

# 機器學習於材料資訊的應用 Machine Learning on Material Informatics

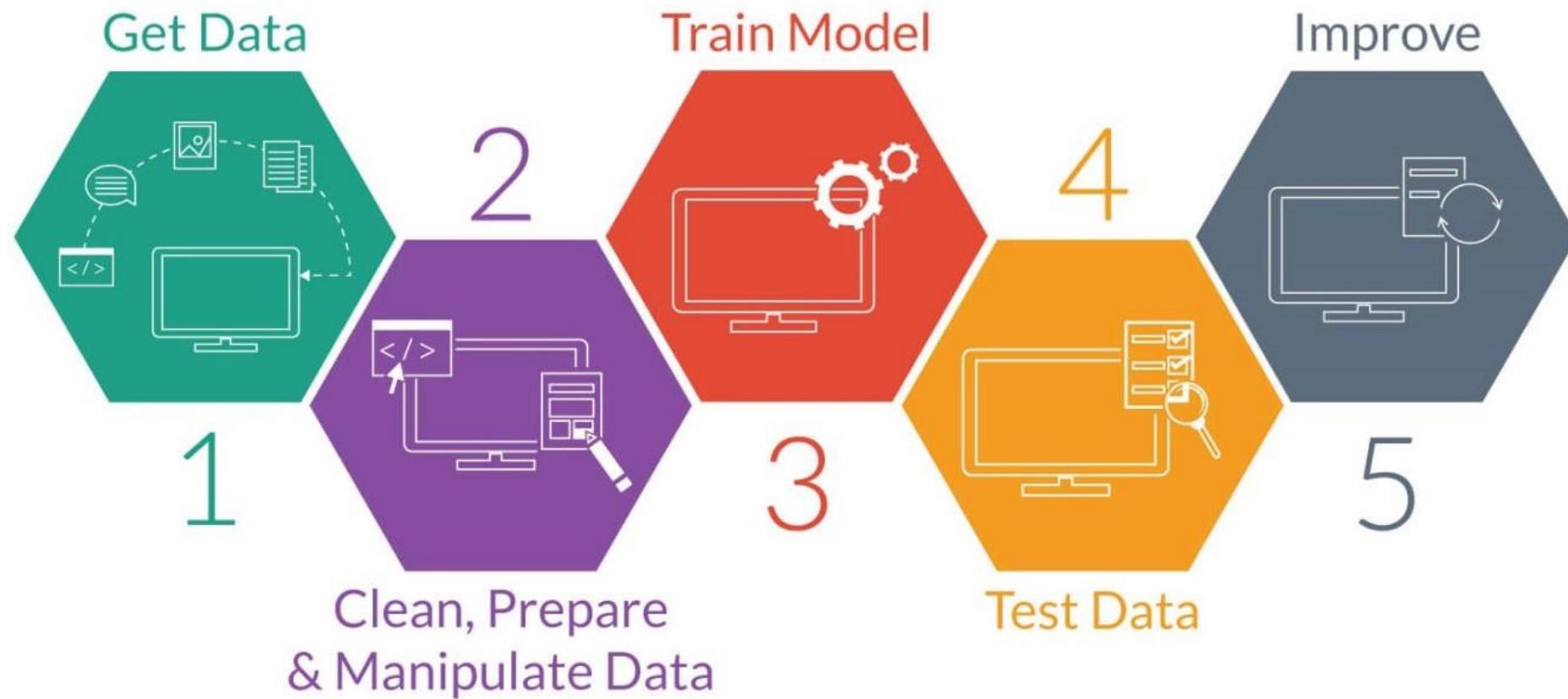
---

陳南佑(NAN-YOW CHEN)

楊安正(AN-CHENG YANG)

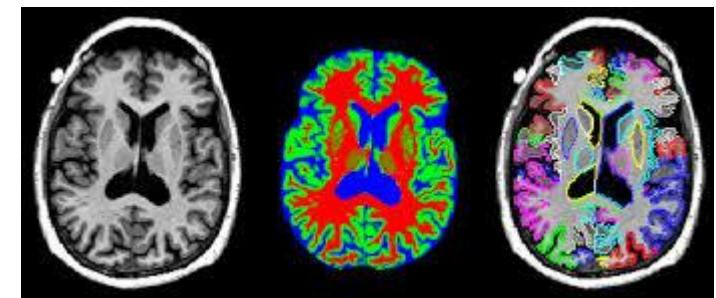
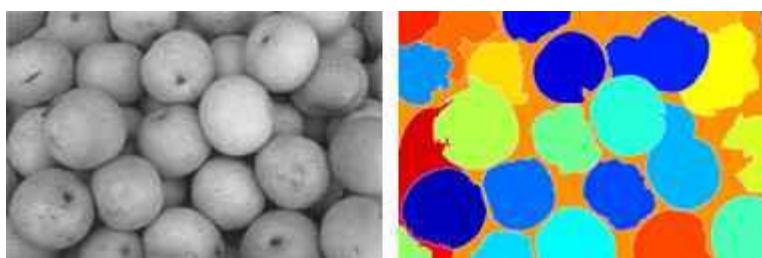
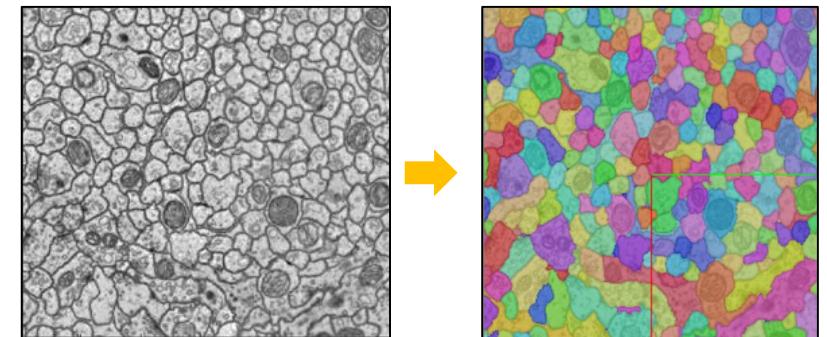
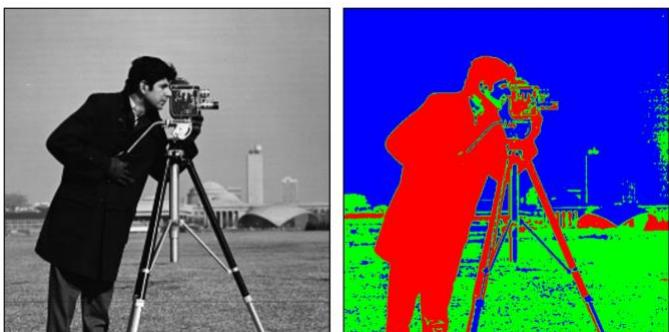
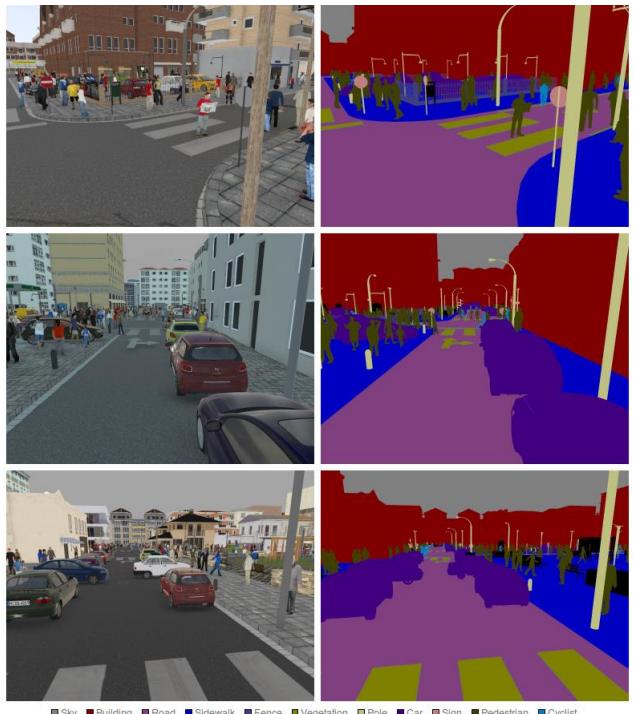
# Work flow for ML

---



# Image segmentation

# Image segmentation

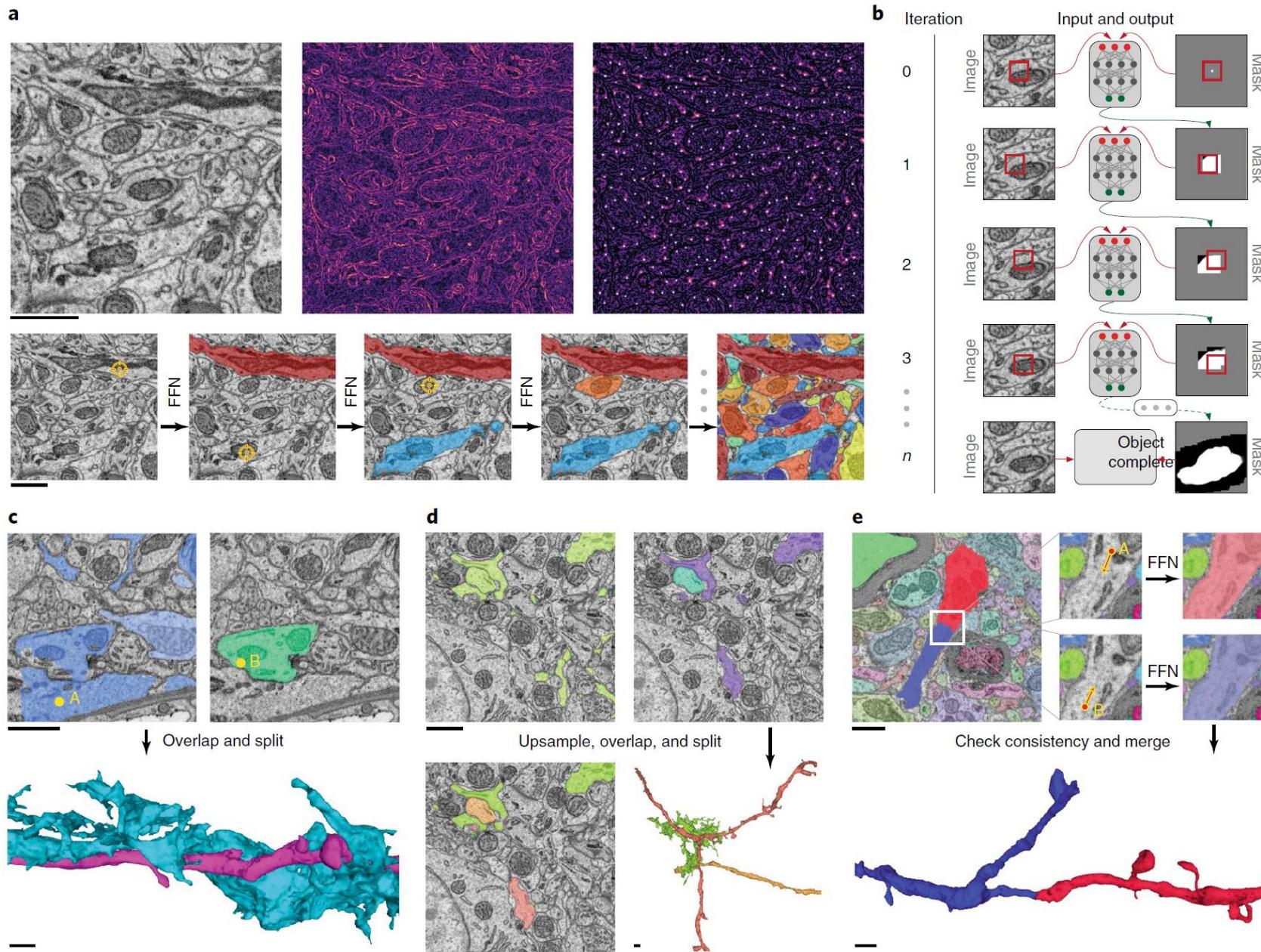


# High-precision automated reconstruction of neurons with flood-filling networks



# System flow

FFN (Flood-filling-network)

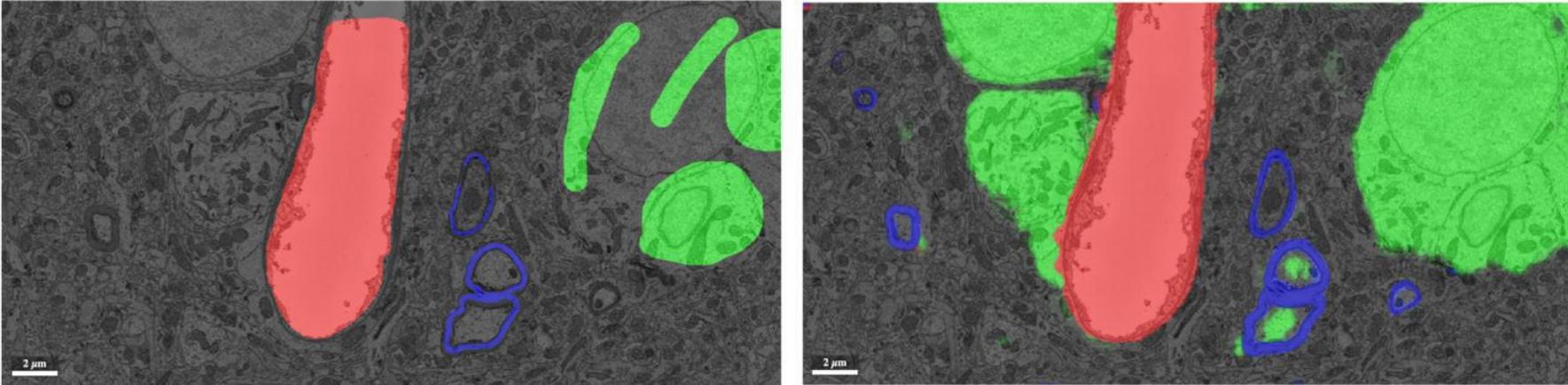


# Segmentation pipeline

---

- Fine alignment
- Cell body segmentation
  - **Tissue-classification CNN** (manually placed into all 454 somas in this paper, potentially 0.97 **precision** and 0.96 **recall**)
  - Explicit handling of cell body is necessary: average diameter, 9 $\mu$ m
- Neuropil segmentation
  - **Flood-filling-network (FFN)** (5 times: Standard Seed/Reversed Seed @ 9x9x20, Standard Seed/Reversed Seed @ 18x18x20 and Standard Seed @ 36x36x40)
- Over-segmentation consensus (開結點)
- Agglomeration (補斷點)
  - Reduce split rate: 44%
  - Increased the run length more than tenfold (1,149%)
- Biological plausibility testing
  - Filtered the merge decision list so that no agglomerated object contained more than one cell body (0.006%)

# Tissue-type classifier



Manually labeled **26.7 million** voxels (0.016% of the volume) at 2x reduced lateral resolution as

1. blood vessel (4.4 million voxels)
2. cell body (**11.5 million** voxels)
3. myelin (1.5 million voxels)
4. neuropil (**7.4 million** voxels)
5. 'out-of-tissue' (1.8 million voxels)

Manual annotations (**5h of human time**) were sparsely created on **every 500th** slice by two authors (V.J. and M.J.) with a custom **web-based tool** that enabled them to **manually paint voxels** with a modifiable brush size

**Manual annotations** (left) and **convolutional network inference** (right) of a subset of the labeled voxel classes: blood vessel (red), myelin (blue), and cell body (green)

False positive identifications of cell body voxels are visible in the automated inference (inside the myelinated area).

