

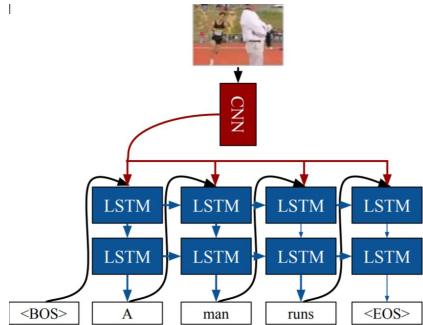
# Model interpretability as a tool for discovery

Subhashini Venugopalan



# Background in Language and Vision

## Image Captioning



LRCN: Long-term Recurrent Convolutional Networks for Visual Recognition and Description

Donahue et. al. CVPR'15

## Video Description



S2VT: Sequence to Sequence Video to Text.  
 Venugopalan et. al. ICCV'15

## Describing “unseen” objects



A **woodpecker** sitting on a tree branch in the woods.

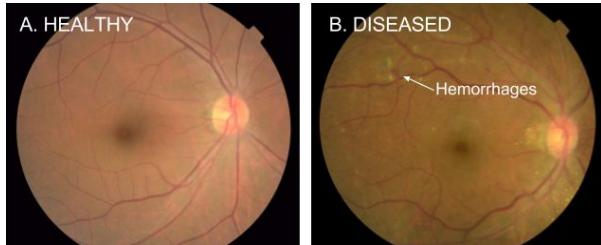


A **orca** is riding a small wave in the water.

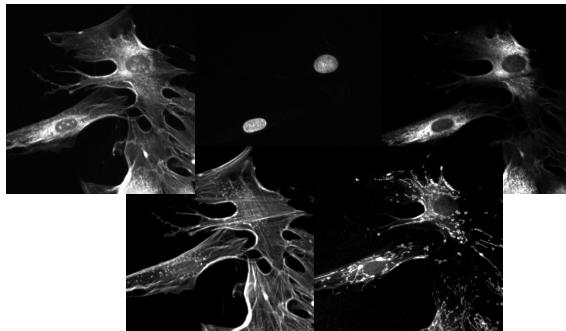
NOC: (Novel Object Captioner) Captioning Images with Diverse Objects

Venugopalan et. al. CVPR'17

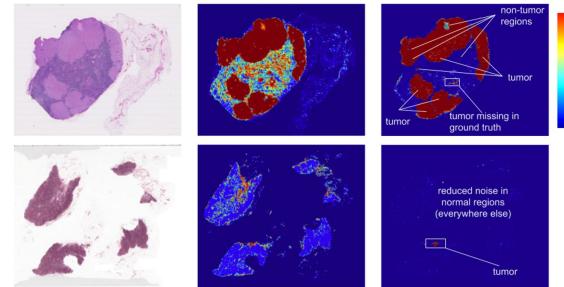
# ML (transfer learning) for medically relevant problems



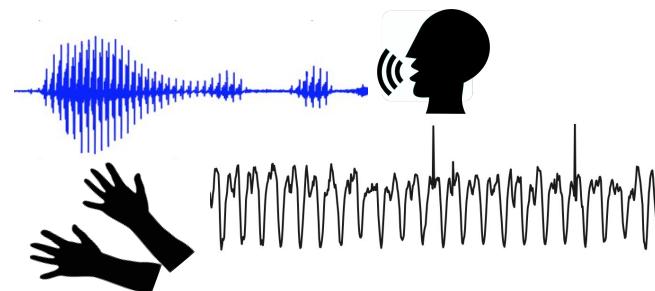
Deep Learning for Detection of Diabetic Retinopathy  
(Gulshan et. al. JAMA'16)



Searching for biomarkers from microscopy images. (Yang et. al. SLAS Discovery '19)



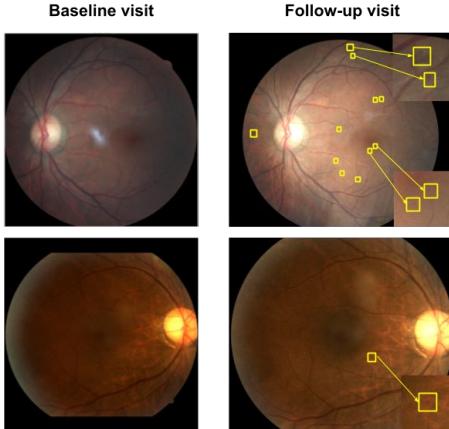
Detecting cancer metastases on pathology images. (Liu et. al. 2017)



ALS disease progression from voice and accelerometer samples.

# Better source of truth leads to novel signals, superhuman perf

future outcome  
novel signal



A

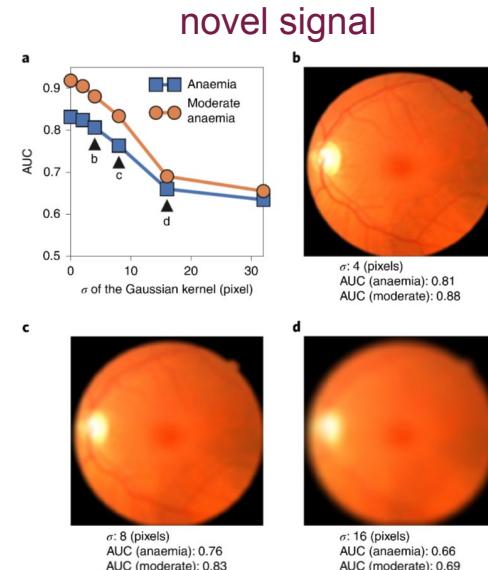
B

Predicting risk of developing diabetic retinopathy using deep learning

Ashish Bora, Siva Balasubramanian, Boris Babenko, Sunny Virmani, Subhashini Venugopalan, Akinori Mitani, Guilherme de Oliveira Marinho, Jorge Cuadros, Paisan Ruamviboonsuk, Greg S Corrado, Lily Peng, Dale R Webster, Avinash V Varadarajan, Naama Hammel, Yun Liu, Pinal Bawishi

Lancet Digital Health (to appear)

different modality label

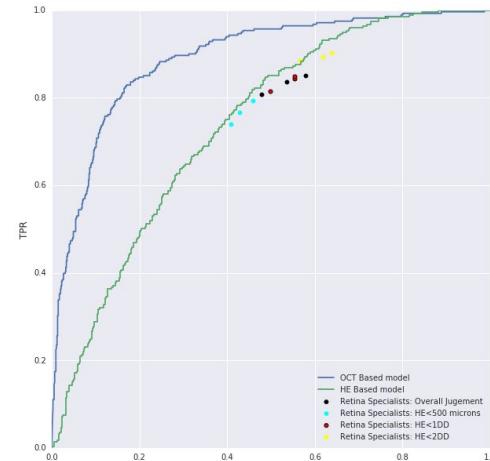


Detection of anaemia from retinal fundus images via deep learning

Akinori Mitani, Abigail Huang, Subhashini Venugopalan, Greg S. Corrado, Lily Peng, Dale R. Webster, Naama Hammel, Yun Liu & Avinash V. Varadarajan

*Nature Biomedical Engineering* 4, 18–27(2020) | Cite this article

different modality label  
strongly exceeds

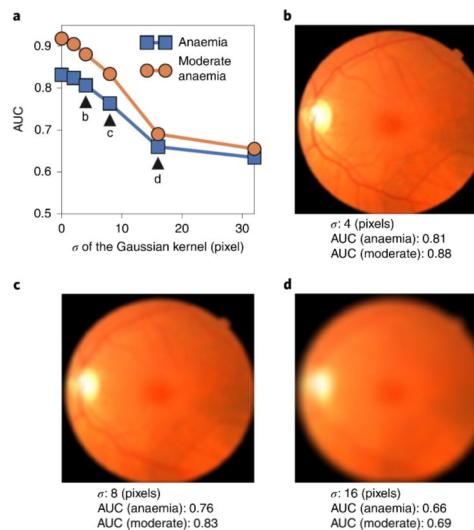


Predicting optical coherence tomography-derived diabetic macular edema grades from fundus photographs using deep learning

Avinash V. Varadarajan, Pinal Bawishi, Paisan Ruamviboonsuk, Peranut Chotcomwongse, Subhashini Venugopalan, Arunachalam Narayanaswamy, Jorge Cuadros, Kuniyoshi Kanai, George Bresnick, Mongkol Tadarati, Sukhum Silpa-archa, Jirawut Limwattanayingyong, Varia Nganthavee, Joseph R. Ledsam, Pearce A. Keane, Greg S. Corrado, Lily Peng & Dale R. Webster

*Nature Communications* 11, Article number: 130 (2020) | Cite this article

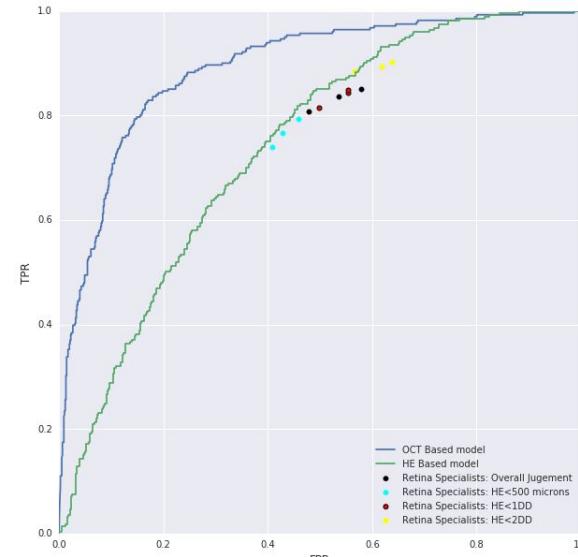
# Learning from outcome - novel signals, outperforming humans



## Detection of anaemia from retinal fundus images via deep learning

Akinori Mitani , Abigail Huang, Subhashini Venugopalan, Greg S. Corrado, Lily Peng, Dale R. Webster, Naama Hammel, Yun Liu & Avinash V. Varadarajan

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## Predicting optical coherence tomography-derived diabetic macular edema grades from fundus photographs using deep learning

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*Nature Communications* 11, Article number: 130 (2020) | [Cite this article](#)

## \* Background

## \* Scientific Discovery by Generating Counterfactuals using Image Translation

Narayanaswamy\*, Venugopalan\*, et. al. MICCAI 2020

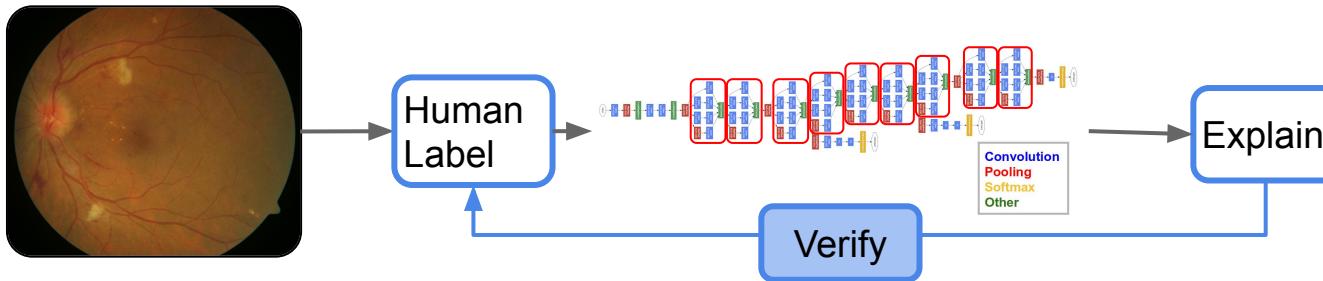
## \* Attribution in Scale and Space

Xu, Venugopalan, Sundararajan CVPR 2020

## \* Predicting risk of developing diabetic retinopathy using deep learning

Bora et. al. Lancet Digital Health 2021

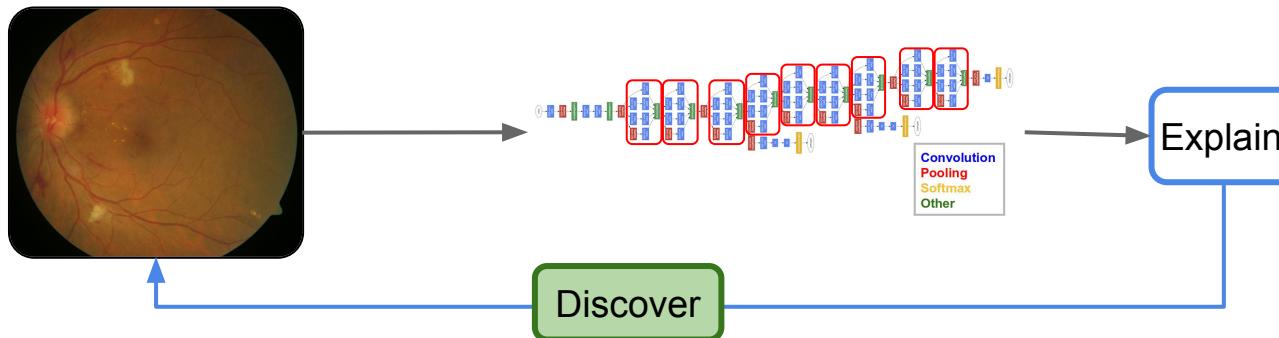
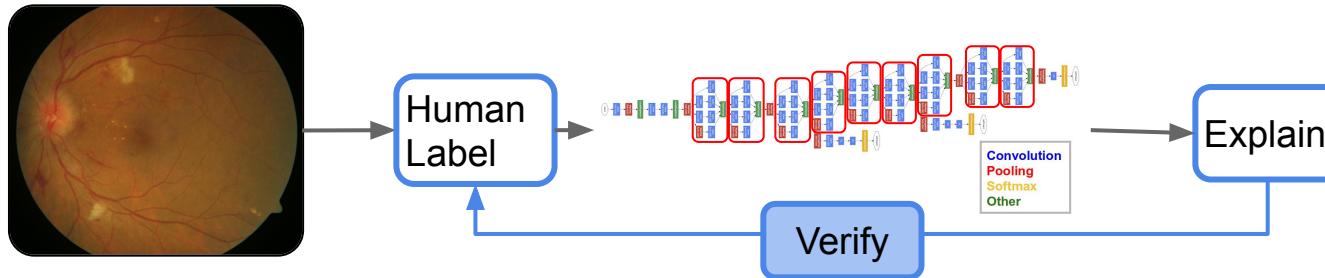
# Prediction to Explanation



Validation → Is the model making predictions for the right reasons?

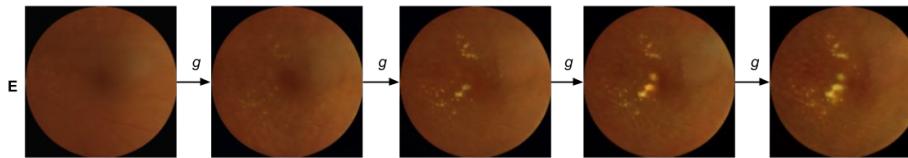
Does it conform to how humans choose a label? (Builds trust)

# Prediction to Explanation to Discovery



# Discovery? Identify properties to teach humans

Progressively exaggerate the kind of things that the model is looking at.



Translate what we can learn into a simple set of properties / features  
to enable experts to perform better  
or improve our understanding of the disease.

# Diabetic Macular Edema - case study

Diabetic Macular Edema (DME)

- late stage of diabetic eye disease.
- characterized by retinal thickening in the macula.
- often results in vision loss.

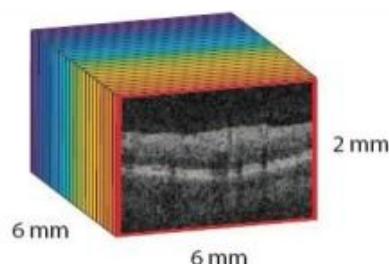
# Diabetic Macular Edema - 2 sources of labels

Diabetic Macular Edema (DME)

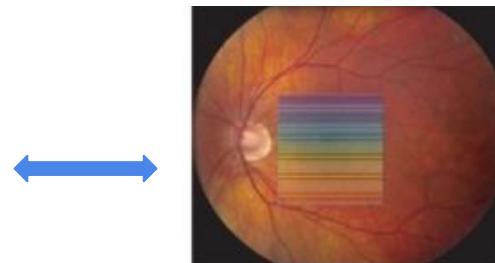
- late stage of diabetic eye disease.
- characterized by retinal thickening in the macula.
- often results in vision loss.

Diagnosis:

- referral based on fundus image. (>80% FP rate)
- confirmation based on measuring retinal thickness in optical coherence tomography (OCT) image (3D).



