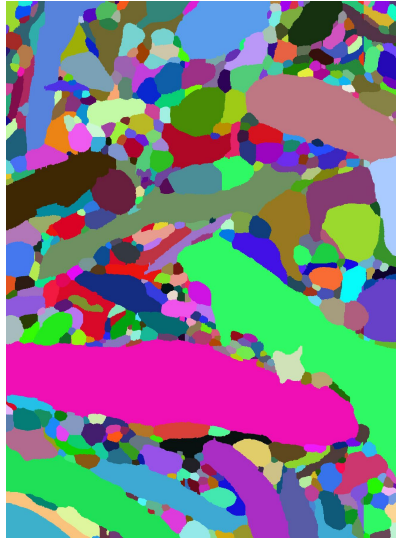
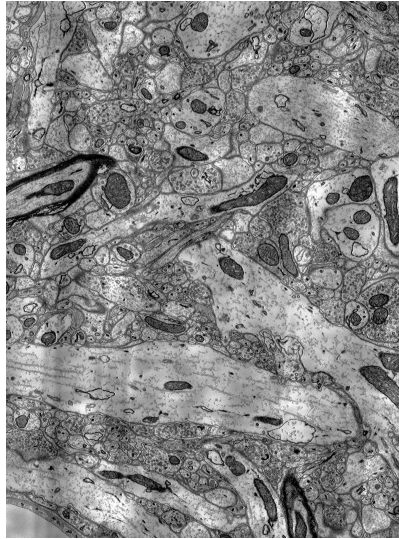


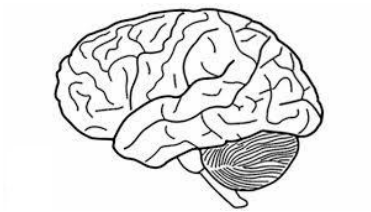
# Segmentation of Electron Microscopy Images in Connectomics



Brian Matejek  
Advisor: Hanspeter Pfister

# Connectomics

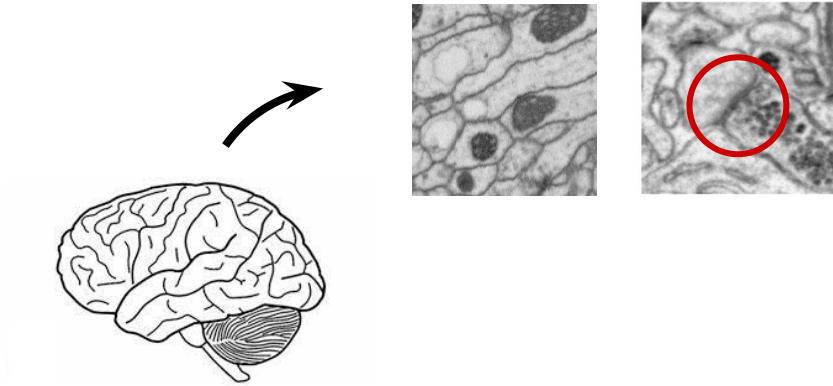
Goal: Extract the wiring diagram from a brain



# Connectomics

Goal: Extract the wiring diagram from a brain

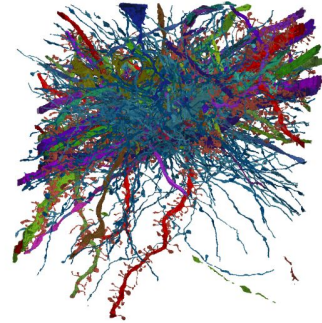
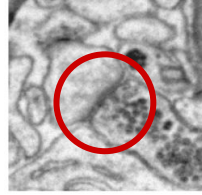
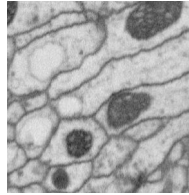
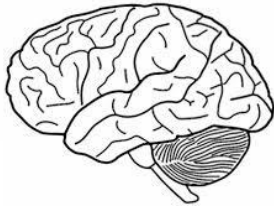
Nano-resolution Imaging



# Connectomics

Goal: Extract the wiring diagram from a brain

Nano-resolution Imaging

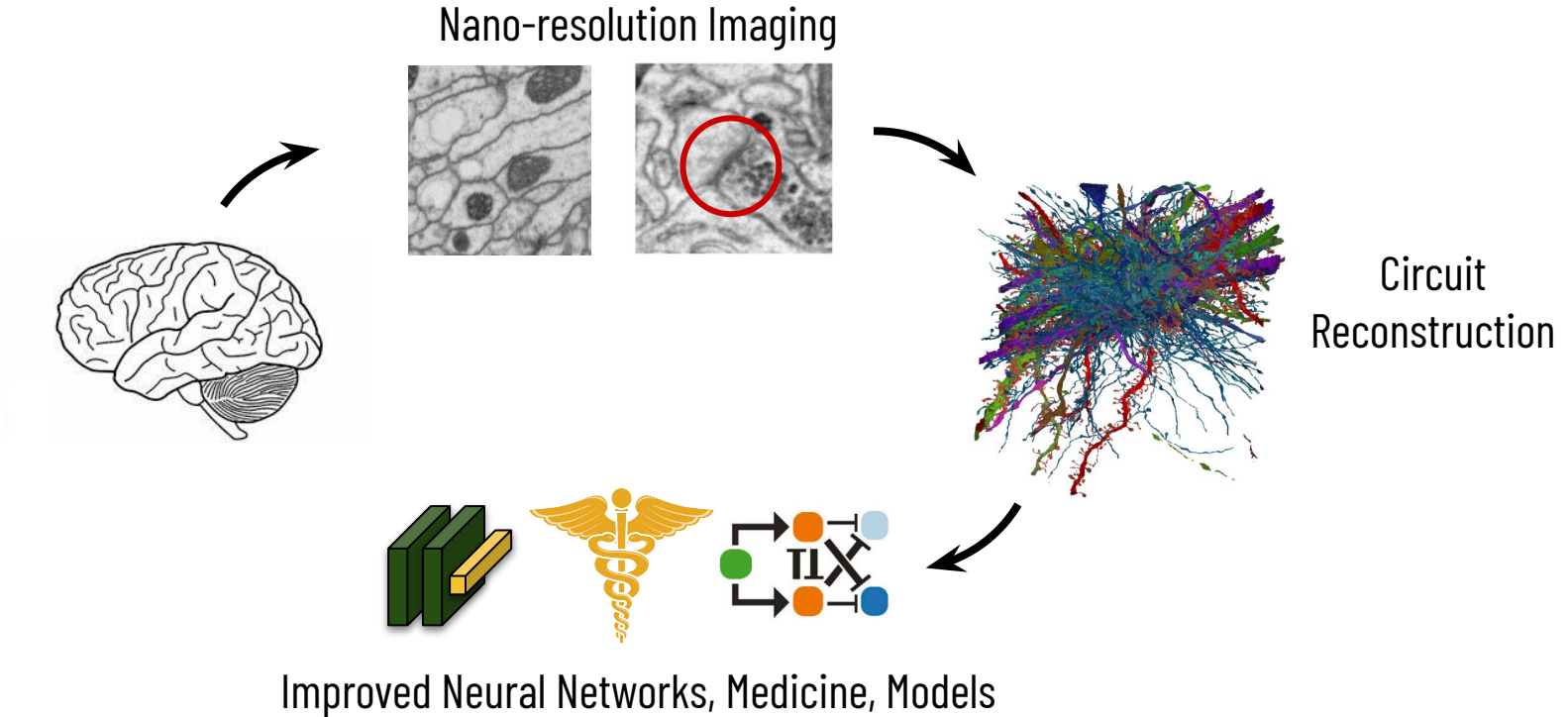


Circuit  
Reconstruction



# Connectomics

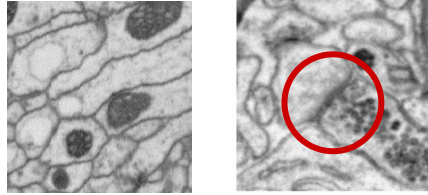
Goal: Extract the wiring diagram from a brain



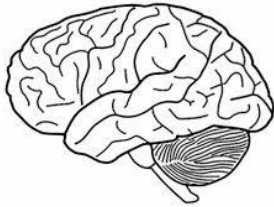
# Connectomics

Goal: Extract the wiring diagram from a brain

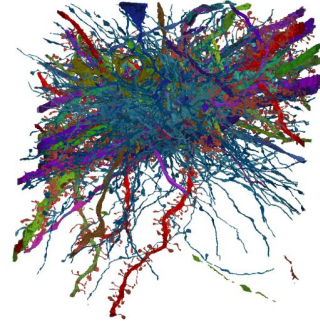
Nano-resolution Imaging



Better  
Understanding



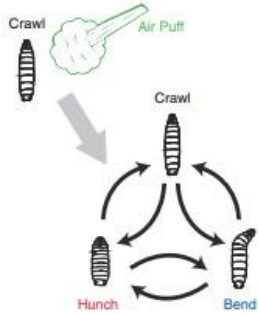
Circuit  
Reconstruction



Improved Neural Networks, Medicine, Models

# Connectomics

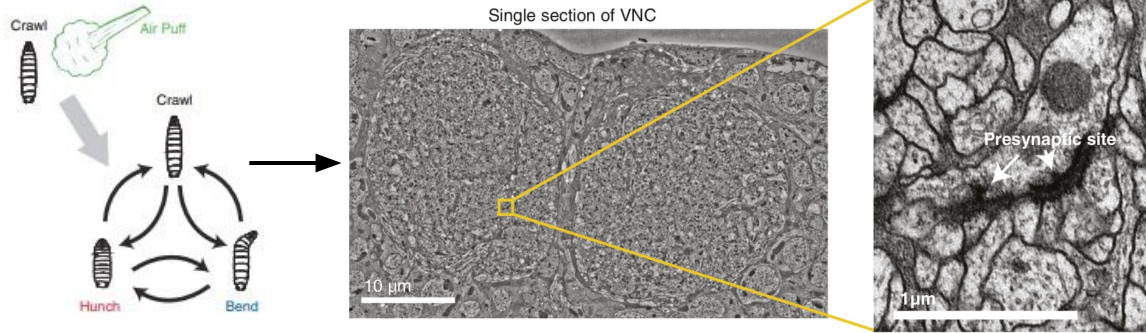
Goal: Extract the wiring diagram from a brain



Behavior

# Connectomics

Goal: Extract the wiring diagram from a brain

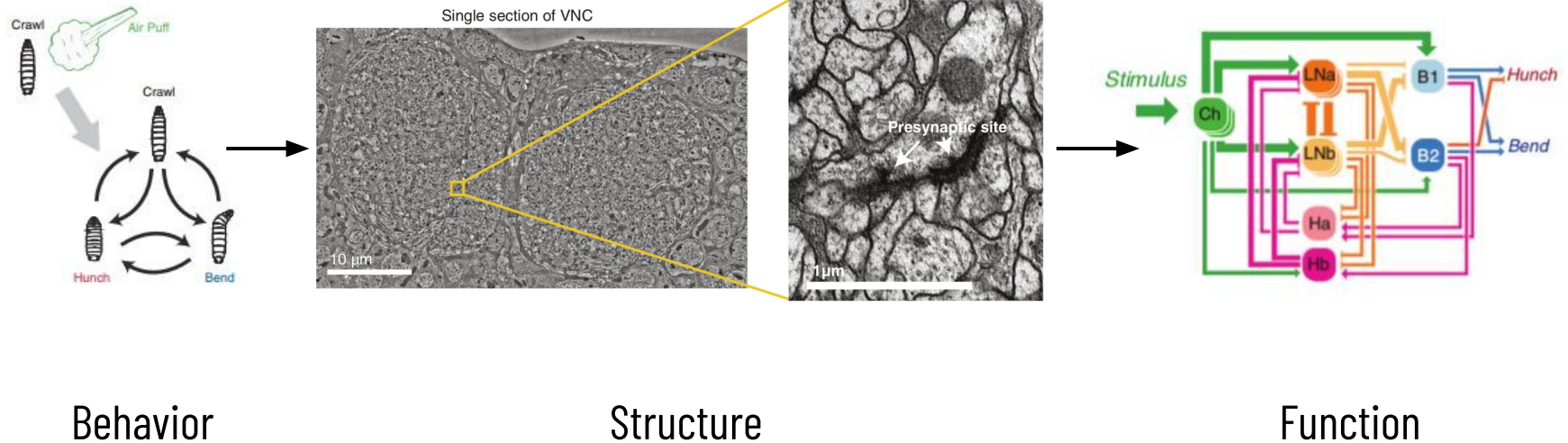


Behavior

Structure

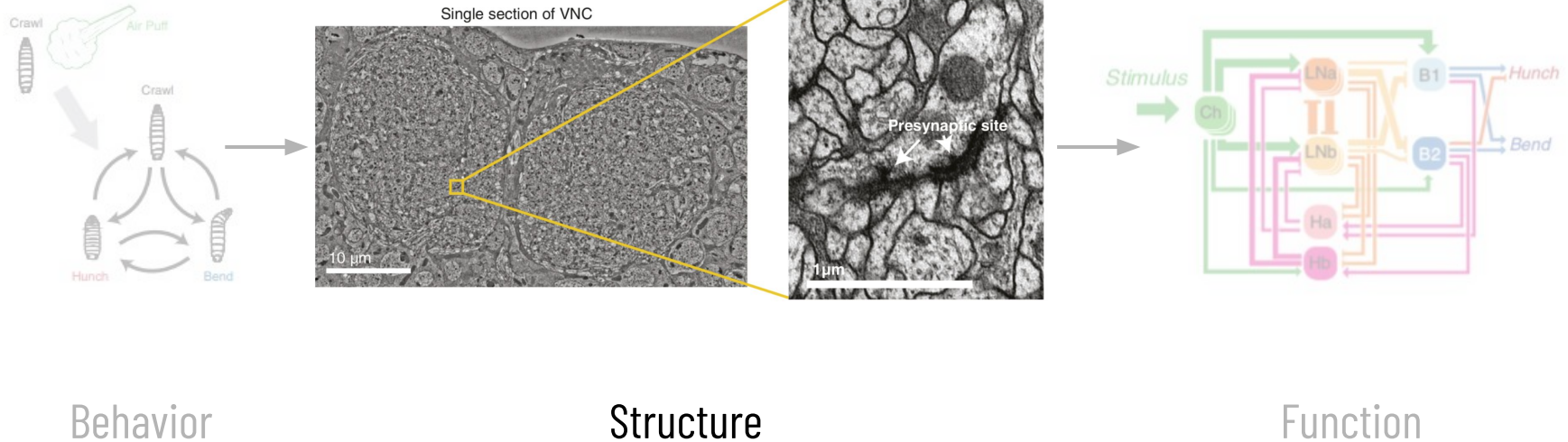
# Connectomics

Goal: Extract the wiring diagram from a brain

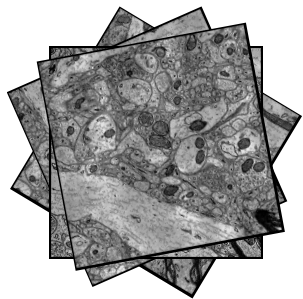


# Connectomics

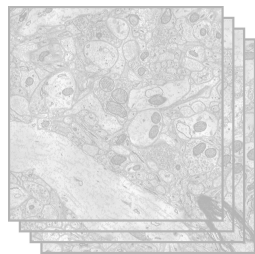
Goal: Extract the wiring diagram from a brain



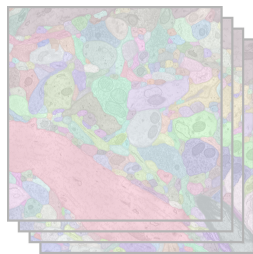
# Connectomics Pipeline



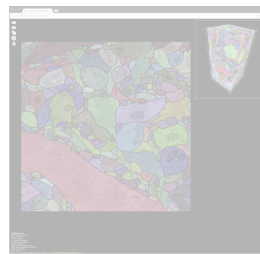
Acquisition



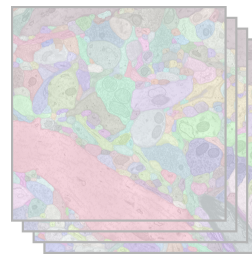
Registration



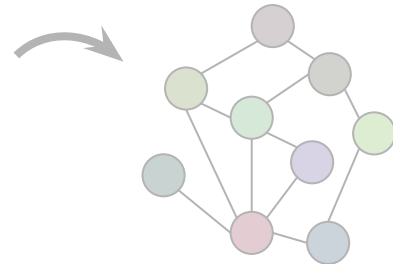
Segmentation



Proofreading



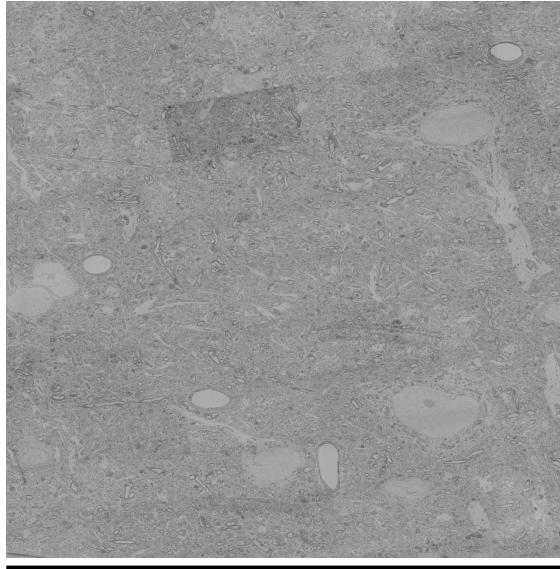
Network Analysis



Suissa-Peleg et al., Automatic Neural Reconstruction from Petavoxel of Electron Microscopy, Microscopy and Microanalysis 2016  
Schalek et al., Imaging a 1 mm<sup>3</sup> Volume of Rat Cortex Using a MultiBeam SEM, Microscopy and Microanalysis, 2016

# Image Acquisition

Multi-beam electron microscopes collect 1 TB of raw image data every hour



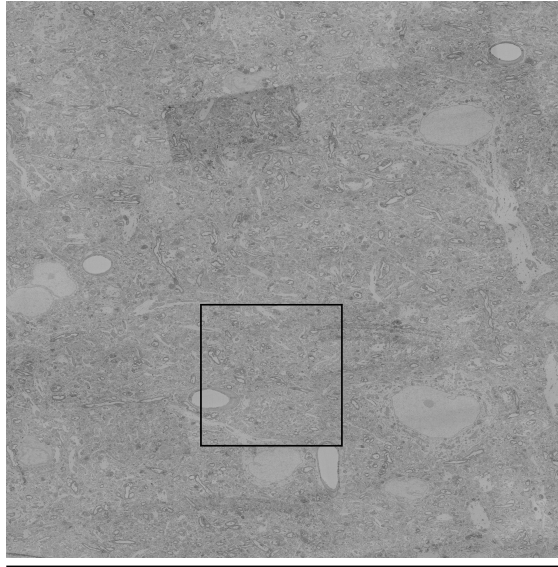
100  $\mu\text{m}$



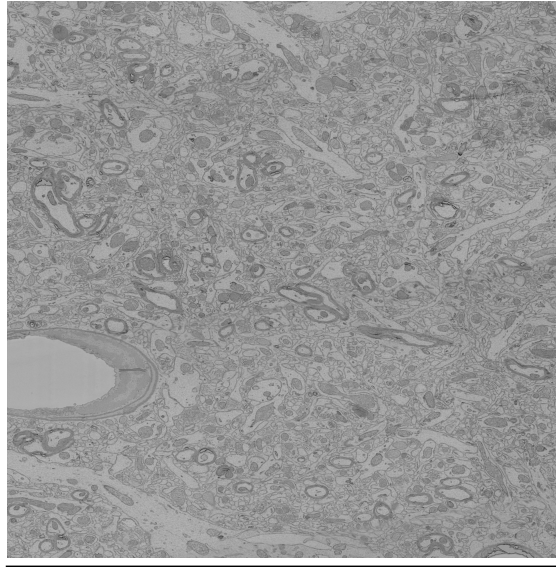
# Image Acquisition

Multi-beam electron microscopes collect 1 TB of raw image data every hour

Can image  $1 \text{ mm}^3$  of image data (2 PB) in 6 months



100  $\mu\text{m}$

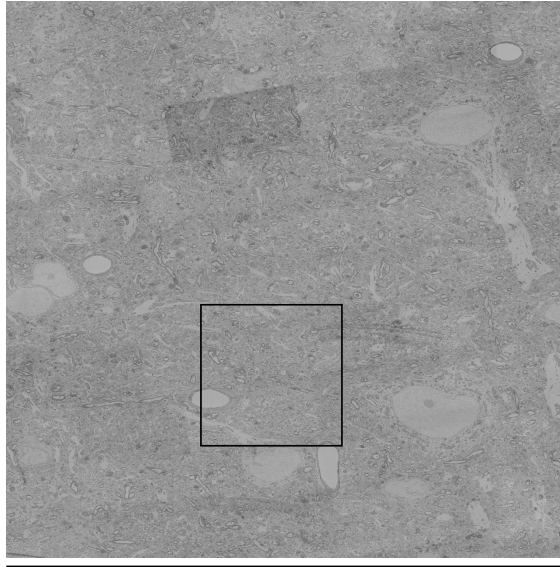


25  $\mu\text{m}$

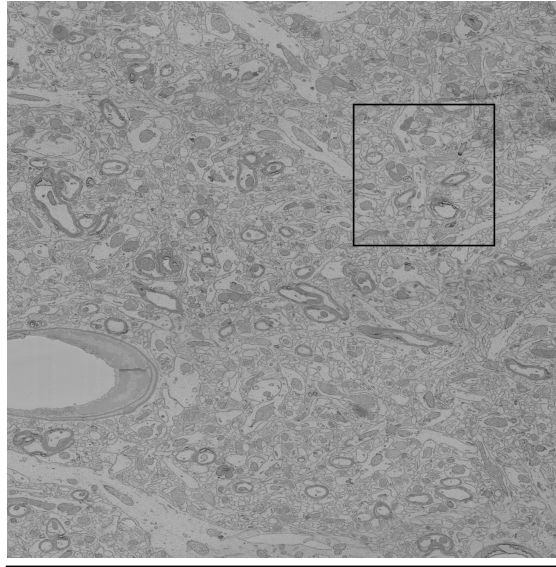
# Image Acquisition

Multi-beam electron microscopes collect 1 TB of raw image data every hour

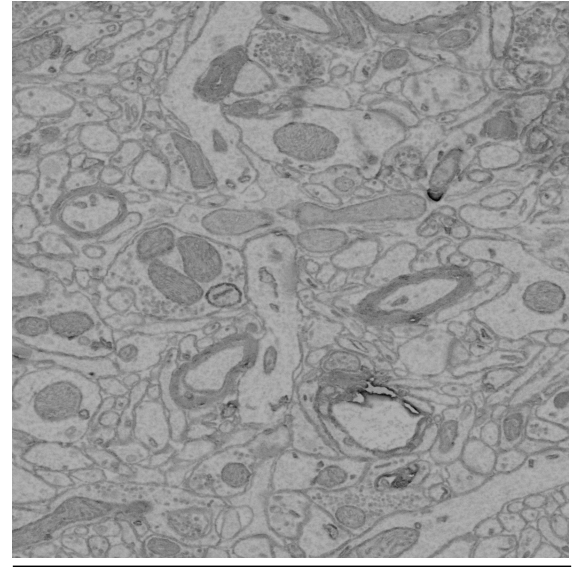
Can image  $1 \text{ mm}^3$  of image data (2 PB) in 6 months



100  $\mu\text{m}$

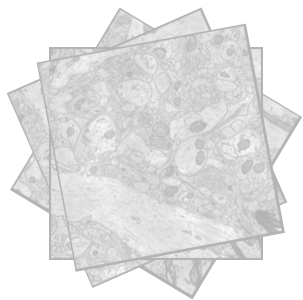


25  $\mu\text{m}$

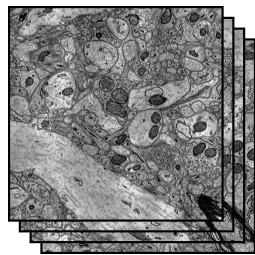


6250 nm

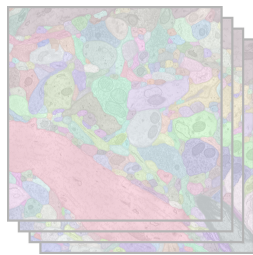
# Connectomics Pipeline



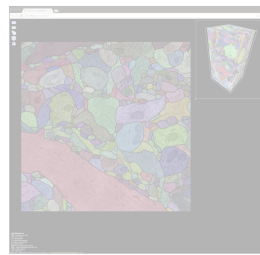
Acquisition



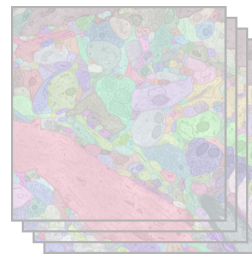
Registration



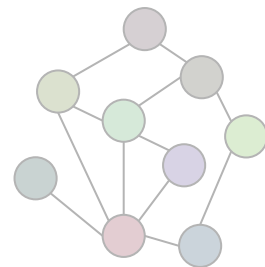
Segmentation



Proofreading

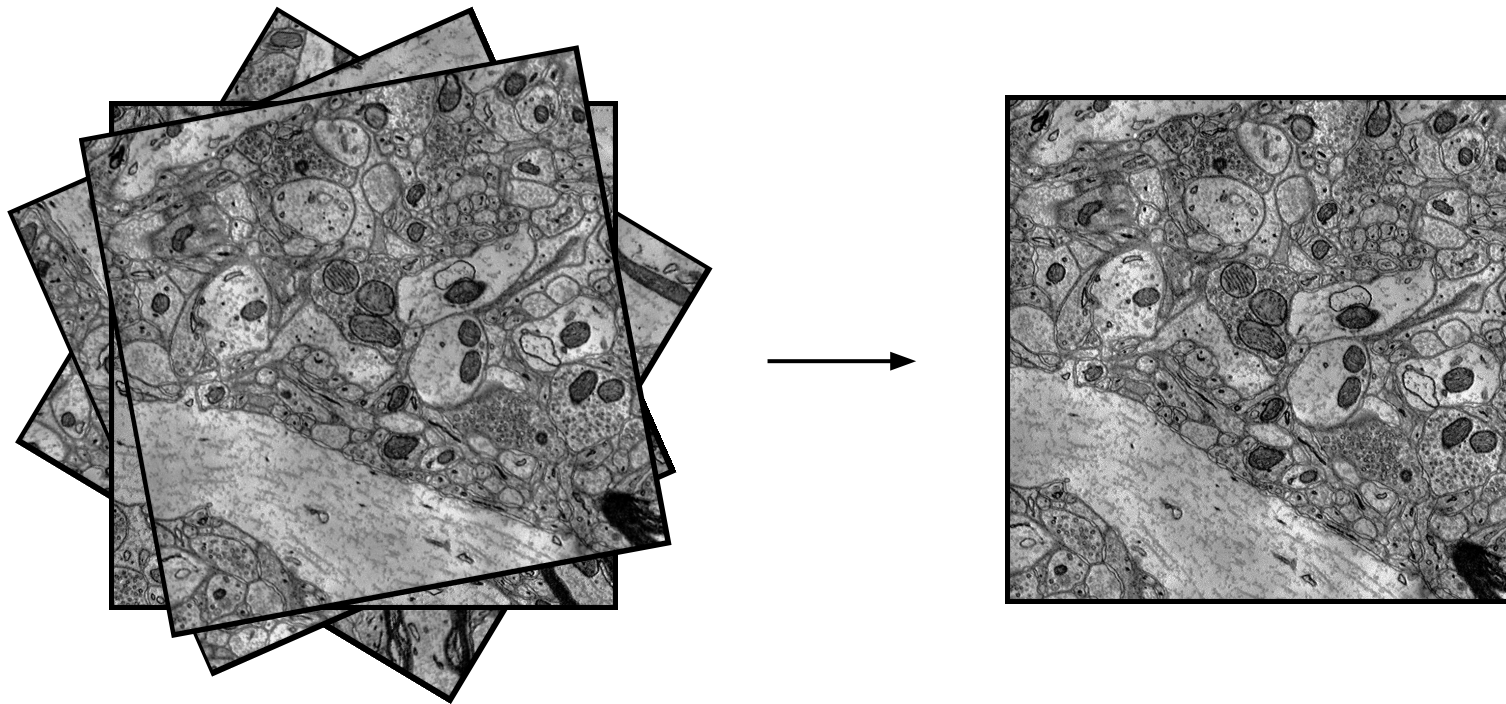


Network Analysis

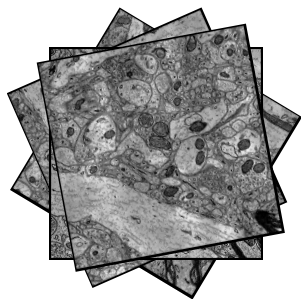


Saalfeld et al., Elastic Volume Reconstruction from Series of Ultra-thin Microscopy Sections, Nature 2012  
Khairy et al., Joint Deformable Registration of Large EM Image Volumes: A Matrix Solver Approach, 2018

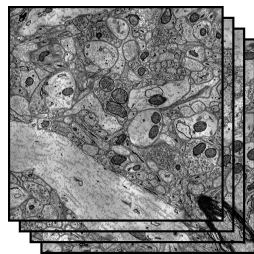
# Registration



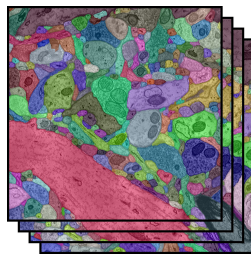
# Connectomics Pipeline



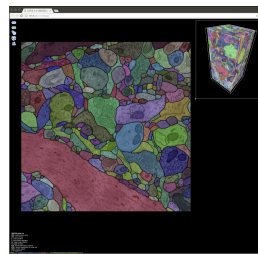
Acquisition



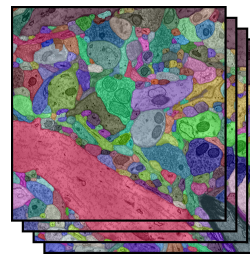
Registration



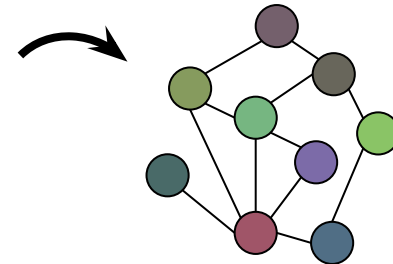
Segmentation



Proofreading



Network Analysis



Nunez-Iglesias et al., Machine Learning of Hierarchical Clustering to Segment 2D and 3D Images, PLoS ONE 2014

Cicek et al., 3D U-Net: Learning Dense Volumetric Segmentation from Sparse Annotation, MICCAI 2016

Januszewski et al., Flood-Filling Networks, 2016

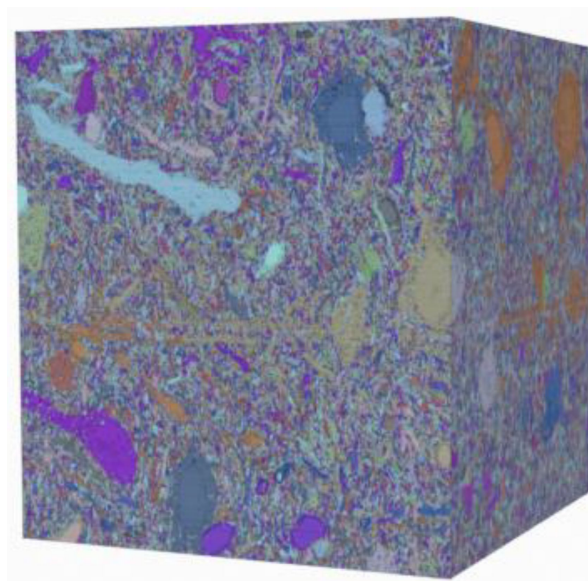
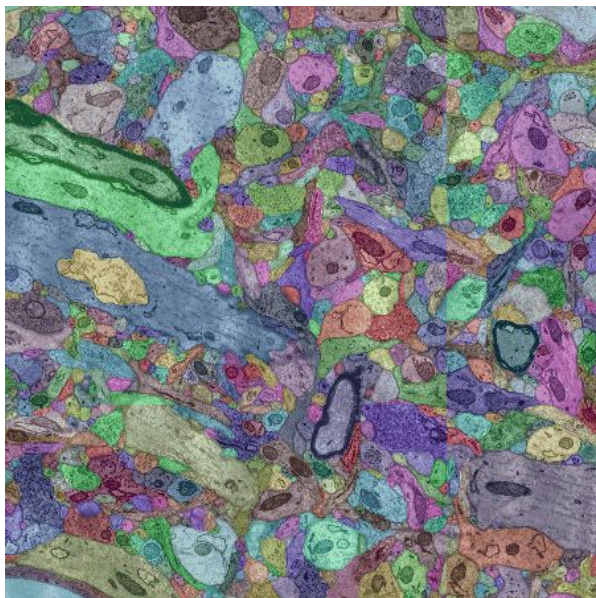
Zeng et al., DeepEM3D: Approaching Human-Level Performance on 3D Anisotropic EM Image Segmentation, Bioinformatics 2017

Pape et al., Solving Large Multicut Problems for Connectomics via Domain Decomposition, ICCV 2017