# Tissue-type classifier

---

- Training sets

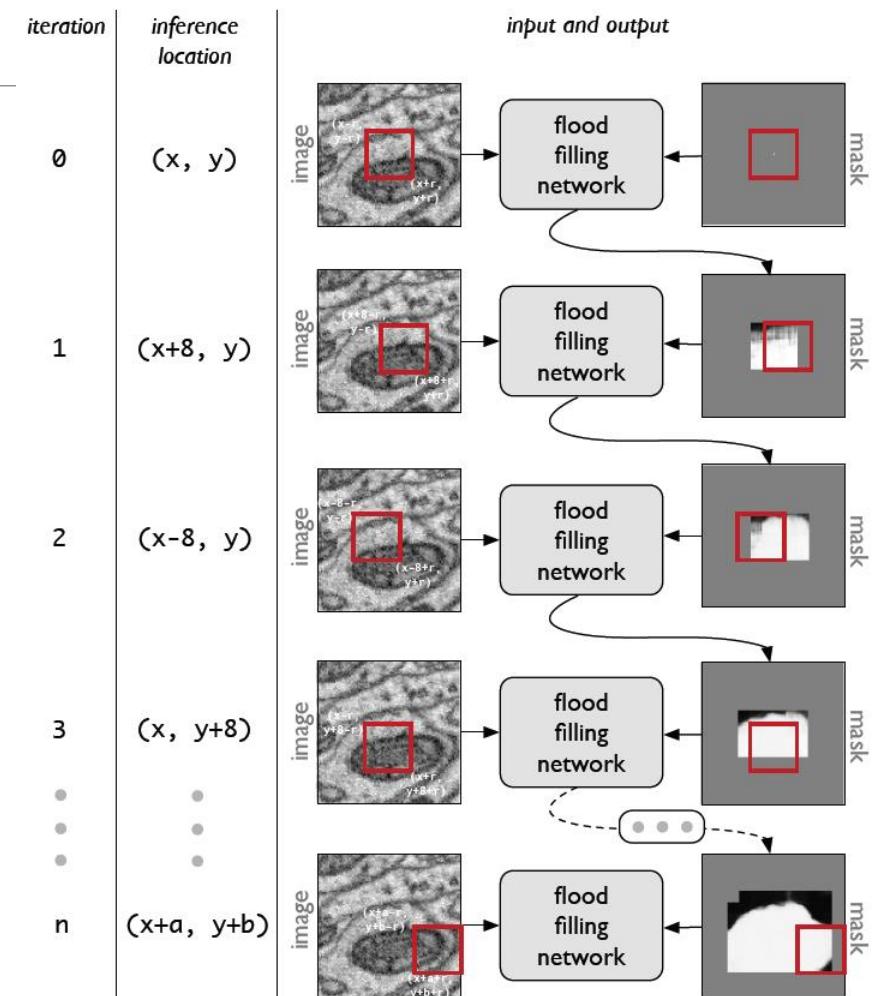
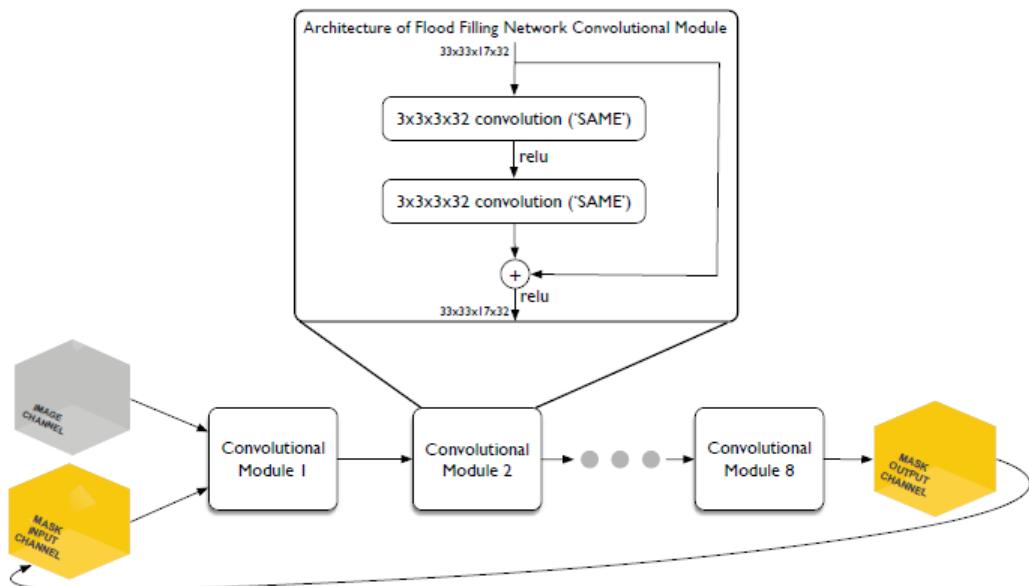
- **65 x 65 x 65** patch on each manually labeled voxel

- CNN setting

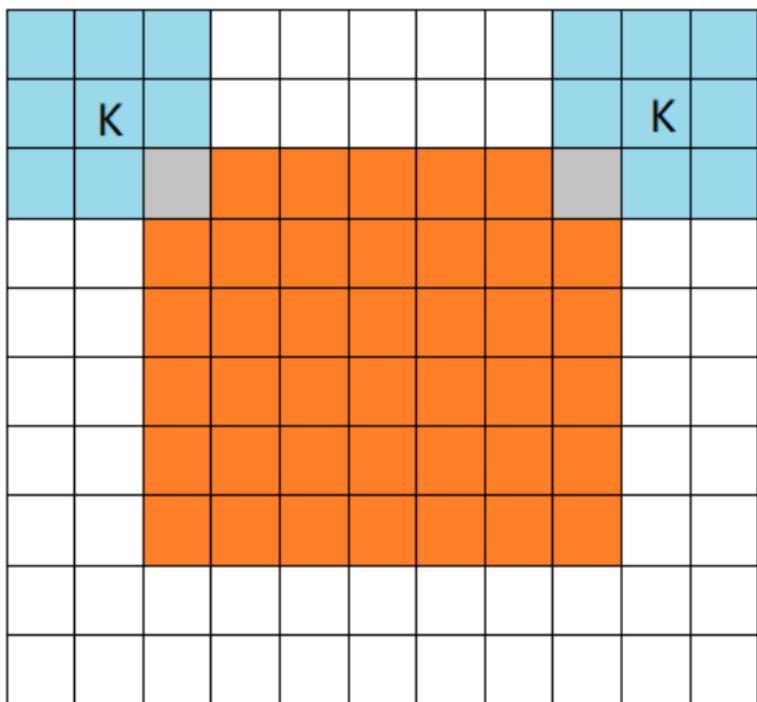
- 3 convolution layer (3 x 3 x 3 kernel size, 64 feature maps, VALID mode)
  - 1 additional convolution layer (3 x 3 x 3 kernel size, 16 features, VALID mode)
  - Fully connected layer (512 nodes)
  - Softmax (6 class)

# Flood-filling-network

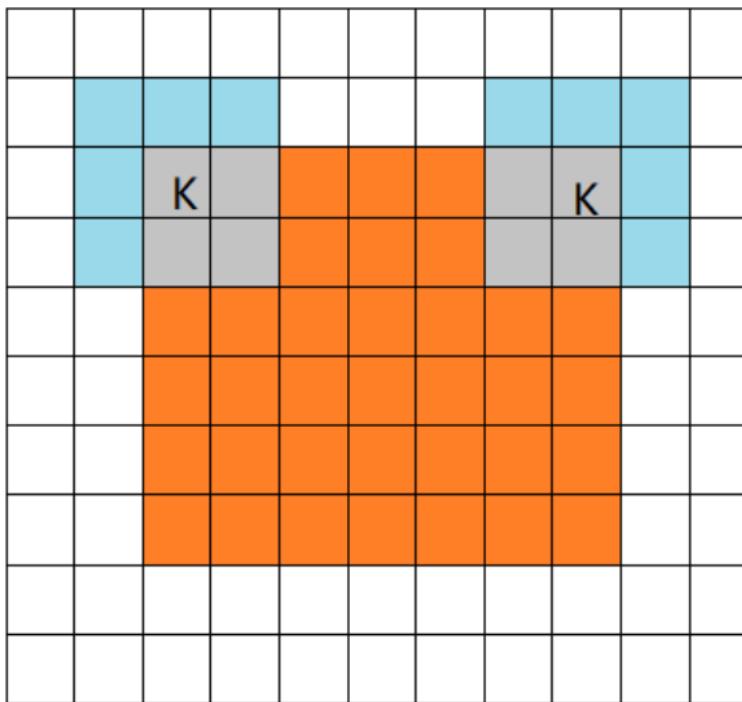
- Similar to PixelCNN model  
(<https://arxiv.org/pdf/1601.06759.pdf>)
- The SAME mode for each convolutional layer
- No pooling



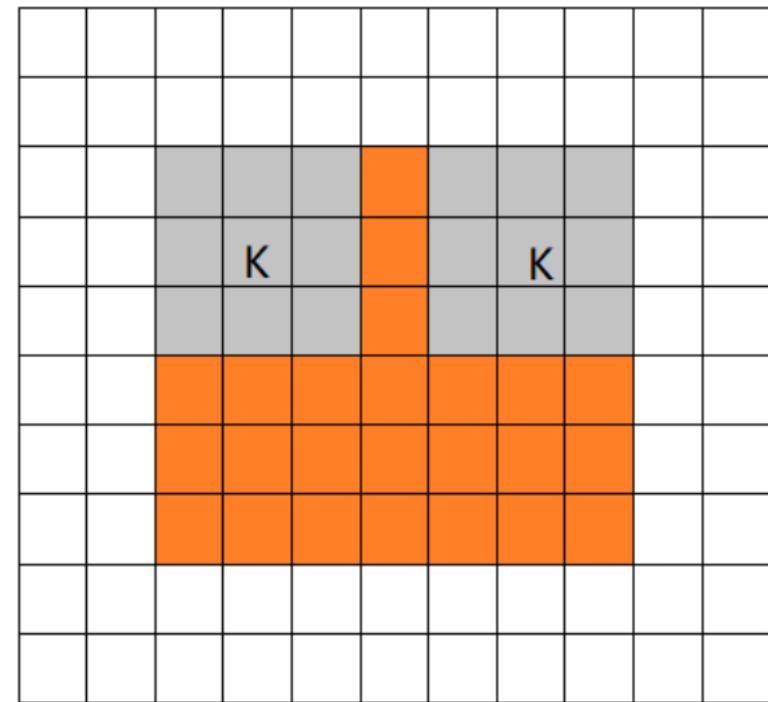
# Padding mode in CNN



Full mode



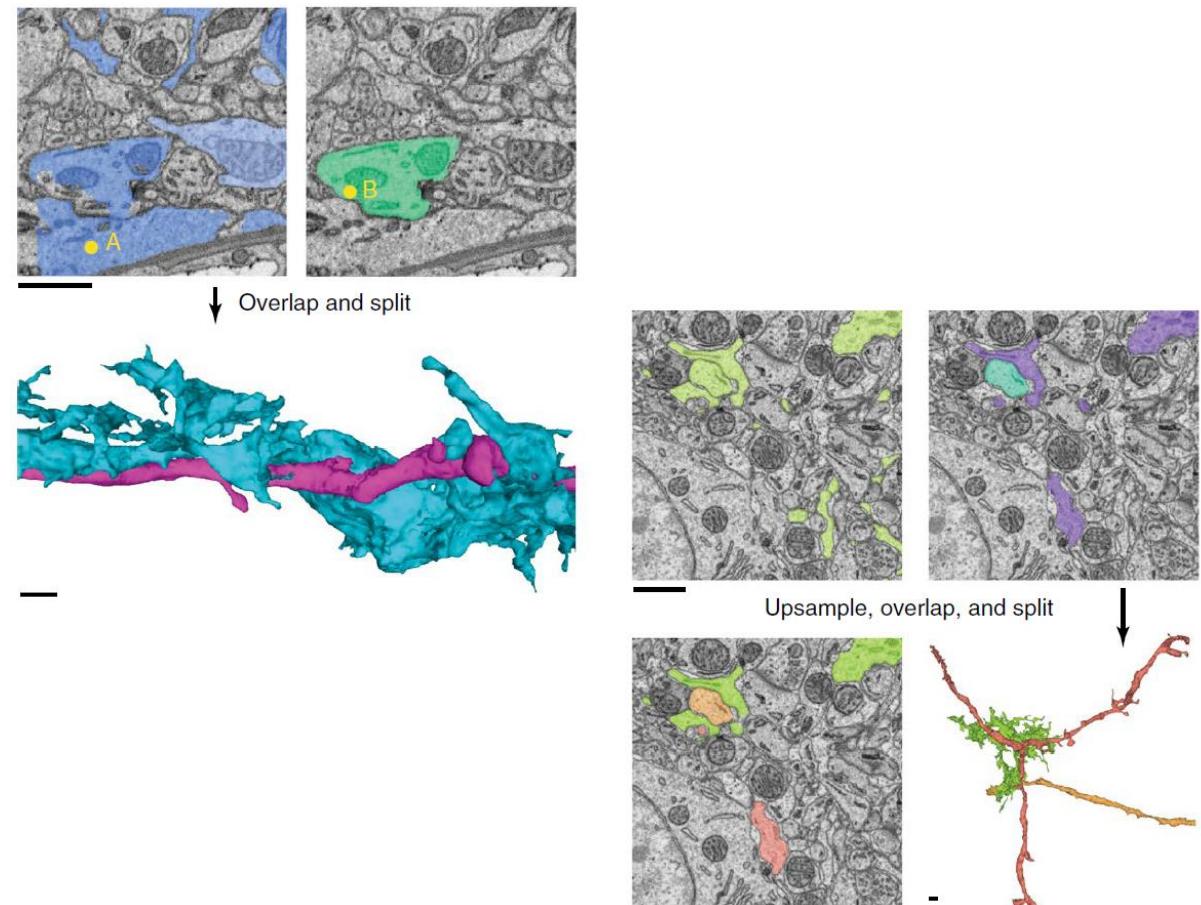
Same mode



Valid mode

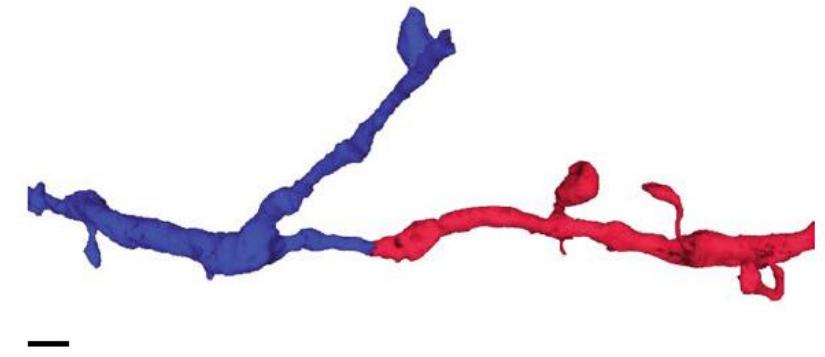
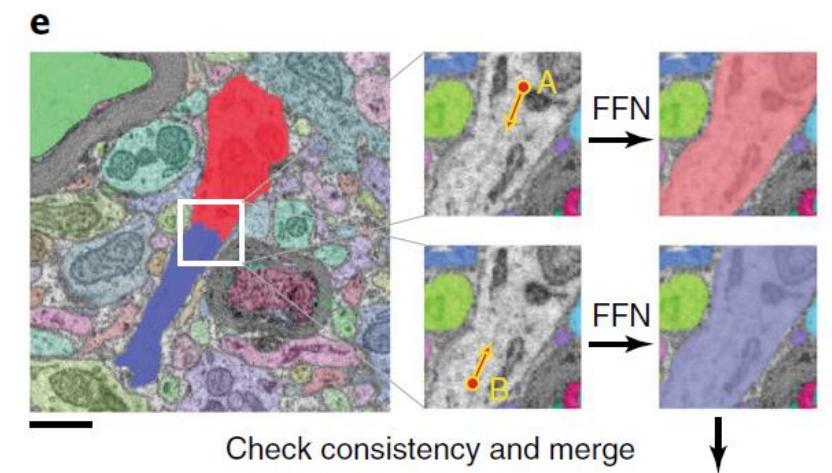
# Hysteresis and approximate scale invariance

- Forward segmentation + reverse segmentation
  - Reverse the seed list
  - Accept all splits as real (the **over-segmentation consensus**)
- Reseeding with resampling at different resolution
- 82-fold reduction mergers with only 2-fold splits increase
  - 9x9x20 nm: Standard Seed + Reversed Seed
  - 18x18x20 nm: Standard Seed + Reversed Seed
  - 36x36x40 nm: Standard Seed
- Conceptually similar to the process of ensemble learning



# Flood-filling-network agglomeration

- Trained classifiers to find split errors (x)
- Use FFN model itself to perform agglomeration (o)
  - Extract  $1\mu\text{m}^3$  subvolume around the point of the segment pair's closest approach, placed seeds in the two objects, and then performed two independent FFN
  - If resulting POMS (predict object mask) overlapped to a high degree, the objects were combined

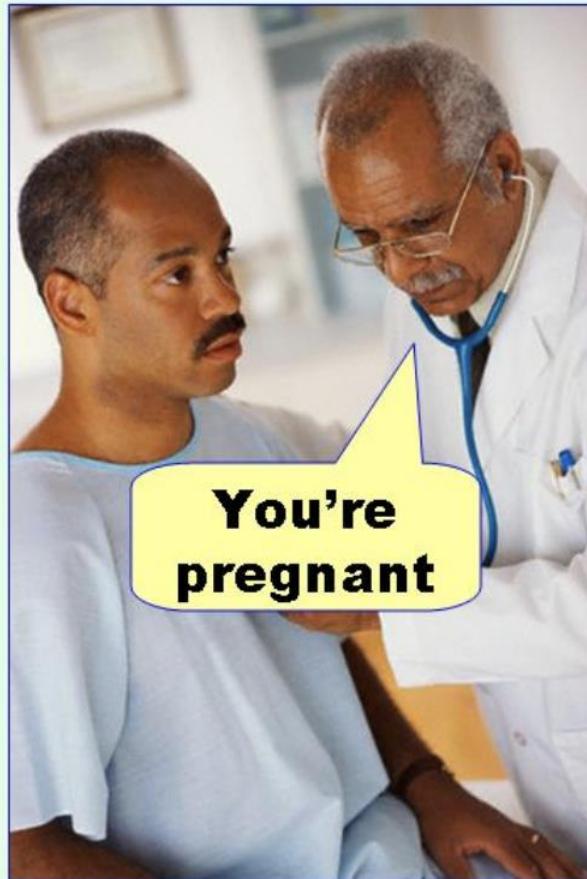


# Confusion matrix

		Predicted Class		
		Positive	Negative	
Actual Class	Positive	True Positive (TP)	False Negative (FN) <b>Type II Error</b>	Sensitivity $\frac{TP}{(TP + FN)}$
	Negative	False Positive (FP) <b>Type I Error</b>	True Negative (TN)	Specificity $\frac{TN}{(TN + FP)}$
	Precision $\frac{TP}{(TP + FP)}$	Negative Predictive Value $\frac{TN}{(TN + FN)}$	Accuracy $\frac{TP + TN}{(TP + TN + FP + FN)}$	