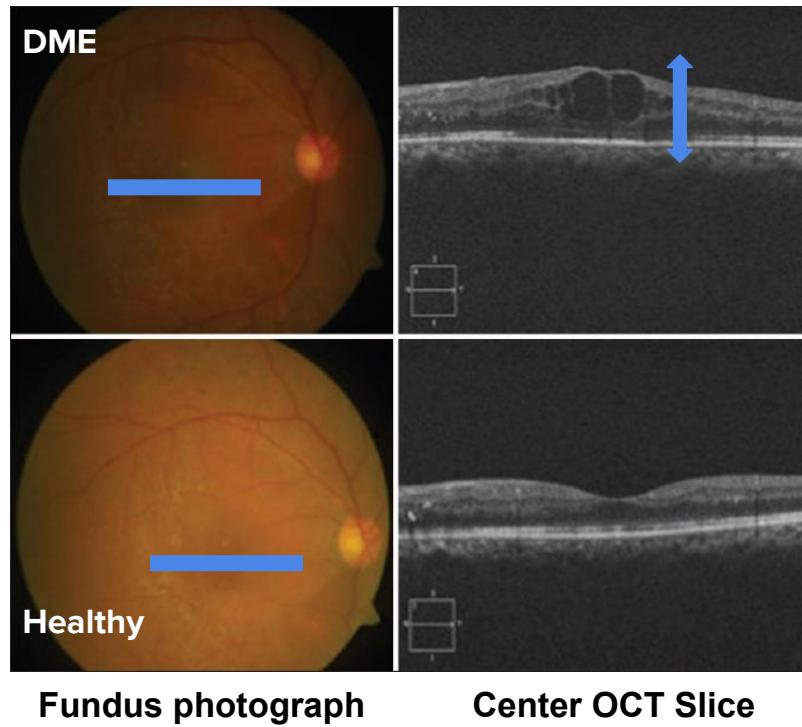
**OCT Slices (3D)**



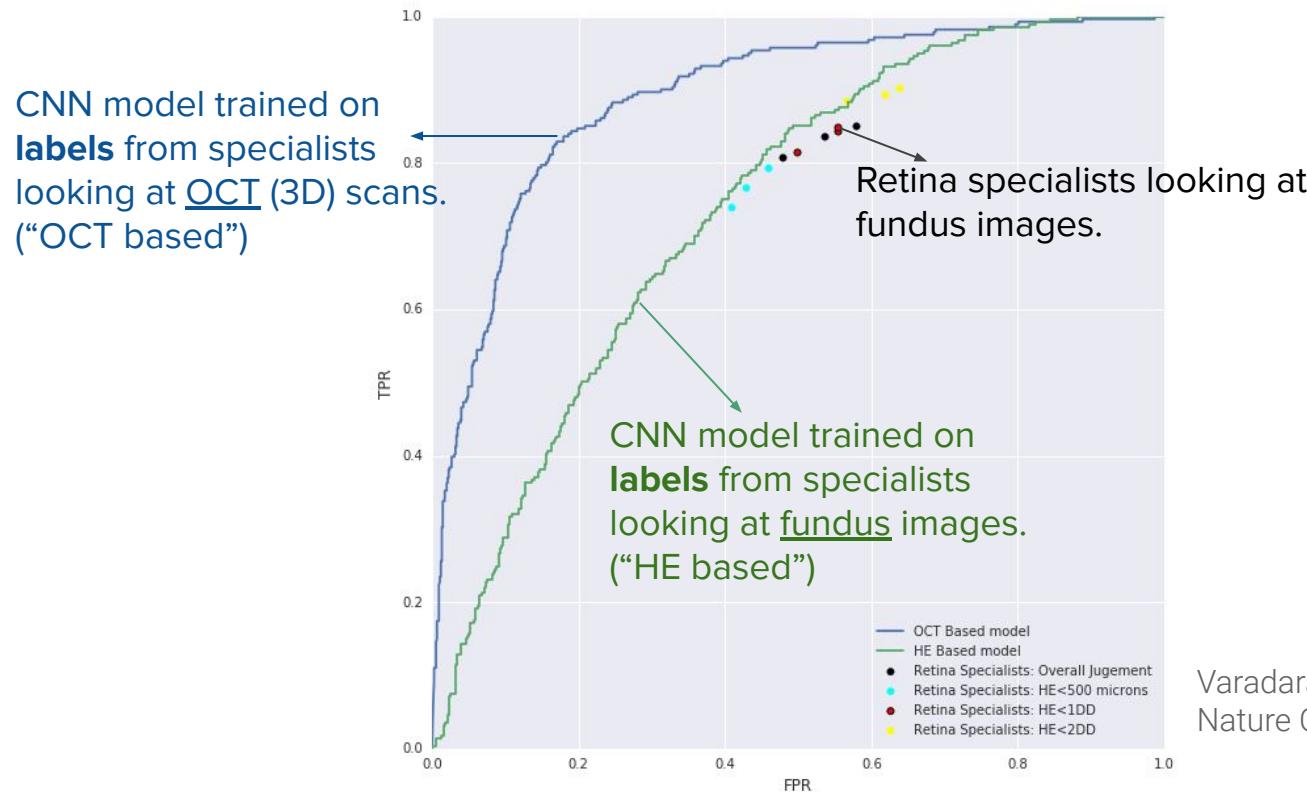
**Fundus photograph (2D)**

Source: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3785070/>

# Diabetic Macular Edema - 2 sources of labels



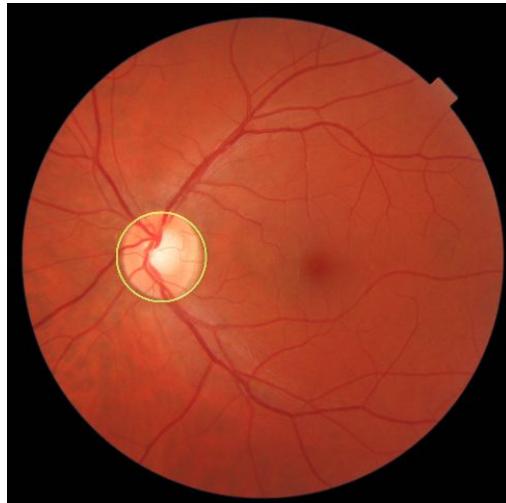
# CNNs see more from 2d fundus images than specialists



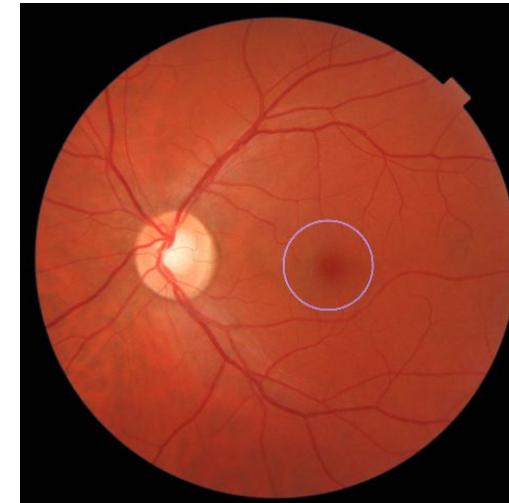
Varadarajan et. al.  
Nature Comms. '20

# Validation - Is the signal in a specific region?

Collect labels to ablate image regions and evaluate performance.



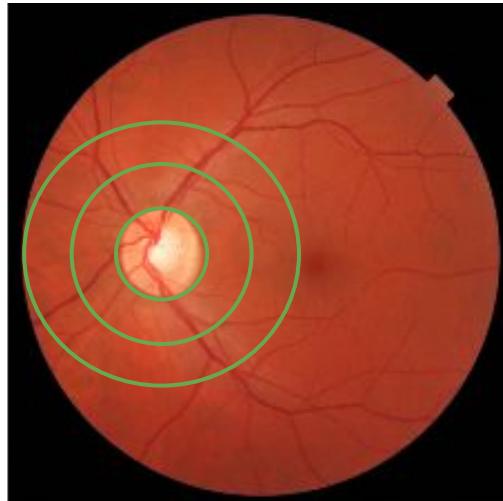
Optic Disc



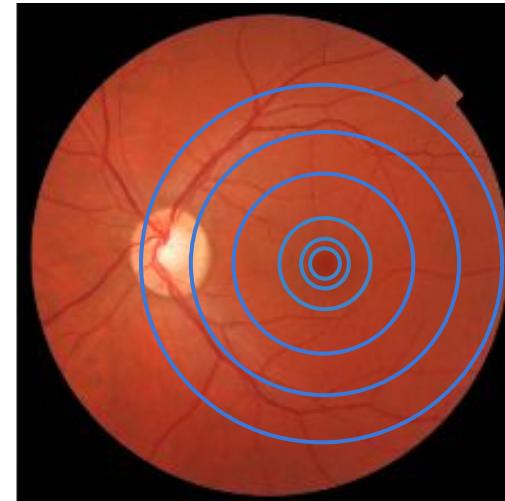
Fovea / Macula

# Validation - Is the signal in a specific region?

Extract crops in multiples of the optic disc diameter and train models.

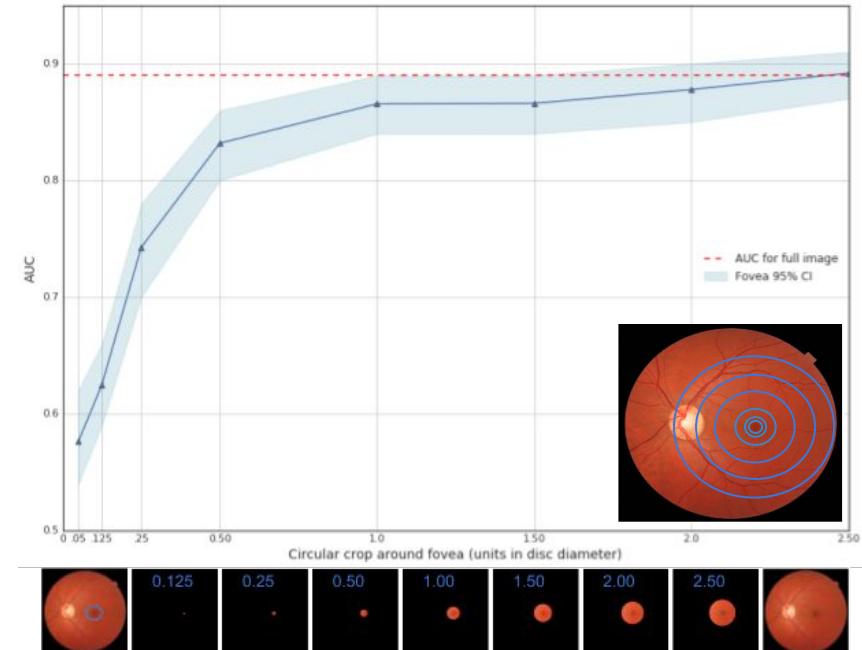
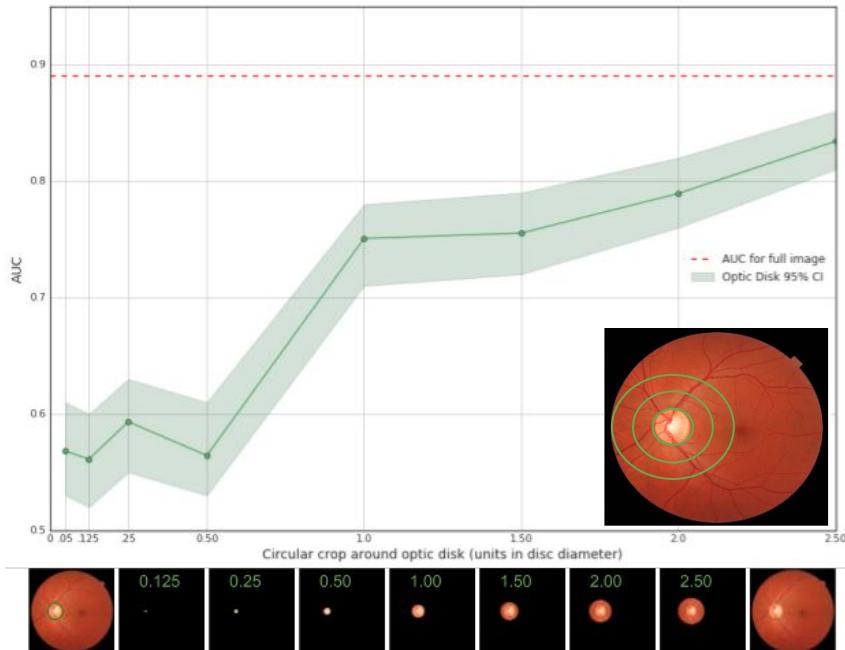


Optic Disc



Fovea / Macula

# Region around fovea accounts for performance.



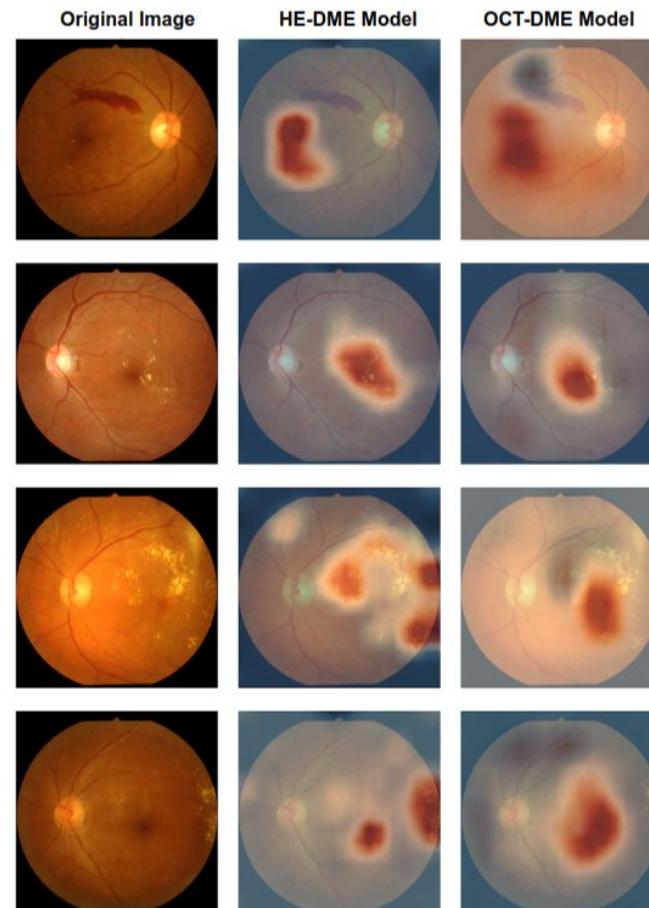
# Saliency maps - Where is it looking?

Middle column - HE-DME: CNN trained on specialist labels on fundus images (2d)

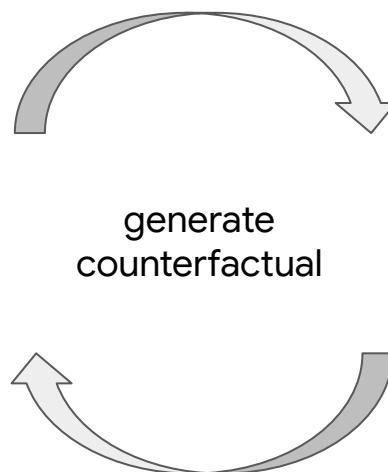
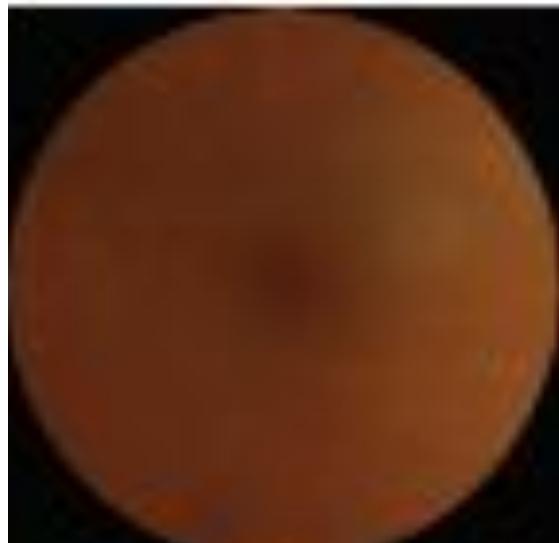
- Hard exudates (HE) yellow lesions

Last column - OCT-DME: CNN trained on specialist labels from OCT scans (3d)

