


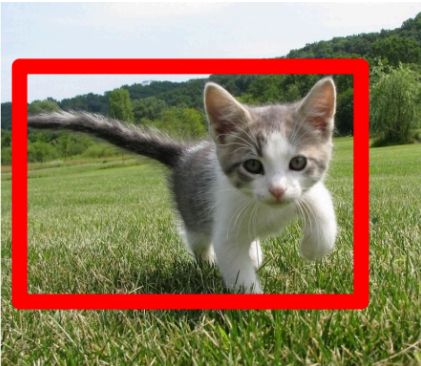
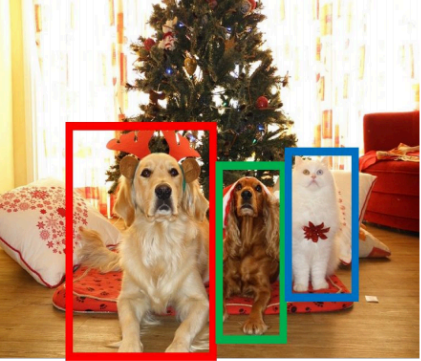

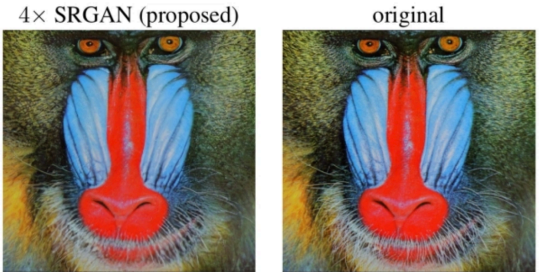
# Lecture 16: Beyond classification – segmentation and autoencoders

Machine Learning and Imaging

BME 548L

Roarke Horstmeyer

# Other Computer Vision Tasks

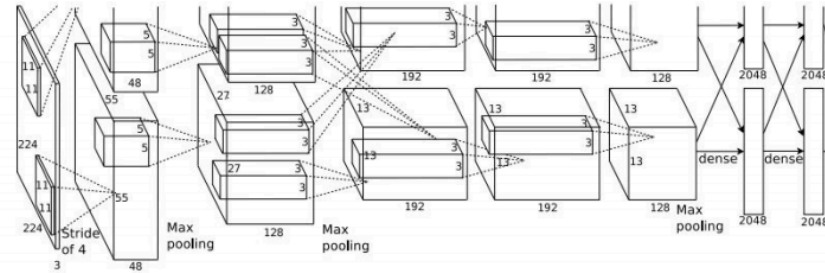
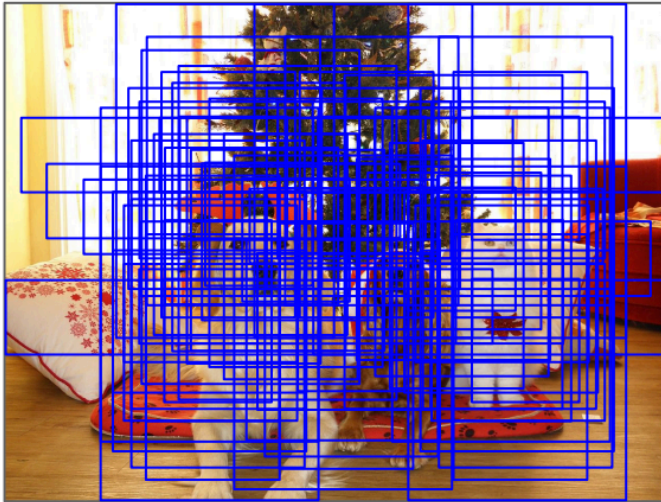
Semantic Segmentation	Classification + Localization	Object Detection	Instance Segmentation	Super-resolution
 <p>GRASS, CAT, TREE, SKY</p> <p>No objects, just pixels</p>	 <p>CAT</p> <p>Single Object</p>	 <p>DOG, DOG, CAT</p>	 <p>DOG, DOG, CAT</p>	 <p>4x SRGAN (proposed)      original</p>
<p>Balanced equation</p>		<p>Over-determined</p>		<p>Under-determined</p>

This image is CC0 public domain

Figure 1: Super-resolved image (left) is almost indistinguishable from original (right). [4x upscaling]

# Object Detection as Classification: Sliding Window

Apply a CNN to many different crops of the image, CNN classifies each crop as object or background

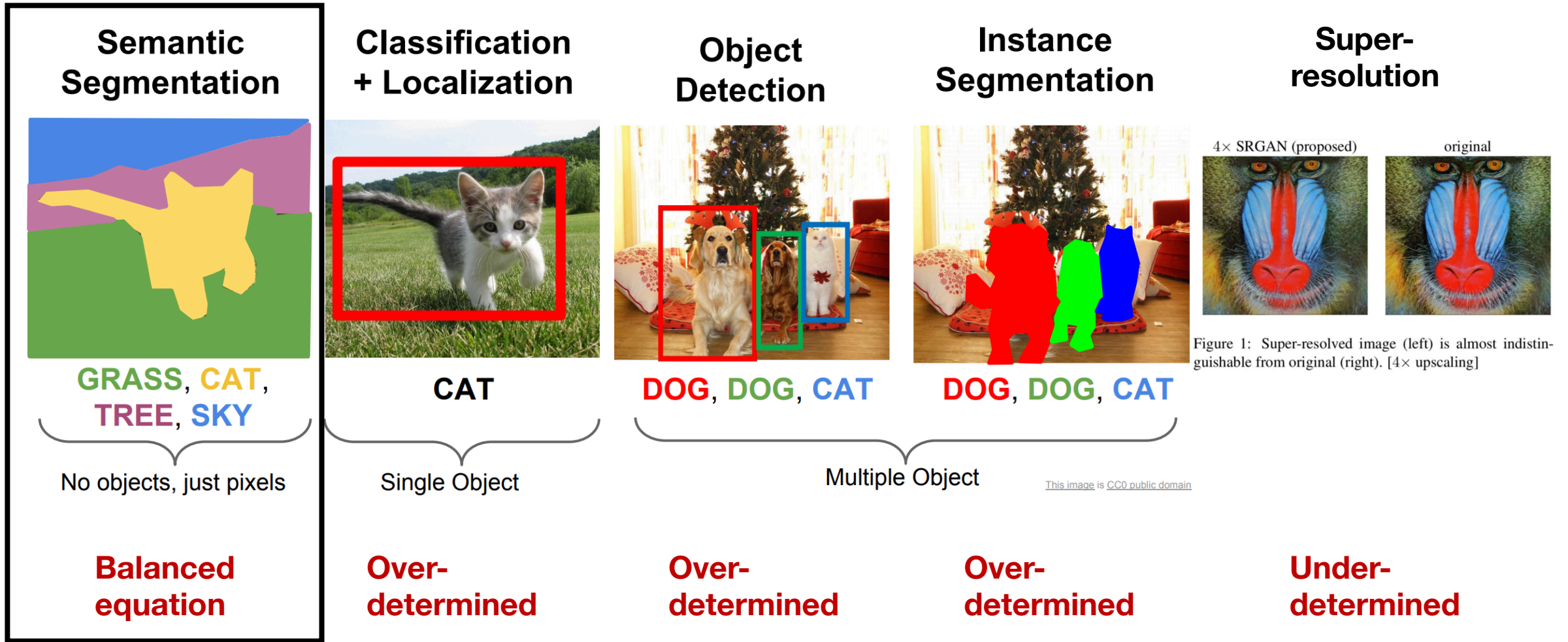


Dog? NO  
Cat? YES  
Background? NO

**Problem: Need to apply CNN to huge number of locations, scales, and aspect ratios, very computationally expensive!**

More information provided in ~20 minute recording posted to:  
<https://deepimaging.github.io/lectures/>

# Other Computer Vision Tasks



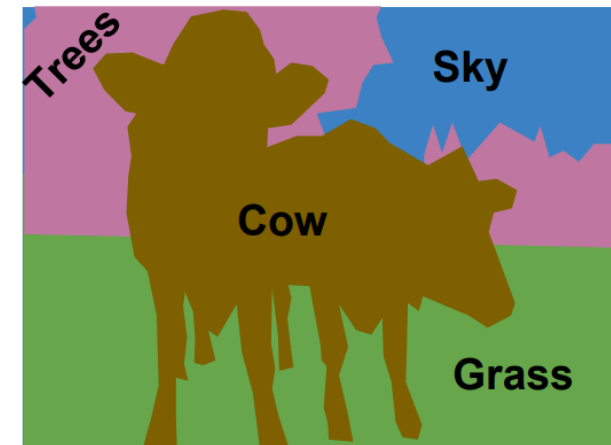
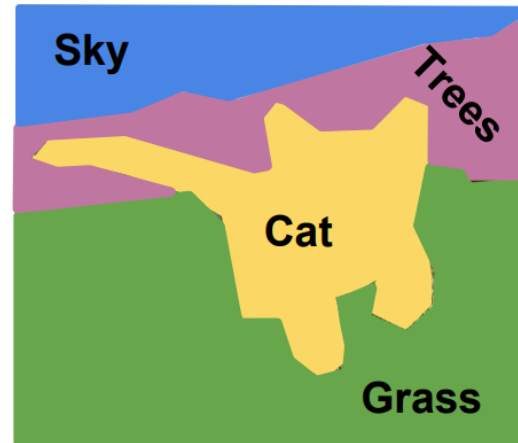
This image is CC0 public domain




# Semantic Segmentation

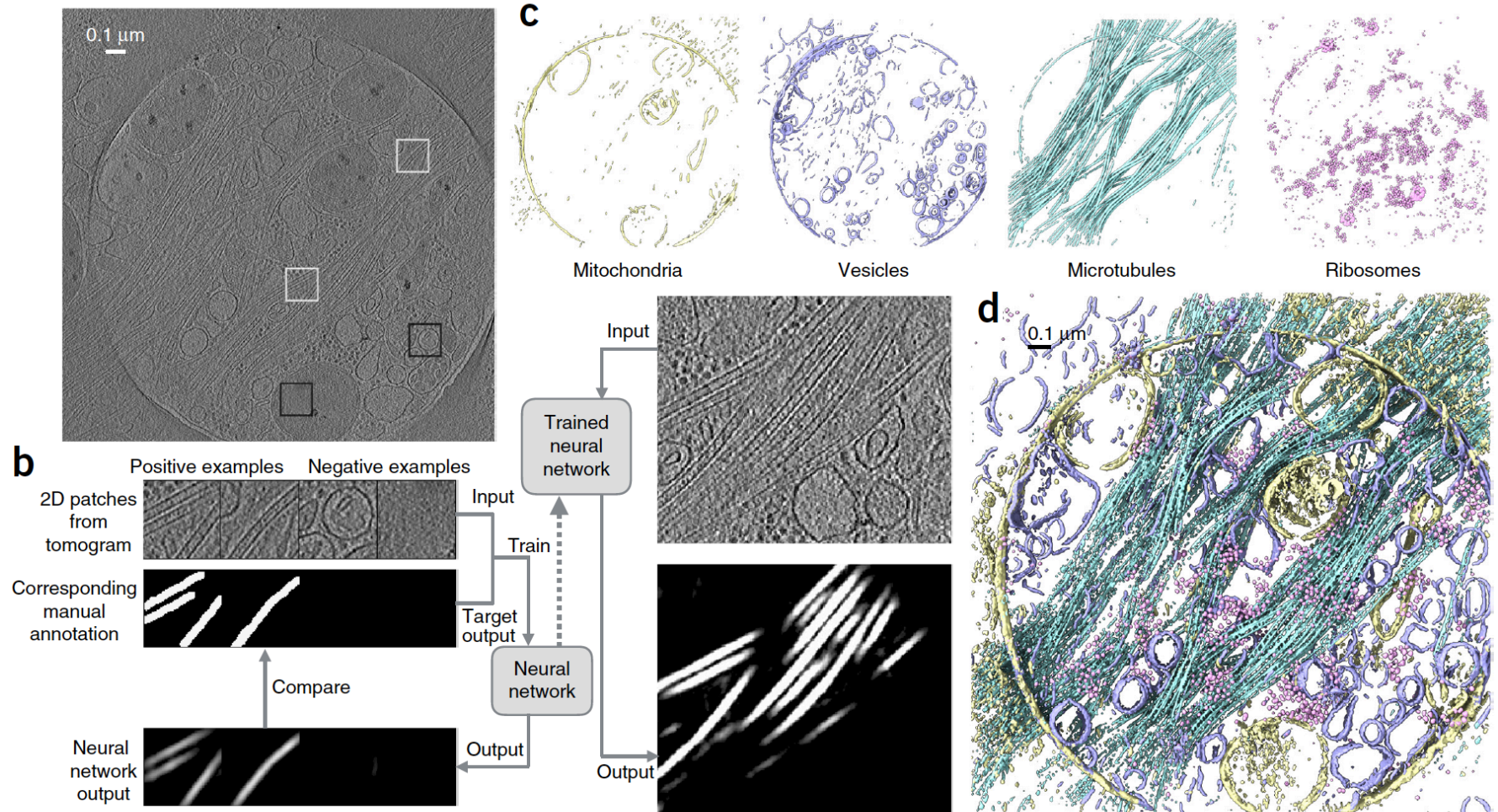
Label each pixel in the image with a category label

