A Novel Approach to Segment Specialized Annotations in Electron Microscopy Images of Glomerular Podocytes

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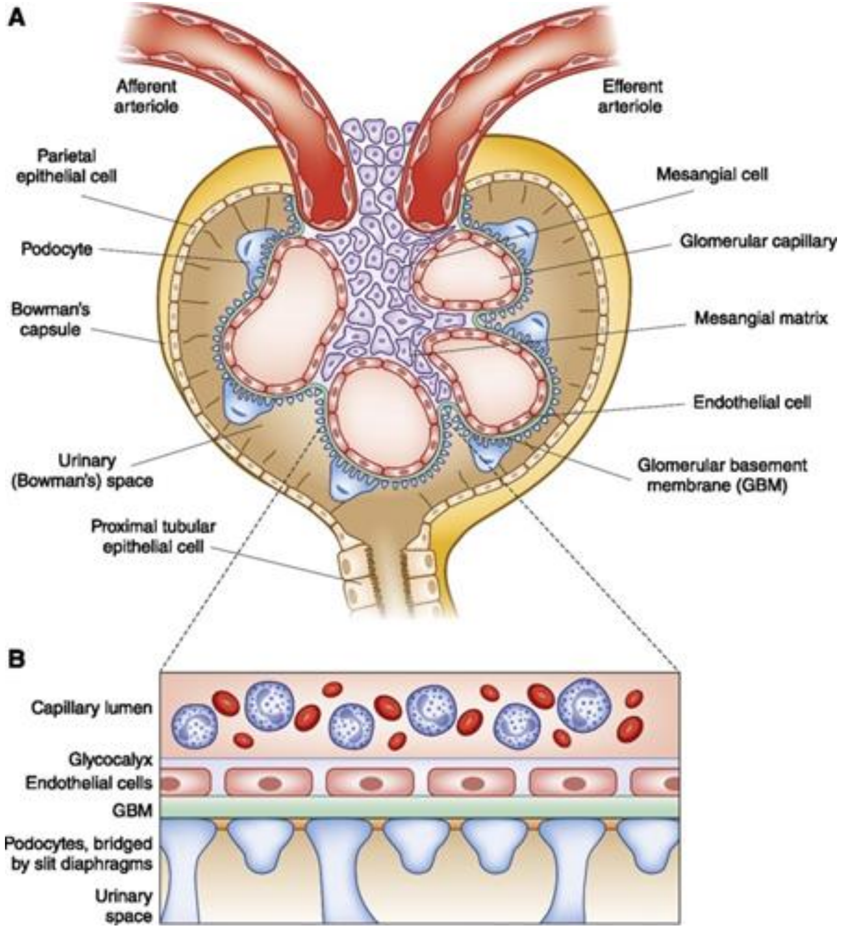
Podocytes: Critical kidney cells with limited regeneration capacity

- The glomerulus is the filtering unit of the kidney.
- Podocytes play a key role in preservation of glomerular structure and function.
- Podocytes are post-mitotic and are not adequately replenished once lost.
- ~80% of diseases causing kidney failure are linked to podocyte injury and loss.
- Measures of podocyte injury are of diagnostic and prognostic significance in various kidney diseases.