- Mostly around macula



# What is different about those regions?

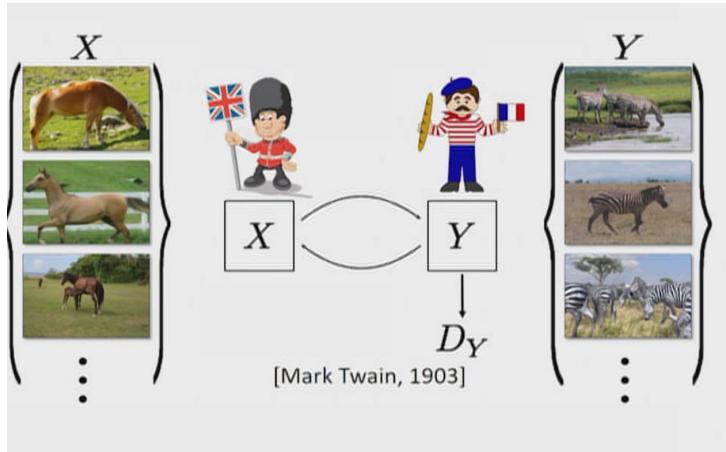


No DME

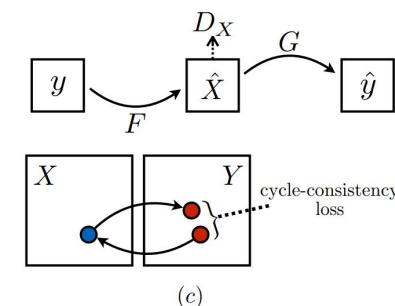
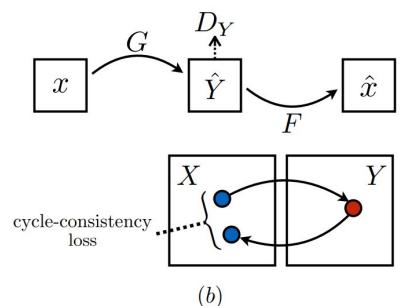
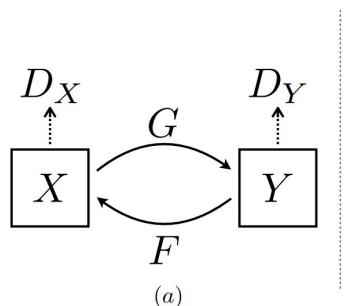


DME

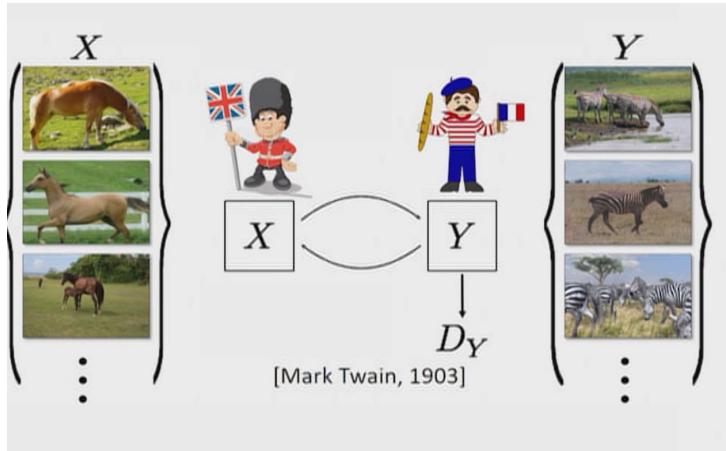
# Image to Image translation (cycleGANs) to the rescue.



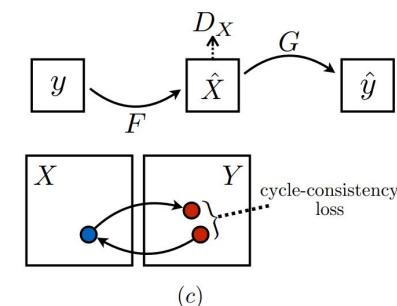
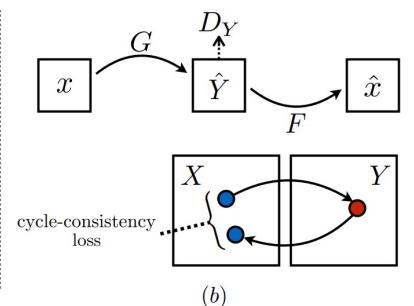
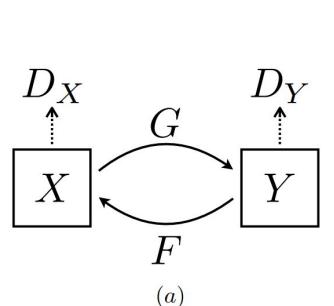
Zhu et. al. ICCV'17 (UC Berkeley)



# Image to Image translation (cycleGANs) to the rescue.



Zhu et. al. ICCV'17 (UC Berkeley)



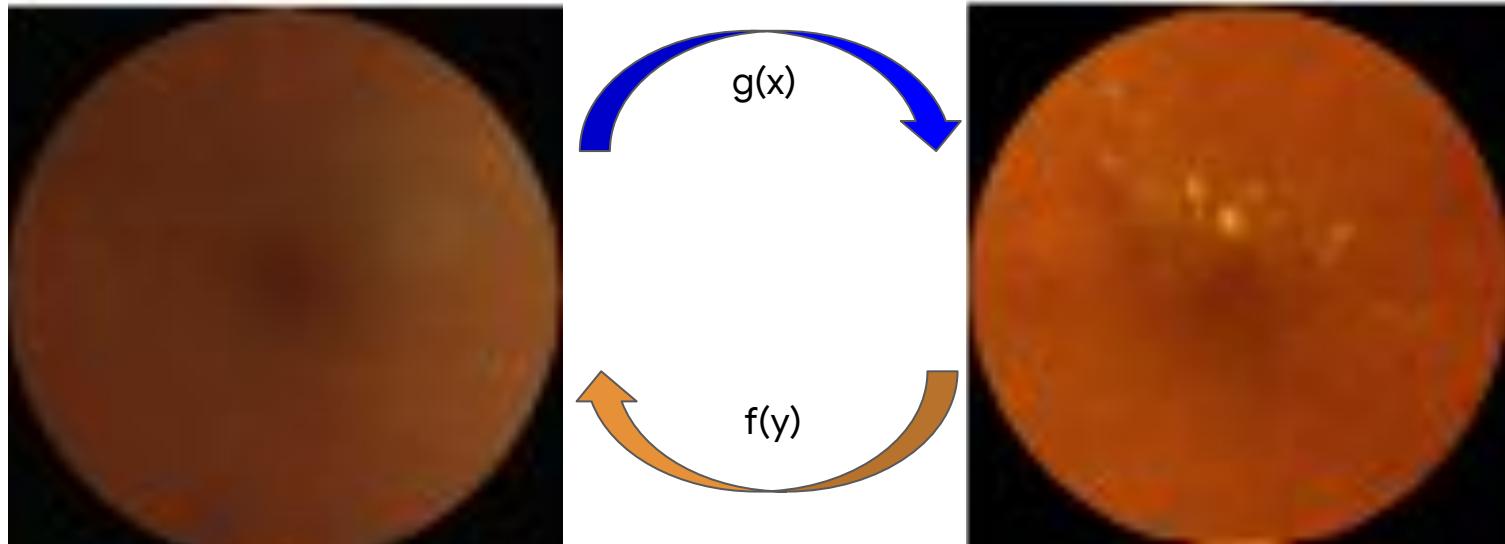
Add 1x1 conv.

Add residual connection.

(easy to copy)

# CycleGANs to visualize the difference

Specifically apply it to region around macula.



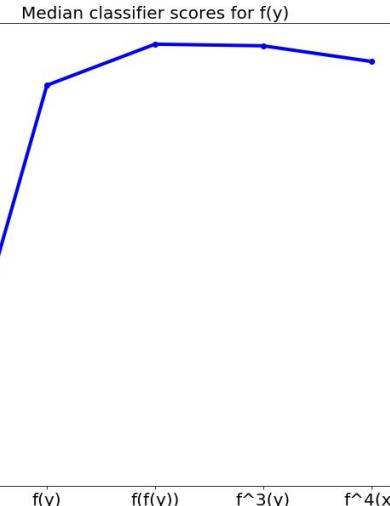
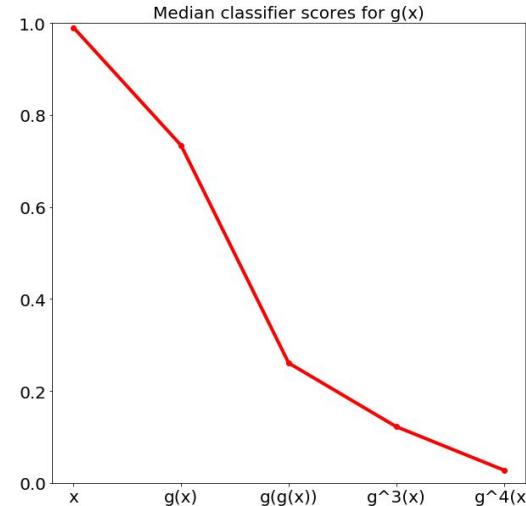
No DME

DME

# Verify that the cycleGAN is “faithful” to the model

Verify that the independently trained classifier AUC changes as expected when we convert/translate images from one class to another.

**No DME**



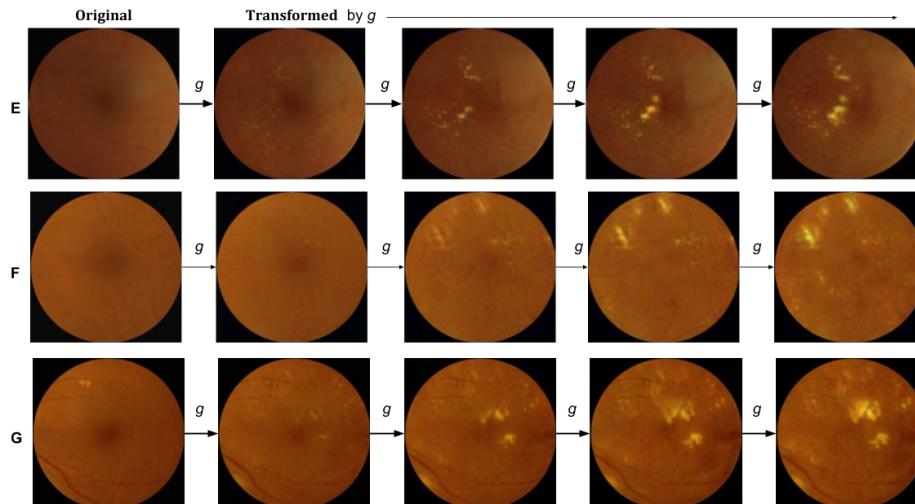
**DME**

Input	AUC [95% CI range]
$(x, y)$	0.804 [0.746 - 0.862]
$g(x), f(y)$	0.374 [0.294 - 0.450]
$g^2(x), f^2(y)$	0.180 [0.139 - 0.241]
$g^3(x), f^3(y)$	0.130 [0.087 - 0.186]
$g^4(x), f^4(y)$	0.106 [0.060 - 0.156]

# Observe transformations

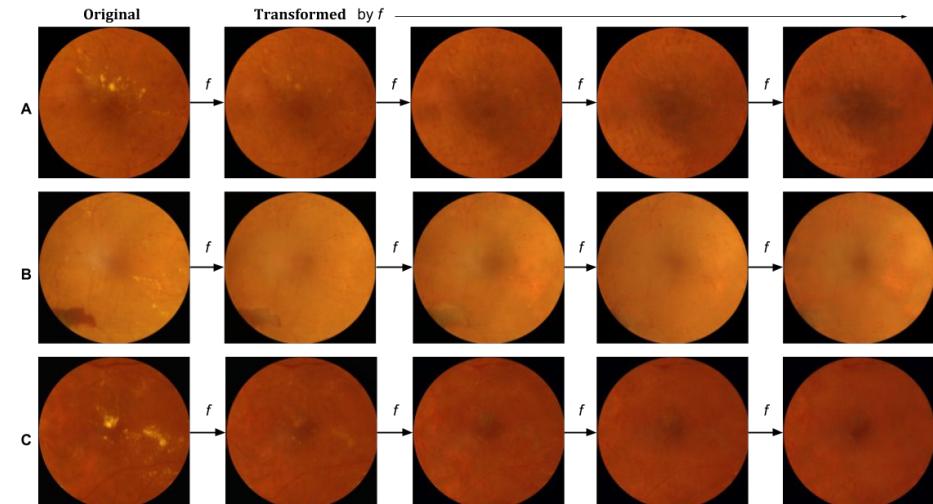
$g(x)$  (i.e. No DME to DME):

1. Adds hard exudates (yellow lesions)
2. Lightens fovea



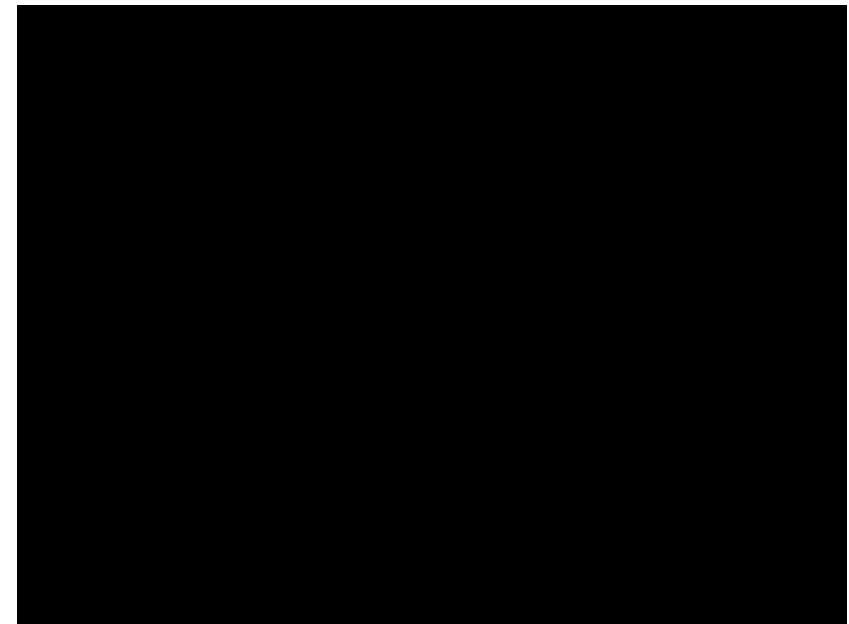
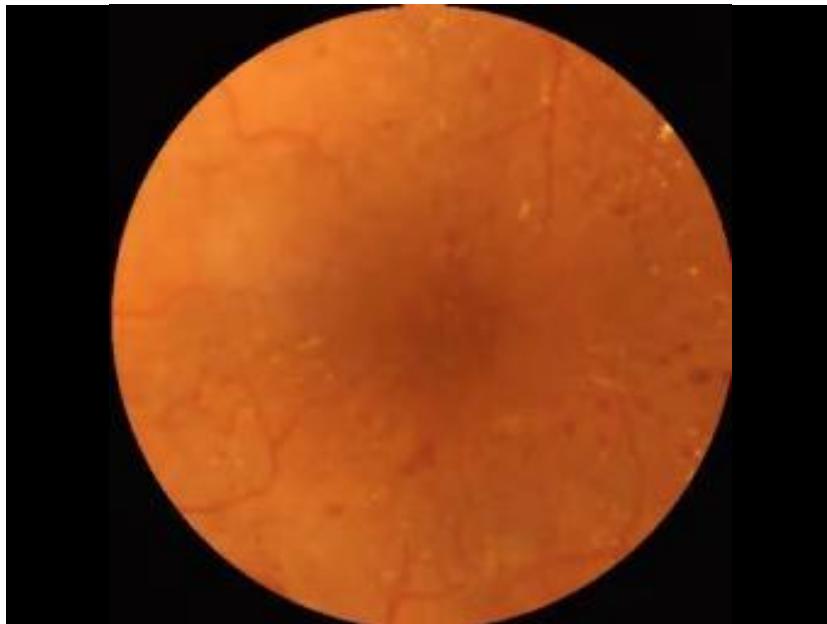
$f(y)$  (i.e. DME to No DME):

1. Removes hard exudates
2. Darkens fovea (very subtle)



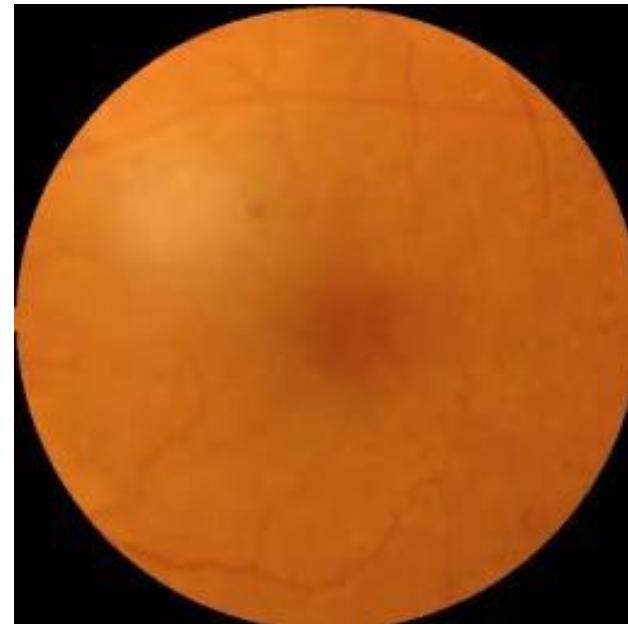
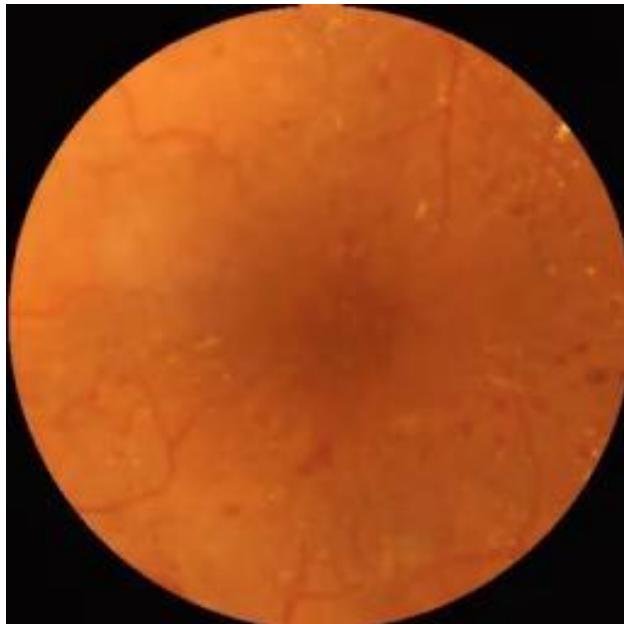
## Observe transformations (loop)

Alpha-blended images applying the transformation and back.



