Medical Image Analysis with CNNs

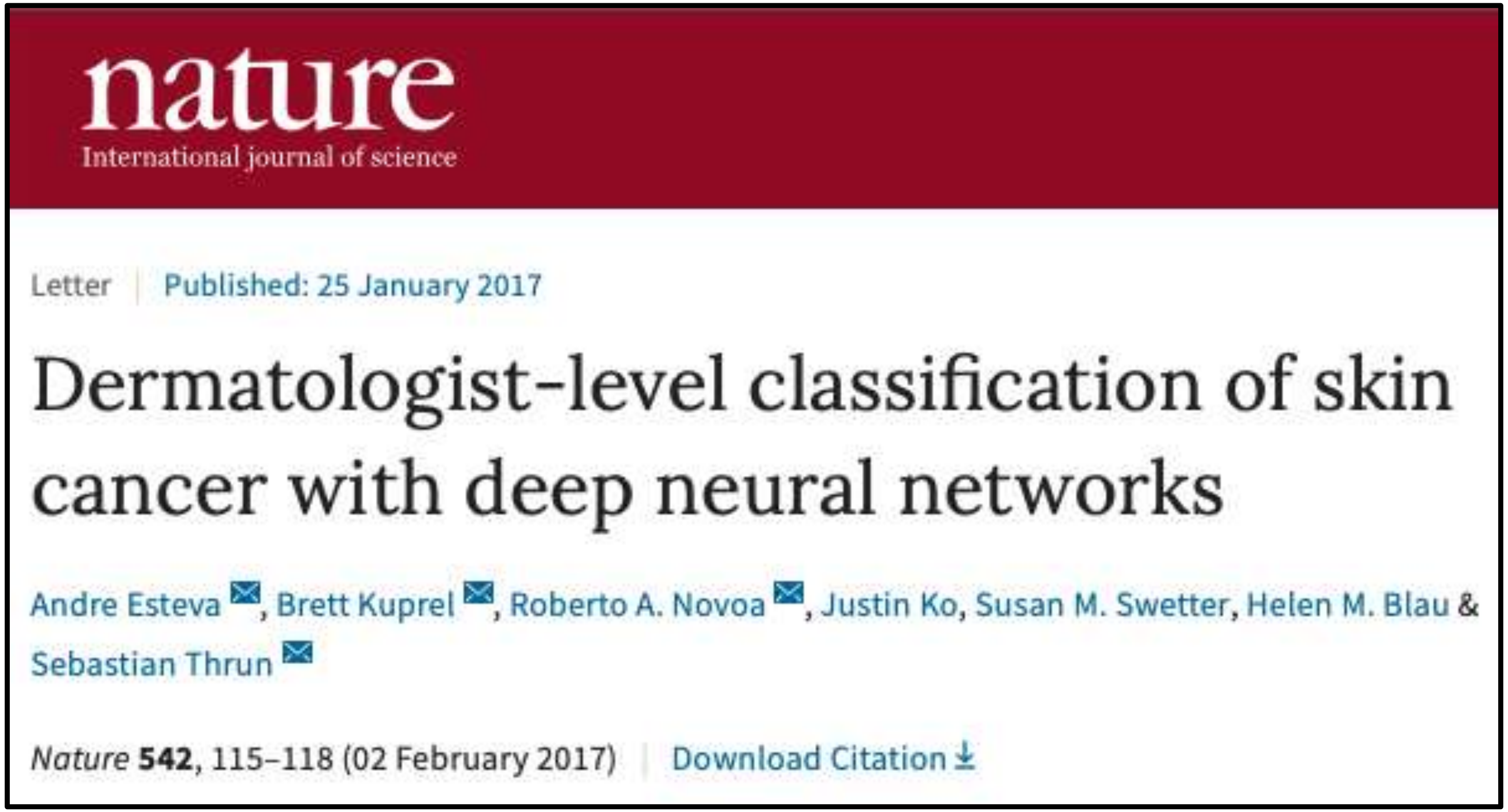
09 July, 2019

Duke/Duke-NUS
Machine Learning Summer School

Matthew Engelhard

Identifying Skin Cancer

MEDICAL IMAGE CLASSIFICATION



nature
International journal of science

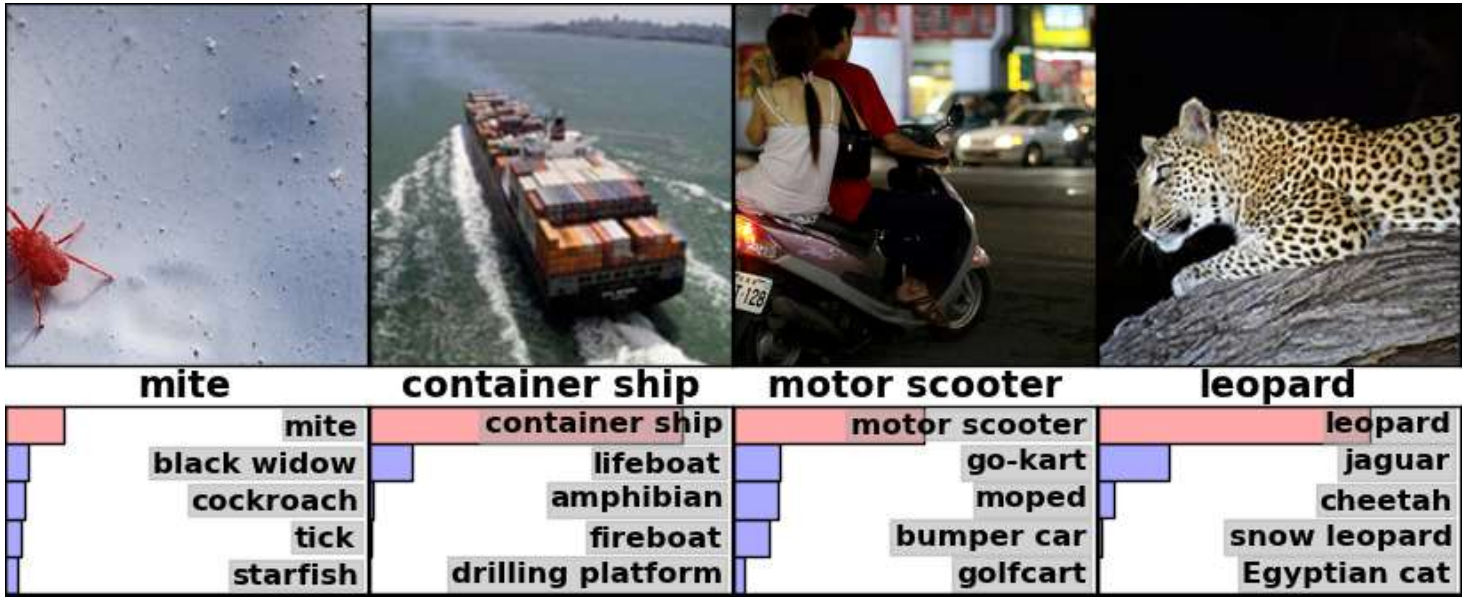
Letter | Published: 25 January 2017

Dermatologist-level classification of skin cancer with deep neural networks

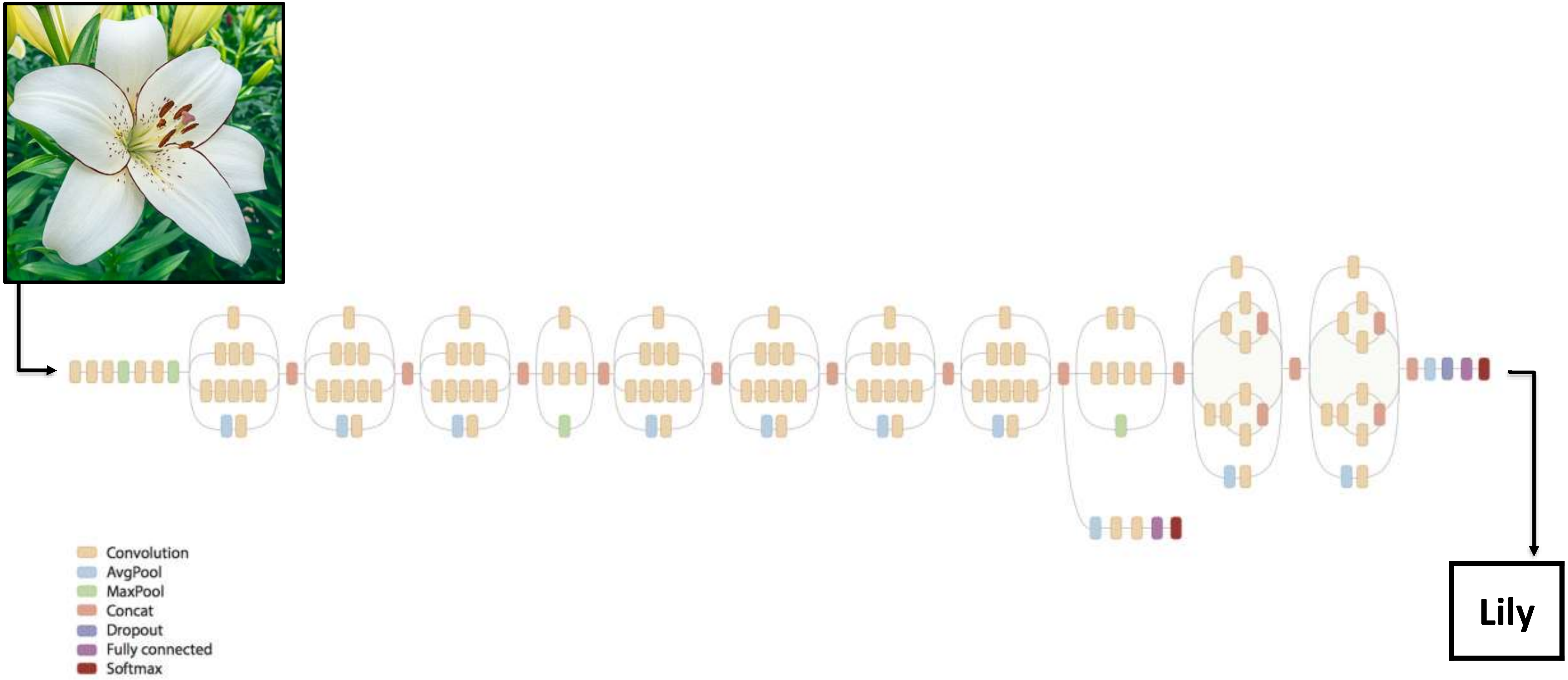
Andre Esteva ✉, Brett Kuprel ✉, Roberto A. Novoa ✉, Justin Ko, Susan M. Swetter, Helen M. Blau & Sebastian Thrun ✉

Nature **542**, 115–118 (02 February 2017) | Download Citation ⤓

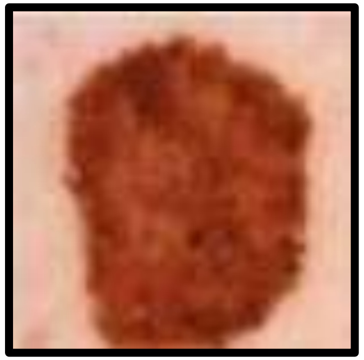
Classification:
predict the label associated with each image

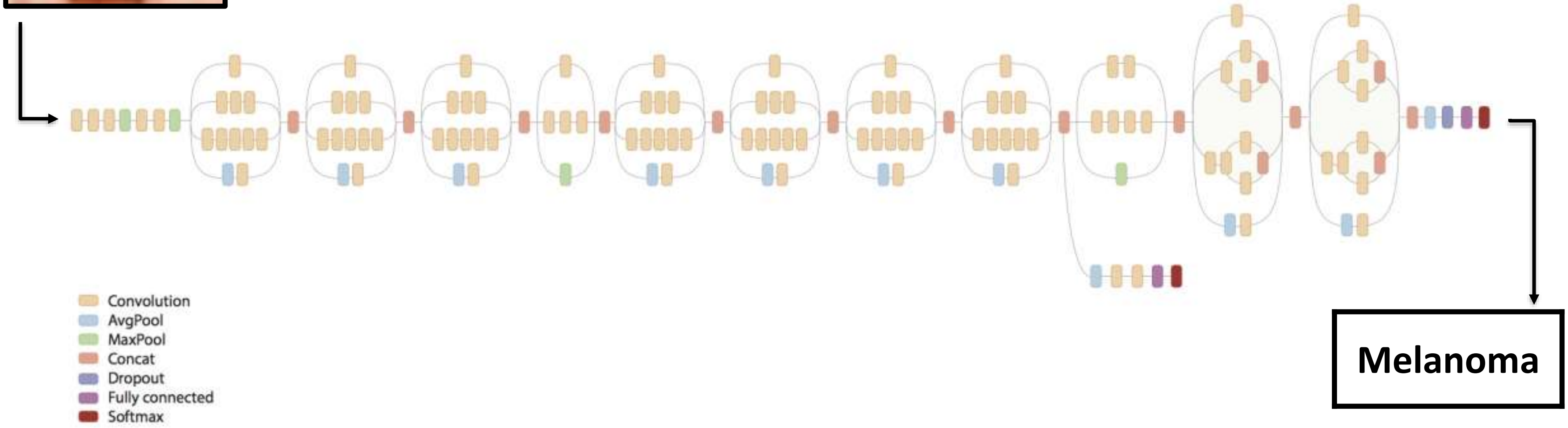


Take a model trained on naturalistic images...



…and repurpose it to evaluate medical images



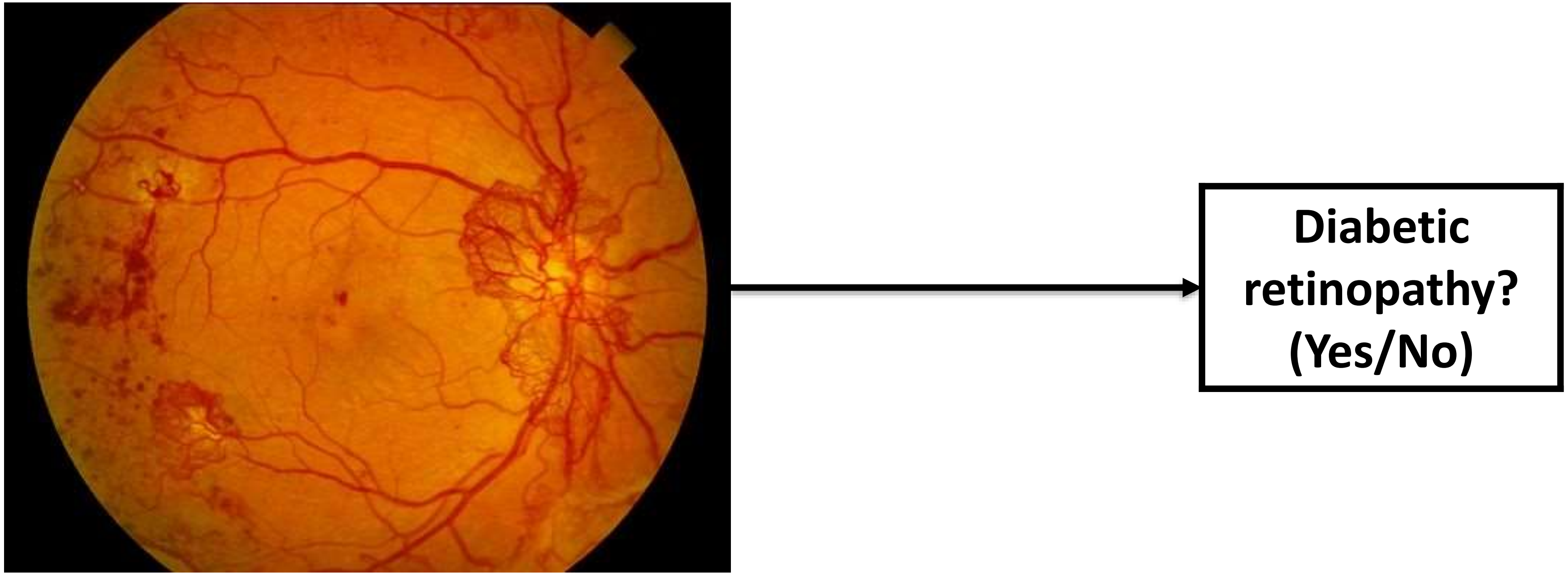


Melanoma

Repurposing our model

- Step 1: Modify the **architecture**
- Step 2: Fine-tune the **parameters**

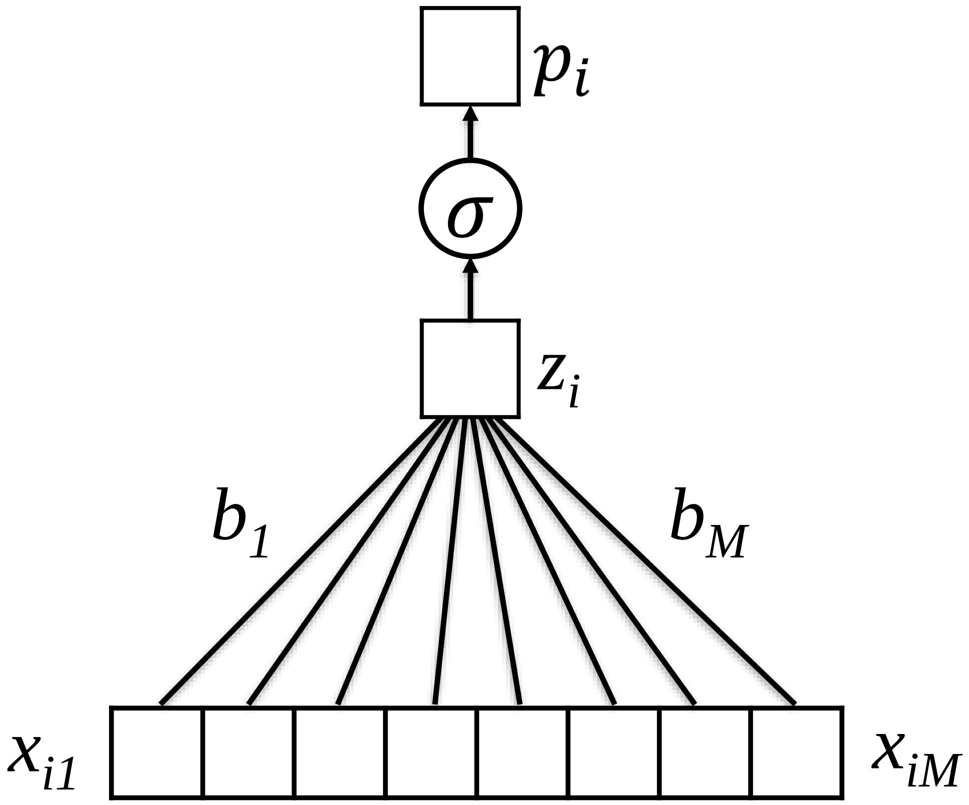
Classifier Output:
Two-Class (e.g. Yes/No)



Diabetic retinopathy? (Yes/No)

Gulshan et al. *JAMA* (2016)

