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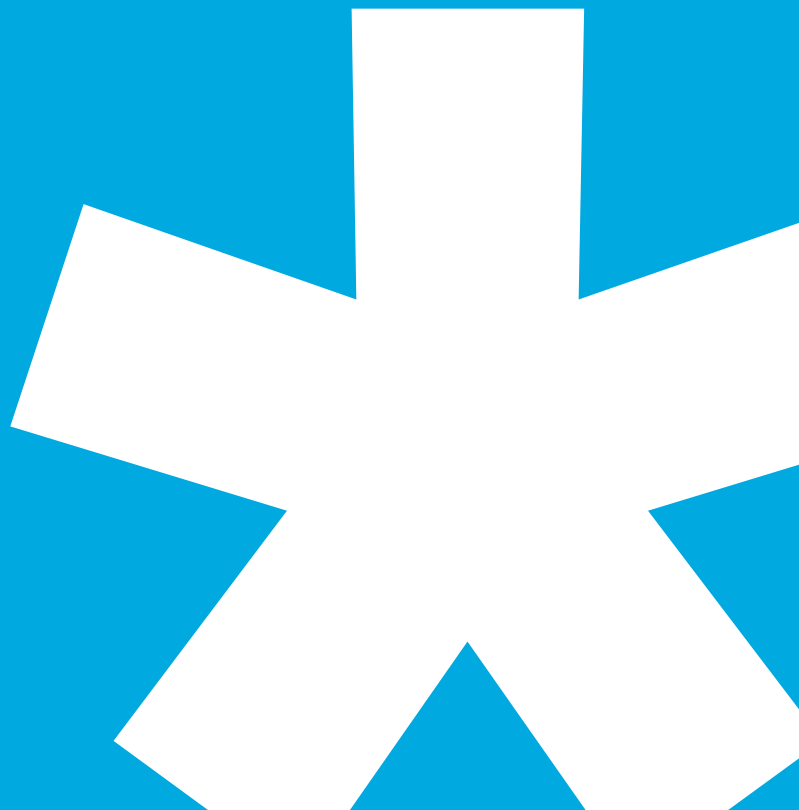
Nuclei Detection

Sangyu Shen



Agenda

1. Goals of the project
2. Segmentation – Semantic vs Instance
3. Unet Model
4. Mask RCNN Model
5. Model Result
6. Conclusion

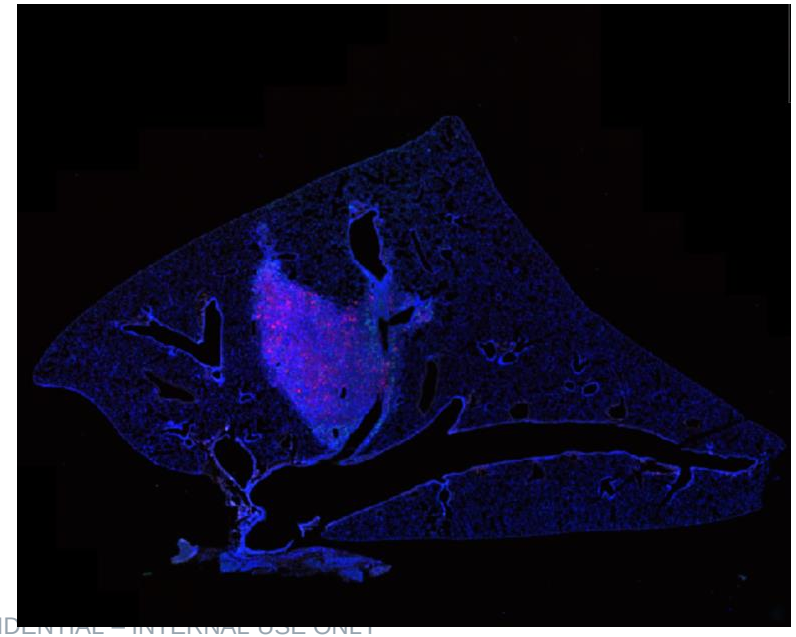
Goals

Nuclei Segmentation

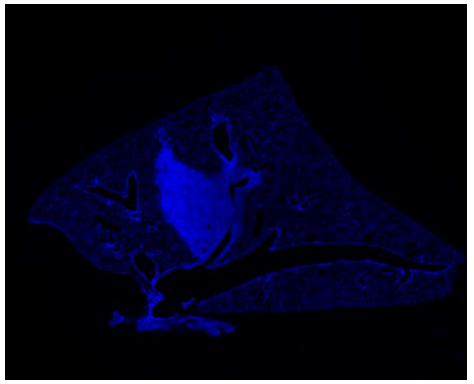
- **Project Goal:** Count and segment nuclei from microscope images

