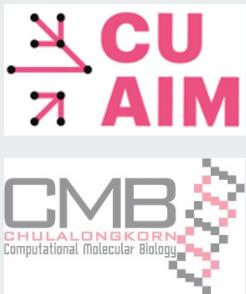


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# 3050571 Practical Clin Data Sci

## Session 13: Artificial intelligence

February 27, 2024

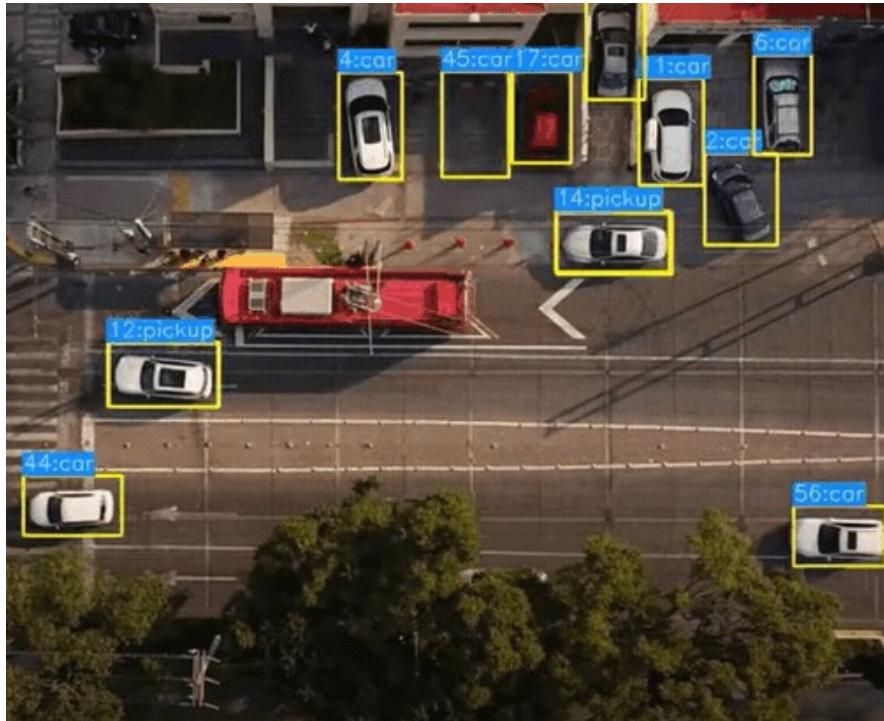


**Sira Sriswasdi, PhD**

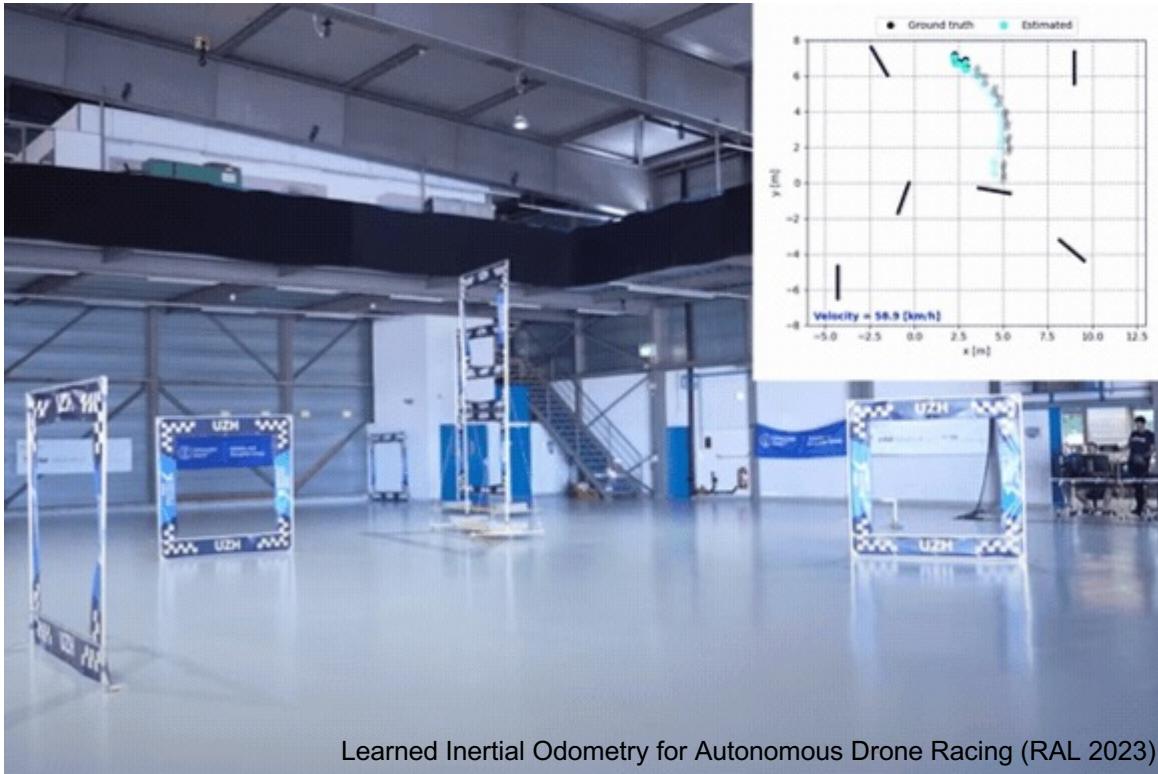
- Research Affairs
- Center of Excellence in Computational Molecular Biology (CMB)
- Center for Artificial Intelligence in Medicine (CU-AIM)

# Real-time object recognition

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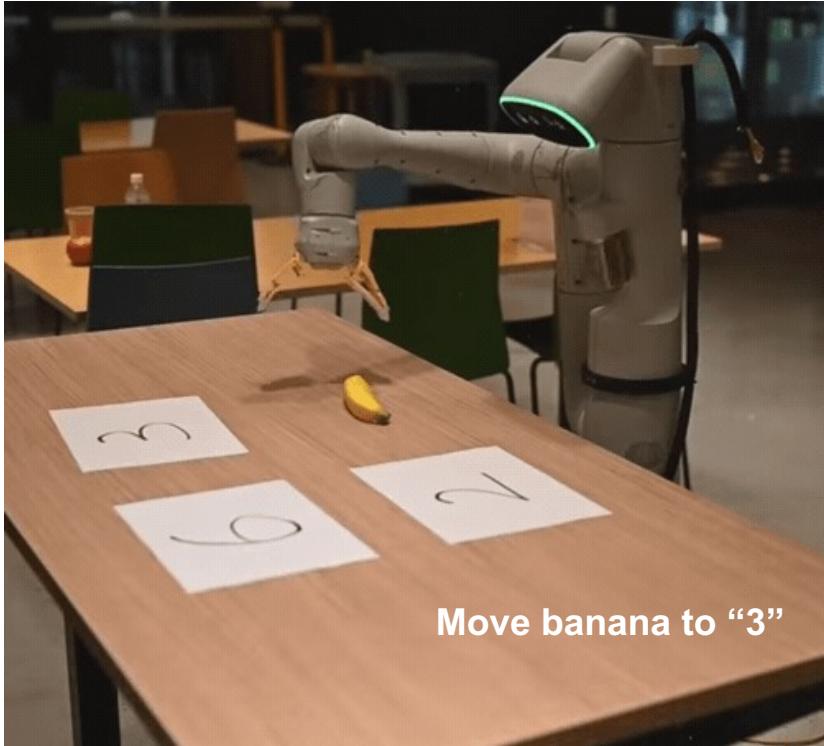
# Interaction with real-world environment



Google DeepMind's AlphaGo computer beats top player Lee Sedol for third time to sweep competition

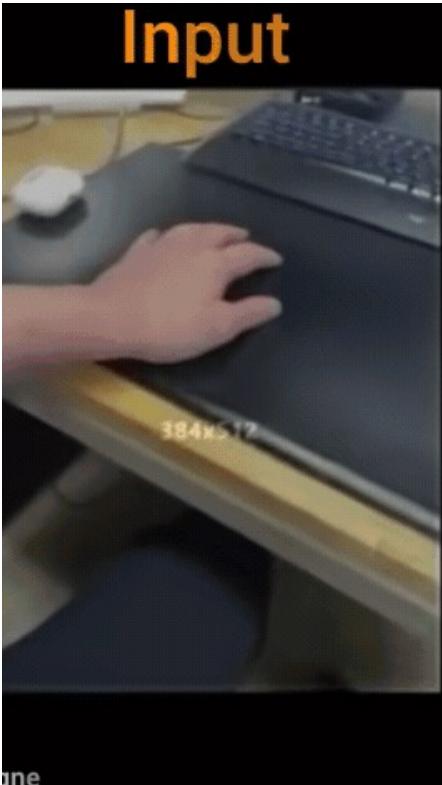
# Text to action: Google RT-2

---



# Art and deepfake

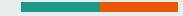
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Talking head anime: <https://github.com/pkhungurn>

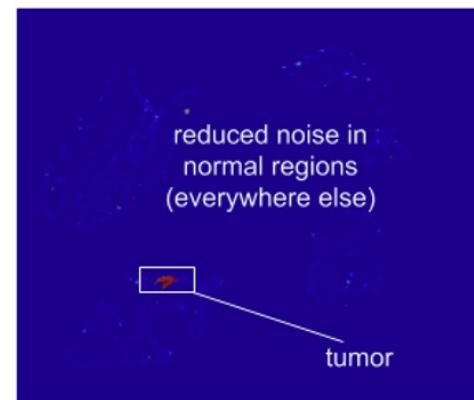
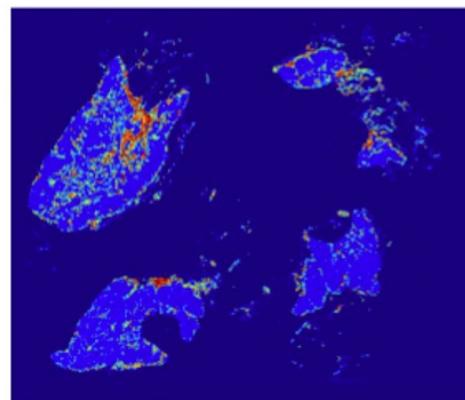
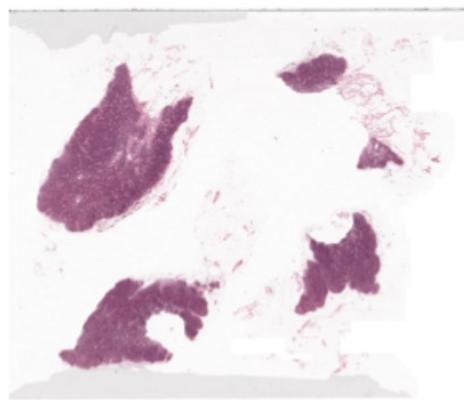
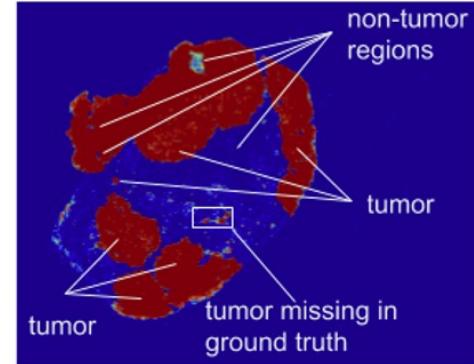
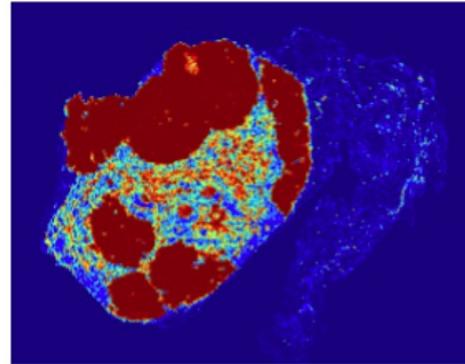
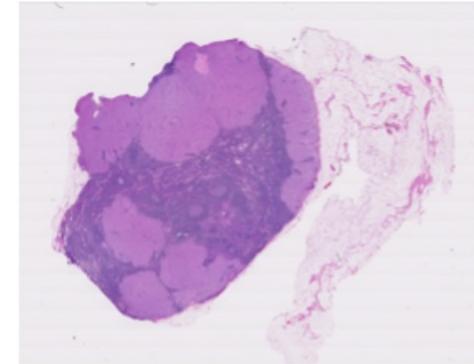