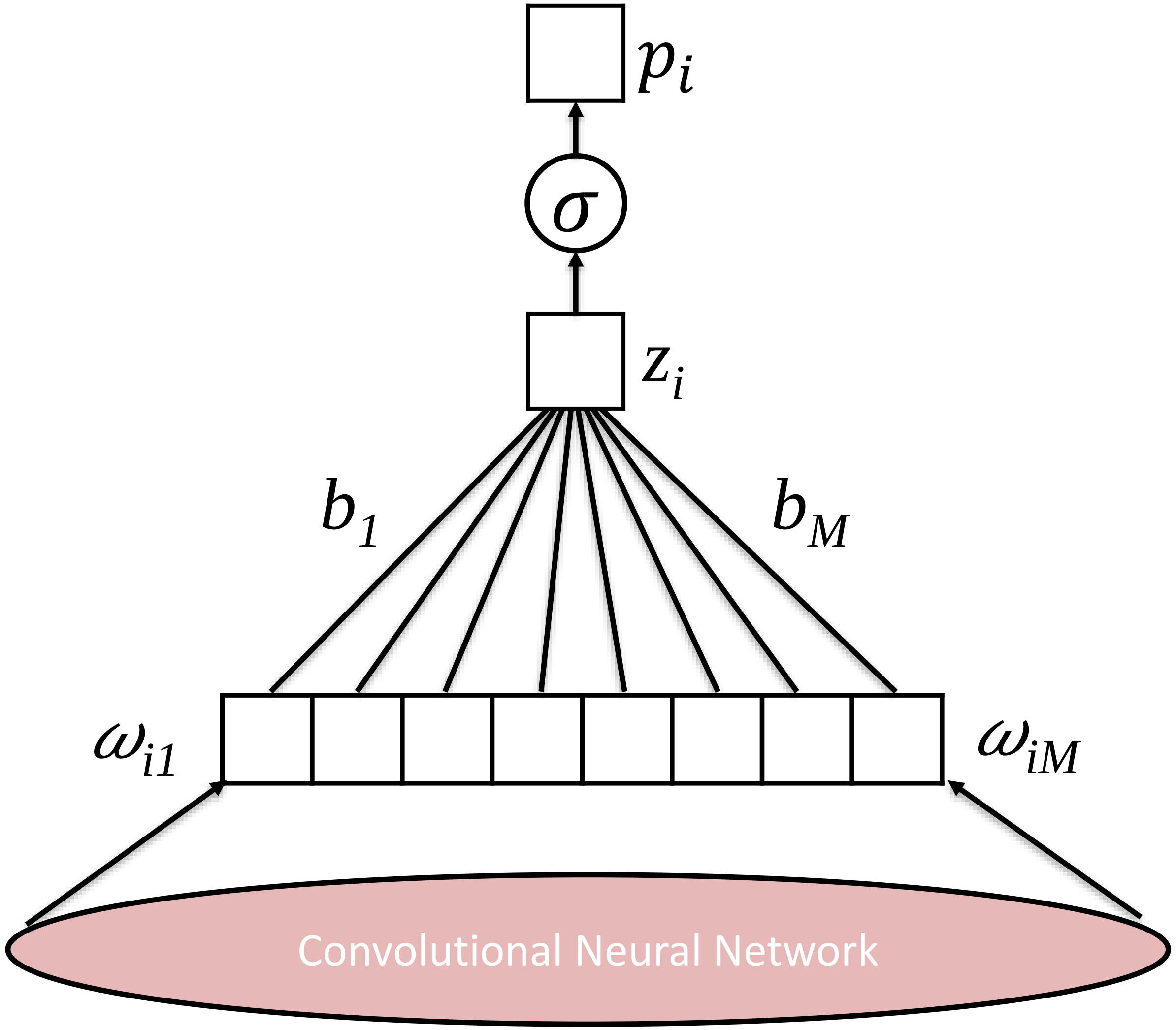
Two-Class Predictions



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

In logistic regression, x_i is a vector of predictor variables

Two-Class Predictions



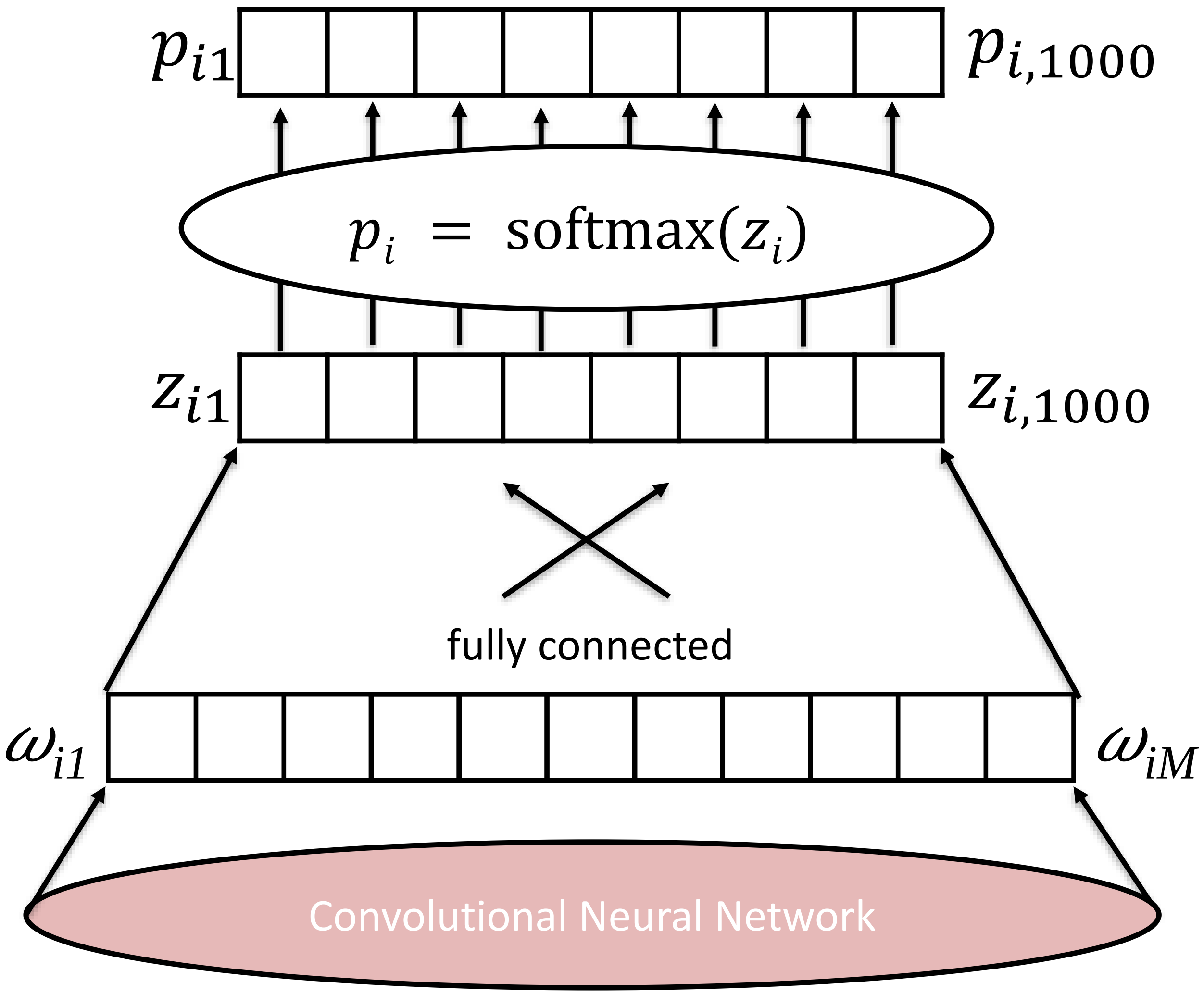
$$\sigma(z_i) = \frac{e^{z_i}}{1 + e^{z_i}}$$

When identifying diabetic retinopathy, consider ω_i , a vector of high-level features extracted by the CNN

Classifier Output:
Multi-Class (ImageNet)

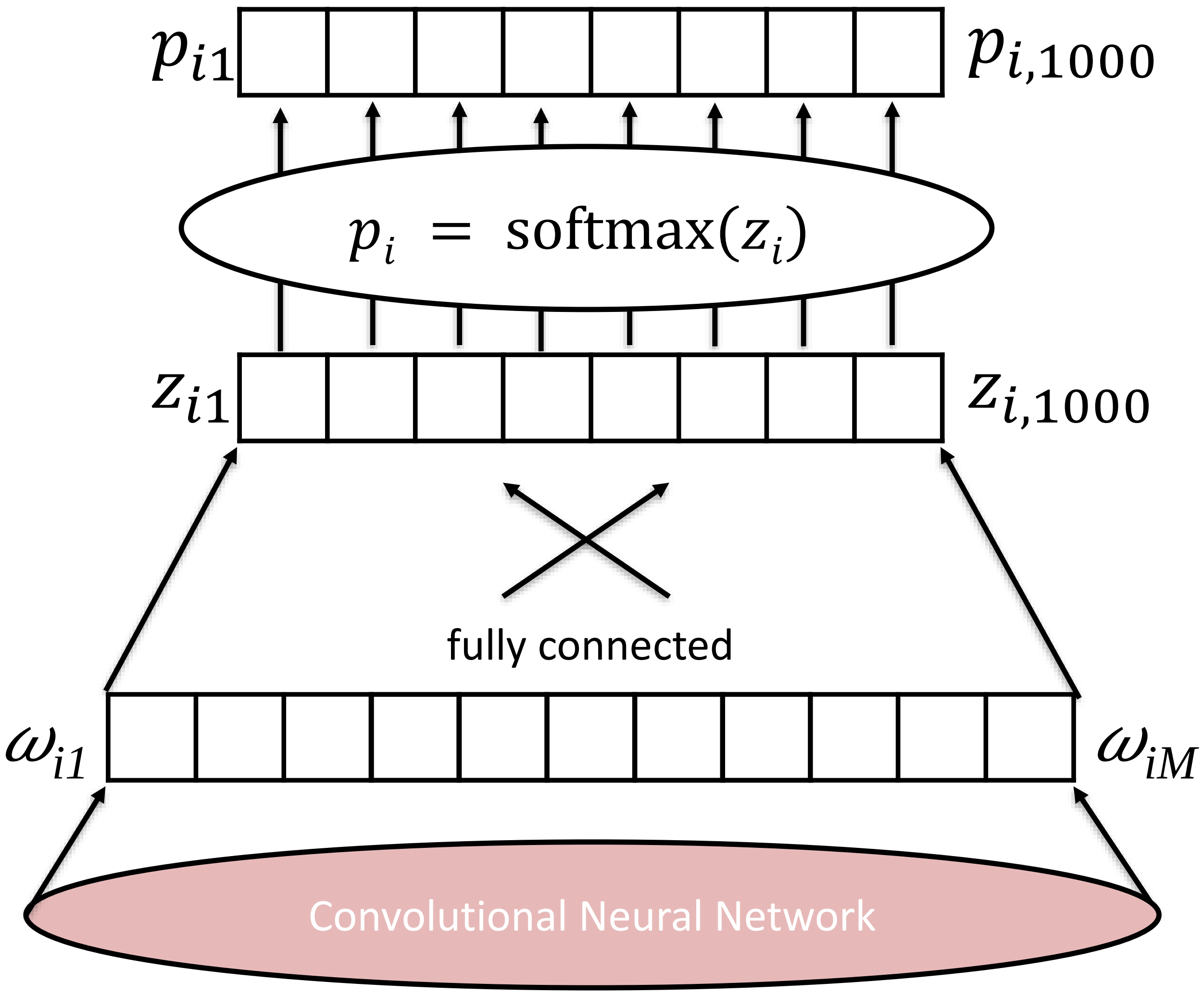
Image Label?
(1000 classes)

Multi-Class Predictions



ω_i is a vector of high-level features extracted by the CNN

Multi-Class Predictions



$$p_{ij} = \frac{e^{z_{ij}}}{\sum_{c=1}^{1000} e^{z_{ic}}}$$

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

z_i are log-odds scores for each class

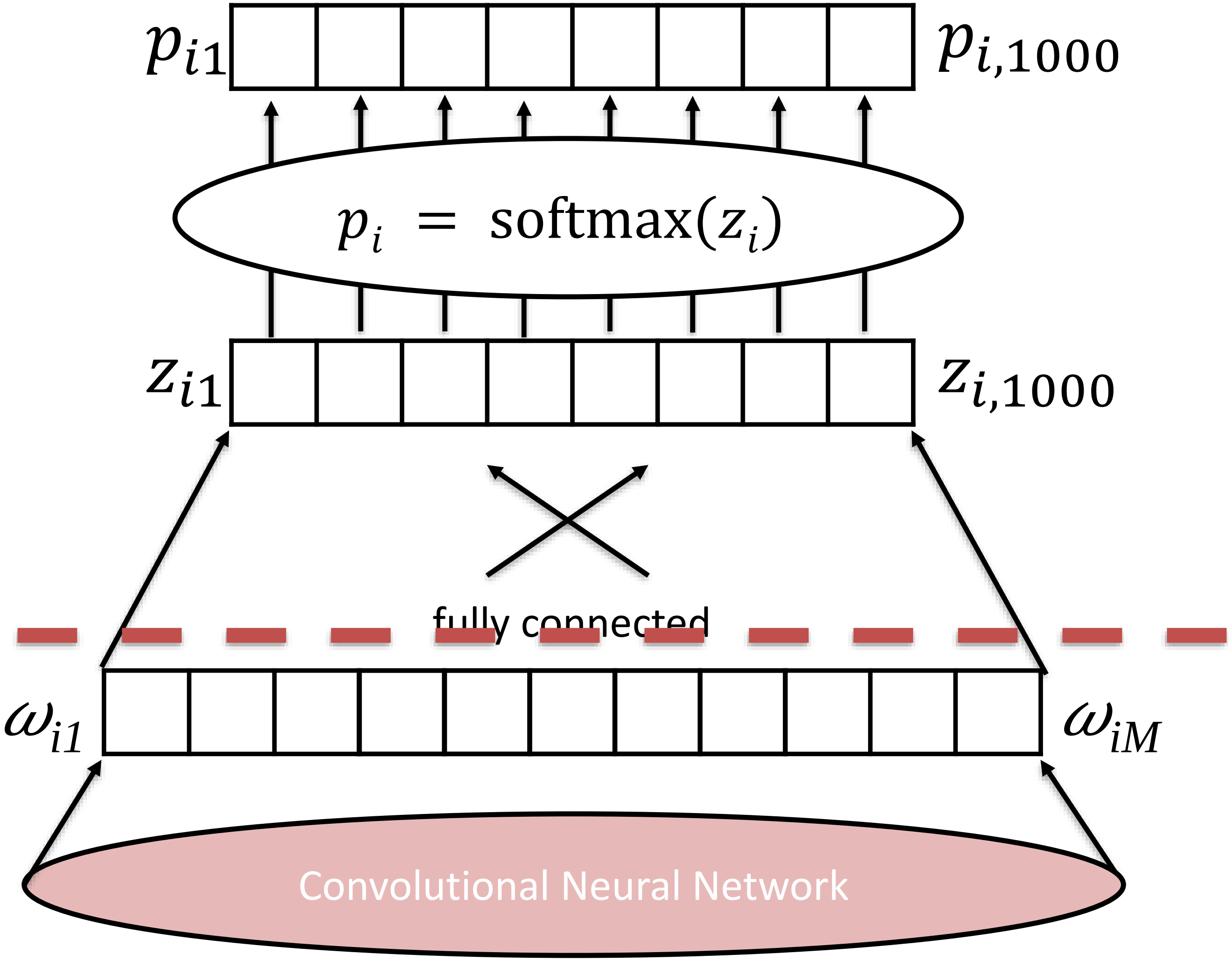
ω_i is a vector of high-level features extracted by the CNN

Classifier Output:
Multi-Class (Lesion Type)

Type of Skin Lesion?
(757 classes)

Esteva et al. *Nature* (2017)

Step 1: Modify the Architecture



1000 training classes

757 training classes

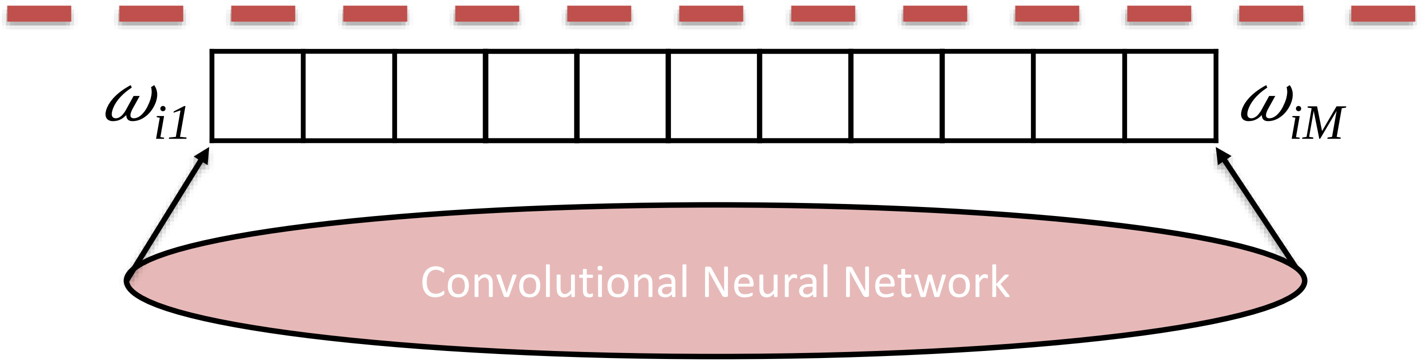
ω_i is a vector of high-level features extracted by the CNN

