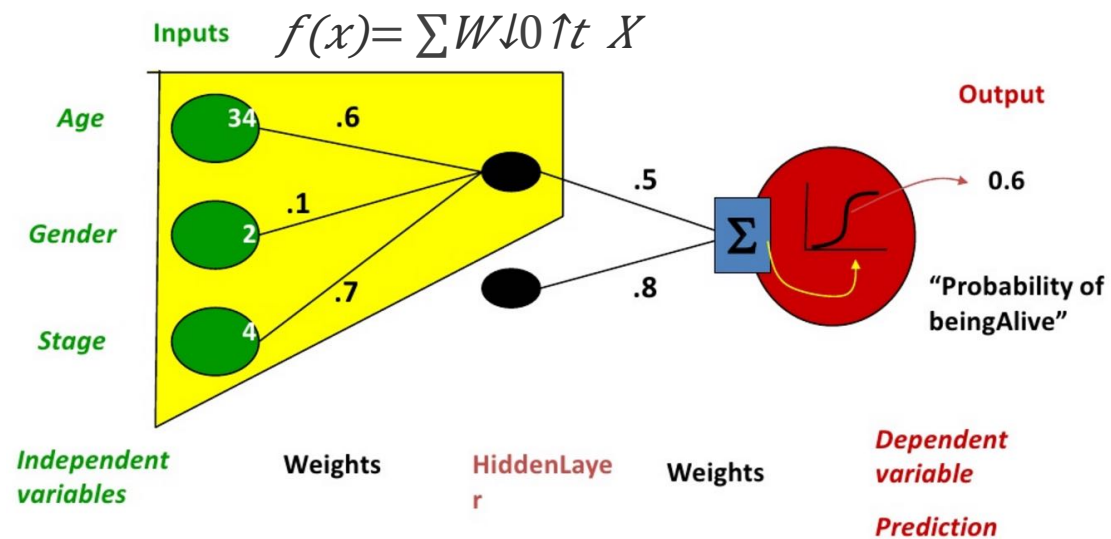
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## Example

=0.6

=0.1

=0.7



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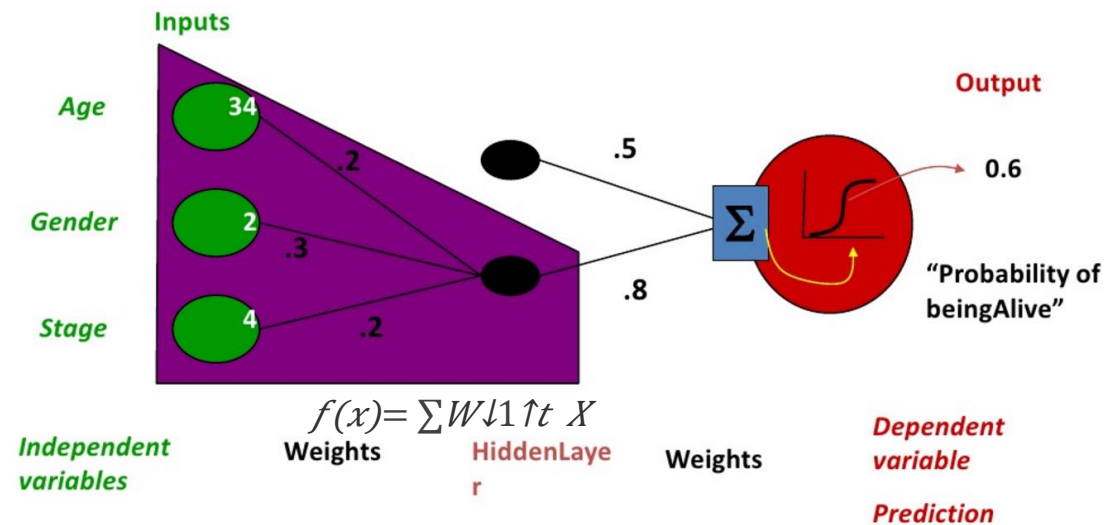
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## Example

$$W_{111} = 0.2$$

$$W_{112} = 0.3$$

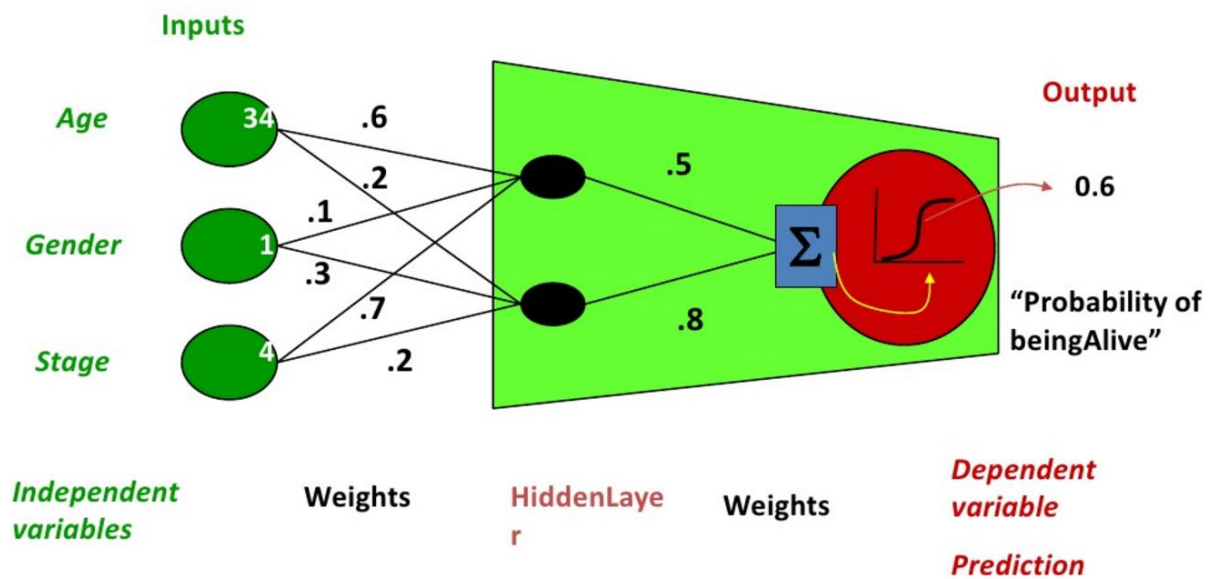
$$W_{113} = 0.2$$



### Medical Image Analysis by Deep Learning

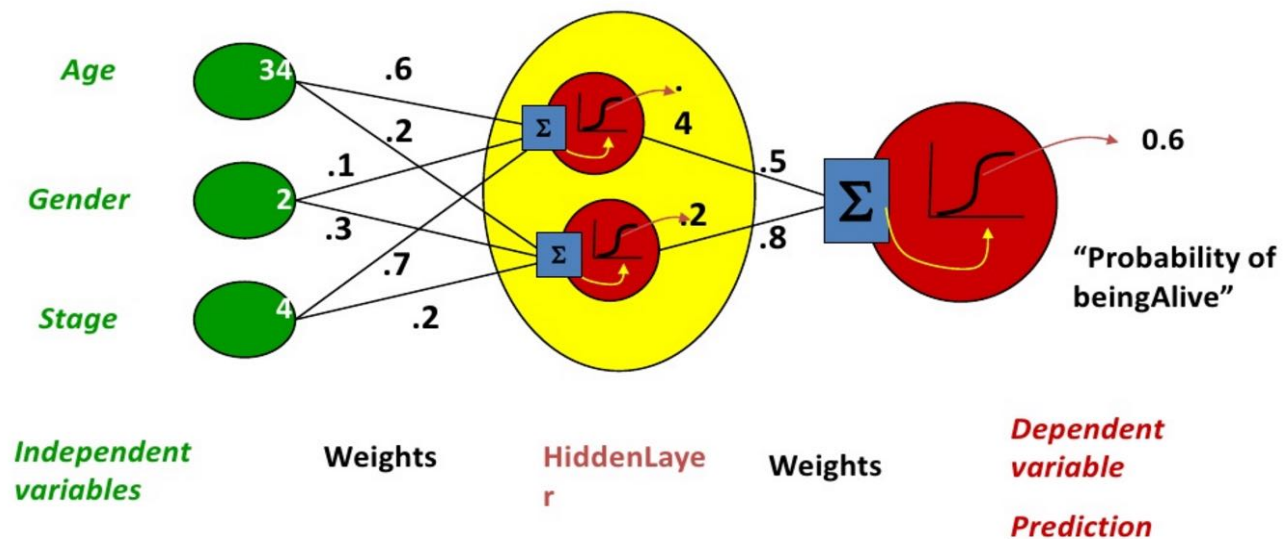
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## Example