Counting cells

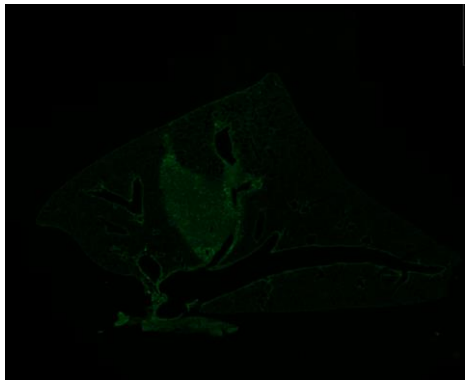
- The first step for many clinical purposes
- Enable extraction of high quality features for analysis in pathology



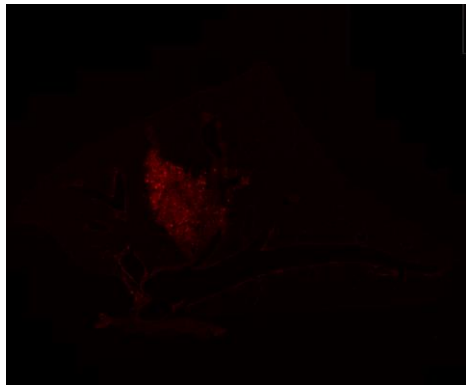
Fluorescently stained with different markers



DAPI: Nuclei



FITC: T cell



Cy3: Tumor

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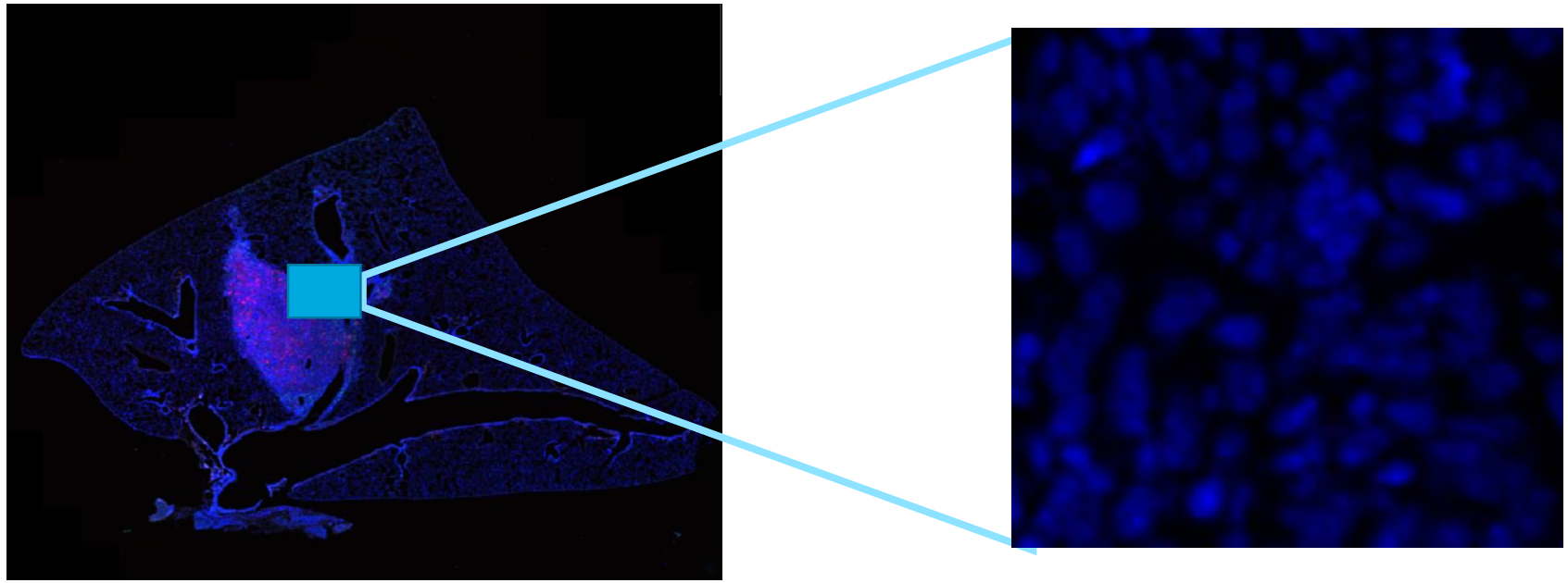
Nuclei Segmentation

