VISUM Summer School

VISion Understanding and Machine intelligence

Interpretability Methodologies for Machine Learning in Medical Imaging

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Healthcare Imaging A.I.

University of Bern/ Insel Data Science Center

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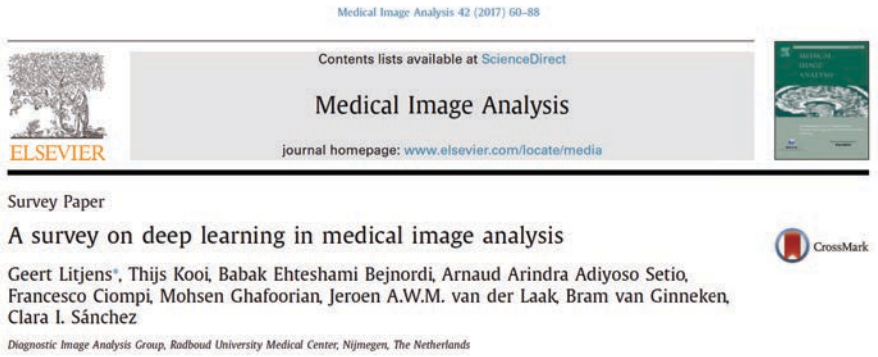
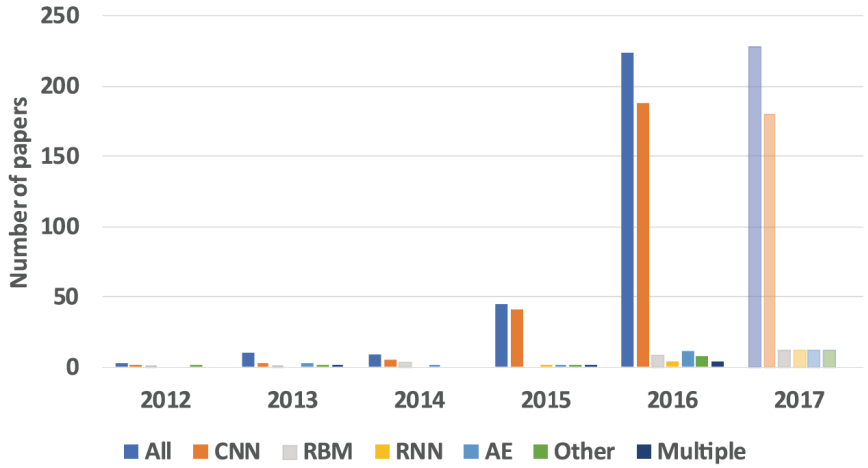
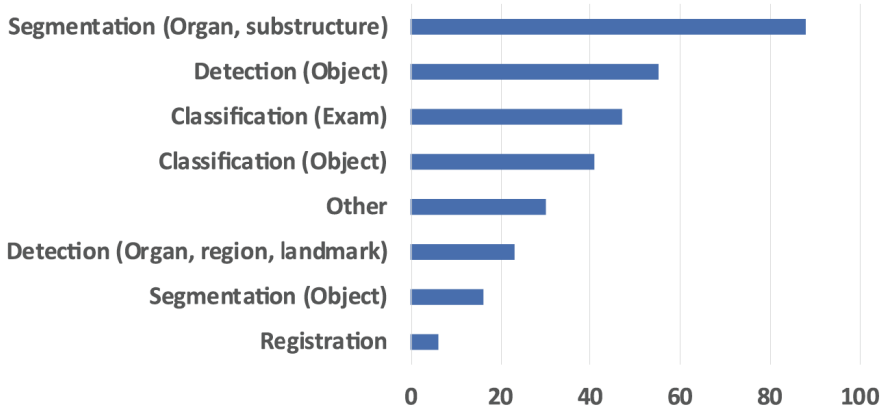
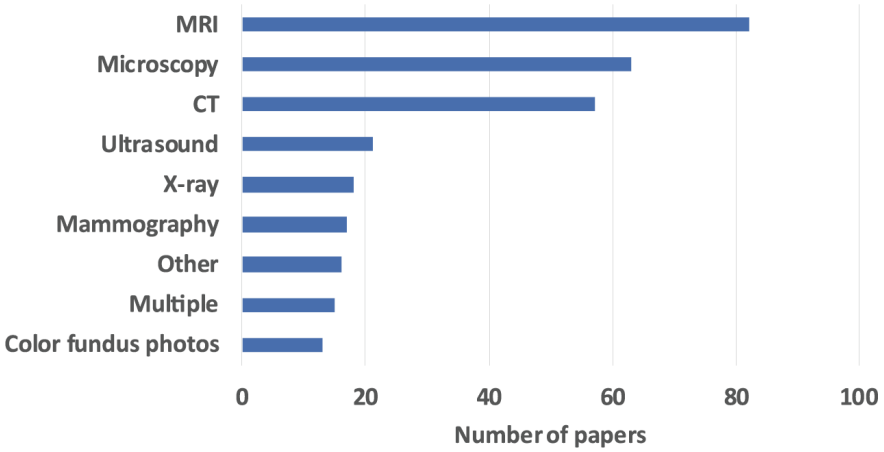
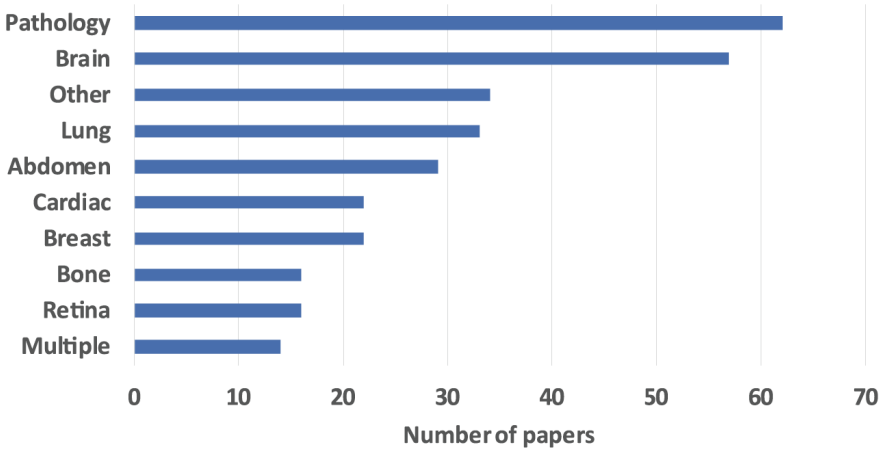
DL in Medical Imaging







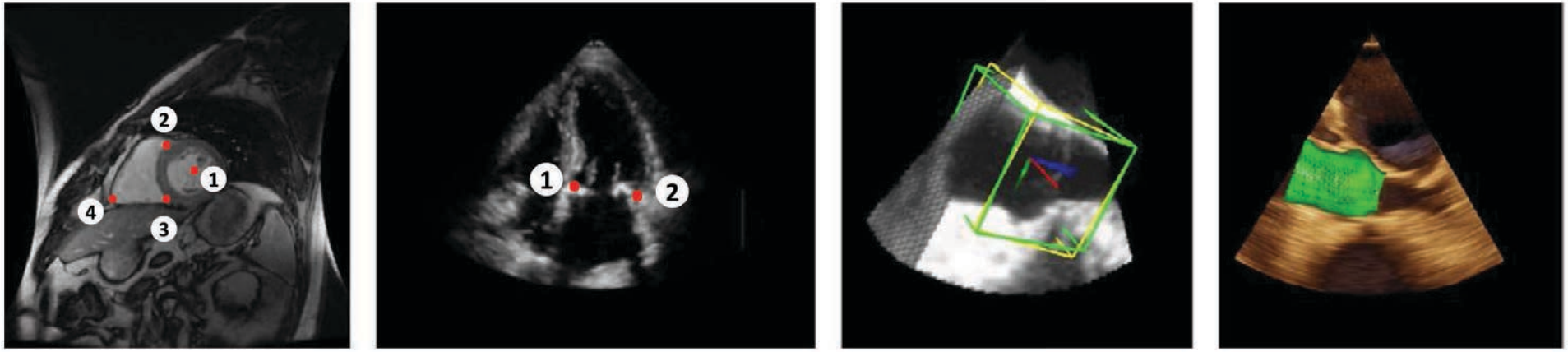


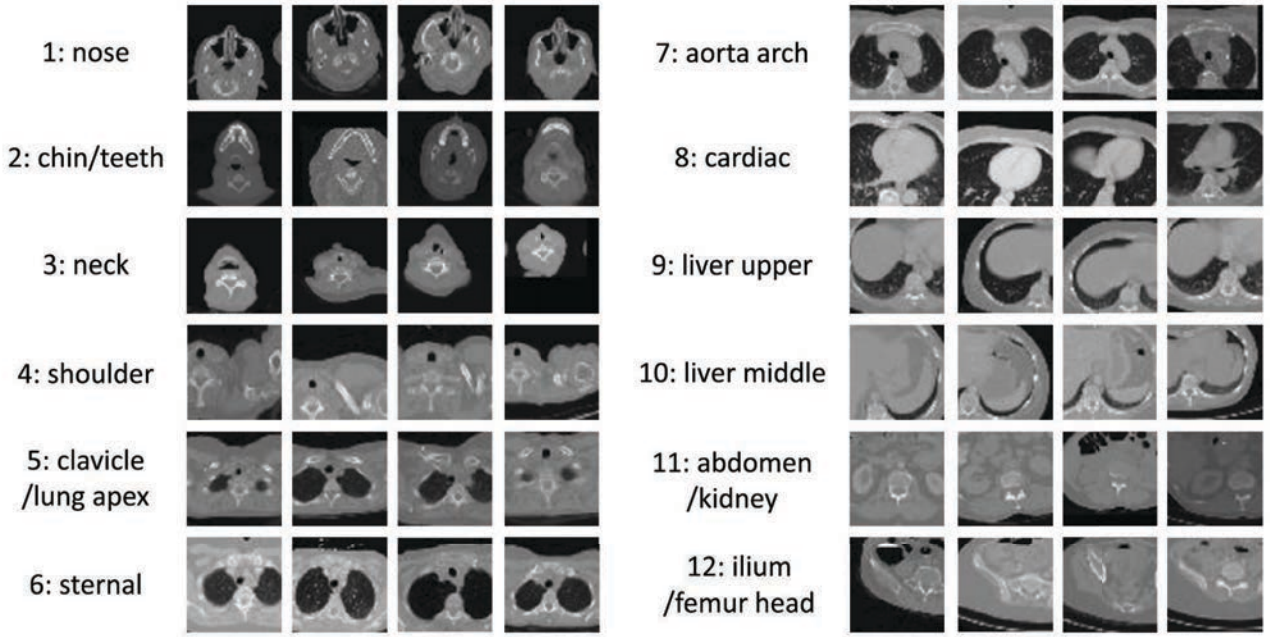


Source: Litjens et al. 2017

DL in Medical Imaging

Medical Image parsing



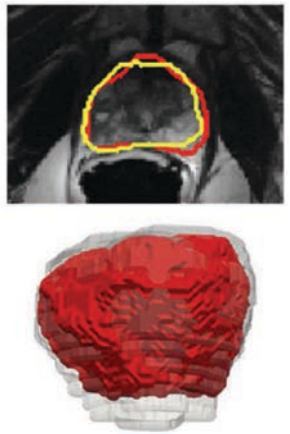


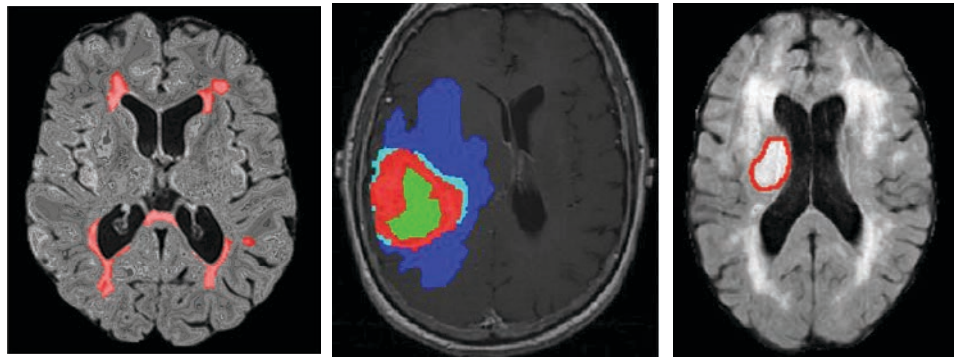
Source: Zhou et al. 2017

DL in Medical Imaging: Versatility

Medical Image Segmentation

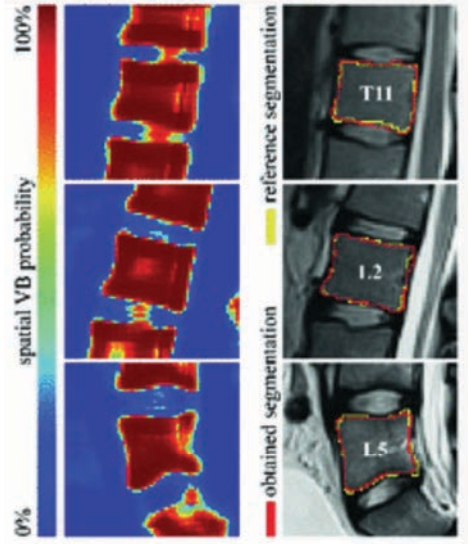
Prostate



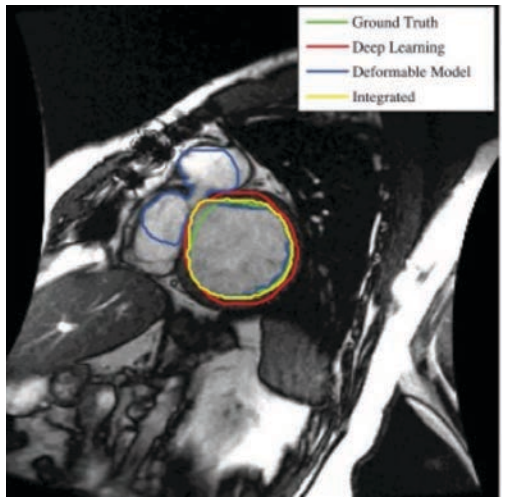


M.S Oncology Stroke

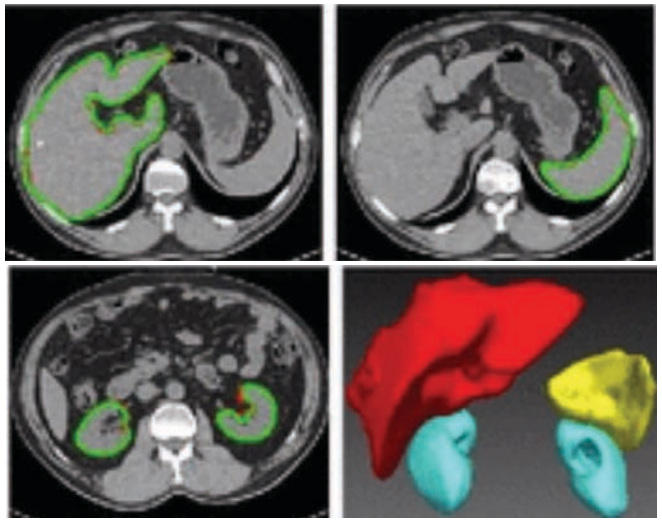
Musculoskeletal



Cardiac



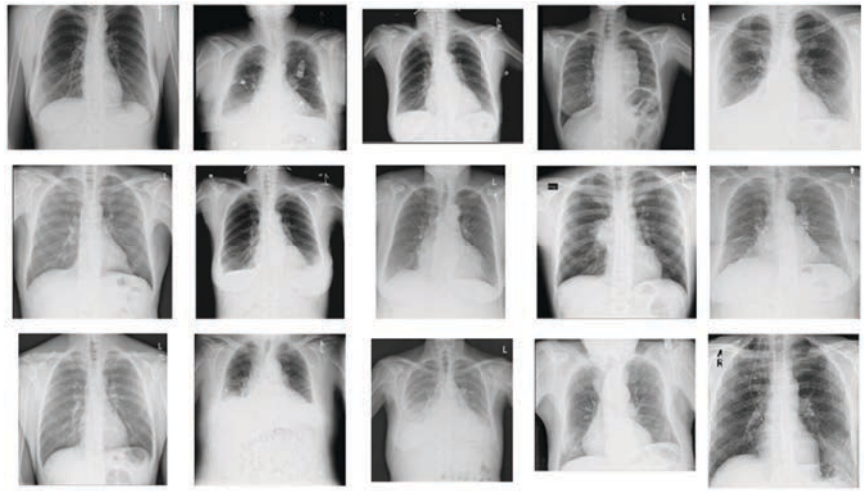
Abdominal



Source: Zhou et al. 2017

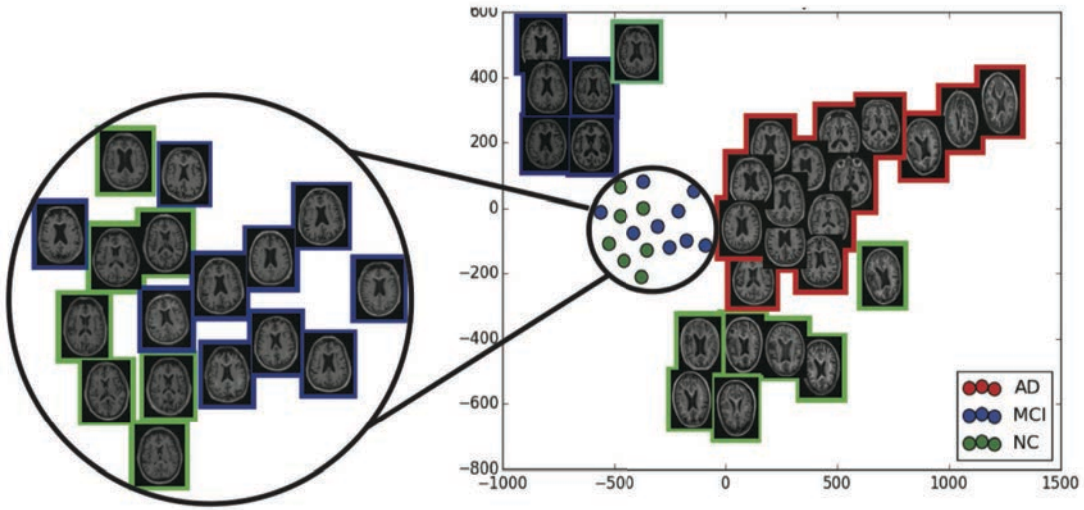
DL in Medical Imaging

Medical Image Classification



Healthy L/R Pleural effusion cardiomegaly enlarged mediastum L/Rconsolidation

Chest image classification



Alzheimer detection

mauricio

Source: Zhou et al. 2017

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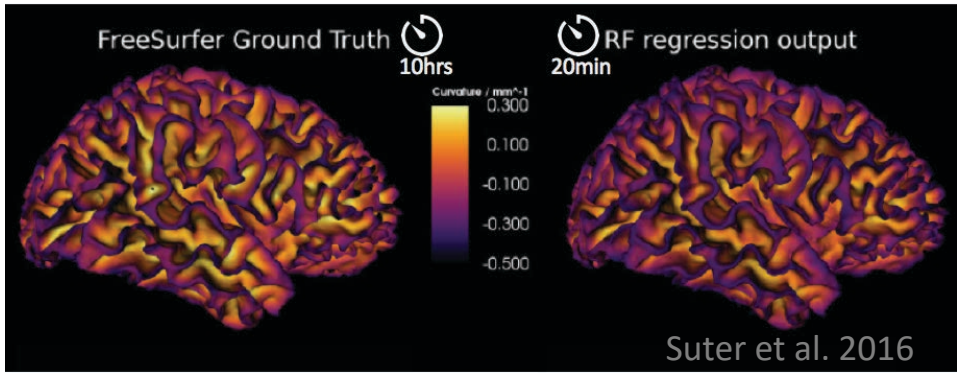
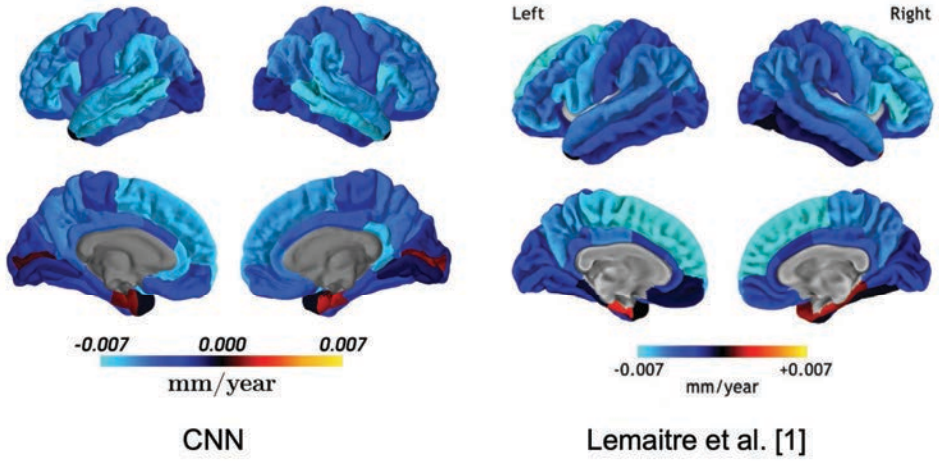
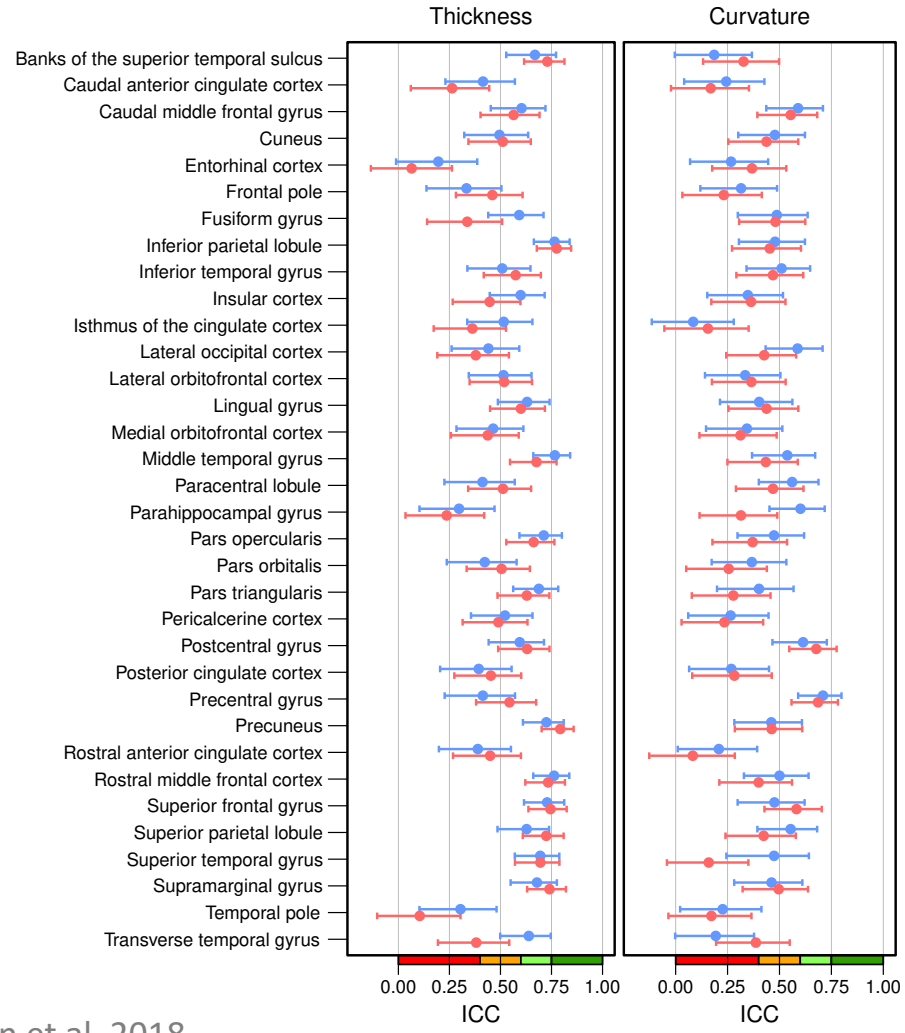
Medical Image Quantification







Rebsamen et al. 2018

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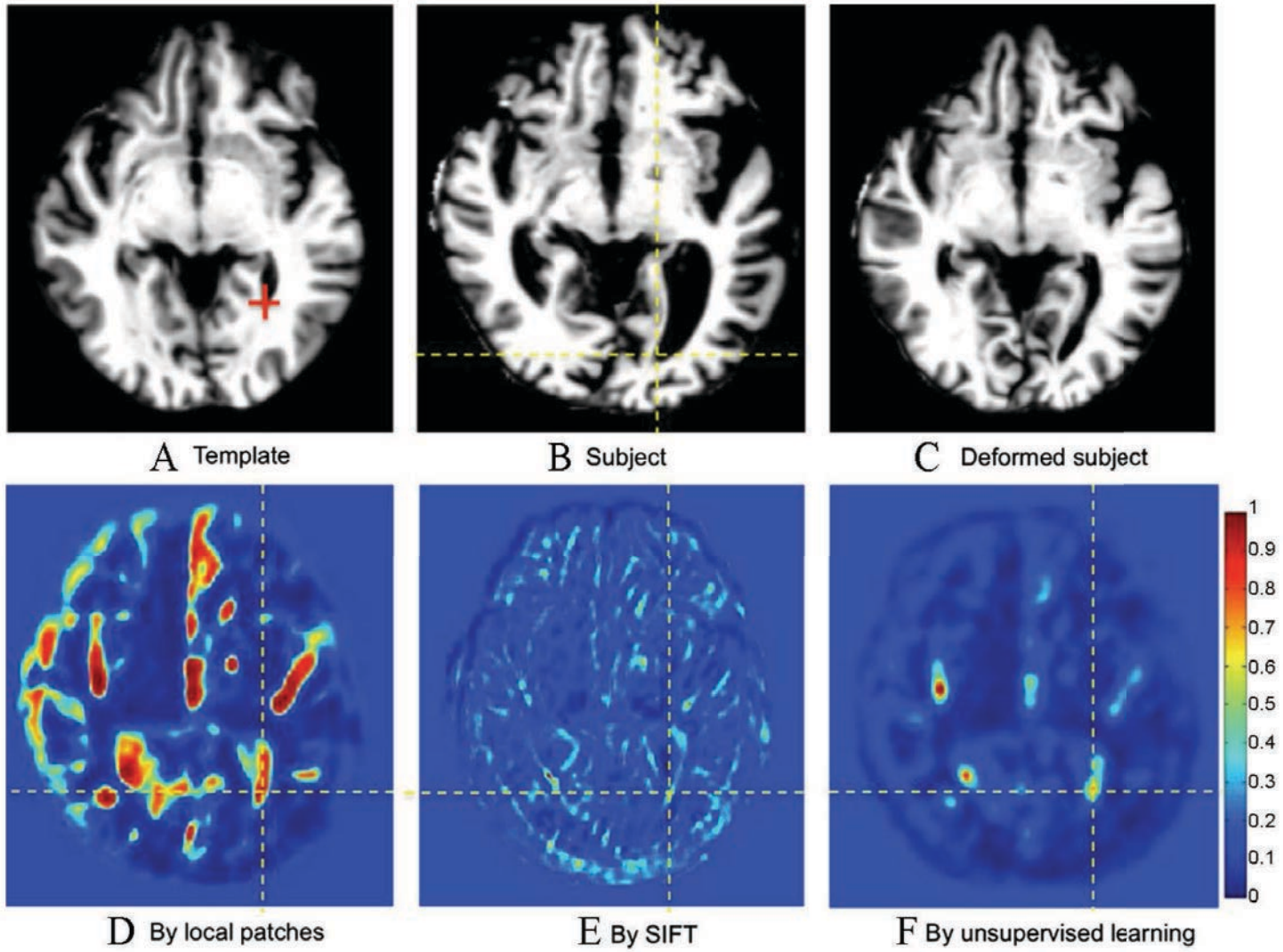
Medical Image Registration



Source: Zhou et al. 2017

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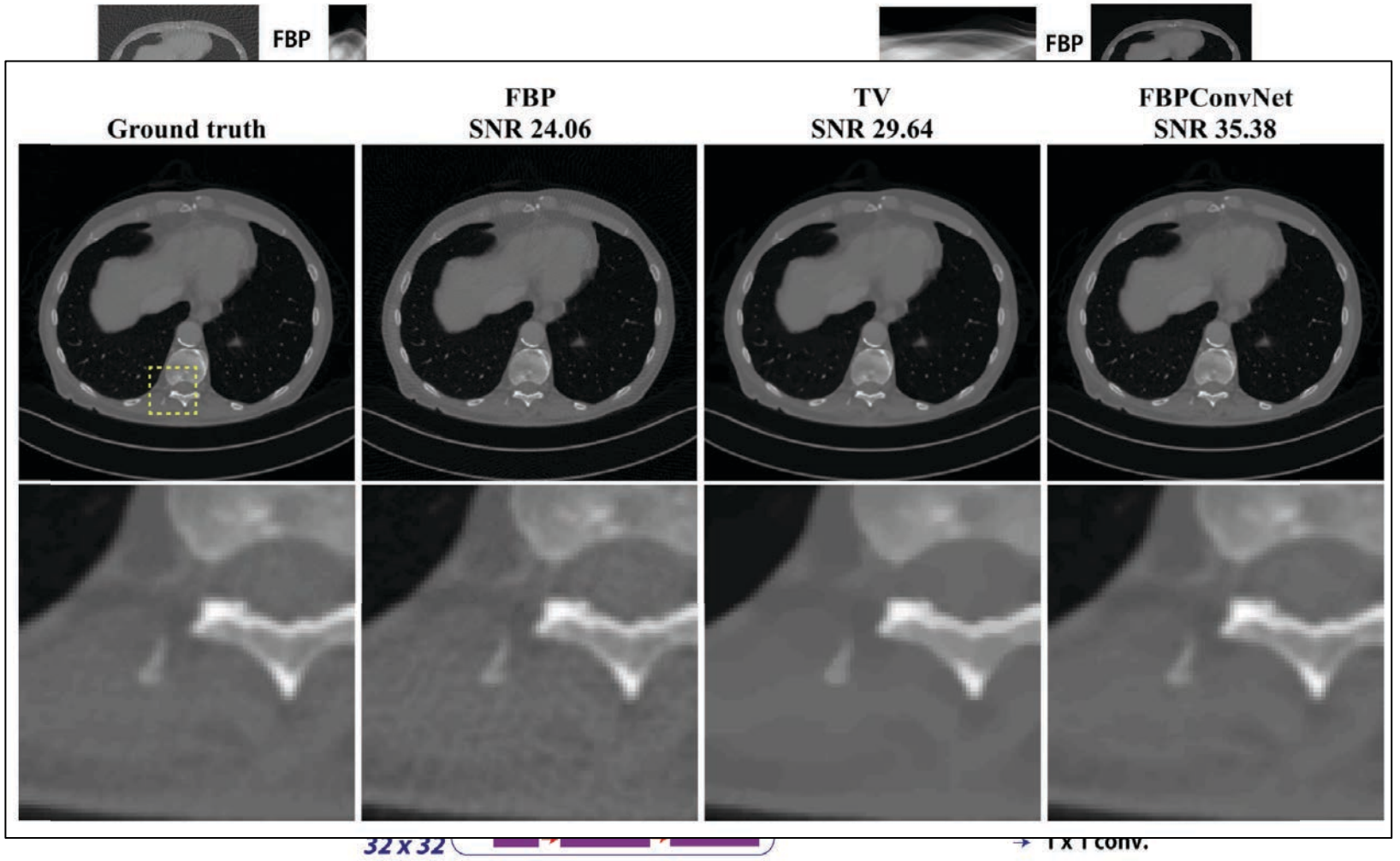
Medical Image Reconstruction

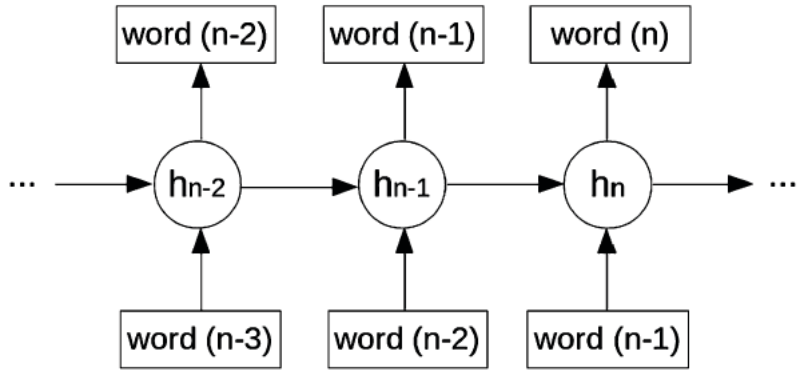


Source: Hwan-Jin TMI et al. 2017

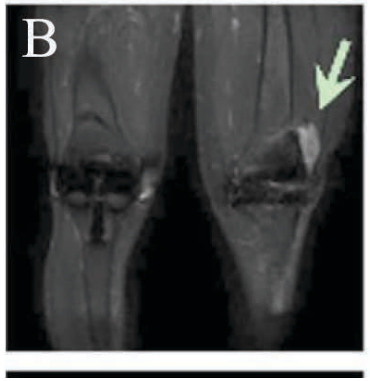
DL in Medical Imaging

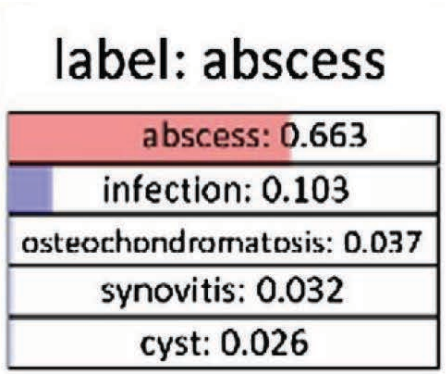
Automated Image Interpretation

"heart"		"brain"		"liver"	
lungs	0.526600	t1	0.615066	spleen	0.759884
mediastinum	0.517008	mri	0.595027	gallbladder	0.648075
consolidating	0.486605	sagittal	0.580841	hepatomegaly	0.642022
pa	0.449816	flair	0.565445	gallstones	0.611837
chest	0.433362	t2	0.555053	pancreas	0.608356
infiltrates	0.428404	axial	0.554040	gallstone	0.606063
hyperinflated	0.413326	spgr	0.520954	steatosis	0.601081
cardiomegaly	0.410785	weighted	0.502047	dome	0.594812
hyperlucent	0.400836	technique	0.487768	portal	0.570008
pectus	0.396142	astrocytoma	0.480527	ascites	0.551869
great	0.395712	gbm	0.476956	hepatosplenomegaly	0.540501
ectatic	0.394560	gradient	0.476593	hepatic	0.537453
shifted	0.389205	oligodendroglioma	0.465892	cirrhosis	0.530389
ray	0.389091	postcontrast	0.463686	fatty	0.522134



Word neural embeddings





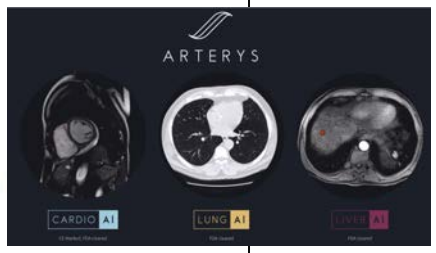
... for example series 701 image 12 and series 401 image 27 with **findings** suggesting minimally enhancing rim laterally for example series 1101 image 21 may ... the **findings** suggest a fluid collection with ... the location suggests possibility of a **synovial** collection **synovial** thickening as the appearance is nonspecific correlation with clinical findings is recommended regarding the possibility of an **infection** **abscess**

Source: Zhou et al. 2017

Feb. 2018

Arterys Receives First FDA Clearance for Broad Oncology Imaging Suite with Deep Learning

FDA clearance covers all solid tumors. Initial launch will include Liver AI and Lung AI oncology software to empower clinicians to quickly measure and track lesions and nodules in MRI and CT scans



As FDA signals wider AI approval, hospitals have a role to play

By Mike Miliard | May 31, 2018 | 03:27 PM

With more machine learning tools expected to get the go-ahead soon, health systems should be partnering with vendors to supply data for better algorithms.

Credit: FDA.gov

April. 2018

FDA Approves First A.I. Device To Detect Diabetic Retinopathy

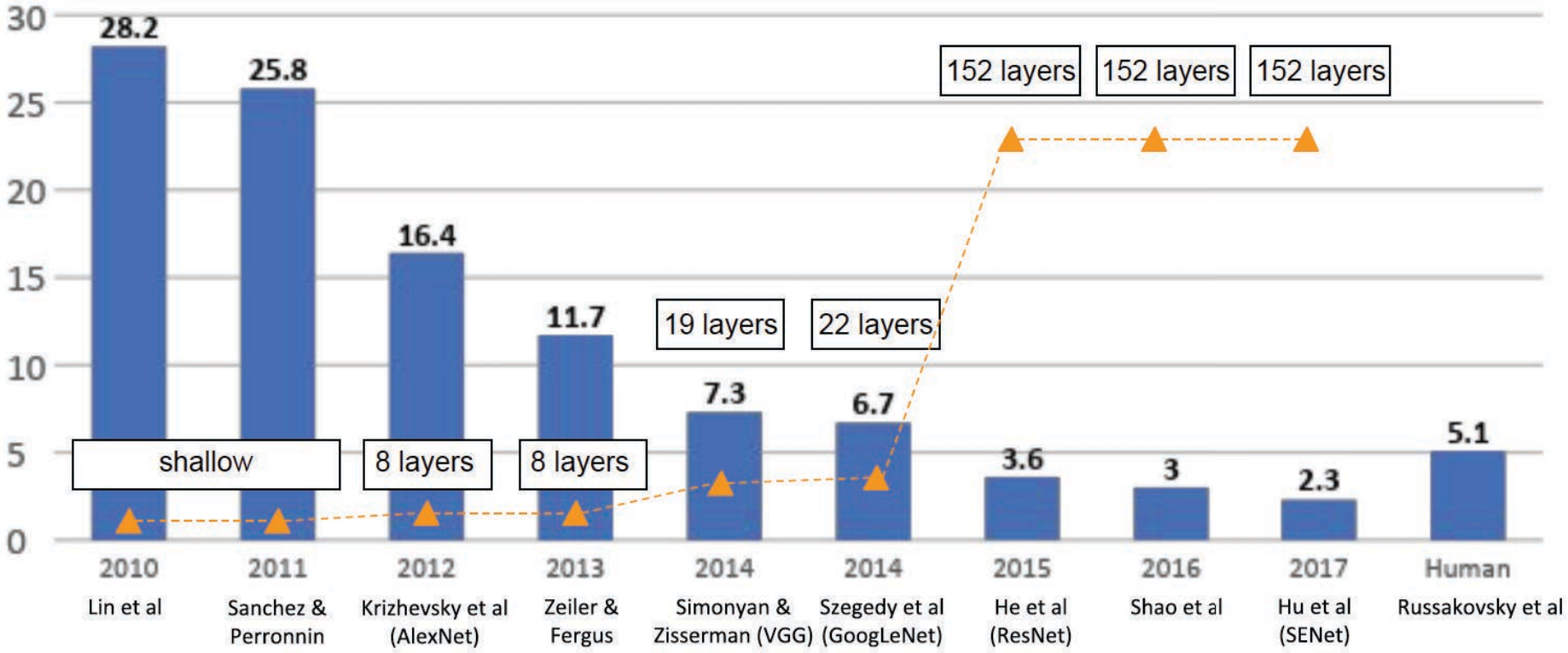

The IDx AI tool in clinical use at University of Iowa Health Care. Credit: YouTube

"A.I. holds enormous promise for the future of medicine, and we're actively developing a new regulatory framework to promote innovation in this space and support the use of AI-based technologies".