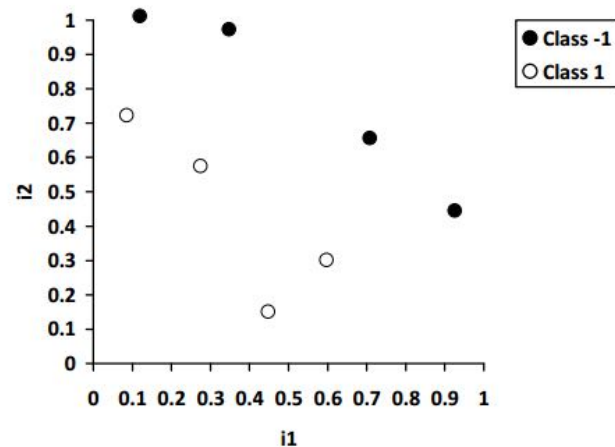


## Example



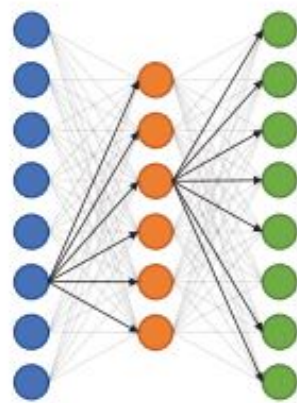
## Example

The chart below shows a set of two-dimensional input samples from two classes:

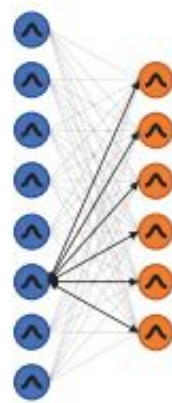


1. How many samples are misclassified for both classes?
2. Calculate the new weights from each class?
3. How many samples are missclassified with new updated weights?

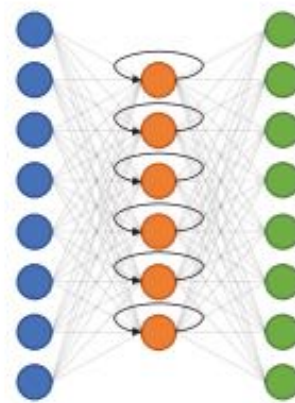
# Popular Neural Network Architecture



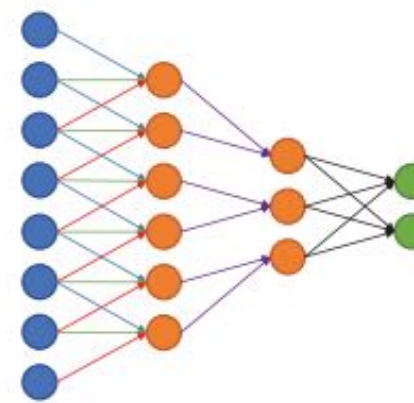
Auto Encoder



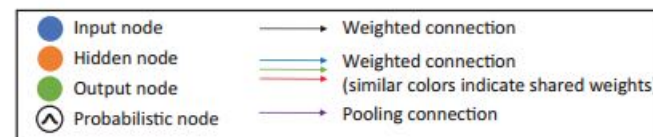
Restricted Boltzmen  
Machine



Recurrent Neural  
Network



Convolution Neural  
Network



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## Deep Learning Frameworks

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Caffe



DEEPLARNING4J

dmlc  
*mxnet*



TensorFlow

theano



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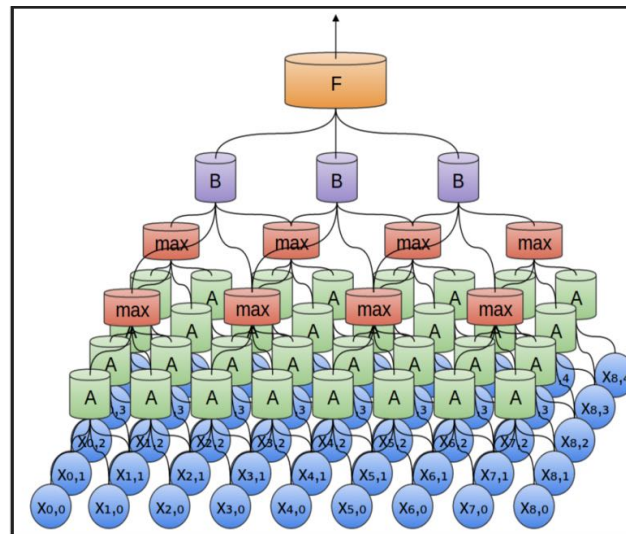
# Classification Model

```
from caffe import layers as L
from caffe import params as P

def lenet(lmdb, batch_size):
    # our version of LeNet: a series of linear and simple nonlinear transformations
    n = caffe.NetSpec()
    n.data, n.label = L.Data(batch_size=batch_size, backend=P.Data.LMDB, source=lmdb,
                             transform_param=dict(scale=1./255), ntop=2)
    n.conv1 = L.Convolution(n.data, kernel_size=5, num_output=20, weight_filler=dict(type='xavier'))
    n.pool1 = L.Pooling(n.conv1, kernel_size=2, stride=2, pool=P.Pooling.MAX)
    n.conv2 = L.Convolution(n.pool1, kernel_size=5, num_output=50, weight_filler=dict(type='xavier'))
    n.pool2 = L.Pooling(n.conv2, kernel_size=2, stride=2, pool=P.Pooling.MAX)
    n.ip1 = L.InnerProduct(n.pool2, num_output=500, weight_filler=dict(type='xavier'))
    n.relu1 = L.ReLU(n.ip1, in_place=True)
    n.ip2 = L.InnerProduct(n.ip1, num_output=10, weight_filler=dict(type='xavier'))
    n.loss = L.SoftmaxWithLoss(n.ip2, n.label)
    return n.to_proto()

with open('examples/mnist/lenet_auto_train.prototxt', 'w') as f:
    f.write(str(lenet('examples/mnist/mnist_train_lmdb', 64)))

with open('examples/mnist/lenet_auto_test.prototxt', 'w') as f:
    f.write(str(lenet('examples/mnist/mnist_test_lmdb', 100)))
```



Picture source: [Christopher Olah's Blog](#)

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# Why Is Deep Learning So Popular?

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New layer-wise training algorithm [Science 2006], i.e. train on atomic task

Big data, compared to 20 years ago

Powerful computers

- Previous algorithms may be theoretically working, but not practically
- not converged to good local minima with the previous less powerful computers

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## Why Is Deep Learning So Popular?

---

- New layer-wise training algorithm [Science 2006], i.e. train on atomic task
- Big data, compared to 20 years ago
- Powerful computers
  - Algorithms were working but impractical
  - Algorithms did not converge to good local minima



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# Deep Learning; Advantages and Disadvantages

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## Advantages

- High performance on multiple domains problems, e.g. speech, language, vision, games, etc.
- Reduces the need for feature engineering
- Can be adapted to new problems with new architecture, e.g. vision, time series, language, etc. using convolutional neural networks, recurrent neural networks, long short-term memory, etc.

## Disadvantages

- Requires a large amount of data .
- Is extremely computationally expensive to train.
- No strong theoretical foundation
- Determining the topology, training method, hyper parameters for deep learning is considered as black magic

# Deep Learning Application on Medical Imaging

## Segmentation

- Hippocampus Segmentation

## Registration

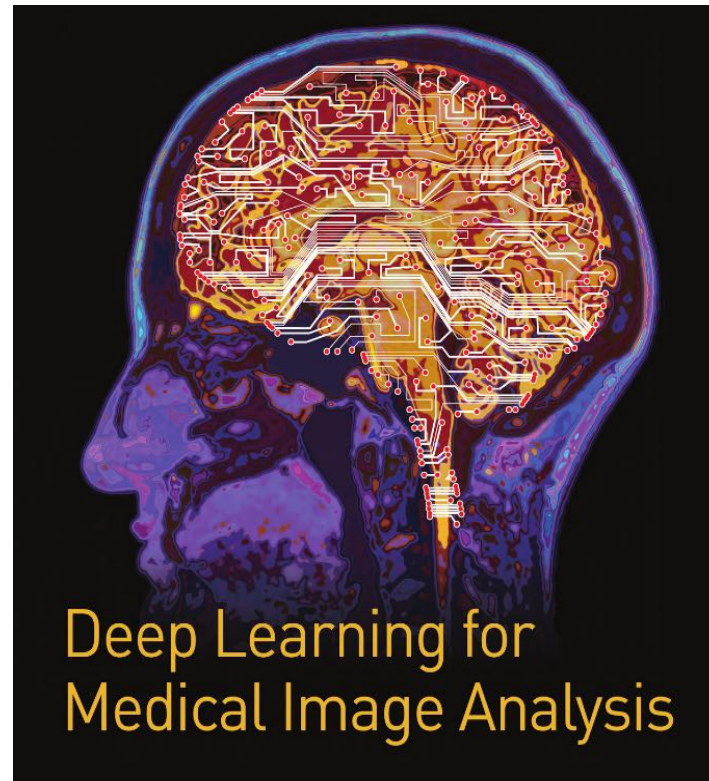
- Brain MRI Registration

## Computer-aided Diagnosis

- AD/MCI Diagnosis
- Skin Cancer Detection

## Image Synthesis

- Estimating CT from MRI



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# Medical Imaging Examples

- CT scan produces up to 2000 images within 25s
- PET/CT requires review of up to 6000 images
- Breast ultrasound can create 5000 images\*