Don't differentiate instances, only care about pixels

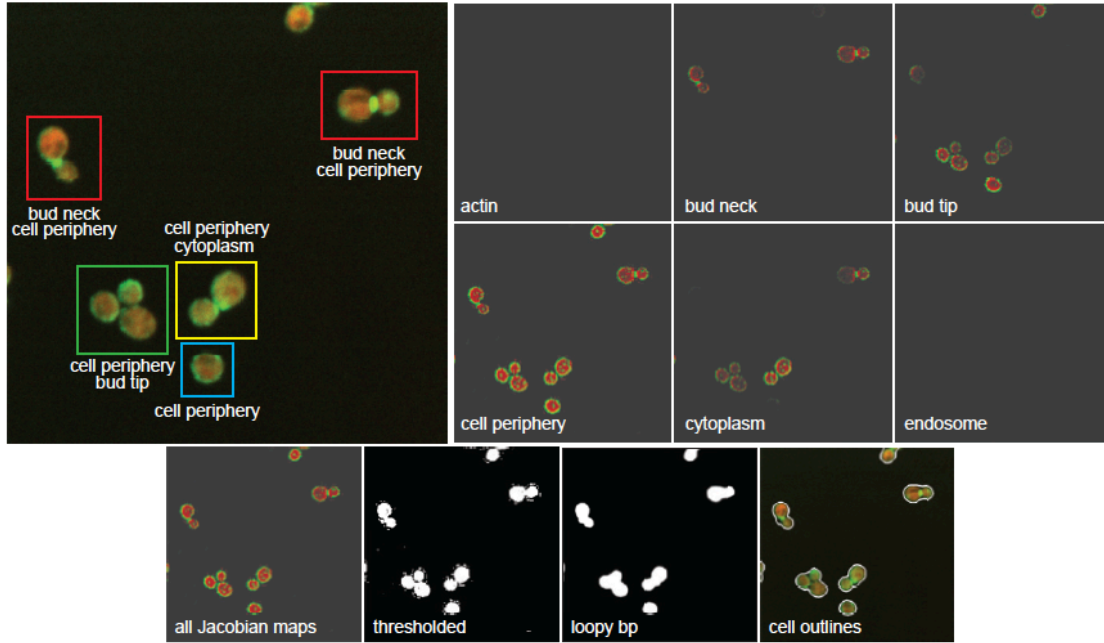


# Convolutional neural networks for automated annotation of cellular cryo-electron tomograms

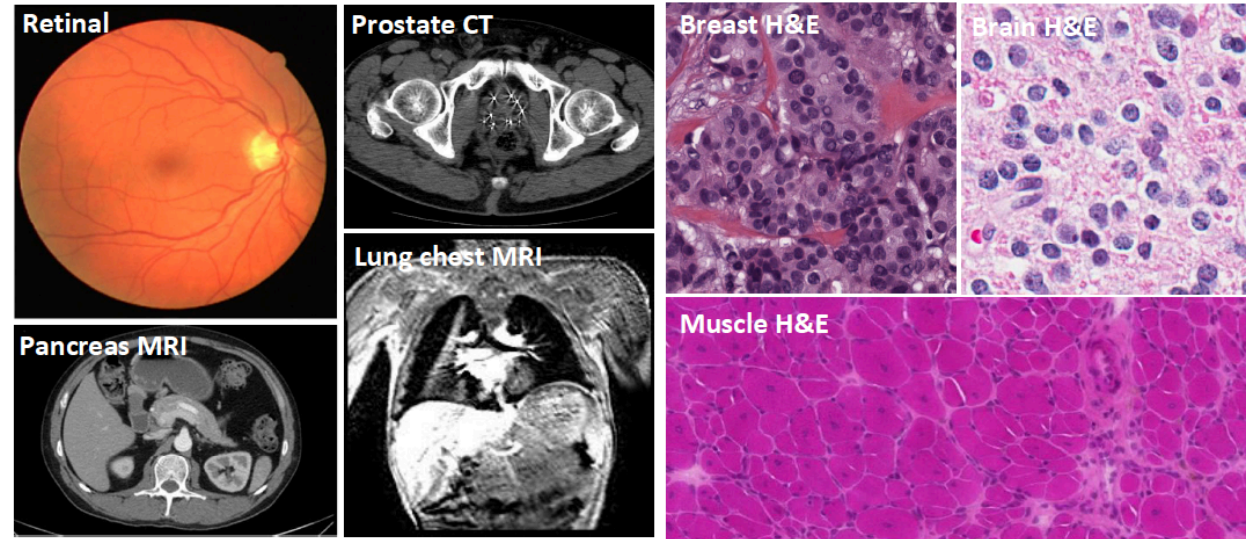
Muyuan Chen<sup>1,2</sup>, Wei Dai<sup>2,4</sup>, Stella Y Sun<sup>2</sup>,  
 Darius Jonasch<sup>2</sup>, Cynthia Y He<sup>3</sup>, Michael F Schmid<sup>2</sup>,  
 Wah Chiu<sup>2</sup> & Steven J Ludtke<sup>2</sup> 



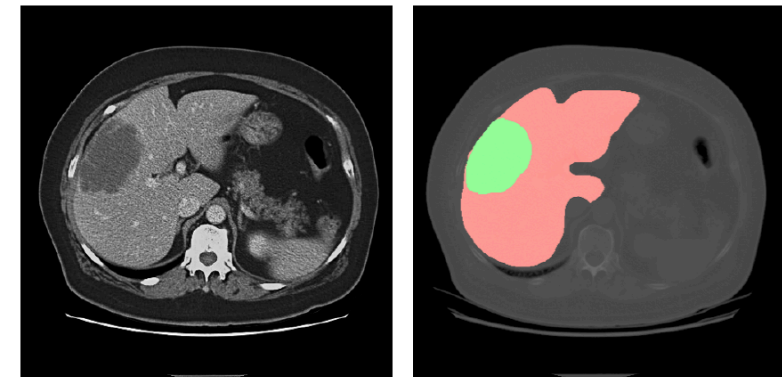
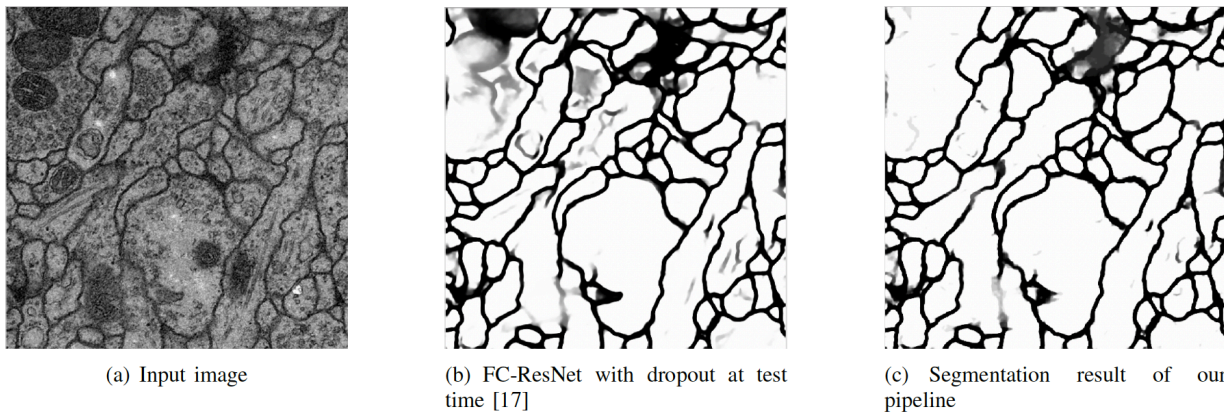




Other possible examples:



Oren Z. Kraus et al., "Classifying and Segmenting Microscopy Images Using Convolutional Multiple Instance Learning," arXiv 2015

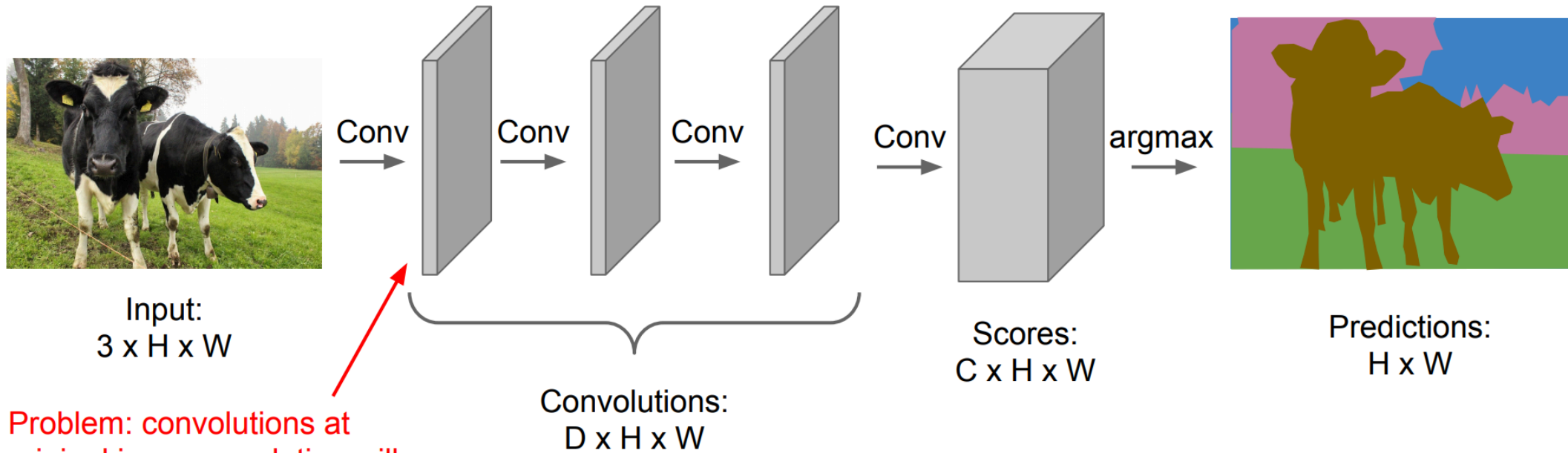


M. Drozdal et al., Learning Normalized Inputs for Iterative Estimation in Medical Image Segmentation (2017)

Z. Zhang et al., Recent Advances in the Applications of Convolutional Neural Networks to Medical Image Contour Detection (2017)

# Semantic Segmentation Idea: Fully Convolutional ?

Design a network as a bunch of convolutional layers to make predictions for pixels all at once!