- **Project Goal:** Count and segment nuclei from microscope images



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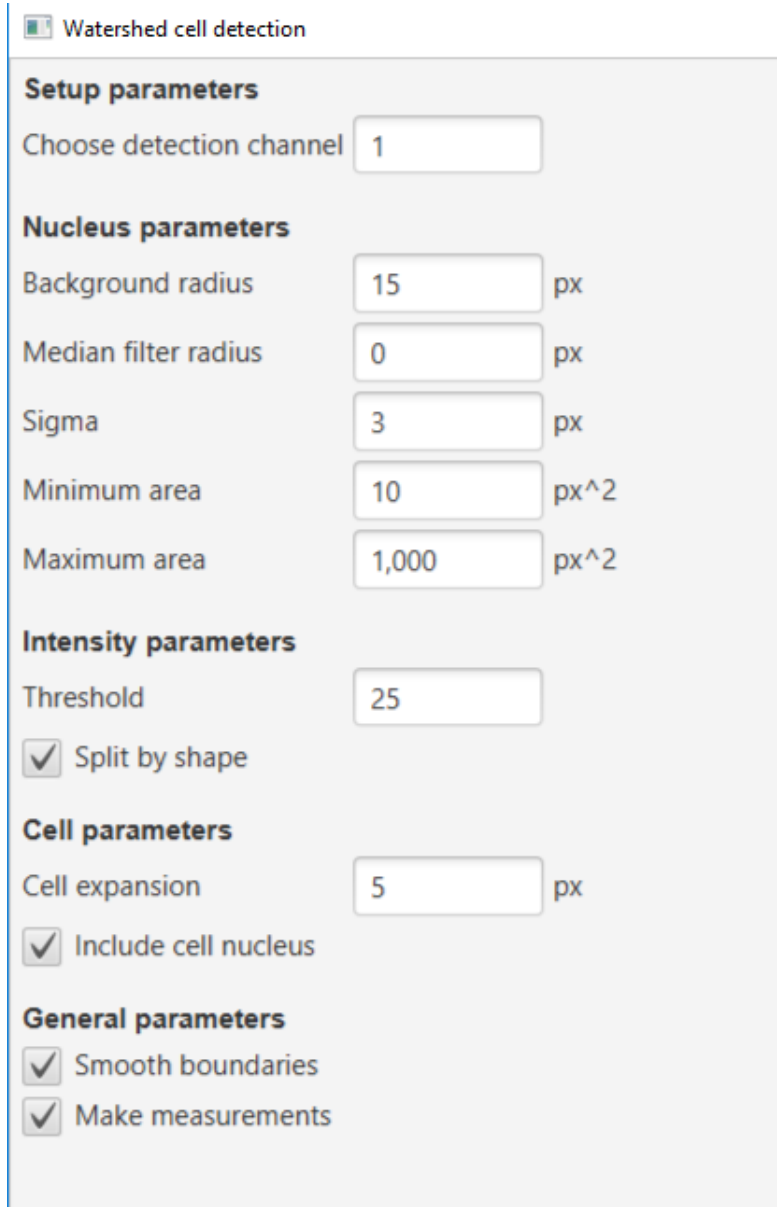
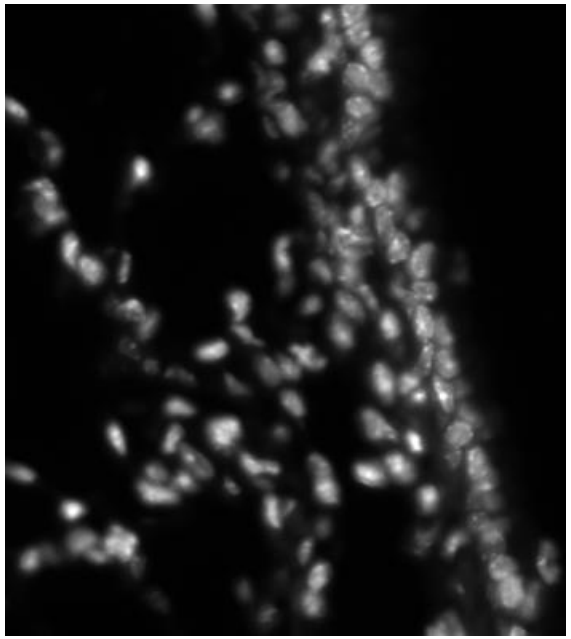
Previous Approach

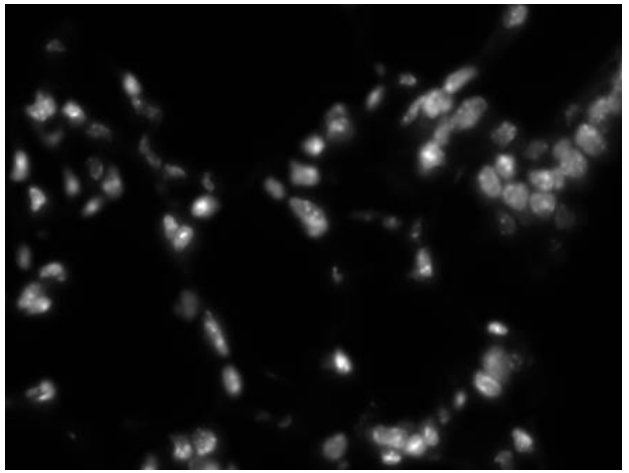
- QuPath
  - Open source software for quantitative pathology (scriptable)
  - Segment cells with filters and thresholds (traditional image processing)
  - Tunable parameters
  - Further analysis pipeline after segmentation



