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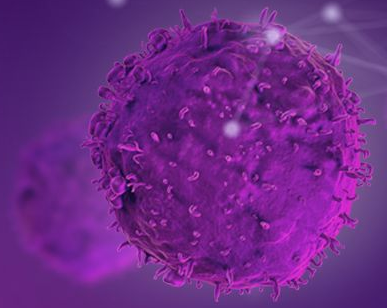
Artificial Intelligence
& Bioinformatics
for Precision Medicine



Deep Learning Segmentation for Nucleus Detection

PyData Warsaw 2018

Dawid Rymarczyk, Data Scientist

November 19th 2018

ardigen.com

Agenda

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1. Nucleus detection problem - Kaggle Data Science Bowl 2018
2. Instance and Semantic segmentation - application to the problem
3. U-Net and Mask R-CNN architecture
4. Enhancements
5. Winning solution
6. Summary

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Nucleus detection problem

Kaggle Data Science Bowl 2018

Nucleus detection problem

Timeline

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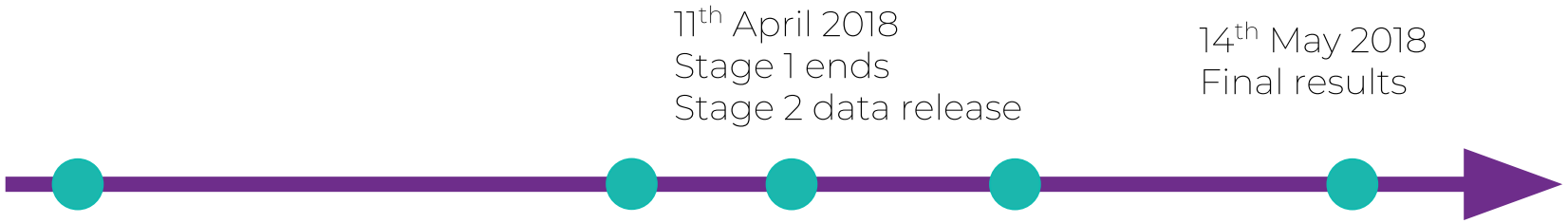


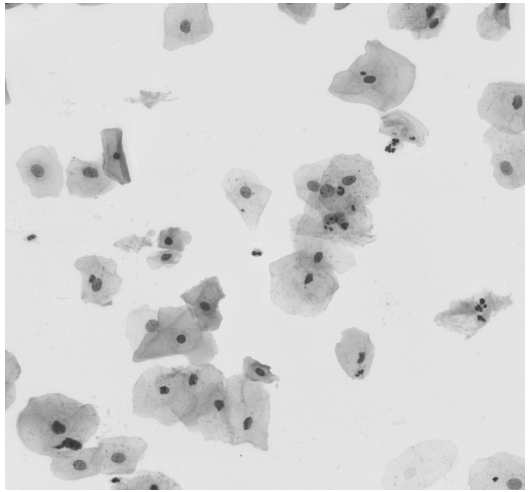
Nucleus detection problem

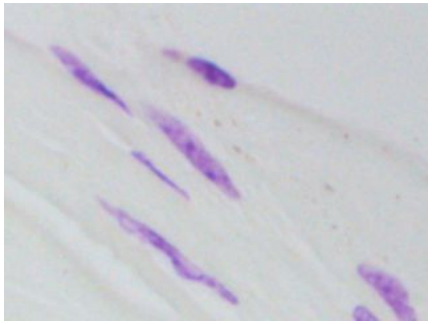
Motivation

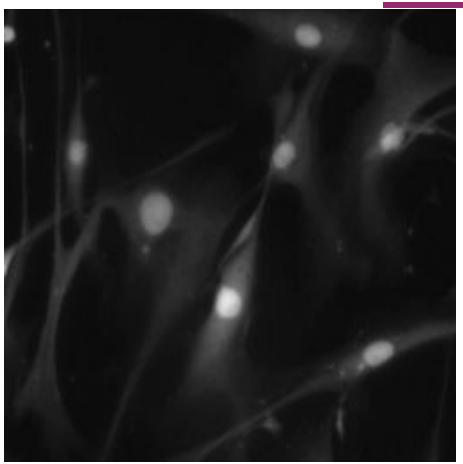
Source: kaggle.com

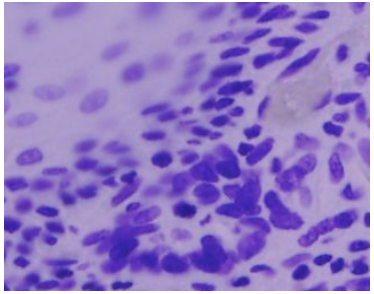
Nucleus detection problem

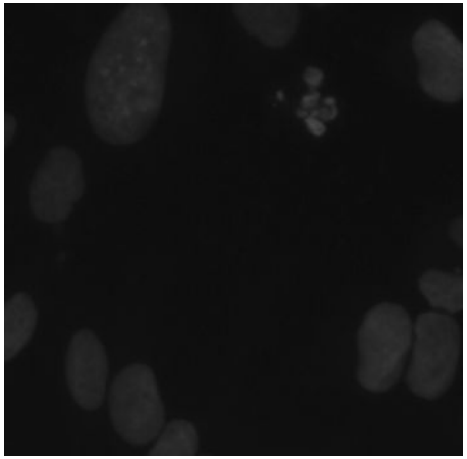
Dataset: 670 images for training

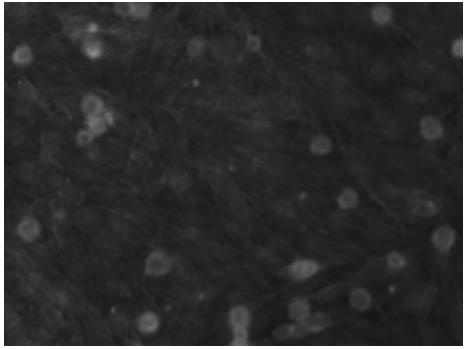






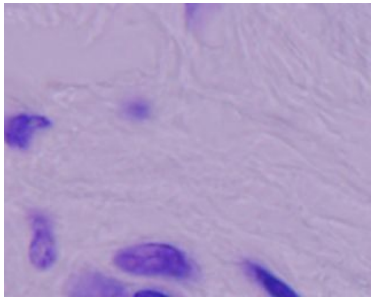






Nucleus detection problem

Definition




Where is the nuclei? Which pixel corresponds to it?




Nucleus detection problem

Evaluation

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Mean Average Precision at different Intersection over Union (IoU) $IoU(A,B) = \frac{A \cap B}{A \cup B}$

Threshold for IoU, *t: {0.5, 0.55, 0.6, 0.65, 0.7, 0.75, 0.8, 0.85, 0.9, 0.95}*

For each threshold t: $\frac{TP(t)}{TP(t) + FP(t) + FN(t)}$

True positive is when the IoU is above the threshold
False positive is when the predicted object has no associated ground truth object
False negative is when the ground truth object has no associated predicted object.

The average precision of a single image is then calculated as the mean of the above precision values at each IoU threshold: $\frac{1}{|thresholds|} \sum_t \frac{TP(t)}{TP(t) + FP(t) + FN(t)}$

Overall score is the mean from all images

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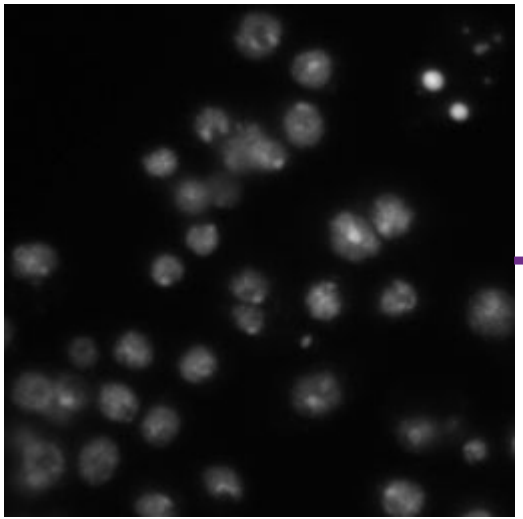
Semantic segmentation

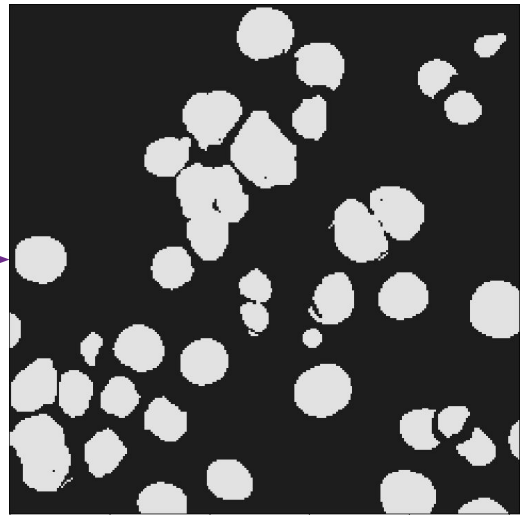
Instance and Semantic segmentation

Semantic

Image



Mask



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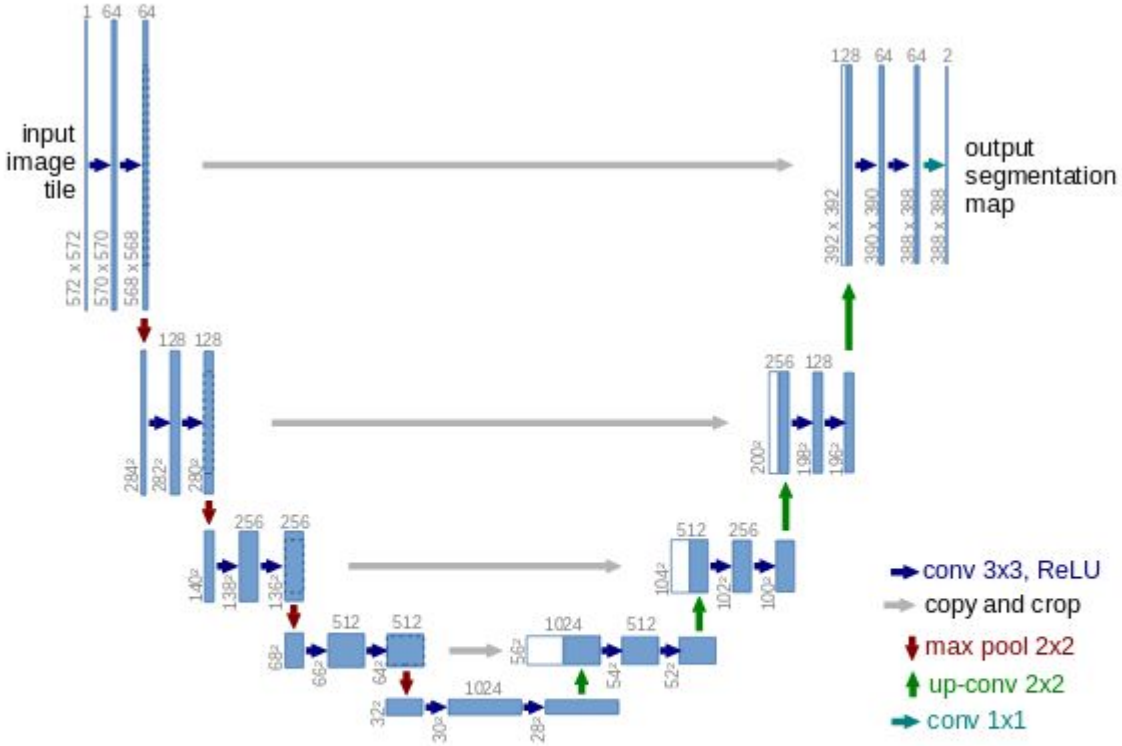
U-Net

