

Lecture 3: Medical Imaging

CSCI6XXX/CHE6XXX/CSCI4XXX
(CSCI6093)

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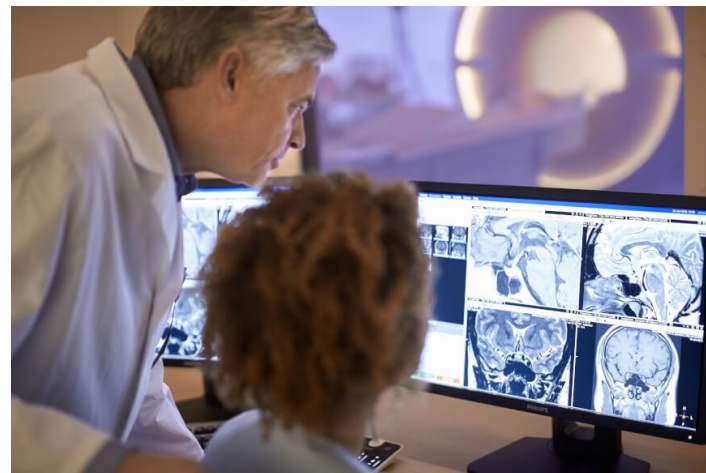
Learning Overview

- Many types of medical imaging data and their respective formats
- DICOM file format is ubiquitous but complex
- Medical imaging data analysis involves many different questions
- Lots of different machine learning paradigms are used to handle challenges of medical image data
- Traditional computer vision approaches
- Deep learning enables learning features/representations
- Convolutions key to capturing spatial relationships
- Augmentation and generative models enable better training with limited data
- Transfer learning and joint-transformer models hugely expand training options
- Machine learning in medical image analysis is very promising but has several major hurdles to broad acceptance

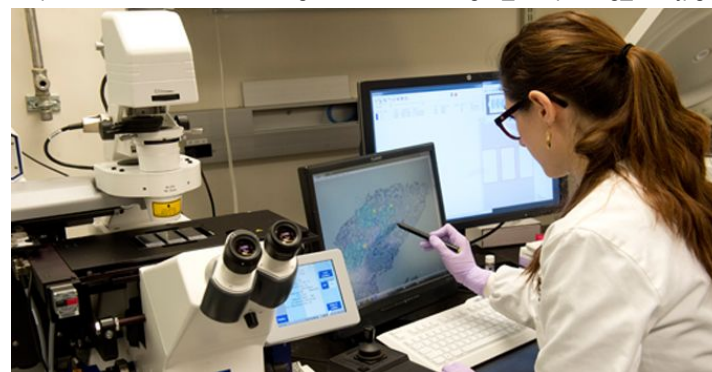
What kind of image data is there in medicine?

Imaging intensive specialties: Radiology & Pathology

- **Radiologists:** collection and interpretation of medical imaging data (including using imaging to guide minimally-invasive procedures). Often specialise in body parts or types of imaging.
- **Nuclear Medicine:** imaging/intervention involving radioisotopes
- Medical Physicists, Technologists, Sonographers, Technician
- **Pathologists:** study of tissue/samples taken from human body, extensive use of microscopy and staining. Often specialise in body parts and/or analysis methods (e.g., molecular pathology)
- **Other specialties:** many other specialties use imaging/image data emergency medicine



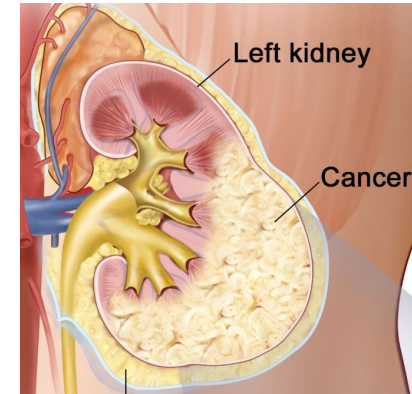
https://commons.wikimedia.org/wiki/File:Radiologist_interpreting_MRI.jpg



Patient can have many imaging modalities

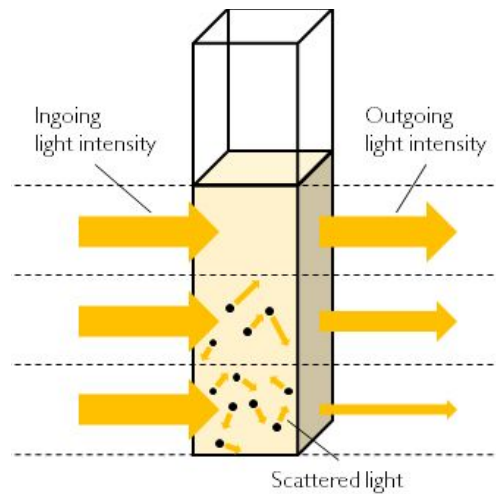
45 year old male presents to Emergency with abdominal pain:

1. Emergency performs **ultrasound** finding a kidney lesion
2. Radiology performs **CT** on lesion suggestive of renal cancer needing resectioning by Urology
3. Given tumour size Radiology performs pre-operative **MRI** to guide surgery
4. Oncology request **PET-CT** to check for metastasis but no evidence
5. Urology resect tumour and send to Pathology who perform **histopathological slide imaging** to confirm renal cell carcinoma
6. Due to high-patient risk, regular follow up **PET-CT** performed by Radiology
7. Patient returns to Emergency with leg weakness 1-2 years later
8. Radiology performs **MRI** and identifies a malignant spinal cord compression.
9. Radiation oncology perform **CT-guided** emergency radiotherapy

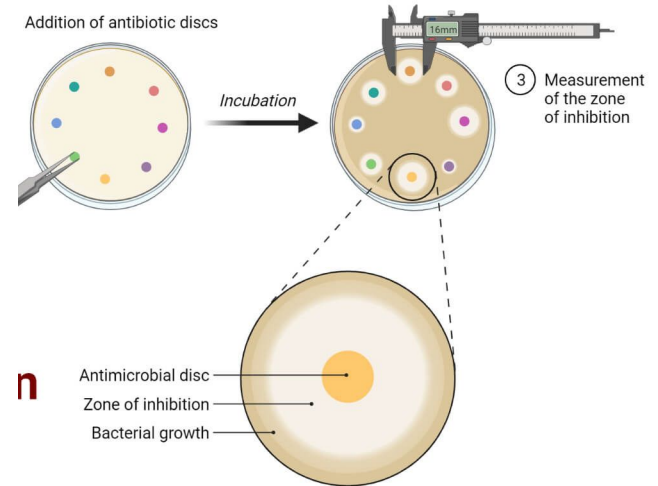


1-dimensional “image data”

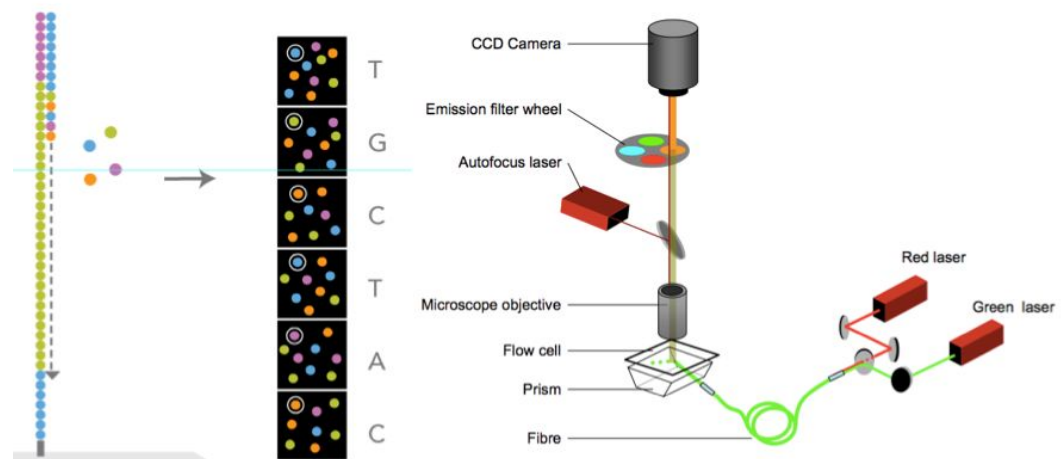
- Many diagnostic tests involve imaging (***culture density, ELISA, antibiotic susceptibility testing, Illumina DNA sequencing***)
- Images can be an intermediate format
- Intermediate formats don't always need stored/further analysed.
- Image analysis trivial and/or hard-coded into machine



aquila biolabs 2020



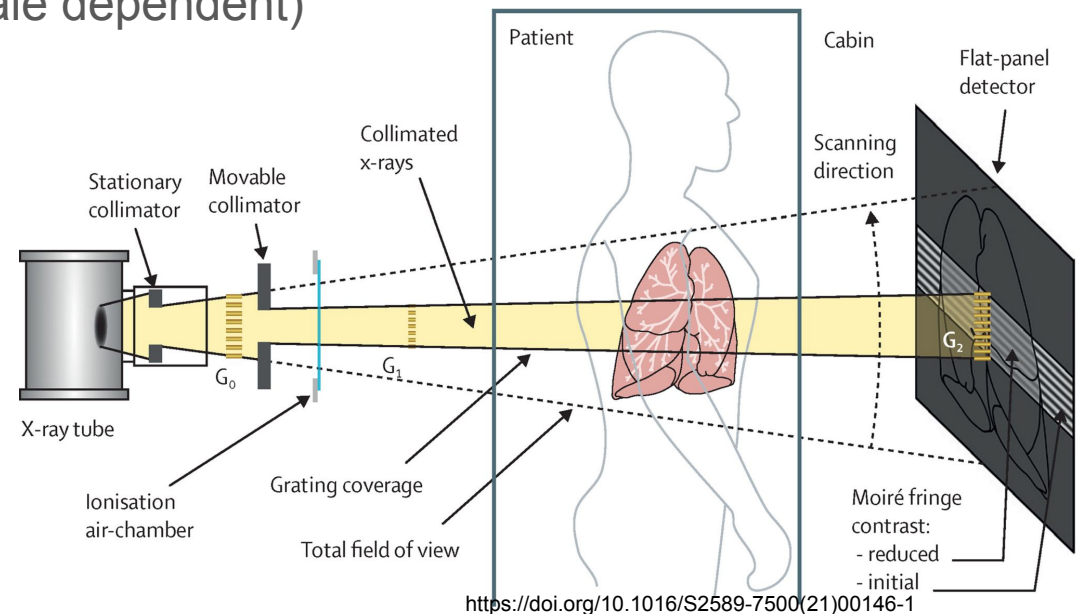
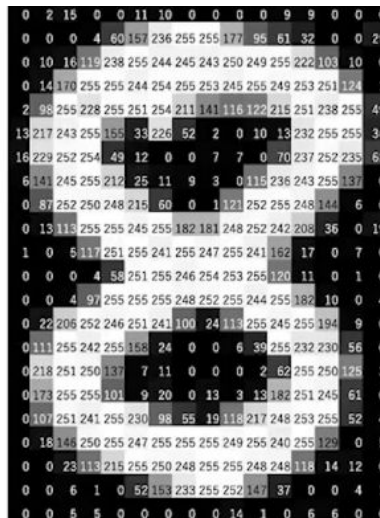
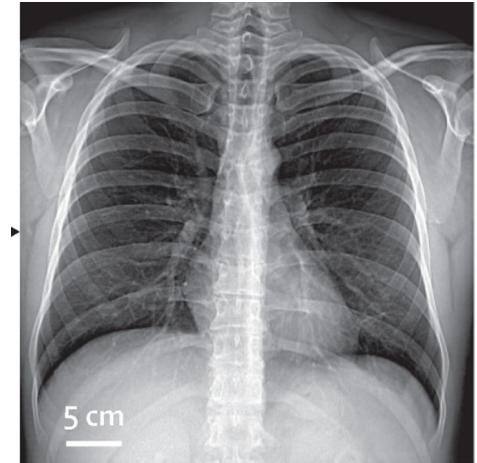
<https://microbenotes.com/kirby-bauer-disc-diffusion/>



<http://enseqlopedia.com/2014/01/nextseq-500s-new-chemistry-described/>

2-dimensional grayscale images: X-ray

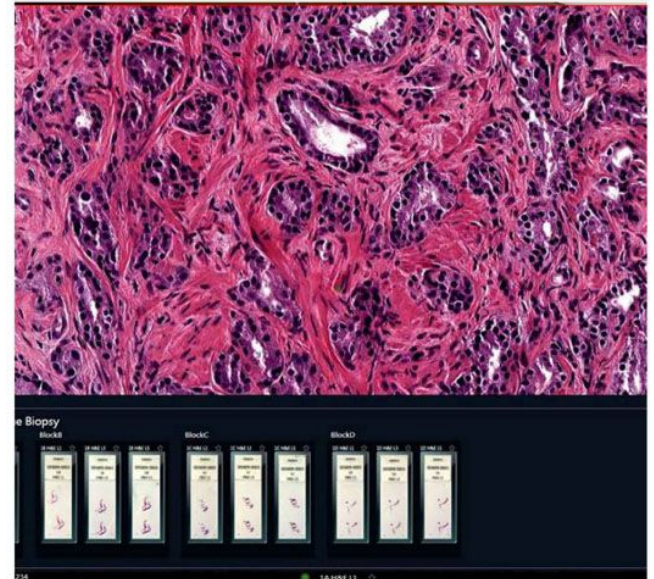
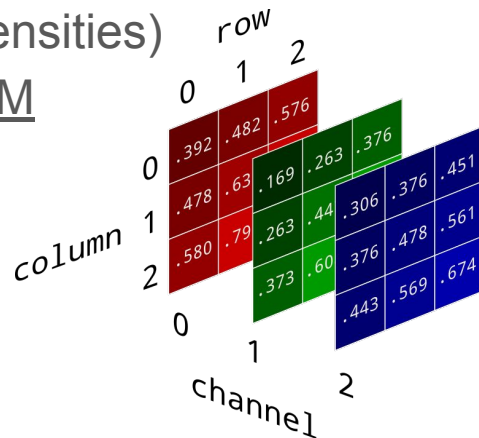
- Use of **x-rays** to image bone and soft tissue anatomy
- **Pro:** low radiation dose, cheap, common, quick
- **Con:** limited tissue density range
- **Data type:** grayscale image (2D matrix of whiteness intensities), many formats but Digital Imaging and Communications in Medicine (DICOM) standard (size is device/scale dependent)