Lee et al., Superhuman Accuracy on the SNEMI3D Connectomics Challenge, 2017

# Label Volumes

Two voxels have the same label only if they belong to the same neuron

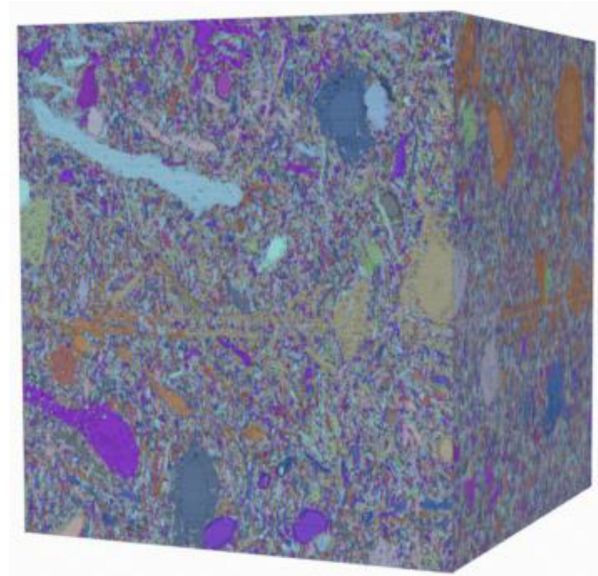
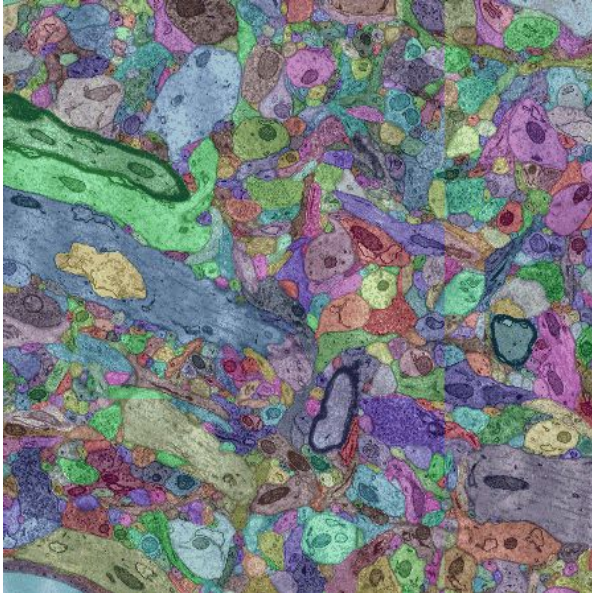




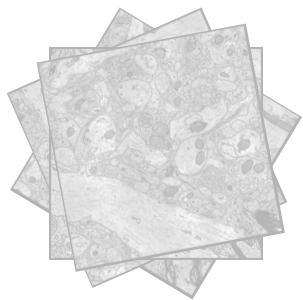
# Label Volumes

Two voxels have the same label only if they belong to the same neuron

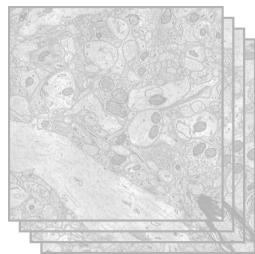
Typically use 64 bits per voxel to label each segment uniquely



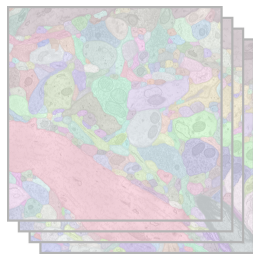
# Connectomics Pipeline



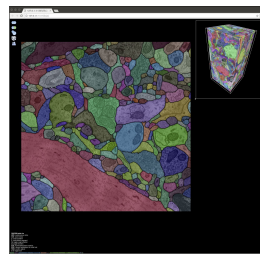
Acquisition



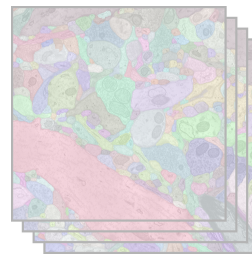
Registration



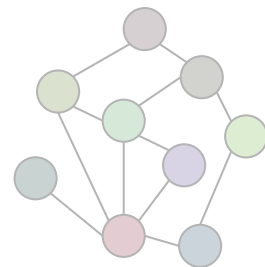
Segmentation



Proofreading



Network Analysis

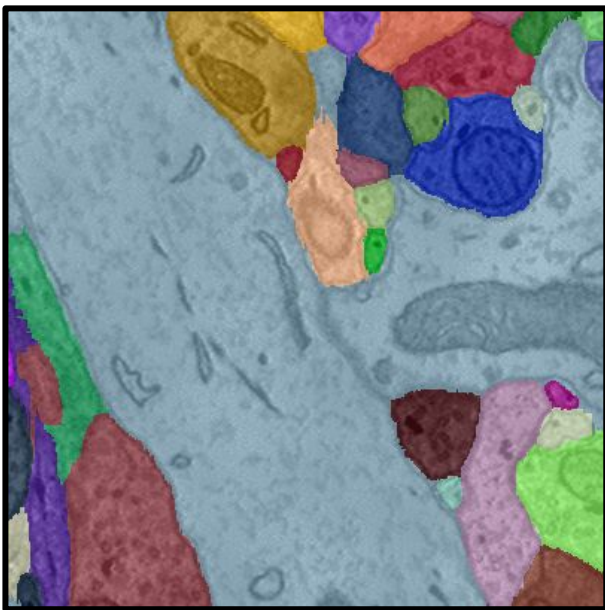


Haehn et al., Design and Evaluation of Interactive Proofreading Tools for Connectomics, IEEE VIS 2014  
Zung et al., An Error Detection and Correction Framework for Connectomics, NIPS 2017  
Haehn et al., Guided Proofreading of Automatic Segmentations for Connectomics, CVPR 2018

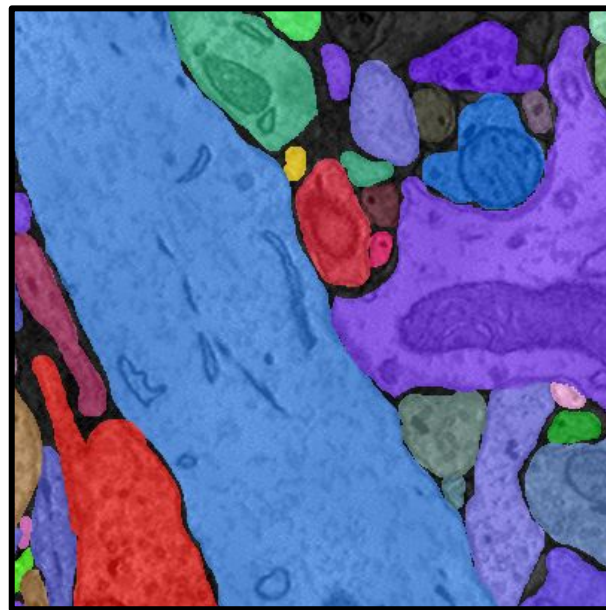


# Merge Errors

Automatic Segmentation

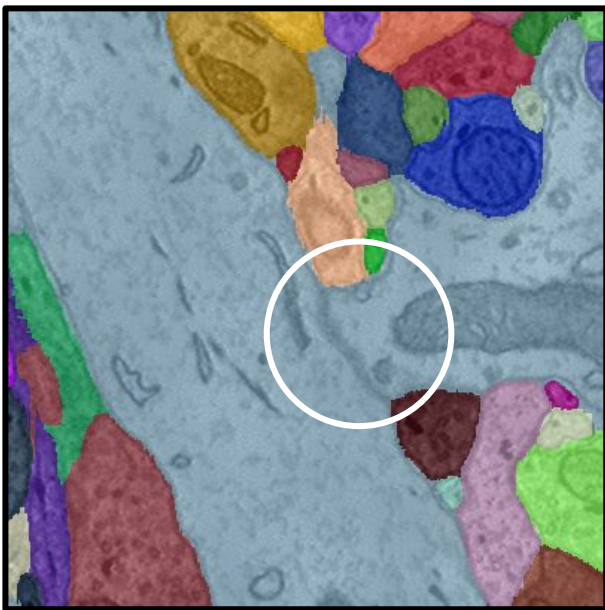


Ground Truth

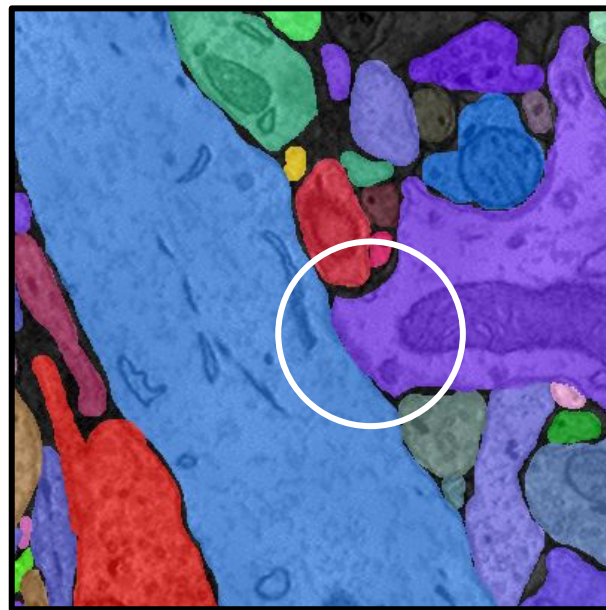


# Merge Errors

Automatic Segmentation

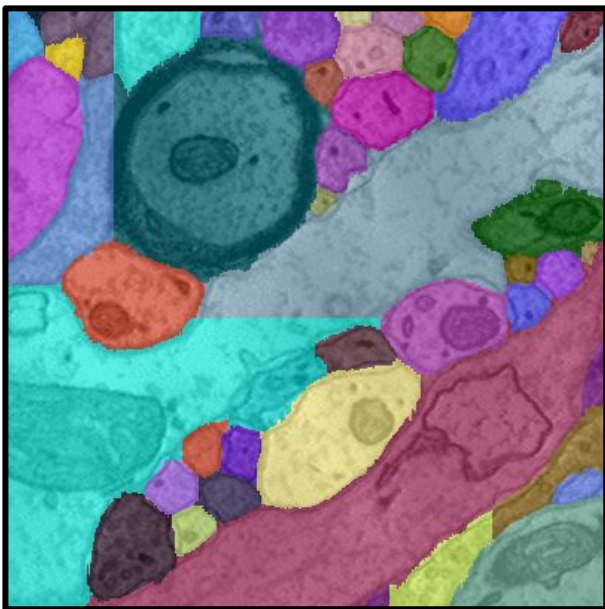


Ground Truth

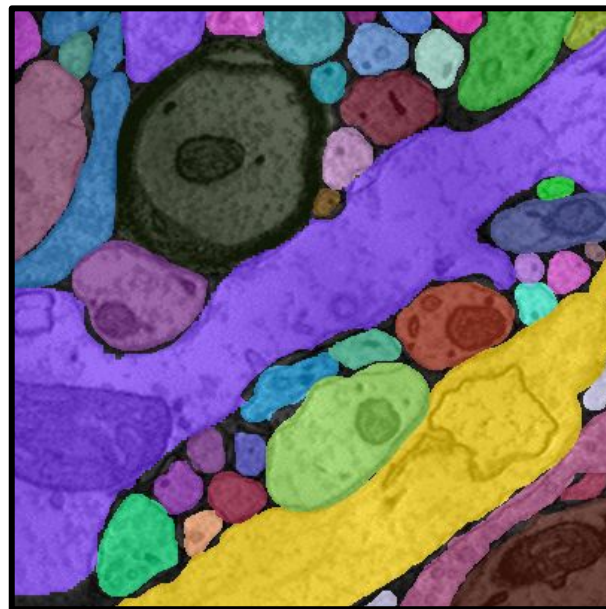


# Split Errors

Automatic Segmentation

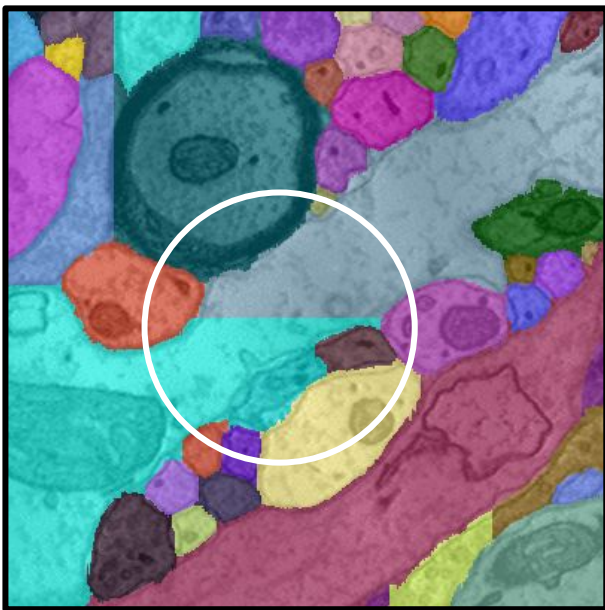


Ground Truth

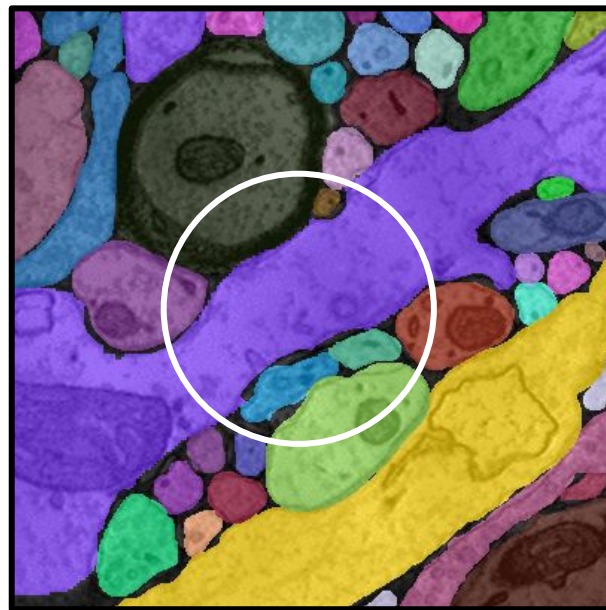


# Split Errors

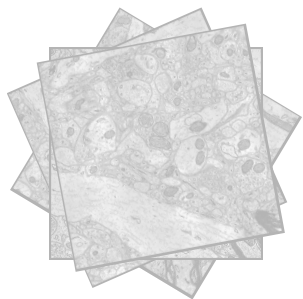
Automatic Segmentation



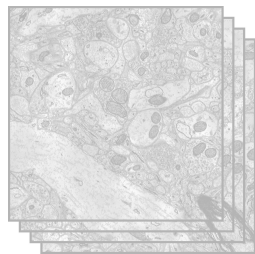
Ground Truth



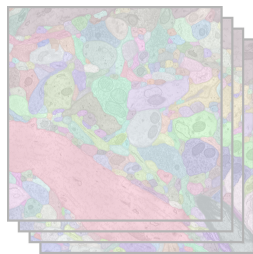
# Connectomics Pipeline



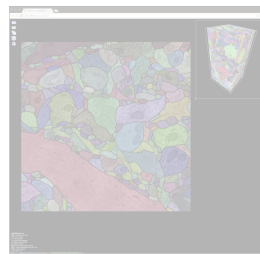
Acquisition



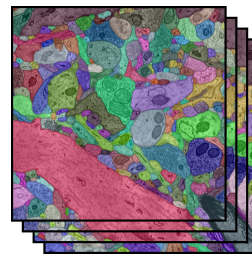
Registration



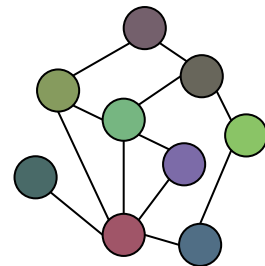
Segmentation



Proofreading



Network Analysis



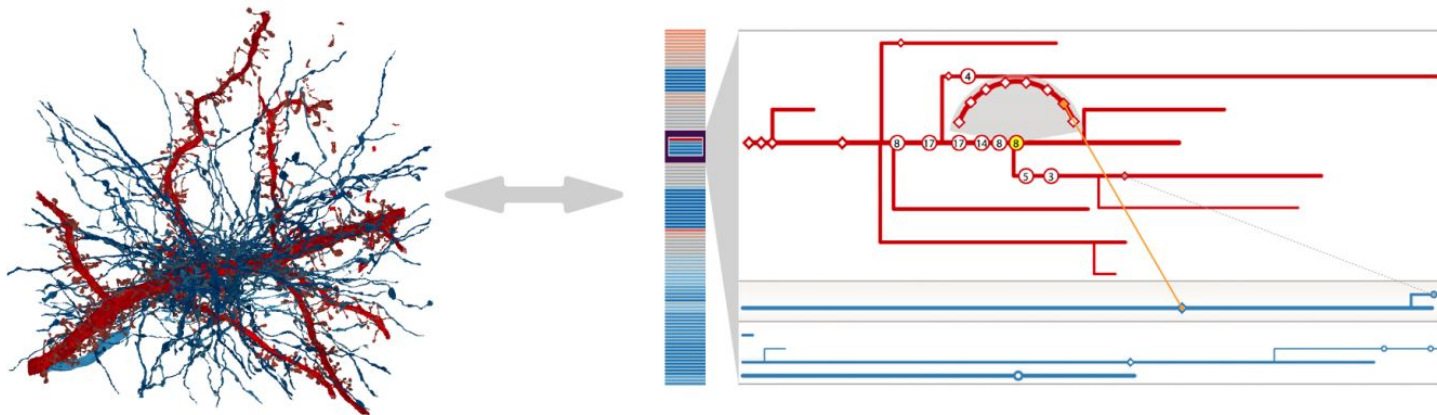
Sorger et al., neuroMAP - Interactive Graph-Visualization of the Fruit Fly's Neural Circuit, BioVIS 2013

Al-Awami et al., NeuroLines: A Subway Map Metaphor for Visualizing Nanoscale Neuronal Connectivity, IEEE VIS 2014

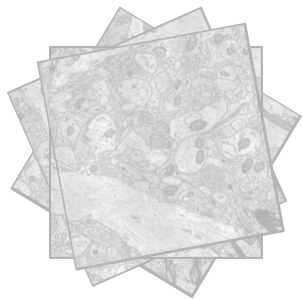
Haehn et al., Scalable Interactive Visualization for Connectomics, MDPI Informatics 2017



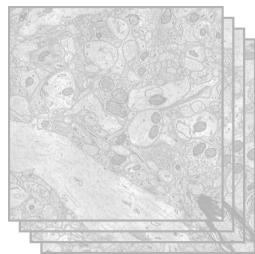
# Network Analysis



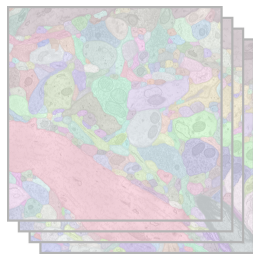
# Connectomics Pipeline



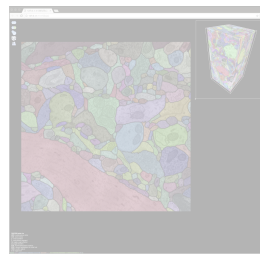
Acquisition



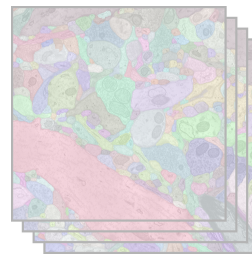
Registration



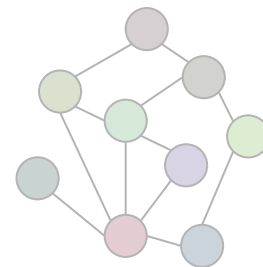
Segmentation



Proofreading

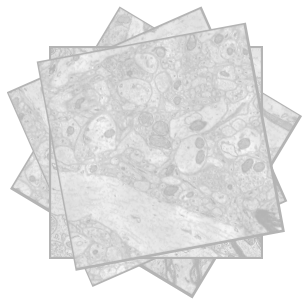


Network Analysis

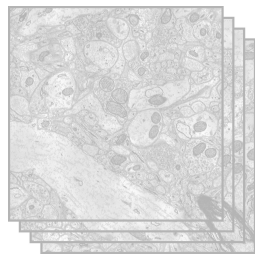


# Connectomics Pipeline

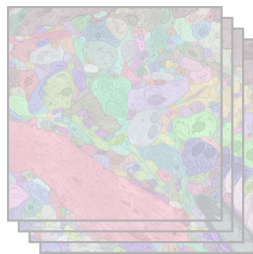
## Compression



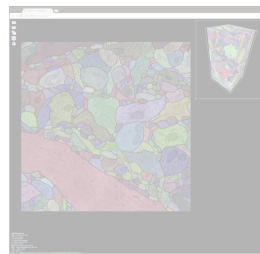
Acquisition



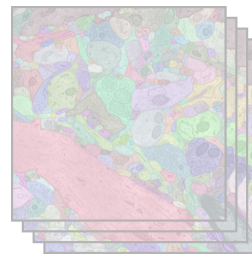
Registration



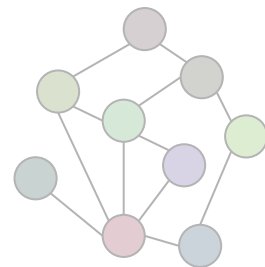
Segmentation



Proofreading

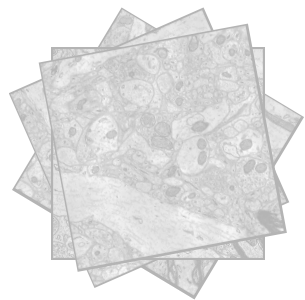


Network Analysis

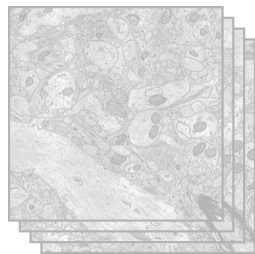




# Connectomics Pipeline

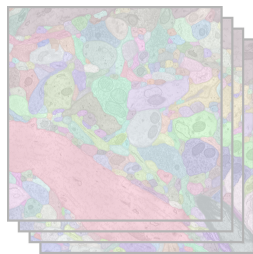


Acquisition

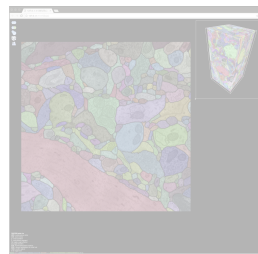


Registration

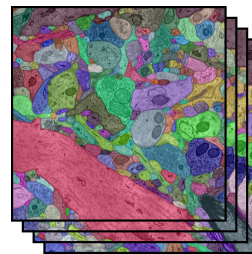
## Compression



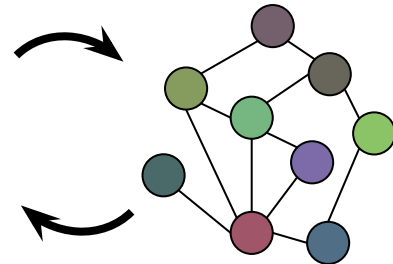
Segmentation



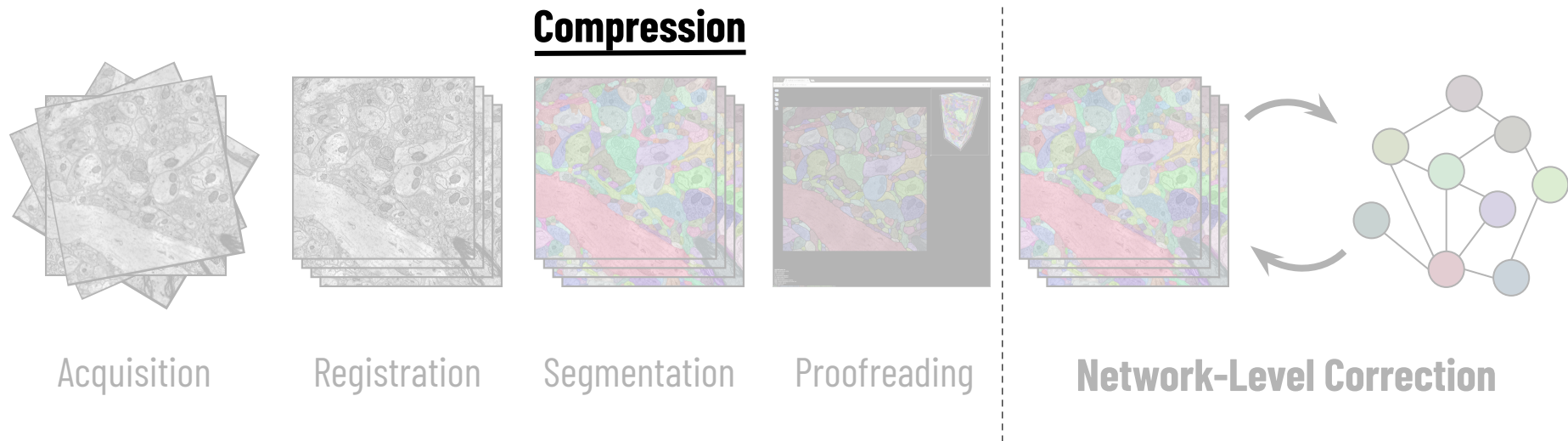
Proofreading



**Network-Level Correction**

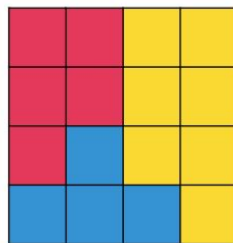


# Connectomics Pipeline



# Compresso: Efficient Compression of Segmentation Data for Connectomics

Brian Matejek, Daniel Haehn, Fritz Lekschas, Michael Mitzenmacher, Hanspeter Pfister



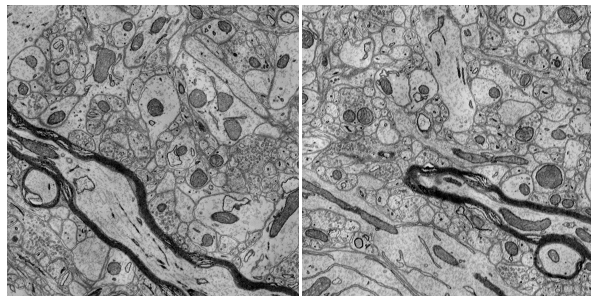
0	1	2	3
4	5	6	7
8	9	10	11
12	13	14	15

$$\sum_{i=0}^{n-1} \mathbb{I}(i) 2^i$$

$$2^1 + 2^5 + 2^8 + 2^9 + 2^{10} + 2^{14} + 2^{15} = 50978$$

# Increasing Scales of Challenge Datasets

SNEMI

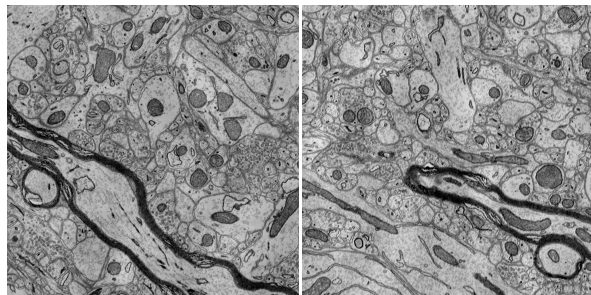


210 MB

2013

# Increasing Scales of Challenge Datasets

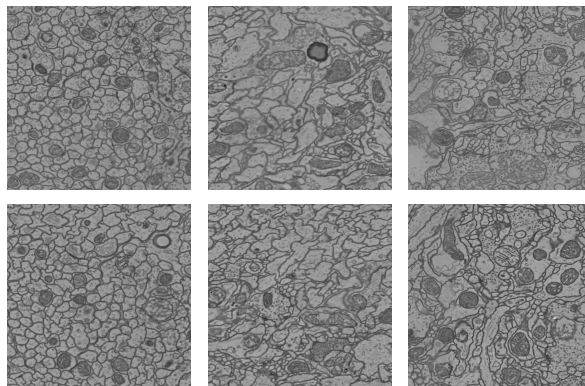
SNEMI



210 MB

2013

CREMI

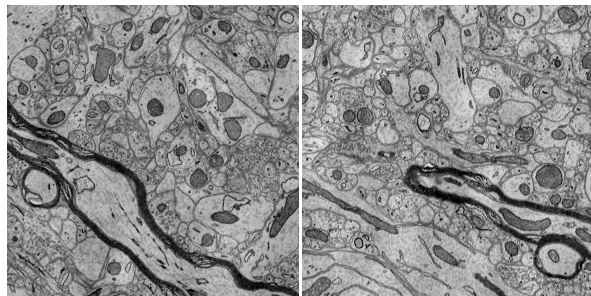


1.2 GB

2016

# Increasing Scales of Challenge Datasets

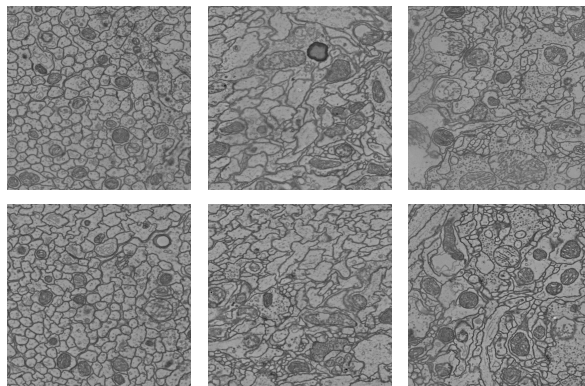
SNEMI



210 MB

2013

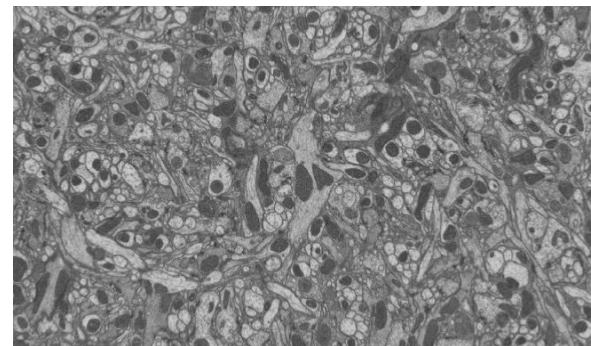
CREMI



1.2 GB

2016

FIB-25

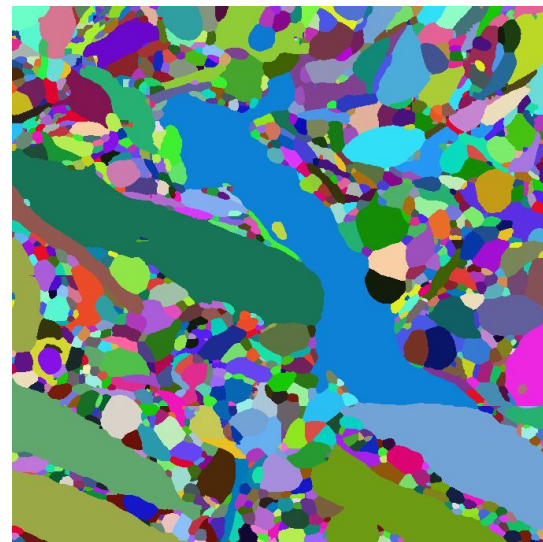
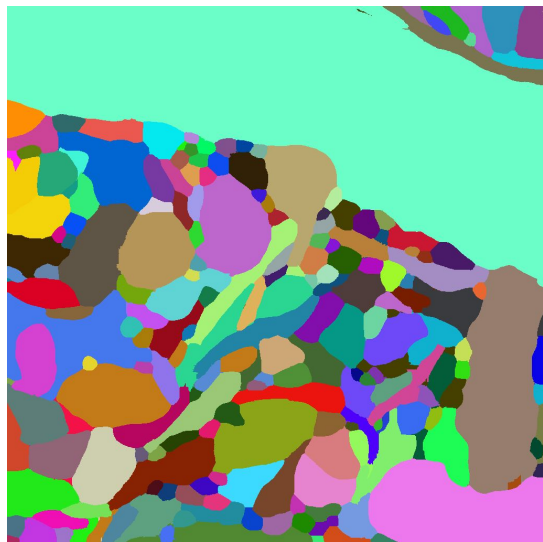


15.7 GB

2017

# Connectomics Label Volumes

Large invariant regions without natural relationships between labels

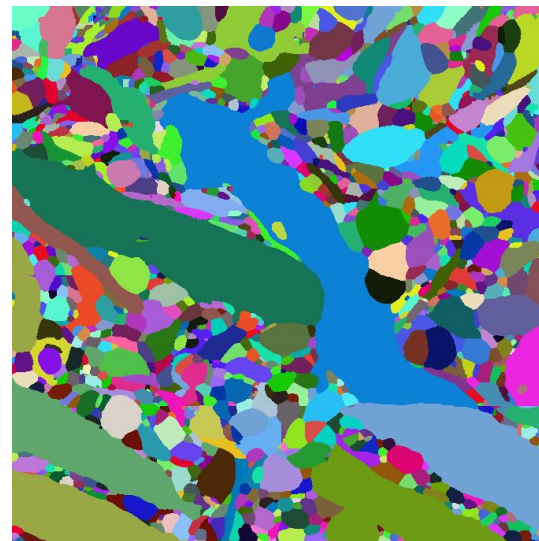


# Existing Compression Schemes

General-purpose compression schemes

BZ2, GZIP, LZMA, LZW, ZLIB, etc.

Not optimized for these unique label volumes





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General-purpose compression schemes

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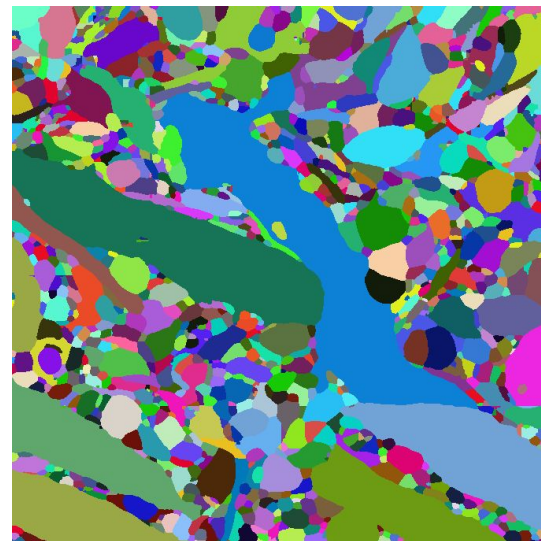
Not optimized for these unique label volumes

Image compression schemes

JPEG, JPEG2000, PNG, etc.