Semantic Segmentation algorithm

U-Net
Architecture



Source: https://arxiv.org/pdf/1505.04597.pdf

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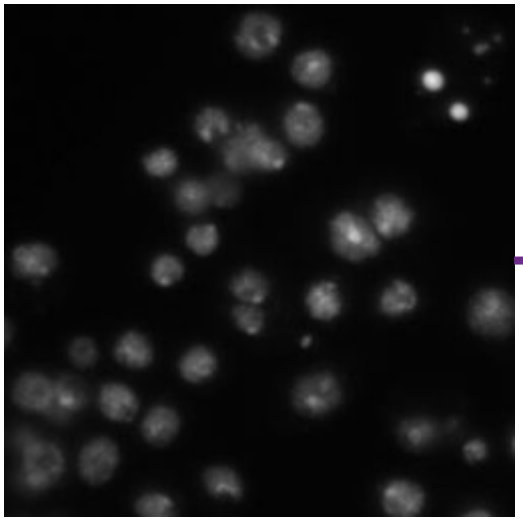
Instance segmentation

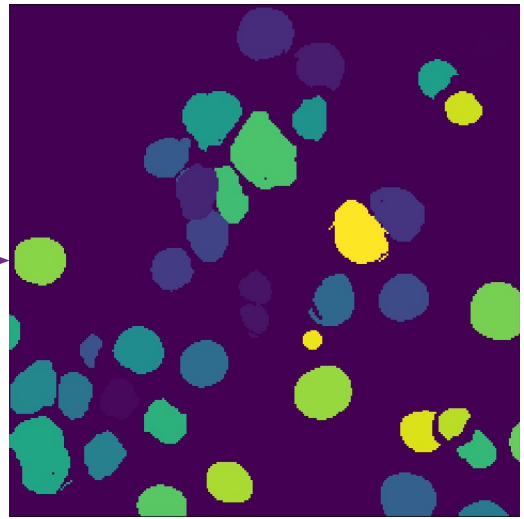
Instance and Semantic segmentation

Instance

Image



Mask



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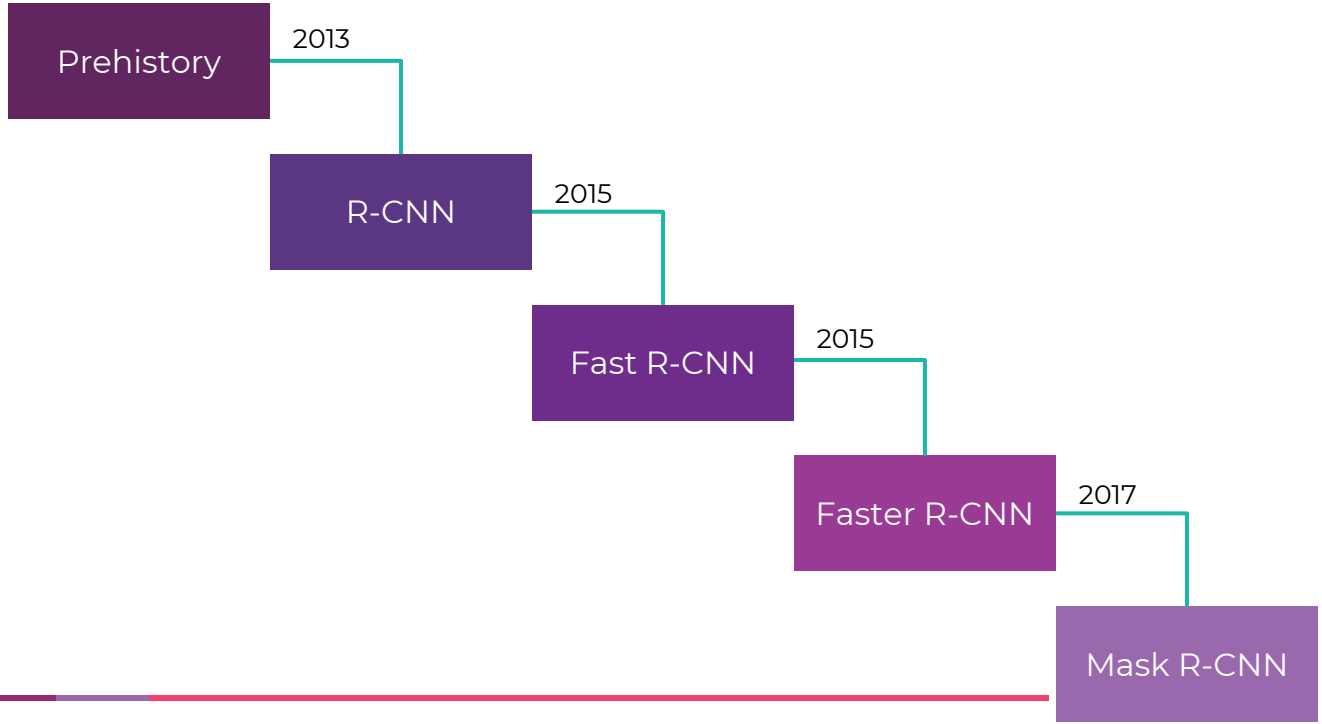
Mask R-CNN

Instance Segmentation algorithm

Mask R-CNN

History of the model

Milestones leading to Mask R-CNN developed by Facebook AI:



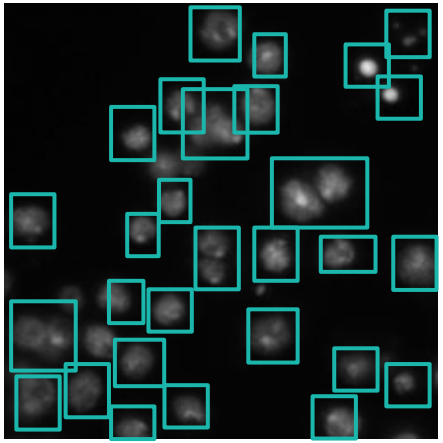
Mask R-CNN

R-CNN

Key steps of the model:

- Region proposals (Selective Search)
- Feature extraction (AlexNet)
- Classifiers (SVM)

Image with Region Proposals



Mask R-CNN

R-CNN

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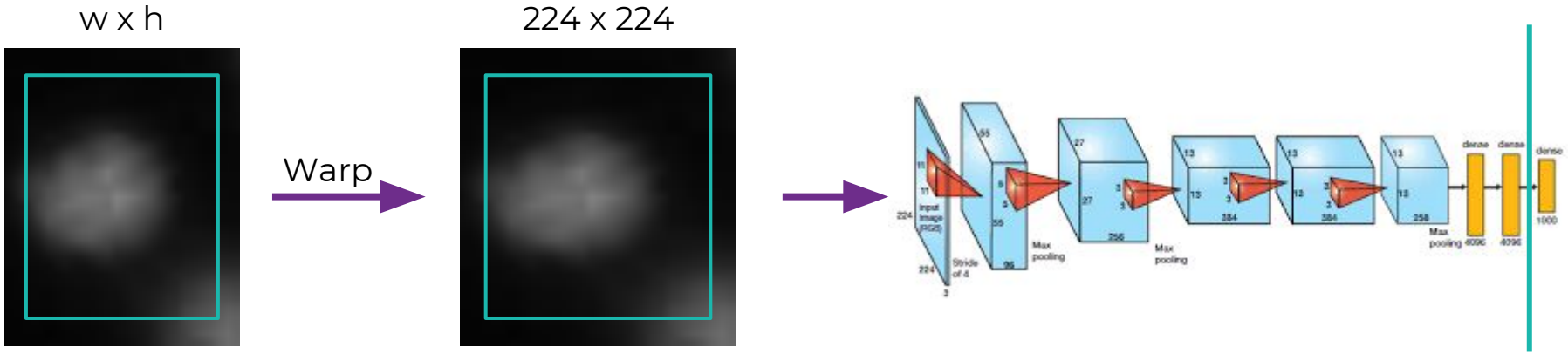

Source: CV-Tricks.com

Mask R-CNN

Fast R-CNN

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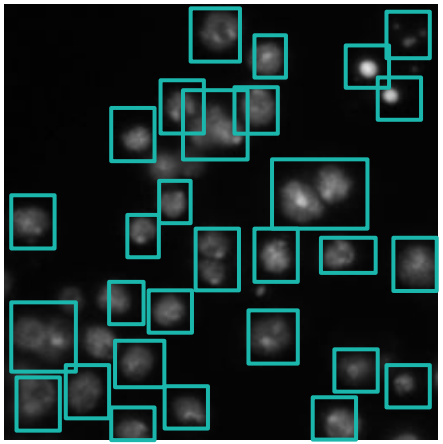
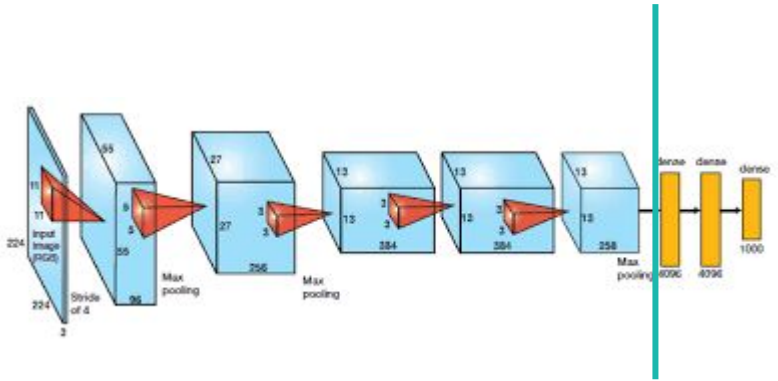
Enhancement:

- Whole image is passed to a network
- End to end training

Image with Region Proposals





Source: CV-Tricks.com

Mask R-CNN

Fast R-CNN

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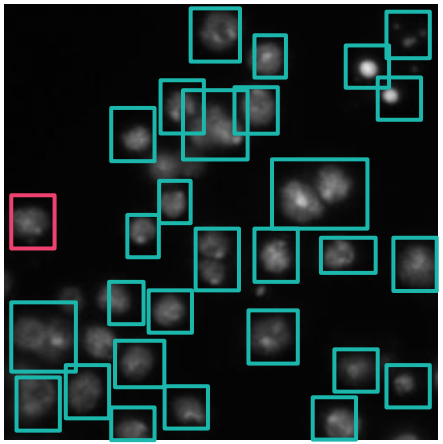
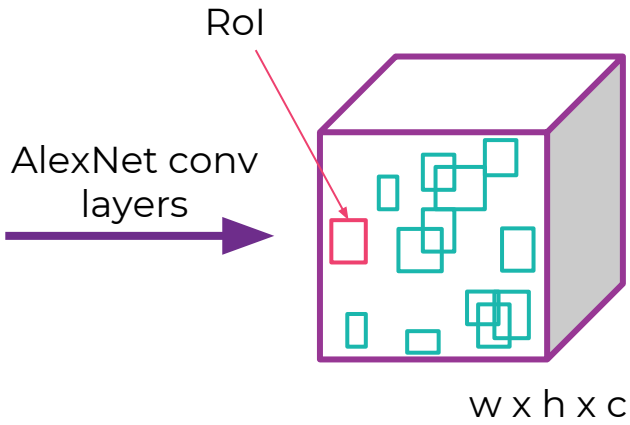
Image with Region Proposals



AlexNet conv layers



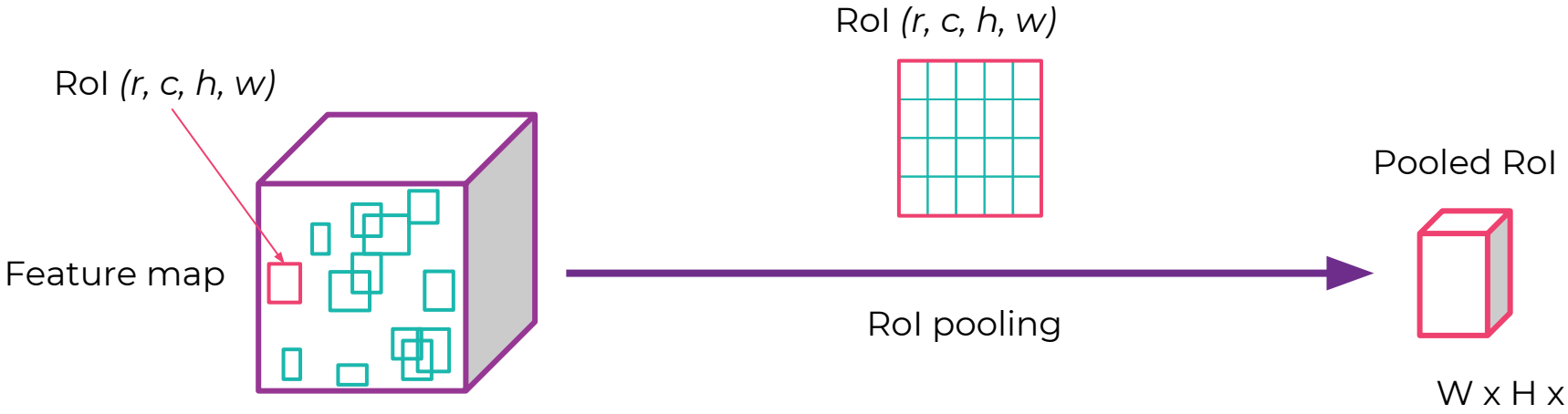
Feature map

Mask R-CNN

Fast R-CNN

Enhancement:

- Whole image is passed to a network
- End to end training



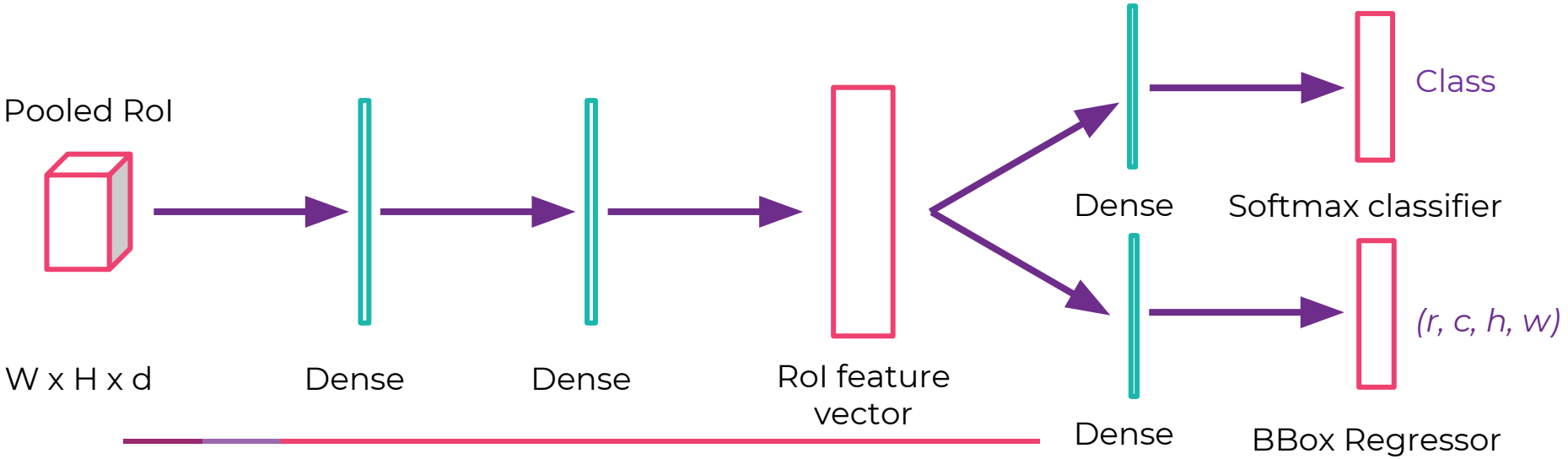
Mask R-CNN

Fast R-CNN

ardigen

Enhancement:

- Whole image is passed to a network
- End to end training



Mask R-CNN

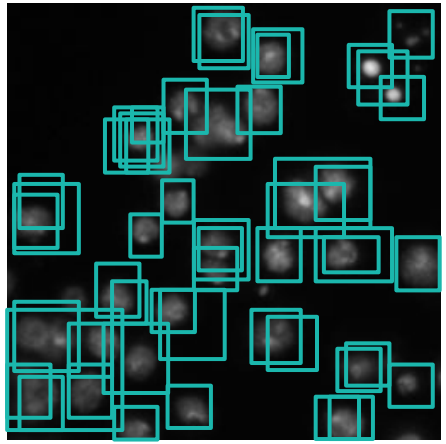
Fast R-CNN

ardigen

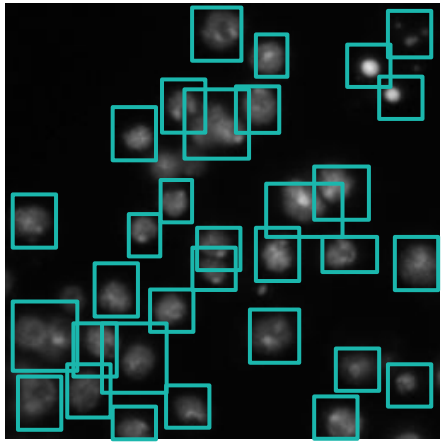
Enhancement:

- Whole image is passed to a network
- End to end training

Image with Region Proposals



NMS
IoU threshold

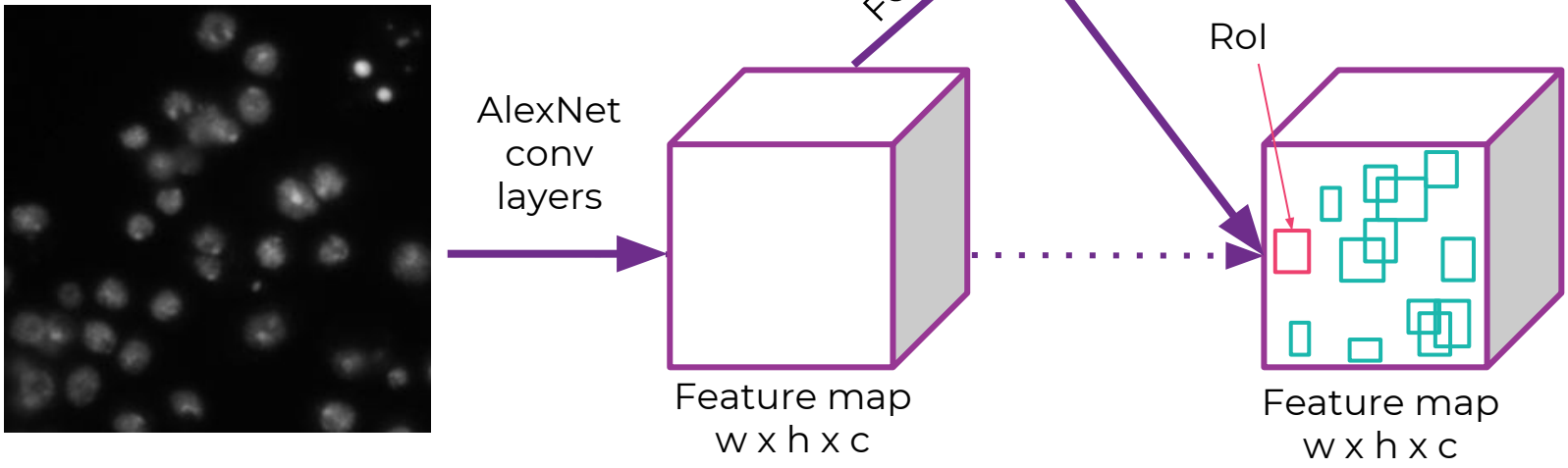


Mask R-CNN

Faster R-CNN

Enhancement:

- Region Proposal Network
- Anchors

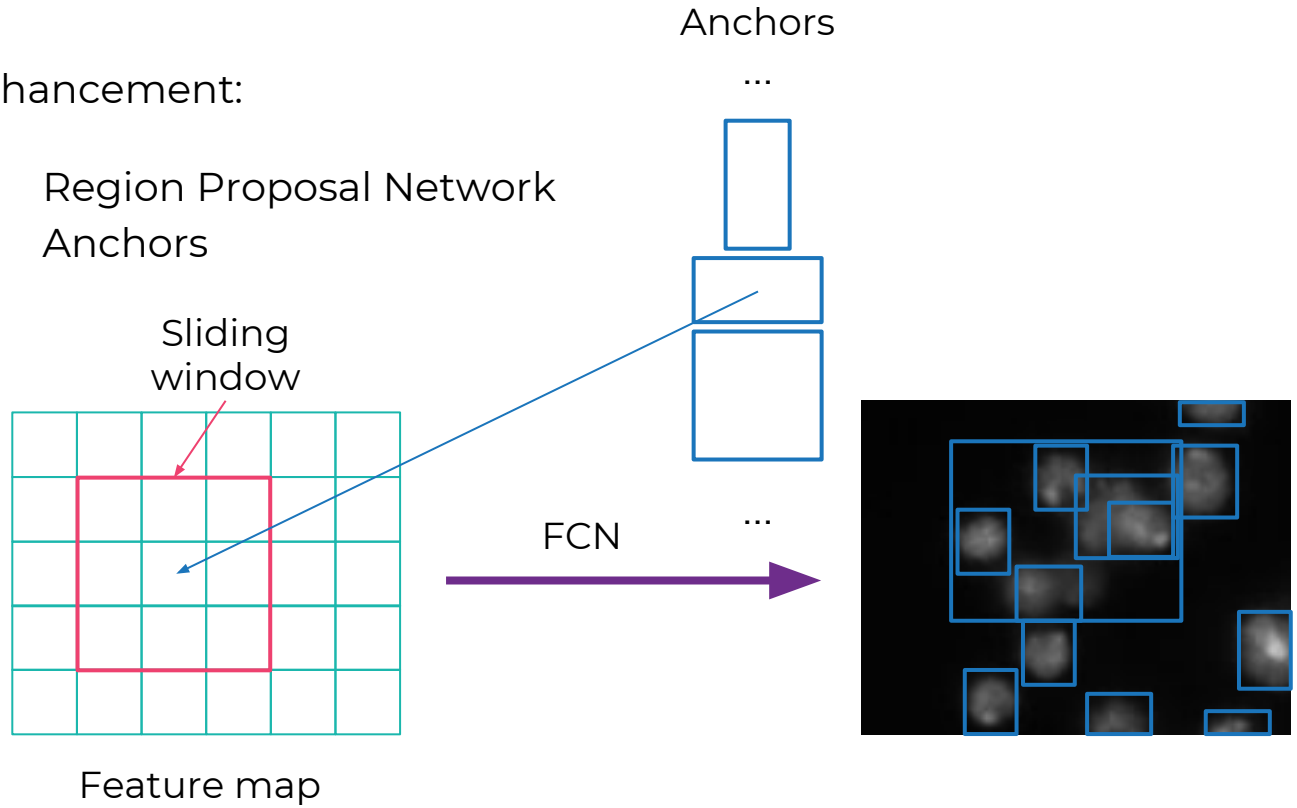


Mask R-CNN

Faster R-CNN

Enhancement:

- Region Proposal Network
- Anchors

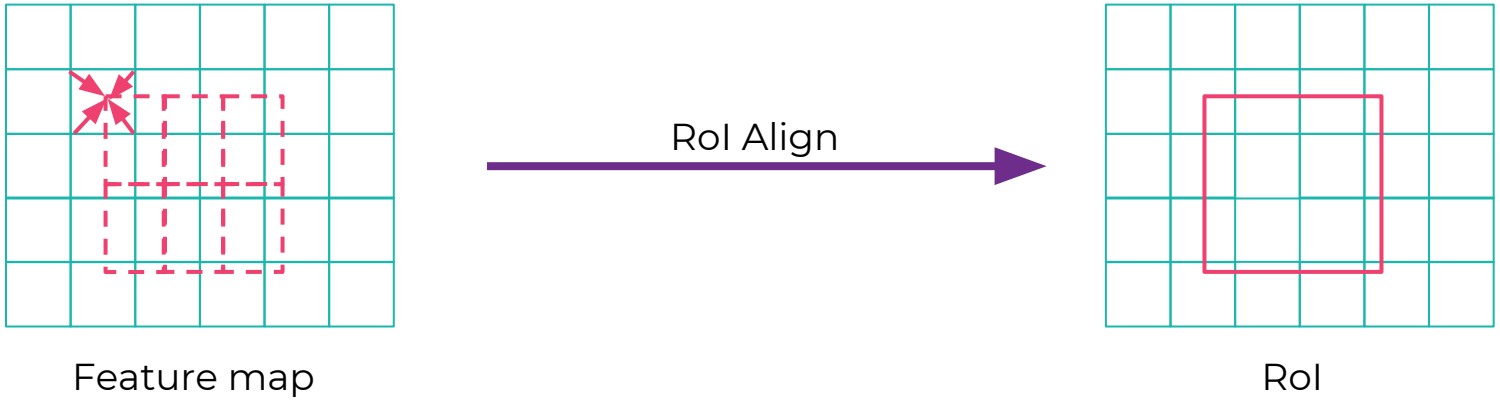


Mask R-CNN

Mask R-CNN

Enhancement:

- Multi task for mask generation
- RoI Align

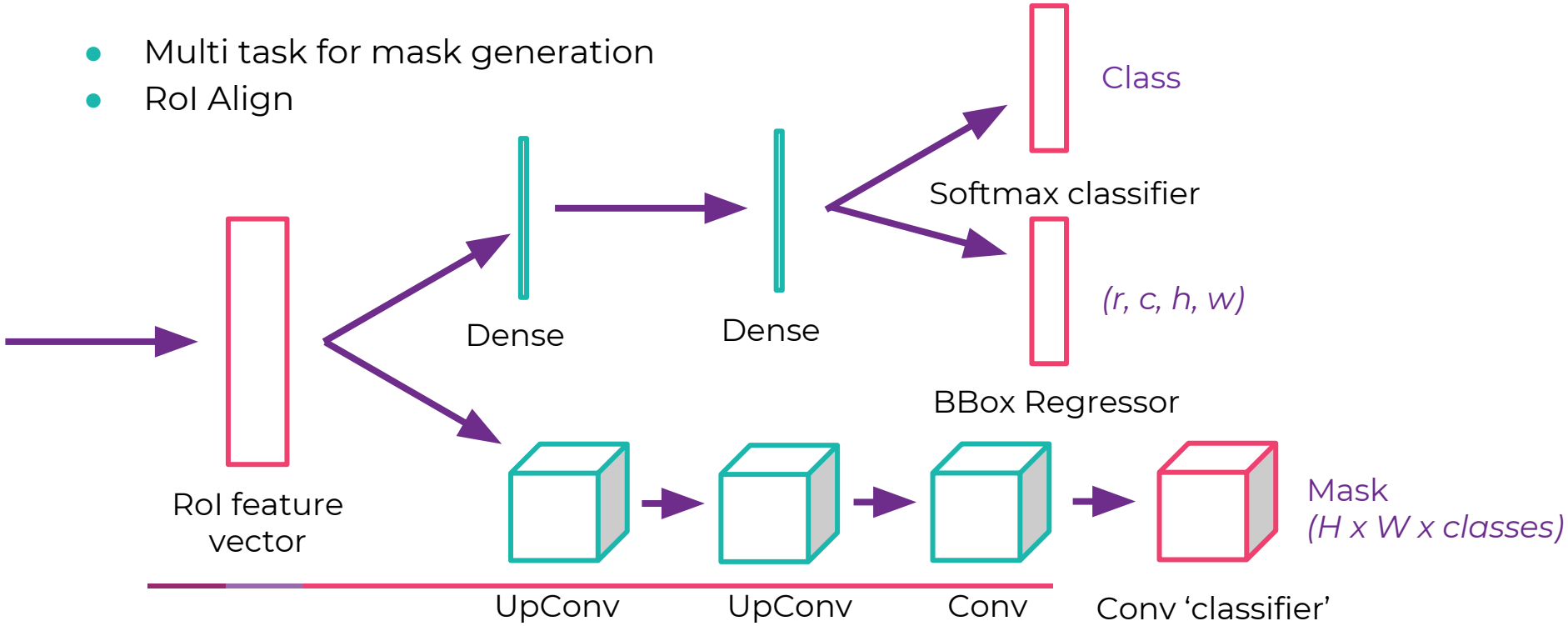


Mask R-CNN

Mask R-CNN

Enhancement:

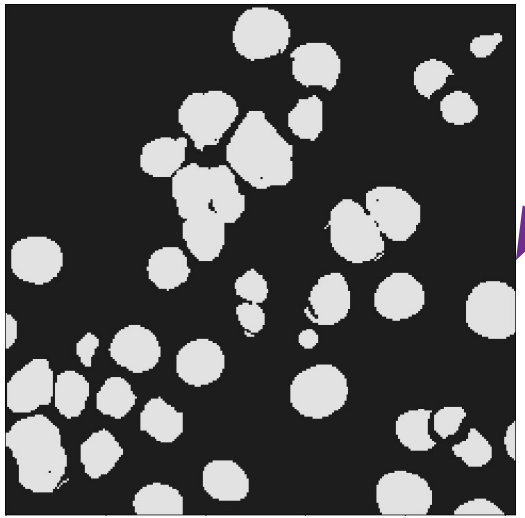
- Multi task for mask generation
- RoI Align