2-dimensional colour images: Whole Slide Imaging

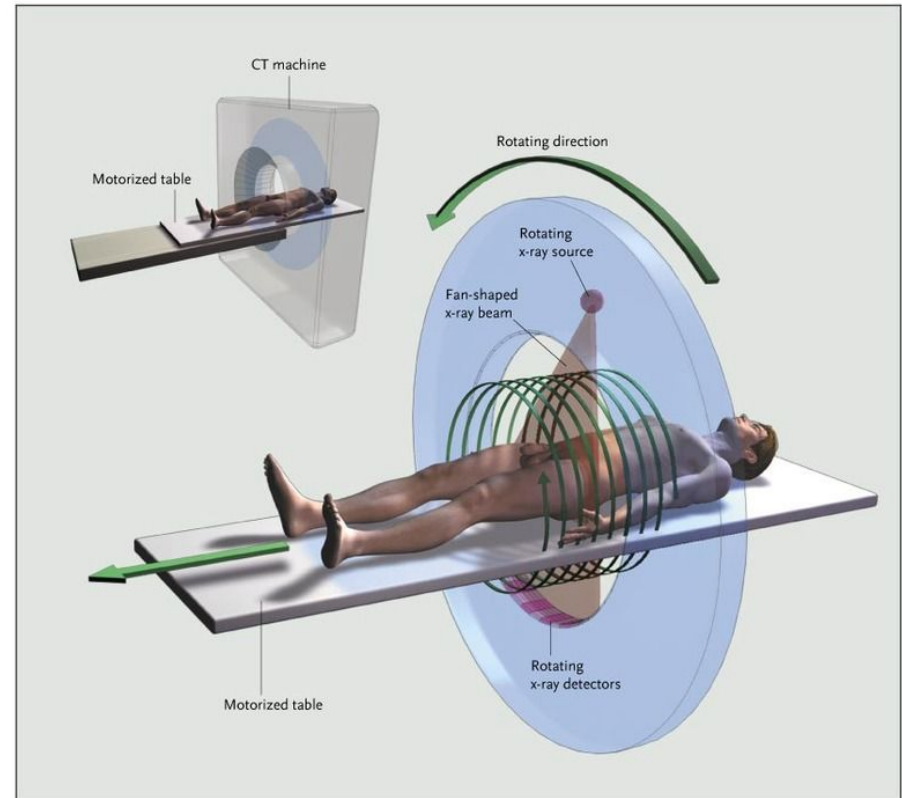
- Digital **scanning/photography** of microscopy slides (including staining/fluorescence)
- **Pro**: sharing/embedded reports, automated analyses, reproducibility
- **Con**: large images (>10GB), sensitive to scanner/preparation
- **Data type**: 3-channel colour image (3D tensor with R,G,B intensities)

TIF/JPEG2000/DICOM



Tomographic/2D slices: Computed Tomography (CT)

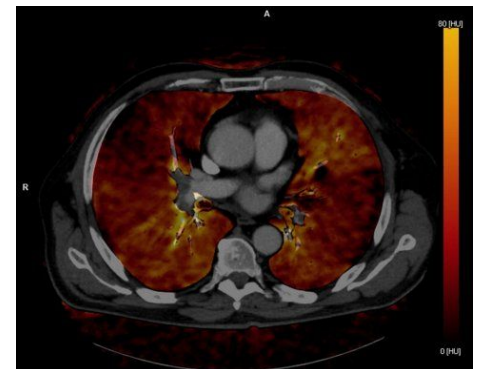
- **X-rays** in 1000-5000 slices/helical pattern computationally processed into pseudo-3D for any organ system
- **Pro:** great capture of anatomical detail, fast, broader than X-ray (contrast capture of organ/vessels)
- **Con:** higher radiation dose, relatively expensive
- **Data Type:** reconstructed grayscale image (3D matrix of whiteness intensities); multiple individual 2D grayscale slides; DICOM



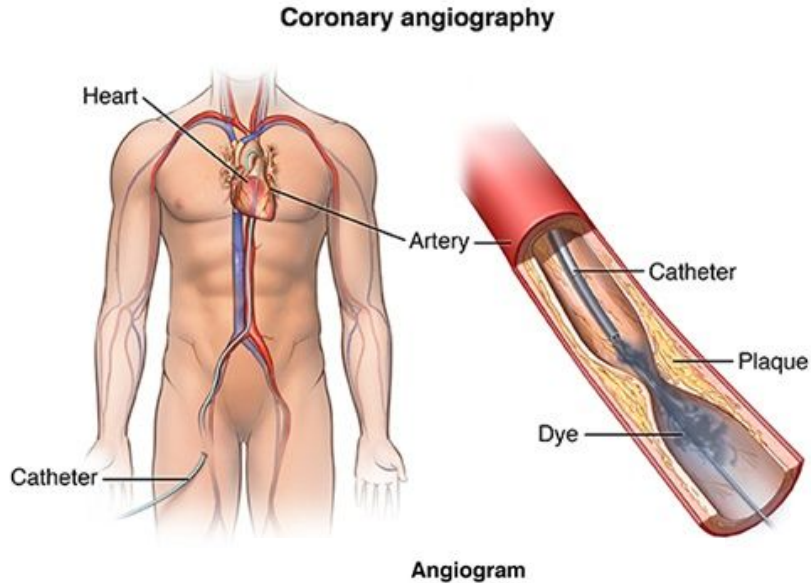
10.1056/NEJMra072149

*Pseudo-coloured
Dual Energy
Contrast CT*

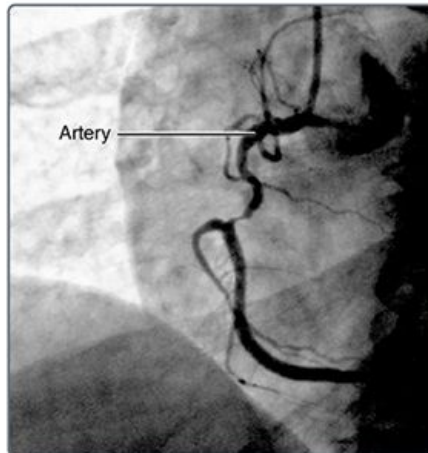
Clínica Universidad de Navarra,
Pamplona, Spain / Siemens
Healthineers



2D video: Fluoroscopy



Angiogram



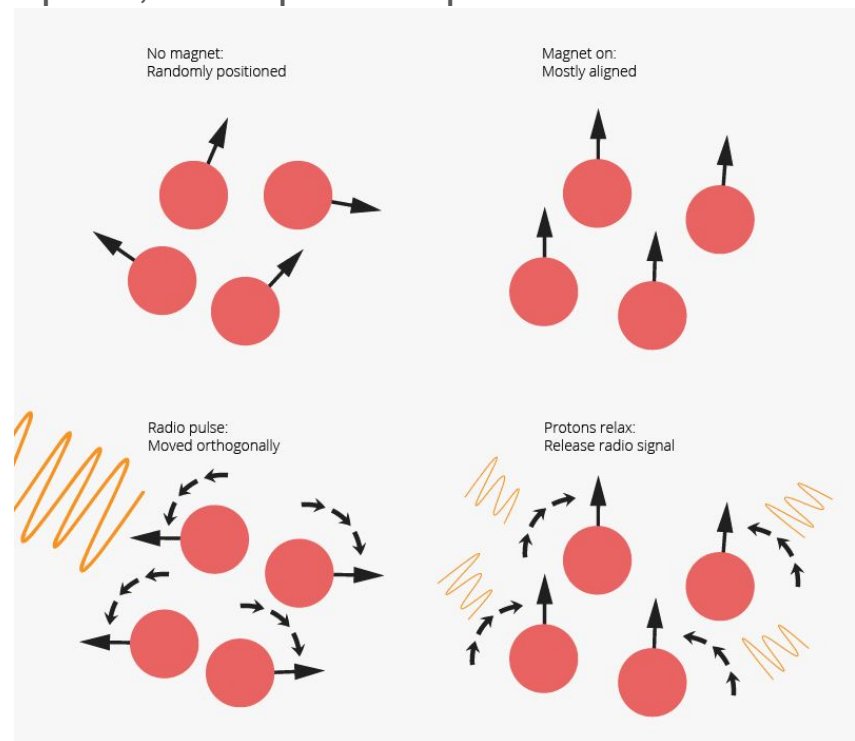
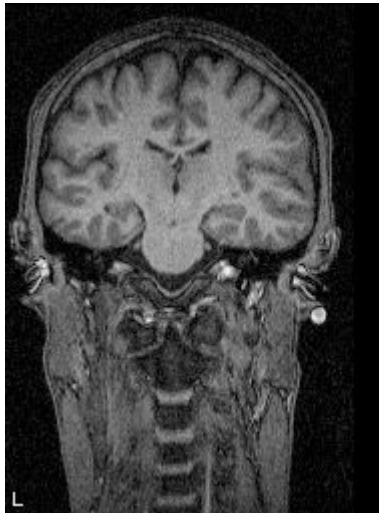
<https://www.hopkinsmedicine.org/health/treatment-tests-and-therapies/cardiac-catheterization>

- **X-ray** collected in a **time-series** with contrast medium used to guide procedures or evaluate change over time (angio).
- **Pro**: real-time imaging, widely available, relatively cheap
- **Con**: more expensive and higher radiation dose than X-ray alone
- **Data**: Series of 2D grayscale (3D tensor): DICOM

3D imaging: Magnetic Resonance Imaging (MRI)

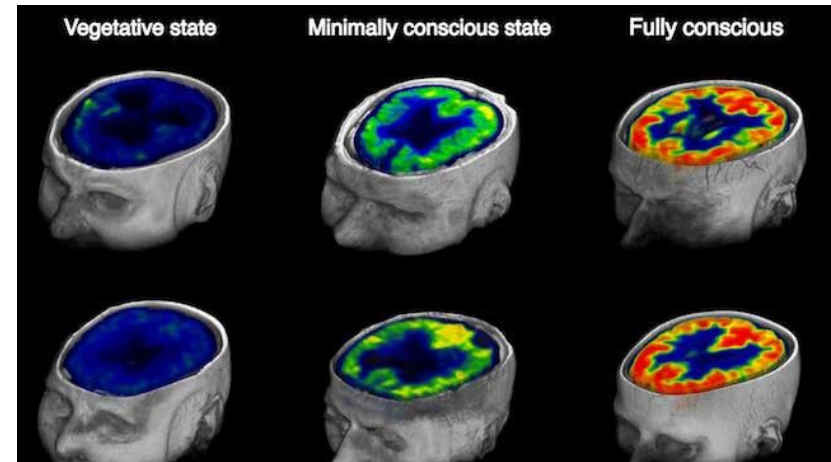
- 3D images constructed from **radiofrequency pulse** perturbation of body atoms (with a magnetic moment protons>neutrons) aligned by strong **magnetic field** (with or without contrast). Can be optimised for blood flow (fMRI)
- **Pro:** detailed multiplanar/3D imaging without contrast, better depiction of soft-tissue than CT, no radiation, painless
- **Con:** Expensive, noisy, lots of required space, susceptible to patient movement => can require sedation.
- **Data:** 3D grayscale tensor; 2D grayscale slices; 4D timeseries;

DICOM

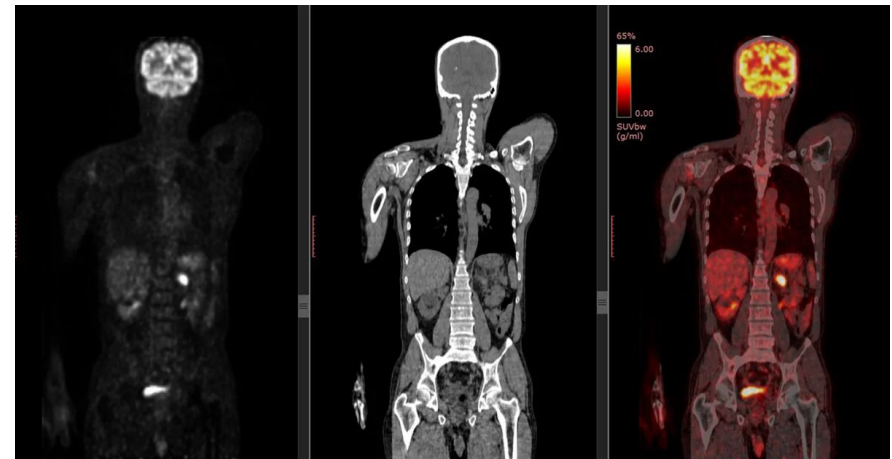


4D imaging: Positron Emission Tomography (PET)

- Time-series of detected **positrons** from radiolabelled fludeoxyglucose or O-15 to detect tissue/lesions with high metabolic activity
- **Pro:** measures function, painless
- **Con:** poor anatomy resolution (combine with CT/MRI), very expensive, radioactive tracer
- **Data:** 4D tensor DICOM (5D colour PET-CT/MRI or 3D fixed time-point).
- SPECT and fMRI also offer dynamic functional imaging options

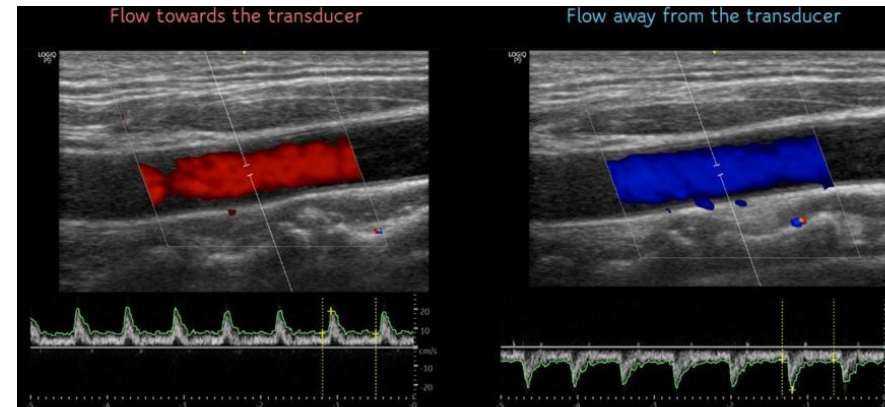
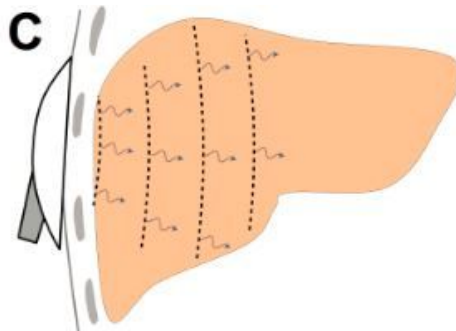
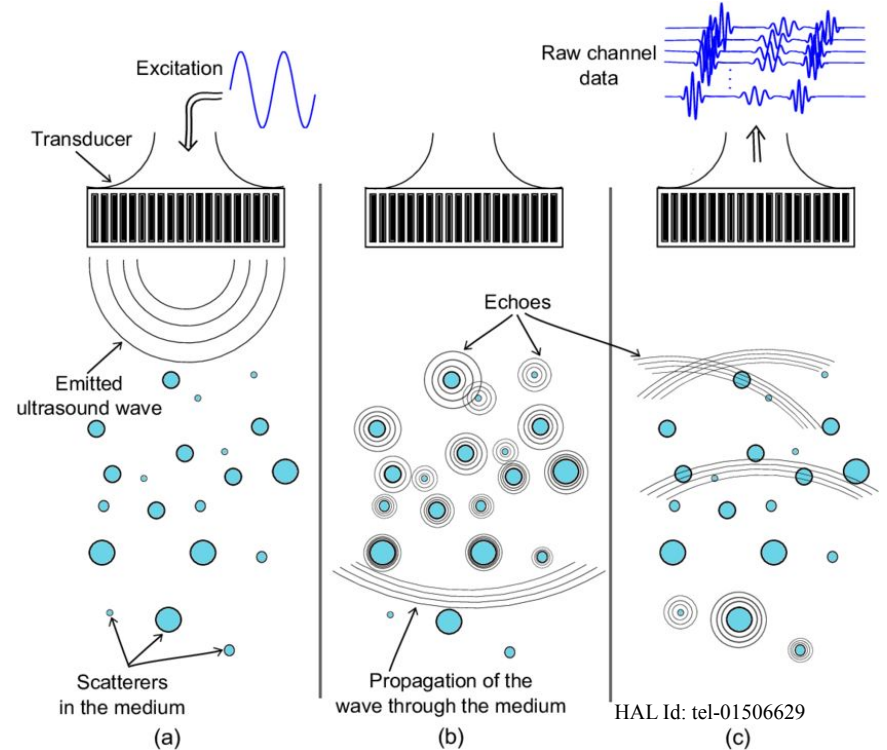