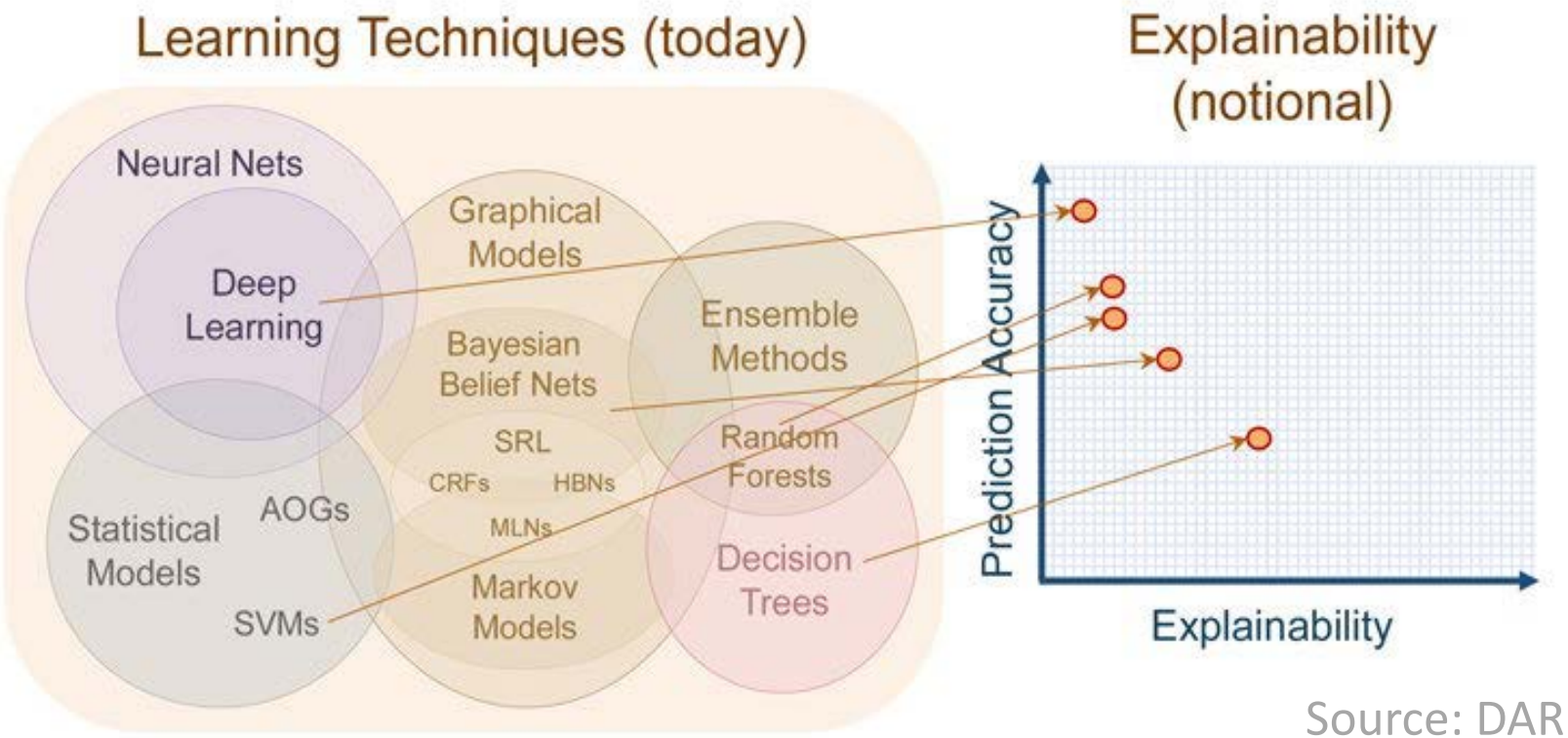
Scott Gottlieb, FDA commissioner

Going deeper

error rate



Explainable A.I



Source: DARPA

Definitions

- What is Interpretability?

An interpretable machine learning algorithm is described as one where the **link between the features** used by the machine learning and the **prediction** itself **can be understood by a human**

Another definition

- Produce explanations without sacrificing accuracy
  - Simpler is easier to understand
  - But oversimplified is typically from an accuracy point of view, not interesting

Barocas, S., Friedler, S., Hardt, M., Kroll, J., Venka-Tasubramanian, S., & H. Wallach, H. (2018). The FAT-ML Workshop Series on Fairness, Accountability, and Transparency in Machine Learning.

Explainability and Interpretability

- Used interchangeably
- Explainability → “What’s the process behind” (e.g. Apple falling from a tree: gravity)
- Interpretability → “understanding/predicting causal/effect phenomena” (what happens if I cut the apple from the tree: it will fall)

Why do we need Interpretability?

- Accountability
- Trust
- Quality Control
- Quality Assurance
- Ethical aspects
- Data exploration

Why do we need Interpretability?

- Accountability
  - System Liability

European Union regulations on algorithmic decision-making and a "right to explanation"

Bryce Goodman, Seth Flaxman

(Submitted on 28 Jun 2016 (v1), last revised 31 Aug 2016 (this version, v3))

We summarize the potential impact that the European Union's new General Data Protection Regulation will have on the routine use of machine learning algorithms. Slated to take effect as law across the EU in 2018, it will restrict automated individual decision-making (that is, algorithms that make decisions based on user-level predictors) which "significantly affect" users. The law will also effectively create a "right to explanation," whereby a user can ask for an explanation of an algorithmic decision that was made about them. We argue that while this law will pose large challenges for industry, it highlights opportunities for computer scientists to take the lead in designing algorithms and evaluation frameworks which avoid discrimination and enable explanation.

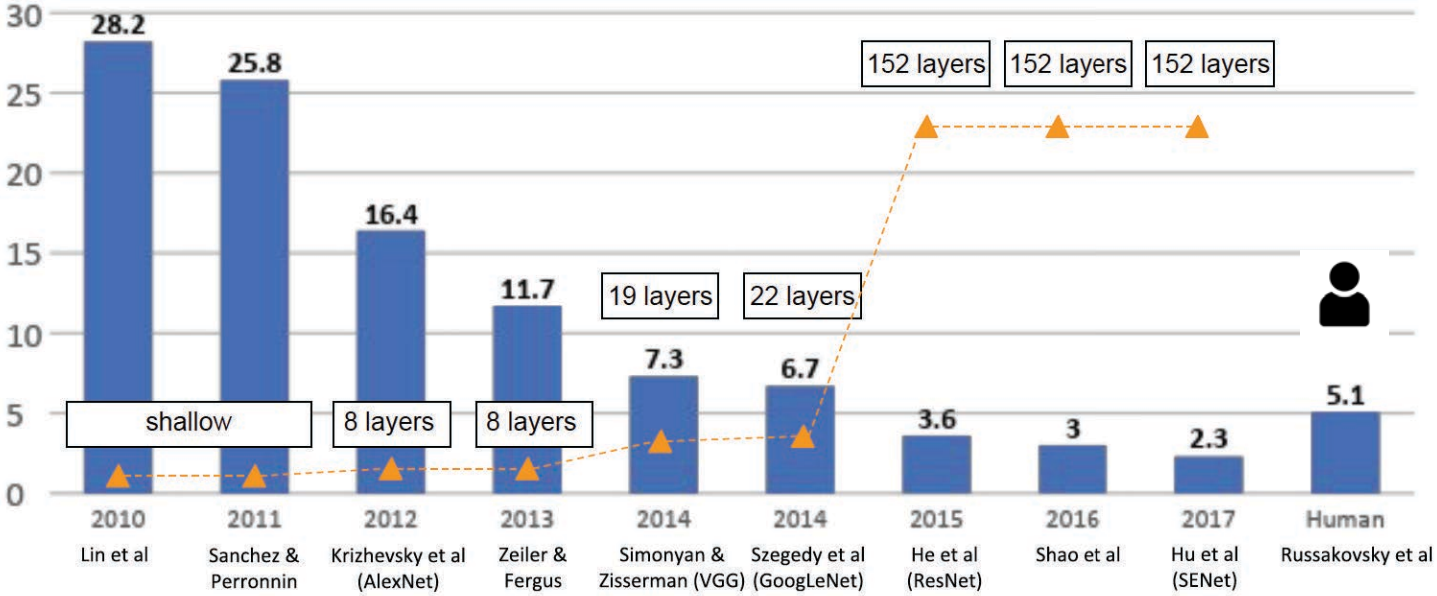
Comments: presented at 2016 ICML Workshop on Human Interpretability in Machine Learning (WHI 2016), New York, NY

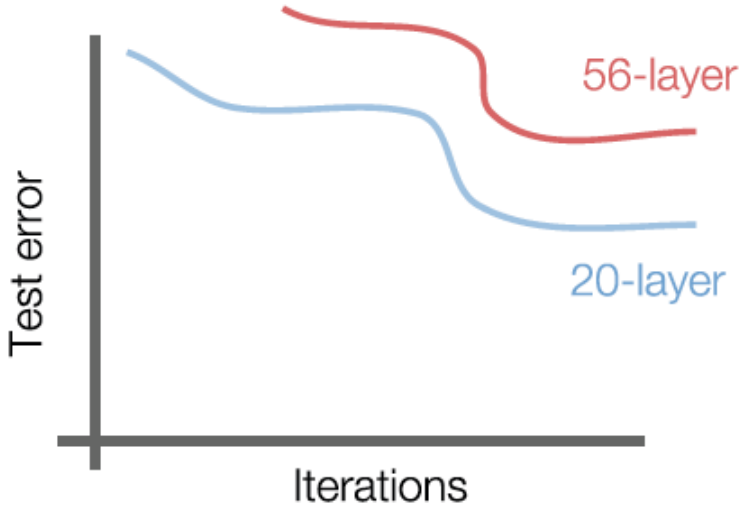
Why do we need Interpretability?

- Quality Assurance: Thorough evaluation of a model's performance
- Ensuring robustness and knowledge of breaking points of an algorithm

Interpretability is needed to leverage Quality Control (QC) of A.I. systems

Solution featuring “high degrees of freedom”



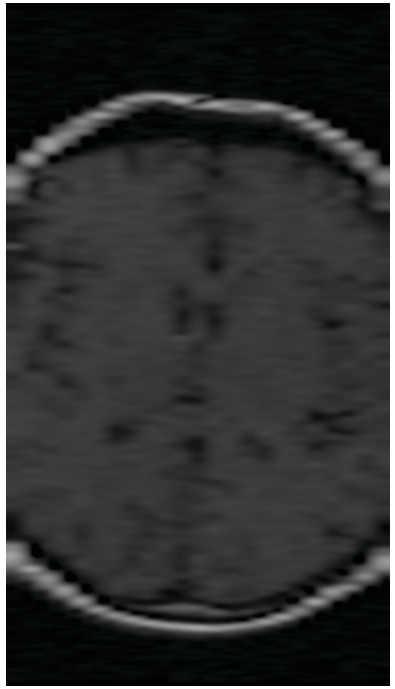


Why do we need Interpretability?

- Quality Control

flawed orientation

flawed orientation



low resolution

A.I. technology is as good as the training data characterizing the task

Why do we need Interpretability?

- Trust
  - Essential in fields such as medicine where technology can play a crucial role
  - In radiology, AI and the potential of restructuring the radiologist’s workflow

DeepFool: a simple and accurate method to fool deep neural networks

Seyed-Mohsen Moosavi-Dezfooli, Alhussein Fawzi, Pascal Frossard
École Polytechnique Fédérale de Lausanne
{seyed.moosavi,alhussein.fawzi,pascal.frossard} at epfl.ch

Full Citation: Nguyen A, Yosinski J, Clune J. *Deep Neural Networks are Easily Fooled: High Confidence Predictions for Unrecognizable Images*. In Computer Vision and Pattern Recognition (CVPR '15), IEEE, 2015.

**Deep Neural Networks are Easily Fooled:
High Confidence Predictions for Unrecognizable Images**

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Published as a conference paper at ICLR 2019

IMAGENET-TRAINED CNNS ARE BIASED TOWARDS TEXTURE; INCREASING SHAPE BIAS IMPROVES ACCURACY AND ROBUSTNESS

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PLOS MEDICINE

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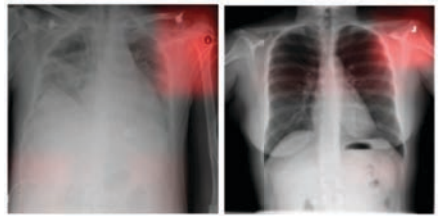
RESEARCH ARTICLE

Variable generalization performance of a deep learning model to detect pneumonia in chest radiographs: A cross-sectional study

John R. Zech, Marcus A. Badgeley, Manway Liu, Anthony B. Costa, Joseph J. Titano, Eric Karl Oermann

Published: November 6, 2018 • https://doi.org/10.1371/journal.pmed.1002683



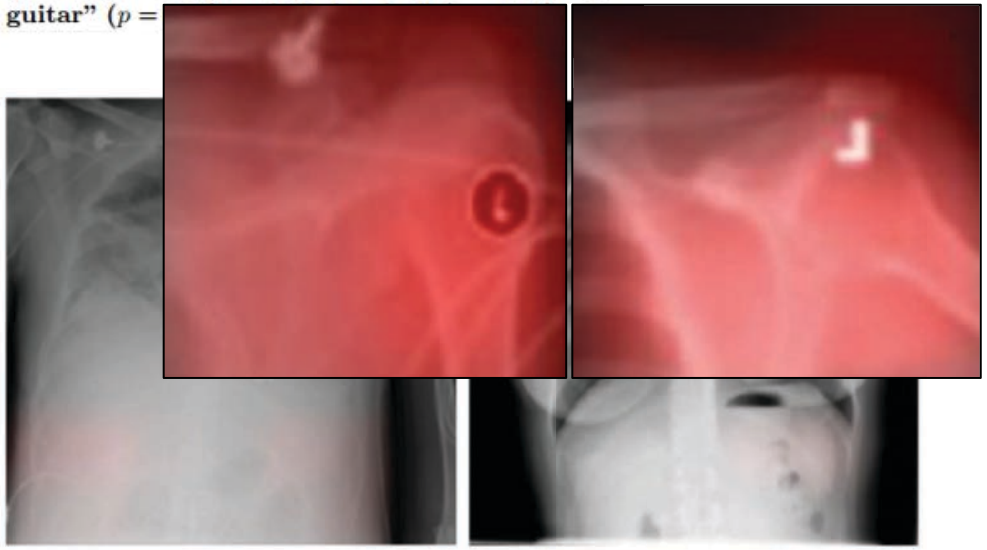
Explaining DL decisions via attention maps

(a) Original Image (b) Explaining *Electric guitar* (c) Explaining *Acoustic guitar* (d) Explaining *Labrador*

Figure 4: Explaining an image classification prediction made by Google's Inception neural network. The top 3 classes predicted are "Electric Guitar" ($p = 0.32$), "Acoustic guitar" ($p =$

(a) Husky classified as wolf (b) Explanation

Figure 11: Raw data and explanation of a bad model's prediction in the "Husky vs Wolf" task.



DL learned to detect clinical site!

Source: Ribeiro et al. 2017, Zech et al. 2018

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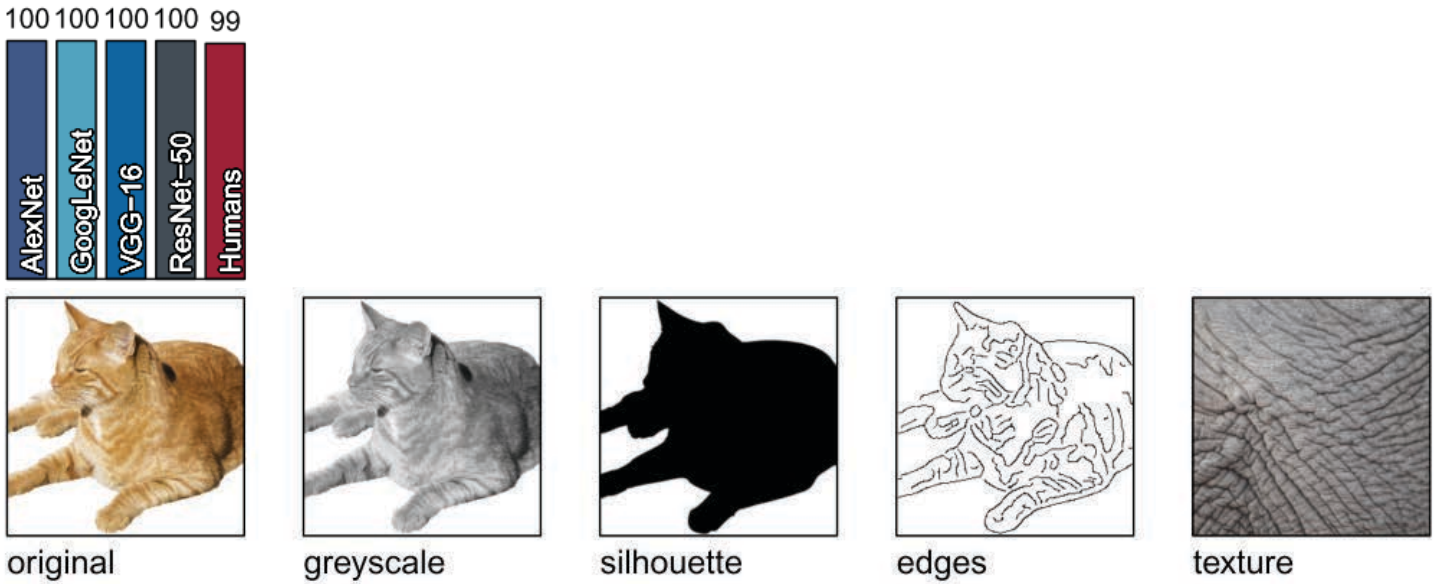

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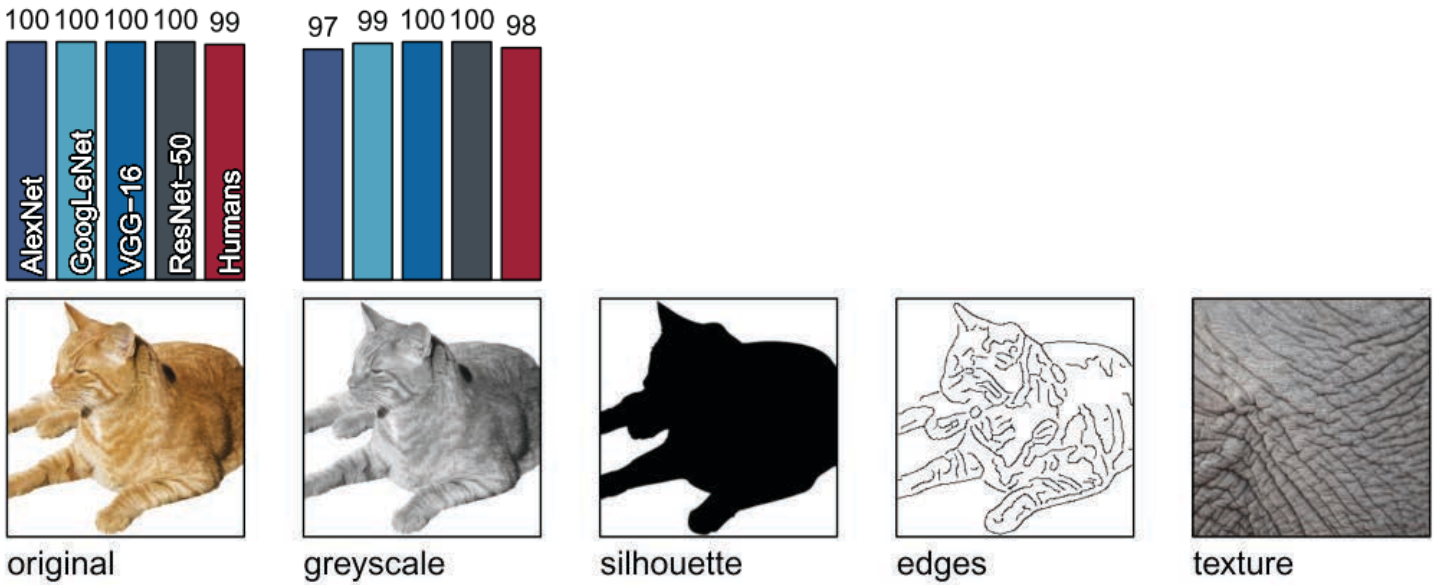

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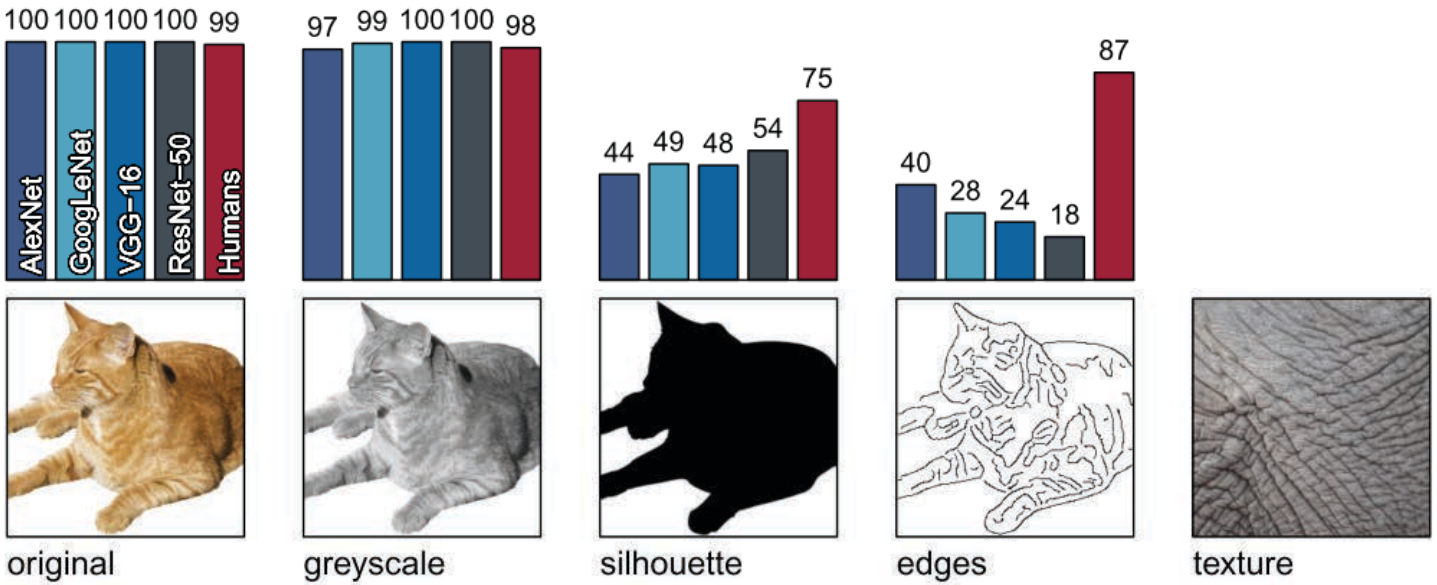

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IMAGENET-TRAINED CNNS ARE BIASED TOWARDS TEXTURE; INCREASING SHAPE BIAS IMPROVES ACCURACY AND ROBUSTNESS

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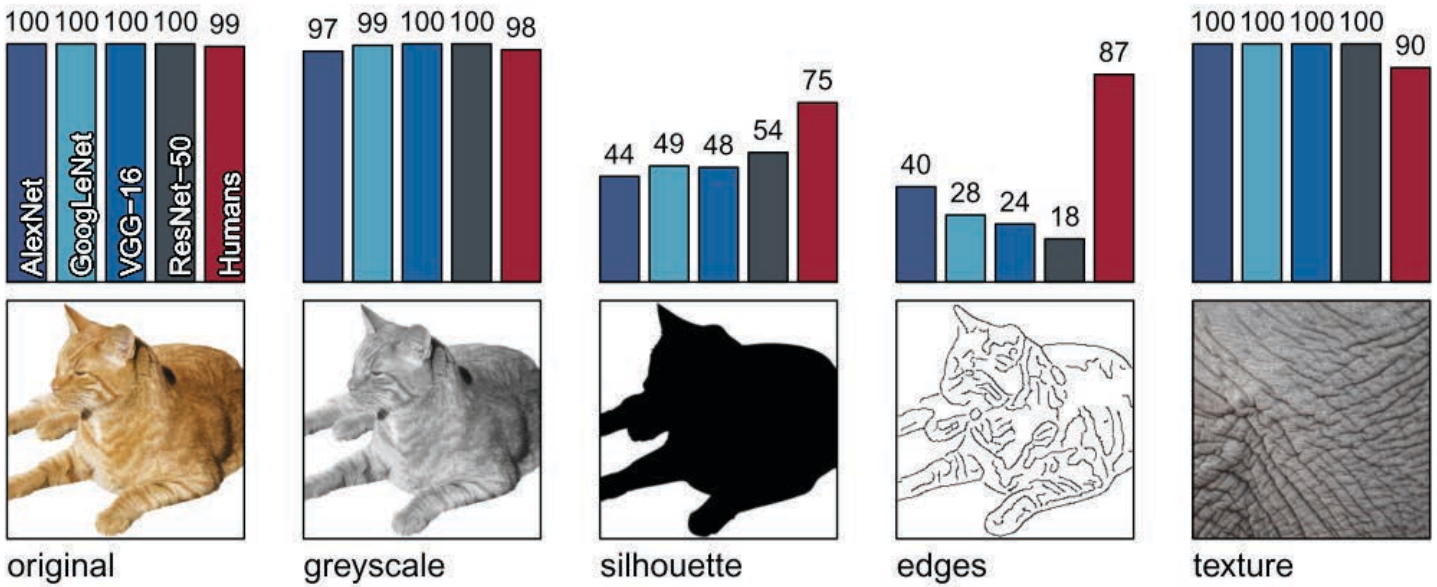


Ethics of AI in Radiology: European and North American Multisociety Statement

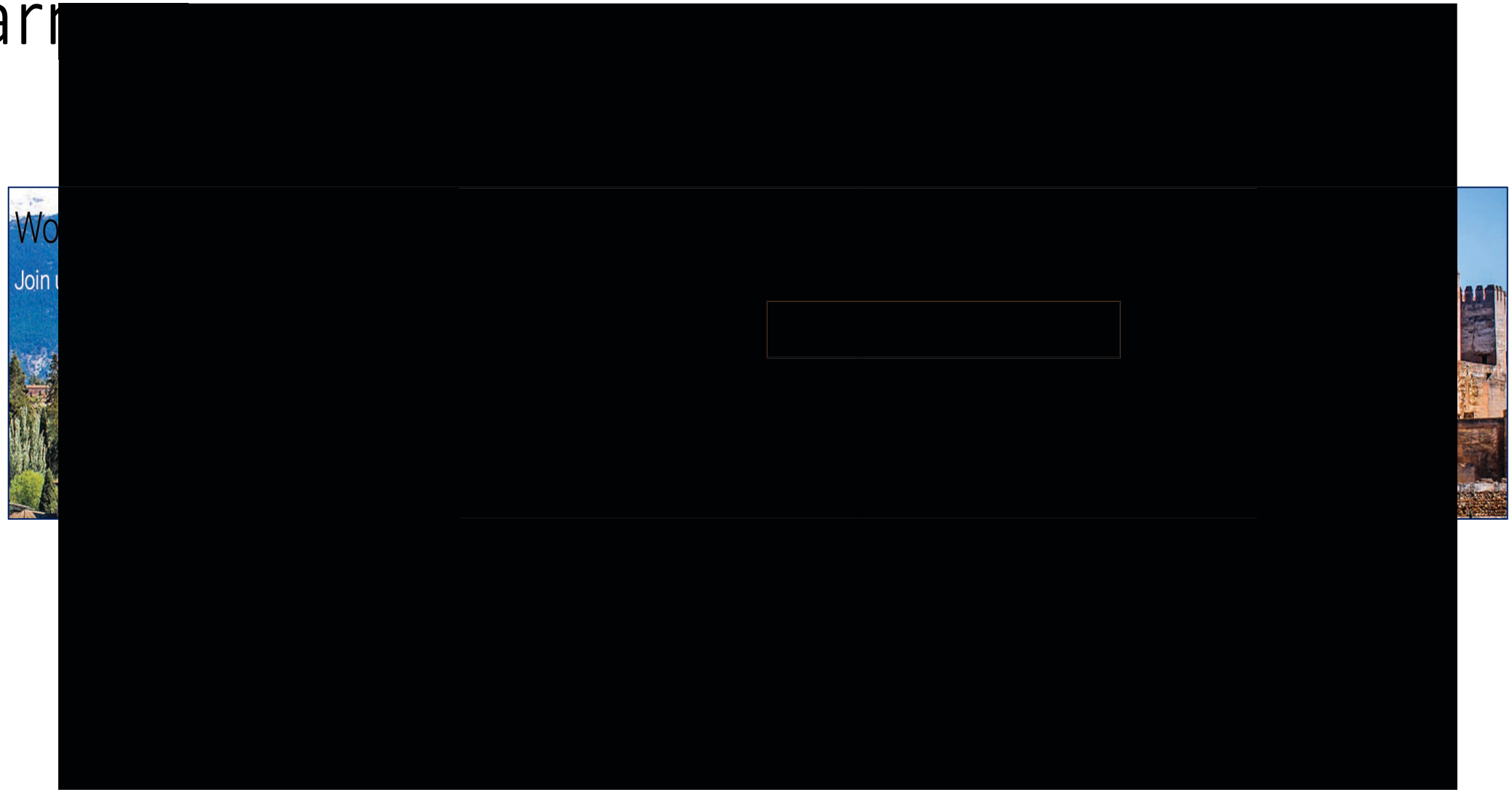
Transparency, interpretability, and explainability

*Transparency, interpretability, and explainability are **necessary to build patient and provider trust**. When a radiologist makes a mistake, we want to know why, in part because we want to know whether the mistake is excusable. We want to know whether the mistake reflects malintent or negligence, or occurred due to other factors.*

*Similarly, if an algorithm fails or contributes to an adverse clinical event or malpractice, radiologists need to be able to understand **why** it produced the result that it did, and **how** it reached a decision.*

https://www.acr.org/-/media/DSI/Files/PDFs/Ethics-of-AI-in-Radiology-Statement_RFC.pdf?la=en

Enhancing Interpretability of machine learn



Taxonomy

- **Black-boxes** operating methods: No need to have “access” to the internal of models. Also referred to as model-agnostic.
- **White-boxes**: These are methods that require access to the internals of the models. Gradient-based models are one example of white box interpretability models.
- By **output**:
  - Visualization, or saliency maps: Provide pixel-wise values reflecting their importance to the performance of the model being interpreted
  - Concepts: summary statement or keyword.
  - Feature importance: explain models by expressing importance of features E.g. high weights of a model.

Let’s check some of these approaches

Partial Dependence Plot (PDP) – Friedman et al. 2001

- shows the marginal effect that one or two features have on the predicted outcome of a machine learning model
- PDP can show whether the relationship between the target and a feature is linear, monotonous or more complex.

$$\hat{f}_{x_S}(x_S) = E_{x_C}\left[\hat{f}(x_S, x_C)\right] = \int \hat{f}(x_S, x_C) d\mathbb{P}(x_C) \quad = \quad \hat{f}_{x_S}(x_S) = \frac{1}{n}\sum_{i=1}^{n} \hat{f}(x_S, x_C^{(i)})$$

Feature being explained – variable

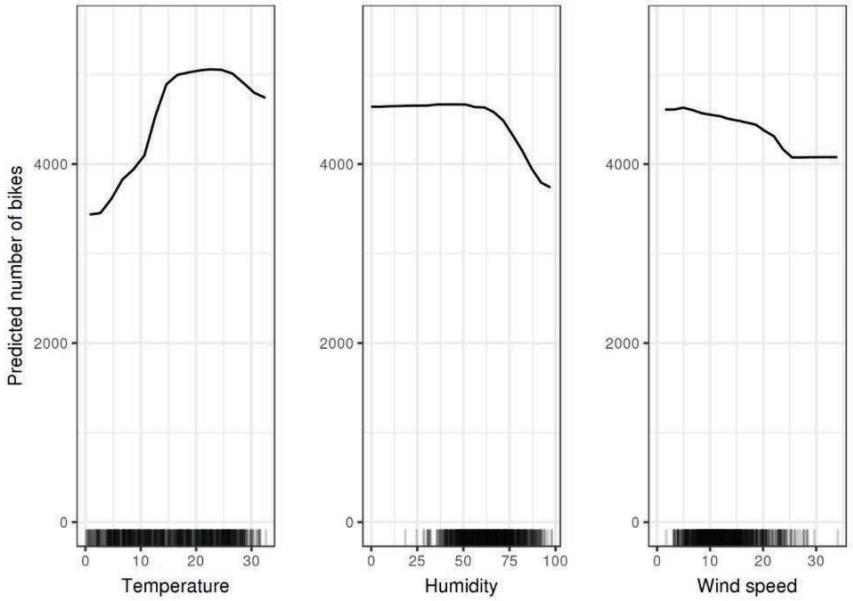
Marginalized over other features – Actual values

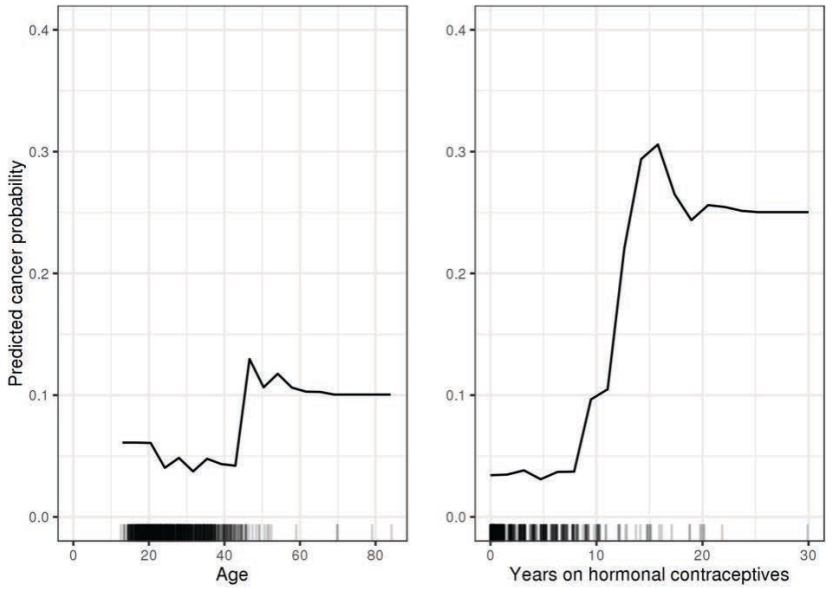
- Global method: The method considers all instances and gives a statement about the global relationship of a feature with the predicted outcome.

Source: Molnar, Christoph. "Interpretable machine learning. A Guide for Making Black Box Models Explainable", 2019. https://christophm.github.io/interpretable-ml-book/.

Partial Dependence Plot (PDP) – Friedman et al. 2001

Example: bike rental – Relation to temperature, humidity, windspeed





<u>Pros/Cons of PDP:</u>

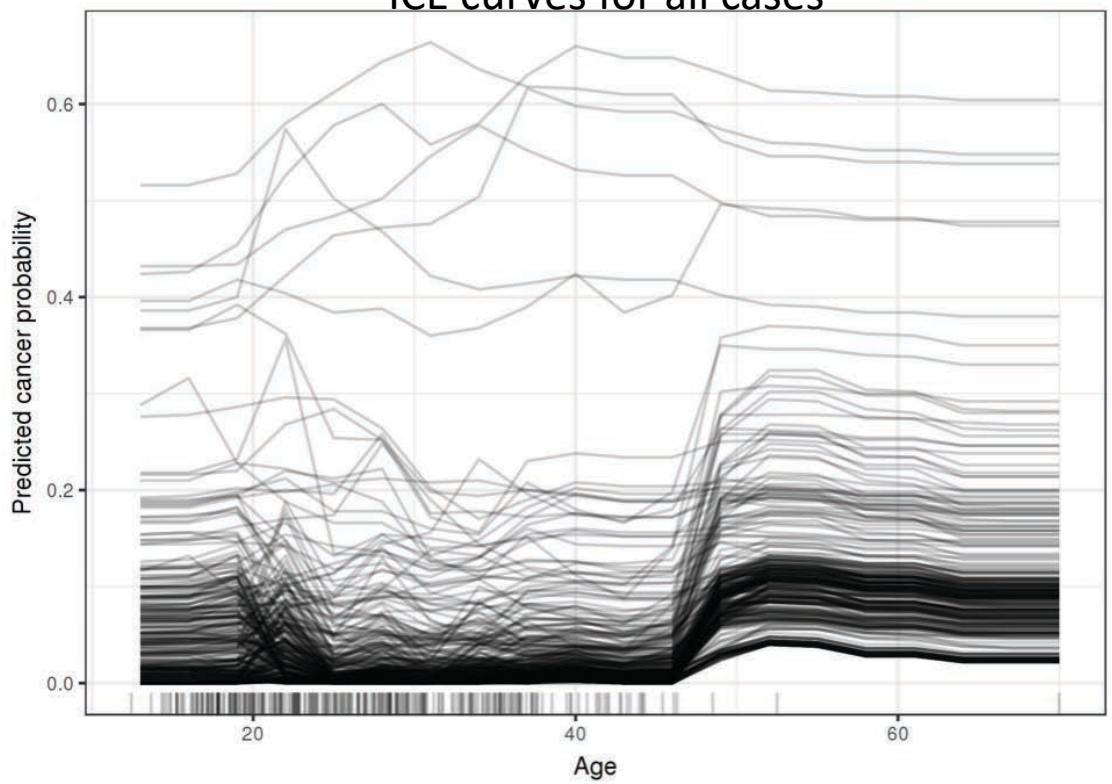
- Simple
- Easy to implement
- Does not account for correlated features
- More than 3 features is hard to visualize
- Doesn't show feature distribution
- Effects might cancel out

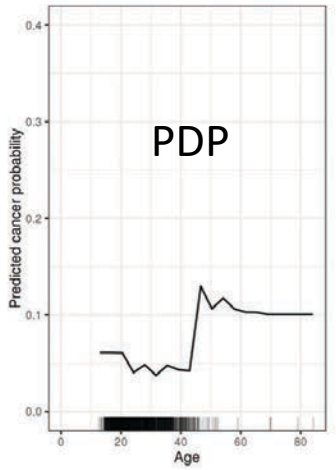
Source: Molnar, Christoph. "Interpretable machine learning. A Guide for Making Black Box Models Explainable", 2019. https://christophm.github.io/interpretable-ml-book/.