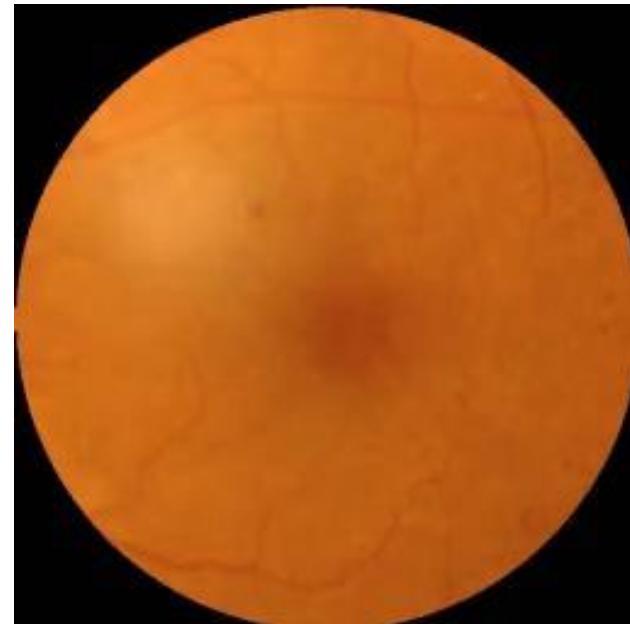
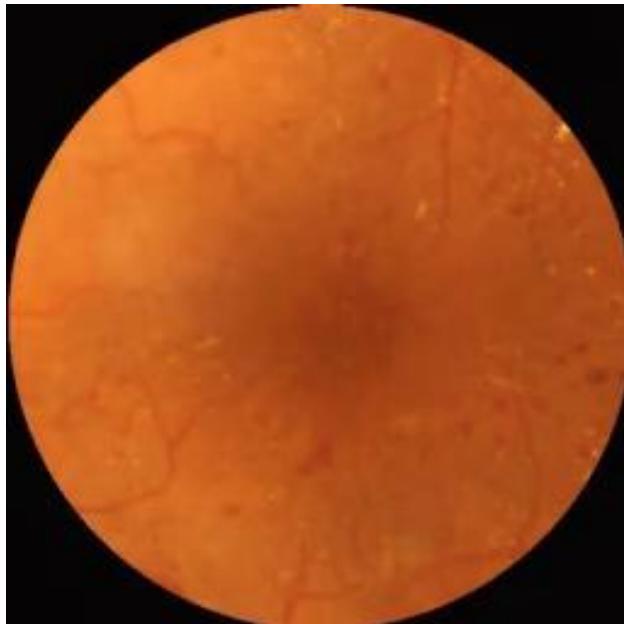
## Observe transformations (loop)

Alpha-blended images applying the transformation and back.

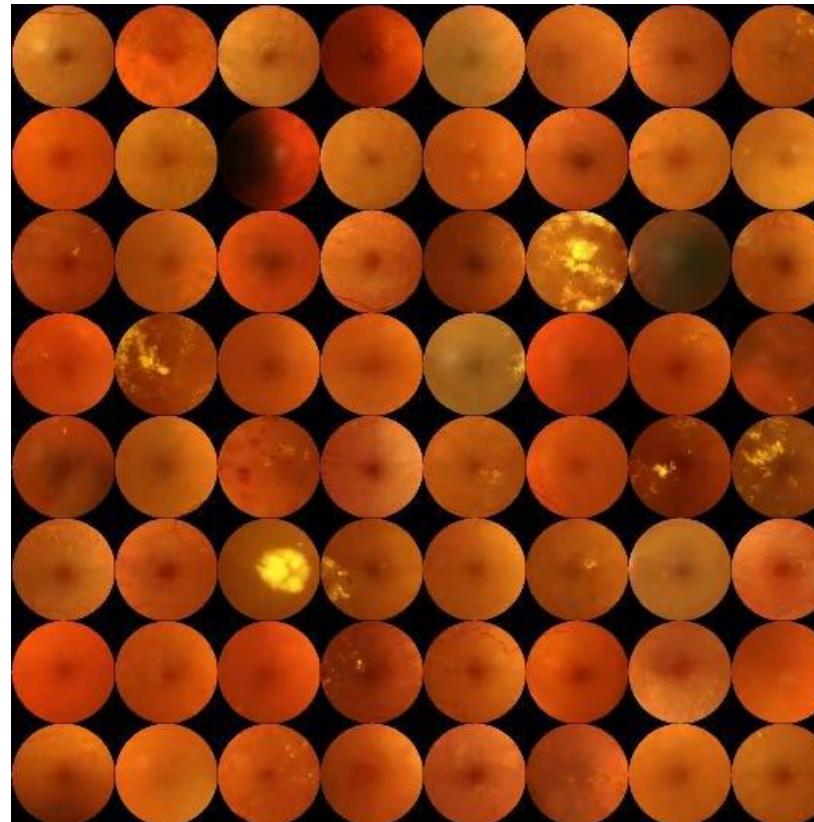


## Observe transformations (loop)

Alpha-blended images applying the transformation and back.



Observe lots of transformations



# Hand engineer features to explain performance

On the full image

- Are hard exudates (yellow lesions) present or not? --- Easy for humans
- Hand-engineered features - mean intensities of pixels (at concentric circles around fovea) [10 (x3) values]
  - fit functional form from weights of a linear model

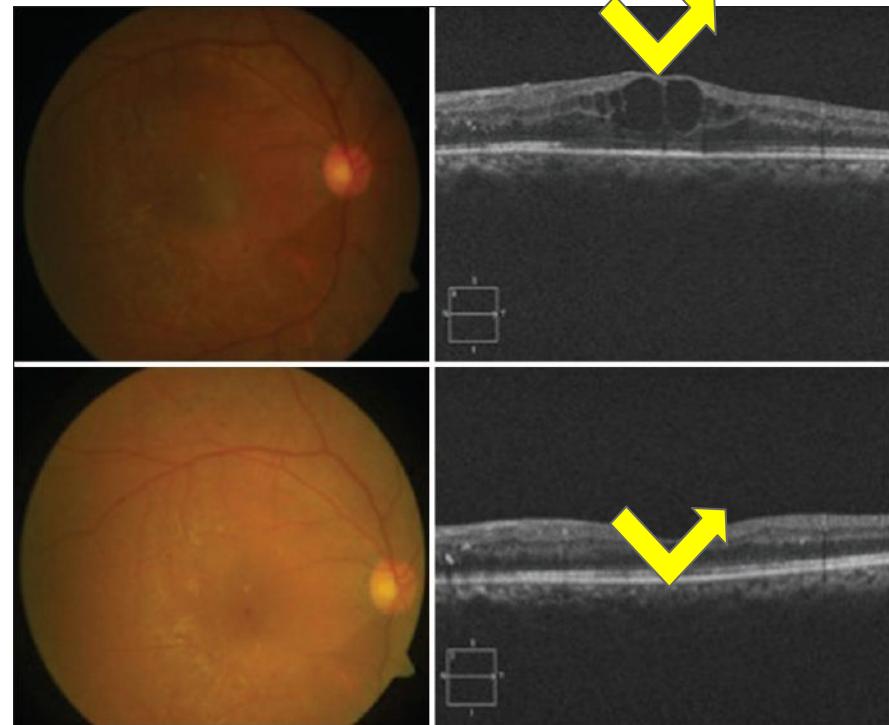
Features	AUC	
	SVM	MLP
Hand-engineered features alone	$72.4 \pm 0.0$	$76.3 \pm 0.3$
Presence of hard exudates alone	$74.1 \pm 0.0$	$74.1 \pm 0.0$
Hand-engineered features + hard exudates' presence	<b><math>81.4 \pm 0.0</math></b>	<b><math>82.2 \pm 0.2</math></b>
<i>M</i> (raw pixels single task on cropped image)	CNN: 84.7	

# Light bounces differently off the surface

Hypothesis (validating in simulation)

- Deeper fovea leads to darker macula
- Flatter fovea leads to lighter macula

Essentially use prediction models, and explanations to generate hypotheses (hopefully leading to discoveries)



# Appearing in MICCAI 2020

Google Research and Google AI Healthcare



Arun Narayanaswamy



Subhashini  
Venugopalan



Philip Nelson



Michael Brenner



Rory Sayres



Lily Peng



Pinal Bavishi



Abigail Huang



Dale Webster



Avinash Varadarajan

## \* Background

## \* Scientific Discovery by Generating Counterfactuals using Image Translation

Narayanaswamy\*, Venugopalan\*, et. al. MICCAI 2020

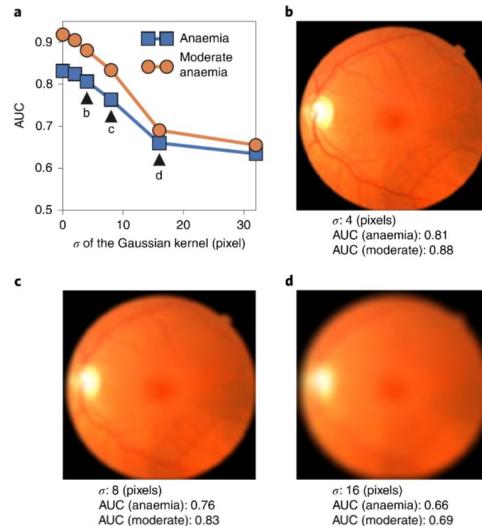
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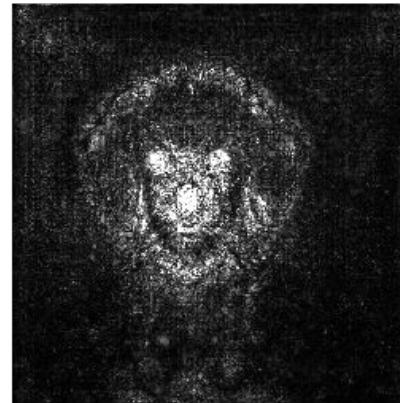
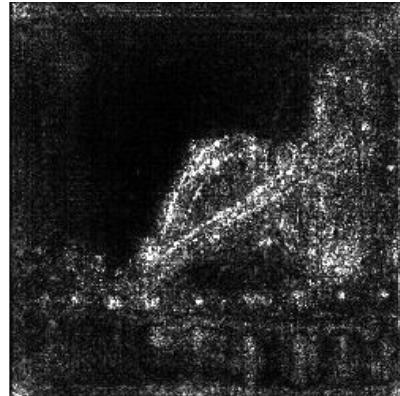
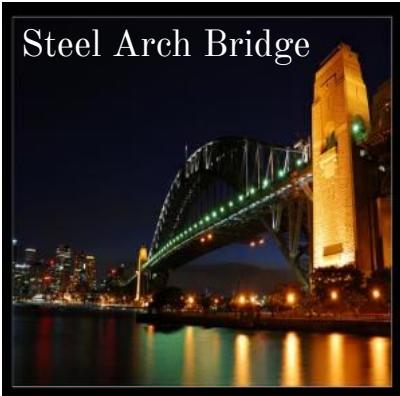
Bora et. al. Lancet Digital Health 2021

# At what scale/frequency does a network recognize signal?

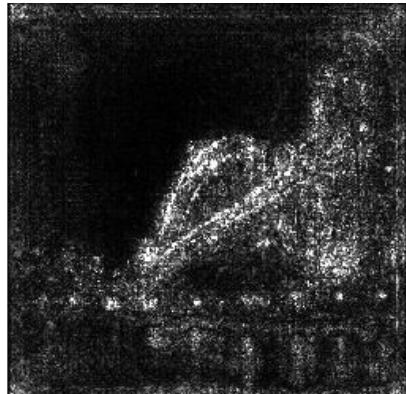
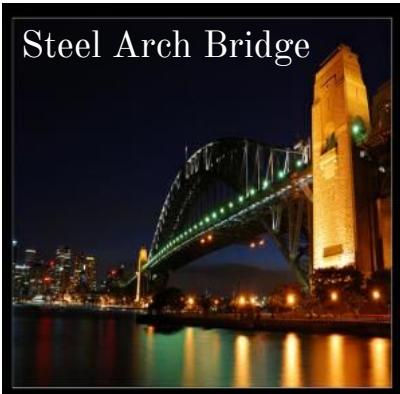


Mitani et. al. Nature BME '20

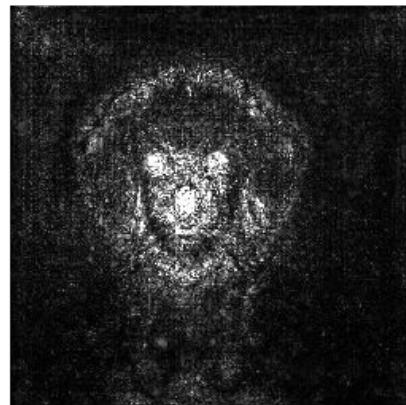
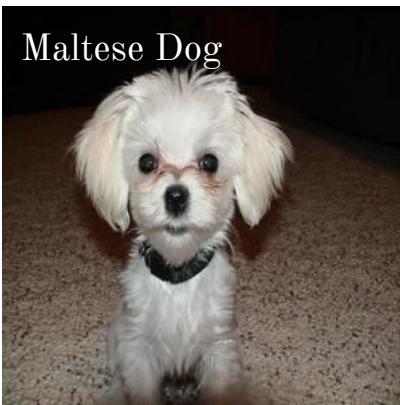
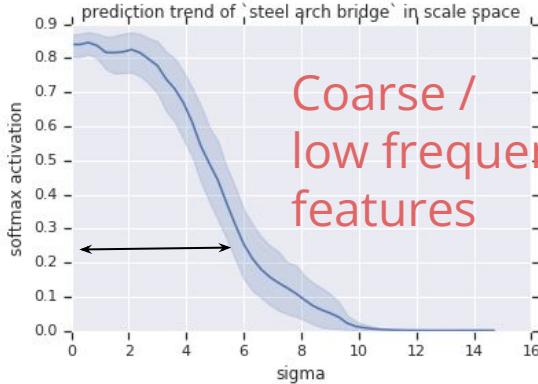
## Existing explanations **localize in space** (i.e. pixels)



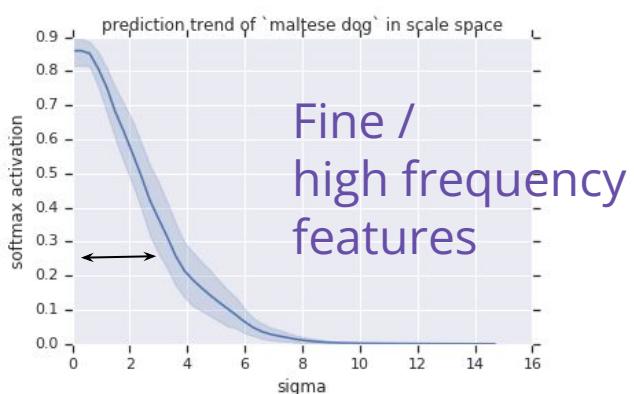
# Can we also localize in scale/frequency?



