



Convolutional neuronal networks

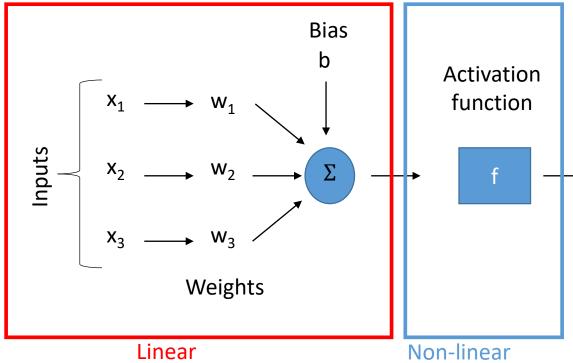
Johannes Müller

With Material from
Robert Haase, PoL
Alex Krull, MPI CBG
Martin Weigert, EPFL Lausanne
Uwe Schmidt, MPI CBG
Ignacio Arganda-Carreras, Universidad del Pais Vasco



Convolutional neural networks





Single neuron output calculation

$$y = w_1 x_1 + w_2 x_2 + w_3 x_3 + b = w^T x + b$$

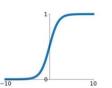
Output

Sigmoid

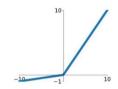
tanh

tanh(x)

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



Leaky ReLU $\max(0.1x, x)$



For image data, the values $x_1, x_2,...$ would be

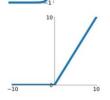
Pixel intensities

Filter kernel entries



Pixel coordinates

ReLU $\max(0, x)$



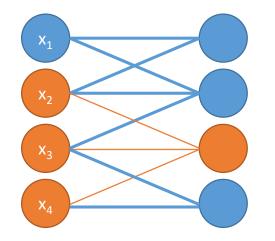
$$\mathbf{Maxout} \\ \max(w_1^T x + b_1, w_2^T x + b_2)$$

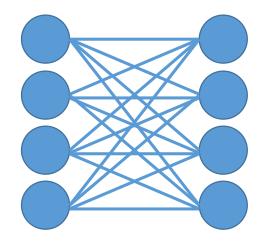


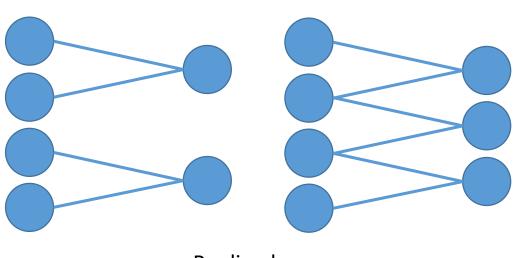
Convolutional neural networks



Layers







Convolutional layer

Fully connected layer

Previously:

Defined filter kernels

1/16	1/8	1/16	
1/8	1/4	1/8	
1/16	1/8	1/16	

Now:

Undefined filter kernels

W ₁₁	W ₁₂	W ₁₃
W ₂₁	W ₂₂	W ₂₃
W ₃₁	W ₃₂	W ₃₃

Pooling layer ("Max pool", "Average pool") Pooling maximal values

3	15	1	13	1 Aver	15	13	
9	7	0	10		11	9	
11	5	5	3		veragin 8.5	g value	25
1	8	9	6		6.3	5.8	

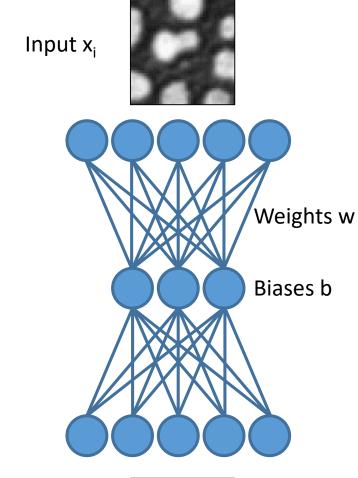
Learning: Back propagation

Pol Physics of Life TU Dresden

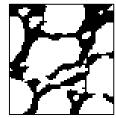
- Learning is an optimization problem
- Step 0: Initialize the network randomly
 - Weights
 - Bias
- Step 1: Forward pass the input through the network, get an initial prediction (Images 0...M)
- Step 2: Compare the output with the ground truth, computer the error (loss function)
 - The loss function can be freely defined.
 - Mean squared error:

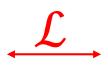
$$\mathcal{L}(y, \hat{y}) = \frac{1}{M} \sum_{i=1}^{M} (\hat{y}_i - y_i)^2$$

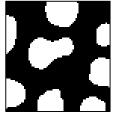
• Step 3: Update weights



Prediction y_i







Ground truth $\hat{y_i}$

Back-Propagation Algorithm



The loss function can be expanded from

$$\mathcal{L}(y, \hat{y}) = \frac{1}{M} \sum_{i=1}^{M} (\hat{y}_i - \mathbf{y}_i)^2$$

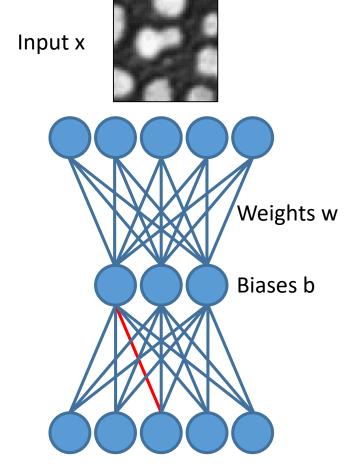
as the prediction depends on inputs x weights w and bias b

$$\mathcal{L}(\hat{y}, x, w) = \frac{1}{M} \sum_{i=1}^{M} (\hat{y}_i - (w^T x_i + b))^2$$

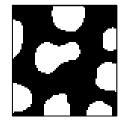
We can calculate derivatives with respect to w and b to find their optimal values

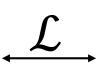
→ Derivatives tell us how to change w & b in order to improve the prediction

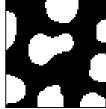
Repeat this n times, each time update weights w



Prediction y





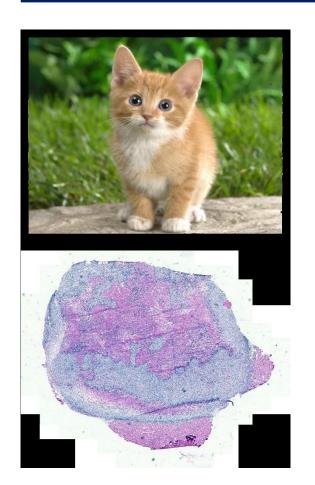


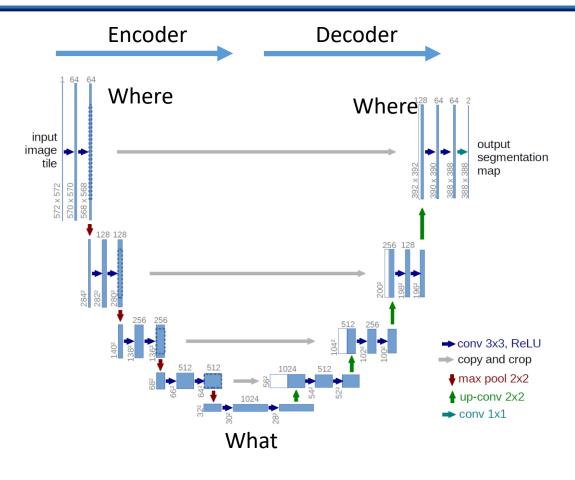
Ground truth \hat{y}

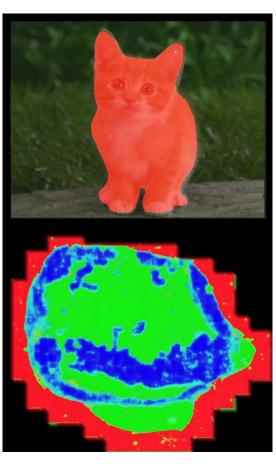


Image segmentation









- The **U-net** is the most used network architecture in biological image processing using CNNs.
 - Encoder: Increase the "What", decrease the "Where"
 - Decoder: Increase the "Where", decrease the "What"