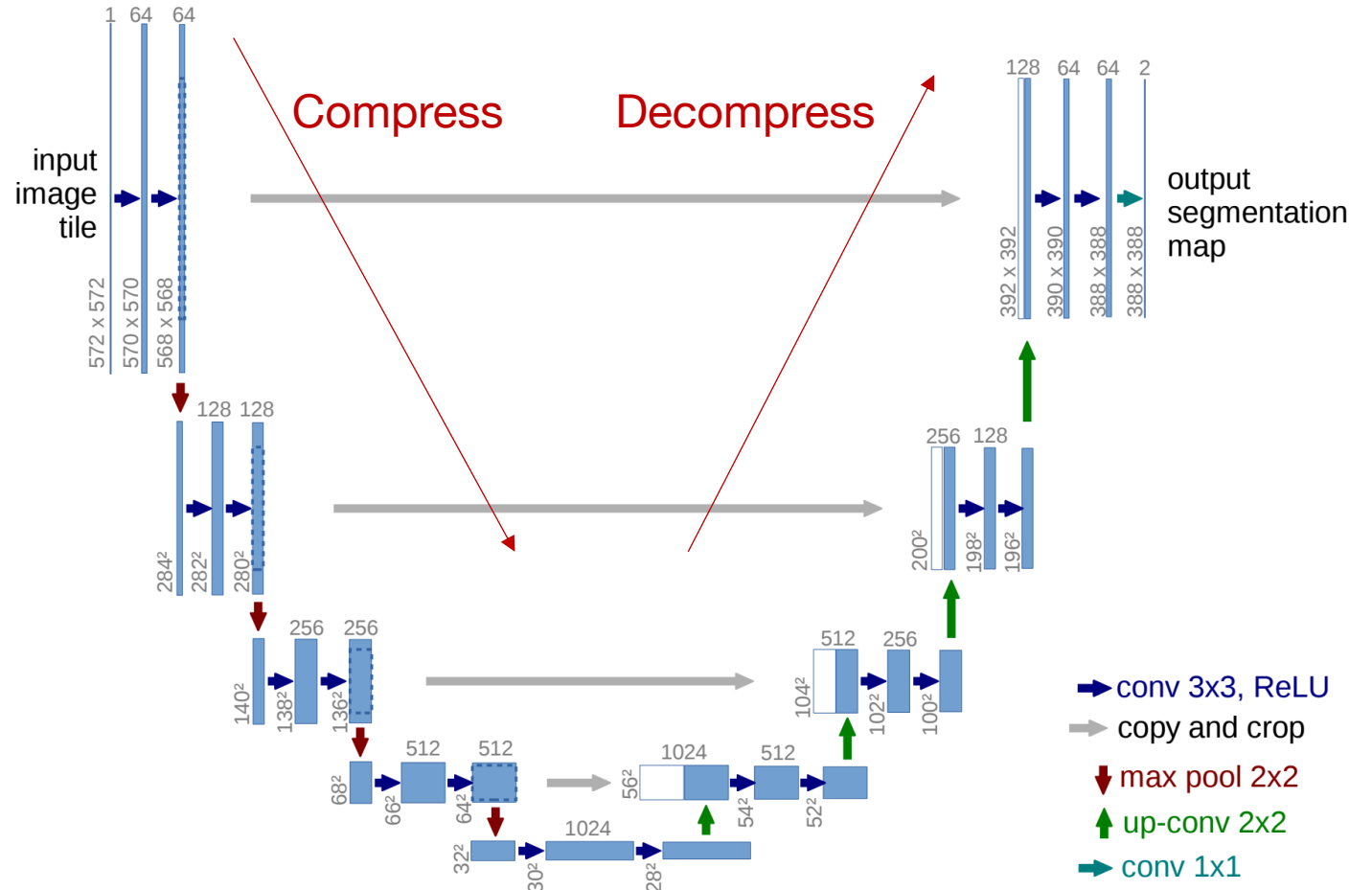
Problem: convolutions at original image resolution will be very expensive ...



# Instead, *compress x-y dimensions of input image*

- Compress spatial features into learned filters
- Then, decompress learned filters back into same spatial dimensions

## U-Net Architecture



## U-Net: Convolutional Networks for Biomedical Image Segmentation

Olaf Ronneberger, Philipp Fischer, and Thomas Brox

Computer Science Department and BIOS Centre for Biological Signalling Studies,  
University of Freiburg, Germany  
ronneber@informatik.uni-freiburg.de,  
WWW home page: <http://lmb.informatik.uni-freiburg.de/>

# Semantic Segmentation Idea: Fully Convolutional

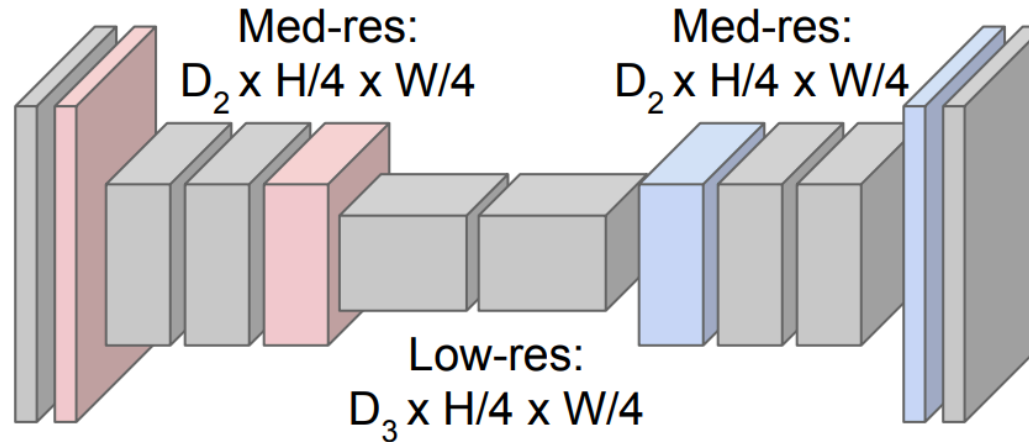
**Downsampling:**  
Pooling, strided convolution

Design network as a bunch of convolutional layers, with **downsampling** and **upsampling** inside the network!

**Upsampling:**  
???



Input:  
 $3 \times H \times W$



High-res:  
 $D_1 \times H/2 \times W/2$

High-res:  
 $D_1 \times H/2 \times W/2$



Predictions:  
 $H \times W$

Long, Shelhamer, and Darrell, "Fully Convolutional Networks for Semantic Segmentation", CVPR 2015

Noh et al, "Learning Deconvolution Network for Semantic Segmentation", ICCV 2015

# In-Network upsampling: “Unpooling”

**Nearest Neighbor**

1	2
3	4



1	1	2	2
1	1	2	2
3	3	4	4
3	3	4	4

Input: 2 x 2

Output: 4 x 4

**“Bed of Nails”**

1	2
3	4



1	0	2	0
0	0	0	0
3	0	4	0
0	0	0	0

Input: 2 x 2

Output: 4 x 4

# In-Network upsampling: “Max Unpooling”

## Max Pooling

Remember which element was max!

1	2	6	3
3	5	2	1
1	2	2	1
7	3	4	8

Input: 4 x 4



5	6
7	8

Output: 2 x 2



Rest of the network

## Max Unpooling

Use positions from pooling layer

1	2
3	4

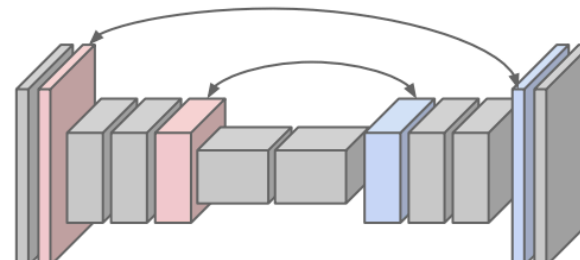
Input: 2 x 2



0	0	2	0
0	1	0	0
0	0	0	0
3	0	0	4

Output: 4 x 4

Corresponding pairs of downsampling and upsampling layers

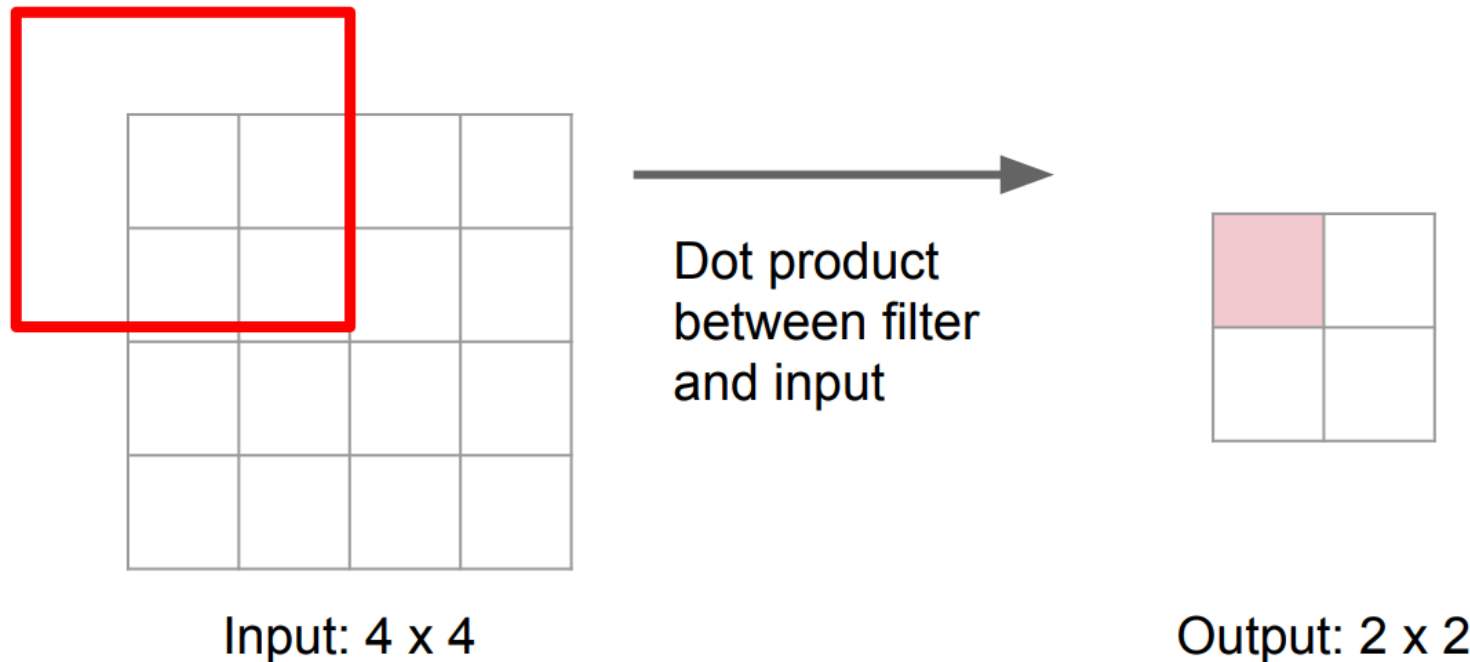






# Learnable Upsampling: Transpose Convolution

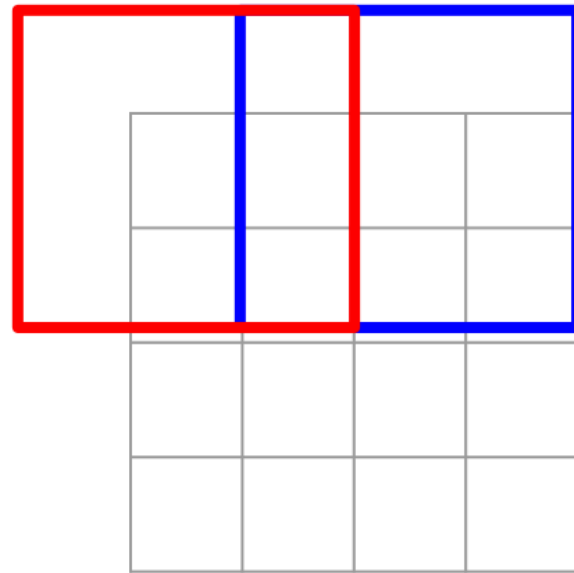
**Recall:** Normal 3 x 3 convolution, stride 2 pad 1





# Learnable Upsampling: Transpose Convolution

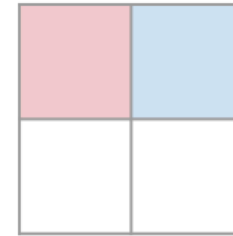
**Recall:** Normal 3 x 3 convolution, stride 2 pad 1