Step 1: Modify the Architecture

1000 training classes

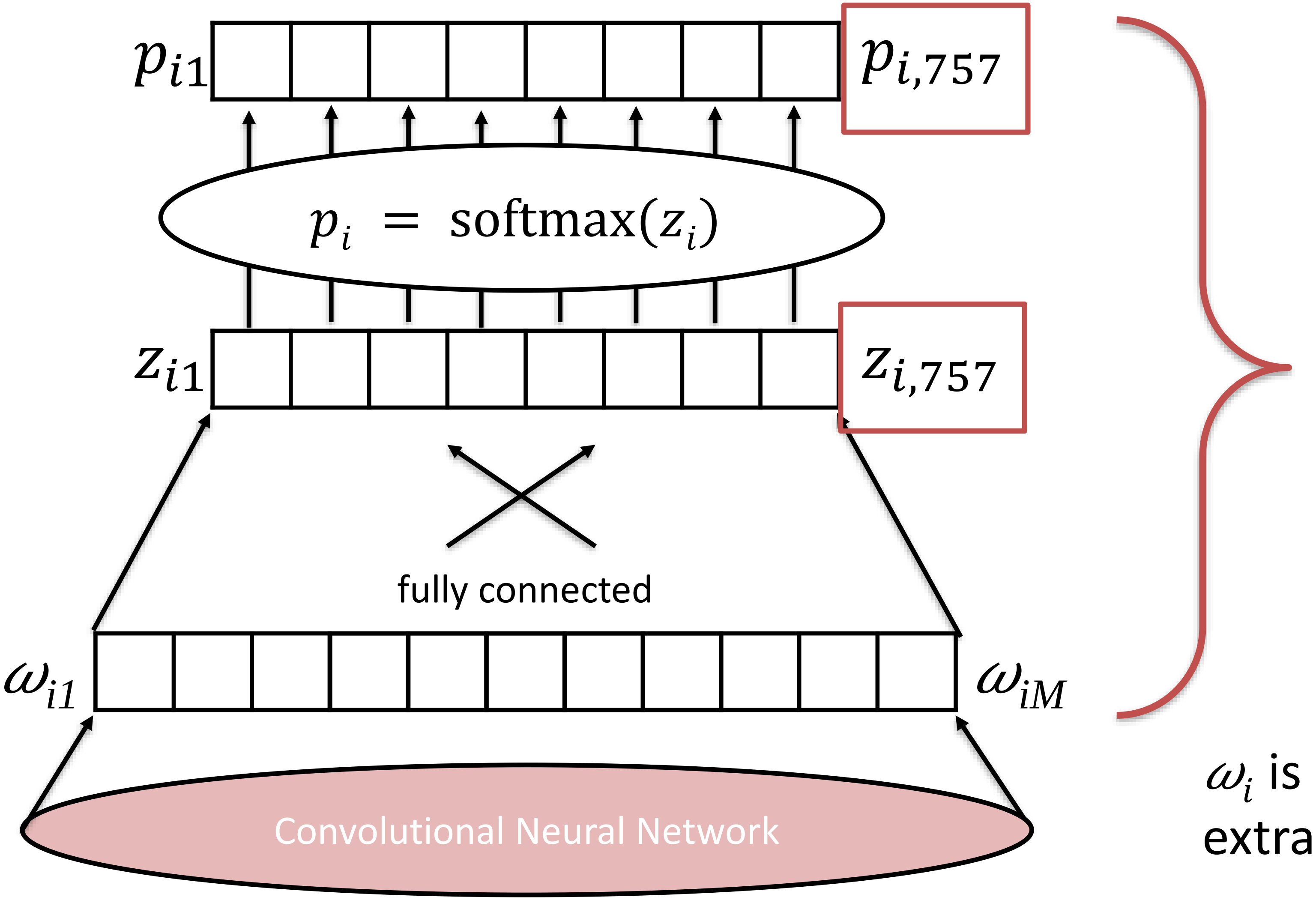
↓

757 training classes



ω_i is a vector of high-level features extracted by the CNN

Step 1: Modify the Architecture

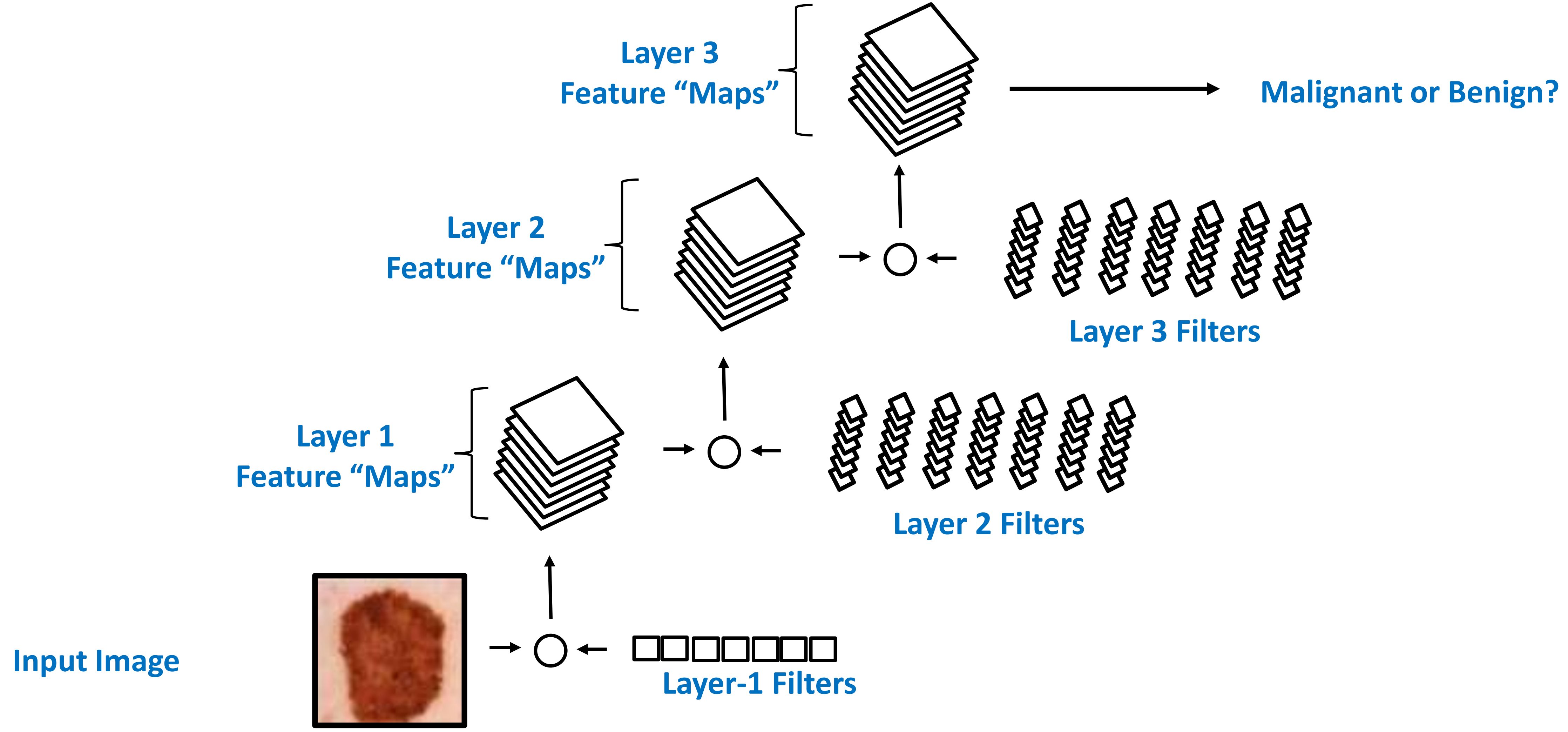


New layers with randomly initialized weights

ω_i is a vector of high-level features extracted by the CNN

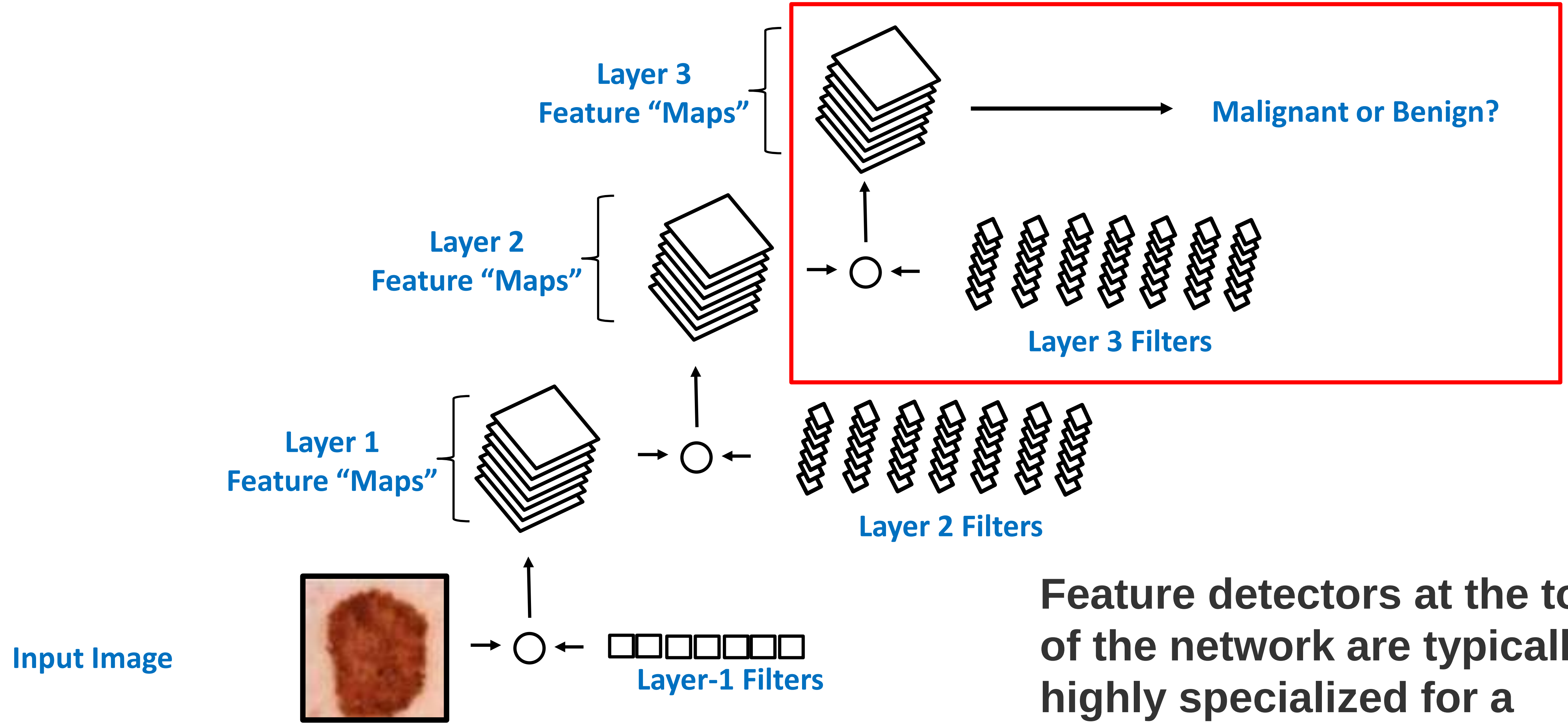
Step 2: Fine-tune the Parameters

“pre-training”, or “transfer learning”



Step 2: Fine-tune the Parameters

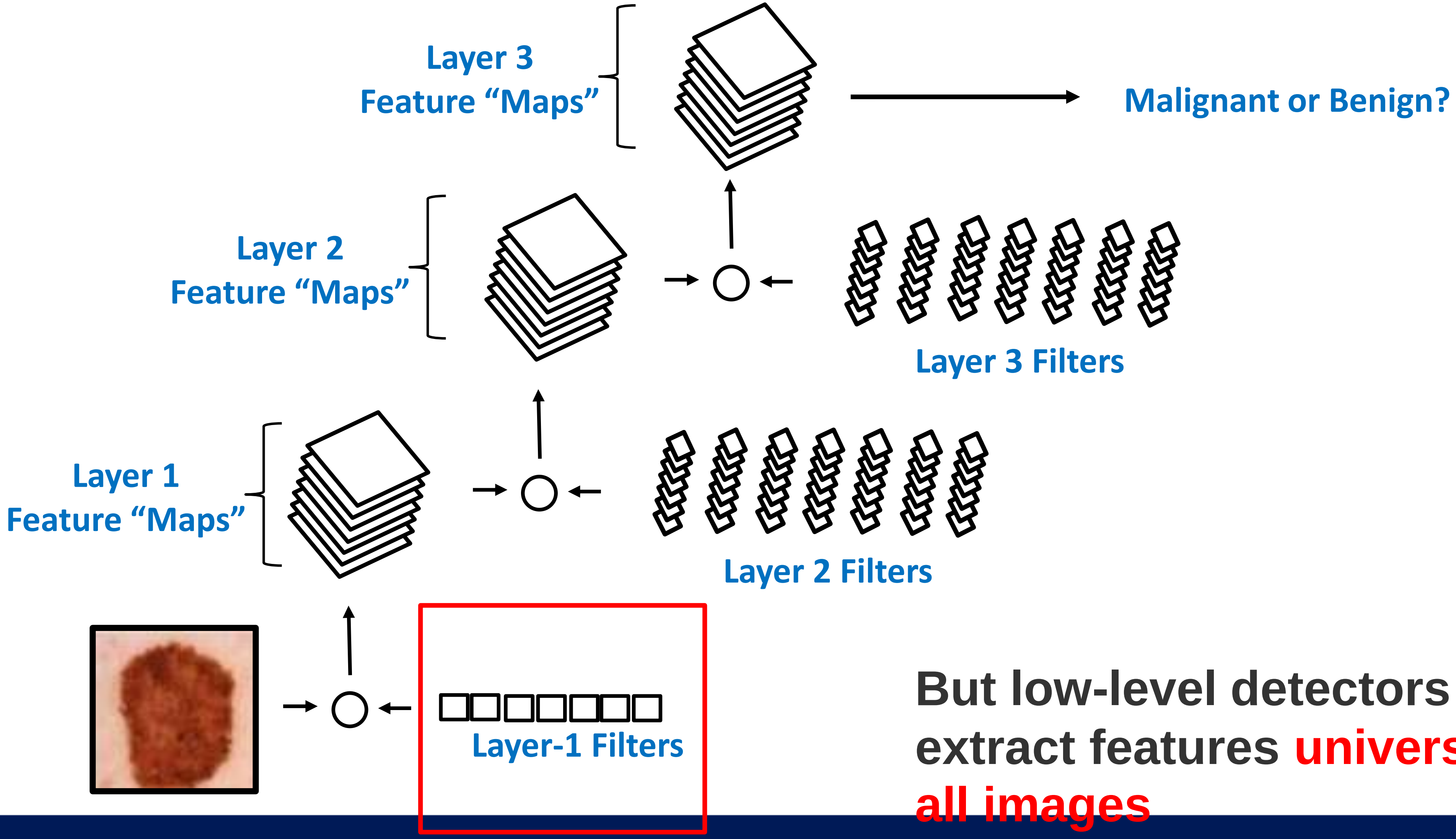
“pre-training”, or “transfer learning”



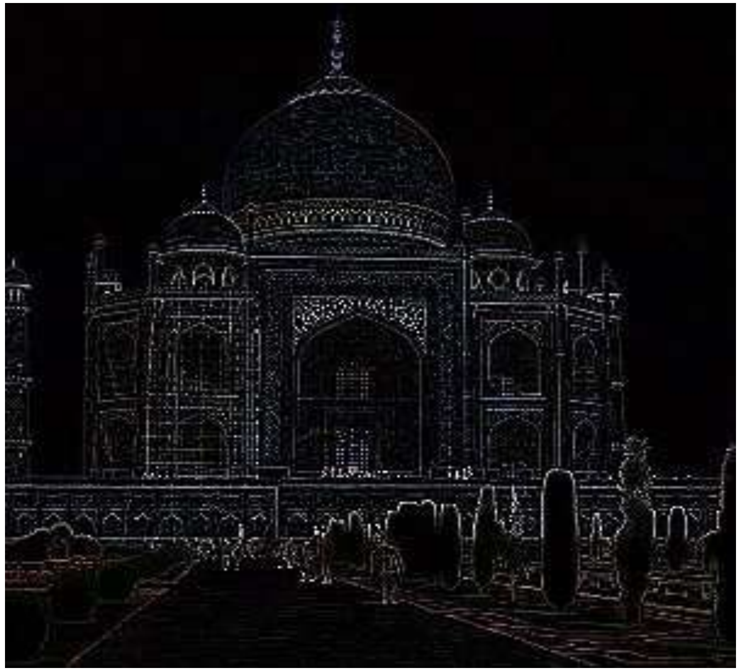
Feature detectors at the top of the network are typically highly specialized for a particular task

Step 2: Fine-tune the Parameters

“pre-training”, or “transfer learning”



But low-level detectors extract features **universal to all images**



https://docs.gimp.org/en/plug-in-convmatrix.html

A filter that detects edges may be useful for many classification tasks.

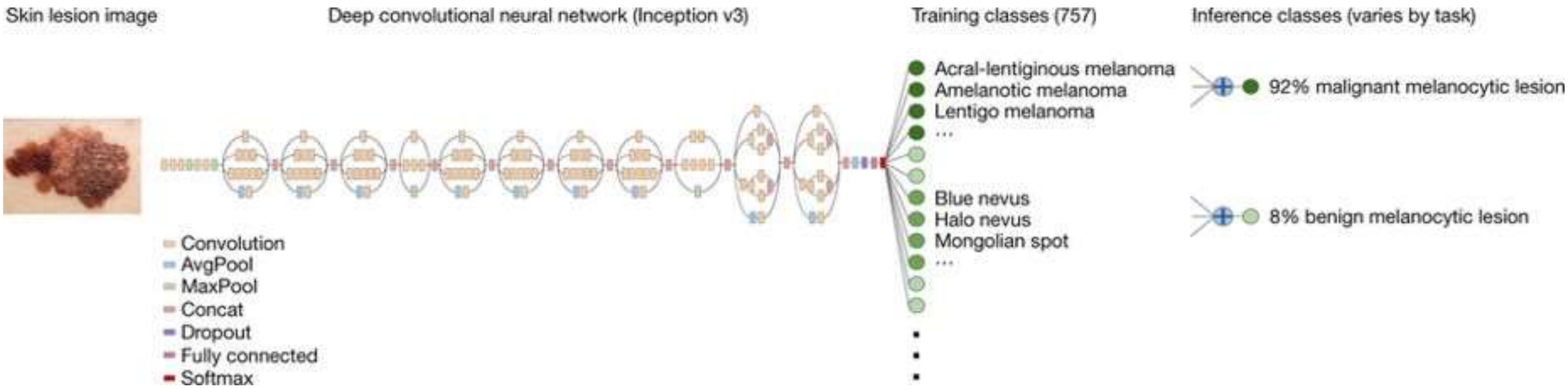
Pre-training, in brief

1) fine-tuning a pre-trained model tends to be **at least as good as learning from scratch**
   (empirical result)

2) freeze early layers and fine-tune later layers
   more data → fine-tune more layers

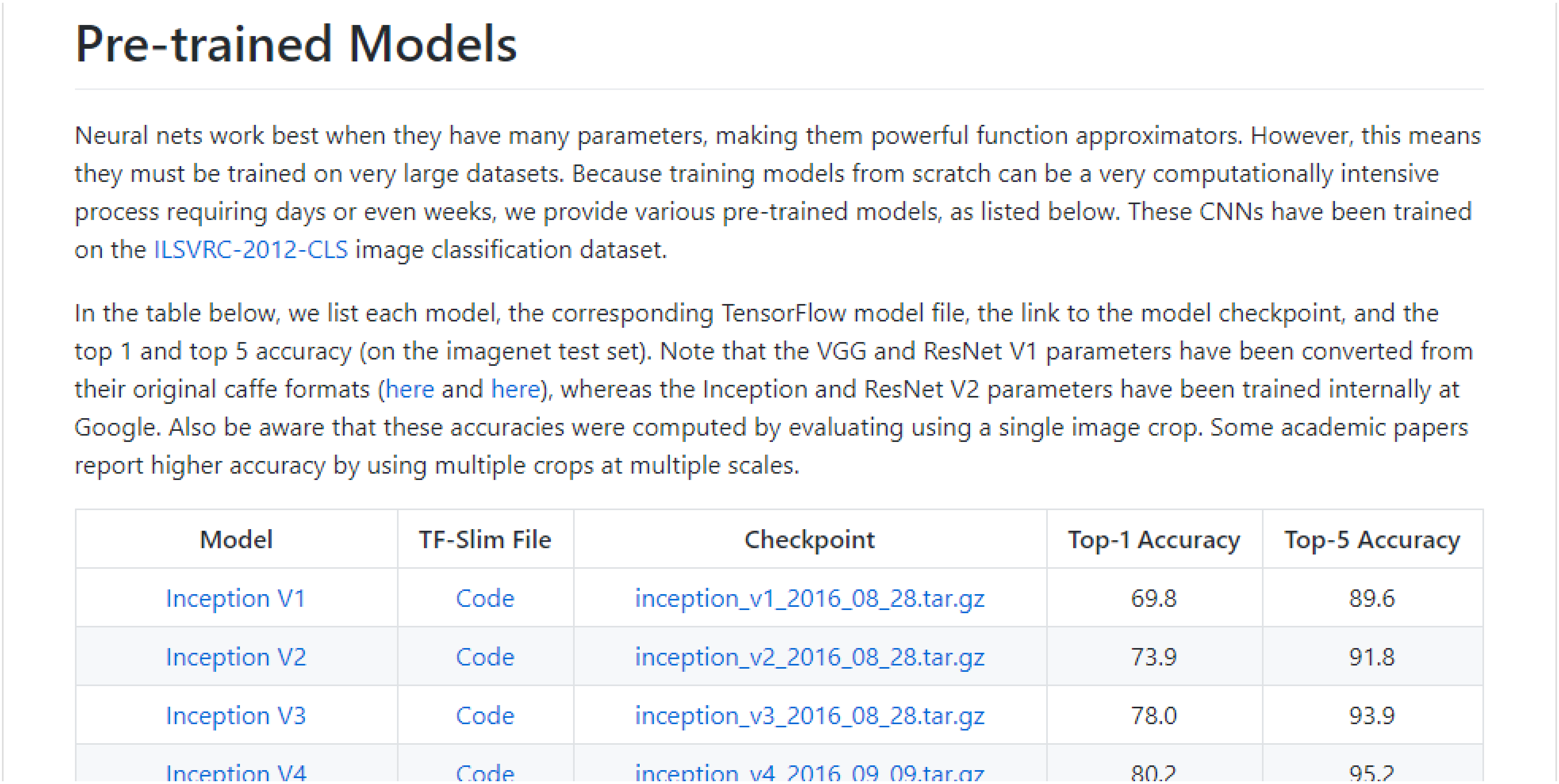
3) best tuning depth depends on the application, and should be explored

Repurposing the Inception v3 CNN



- Begin with a model trained on ImageNet (to classify everyday images)
- Modify the architecture to match the new number of training classes
- Fine-tune parameters using images of skin lesions

Inception v3 and many other models are freely available



Pre-trained Models

Neural nets work best when they have many parameters, making them powerful function approximators. However, this means they must be trained on very large datasets. Because training models from scratch can be a very computationally intensive process requiring days or even weeks, we provide various pre-trained models, as listed below. These CNNs have been trained on the ILSVRC-2012-CLS image classification dataset.

In the table below, we list each model, the corresponding TensorFlow model file, the link to the model checkpoint, and the top 1 and top 5 accuracy (on the imagenet test set). Note that the VGG and ResNet V1 parameters have been converted from their original caffe formats (here and here), whereas the Inception and ResNet V2 parameters have been trained internally at Google. Also be aware that these accuracies were computed by evaluating using a single image crop. Some academic papers report higher accuracy by using multiple crops at multiple scales.