Individual Conditional Expectation (ICE)

- ICE shows how the instance's prediction changes when a feature changes. One feature at a time
- PDP is the average of ICE over all features

ICE curves for all cases





Actual values for other features

$$\hat{f}_{x_S}(x_S) = \left\{ \hat{f}(x_S, x_C) \right\}_{i=1..,N}$$

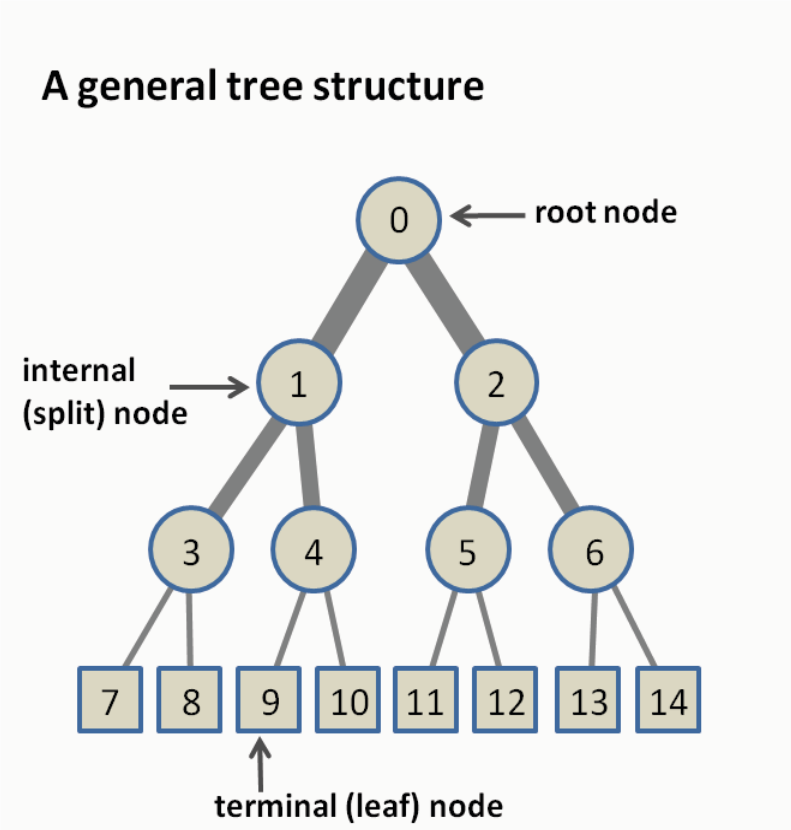
Variable - e.g. grid search

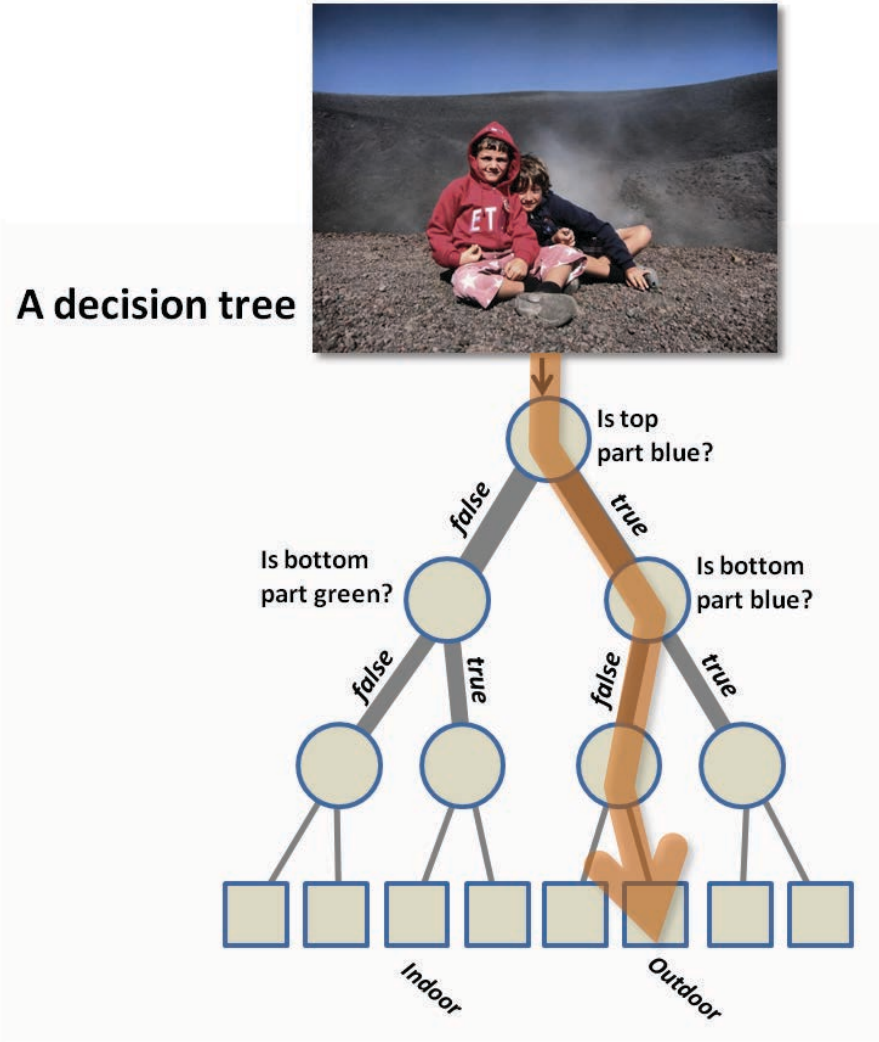
i^{th} case

Source: Molnar, Christoph. "Interpretable machine learning. A Guide for Making Black Box Models Explainable", 2019. https://christophm.github.io/interpretable-ml-book/.

Decision trees

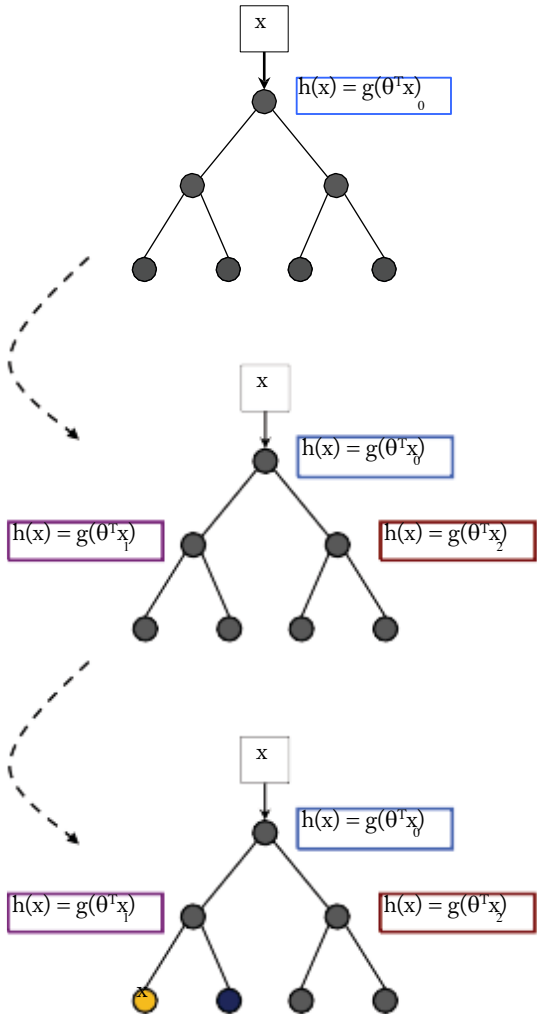
General Concept

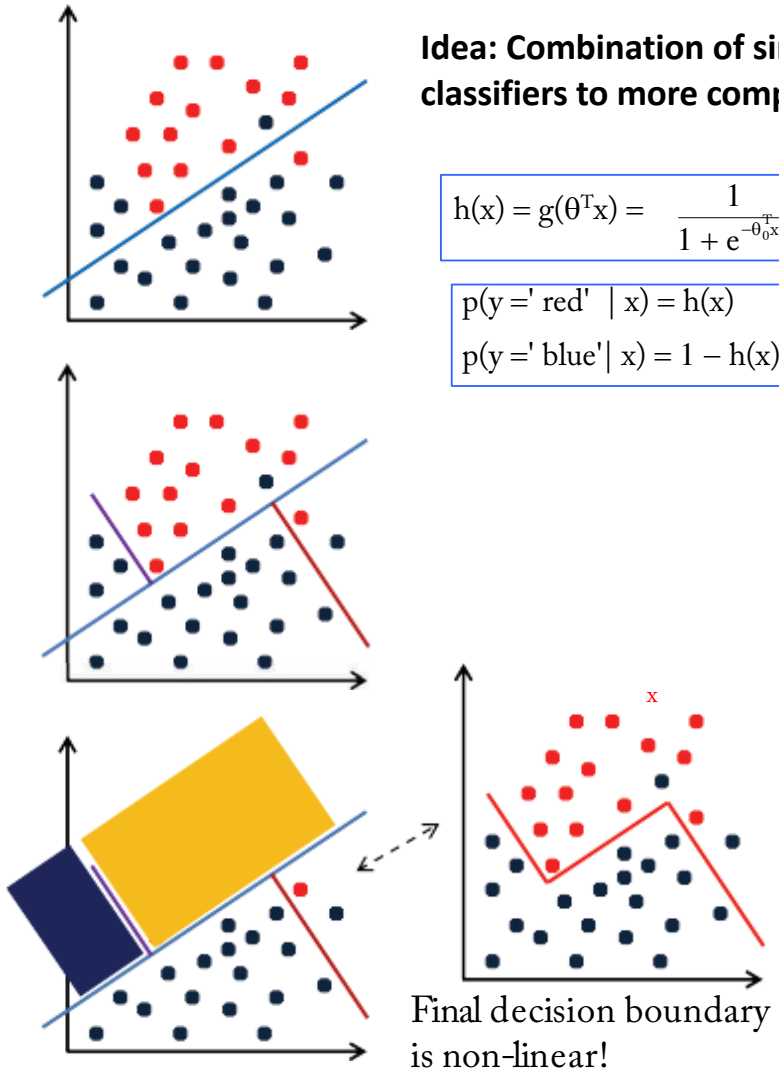




Transitioning from linear to non-linear classifier

- *Small* trees structure are interpretable
- Good for visualization
- Capture interactions among features
- However, subject to depth (D): number of terminal nodes is 2^D





Idea: Combination of simple classifiers to more complex ones

$$h(x) = g(\theta^T x) = \frac{1}{1 + e^{-\theta_0^T x}}$$

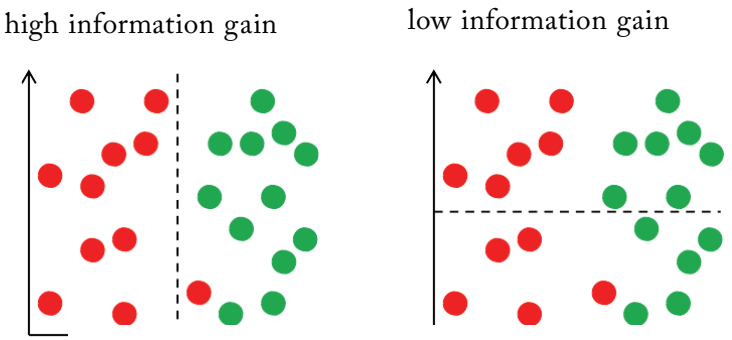
$$p(y = \text{' red'} \mid x) = h(x)$$
$$p(y = \text{' blue'} \mid x) = 1 - h(x)$$

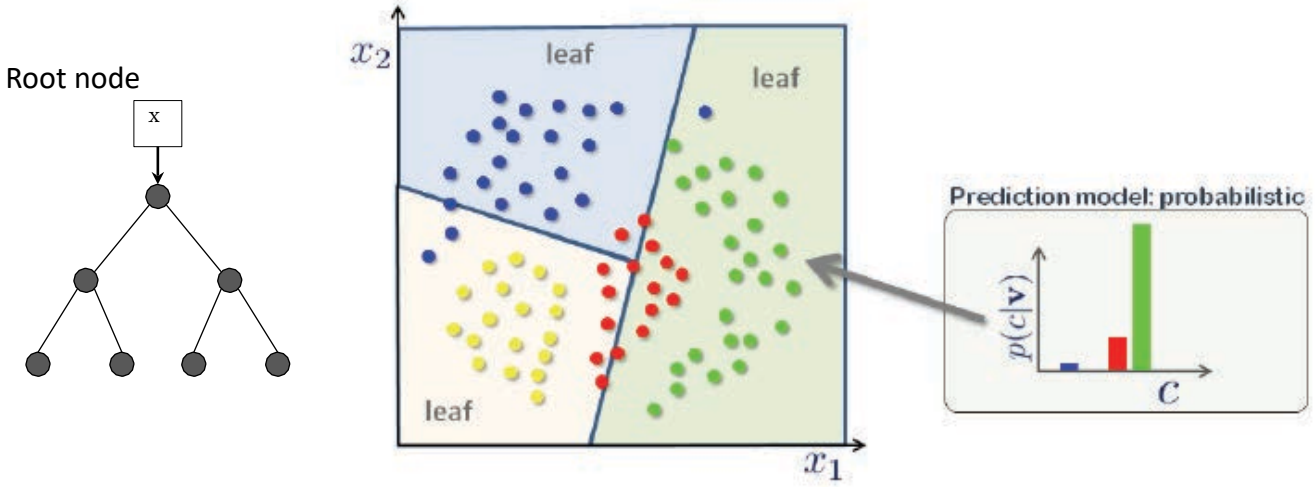
x

Final decision boundary is non-linear!

Interpretation of Decision Trees

- A model can be interpreted by analyzing the feature importance
- A feature is important when it maximally reduces impurity of split data
- Tree structure describes feature importance (e.g. root node features are most important)





Information Gain - IG

$$IG = H(\mathcal{S}) - \sum_{i \in \{L,R\}} \frac{|\mathcal{S}^i|}{|\mathcal{S}|} H(\mathcal{S}^i)$$

Entropy

$$H(\mathcal{S}) = \sum_{y \in \mathcal{Y}} p(y) \log p(y).$$

Alternative, Gini Index

$$\text{GI} = 1 - \sum p(y)$$

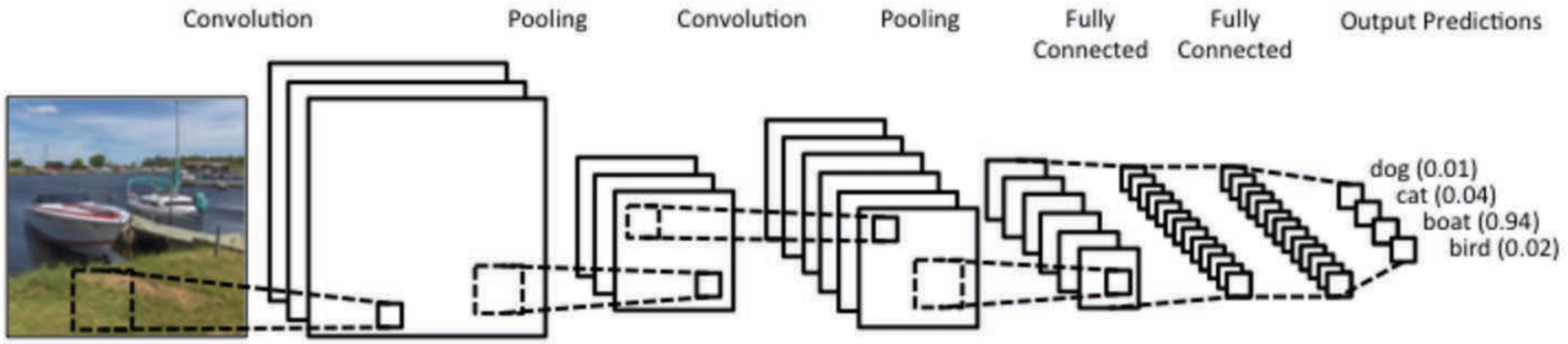
- IG favors smaller but varied partitions; GI favors larger partitions

Interpretable DL

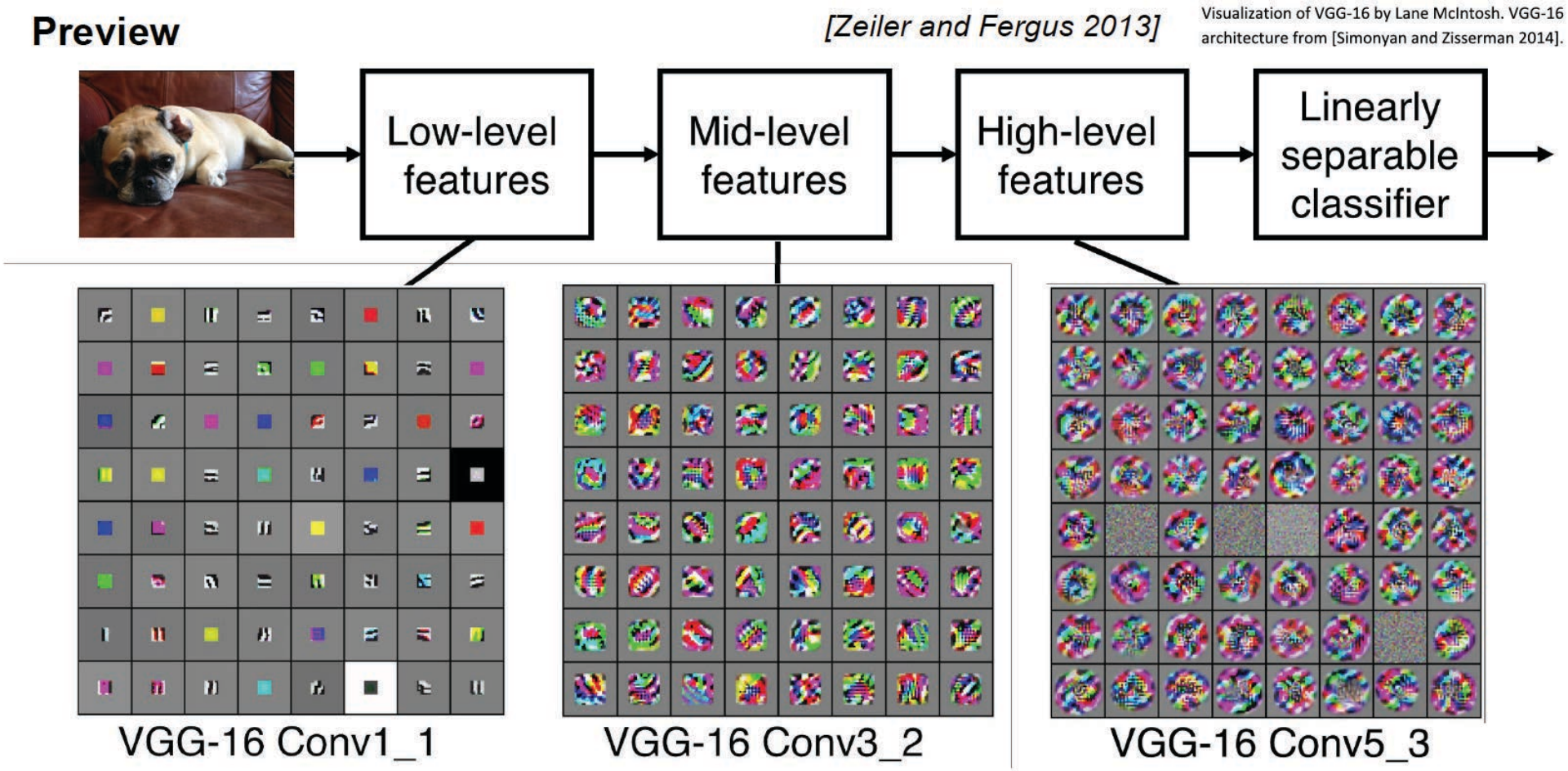
Convolutional Neural Networks

Typical structure:

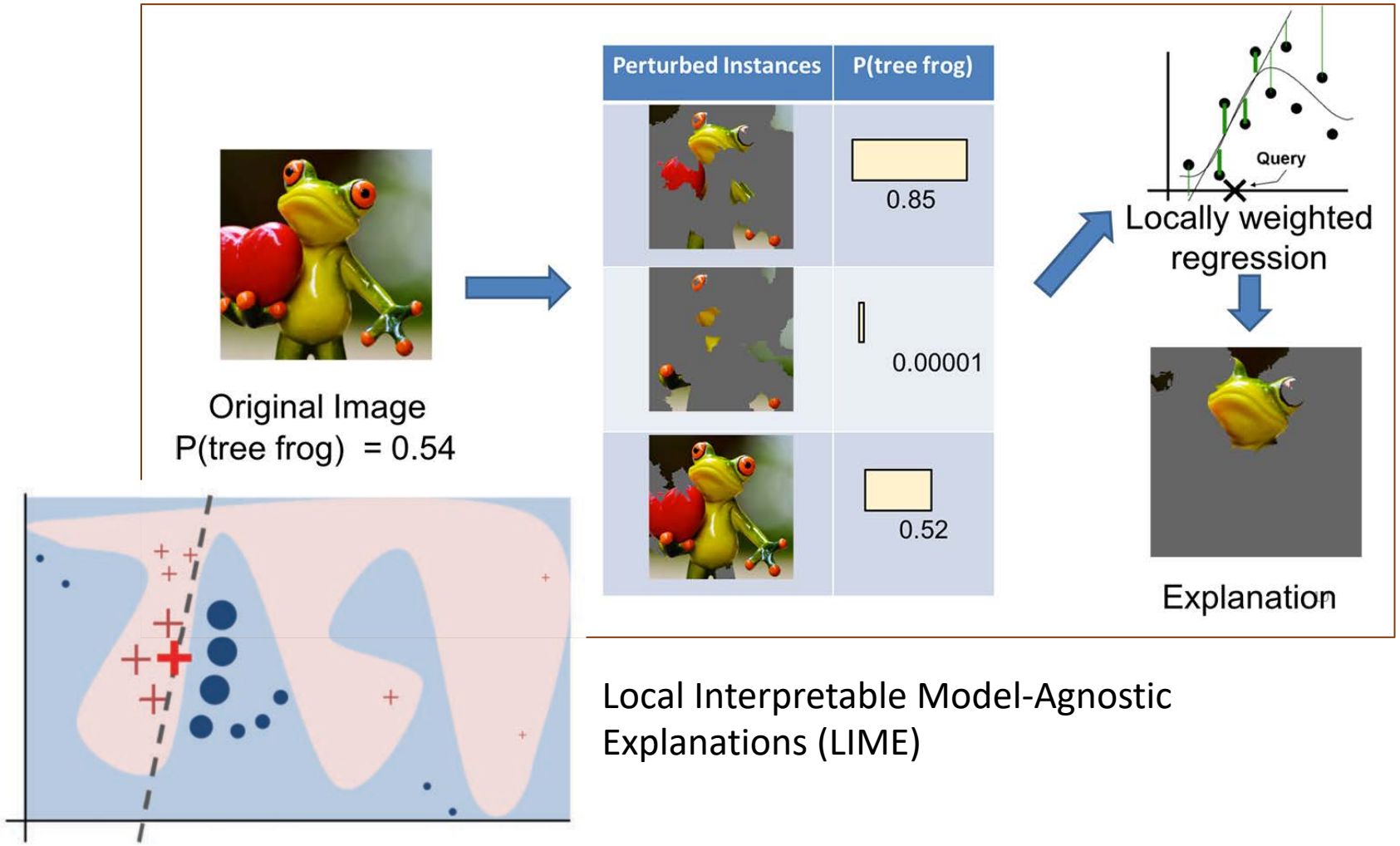
- Convolution layers
- Pooling or subsampling layers
- Fully connected layers



Convolutional Neural Networks



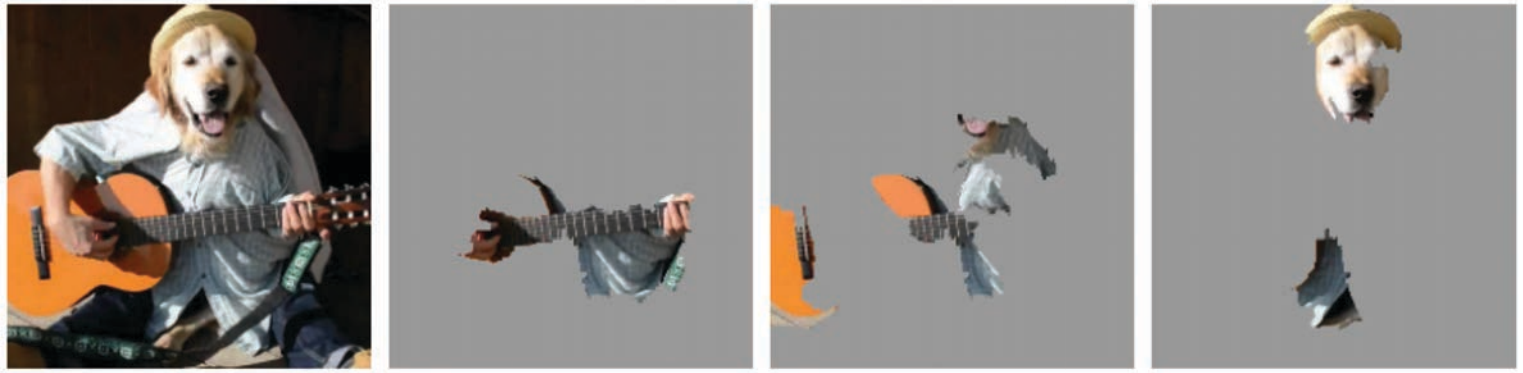
“Why Should I Trust You?” Explaining the Predictions of Any Classifier: Local Interpretable Model-agnostic Explanations (LIME) – Ribeiro et al . 2017



Local Interpretable Model-Agnostic Explanations (LIME)

Source: Ribeiro et al. 2017

“Why Should I Trust You?” Explaining the Predictions of Any Classifier: Local Interpretable Model-agnostic Explanations (LIME) – Ribeiro et al . 2017



(a) Original Image (b) Explaining *Electric guitar* (c) Explaining *Acoustic guitar* (d) Explaining *Labrador*

Figure 4: Explaining an image classification prediction made by Google’s Inception neural network. The top 3 classes predicted are “Electric Guitar” ($p = 0.32$), “Acoustic guitar” ($p = 0.24$) and “Labrador” ($p = 0.21$)

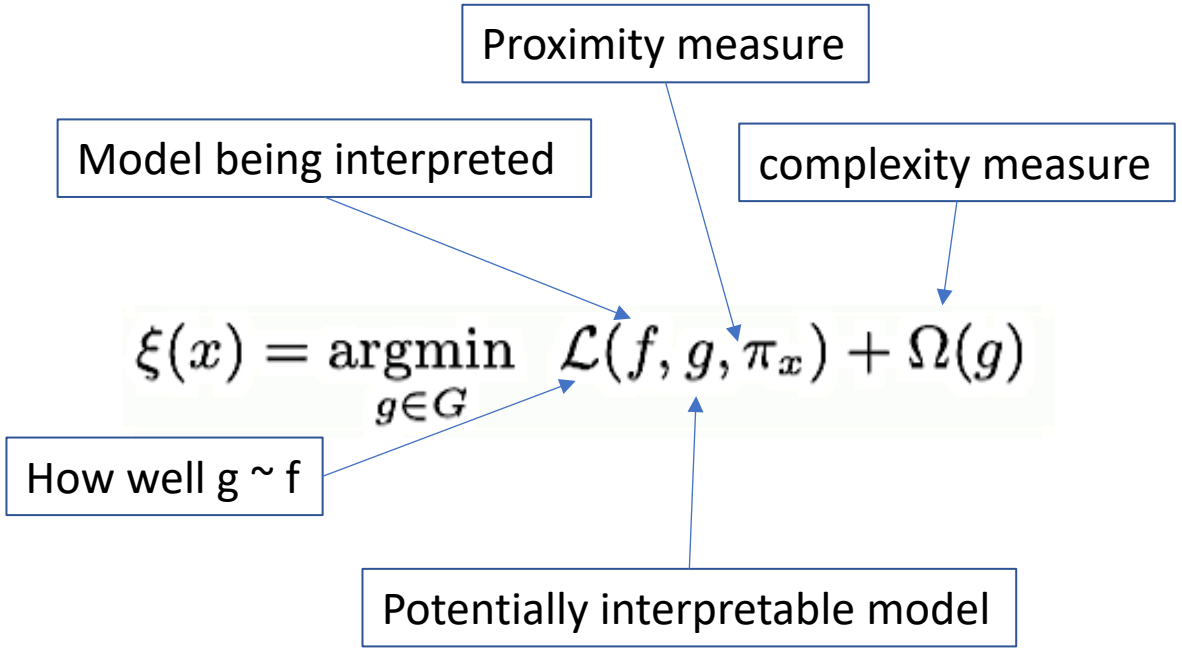
(a) Husky classified as wolf (b) Explanation

Figure 11: Raw data and explanation of a bad model’s prediction in the “Husky vs Wolf” task.

Source: Ribeiro et al. 2017

“Why Should I Trust You?” Explaining the Predictions of Any Classifier: Local Interpretable Model-agnostic Explanations (LIME) – Ribeiro et al . 2017

Local Interpretable Model-Agnostic Explanations (LIME)



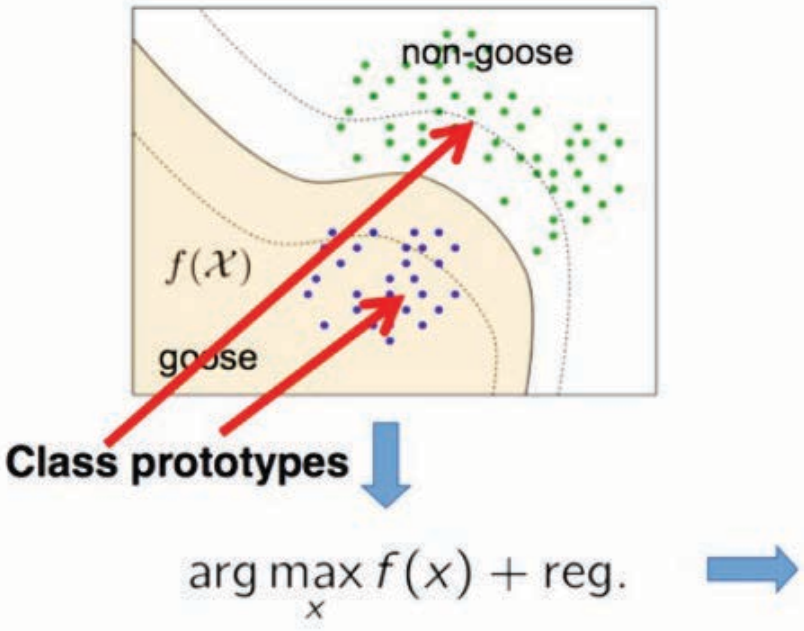
Algorithm 1 Sparse Linear Explanations using LIME

Require: Classifier f, Number of samples N
Require: Instance x, and its interpretable version x'
Require: Similarity kernel π_x, Length of explanation K

$\mathcal{Z} \leftarrow \{\}$
for $i \in \{1, 2, 3, ..., N\}$ **do**
  $z'_i \leftarrow sample\_around(x')$
  $\mathcal{Z} \leftarrow \mathcal{Z} \cup \langle z'_i, f(z_i), \pi_x(z_i) \rangle$
end for
$w \leftarrow$ K-Lasso$(\mathcal{Z}, K)$ ▷ with z'_i as features, $f(z)$ as target
return w

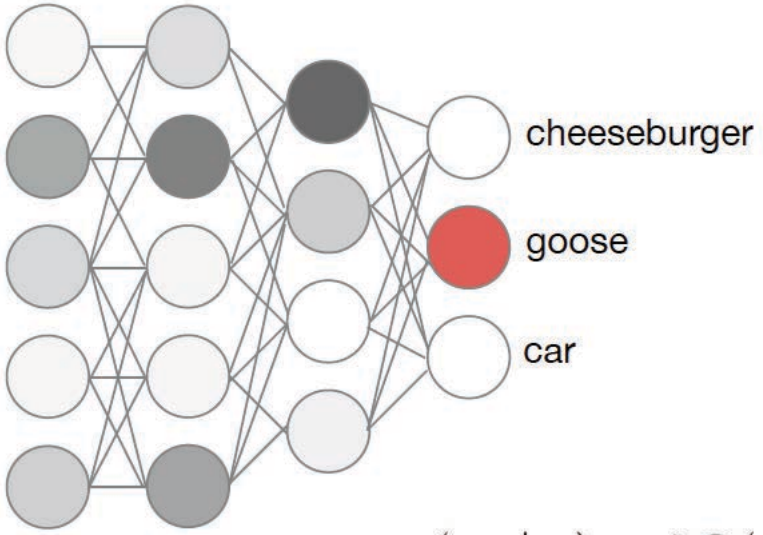
Source: Ribeiro et al. 2017

Explaining by finding prototype class members



Simonyan et al. 2013

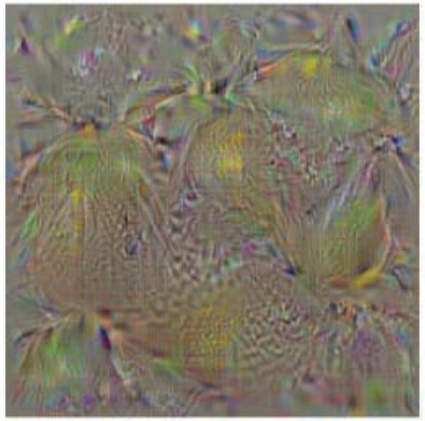
- Global explanation technique
- Find pattern maximizing class activation
- Not-necessarily a real image



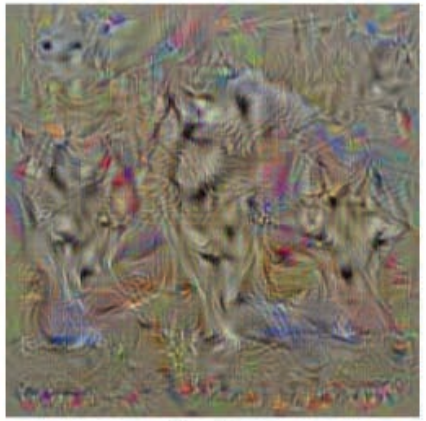
$$\max_{x \in \mathcal{X}} p_\theta(\omega_c \mid x) + \lambda \Omega(x)$$

Simonyan et al. 2013. Deep Inside Convolutional Networks: Visualising Image Classification Models and Saliency Maps

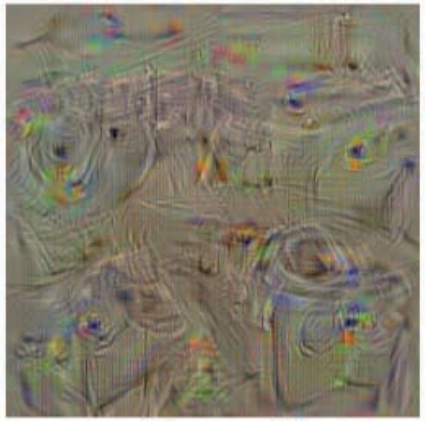
bell pepper



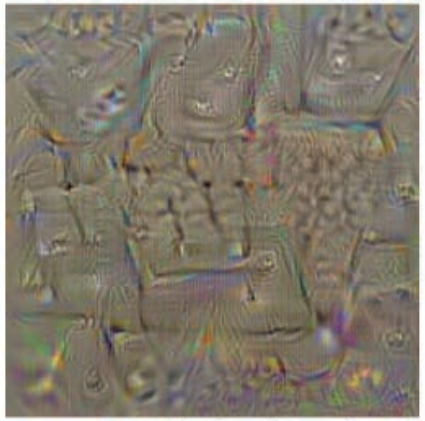
lemon



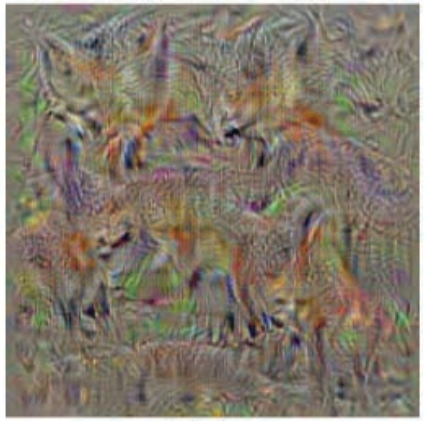
husky



washing machine



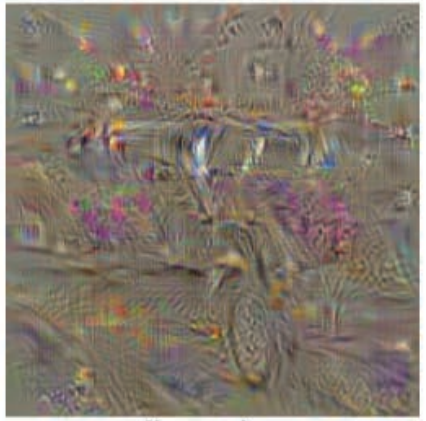
computer keyboard



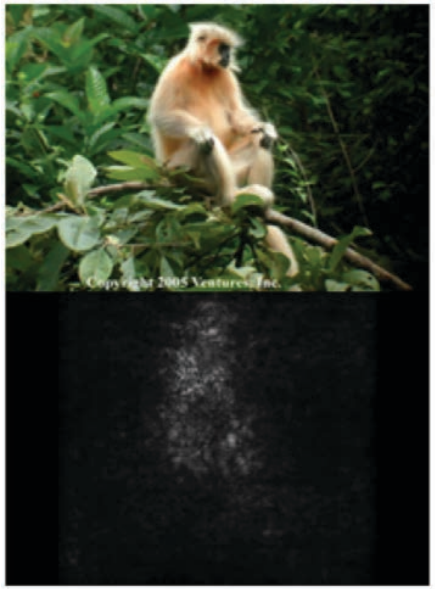
kit fox

goose

ostrich



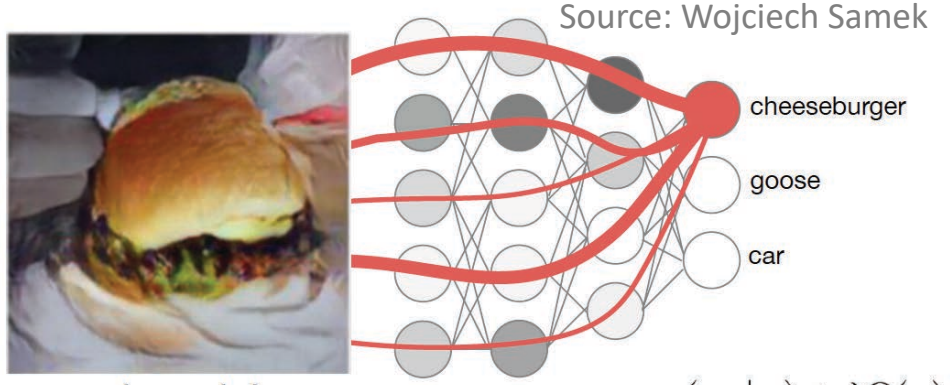
limousine



Simonyan et al. 2013. Deep Inside Convolutional Networks: Visualising Image Classification Models and Saliency Maps