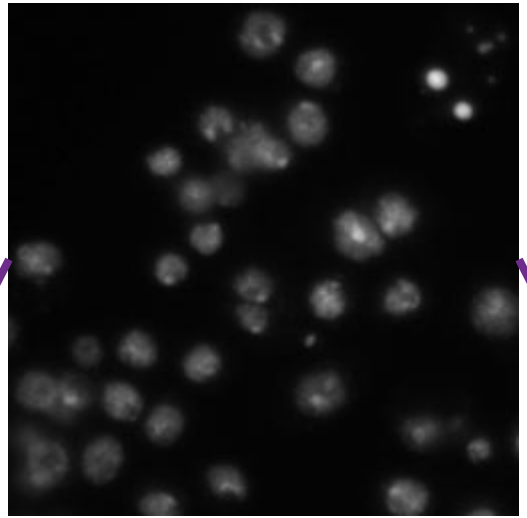


Instance and Semantic segmentation

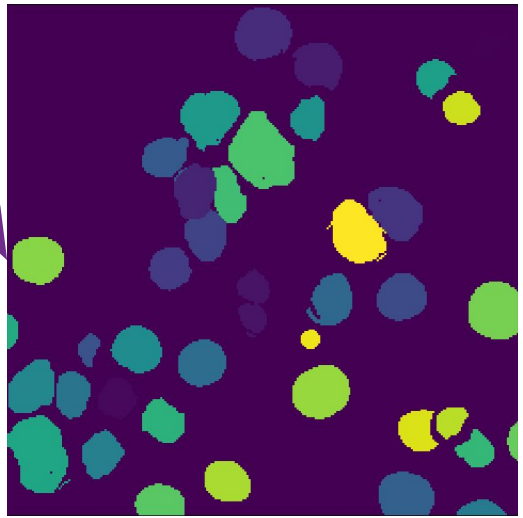
Comparison

Semantic





Instance



Instance and Semantic segmentation

Comparison

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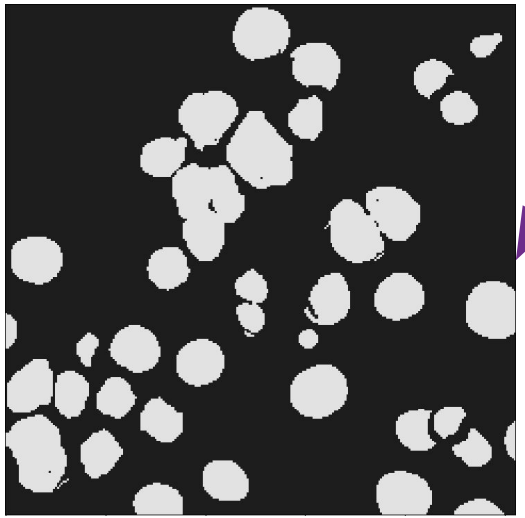
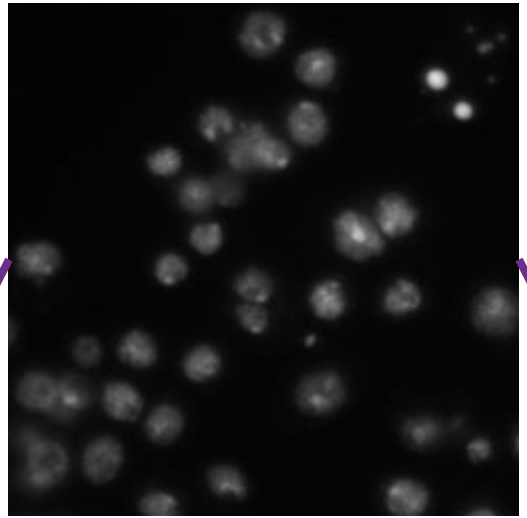
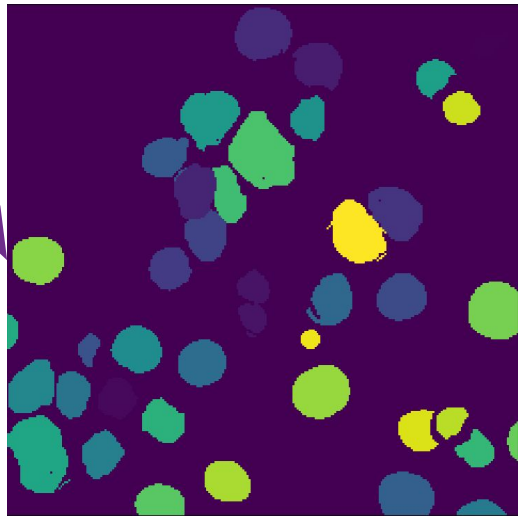
Semantic





Instance



Which approach was the winning one?

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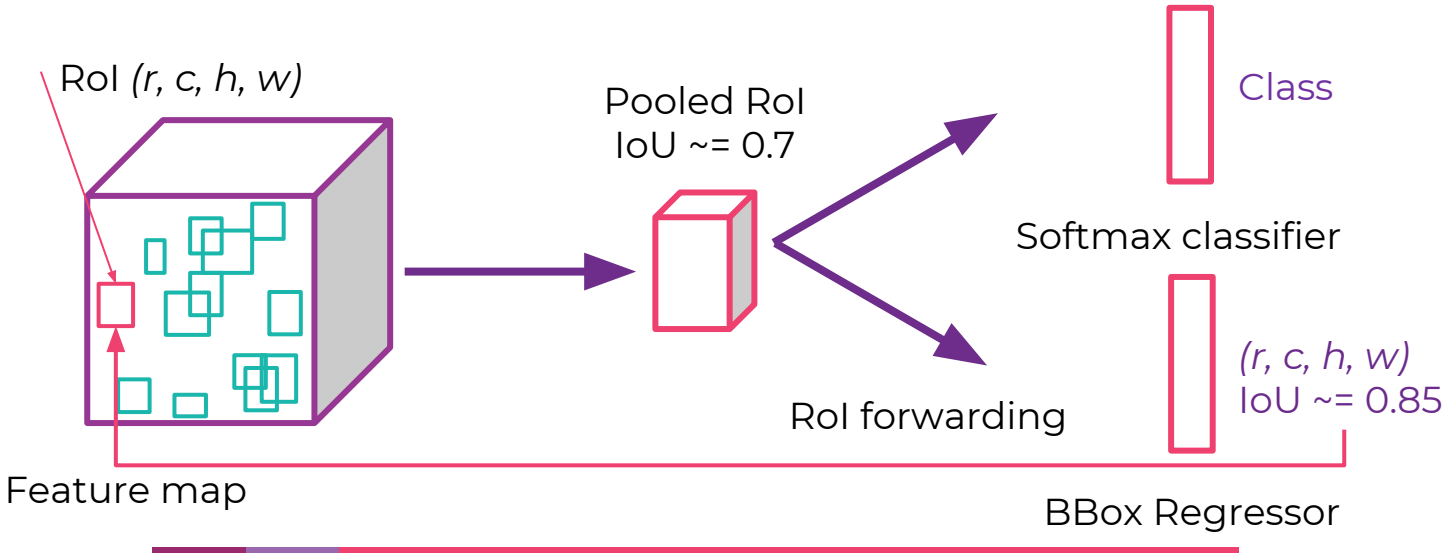
General enhancements

General enhancements

Cascade R-CNN

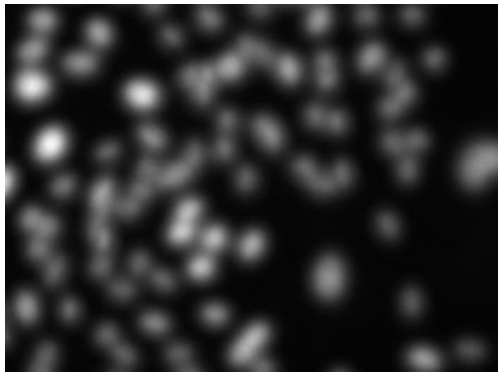
Enhancement:

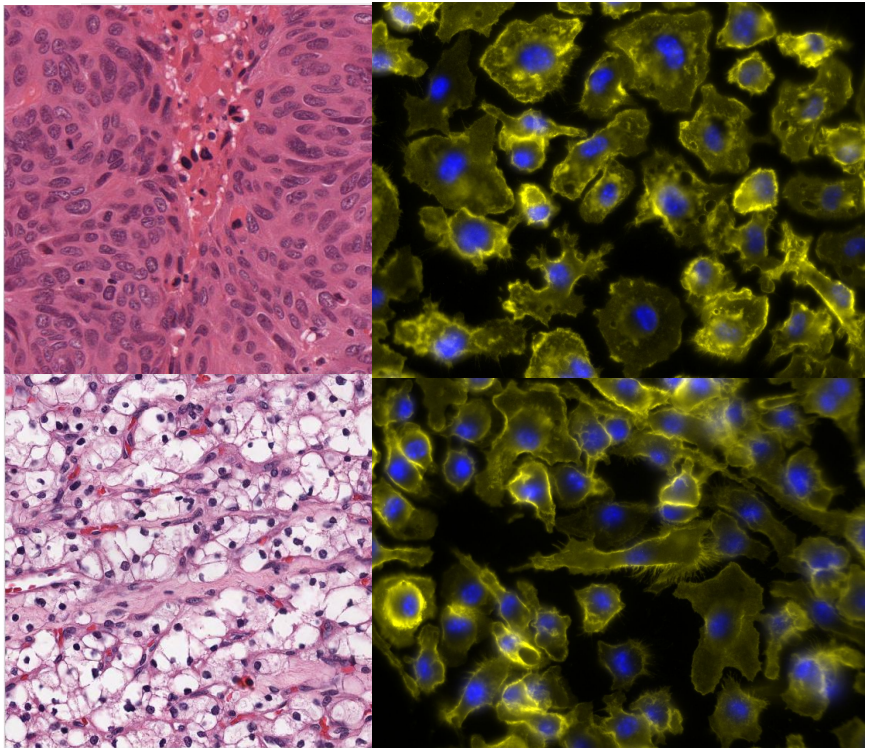
- Prevention of overfitting for different IoU threshold



External Data

- Hematoxylin and eosin (H&E) stain [https://nucleisegmentationbenchmark.weebly.com/]
- Broad Bioimage Benchmark Collection [https://data.broadinstitute.org/bbbc/image_sets.html]
  - Human U2OS cells (out of focus)
  - Bone-marrow derived macrophages from C57BL/6 mice

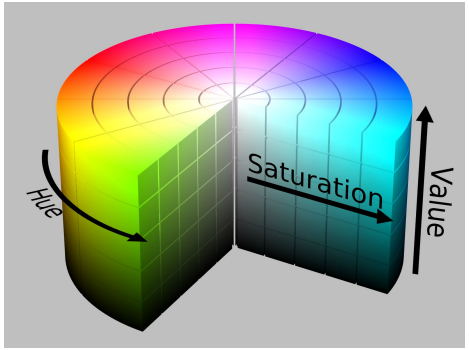




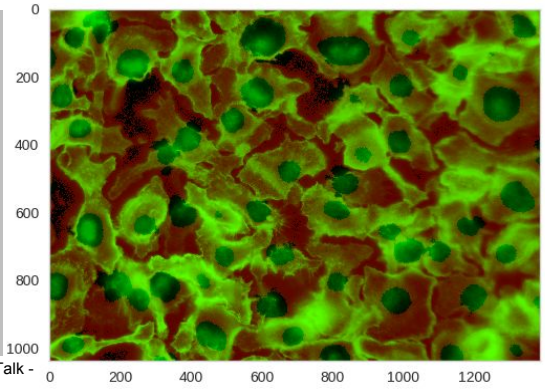
NORMALIZATION

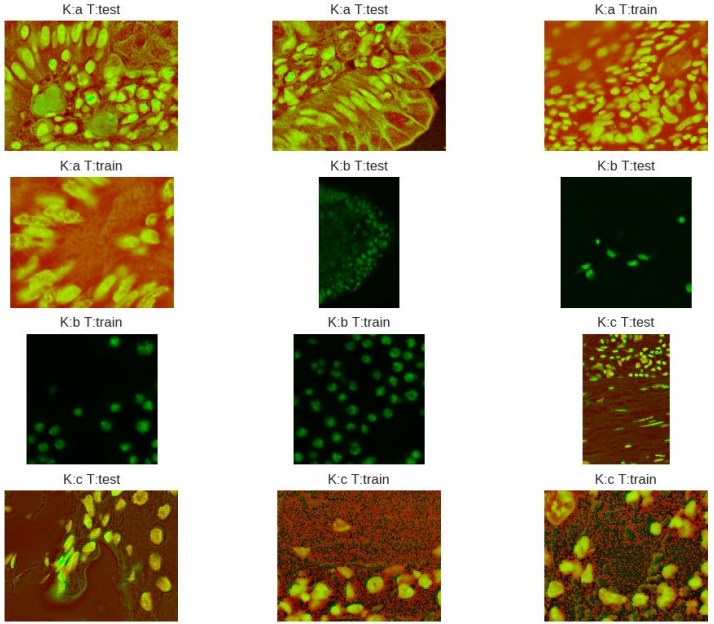
How **not** to train a separate NN for each image type