Model	TF-Slim File	Checkpoint	Top-1 Accuracy	Top-5 Accuracy
Inception V1	Code	inception_v1_2016_08_28.tar.gz	69.8	89.6
Inception V2	Code	inception_v2_2016_08_28.tar.gz	73.9	91.8
Inception V3	Code	inception_v3_2016_08_28.tar.gz	78.0	93.9
Inception V4	Code	inception_v4_2016_09_09.tar.gz	80.2	95.2

TF-Slim Code: Defines the model architecture

Checkpoint File: Trained model parameters

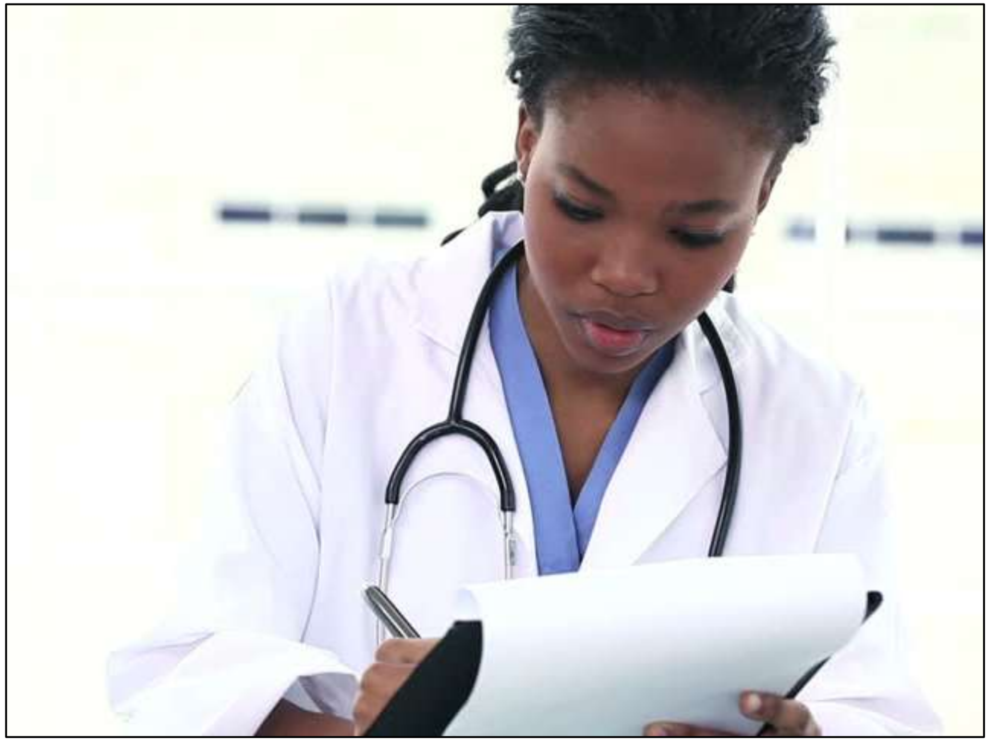
https://github.com/tensorflow/models/tree/master/research/slim#Pretrained

What are the labels?

“GROUND TRUTH” IN MEDICINE

Esteva et al: Two Types of Labels

All images: dermatologists' annotations



Some images: biopsy results

Two Rounds of Evaluation

1. Model development: predict dermatologists’ annotations:
   - Three-class disease partition
   - Nine-class disease partition

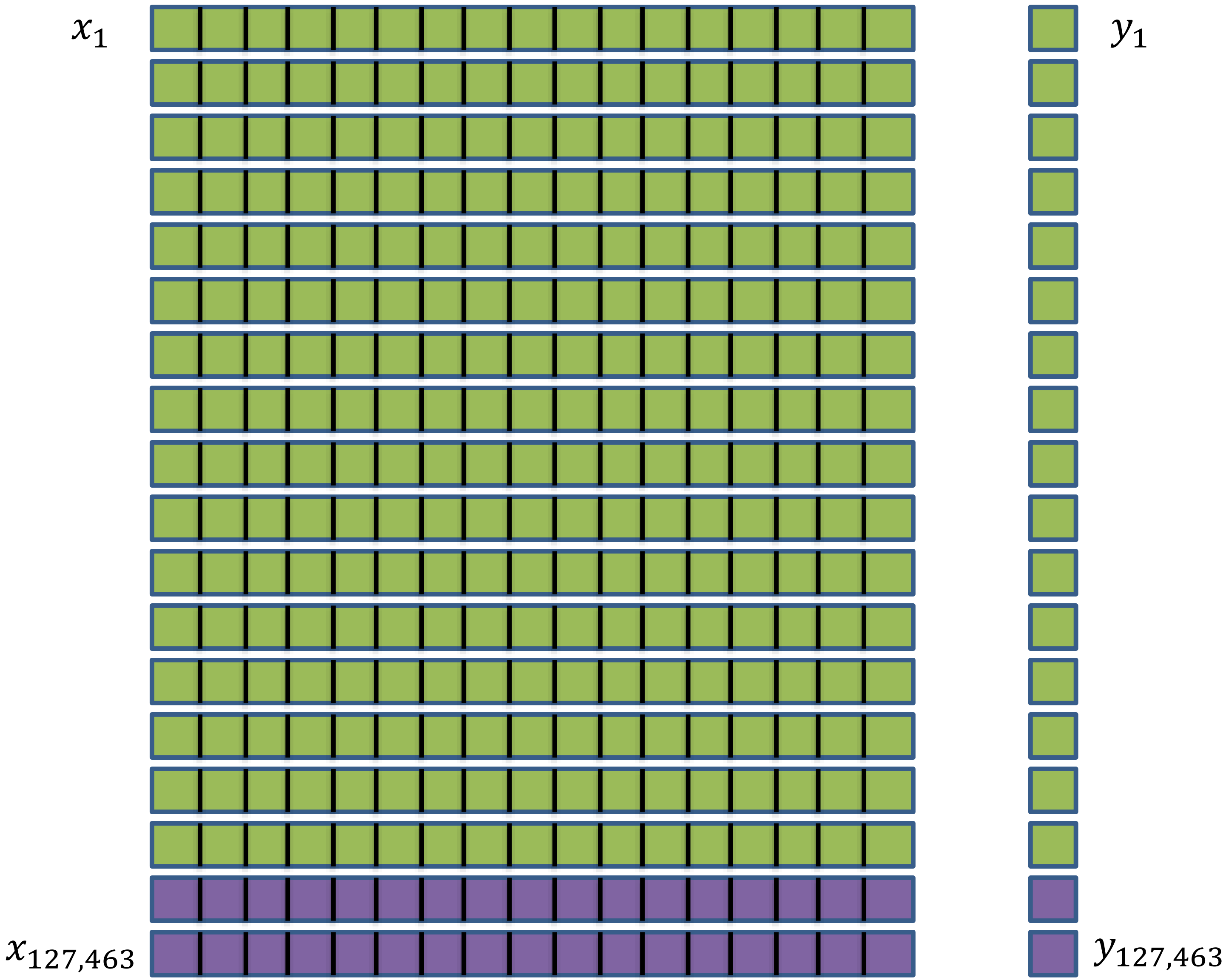
2. Model evaluation: predict biopsy result (benign vs malignant)
   - Keratinocyte carcinoma vs benign seborrheic keratosis
   - Malignant melanoma vs benign nevus
     - Standard images
     - Dermoscopy

Model Development:

Predict dermatologists' annotations

- 9-fold cross-validation
  - 757 training classes derived from dermatologists' annotations
  - 3 and 9-class validation partitions
  - two dermatologists

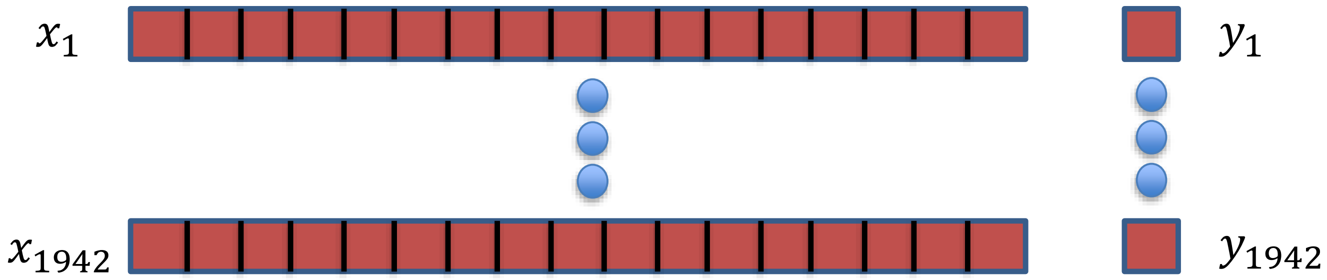
training set **validation set**



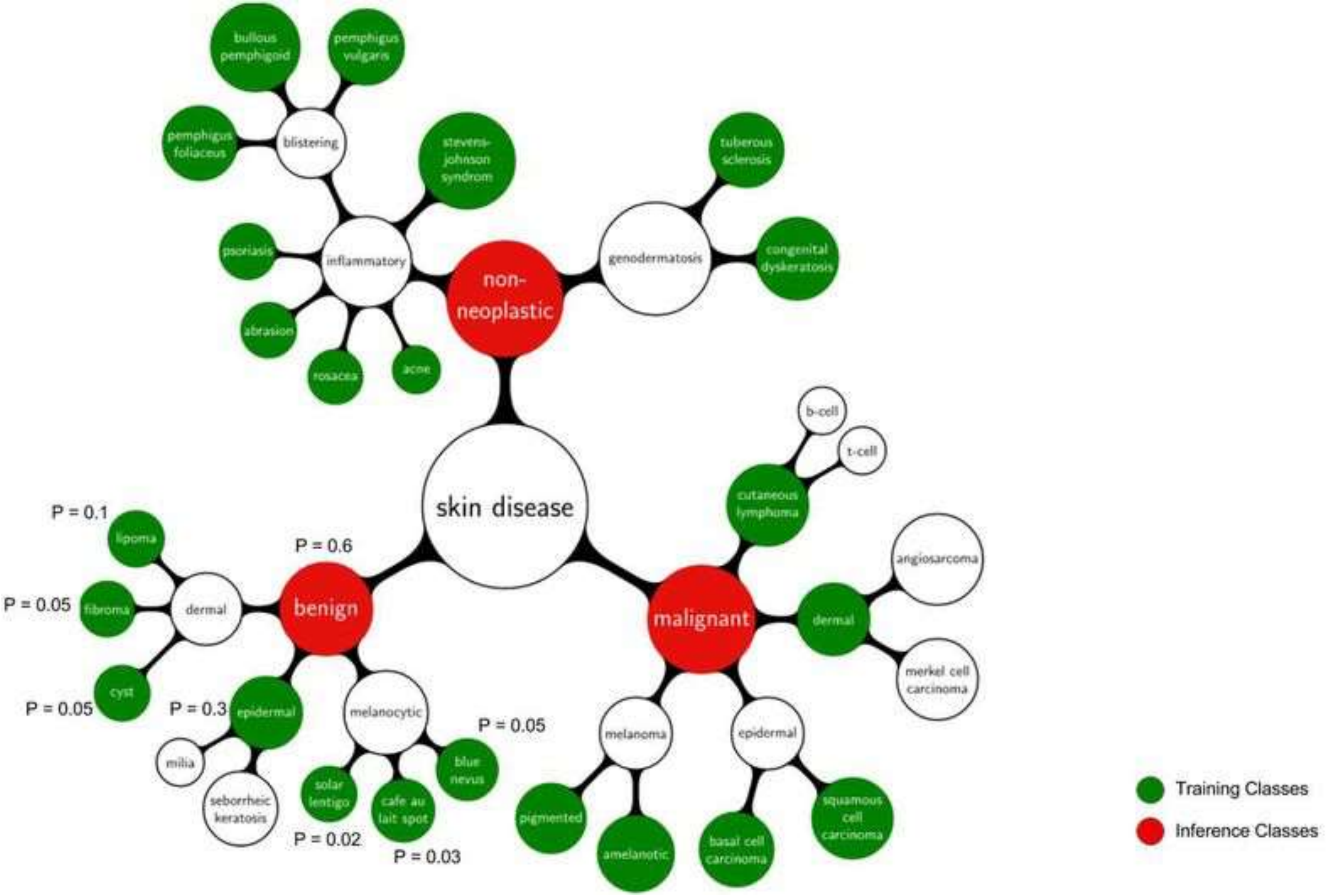
Model Evaluation: Predict Biopsy Result

Performance of the trained model is compared to 21 dermatologists on a test set of biopsy-proven images

test set of 1942 biopsy-proven images



Specifying training classes based on taxonomy of lesions

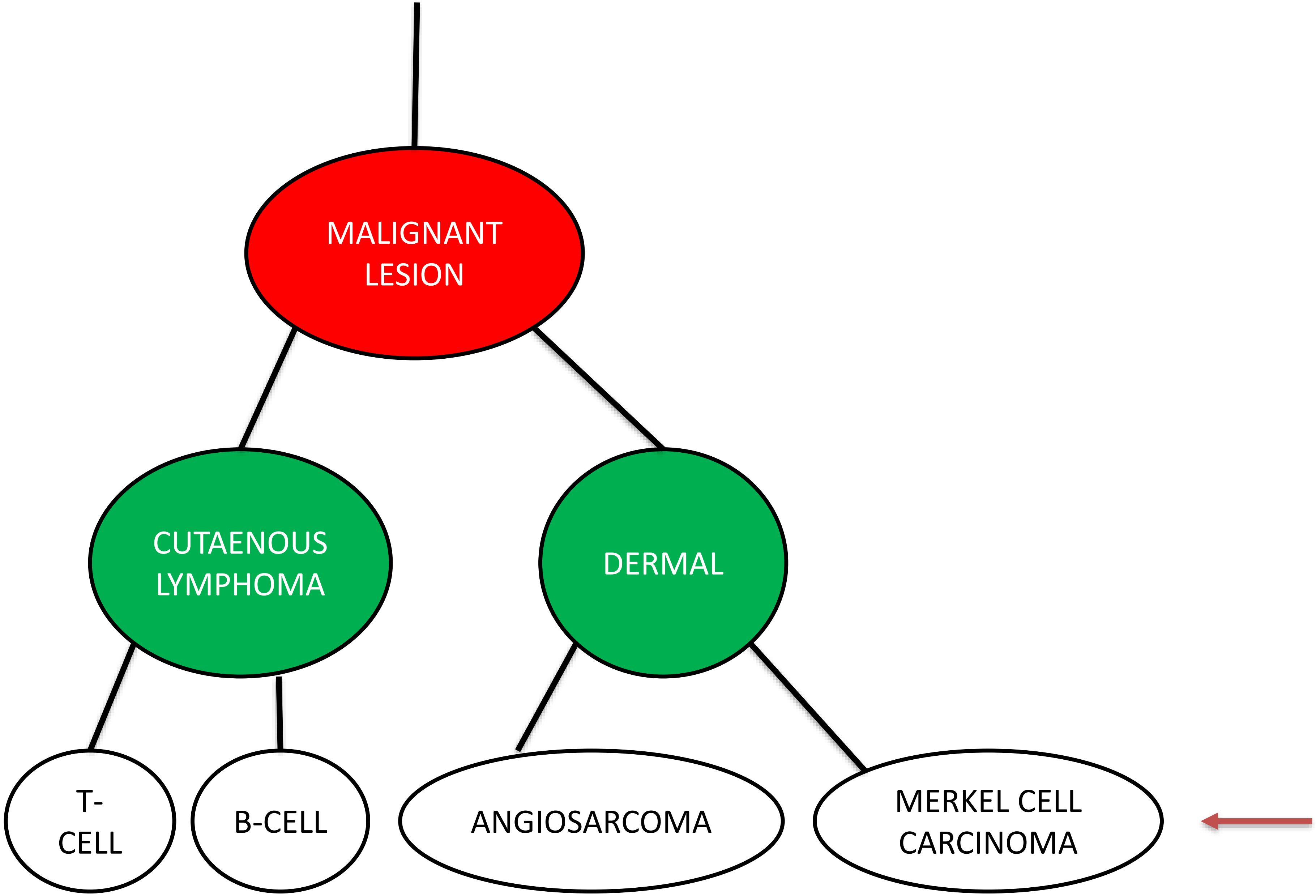


Disease Partitioning Algorithm:

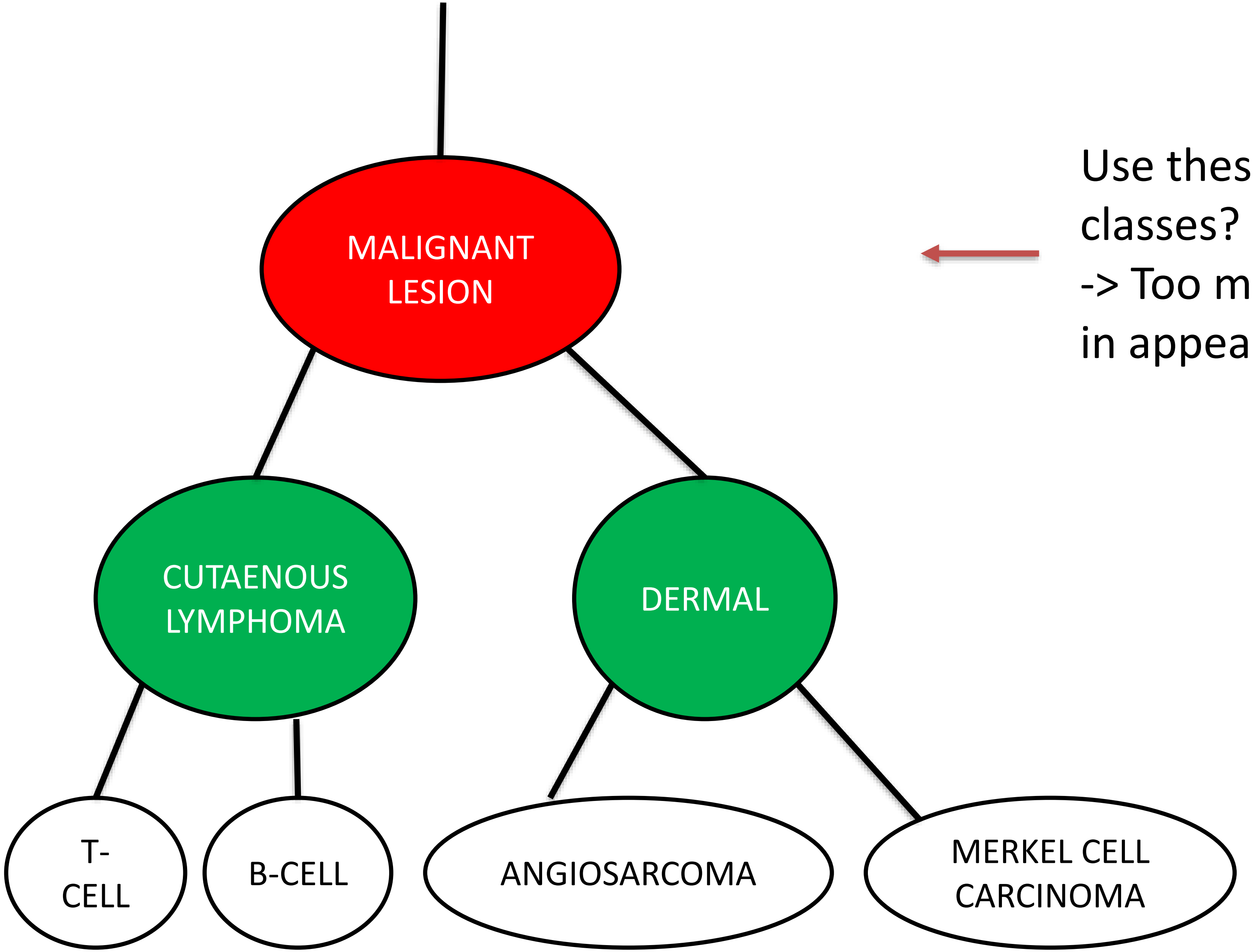
- Ascend the tree until the current node contains <1000 images across all child nodes. Add these images as a distinct training class.

- This resulted in 757 training classes.