- Sensitivity, **Recall**, hit rate, or true positive rate (TPR)
- Specificity, selectivity or true negative rate (TNR)
- **Precision** or positive predictive value (PPV)
- Negative predictive value (NPV)
- **Accuracy** (ACC)
- FNR, FPR, FDR, FOR, TS, ... etc.  
([https://en.wikipedia.org/wiki/Confusion\\_matrix](https://en.wikipedia.org/wiki/Confusion_matrix))

**Type I error**  
(false positive)



**Type II error**  
(false negative)



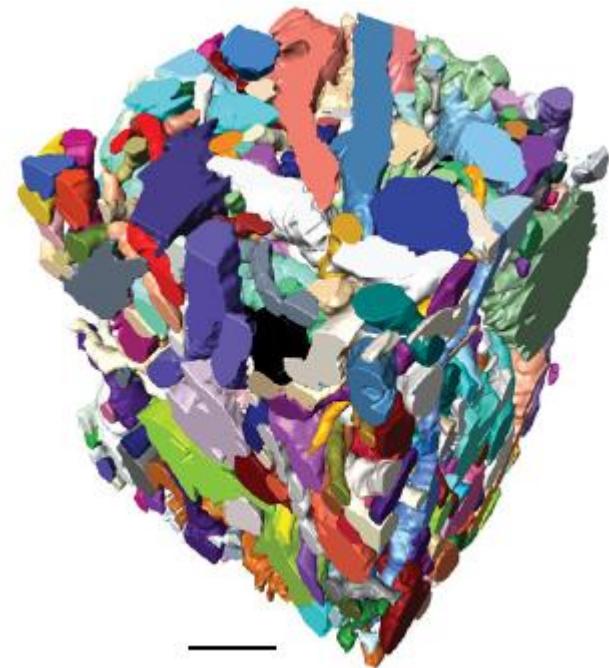
# Large-scale segmentation accuracy

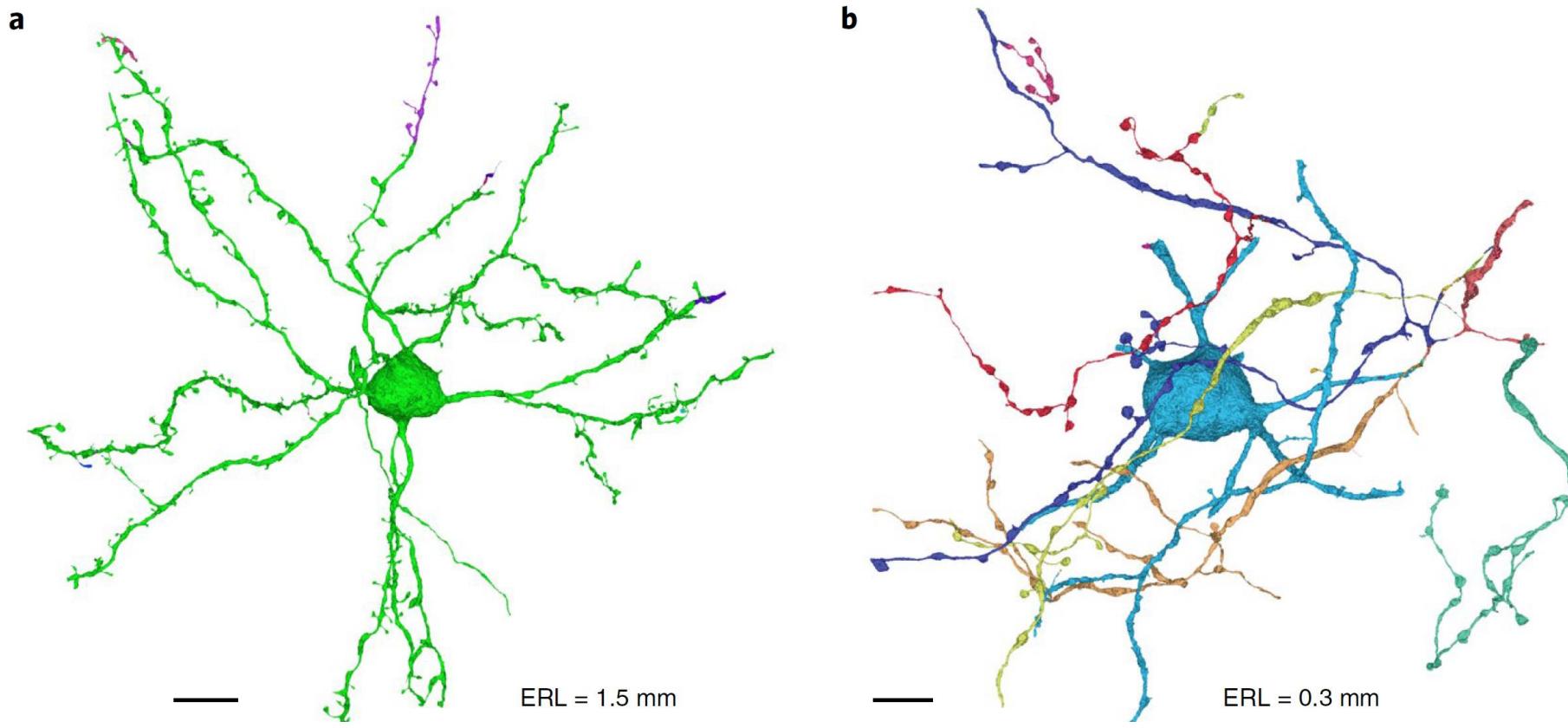
## □ Tuning set

- 12 neurons (median 0.8mm)
- Total path length: 13.5mm (27% axon)

## □ Testing set

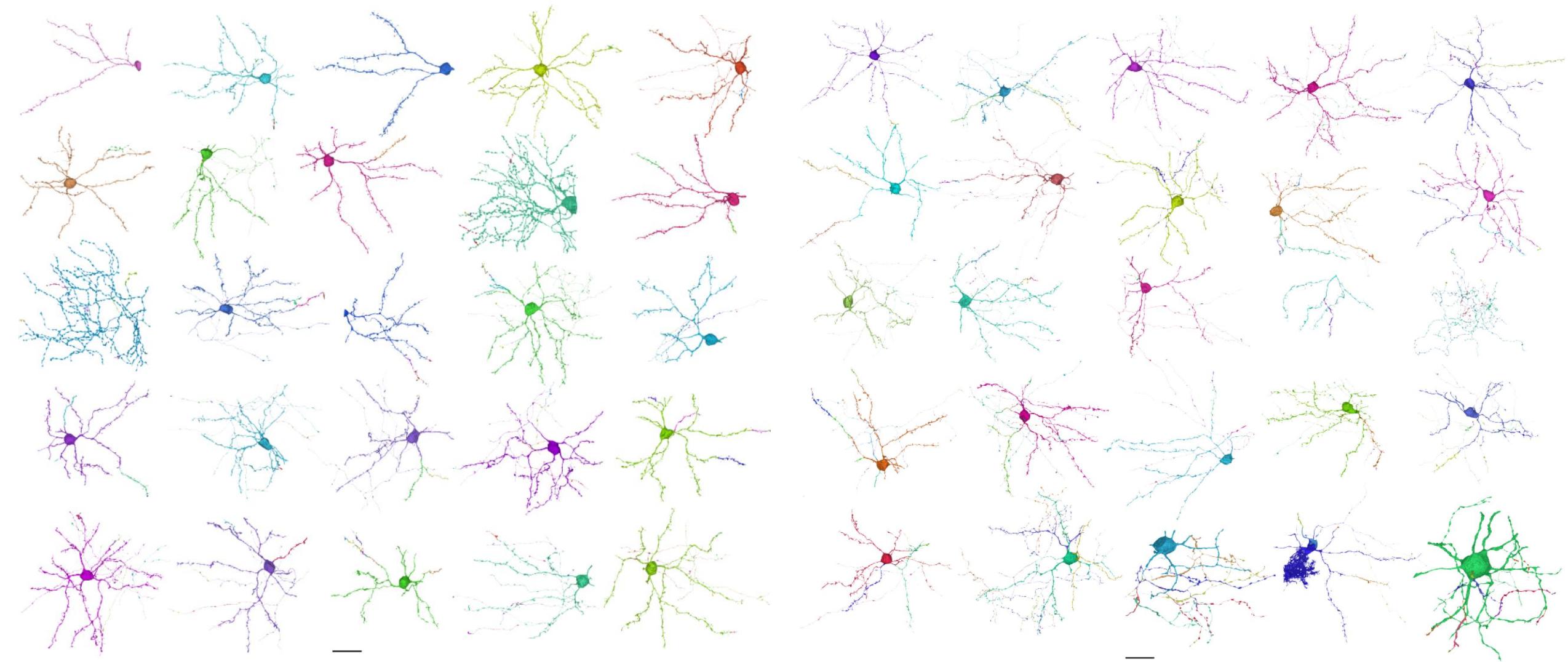
- 50 neurons (median 1.9mm)
  - Total path length: 97mm (34% axon)
- Compare the automatic segmentation to the manually generated skeleton
  - 8 mergers
  - 66 splits (mostly missed dendritic spines)

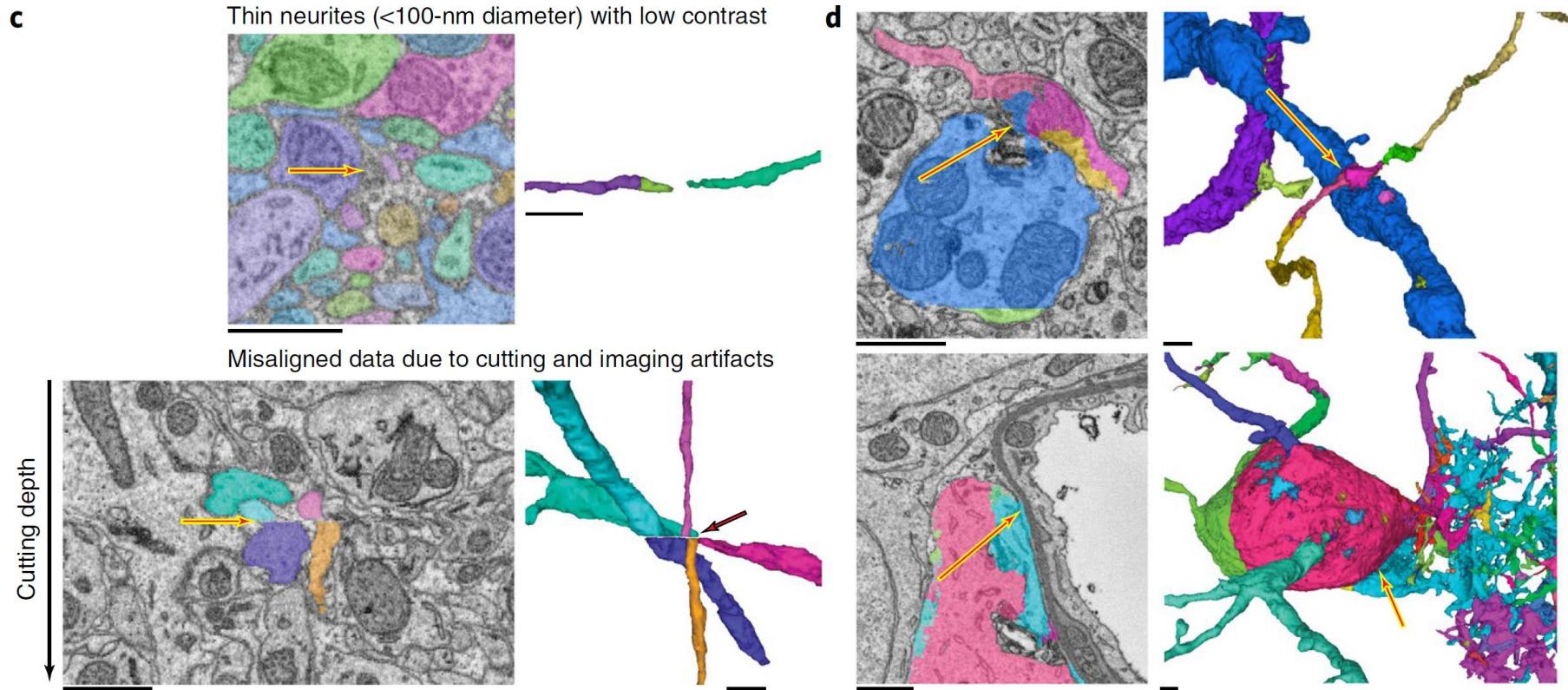




FFNc: max ERL and min ERL

FFNc: total ERL: 1.1mm (test medium 1.9mm), and 4 mergers (total 97 mm)





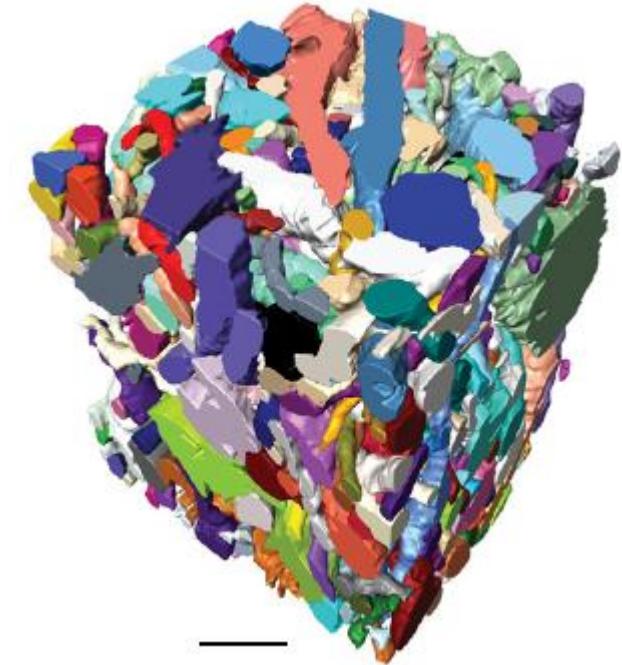
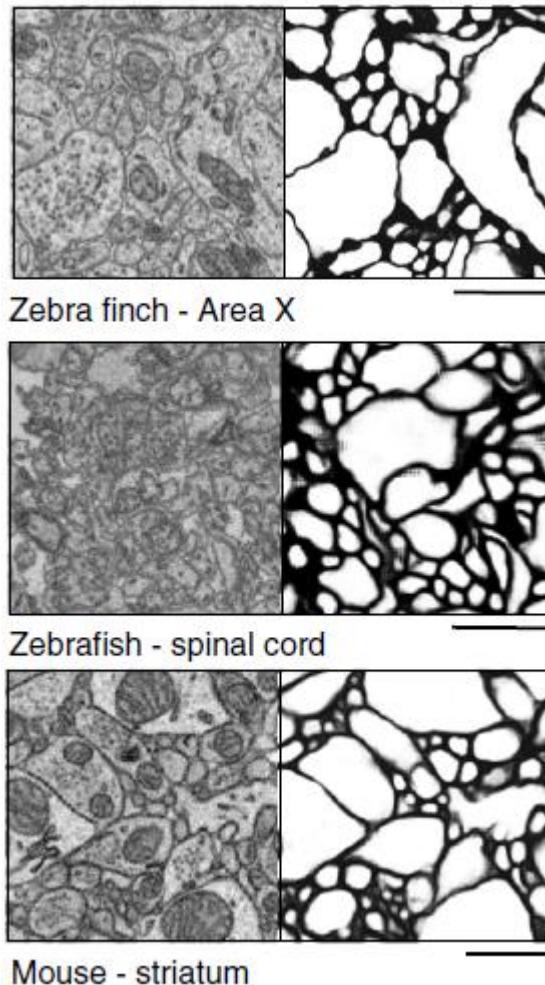
**c**, Zoomed-in views of splits (indicated by arrows) caused by low contrast (top) and slice misalignment (bottom).

**d**, Supervoxel mergers (indicated by arrows) between a dendrite and an axon (top) and between a neuronal cell body and a glial process (bottom).

Scale bars, 1 $\mu$ m (**c,d**).