Rely on frequency reduction and value prediction

Not useful with large invariant regions



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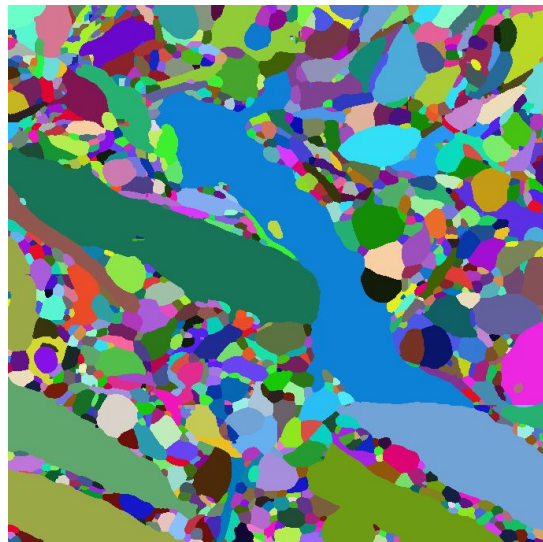
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Video compression schemes

H.264, H.265, MPEG, etc.

Color space optimizations do not translate



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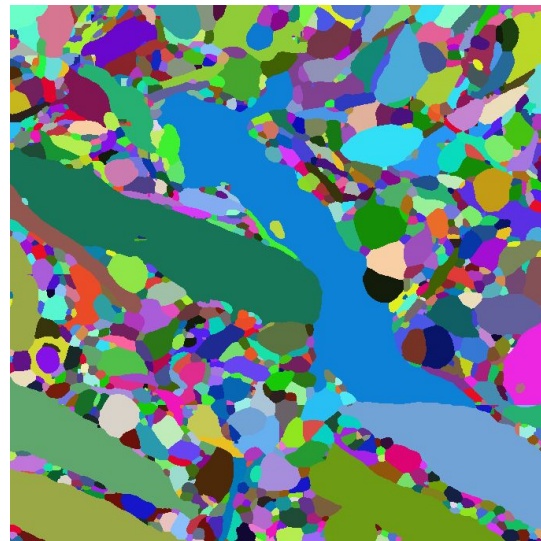
Video compression schemes

H.264, H.265, MPEG, etc.

Color space optimizations do not translate

Neuroglancer compression scheme

Specifically designed for label volumes



# Neuroglancer

Specifically designed for label volumes

Exploits homogeneity by creating small blocks with  $N$  labels

Reduces local entropy to  $\log_2(N)$

Lookup tables decode the values  $[0, N)$  to the original 64-bit labels

Blocks are typically  $8 \times 8 \times 8$  voxels each



Google Open Source

<https://opensource.google.com/projects/neuroglancer>

Compression

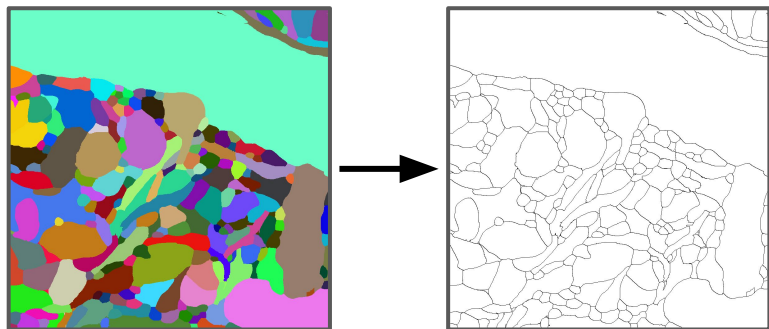
# Compresso Overview

Lossless compression

# Compresso Overview

Lossless compression

Decouple per-segment shapes and per-pixel labels

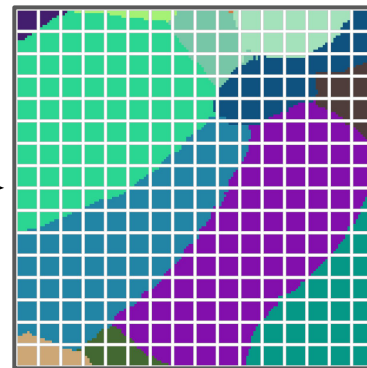
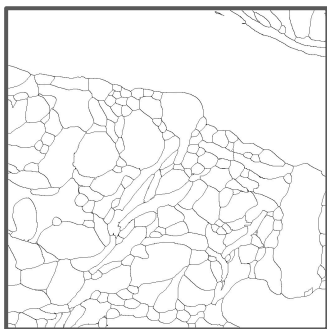
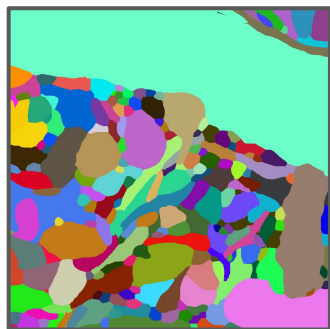


# Compresso Overview

Lossless compression

Decouple per-segment shapes and per-pixel labels

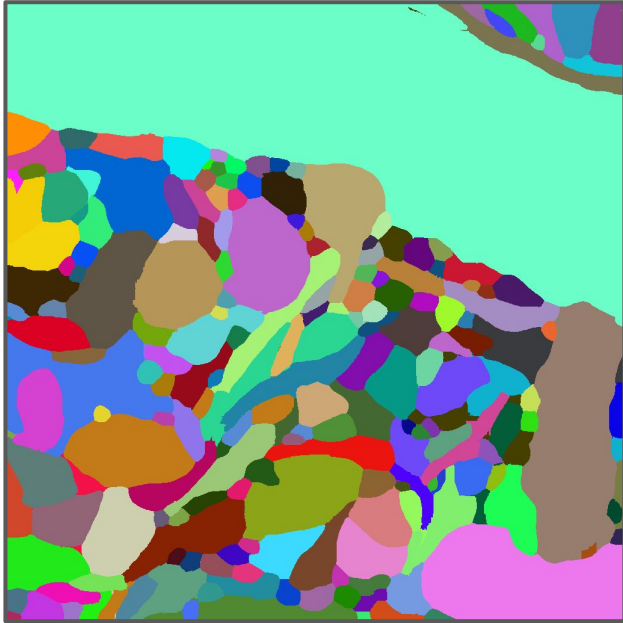
Divide the volume into non-overlapping congruent 3D windows

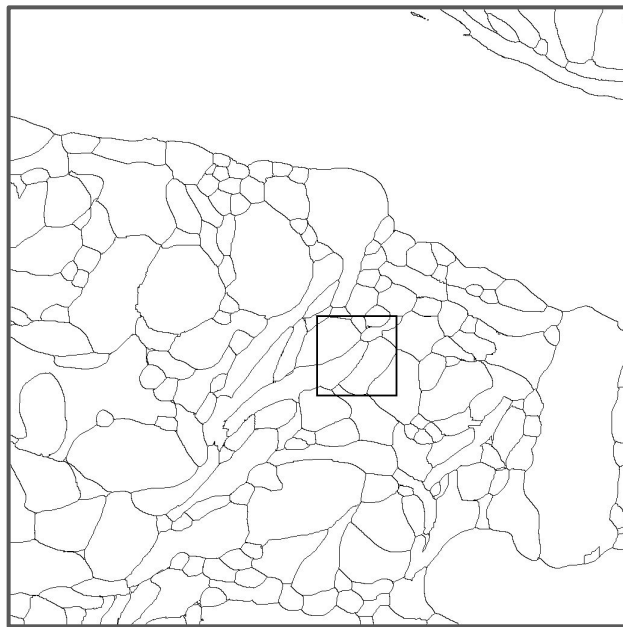
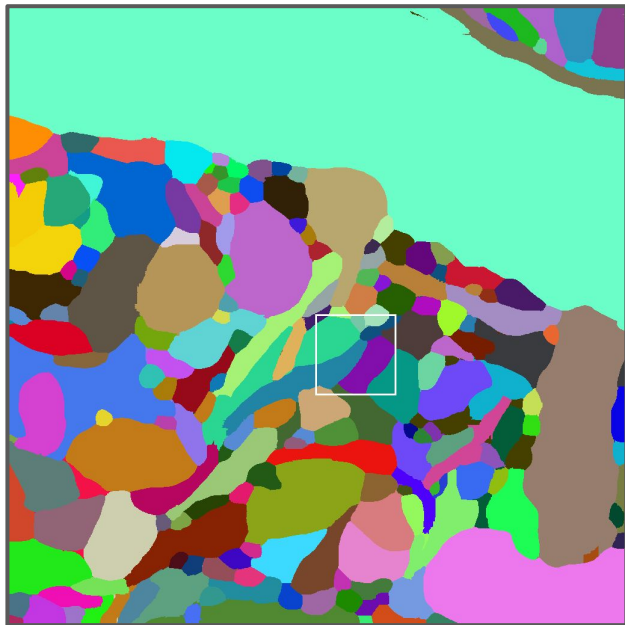




# Boundary Map Generation

A pixel  $(x, y, z)$  is 1 if its neighbor  $(x + 1, y, z)$  or  $(x, y + 1, z)$  belongs to a different segment



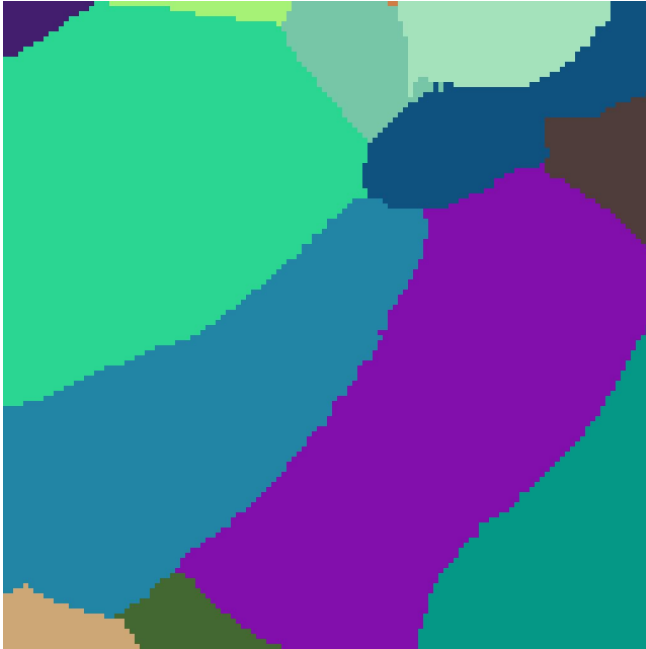


Boxed region divided into congruent windows

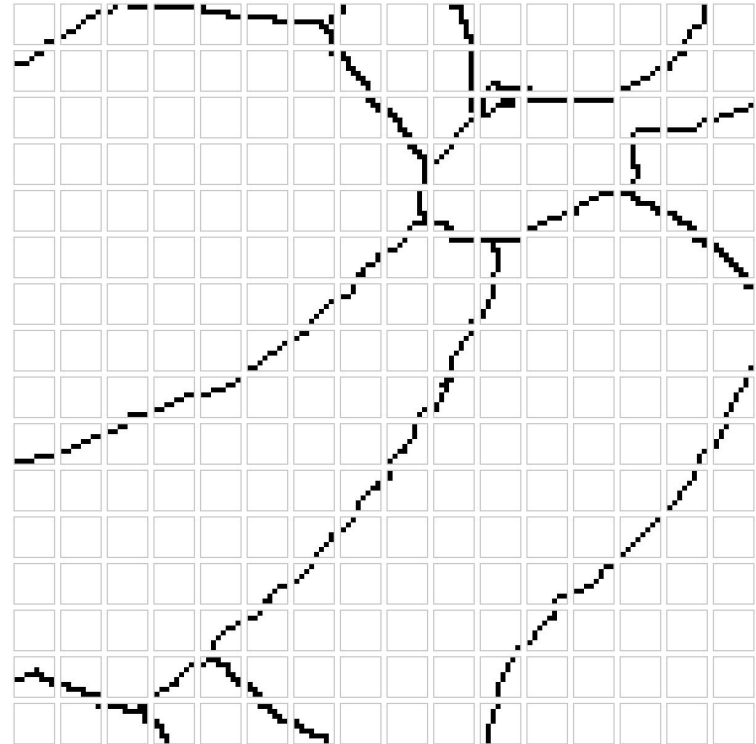
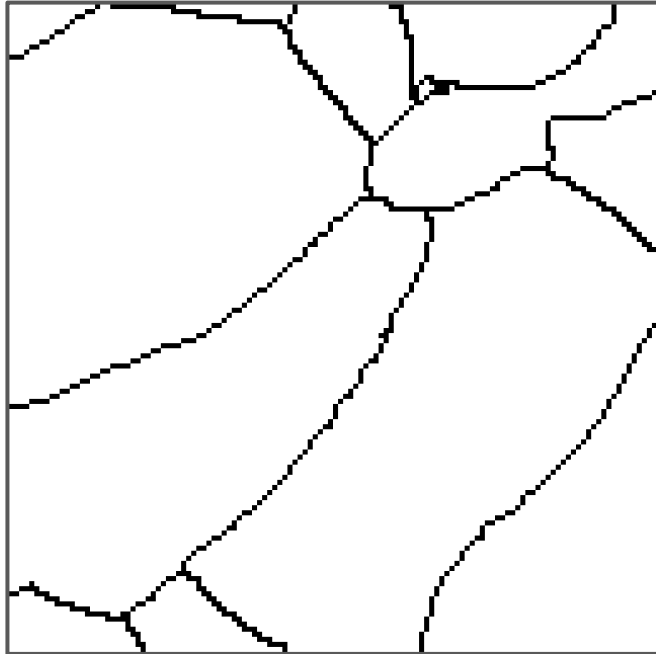


Boxed region divided into congruent windows

Each window is 8 x 8 x 1 voxels

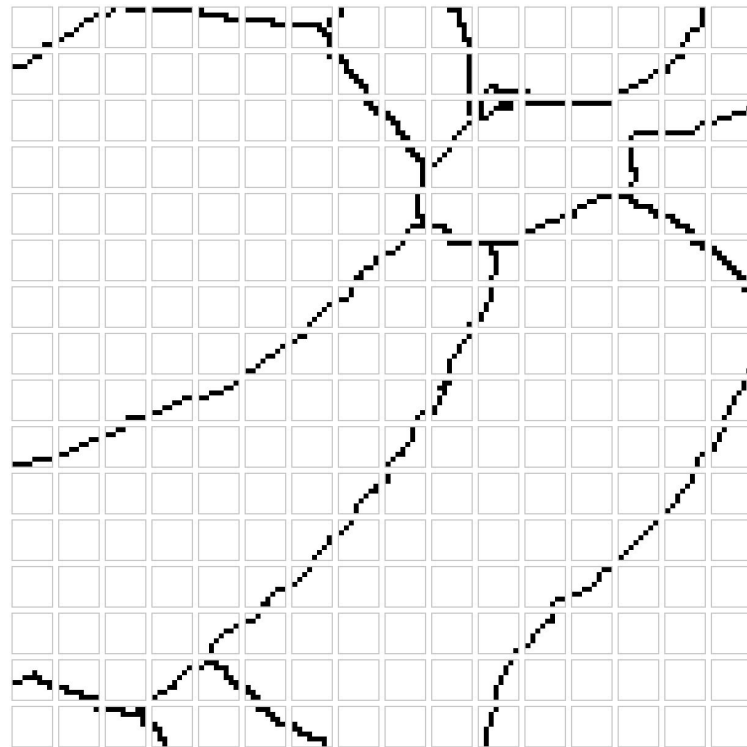
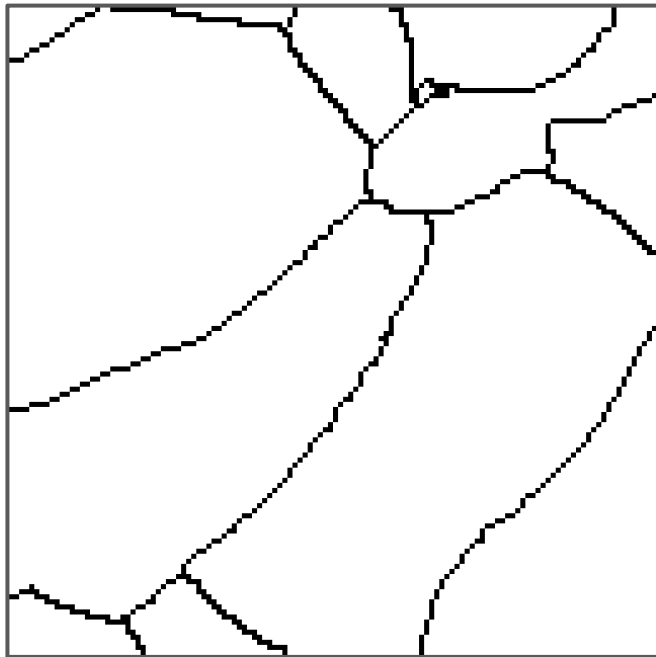


Accompanying boundary map

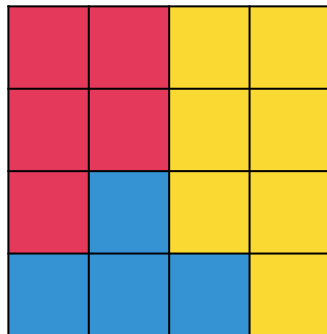


Accompanying boundary map

Goal: Store one 64-bit integer per window



# Assigning Values to Windows



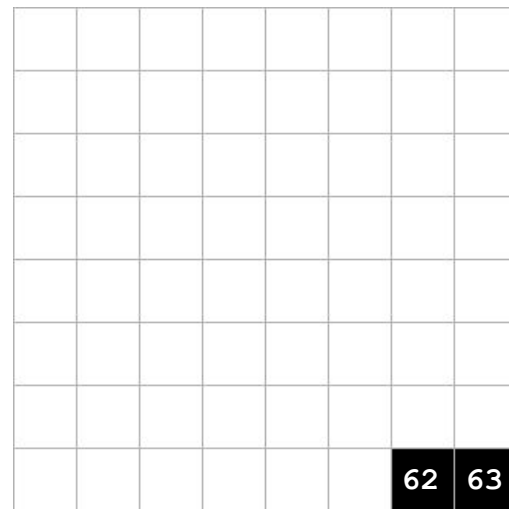
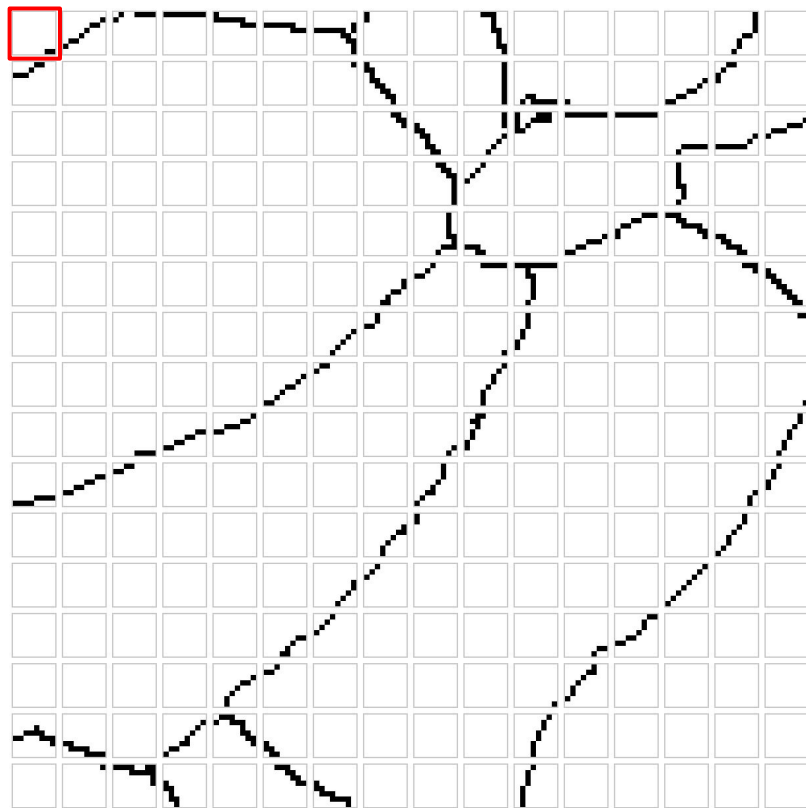
0	1	2	3
4	5	6	7
8	9	10	11
12	13	14	15

$$\sum_{i=0}^{n-1} \mathbb{I}(i) 2^i$$

$$2^1 + 2^5 + 2^8 + 2^9 + 2^{10} + 2^{14} + 2^{15} = 50978$$

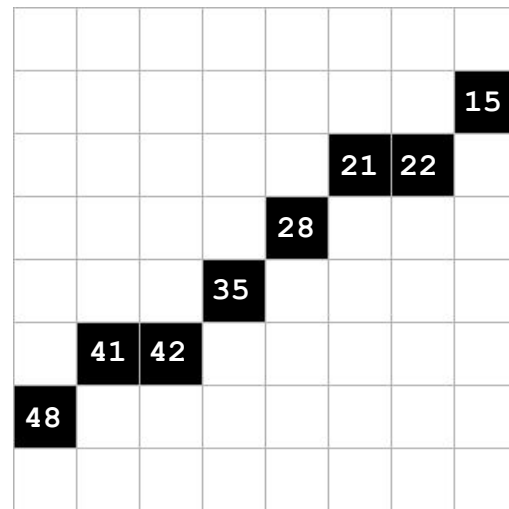
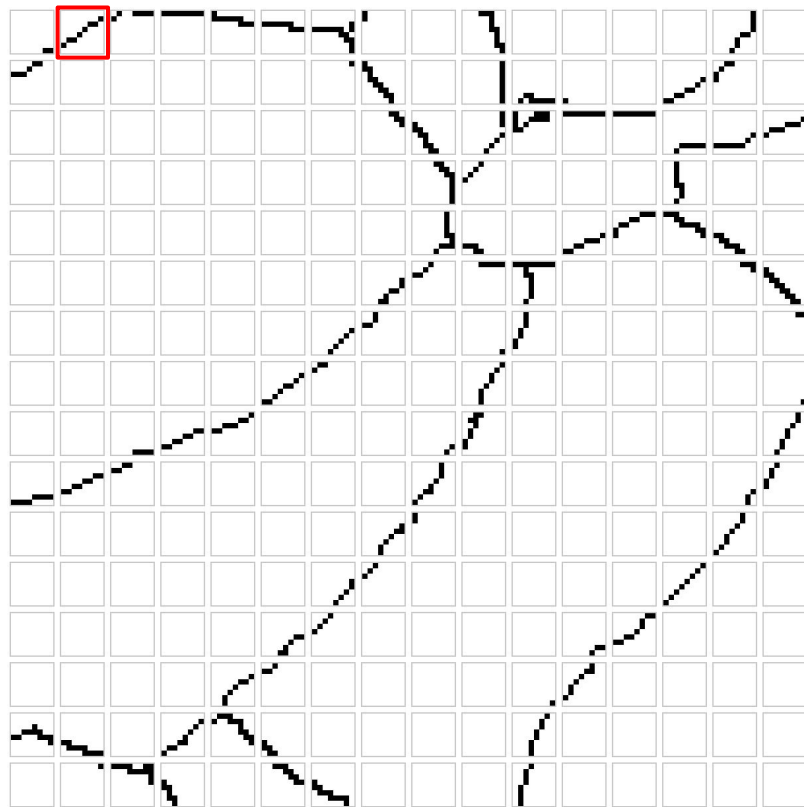


# Boundary Encoding



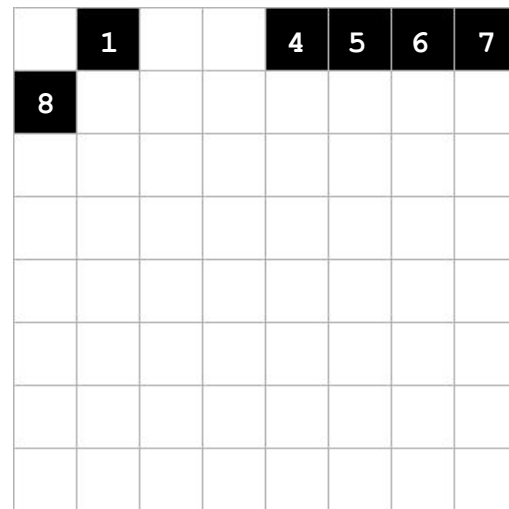
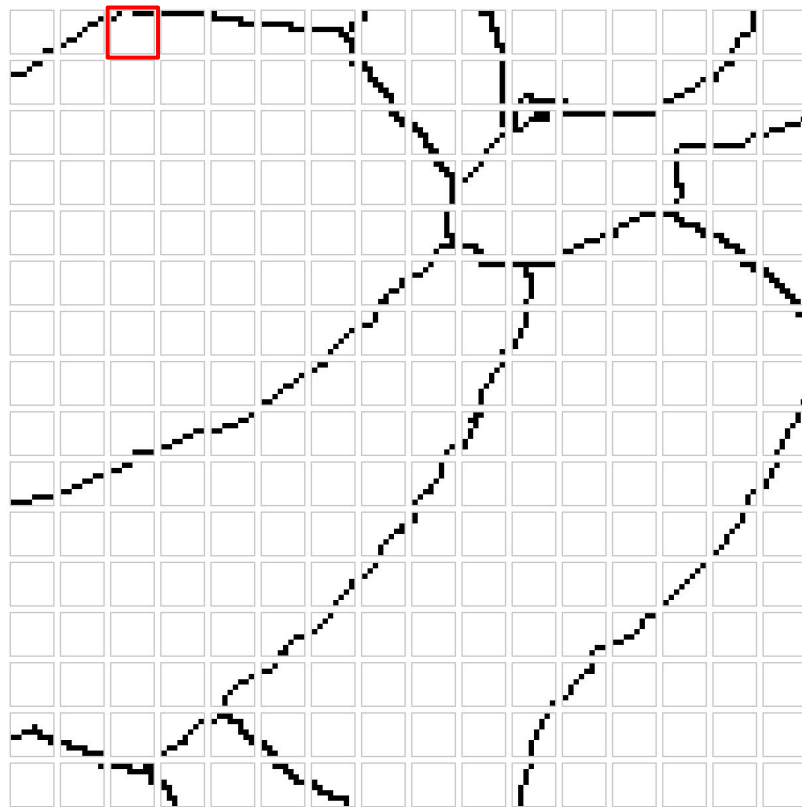
$$2^{62} + 2^{63} = 13835058055282163712$$

# Boundary Encoding



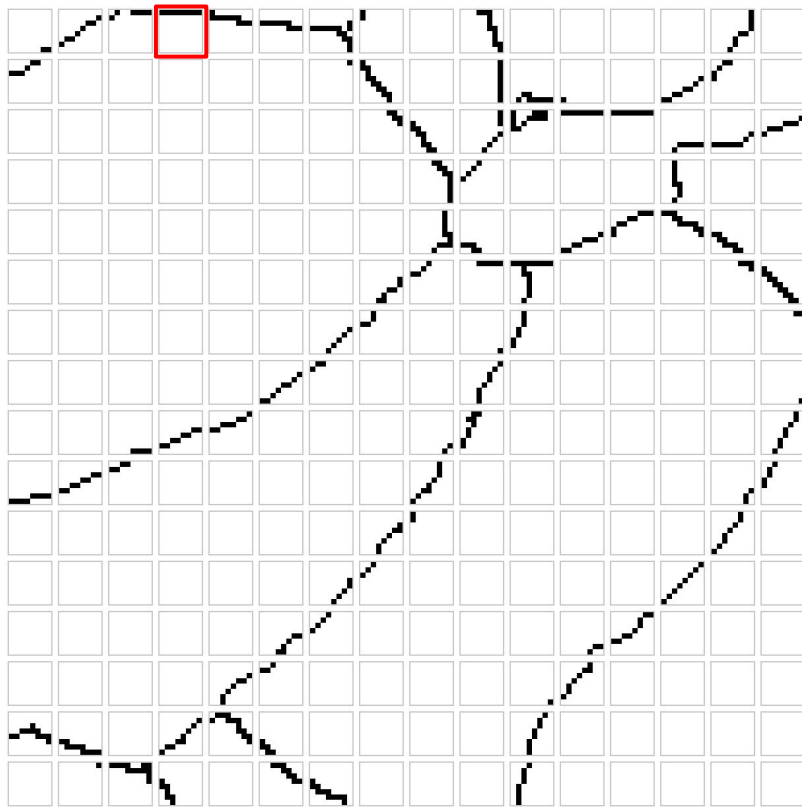
$$2^{15} + 2^{21} + 2^{22} + 2^{28} + 2^{35} + 2^{41} + 2^{42} + 2^{48} = 288106680975360$$

# Boundary Encoding



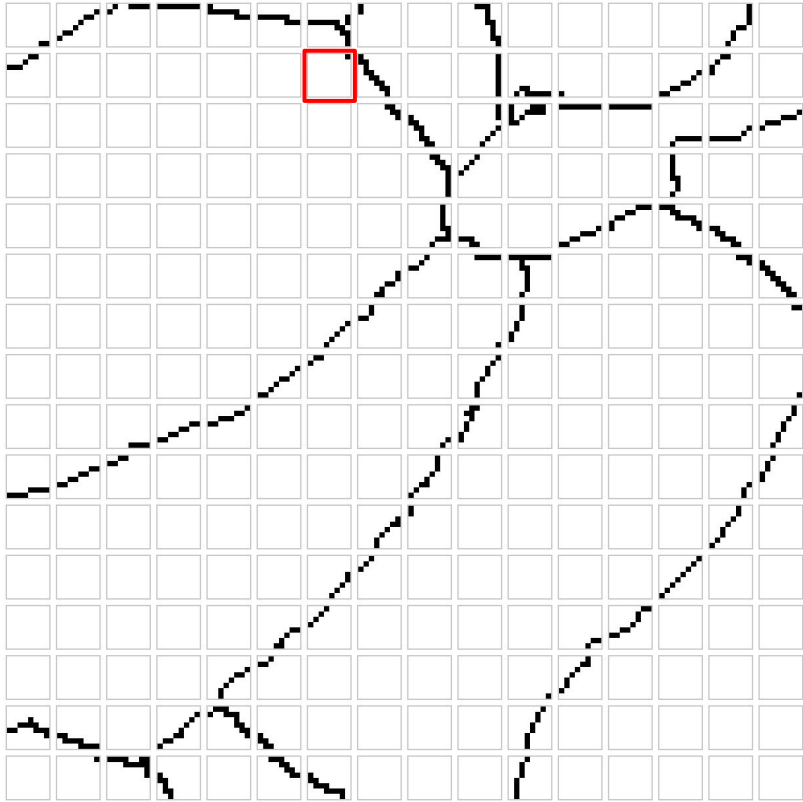
$$2^1 + 2^4 + 2^5 + 2^6 + 2^7 + 2^8 = 498$$

# Boundary Encoding

[illegible]

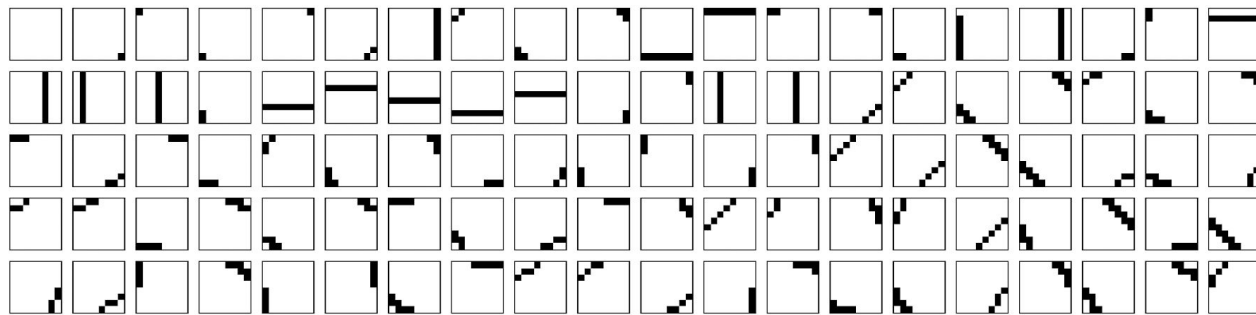
$$2^0 + 2^1 + 2^2 + 2^3 + 2^4 + 2^5 + 2^6 + 2^7 = 255$$

# Boundary Encoding



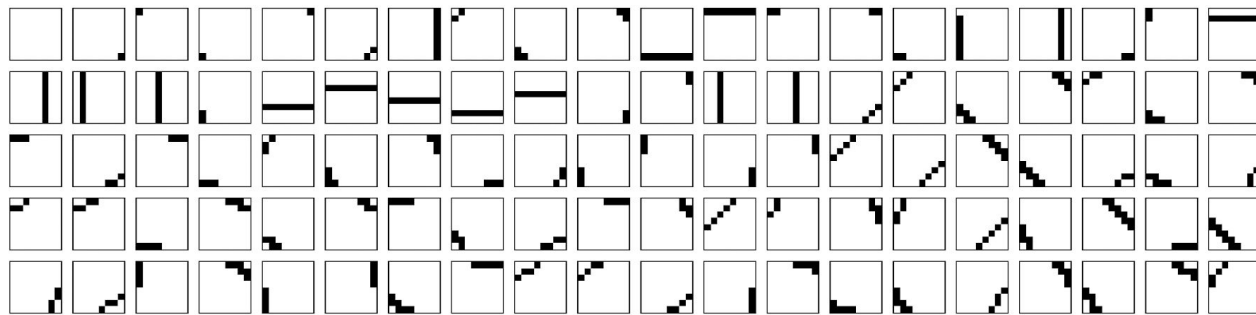
13835058055282163712  
288106680975360  
498  
255  
14696193  
3762225152  
9259612355635970048  
257  
0  
9277485877618024504  
0  
0  
0  
0  
580982358589603968  
0  
460848  
0  
0  
0  
0  
0  
128  
.  
.  
.