Challenges

- Manual counting
  - Time consuming
  - Labor intensive
  - Impossible to count a whole tissue slice
  - Difficult quality control – sampling and random errors
- Thresholding techniques
  - Various staining conditions, cell types
  - Difficult to count overlapping cells
  - No standard requirements
  - Threshold parameters: not one size fits all





Need new method – fast, robust, general

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Background

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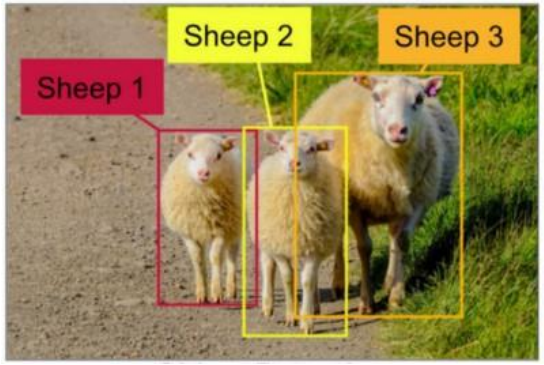
Image Processing Problem

- Classification

➡ CAT

- Object Detection

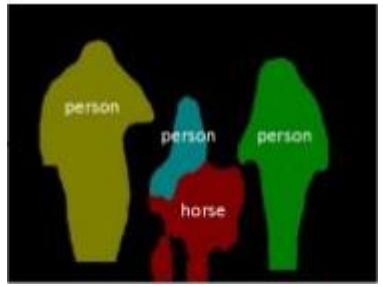


- Semantic Segmentation

➡

- Instance Segmentation

➡



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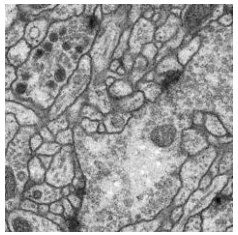
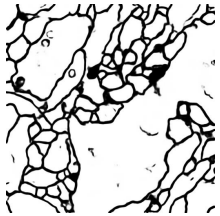
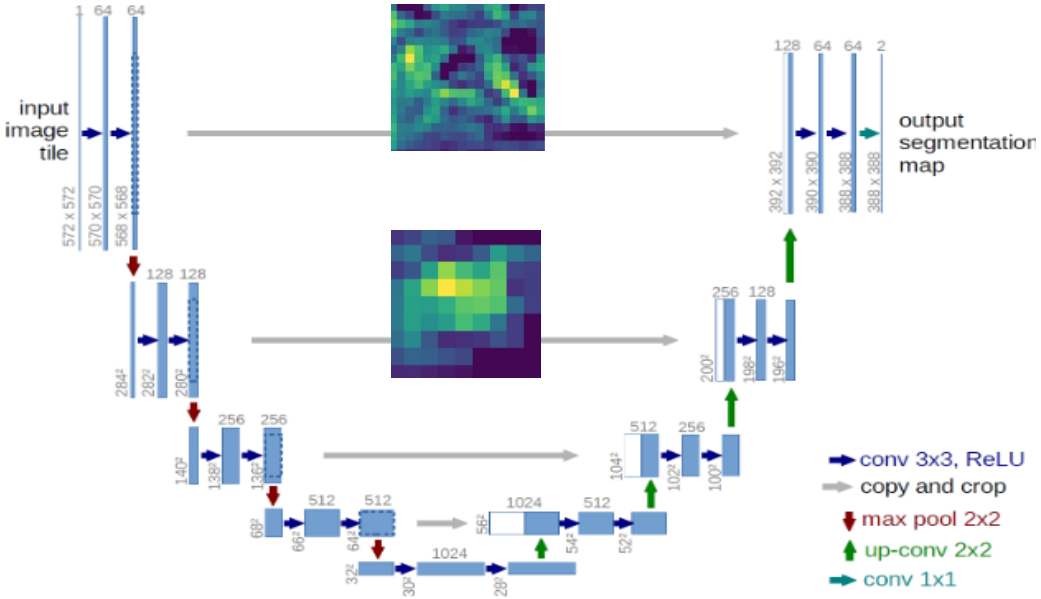
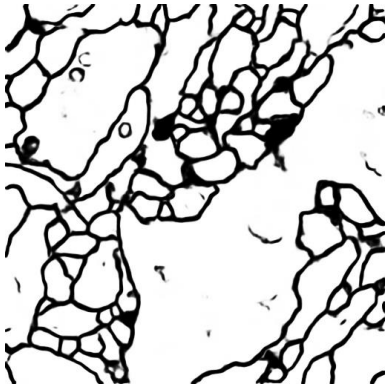
Segmentation Algorithm - Unet

- Unet algorithm – semantic segmentation
  - Convolutional Networks for Biomedical Image Segmentation
  - Created by Olaf Ronneberger, Philipp Fischer, Thomas Brox in 2015