Input: 4 x 4



Dot product  
between filter  
and input



Output: 2 x 2

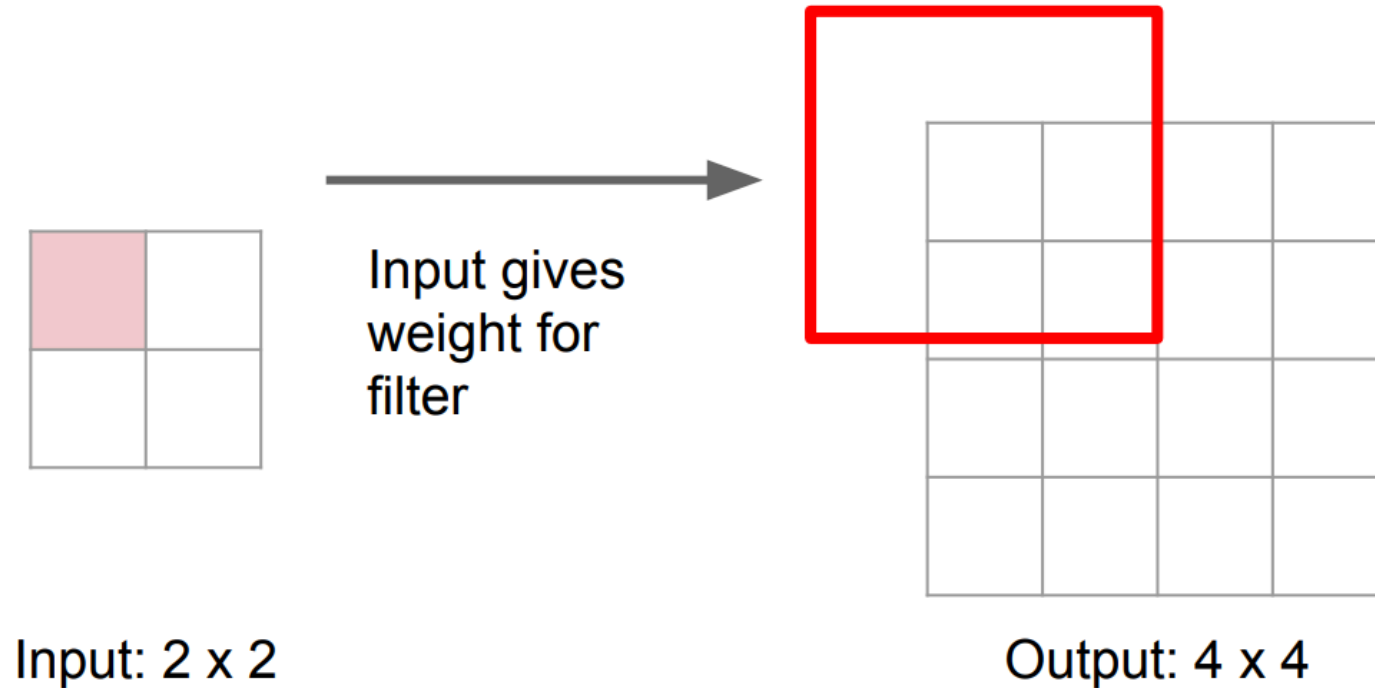
Filter moves 2 pixels in  
the input for every one  
pixel in the output

Stride gives ratio between  
movement in input and  
output



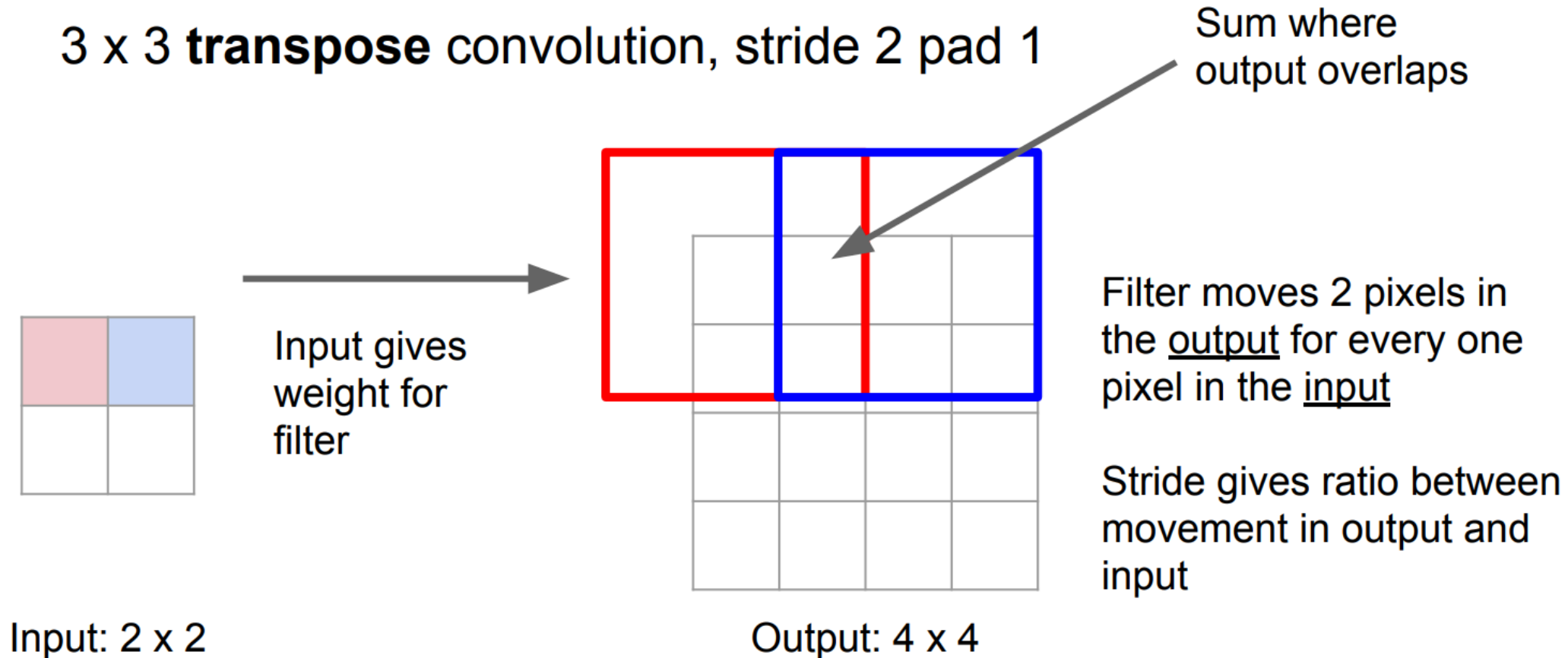
# Learnable Upsampling: Transpose Convolution

3 x 3 **transpose** convolution, stride 2 pad 1

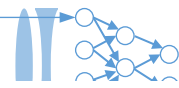


# Learnable Upsampling: Transpose Convolution

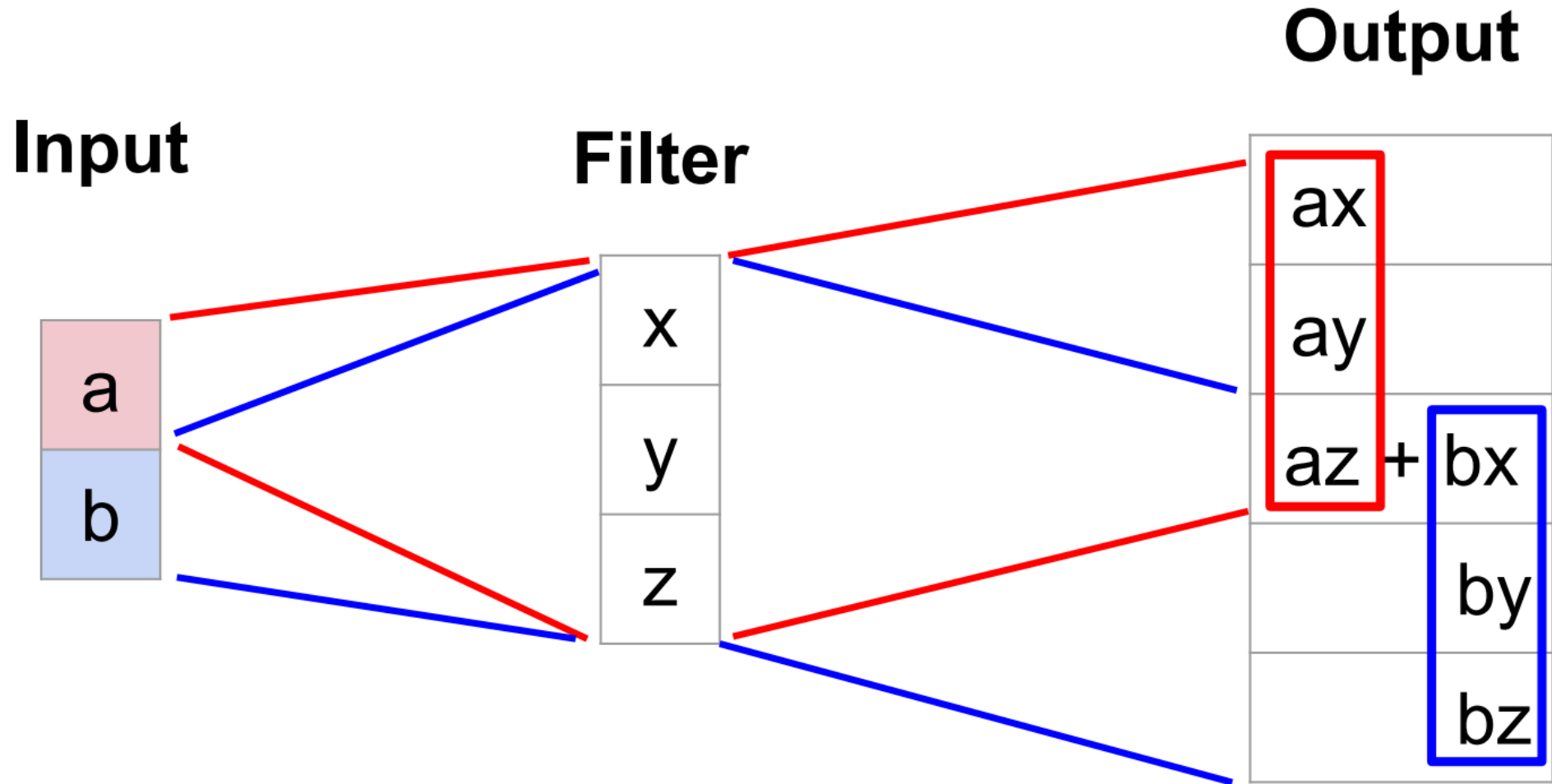
3 x 3 **transpose** convolution, stride 2 pad 1







# Learnable Upsampling: 1D Example



Output contains copies of the filter weighted by the input, summing at where it overlaps in the output

Need to crop one pixel from output to make output exactly 2x input



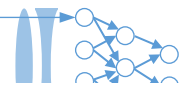
# Convolution as Matrix Multiplication (1D Example)

We can express convolution in terms of a matrix multiplication

$$\vec{x} * \vec{a} = X \vec{a}$$

$$\begin{bmatrix} x & y & x & 0 & 0 & 0 \\ 0 & x & y & x & 0 & 0 \\ 0 & 0 & x & y & x & 0 \\ 0 & 0 & 0 & x & y & x \end{bmatrix} \begin{bmatrix} 0 \\ a \\ b \\ c \\ d \\ 0 \end{bmatrix} = \begin{bmatrix} ay + bz \\ ax + by + cz \\ bx + cy + dz \\ cx + dy \end{bmatrix}$$

Example: 1D conv, kernel size=3, stride=1, padding=1



# Convolution as Matrix Multiplication (1D Example)

We can express convolution in terms of a matrix multiplication

$$\vec{x} * \vec{a} = X \vec{a}$$

$$\begin{bmatrix} x & y & x & 0 & 0 & 0 \\ 0 & x & y & x & 0 & 0 \\ 0 & 0 & x & y & x & 0 \\ 0 & 0 & 0 & x & y & x \end{bmatrix} \begin{bmatrix} 0 \\ a \\ b \\ c \\ d \\ 0 \end{bmatrix} = \begin{bmatrix} ay + bz \\ ax + by + cz \\ bx + cy + dz \\ cx + dy \end{bmatrix}$$

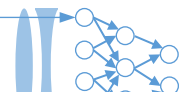
Example: 1D conv, kernel size=3, stride=1, padding=1

Convolution transpose multiplies by the transpose of the same matrix:

$$\vec{x} *^T \vec{a} = X^T \vec{a}$$

$$\begin{bmatrix} x & 0 & 0 & 0 \\ y & x & 0 & 0 \\ z & y & x & 0 \\ 0 & z & y & x \\ 0 & 0 & z & y \\ 0 & 0 & 0 & z \end{bmatrix} \begin{bmatrix} a \\ b \\ c \\ d \end{bmatrix} = \begin{bmatrix} ax \\ ay + bx \\ az + by + cx \\ bz + cy + dx \\ cz + dy \\ dz \end{bmatrix}$$

