Automated Identification of Different Tissue Regions in H&E and IHC Stained Slides Using Deep Learning

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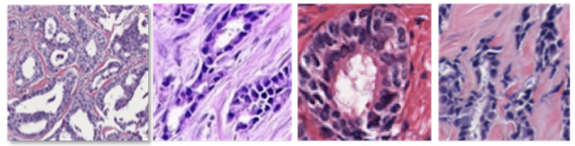
1 – Background

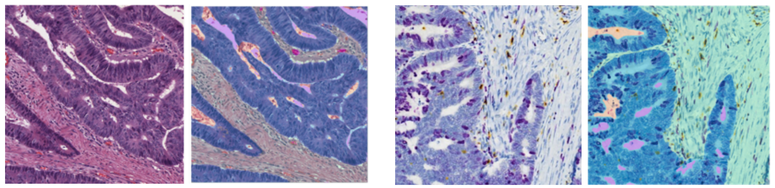
Identifying tumor epithelial, tumor stroma, and necrosis and characterizing their spatial relationships can add prognostic value in a clinical practice. It also enables studying spatial location of different cell types in different tissue regions which can support new biomarker discovery for drug development.

The variation in the size, shape and number of different tissue areas across Whole Slide Images (WSIs) makes their manual annotation an error-prone and time-consuming task.



Example of stain variations across different H&E slides

Objective: Develop deep learning algorithms for segmenting **tumor**, **stroma**, **necrosis**, and **other** (background, blood, muscle, etc) in H&E and IHC (Ki67/CD8) stained CRC slides.



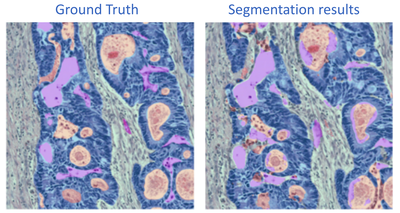
2 – Methods

Data

- Fields of view (FOVs) randomly generated on whole slide images (mainly CRC tissue)
- Different tissue regions in the FOVs are annotated by a pathologist

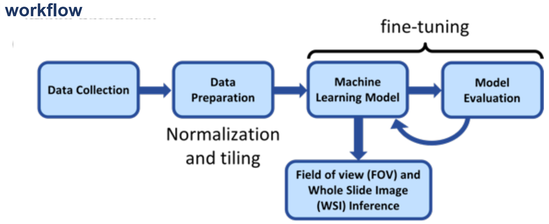
Training set for H&E Segmentation model
- H&E stained biopsy and surgical sections
- Number of slides: 77
- Number of FOVs: 221
- Size of FOV: ~1024x1024 pixels (~500x500 micron)

Training set for IHC segmentation model:
- Ki67/CD8 stained biopsy and surgical sections
- Number of slides: 60
- Number of FOVs: 238
- Size of FOV: ~1024x1024 pixels (~500x500 micron)



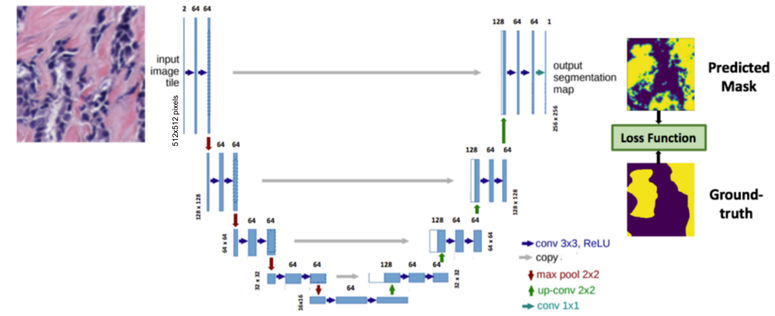
Dice Similarity Coefficient (Av. of 4 classes): 0.72
Intersection_Over_Union (Av. of 4 classes): 0.58

Automated workflow



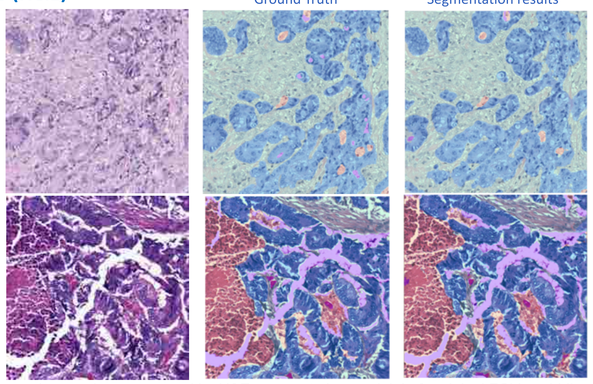
3 – Methods

ResU-Net architecture. U-Net is simple, fast to train, gives reasonable results with less amount of training data. U-Net and its variants have achieved state-of-the-art results for medical image segmentation.