# Window Repetition



These 100 windows account for over 82% of all windows on a representative connectomics dataset

# Window Repetition

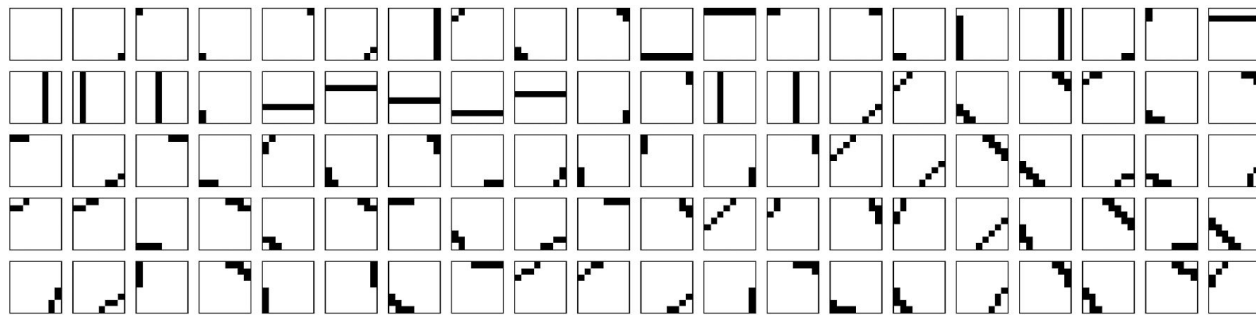


These 100 windows account for over 82% of all windows on a representative connectomics dataset

Typically there are only 100,000 unique windows in a given label volume



# Window Repetition



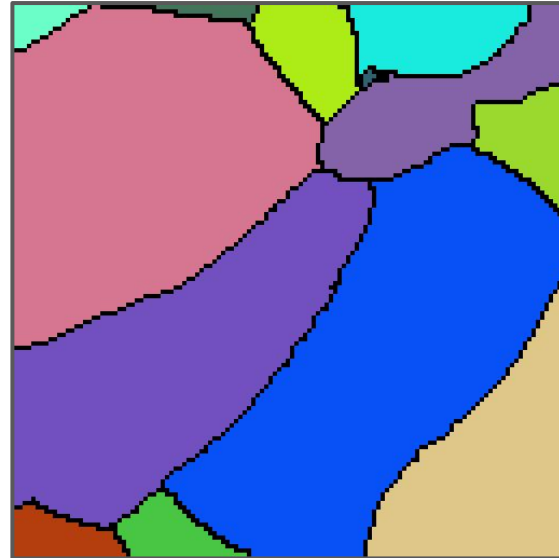
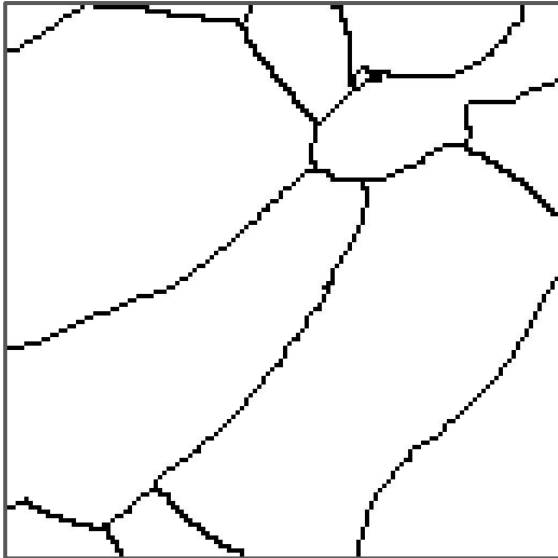
These 100 windows account for over 82% of all windows on a representative connectomics dataset

Typically there are only 100,000 unique windows in a given label volume

Map window values to this smaller subset to use 3 bytes per window

# Compressing Per-Pixel Labels

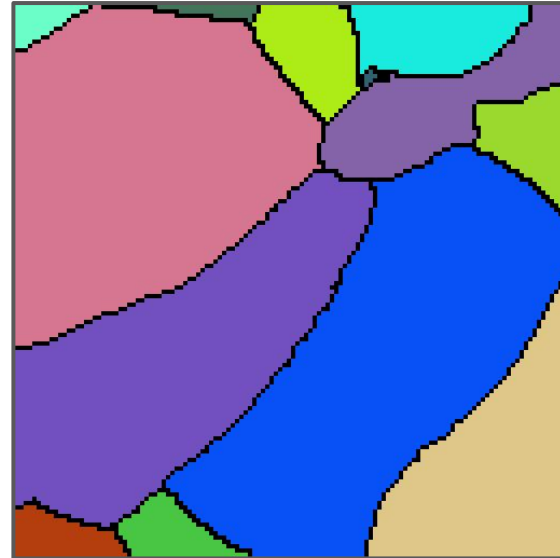
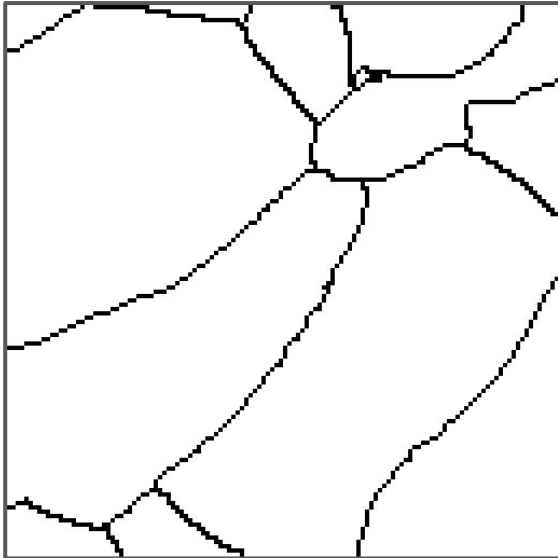
Goal: Store one 64-bit label per component



# Compressing Per-Pixel Labels



Goal: Store one 64-bit label per component

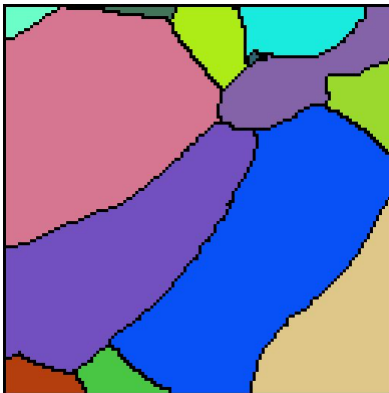
Solution: Identify continuous regions using a connected components algorithm



# Per-Pixel Label Encoding



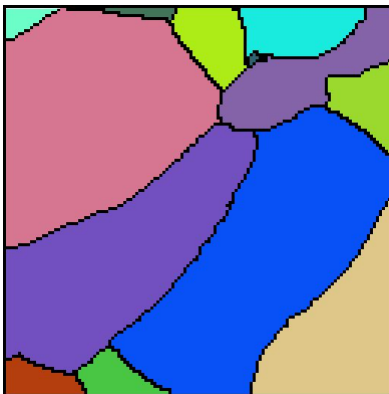
1   $\longrightarrow$   1381



# Per-Pixel Label Encoding




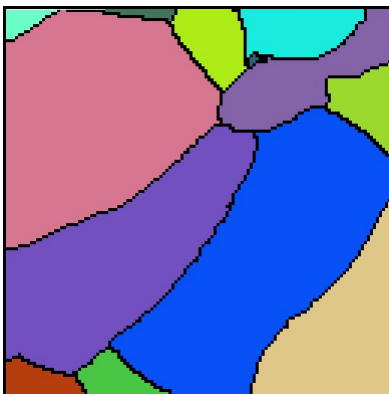
1   $\longrightarrow$   1381  
2   $\longrightarrow$   836



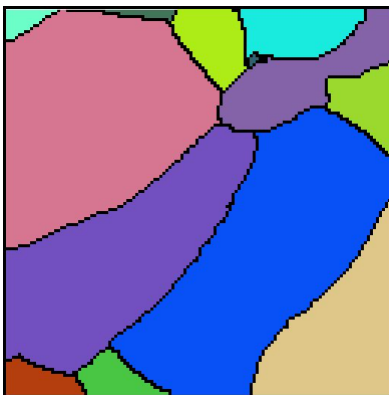
# Per-Pixel Label Encoding











1		→		1381
2		→		836
3		→		538



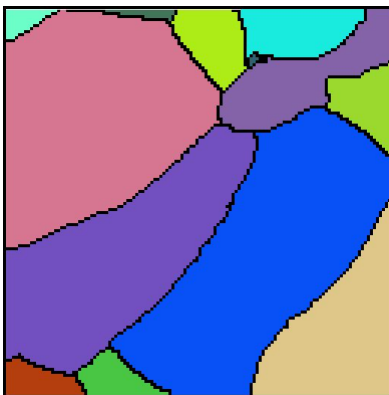
# Per-Pixel Label Encoding













1		→		1381
2		→		836
3		→		538
4		→		1617

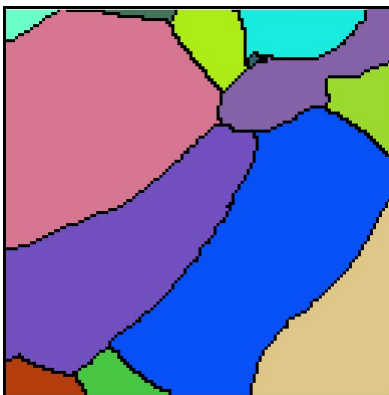














# Per-Pixel Label Encoding



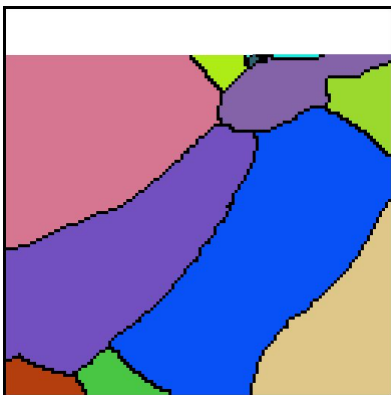
1		→		1381
2		→		836
3		→		538
4		→		1617
5		→		1709




# Per-Pixel Label Encoding



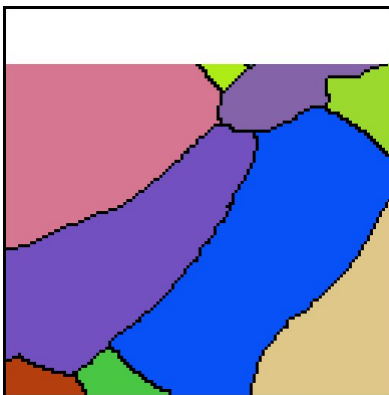
1		→		1381
2		→		836
3		→		538
4		→		1617
5		→		1709
6		→		1688

# Per-Pixel Label Encoding



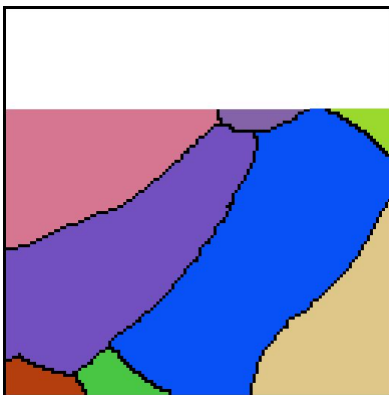
1		→		1381
2		→		836
3		→		538
4		→		1617
5		→		1709
6		→		1688
7		→		1617
















# Per-Pixel Label Encoding



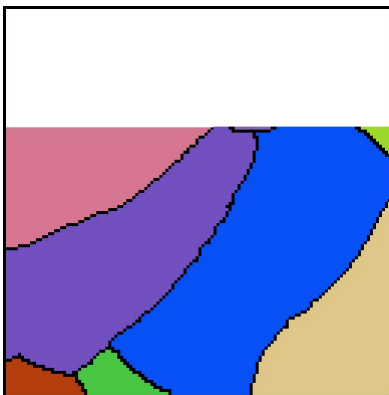
1		→		1381
2		→		836
3		→		538
4		→		1617
5		→		1709
6		→		1688
7		→		1617
8		→		1619





















# Per-Pixel Label Encoding



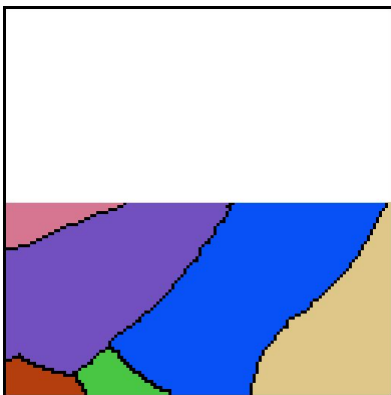
1		→		1381
2		→		836
3		→		538
4		→		1617
5		→		1709
6		→		1688
7		→		1617
8		→		1619
9		→		1020














# Per-Pixel Label Encoding



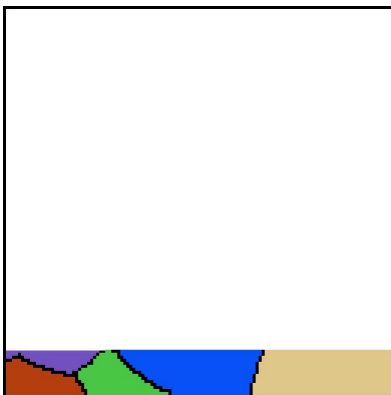
1		→		1381
2		→		836
3		→		538
4		→		1617
5		→		1709
6		→		1688
7		→		1617
8		→		1619
9		→		1020
10		→		827

























# Per-Pixel Label Encoding



1		→		1381
2		→		836
3		→		538
4		→		1617
5		→		1709
6		→		1688
7		→		1617
8		→		1619
9		→		1020
10		→		827
11		→		1723

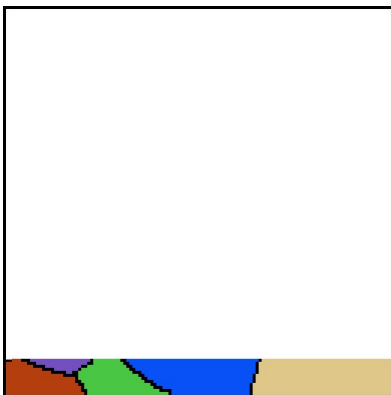
# Per-Pixel Label Encoding

















1		→		1381
2		→		836
3		→		538
4		→		1617
5		→		1709
6		→		1688
7		→		1617
8		→		1619
9		→		1020
10		→		827
11		→		1723
12		→		1246

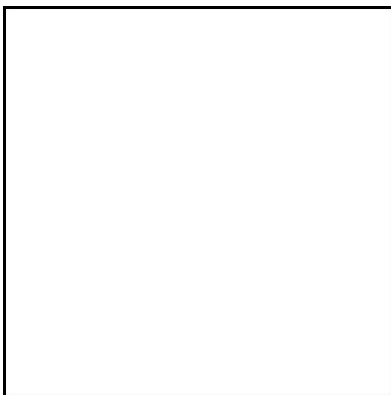















# Per-Pixel Label Encoding



1		→		1381
2		→		836
3		→		538
4		→		1617
5		→		1709
6		→		1688
7		→		1617
8		→		1619
9		→		1020
10		→		827
11		→		1723
12		→		1246
13		→		1258

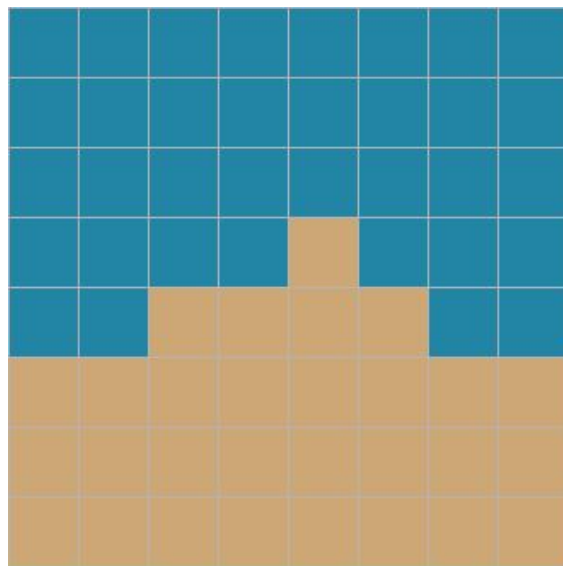
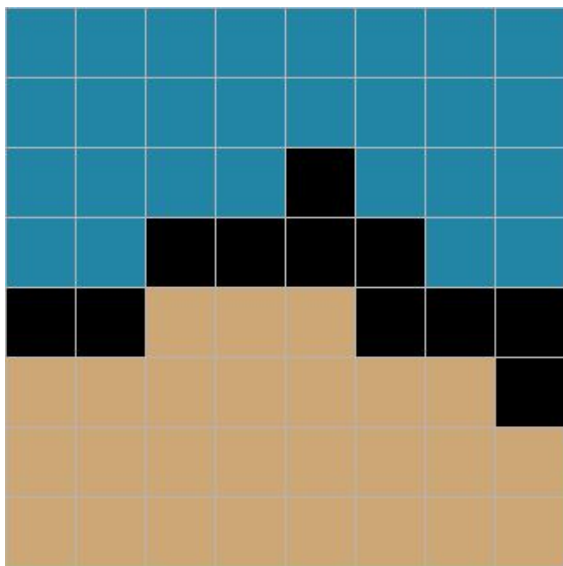
# Per-Pixel Label Encoding



1		→		1381
2		→		836
3		→		538
4		→		1617
5		→		1709
6		→		1688
7		→		1617
8		→		1619
9		→		1020
10		→		827
11		→		1723
12		→		1246
13		→		1258

# Indeterminate Locations

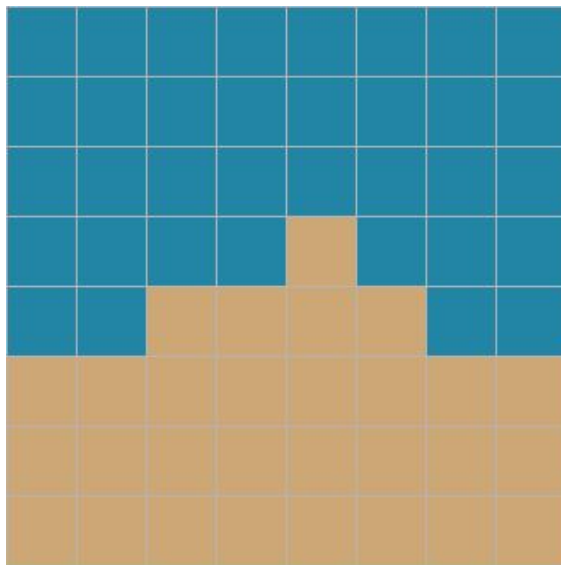
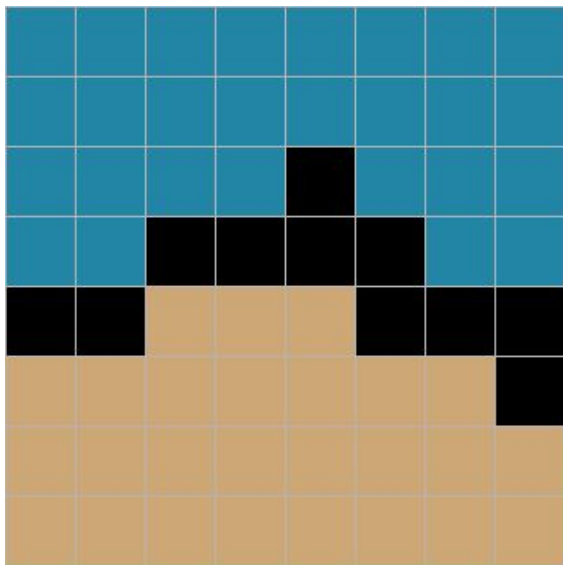
So far, we assumed the boundary map and connected component mapping is enough for decompression



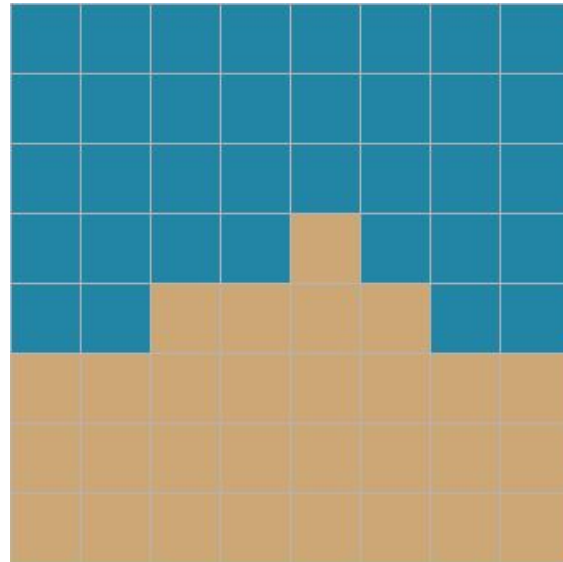
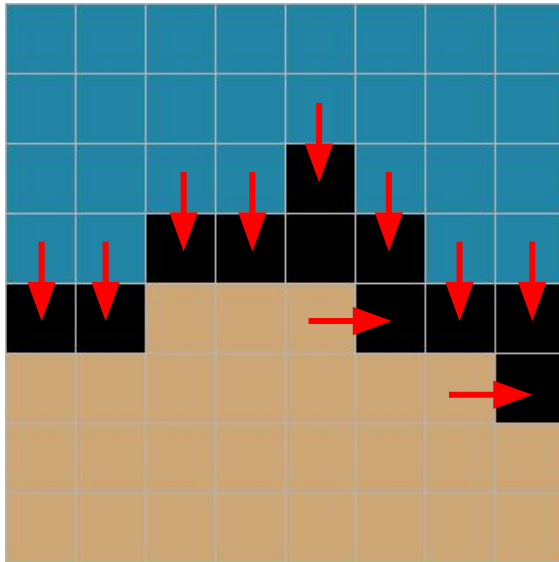
# Indeterminate Locations

So far, we assumed the boundary map and connected component mapping is enough for decompression

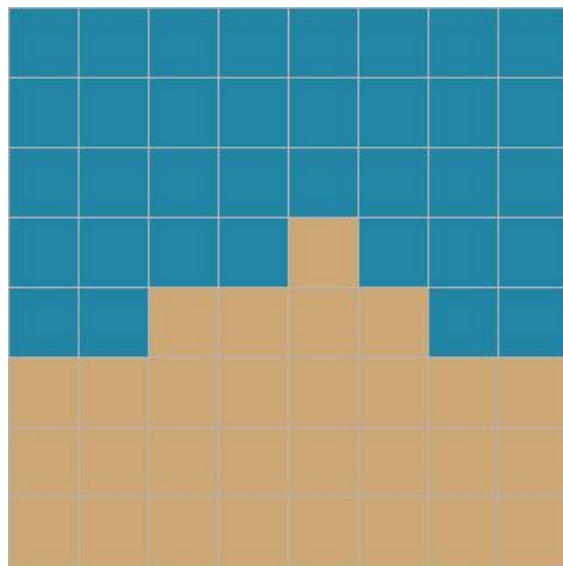
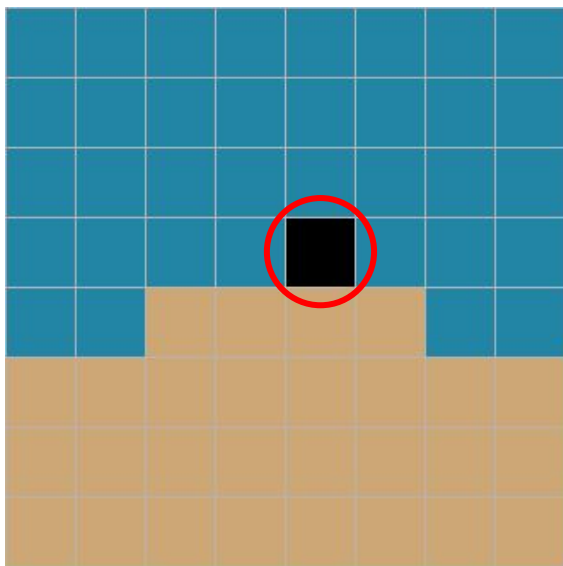
One additional corner case to consider:



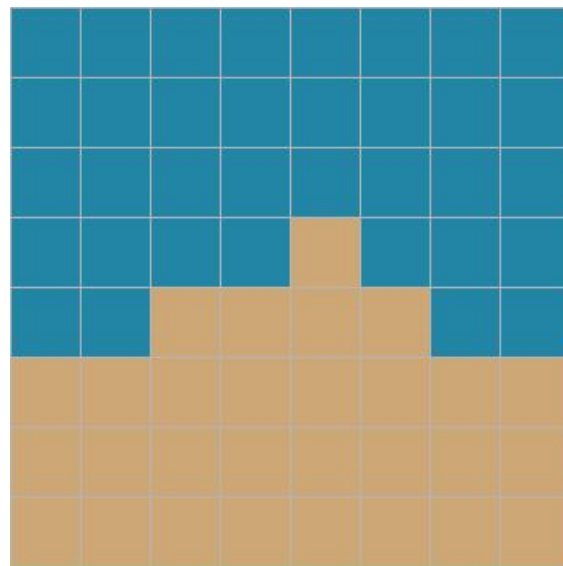
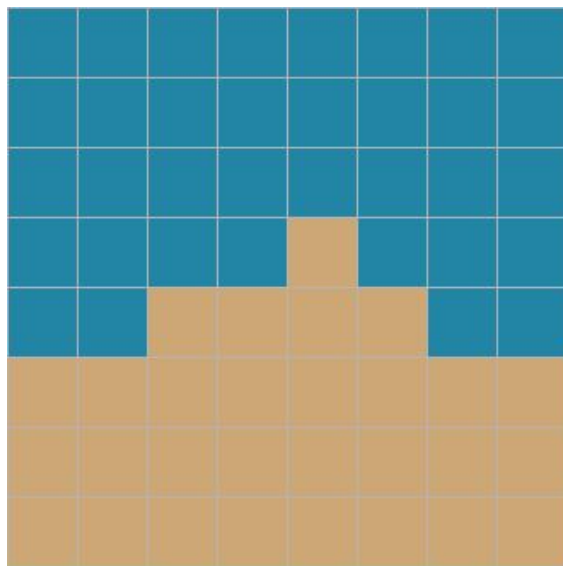
# Indeterminate Locations



# Indeterminate Locations



# Indeterminate Locations



Decompression



# Decompressing Boundary Map

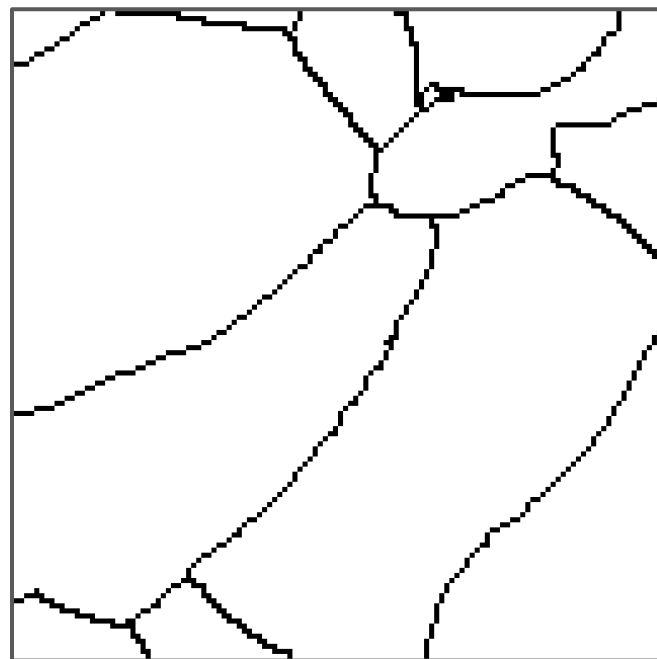
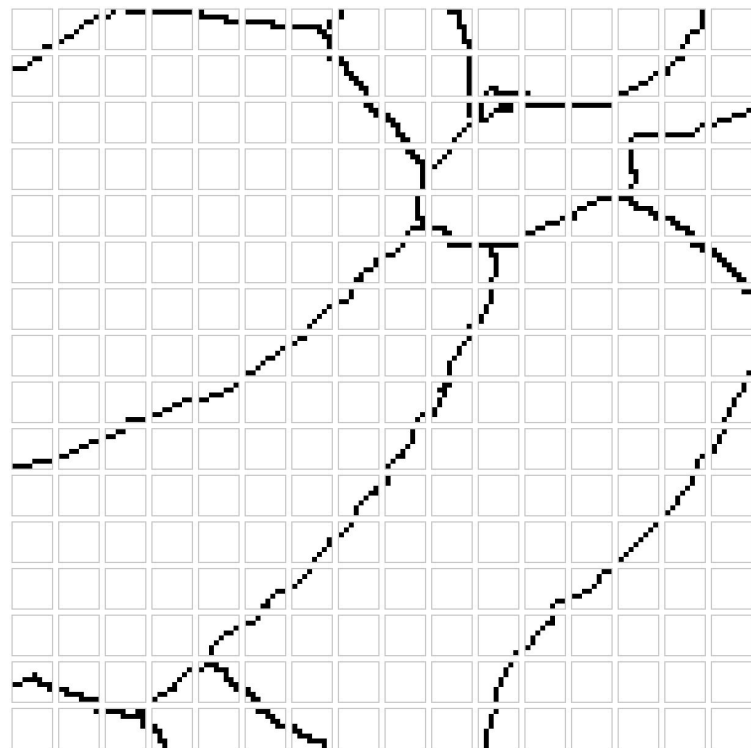
13835058055282163712  
288106680975360  
498  
255  
14696193  
3762225152  
9259612355635970048  
257  
0  
9277485877618024504  
0  
0  
0  
0  
580982358589603968  
0  
460848  
0  
0  
0  
0  
0  
0  
128  
.  
.  
.