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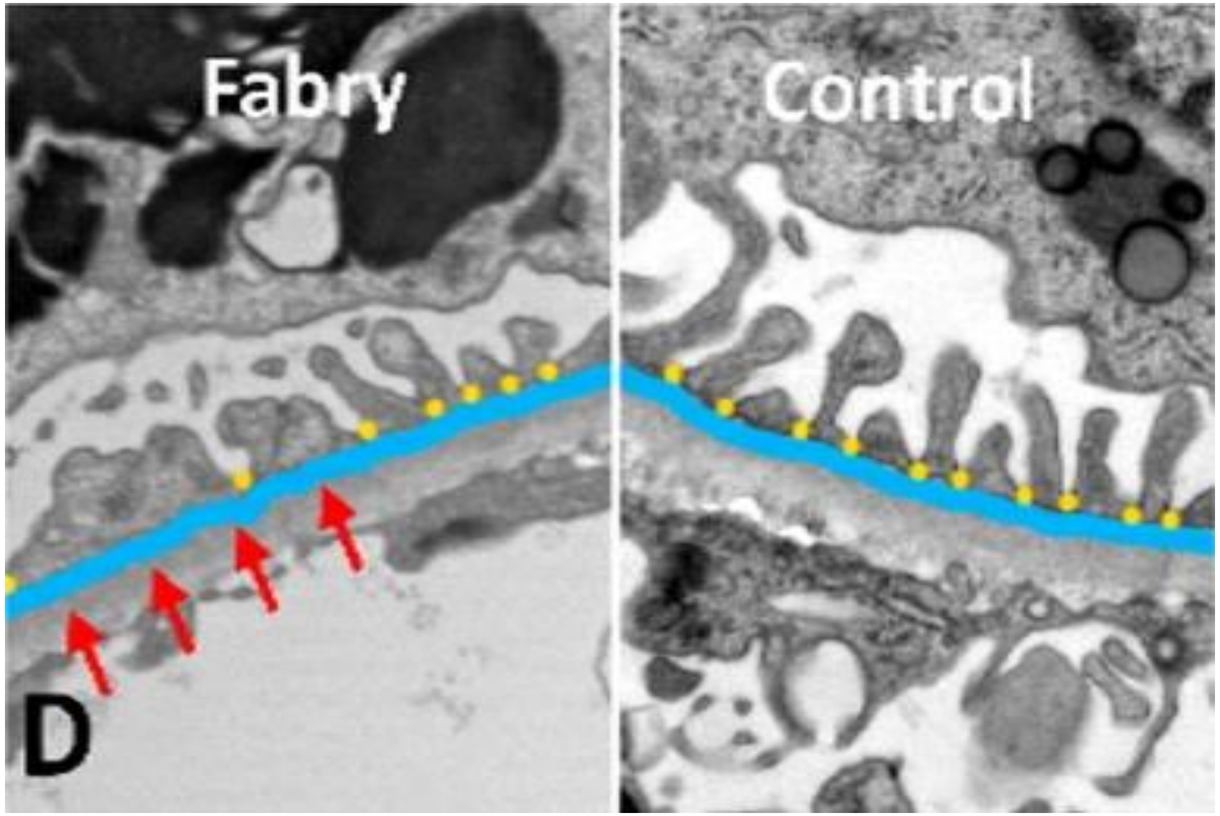
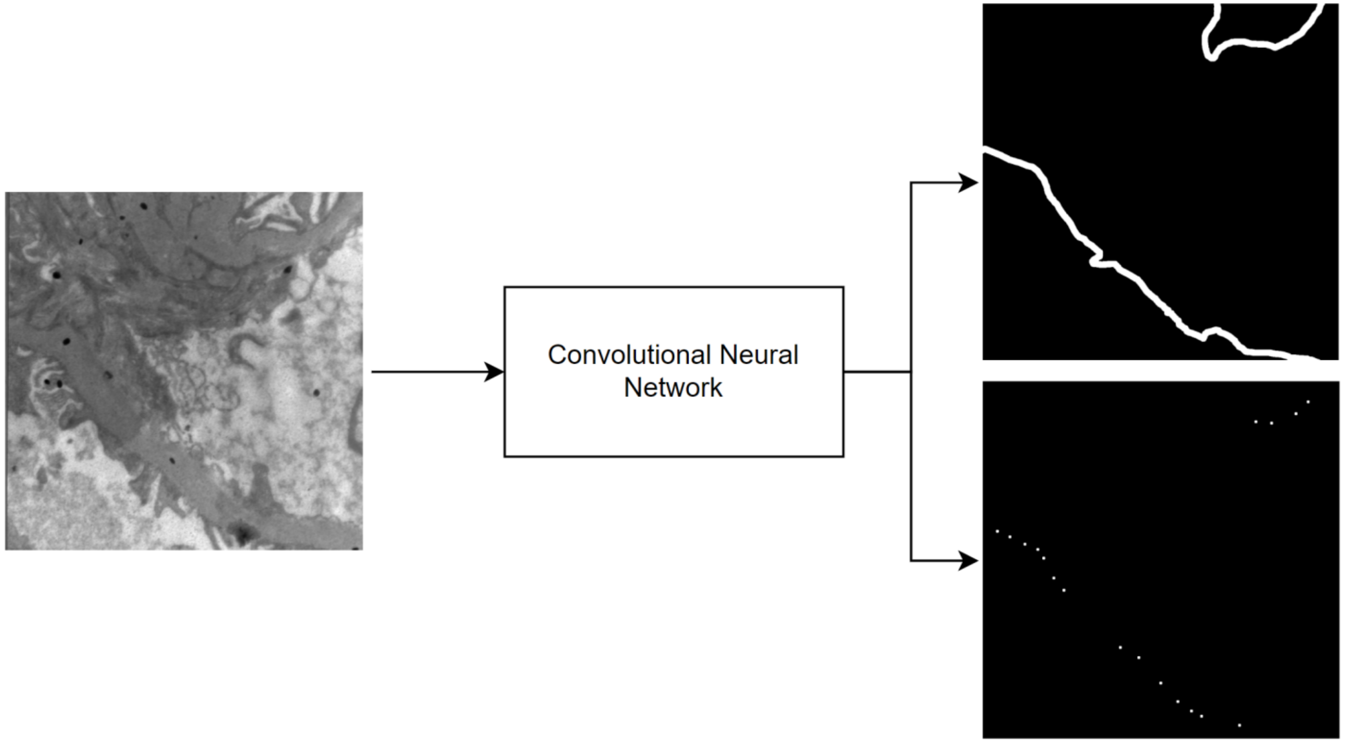
Context: Foot Process Width

- Foot Process Width (FPW) is a well-known indicator for disease progression
- The average distance between slits (yellow dots) increases as the disease progresses
- We generally measure the distance along the membrane edge (blue line)



Standard Modeling Approach

Standard segmentation pipeline: A convolutional neural network takes in the EM image and outputs several relevant segmentation masks.



Standard Modeling Approach

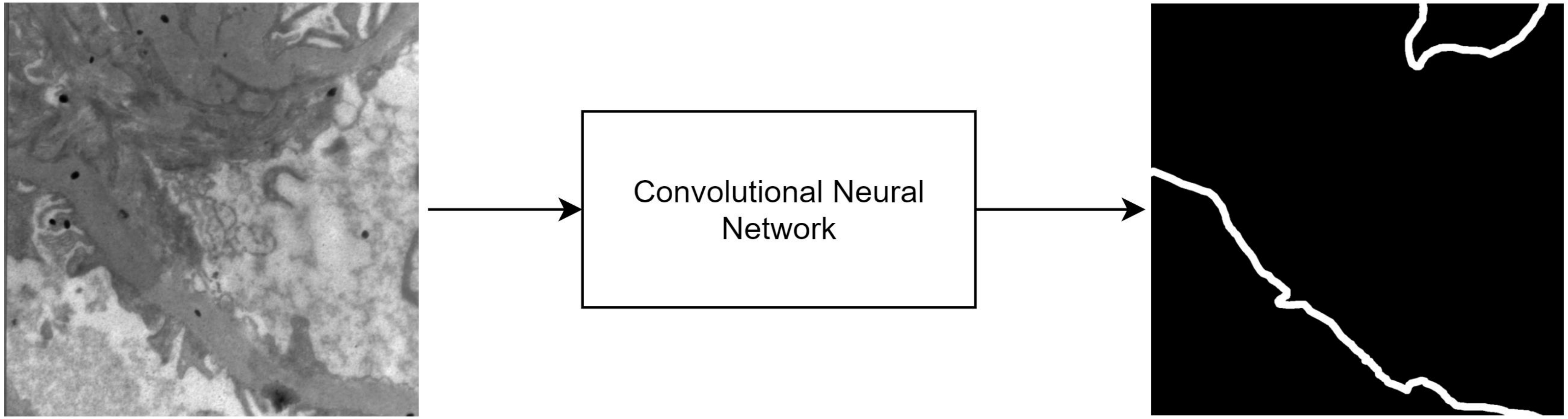
Barriers to accurate slit segmentation:

- *Overwhelming context*. There is much more information given in the image than is needed to segment slits.
- *Small/specialized annotation*. The number of positive pixels is significantly smaller than the number of negative pixels.
- *Imbalanced masks.* The membrane layer and slit layer have segmented areas that are very different in terms of area making a single IoU technique difficult without averaging or weighting.