arch bridge

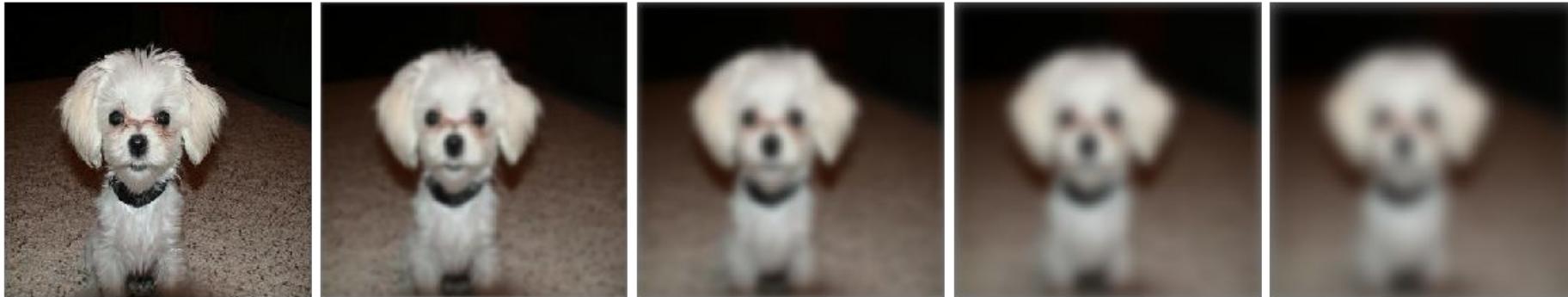


dog breed

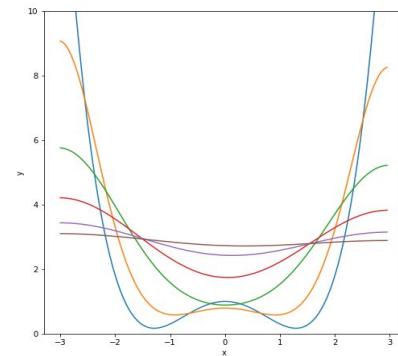


# Key idea from scale-space theory

To handle image structures at different scales, **represent an image as a one-parameter family of smoothed images.** Burt and Adelson '81, T. Lindberg '90



**Gaussian blur perturbation only destroys information!  
Ensures explanation is free of artifacts.**



# How? Integrate gradients, progressively reducing blur

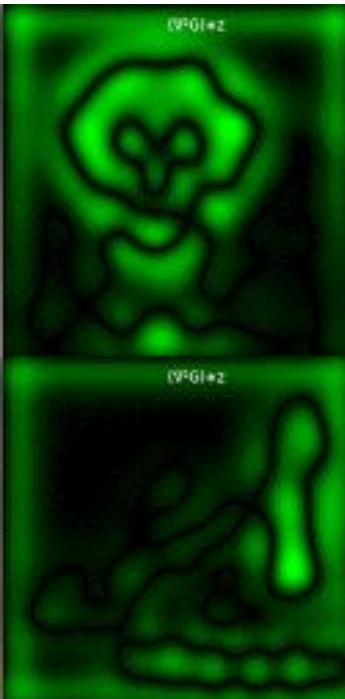
Original image



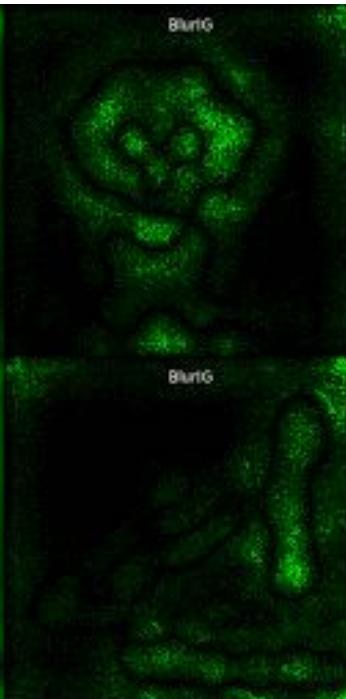
Gaussian filtered image



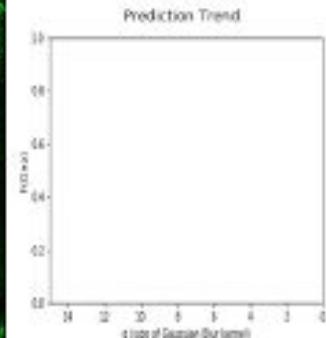
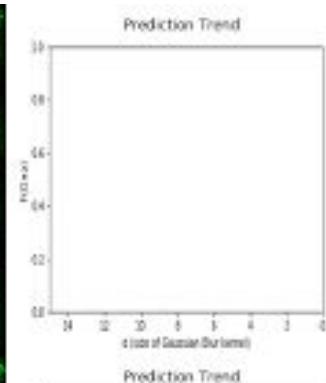
Gaussian derivatives localize attributions in scale



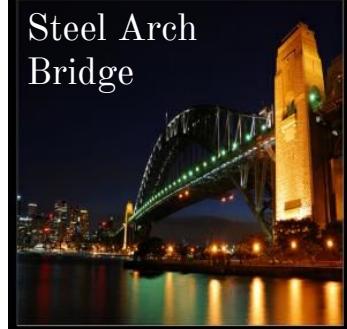
Model derivatives localize attributions in space



Evolution of prediction scores



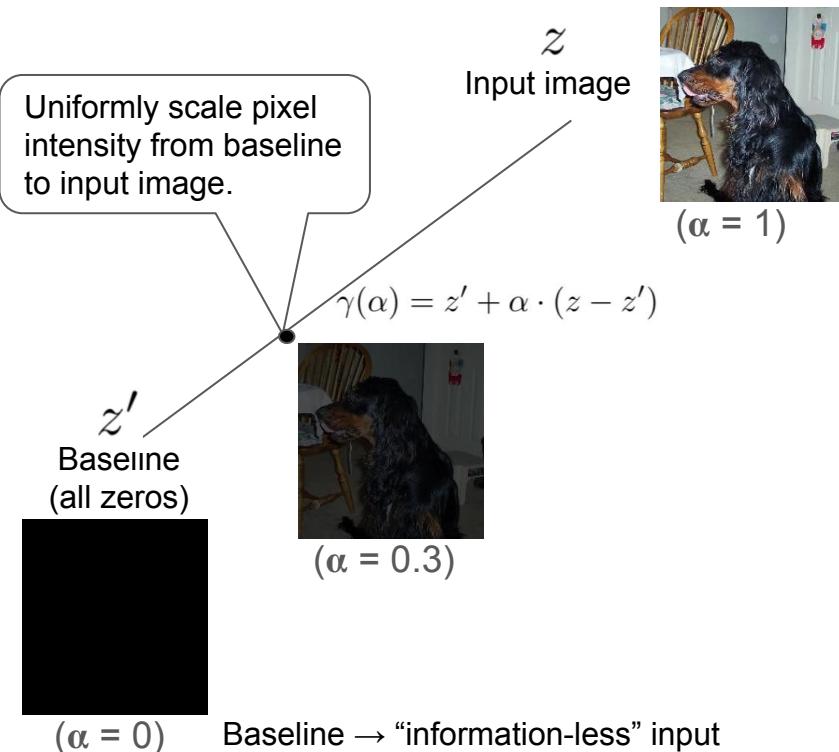
Steel Arch Bridge



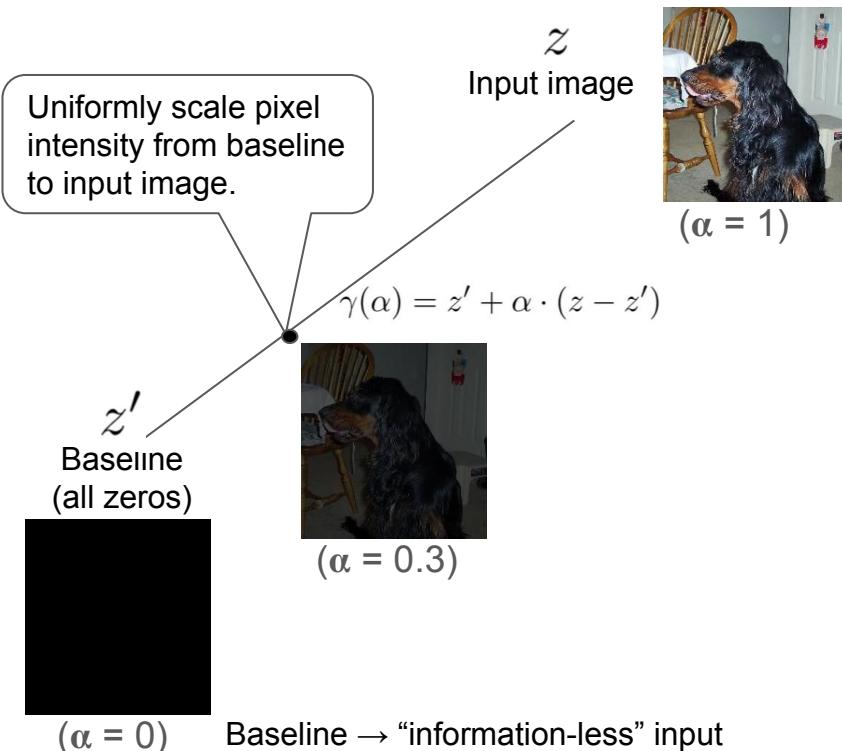
# BlurIG: Blur Integrated Gradients



# Integrated Gradients: Intensity path



# Integrated Gradients: Localize attributions in space



$$IG(\text{image}) = (z - z') \cdot \int_{\alpha=0}^1 \underbrace{\frac{\partial F(z' + \alpha \cdot (z - z'))}{\partial \gamma(\alpha)}}_{\text{gradient}} d\alpha$$

model

gradient

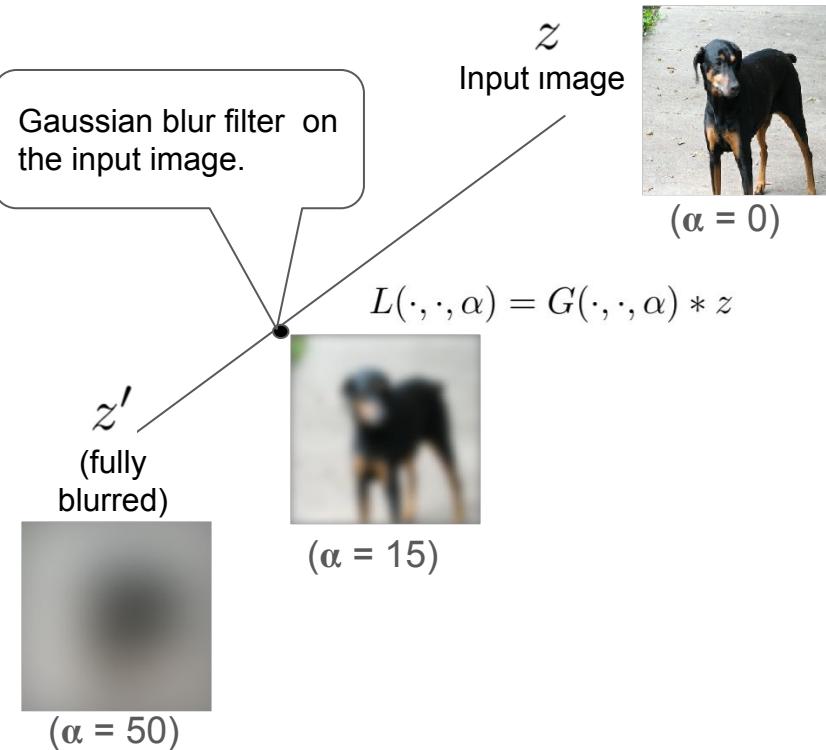
$F$  is the prediction function for the label.

Attribution is per pixel, but I'm ignoring subscripts.

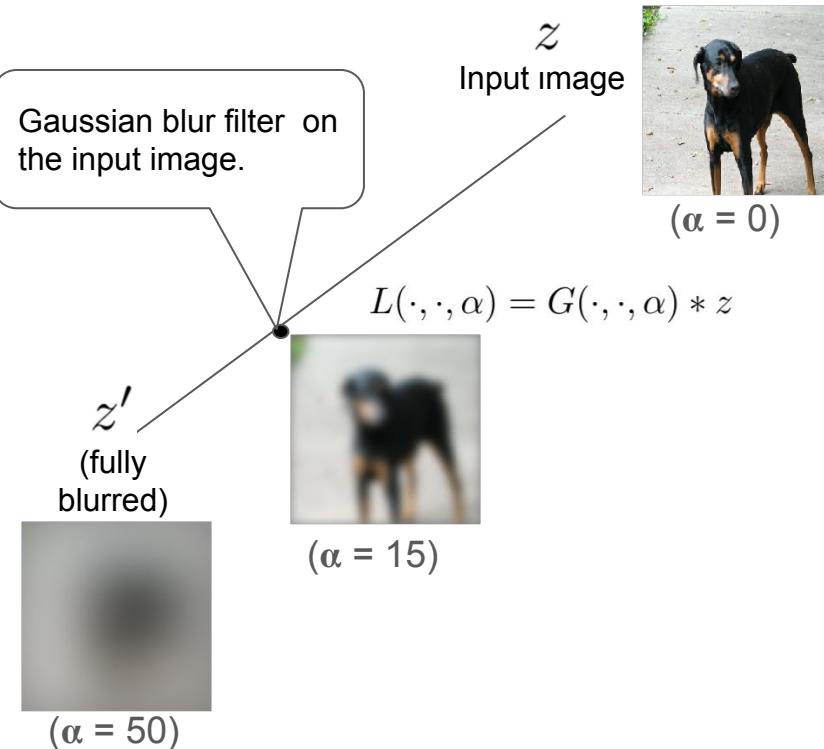
Why integral? Why not just gradient?

--Sundararajan et. al. ICML'17

# BlurIG: Gaussian Blur path



# BlurIG: Gaussian Blur path



model

$$\text{BlurIG}(x, y) := \int_{\alpha=\infty}^0 \underbrace{\frac{\partial F(L(x, y, \alpha))}{\partial L(x, y, \alpha)} \frac{\partial L(x, y, \alpha)}{\partial \alpha}}_{\text{gradient LoG filtering}} d\alpha$$

$F$  is the prediction function for the label.

Attribution is per pixel indicated by  $(x, y)$ .

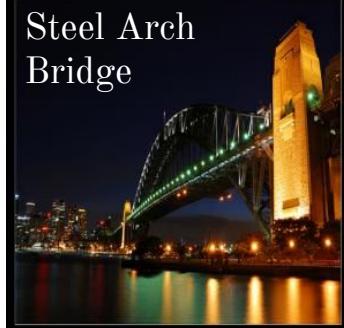
LoG  $\rightarrow$  Laplacian of Gaussian (blob detector!)

# BlurIG: Integrated gradients along the Gaussian blur path

Original image



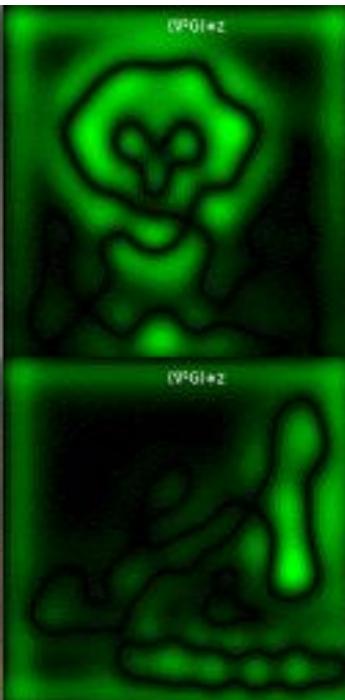
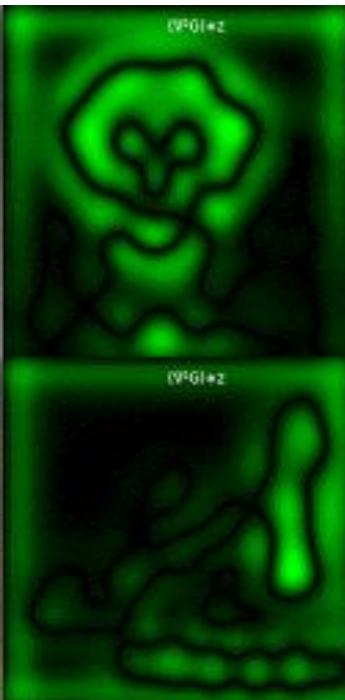
Steel Arch Bridge



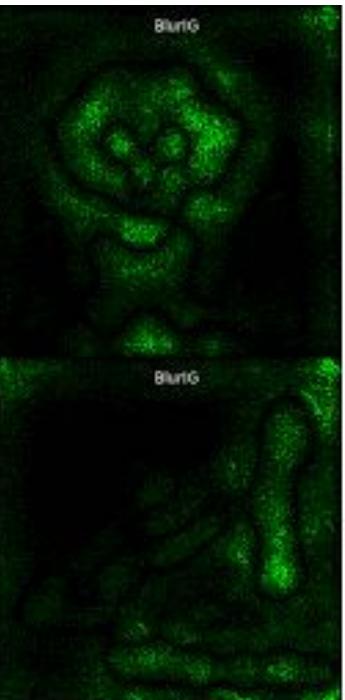
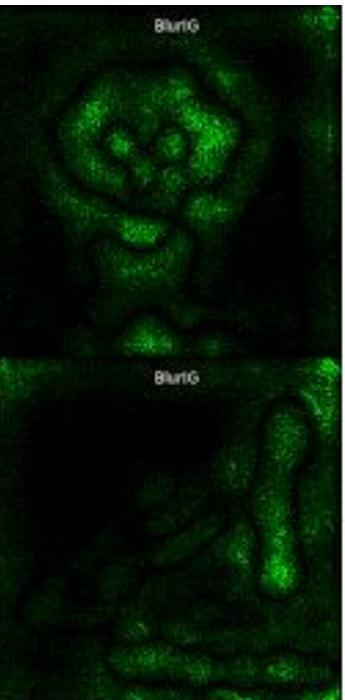
Gaussian filtered image



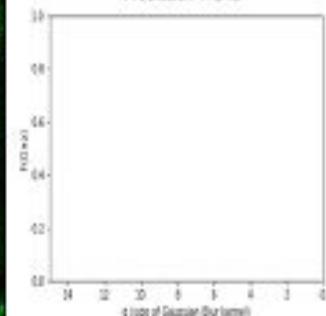
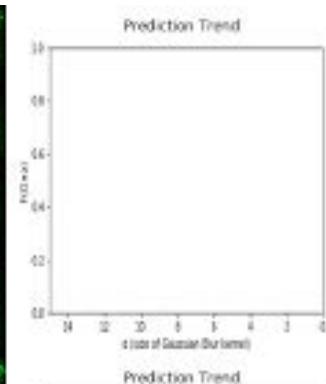
Gaussian derivatives localize attributions in scale



Model derivatives localize attributions in space



Evolution of prediction scores

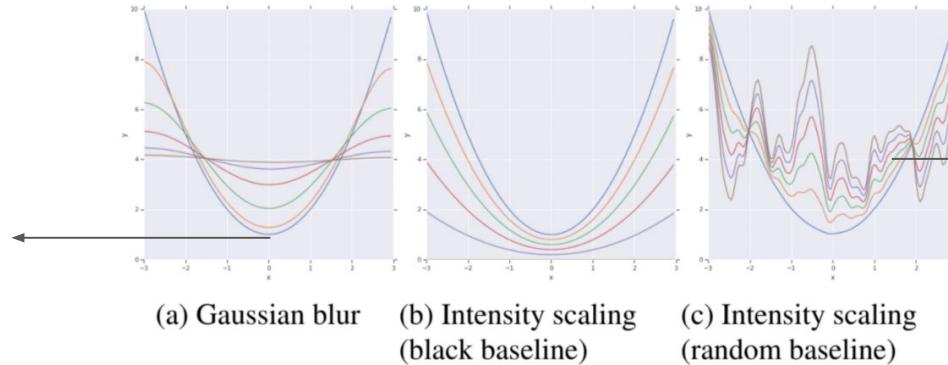


# Scale-space axioms - attractive properties for explanation



Gaussian blur perturbation only destroys information!  
Does not introduce artifacts.