  - Encoder: captures context from image
  - Decoder: enables precise localization

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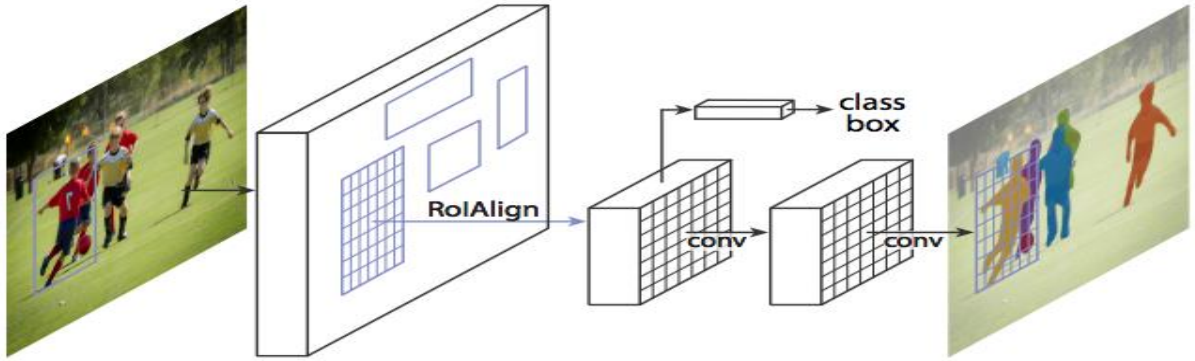
Segmentation Algorithm – Mask RCNN

- Mask R CNN algorithm – instance segmentation
  - Created by Facebook AI research, 2017
  - Generates bounding boxes and segmentation masks for each instance of an object in the image



  - Region Proposal Network: proposes candidate object bounding boxes
  - Feature Extraction and Prediction: extracts from each candidate box; classify and re-define bounding-box
  - Mask: also outputs a binary mask for each box

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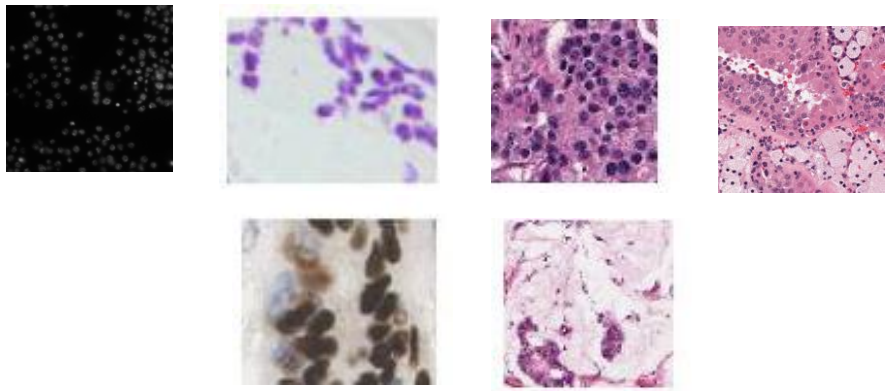
Methodology

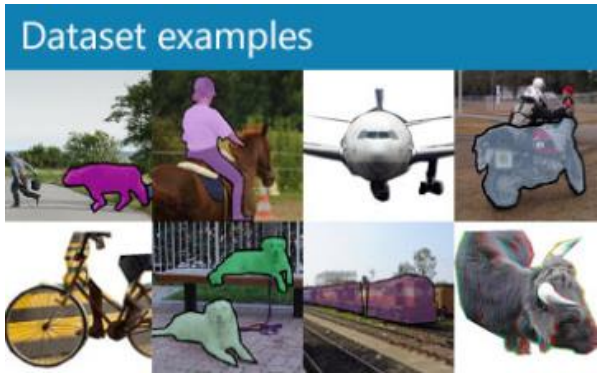
Nuclei Segmentation Training

- Dataset:
  - Booz Allen Hamilton Nuclei Segmentation Dataset
    - ~900 images with masks
    - a variety of conditions, e.g, cell type, magnification, and imaging modality (brightfield vs. fluorescence)



  - Augmentation:
    - horizontal or vertical flips
    - Random rotation: 90 or (-10, 10) degrees
    - Random resize image

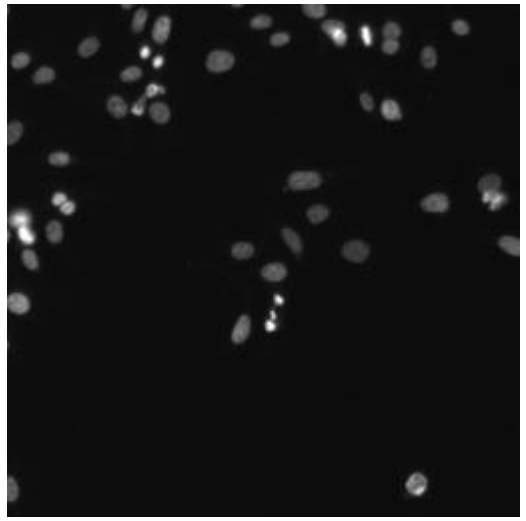
- Pre-train Weights:
  - Computed based on COCO dataset
  - Provided a better starting point