Synthesizing the preferred inputs for neurons in neural networks via deep generator networks
 - Nguyen et al. 2016

Source: Wojciech Samek

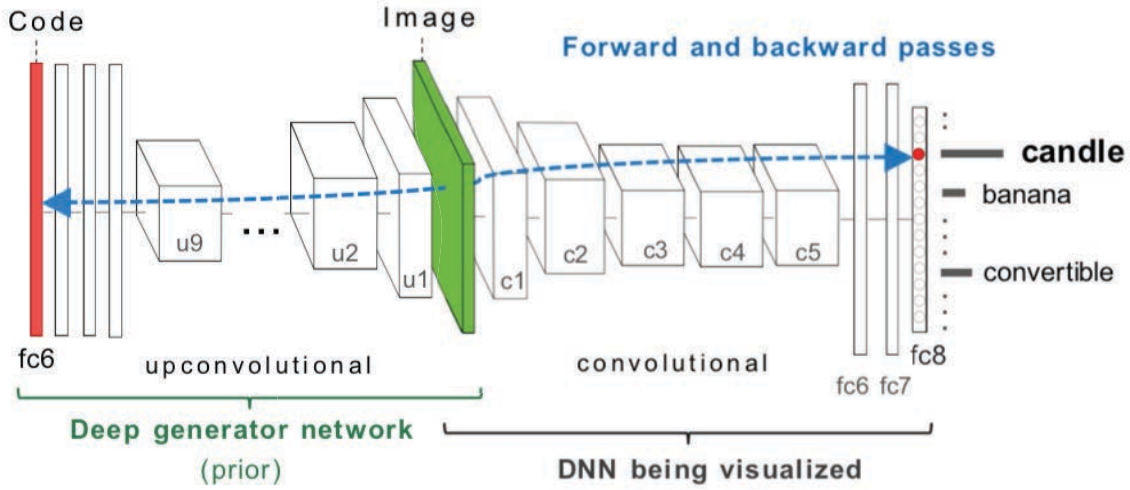


complex regularizer
(Nguyen et al. 2016)

$$\max_{x \in \mathcal{X}} p_\theta(\omega_c \mid x) + \lambda \Omega(x)$$

Regularization via generative adversarials

1.- Forwards pass of gradients
2- Detect maximum activation
3.- Backwark pass of “FC6” into encoder

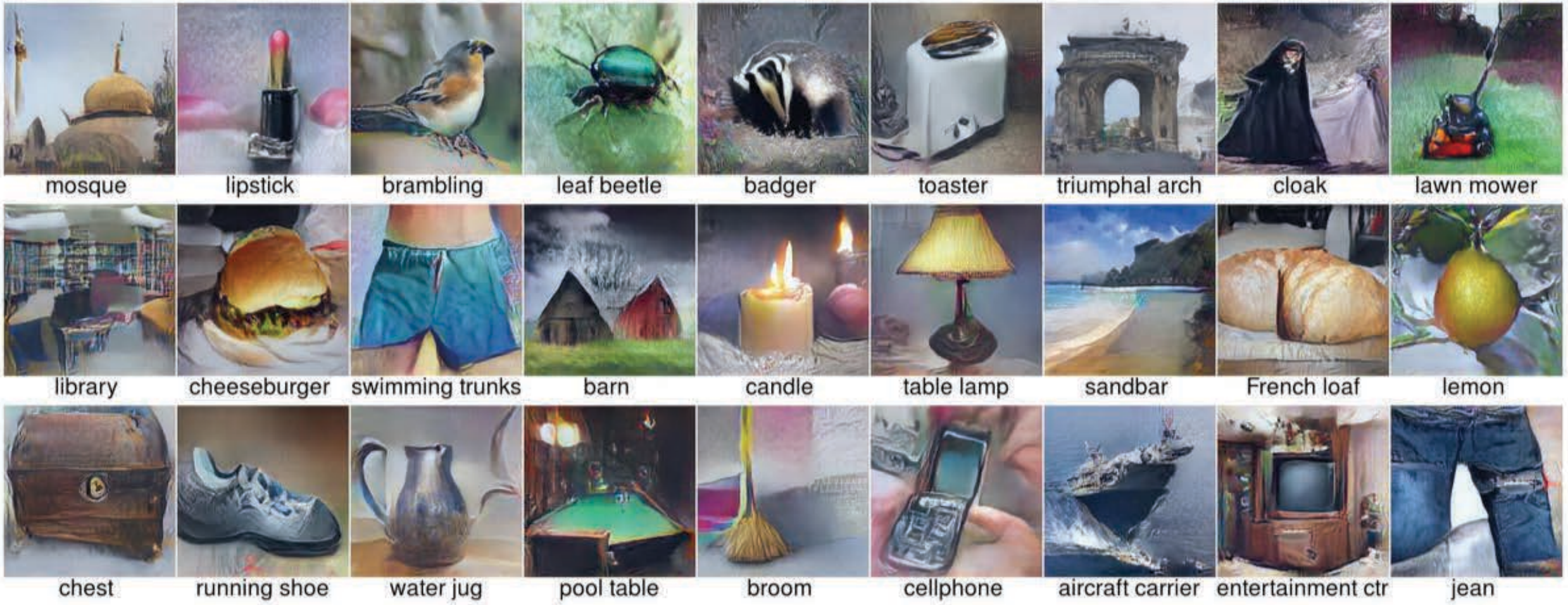


Feature vector | classifier | generator

$$\hat{\mathbf{y}}^l = \arg\max_{\mathbf{y}^l} (\Phi_h(G_l(\mathbf{y}^l)) - \lambda \|\mathbf{y}^l\|)$$

- Prior generator and DNN can be trained separately

Synthesizing the preferred inputs for neurons in neural networks via deep generator networks
- Nguyen et al. 2016



Gradient-based methods

- Idea: magnitude of gradient reflects importance (attribution) of input to output scores

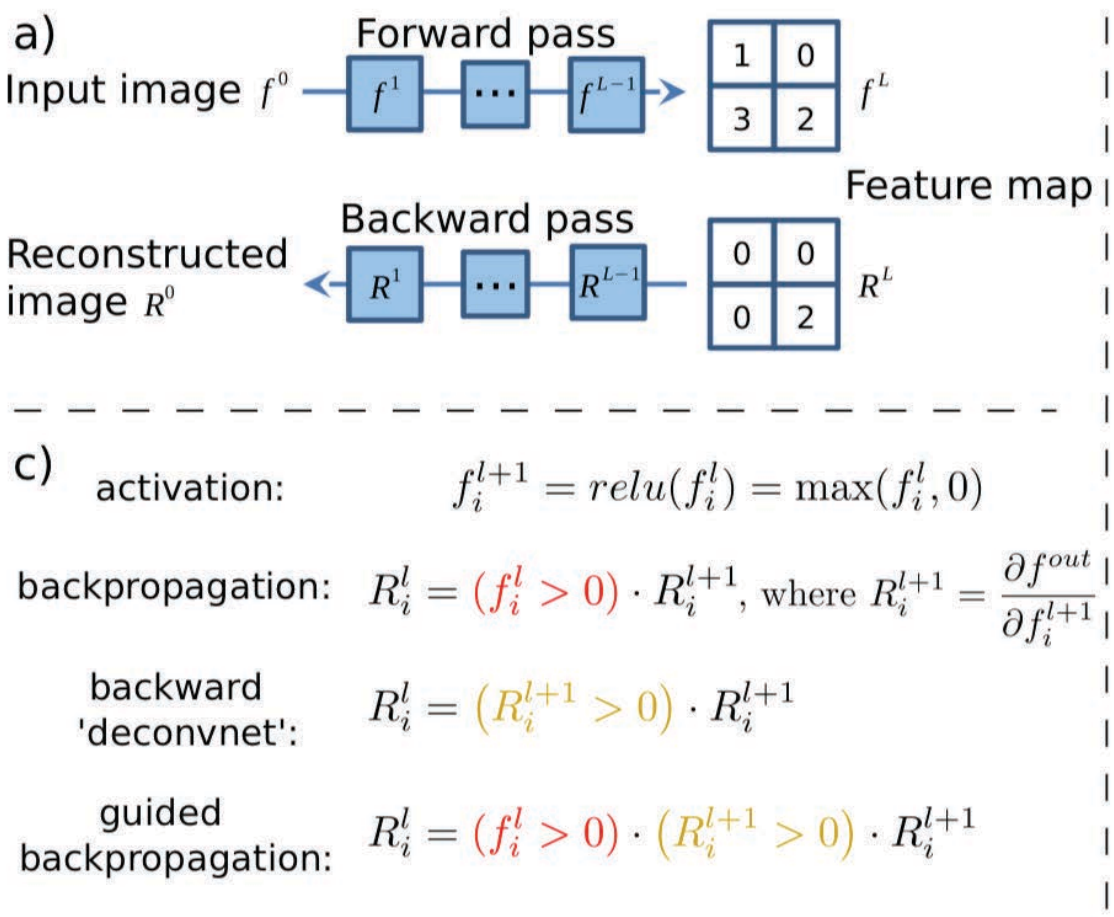
$$R = \sum \left(\frac{\delta S}{\delta x_i} \right)^2$$

Variations:

- Input * Gradient $x * \frac{\delta f}{\delta x_i}$ → Addresses gradient saturation and reduces diffusivity – Shrikumar et al. 2016
- Deconvnet: inverts direction of applying activation; zero outs negative activations– Zeiler et al. 2014
- Guided-backpropagation: deconvnet + filters out negative forward activations - Springenberg et al. 2015
- Integrated gradients: sums over scaled versions of input; addresses gradient saturation – Sundararajan et al. 2017
- Grad-CAM: includes a neuron importance weight (detailed later) - Selvaraju et al. 2017

Image source: Samek et al. 2018

Differences between backprop, deconvnet and guided-backpropagation



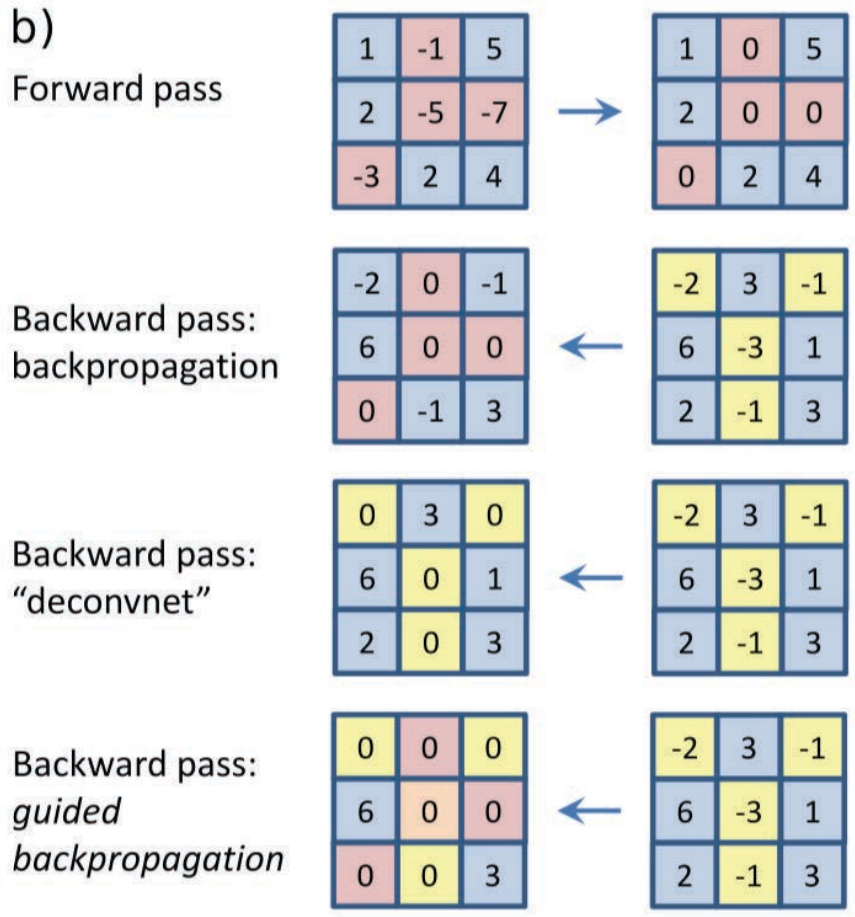


Image source: Springenberg et al. ICLR 2015

Gradients

Sensitivity
(Baehrens et al. 2010)

Sensitivity
(Morch et al., 1995)

Sensitivity
(Simonyan et al. 2014)

Gradient vs. Decomposition
(Montavon et al., 2018)

Gradient times input
(Shrikumar et al., 2016)

DeepLIFT
(Shrikumar et al., 2016)

Grad-CAM
(Selvaraju et al., 2016)

Integrated Gradient
(Sundararajan et al., 2017)

Decomposition

LRP for LSTM
(Arras et al., 2017)

Optimization

LIME
(Ribeiro et al., 2016)

Meaningful Perturbations
(Fong & Vedaldi 2017)

PatternLRP
(Kindermans et al., 2017)

Deconvolution

Deconvolution
(Zeiler & Fergus 2014)

Guided Backprop
(Springenberg et al. 2015)

Understanding the Model

Deep Visualization
(Yosinski et al., 2015)

Synthesis of preferred inputs
(Nguyen et al. 2016)

Inverting CNNs
(Dosovitskiy & Brox, 2015)

Feature visualization
(Erhan et al. 2009)

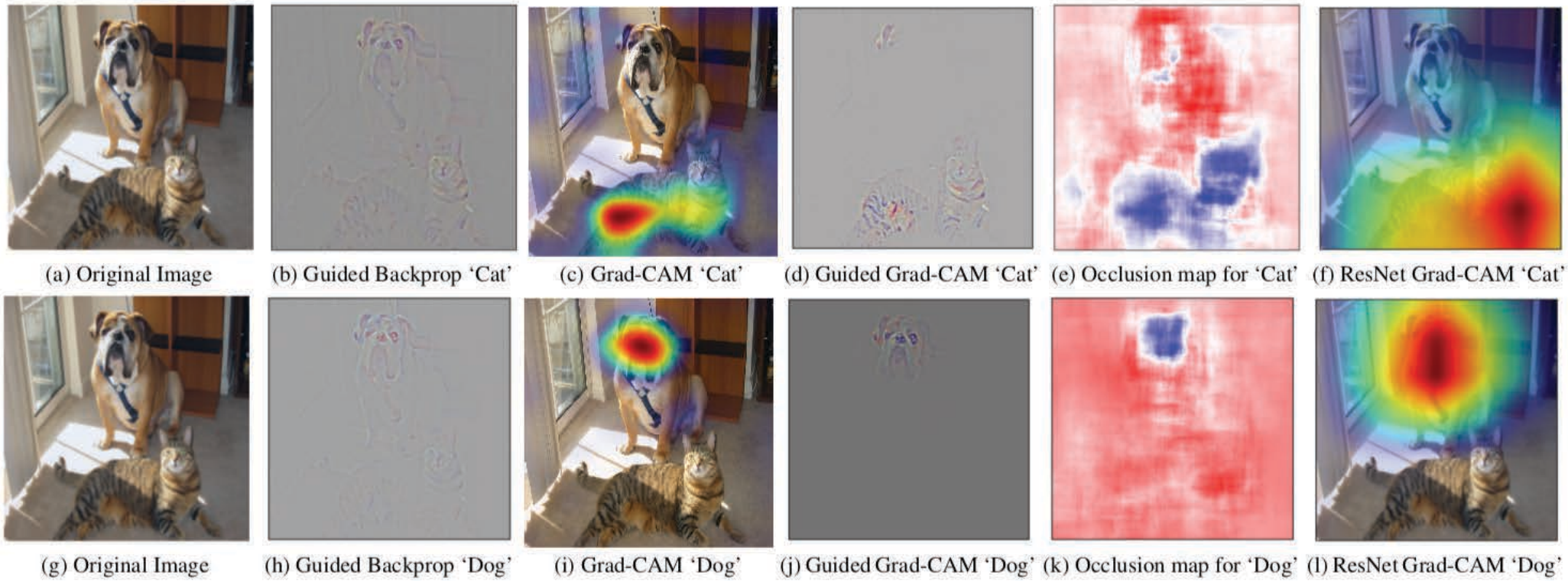
Inverting CNNs
(Mahendran & Vedaldi, 2015)

RNN cell state analysis
(Karpathy et al., 2015)

Network Dissection
(Zhou et al. 2017)

Grad-CAM: Visual Explanations from Deep Networks via Gradient-based Localization - Selvaraju et al. 2017

- Generalization of CAM: Zhou et al. Learning Deep Features for Discriminative Localization. In *CVPR*, 2016.
  - Applicable to any CNN-based (CAM requires conv feature maps → global average pooling → softmax layer)
- Motivation – Good visualization is class-specific and detailed

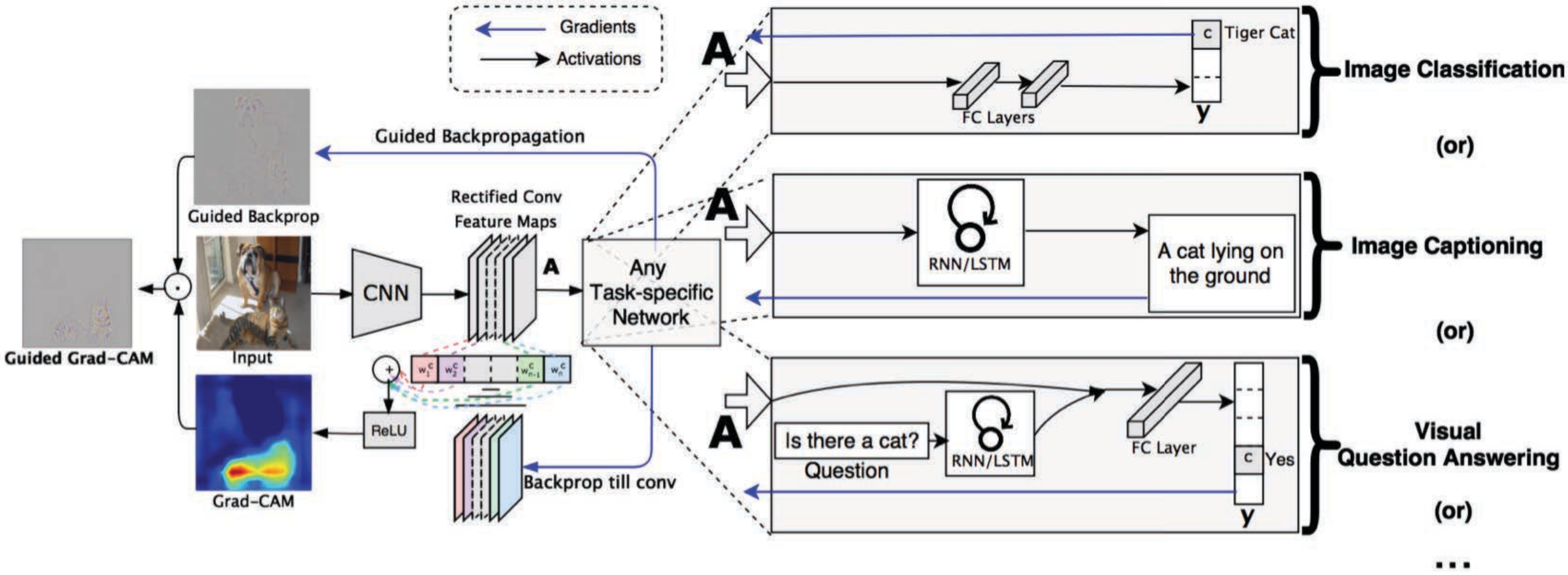


(a) Original Image (b) Guided Backprop 'Cat' (c) Grad-CAM 'Cat' (d) Guided Grad-CAM 'Cat' (e) Occlusion map for 'Cat' (f) ResNet Grad-CAM 'Cat'

(g) Original Image (h) Guided Backprop 'Dog' (i) Grad-CAM 'Dog' (j) Guided Grad-CAM 'Dog' (k) Occlusion map for 'Dog' (l) ResNet Grad-CAM 'Dog'

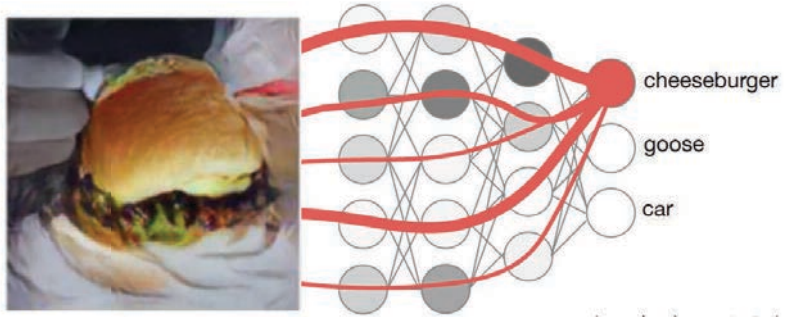
Grad-CAM: Visual Explanations from Deep Networks via Gradient-based Localization - Selvaraju et al. 2017

Guided-Grad-CAM: Uses Grad-CAM ask mask for Guided Backprop



Grad-CAM: Visual Explanations from Deep Networks via Gradient-based Localization - Selvaraju et al. 2017

Single forward and (partial) backward pass



Source: Wojciech Samek

Neuron importance weights $\alpha_k^c = \overbrace{\frac{1}{Z}\sum_i\sum_j}^{\text{global average pooling}} \underbrace{\frac{\partial y^c}{\partial A_{ij}^k}}_{\text{gradients via backprop}}$

A^k: kth feature map

y^c: score for class c (before softmax)

$$L^c_{\text{Grad-CAM}} = ReLU\underbrace{\left(\sum_k \alpha_k^c A^k\right)}_{\text{linear combination}}$$

Grad-CAM: Visual Explanations from Deep Networks via Gradient-based Localization - Selvaraju et al. 2017

Robustness to adversarial examples: Examples where VGG got “fooled”

Boxer: 0.40 Tiger Cat: 0.18

(a) Original image

Airliner: 0.9999

(b) Adversarial image

Boxer: 1.1e-20

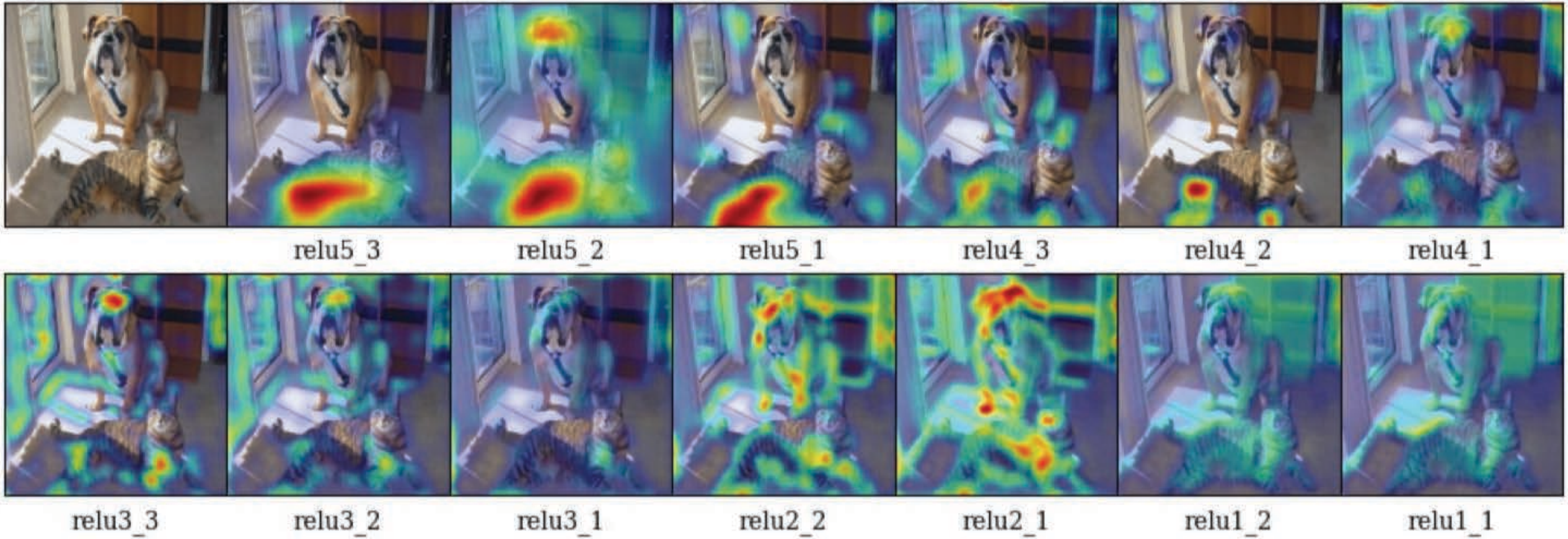
(c) Grad-CAM “Dog”

Tiger Cat: 6.5e-17

(d) Grad-CAM “Cat”

Grad-CAM: Visual Explanations from Deep Networks via Gradient-based Localization - Selvaraju et al. 2017

Layer-wise analysis



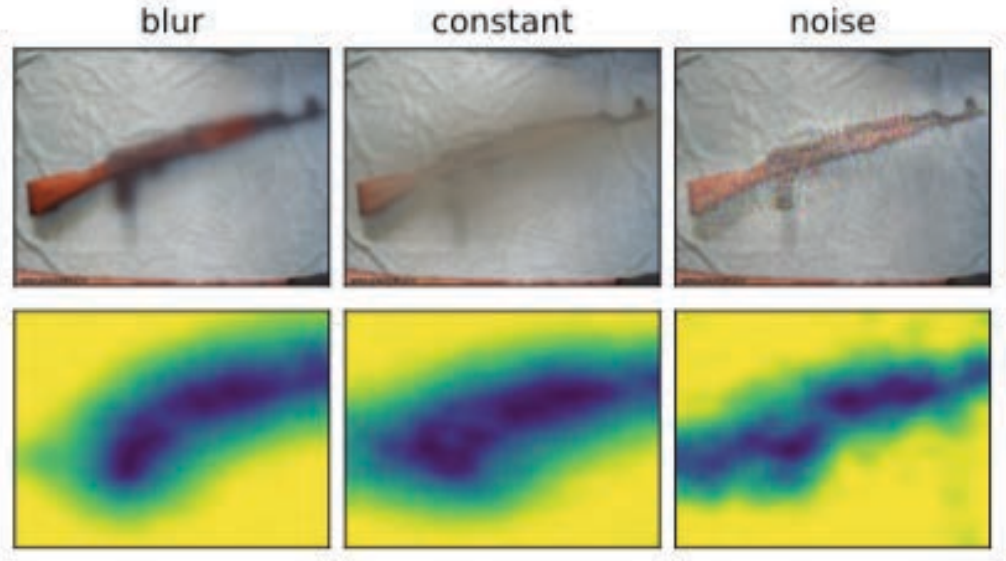
Interpretable Explanations of Black Boxes by Meaningful Perturbation - Fong et al. 2018

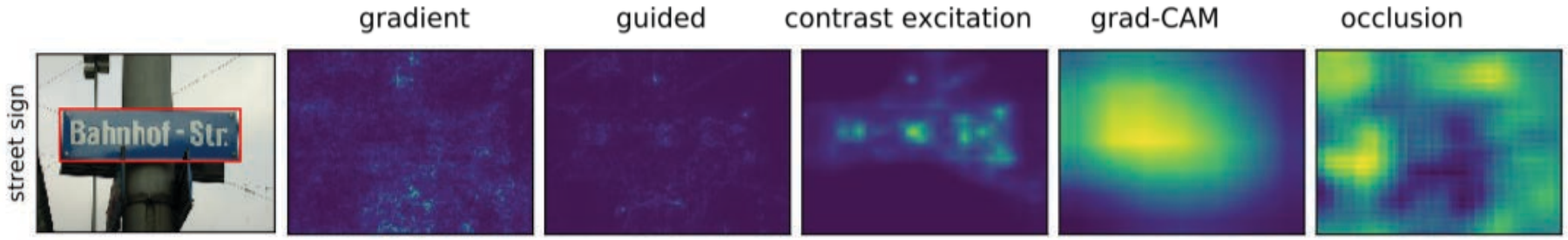
Motivation: Saliency (gradient-based) approaches are not specific enough

Key idea: select the right perturbation* to study the effect on the prediction function f(x)

Meaning of an explanation depends on the meaning of the changes applied to the input x

*Perturbation ←→ type of information deletion





Interpretable Explanations of Black Boxes by Meaningful Perturbation - Fong et al. 2018

Optimal "information deletion" mask

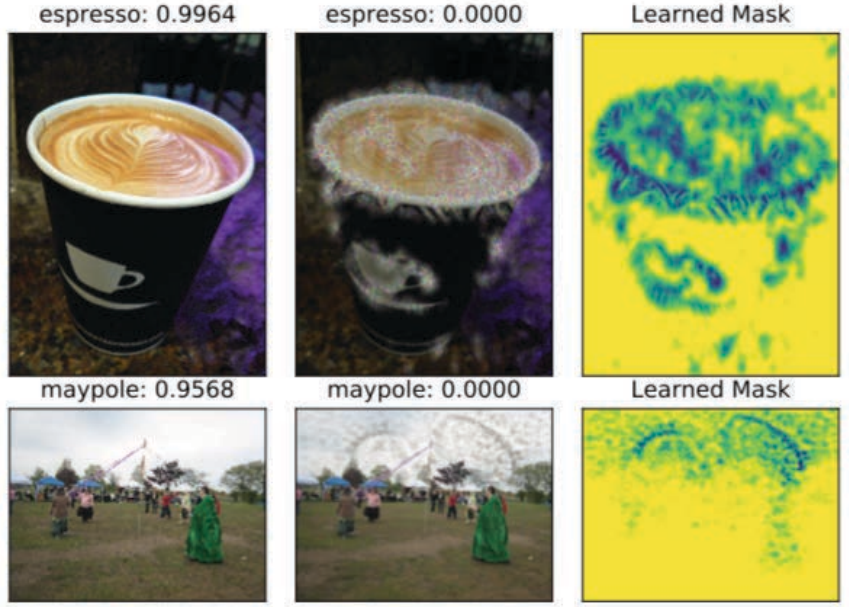
Enforces minimal mask size

perturbator

Input image

$$m^* = \underset{m \in [0,1]^\Lambda}{\operatorname{argmin}} \lambda \|\mathbf{1} - m\|_1 + f_c(\Phi(x_0; m))$$

Predictor for class c being interpreted



Can lead to unnatural perturbations → against explanations

Interpretable Explanations of Black Boxes by Meaningful Perturbation - Fong et al. 2018

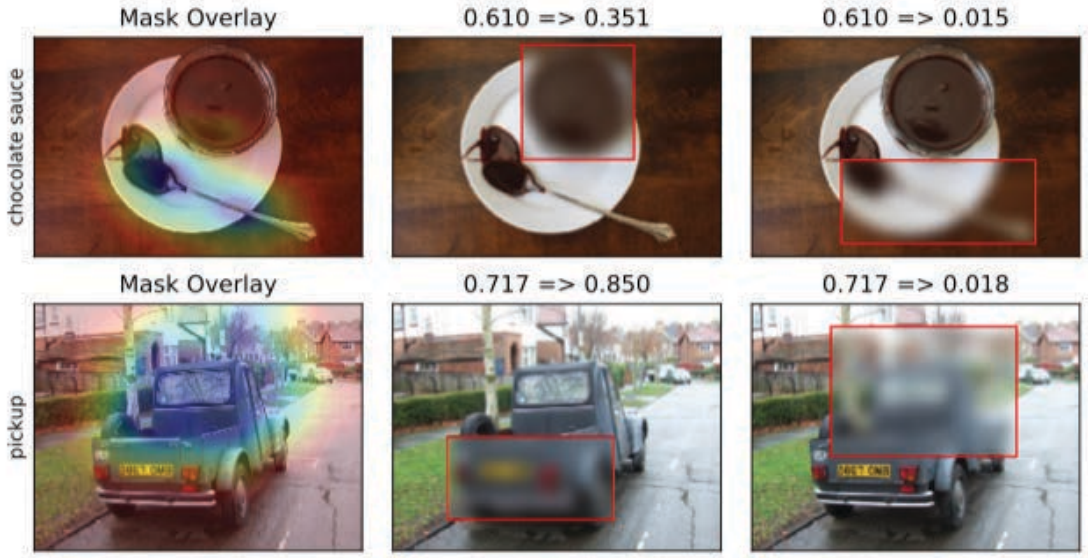
Enforces minimal mask size

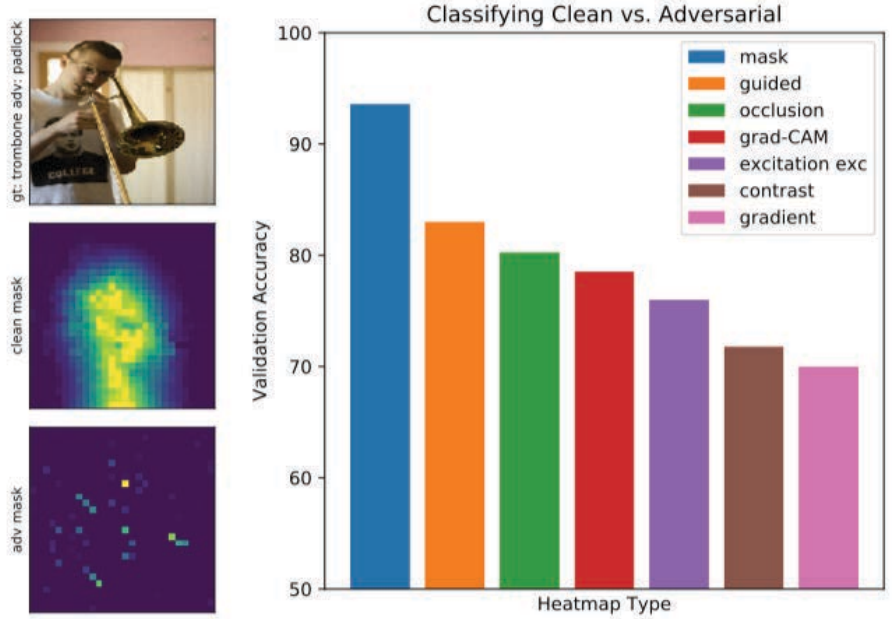
Enforces simplicity of the mask

$$\min_{m \in [0,1]^\Lambda} \lambda_1 \|\mathbf{1} - m\|_1 + \lambda_2 \sum_{u \in \Lambda} \|\nabla m(u)\|_\beta^\beta + \mathbb{E}_\tau [f_c(\Phi(x_0(\cdot - \tau), m))]$$

Expectation

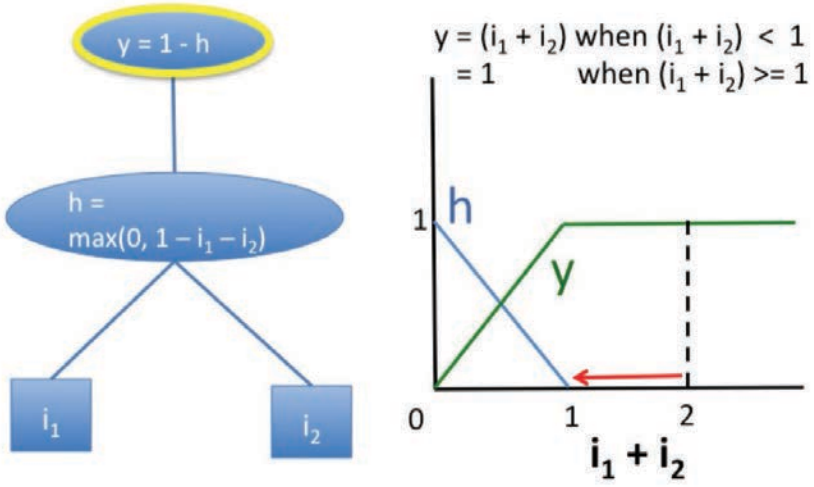
Add variability to the mask (via jitter)

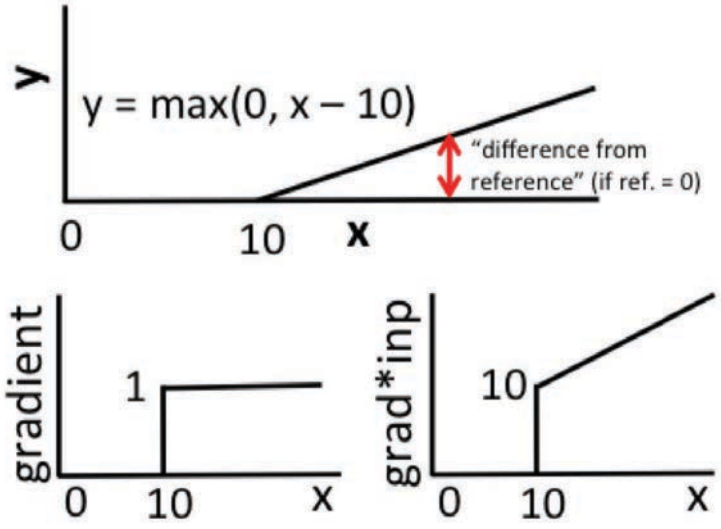




DeepLift - Learning Important Features Through Propagating Activation Differences – Shrikumar et al. 2017