A Novel Approach for Slit Segmentation

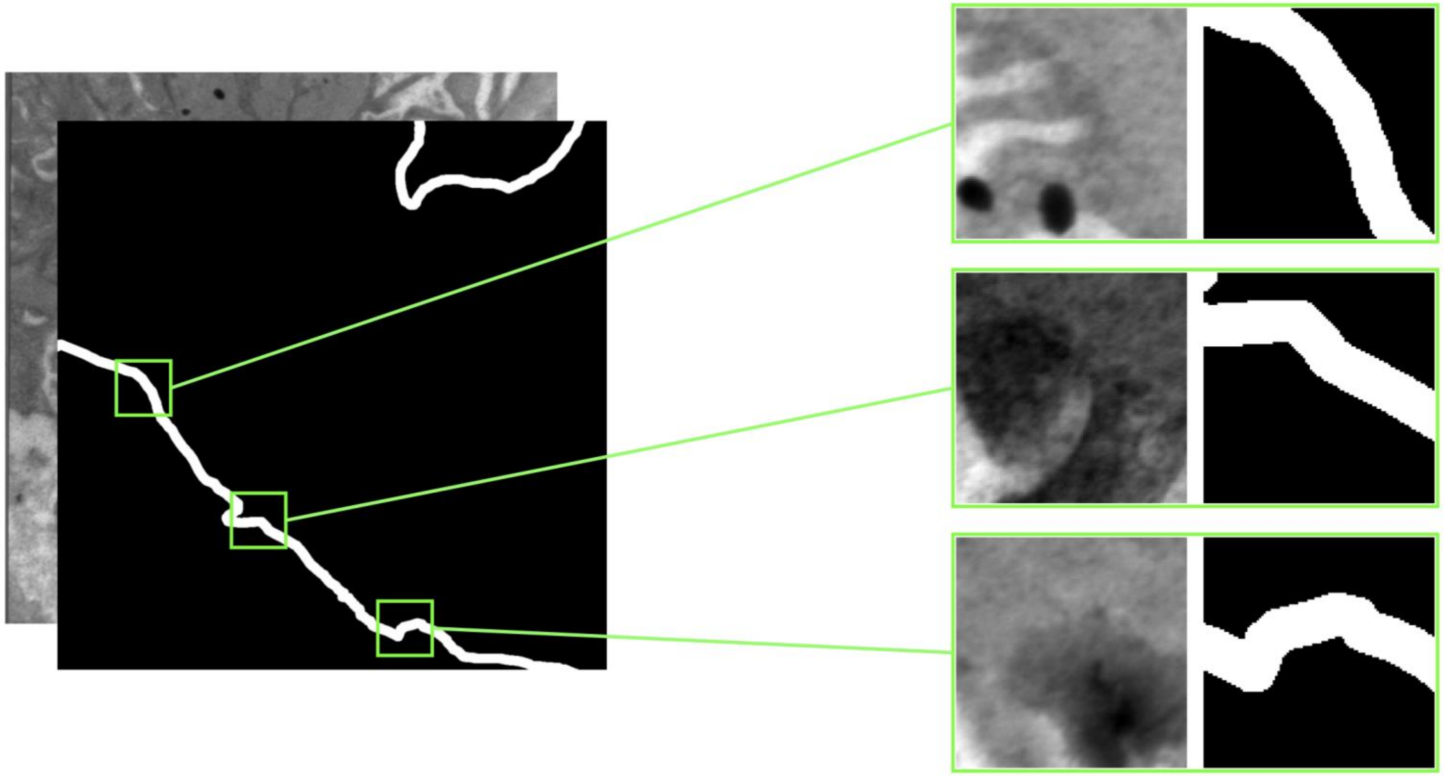
Multi-Stage Approach

Stage I. Segment the membrane mask alone.