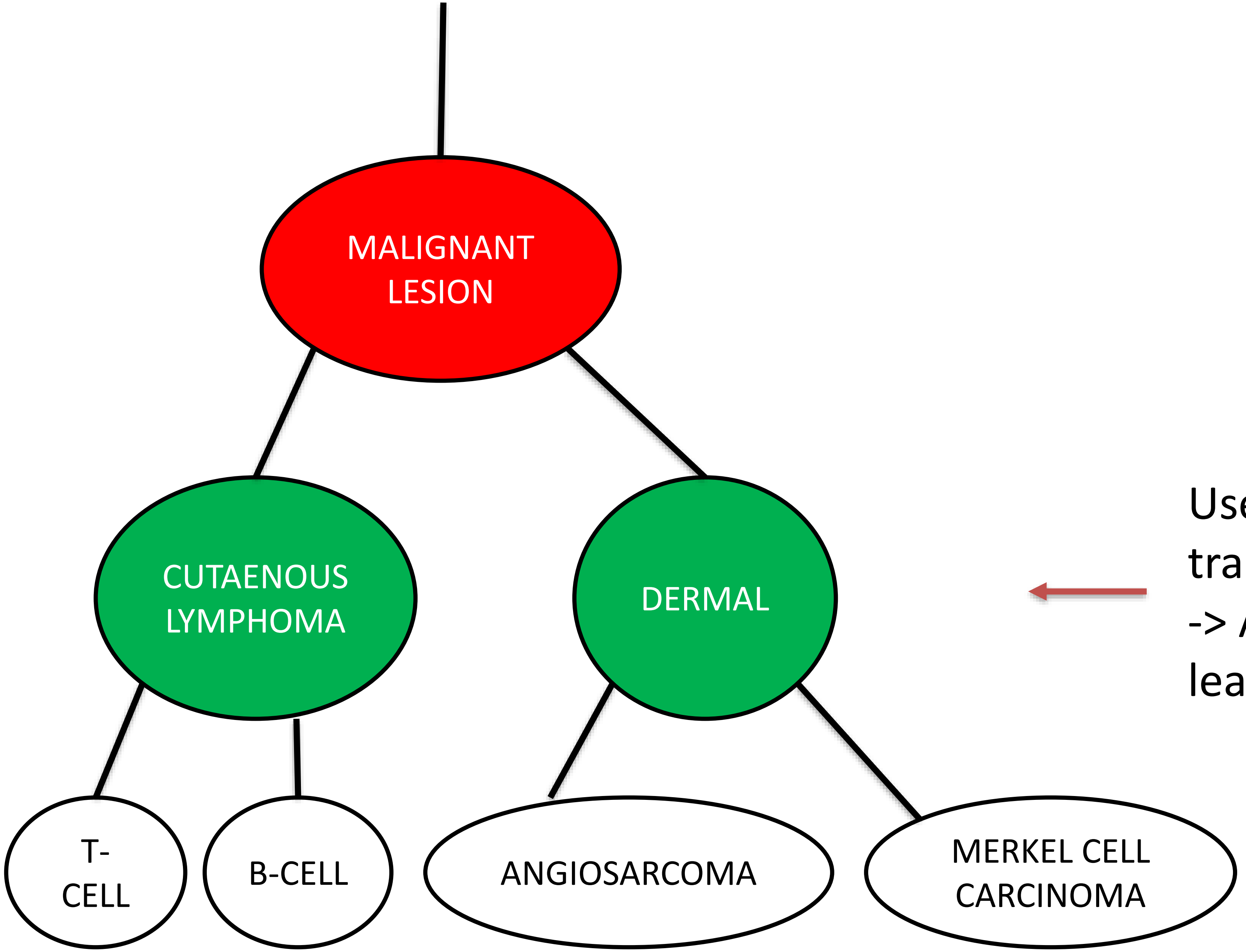
- However, performance was assessed based on higher-level nodes.



Use these as training classes?
-> Too few examples to learn effectively



Use these as training classes?
-> Too much variability in appearance

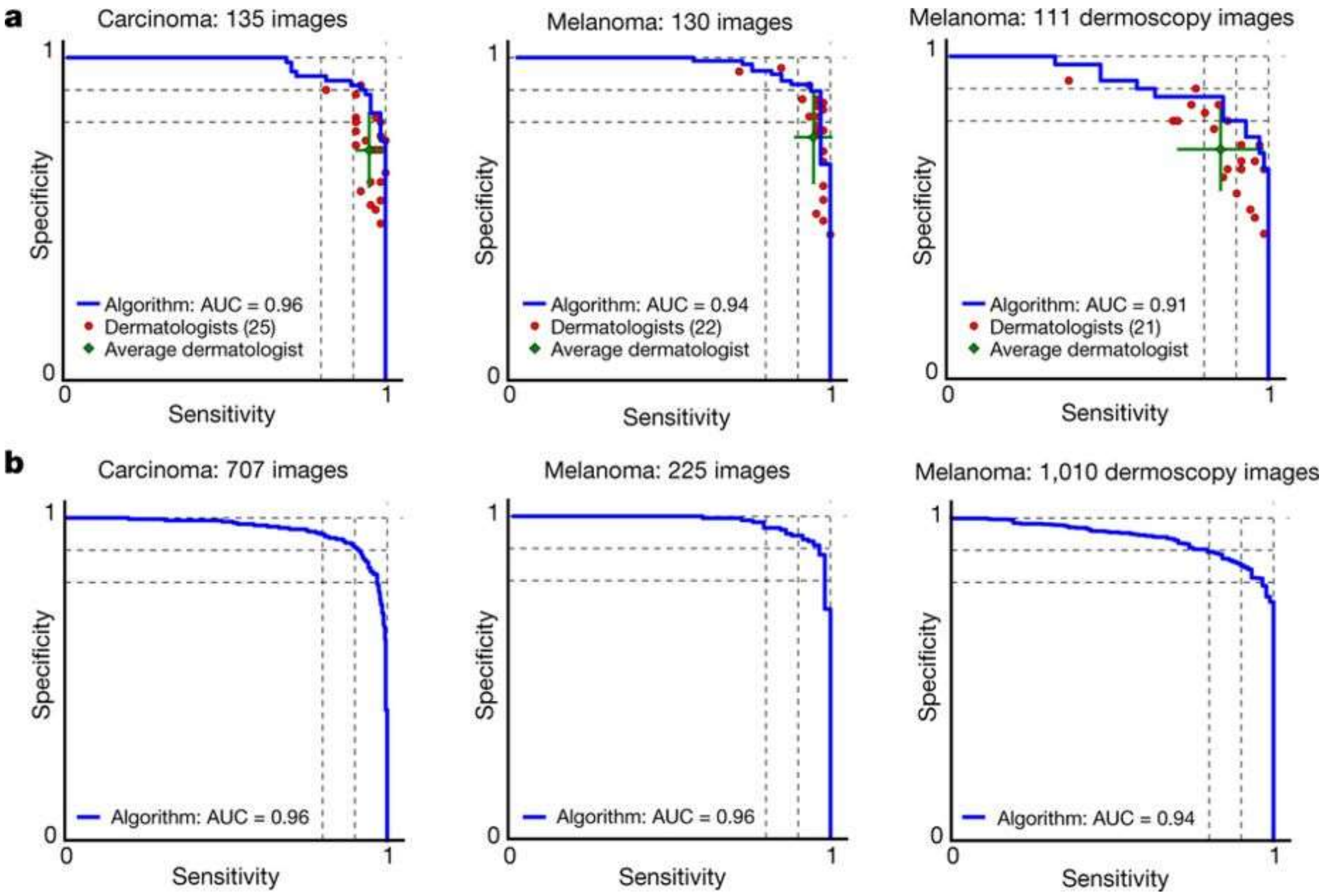


Use these as training classes.
-> Allows effective learning

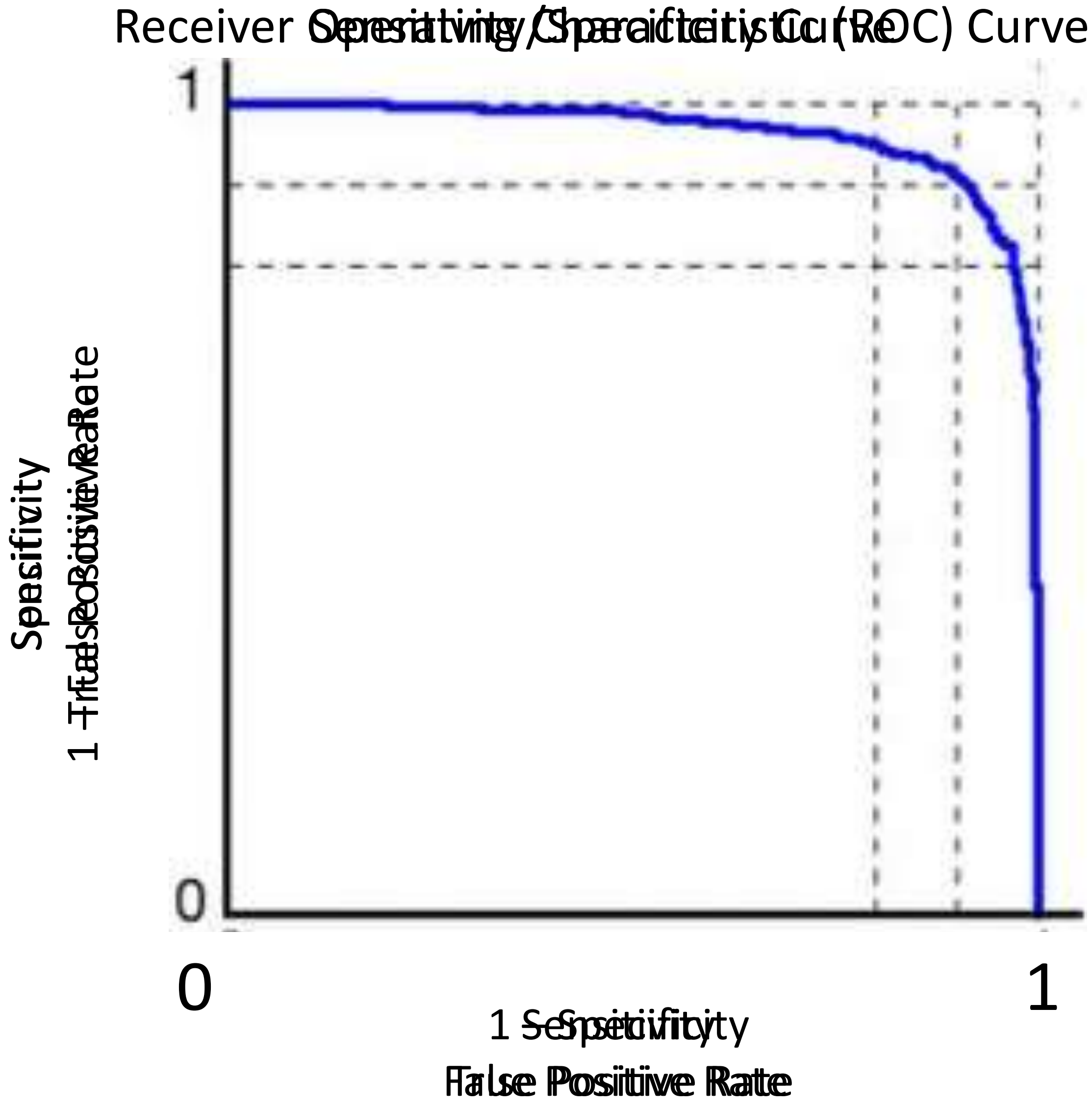
Interpreting the ROC Curve

CLASSIFICATION RESULTS

Results: CNN Performance vs Dermatologists



Evaluation Measures: Classification



Sensitivity, or True Positive Rate:

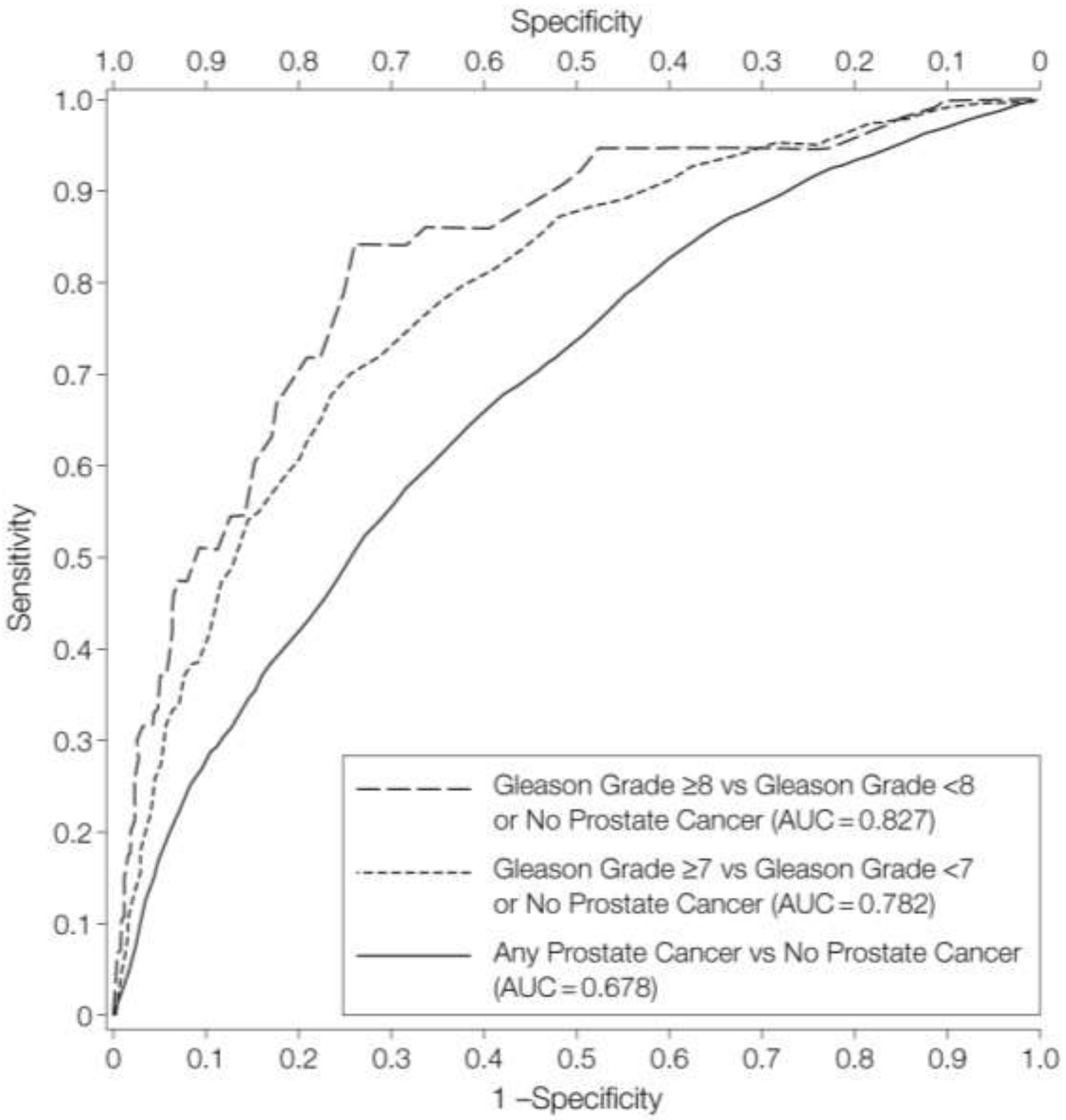
$$\frac{\text{true positives}}{\text{all condition positives}}$$

Specificity, or (1 – False Positive Rate):

$$\frac{\text{true negatives}}{\text{all condition negatives}}$$

Accuracy:

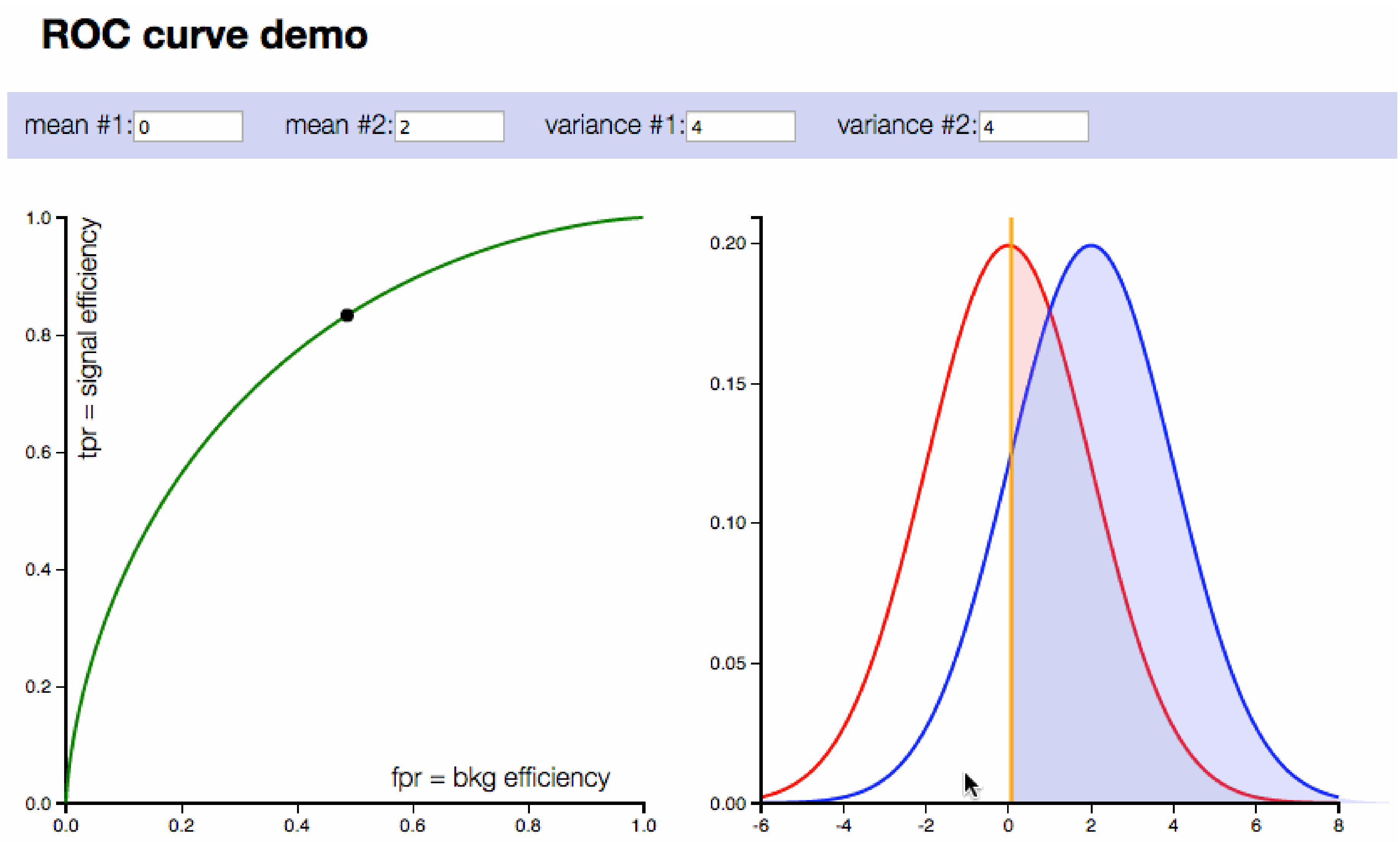
$$\frac{\text{true positives} + \text{true negatives}}{\text{total cases}}$$



Receiver Operating Characteristic Curve for Prostate-Specific Antigen (PSA)

Thompson IM, Ankerst DP, Chi C, et al. Operating Characteristics of Prostate-Specific Antigen in Men With an Initial PSA Level of 3.0 ng/mL or Lower. *JAMA.* 2005;294(1):66–70. doi:10.1001/jama.294.1.66

Set a “classification threshold” to distinguish between groups



ROC curve demo

mean #1: 0 mean #2: 2 variance #1: 4 variance #2: 4

http://arogozhnikov.github.io/2015/10/05/roc-curve.html

Once a threshold is set, we get a “confusion matrix”

	Condition Positive	Condition Negative
Prediction Positive	True Positive	False Positive
Prediction Negative	False Negative	True Negative

Sensitivity, or True Positive Rate:

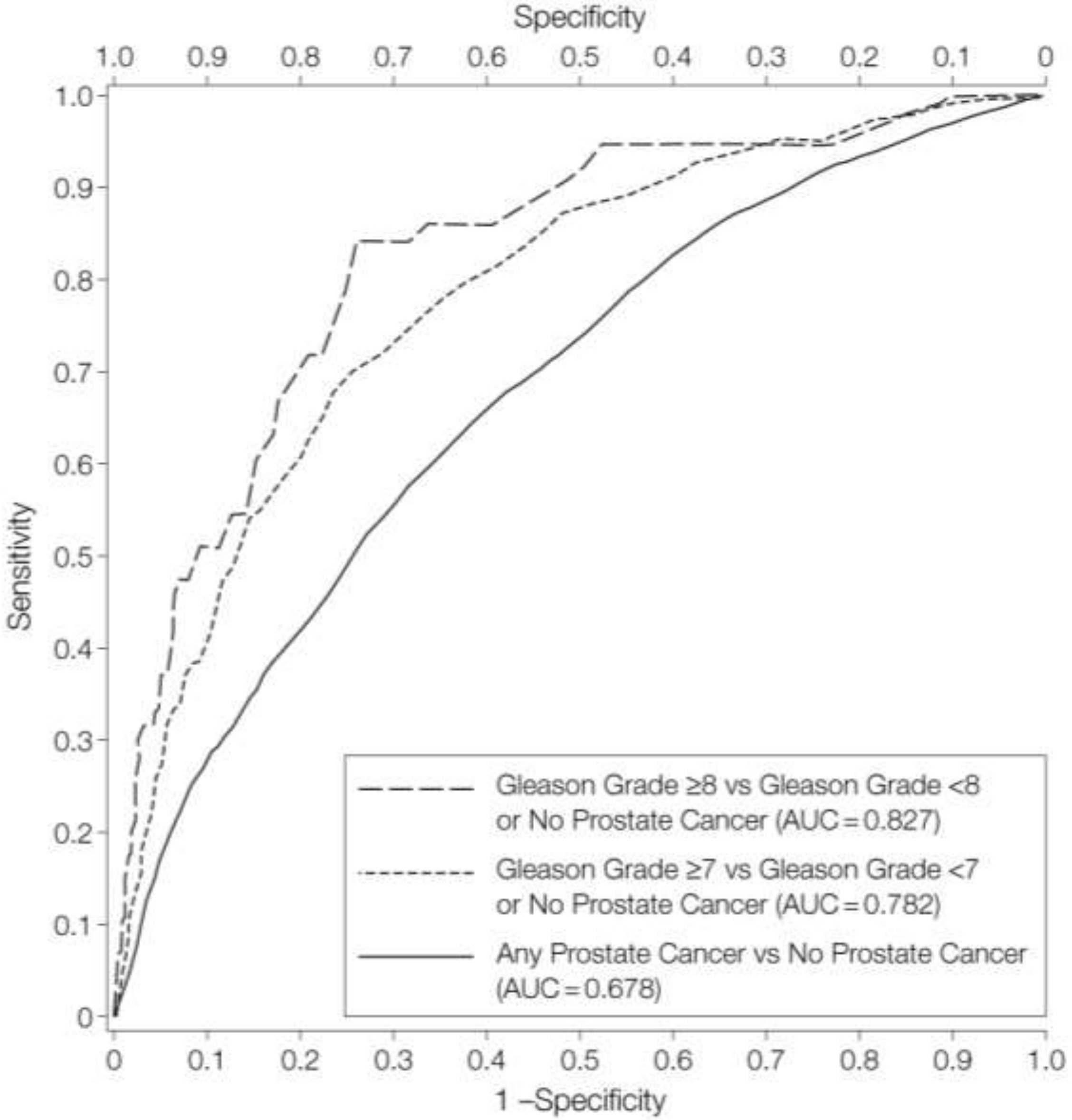
$$\frac{\text{true positives}}{\text{all condition positives}}$$

Specificity, or (1 – False Positive Rate):

$$\frac{\text{true negatives}}{\text{all condition negatives}}$$

Accuracy:

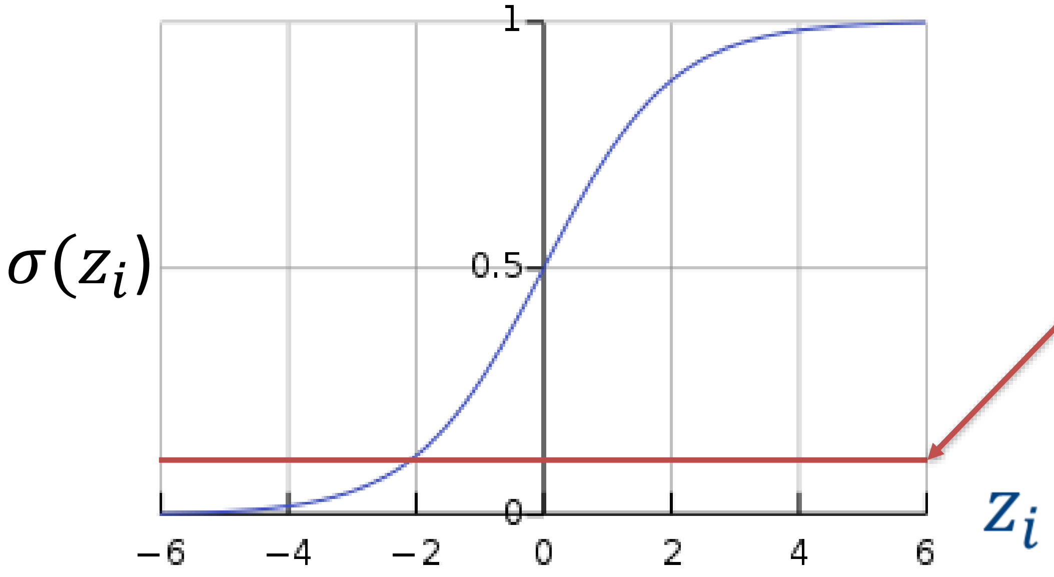
$$\frac{\text{true positives} + \text{true negatives}}{\text{total cases}}$$



1) Set a threshold on PSA
2) Make predictions:
    - Above threshold: cancer-positive
    - Below threshold: cancer-negative
3) Count true positives, true negatives, false positives, and false negatives
4) Calculate sensitivity and specificity
5) Plot point and repeat

Set a threshold on classifier predictions

$$p(y_i = 1|x_i) = \sigma(z_i)$$

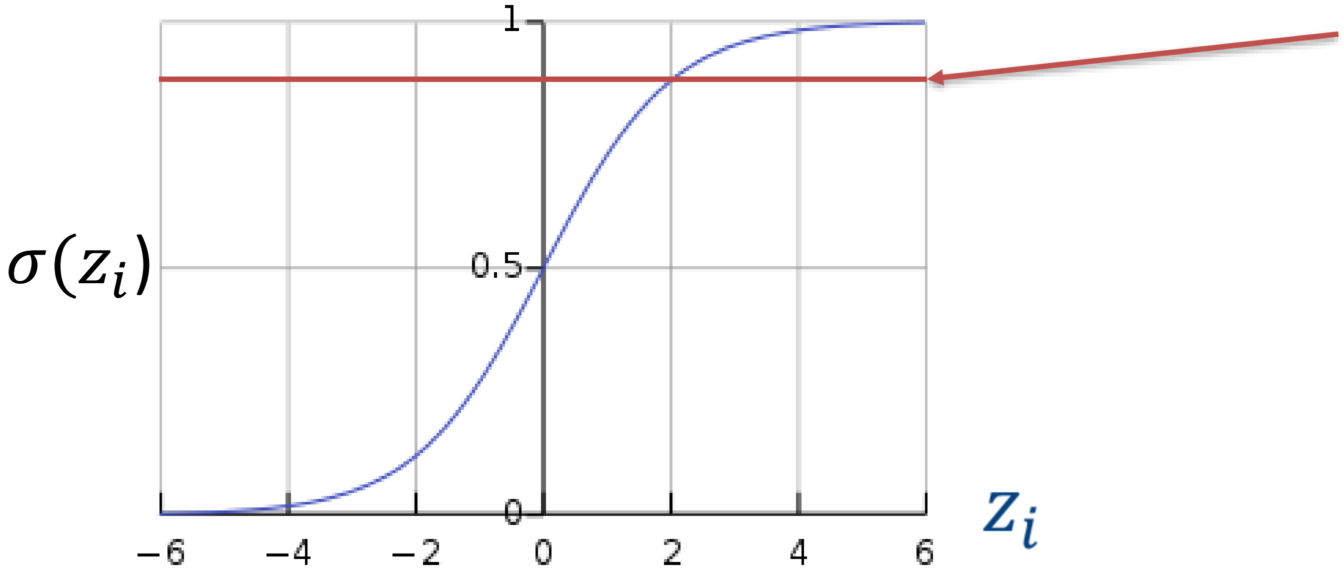


classification threshold

A low threshold favors sensitivity, because more points are predicted to be ones

Set a threshold on classifier predictions

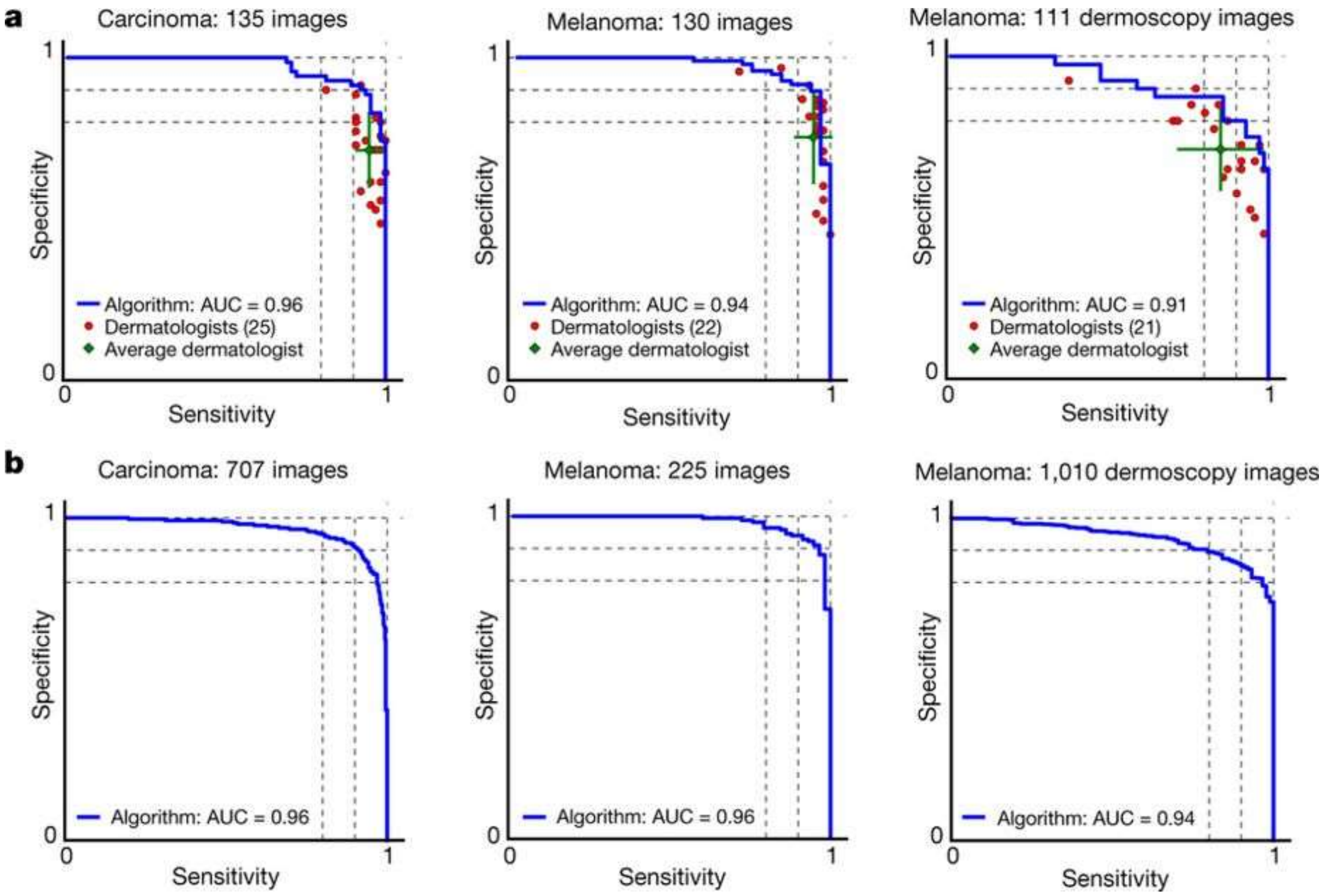
$$p(y_i = 1|x_i) = \sigma(z_i)$$



classification threshold

A high threshold favors specificity, because more points are predicted to be zeros

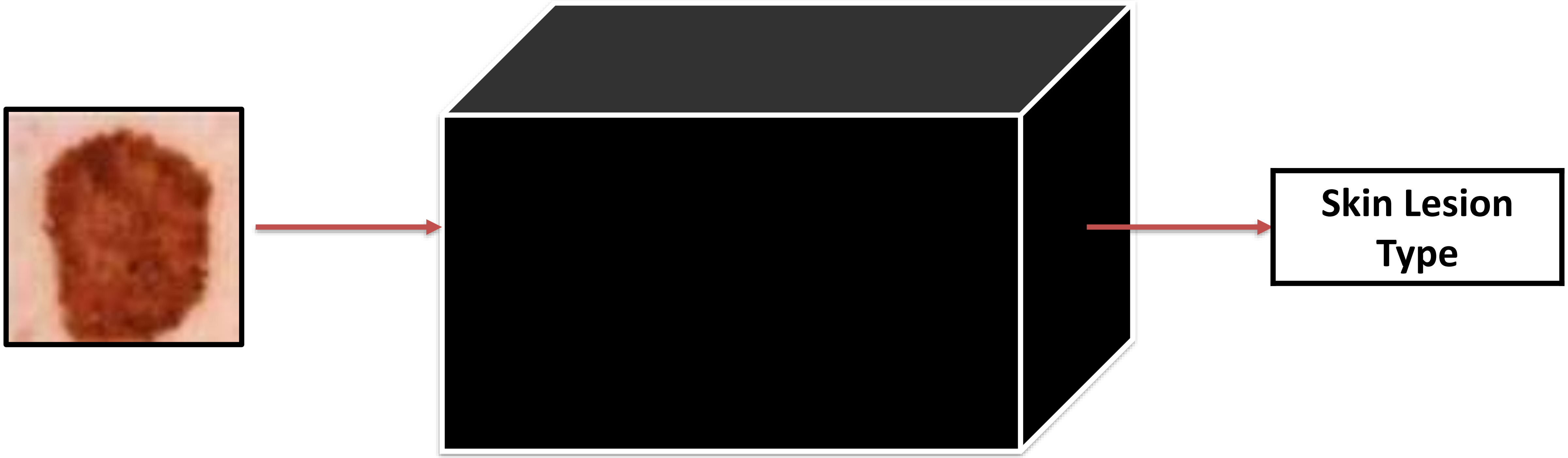
Results: CNN Performance vs Dermatologists



How do the authors attempt to look inside the “black box”?

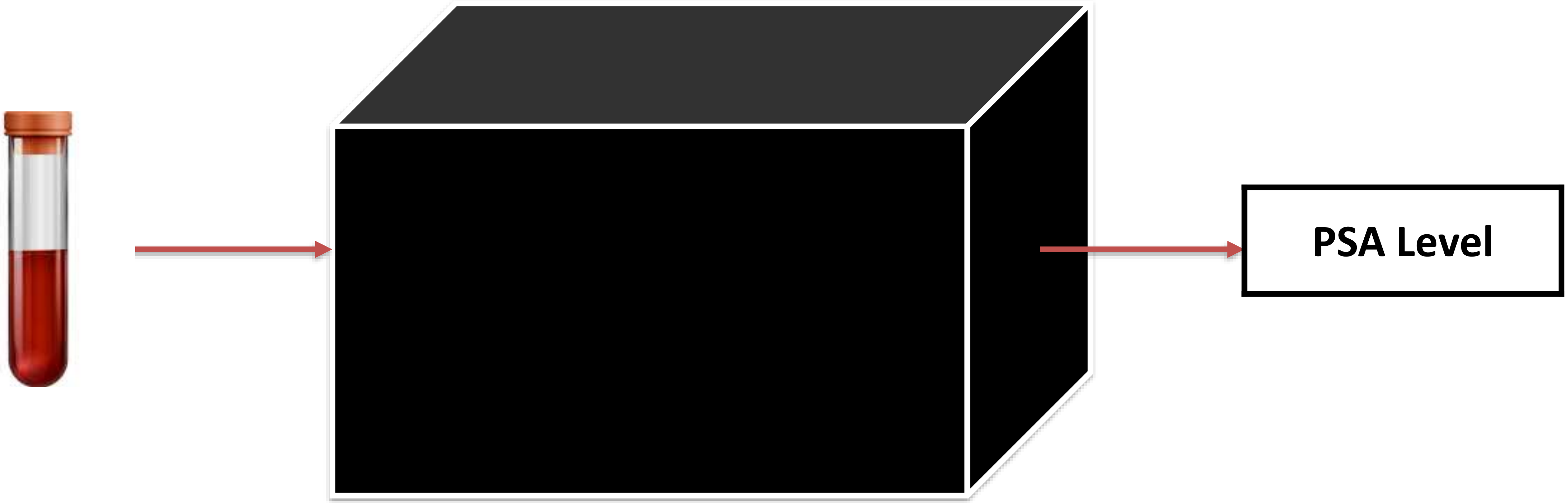
MODEL INTERPRETATION

Machine Learning: A Black Box?



Skin Lesion Type

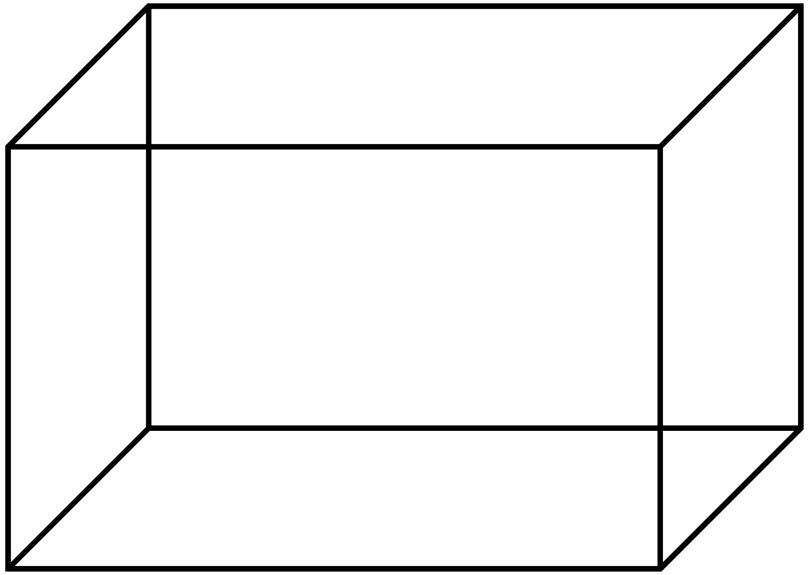
Prostate-specific antigen measurement: A Black Box?