## Decompressing Boundary Map

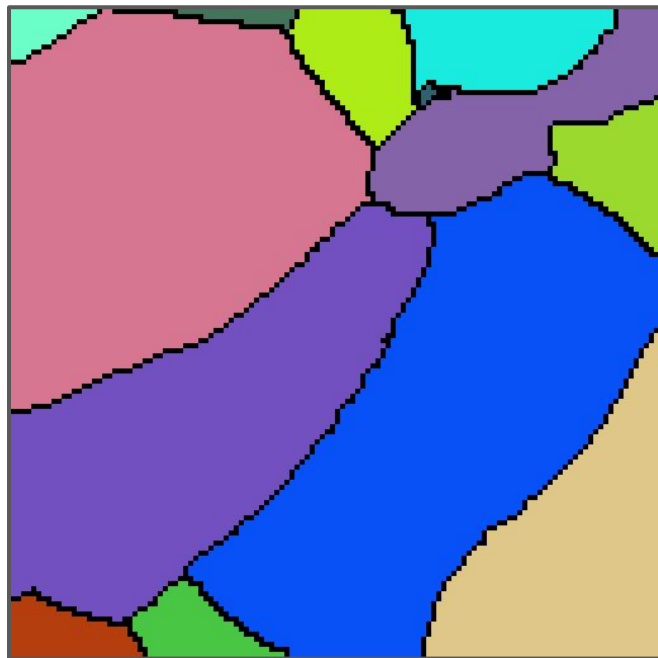
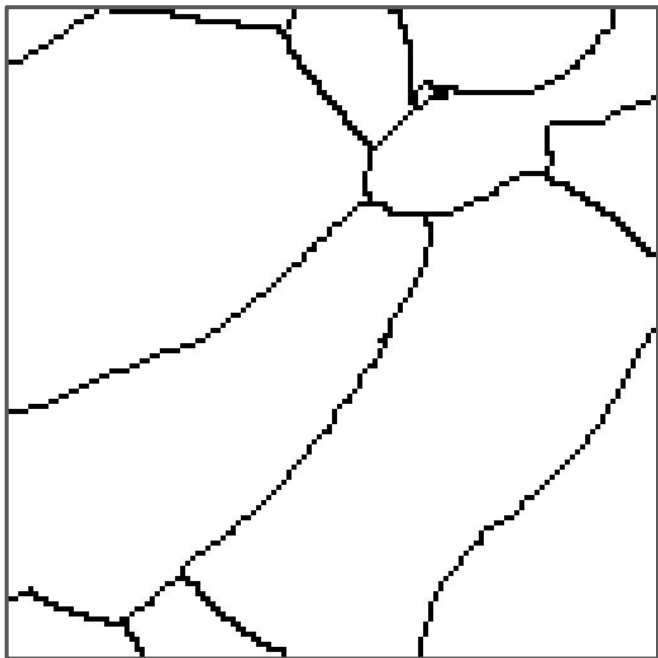
[illegible]

## Decompressing Boundary Map

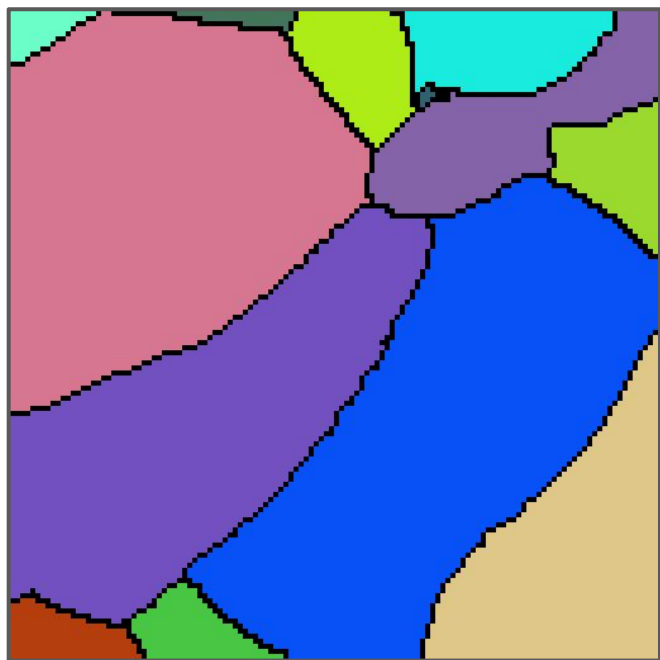
[illegible][illegible]





























## Decompressing Per-Pixel Labels



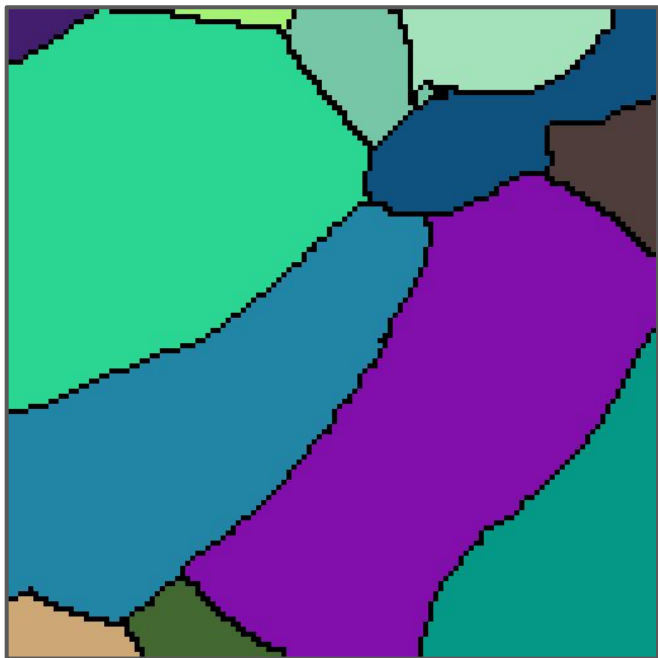
# Decompressing Per-Pixel Labels



1		→		1381
2		→		836
3		→		538
4		→		1617
5		→		1709
6		→		1688
7		→		1617
8		→		1619
9		→		1020
10		→		827
11		→		1723
12		→		1246
13		→		1258



# Decompressing Per-Pixel Labels



# Variable 3D Window Sizes

Compresso can use different sized windows depending on the input data

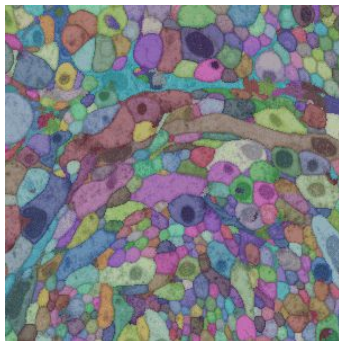


# Variable 3D Window Sizes

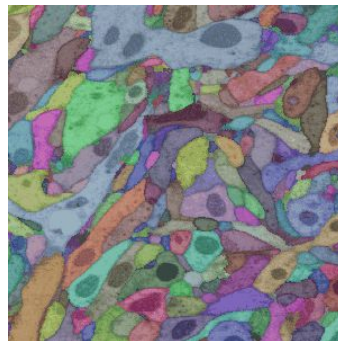
Compresso can use different sized windows depending on the input data

4x4x4 windows outperform 8x8x1 windows by 12.5% on an isotropic dataset

Isotropic Data

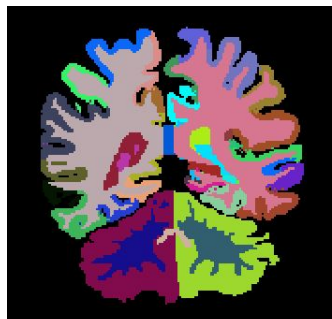


XY-plane



YZ-plane

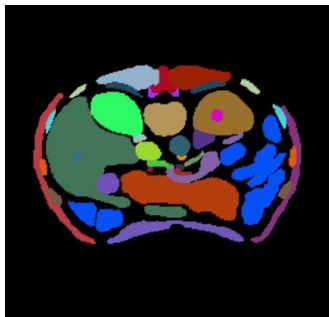
## Extends to Other Segmentation Datasets



SPL Brain Atlas



SPL Knee Atlas



SPL Abdominal Atlas



Berkeley Segmentation  
Dataset



PASCAL Visual Object  
Classes Dataset

# Results

# Two Stage Compression with LZMA

Follow Compresso with a general-purpose compression scheme such as LZMA

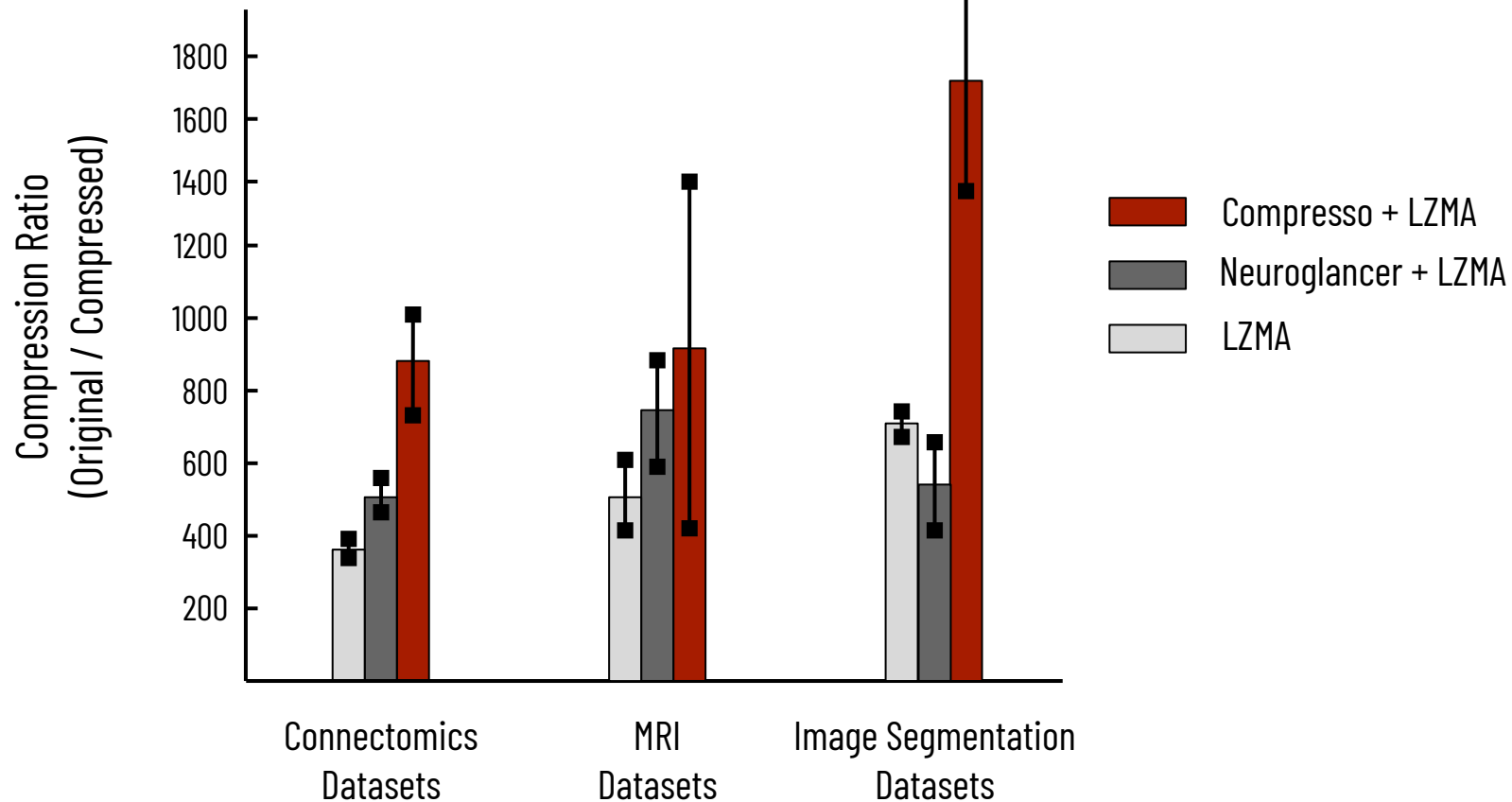
# Two Stage Compression with LZMA

Follow Compresso with a general-purpose compression scheme such as LZMA

LZMA uses complex models for probability predictions of bits

Dataset	Uncompressed	Neuroglancer + LZMA	Compresso + LZMA
AC3 Mouse cortex, EM	1.26 GB	550x	<b>771x</b>
AC4 Mouse cortex, EM	838.86 MB	479x	<b>660x</b>
CREMI A, B, C Drosophila brain, EM	1.56 GB	465x, 629x, 496x	<b>804x, 1158x, 899x</b>
L. Cylinder Mouse cortex, EM	10.07 GB	425x	<b>889x</b>
SPL Brain Atlas T1/T2-weighted MRI	135.27 MB	<b>764x</b>	645x
SPL Knee Atlas MRI	249.56 MB	1172x	<b>1562x</b>
SPL Abdominal Atlas CT	59.24 MB	417x	<b>482x</b>

# Compression Ratio



Method	Compression Speed	Decompression Speed
LZMA	9.89 MB / s	366.13 MB / s
Neuroglancer + LZMA	43.80 MB / s	164.32 MB / s
Compresso + LZMA	131.15 MB / s	206.60 MB / s



# Complexity

$P$  is the number of pixels;  $N$  is the number of distinct window values;  $X$  and  $Y$  are the size of the  $x$  and  $y$  dimensions of the input data; and  $\alpha$  is the inverse Ackermann function.

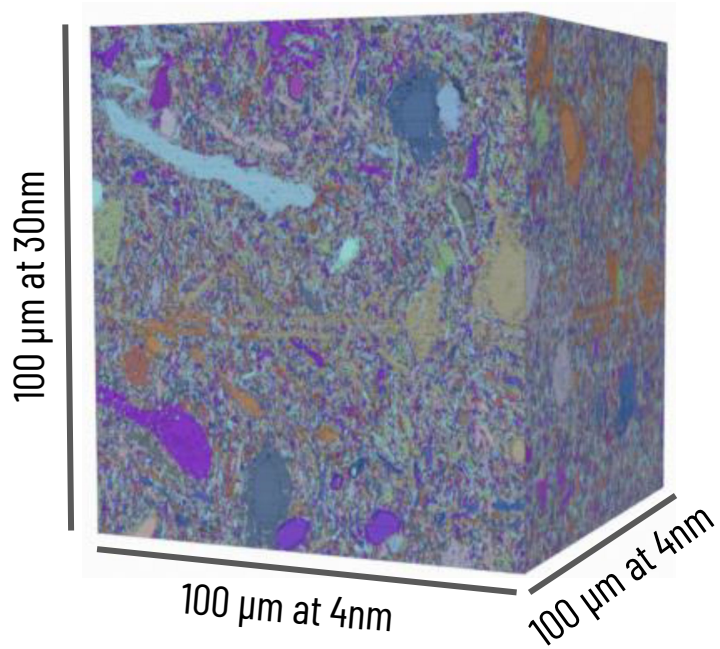
Compression:

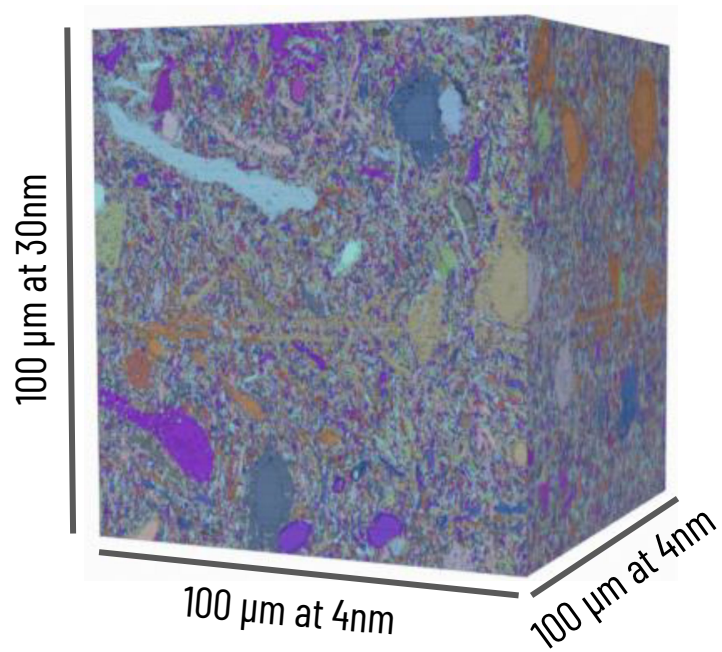
$$O(P(1 + \alpha(XY)) + N \log N)$$

Decompression:

$$O(P(1 + \alpha(XY)))$$

# Compression of 100 microns cubed

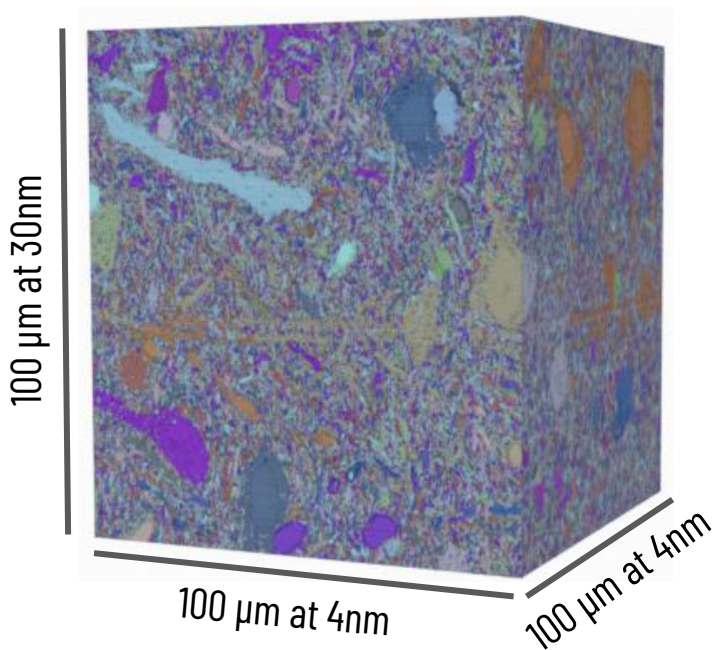




Uncompressed:

19.25 terabytes

# Compression of 100 microns cubed

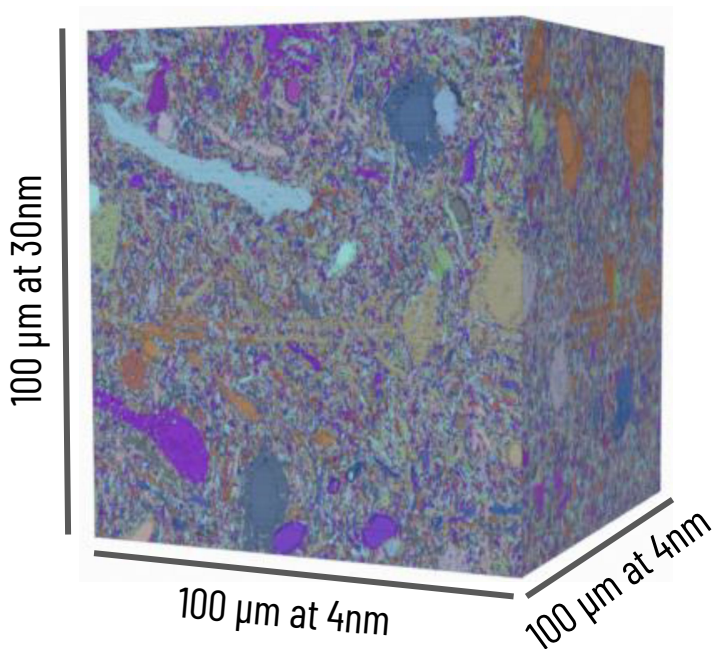


Uncompressed: 19.25 terabytes

With Compresso + LZMA: 25.94 gigabytes

Ratio: 742x

# Compression of 100 microns cubed



Uncompressed: 19.25 terabytes

With Compresso + LZMA: 25.94 gigabytes

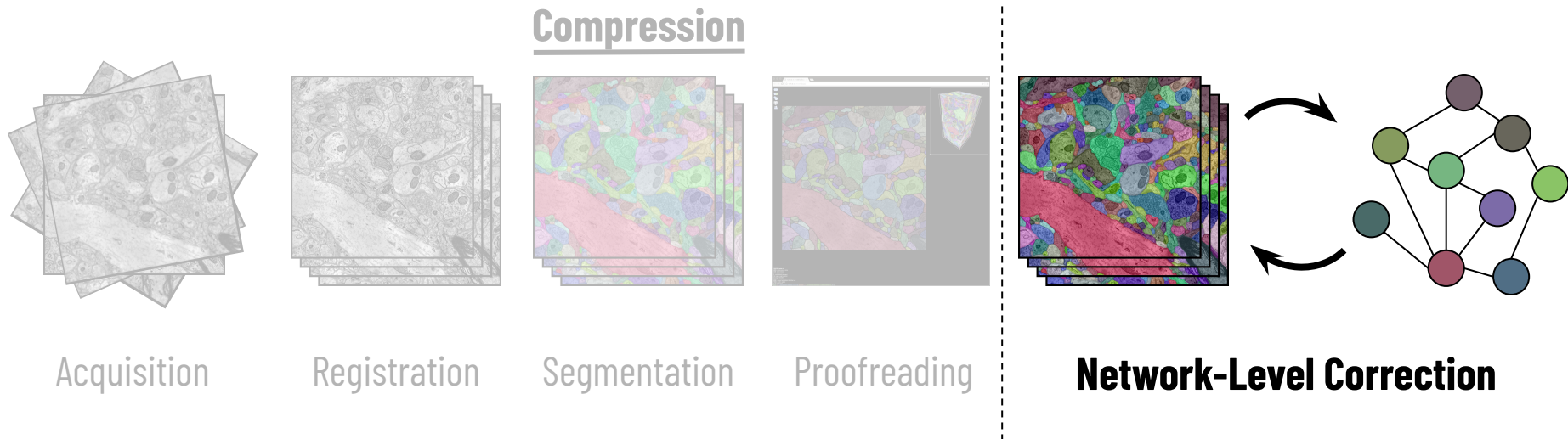
Ratio: 742x

AWS Storage Costs (S3 Standard Storage):

Uncompressed: \$442.75 / month

Compressed: \$0.60 / month

# Connectomics Pipeline



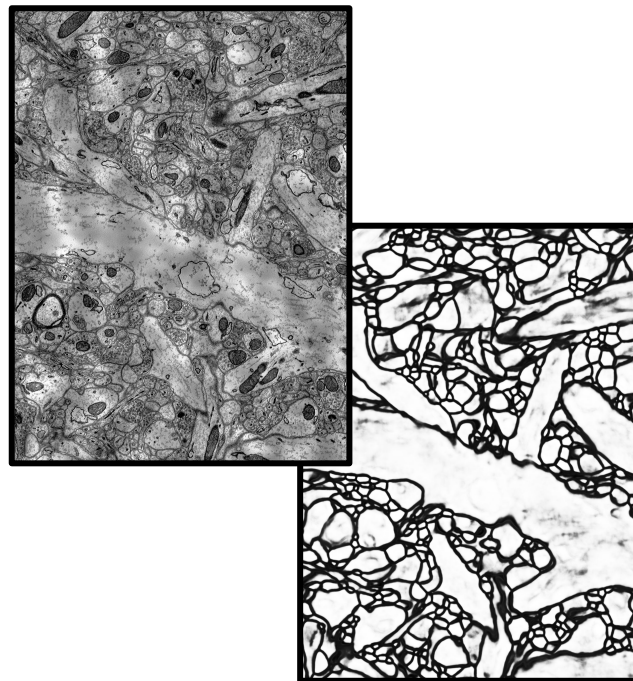
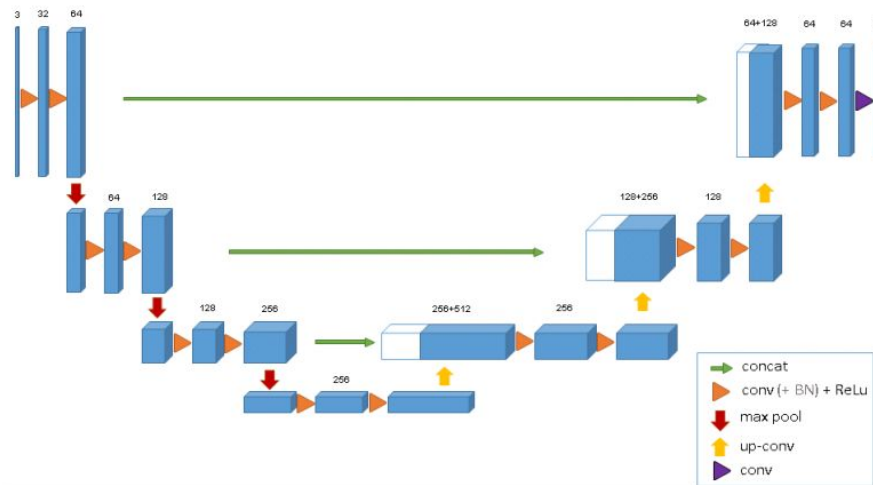
# Biologically-Constrained Region Merging for Connectome Reconstruction

Brian Matejek, Daniel Haehn, Donglai Wei, Toufiq Parag, Hanspeter Pfister



Under Review, ECCV 2018

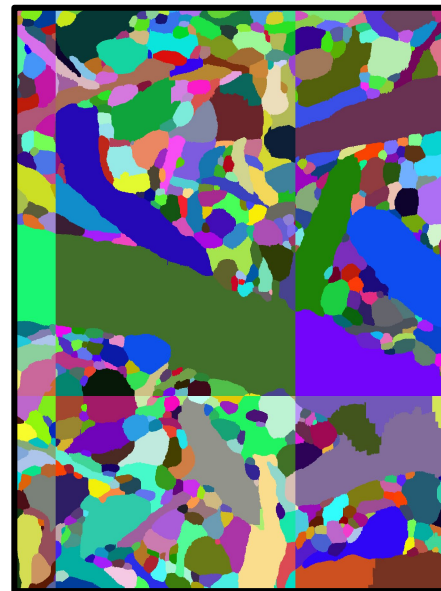
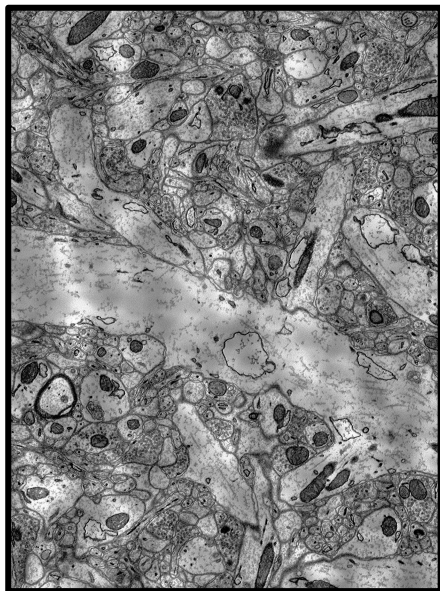
# U-Net



Ronneberger et al., U-Net: Convolutional Networks for Biomedical Image Segmentation, MICCAI 2015  
Cicek et al., 3D U-Net: Learning Dense Volumetric Segmentation from Sparse Annotation, MICCAI 2016



# 3D Watershed on Affinities

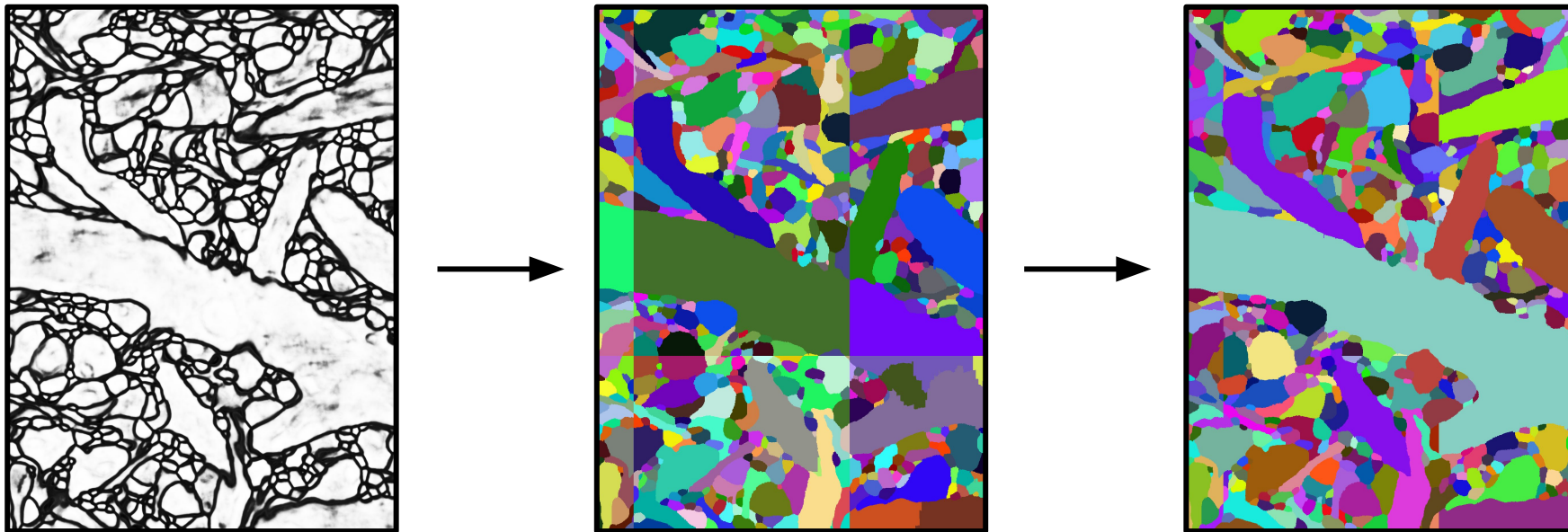


Zlateski et al., Image Segmentation by Size-Dependent Single Linkage Clustering of a Watershed Basin Graph, 2015

Funke et al., A Deep Structured Learning Approach Towards Automating Connectome Reconstruction from 3D Electron Micrographs, 2017

Zeng et al., DeepEM3D: Approaching Human-Level Performance on 3D Anisotropic EM Image Segmentation, Bioinformatics 2017

# Context-Aware Delayed Agglomeration

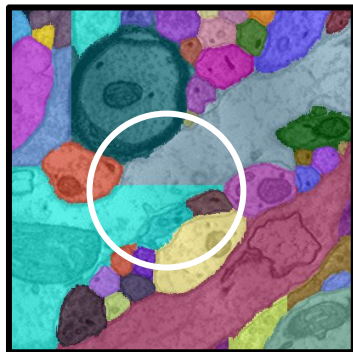


Nunez-Iglesias et al., Machine Learning of Hierarchical Clustering to Segment 2D and 3D Images, PLoS ONE, 2013

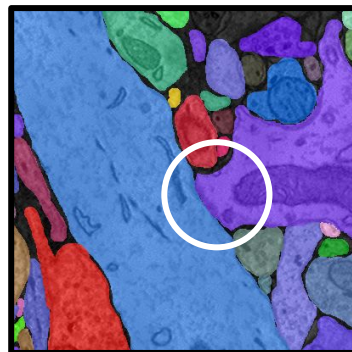
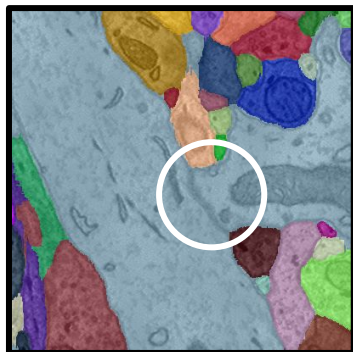
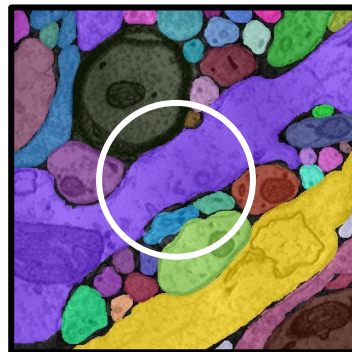
Parag et al., A Context-Aware Delayed Agglomeration Framework for Electron Microscopy Segmentation, PLoS ONE 2015

# Errors

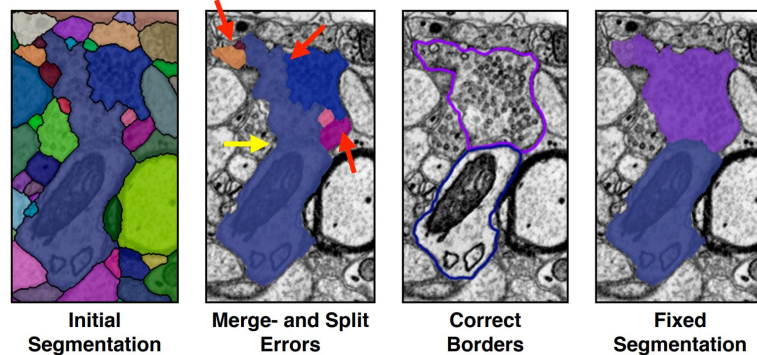
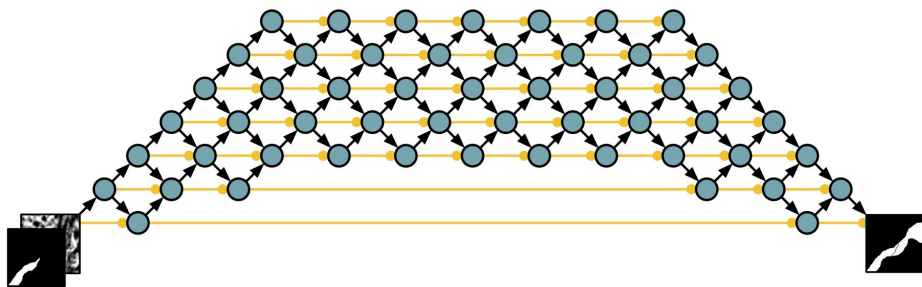
Automatic Segmentation



Ground Truth



# Proofreading and Error Correction



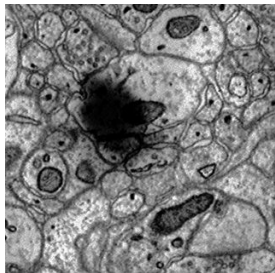
Zung et al., An Error Detection and Correction Framework for Connectomics, NIPS 2017

Haehn et al., Guided Proofreading of Automatic Segmentations for Connectomics, CVPR 2018

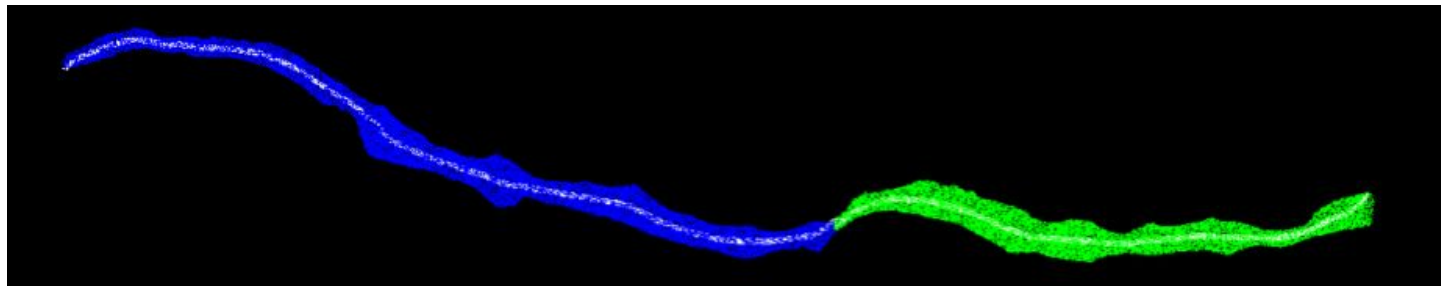
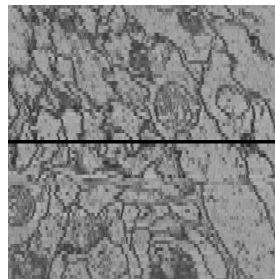


# Need for Global Context

Stained Images

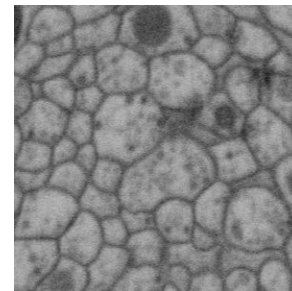
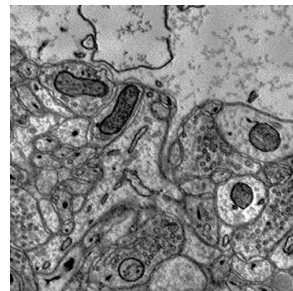
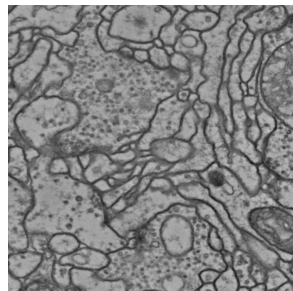
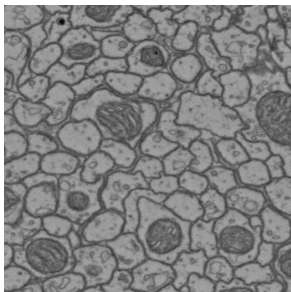


Missing Sections

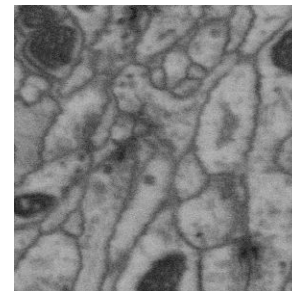
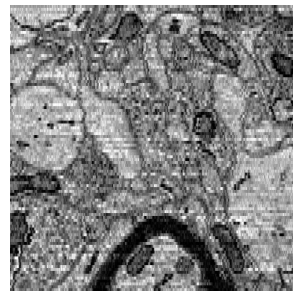
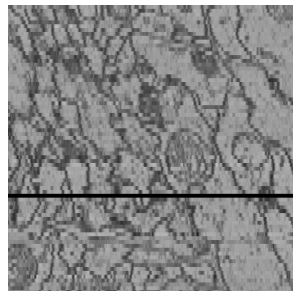
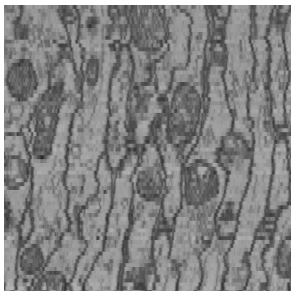