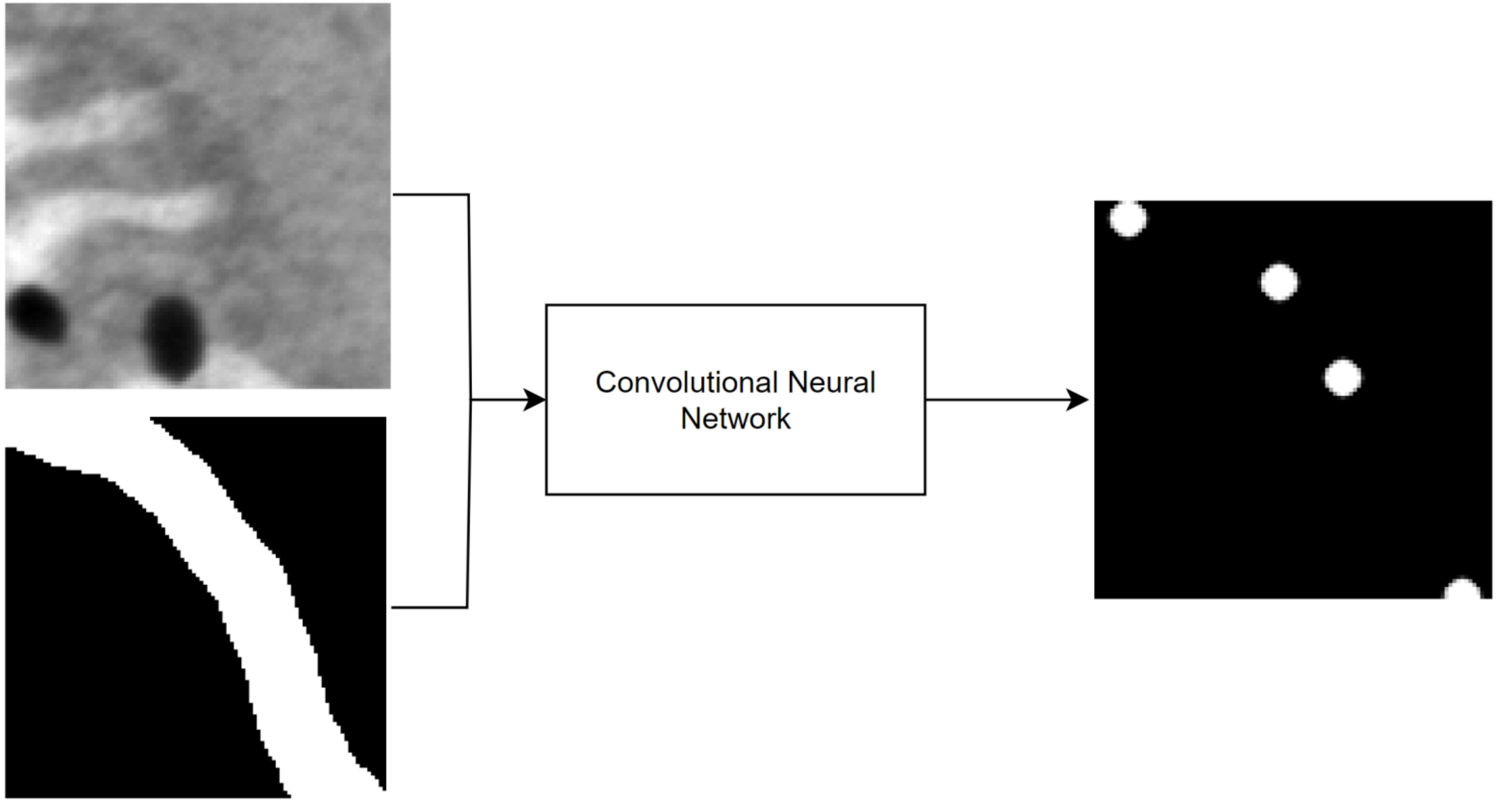
Multi-Stage Approach

Stage II. Obtain 'window snapshots' along the membrane.



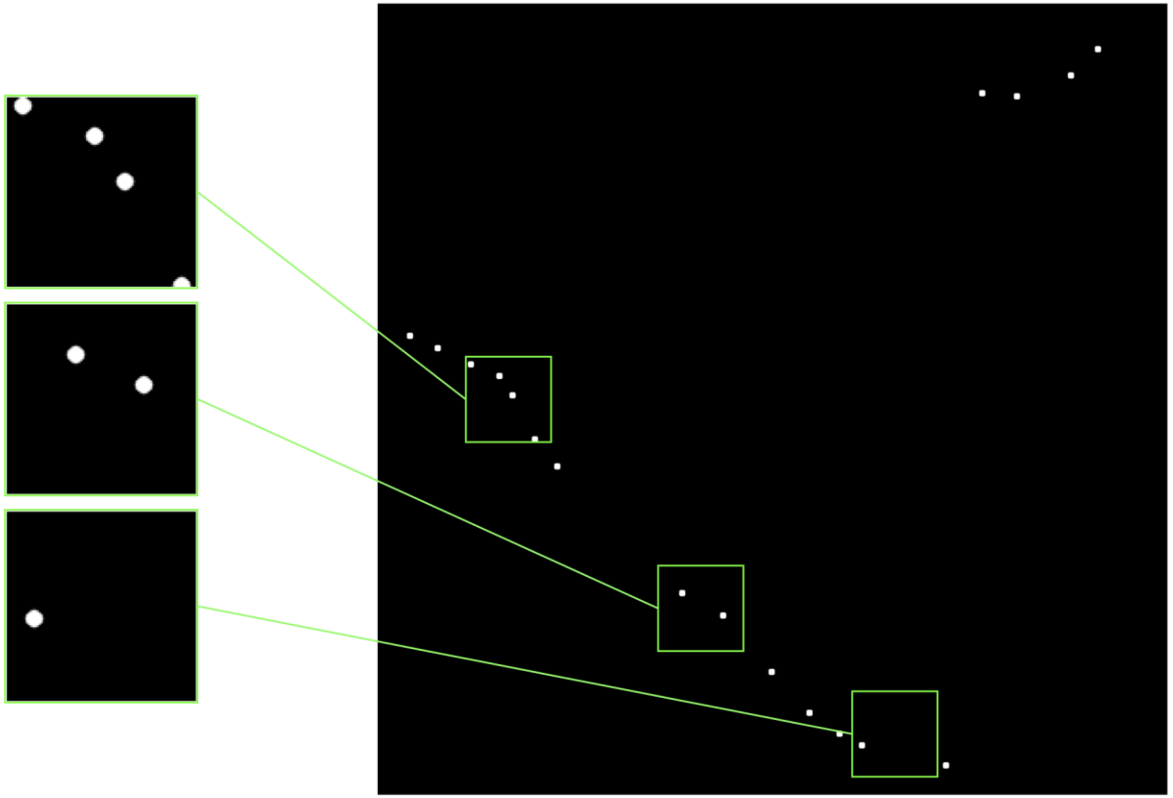
Multi-Stage Approach

Stage III. Segment the slits within each window.