- Use CLAHE (Contrast Limited Adaptive Histogram Equalization):
  - BGR → LAB (L - lightness)
  - CLAHE on L channel
  - Use only the L channel
- Add H-channel from HSV to account for the contrast in color



By HSV_color_solid_cylinder.png: SharkDderivative work: SharkD Talk - HSV_color_solid_cylinder.png, CC BY-SA 3.0, https://commons.wikimedia.org/w/index.php?curid=9801673





Test Time Augmentation

Testing matters too

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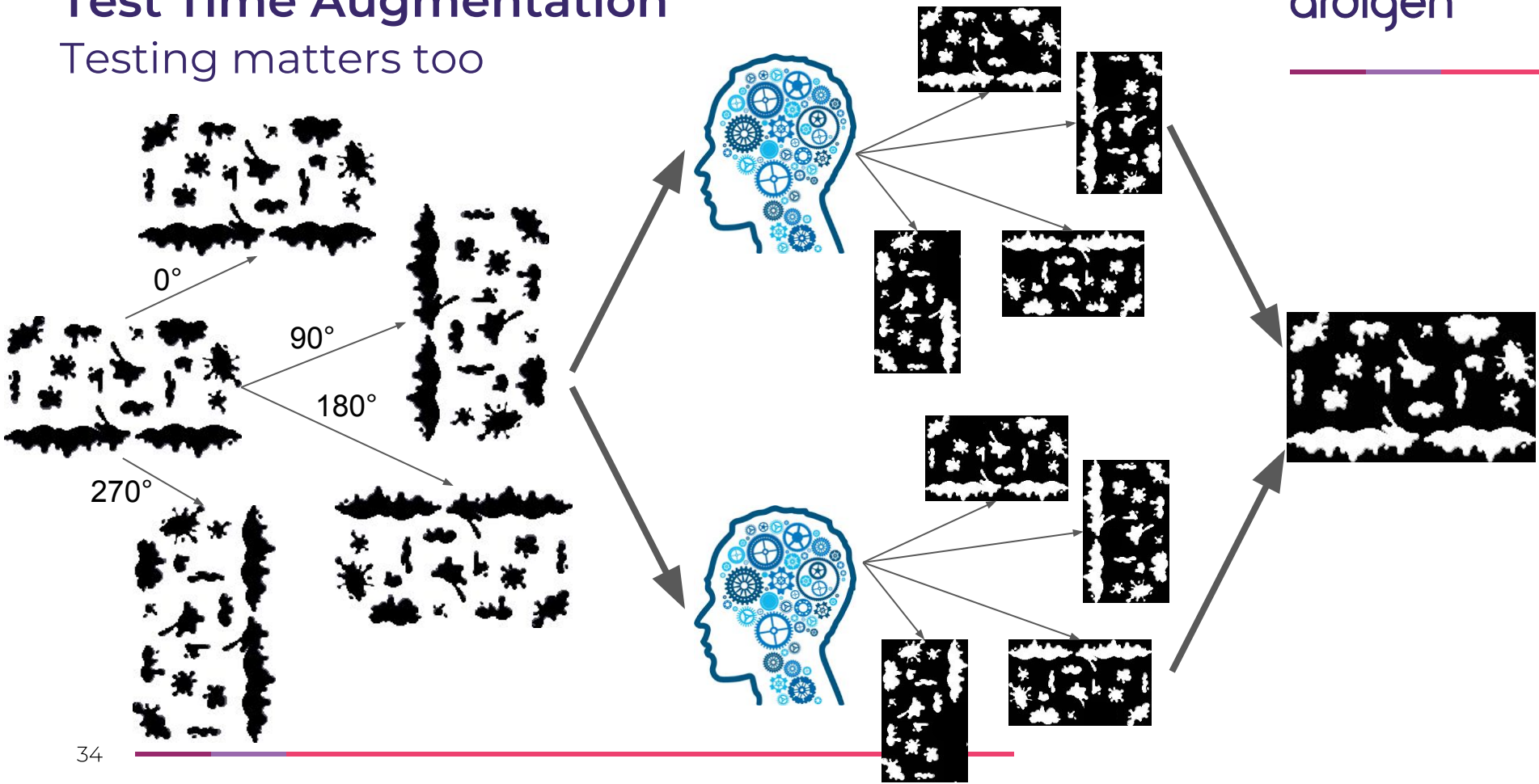
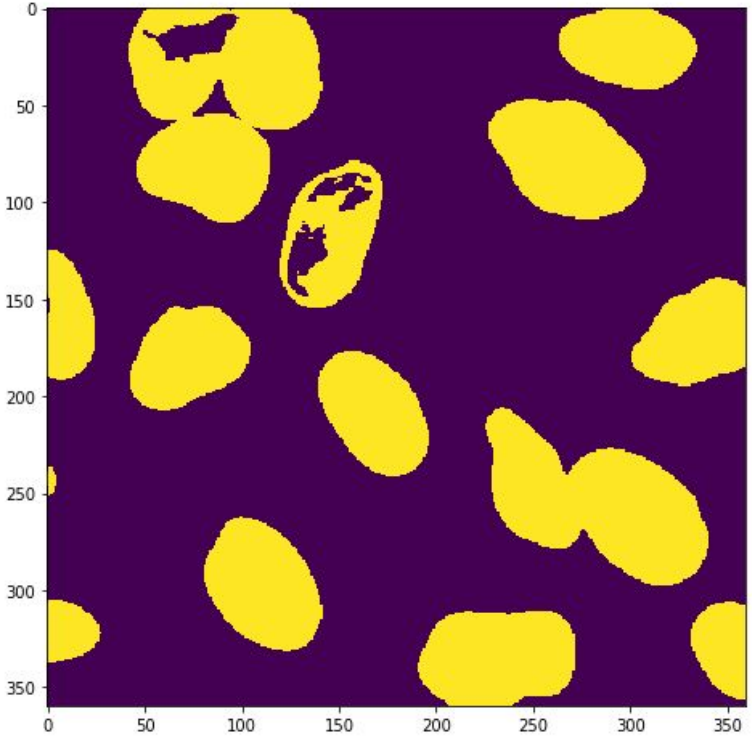
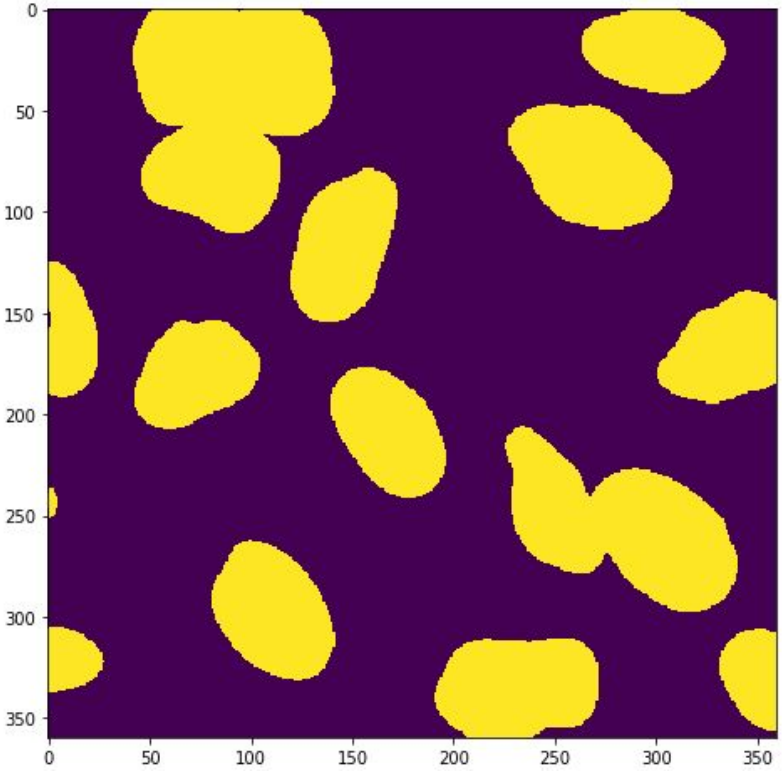


Post Processing

Filling holes and closing

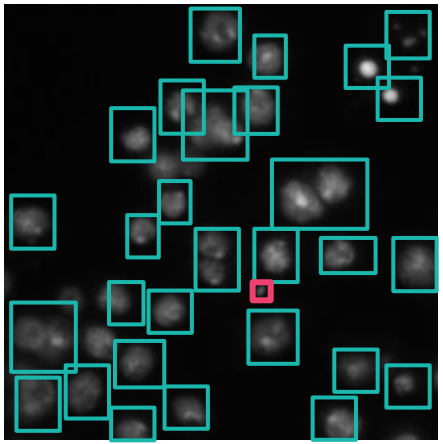




General enhancements

Other

1. Effective use of dilated convolutions
2. Focal Loss function
3. Different mask sizes
4. Data balancing
5. Auxiliary tasks
6. Data augmentation