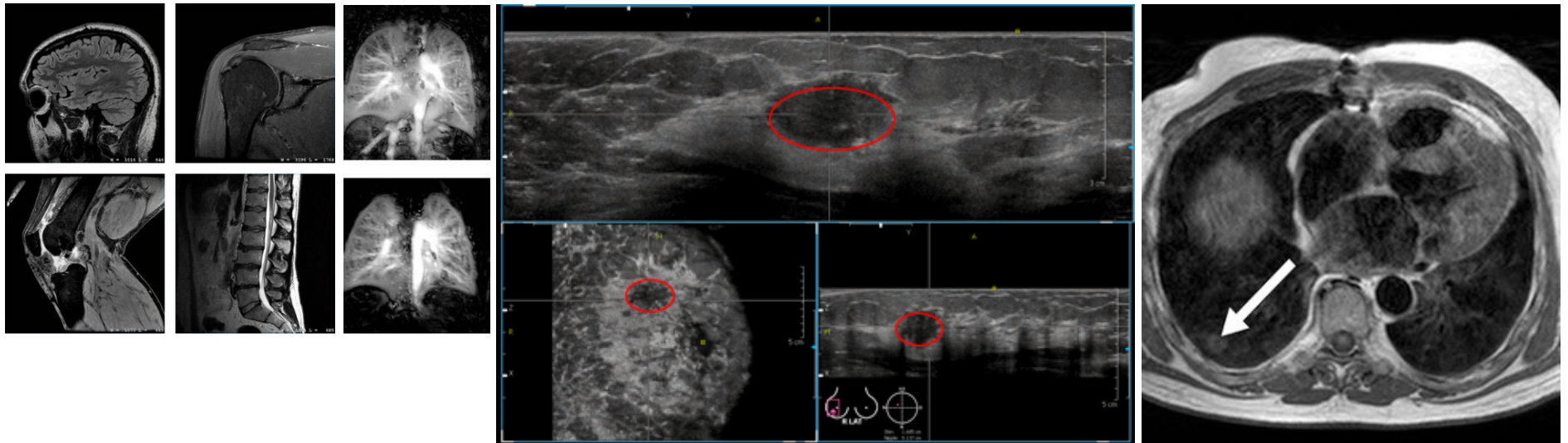
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\*<http://www.cancer.org>

# Medical Imaging Examples



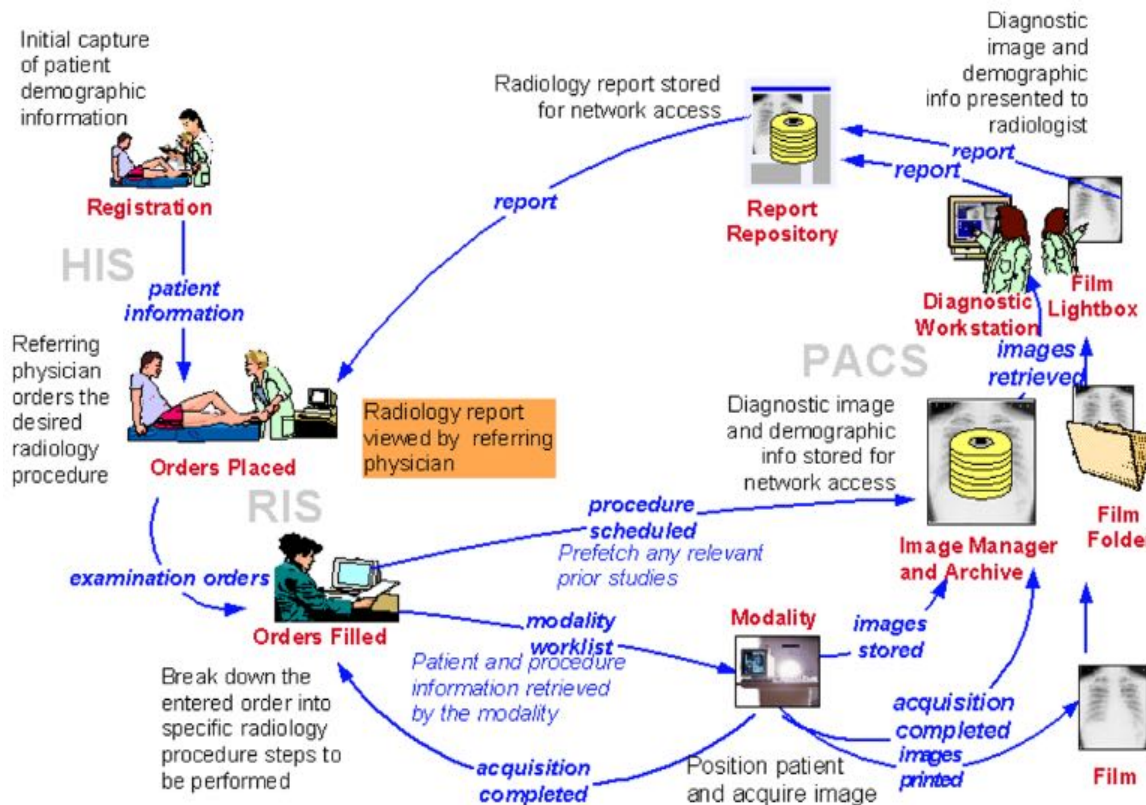
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\*<http://www.cancer.org>

## Current Radiologist's Workflow



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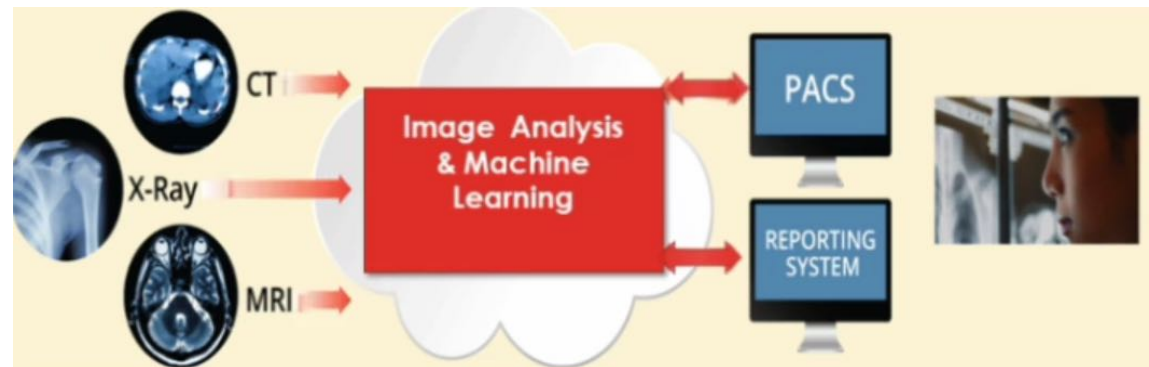
# Image Analysis & Machine Learning

- Challenges in Image Analysis:

- Time consuming
- Missed findings

- Machine learning may assist radiologist in:

- Formulating findings
- Taking measurements
- Characterization
- Work more efficiently