Stable Diffusion: 8



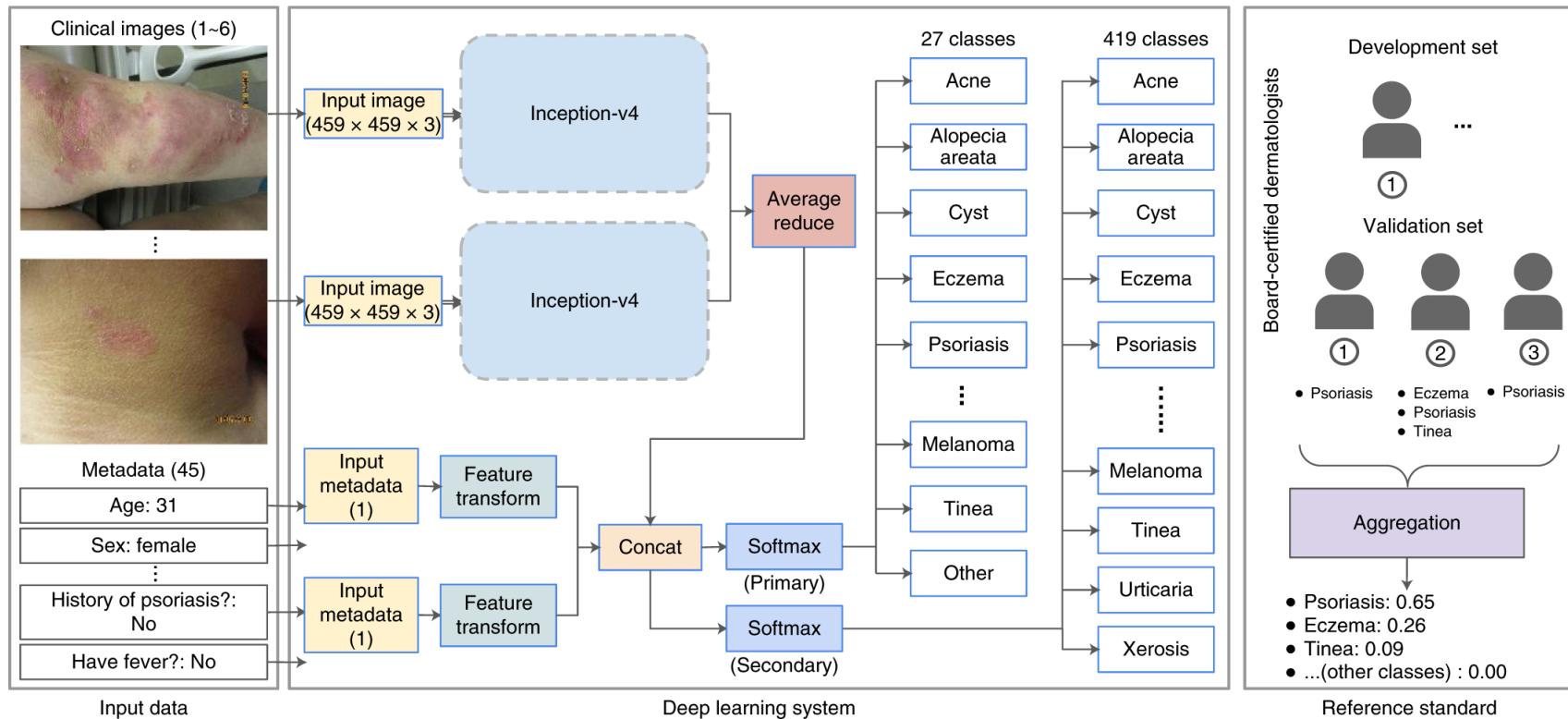
# AI in medicine and healthcare

# Tumor segmentation



# Skin lesion assessment

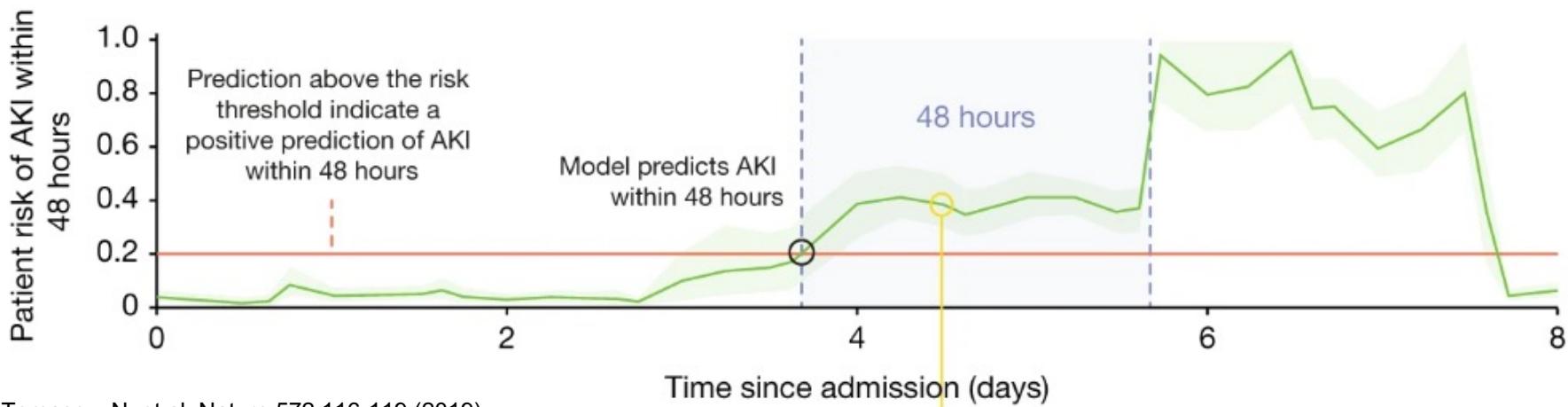
Liu, Y. et al. Nature Medicine 26:900-908 (2020)



# Early warning for acute kidney injury

- Inputs
  - Medical record
  - Blood tests
- Outputs
  - Risk of AKI in the next 48h

Using AI to give doctors a 48-hour head start on life-threatening illness



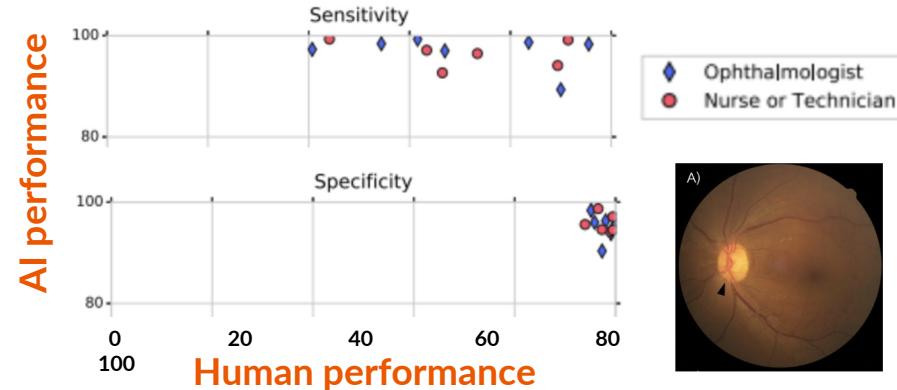
# National diabetic retinopathy screening

---



ARTICLE OPEN

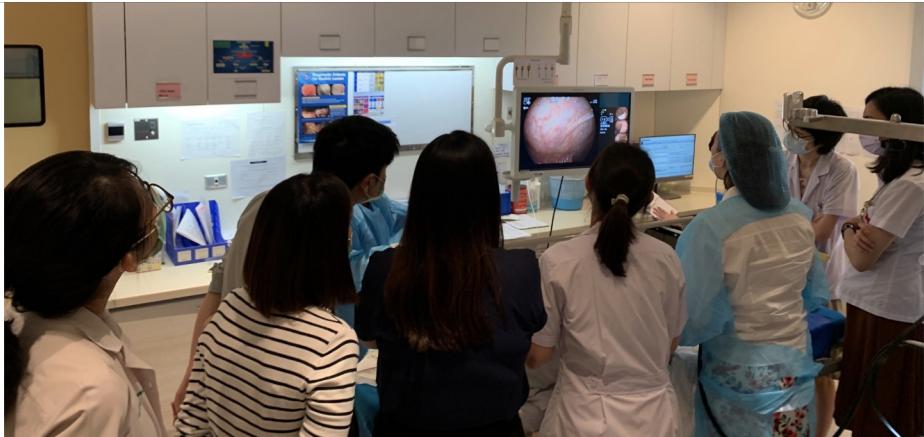
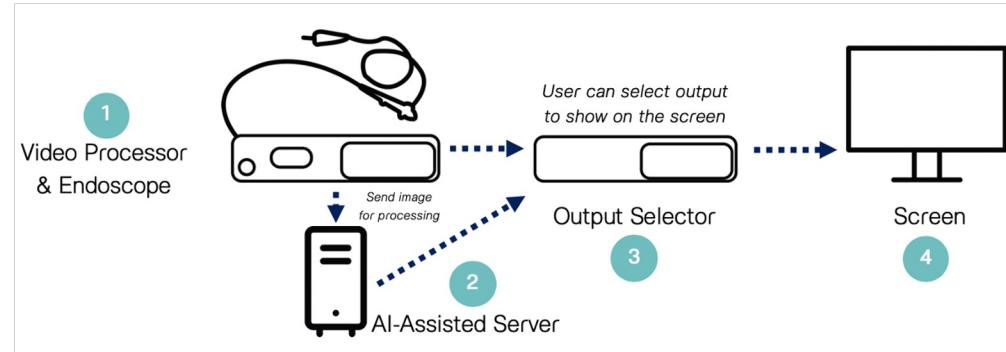
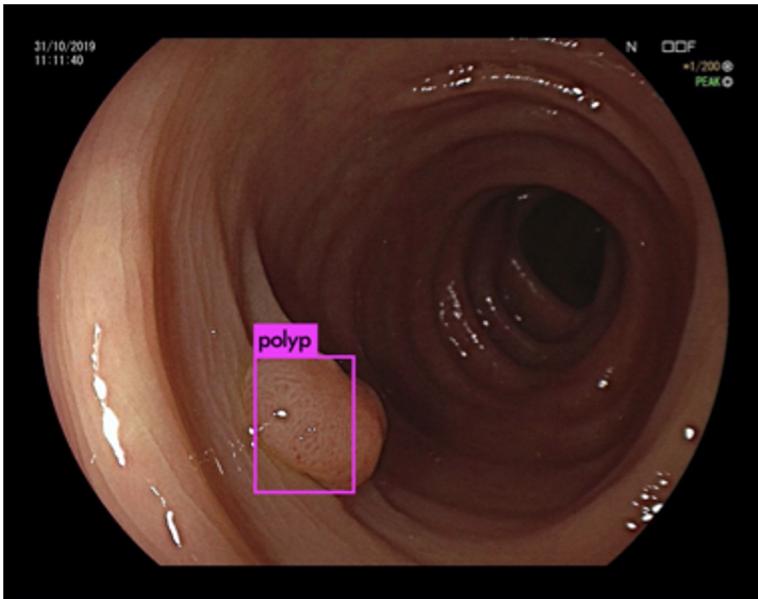
Deep learning versus human graders for classifying diabetic retinopathy severity in a nationwide screening program



- 25k fundus images from 7,517 patients in Thailand

# AI-assisted endoscopy

## Real-time polyp detection



# Question answering service via ChatGPT



## Domain-specific information

A screenshot of a mobile application interface for a domain-specific question and answer service.