YOLO: You only look once

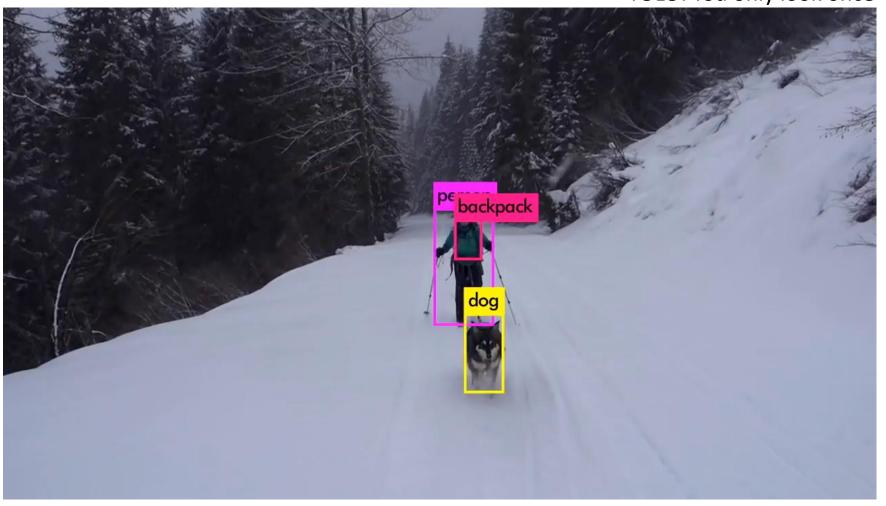


Image denoising



- CARE: content-aware restoration
- Image acquisition of pairs of images: A high-quality and a low-quality image.
- Problem: Shot noise, Biology moves!
- Trained model only applicable to image data of the same conditions (biological system, microscope, etc)

5 example validation patches top row: input (source), middle row: target (ground truth), bottom row: predicted from source

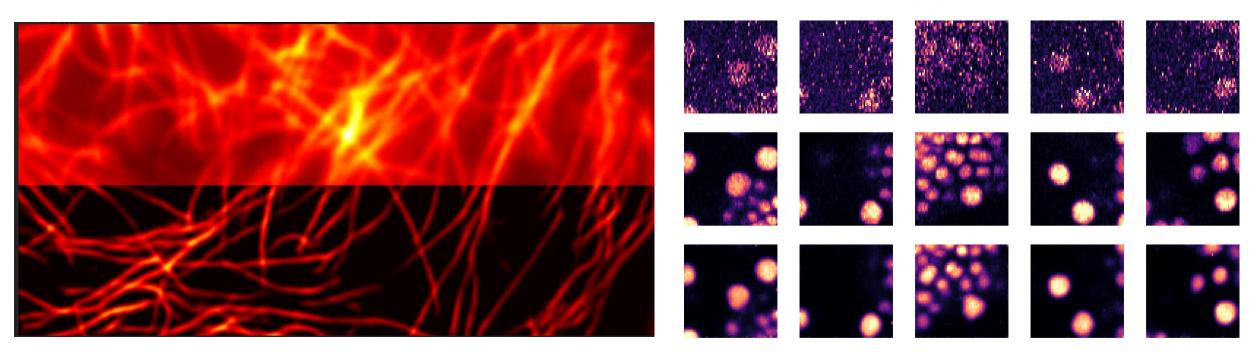


Image denoising









Strategy:

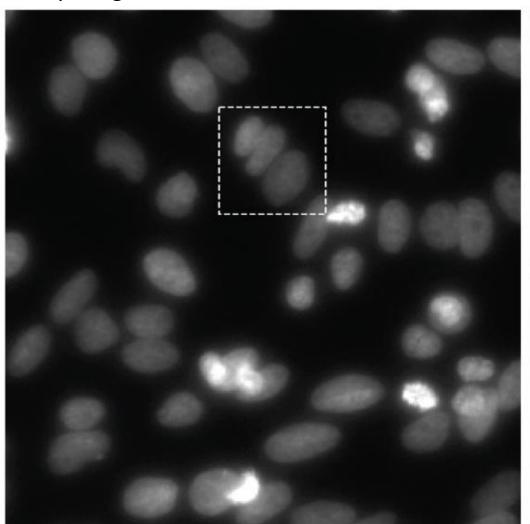
- → Try to predict intensity of pixel y from surrounding pixels x
- → CNN fails to predict noise component → N2V can only reproduce signal from the surroundings of y
- → Only **random** noise can be removed, otherwise artifacts occur

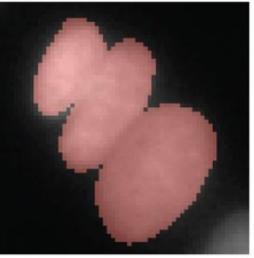
https://github.com/juglab/n2v

https://forum.image.sc/t/n2v-artefacts-in-training-data/70686

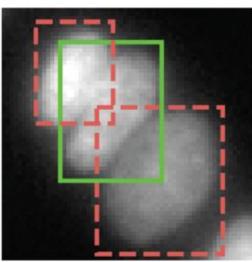


Noisy images + Crowded cells = Common source of segmentation errors





Dense Segmentation (e.g. U-Net)

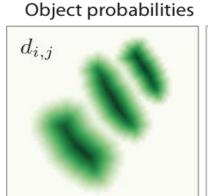


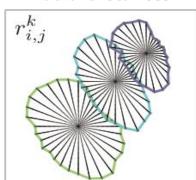
Bounding box based methods (e.g. Mask-RCNN)

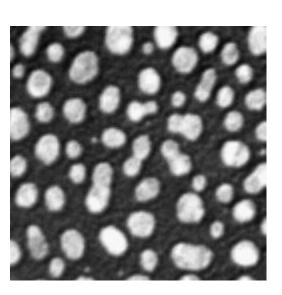
Pol Physics of Life TU Dresden Radial Distances

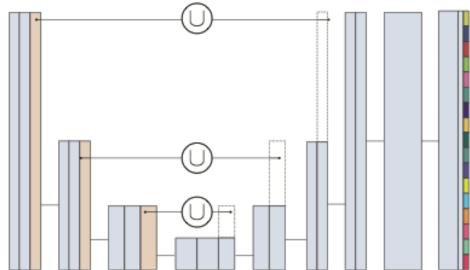
Strategy:

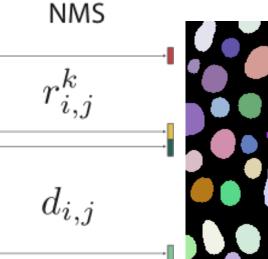
- → Add additional information to prediction
- → Member pixels of objects (nuclei) can be reached via a straight line from the center













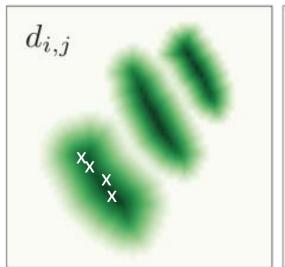
Dense Polygon Prediction (e.g. U-Net, ResNet)

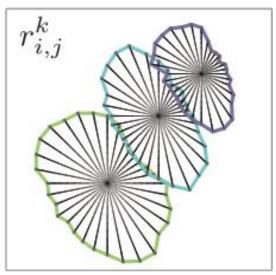
Polygon Selection (Non-Maximum Suppression NMS)

Pol Physics of Life TU Dresden

Object probabilities

Radial Distances





Non-maximum-suppression (NMS):