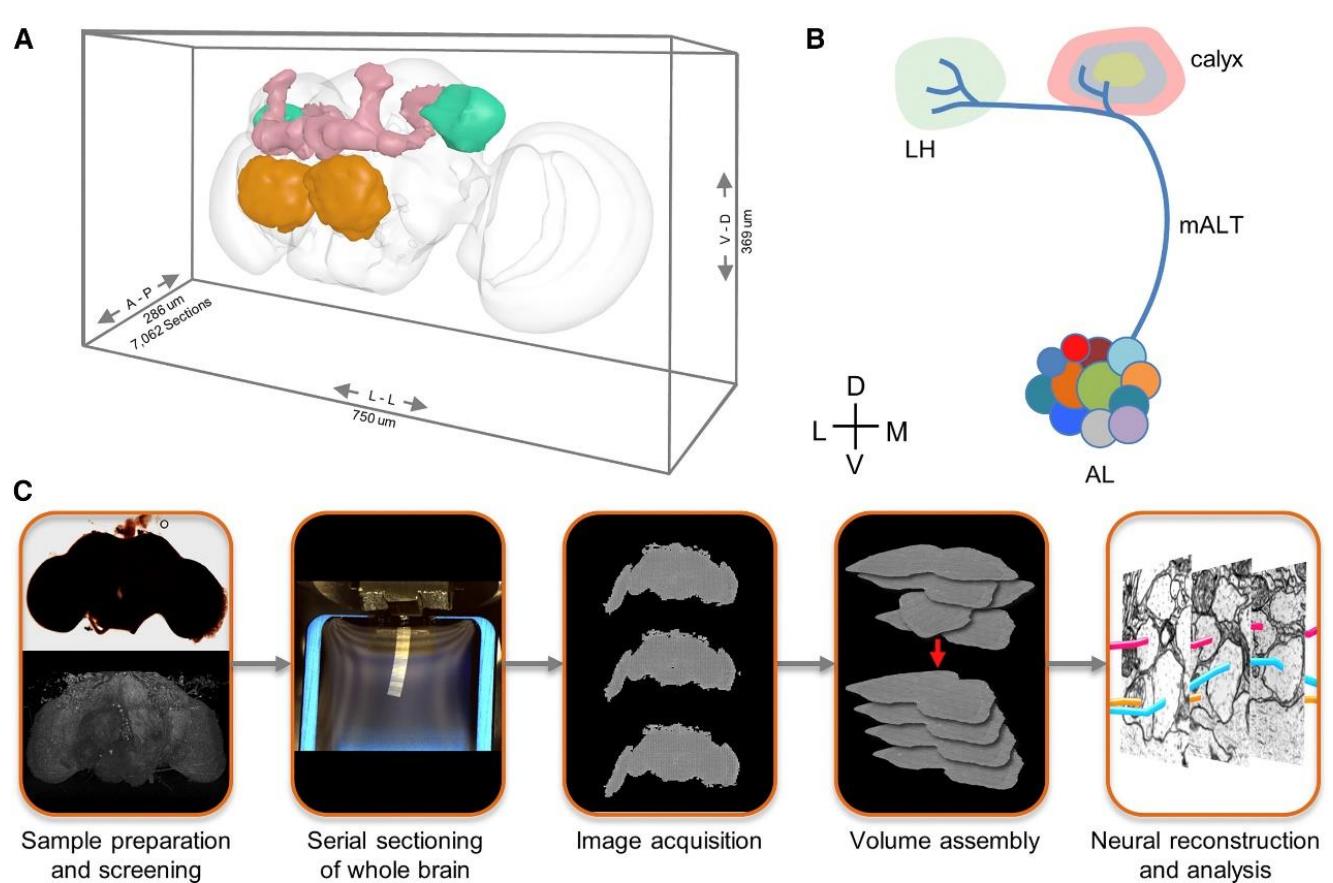
# Automated synaptic connectivity inference for volume electron microscopy

Machine learning segmentation,  
3D CNN



# Janelia Farm's EM data

- One slice :  $8192 \times 8192$  @ 8bits
- Total slices : ~ 107 million
- Real size :  $750 \times 350 \times 282 \mu\text{m}^3$
- Total storage size : ~ 26 TB



# Image segmentation exercise

# CREMI

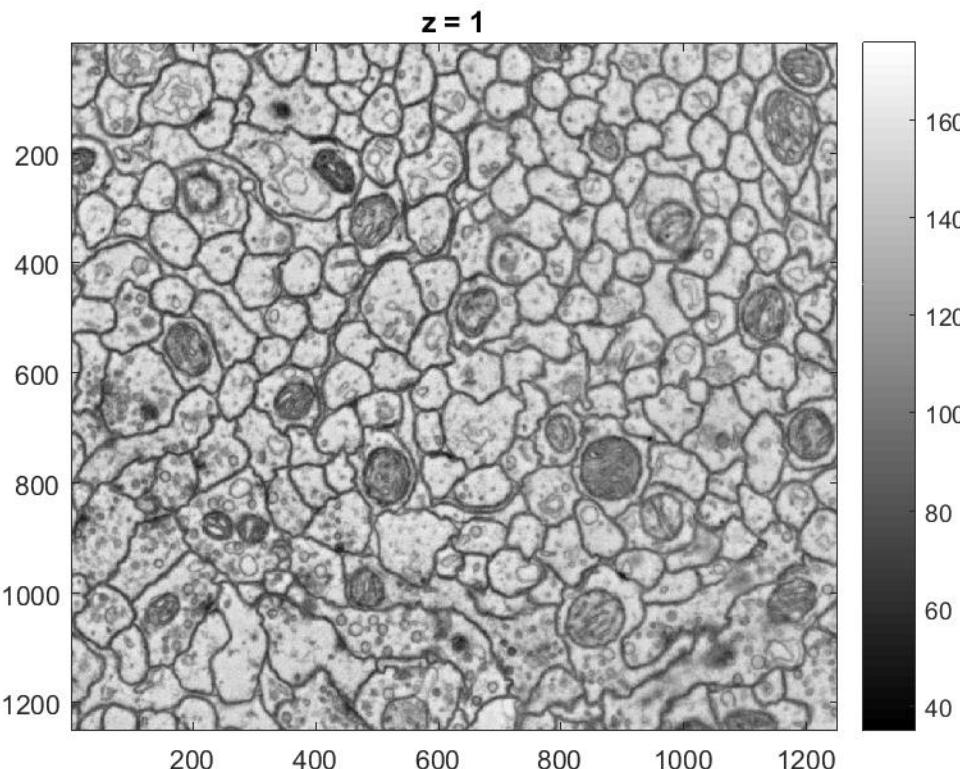
---

- <https://cremi.org/data/>
- **MICCAI Challenge on Circuit Reconstruction from Electron Microscopy Images**
- CREMI provide three datasets, each consisting of two  $(5 \mu\text{m})^3$  volumes ([training](#) and testing, each 1250 px  $\times$  1250 px  $\times$  125 px) of serial section EM of the adult fly brain. Each volume has neuron and synapse labelings and annotations for pre- and post-synaptic partners.
- **sample\_A\_20160501.hdf, 167MB, 1250 px  $\times$  1250 px  $\times$  125 px**

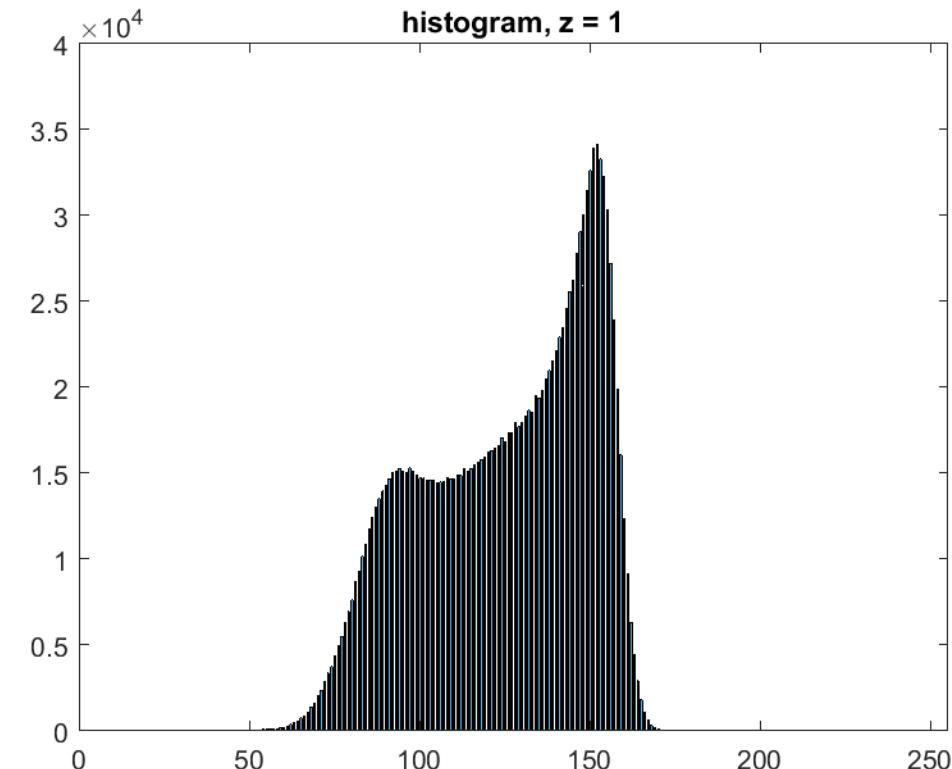
# sample\_A\_20160501

---

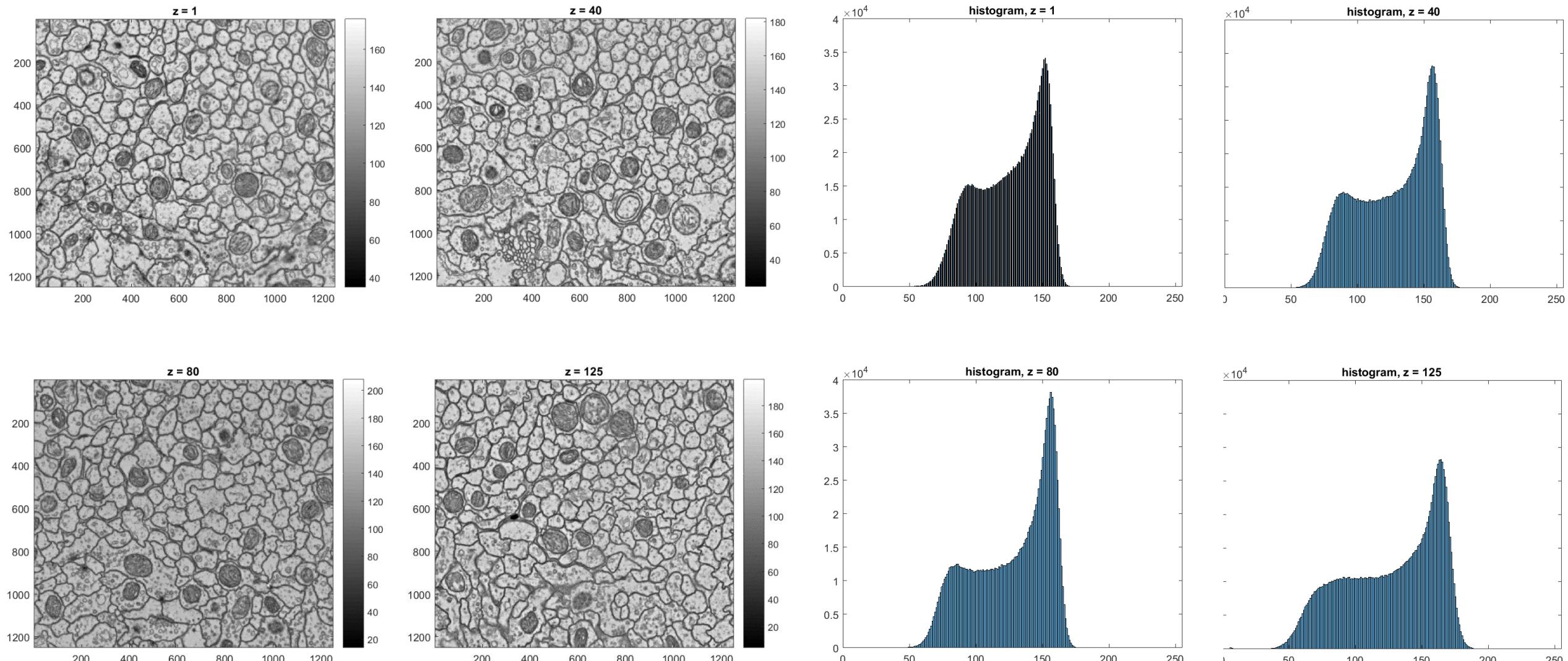
$z=1$ , image



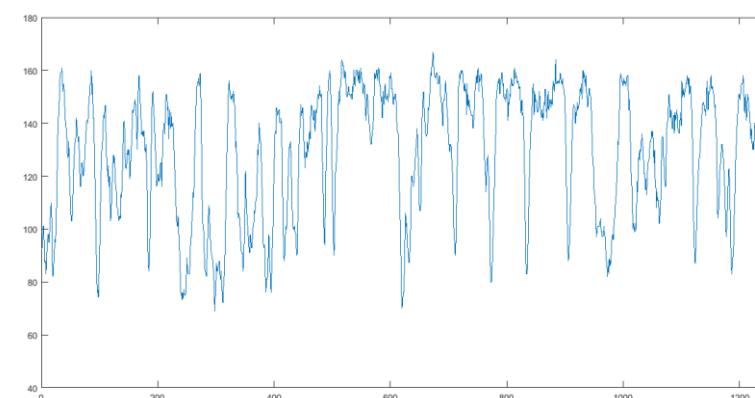
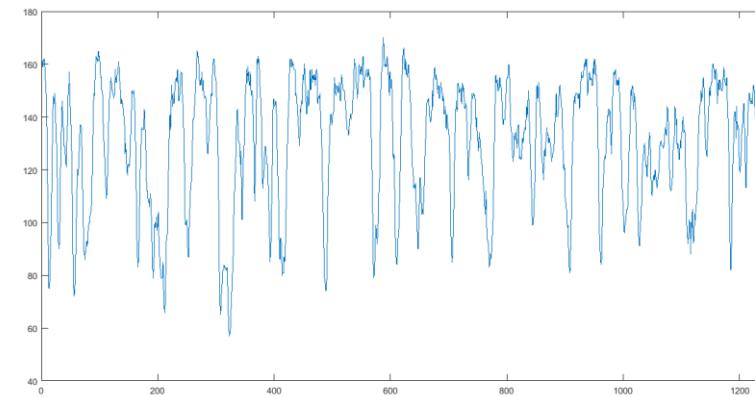
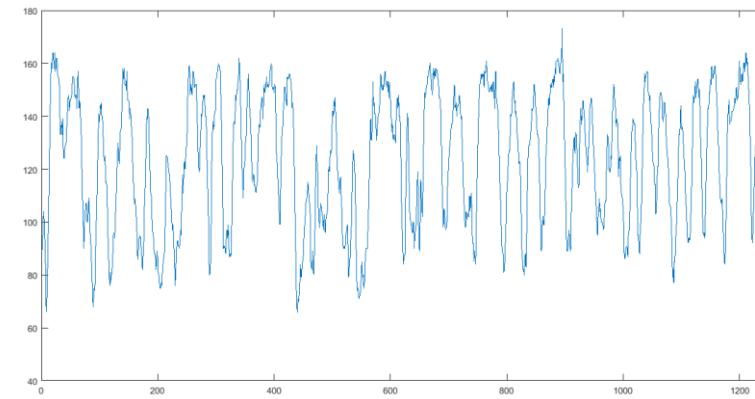
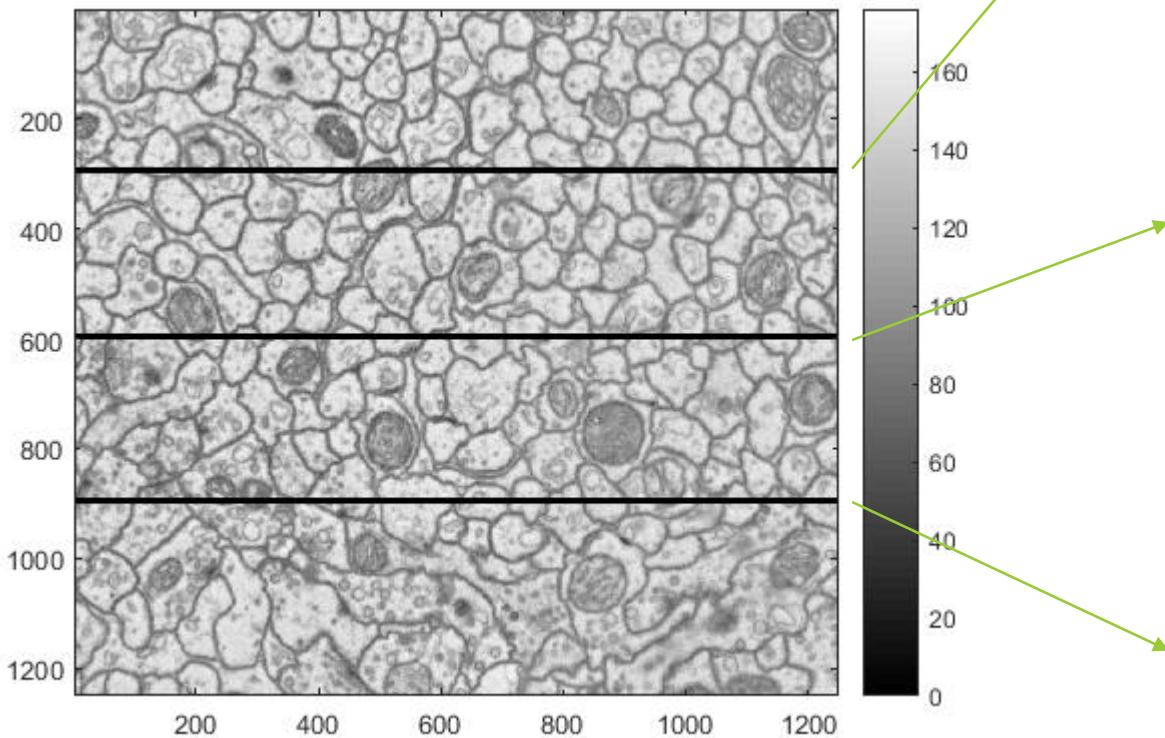
$z=1$ , density histogram