<https://sciencebasedmedicine.org/pet-scans-predict-coma-outcome/>



Many formats: Ultrasound

- Uses **sound waves** and echo pattern to image internal structures (soft tissue/organ/vessels)
- **Pro:** real-time imaging, no radiation, portable
- **Con:** operator skill dependent, patient anatomy, more expensive than X-ray
- **Many types:** *elastography, doppler, triplex, transvaginal, endoscopic*
- **Data type:** be rendered as 2D, 2D-slices, 3D or 4D! DICOM



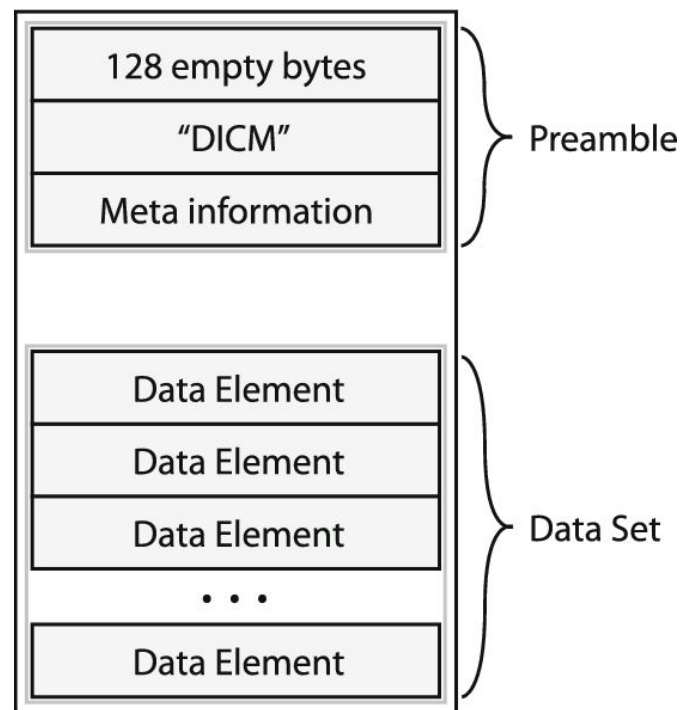
Overview of medical image data

- Point measure (1D - single value): optical density/turbidity/fluorescence
- Project/Planar imaging (2D matrix of pixels): X-ray
- Tomographic/Multislice Imaging (3D tensor of pixels): a series of images representing slices through a volume: CT
- 3-dimensional/Volume (3D tensor of voxels): MRI
- Dynamic Series (4D tensor of voxels): fMRI/PET-CT/MRI

- 45 year old male presents to Emergency with abdominal pain: 100-1000s of GB of imaging data in a variety of different imaging formats/modalities (mostly as DICOM files)

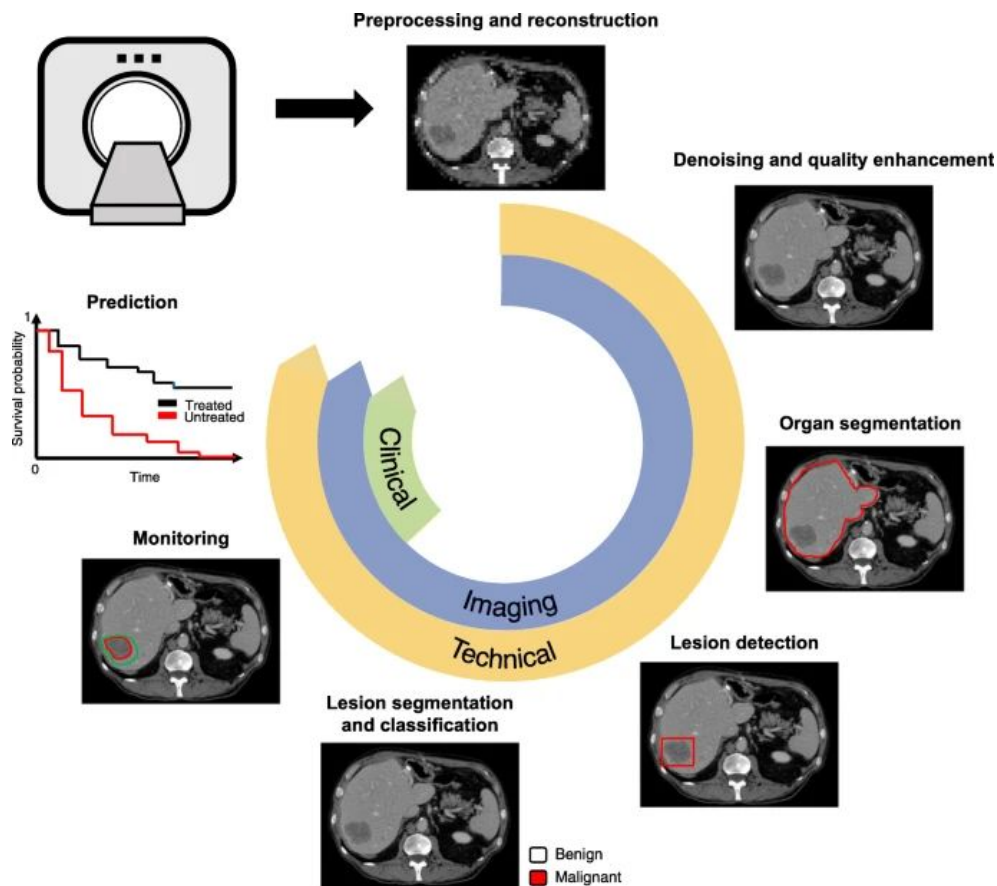
DICOM Data Format

- Standardised file format split into preamble and image information
- Preamble contains key metadata:
 - **Pixel depth:** number of bits encoding each pixel/voxel (e.g., 8/32/64-bits)
 - **Samples per Pixel/Number of Channels:** number of values encoding each pixel/voxel e.g., monochrome = 1 channel, colour = 3 channels (R,G,B)
 - **Spatial resolution:** size of smallest discernible feature
 - **Other Embedded Metadata:** capture frequency/contrast/capture model/patient size (important for normalising across your data)
- Image data: image matrix/tensors (nominally integer only although scaling is possible)
- Many other proprietary formats exist but DICOM is mostly successful as a standard



What kind of analysis task would we want to do using these images?

Lots of things we may want to do using medical images



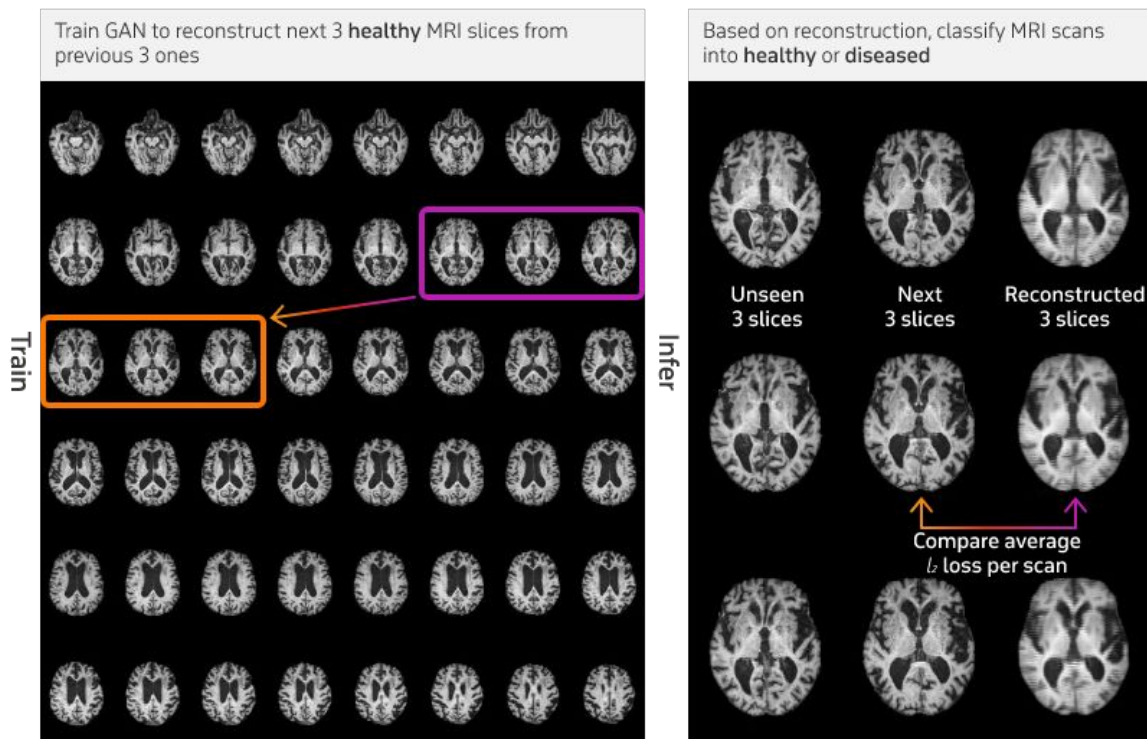
- **Image preprocessing:** super resolution, densification
- **Registration:** align spatial coordinates of images into 1 common system (PET + MRI)
- **Detection:** highlighting specific elements (anomaly/lesion)
- **Segmentation:** delineation or volume extraction of target object (organ/lesion)
- **Classification:** distinguish classes of objects (benign vs malignant lesion)
- **Monitoring:** longitudinal measurement of lesion (% of organ impacted by lesion)
- **Prediction:** predicting outcome based on image (success of chemotherapy)

Medical image data is intrinsically challenging

- Lots of modalities with very large image size (but small datasets)
- Non-standardised acquisition (varied devices, set-ups etc)
- Disease patterns in images are very long-tailed
- Labels are sparse and noisy
- Samples are heterogeneous and imbalance
- Subjectivity in growth-truth
- Can be impossible to de-identify e.g., facial scans

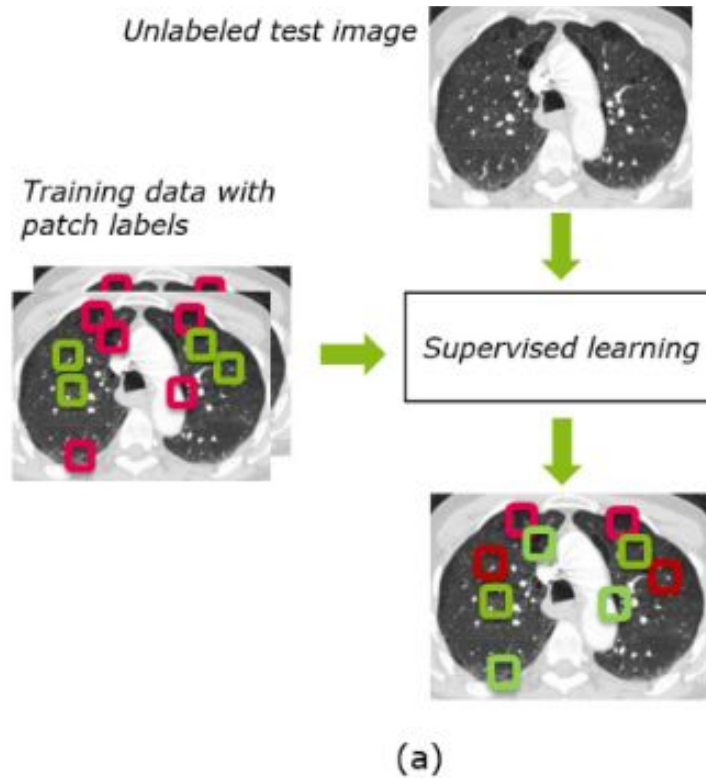
Unsupervised learning

Example of unsupervised medical anomaly detection



Data source: bmcbioinformatics.biomedcentral.com—MADGAN: unsupervised medical anomaly detection GAN using multiple adjacent brain MRI slice reconstruction, 2021

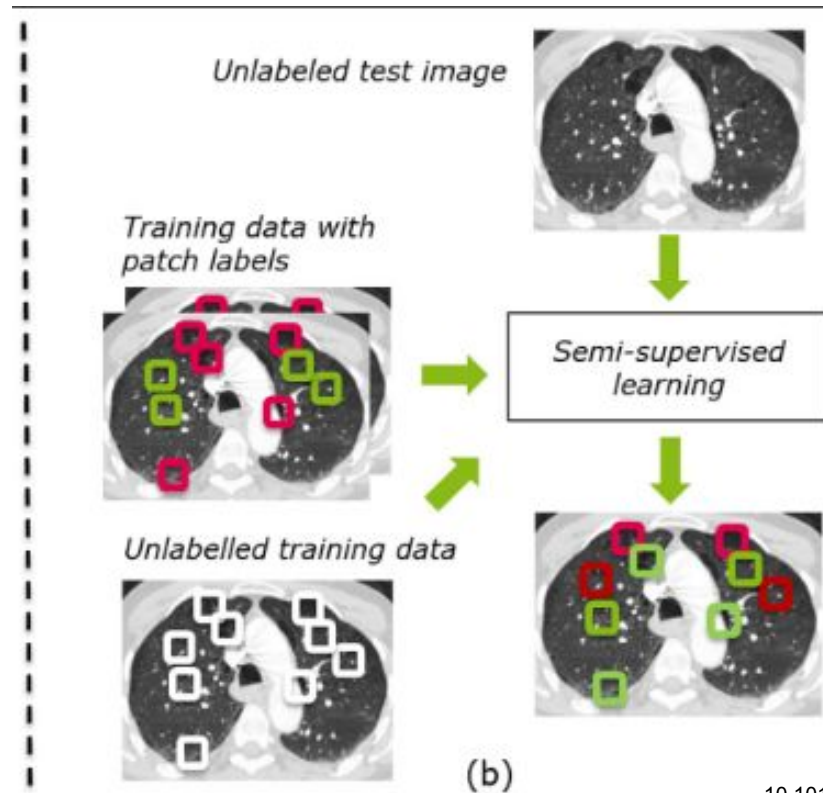
Label challenges require alternative training paradigms