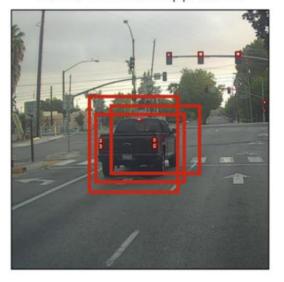
 Intersection over Union (IoU) threshold τ determines "conservativeness":
 High τ: Objects tend to be considered as separate objects

Low τ : Objects tend to be considered as the same objects

Problem:

- → Multiple candidate points for nucleus center
- → Overlapping instance predictions

Before non-max suppression





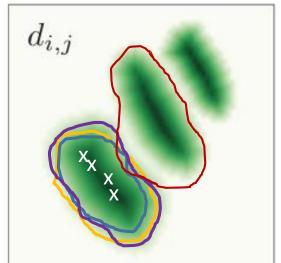
After non-max suppression

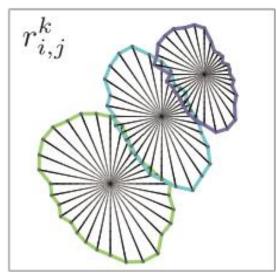




Object probabilities

Radial Distances





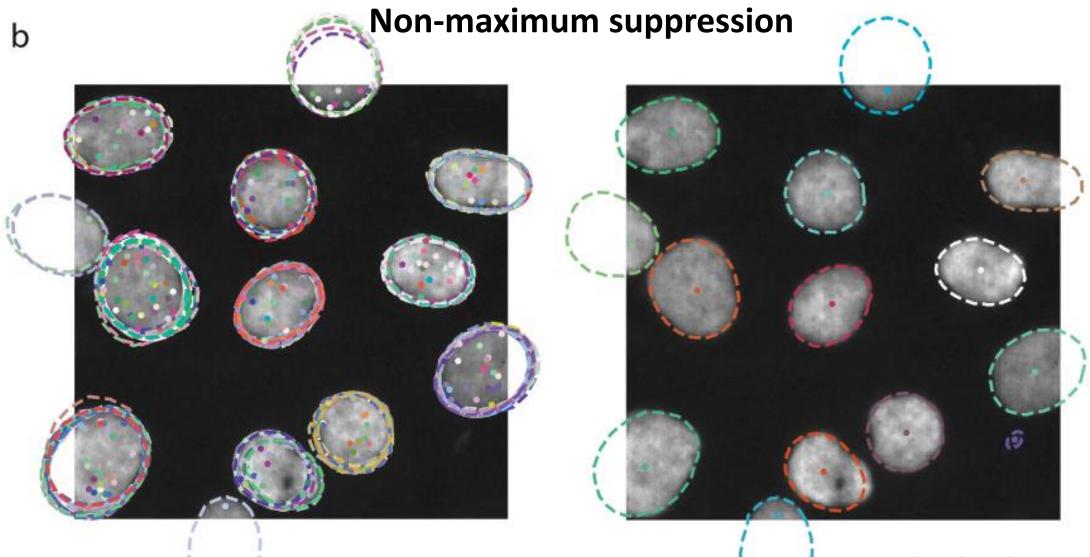
Non-maximum-suppression (NMS):

- → Object probabilities: Probability that pixel belongs to class "nucleus"
- → Multiple maxima lead to multiple possible polygons for the same nucleus

Algorithm:

- → Select polygon with highest object probability inside: <a>\bigc\rightarrow\$
- \rightarrow Look at other polygons: Is the overlap of \bigcirc with \bigcirc larger than threshold τ ?
 - → Yes: and are actually the same object, drop ○
 - → No: and ◇ are separate nuclei
- \rightarrow Setting τ very high leads to many false positives!