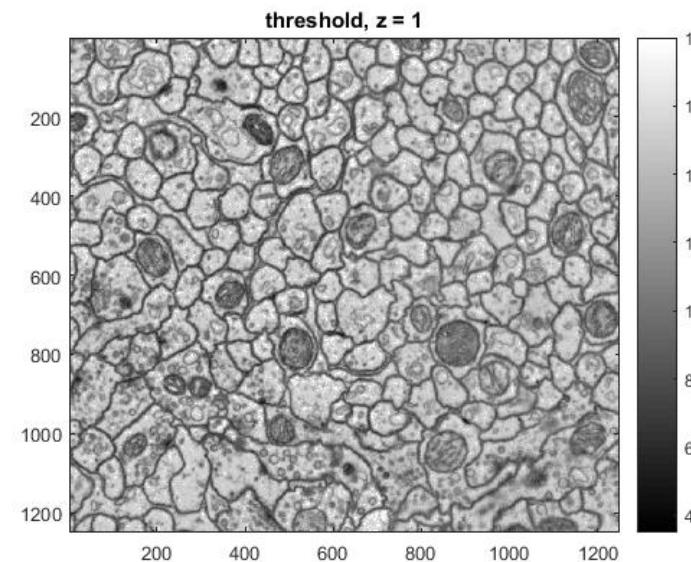
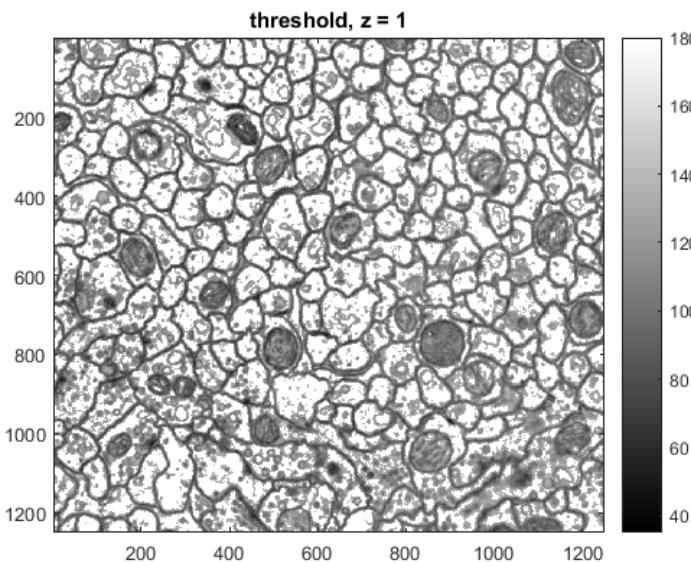
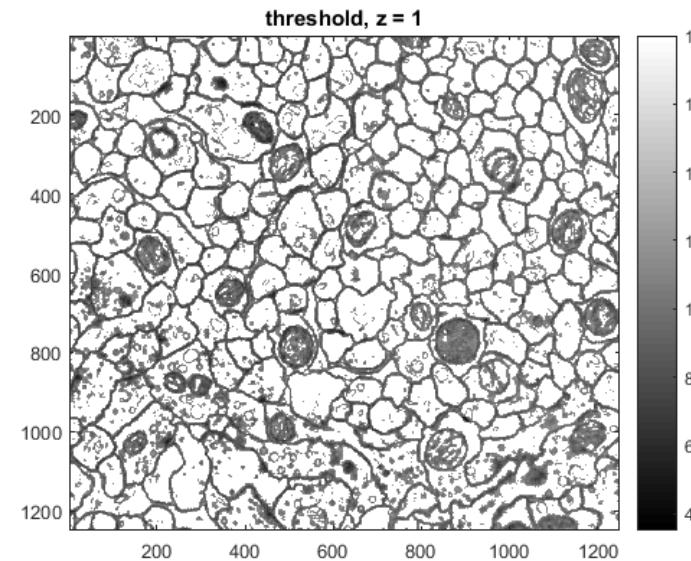
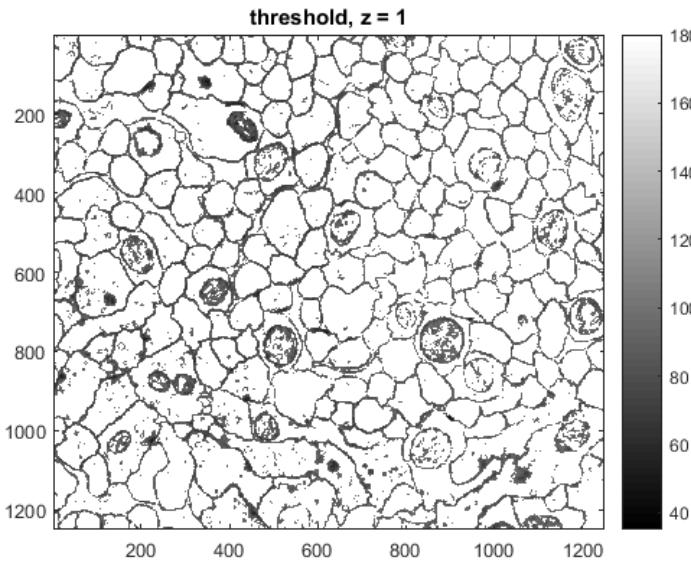
$z = 1, 40, 80, 125$



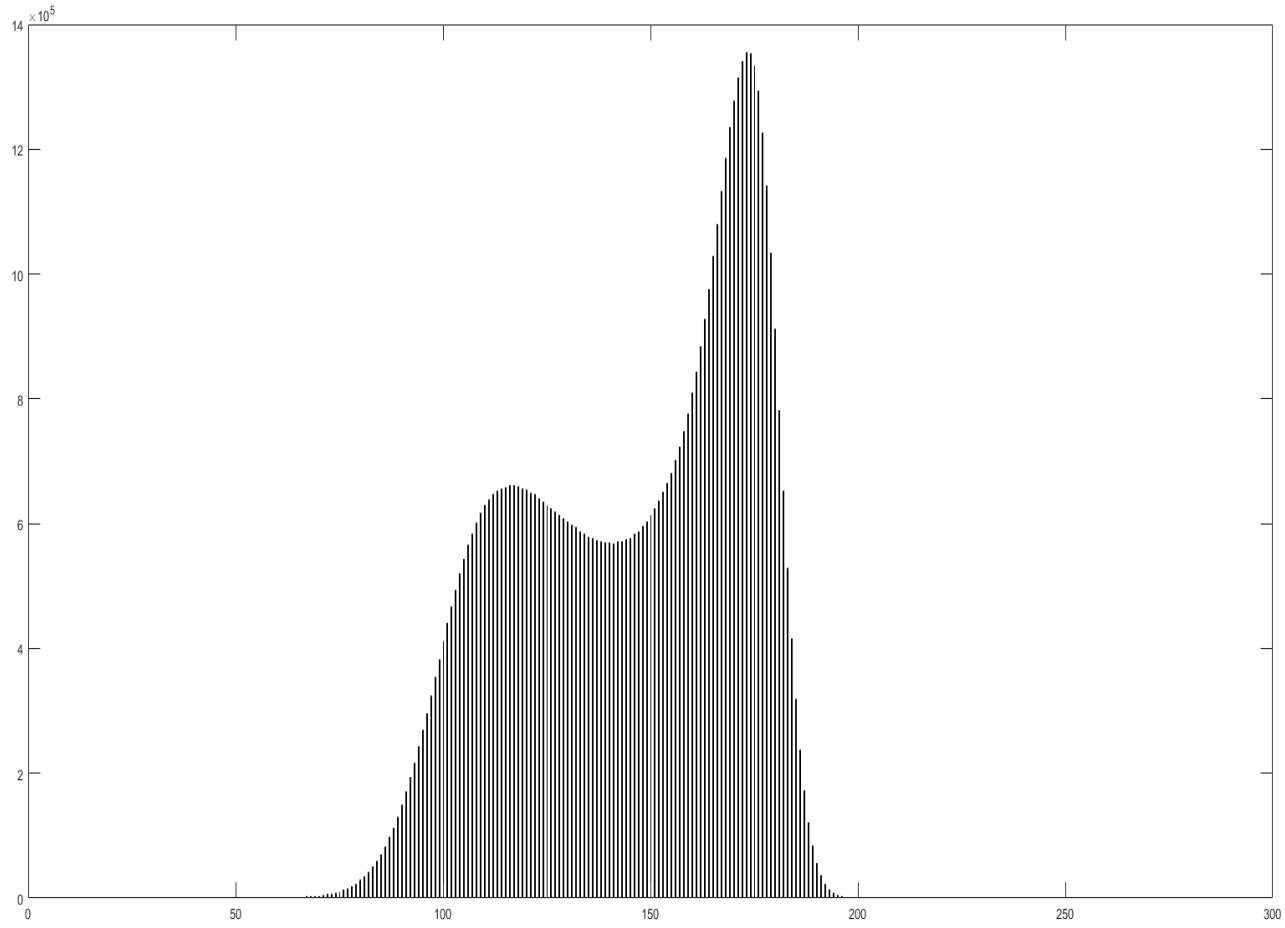
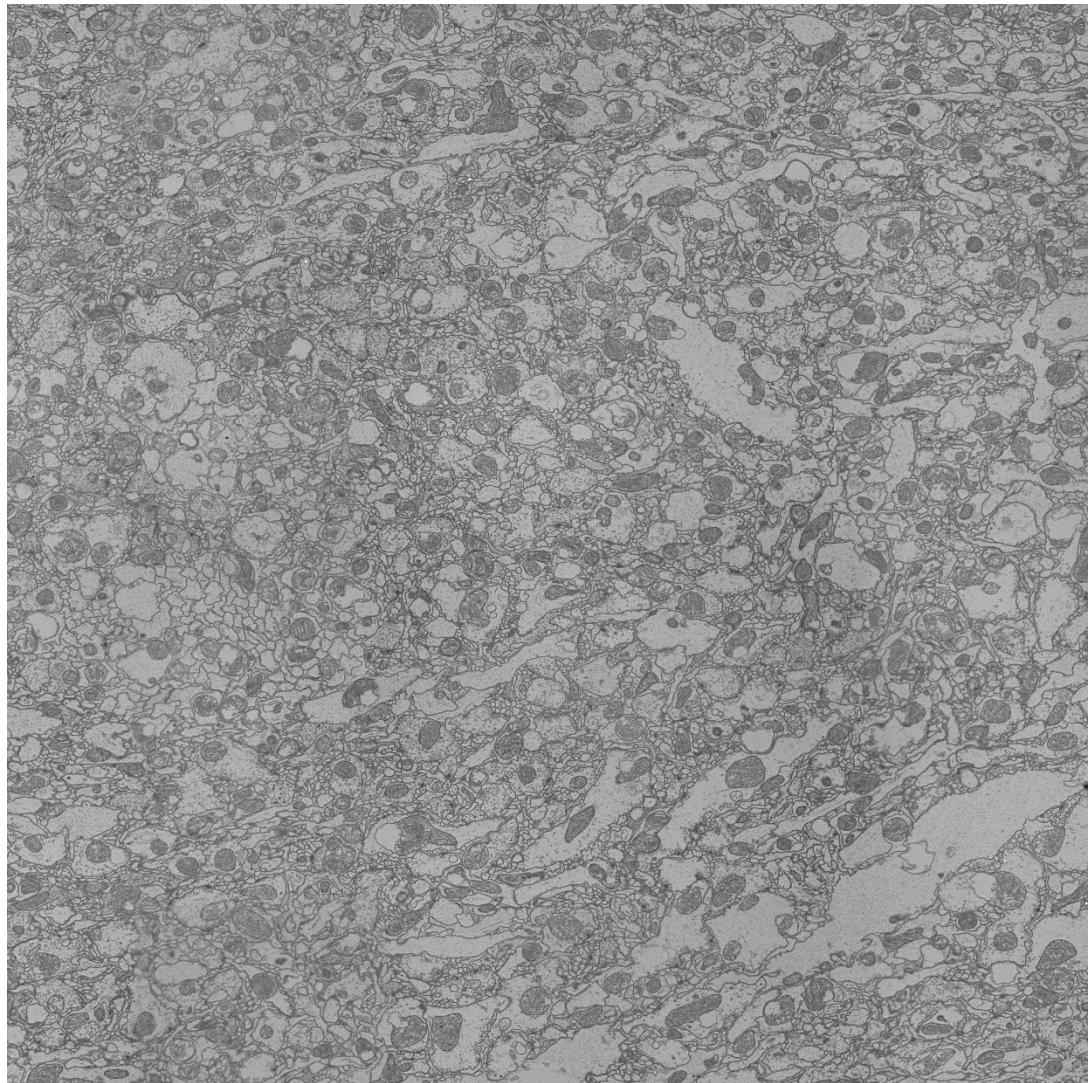
# Cross-section@z=1, y=300, 600, 900