10.1016/j.media.2019.03.009

Supervised learning

Label challenges require alternative training paradigms

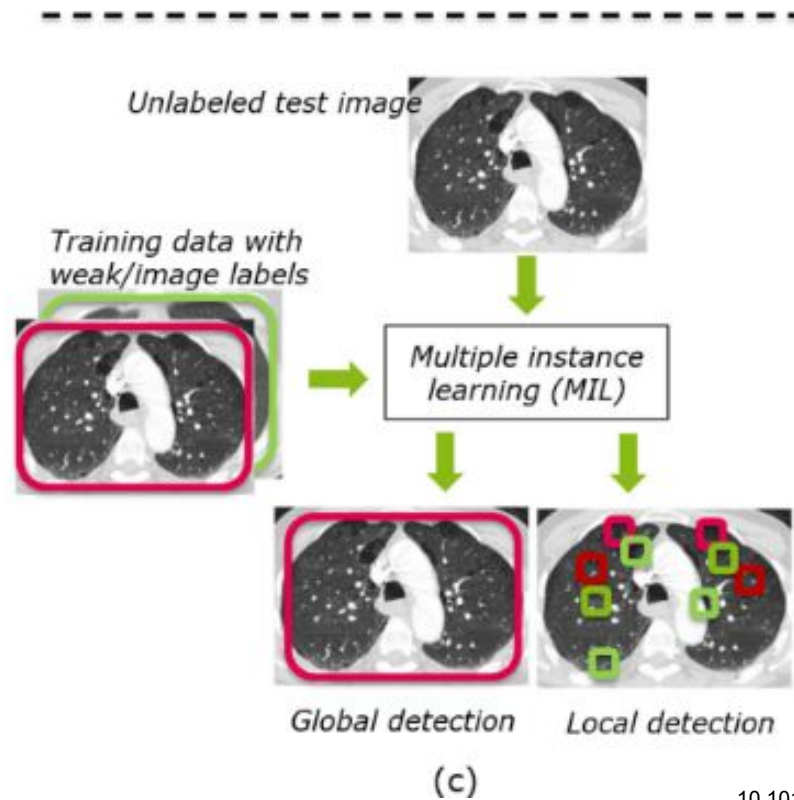


10.1016/j.media.2019.03.009

Supervised learning

Semi-supervised learning

Label challenges require alternative training paradigms



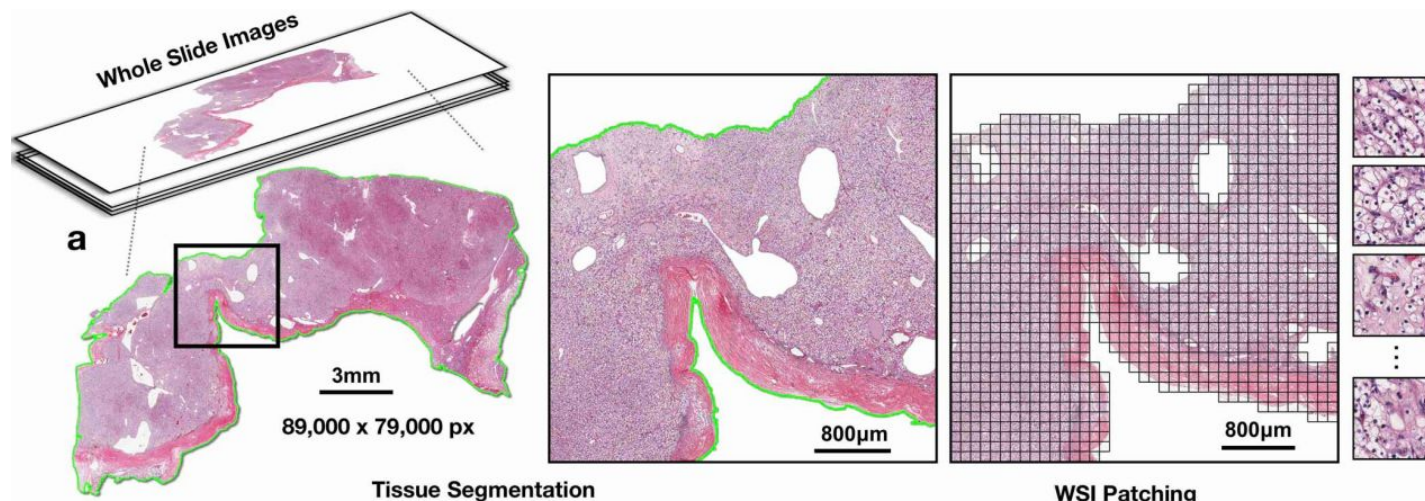
10.1016/j.media.2019.03.009

Supervised learning

Semi-supervised learning

Multiple Instance Learning

Label challenges require alternative training paradigms



Multi-Instance Learning

Whole Pathology Image

Normal

Cancerous

Image is labelled as cancerous because of one part

Broken up into patches ("instances")

Entire "bag" of "instances" still labelled as cancerous

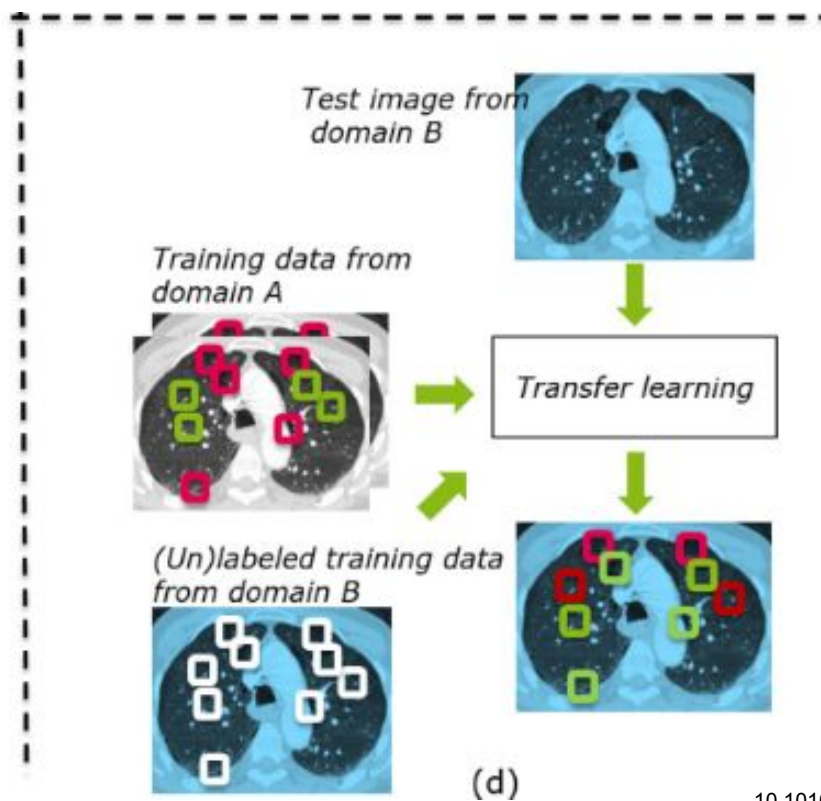
But now we can learn features based on the instances

Supervised learning

Semi-supervised learning

Multiple Instance Learning

Label challenges require alternative training paradigms



10.1016/j.media.2019.03.009

Supervised learning

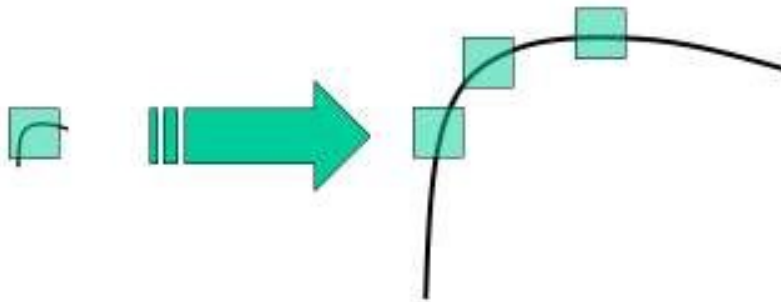
Semi-supervised learning

Multiple Instance Learning

Transfer Learning

Traditional Computer Vision

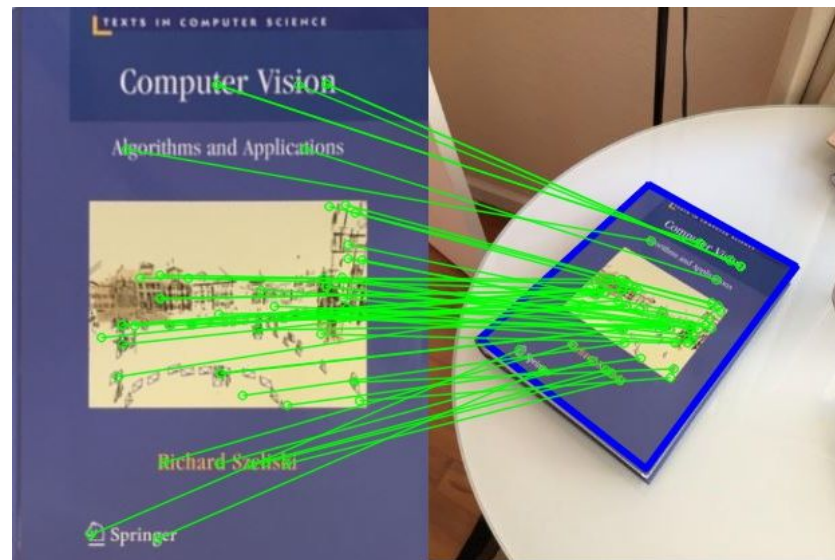
- Thresholding: pixels \geq certain set to max
- Edge detection: changes in brightness
- Segmenting: grouping thresholded areas enclosed by edges
- Curve detection: edges adjacent to one another
- Optical flow: detection of movement



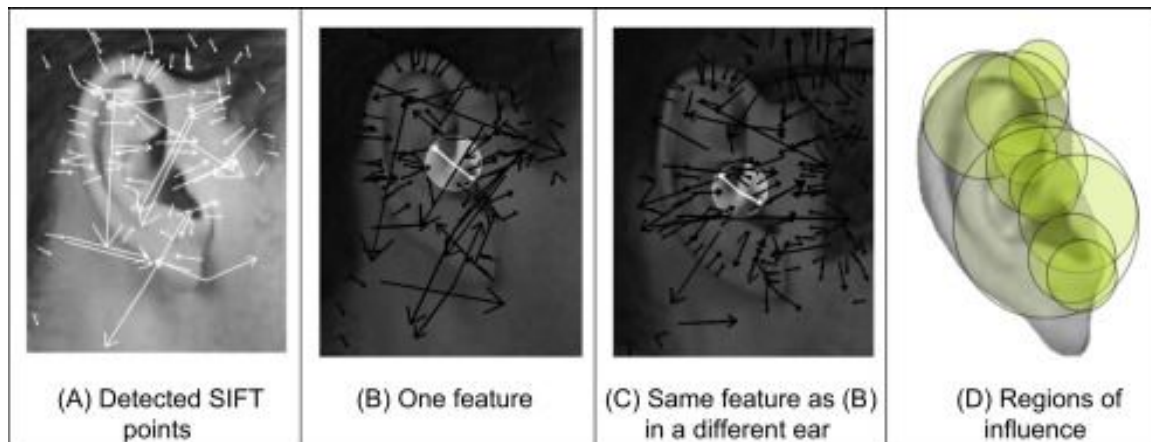
<https://pyimagesearch.com/2021/04/28/open-cv-thresholding-cv2-threshold/>

More complex traditional methods

- Scale-Invariant Feature Transform (SIFT)
- Speeded Up Robust Features (SURF)
- BUT, manual feature engineering is difficult, time-consuming, and often doesn't generalise well



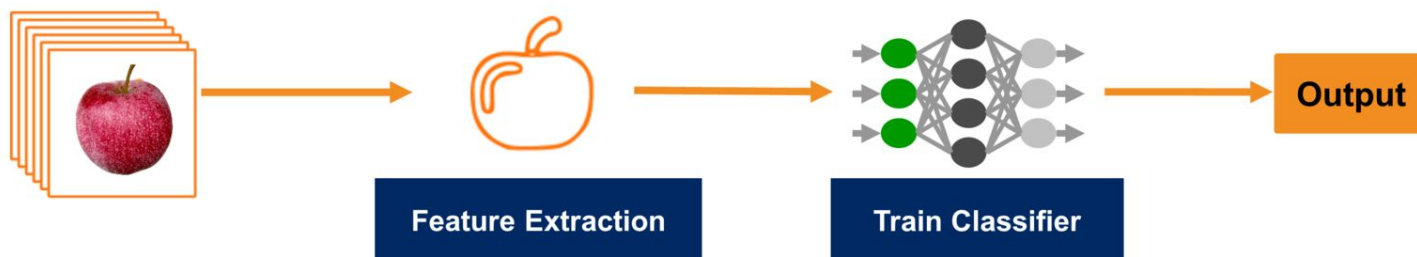
<https://stackoverflow.com/questions/51693427/sift-object-matching-in-python>



How do we do analyse images without
feature engineering?