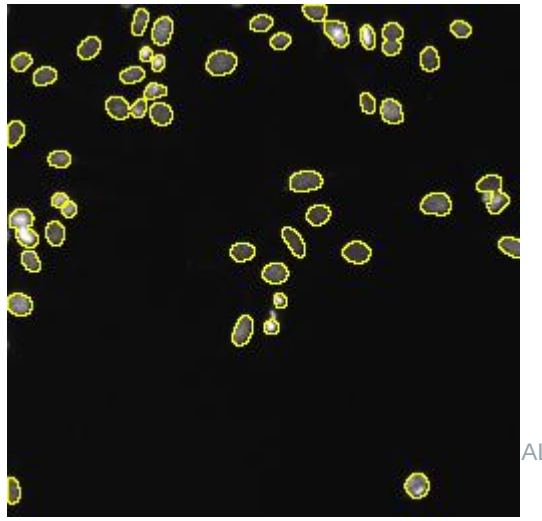
  - a large-scale object detection, segmentation, and captioning dataset.
  - 330K images (>200K labeled)
  - 1.5 million object instances
  - 80 object categories

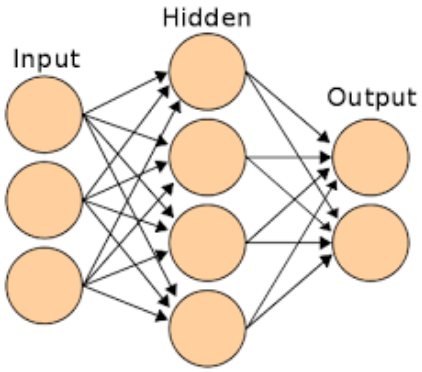
Nuclei Segmentation Training

Image



Ground Truth



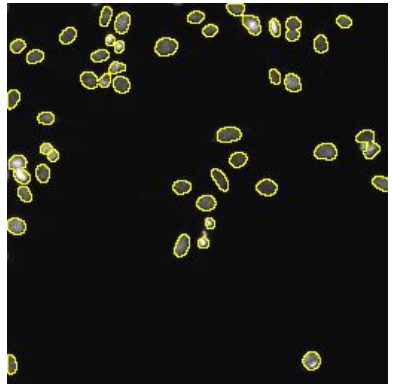


Prediction

Image ID	Pixels
Image-2019-01	59776 8 60126 12 60469 22 60820 24 61171 26 61523 27 61875 27 62227
Image-2019-01	5233 3 5583 7 5934 9 6286 9 6637 11 6989
…	…

rows = total cells

Mask Visualization



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Result

Nuclei Segmentation Training

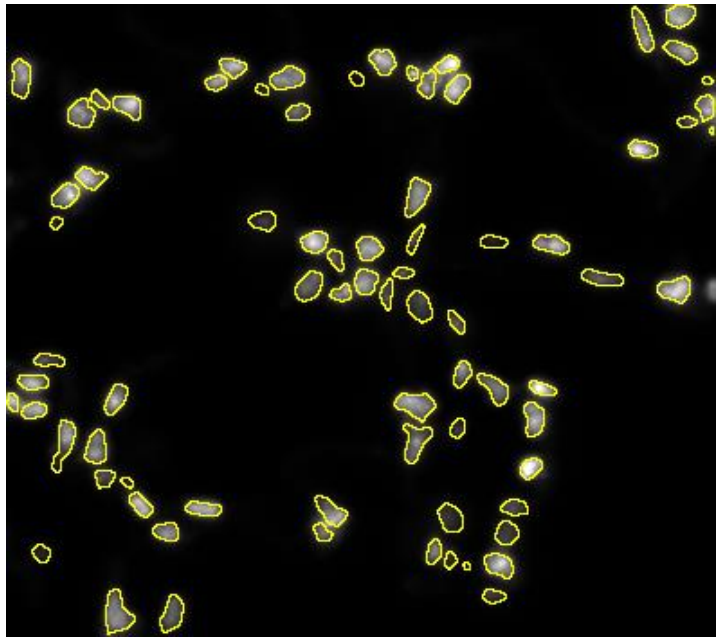
Model	Training Time	Prediction Time	Complete Prediction	# total cells
Unet	< 24 hours	~ 40s	~ 24 hours *	-
Mask RCNN	~ 2 days	<1s	~ 2.5 hours	~ 150,000 *

* Estimated – 6 batches in 3 hours (total 49 batches)