## Medical Image Analysis by Deep Learning

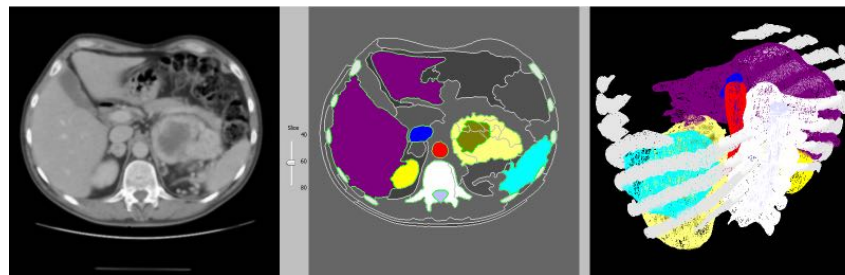
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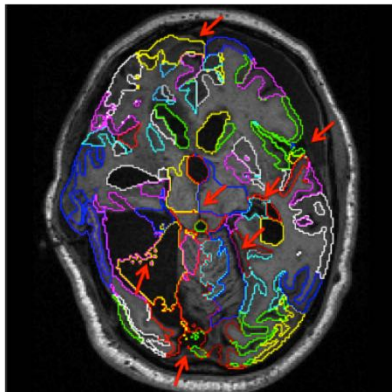
## Application Example: Medical Image Segmentation

**Segmentation** is the process of partitioning an image into different meaningful segments.

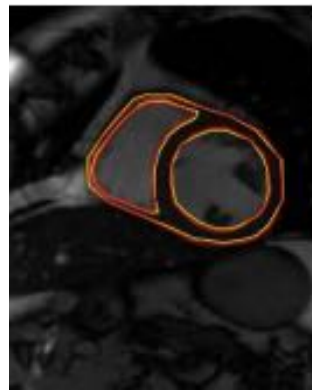
In medical imaging, these segments often correspond to different tissue classes, organs, pathologies, or other biologically relevant structures.



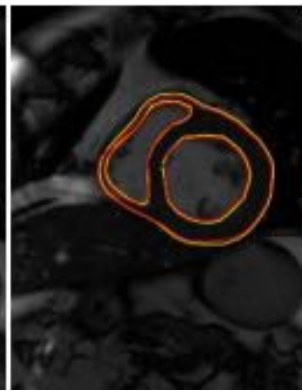
abdominal CT scan.  
the rib cage, liver, kidneys, spleen, blood vessels and a renal tumor



whole-brain segmentation  
C. Ledig 2015



endocardium and epicardium at end of  
diastole and systole. M.Rezaei 2013



Retina segmentation  
M.Rezaei 2014

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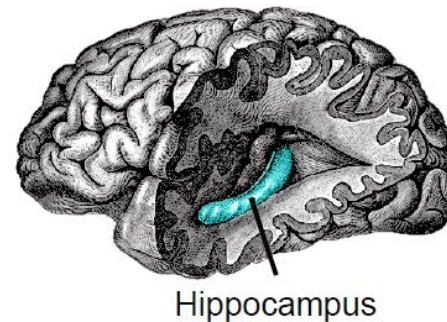
## Hippocampus Segmentation

### Importance

- The volume of the hippocampus is an important trait for early diagnosis of neurological diseases (e.g., Alzheimer's disease)

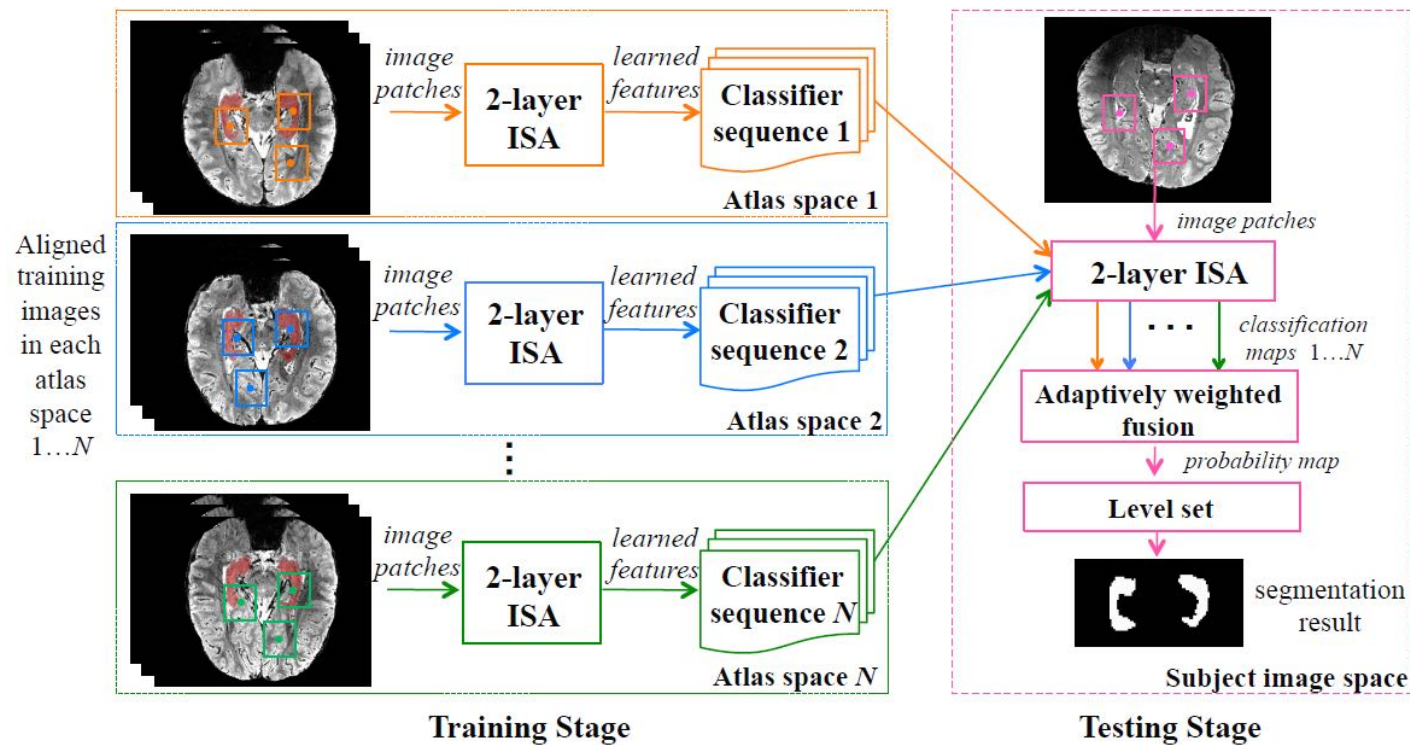
### Challenges

- The hippocampus is small ( $\approx 35 \times 15 \times 7 \text{ mm}$ )
- The hippocampus is surrounded by complex structures
- Low imaging resolution ( $\approx 1 \times 1 \times 1 \text{ mm}$ ) of 1.5T or 3T MRI scanners





# Deep Learning Solution for Hippocampus Segmentation



ISA: Independent Subspace Analysis

UNC, Dinggang Shen-2017

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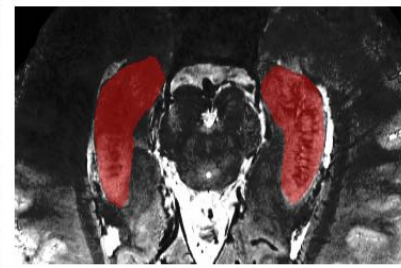
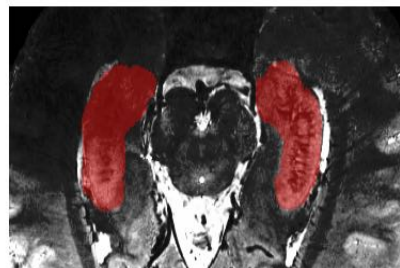
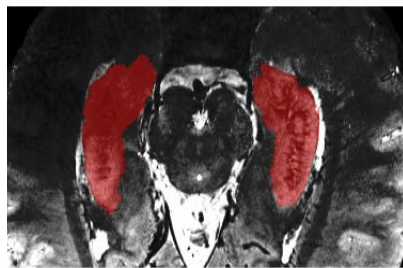
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## Evaluation

	P	R	RO	SI
Hand-Crafted Haar + Texture Features	0.843	0.847	0.772	0.865
Hierarchical Patch Representations	<b>0.883</b>	<b>0.881</b>	<b>0.819</b>	<b>0.894</b>

$V(A)$  : The volume of the ground-truth (manual segmentation)