- Also part of the “gradient backpropagation” family of methods
- Motivation: zero gradients not necessarily mean no attribution; consider positive and negative attributions
- Idea: measure importance by assessing difference to a “reference”





DeepLift - Learning Important Features Through Propagating Activation Differences – Shrikumar et al. 2017

- "reference"? → default or neutral state ?(e.g. black image)

Difference between neuron output and its reference value

$$\sum_{i=1}^{n} C_{\Delta x_i \Delta t} = \Delta t$$

Contribution measure: difference to delta_t attributed to differences in input x

Positive and negative contributions

$$\Delta x_i = \Delta x_i^+ + \Delta x_i^-$$

$$C_{\Delta x_i \Delta t} = C_{\Delta x_i^+ \Delta t} + C_{\Delta x_i^- \Delta t}$$

Dense and conv. layers

$$C_{\Delta x_i^+ \Delta y^+} = 1\{w_i \Delta x_i > 0\} w_i \Delta x_i^+$$

$$C_{\Delta x_i^- \Delta y^+} = 1\{w_i \Delta x_i > 0\} w_i \Delta x_i^-$$

$$C_{\Delta x_i^+ \Delta y^-} = 1\{w_i \Delta x_i < 0\} w_i \Delta x_i^+$$

$$C_{\Delta x_i^- \Delta y^-} = 1\{w_i \Delta x_i < 0\} w_i \Delta x_i^-$$

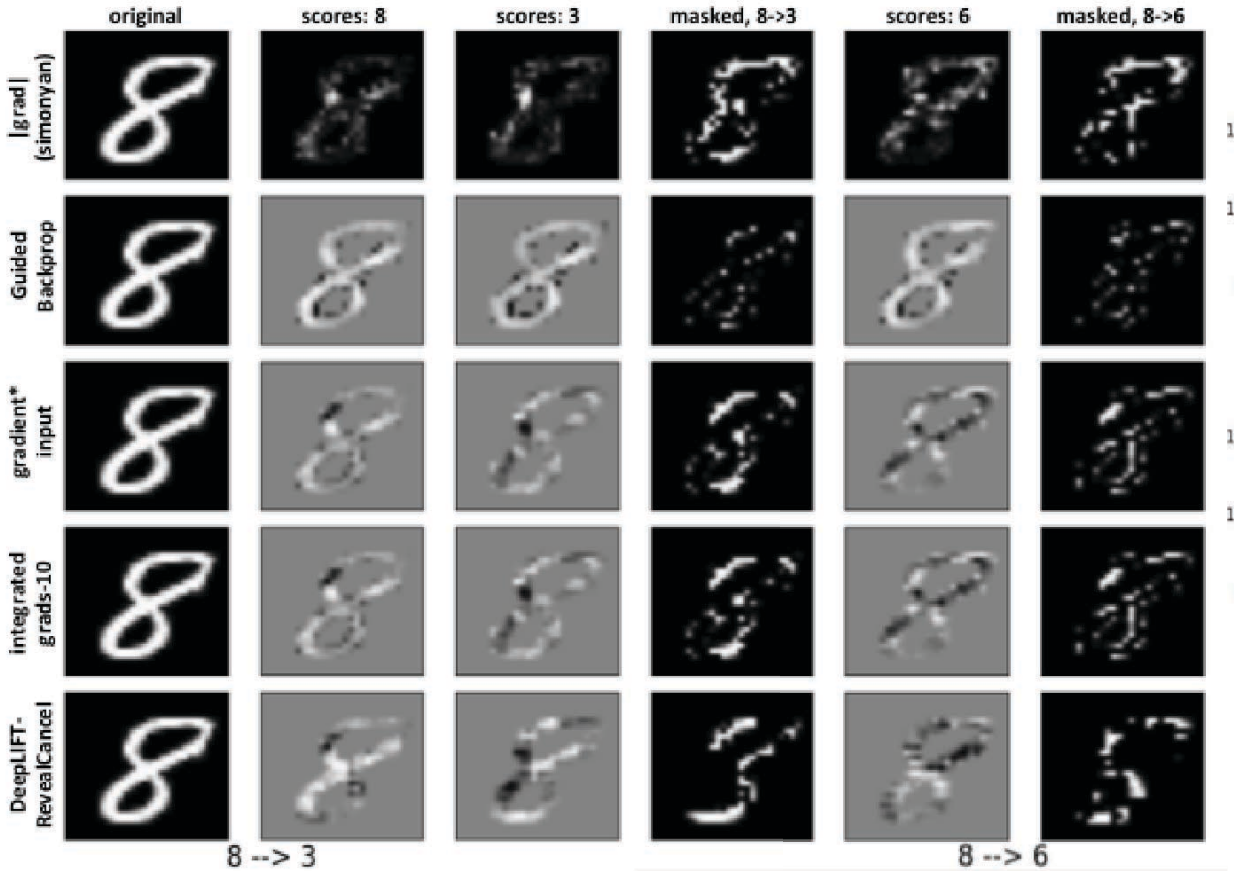
Non-linear (e.g.ReLU)

$$C_{\Delta x \Delta y} = \Delta y$$

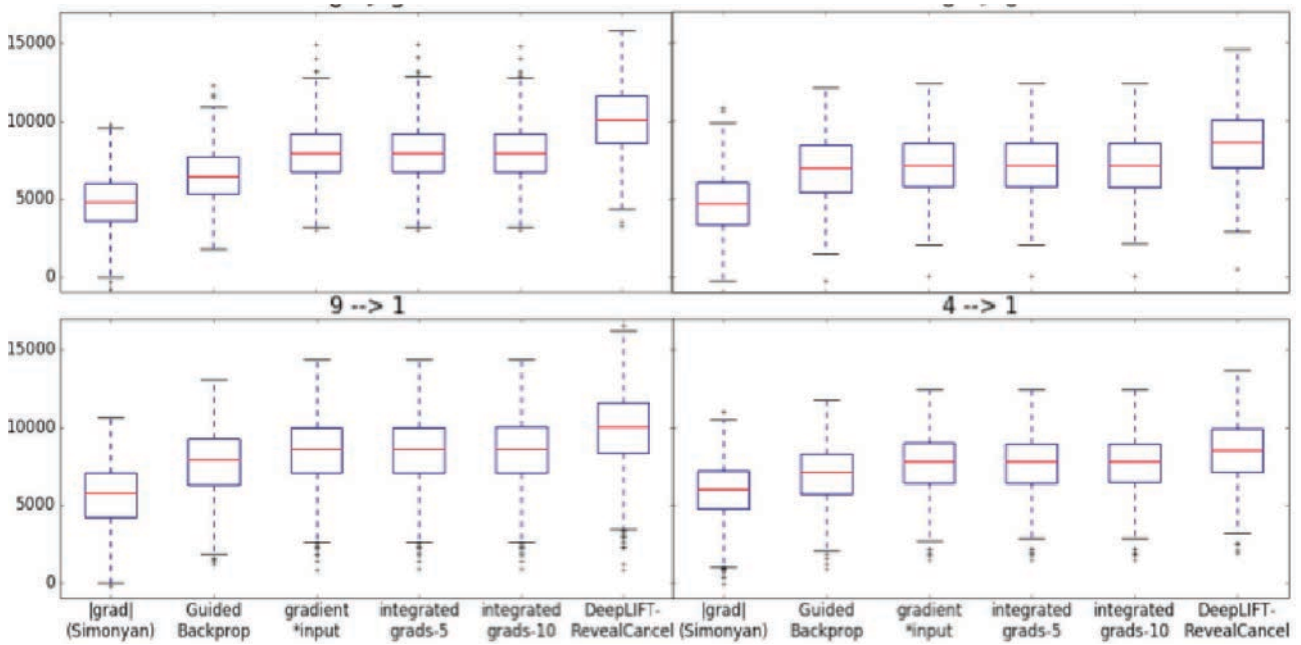
Approximates gradient

DeepLift - Learning Important Features Through Propagating Activation Differences – Shrikumar et al. 2017

Evaluation on MNIST: maximizing transition between digits



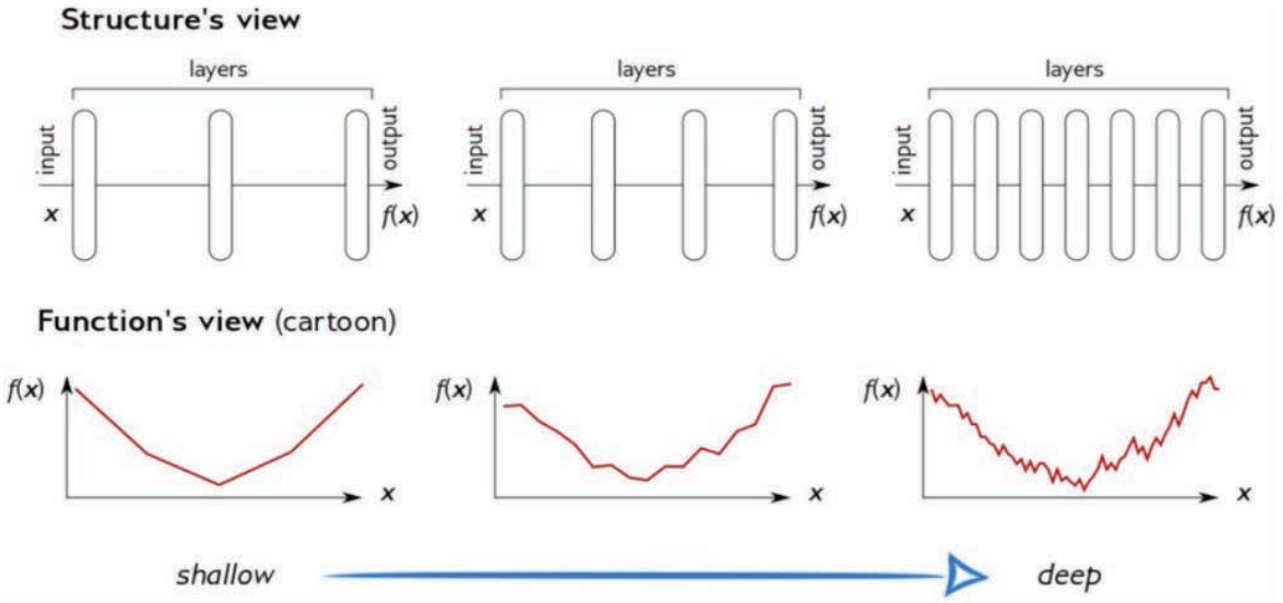
log-odds scores of target vs. original class after the mask is applied



Layer-wise Relevance Propagation (LRP) -

Bach et al., PLOS ONE, 2015

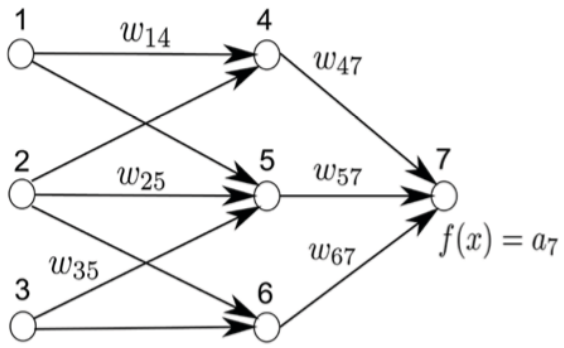
- Motivation: Gradient methods suffering from shattered gradient problem → depth affects reliability of computed input gradients
- Sensitivity explains changes to the prediction function, not the function's value itself.



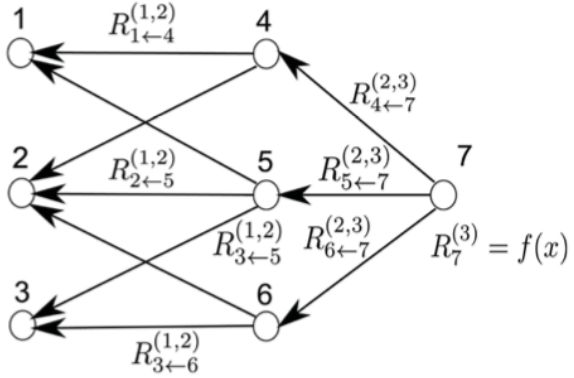
Source: Wojciech Samek

Layer-wise Relevance Propagation (LRP) -

Bach et al., PLOS ONE, 2015



Testing



Relevance propagation

Conditions

$$R_7^{(3)} = R_{4\leftarrow 7}^{(2,3)} + R_{5\leftarrow 7}^{(2,3)} + R_{6\leftarrow 7}^{(2,3)}$$

$$R_4^{(2)} = R_{1\leftarrow 4}^{(1,2)} + R_{2\leftarrow 4}^{(1,2)}$$

$$R_5^{(2)} = R_{1\leftarrow 5}^{(1,2)} + R_{2\leftarrow 5}^{(1,2)} + R_{3\leftarrow 5}^{(1,2)}$$

$$R_6^{(2)} = R_{2\leftarrow 6}^{(1,2)} + R_{3\leftarrow 6}^{(1,2)}$$

As a function of activations “a” and neuron weights “w”. Example:

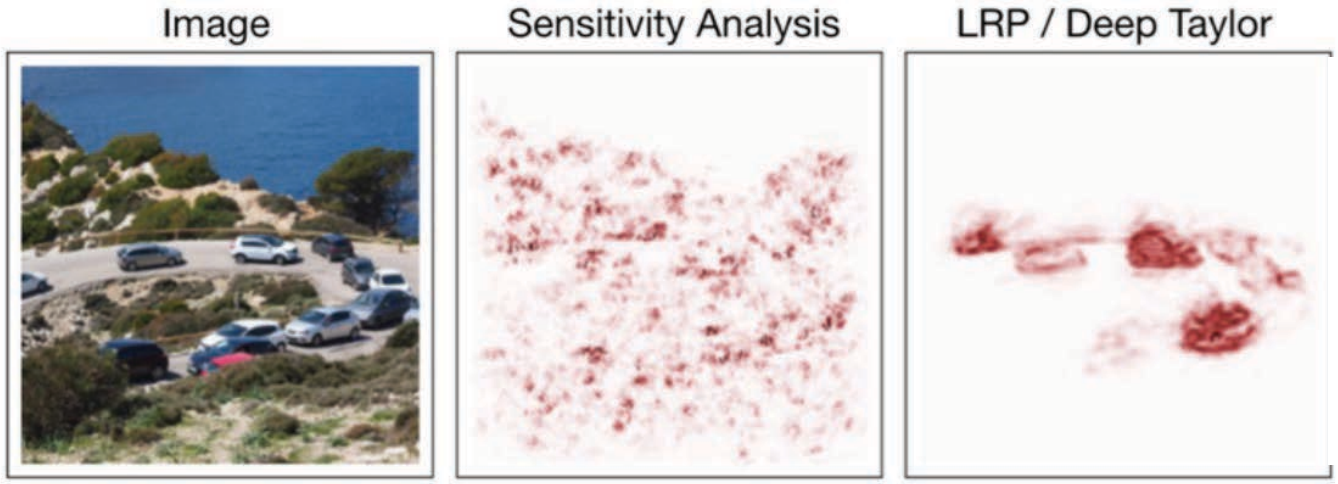
$$R_4^{(2)} = R_4^{(2)} \frac{a_1 w_{14}}{\sum_{i=1,2} a_i w_{i4}} + R_4^{(2)} \frac{a_2 w_{24}}{\sum_{i=1,2} a_i w_{i4}}$$

General formulation

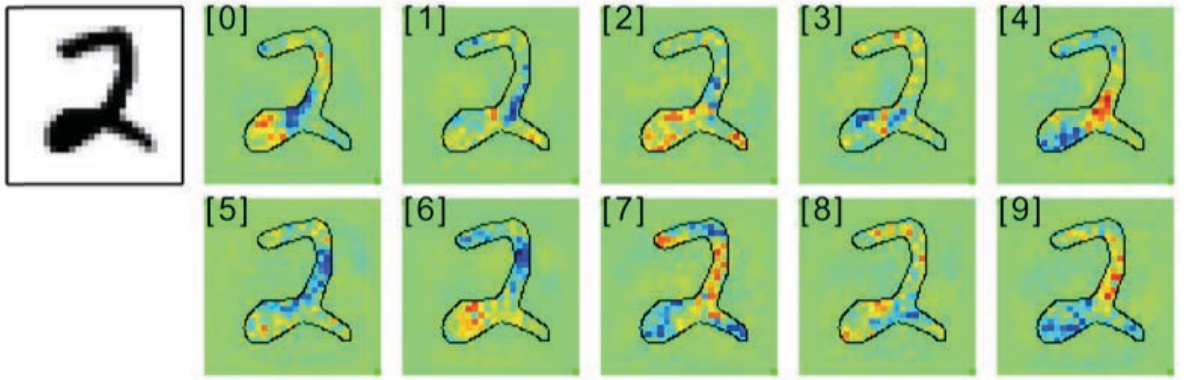
$$R_{i\leftarrow k}^{(l,l+1)} = R_k^{(l+1)} \frac{a_i w_{ik}}{\sum_h a_h w_{hk}}$$

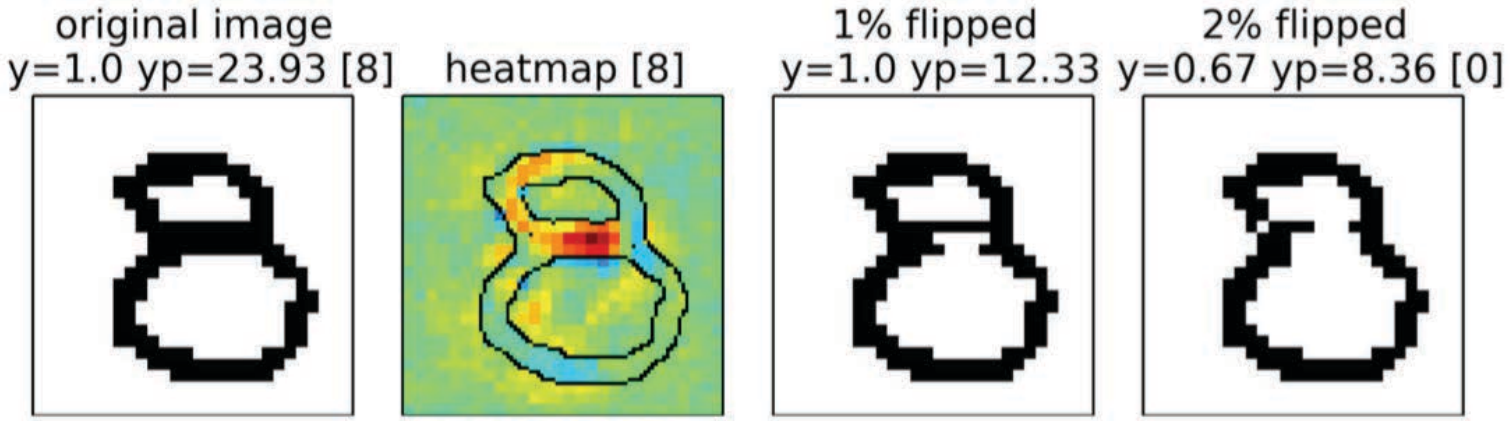
Layer-wise Relevance Propagation (LRP) -

Bach et al., PLOS ONE, 2015



Interpreting MNIST predictions

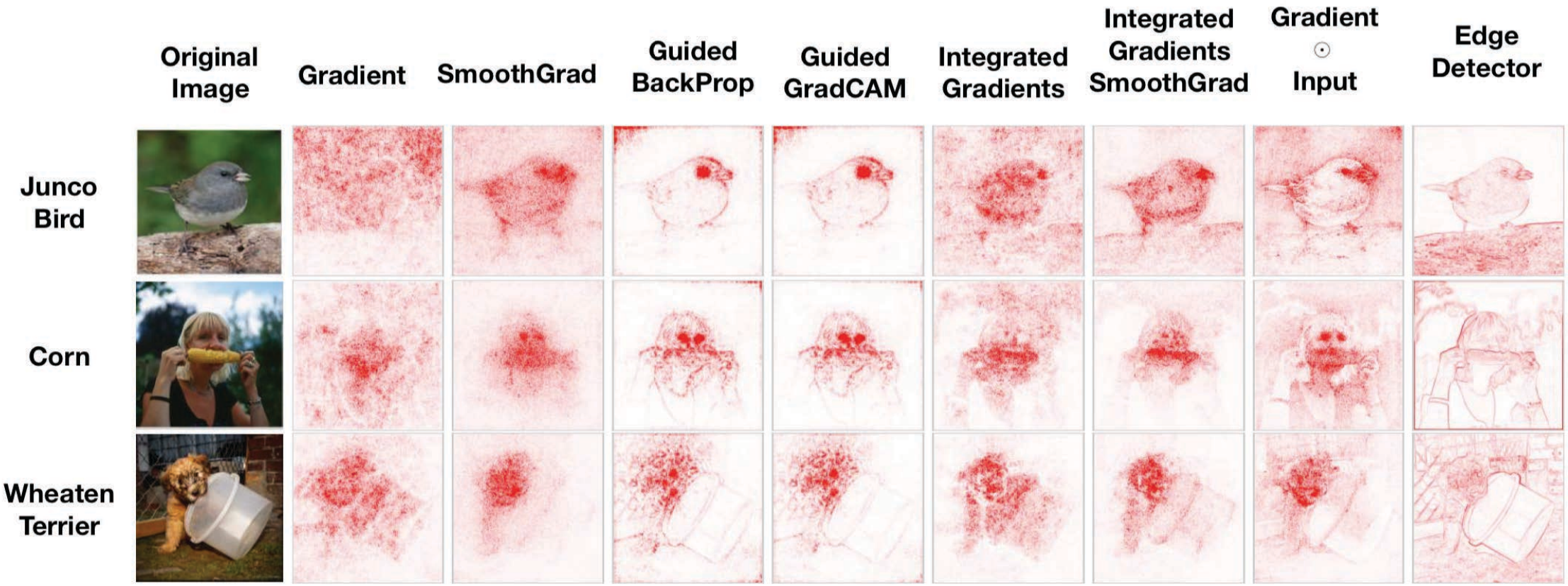




Sanity Checks for Saliency Maps

Julius Adebayo,* **Justin Gilmer**♯, **Michael Muelly**♯, **Ian Goodfellow**♯, **Moritz Hardt**♯†, **Been Kim**♯
juliusad@mit.edu, {gilmer,muelly,goodfellow,mrtz,beenkim}@google.com
♯Google Brain
†University of California Berkeley

Motivation: Objective Evaluation of Interpretability Methods
Observation: Some methods are independent of the model and data processing.



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juliusad@mit.edu, {gilmer,muelly,goodfellow,mrtz,beenkim}@google.com
♯Google Brain
†University of California Berkeley

Sanity checks

Observation: Some methods are independent of the model and data generating process

- The **model parameter randomization test**: perturbations to model parameters
- **The data randomization test** : perturbations to labels

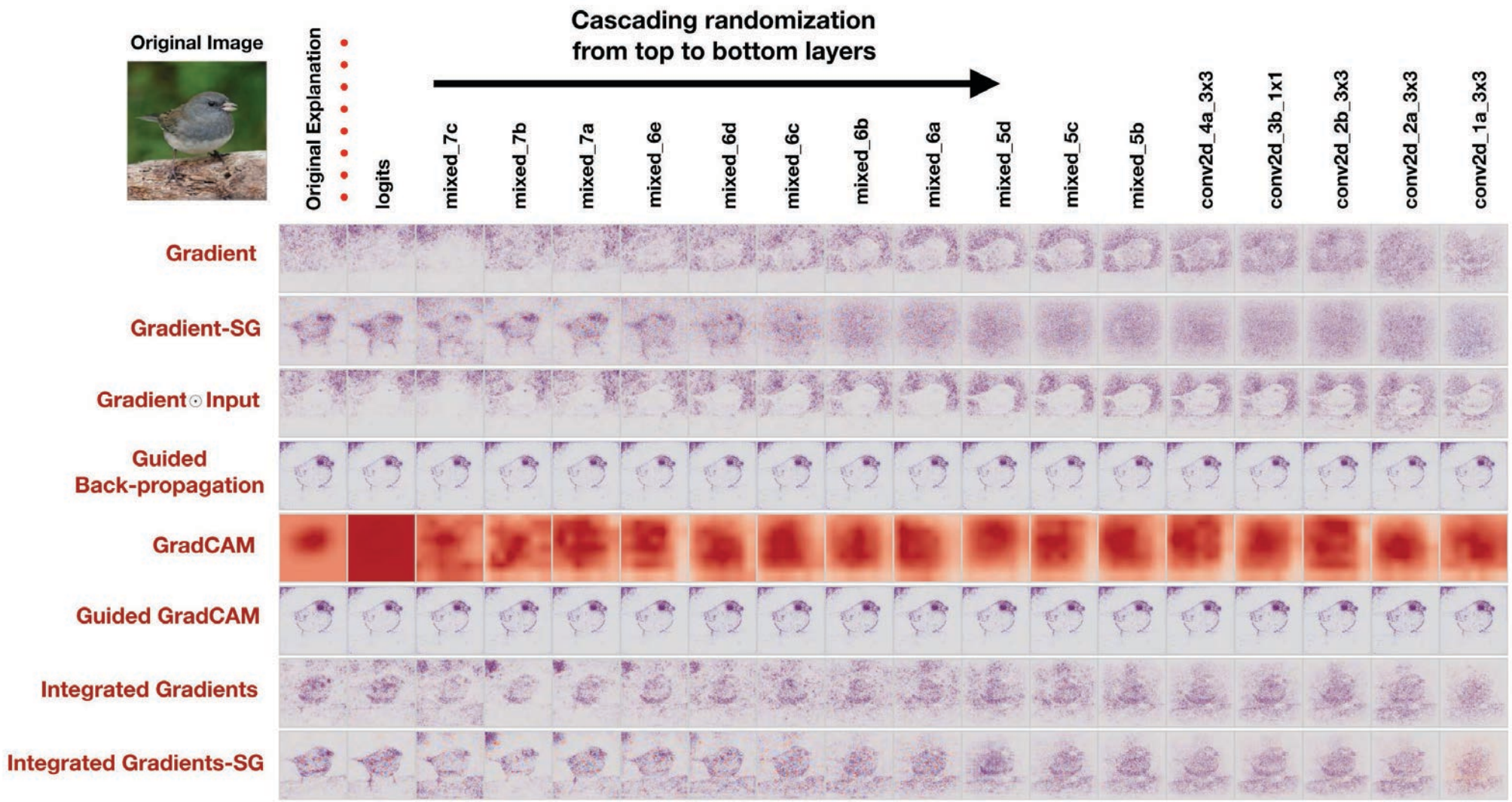
Other quantitative ways include:

- "Fragility": find adversarial examples that most affect the saliency maps
- As surrogate for image classification, i.e. thresholded saliency maps used as localization ROI

Assessing similarity among maps

- Structural similarity maps – SSIM
- Spearman rank correlation
- Pearson correlation of the histogram of gradients (HOGs)

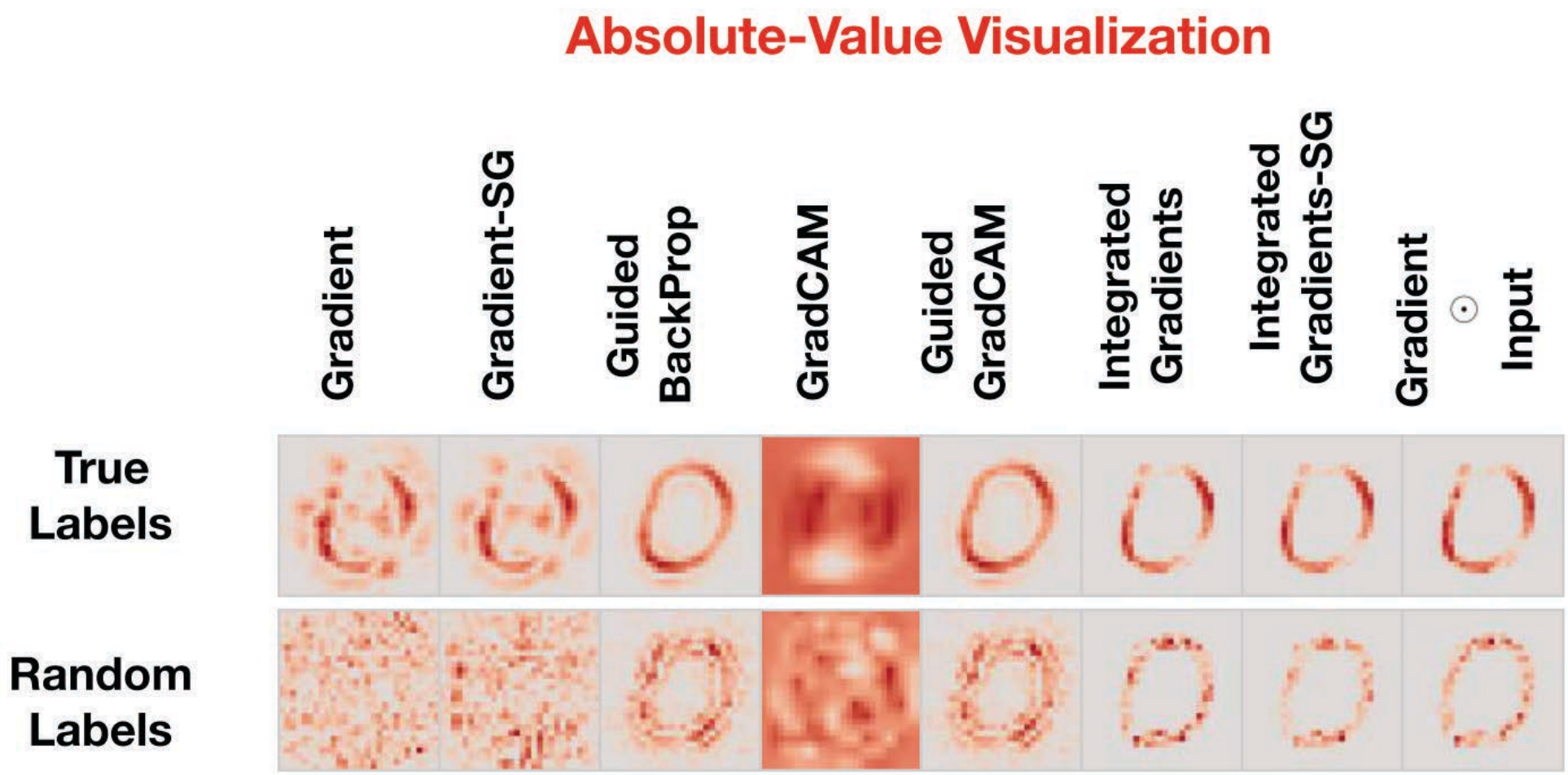
Sanity Checks for Saliency Maps



Cascaded randomization on Inception v3

Findings:
Gradients & GradCAM passed the sanity checks, while Guided BackProp & Guided GradCAM fail

Sanity Checks for Saliency Maps



Explanations of "zero" on true vs randomized labels

Findings:
Gradients & GradCAM passed the sanity checks, while Guided BackProp & Guided GradCAM fail

Sanity Checks for Saliency Maps

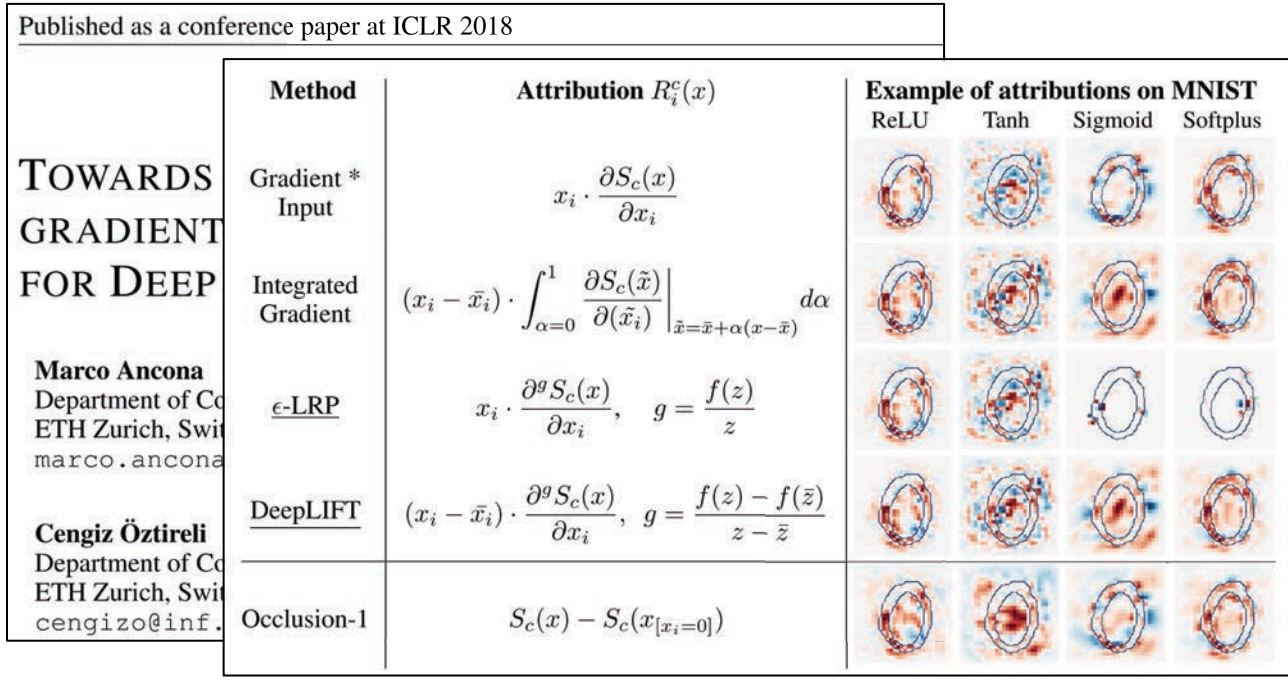
Julius Adebayo,* Justin Gilmer[♯], Michael Muelly[♯], Ian Goodfellow[♯], Moritz Hardt[♯†], Been Kim[♯]
juliusad@mit.edu, {gilmer,muelly,goodfellow,mrtz,beenkim}@google.com
[♯]Google Brain
[†]University of California Berkeley

Other findings/confirmation from previous works:

- LRP and DeepLIFT are equivalent to (input *gradient) for ReLU network w/o positive biases.
- Explanations of methods of the type “input * gradient” are heavily based on input structure → edge detector effect
- Explanations that do not depend on model parameters or training data might still depend on the model architecture, and thus provide some useful information about the prior incorporated in the model architecture.

See more benchmarking here:

- DeepLIFT often approximates Integrated gradients (IG)
- DeepLIFT != IG and fail to produce meaningful results when applied to RNNs with multiplicative interactions (e.g. LSTM)

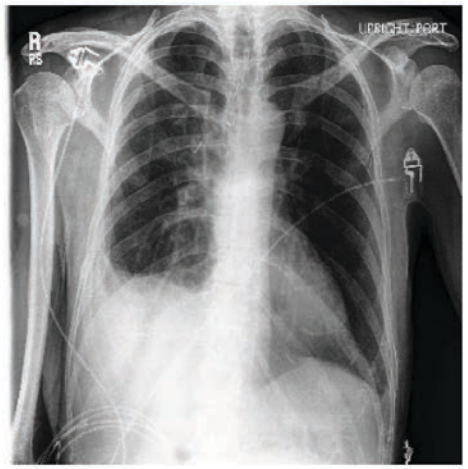


Wrap-up saliency methods

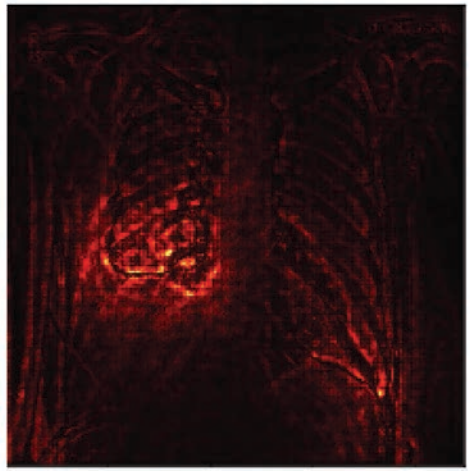
- Many approaches have been proposed!
- Visual evaluation alone can be misleading
- Recent findings on deficiencies and similarities of gradient-based approaches
- (Recall) all these methods require access to the model architecture
- Assessment of methods is an active field of research
- Seemingly lack of integration of expert-knowledge (e.g. more methodological way of defining “reference” points for interpretability)

Saliency maps – beyond explanations
Silva et al. MICCAI 2020

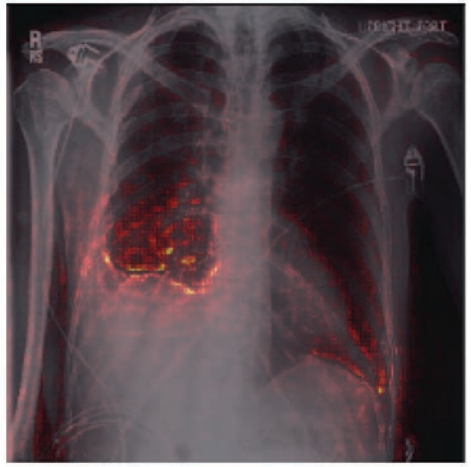
- Observation: The information contained in saliency maps, explaining a classifier's decisions, can be **used for image retrieval** (given input, find most similar images)



(a) Test Image



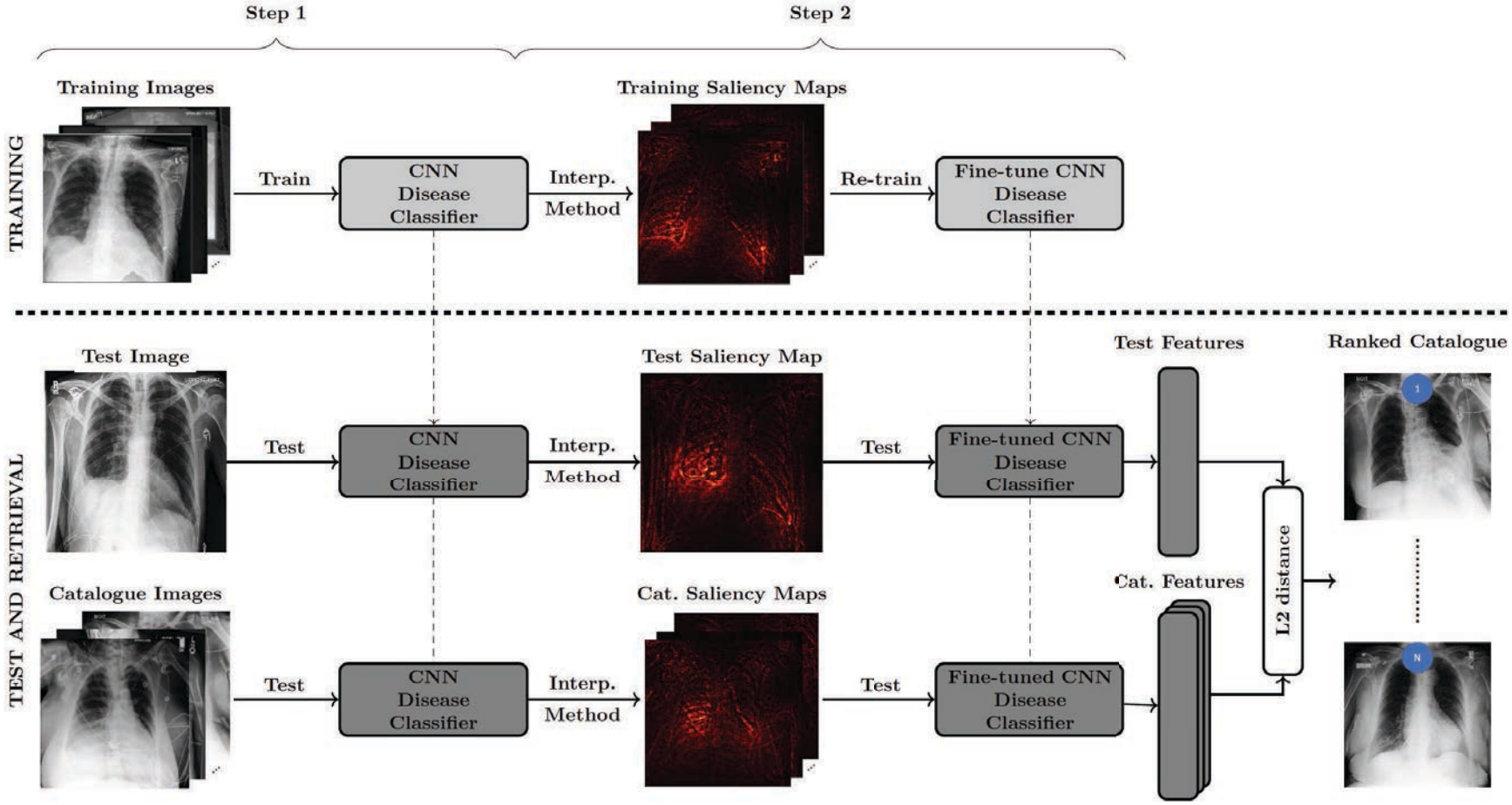
(b) Saliency Map



(c) Image with Saliency

- Motivation: Explanations inform about **medical condition**, which is needed for comparing images in a retrieval process!