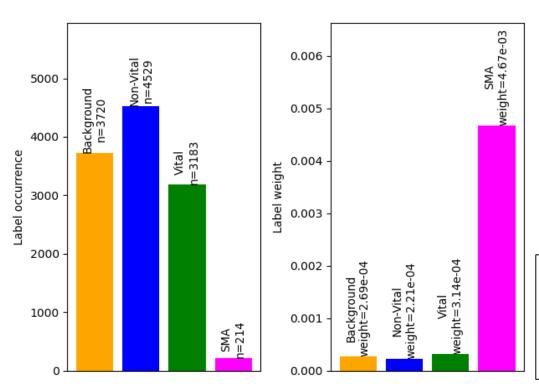
Things to consider



Encoder

Many prediction frameworks use UNets – similar weak points Receptive field:

- → Neurons in deeper layers can only "see" parts of the raw image
- →Objects must be smaller than receptive field to be detectable



Unbalanced training data:

- → Heterogeneous occurrence of labels in training data
- →Rare events will not be caught because they don't harm accuracy much
- → Weighted data sampling

Is the iPhone racist? Chinese users claim iPhoneX face recognition can't tell them apart

APPLE has come under fire following numerous complaints from Chinese users who claim the iPhone X face recognition can't tell them apart.



Implementation aspects



Popular frameworks: https://www.pytorch.org/





Hardware requirements: Nvidia (CUDA-capable) graphics card (GPU)

Memory: GPU memory limits < RAM memory \rightarrow Images are tiled and passed through the network in *batches*

Batch dimension

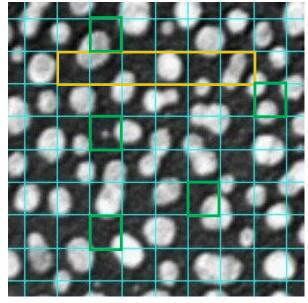
Batch-processing:

/ Channel dimension

- \rightarrow For 2D multichannel image: data.shape = [B, C, Y, X]
- ⇒Batch normalization: Data in batch is normalized from $[-\sigma, \sigma]$ → [-1, 1] Higher batch size, smaller tiles → Better generalization of image statistics Lower batch size, bigger tiles → Potentially larger receptive field

Train/test/validation split:

- → During training: Measure performance ("loss") of network, update weights
- → During testing: Measure performance of updated network, **keep weights**
- → Validation: Measure performance in **unseen** validation dataset



Tiles in batch

epoch

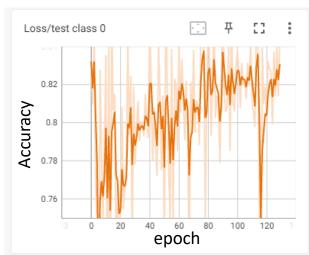
Tiles in batch

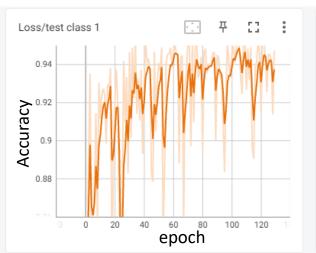
Implementation aspects

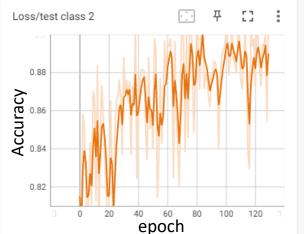


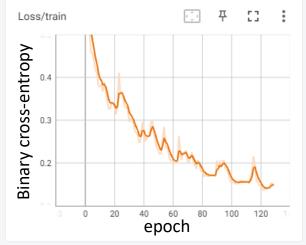


Training loss: Binary cross-entropy (Measure for information in image A contained in image B)







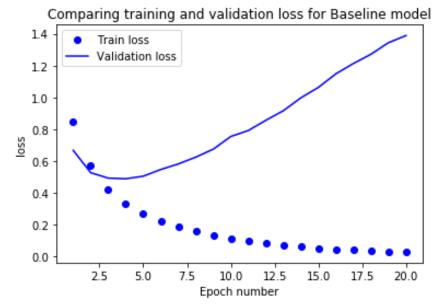


Test loss: Label-wise accuracy

→ We use different metrics in training/testing!