When stride=1, convolution transpose is just a regular convolution (with different padding rules)



# Convolution as Matrix Multiplication (1D Example)

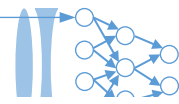
We can express convolution in terms of a matrix multiplication

$$\vec{x} * \vec{a} = X \vec{a}$$

$$\begin{bmatrix} x & y & x & 0 & 0 & 0 \\ 0 & 0 & x & y & x & 0 \end{bmatrix} \begin{bmatrix} 0 \\ a \\ b \\ c \\ d \\ 0 \end{bmatrix} = \begin{bmatrix} ay + bz \\ bx + cy + dz \end{bmatrix}$$

Example: 1D conv, kernel size=3, stride=2, padding=1





# Convolution as Matrix Multiplication (1D Example)

We can express convolution in terms of a matrix multiplication

$$\vec{x} * \vec{a} = X \vec{a}$$

$$\begin{bmatrix} x & y & z & 0 & 0 & 0 \\ 0 & 0 & x & y & z & 0 \end{bmatrix} \begin{bmatrix} 0 \\ a \\ b \\ c \\ d \\ 0 \end{bmatrix} = \begin{bmatrix} ay + bz \\ bx + cy + dz \end{bmatrix}$$

Example: 1D conv, kernel size=3, stride=2, padding=1

Convolution transpose multiplies by the transpose of the same matrix:

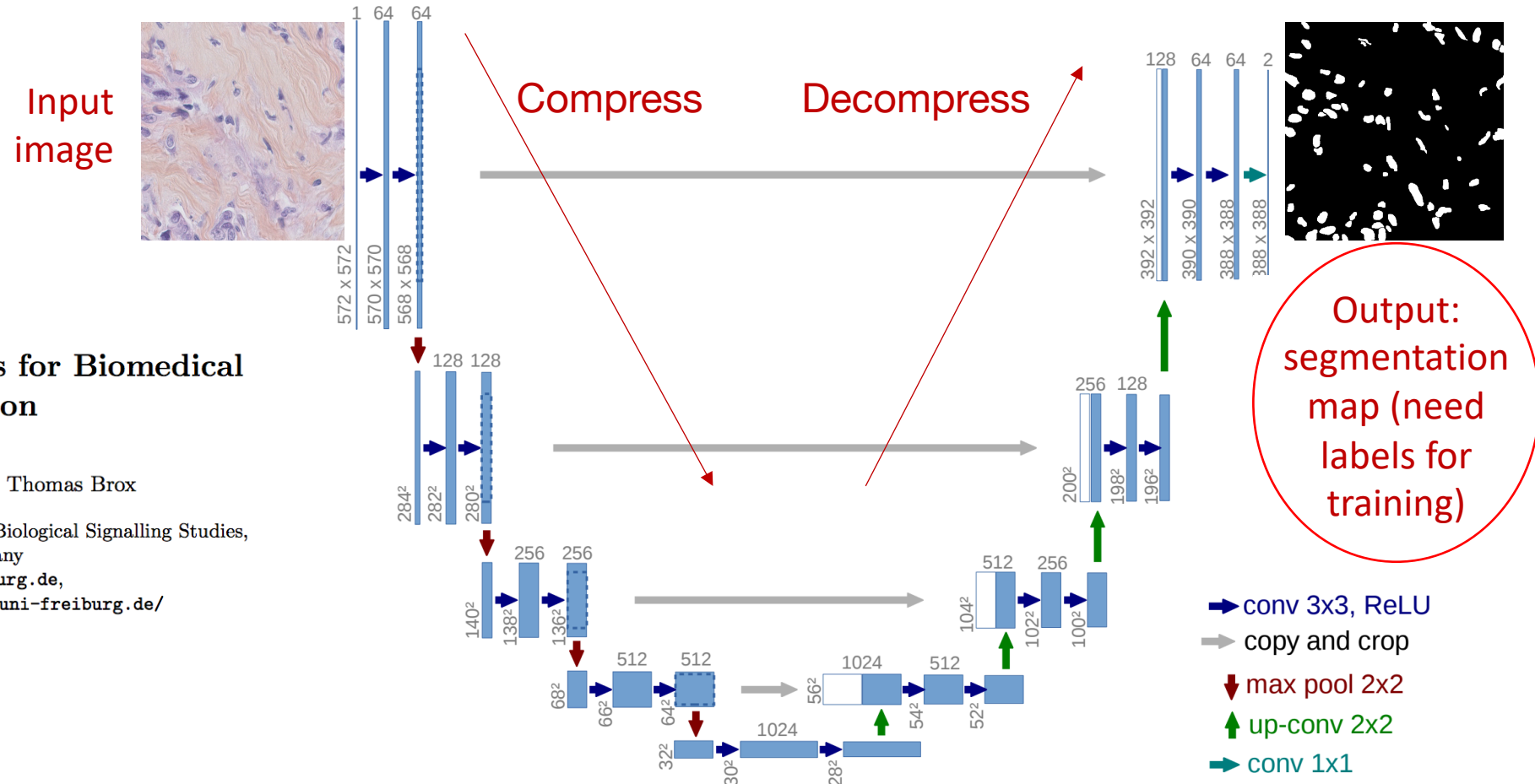
$$\vec{x} *^T \vec{a} = X^T \vec{a}$$

$$\begin{bmatrix} x & 0 \\ y & 0 \\ z & x \\ 0 & y \\ 0 & z \\ 0 & 0 \end{bmatrix} \begin{bmatrix} a \\ b \end{bmatrix} = \begin{bmatrix} ax \\ ay \\ az + bx \\ by \\ bz \\ 0 \end{bmatrix}$$

When stride>1, convolution transpose is no longer a normal convolution!

# Segmentation: need a map of classes for label

## U-Net Architecture



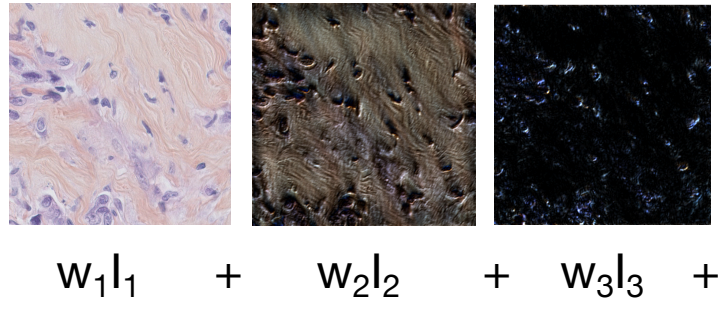
### U-Net: Convolutional Networks for Biomedical Image Segmentation

Olaf Ronneberger, Philipp Fischer, and Thomas Brox

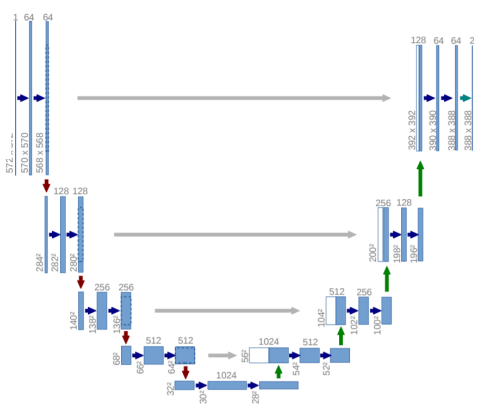
Computer Science Department and BIOS Centre for Biological Signalling Studies,  
 University of Freiburg, Germany  
 ronneber@informatik.uni-freiburg.de,  
 WWW home page: <http://lmb.informatik.uni-freiburg.de/>

# Learned sensing for improved image segmentation

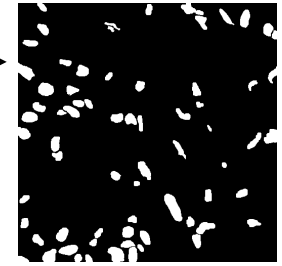
Variably illuminated images from different LEDs



U-Net CNN

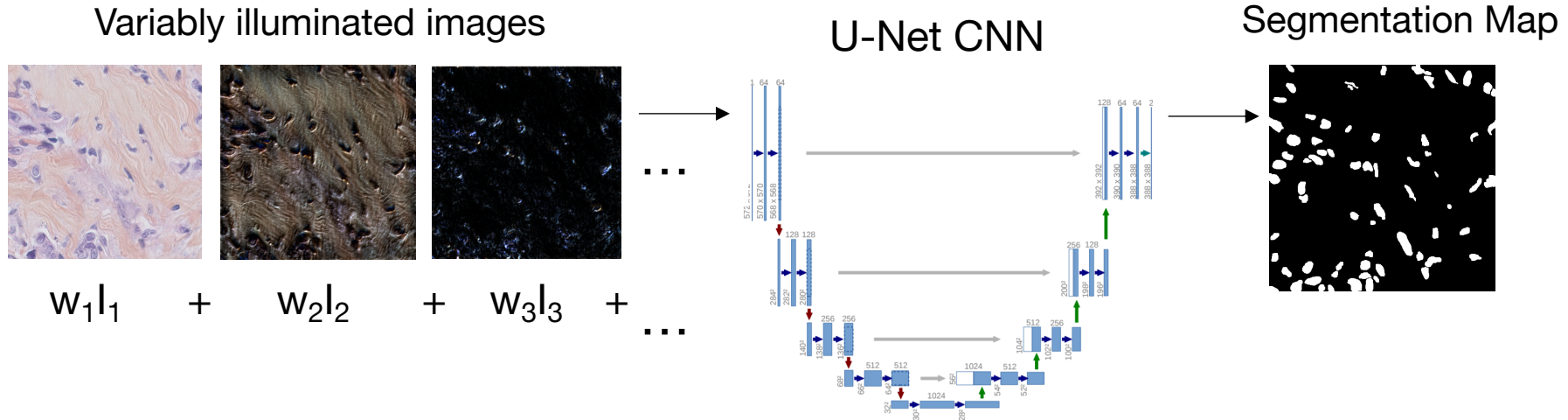


Segmentation Map

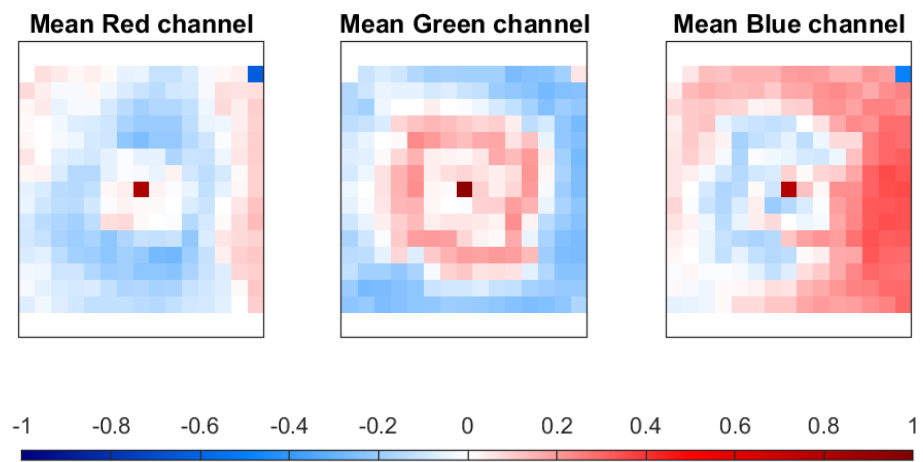


\*If we allow  $w$ 's here to be trainable weights, then we can find ideal brightnesses for the different LEDs!