Deep Learning discovers feature representations

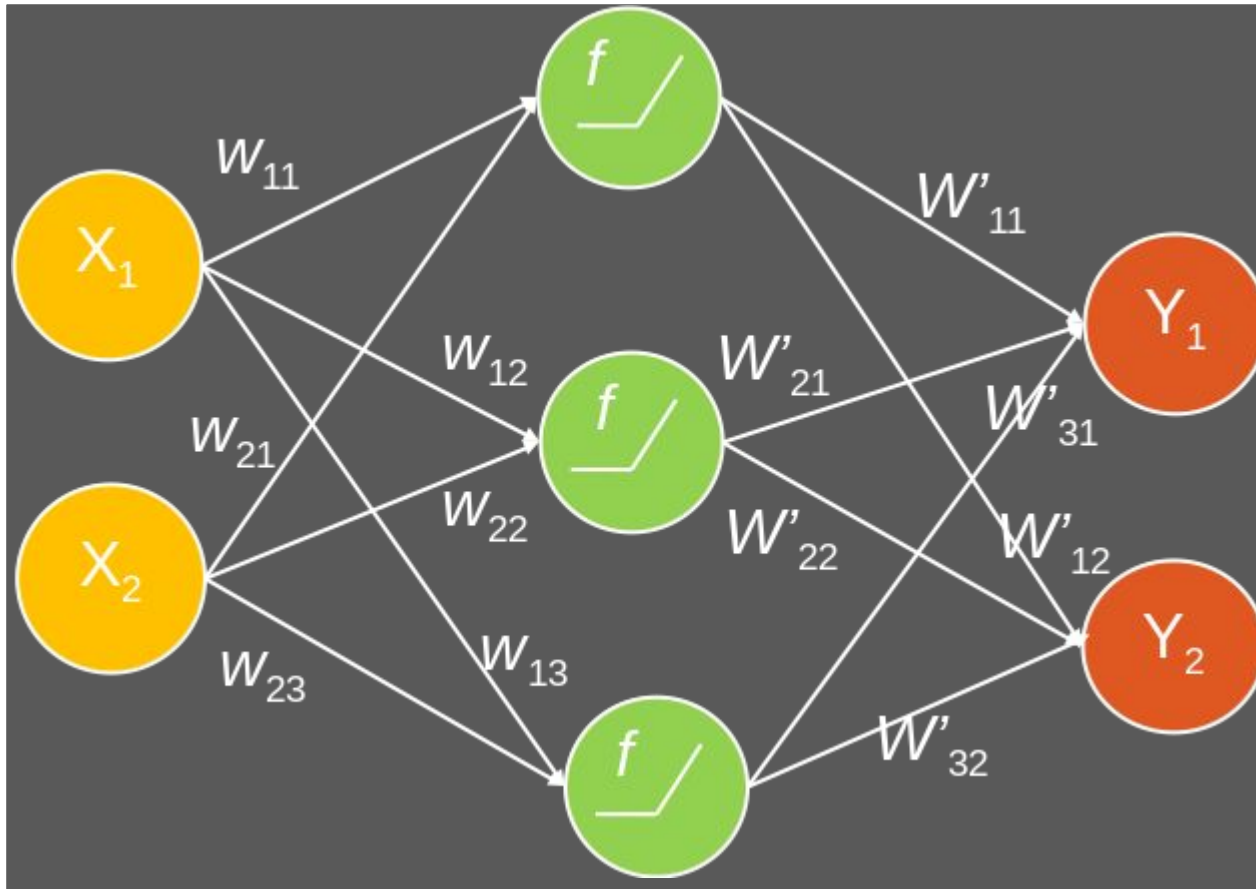
Classic Machine Learning



Deep Learning



Artificial Neural Network

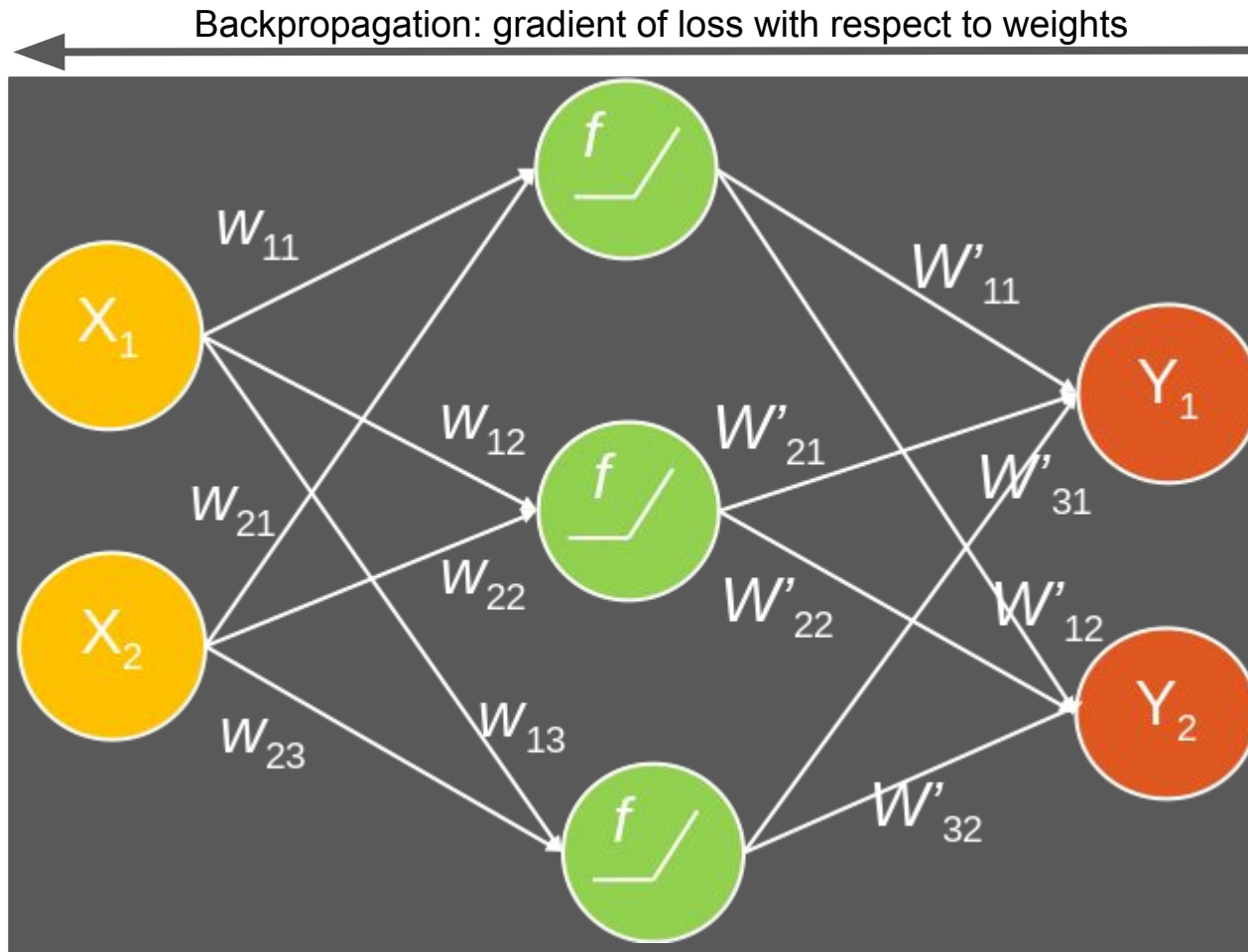


$$Y_1 = f(x_1 w_{11} + x_2 w_{21}) w'_{11} + f(x_1 w_{12} + x_2 w_{22}) w'_{21} + f(x_1 w_{13} + x_2 w_{23}) w'_{31}$$

$$Y_2 = f(x_1 w_{11} + x_2 w_{21}) w'_{12} + f(x_1 w_{12} + x_2 w_{22}) w'_{22} + f(x_1 w_{13} + x_2 w_{23}) w'_{32}$$

Slide by Dr. Maria
Valdes Hernandez

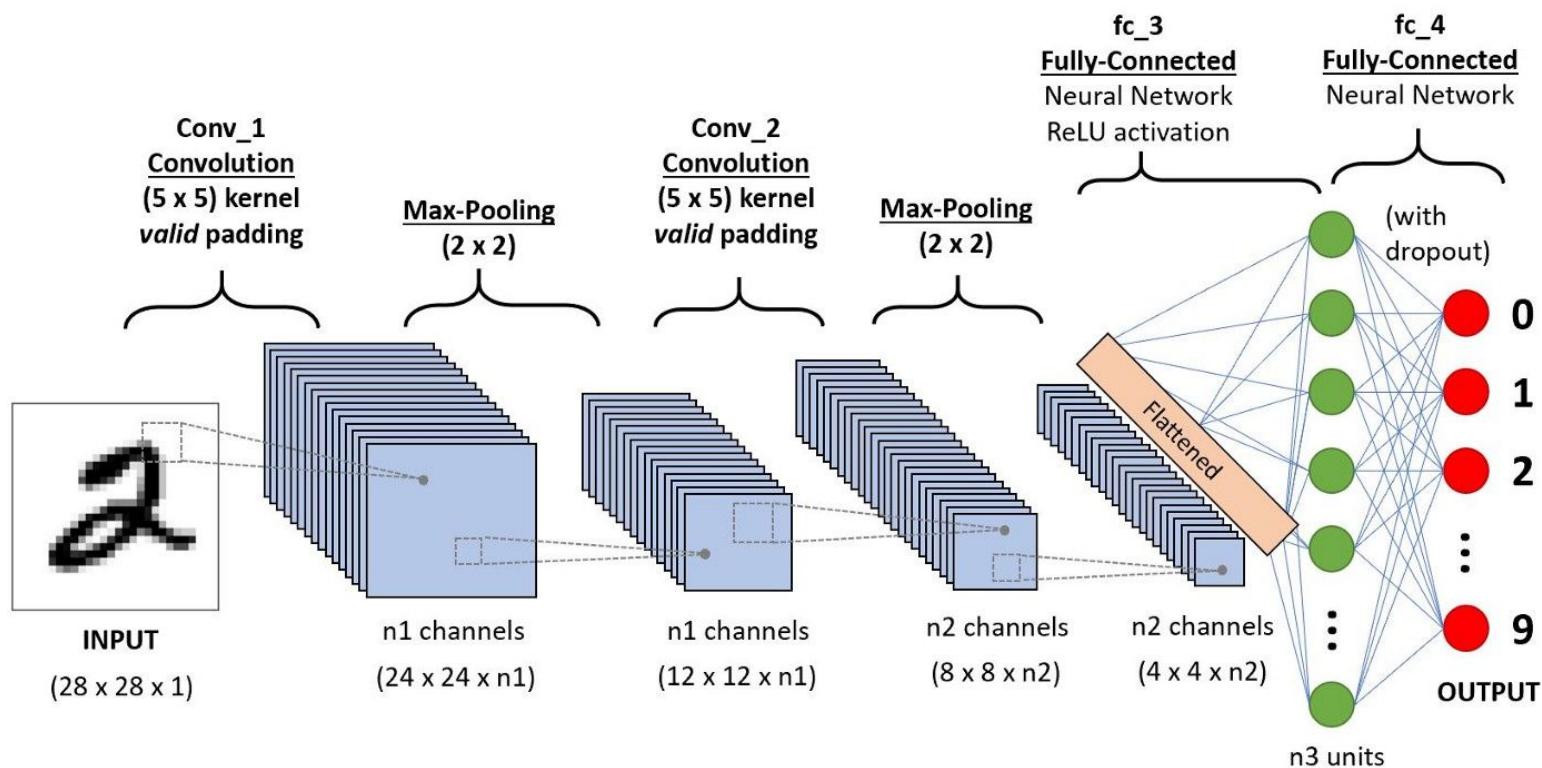
Artificial Neural Network



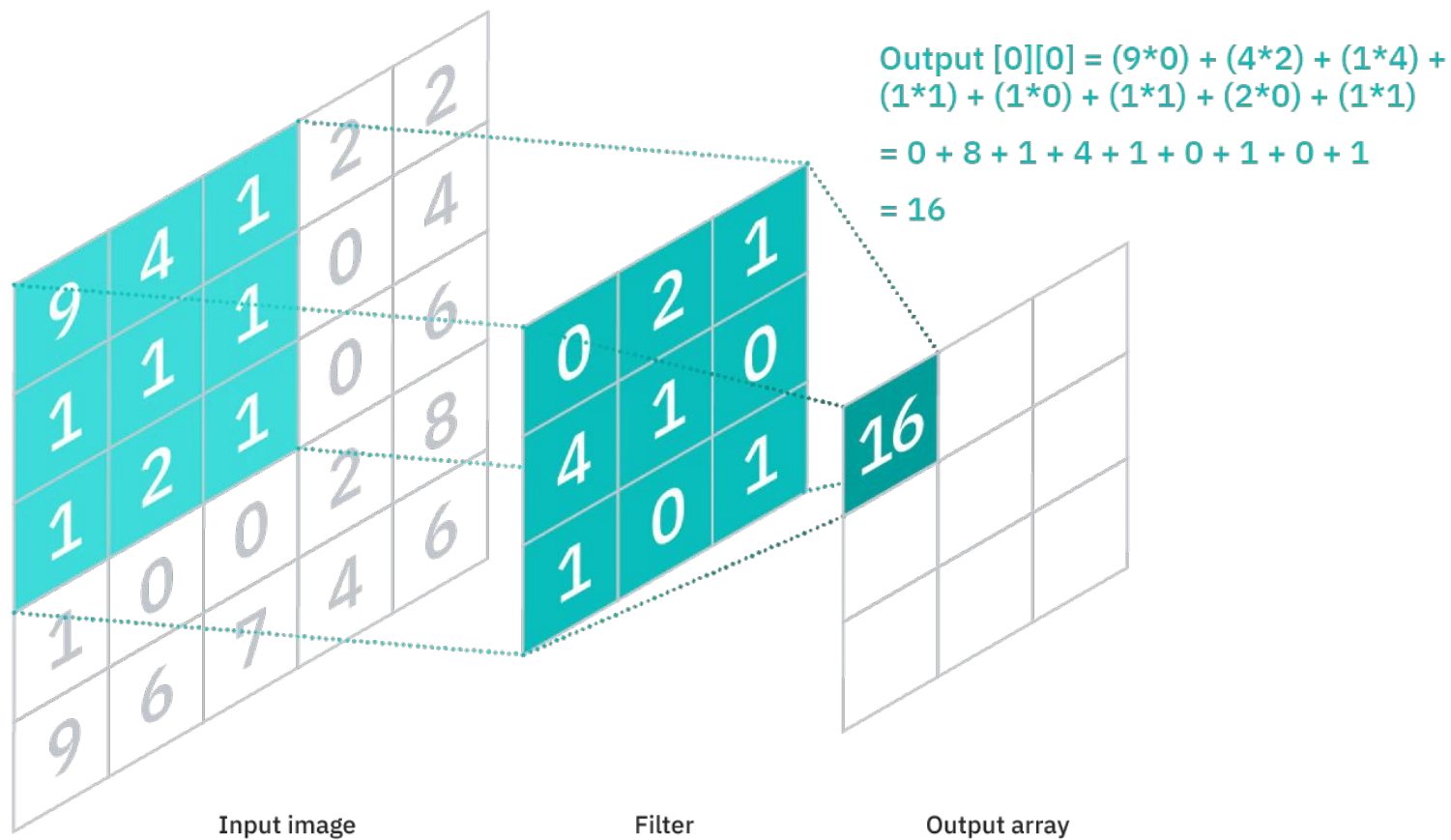
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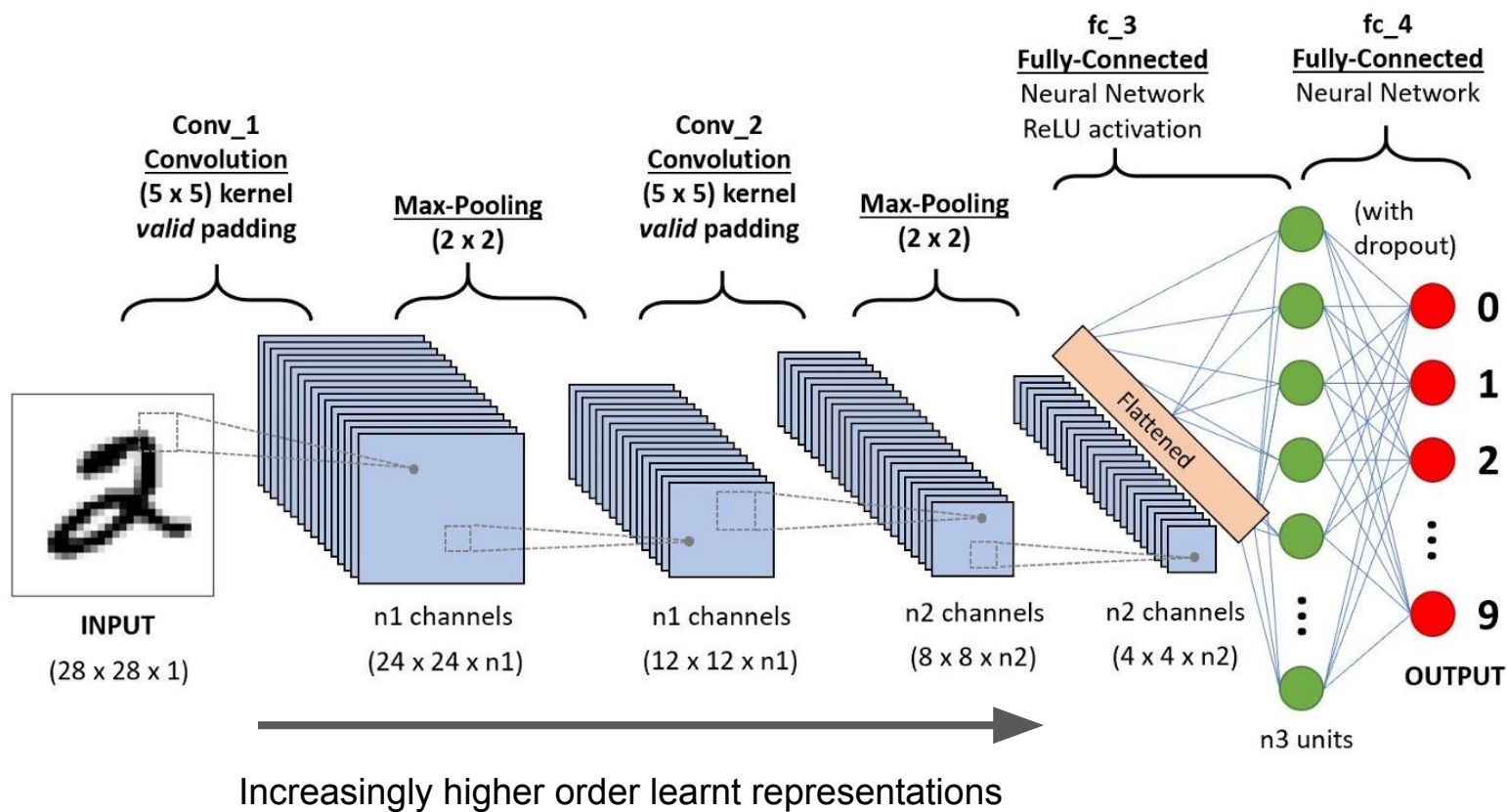
Convolutions capture spatial relations