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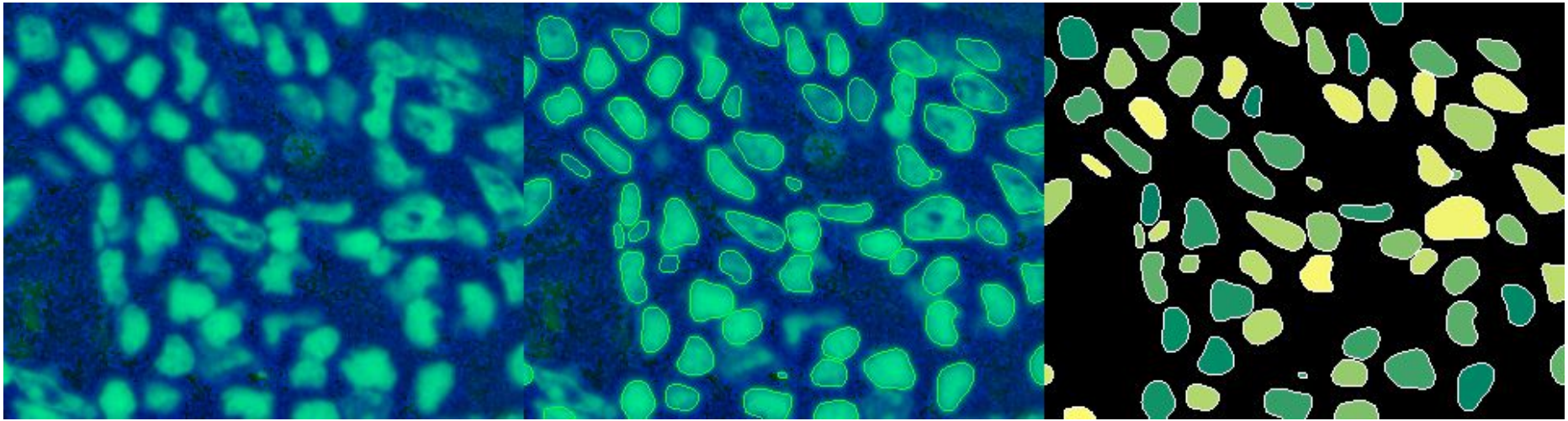
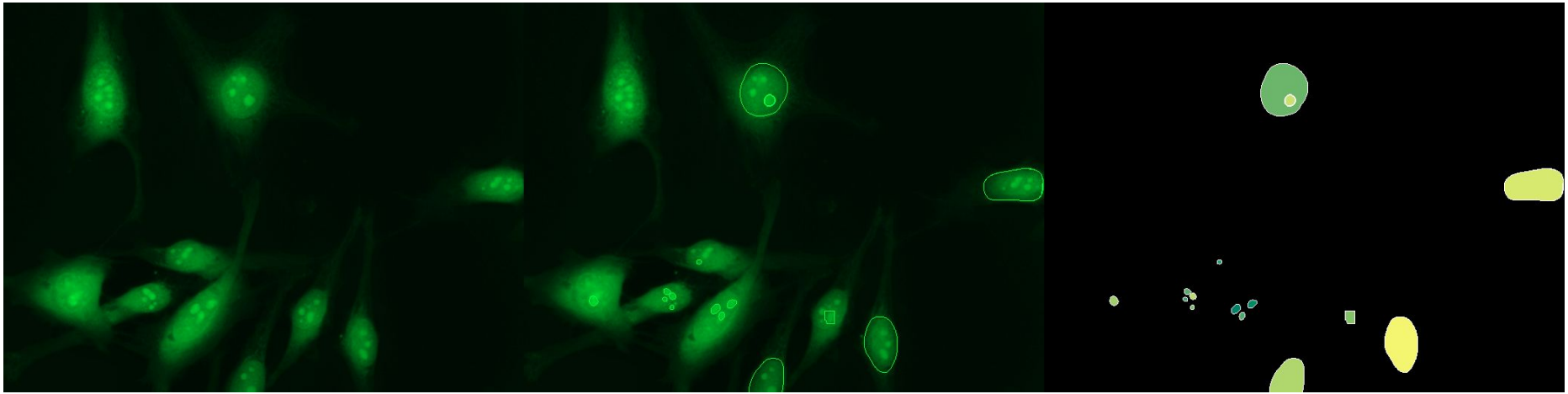
Examples of results