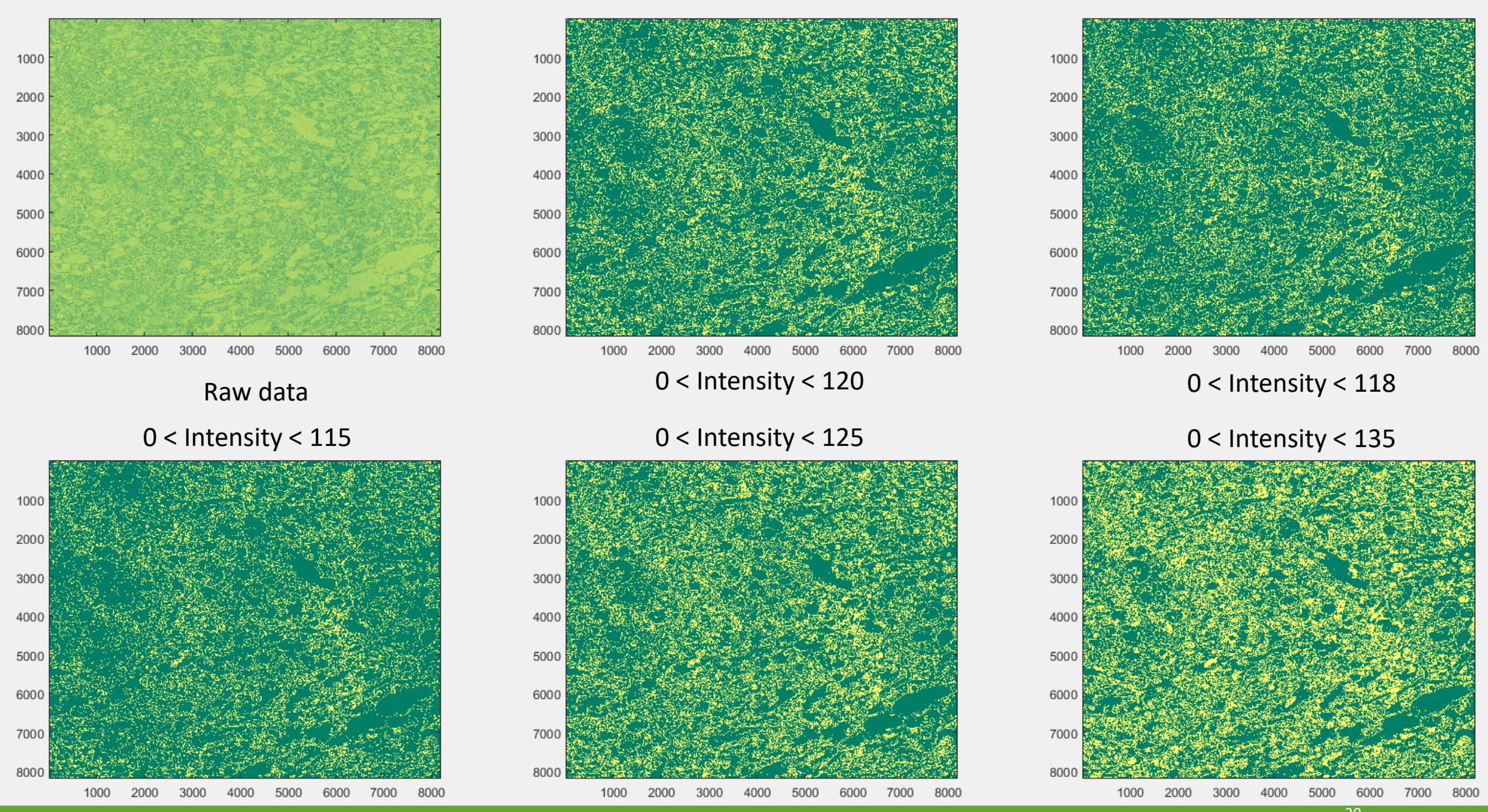


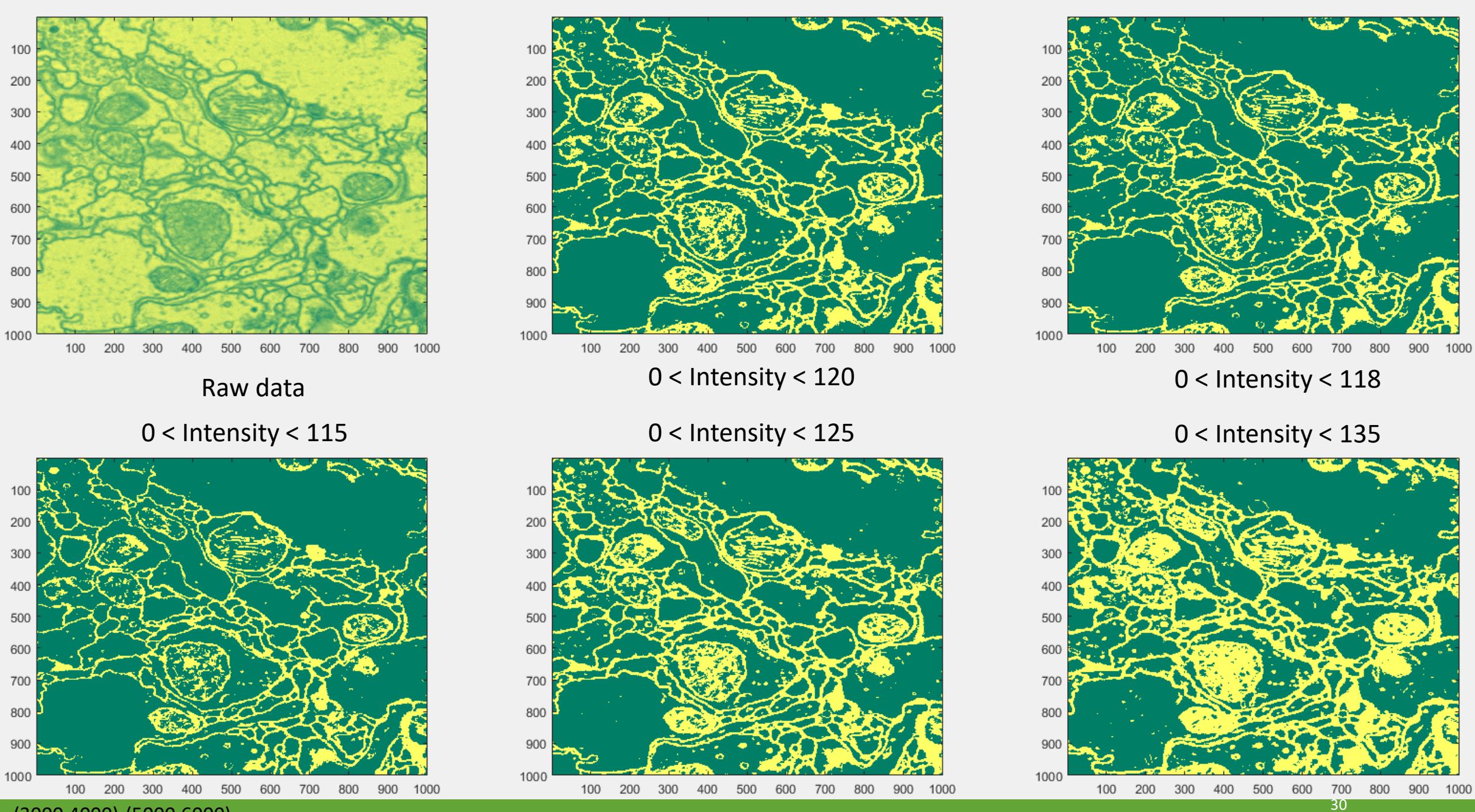
# Threshold@z=1, 100,120,140,160<T<180

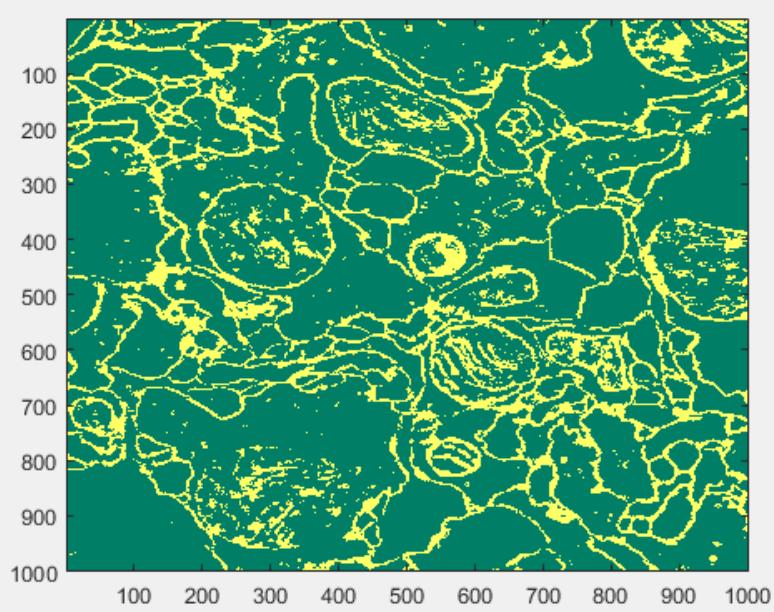
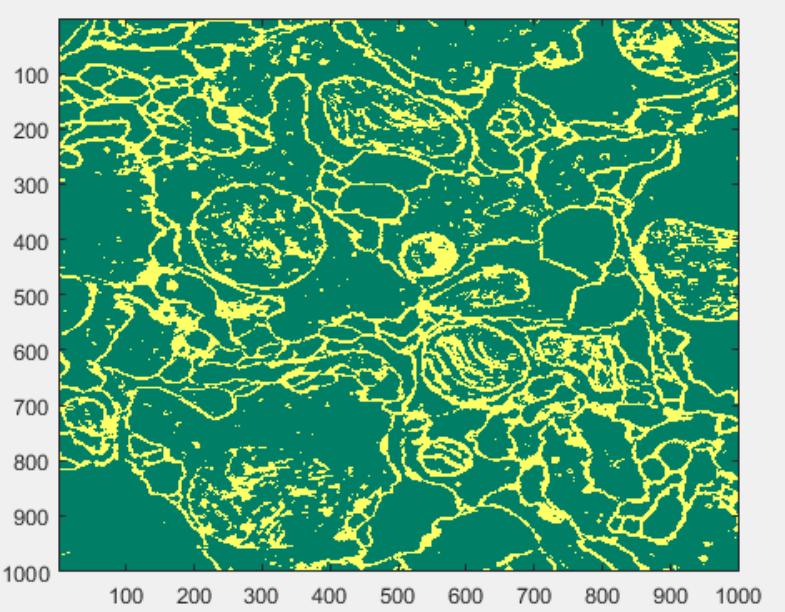
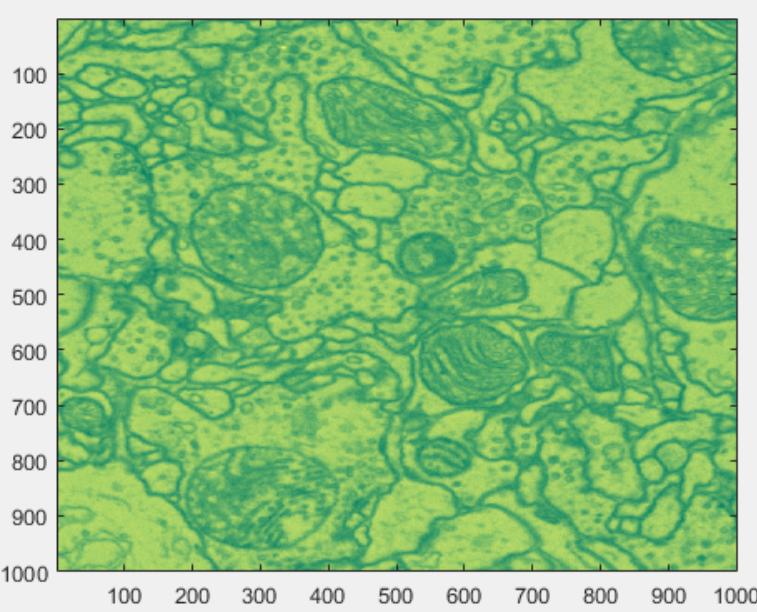


# 4224.0.8.17.png



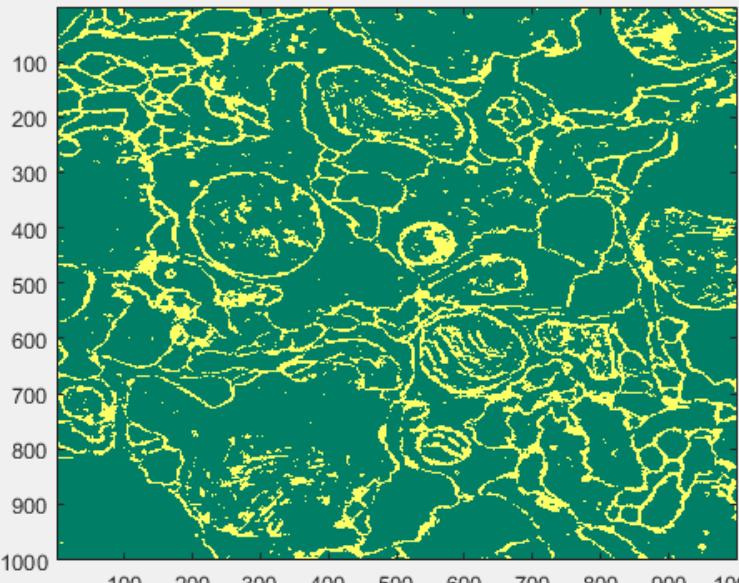






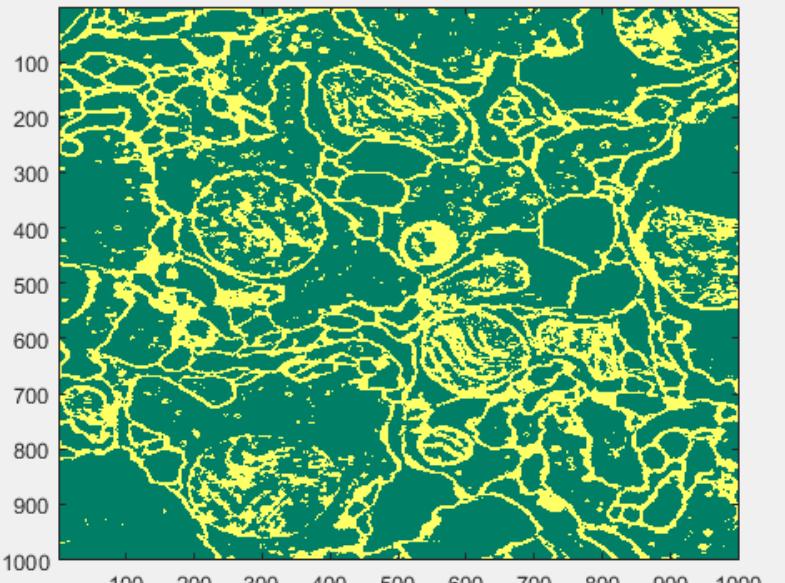
Raw data

$0 < \text{Intensity} < 115$



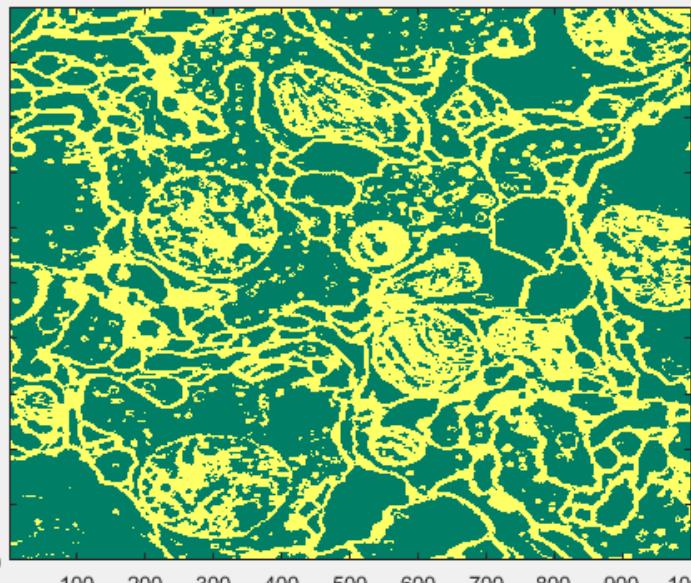
$0 < \text{Intensity} < 120$

$0 < \text{Intensity} < 125$



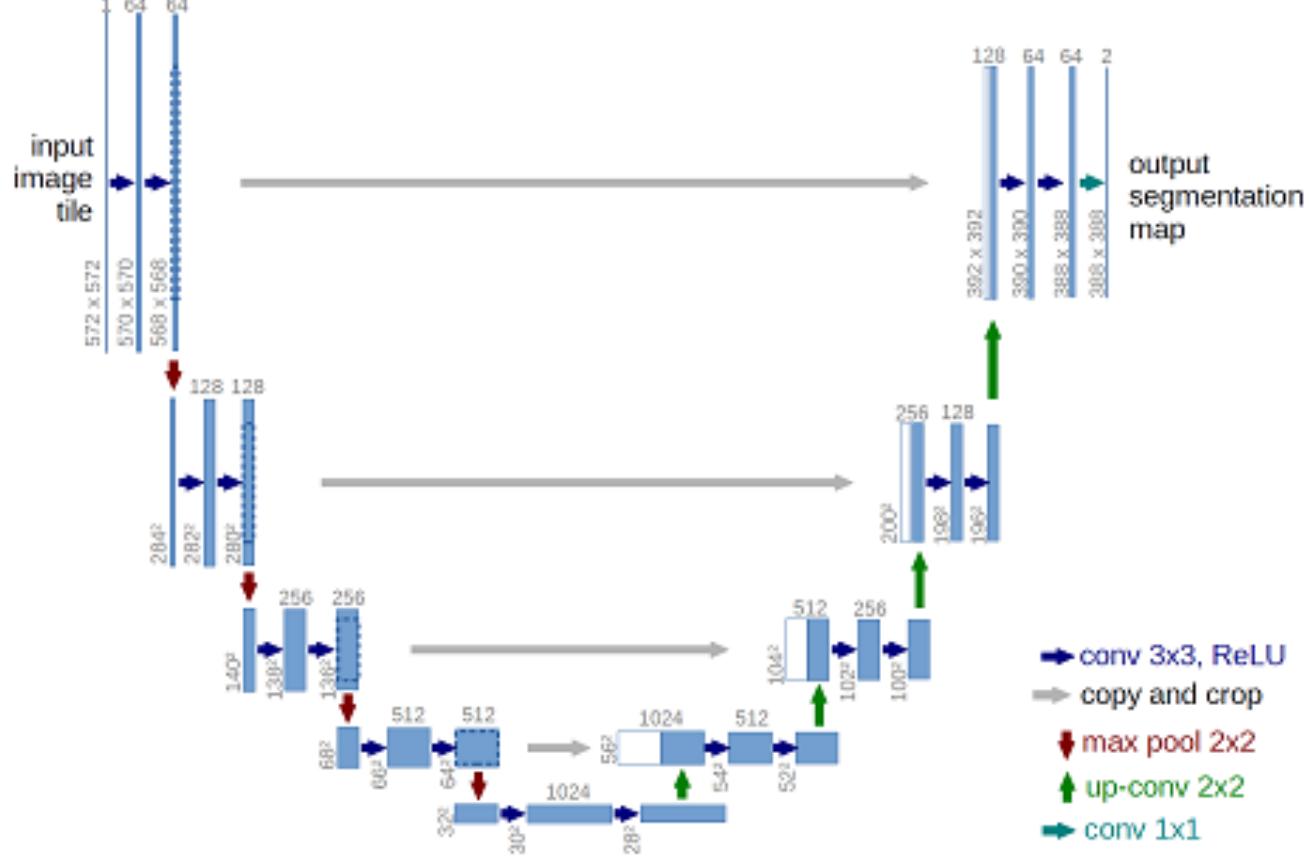
$0 < \text{Intensity} < 118$

$0 < \text{Intensity} < 135$



# U-Net

- <https://arxiv.org/abs/1505.04597>
- Nature Methods 16, 67–70 (2019)
- <https://github.com/zxhuo/unet>



# U-net: Convolutional Networks for Biomedical Image Segmentation

---

Olaf Ronneberger, Philipp Fischer, and Thomas Brox

Computer Science Department and  
BIOSS Centre for Biological Signalling Studies  
University of Freiburg, Germany

Olaf Ronneberger, University of Freiburg, Germany, 22.5.2015

## Leaderboard Neuron Segmentation

Results for the neuron segmentation category, averaged over all samples.