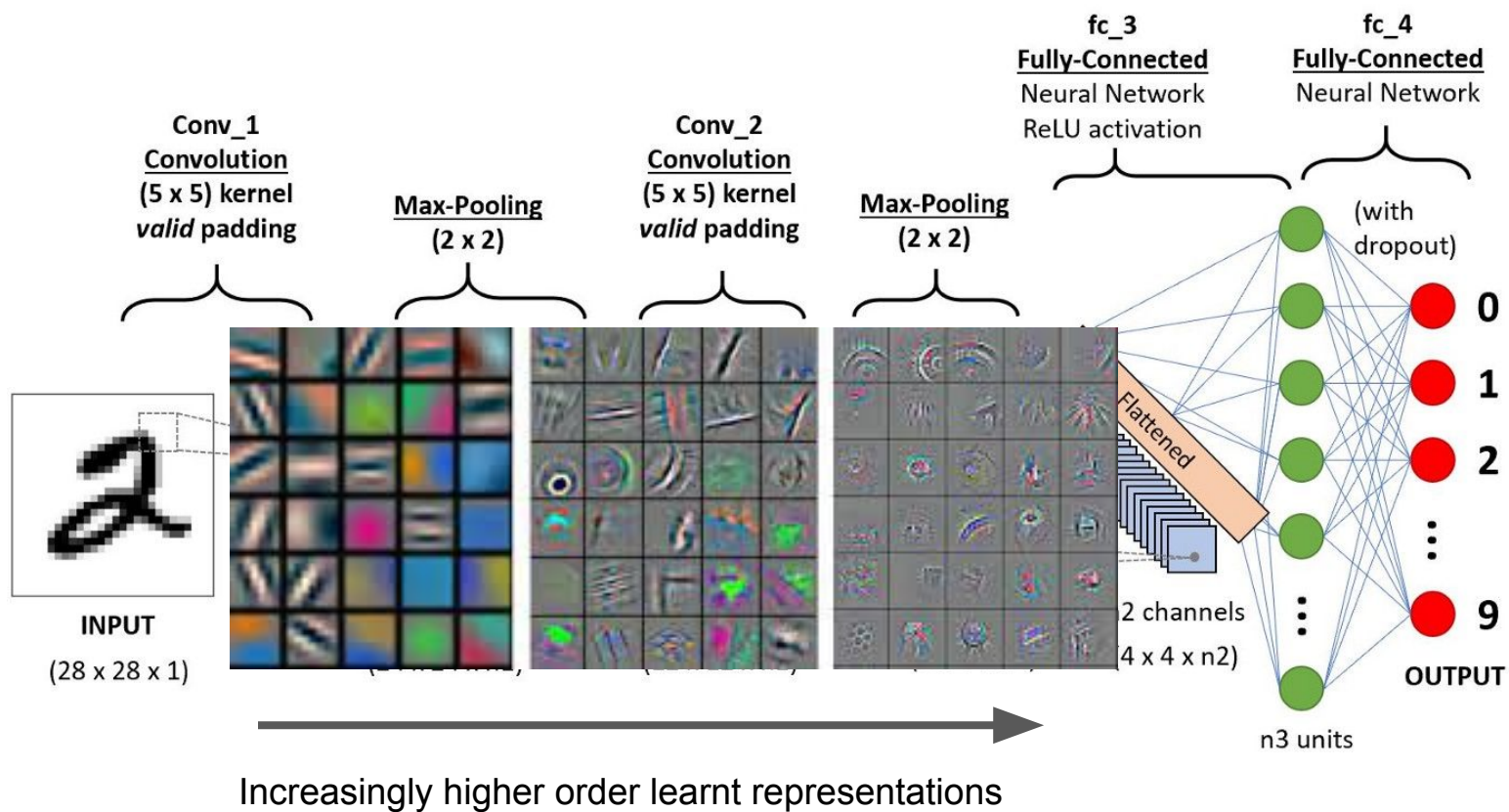
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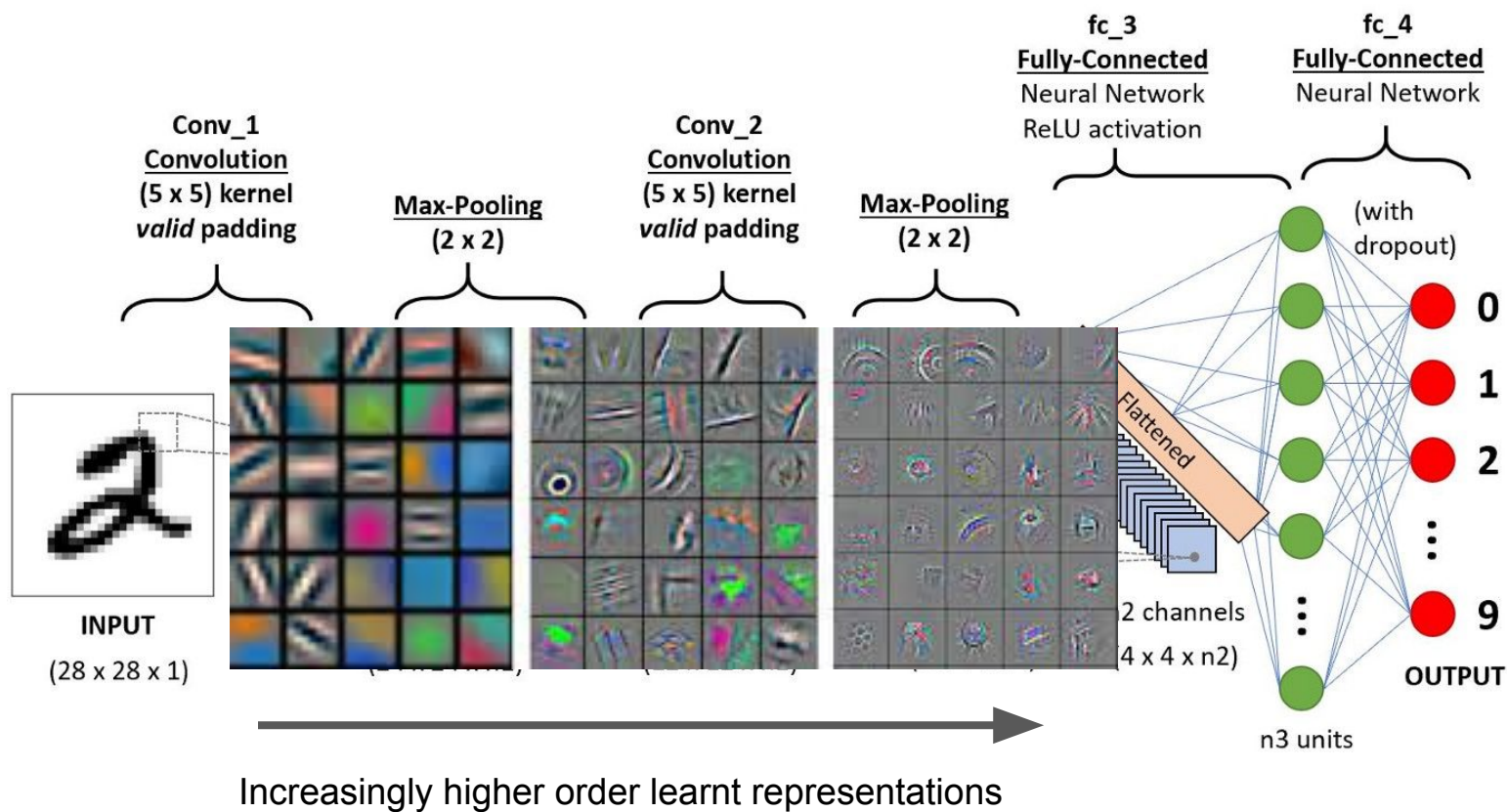
Convolutions capture spatial relations



Convolutions capture spatial relations



Convolutions capture spatial relations

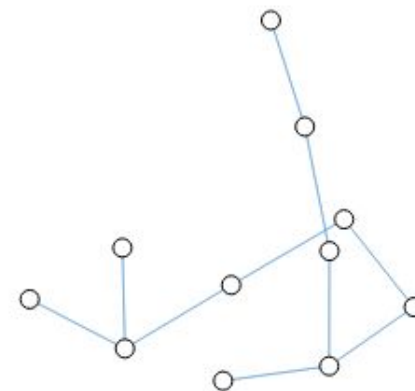
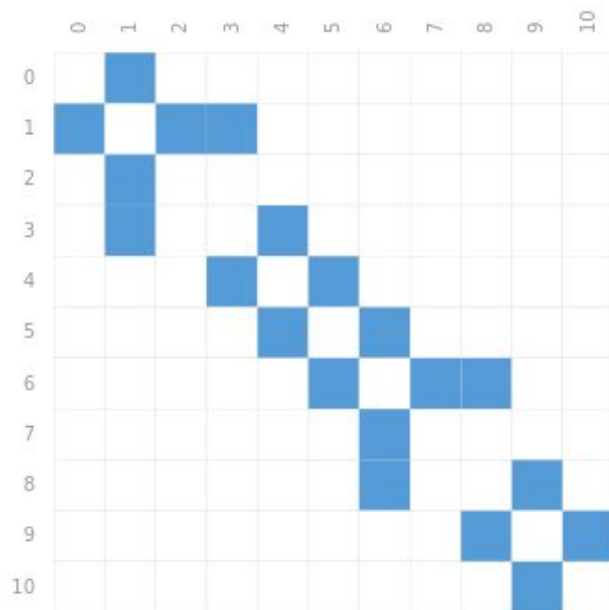


- Can use convolutions in more complex architectures (attention, resnets, transformers etc).

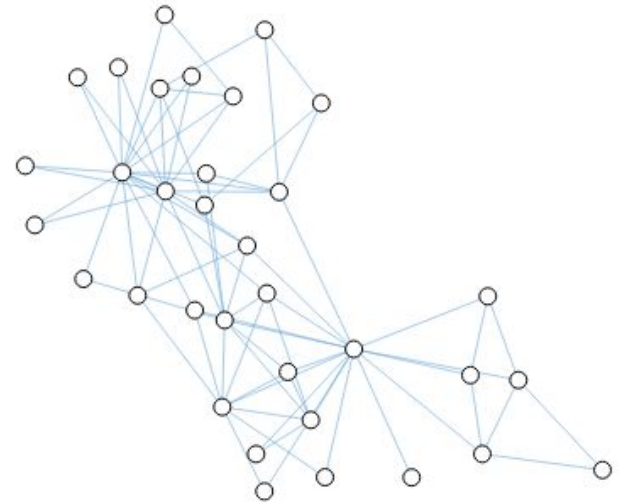
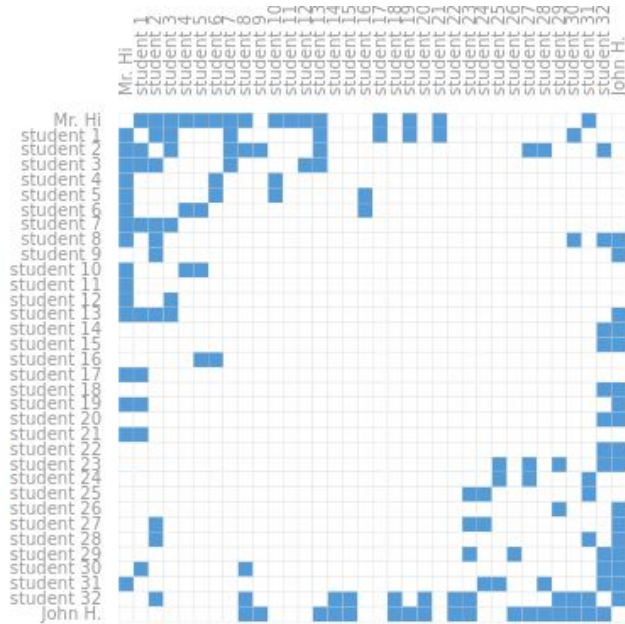
Aside: CNNs can be used for non-image spatial data