# Variable Image Data

xy-slice



yz-slice



CreMi Vol. A

*Drosophila melanogaster*

$4 \times 4 \times 40 \text{ nm}^3 / \text{vx}$

CreMi Vol. C

*Drosophila melanogaster*

$4 \times 4 \times 40 \text{ nm}^3 / \text{vx}$

Kasthuri

*Mouse*

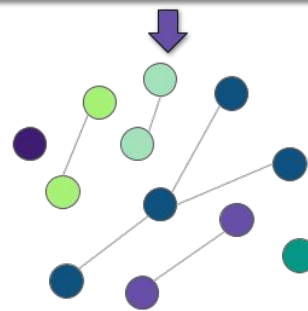
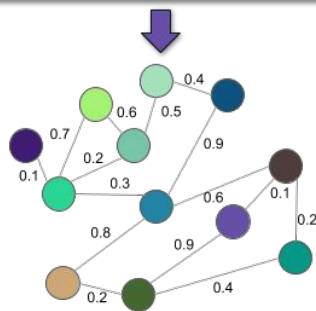
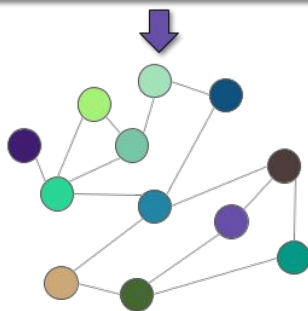
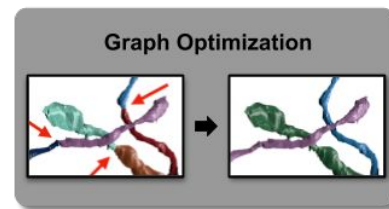
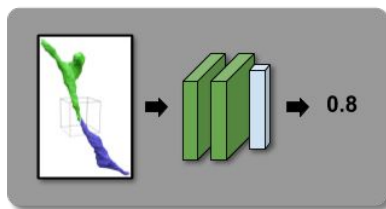
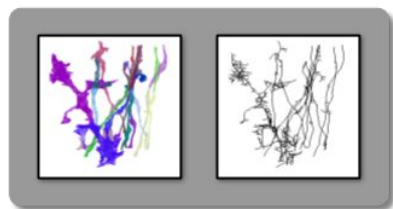
$6 \times 6 \times 30 \text{ nm}^3 / \text{vx}$

FlyEM

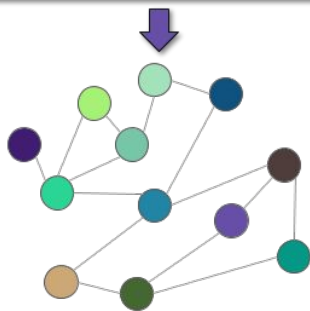
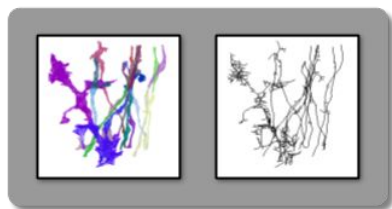
*Drosophila melanogaster*

$10 \times 10 \times 10 \text{ nm}^3 / \text{vx}$

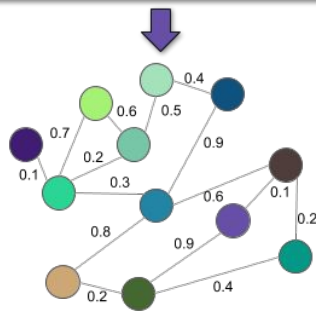
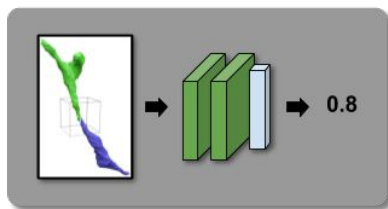
# Proposed Region Merging



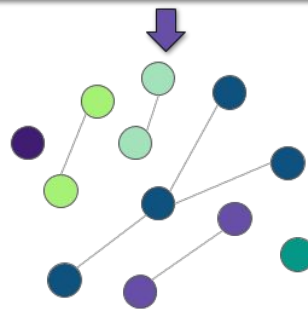
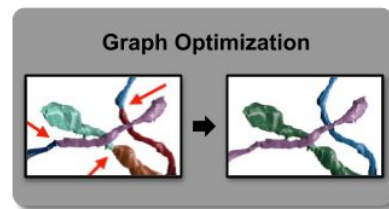
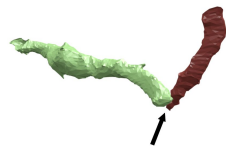
# Proposed Region Merging with Biological Constraints



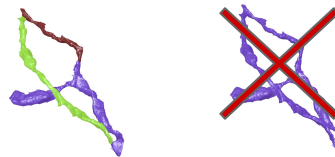
Geometric Priors



Learned Constraints

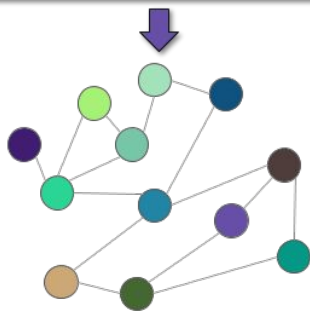
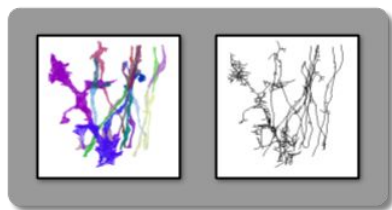


Topological Restrictions





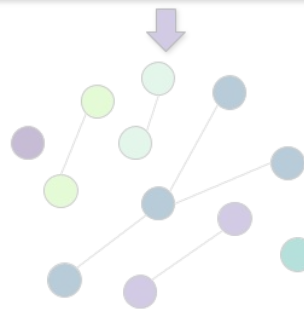
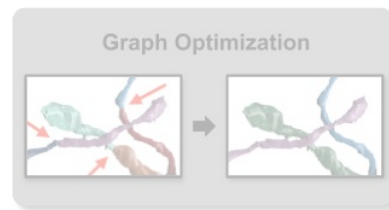
# Goal: Construct a graph with as few extra edges as possible



Geometric Priors



Learned Constraints



Topological Restrictions



# Adjacency Graphs

Every segment in the label volume receives a node

Segments with a pair of neighboring voxels receive an edge between the corresponding nodes

# Adjacency Graphs

Every segment in the label volume receives a node

Segments with a pair of neighboring voxels receive an edge between the corresponding nodes

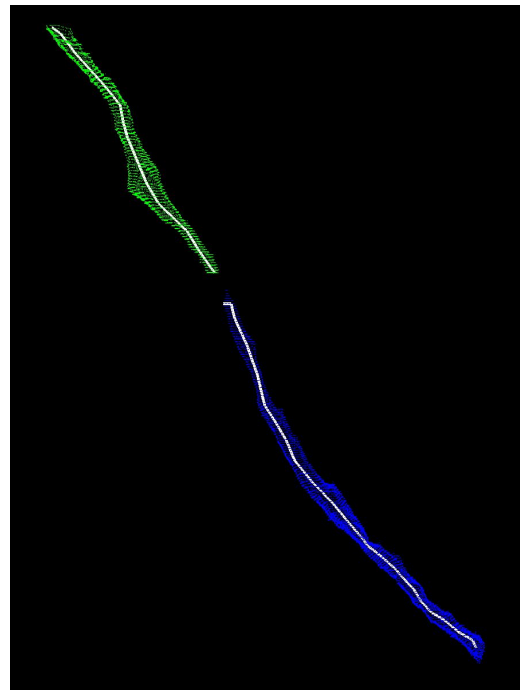
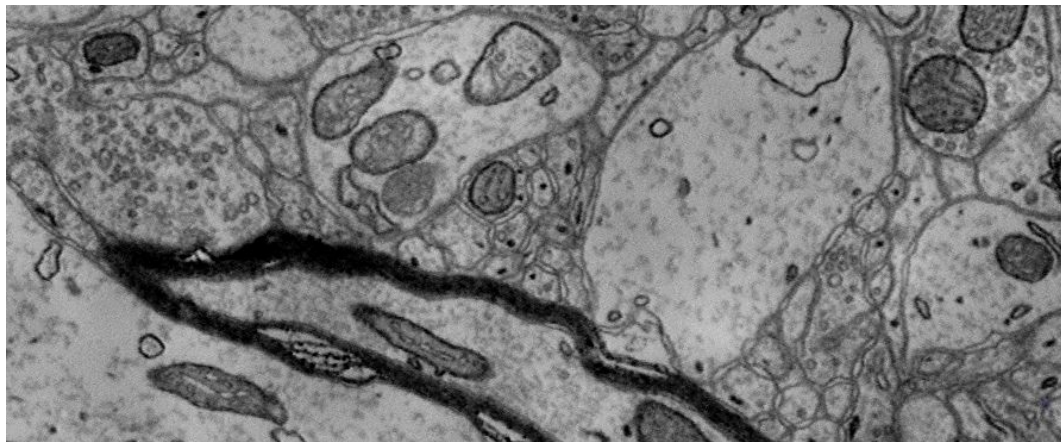


Typical Segment

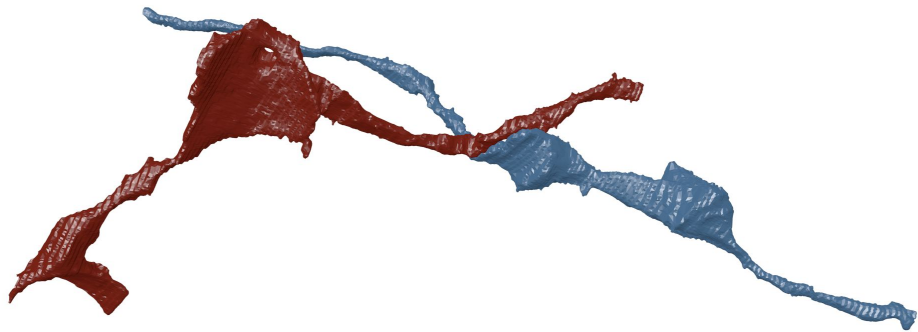


103 Adjacent Neighbors

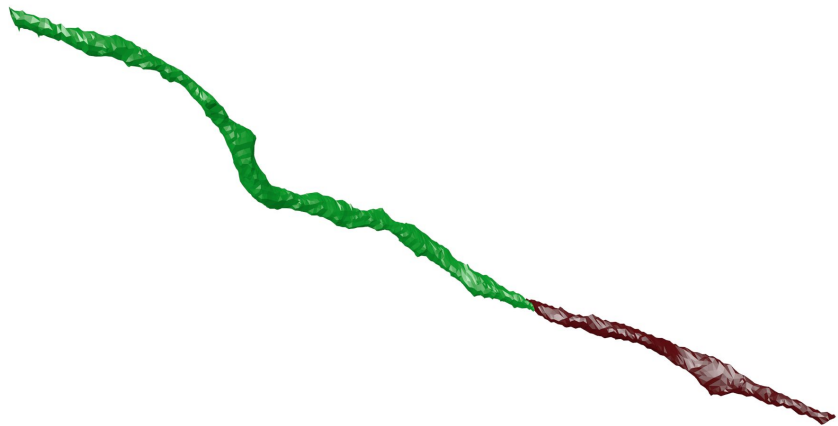
# Non-Adjacent Split Errors



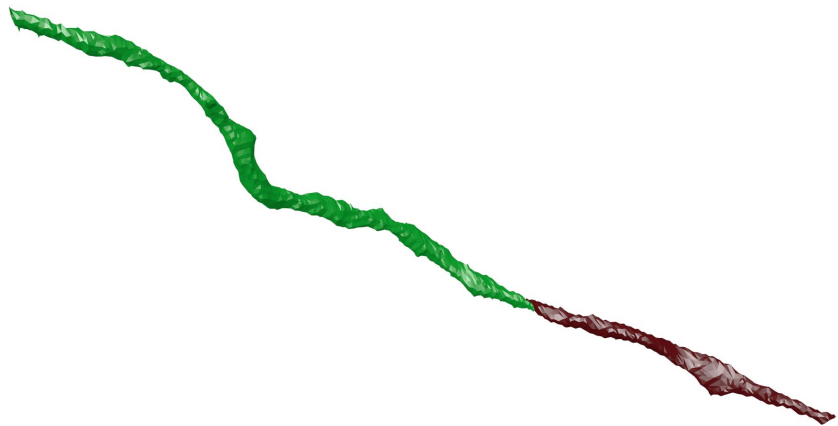
Correctly Segmented



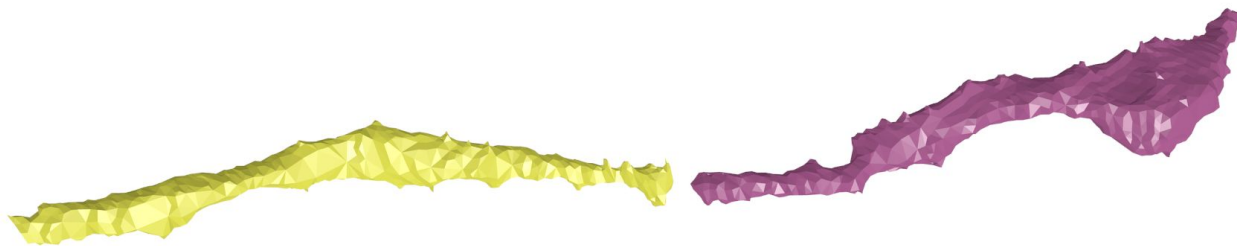
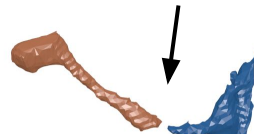
Incorrectly Split



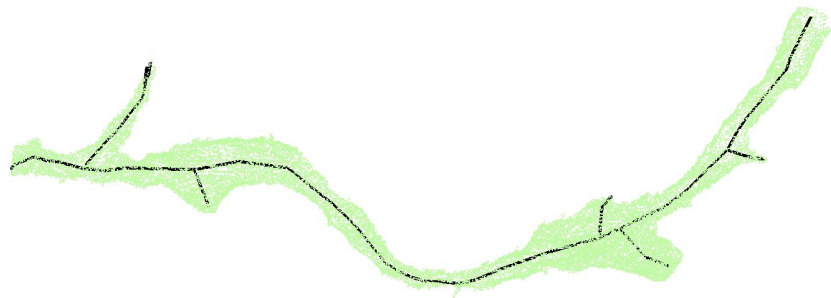
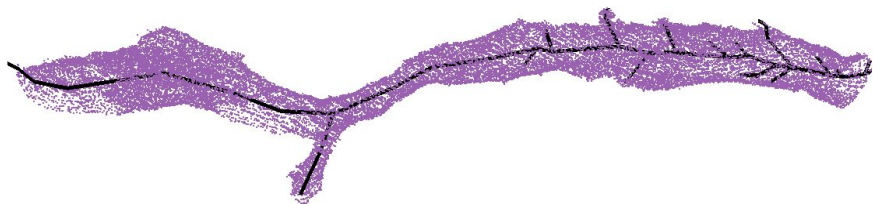
Incorrectly Split



Dendritic Spine

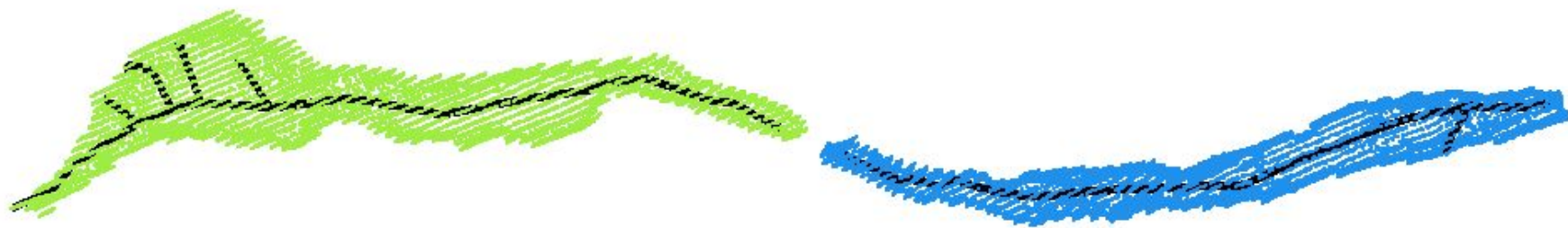


# Skeletonization

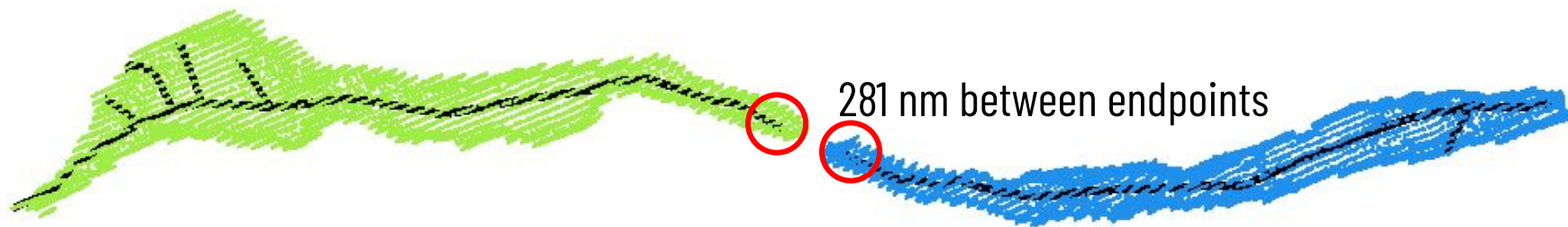




# Merge Candidate



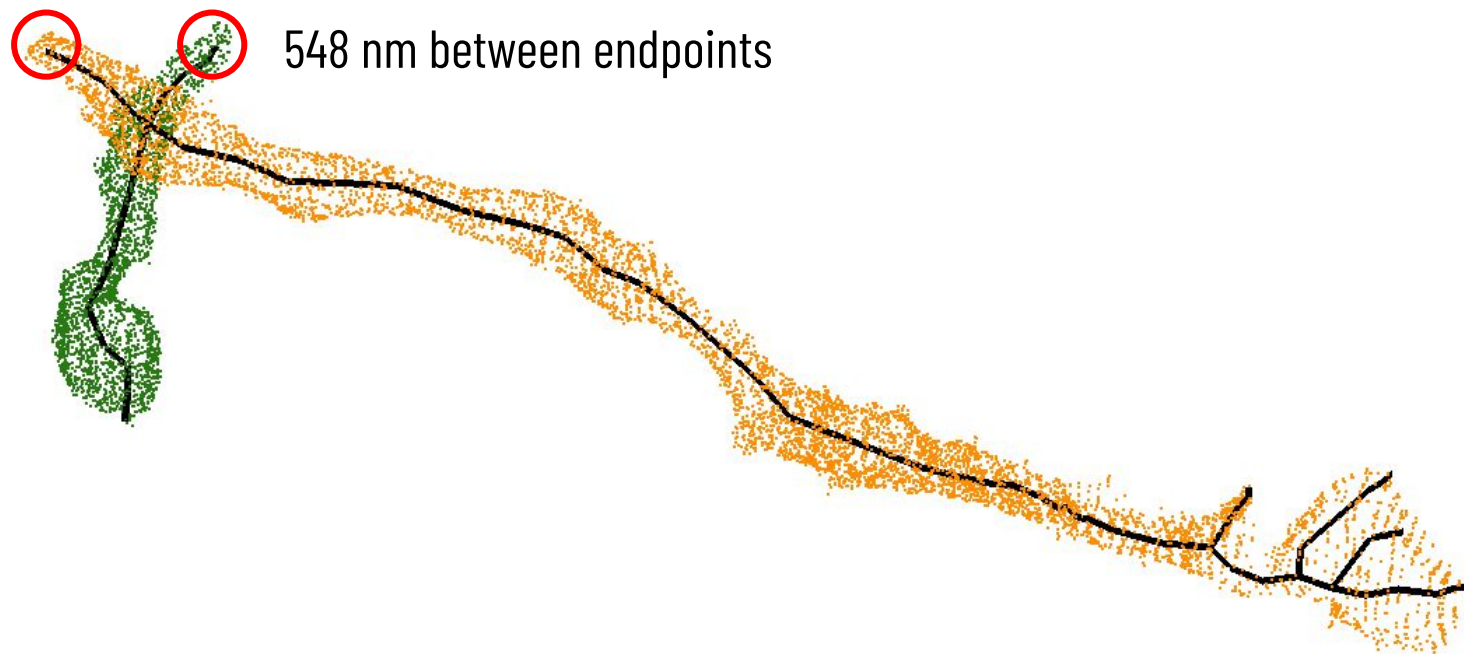
# Merge Candidate



# Pruned Candidate



# Pruned Candidate



Number of Edges



Typical Segment



103

**Before**

## Number of Edges

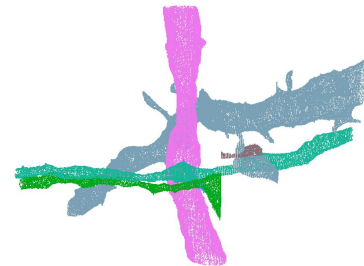


Typical Segment



103

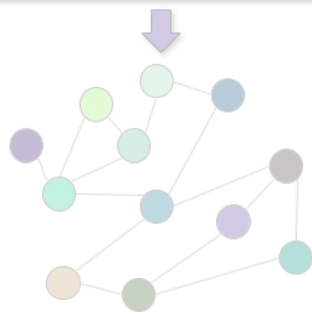
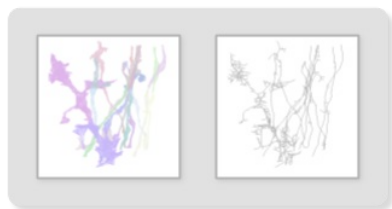
**Before**



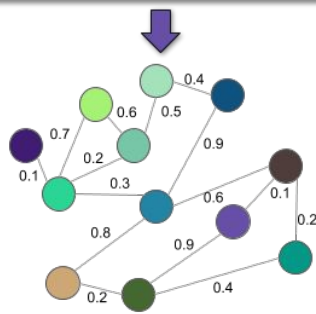
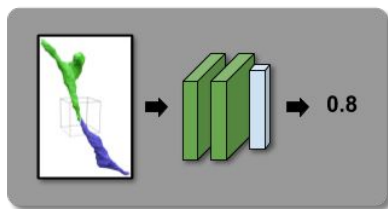
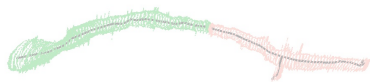
5

**After**

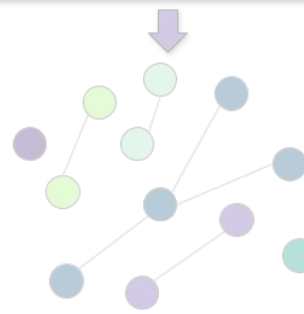
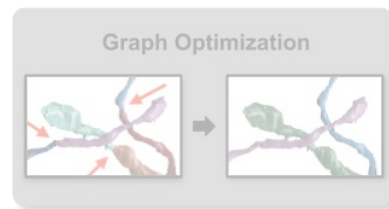
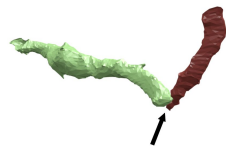
# Goal: Populate edge weights for the graph



Geometric Priors



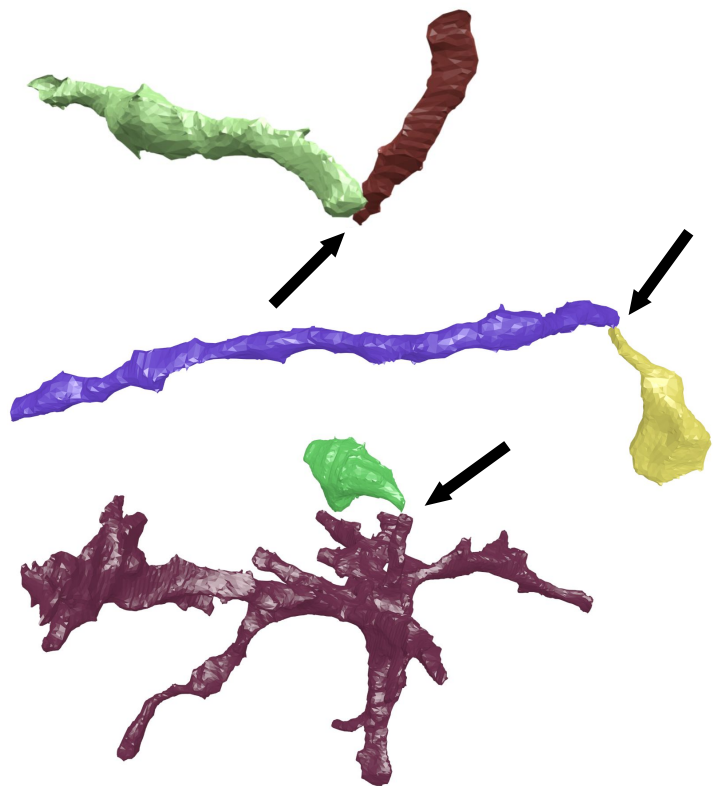
Learned Constraints



Topological Restrictions

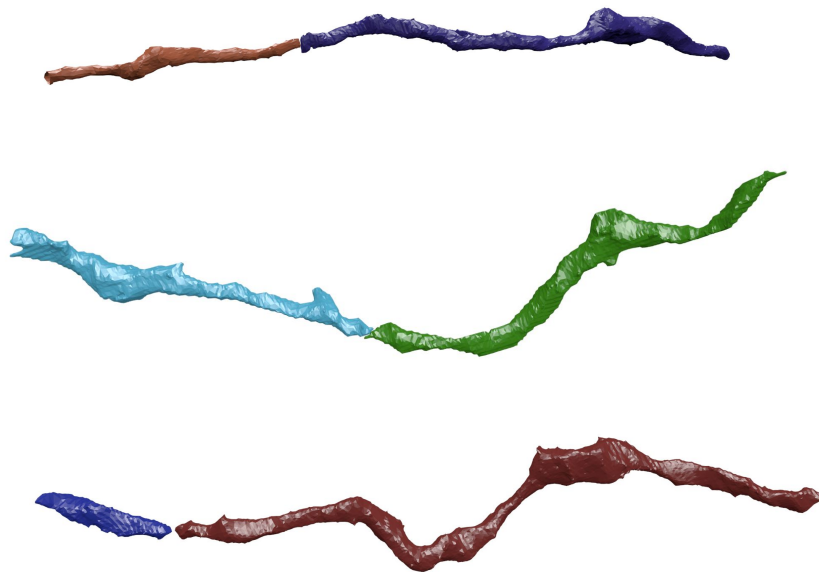
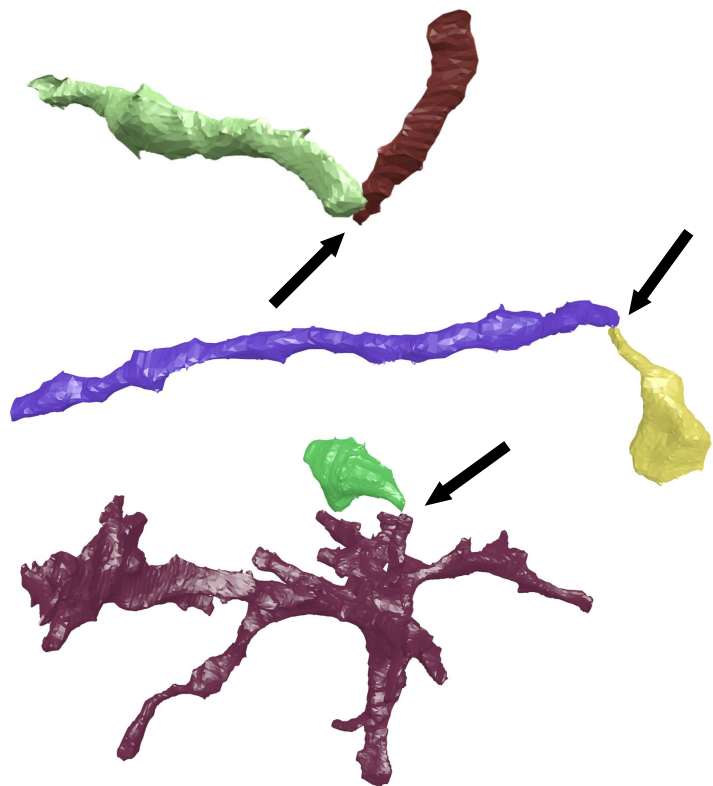