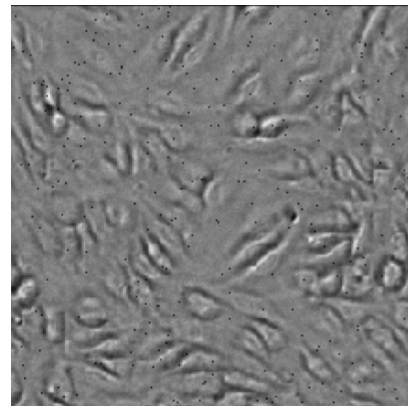
# Learned sensing for improved image segmentation



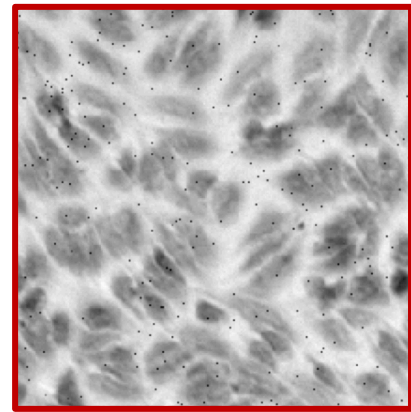
## Optimized illumination for nuclei segmentation



Standard illumination



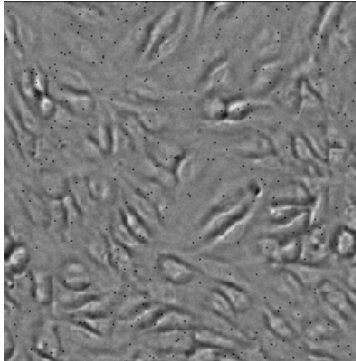
Learned illumination



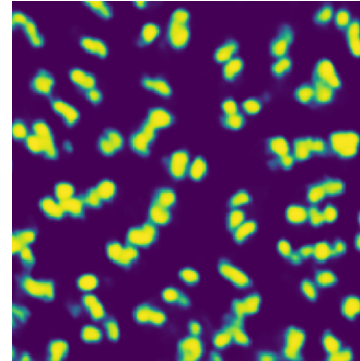
+5-10% accuracy

# Image segmentation –current workflow

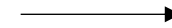
**Capture:** BF images



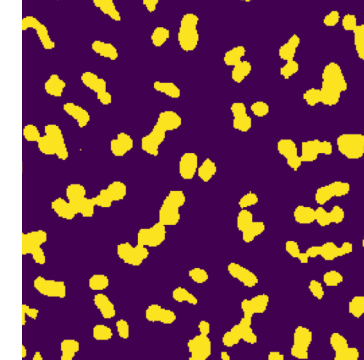
**Capture:** Fluorescence



Threshold



**Segmentation Mask**

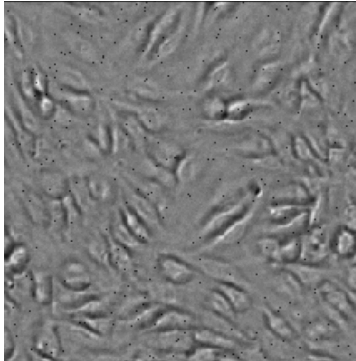


(e.g., DAPI-stained nuclei)

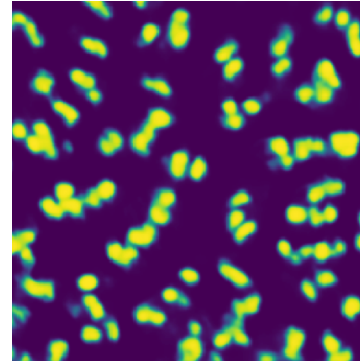


# Image segmentation –current workflow

Capture: BF images



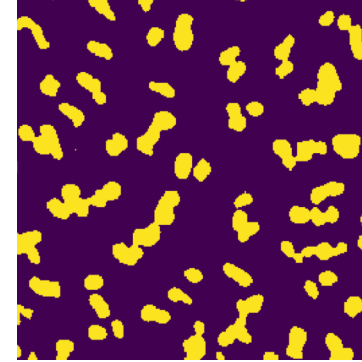
Capture: Fluorescence



Threshold

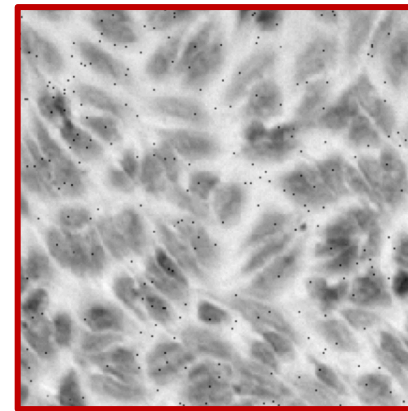
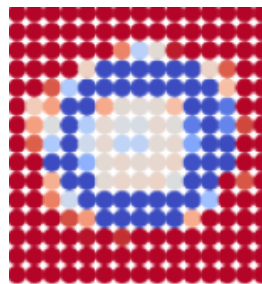


Segmentation Mask



(e.g., DAPI-stained nuclei)

Learned illumination



Inference via a trained U-Net

Optimally illuminated

# *in silico* labeling: fluorescence image inference from bright-field data

## *In Silico* Labeling: Predicting Fluorescent Labels in Unlabeled Images

Eric M. Christiansen,<sup>1,11,\*</sup> Samuel J. Yang,<sup>1</sup> D. Michael Ando,<sup>1,9</sup> Ashkan Javaherian,<sup>2,9</sup> Gaia Skibinski,<sup>2,9</sup> Scott Lipnick,<sup>3,4,8,9</sup> Elliot Mount,<sup>2,10</sup> Alison O’Neil,<sup>3,10</sup> Kevan Shah,<sup>2,10</sup> Alicia K. Lee,<sup>2,10</sup> Piyush Goyal,<sup>2,10</sup> William Fedus,<sup>1,6,10</sup> Ryan Poplin,<sup>1,10</sup> Andre Esteva,<sup>1,7</sup> Marc Berndl,<sup>1</sup> Lee L. Rubin,<sup>3</sup> Philip Nelson,<sup>1,\*</sup> and Steven Finkbeiner<sup>2,5,\*</sup>

<sup>1</sup>Google, Inc., Mountain View, CA 94043, USA

<sup>2</sup>Taube/Koret Center for Neurodegenerative Disease Research and DaedalusBio, Gladstone Institutes, San Francisco, CA 94158, USA

<sup>3</sup>Department of Stem Cell and Regenerative Biology, Harvard University, Cambridge, MA 02138, USA

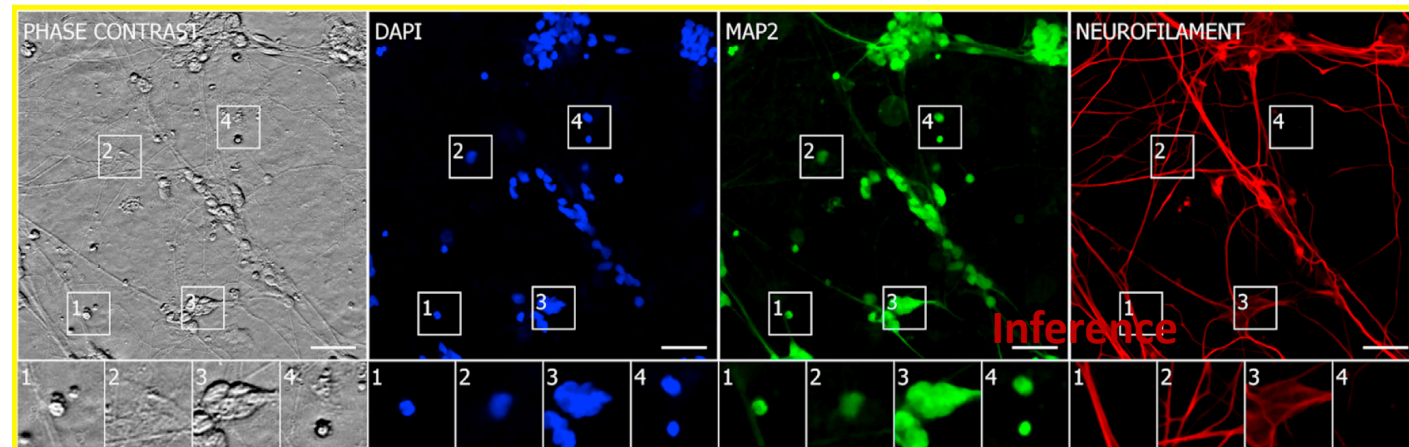
<sup>4</sup>Department of Biomedical Informatics, Harvard Medical School, Boston, MA 02115, USA

<sup>5</sup>Departments of Neurology and Physiology, University of California, San Francisco, 94158, USA

<sup>6</sup>Montreal Institute of Learning Algorithms, University of Montreal, Montreal, QC, Canada

<sup>7</sup>Department of Electrical Engineering, Stanford University, Stanford, CA 94305, USA

<sup>8</sup>Center for Assessment Technology and Continuous Health, Massachusetts General Hospital, Boston, MA 02114, USA

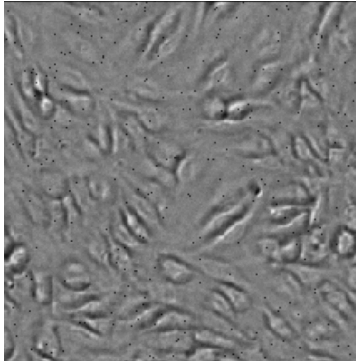


**BF Focal stack  
(26+ images)**

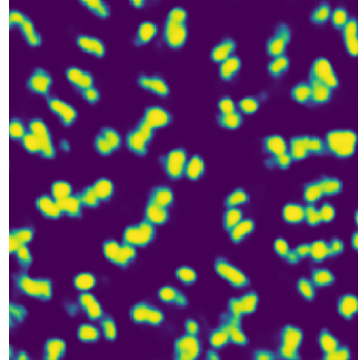
**Task: bright-field to fluorescence image Inference**

# Image segmentation versus *in silico* labeling (fluorescence inference)

Capture: Bright field



Capture: Fluorescence



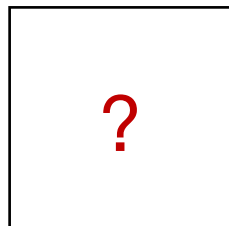
Threshold



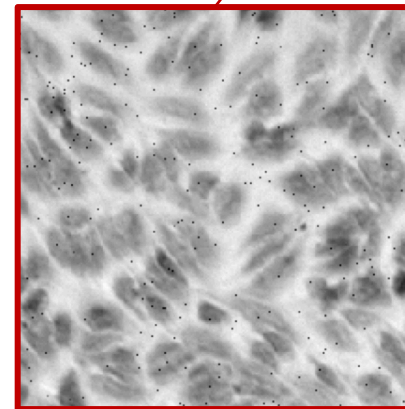
Segmentation Mask



Learned illumination for fluorescent image inference?