<https://distill.pub/2021/gnn-intro>



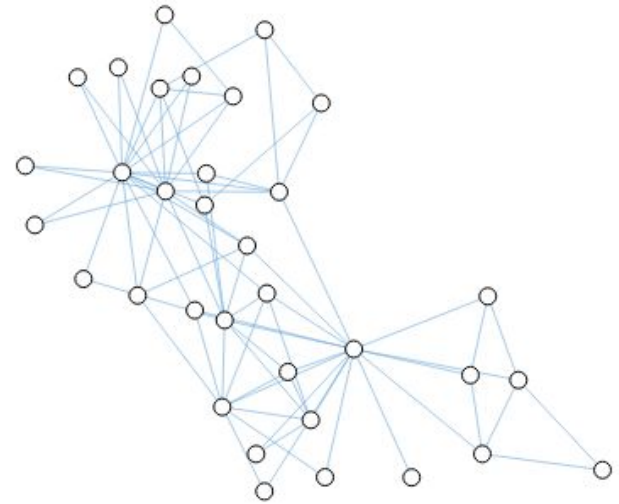
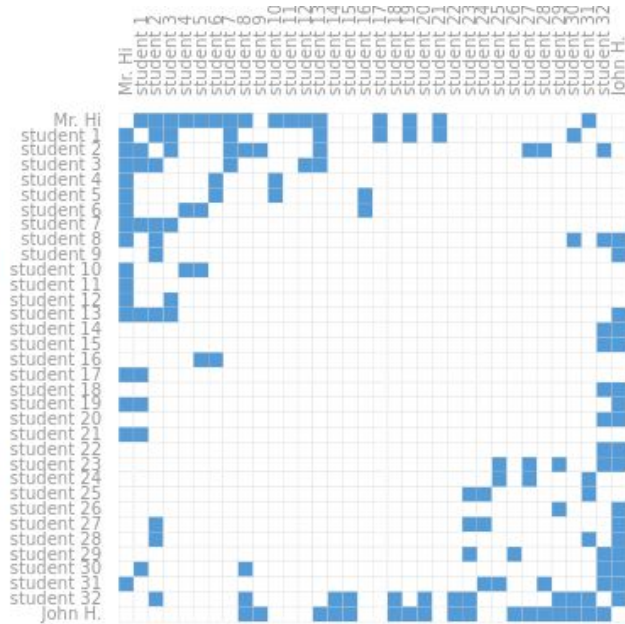
Aside: CNNs can be used for non-image spatial data



<https://distill.pub/2021/gnn-intro>

- Graph neural networks

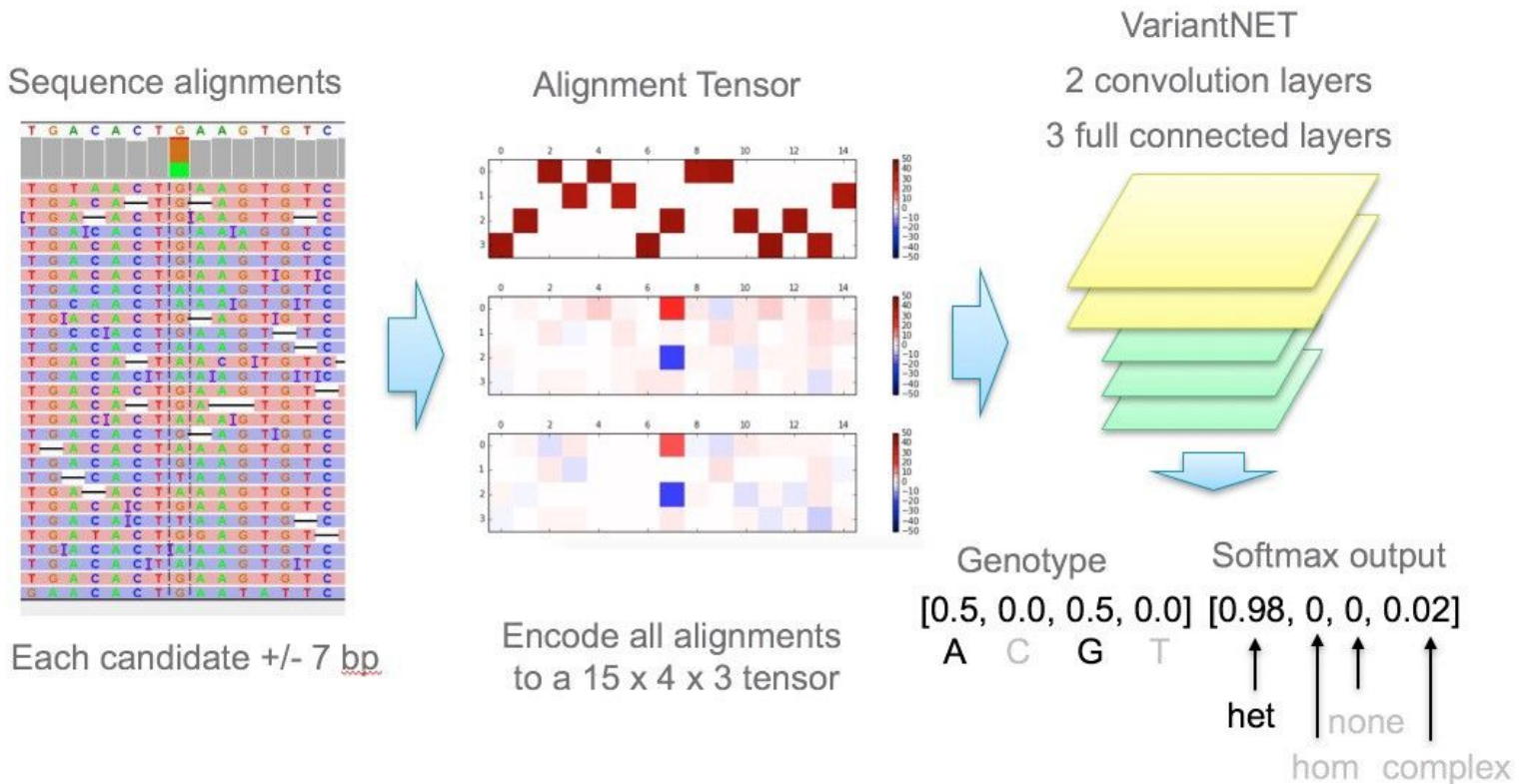
Aside: CNNs can be used for non-image spatial data



<https://distill.pub/2021/gnn-intro>

- Graph neural networks
- Text data (semantic networks)

Aside: CNNs can be used for non-image spatial data

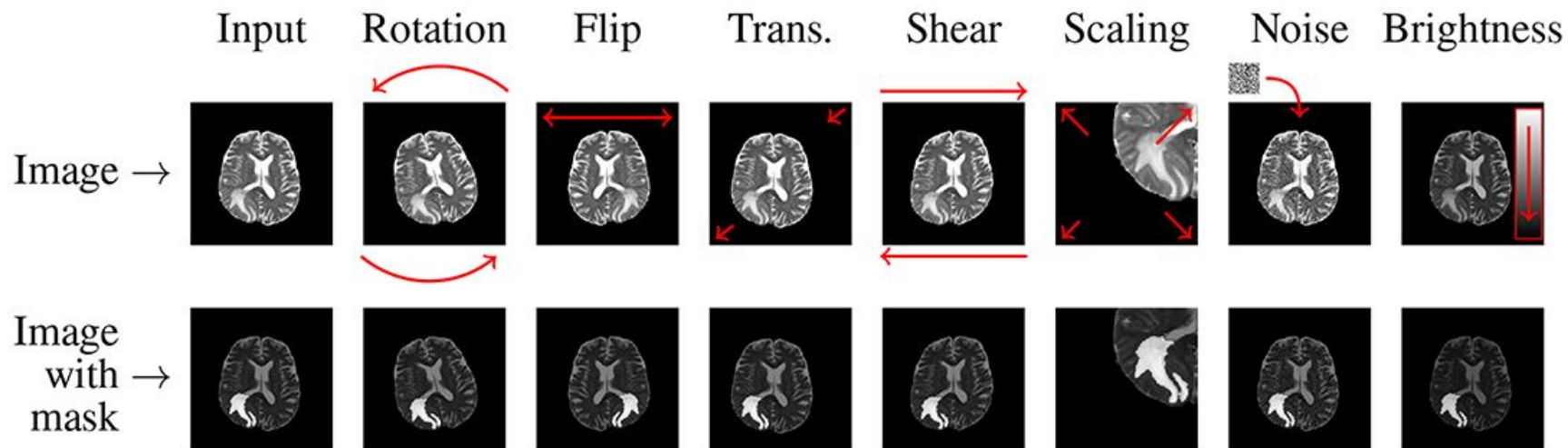


- Graph neural networks
- Text data (semantic networks)
- Mutation calling...

Didn't you say training data is hard to get?

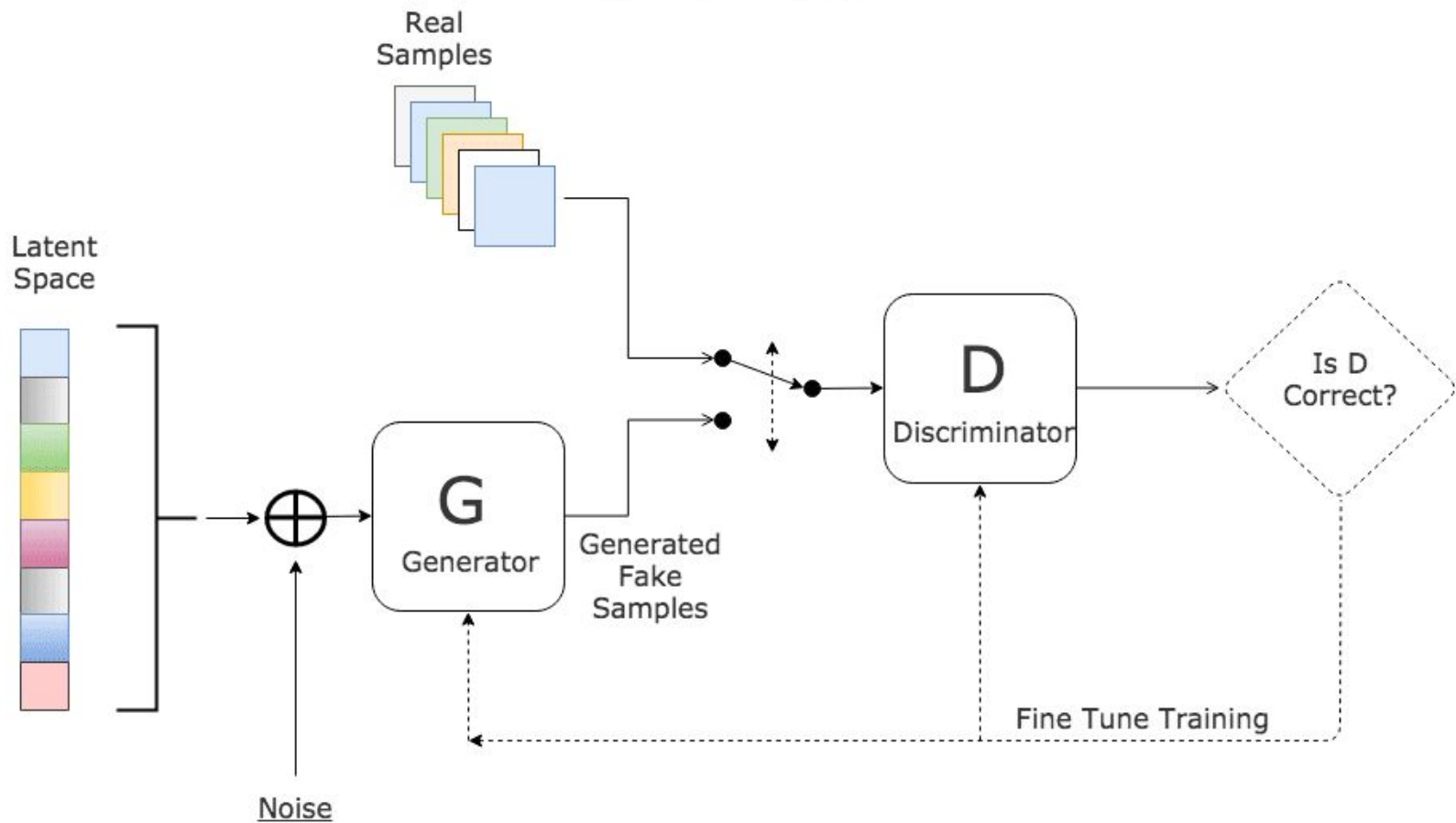
Making your data go further: augmentation

- Apply affine and pixel transformations to your data -> more training samples



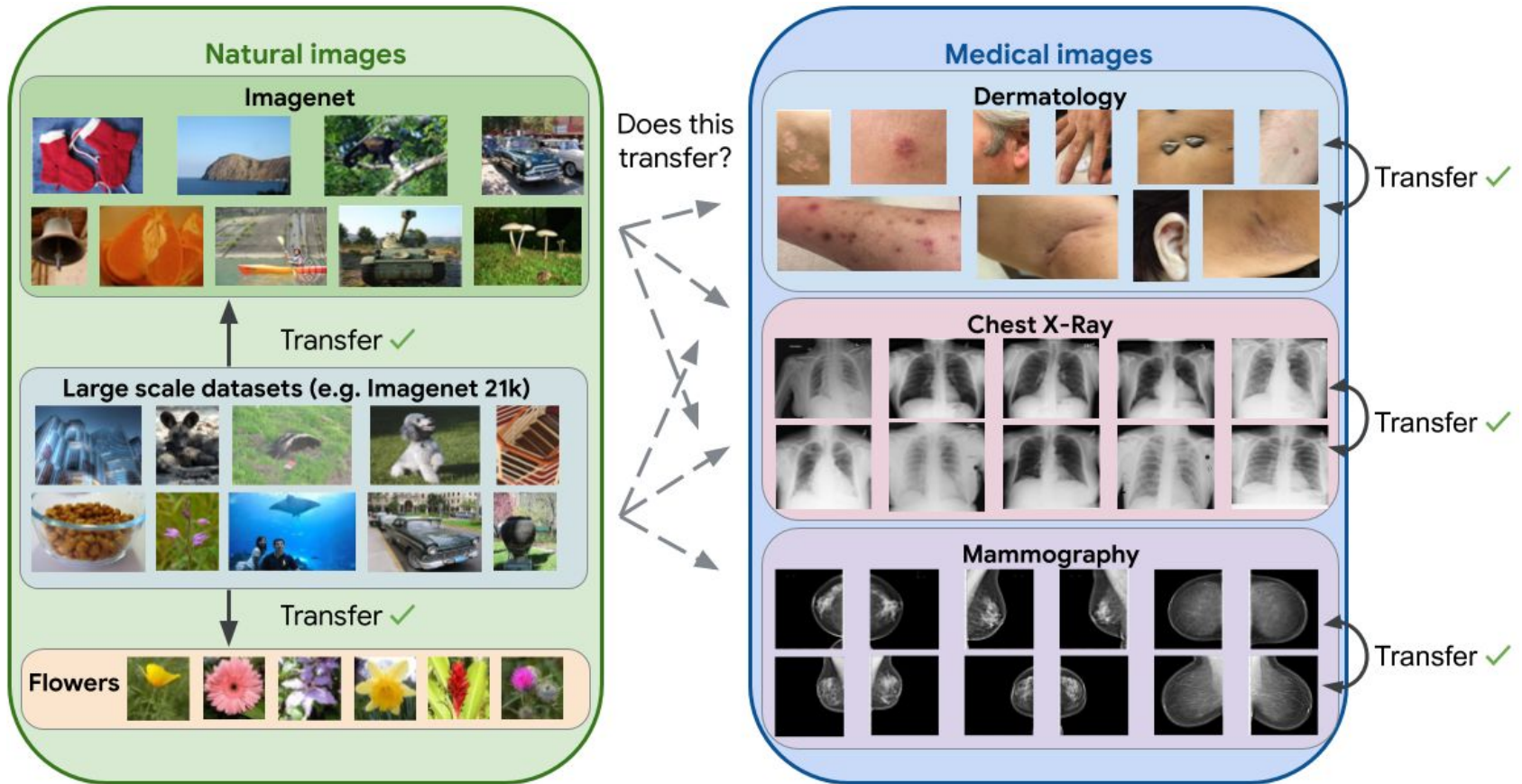
Feels a bit like manual feature engineering,
can we automate this?