Primary Question	Labels	Variations	Answer	Last Updated
What is an Endoscopy procedure	endoscopy	2	17 days ago Orbita Health	...
Can I exercise after my colonoscopy?	exercise gym	18	5 months ago Orbita Health	...

Interpreting question and formulating answer using ChatGPT

### GPT-3.5, Prompt, Context, Question

Answer the question based on the context below.  
If the question cannot be answered using the information provided answer with 'I don't know'

Context:

TEXT of Article from Vector DB



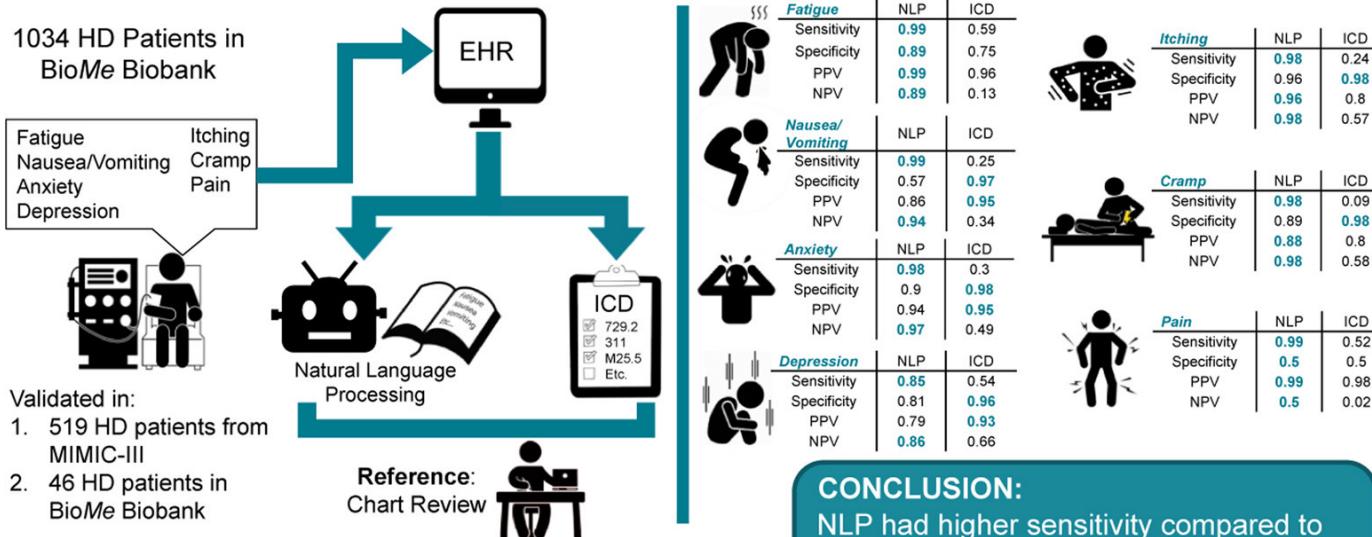
Where is your office

Our headquarter are located at 77 Sleeper St, Boston, MA 02210

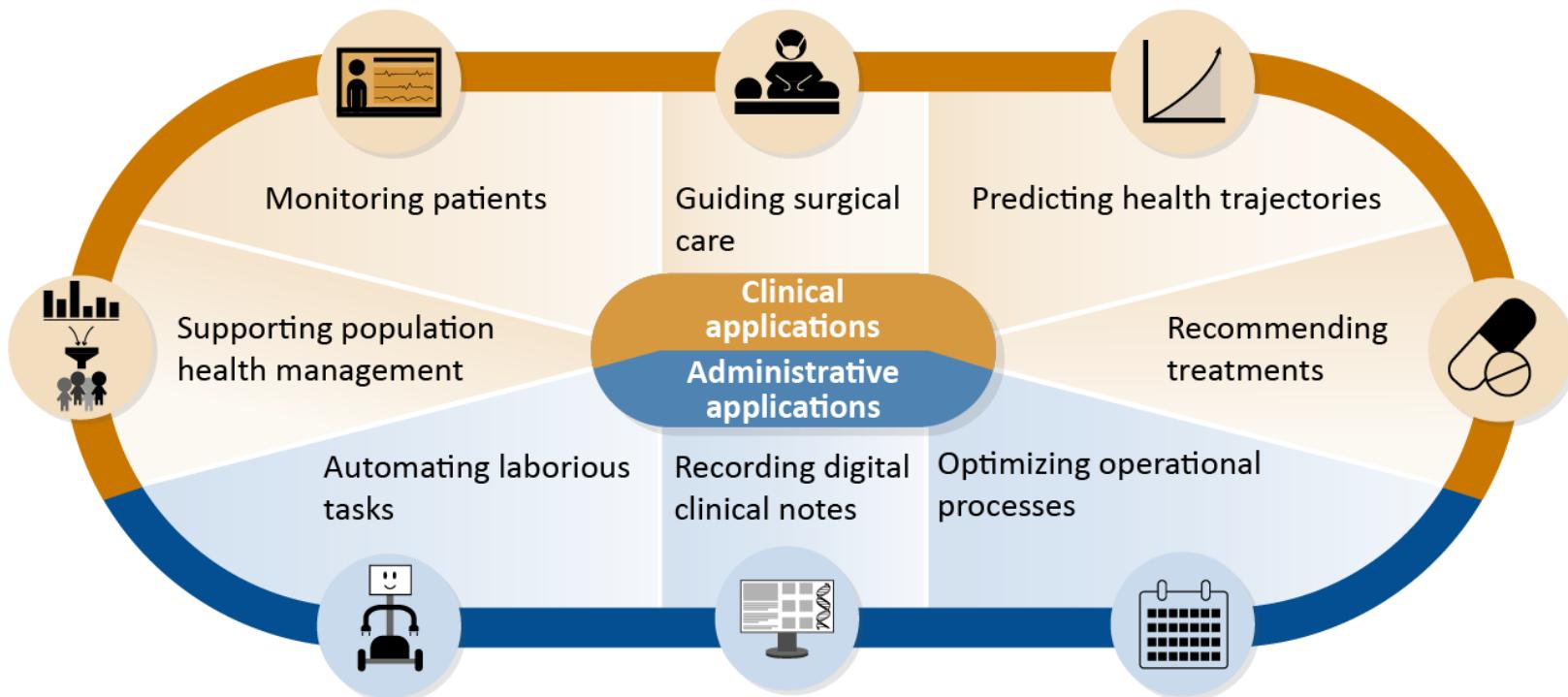
# Information extraction from electronic health record

Chan, L. et al. Kidney International 97:383-392 (2020)

Natural language processing of electronic health records is superior to billing codes to identify symptom burden in hemodialysis patients.



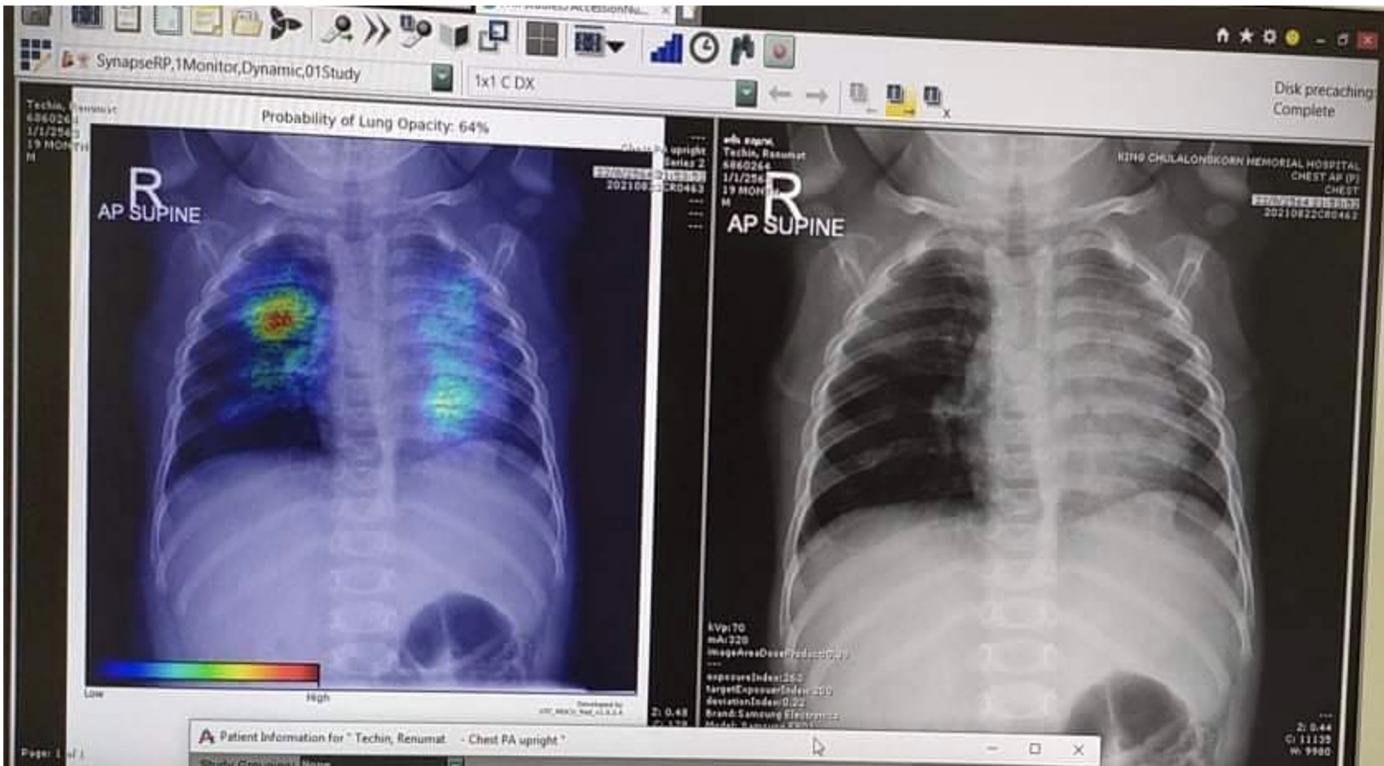
# Use cases for AI in healthcare



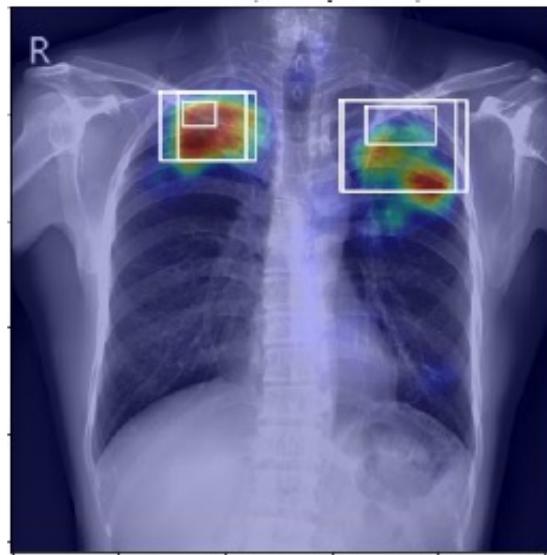
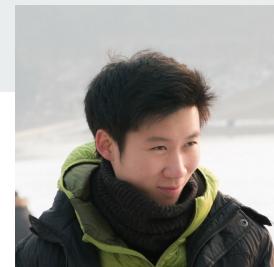