Saliency maps – beyond explanations
Silva et al. MICCAI 2020

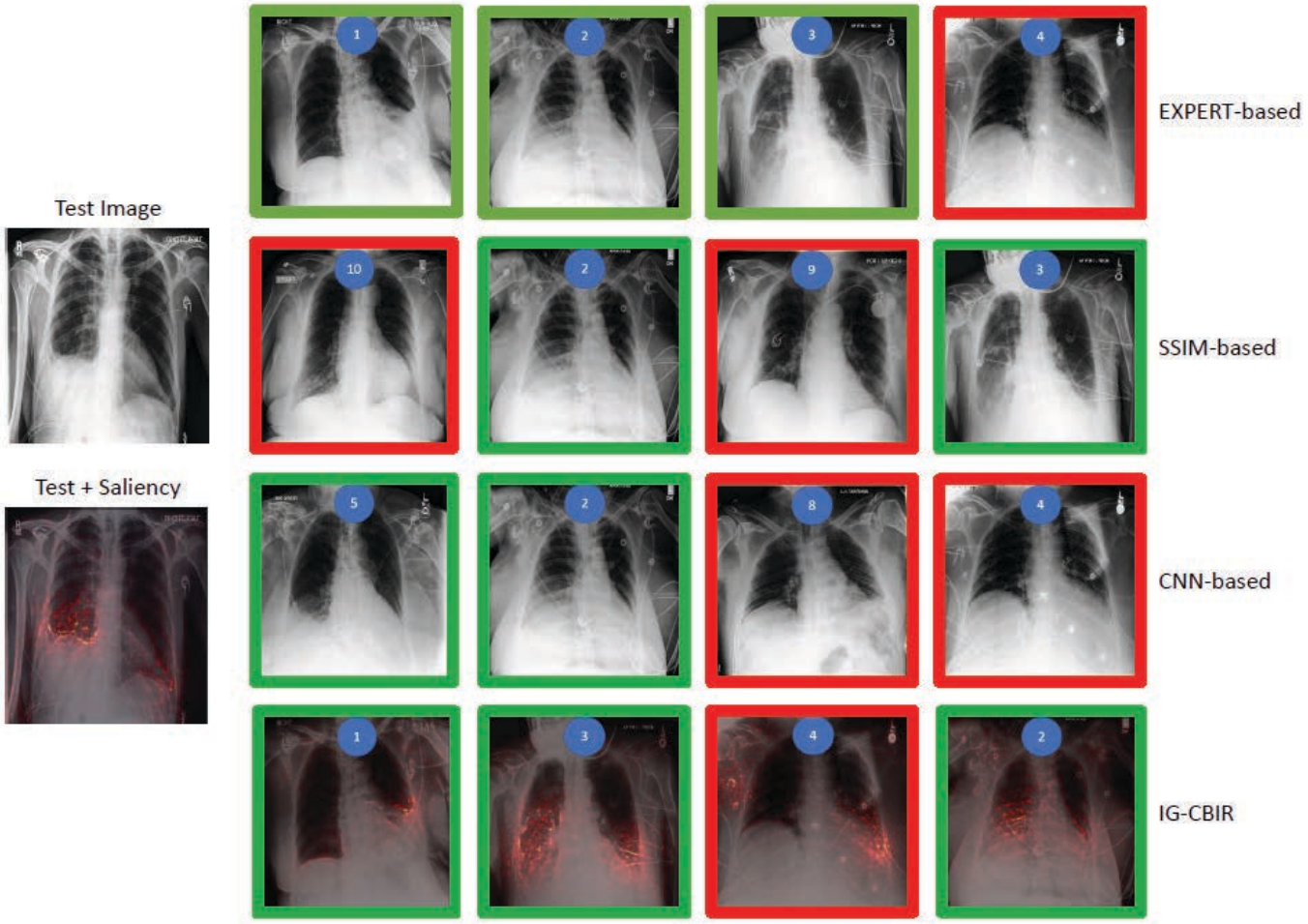


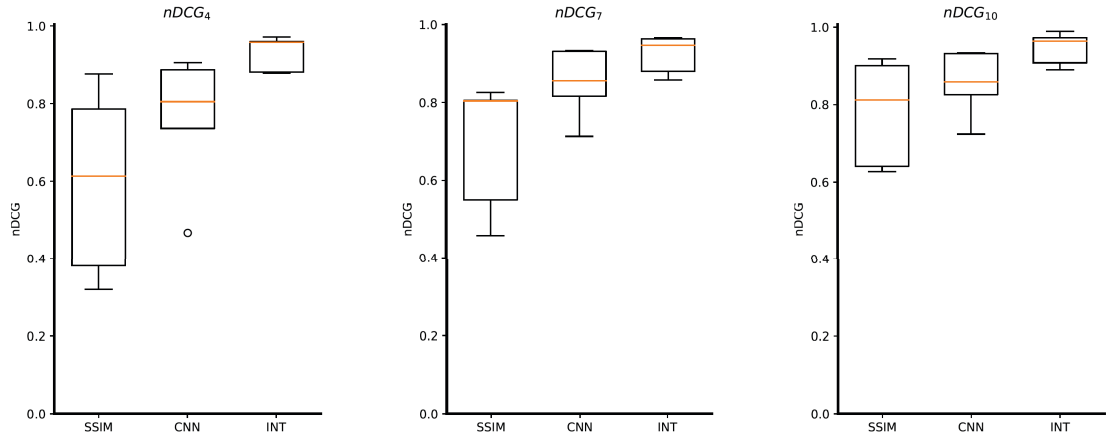
See also:

The Unreasonable Effectiveness of Deep Features as a Perceptual Metric

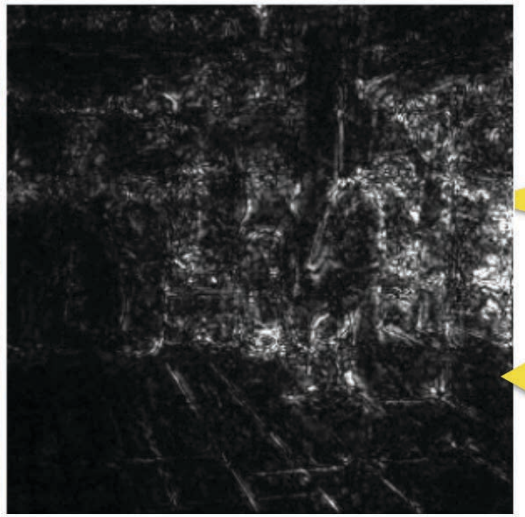
Richard Zhang[1] Phillip Isola[12] Alexei A. Efros[1] Eli Shechtman[3] Oliver Wang[3]
[1]UC Berkeley [2]OpenAI [3]Adobe Research
{rich.zhang, isola, efros}@eecs.berkeley.edu {elishe,owang}@adobe.com

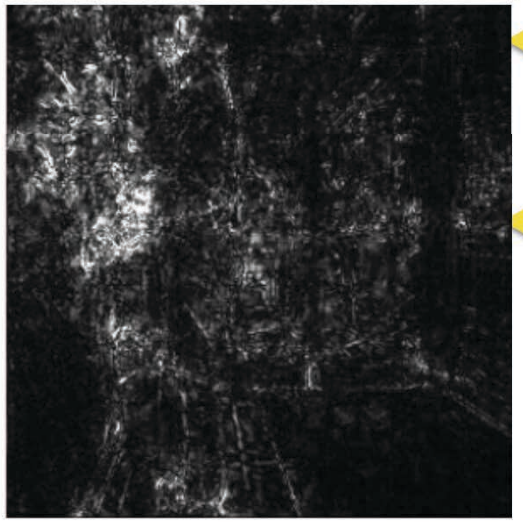
Saliency maps – beyond explanations
Silva et al. MICCAI 2020





Testing with Concept Activation Vectors – TCAV – Kim et al. 2017





Were there more pixels on the cash machine than on the person?

Did the 'human' concept matter? Did the 'glasses' or 'paper' matter?

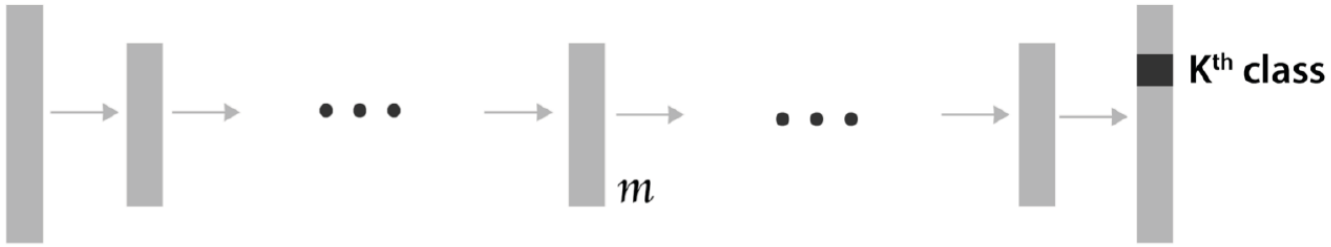
Which concept mattered more?

Is this true for all other cash machine predictions?

Wouldn't it be great if we can **quantitatively** measure how important *any* of these **user-chosen concepts** are?

Image source: Kim Been

Testing with Concept Activation Vectors – TCAV – Kim et al. 2017



Quantitative explanation: how much a concept (e.g., gender, race) was important for a prediction in a trained model.

…even if the concept was not part of the training.

Image source: Kim Been

Testing with Concept Activation Vectors – TCAV – Kim et al. 2017

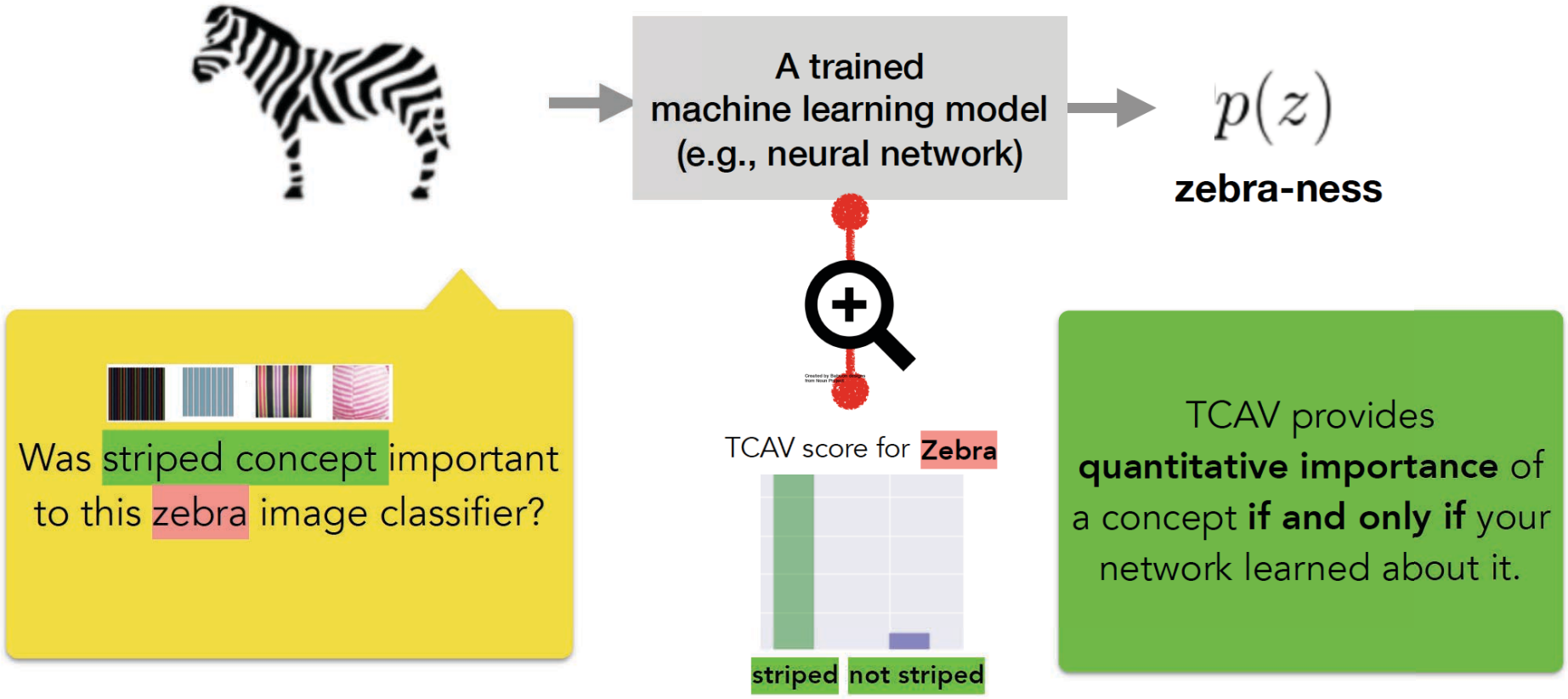


Image source: Kim Been

Testing with Concept Activation Vectors – TCAV – Kim et al. 2017

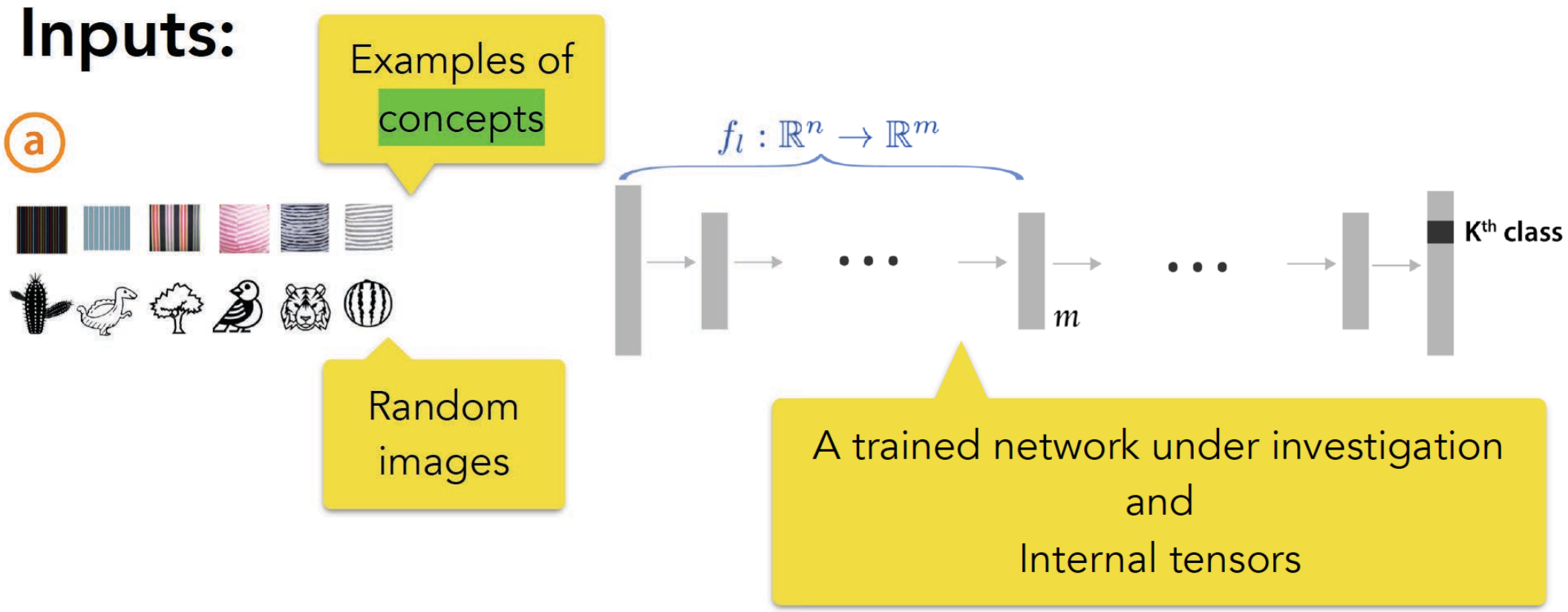


Image source: Kim Been

Testing with Concept Activation Vectors – TCAV – Kim et al. 2017

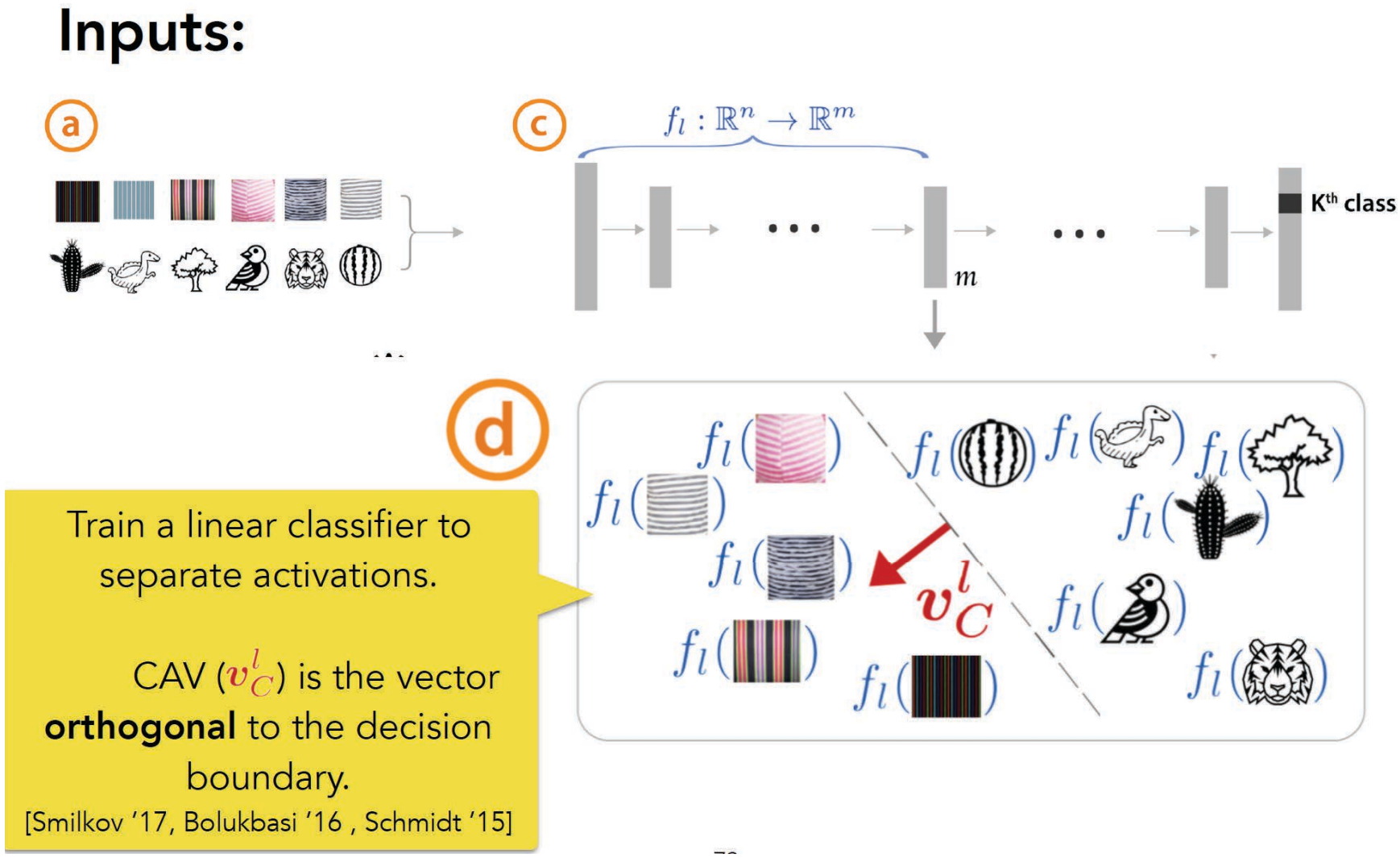


Image source: Kim Been

Testing with Concept Activation Vectors – TCAV – Kim et al. 2017

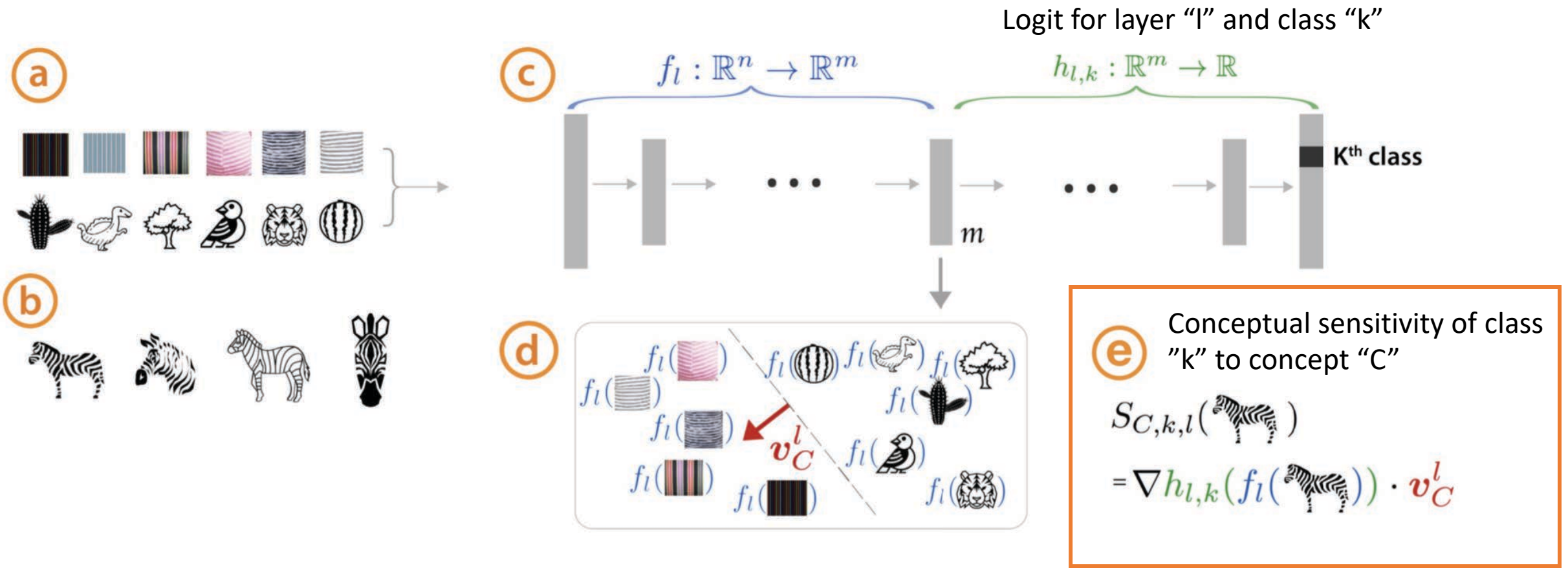


Image source: Kim Been

Testing with Concept Activation Vectors – TCAV – Kim et al. 2017

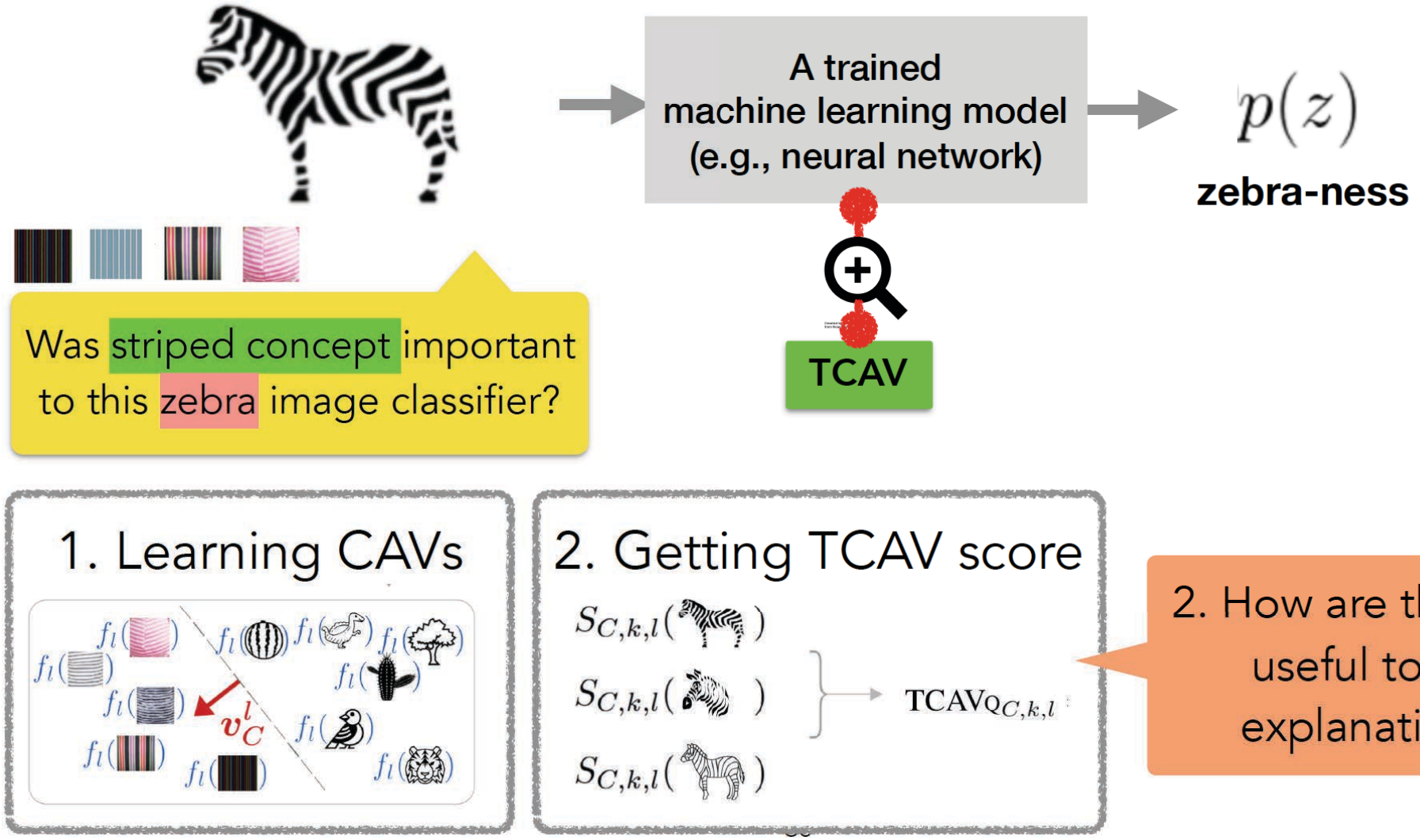
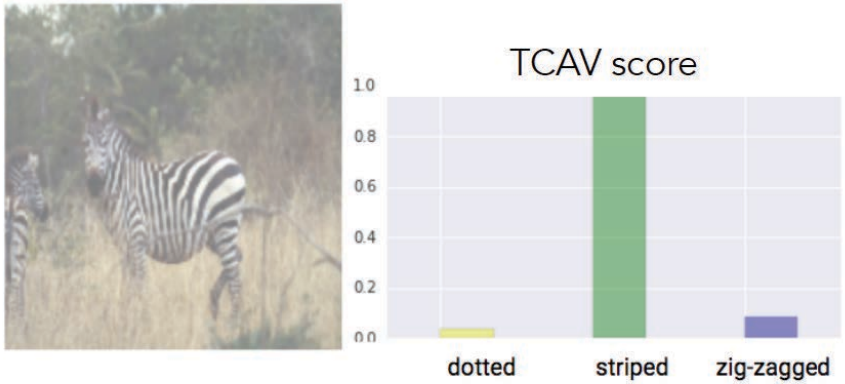


Image source: Kim Been

Testing with Concept Activation Vectors – TCAV – Kim et al. 2017

TCAV



zebra-ness → $\frac{\partial p(z)}{\partial \boldsymbol{v}_C^l} = S_{C,k,l}(\boldsymbol{x})$

striped CAV →

Directional derivative with CAV

$S_{C,k,l}($  $)$

$S_{C,k,l}($  $)$

$S_{C,k,l}($  $)$

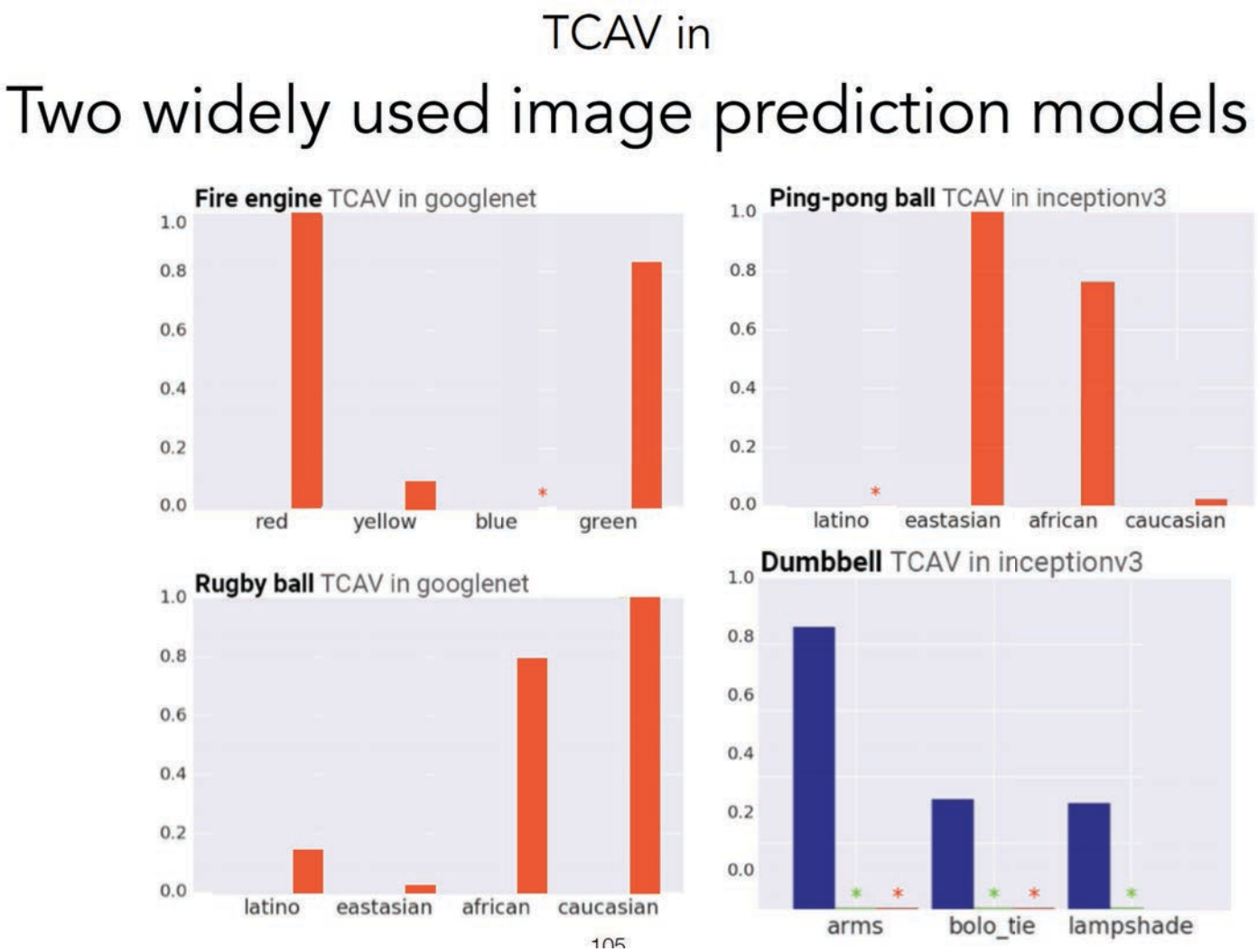
$S_{C,k,l}($  $)$

$$\text{TCAVQ}_{C,k,l} = \frac{|\{\boldsymbol{x} \in X_k : S_{C,k,l}(\boldsymbol{x}) > 0\}|}{|X_k|}$$

fraction of k-class inputs whose l-layer activation vector was positively influenced by concept C

Image source: Kim Been

Testing with Concept Activation Vectors – TCAV – Kim et al. 2017



TCAV facilitates spotting of biases in the datasets

Image source: Kim Been

Testing with Concept Activation Vectors – TCAV – Kim et al. 2017

Example application to Diabetic Retinopahty (DR)

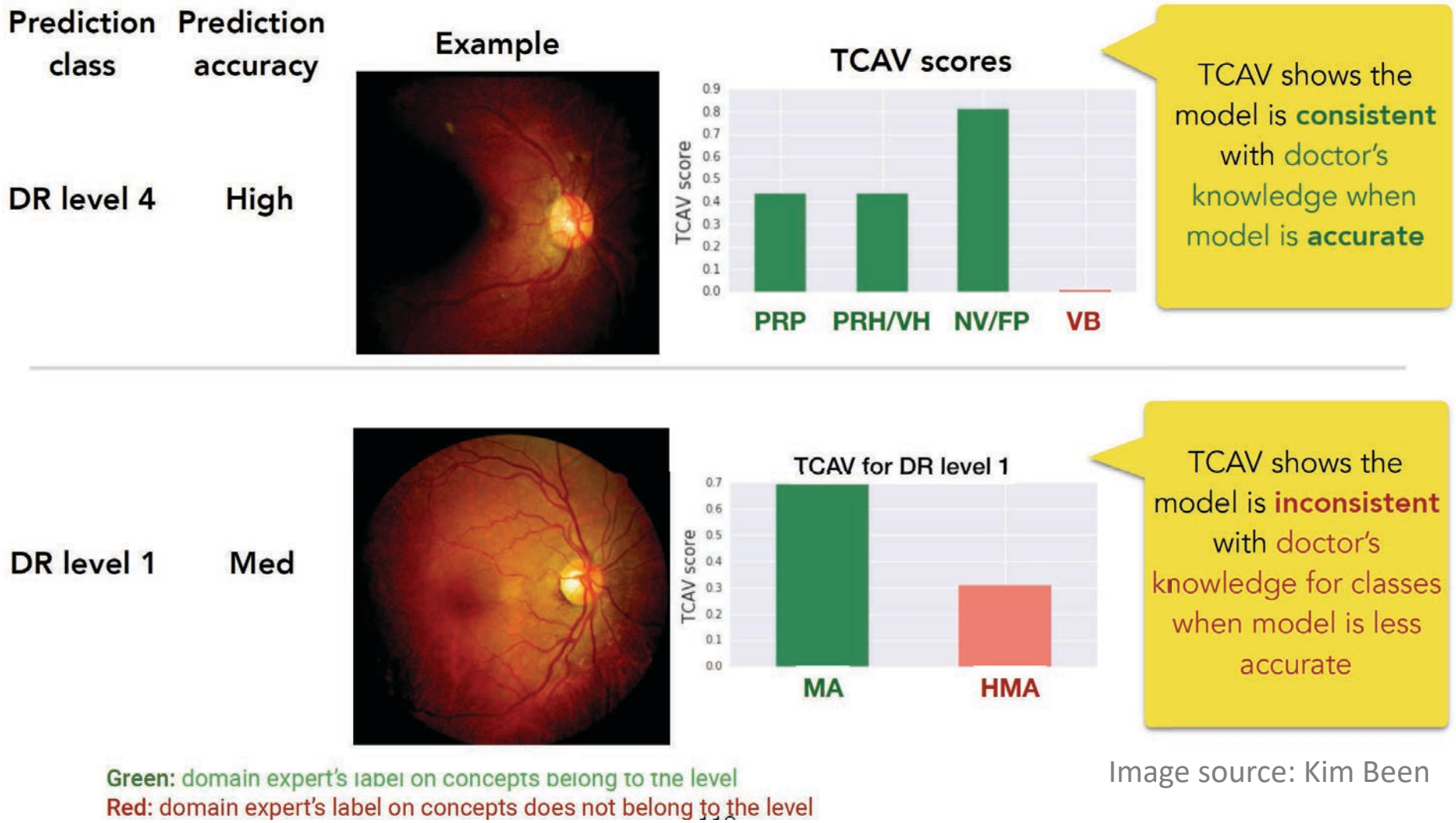
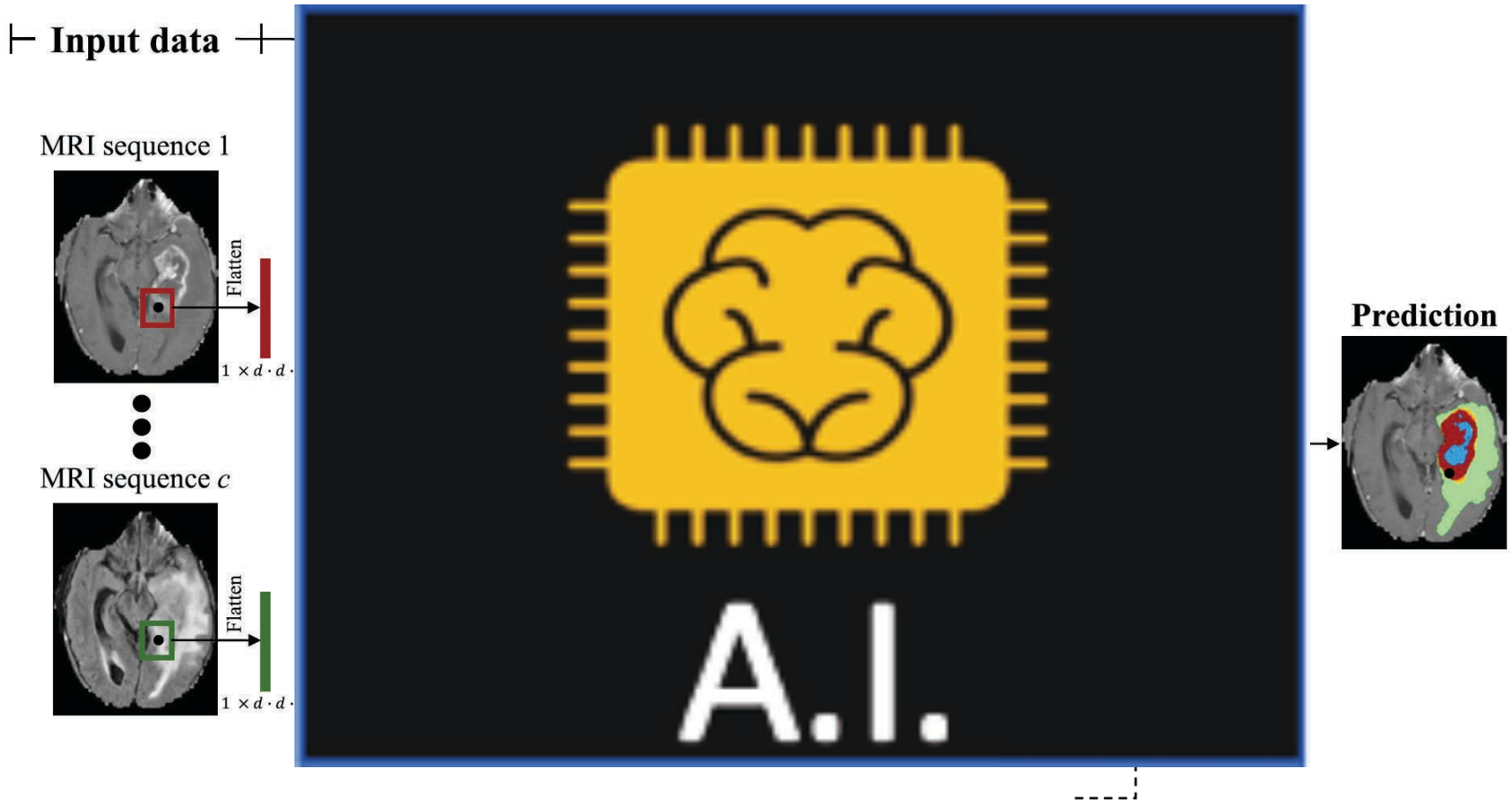