# Learned Constraints

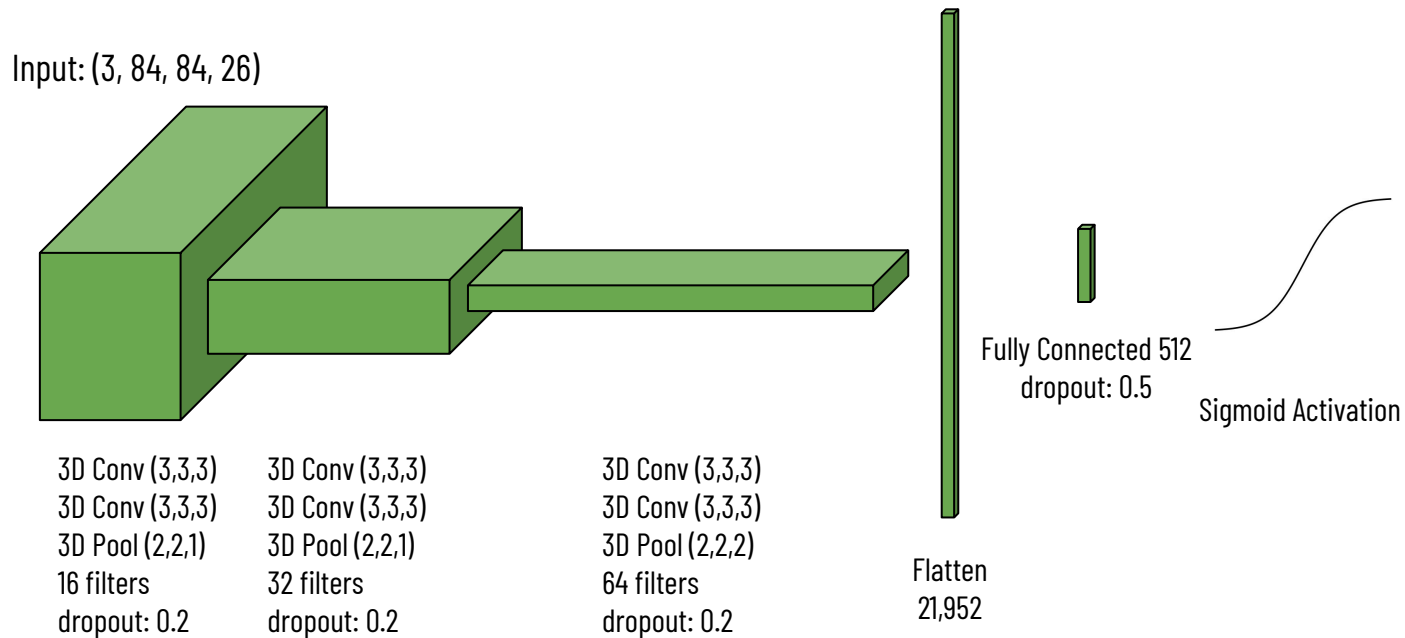




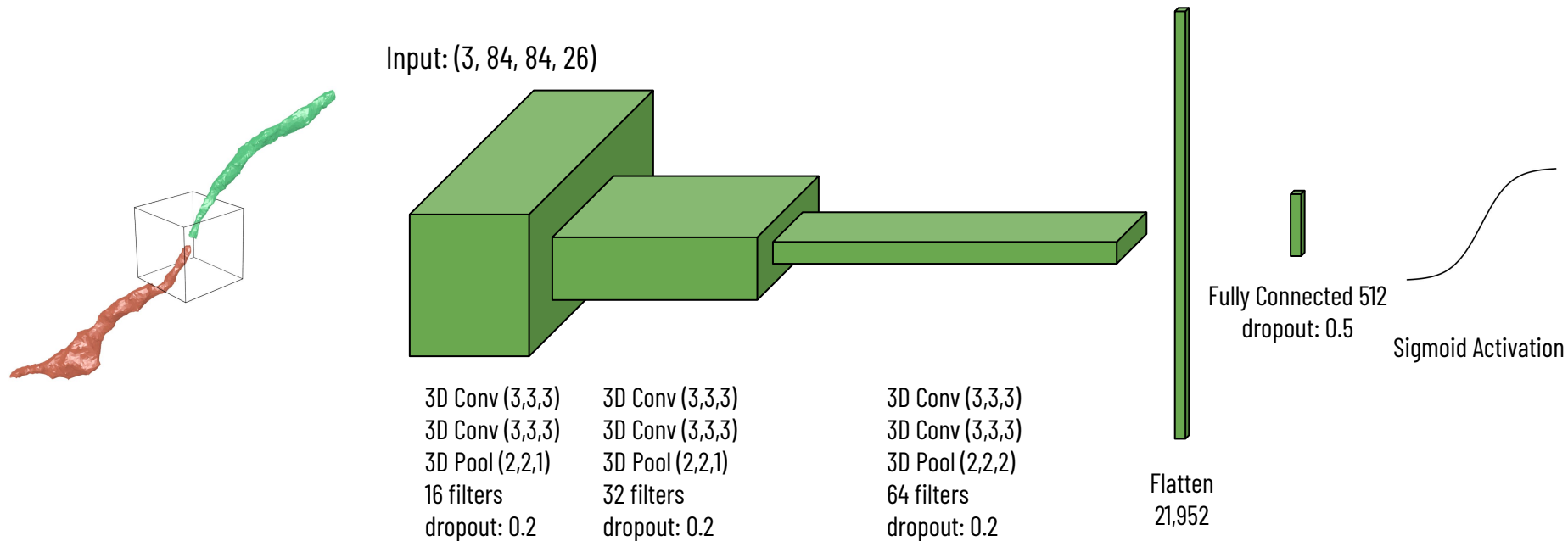
# Learned Constraints



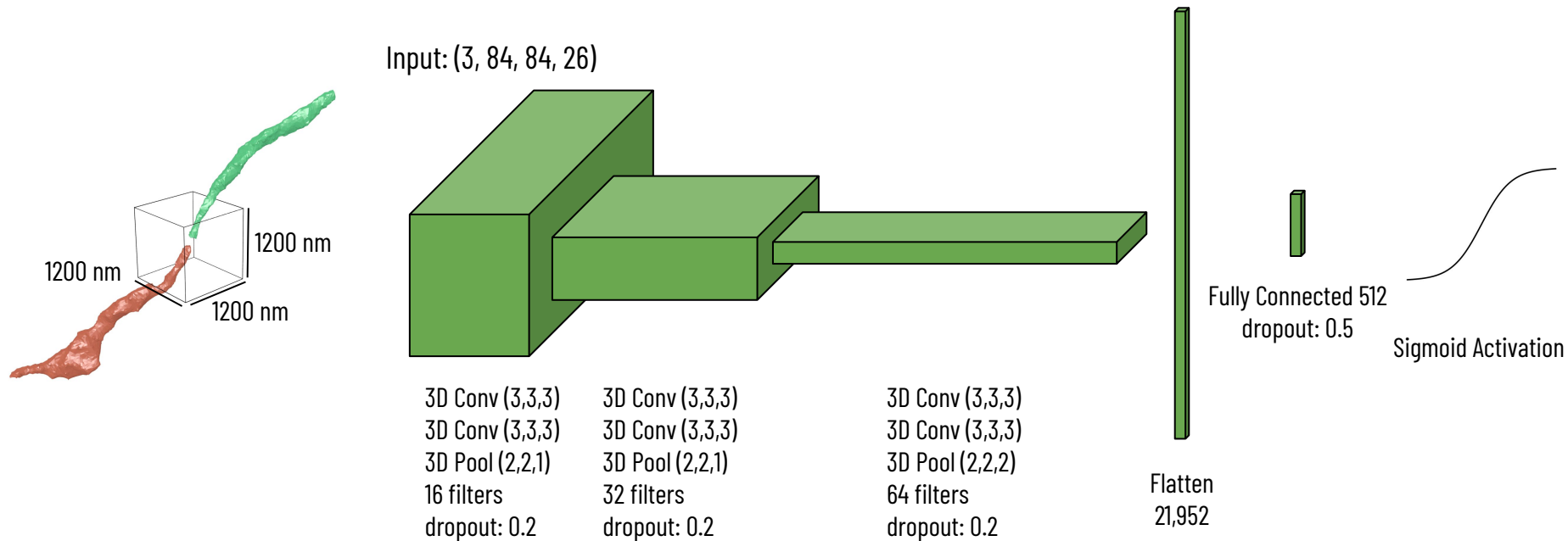
# Architecture and Training Parameters



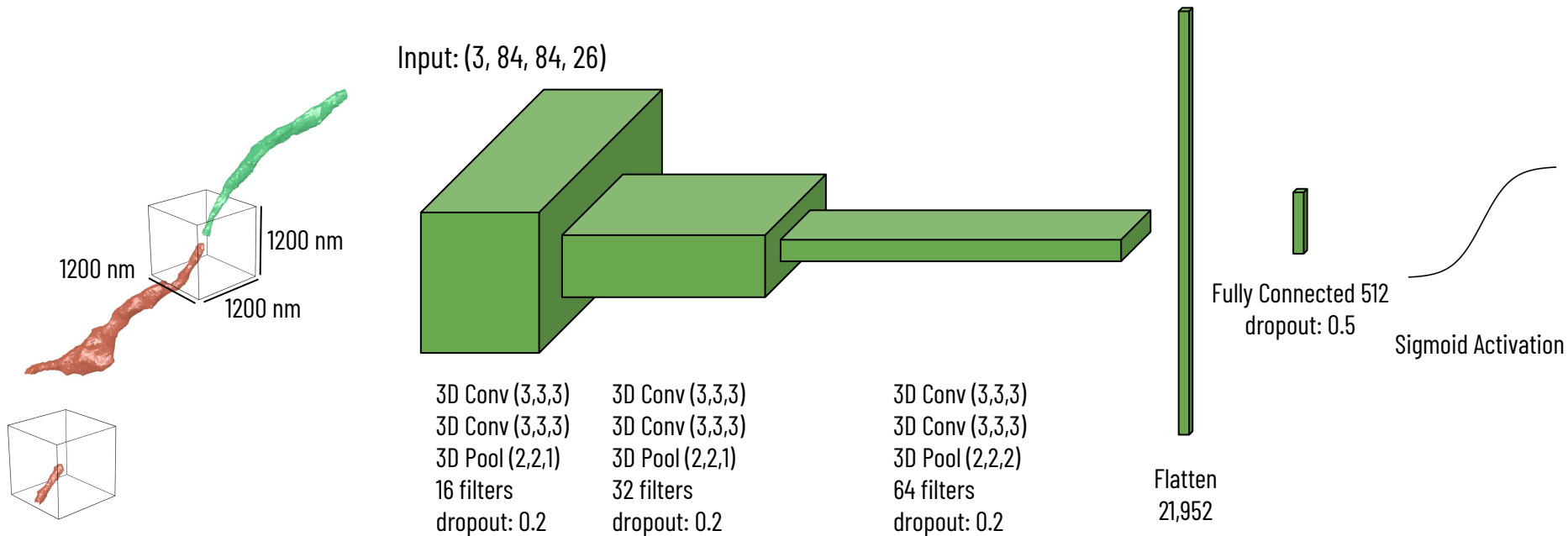
# Architecture and Training Parameters



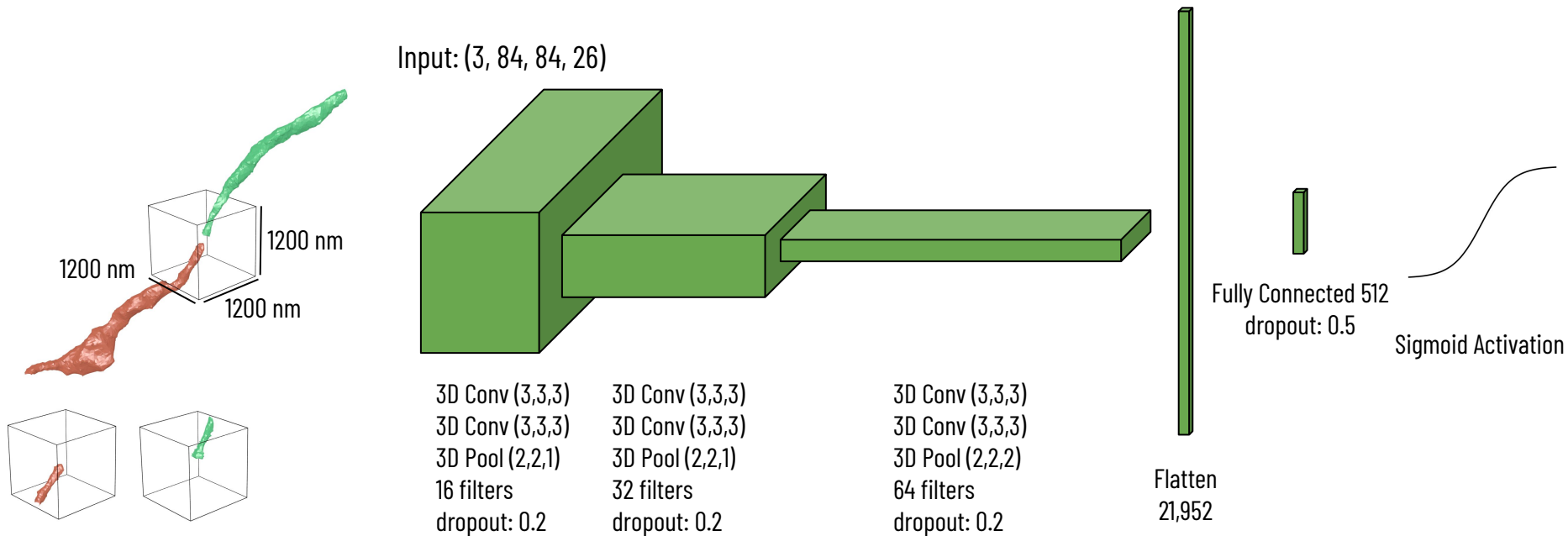
# Architecture and Training Parameters



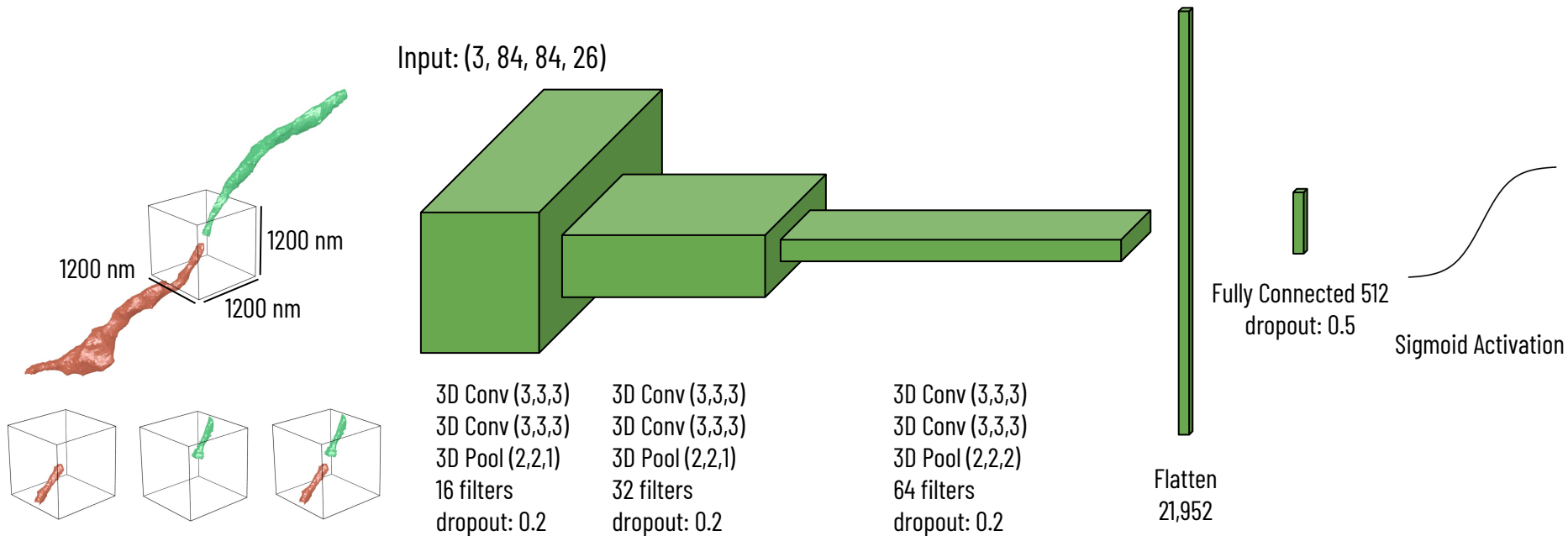
# Architecture and Training Parameters



# Architecture and Training Parameters



# Architecture and Training Parameters



# Parameters

Parameters	Values
Loss Function	Mean Squared Error
Optimizer	SGD with Nesterov Momentum
Momentum	0.9
Initial Learning Rate	0.01
Decay Rate	$5 * 10^{-8}$
Activation	LeakyReLU ( $\alpha = 0.001$ )
Kernel Sizes	$3 \times 3 \times 3$
Filter Sizes	$16 \rightarrow 32 \rightarrow 64$

Table 1: Training parameters.

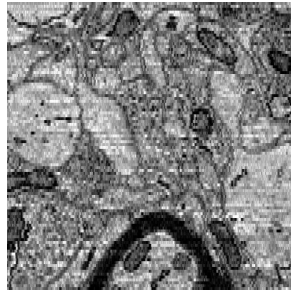
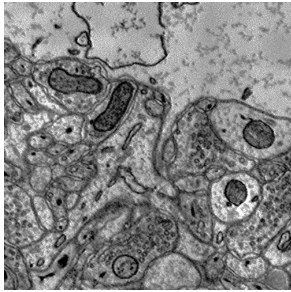


# Architectures

Depth	Input Size	No. Parameters	Output Size	Accuracy	Precision	Recall
3	(3, 18, 52, 52)	1,101,553	(64, 3, 3, 3)	91.30	58.06	92.81
3	(3, 20, 60, 60)	2,313,969	(64, 4, 4, 4)	92.41	61.70	92.41
3	(3, 22, 68, 68)	4,312,817	(64, 5, 5, 5)	92.33	61.49	92.34
3	(3, 24, 76, 76)	7,294,705	(64, 6, 6, 6)	93.51	65.78	93.13
<b>3</b>	<b>(3, 26, 84, 84)</b>	<b>11,456,241</b>	<b>(64, 7, 7, 8)</b>	<b>95.38</b>	<b>74.43</b>	<b>92.34</b>
3	(3, 28, 92, 92)	16,994,033	(64, 8, 7, 8)	91.87	59.70	94.22
3	(3, 30, 100, 100)	24,104,689	(64, 9, 9, 9)	92.01	60.24	93.75
4	(3, 28, 92, 92)	1,404,913	(128, 2, 2, 2)	91.70	60.24	85.94
4	(3, 32, 108, 108)	2,650,097	(128, 3, 3, 3)	92.80	64.28	86.88

**Table 2.** The results of various network architectures trained on the Kasthuri data.

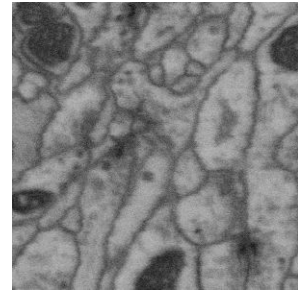
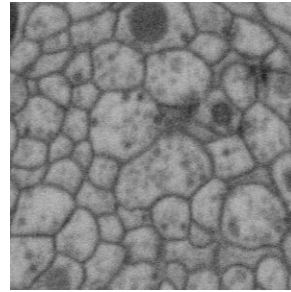
# Independent of Image Data



Kasthuri

*Mouse*

$6 \times 6 \times 30 \text{ nm}^3 / \text{vx}$



FlyEM

*Drosophila melanogaster*

$10 \times 10 \times 10 \text{ nm}^3 / \text{vx}$

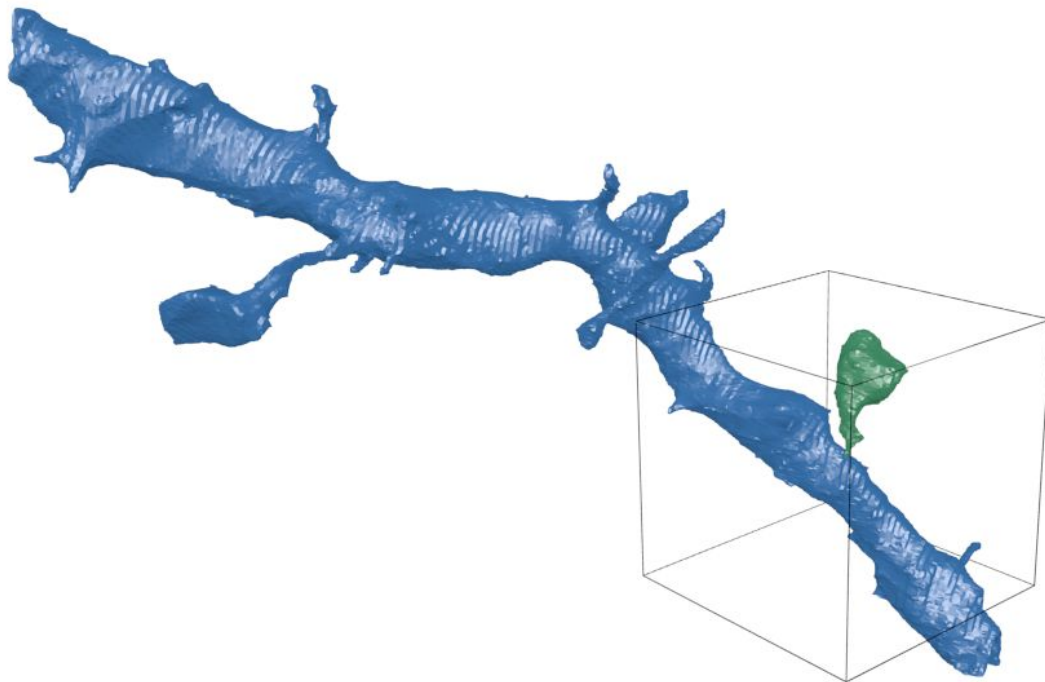
# Regions of Interest

Too small and there is not enough local context



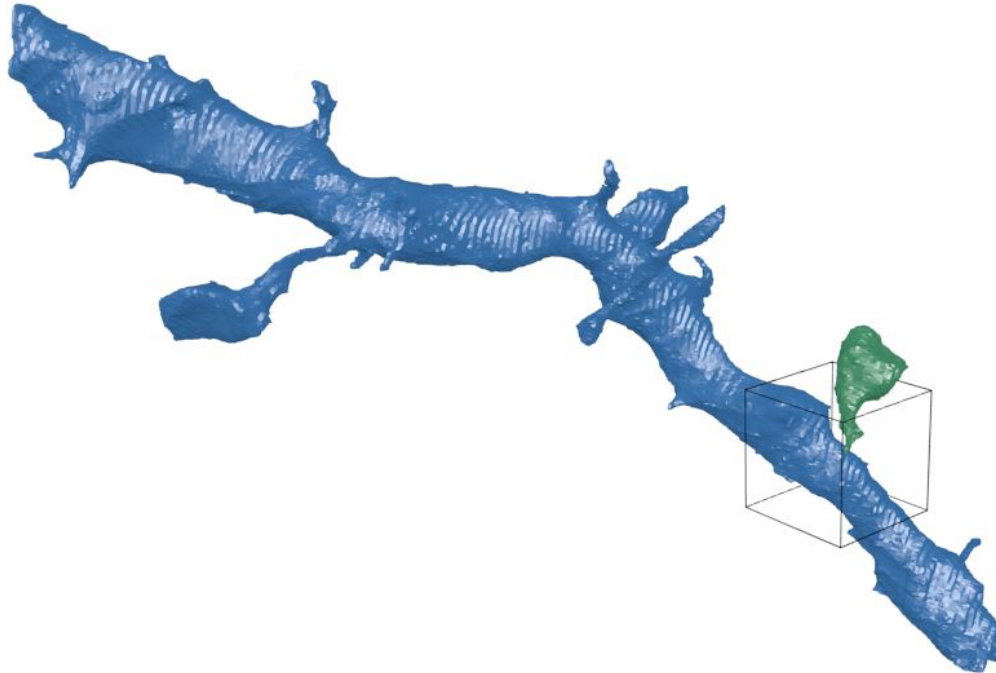
# Regions of Interest

Too large and unnecessary detail inhibits learning



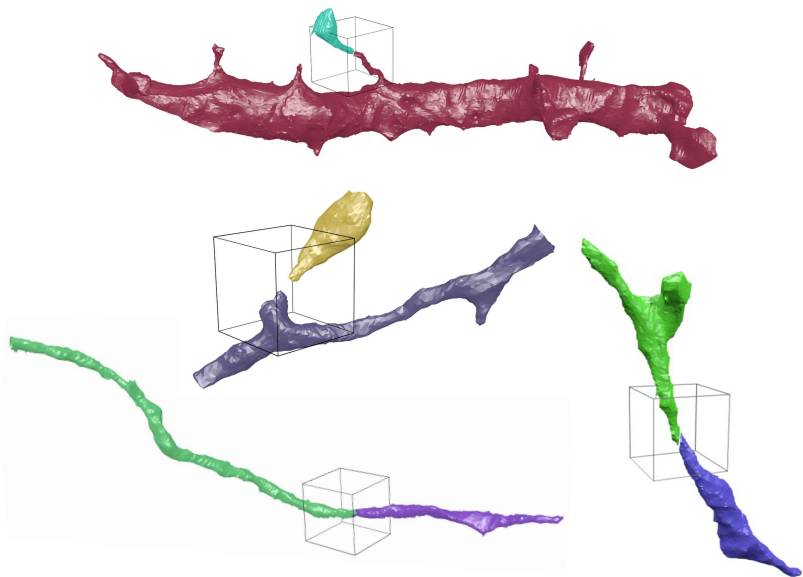
# Regions of Interest

Found that cubes of size  $1200 \times 1200 \times 1200 \text{ nm}^3$  work well



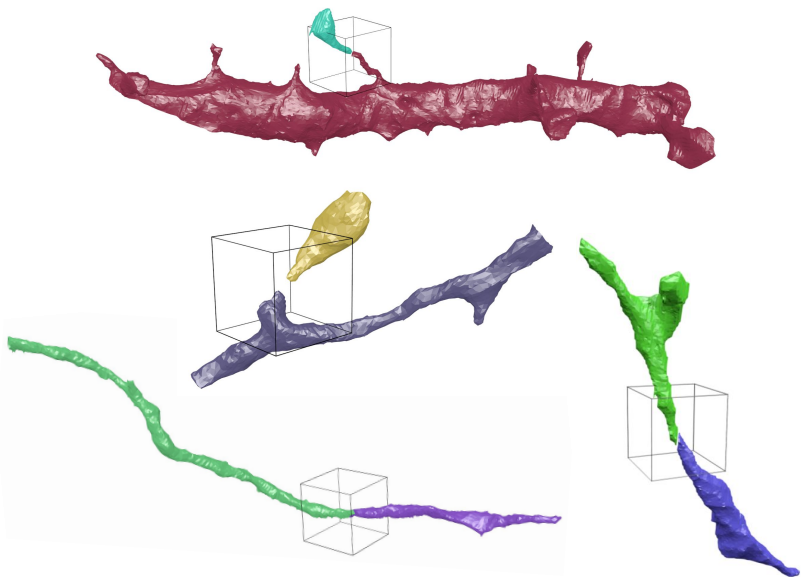
# Input Examples

Should Merge

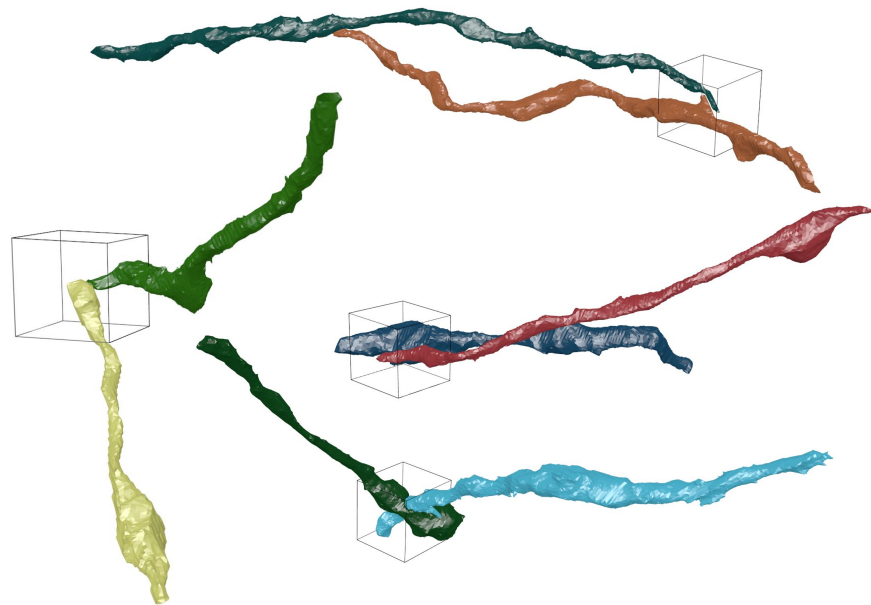


# Input Examples

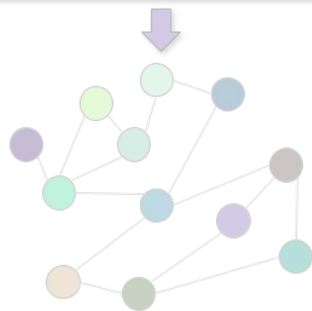
Should Merge



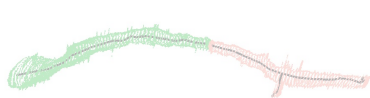
Should Not Merge



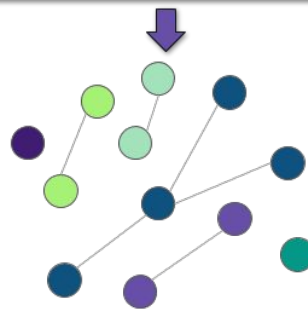
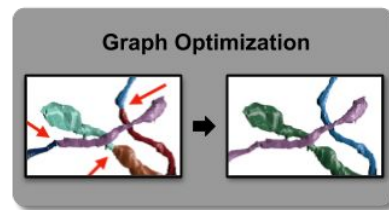
# Goal: Partition the graph into individual neurons



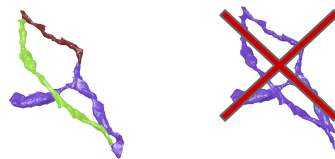
Geometric Priors



Learned Constraints



Topological Restrictions





# Multicut

Reformulate the segmentation problem as a multicut graph partitioning one

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Reformulate the segmentation problem as a multicut graph partitioning one

The final number of segments is not predetermined

# Multicut

Reformulate the segmentation problem as a multicut graph partitioning one

- The final number of segments is not predetermined

- Guarantees a globally consistent solution

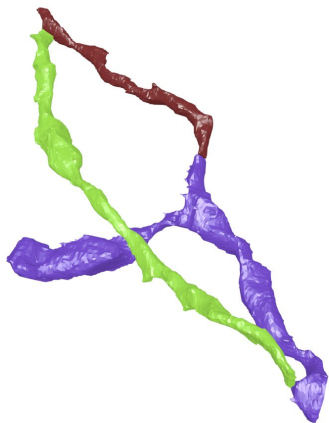
# Multicut

Reformulate the segmentation problem as a multicut graph partitioning one

- The final number of segments is not predetermined

- Guarantees a globally consistent solution

Enforce topological constraints on neurons



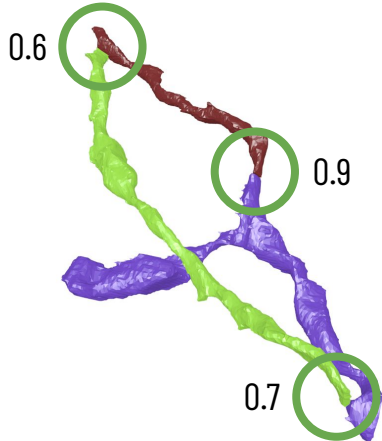
# Multicut

Reformulate the segmentation problem as a multicut graph partitioning one

The final number of segments is not predetermined

Guarantees a globally consistent solution

Enforce topological constraints on neurons



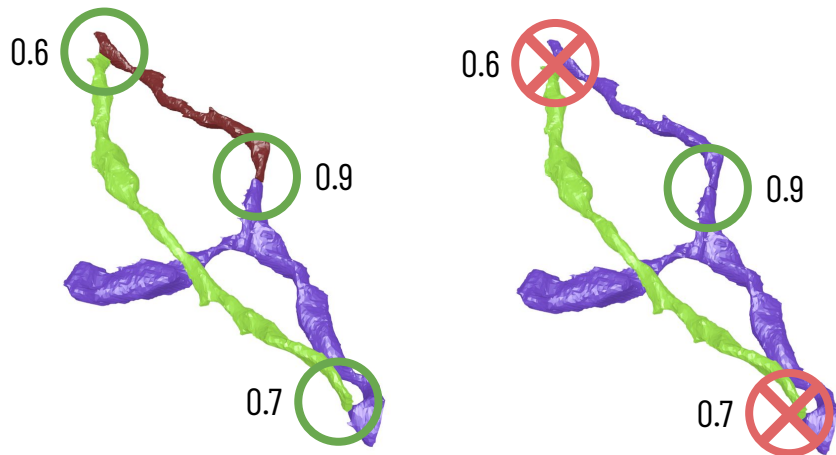
# Multicut

Reformulate the segmentation problem as a multicut graph partitioning one

The final number of segments is not predetermined

Guarantees a globally consistent solution

Enforce topological constraints on neurons



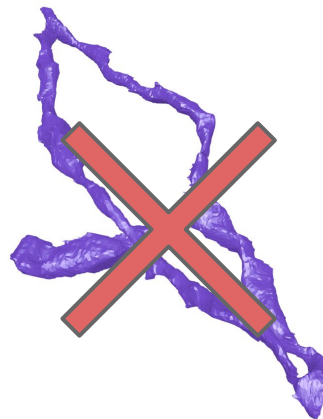
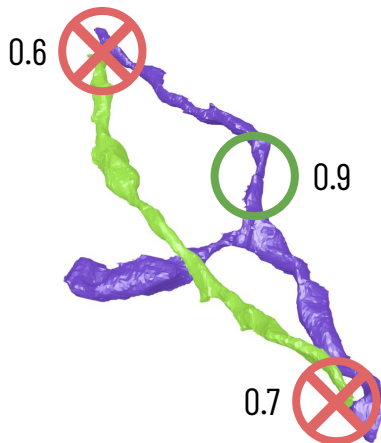
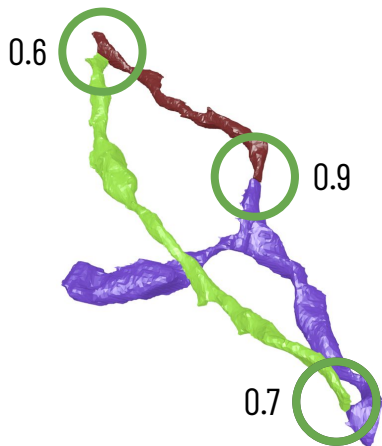
# Multicut

Reformulate the segmentation problem as a multicut graph partitioning one

The final number of segments is not predetermined

Guarantees a globally consistent solution

Enforce topological constraints on neurons



# Multicut

Reformulate the segmentation problem as a multicut graph partitioning one



# Multicut

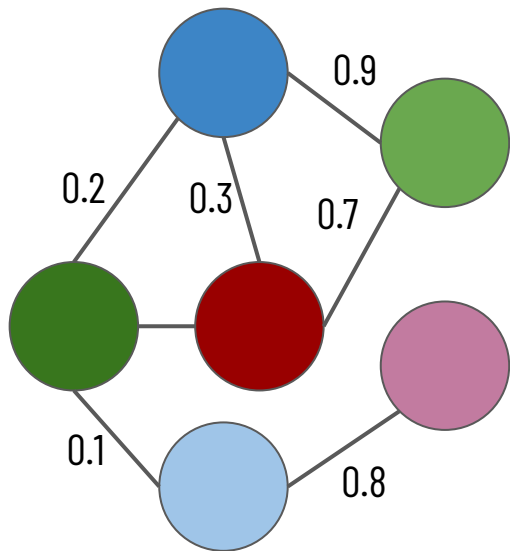
Reformulate the segmentation problem as a multicut graph partitioning one

Guarantees a globally consistent solution

# Multicut

Reformulate the segmentation problem as a multicut graph partitioning one

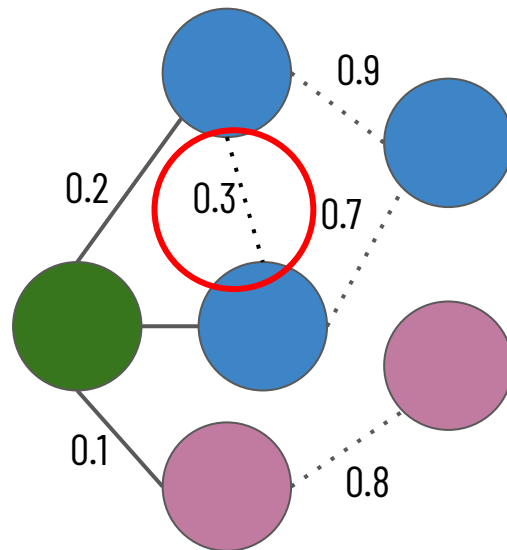
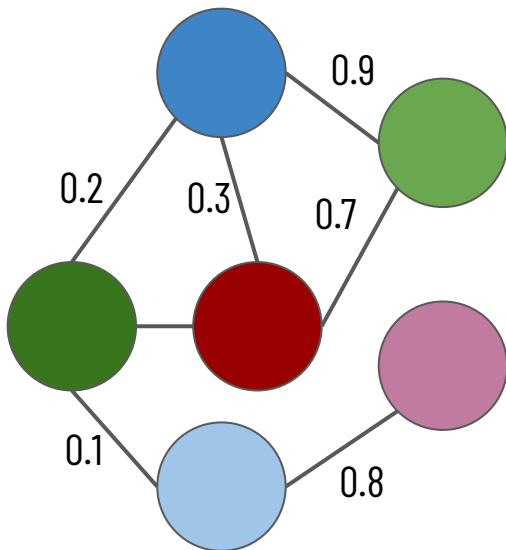
Guarantees a globally consistent solution



# Multicut

Reformulate the segmentation problem as a multicut graph partitioning one

Guarantees a globally consistent solution



# Multicut

Reformulate the segmentation problem as a multicut graph partitioning one

- Guarantees a globally consistent solution

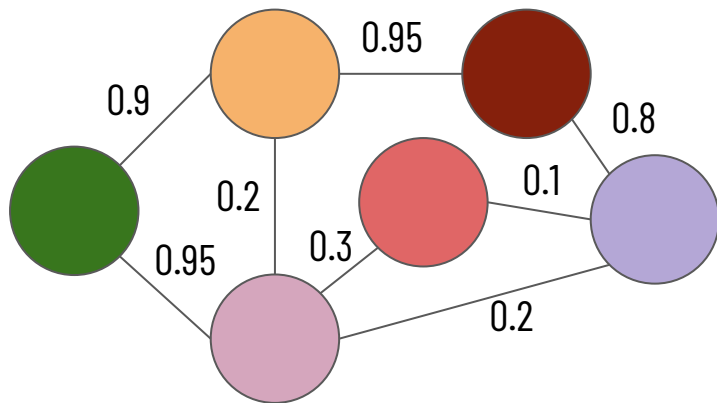
- The final number of segments is not predetermined