Change the view to: [only sample A+](#) [only sample B+](#) [only sample C+](#)

Group	Submission	CREMI score	VOI split	VOI merge	ARAND
IAL	UnetLMC2	<b>0.221</b>	0.339	0.115	0.108
PNI	PNIUNet5	<b>0.228</b>	0.345	0.106	0.116
PNI	PNIUNet7	<b>0.228</b>	0.345	0.106	0.116
PNI	PNIUNet0	<b>0.229</b>	0.350	0.101	0.117
PNI	PNIUNet4	<b>0.237</b>	0.350	0.110	0.122
PNI	PNIUNet6	<b>0.237</b>	0.349	0.114	0.122
PNI	PNIUNet8	<b>0.237</b>	0.349	0.114	0.122
PNI	JRC-UNet	<b>0.239</b>	0.386	0.081	0.123
PNI	PNIUNet3	<b>0.240</b>	0.327	0.124	0.128
IAL	GASP_avg	<b>0.241</b>	0.365	0.096	0.129
IAL	UnetLRIIF	<b>0.242</b>	0.350	0.135	0.121
PNI	PNIUNet2	<b>0.242</b>	0.326	0.127	0.130
IAL	AvgAggLR	<b>0.244</b>	0.372	0.096	0.130
PNI	RS-UNet2	<b>0.246</b>	0.318	0.158	0.127
IAL	CMskMWS2	<b>0.246</b>	0.383	0.107	0.125
PNI	RS-UNet0	<b>0.248</b>	0.376	0.092	0.134
IAL	DunetLR	<b>0.249</b>	0.372	0.142	0.121
PNI	PNIUNet1	<b>0.251</b>	0.344	0.129	0.134
PNI	RS-UNet1	<b>0.258</b>	0.435	0.076	0.130
JRC	MTLSD	<b>0.266</b>	0.380	0.116	0.144
IAL	pEmbUNet	<b>0.268</b>	0.397	0.127	0.139
JRC	MTLR	<b>0.269</b>	0.395	0.130	0.138
PCH	UNet_mis	<b>0.272</b>	0.453	0.113	0.131
PCH	interp	<b>0.275</b>	0.473	0.114	0.129
JRC	MALAMcv2	<b>0.276</b>	0.490	0.089	0.132

Page 1 of 6 [Next](#)

25 of 144 items

## Leaderboard Synaptic Cleft Detection

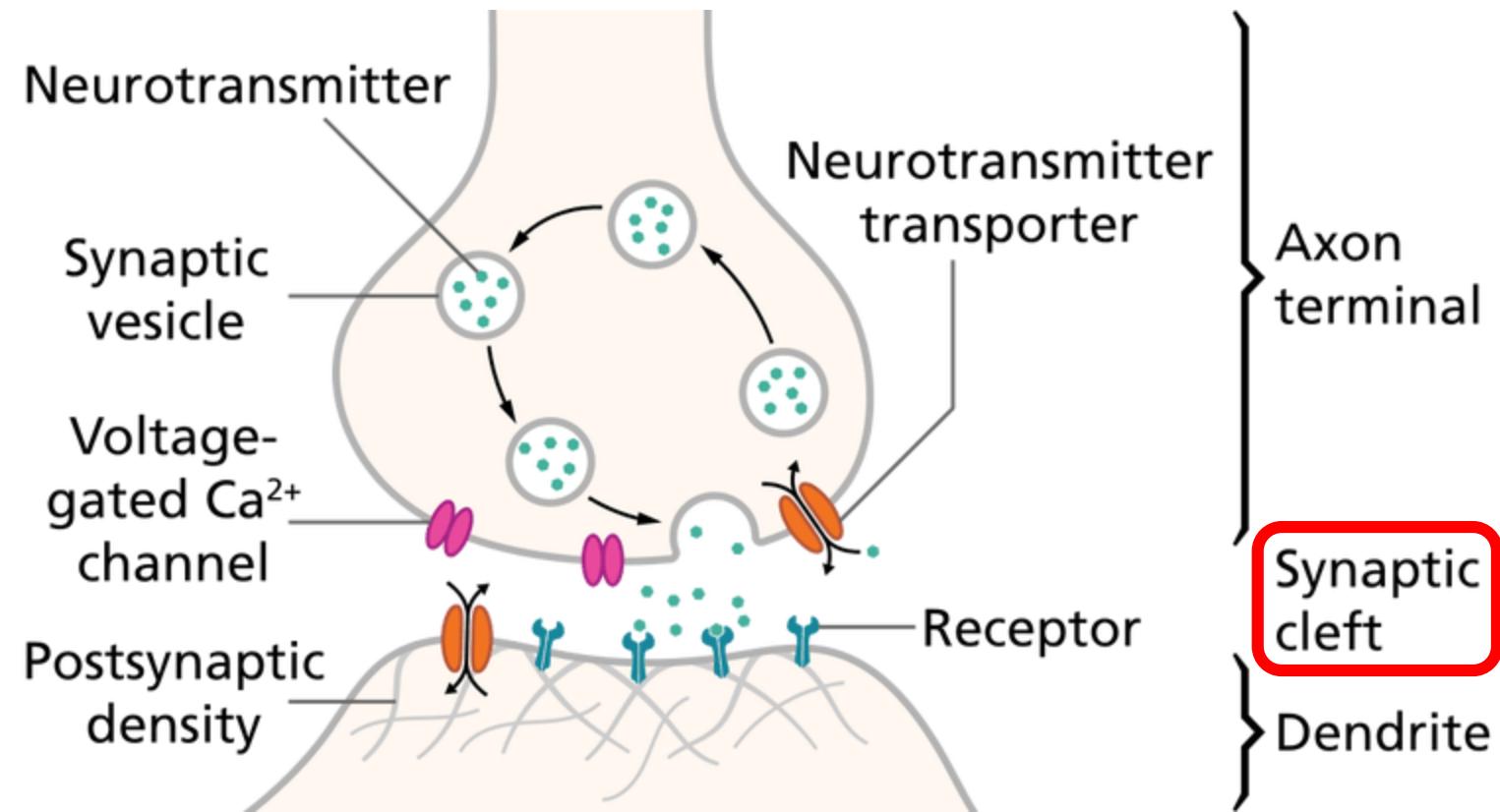
Results for the synaptic cleft detection category, averaged over all samples.

Change the view to: [only sample A+](#) [only sample B+](#) [only sample C+](#)

Group	Submission	CREMI score	FP	FN	1 - F-score	ADGT	ADF
IbdI	Ib_thicc	<b>59.04</b>	107211.3	234.0	0.190	109.17	8.91
SDG	Unet2	<b>63.92</b>	202177.7	13156.0	0.256	97.64	30.19
IbdI	Ib_lst	<b>64.22</b>	118160.0	0.0	0.209	121.50	6.93
I2I	SparSep	<b>66.76</b>	151781.7	11350.3	0.188	87.35	46.17
JRC	DTU-2	<b>67.56</b>	70761.3	10069.3	0.123	109.67	25.46
JRC	DTU-1	<b>72.21</b>	85169.0	13607.3	0.131	106.31	38.11
DKFZ-MIC	nnUNet	<b>74.96</b>	49914.0	18981.3	0.117	64.46	85.46
SDG	Unet1	<b>75.28</b>	185988.3	16897.3	0.230	84.34	66.22
I2I	CSparSep	<b>75.79</b>	71650.0	18918.3	0.140	72.06	79.52
DIVE	SegCleft	<b>77.03</b>	80978.3	20639.3	0.162	121.03	33.03
DIVE	cleft_1	<b>77.03</b>	80978.3	20639.3	0.162	121.03	33.03
DIVE	WeitUNet	<b>78.12</b>	54372.7	24480.3	0.128	71.51	84.73
DIVE	BouUNet	<b>81.45</b>	75985.0	21974.0	0.160	76.66	86.24
DIVE	BesUNet	<b>82.46</b>	131090.7	15589.0	0.206	109.52	55.40
DIVE	cleft	<b>88.46</b>	97220.7	21239.3	0.172	139.74	37.18
HSS	HSZ	<b>90.11</b>	65092.3	25807.3	0.154	99.61	80.61
DIVE	exp19lst	<b>90.80</b>	25114.7	21554.0	0.107	117.39	64.21
IbdI	Cleft_Ib	<b>97.85</b>	227868.0	0.0	0.262	181.08	14.61
DIVE	cleft_hi	<b>107.24</b>	44844.3	52063.7	0.158	94.14	120.33
SDG	Synap0.0	<b>118.10</b>	193580.0	12504.0	0.270	185.62	50.58
SDG	SynapX.0	<b>118.10</b>	193580.0	12504.0	0.270	185.62	50.58
DIVE	CRNNGate	<b>120.36</b>	62609.0	47395.7	0.175	110.06	130.66
SDG	SynapX.X	<b>121.40</b>	204301.0	16302.7	0.286	194.74	48.06
SDG	SnapX.O	<b>124.59</b>	182577.0	17000.7	0.306	205.18	44.01
SDG	SnapF.V	<b>124.59</b>	182577.0	17000.7	0.306	205.18	44.01

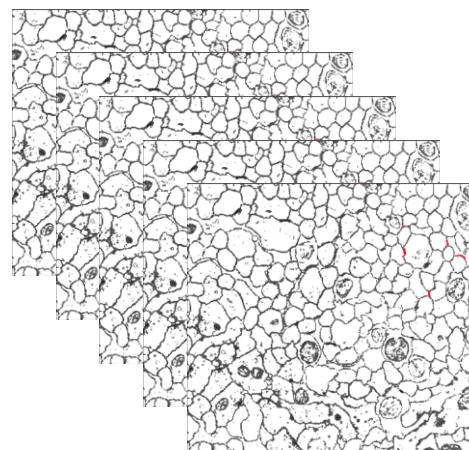
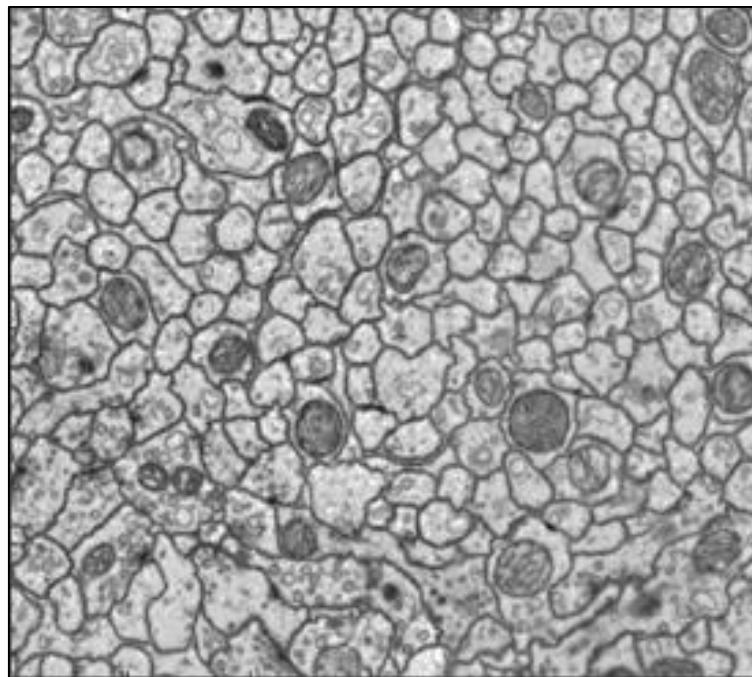
Page 1 of 2 [Next](#)