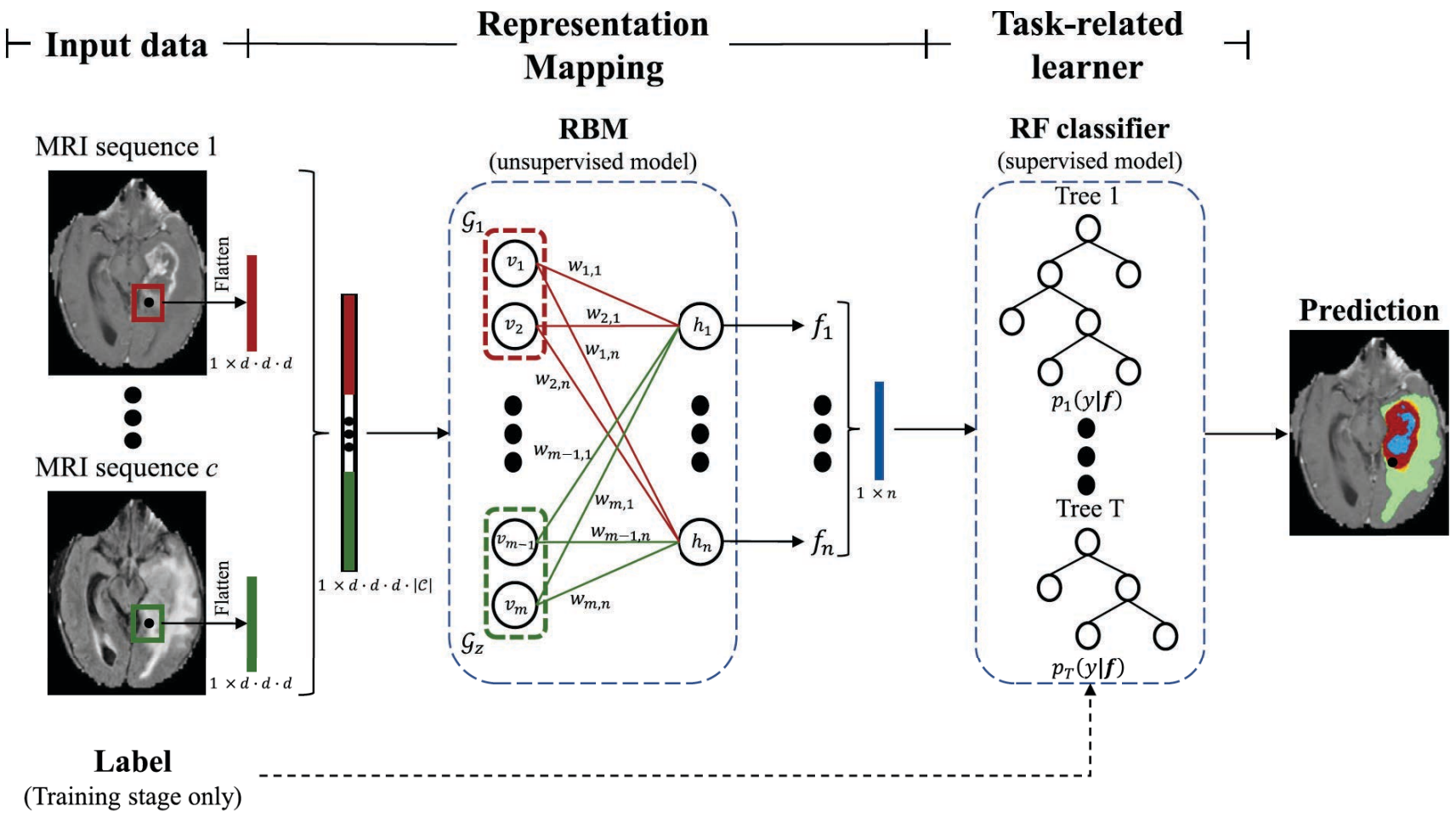
Image source: Kim Been

Enhancing Interpretability of Learned Features in Multisequence-MRI

Example task:
Automated brain tumor segmentation from multisequence MRI



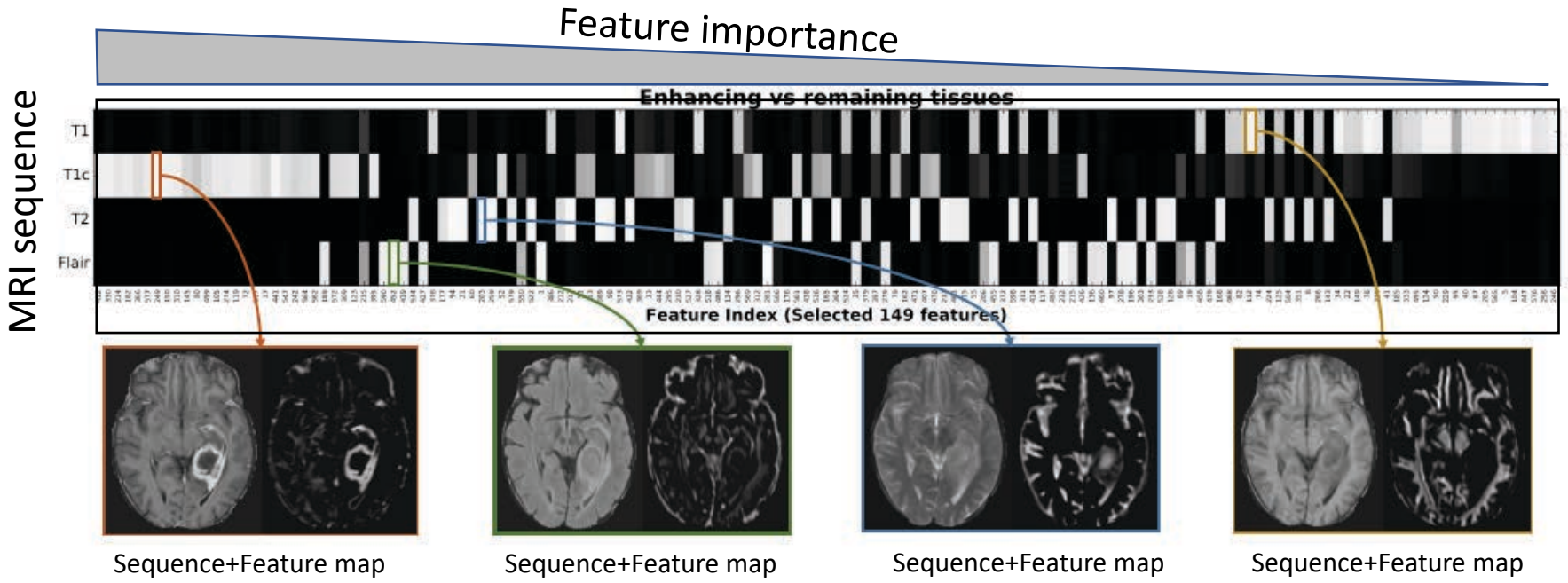
Enhancing Interpretability of Learned Features in Multisequence-MRI



Pereira et al. 2018

Enhancing interpretability of machine learning algorithms

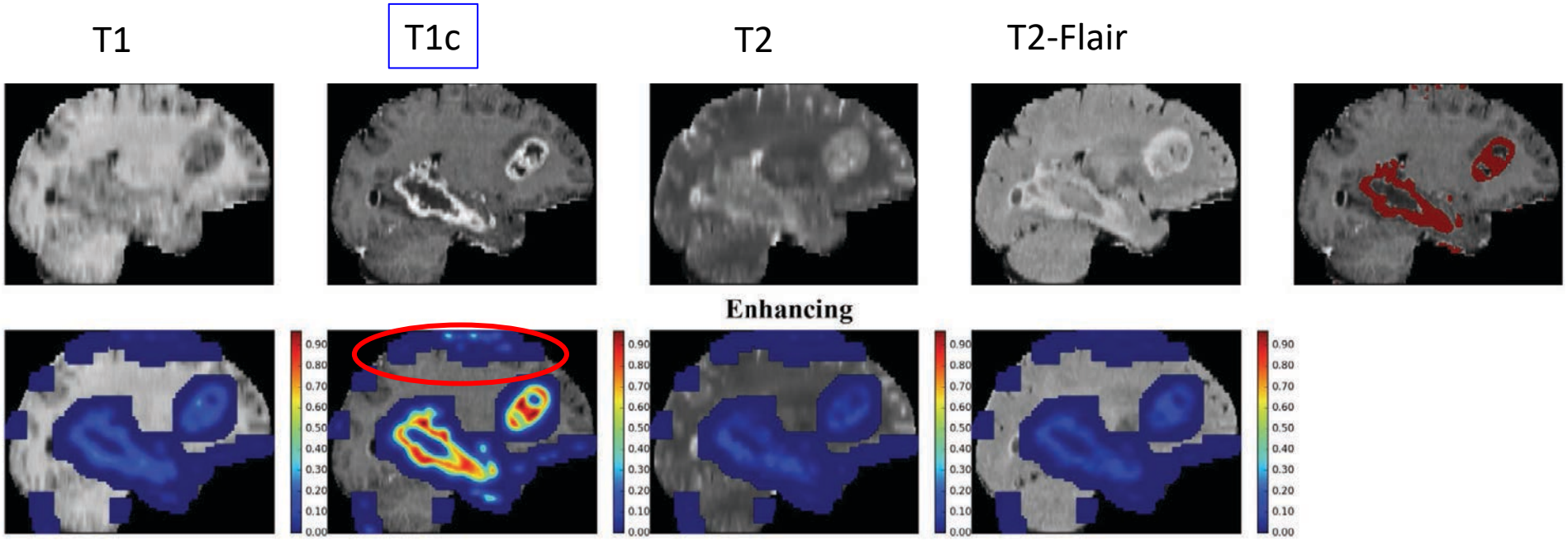
- *How is the machine using the information?*
- *Which sequence is more important?*
- *If it fails, why does it fail?*
- *Quality Certification*



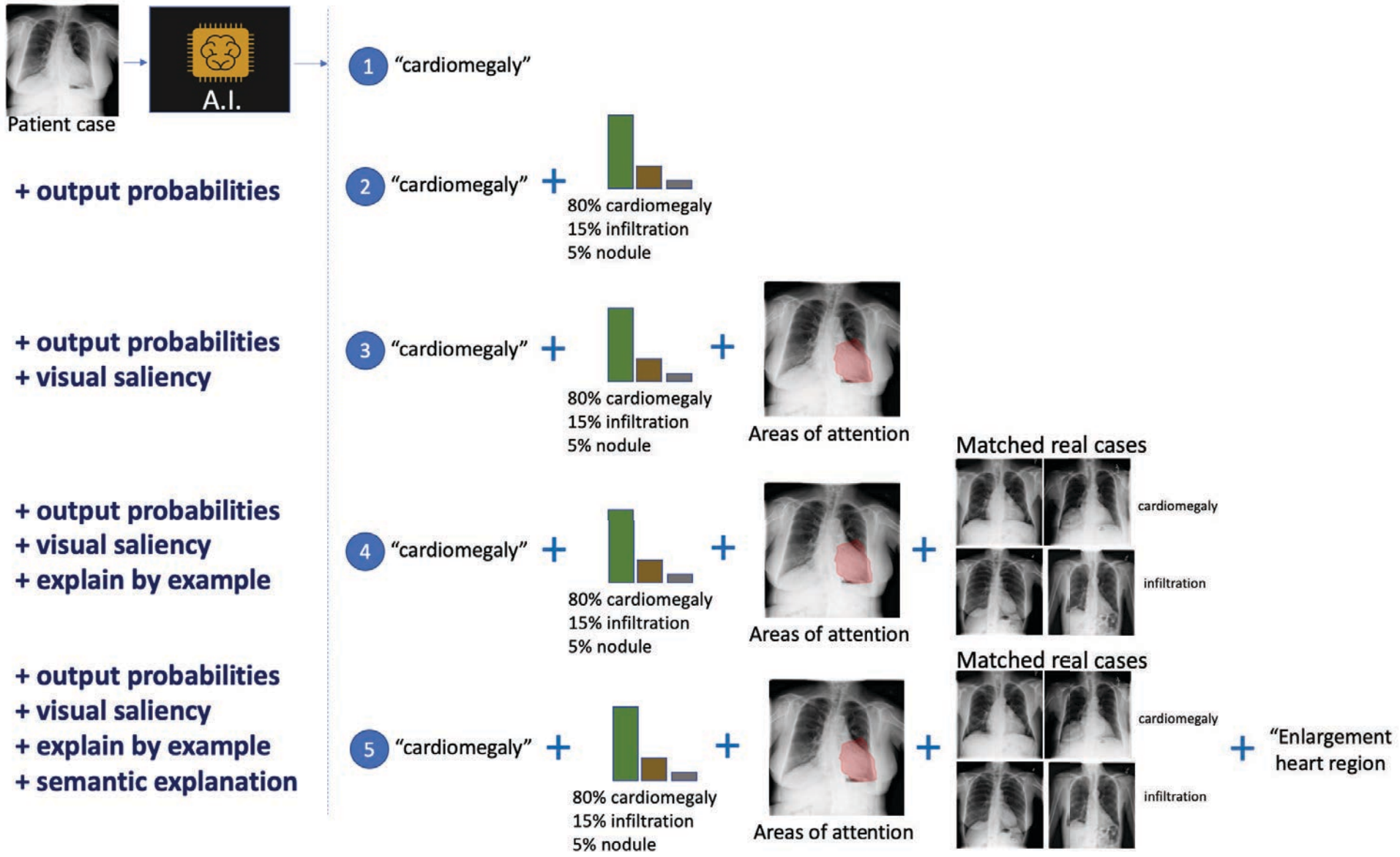
Enhancing interpretability of machine learning algorithms

Which Sequence is used most for the task of tumor-enhancing segmentation?

- *T1c (agrees with clinical practice)*
- *Method also detects bias from pre-processing*



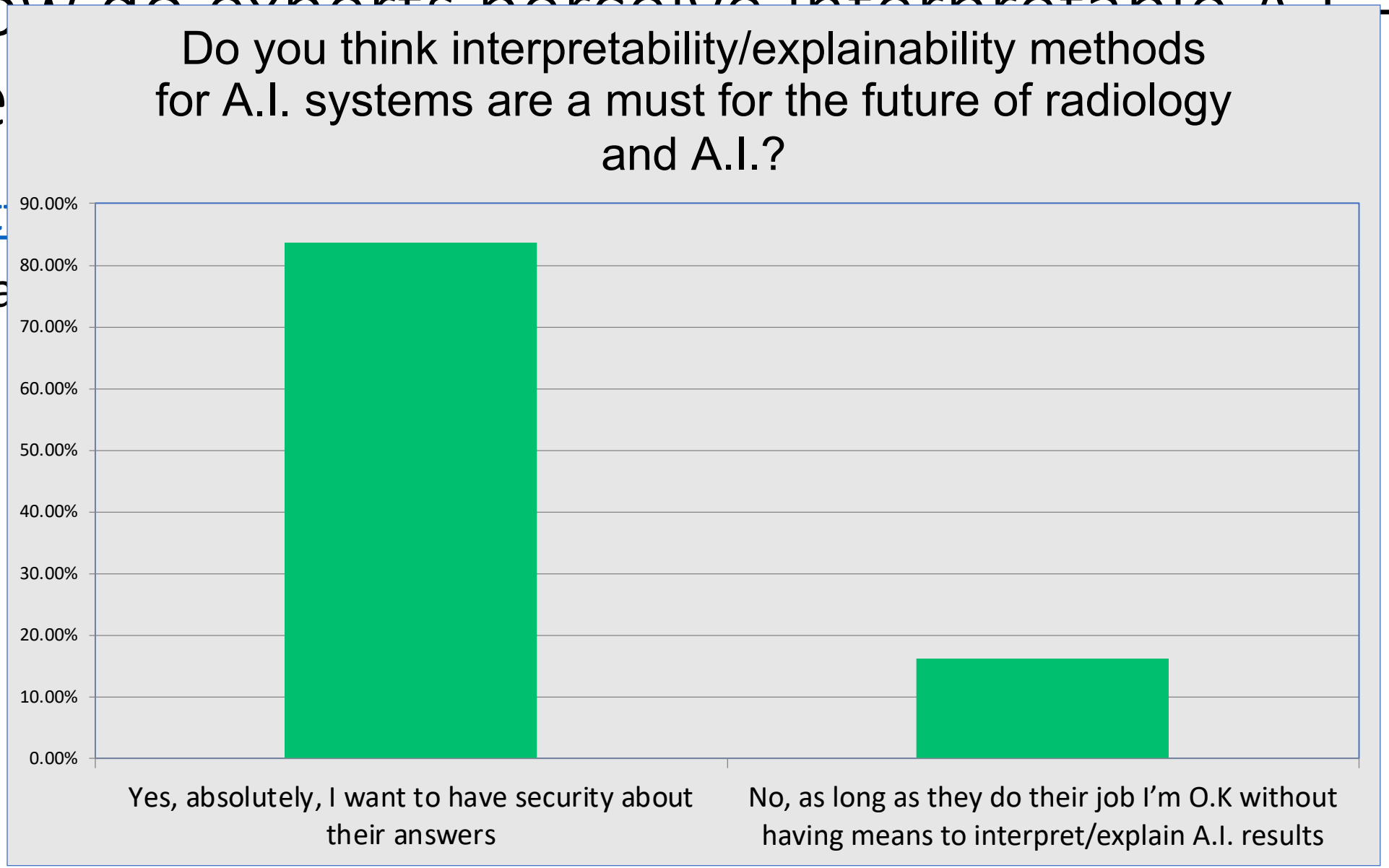
Combining interpretability approaches



How do experts perceive interpretable A.I. – ne

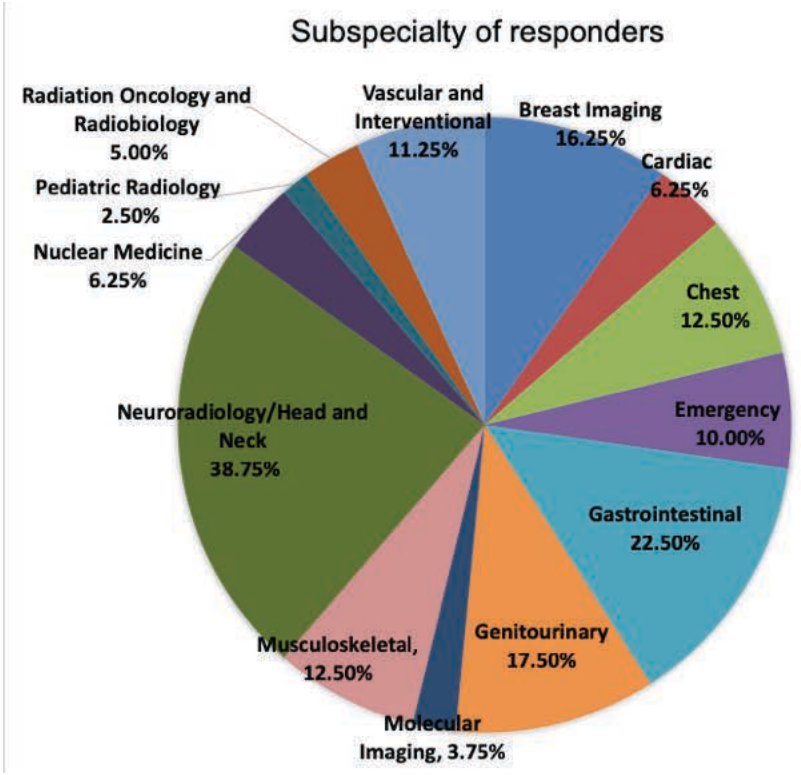
- ht

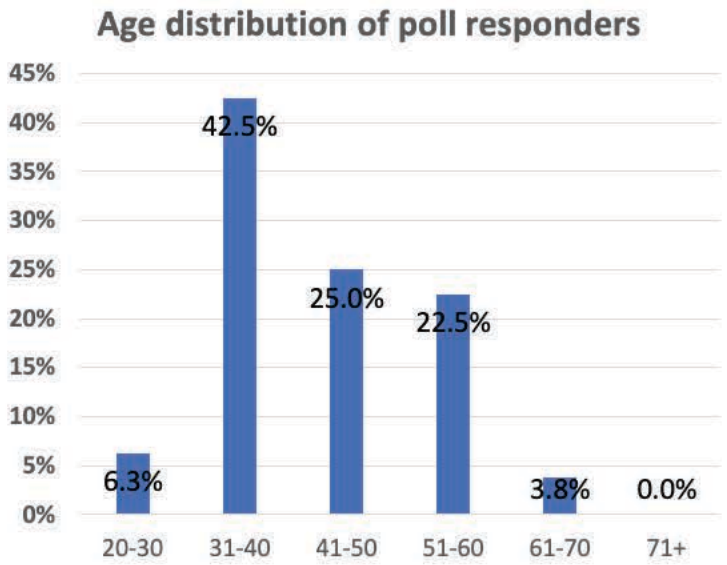
Plea

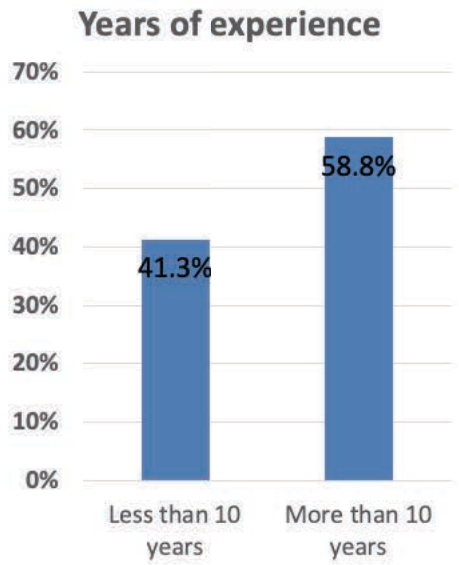


How do experts perceive interpretable A.I. – needed?

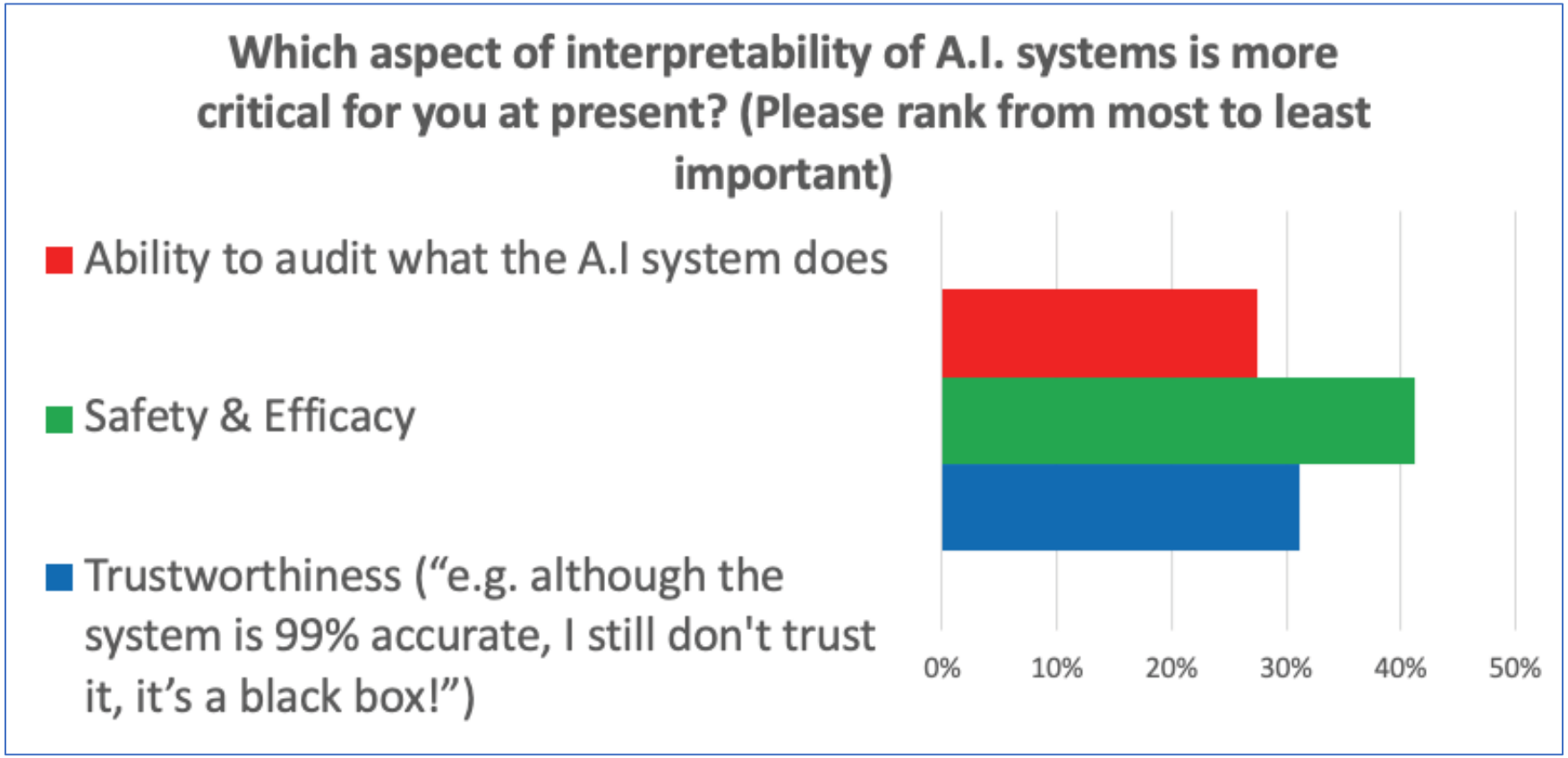
80 responders
Online survey





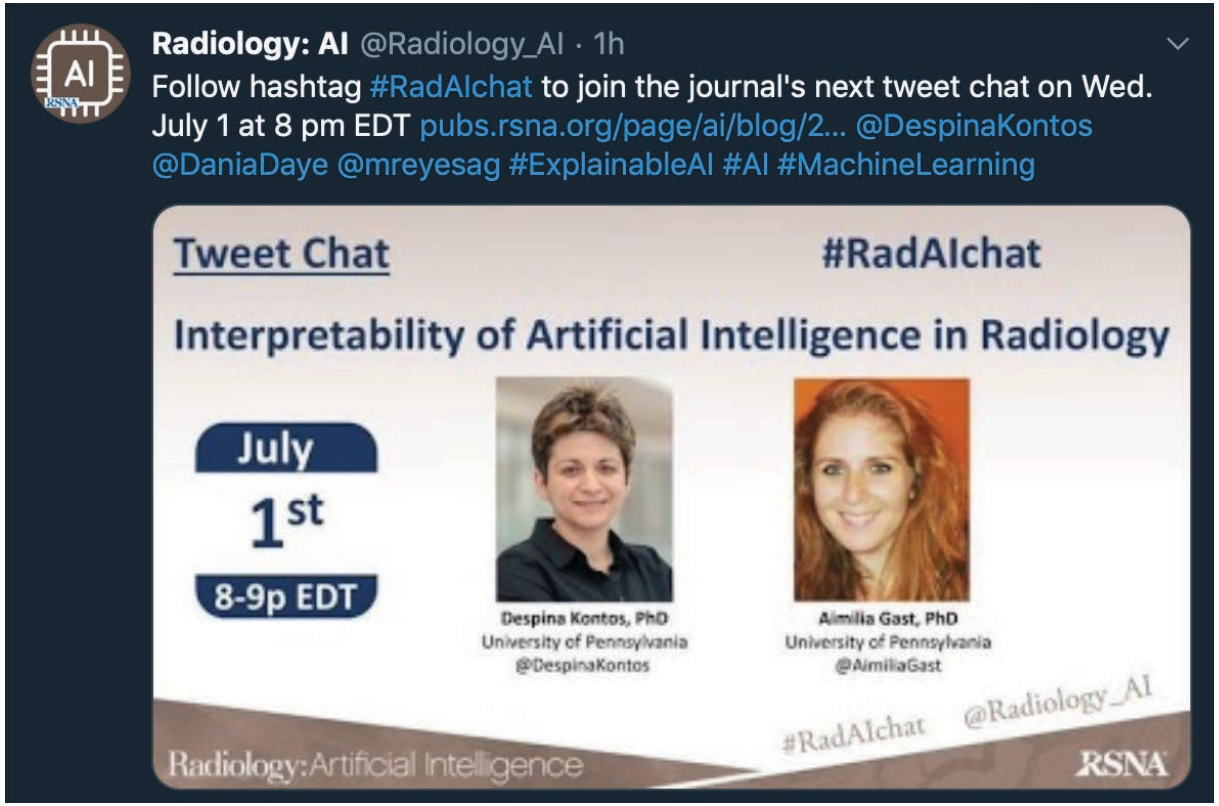


How do experts perceive interpretable A.I. – needed?



"*Primum non nocere – First, to do no harm*"

Interpretability of AI in Radiology: Highlighted work by the Radiology Community



Improved Interpretability: Deep Learning meets Causal Inference

CONTRIBUTED ARTICLES

The Seven Tools of Causal Inference, with Reflections on Machine Learning

By Judea Pearl
Communications of the ACM, March 2019, Vol. 62 No. 3, Pages 54-60
10.1145/3241036

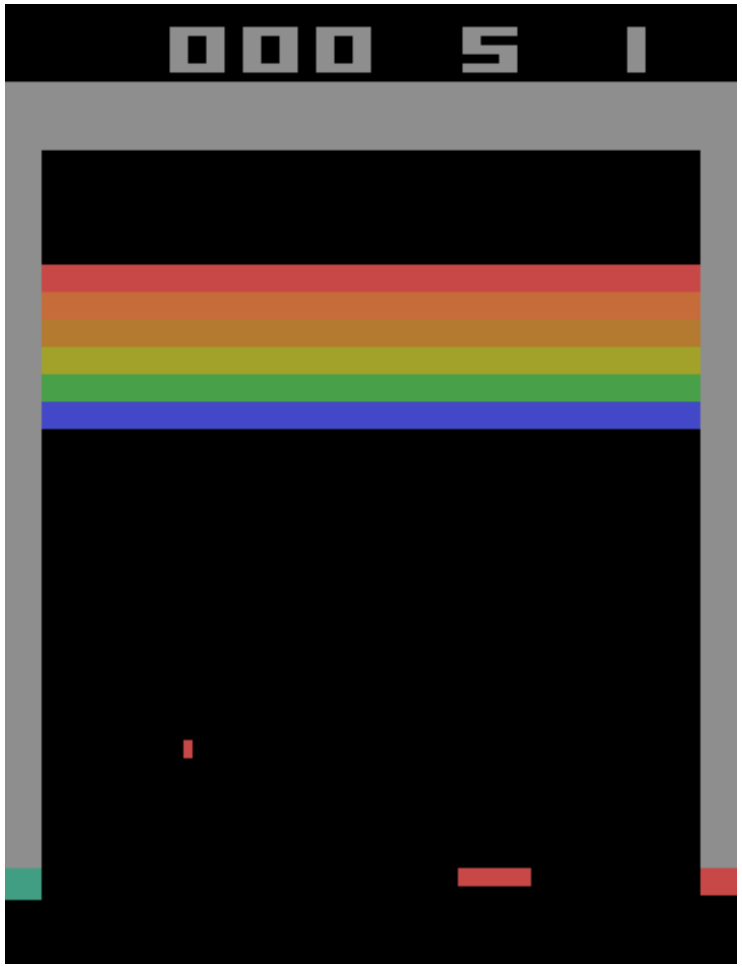
Counterfactual ("Was it X that caused Y"?)
"alternative worlds"

Interventional ("What if?")

Associational ("relation between X and Y")

Counterfactual calls for "alternative worlds" ←→ A.I

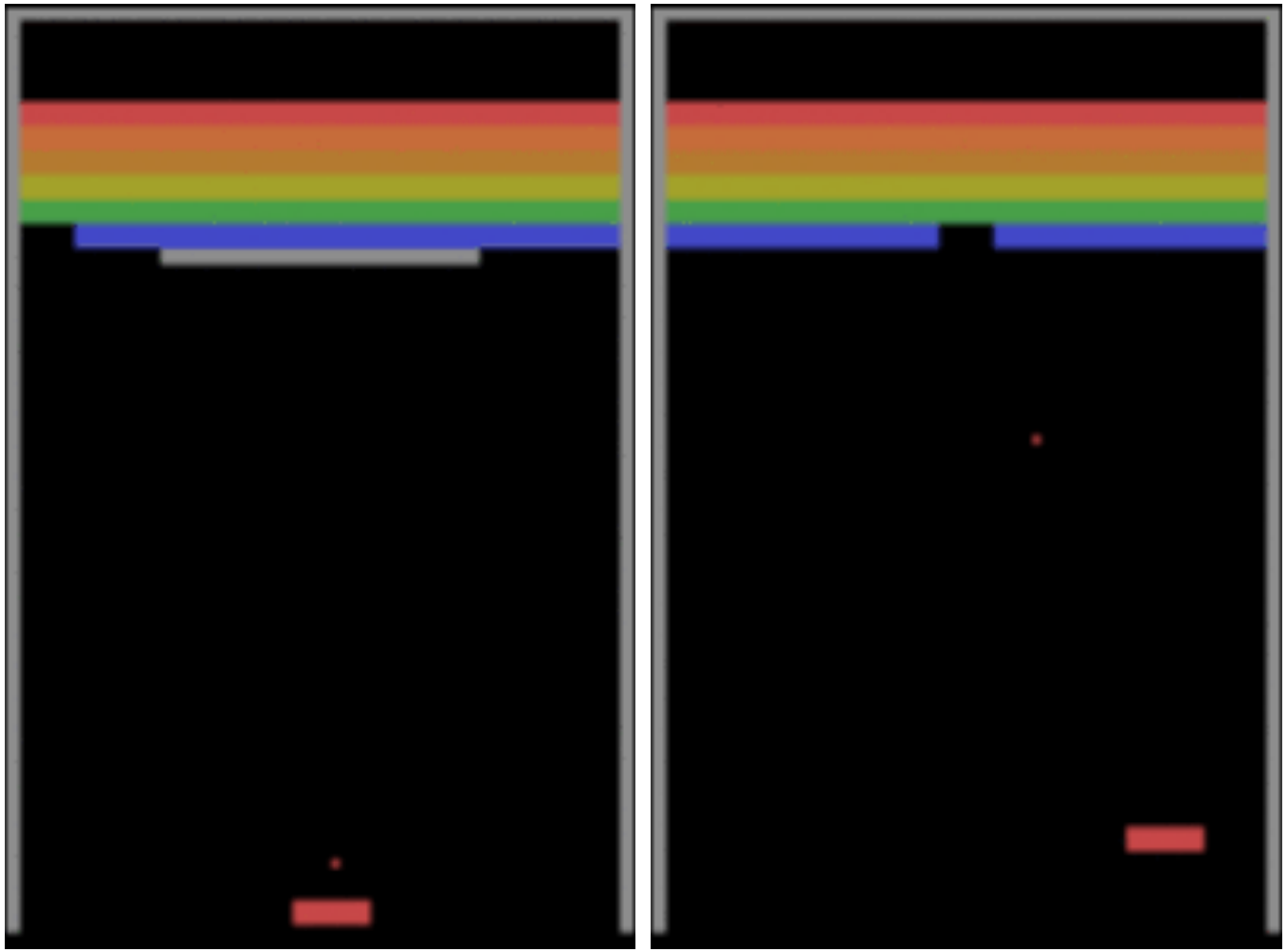
Improved Interpretability: Deep Learning meets Causal Inference



2014 - DeepMind teaches itself to play breakout

..but can the A.I. system adapt to small changes?