# Medical AI at MDCU

# Our local CXR AI



# Accurate lesion localization



- Trustworthy AI must be able to provide evidence supporting prediction

# Automatic radiologist report generation

---

X-ray	Ground truth	LSP
	<p>frontal and lateral views of the chest were obtained. there are streaky linear opacities at the lung bases which are likely due to atelectasis with chronic changes. no definite focal consolidation is seen. there is no pleural effusion or pneumothorax. no pneumothorax is seen. the aorta is calcified and tortuous. the cardiac silhouette is top normal to mildly enlarged. dual-lead left-sided pacemaker is seen with leads in the expected positions of the right atrium and right ventricle. chronic-appearing rib deformities on the right is again seen.</p>	<p>frontal and lateral views of the chest were obtained. there is a small left pleural effusion with overlying atelectasis. there is no focal consolidation, pleural effusion or pneumothorax. the aorta is calcified and tortuous. the heart is mildly enlarged. a left-sided pacemaker is seen with leads in the expected position of the right atrium and right ventricle. the patient is status post median sternotomy and cabg. the lungs are otherwise clear.</p>

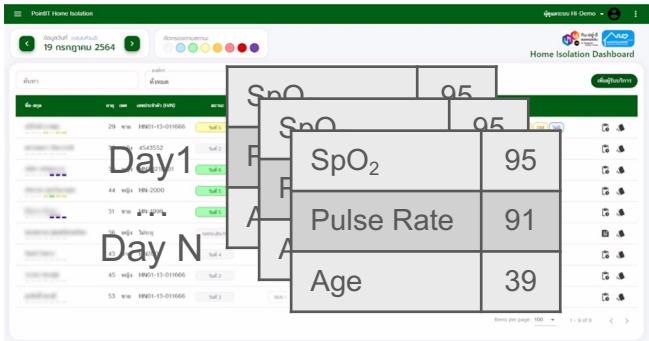


# AI-assisted COVID-19 monitoring

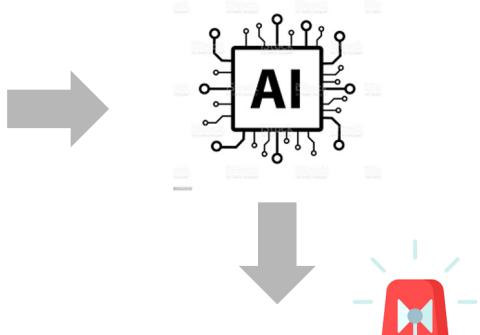
1. Patients send vital sign and symptom data from home



Monitoring dashboard (weSAFE)



2. AI predicts risk of adverse event



5. Conventional healthcare decision making



4. Follow-up for high-risk patients



3. Alert doctors

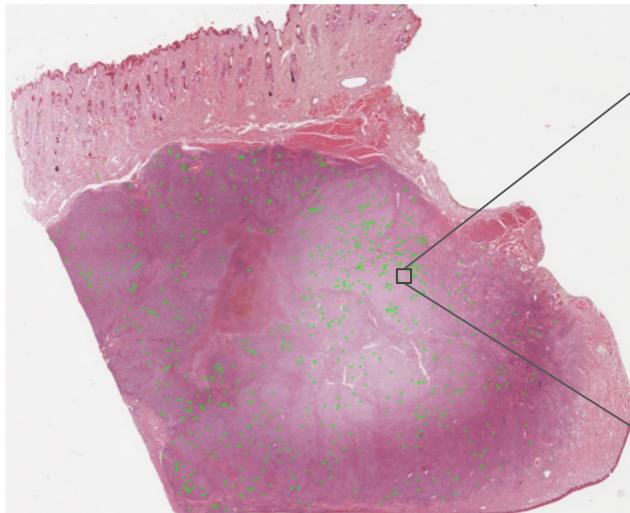




# Digital pathology

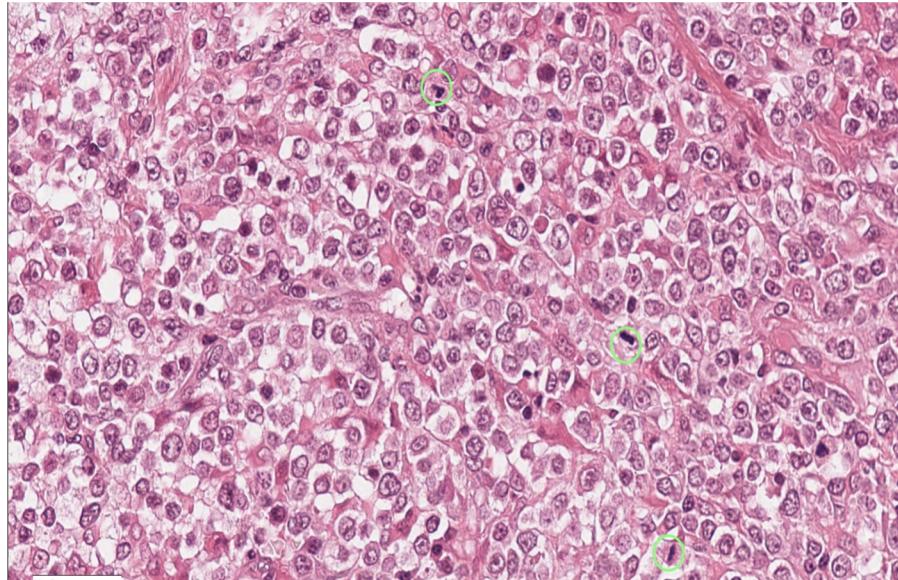
# Pain point: locating ROIs with highest object counts

---



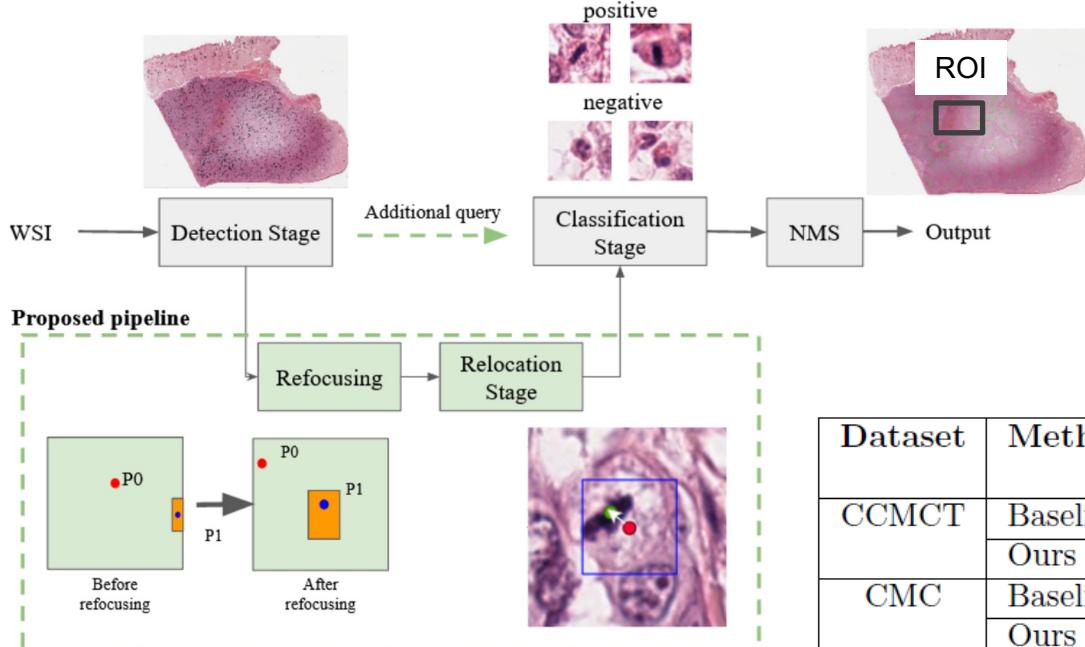
Whole-slide image (150,000 x 150,000 pixels)

40x



Mitotic figures

# Lesson: AI does not have to do everything

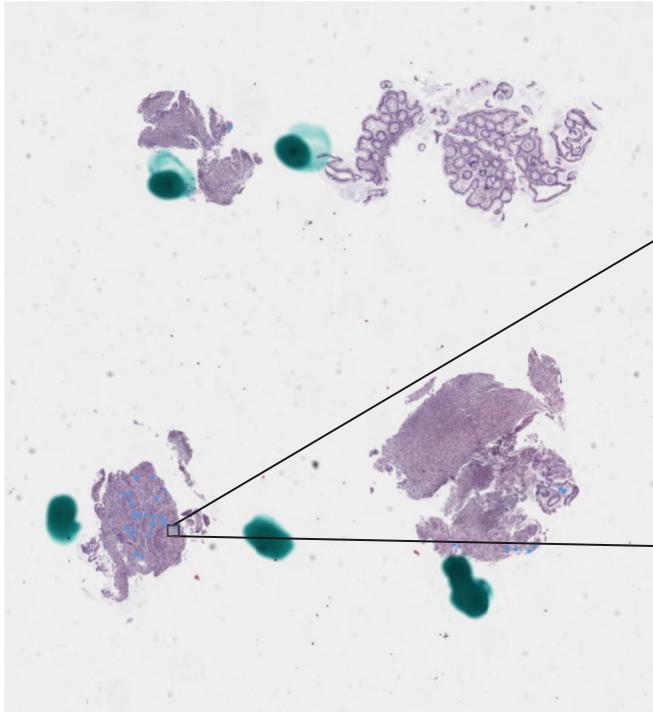


- Minimize ROI search
- <2 mitotic count error when a pathologist is involved

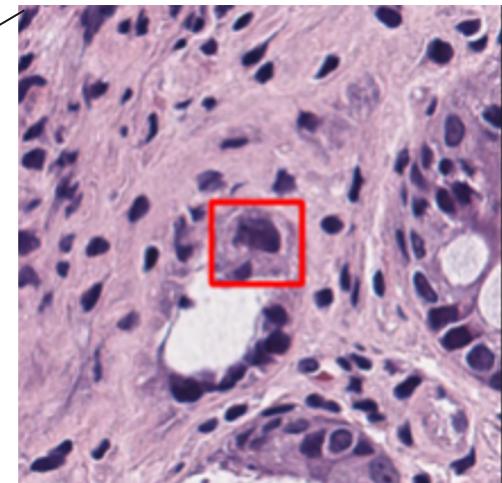
Dataset	Method	Fully-Automated		Human-In-The-Loop	
		MAPE	MAE	MAPE	MAE
CCMCT	Baseline	18.8	10.5	11.2	4.4
	Ours	10.5	8.3	6.8	1.9
CMC	Baseline	7.8	3.1	8.1	2.4
	Ours	5.6	1.9	5.6	1.6

# Pain point: detecting rare infected cells

---



40x



An infected cell

Whole-slide image (150,000 x 150,000 pixels)

# Low sensitivity and confidence of visual inspection

---

Sample	Ground truth	# of infected assessments	# of uninfected assessments	# of unsure assessments
1	Infected	1	2	6
2	Infected	2	3	4
3	Infected	1	6	2
4	Infected	4	3	2
5	Infected	1	8	
6	Uninfected	1	6	2
7	Uninfected		2	7
8	Uninfected		9	1
9	Uninfected		6	3
10	Uninfected	1	6	2
11	Uninfected	2	6	1
12	Uninfected		7	3

# Lesson: AI does not have to be perfect to be useful

---

## Development

- 1,239 annotated infected cells from 68 whole-slide images
- 34.2% F1 score

## Evaluation

- AI proposes the top 10 likely cells per slide
- Pathologists classify whole-slide based on only proposed cells
  - Preliminary result = 100% sensitivity