Loss functions: Binary cross-entropy, Dice similarity coefficient.
• Optimizers: Momentum, Adam.
• Data augmentation: Rotation, Translation, Zoom, Shear, Horizontal flip.

4 – Results (H&E)

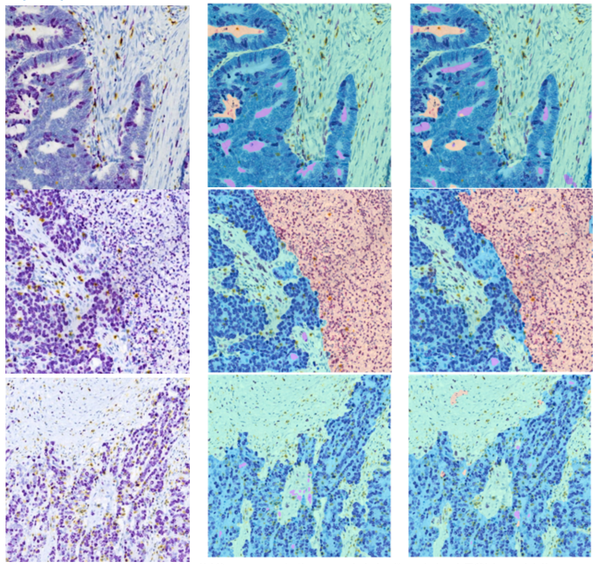


Segmentation overlays generated by H&E segmentation model. Left: original FOVs, middle: ground truth masks, right: algorithm results (blue:; tumor, green: stroma, orange: necrosis, purple: other).

Visual assessment on 80 whole slide images done by a pathologist.

Difference	Necrosis overdetection	Necrosis underdetection	Stroma overdetection	Stroma underdetection	Tumor overdetection	Tumor underdetection
0	34	35	35	48	67	19
Minimal	37	39	44	32	12	60
Moderate	9	6	1	0	1	1
Sum	80	80	80	80	80	80

5 – Results (IHC)

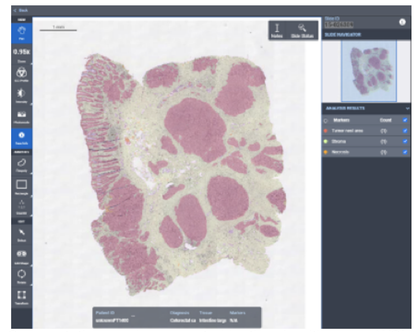


Segmentation overlays generated by IHC segmentation model. Left: original FOVs, middle: ground truth masks, right: algorithm results (blue:; tumor, green: stroma, orange: necrosis, purple: other).

6 – Results (quantitative assessment)

Test set for H&E Segmentation model
- H&E stained slides
- Number of slides (biopsy and surgical): 31
- Number of FOVs: 92
- Size of FOV: ~1024x1024 pixels

Test set for IHC segmentation model:
- Dual Ki67/CD8 stained slides
- Number of slides (biopsy and surgical): 27
- Number of FOVs: 64
- Size of FOV: ~1024x1024 pixels



Segmentation masks generated by the algorithm on a WSI

Quantitative validation metrics for H&E and IHC segmentation models, obtained from comparing the algorithm results with the ground truth annotated by the pathologist on test FOVs.

Model	Av. Accuracy	Av. Dice Coefficient	Av. IOU
H&E Segmentation	0.70	0.71	0.70
IHC Segmentation	0.76	0.75	0.82

7 – Conclusion

We have developed deep learning algorithms for automated segmentation of different tissue regions in the tumor environment. This could potentially enable faster and more reliable assessment of WSIs by eliminating the need for manual annotation from pathologists.