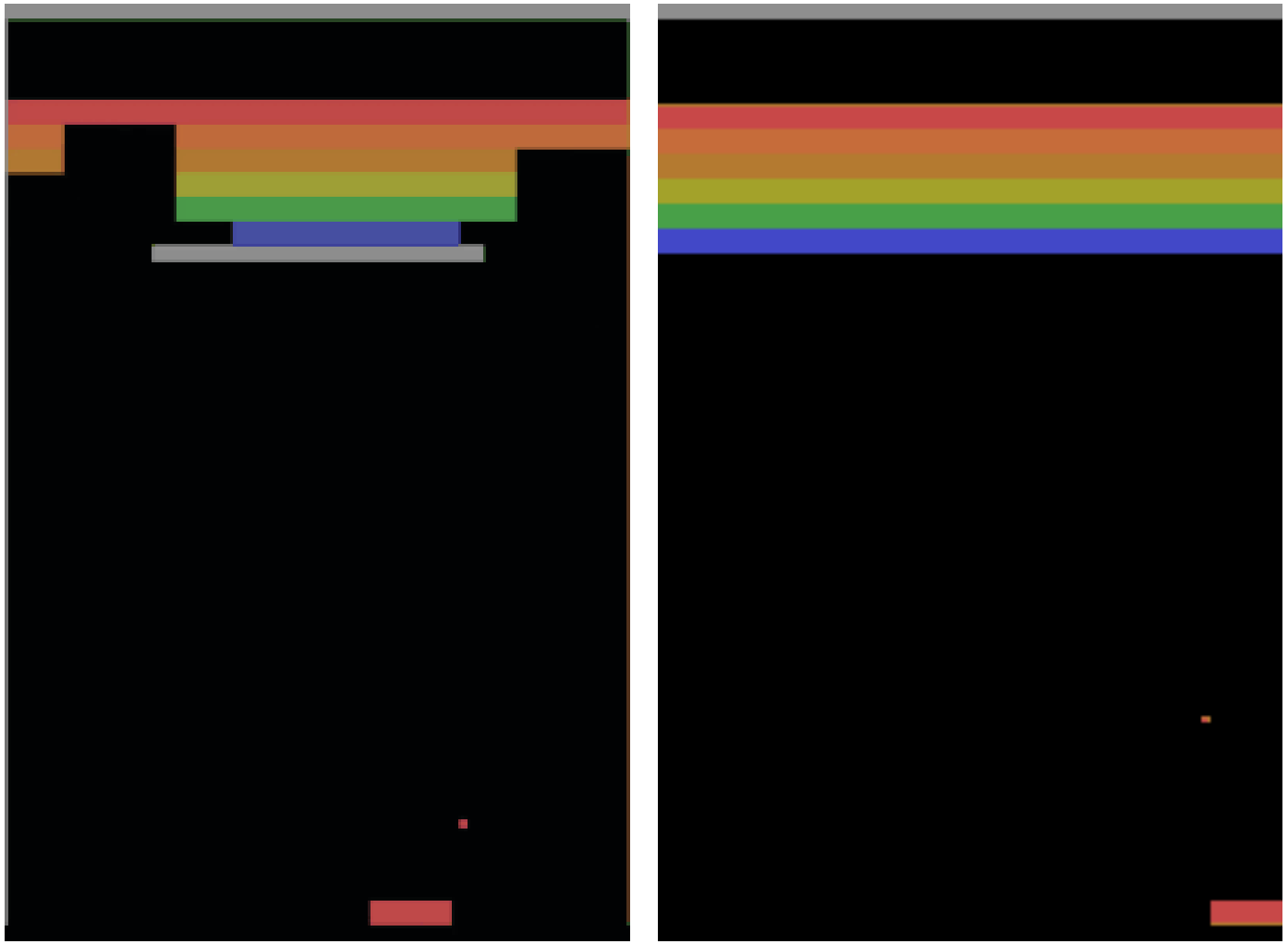
Improved Interpretability: Deep Learning meets Causal Inference



Schema Networks: Zero-shot Transfer with a Generative Causal Model of Intuitive Physics

Ken Kansky Tom Silver David A. Mély Mohamed Eldawy Miguel Lázaro-Gredilla Xinghua Lou
Nimrod Dorfman Szymon Sidor Scott Phoenix Dileep George

Improved Interpretability: Deep Learning meets Causal Inference



Schema Networks: Zero-shot Transfer with a Generative Causal Model of Intuitive Physics

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Nimrod Dorfman Szymon Sidor Scott Phoenix Dileep George

- Better modeling of cause-effect
- Better generalization through a conceptual representation

- Causal-Effect can leverage **better explanations** of systems

Let’s wrap-up

- Interpretability of ML systems is not a new topic, but propelled by new findings from the DL community and efforts to safely translate this technology to (medical) applications. Complexity and Prevalence.
- The goal of interpretability is *NOT* to understand every part but to have enough information for the task at hand.
- Interpretability can leverage: auditability, trust, adoptability, understanding of system’s inner workings.
- Lot of work in visualization techniques; active area of research
- Benchmarking of interpretability methods is still an unexplored area.
- Likely a task-dependent combination of approaches will ultimately succeed. Tradeoff *succinct-yet-rich explanation*

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Resources

- iMIMIC websites
  - 2018 edition, check material section https://imimic.bitbucket.io/resources.html
  - 2019 edition (talks and accepted contributions to be posted)

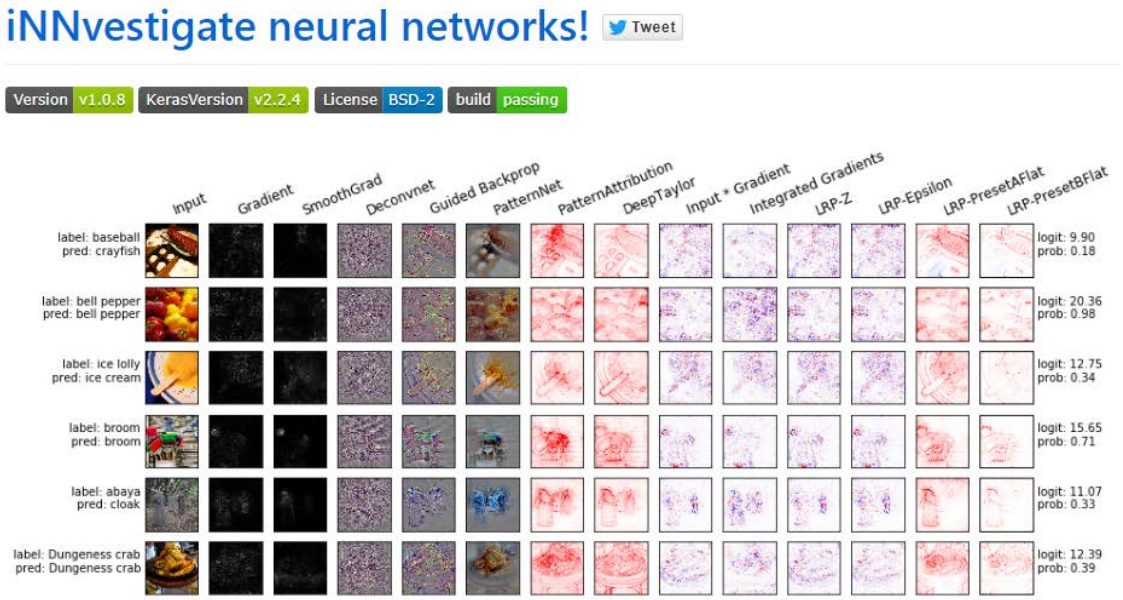
  http://imimic-workshop.com

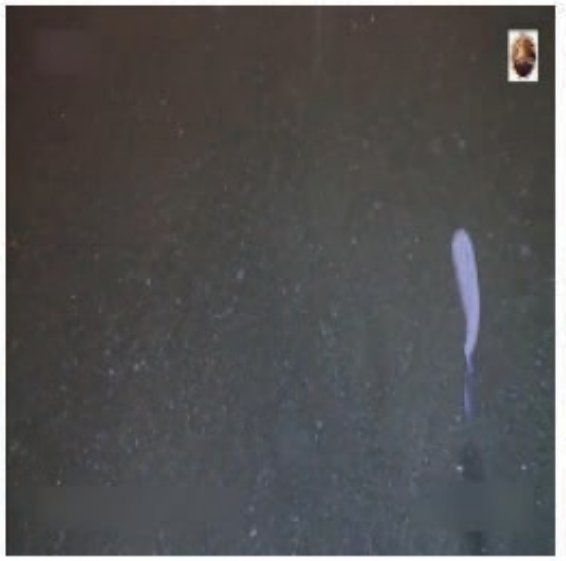
  - Awesome book from Christoph Molnar: https://christophm.github.io/interpretable-ml-book/

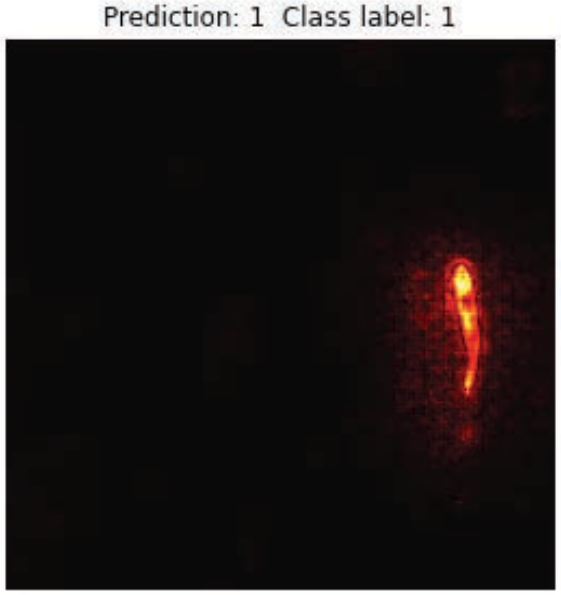
  - INNvestigate - https://github.com/albermax/innvestigate/

Hands-on session

- Using interpretability as a proxy to annotate fish images → semi-supervised approach







VISUM Summer School

VISion Understanding and Machine intelligence

..and a short quiz now

VISUM Summer School

VISion Understanding and Machine intelligence

Interpretability Methodologies for Machine Learning in Medical Imaging

Mauricio Reyes, PhD.

Healthcare Imaging A.I.

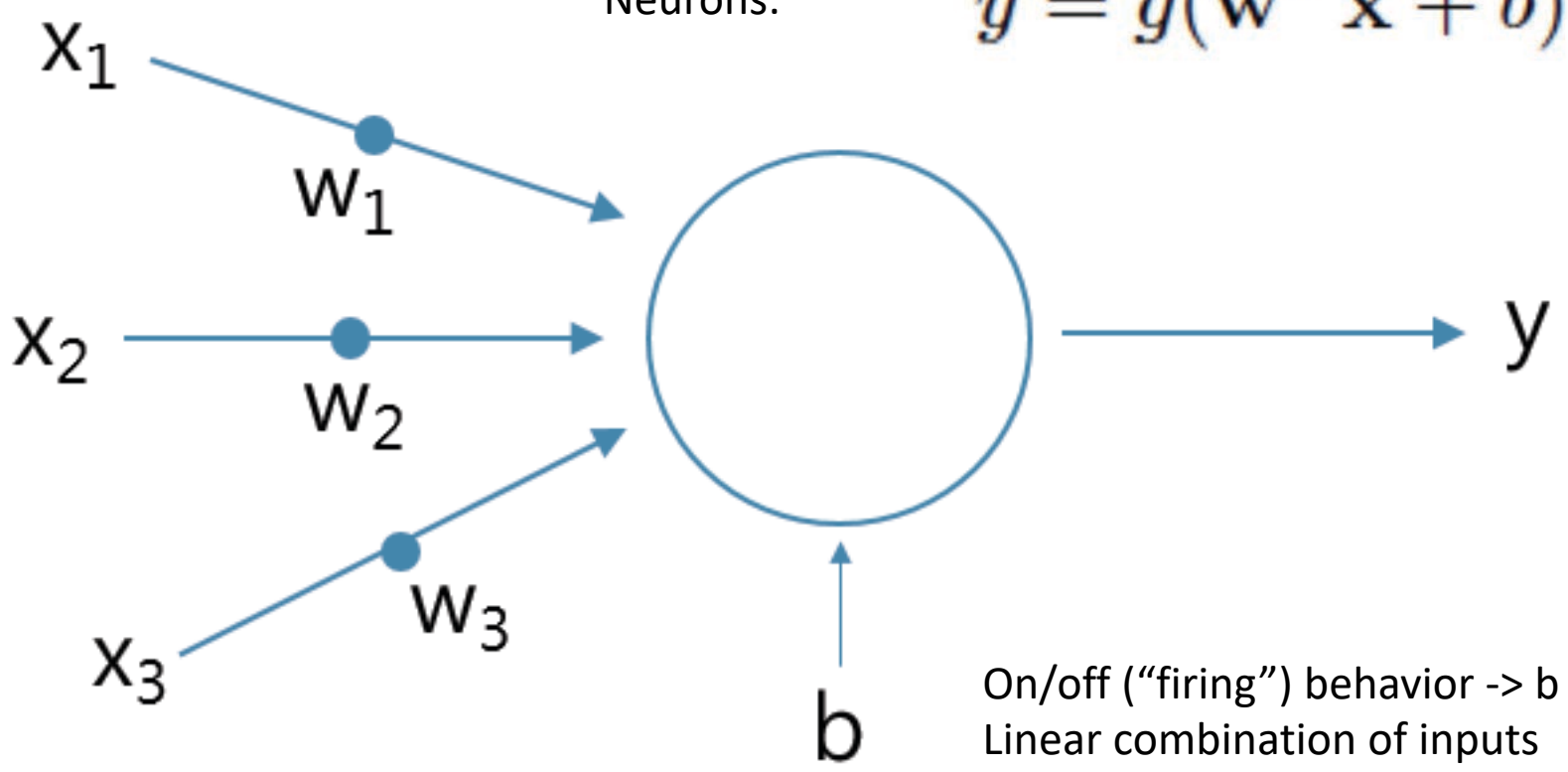
University of Bern/ Insel Data Science Center

Go to **www.menti.com** and use the code **57 91 60**

From neuron to neural nets

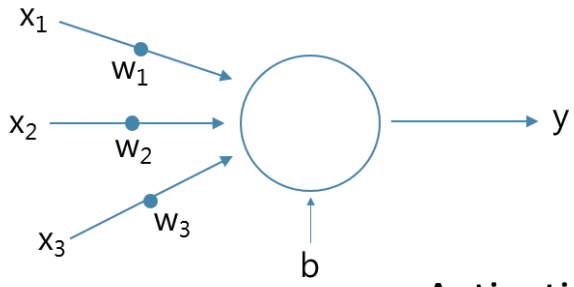
Neurons:

$$y = g(\mathbf{w}^\top \mathbf{x} + b)$$



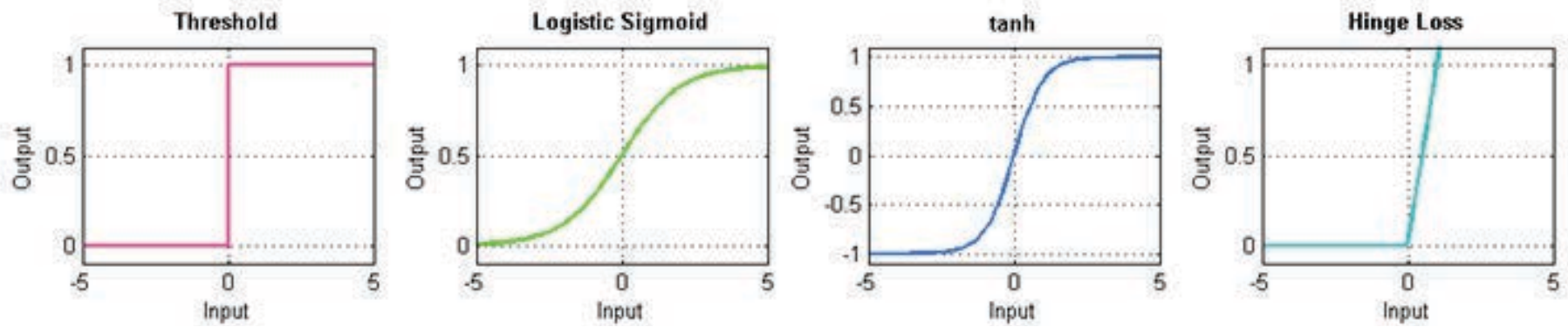
On/off (“firing”) behavior -> b value
Linear combination of inputs

Neural Nets: Activation functions

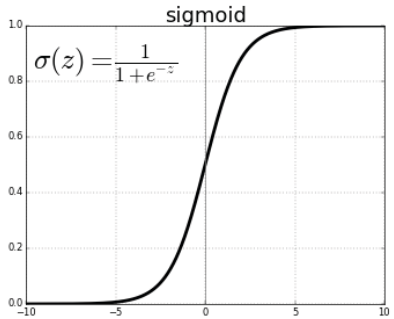


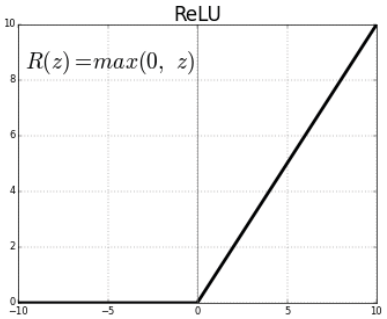
$$y = g(\mathbf{w}^\top \mathbf{x} + b)$$

Activation Function “g”



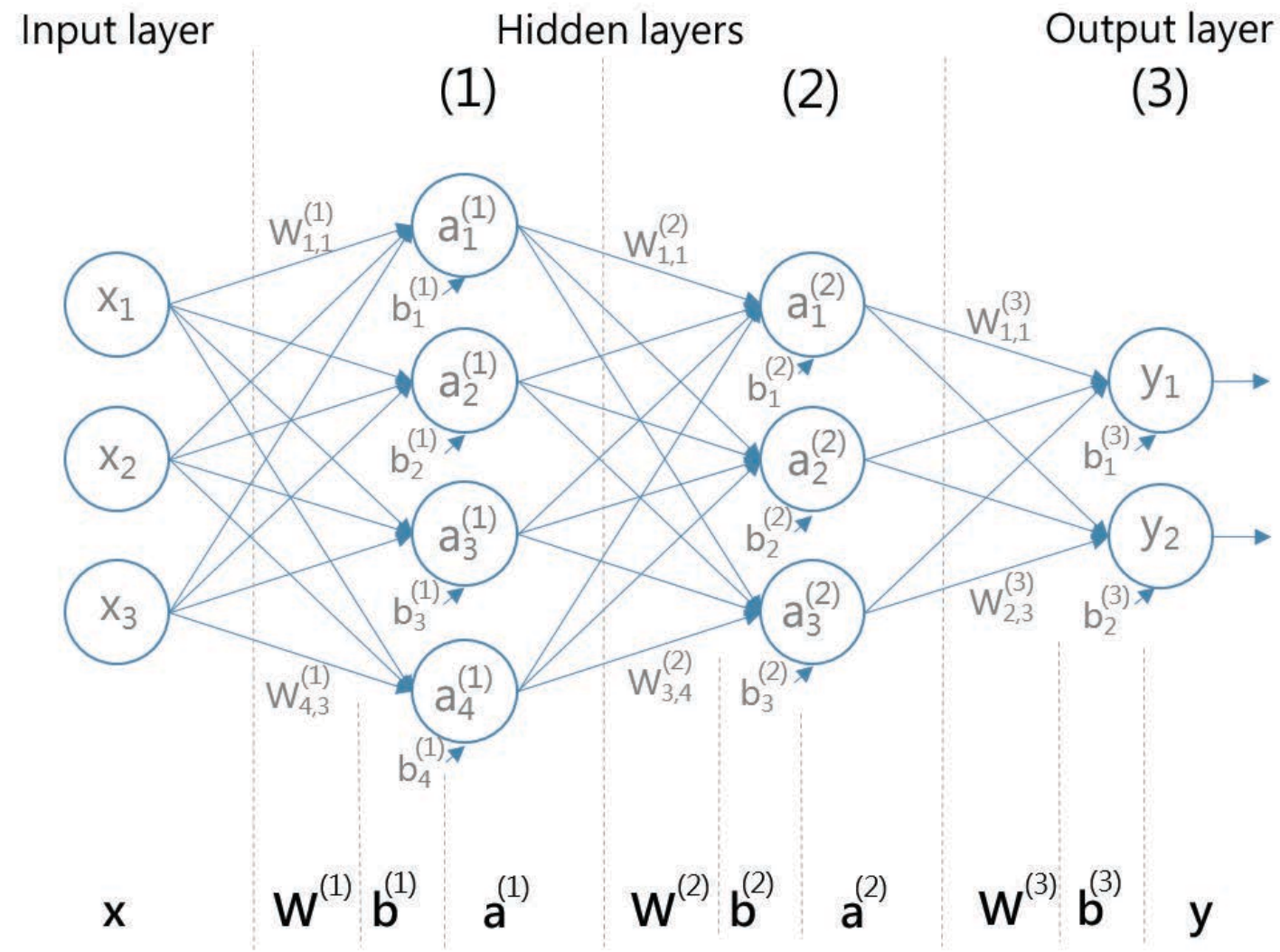
Most used: sigmoid and ReLu





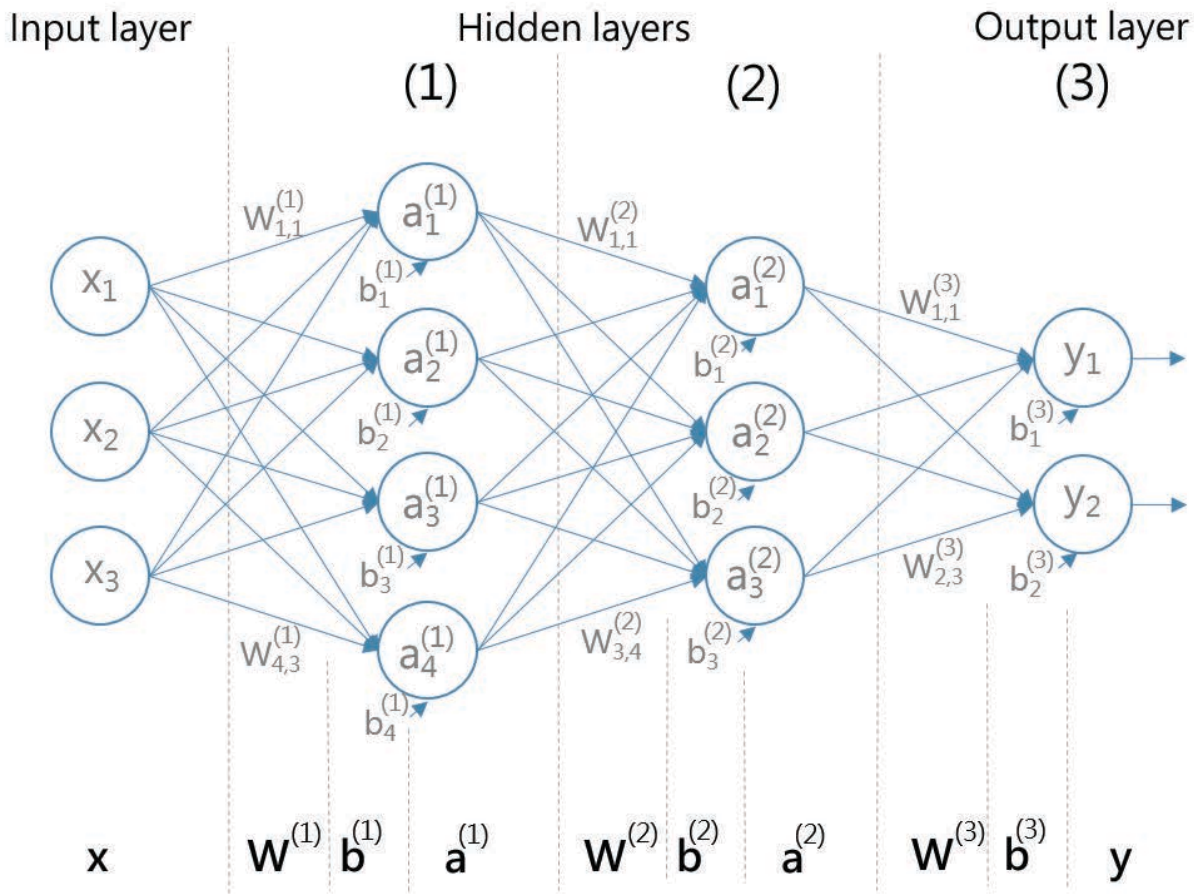
(We’ll talk later about issues with sigmoid)

Neural Nets: Layers



Neural Nets: Math behind layers

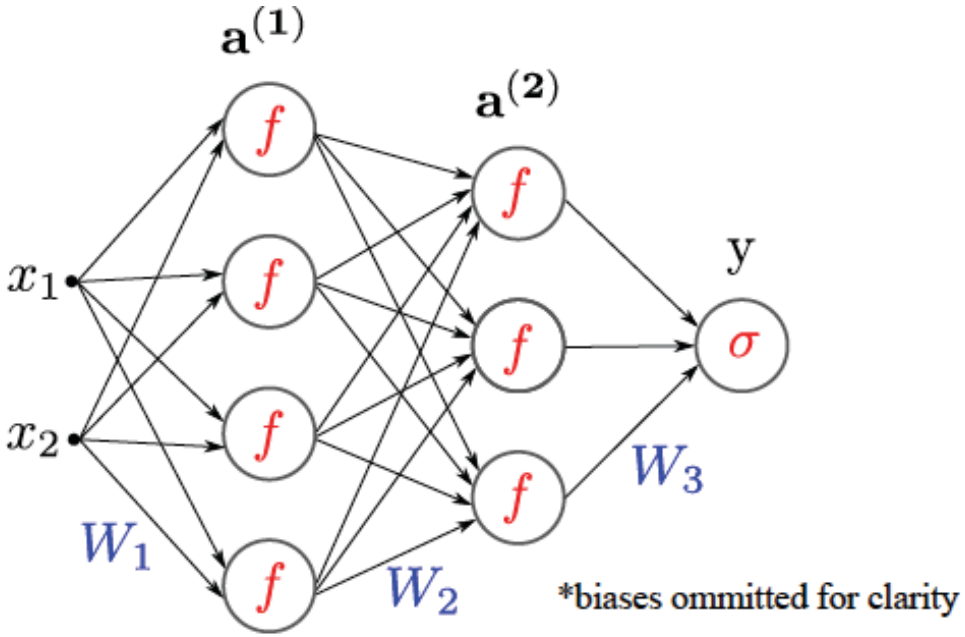
$$\mathbf{a}^{(1)} = g^{(1)}\left(\mathbf{W}^{(1)}\mathbf{x} + \mathbf{b}^{(1)}\right) \qquad \mathbf{a}^{(l)} = g^{(l)}\left(\mathbf{W}^{(l)}\mathbf{a}^{(l-1)} + \mathbf{b}^{(l)}\right)$$



Multilayer Perceptron (MLP)

Characteristics and Training a MLP

- Adjust weights to minimize error -> supervised
- Backpropagation -> backward propagation of errors
- Gradient Descent
- Fully connected: output of a neuron connects to all downstream neurons



Training is an optimization process

- Gradient descent

  Numerical gradient: slow :(, approximate :(, easy to write :) Analytic gradient: fast :), exact :), error-prone :(

  In practice: Derive analytic gradient, check your implementation with numerical gradient

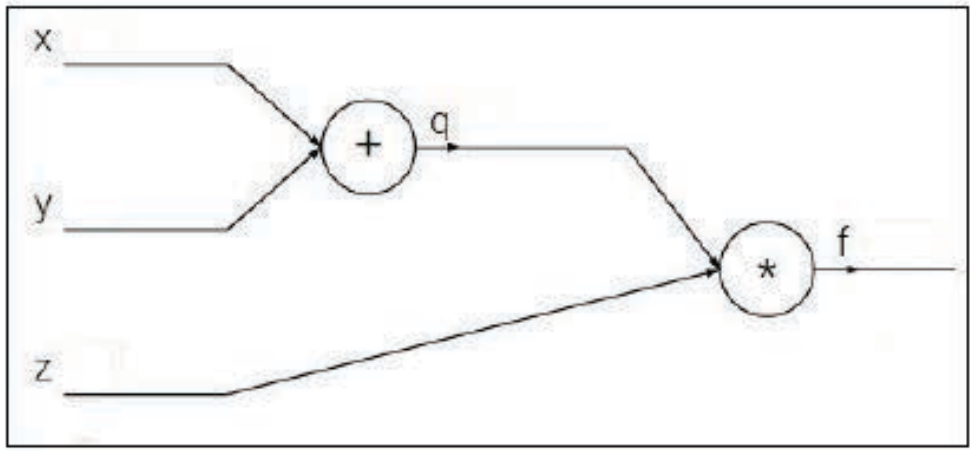
  (Kingma & Ba 2015)

- Adam optimization is the most popular to date

Simple example Backpropagation credits: Fei-Fei CS231

Backpropagation: a simple example

$$f(x, y, z) = (x + y)z$$



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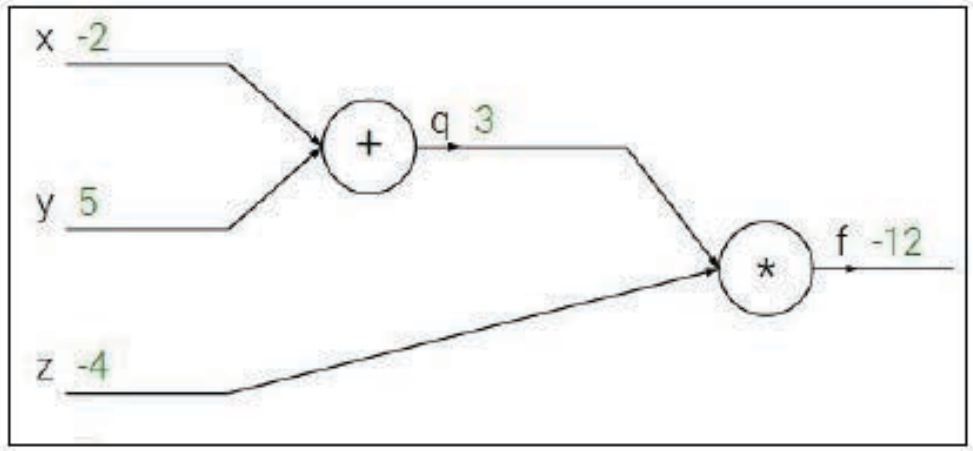
Backpropagation: a simple example

$$f(x, y, z) = (x + y)z$$

e.g. x = -2, y = 5, z = -4



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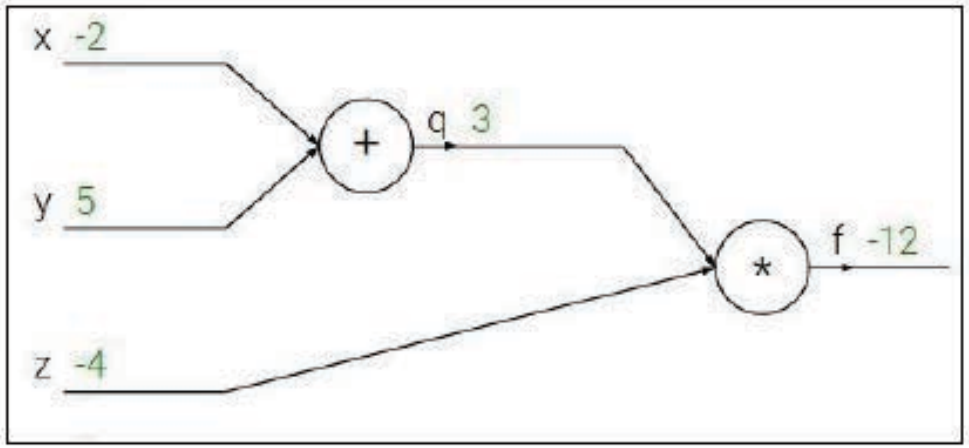
$$f(x, y, z) = (x + y)z$$

e.g. x = -2, y = 5, z = -4

$$q = x + y \qquad \frac{\partial q}{\partial x} = 1, \frac{\partial q}{\partial y} = 1$$

$$f = qz \qquad \frac{\partial f}{\partial q} = z, \frac{\partial f}{\partial z} = q$$

Want: $\frac{\partial f}{\partial x}, \frac{\partial f}{\partial y}, \frac{\partial f}{\partial z}$



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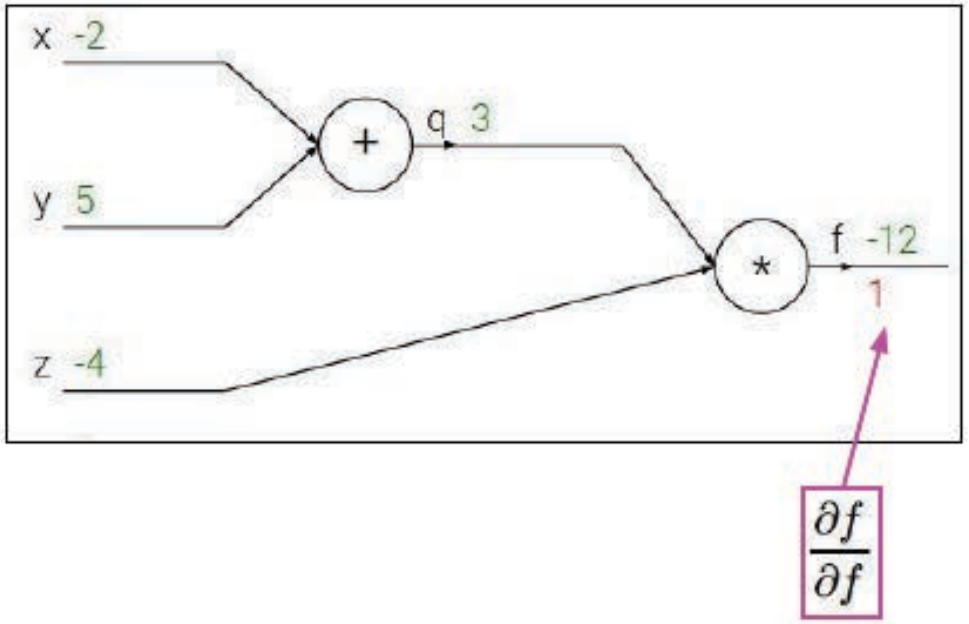

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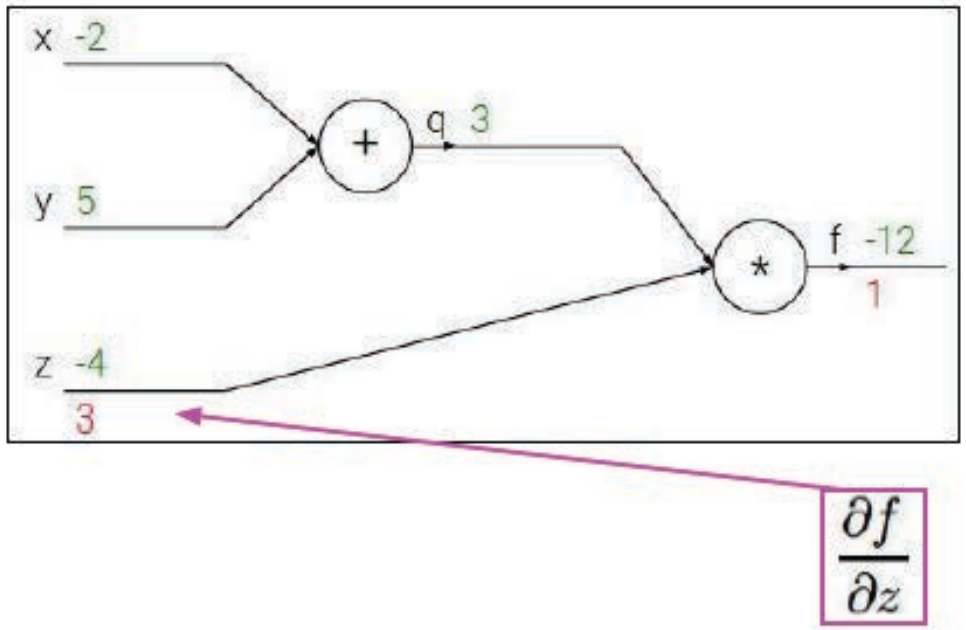

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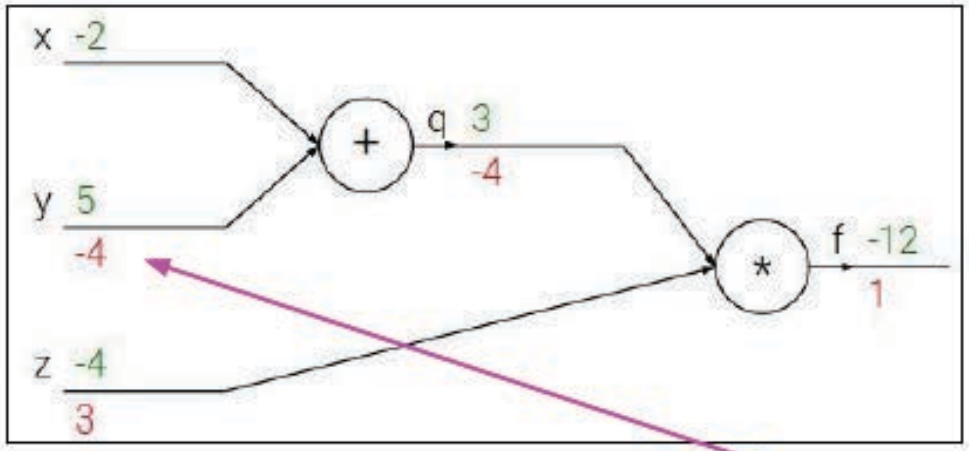

Chain rule:

$$\frac{\partial f}{\partial y} = \frac{\partial f}{\partial q}\frac{\partial q}{\partial y}$$

Upstream gradient

Local gradient

Simple example Backpropagation credits: Fei-Fei CS231