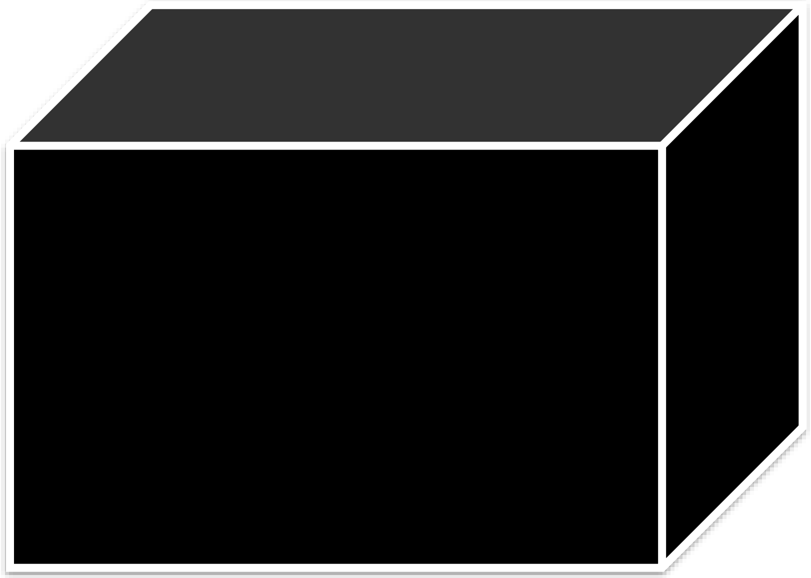
PSA Level

Two competing perspectives

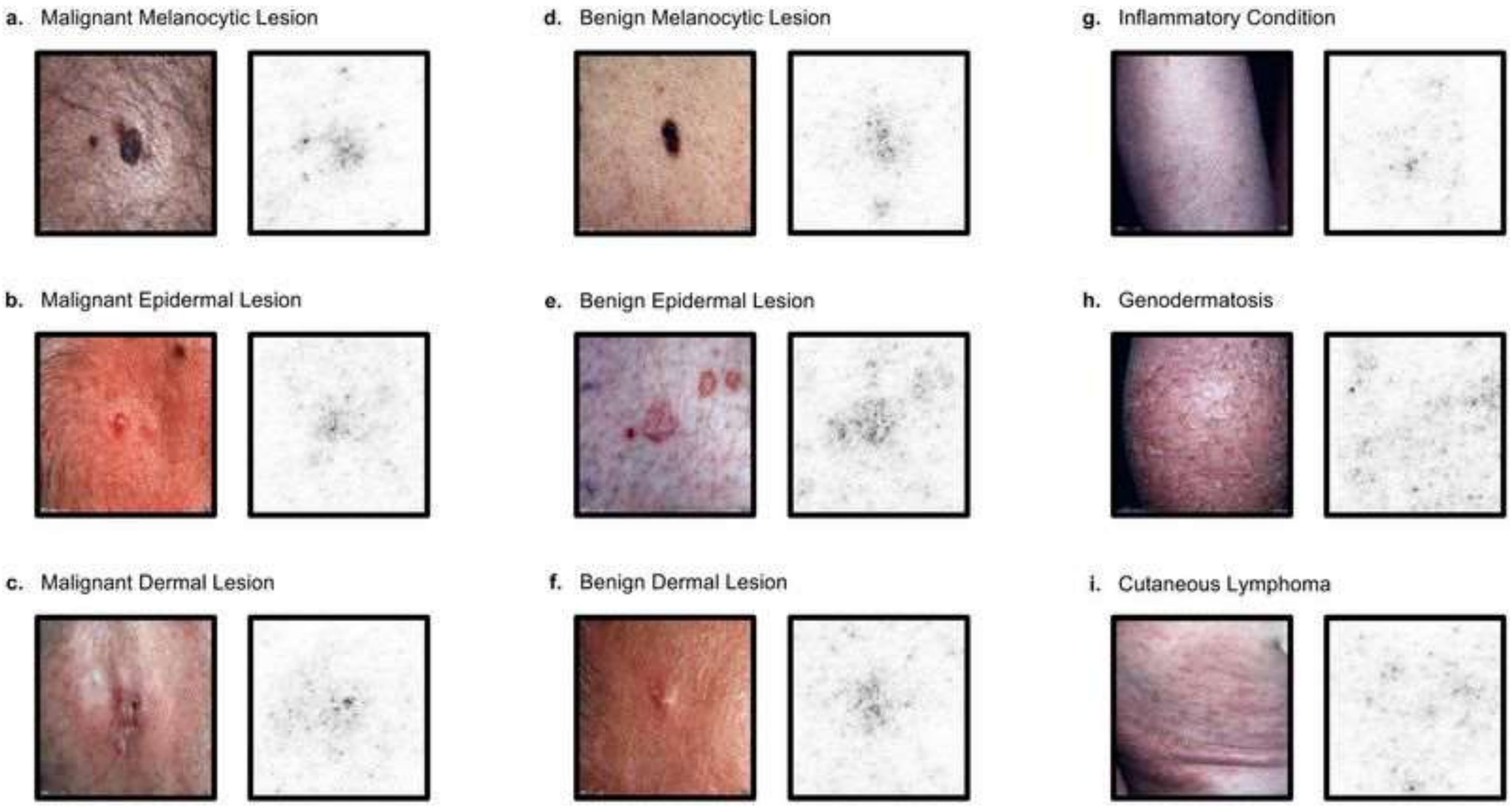
Clinicians must fully understand how their diagnostic tools work



Clinicians must be sure these tools are *valid* and *reliable*



Saliency maps for example images



a. Malignant Melanocytic Lesion
b. Malignant Epidermal Lesion
c. Malignant Dermal Lesion
d. Benign Melanocytic Lesion
e. Benign Epidermal Lesion
f. Benign Dermal Lesion
g. Inflammatory Condition
h. Genodermatosis
i. Cutaneous Lymphoma

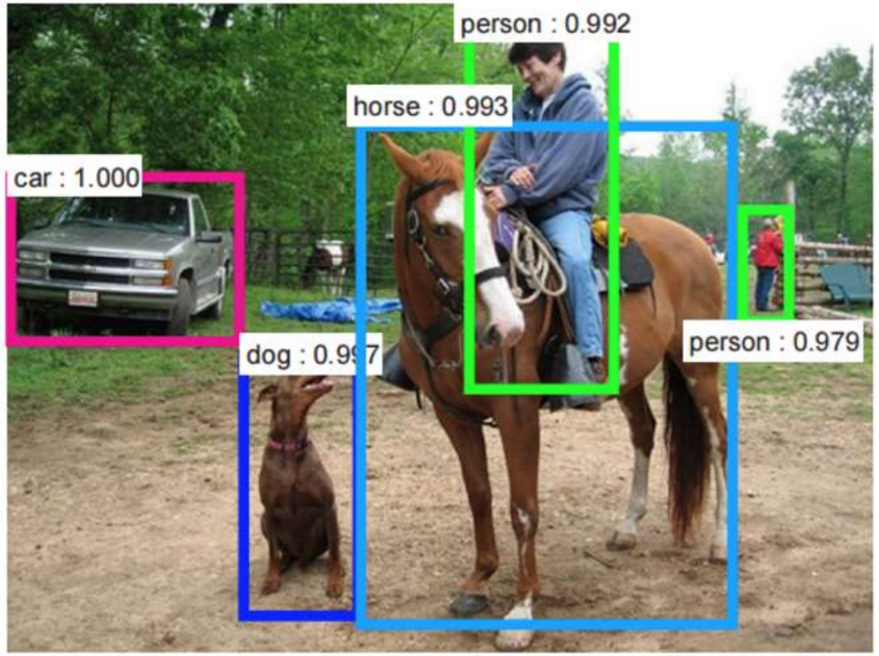
Saliency maps show gradients for each pixel with respect to the CNN’s loss function. Darker pixels represent those with more influence.

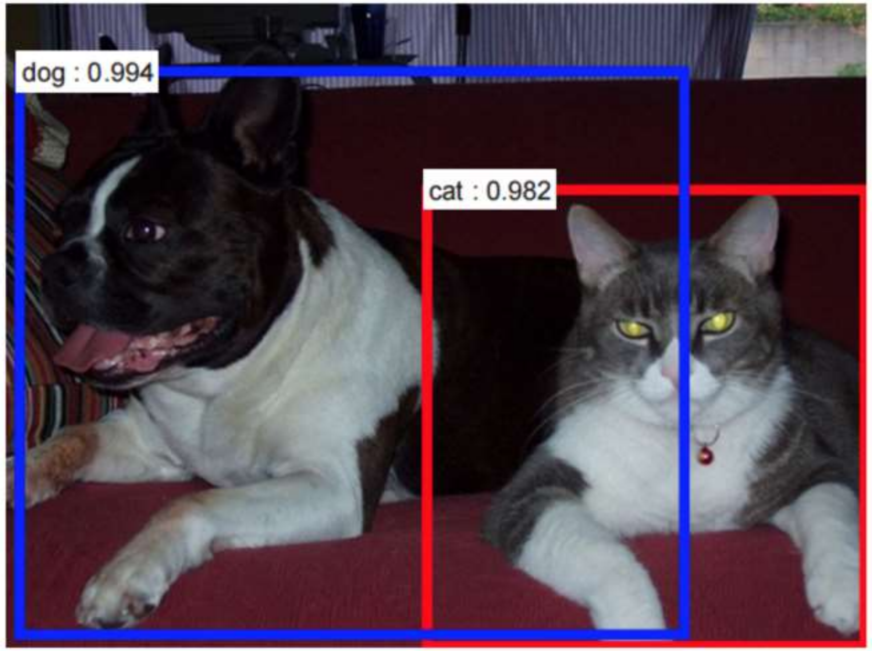
Q: How much does this visualization help us understand the model?

Detection and Segmentation for Medical Images

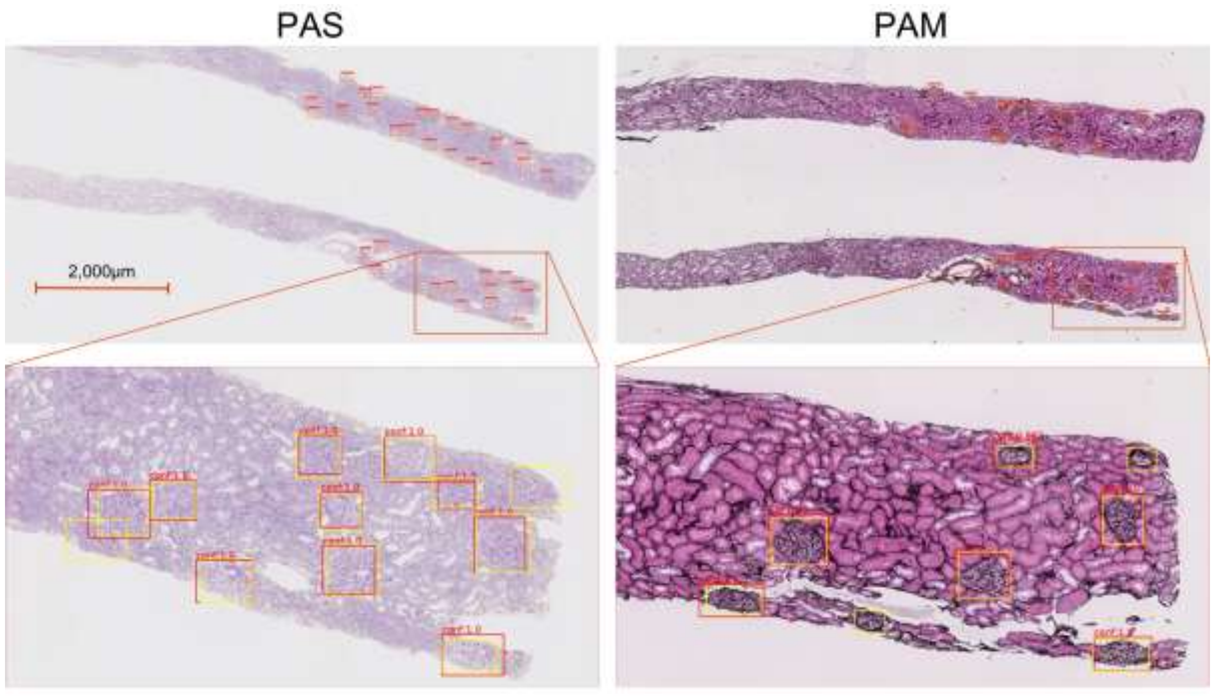
BEYOND CLASSIFICATION

Detection: propose regions and predict their labels



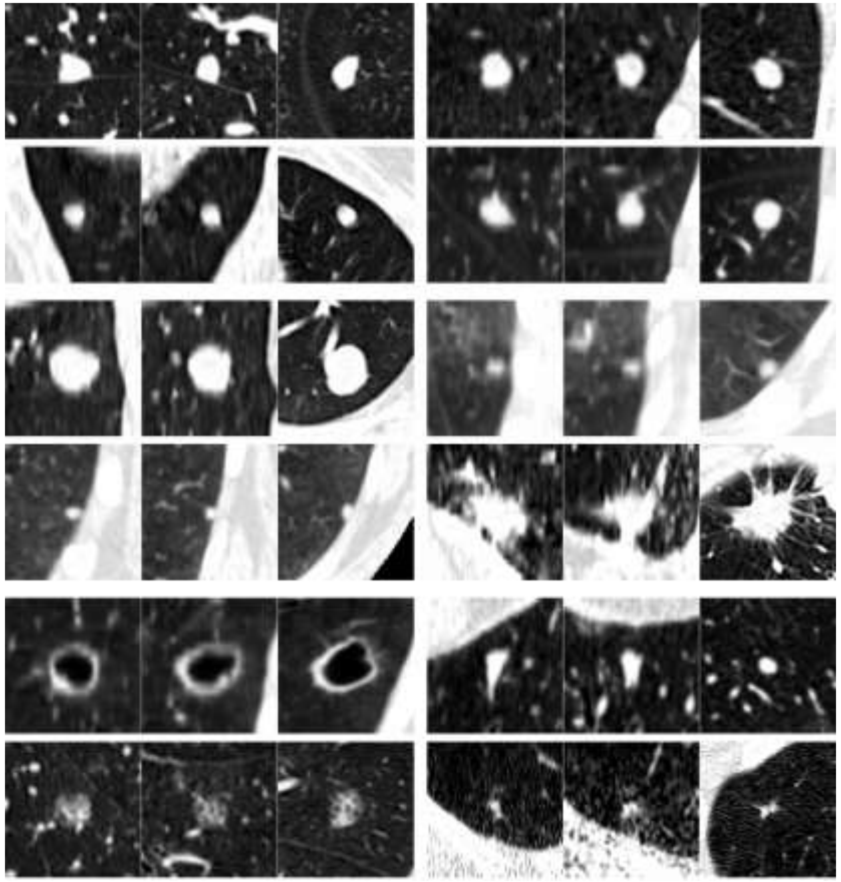


Detection in medicine



Glomerular Detection with Faster-RCNN

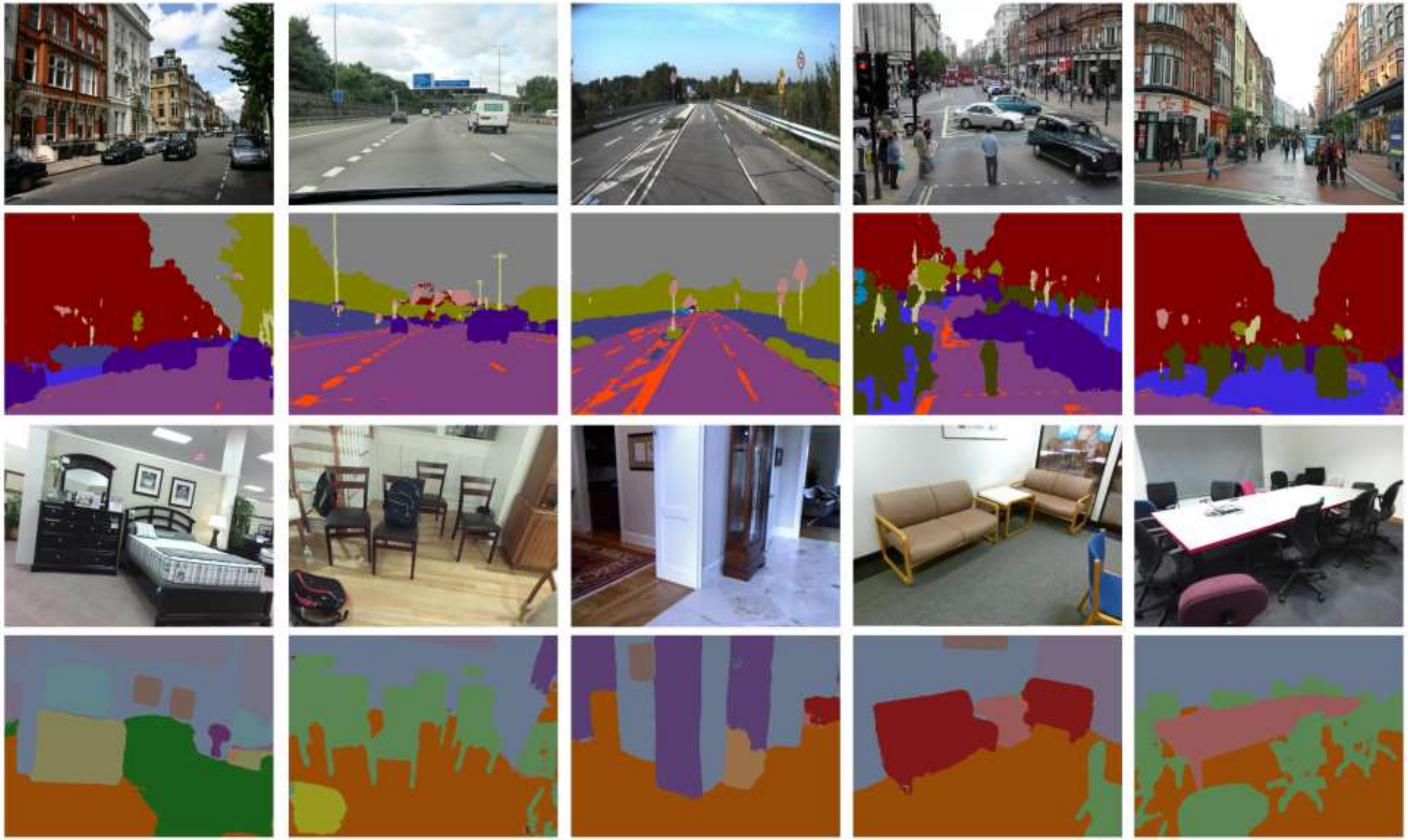
Kawazoe et al., *J. Imaging, 2018*



Pulmonary Nodule detection in CT

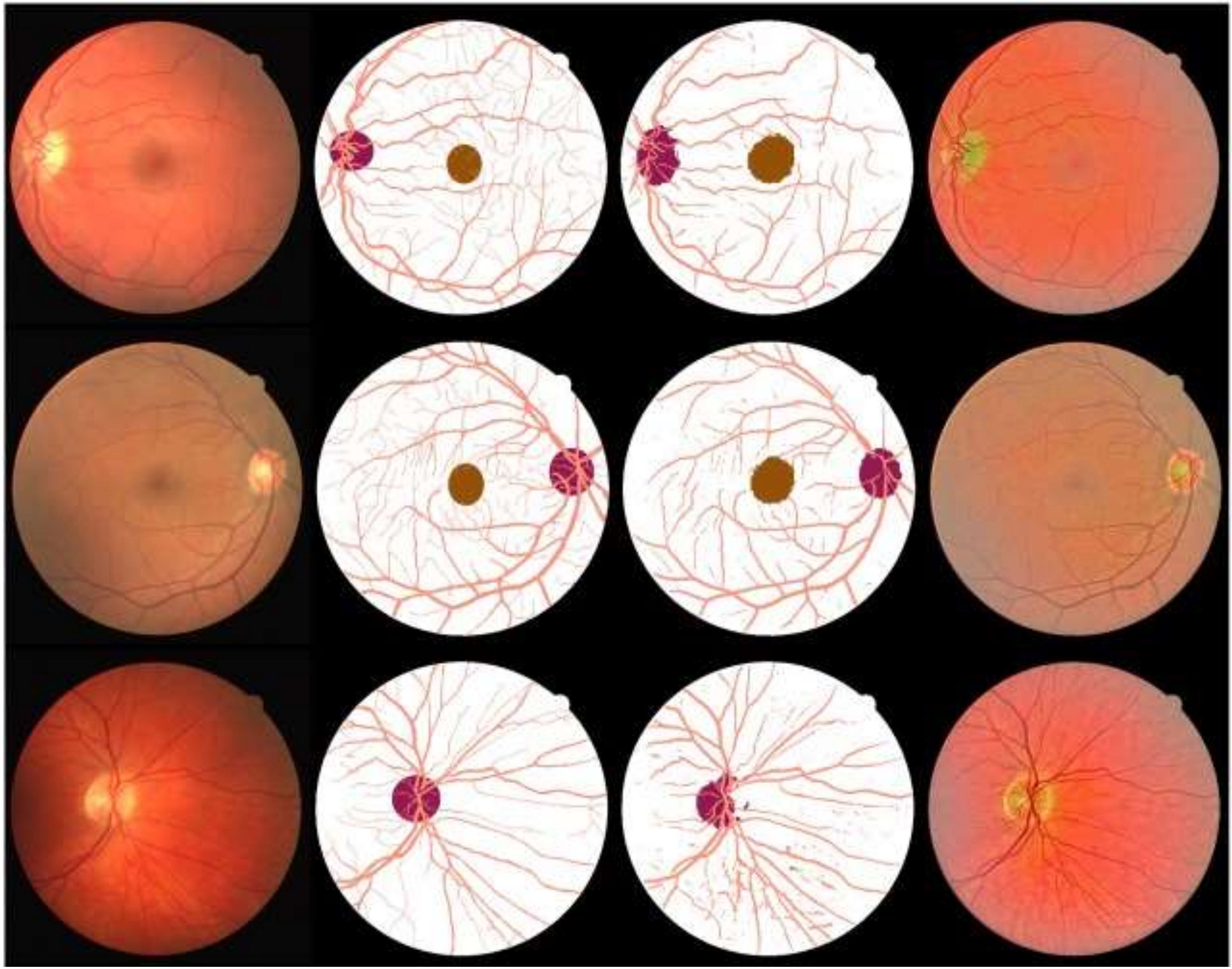
van Ginneken et al., *Biomedical Imaging,* 2015