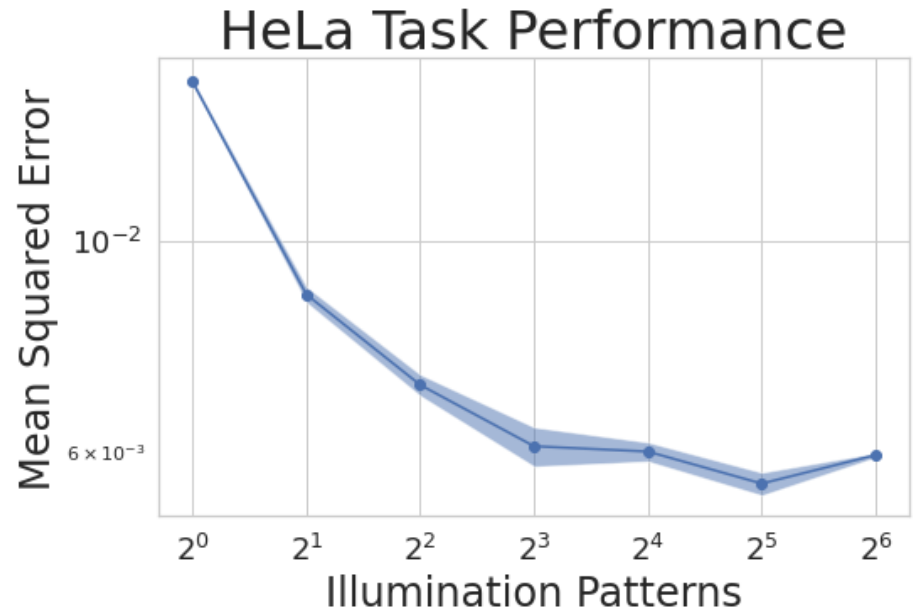
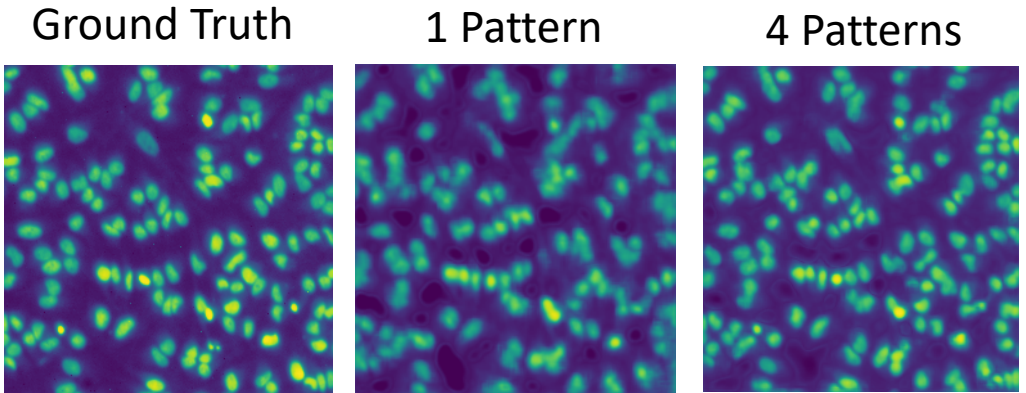
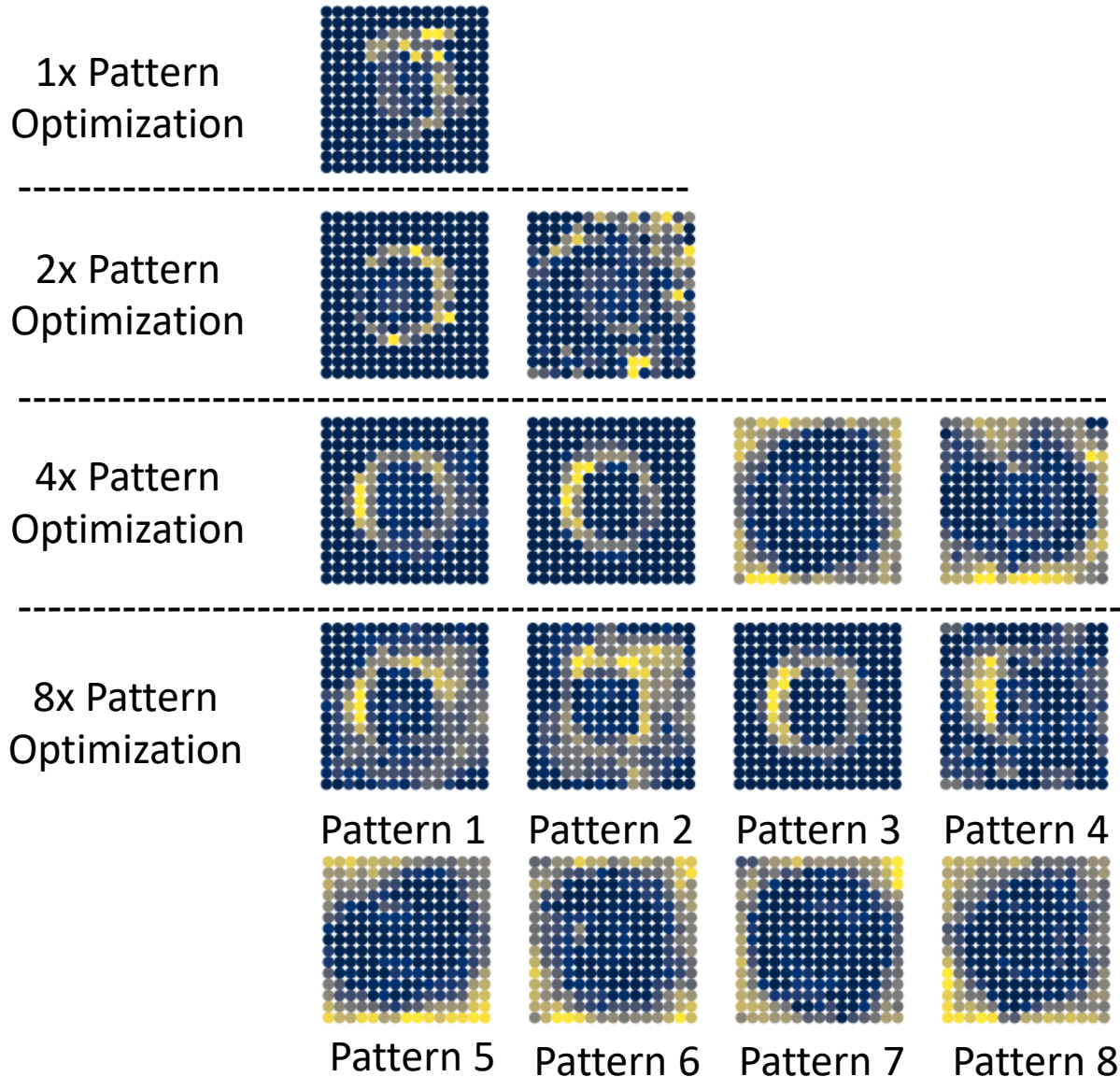


Directly infer the fluorescence image



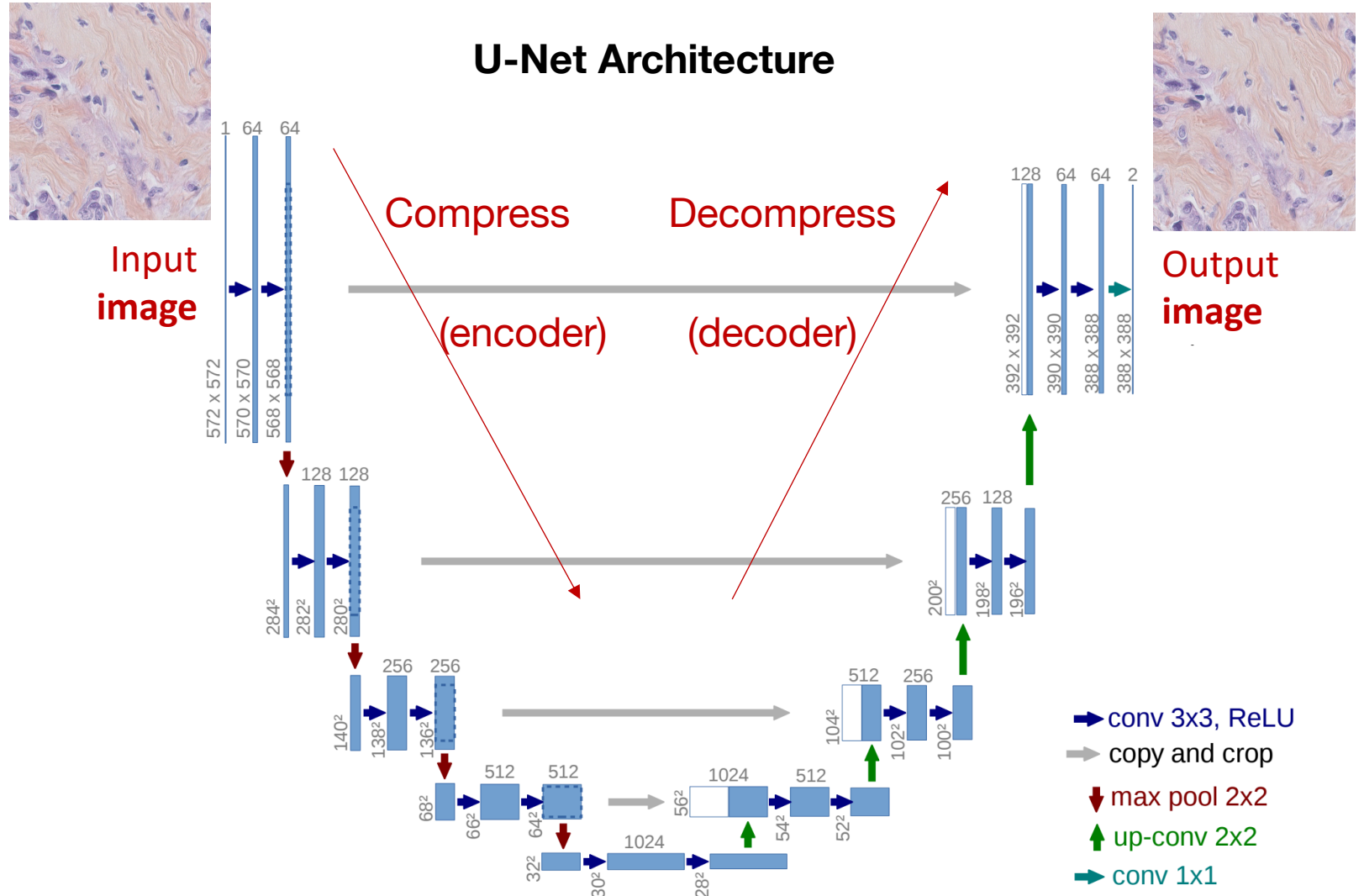
Optimally illuminated

# Multiple Patterns for Fluorescence image inference





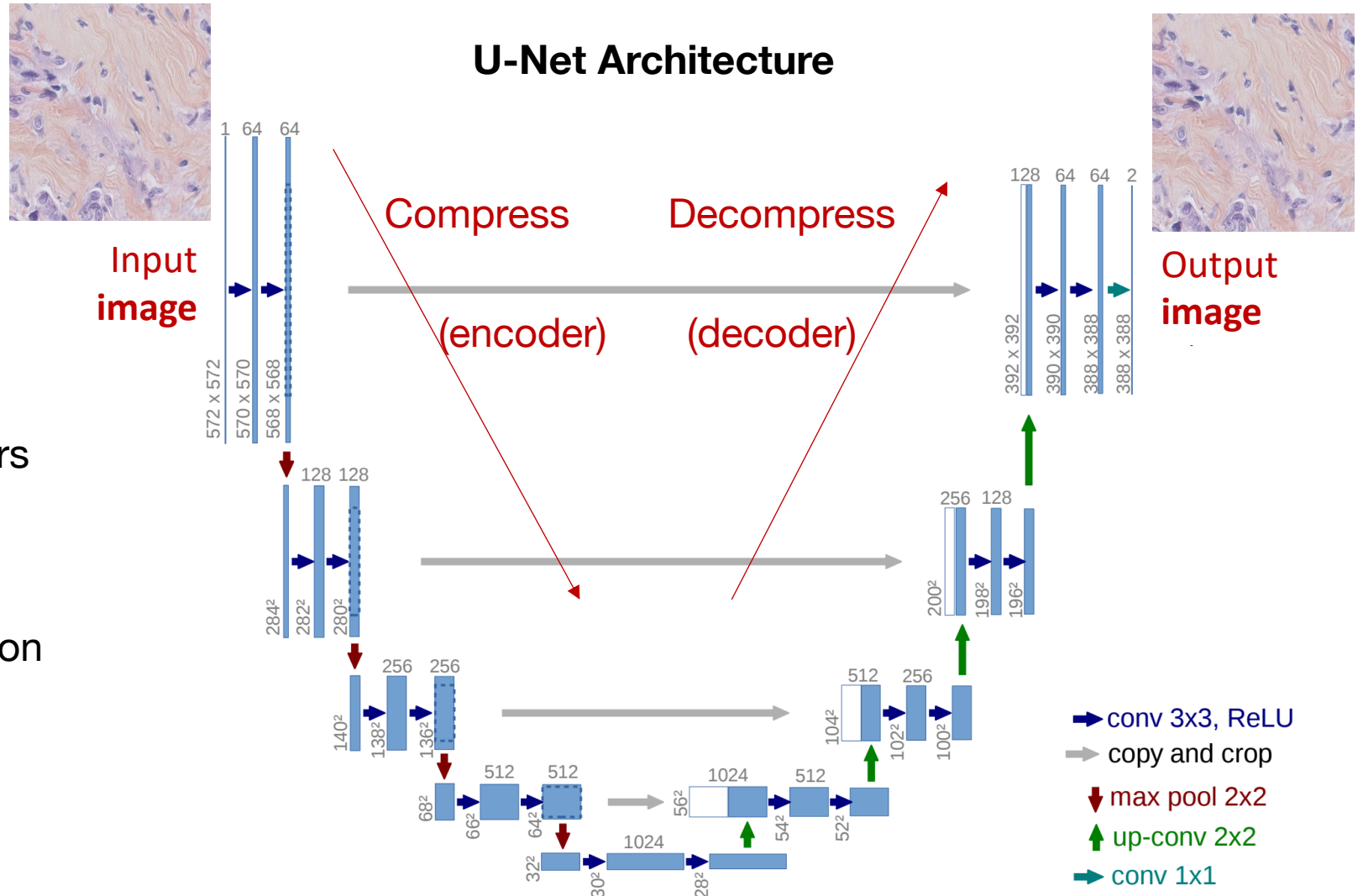
# Instead, *compress x-y dimensions of input image*