$V(B)$  : The volume of the automatic segmentation



Precision

$$P = \frac{V(A \cap B)}{V(B)}$$

Recall

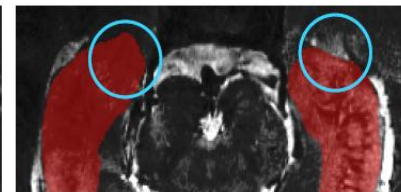
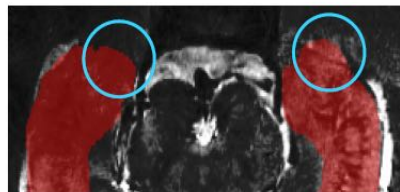
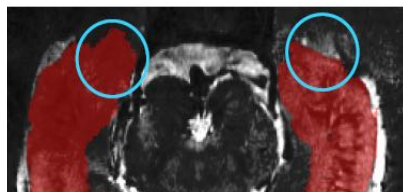
$$R = \frac{V(A \cap B)}{V(A)}$$

Relative overlap

$$RO = \frac{V(A \cap B)}{V(A \cup B)}$$

Similarity index

$$SI = \frac{V(A \cap B)}{\{(V(A) + V(B))/2\}}$$



Ground Truth

Haar + Texture Features

Hierarchical Features

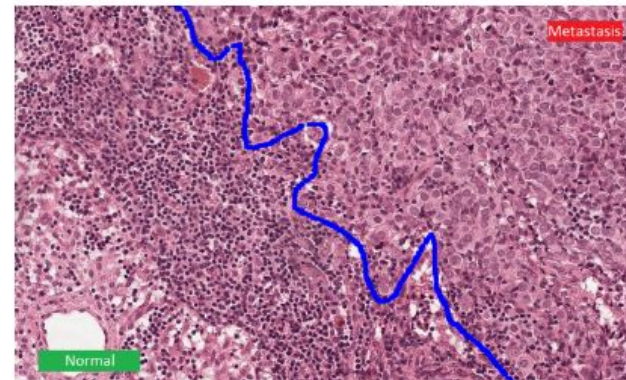
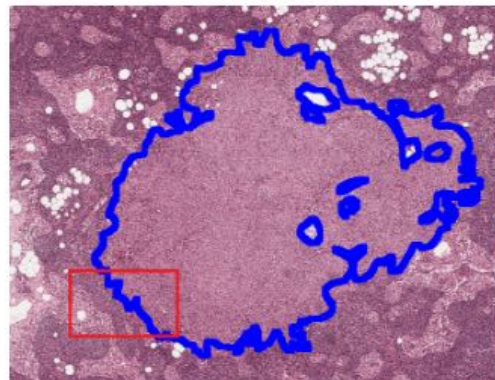
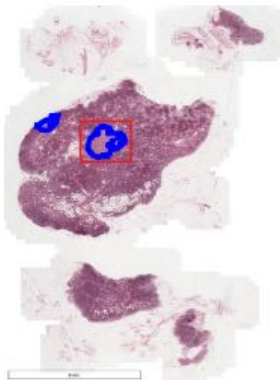
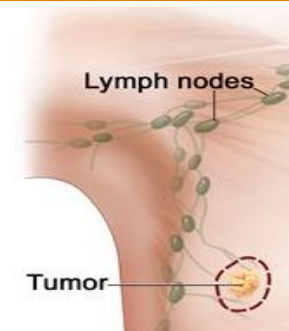
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## Open Challenge: Breast Cancer Metastase Segmentation

- CAMELYON17 is the second grand challenge in pathology



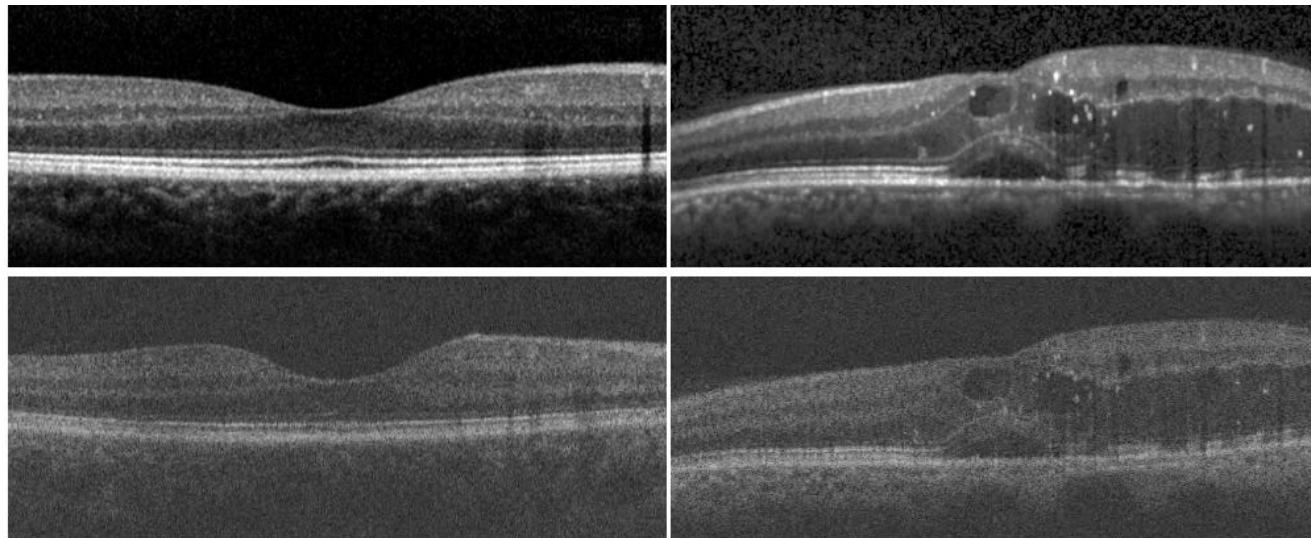
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## Open Challenges: Retinal OCT Fluid

**RETOUCH** is Retinal OCT Fluid Challenge, to segment variety of retinal fluid lesions 2013-2017



Normal retina imaged with OCT from the three manufacturers.  
The three slices come from three different subjects.

Retina with macular edema imaged with OCT from the three manufacturers.  
The slices are of the same patient and approximately at the same anatomical position.

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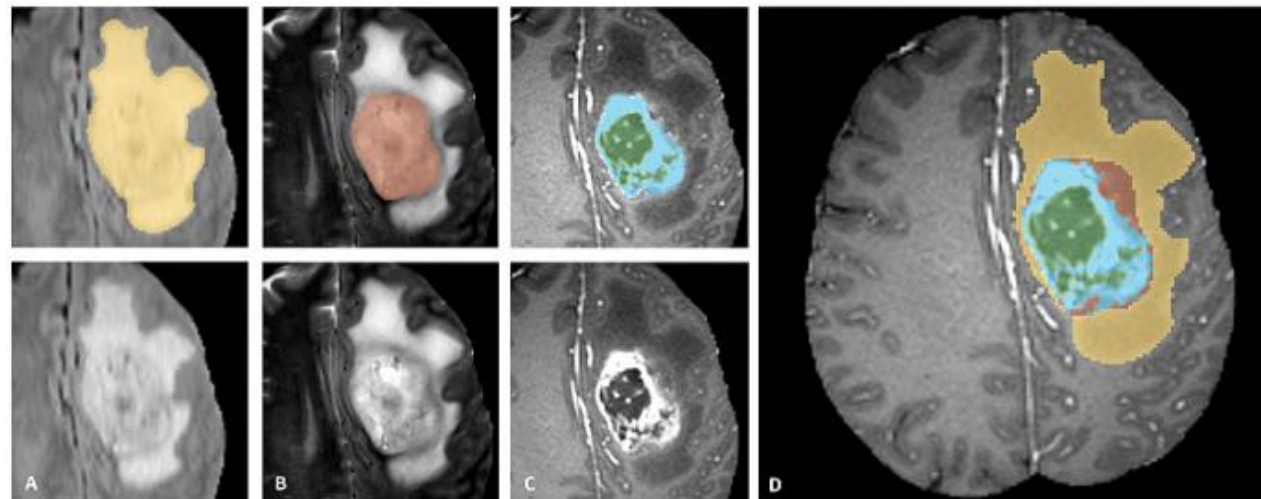
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## Open Challenges: Brain Tumor Segmentation

- BraTS : BraTs Challegnes is Brain Tumor Segmentation Challenges(2012-2017)



**Fig.1: Glioma sub-regions.** Shown are image patches with the tumor sub-regions that are annotated in the different modalities (top left) and the final labels for the whole dataset (right). The image patches show from left to right: the whole tumor (yellow) visible in T2-FLAIR (Fig.A), the tumor core (red) visible in T2 (Fig.B), the enhancing tumor structures (light blue) visible in T1Gd, surrounding the cystic/necrotic components of the core (green) (Fig. C). The segmentations are combined to generate the final labels of the tumor sub-regions (Fig.D): edema (yellow), non-enhancing solid core (red), necrotic/cystic core (green), enhancing core (blue). (Figure taken from the [BraTS IEEE TMI paper](#).)