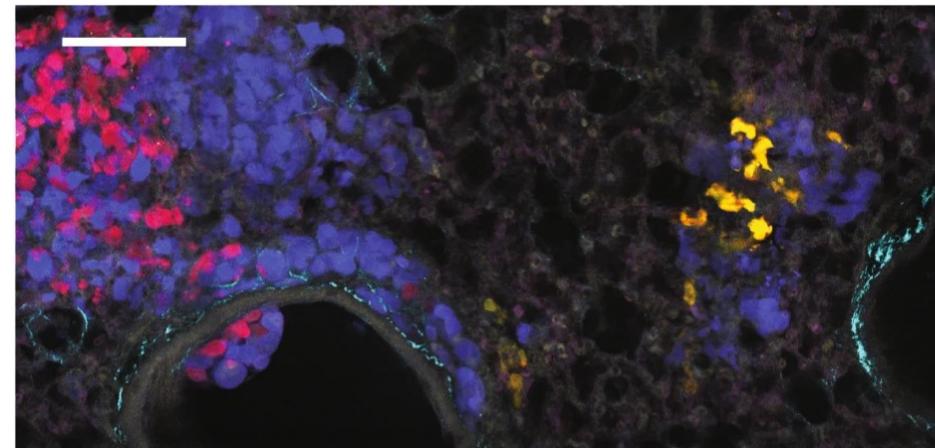


# H&E 2.0

# Spatial omics and multiplexed imaging



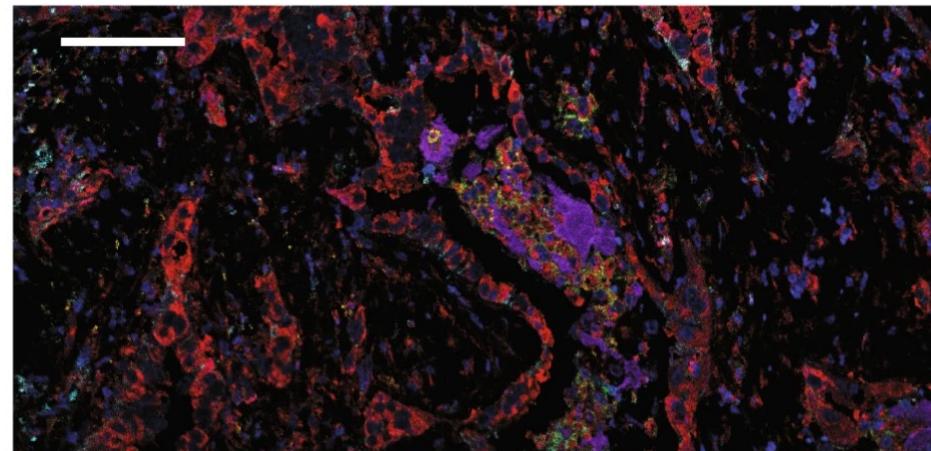
Optical clonal barcoding



● RFP clone    ● YFP clone    ● Cerulean clone    ● Collagen    ● Lectin

Lewis, S.M. et al. Nature Methods 18:997-1012 (2021)

Spatial proteomics

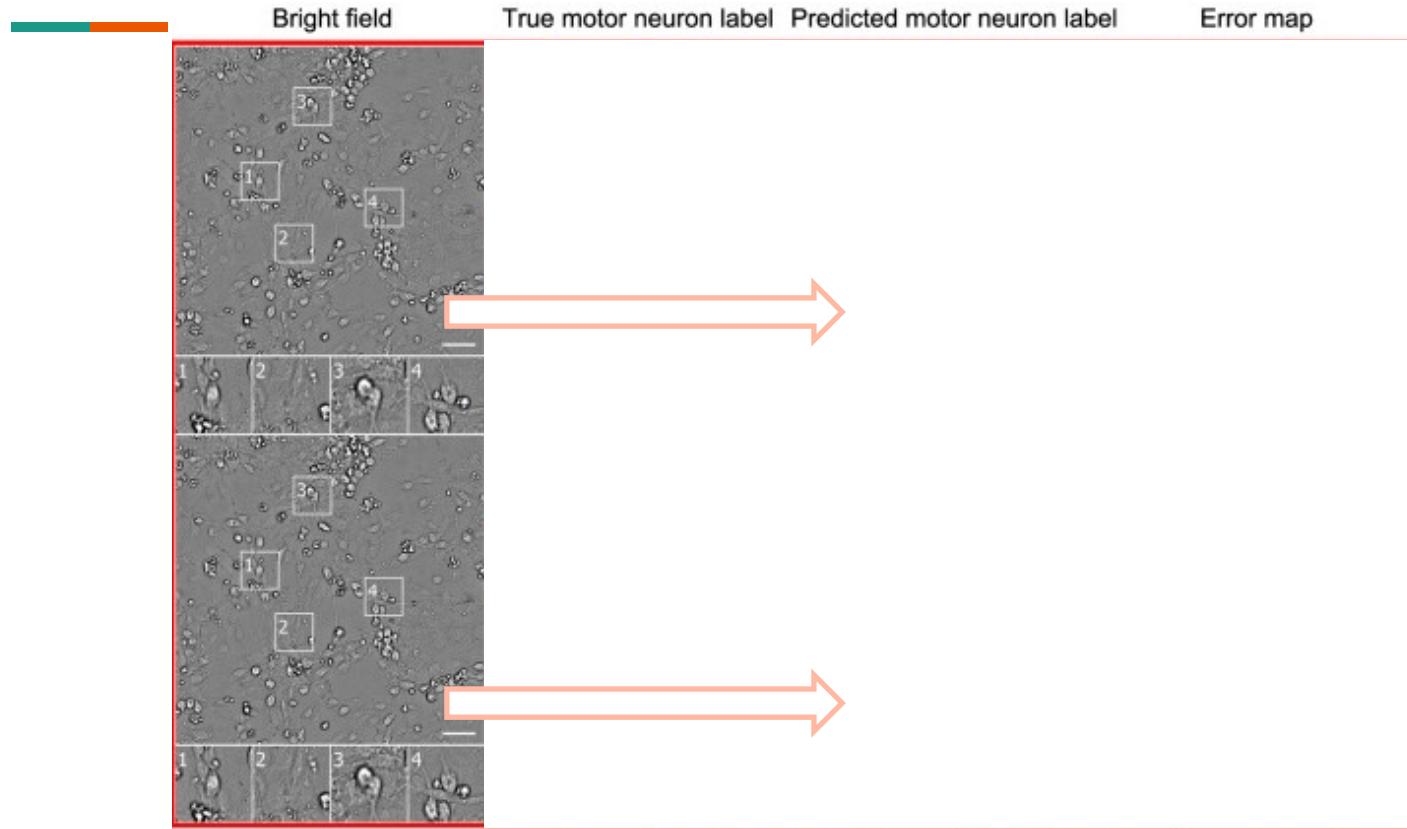


●  $\beta$ -tubulin    ● CD11b    ● CD163    ● CD68    ● dsDNA  
● HLA class 1    ● Keratin    ● Ki-67    ● Vimentin

- Enable single-cell interpretation of tissue images

# *In silico* labeling with AI

Christiansen, E.M. et al. Cell 173:792-803 (2018)

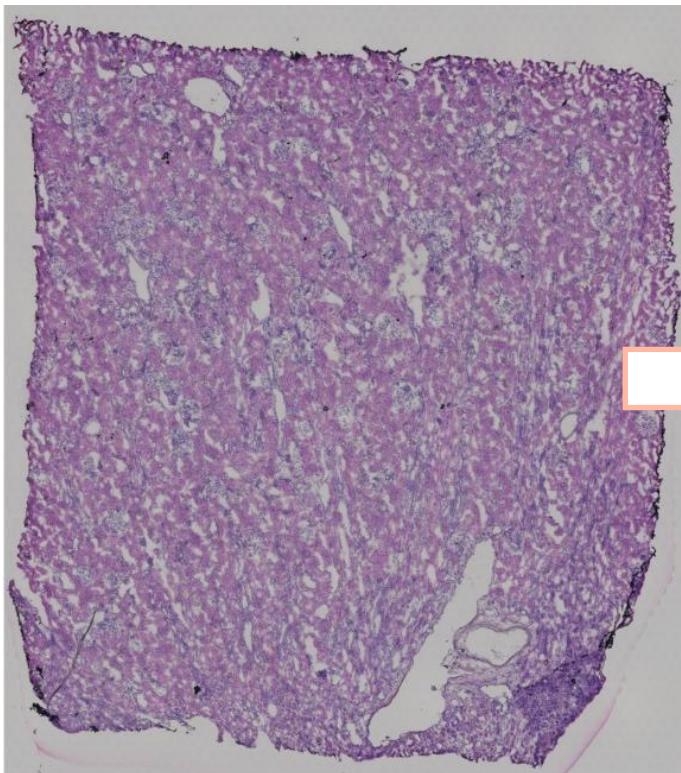


# H&E with AI annotations



Ferrerira, R.M. et al. JCI Insight 6:e147703 (2021)

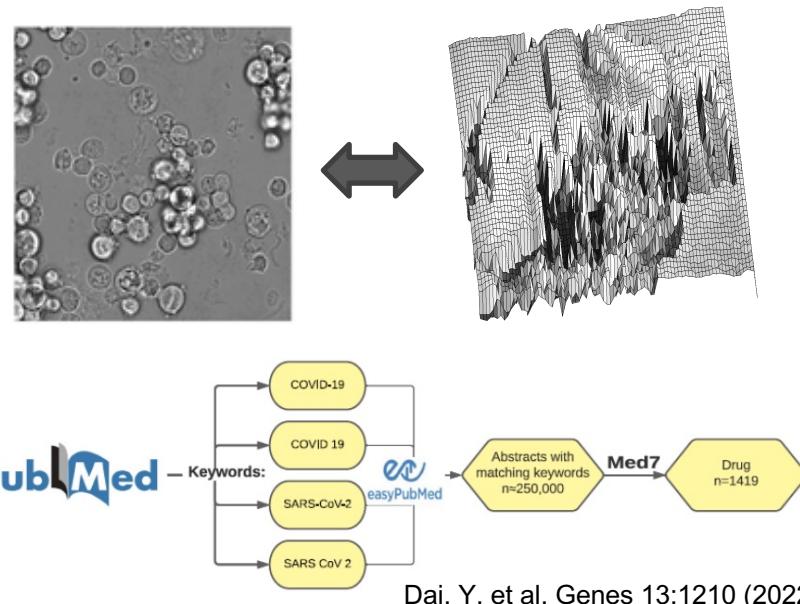
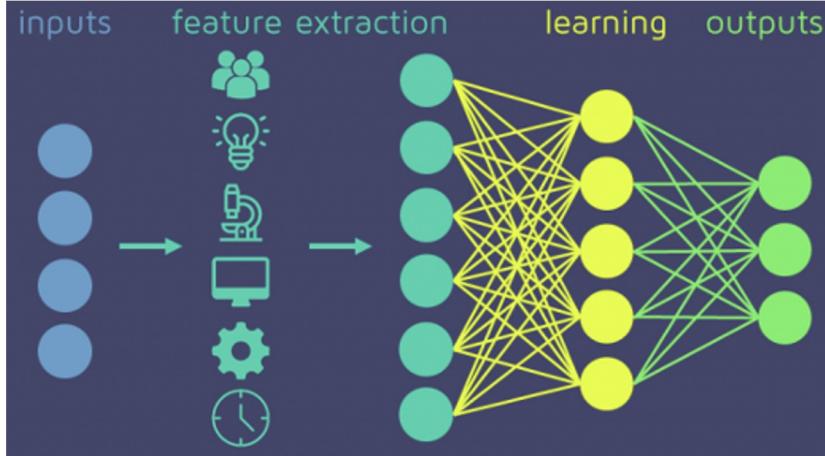
A