Blur path -  
Non-enhancement  
of local extrema.



Intensity path -  
creation of local  
extrema!

Figure 2: Scale space for  $x^2 + 1$  along the Gaussian blur, and intensity scaling (black and random baseline) paths.

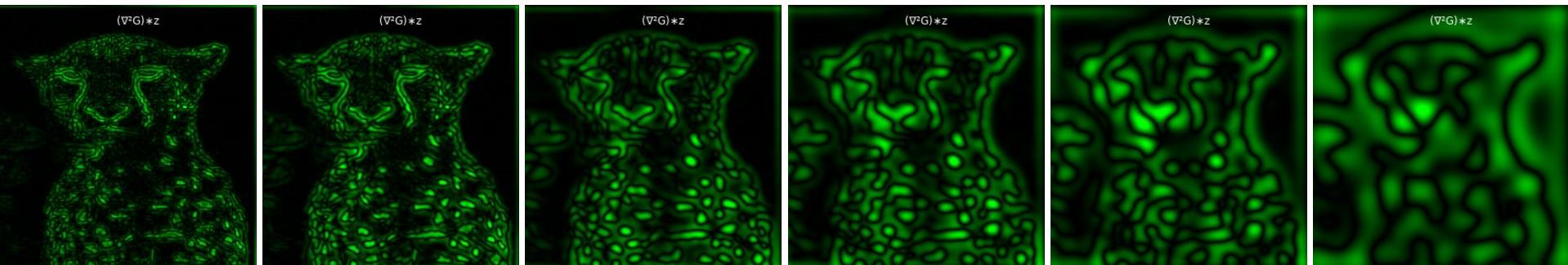
# Scale-space axioms - attractive properties for explanation



Gaussian blur perturbation only destroys information!  
Does not introduce artifacts.



Gaussian operator and Laplacian of Gaussian operator enhance image features - edges, blobs, textures.



# Scale-space axioms - attractive properties for explanation



**Gaussian blur perturbation only destroys information!  
Does not introduce artifacts.**

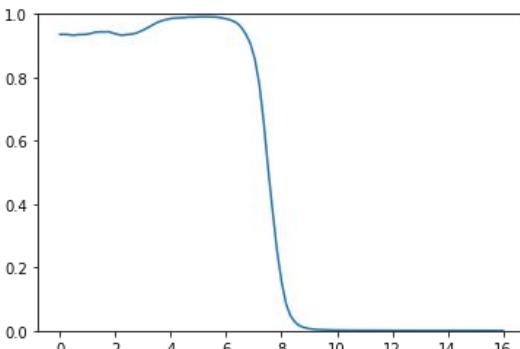
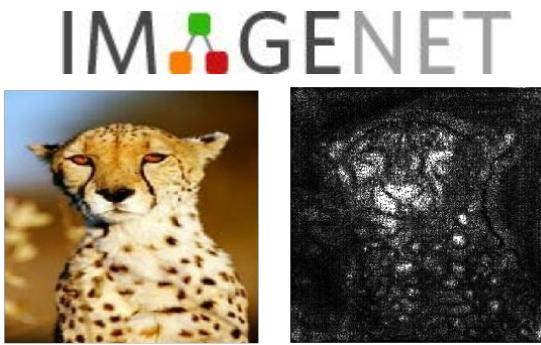


**Gaussian operator and Laplacian of Gaussian operator enhance image  
features - edges, blobs, textures.**

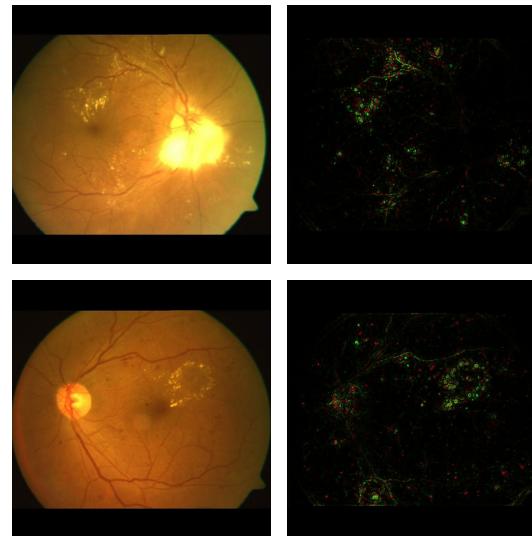


**Gaussian blur path eliminates the need for an “information-less”  
baseline image for Integrated Gradients.**

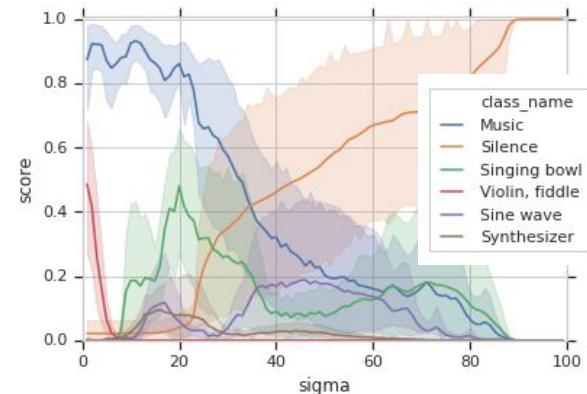
# Applied to 3 classification tasks



### Diabetic Retinopathy



### Audio identification



# Links



Shawn Xu



Subhashini  
Venugopalan



Mukund Sundararajan

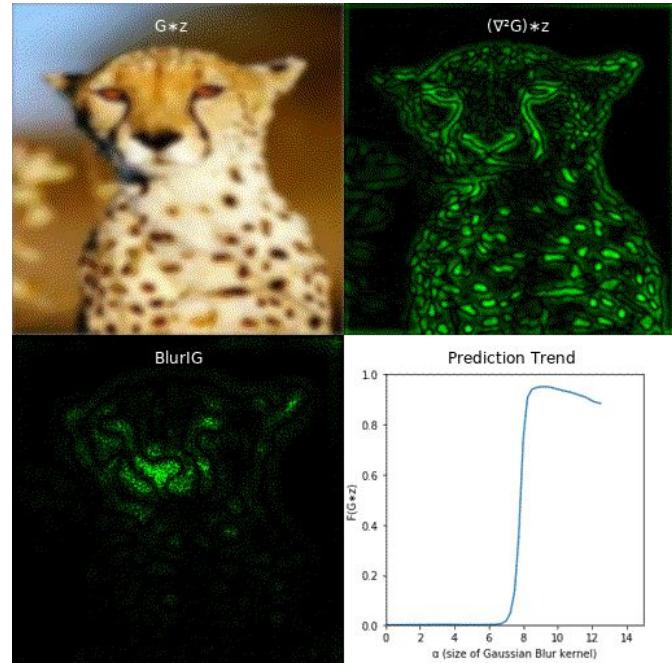
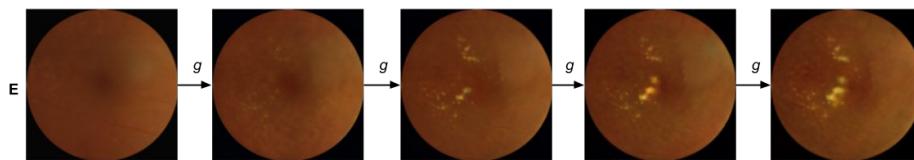
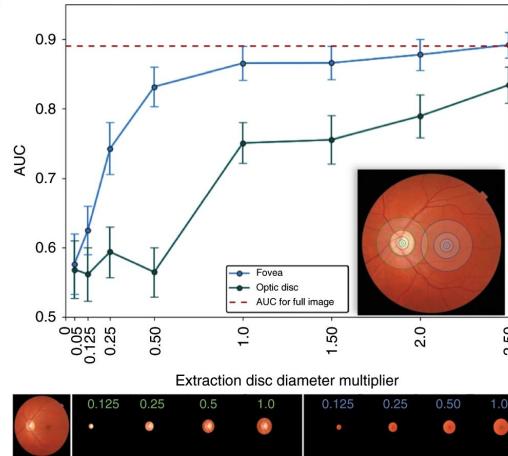
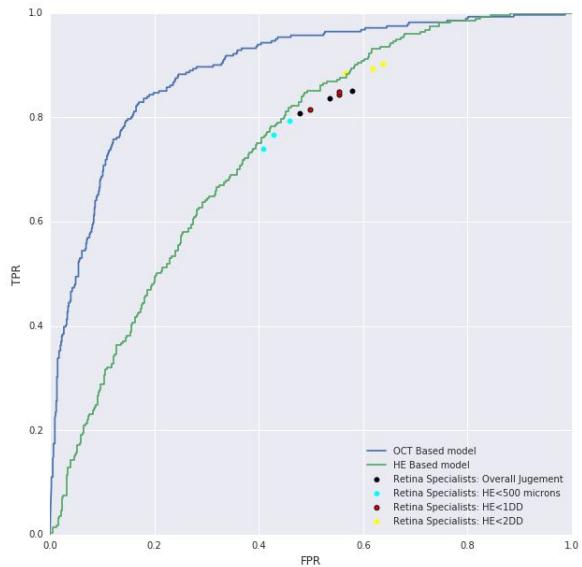
Paper: <https://arxiv.org/abs/2004.03383>

Code: <https://github.com/PAIR-code/saliency>

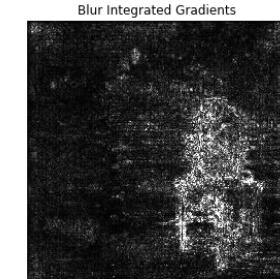
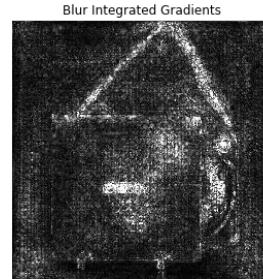
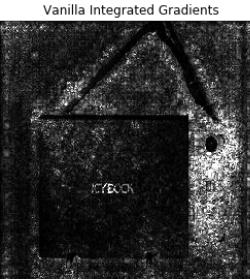
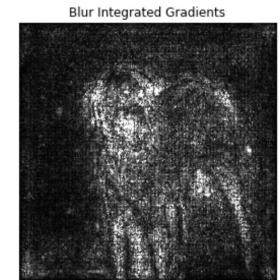
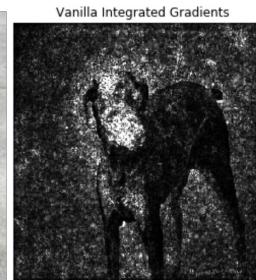
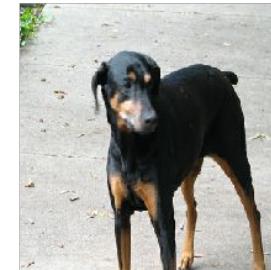
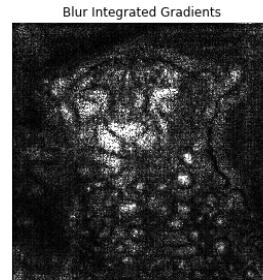
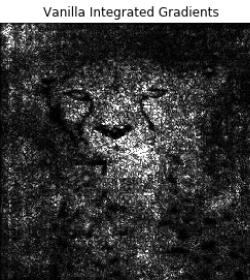
Video:

[https://www.youtube.com/watch?v=0iof\\_BMe1Q0](https://www.youtube.com/watch?v=0iof_BMe1Q0)

# Questions?



# ImageNet (IG vs BlurIG)



IG has color bias from choice of baseline.

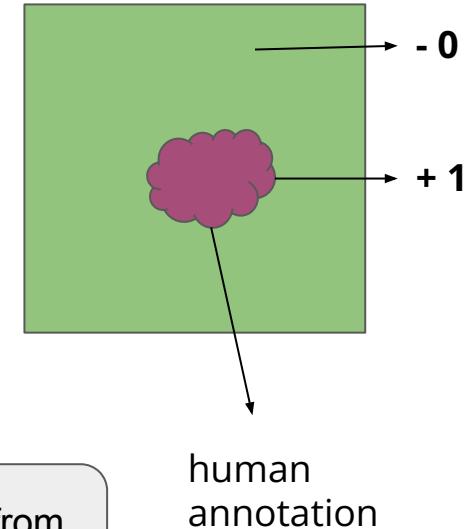
BlurIG has a shape bias.