Segmentation: predict the label for each pixel

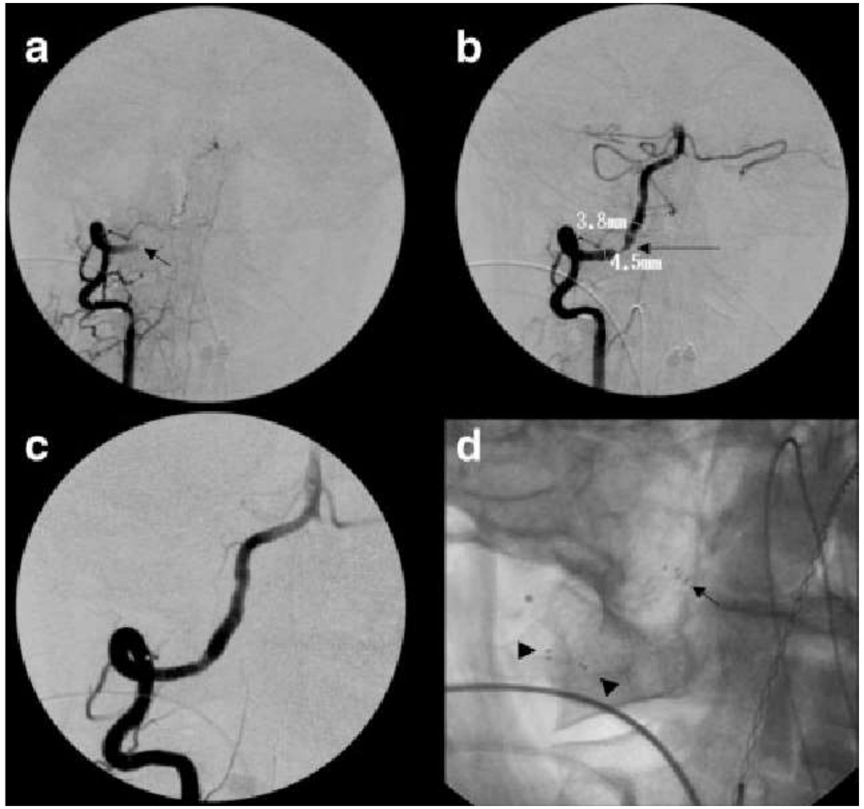


Segmentation of optic disc, fovea and retinal vasculature

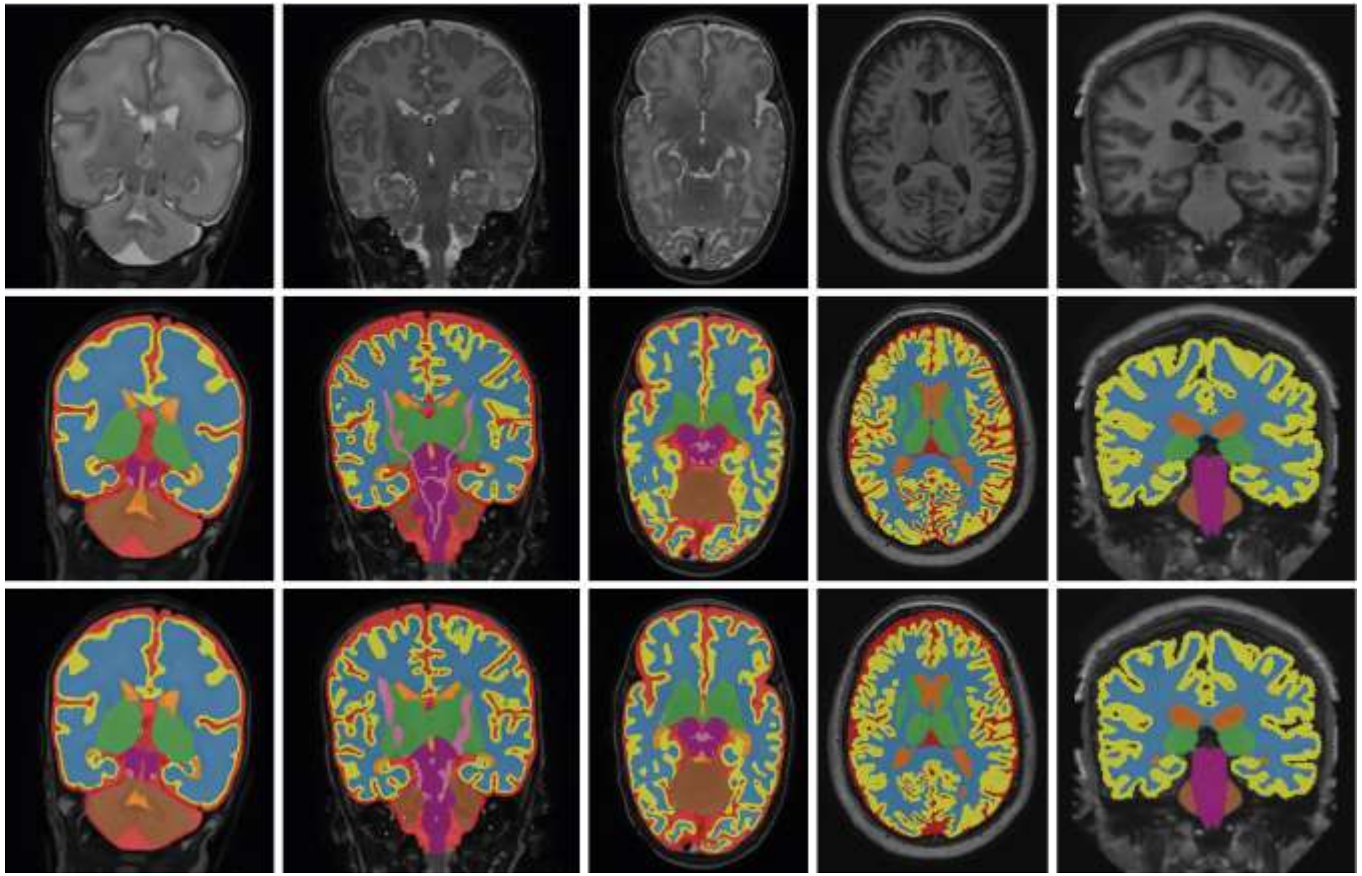
Journal of Computational Science, *20*, 70-79 (2017).



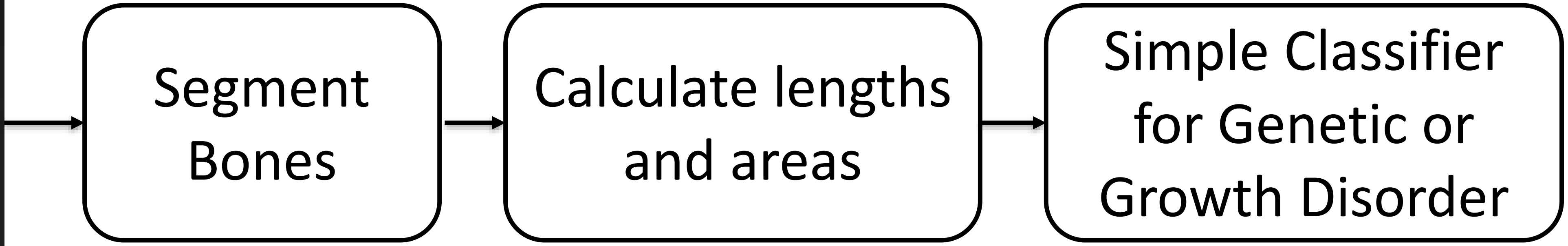
Precisely Identify Boundaries



Determine Areas or Volumes



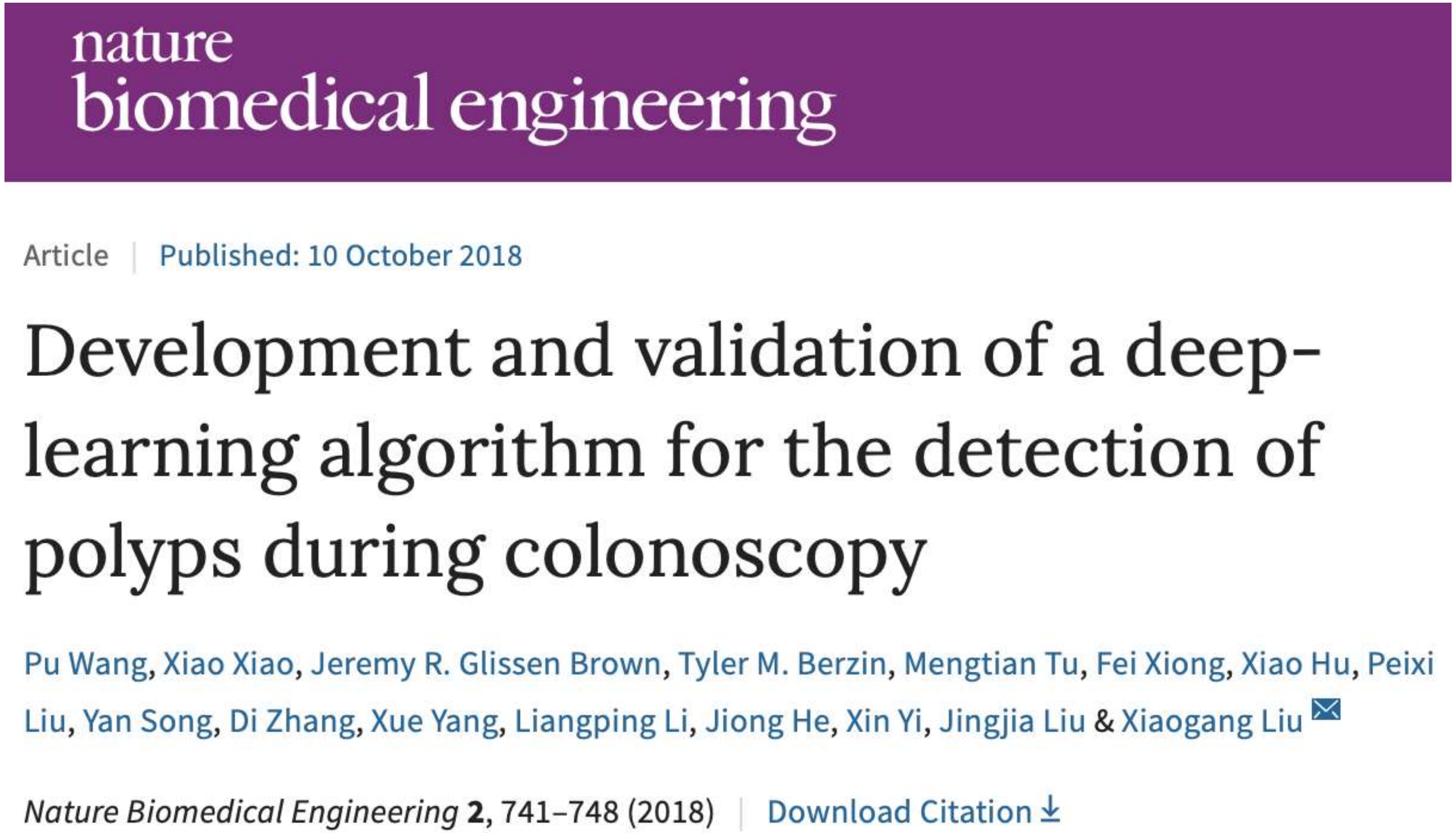
Segmentation-based features when end-to-end classification is not feasible



Segment Bones

Calculate lengths and areas

Simple Classifier for Genetic or Growth Disorder



nature
biomedical engineering

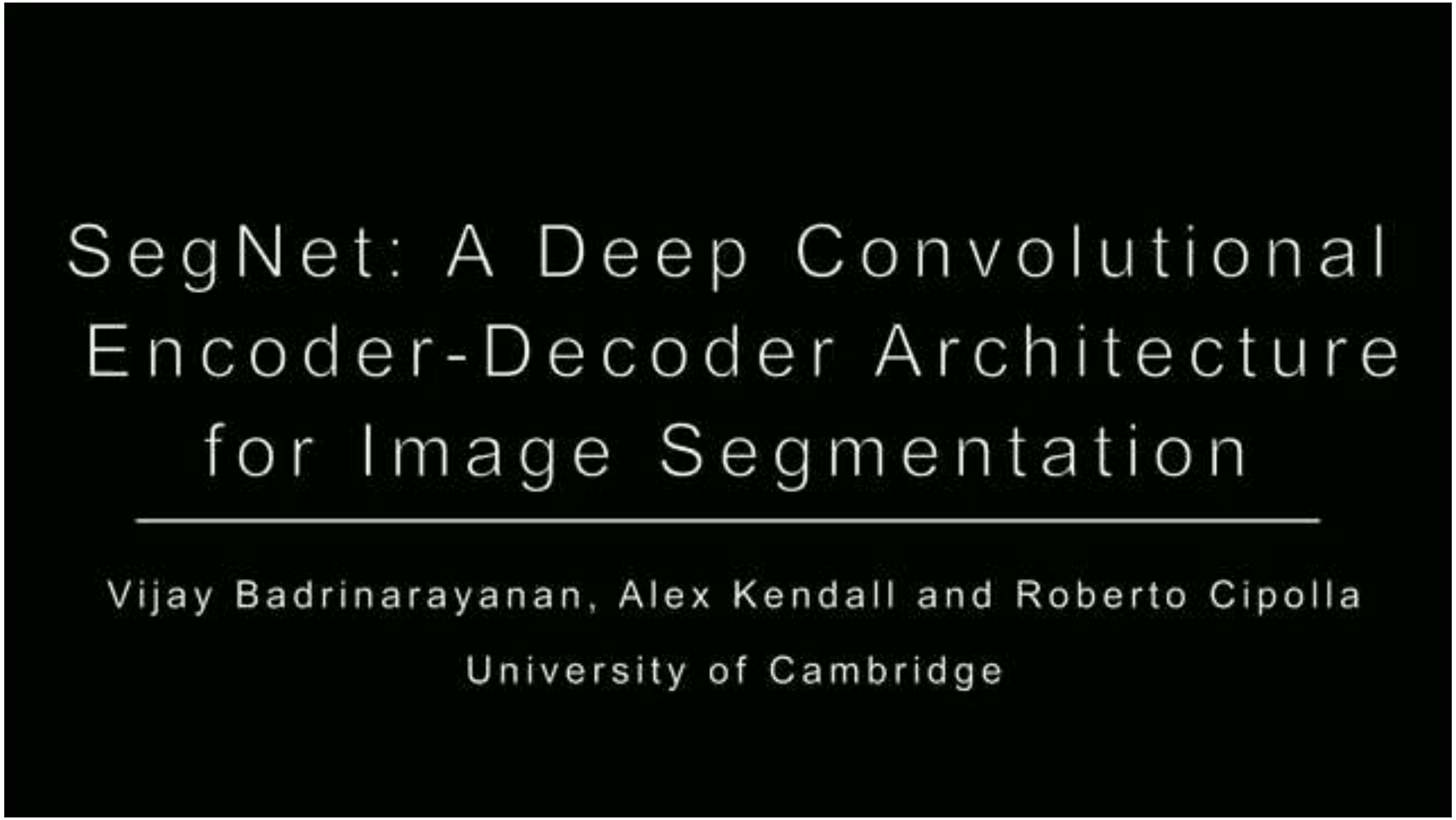
Article | Published: 10 October 2018

Development and validation of a deep-learning algorithm for the detection of polyps during colonoscopy

Pu Wang, Xiao Xiao, Jeremy R. Glissen Brown, Tyler M. Berzin, Mengtian Tu, Fei Xiong, Xiao Hu, Peixi Liu, Yan Song, Di Zhang, Xue Yang, Liangping Li, Jiong He, Xin Yi, Jingjia Liu & Xiaogang Liu ✉

Nature Biomedical Engineering **2**, 741–748 (2018) | Download Citation ⤓

Approach: Start with SegNet (2015)

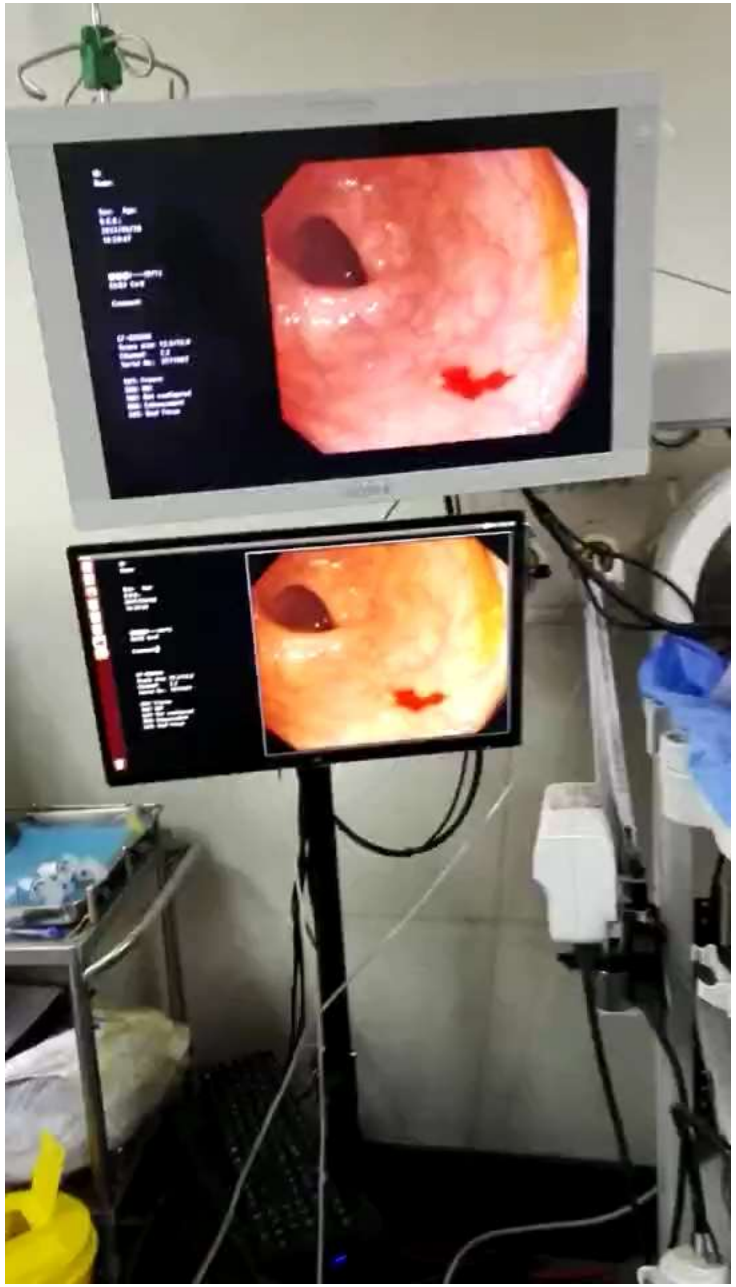


SegNet: A Deep Convolutional Encoder-Decoder Architecture for Image Segmentation

Vijay Badrinarayanan, Alex Kendall and Roberto Cipolla

University of Cambridge

Retrain to segment polyps in real time



THANK YOU!

Questions or ideas? Please contact me at m.engelhard@duke.edu