# How did the magic happen?

# Limitation of classical (non-deep) learning

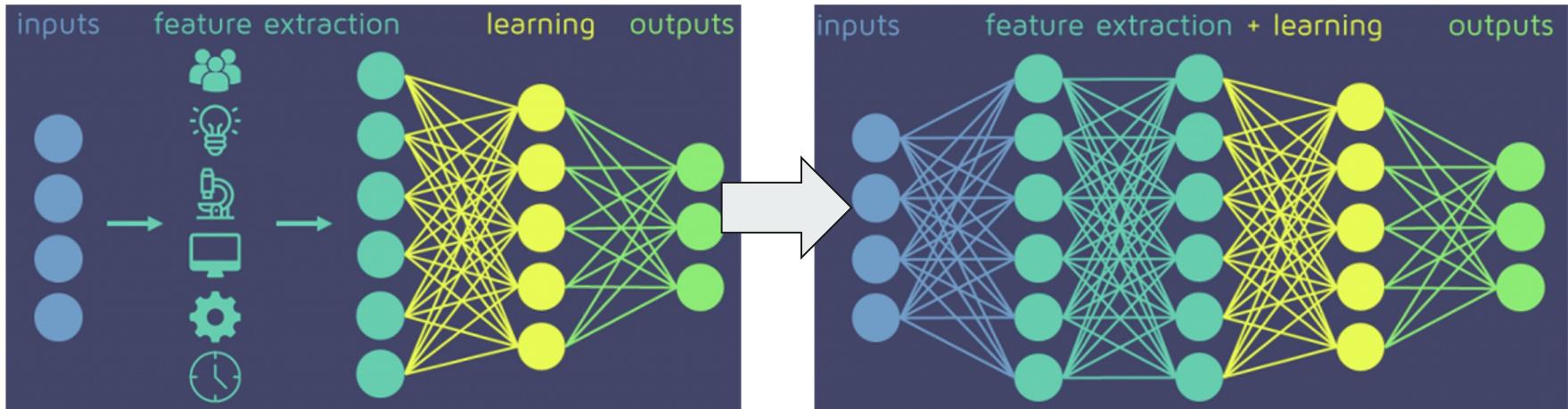


Dai, Y. et al. Genes 13:1210 (2022)

- Classical machine learning requires the input to be formatted and pre-processed by human

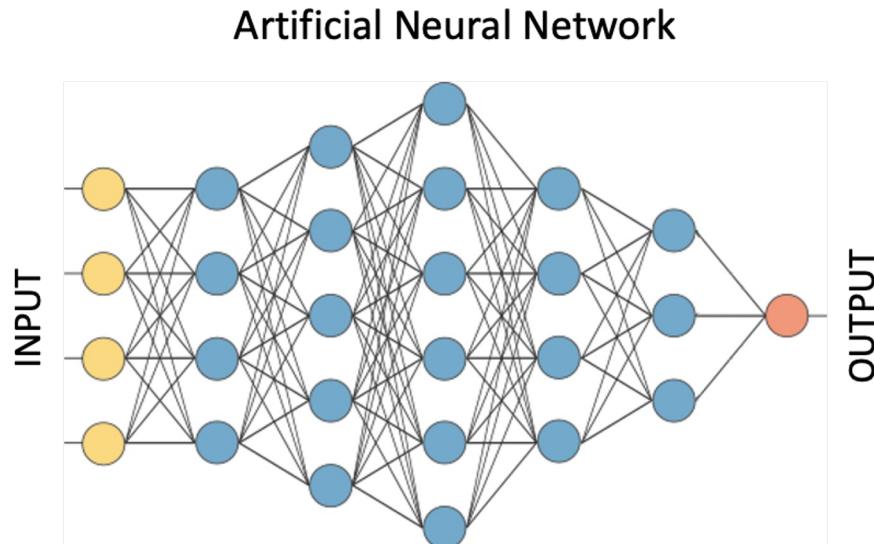
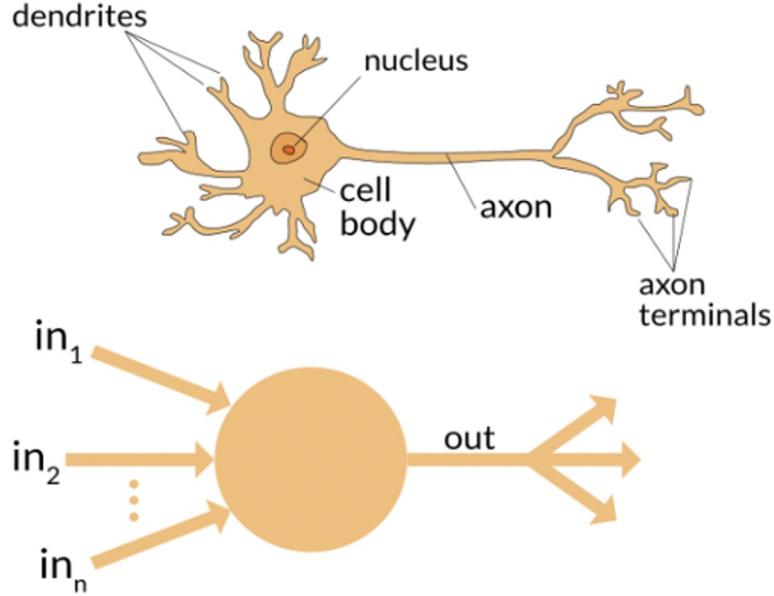
# End-to-end learning

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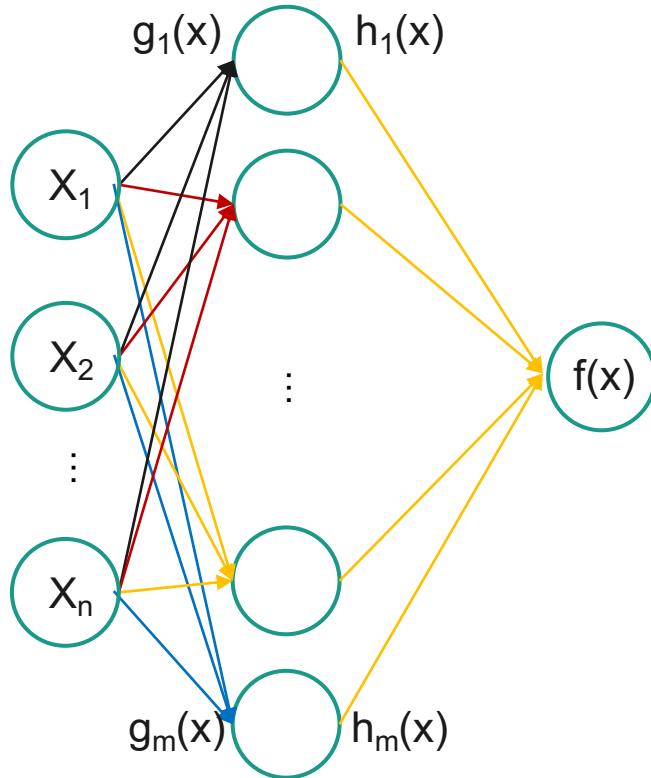
- Deep learning, via **artificial neural network models**, can learn to extract useful information from raw input directly
- **The catch is a lot of data and supervision is needed**

# Artificial neural network



- Network of **simple** computation nodes:  $out = f(w_1in_1 + w_2in_2 + \dots + w_nin_n)$

# Calculations inside neural network



Linear neuron input

- $g_1(x) = w_{1,1}x_1 + \dots + w_{1,n}x_n$
- $g_m(x) = w_{m,1}x_1 + \dots + w_{m,n}x_n$

Sigmoid activation

- $h_1(x) = \frac{1}{1+e^{-g_1(x)}}$
- $h_m(x) = \frac{1}{1+e^{-g_m(x)}}$

Linear aggregated output

- $f(x) = u_1 h_1(x) + \dots + u_m h_m(x)$

# Universal approximation theorem (Cybenko, 1989)

---

**Universal Approximation Theorem:** Fix a continuous function  $\sigma : \mathbb{R} \rightarrow \mathbb{R}$  (activation function) and positive integers  $d, D$ . The function  $\sigma$  is not a polynomial if and only if, for every **continuous** function  $f : \mathbb{R}^d \rightarrow \mathbb{R}^D$  (target function), every **compact** subset  $K$  of  $\mathbb{R}^d$ , and every  $\epsilon > 0$  there exists a continuous function  $f_\epsilon : \mathbb{R}^d \rightarrow \mathbb{R}^D$  (the layer output) with representation

$$f_\epsilon = W_2 \circ \sigma \circ W_1$$

where  $W_2, W_1$  are **composable affine maps** and  $\circ$  denotes component-wise composition, such that the approximation bound

$$\sup_{x \in K} \|f(x) - f_\epsilon(x)\| < \epsilon$$

holds for any  $\epsilon$  arbitrarily small (distance from  $f$  to  $f_\epsilon$  can be infinitely small).

- Neural network with one hidden layer can mimic any mathematical function

# Gradient of a neural network

---

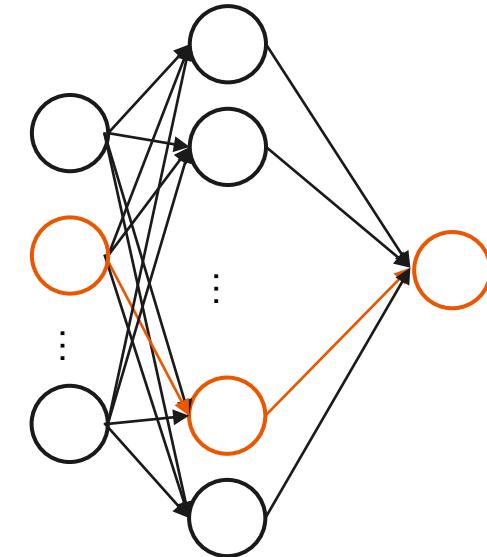
Neuron input:  $g_i(x) = w_{i,1}x_1 + \dots + w_{i,n}x_n$

Sigmoid activation:  $h_i(x) = \frac{1}{1+e^{-g_i(x)}}$

Linear output:  $f(x) = u_1h_1(x) + \dots + u_mh_m(x)$

MSE loss:  $L(f(x), y) = \frac{1}{2} \|f(x) - y\|^2$

Gradient:  $\frac{\delta L}{\delta w_{i,j}} = ?$  ( $w_{i,j}$  is the weight for  $j$ -th feature entering  $i$ -th neuron)



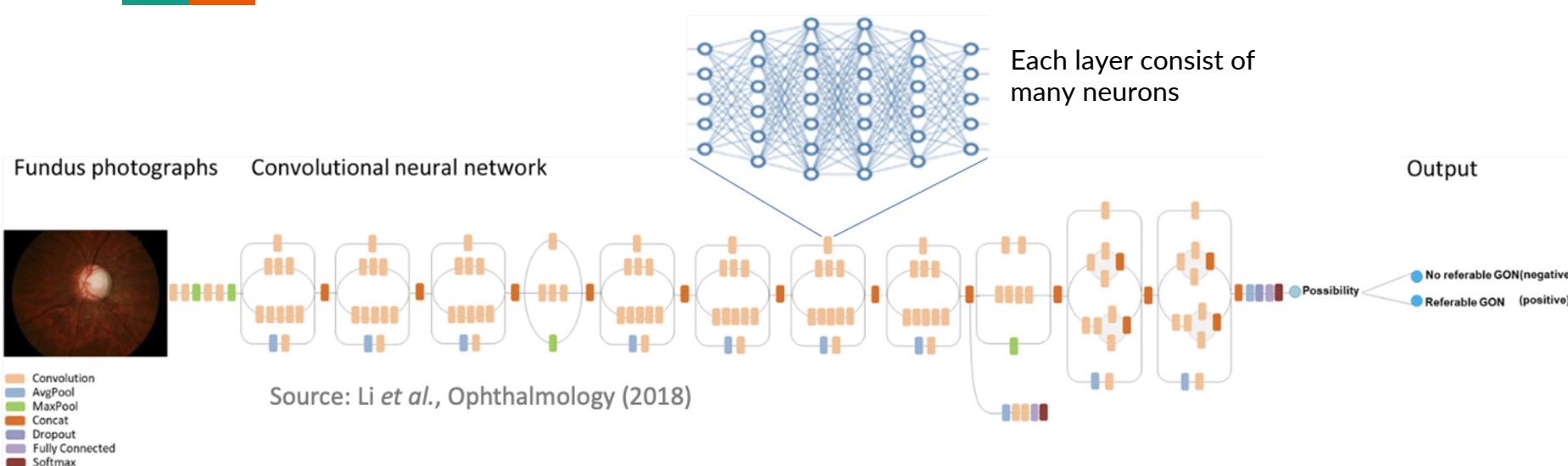
$$\frac{\delta L}{\delta w_{i,j}} = \frac{\delta L}{\delta f} \frac{\delta f}{\delta h_i} \frac{\delta h_i}{\delta g_i} \frac{\delta g_i}{\delta w_{i,j}} = (f(x) - y) \cdot u_i \cdot g_i(x)(1 - g_i(x)) x_j$$