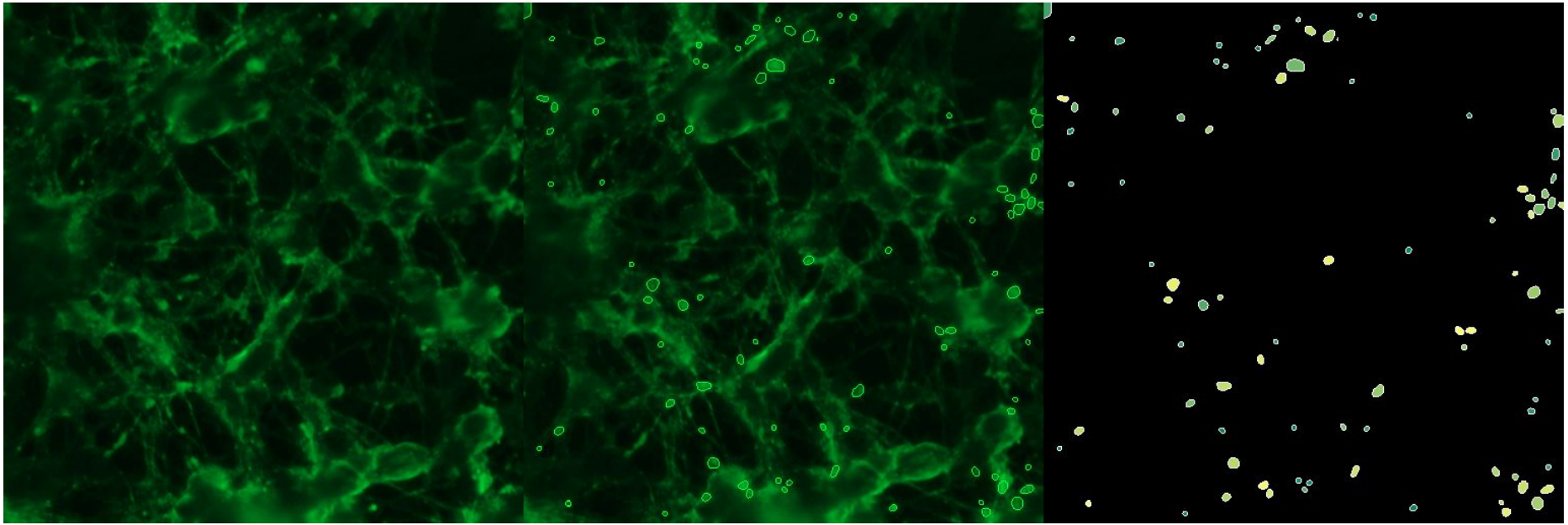
Our results
Visualization



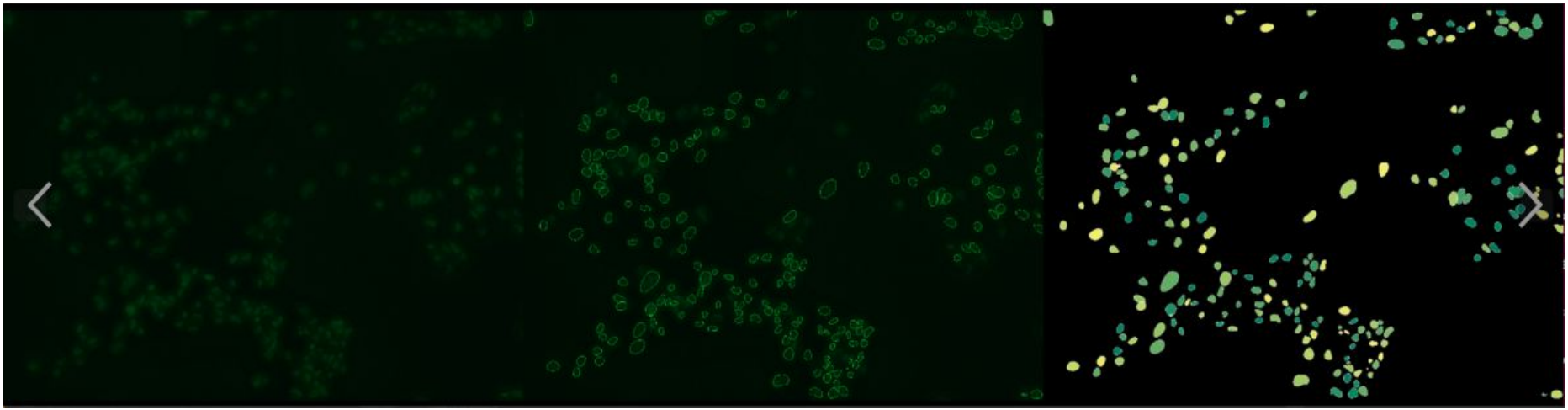
Our results
Visualization



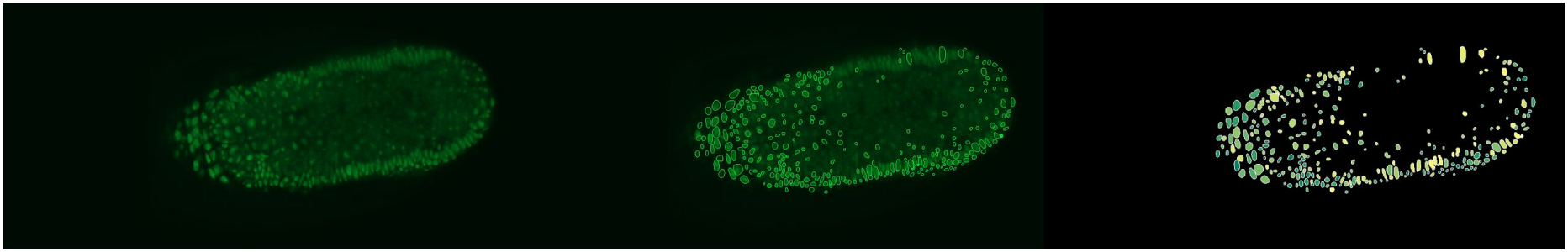
Our results
Visualization



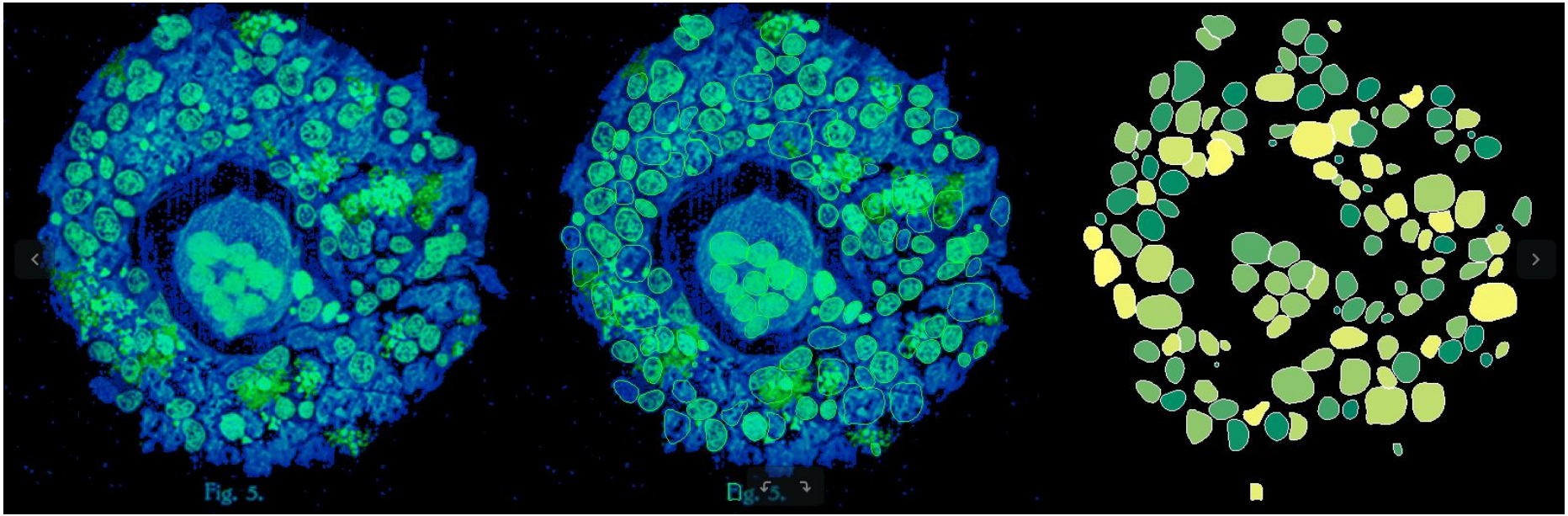
Our results
Visualization



Our results
Visualization



Our results
Visualization



Results:
Top 9%
Bronze Medal
0.445

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Winning solution

And other interesting one

1st place U-Net on steroids LB: 0.631

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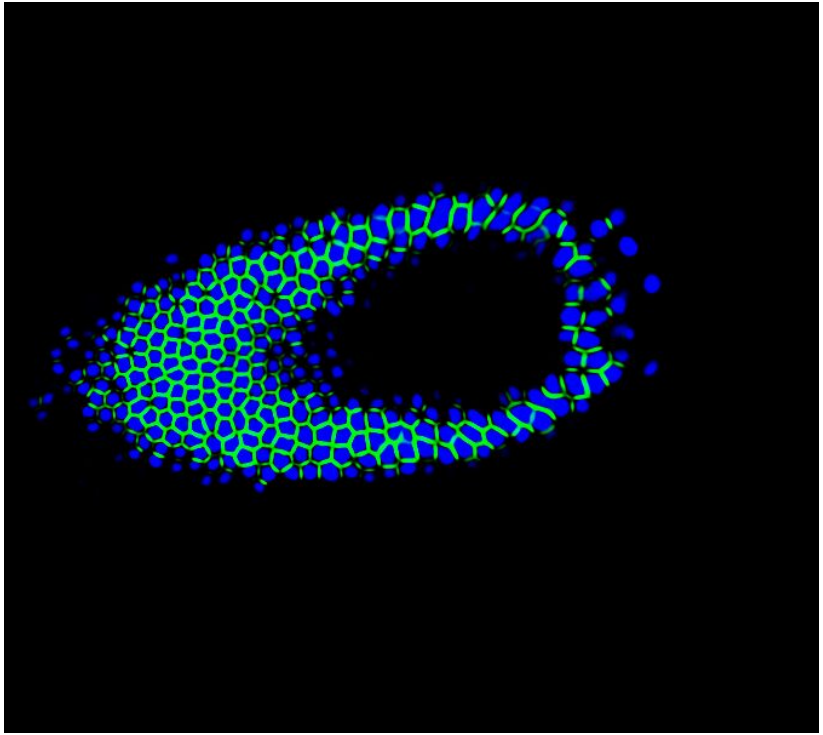
Auxiliary tasks and post processing, deep model and augmentations:

- Clahe, Sharpen, Emboss
- Gaussian Noise
- Color to Gray
- Inverting
- Remapping grayscale to random color images
- Blur, Median Blur, Motion Blur
- contrast and brightness
- random scale, rotates and flips
- Heavy geometric transformations
- Random HSV
- Channel shuffle
- Nucleus copying on images.



Source kaggle.com

Matterport's Mask R-CNN 3rd place LB: 0.614

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- Strong **scaling augmentation**, a lot of zooming in and out and aspect ratio changes.
- Test time augmentation: **15 different augmentations** at test time with different rotations, scalings, channel color shifts, etc. This takes a loooong time (aprox. 2 days for the stage_2 test set) and a **binary dilation post-processing** actually gives a very similar score,
- Matterport's TensorFlow implementation with pretrained weights from ImageNet.

Why U-Net and not Mask R-CNN?
Why Mask R-CNN and not U-Net?

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QA

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General enhancements

Effective use of dilated convolutions

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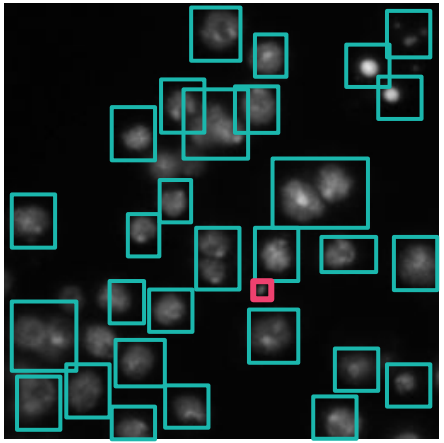
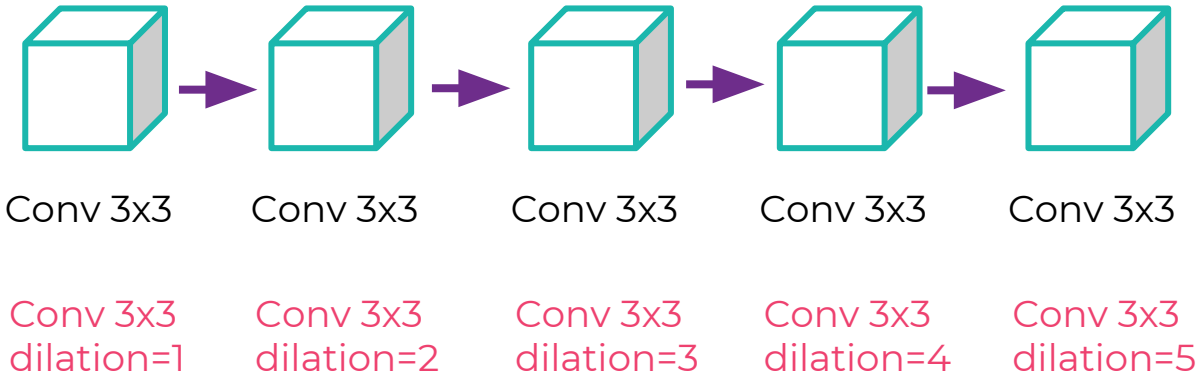
Enhancement:

- Get more context and detect micro nucleus

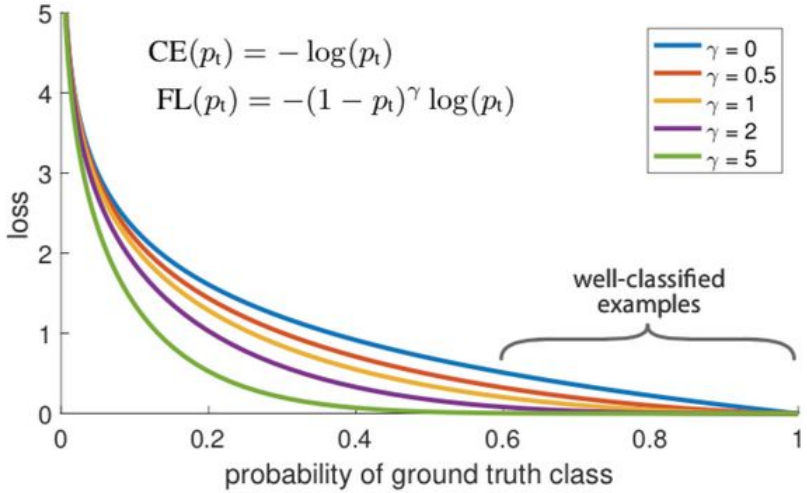




General enhancements
Focal Loss Function

Enhancement:

- Pay more attention to tricky examples



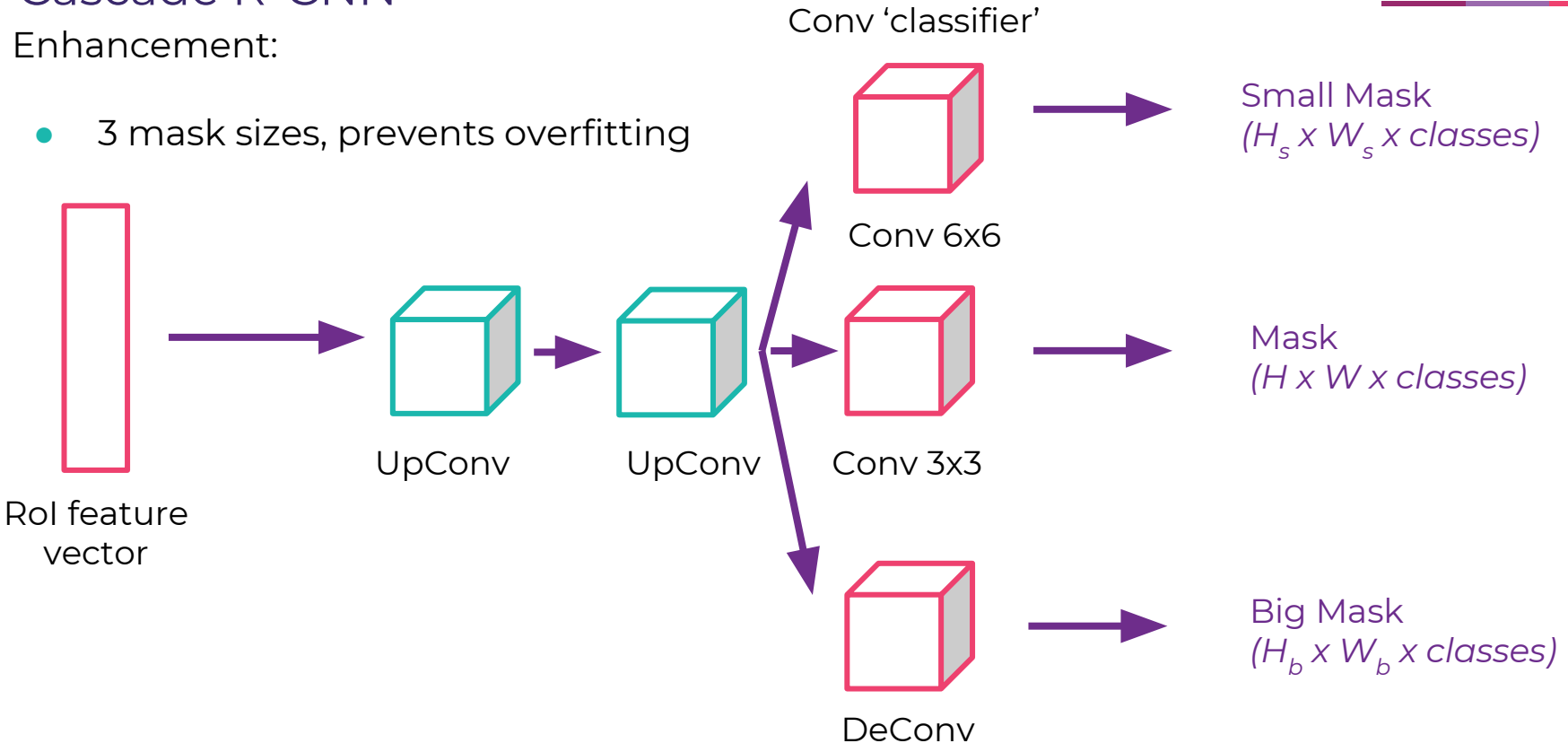
Source: https://arxiv.org/pdf/1708.02002.pdf

General enhancements

Cascade R-CNN

Enhancement:

- 3 mask sizes, prevents overfitting



Data balance

1. Training data were highly imbalanced
2. Moreover we used external data (that was a little bit different than training data)
3. We wanted to create the algorithm that could generalise well, in order to do that we decided to create weighted sampler
    a. Weight of every class from the training data was set to the square root of number of class samples
    b. Weight of every class from external data was set to the smallest weight from training data