Multi-Stage Approach

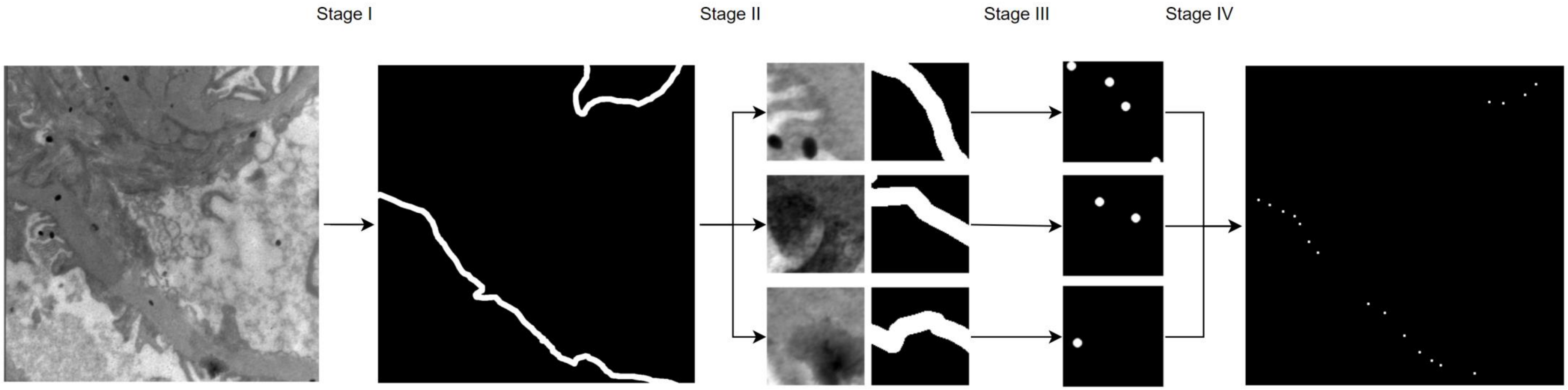
Stage IV. Piece the segmented slit windows together.



Multi-Stage Approach

This approach addresses the primary problems well.

- *Overwhelming context*. By restricting the range of context to relevant areas around the membrane, the model only sees relevant features.
- *Small/specialized annotation*. Each slit is larger w.r.t. the mask without losing on precision, and thus more important in optimization.

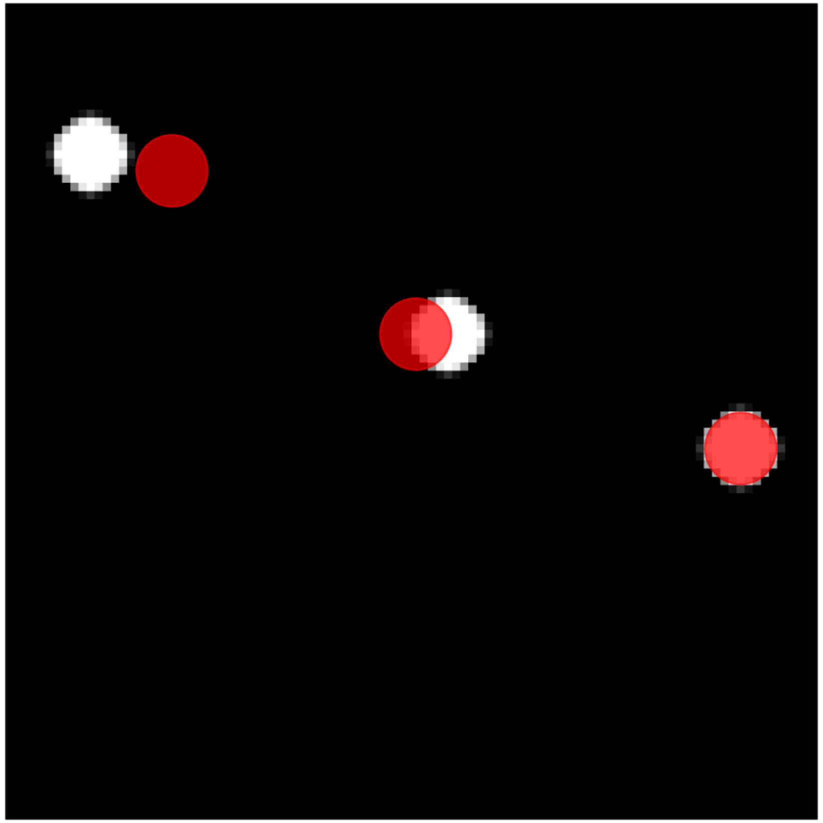


Dynamic Dilation

Slits are still small w.r.t. the window.

Suffers from lack of continuous signals:

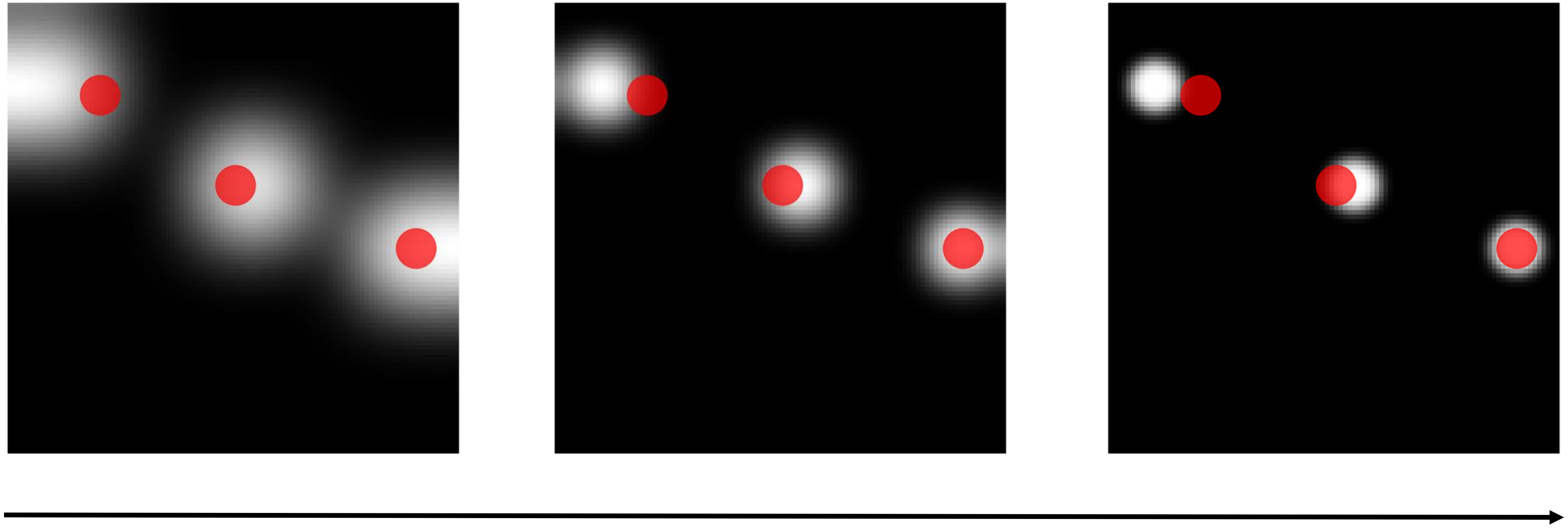
Discoveries are somewhat 'discrete'.