# Quantitative Evaluation - Human Interpretability

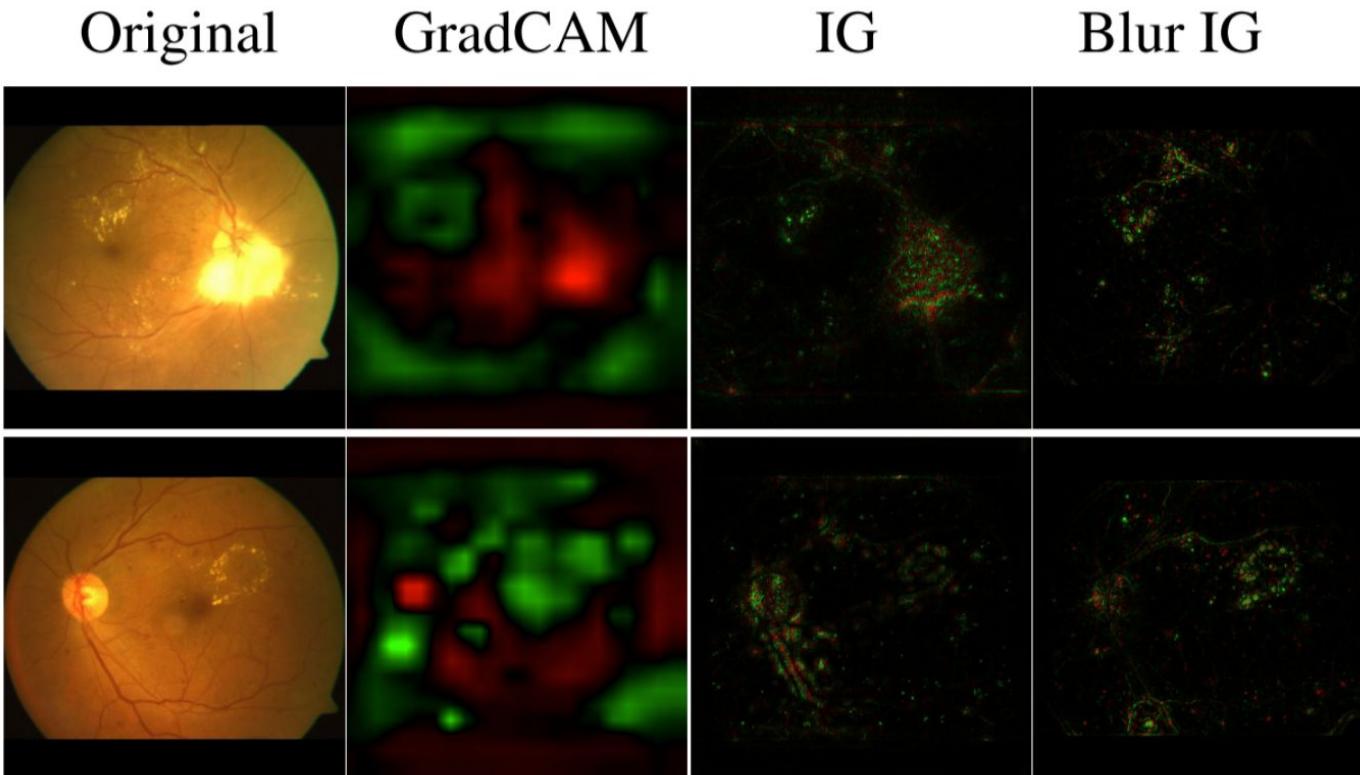
Attribution method	ImageNet			Diabetic Retinopathy		
	AUC ↑	F1 ↑	MAE ↓	AUC ↑	F1 ↑	MAE ↓
XRAI	0.836	0.786	0.149	0.805	0.285	0.068
GradCAM	0.742	0.715	0.194	0.817	0.249	0.058
IG (random-4)	0.709	0.674	0.223	0.827	0.344	0.060
IG (black)	0.710	0.674	0.219	0.828	0.307	0.062
IG (black+white)	0.729	0.681	0.216	0.818	0.296	0.062
<b>Blur IG (ours)</b>	0.738	0.693	0.209	0.831	0.293	0.061

Table 1: Average F1, AUC, and MAE scores for different explanation methods on images from ImageNet validation set (N=9684), and Diabetic Retinopathy dataset (N=141). (↑ indicates higher is better, ↓ indicates lower is better)

DR different from  
“natural” images

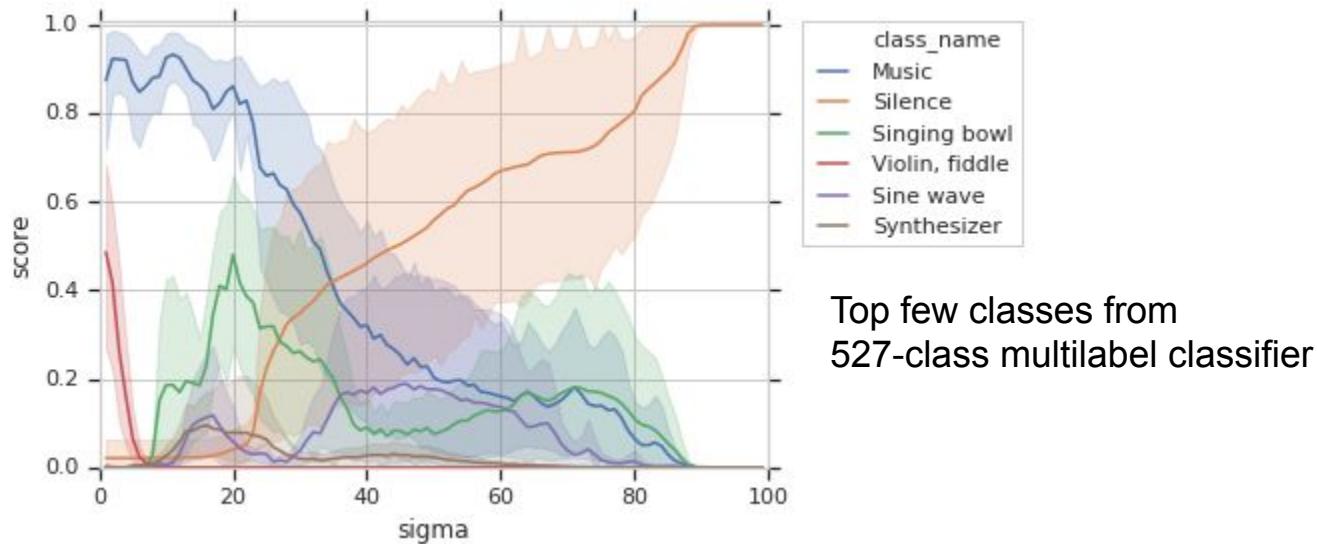


# Diabetic Retinopathy



Green are positive attributions, and red negative.

# AudioSet - Predictions evolve to lower frequency classes.



Visualizing the evolution of class prediction probabilities for prominent categories along the blur integration path from a few (7) violin audio samples. Y axis shows the confidence score, and X axis the sigma for the gaussian blur kernel. Color indicates the class. Initially model has higher confidence on violin and string instrument classes. With increased blur, confidence shifts towards singing bowl, sine wave, and then silence.

# Class conditioning: Prediction is music not because it is violin!

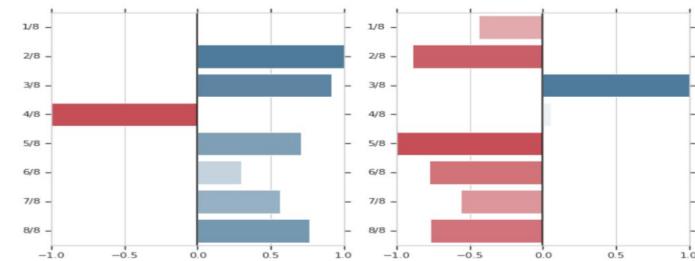
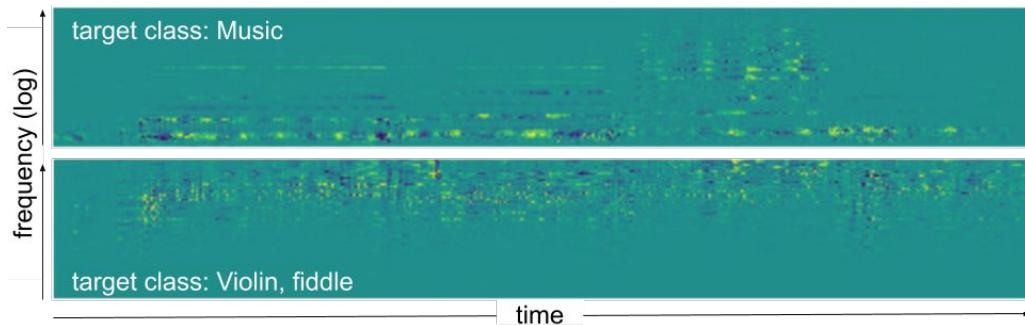
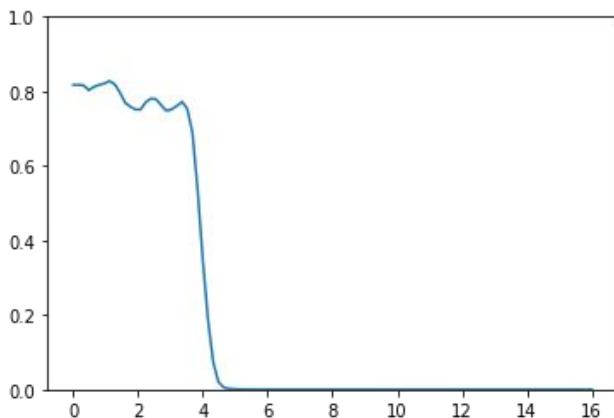
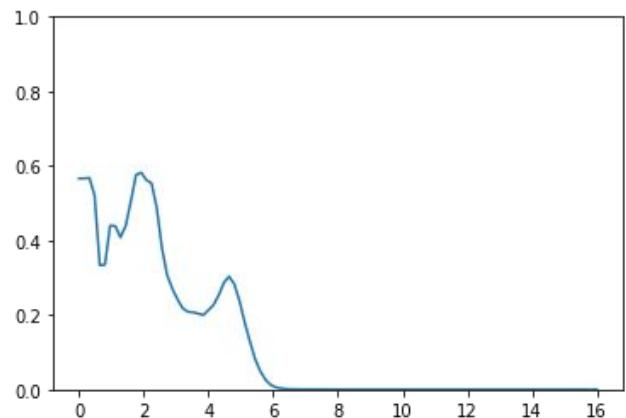
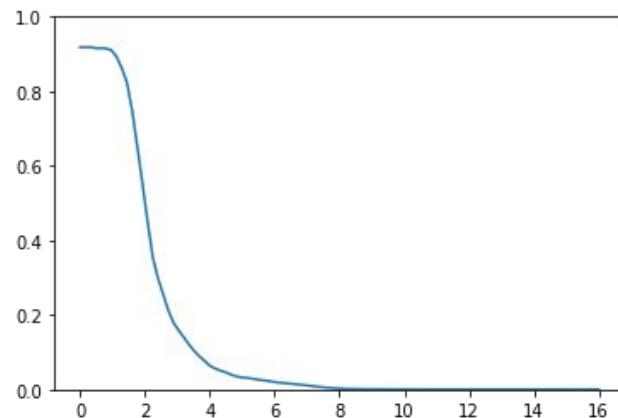
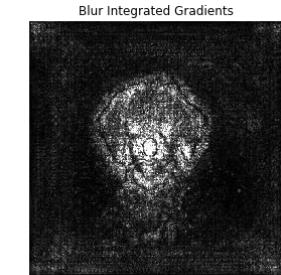
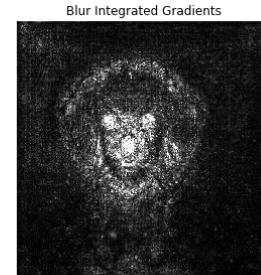
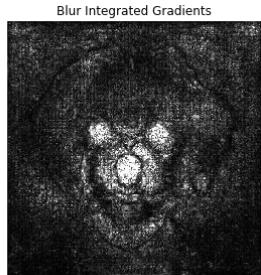


Figure 12: Aggregation of Blur IG contributions on 7 violin audio samples with target class as ‘Music’ (left) and target class as ‘Violin, fiddle’ (right). Y axis depicts the frequency bins, and X axis the integrated gradients. Blue indicates positive gradients/contributions and red the negative gradients. Explanation for class Music shows positive contributions from the lower frequencies while explanation for ‘Violin, fiddle’ shows positive contributions only from the higher frequencies.

# Effect of Crop and Zoom

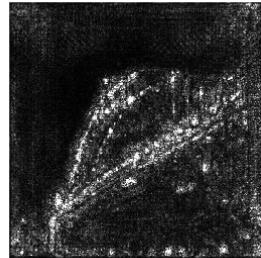


## Effect of crop and zoom

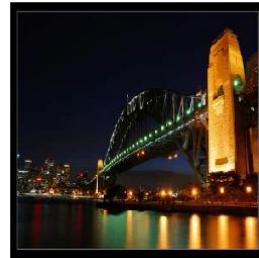
### Original Image



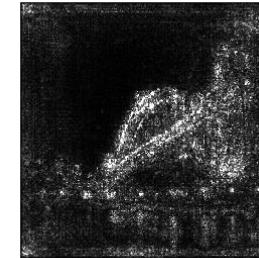
## Blur Integrated Gradients



### Original Image



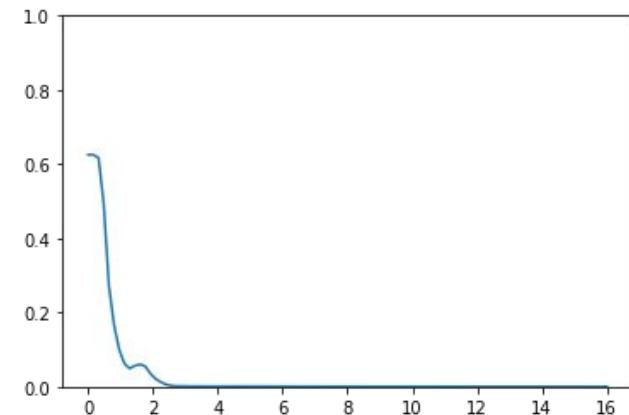
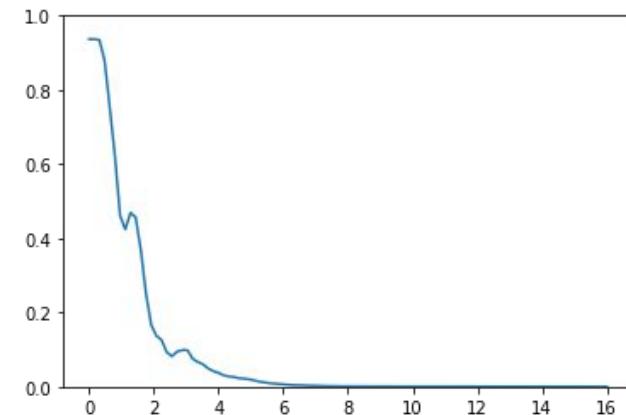
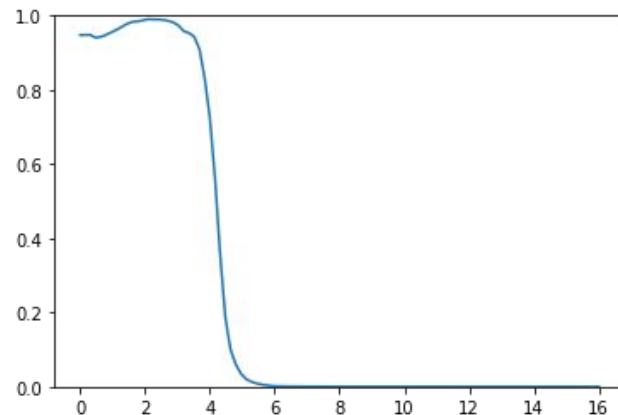
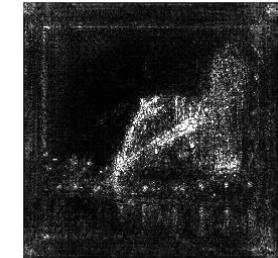
## Blur Integrated Gradients



### Original Image



## Blur Integrated Gradients



## Effect of crop and zoom

### Original Image



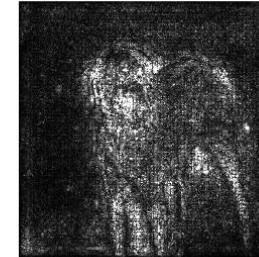
## Blur Integrated Gradients



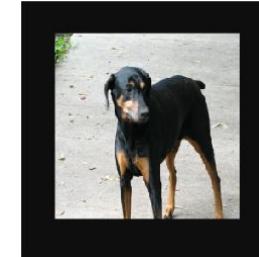
### Original Image



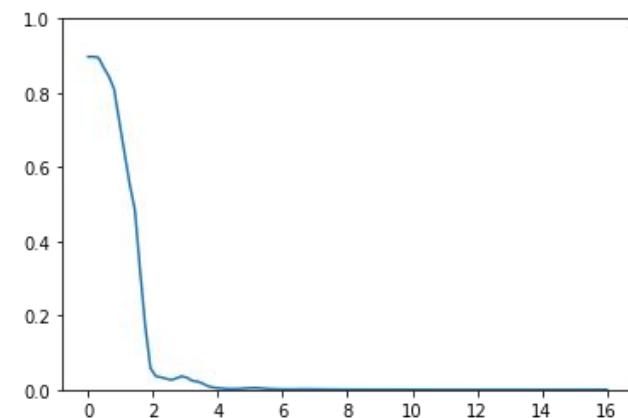
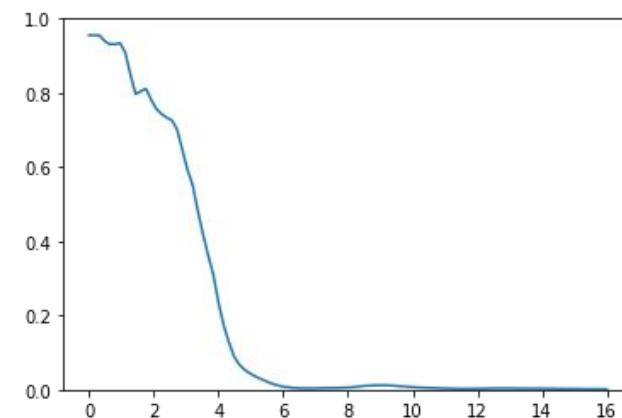
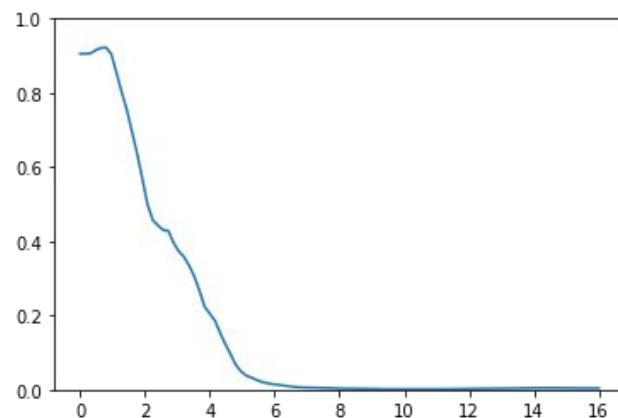
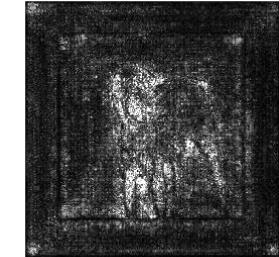
## Blur Integrated Gradients