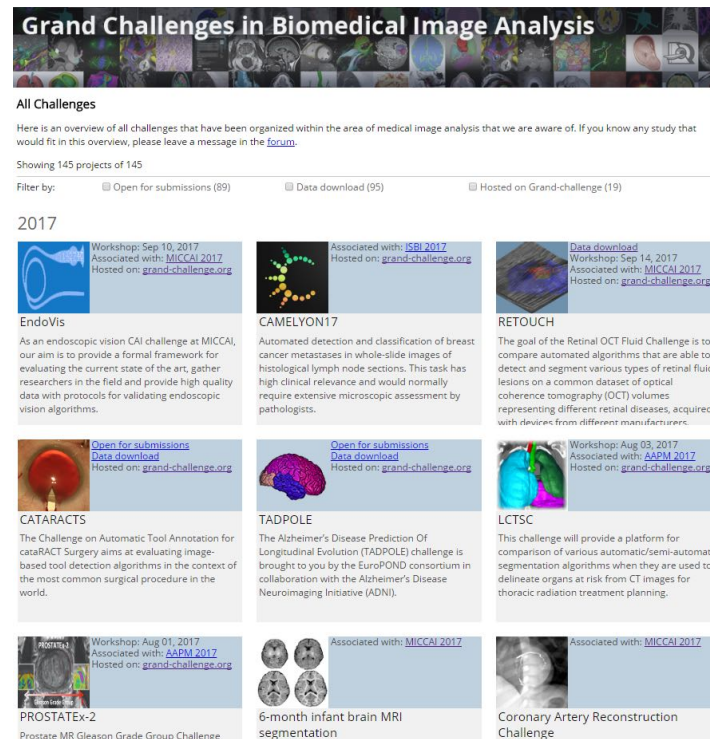
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## Other Challenges

- [https://grand-challenge.org/all\\_challenges/](https://grand-challenge.org/all_challenges/)
- Medical Image Computing and Computer Assisted Interventions Conference-MICCAI
- IEEE Symposium on Bio Medical Imaging (ISBI)
- Artificial Intelligence in Medicine (AIME)



**Grand Challenges in Biomedical Image Analysis**










**All Challenges**

Here is an overview of all challenges that have been organized within the area of medical image analysis that we are aware of. If you know any study that would fit in this overview, please leave a message in the [forum](#).

Showing 145 projects of 145

Filter by: ☐ Open for submissions (89) ☐ Data download (95) ☐ Hosted on Grand-challenge (19)

2017

 <p><b>EndoVis</b></p> <p>Workshop: Sep 10, 2017 Associated with: <a href="#">MICCAI 2017</a> Hosted on: <a href="#">grand-challenge.org</a></p> <p>As an endoscopic vision CAI challenge at MICCAI, our aim is to provide a formal framework for evaluating the current state of the art, gather researchers in the field and provide high quality data with protocols for validating endoscopic vision algorithms.</p>	 <p><b>CAMELYON17</b></p> <p>Associated with: <a href="#">ISBI 2017</a> Hosted on: <a href="#">grand-challenge.org</a></p> <p>Automated detection and classification of breast cancer metastases in whole-slide images of histological lymph node sections. This task has high clinical relevance and would normally require extensive microscopic assessment by pathologists.</p>	 <p><b>RETOUCH</b></p> <p>Data download Workshop: Sep 14, 2017 Associated with: <a href="#">MICCAI 2017</a> Hosted on: <a href="#">grand-challenge.org</a></p> <p>The goal of the Retinal OCT Fluid Challenge is to compare automated algorithms that are able to detect and segment various types of retinal fluid lesions on a common dataset of optical coherence tomography (OCT) volumes representing different retinal diseases, acquired with devices from different manufacturers.</p>
 <p><b>CATARACTS</b></p> <p>Open for submissions Data download Hosted on: <a href="#">grand-challenge.org</a></p> <p>The Challenge on Automatic Tool Annotation for cataract Surgery aims at evaluating image-based tool detection algorithms in the context of the most common surgical procedure in the world.</p>	 <p><b>TADPOLE</b></p> <p>Open for submissions Data download Hosted on: <a href="#">grand-challenge.org</a></p> <p>The Alzheimer's Disease Prediction Of Longitudinal Evolution (TADPOLE) challenge is brought to you by the EuroPOND consortium in collaboration with the Alzheimer's Disease Neuroimaging Initiative (ADNI).</p>	 <p><b>LCTSC</b></p> <p>Workshop: Aug 03, 2017 Associated with: <a href="#">AAPM 2017</a> Hosted on: <a href="#">grand-challenge.org</a></p> <p>This challenge will provide a platform for comparison of various automatic/semi-automatic segmentation algorithms when they are used to delineate organs at risk from CT images for thoracic radiation treatment planning.</p>
 <p><b>PROSTATEX-2</b></p> <p>Workshop: Aug 01, 2017 Associated with: <a href="#">AAPM 2017</a> Hosted on: <a href="#">grand-challenge.org</a></p> <p>Prostate MR Gleason Grade Group Challenge.</p>	 <p><b>6-month infant brain MRI segmentation</b></p> <p>Associated with: <a href="#">MICCAI 2017</a></p>	 <p><b>Coronary Artery Reconstruction Challenge</b></p> <p>Associated with: <a href="#">MICCAI 2017</a></p>

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## Application Example: Medical Image Registration

- Studying temporal changes. (time series study e.g. cognitive processes, heart deformations)
- Combining complementary information from different imaging modalities
- Characterizing a population of subjects.

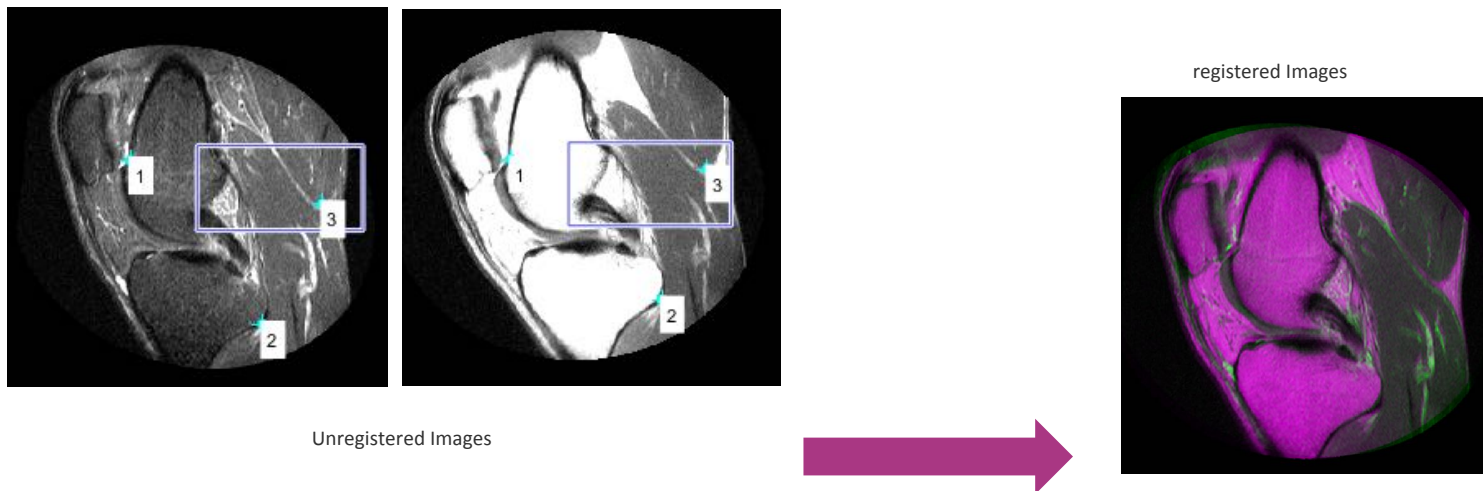
### HOW?