Yes! Generative Adversarial Network



Can we use different image data then tune?

Transfer learning

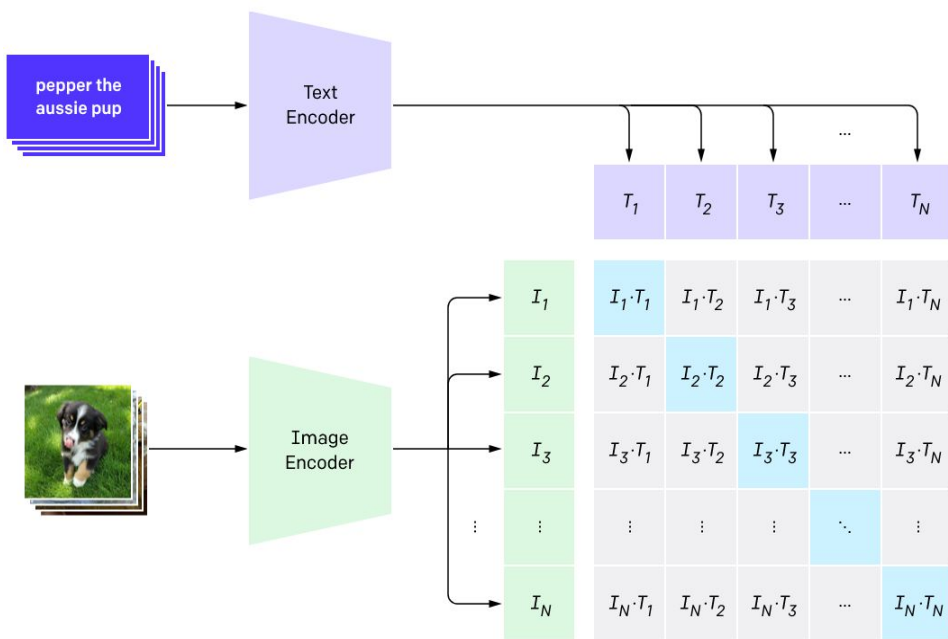


Can we make bad labels better?

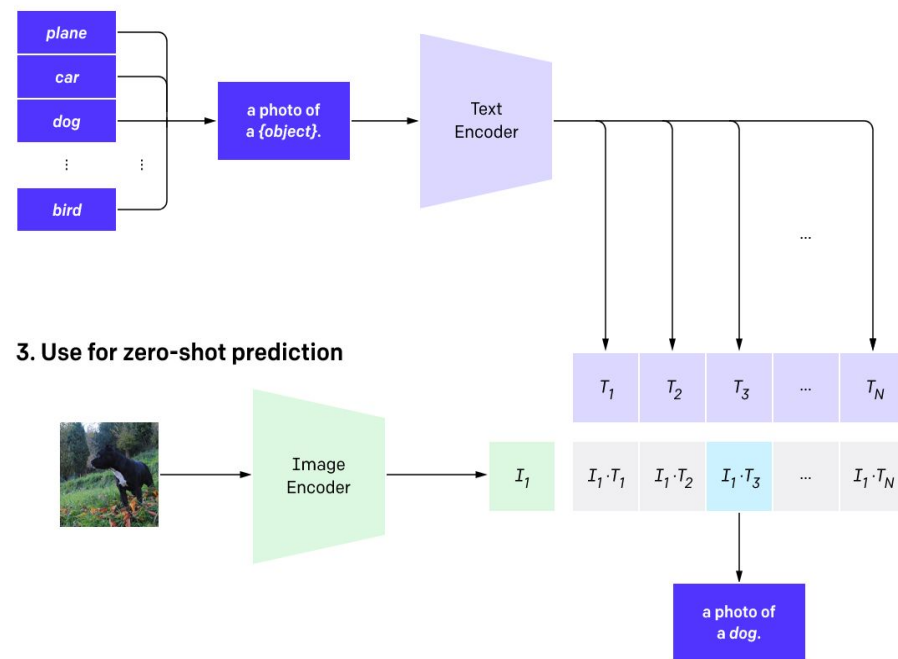
Bad text labels, bad images -> why not embed both?

- OpenAI's Contrastive Language-Image Pre-training (CLIP)
- Use 400 million images trawled from internet (with variable quality labels)
- Initial training: 30 days 592 GPUs -> \$1,000,000 equivalent cost

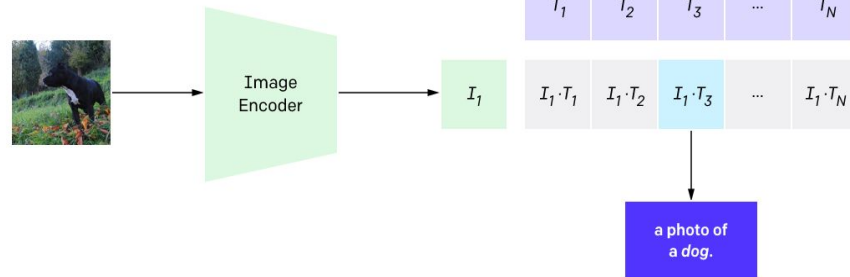
1. Contrastive pre-training



2. Create dataset classifier from label text

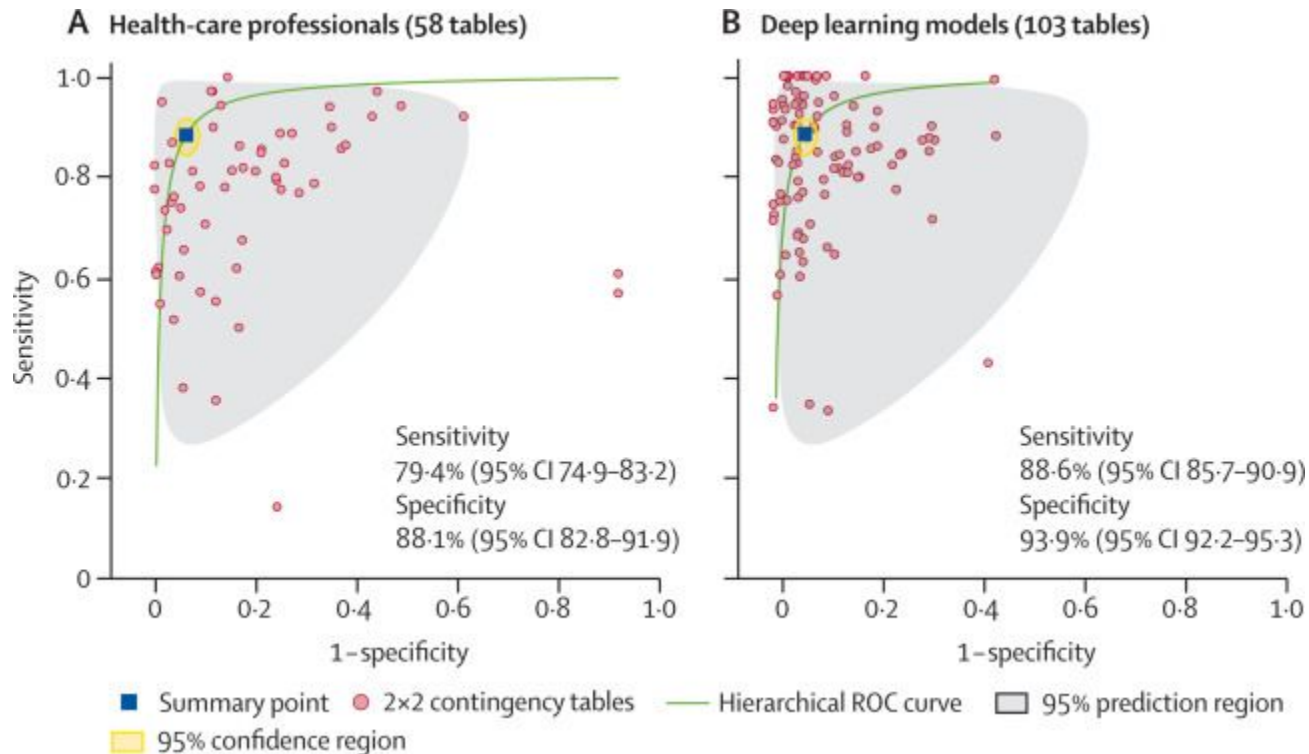


3. Use for zero-shot prediction

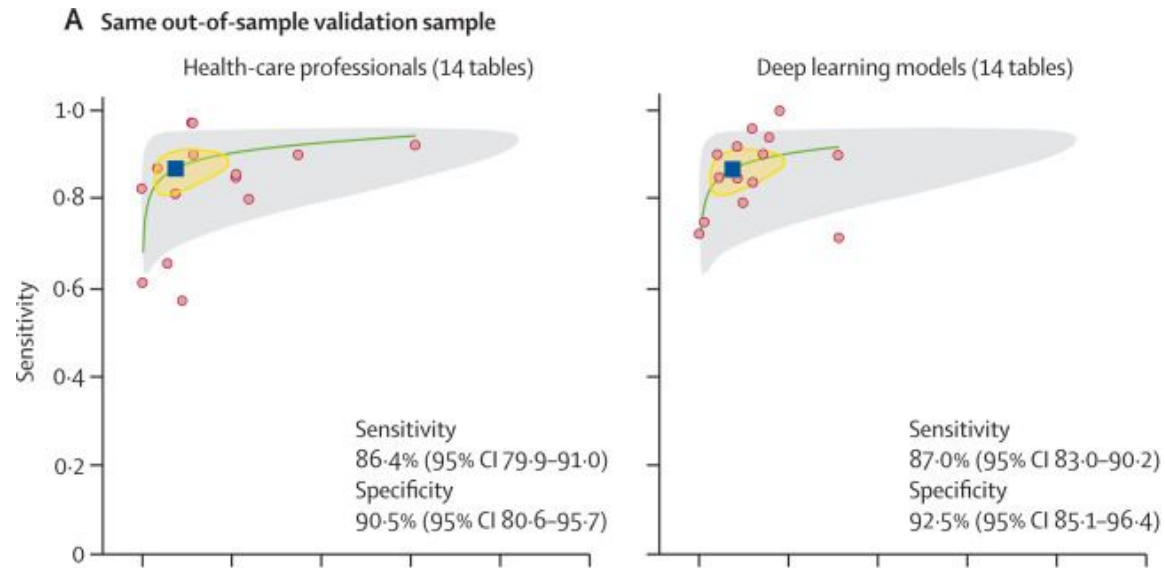


So, can we use these clinically?

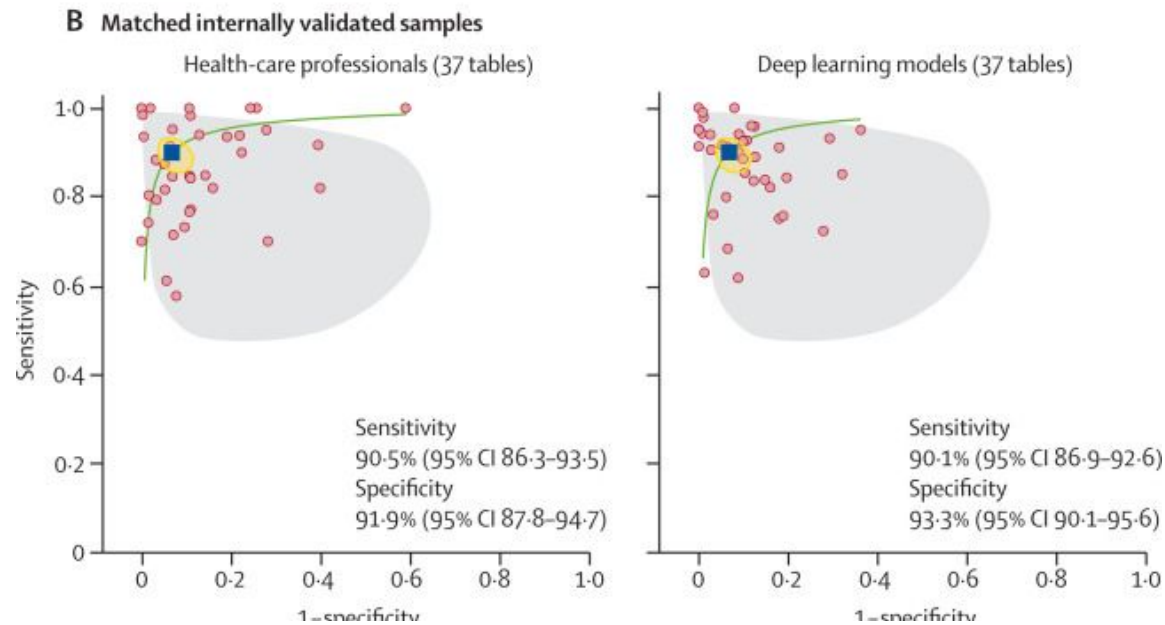
Outperforming humans is possible



Outperforming humans is possible



Outperforming humans is possible



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Great, so why don't we use these all the time?

Legal hurdles are daunting but important

- Commercial software for medical images is a medical device
- Regulated as such.
- Regulatory frameworks actively changing/developing
- Requires explanatory power (still a work-in-progress for deep learning)
- Requires acceptance by clinicians



Learning Overview

- Many types of medical imaging data and their respective formats
- DICOM file format is ubiquitous but complex
- Medical imaging data analysis involves many different questions
- Lots of different machine learning paradigms are used to handle challenges of medical image data
- Traditional computer vision approaches
- Deep learning enables learning features/representations
- Convolutions key to capturing spatial relationships
- Augmentation and generative models enable better training with limited data
- Transfer learning and joint-transformer models hugely expand training options
- Machine learning in medical image analysis is very promising but has several major hurdles to broad acceptance