## Toward deep(er) learning

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# Deep artificial neural network



- Up to billions of parameters
- Deep learning is the technique for developing deep artificial neural network and theory on how such feat is possible

# ImageNet: The rise of deep artificial neural network

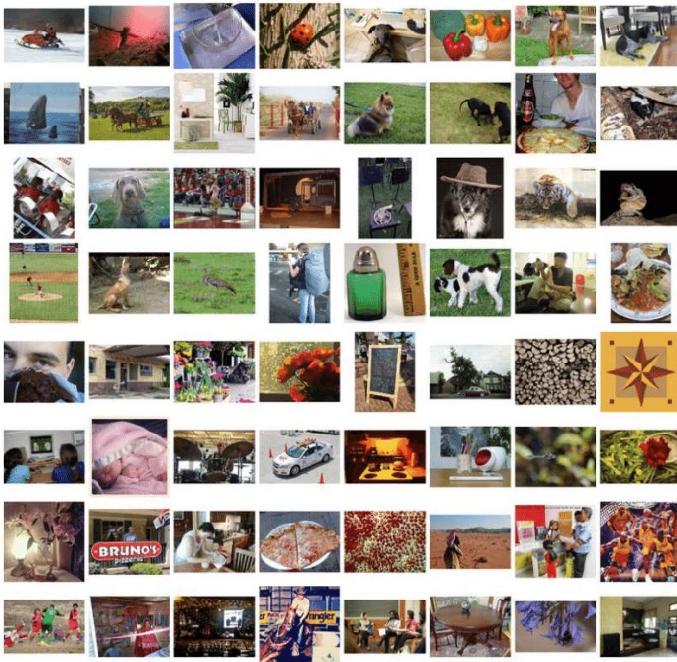
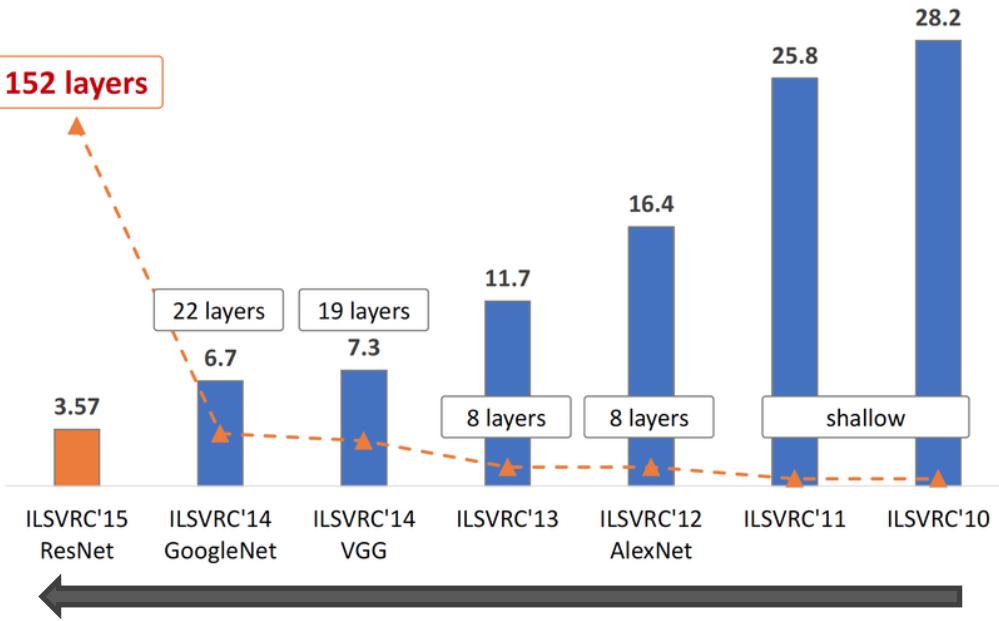
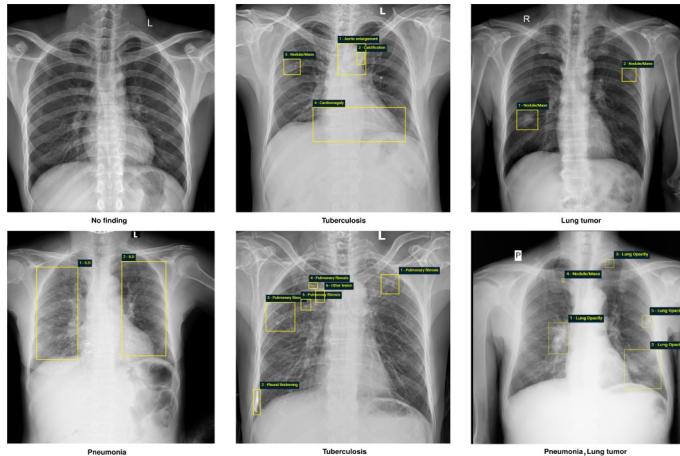


Image classification error



# Medical imaging databases

18,000 annotated CXR images



>1,000,000 CXR images with report

Repository for all imaging data of cancer cases



Dataset	Source Institution	Disease Labeling	# Images	# Reports	# Patients
Open-I	Indiana Network for Patient Care	Expert	8,121	3,996	3,996
Chest-Xray8	National Institutes of Health	Automatic (DNorm + MetaMap)	108,948	0	32,717
CheXpert	Stanford Hospital	Automatic (CheXpert labeler)	224,316	0	65,240
PadChest	Hospital Universitario de San Juan	Expert + Automatic (Neural network)	160,868	206,222	67,625
MIMIC-CXR	Beth Israel Deacones Medical Center	Automatic (CheXpert labeler)	473,057	206,563	63,478

# Graphical processing unit (GPU)

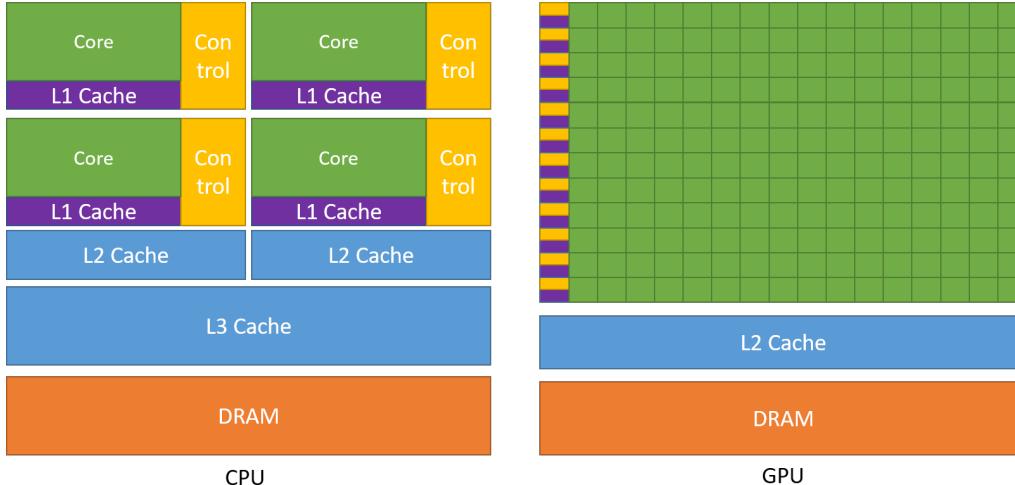


Image from [analyticsvidhya.com](http://analyticsvidhya.com)



- Calculation of gradient for an ANN requires millions of simple operations that can be performed in parallel → Similar to the calculation of graphics



# Representation learning

# Naïve representations



	1	2	3	4	5	6	7	8	9
man	1	0	0	0	0	0	0	0	0
woman	0	1	0	0	0	0	0	0	0
boy	0	0	1	0	0	0	0	0	0
girl	0	0	0	1	0	0	0	0	0
prince	0	0	0	0	1	0	0	0	0
princess	0	0	0	0	0	1	0	0	0
queen	0	0	0	0	0	0	1	0	0
king	0	0	0	0	0	0	0	1	0
monarch	0	0	0	0	0	0	0	0	1

Image from [hackermoon.com](http://hackermoon.com)

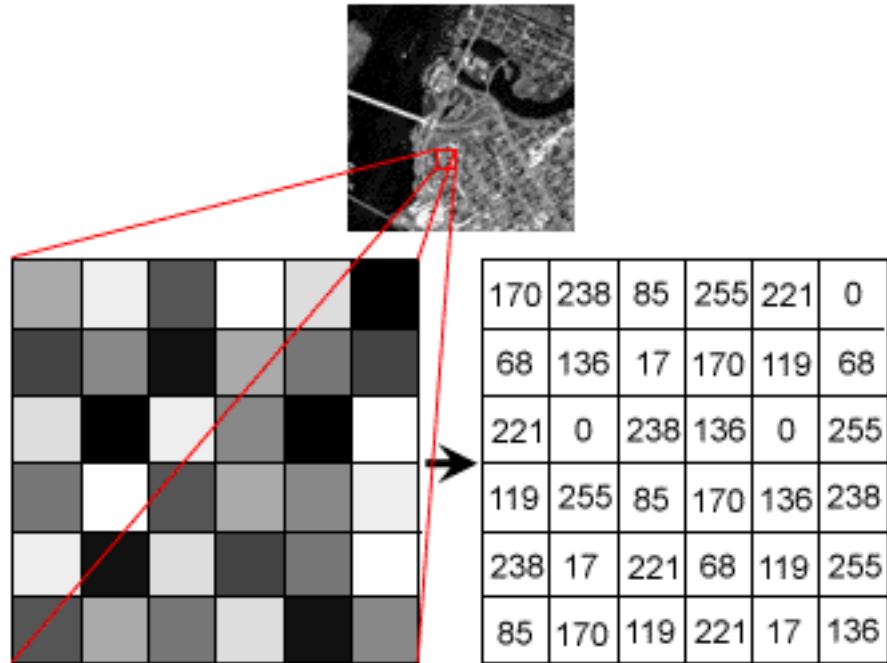
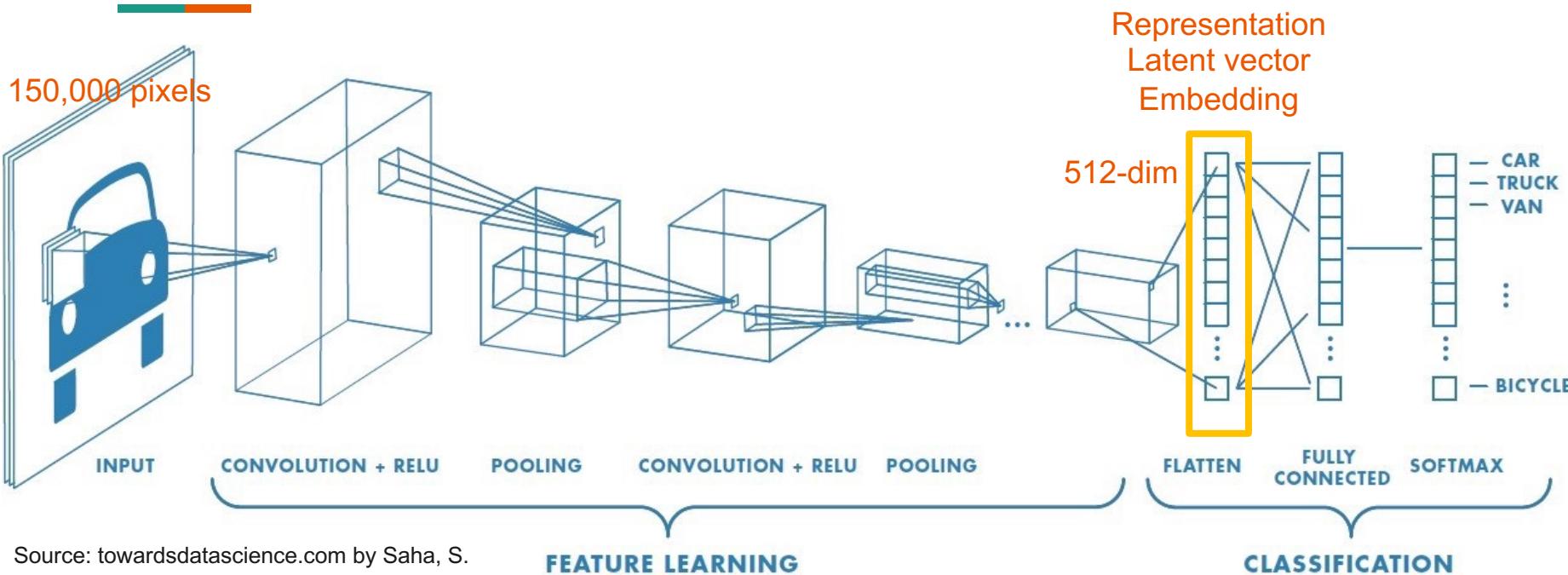