- Transformation model (rigid, affine, deformable)
- similarity metric (sum of squared distance, Correlation coefficient)



Data augmentation by  
registration M.Rezaei 2017

## Affine registration on Knee (MRI-Flair & T1c) –(II)



Reflection, Scale, Rotate, Shear, Identity

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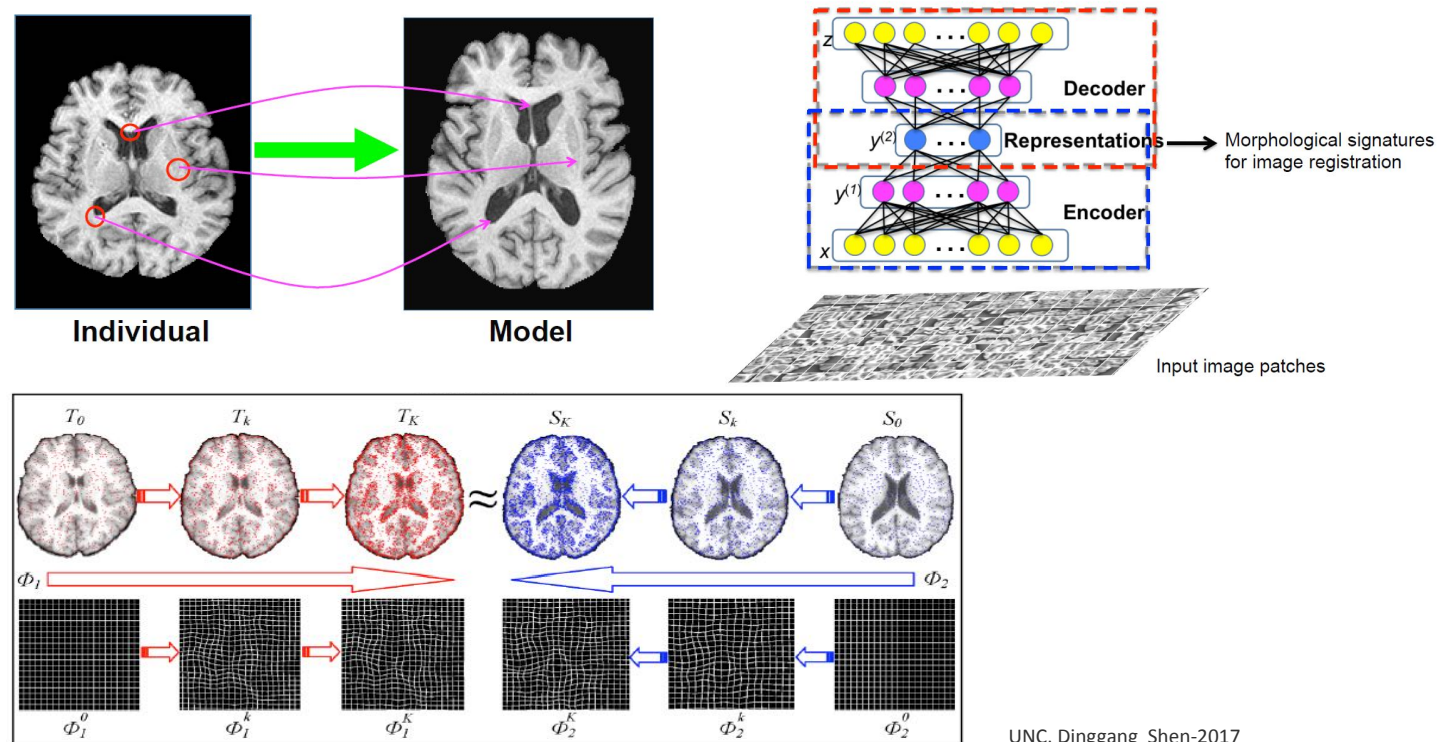
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Mathwork-2014

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# Alzheimer Diseases Detection by Auto-encoder Registration



UNC, Dinggang Shen-2017

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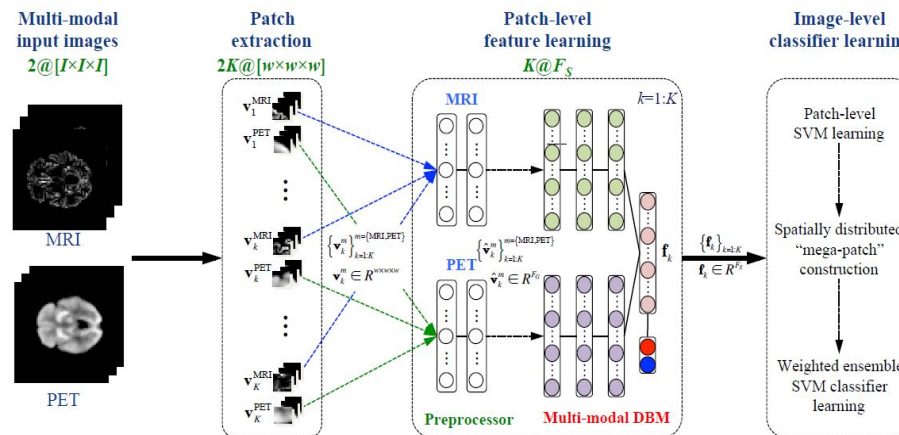
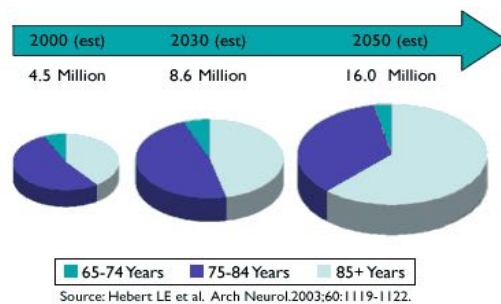
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# Brain and Alzheimer Diseases

15,000 leading cause-of-death in Deutschland

6th leading cause-of-death in US



$I$ : image size,  $w$ : patch size,  $K$ : # of selected patches,  $m$ : modality index,  
 $F_G$ : # of hidden units in Gaussian restricted Boltzmann machine,  
 $F_S$ : # of hidden units in the top-layer of multi-modal Deep Boltzmann Machine (DBM)

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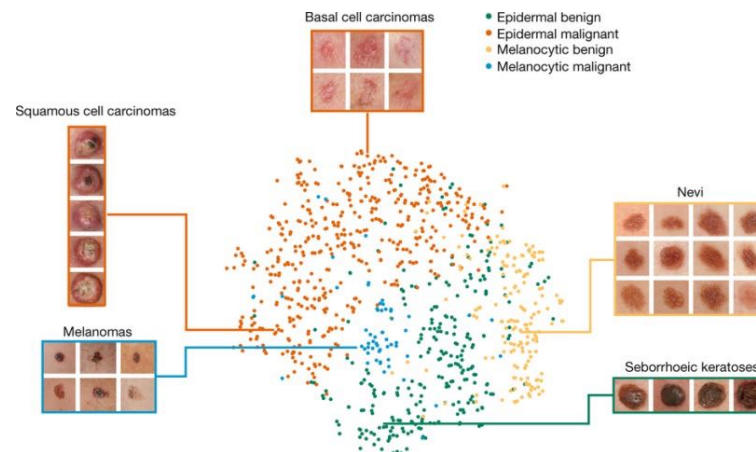
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## Computer-aided Diagnosis

Esteva et al. “Dermatologist-level classification of skin cancer with deep neural networks”, in ***Nature***, 25 January 2017

- Demonstrates capabilities of artificial intelligence in classifying skin cancer with a level of competence comparable to dermatologists



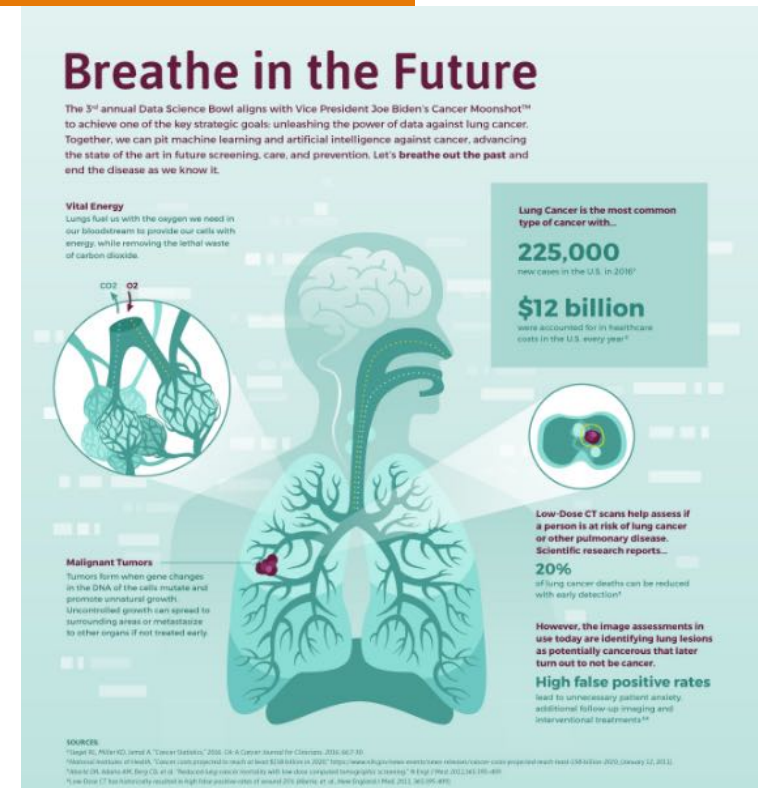
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# Lung Cancer Detection