### Original Image



## Blur Integrated Gradients



## Links

Paper: <https://arxiv.org/abs/2004.03383>

Code: <https://github.com/PAIR-code/saliency>

Video:

[https://www.youtube.com/watch?v=0iof\\_BMe1Q0](https://www.youtube.com/watch?v=0iof_BMe1Q0)

{jinhuaxu@,vsubhashini@,mukunds@}google.com

## \* Background

## \* Scientific Discovery by Generating Counterfactuals using Image Translation

Narayanaswamy\*, Venugopalan\*, et. al. MICCAI 2020

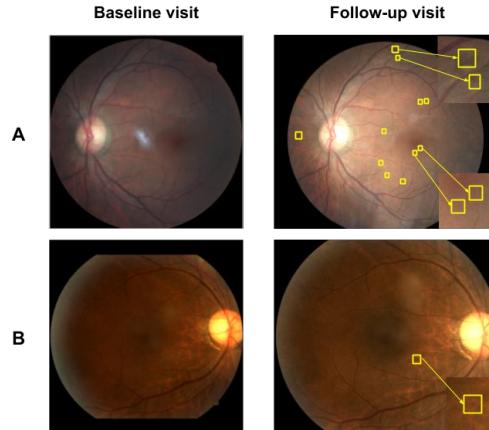
## \* Attribution in Scale and Space

Xu, Venugopalan, Sundararajan CVPR 2020

## \* Predicting risk of developing diabetic retinopathy using deep learning

Bora et. al. Lancet Digital Health 2021

# Predicting risk of DR (6m - 2yrs) before symptoms show



## Predicting risk of developing diabetic retinopathy using deep learning

Ashish Bora, Siva Balasubramanian, Boris Babenko, Sunny Virmani, Subhashini Venugopalan, Akinori Mitani, Guilherme de Oliveira Marinho, Jorge Cuadros, Paisan Ruamviboonsuk, Greg S Corrado, Lily Peng, Dale R Webster, Avinash V Varadarajan, Naama Hammel, Yun Liu, Pinal Bavishi

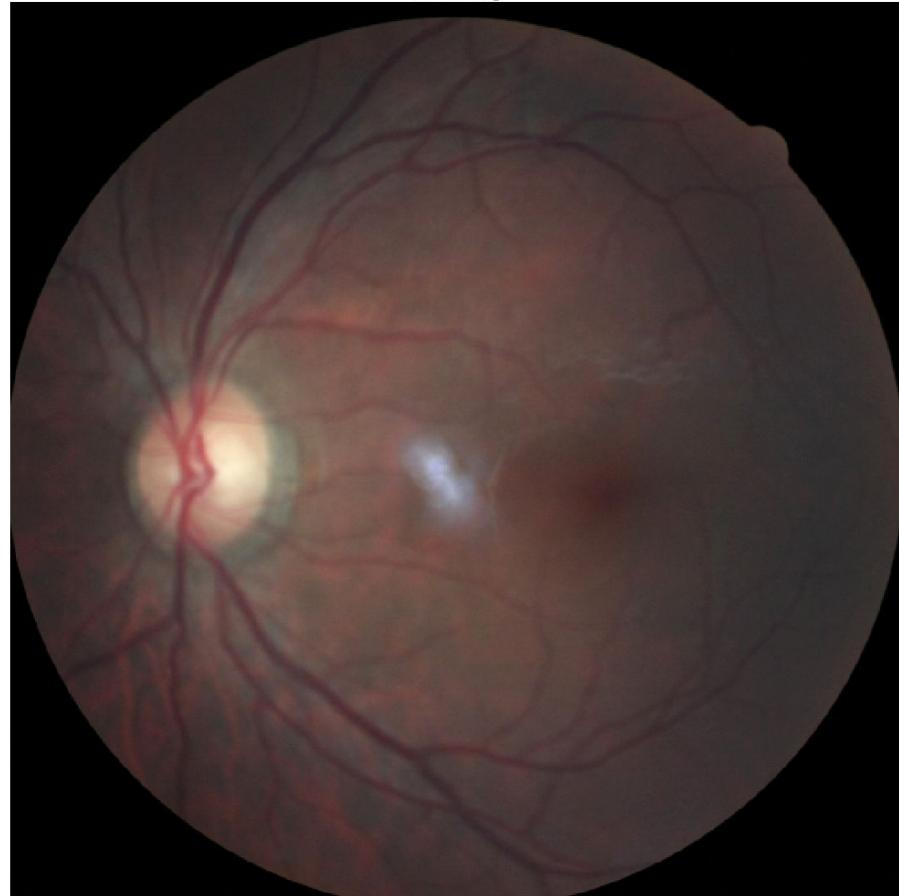
Lancet Digital Health 2021

## Baseline visit - NO DR

At baseline:

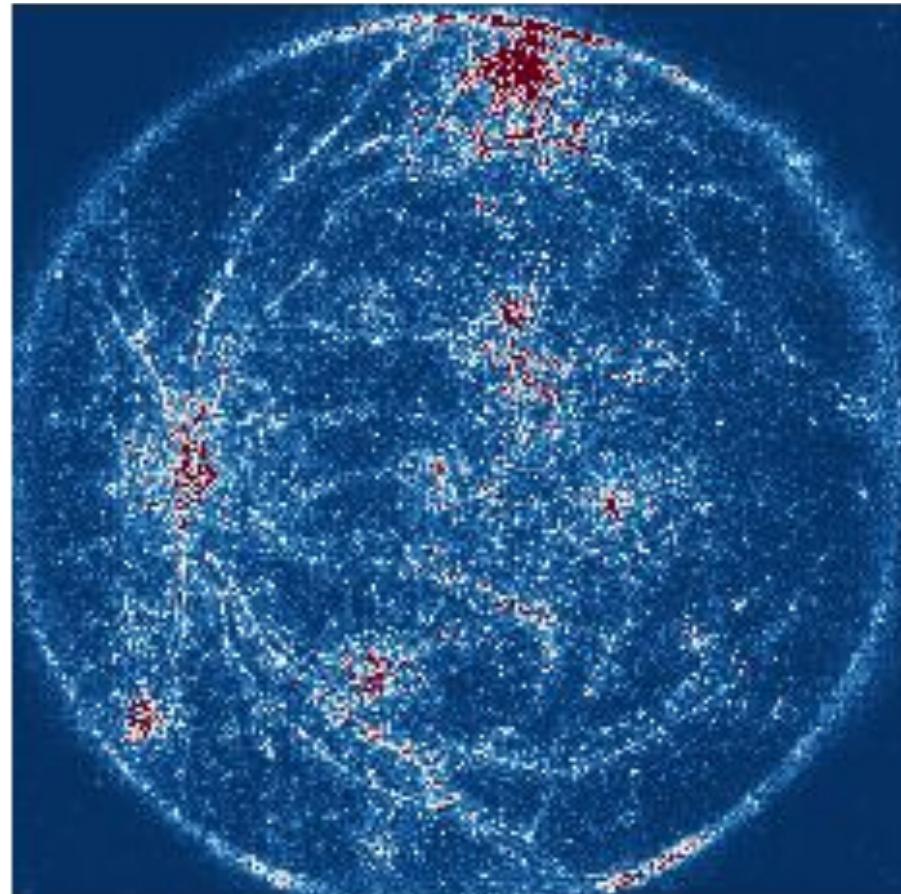
Doctor and DR Model : NO DR

Risk of DR (DR progression model): 0.72



# BlurIG - pixel attribution

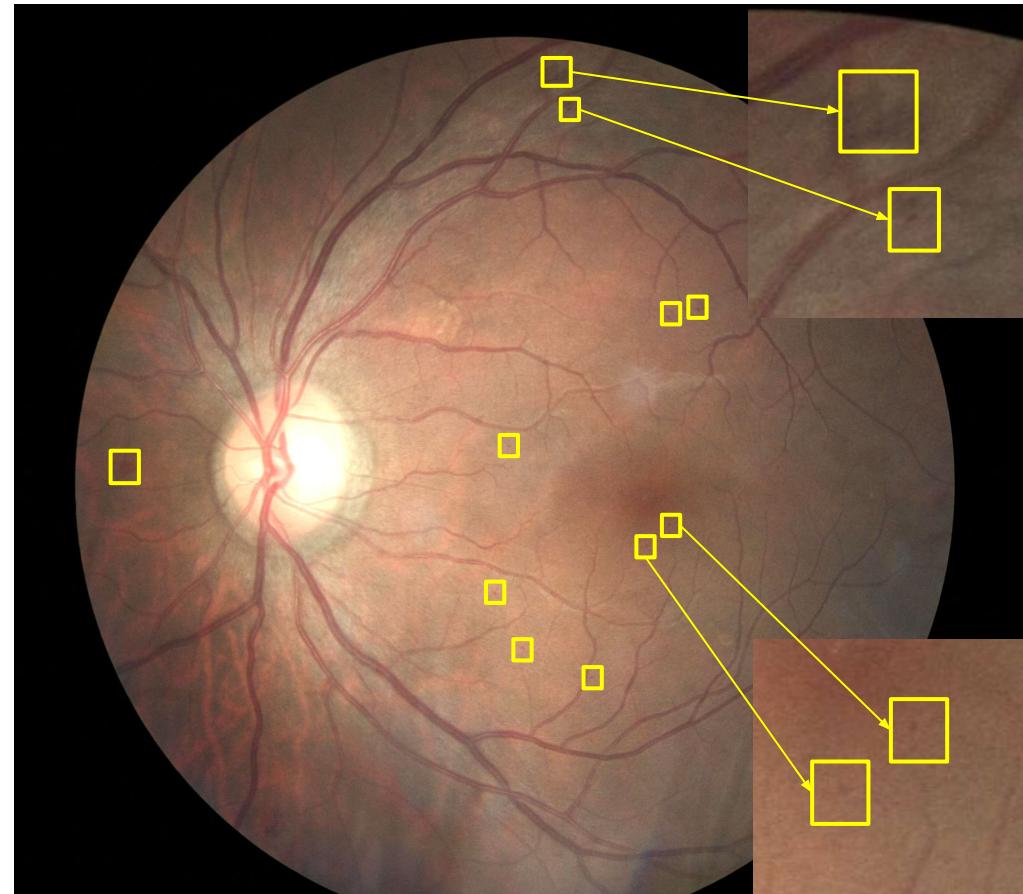
Pixel attribution on image from baseline visit.  
Red indicates regions that the model is looking at.



**Follow-up visit +1.5yrs:  
Attributed regions  
develop symptoms**

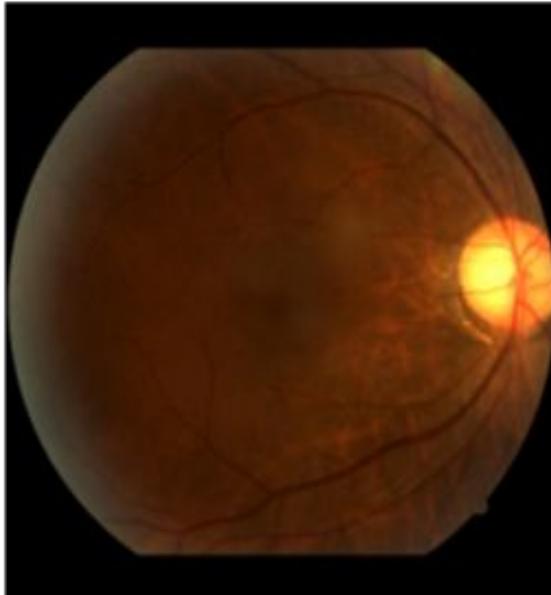
DR Model: Mild+ DR

**Yellow boxes** highlight microaneurysms identified by retina specialist.

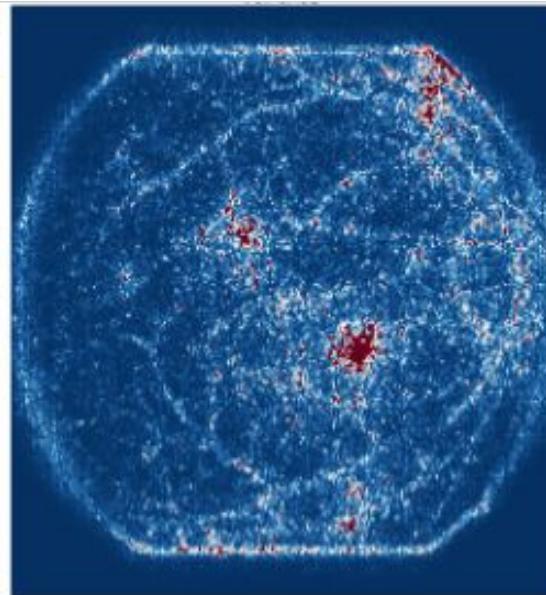


# Attribution highlights where symptoms show-up in future

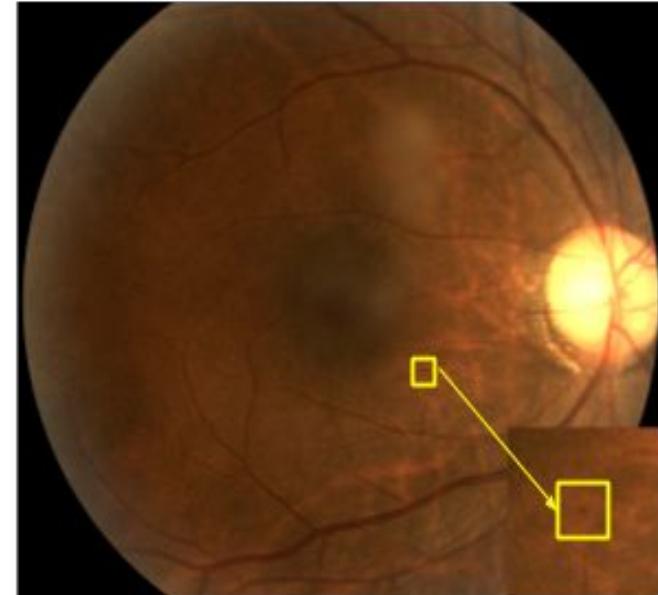
Baseline visit



BlurIG



Follow-up visit



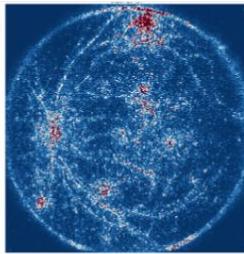
# Predicting risk of DR (6m - 2yrs) before symptoms show

Interpretability techniques (BlurIG and IG) localize on regions where micro-aneurysms develop in the future.  
(At baseline visit patient has NO DR)

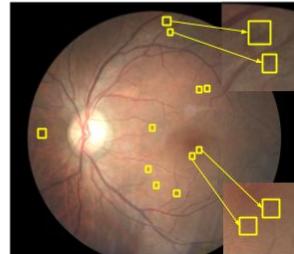
Baseline visit



BlurIG



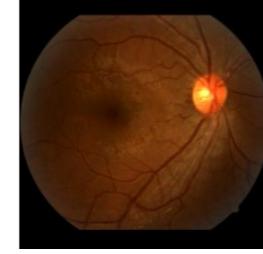
Follow-up visit



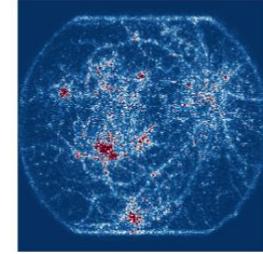
A

B

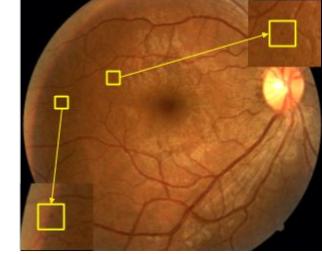
Baseline visit



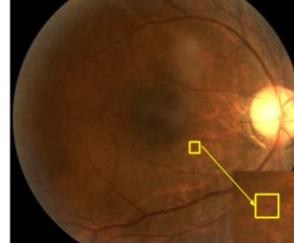
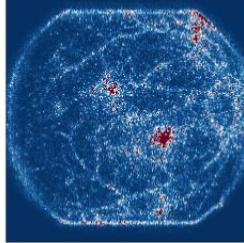
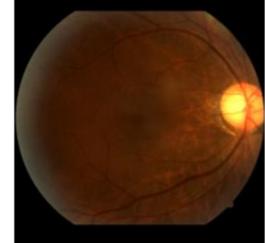
BlurIG



Follow-up visit



C



B

D