Image from [naushardsblog.wordpress.com](http://naushardsblog.wordpress.com)

# Encoder-Decoder view of neural network

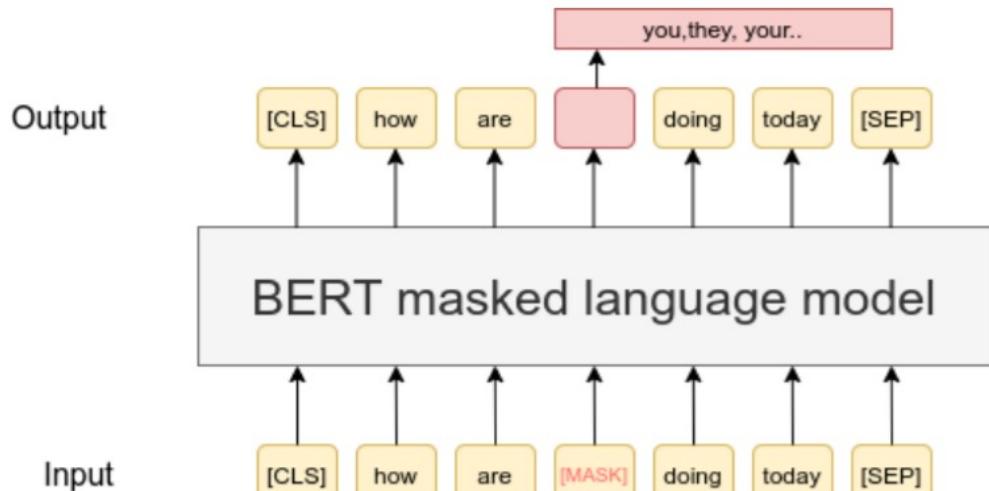


- Encode raw data into useful features → decode features for prediction

# Word representation learning

---

- Transforming words to vectors (**embeddings**) that capture some meanings or characteristics
- The model obtains good embeddings by learning to predict the missing words



[https://www.sbert.net/examples/unsupervised\\_learning/MLM/README.html](https://www.sbert.net/examples/unsupervised_learning/MLM/README.html)

# Meaningful word embedding

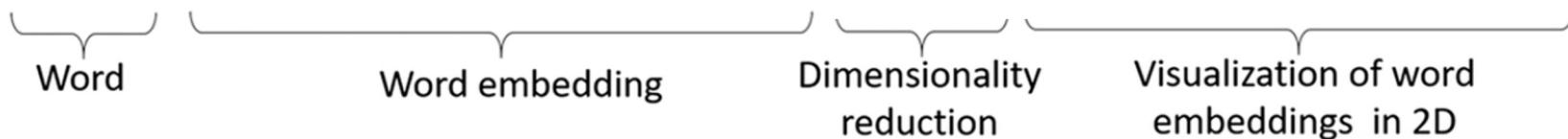


*man* →

*woman* →

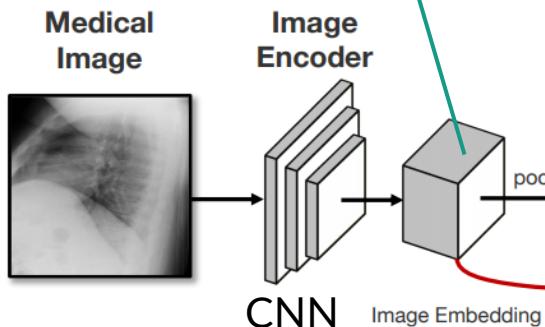
*king* →

*queen* →

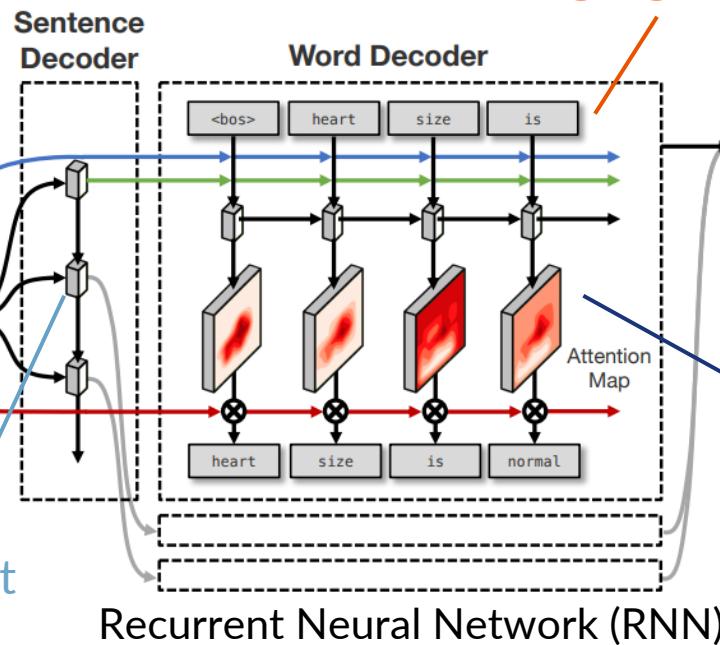


# Combining image and word embeddings

Capture key characteristics about the image – lesions?



Generate embedding that define a sentence's topic



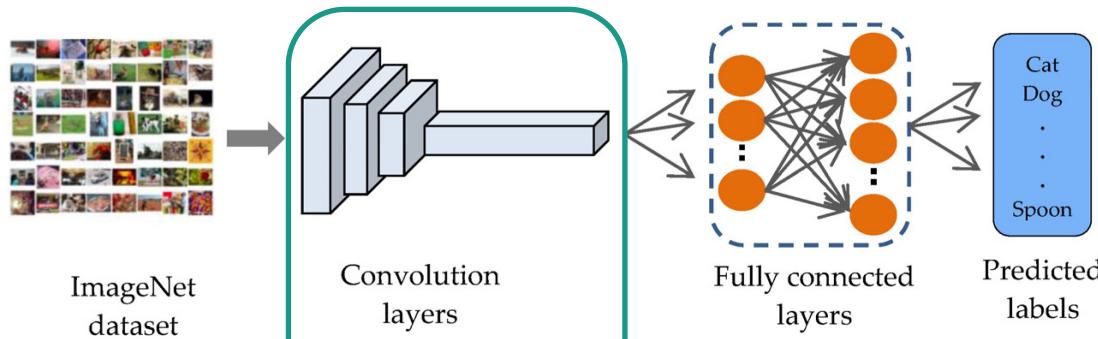
Sequentially generate words that follow the learned language and defined topic

Generated Report

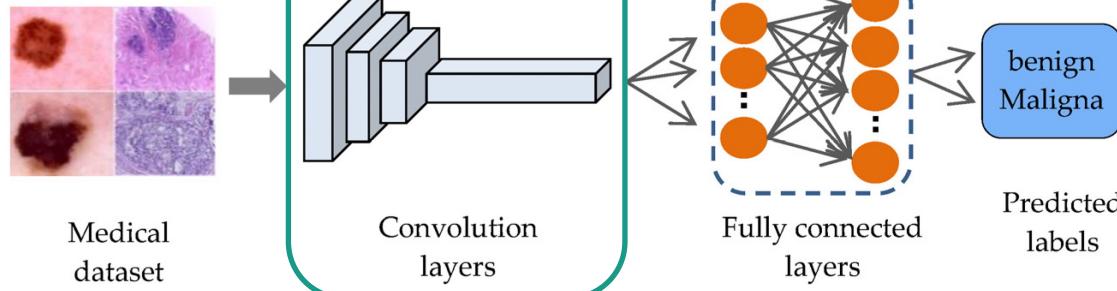
heart size is normal.  
there is no focal consolidation,  
effusion or pneumothorax.  
the lungs are clear.  
there is no acute osseous  
abnormalities.

Co-utilization of image and word embeddings to provide explanation

# Transfer learning reduces data requirement

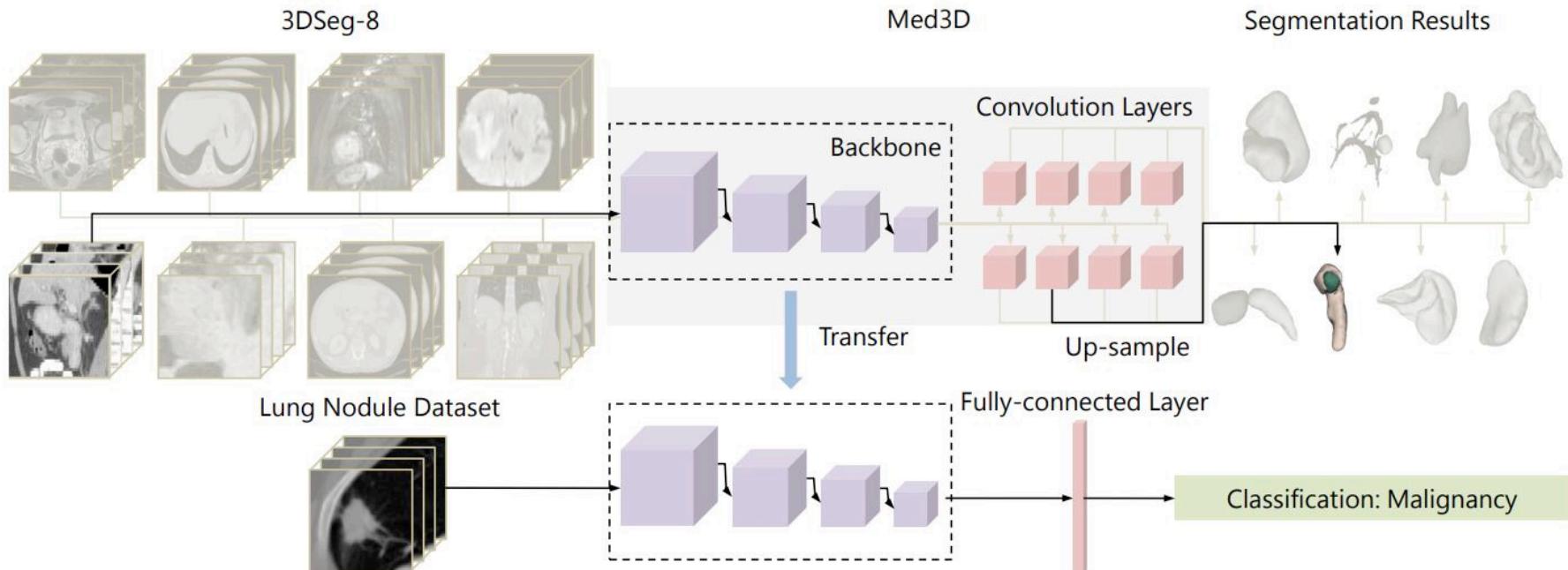


Reuse the front part of the neural network



Retrain the classifier on target task

# Shared encoder for multiple domains



# Any questions?

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See you on February 29<sup>th</sup>