Dynamic Dilation

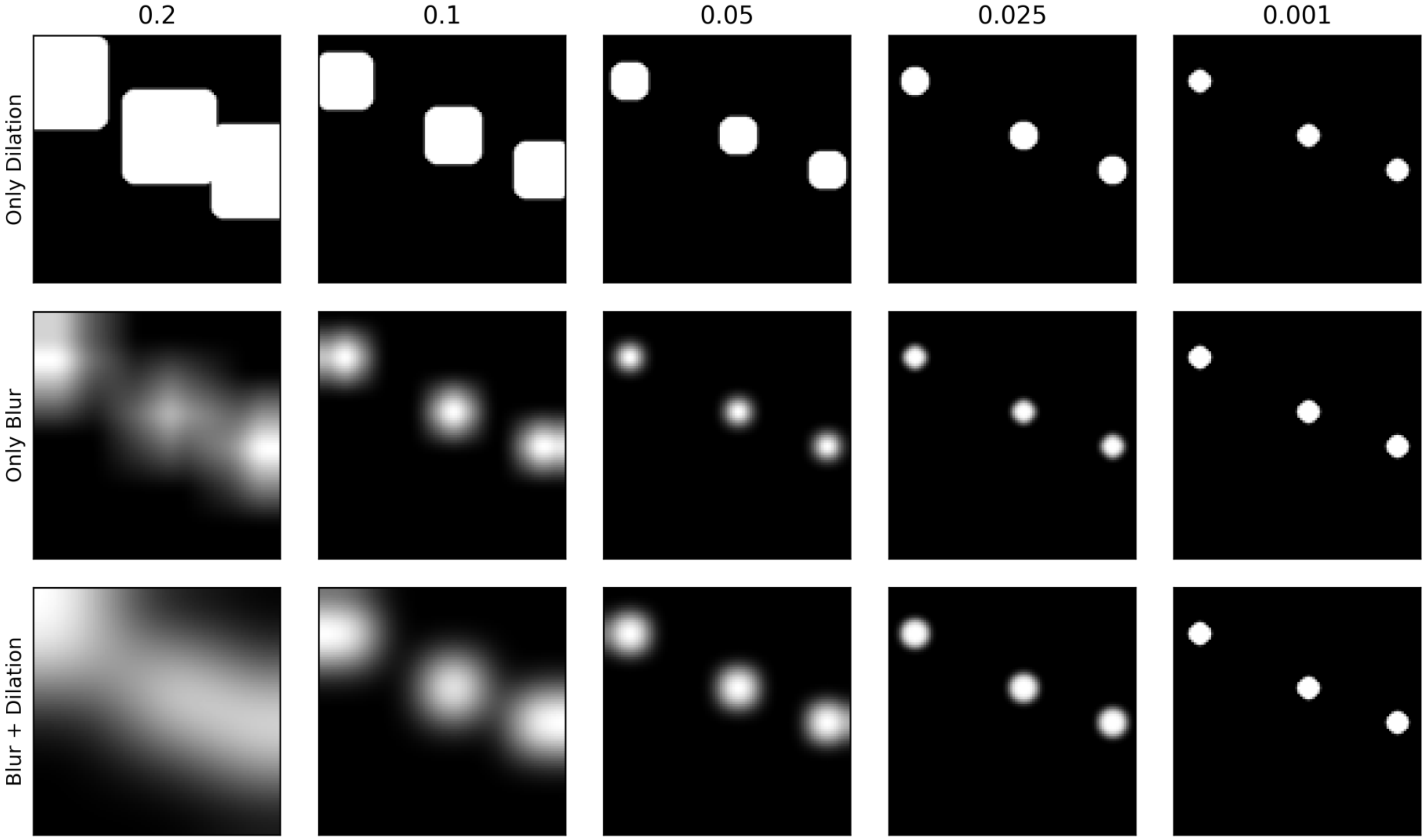
Proposal: begin with softened and larger labels to enable a smoother signal

(after model has been pretrained to predict slit-like segmentations)