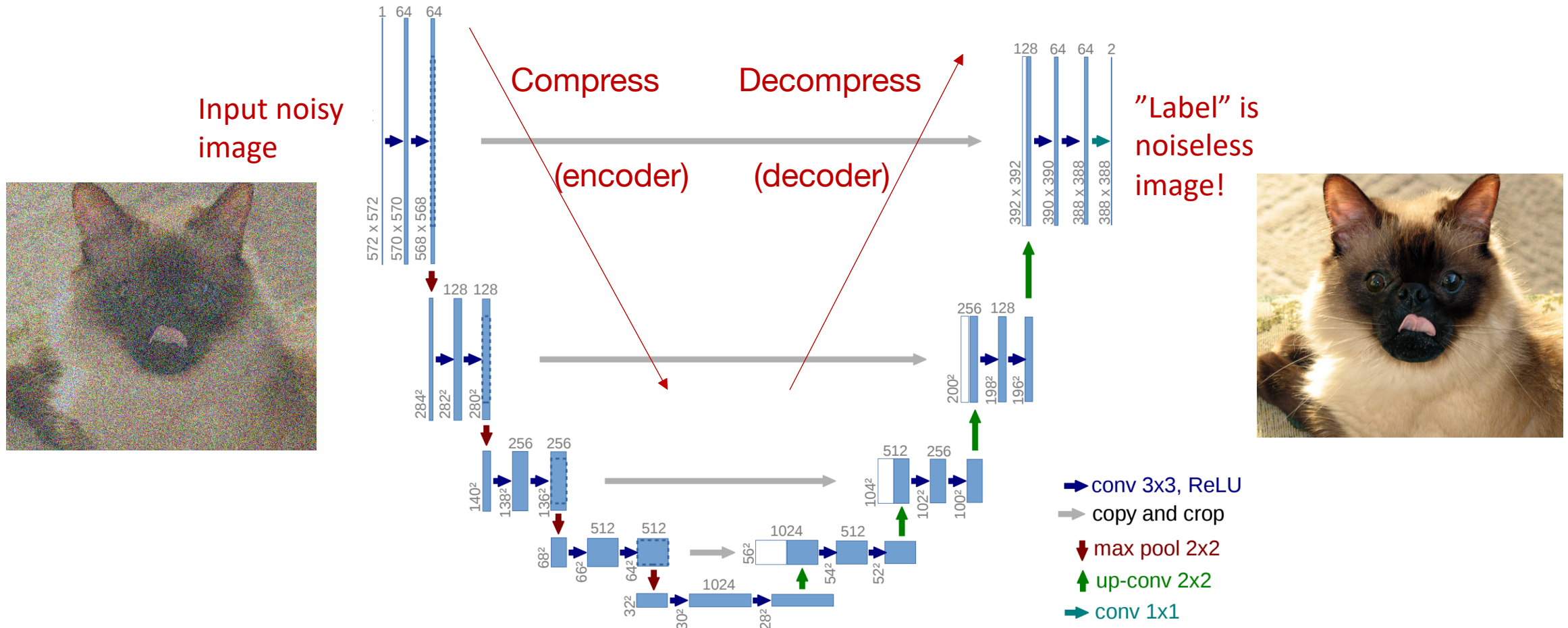
# Instead, *compress x-y dimensions of input image*

- Compress spatial features into learned filters
- Then, decompress learned filters back into same spatial dimensions
- **Termed an autoencoder**
- Analogous to image compression
- A pretty powerful idea...



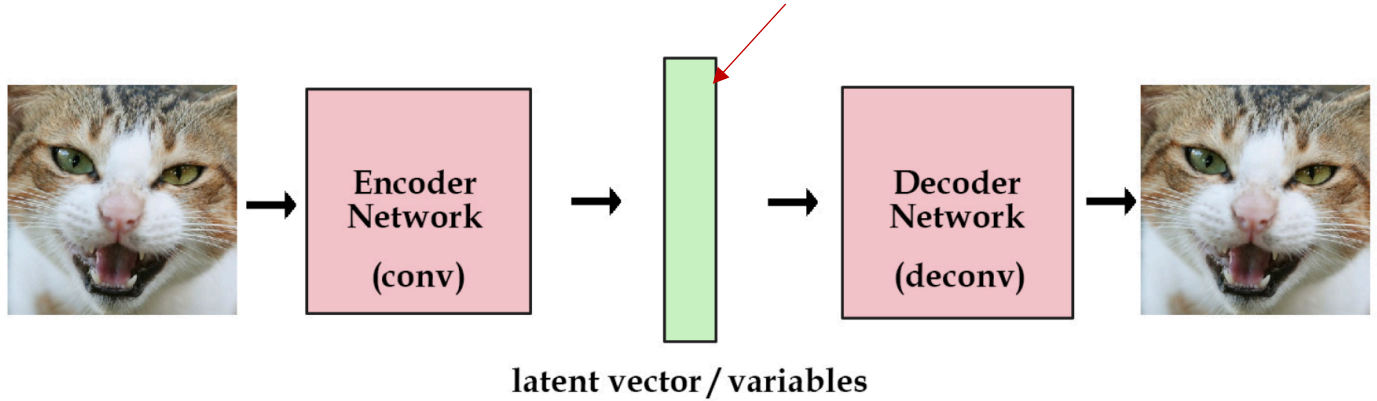
# Another example: Denoising Autoencoder

## U-Net Architecture



# Example: Variational Autoencoder (VAE)

Force this vector to follow a Gaussian PDF



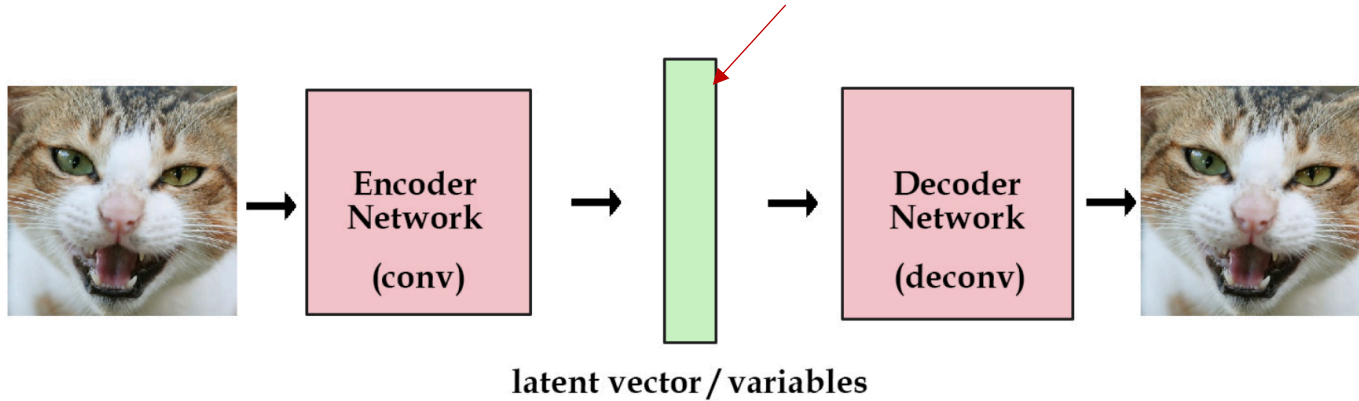
- Good *generative model*
- Have a clean probability distribution to select from to generate new examples

Minimize (KL) distance between latent vector and Gaussian normal



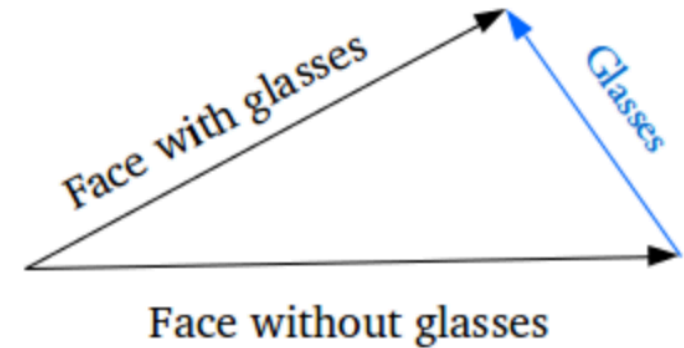
# Example: Variational Autoencoder (VAE)

Force this vector to follow a Gaussian PDF



Minimize (KL) distance between latent vector and Gaussian normal

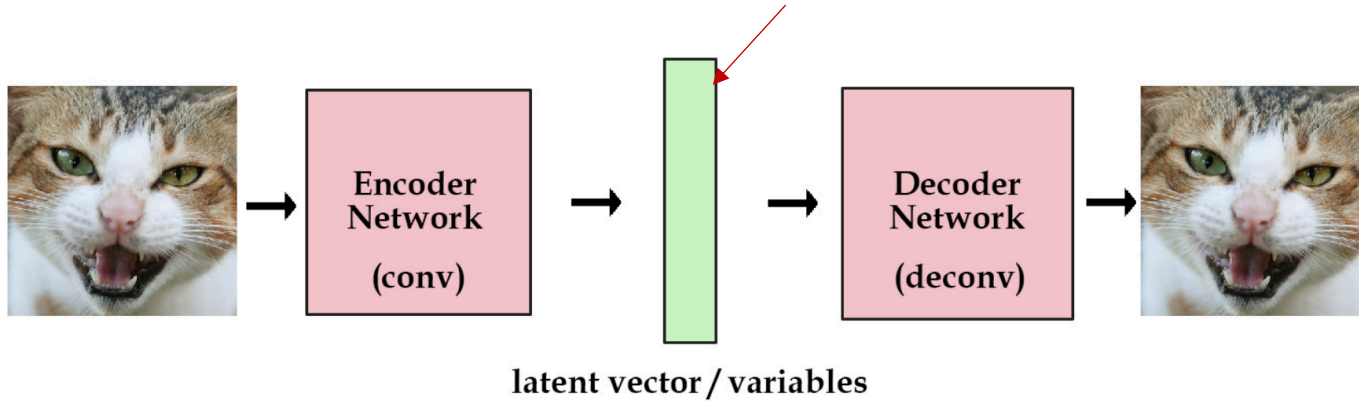
- With Gaussian PDF, can start to add/subtract latent vector in a normalized vector space



Adding new features to samples

# Example: Variational Autoencoder (VAE)

Force this vector to follow a Gaussian PDF

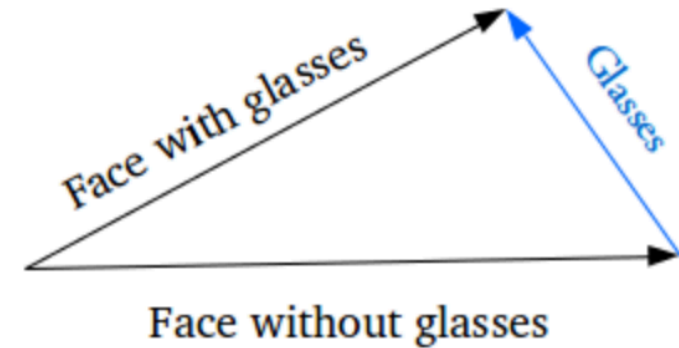


Minimize (KL) distance between latent vector and Gaussian normal

Generative Example (once trained):

- Encode image with glasses, obtain latent vector PDF  $P_g$
- Encode image without glasses, obtain PDF  $P_{ng}$
- Compute  $\mathbf{diff} = P_g - P_{ng}$
- Encode new image to obtain  $P_{new}$ , add in  $\mathbf{diff}$
- Decode  $P_{new} + \mathbf{diff}$  to get guy with glasses!

- With Gaussian PDF, can start to add/subtract latent vector in a normalized vector space



Adding new features to samples

Glasses



Exploring a specific variation of input data[1]



Code review: See the following:

[Jupyter Notebook: A simple Autoencoder in Tensorflow/Keras](#)

<https://deepimaging.github.io/lectures/>