25 of 49 items

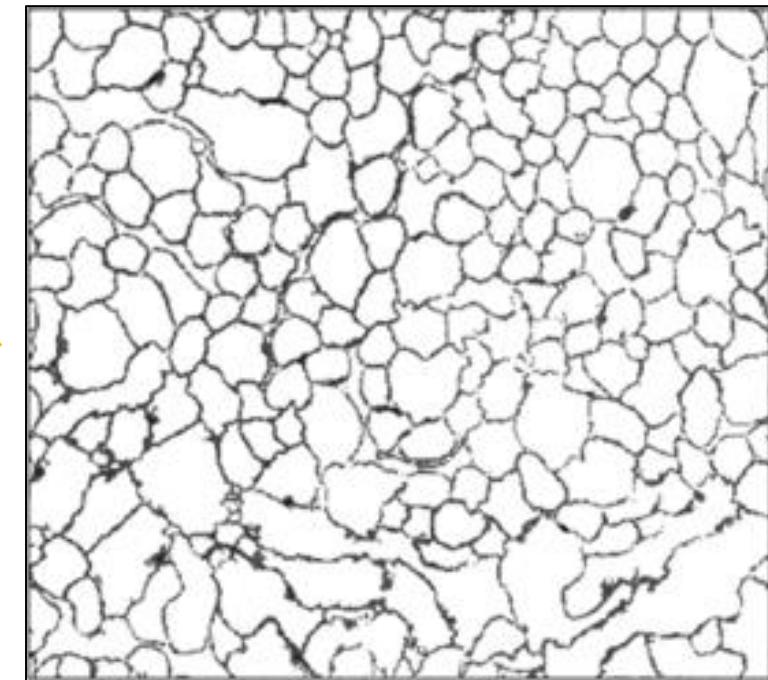


# Proposed workflow - Membrane segmentation

---



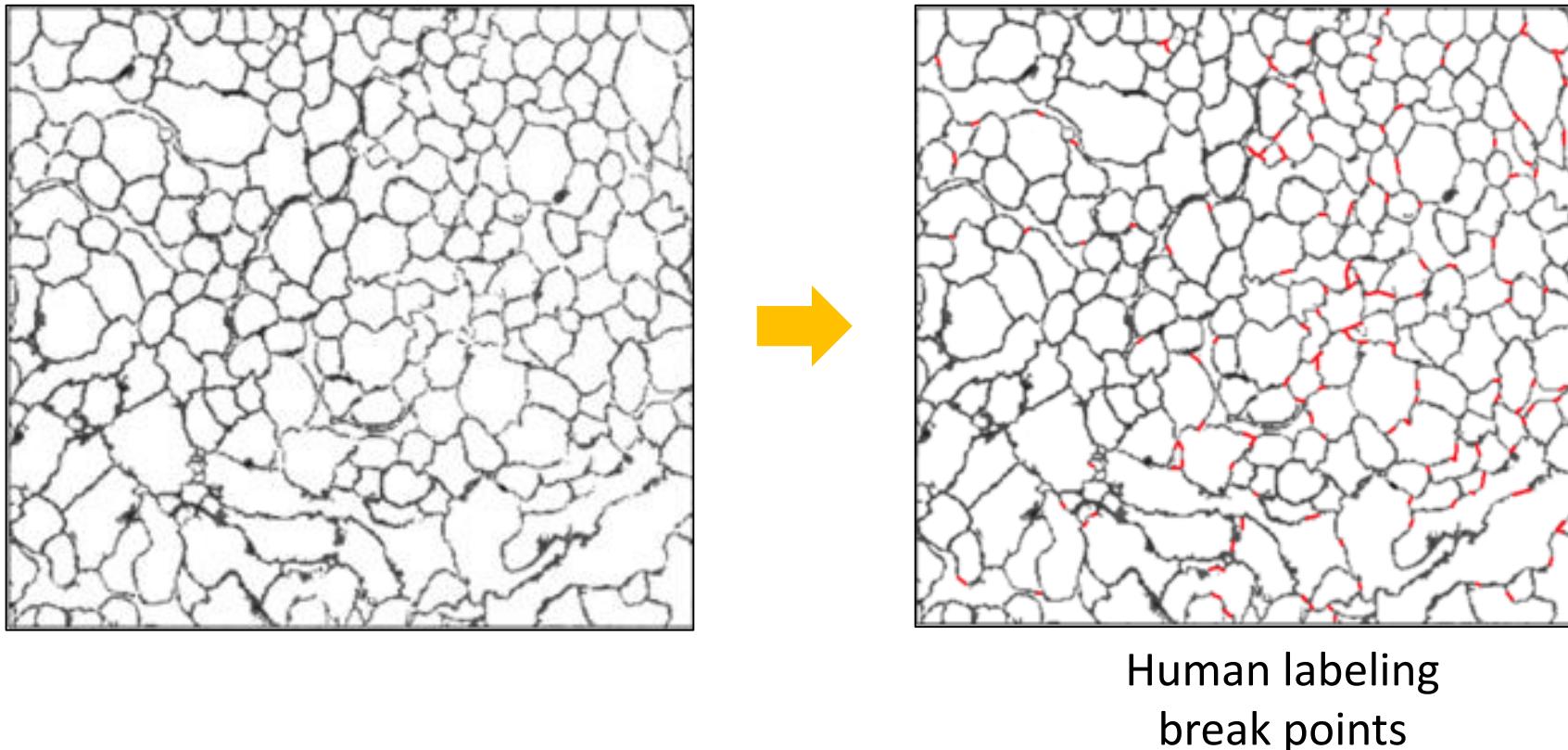
Ensemble learning

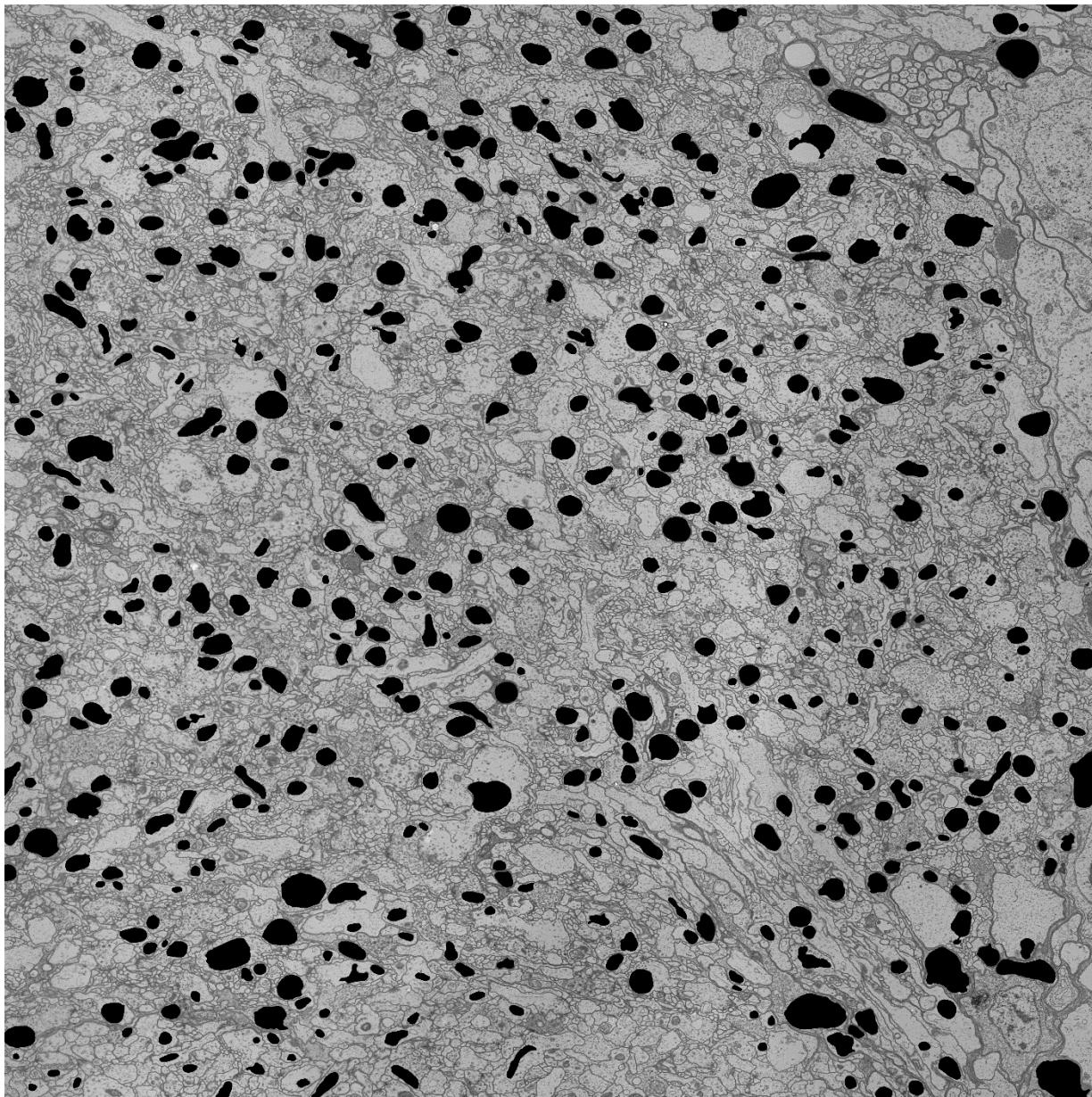


Membrane segmented by U-Net

# Proposed workflow - Break points fixing

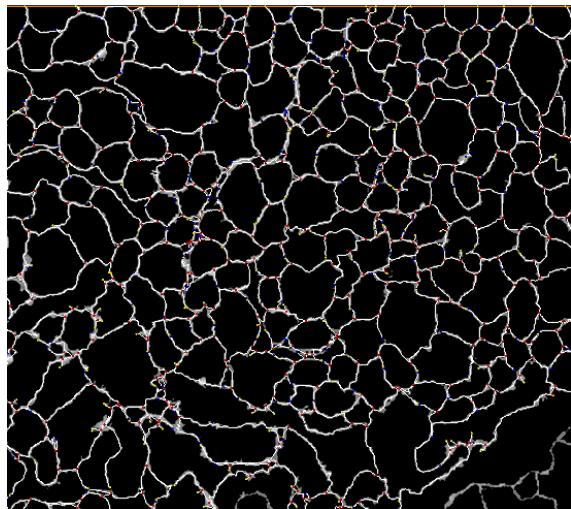
---



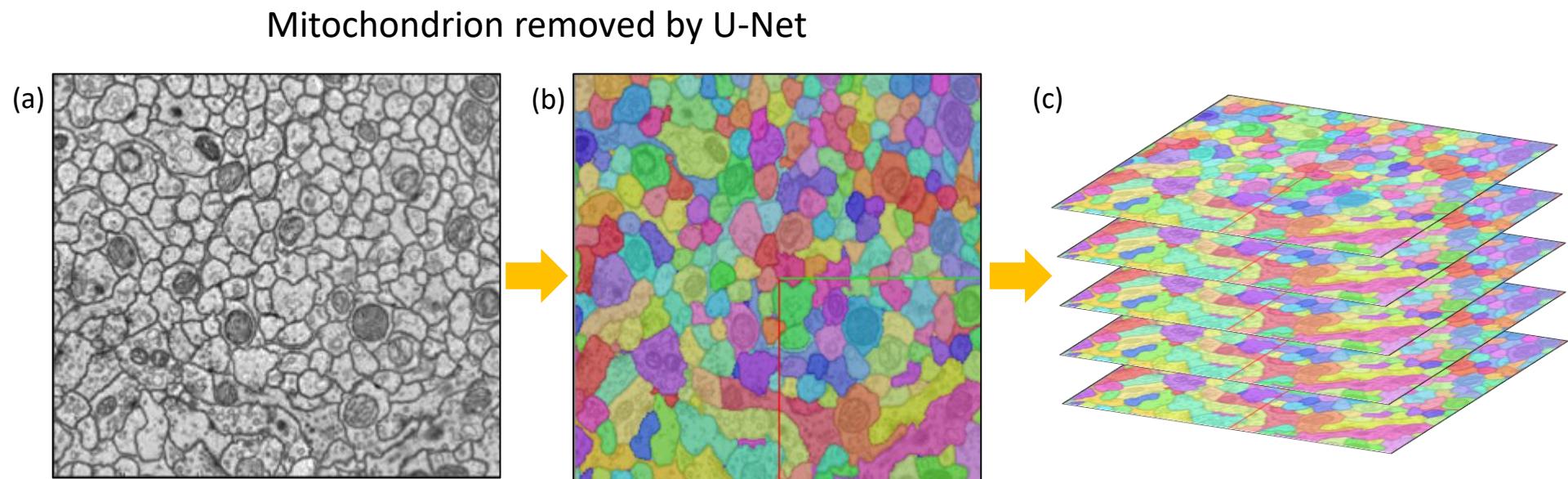


Human labeling  
mitochondrion

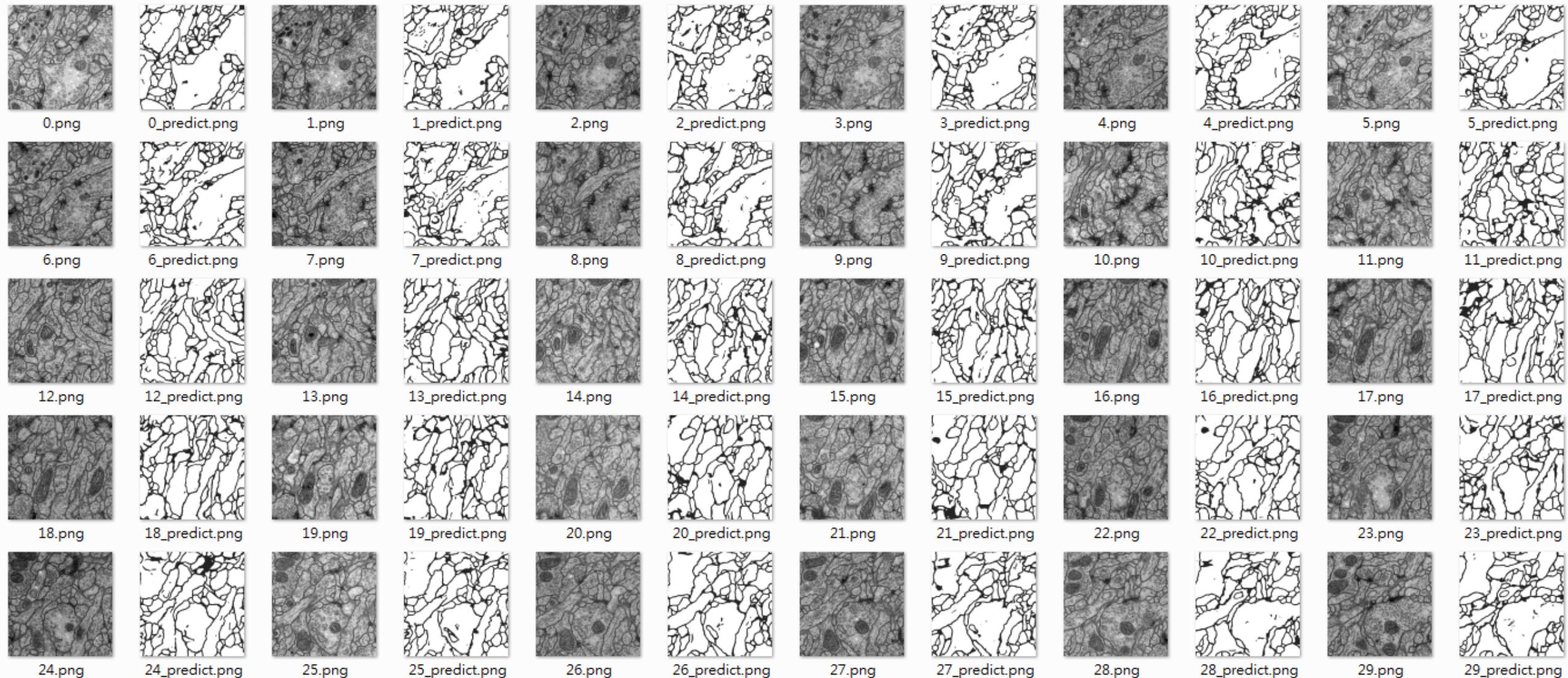
# Proposed workflow - Mitochondrion Removing



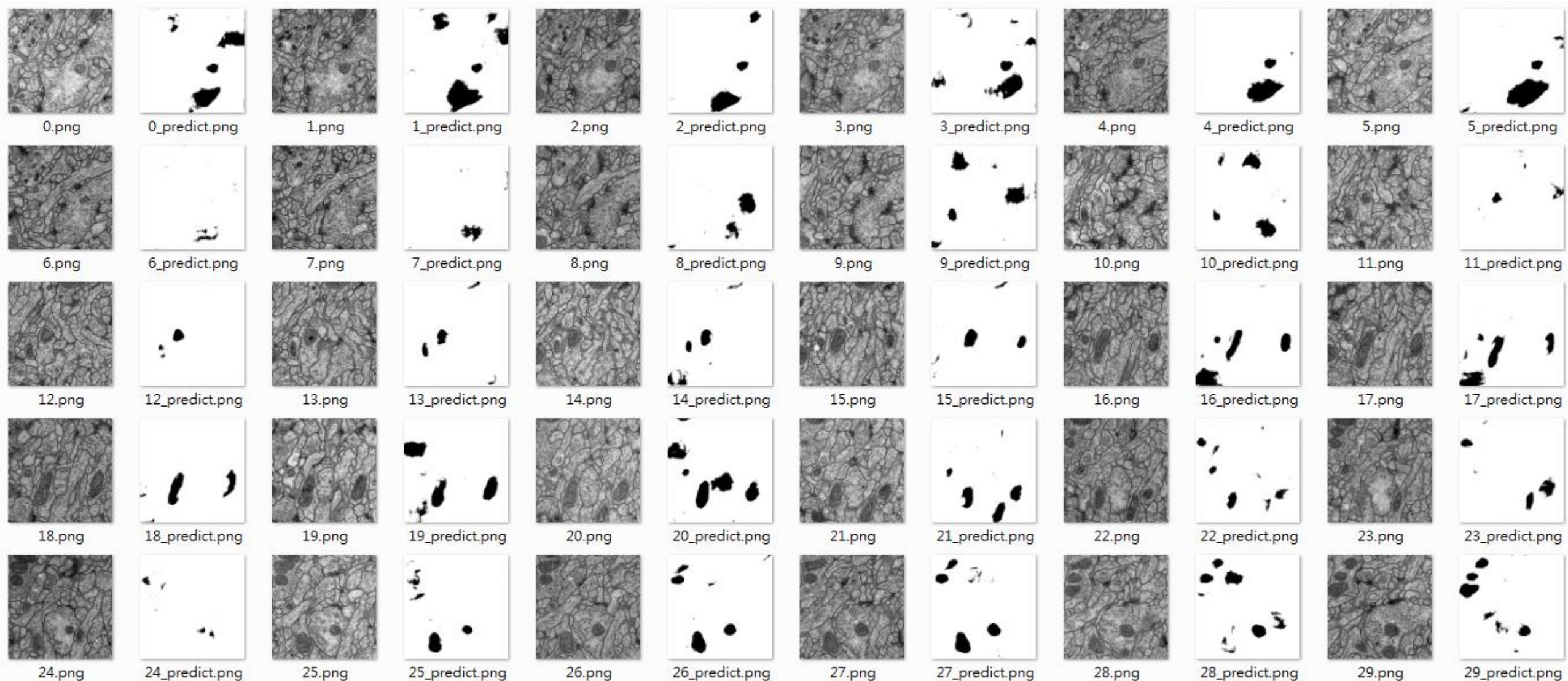
Membrane fixed by U-Net



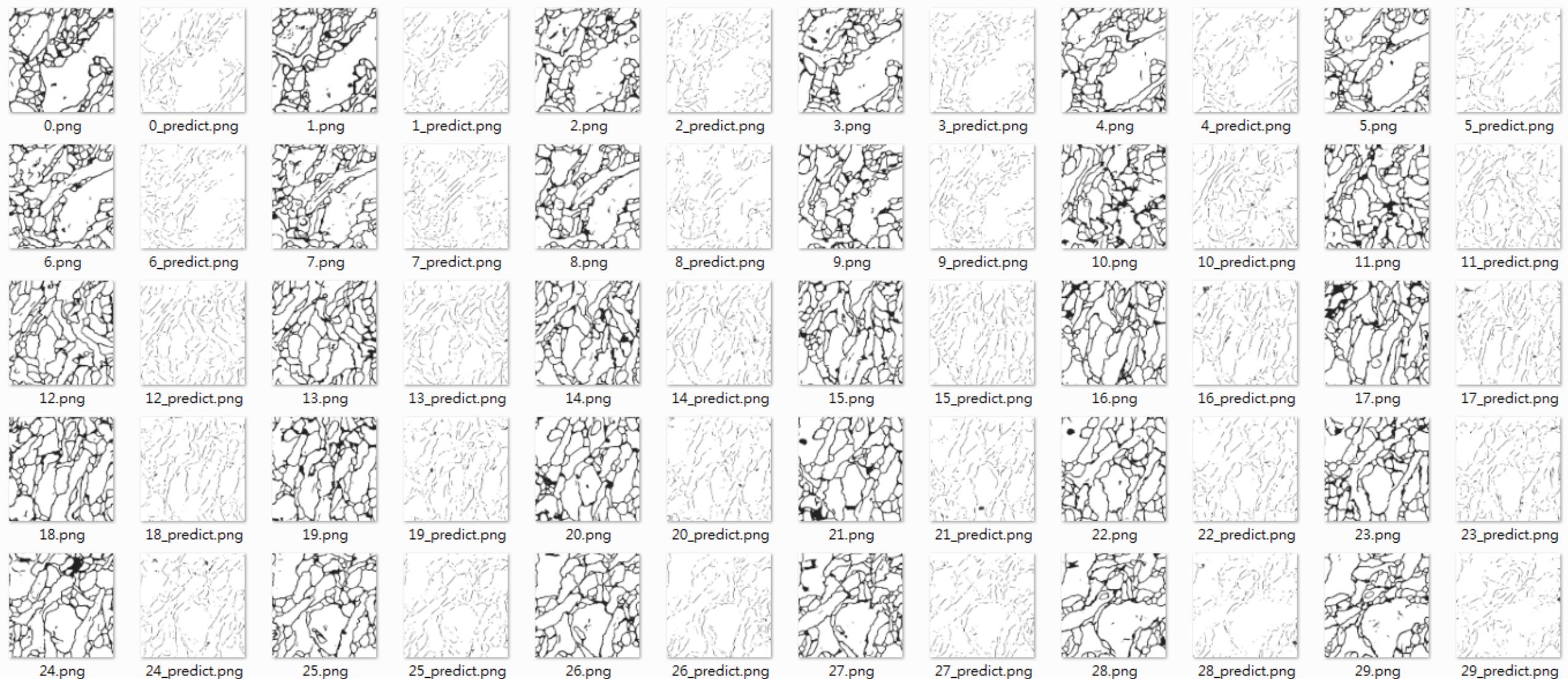
# Membrane segmented results



# Mitochondrion predicted results



# Membrane fixed results



# Janelia Farm's EM data

---

- One slice :  $8192 \times 8192$  @ 8bits
- Total slices :  $\sim 107$  million
- Real size :  $750 \times 350 \times 282 \text{ } \mu\text{m}^3$
- Total storage size :  $\sim 26$  TB
- The very primary results:
  - Do inference for  $512 \times 512 \times 30 \sim 2.079$  sec
  - Do inference for one slice  $\sim (8192 / 512)^2 / 30 * 2.078 \sim 17.7323$  sec
  - Do inference for all slices  $\sim 220$  days!!!
- <https://github.com/google/neuroglancer/blob/master/README.md>

# Next class

---

- Case study