Approaches original labels as training proceeds

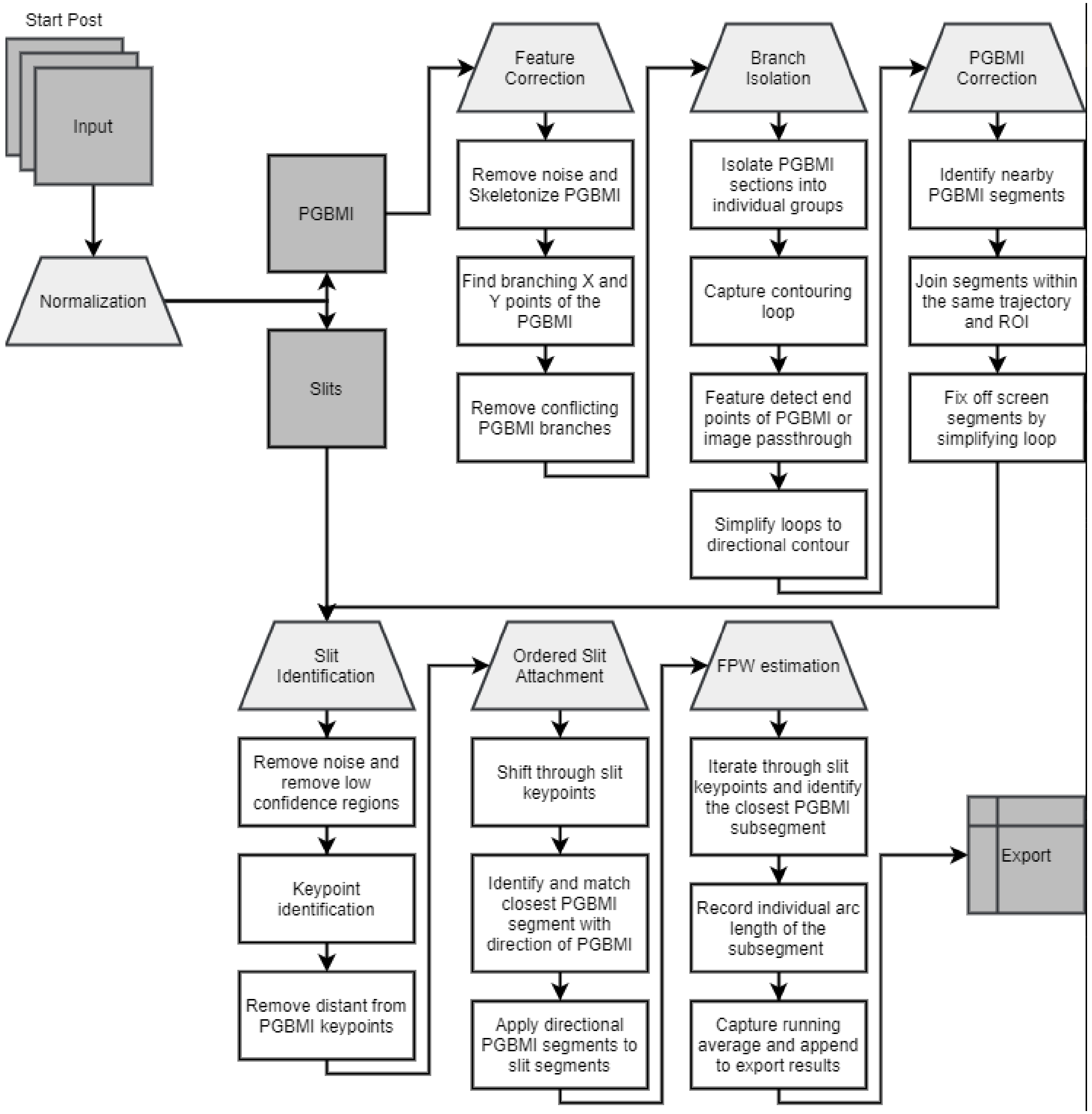
Dynamic Dilation



Post-Processing

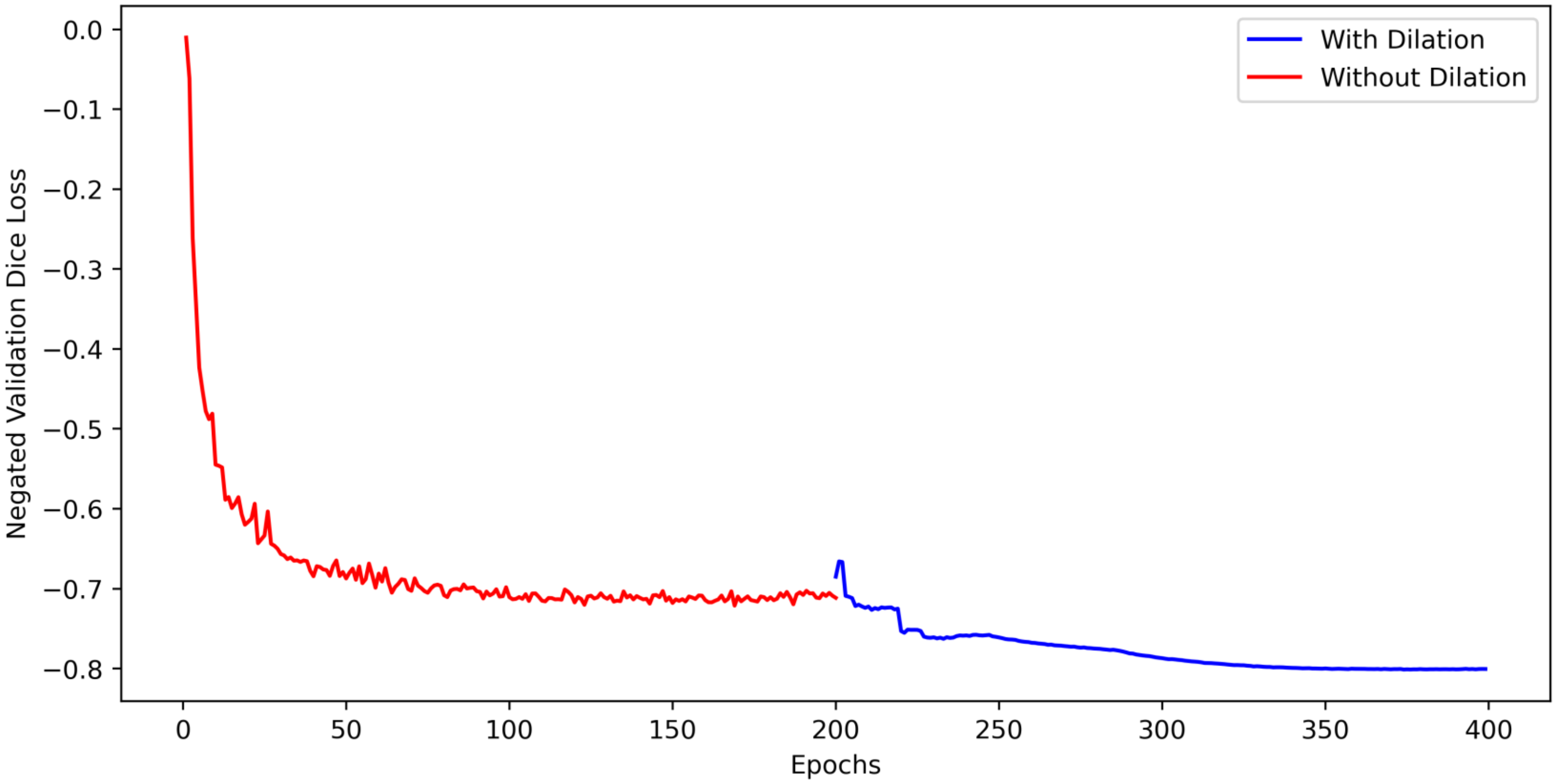
Analysis is still done using traditional computer vision techniques:

- After using ML to generate the segmentation masks (the labeled images) we used some vision techniques to isolate slits to membranes
- After grouping slits to their respective membranes we measured their distance along the membrane.



Results

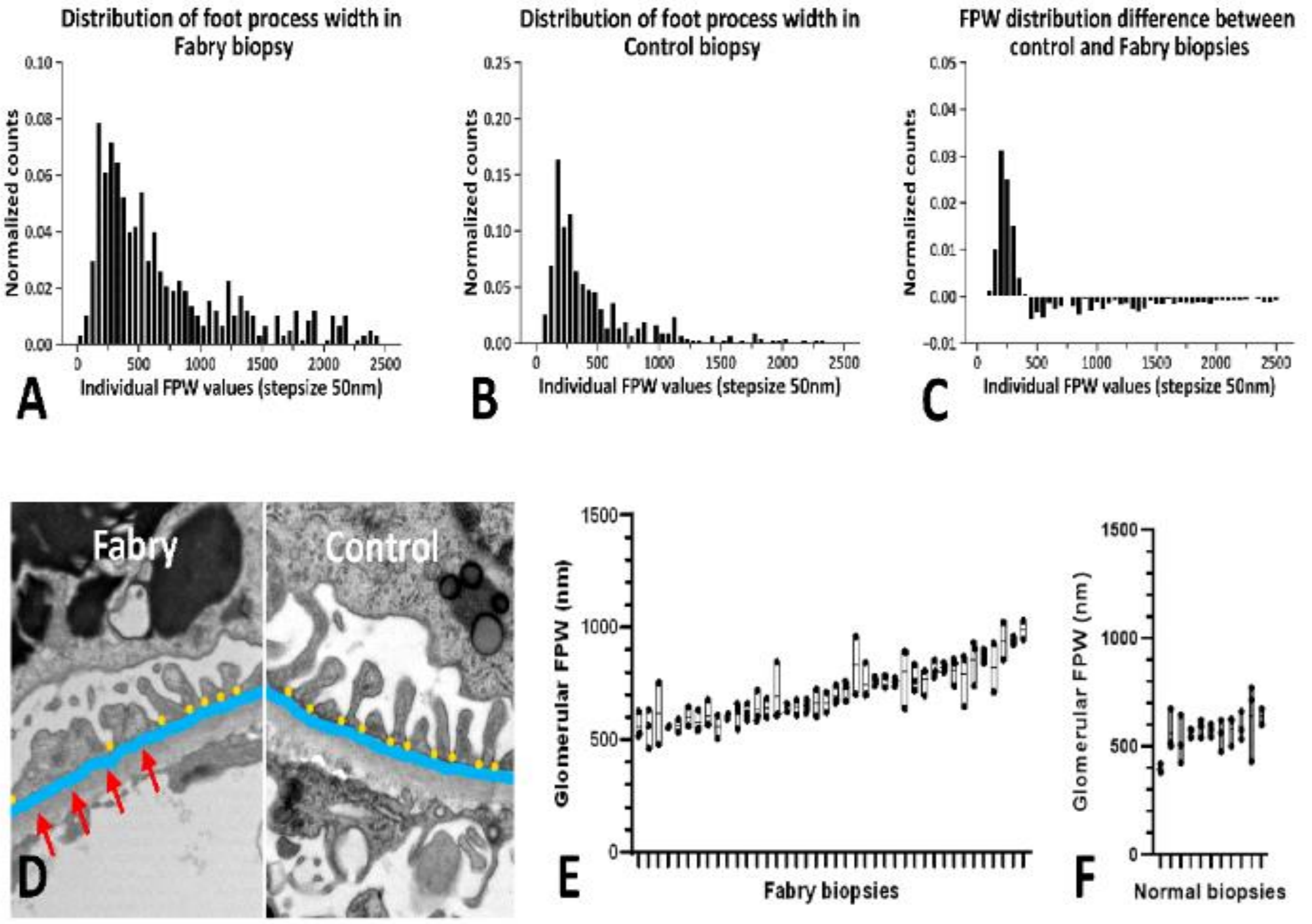
Method	*Validation Dice Loss*
Standard Modeling	0.64
Multi-Stage	0.71
Multi-Stage + Dynamic Dilation	0.80



Results

Preliminary results from older models show how the estimation of FPW, using an automated approach, does indicate clear differences in measurements between patients with Fabry disease and normal patients.

A) histogram of FPW measurements for patients with Fabry
B) histogram of FPW measurements for patients without Fabry
C) Normalized results comparing measurements between Normal and Fabry
D) Sample image showing distance difference
E/F) The FPW distances grouped together by glomerulus (we had on average 3 samples per glomerulus)



Broader Implications

- Provides a general model to approach segmentation of small/imbalanced regions
  - 'Local segmentation' vs. 'global segmentation'
  - Removes 'noise'/irrelevant information from model view
- Demonstrates application of target relaxing for overcoming learning barriers in medical segmentation

Questions