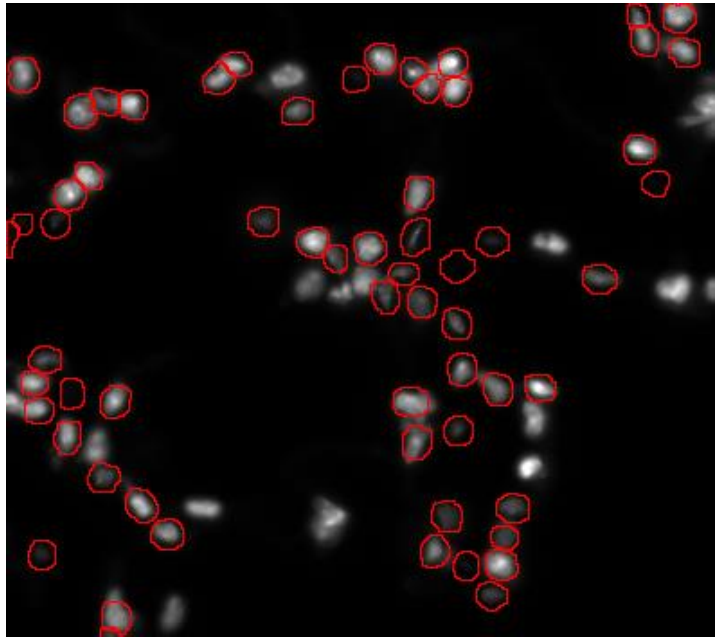
Execution: NVIDIA GK210 GPU 12GB

Testing – Outcome between Unet and Mask RCNN

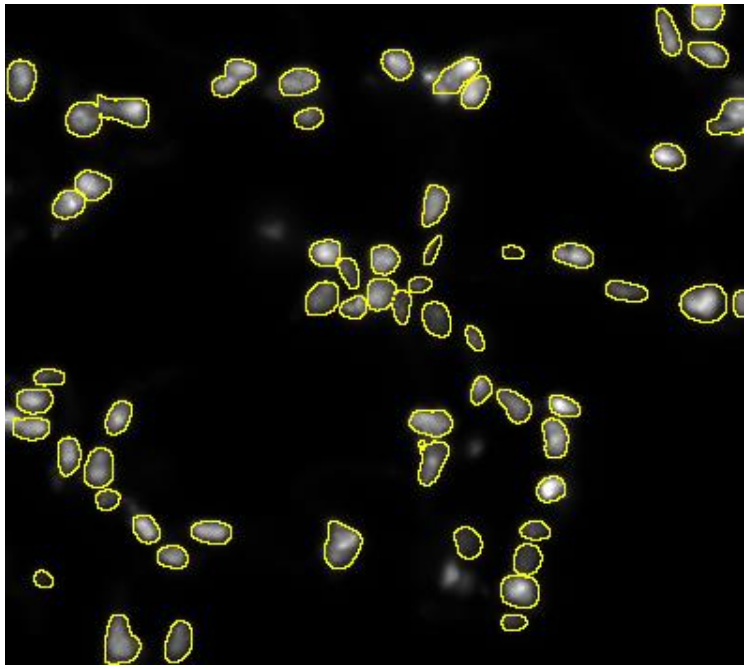
QuPath



Unet



Mask RCNN



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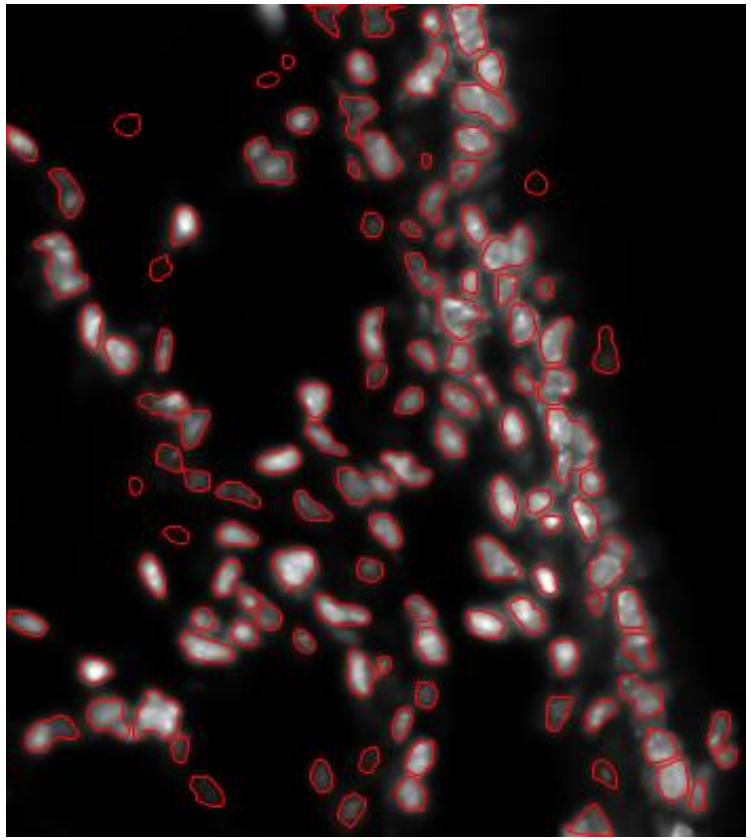
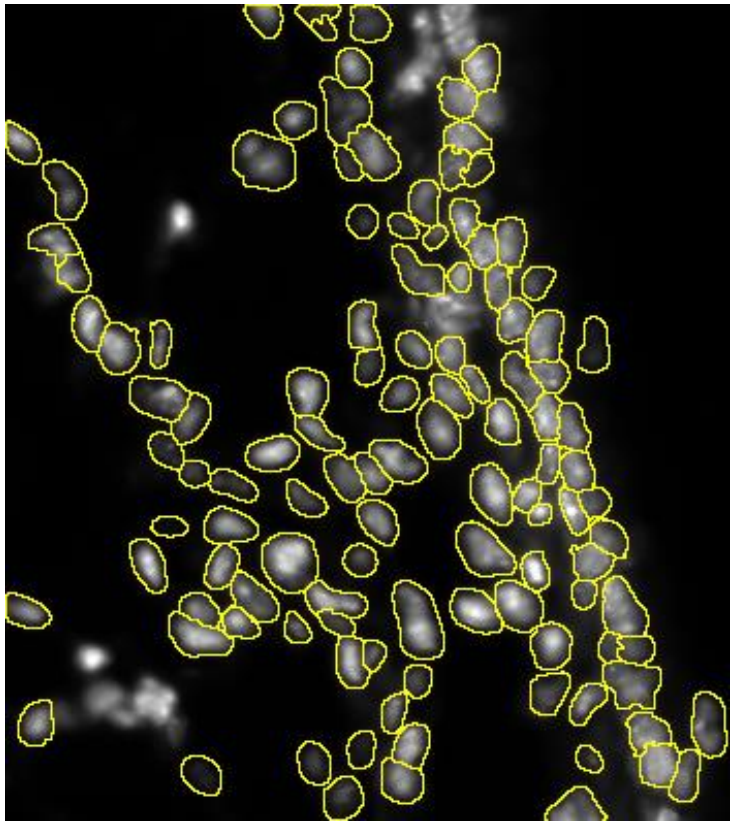
Testing – Outcome between Unet and Mask RCNN

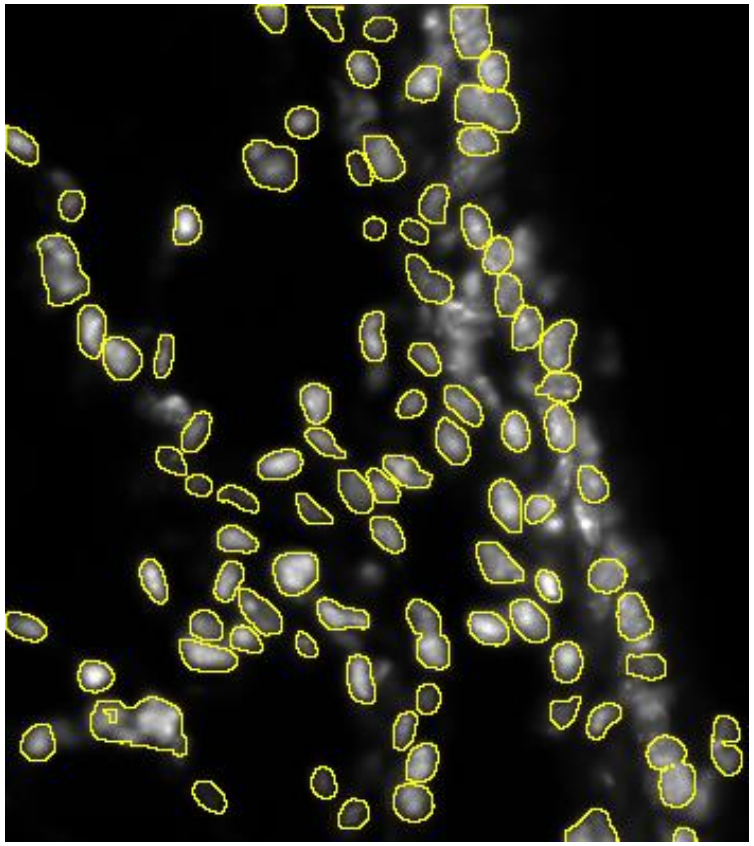
QuPath



Unet



Mask RCNN



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Conclusion

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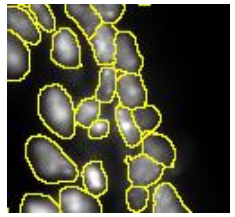
Conclusion

CNN Method:

- Better solution to overlapping cells



- Could perform for a whole image at once
  - Where threshold method fails
- Could be embedded into QuPath framework
- Fast prediction
- Stable and general outcomes
  - User independent
  - Train on various image types
- Framework for future process

Possible Improvement

- More Data
  - Larger training data
  - Tweak by more specific data related to our project

- Validation and hyperparameters tuning – Generalized Ability
  - Stratified validation set
  - Other optimizer
  - More post-processing

(Thank you)