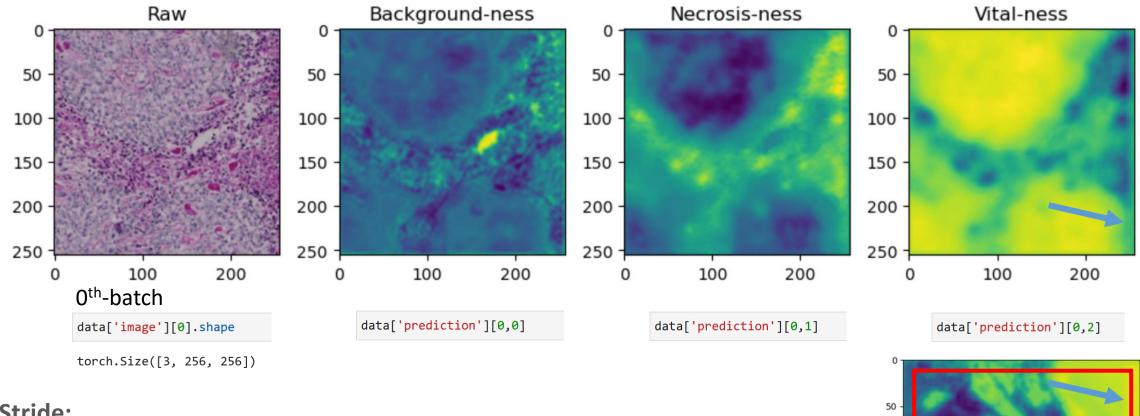
Overfitting:

- → Network is learning things "by heart"
- → Hint at this happening: Updated weights from training fail to perform well in test



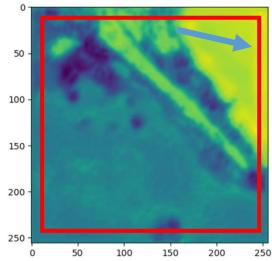
Implementation aspects





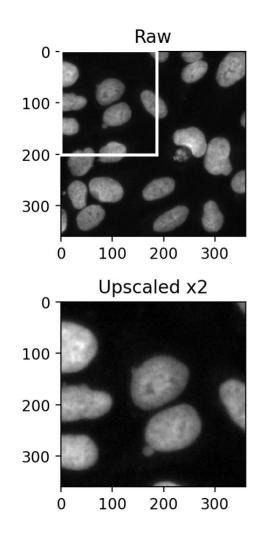
Stride:

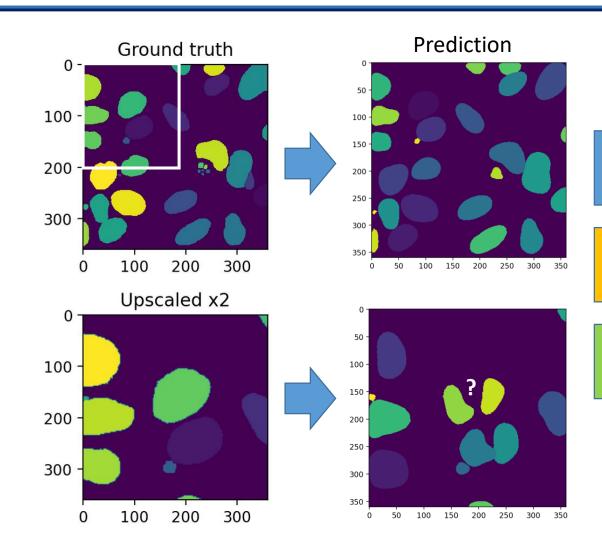
- → Network can not predict accurately at image edges
- → We throw away a X-pixel wide margin at the image edge



Example







What happened here?

Receptive field too small

I used a different resolution than during training

Overfitting

Takeaways



- With great power comes great responsibility: Validate your models well!
- Better data > better model