- Strikes approx. 225,000 people every year just in USA
- Causes approx. USD 12 billion in health care costs.
- Data Science Bowl 2017 Challenges (USD 1,000,000)
- Lung Nodule Detection (2015-2017,ISBI)

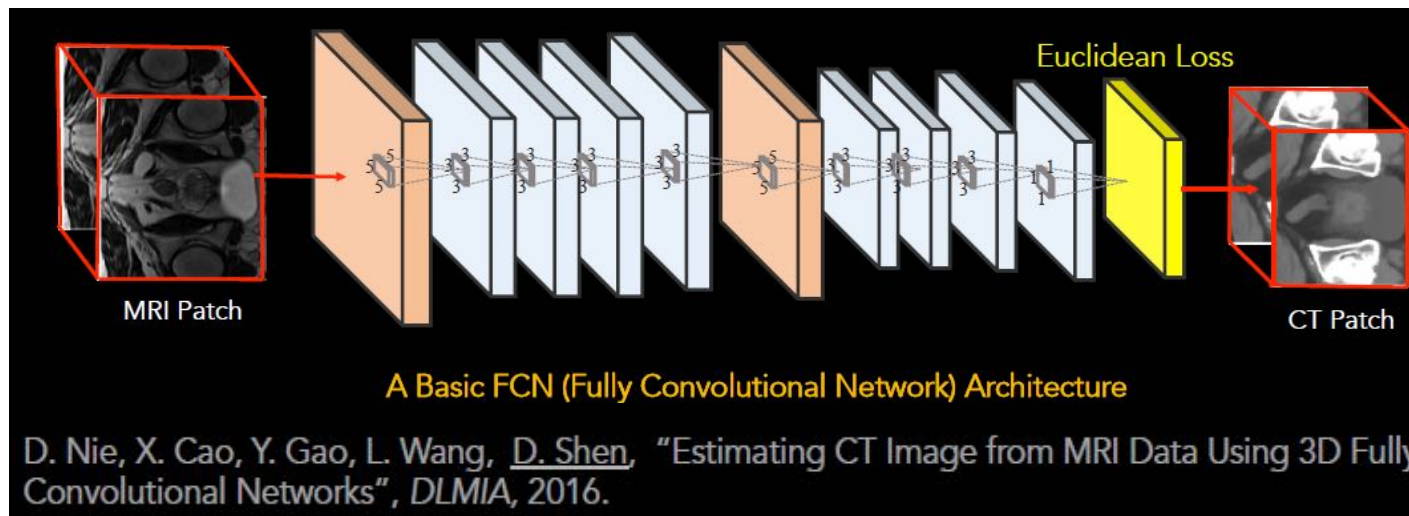


### Estimating CT from MRI with Fully Convolution Neural Network

(+) Bone injuries

(+) Organs in the pelvis, chest and abdomen

(-) CT images use Radiation

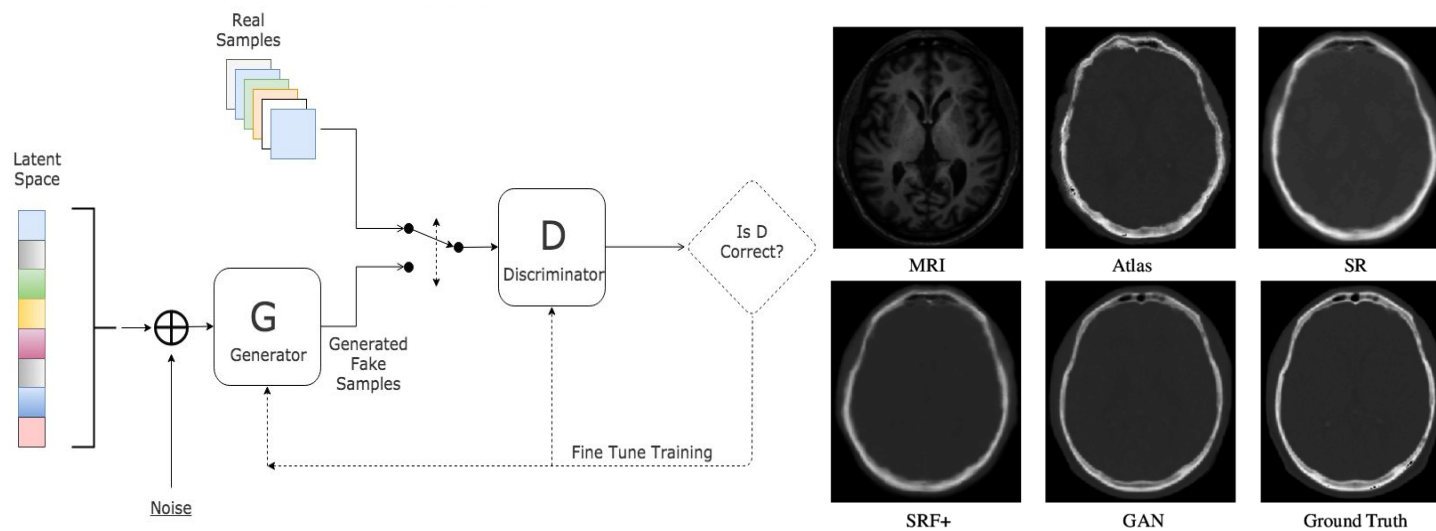


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# Unsupervised Learning for Estimating CT from MRI



(Goodfellow 2016)

UNC, Dinggang Shen-2017

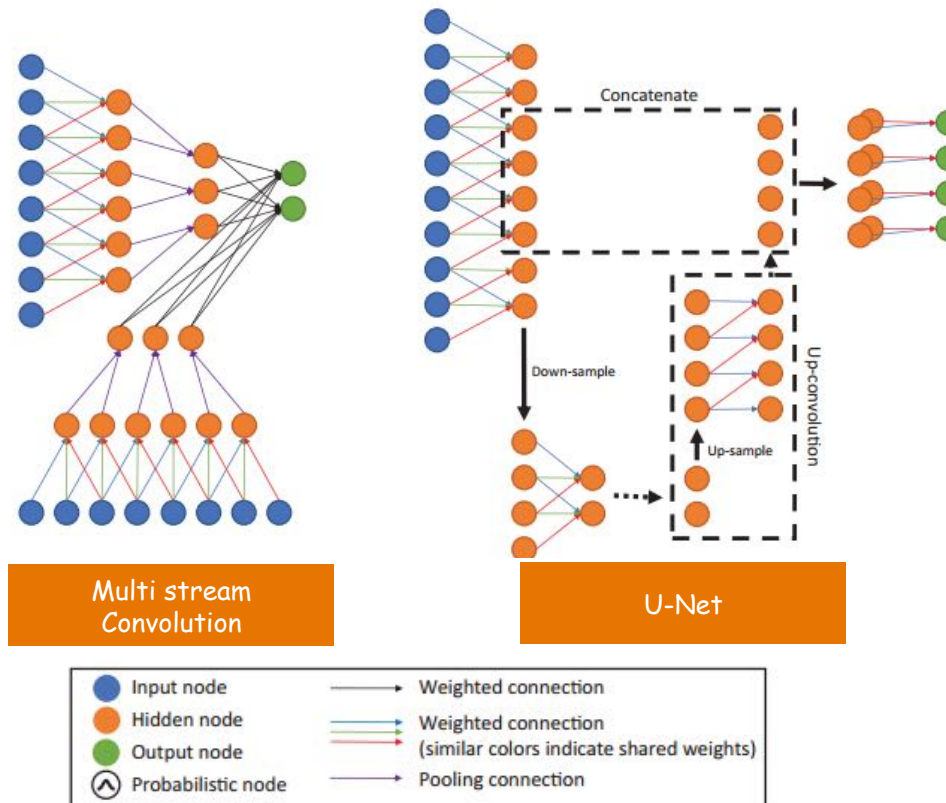
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## Popular Neural Network Architecture in Medical Imaging



### Medical Image Analysis by Deep Learning

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