# Lifted Multicut Extension

Costs associated with segmenting any pair of nodes

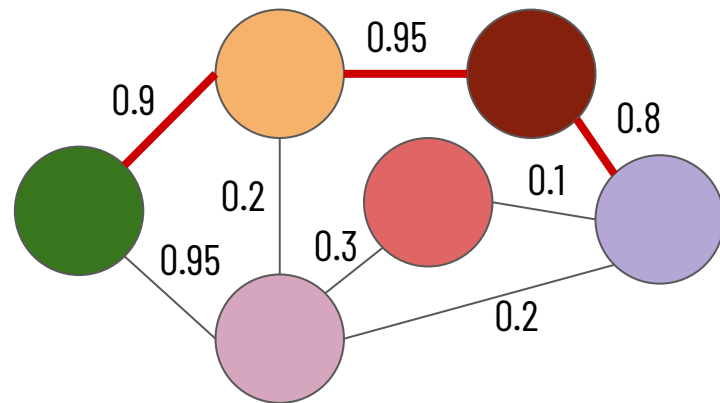
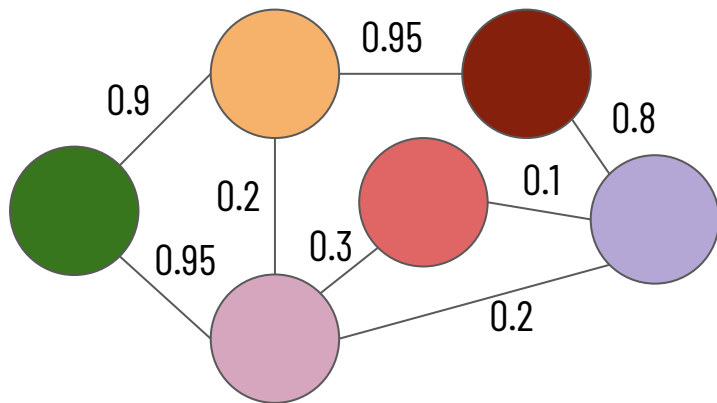
# Lifted Multicut Extension

Costs associated with segmenting any pair of nodes



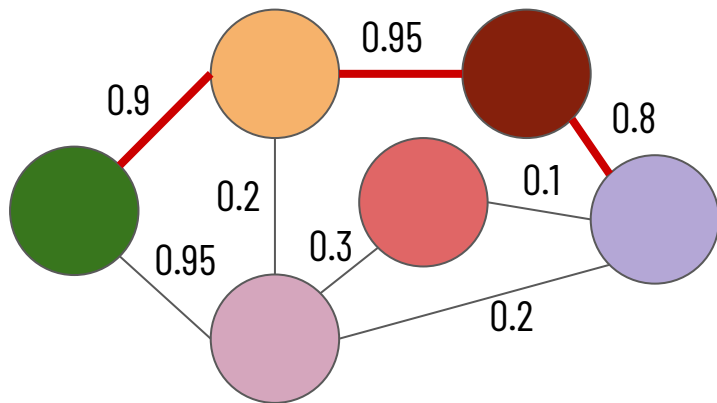
# Lifted Multicut Extension

Costs associated with segmenting any pair of nodes


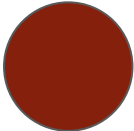

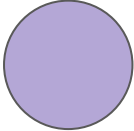
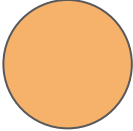
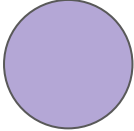


# Lifted Multicut Extension

Costs associated with segmenting any pair of nodes



Penalties

		0.855
		0.684
		0.760

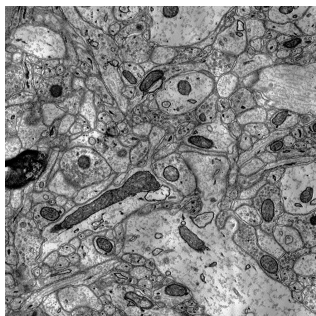


# Results

# Datasets

## Training Data

---



Kasthuri Vol. 1

*Mouse*

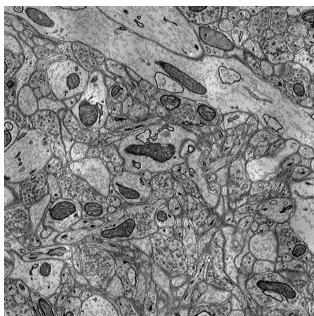
$6 \times 6 \times 30 \text{ nm}^3 / \text{vx}$

$1335 \times 1809 \times 338 \text{ vx}$

$8.01 \times 10.85 \times 10.14 \text{ }\mu\text{m}^3$

## Testing Data

---



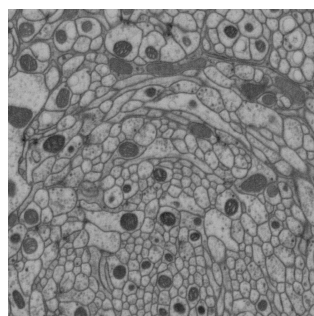
Kasthuri Vol. 2

*Mouse*

$6 \times 6 \times 30 \text{ nm}^3 / \text{vx}$

$1336 \times 1809 \times 338 \text{ vx}$

$8.02 \times 10.85 \times 10.14 \text{ }\mu\text{m}^3$



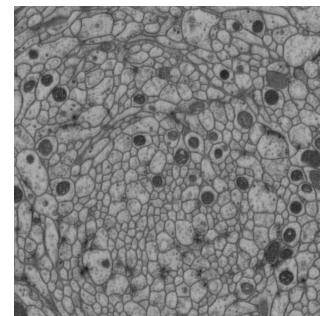
FlyEM Vol. 1

*Drosophila melanogaster*

$10 \times 10 \times 10 \text{ nm}^3 / \text{vx}$

$999 \times 999 \times 998 \text{ vx}$

$9.99 \times 9.99 \times 9.98 \text{ }\mu\text{m}^3$



FlyEM Vol. 2

*Drosophila melanogaster*

$10 \times 10 \times 10 \text{ nm}^3 / \text{vx}$

$999 \times 999 \times 999 \text{ vx}$

$9.99 \times 9.99 \times 9.99 \text{ }\mu\text{m}^3$

# Split Variation of Information

Measure of entropy between segmentation and ground truth

# Split Variation of Information

Measure of entropy between segmentation and ground truth

VI Split: Increases if two voxels from the same neuron have different labels



# Split Variation of Information

Measure of entropy between segmentation and ground truth

VI Split: Increases if two voxels from the same neuron have different labels



VI Merge: Increases if two voxels from different neurons have the same label



# Split Variation of Information

Measure of entropy between segmentation and ground truth

VI Split: Increases if two voxels from the same neuron have different labels

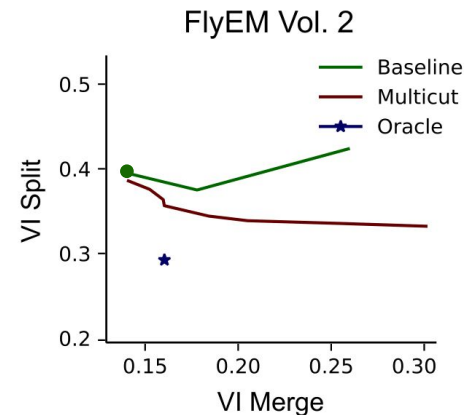
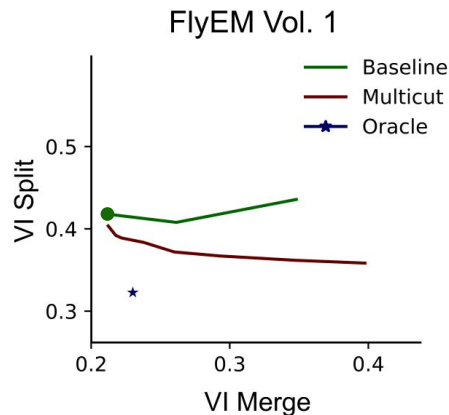
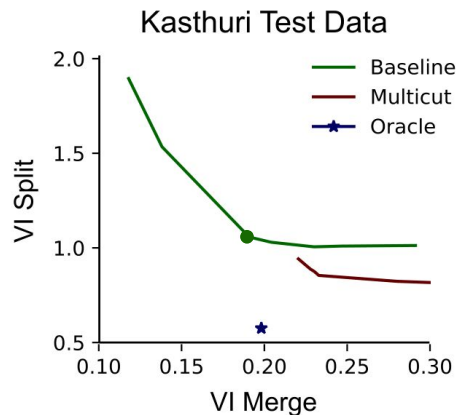


VI Merge: Increases if two voxels from different neurons have the same label



Total Variation of Information = VI Split + VI Merge

# Variation of Information

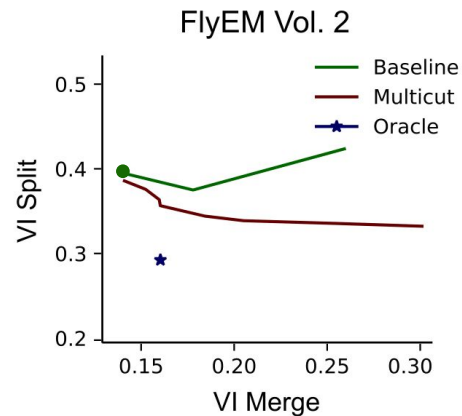
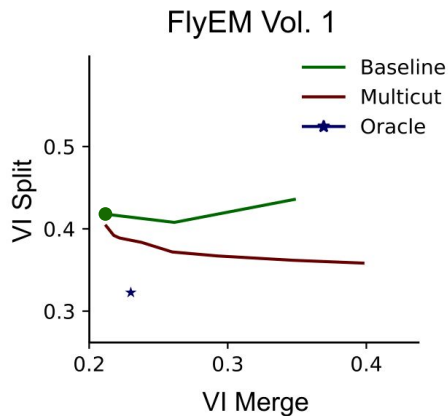
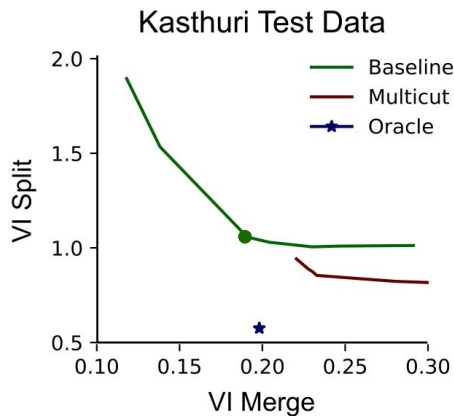


Baseline curve is generated by varying an agglomeration parameter in the Neuroproof algorithm

Green dot represents the input segmentation

Oracle correctly partitions the graph that we extract from the input segmentation

# Variation of Information



Total VI Improvement:

10.4%

8.9%

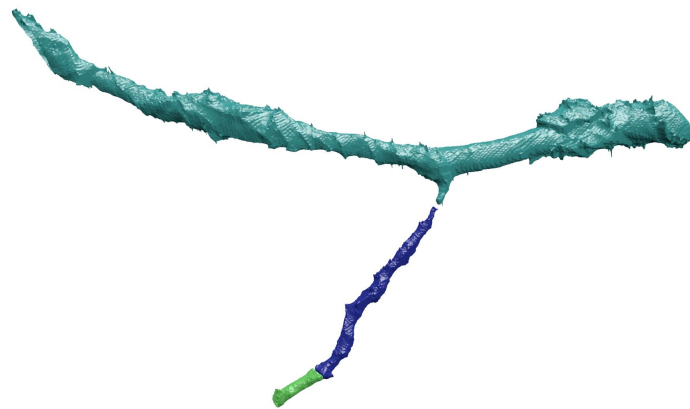
5.4%



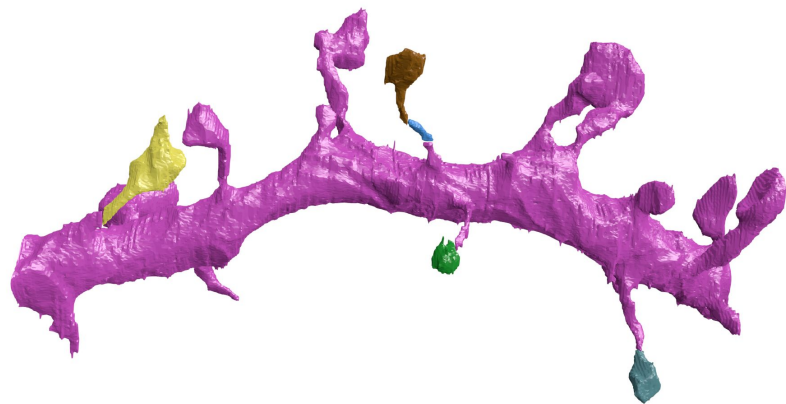
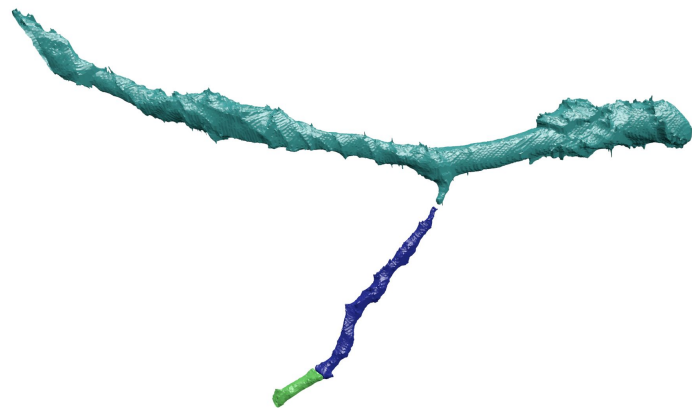
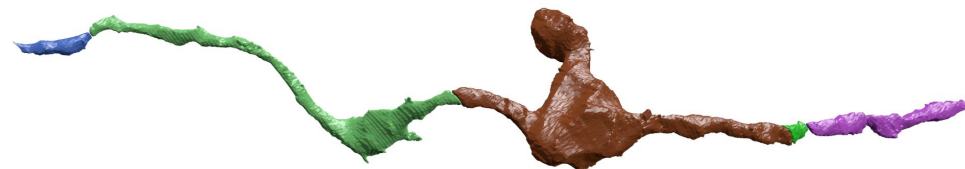
# Qualitative Results



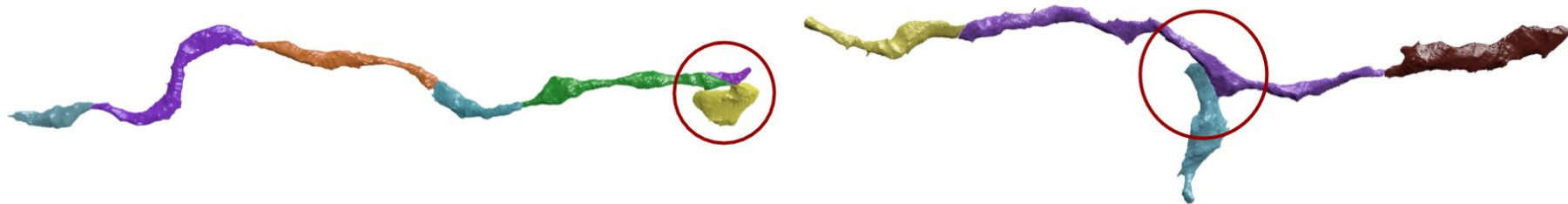
## Qualitative Results



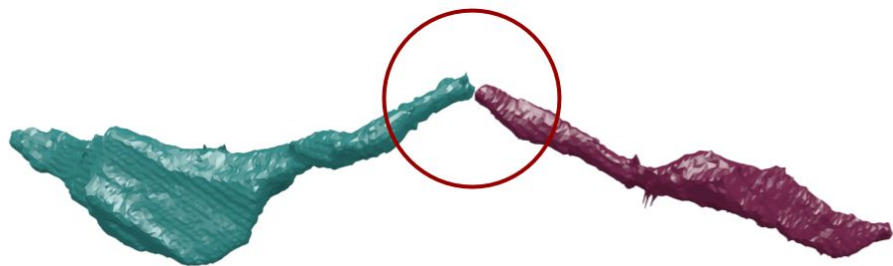
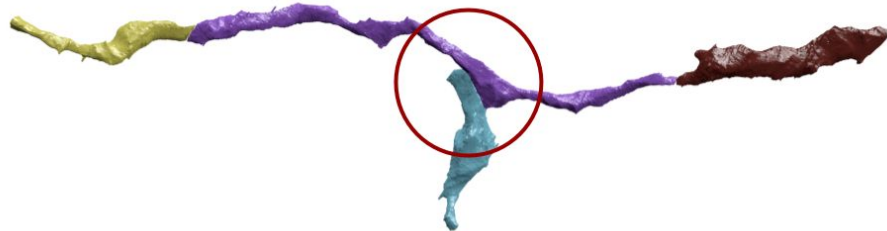
## Qualitative Results



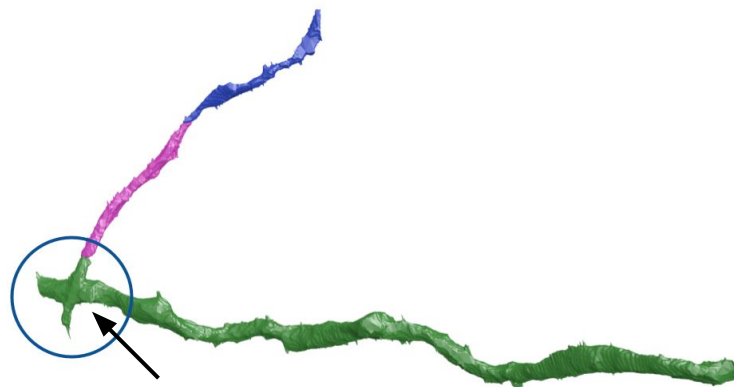
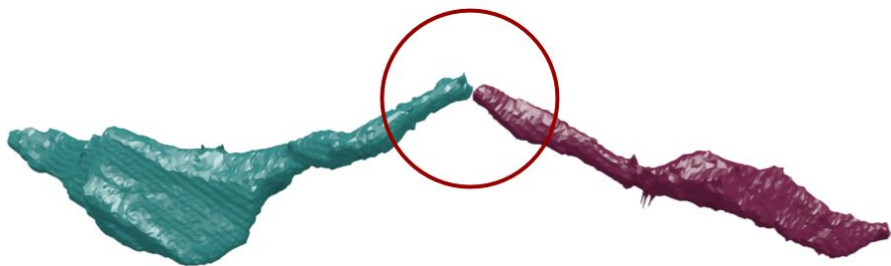
# Failure Cases



# Failure Cases

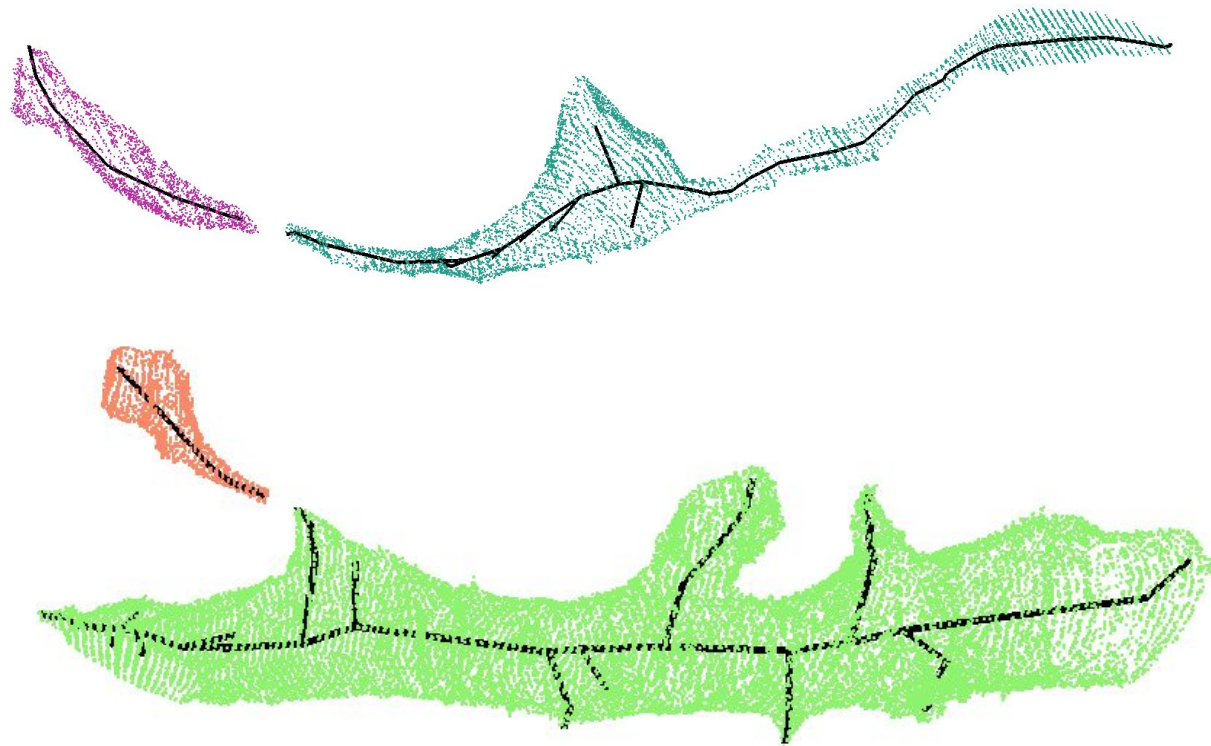


# Failure Cases

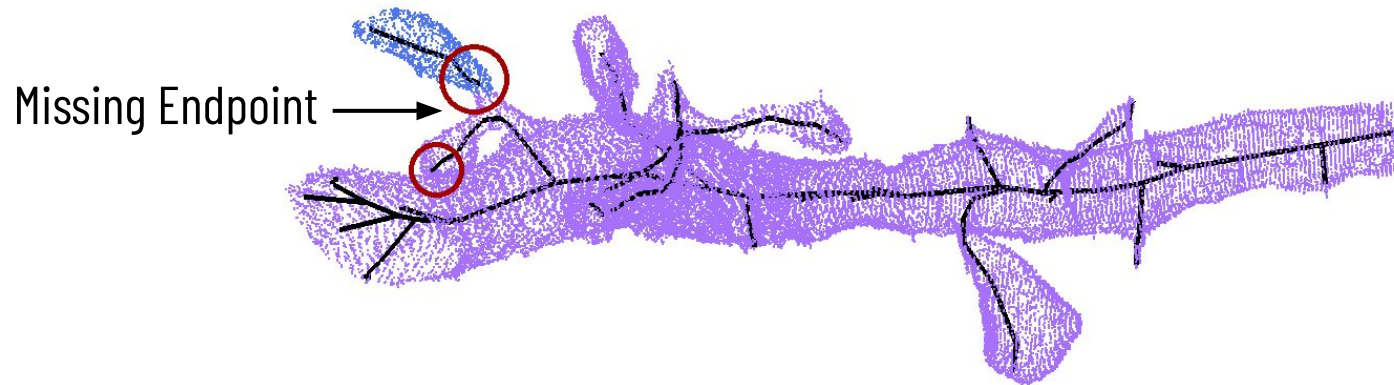
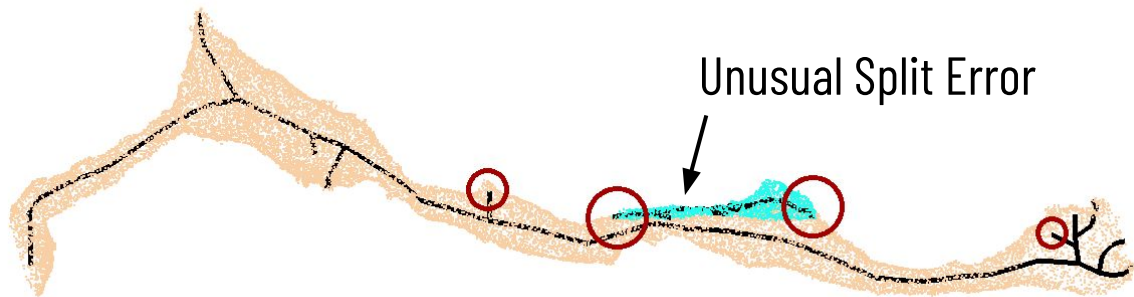


Error in Input Segmentation

# Graph Pruning



# Failure Cases



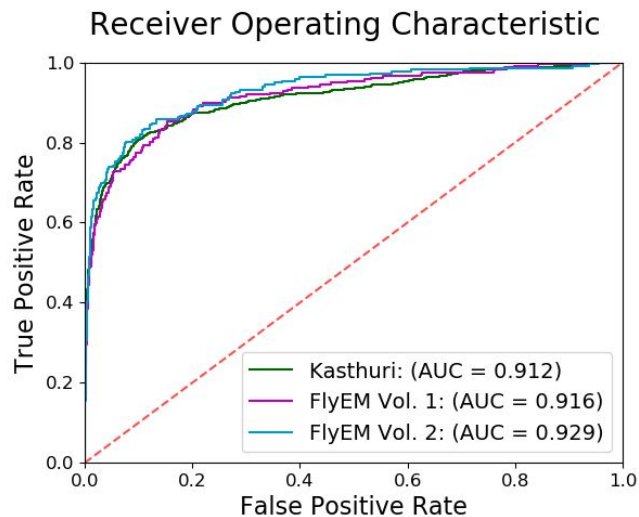


# Graph Extraction Results

Table 1: The results of our graph pruning approach compared to the baseline graph with all adjacent regions. We show the number of true merge locations (e.g., 974) compared to total number of edges in the graph (e.g., 25,798) for each case. The number of missed splits corresponds to the number of split errors that our method misses compared to an adjacency matrix.

<b>Dataset</b>	<b>Segment Adjacency</b>	<b>Skeleton Pruning</b>	<b>Missed Splits</b>	<b>Gained Edges</b>
Kasthuri	974 / 25,798	764 / 6,218	307	97
FlyEM Vol. 1	304 / 15,949	212 / 4,578	105	13
FlyEM Vol. 2	298 / 17,614	197 / 4,366	120	19

# CNN Results



Accuracies:

Kasthuri	90.4%
FlyEM Vol. 1	94.4%
FlyEM Vol. 2	95.2%

# Multicut Results

Table 2: Precision, recall, and accuracy changes between CNN only and CNN paired with graph-optimized reconstructions for the training and three test datasets. The combined method results in better precision and accuracy. The lifted multicut extension provides very slight improvements in recall and accuracy over these three datasets.

<b>Dataset</b>	<b>Multicut</b>			<b>Lifted Multicut</b>		
	$\Delta$ Precision	$\Delta$ Recall	$\Delta$ Accuracy	$\Delta$ Precision	$\Delta$ Recall	$\Delta$ Accuracy
Kasthuri	31.94%	-36.24%	0.71%	-1.01%	0.60%	0.02%
FlyEM Vol. 1	40.87%	-42.37%	1.26%	0.35%	0.85%	0.04%
FlyEM Vol. 2	27.80%	-44.95%	0.33%	0.54%	0.92%	0.04%

# Running Times

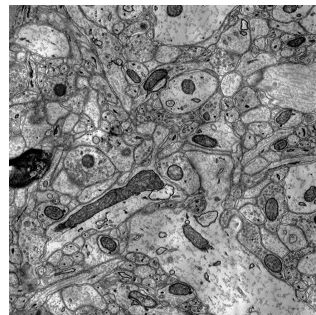
Skeletonization: 0.56 seconds per segment on average

Graph Extraction: 31 seconds

CNN Inference: 124 seconds

Multicut: 37 seconds

**~45 minutes**



Kasthuri Vol. 1

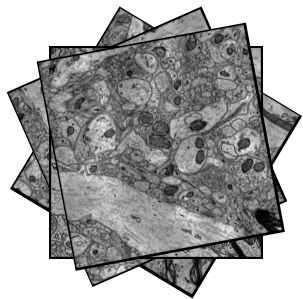
*Mouse*

$6 \times 6 \times 30 \text{ nm}^3 / \text{vx}$

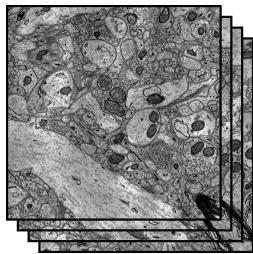
$1335 \times 1809 \times 338$

$8.01\mu\text{m} \times 10.85\mu\text{m} \times 10.14\mu\text{m}$

# Connectomics Pipeline

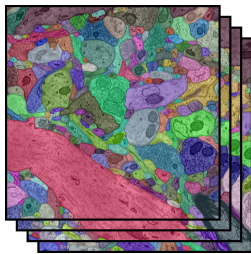


Acquisition

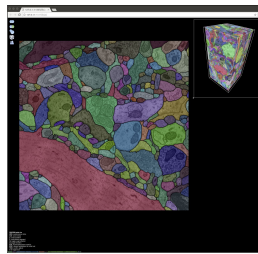


Registration

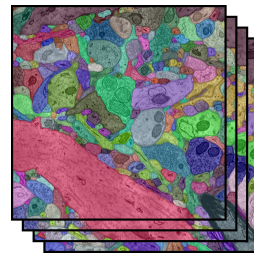
## Compression



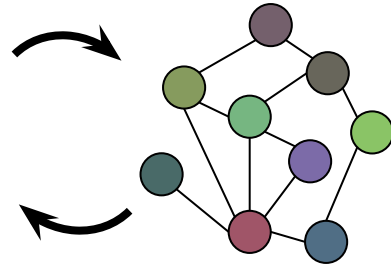
Segmentation



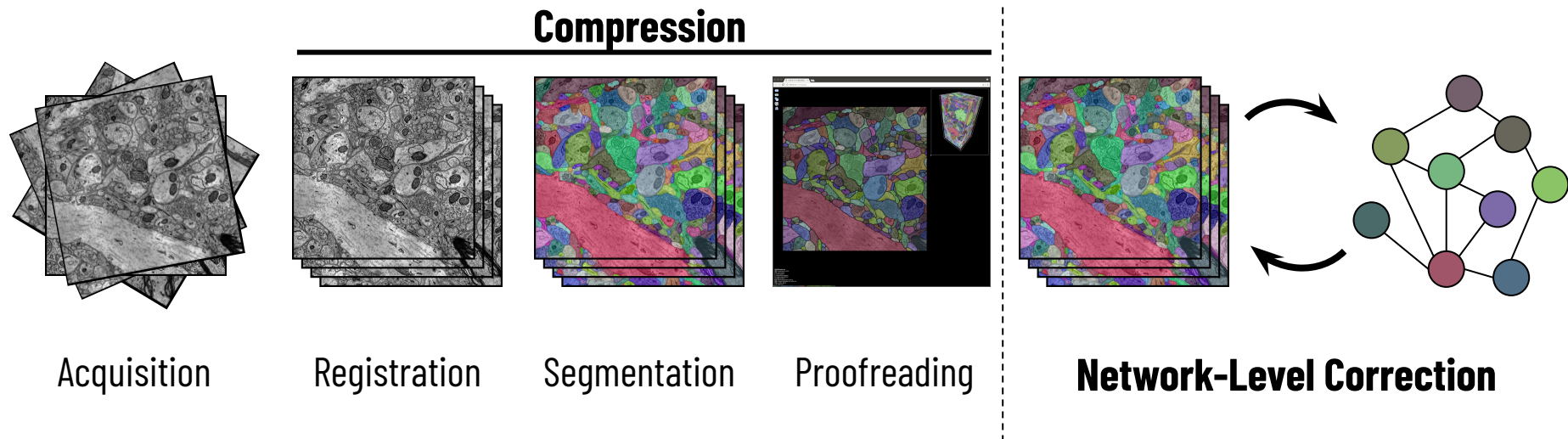
Proofreading



**Network-Level Correction**

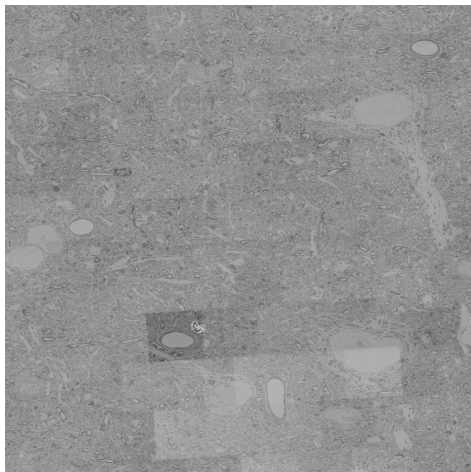


# Connectomics Pipeline



# Compression Future Work

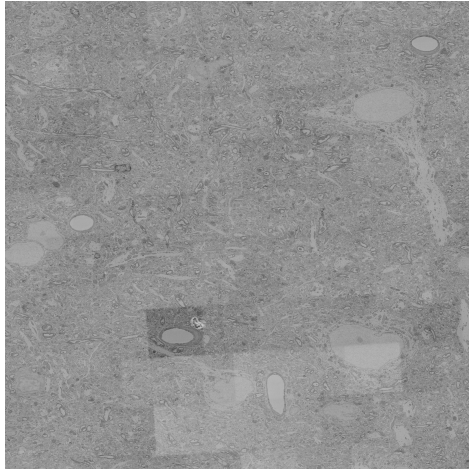
Specialized compression techniques for raw images (currently use JPEG 2000)



# Compression Future Work

Specialized compression techniques for raw images (currently use JPEG 2000)

Use convolutional neural networks to improve compression of images



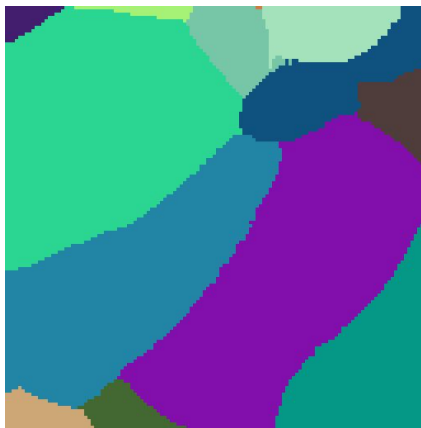
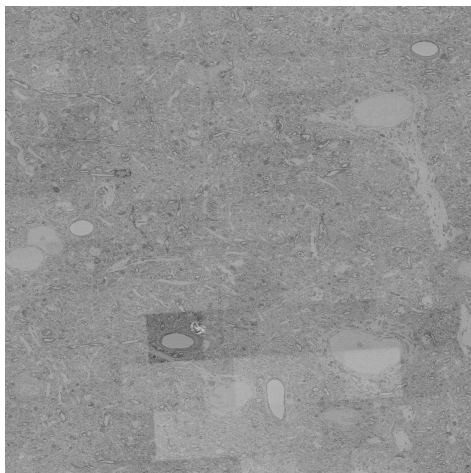


# Compression Future Work

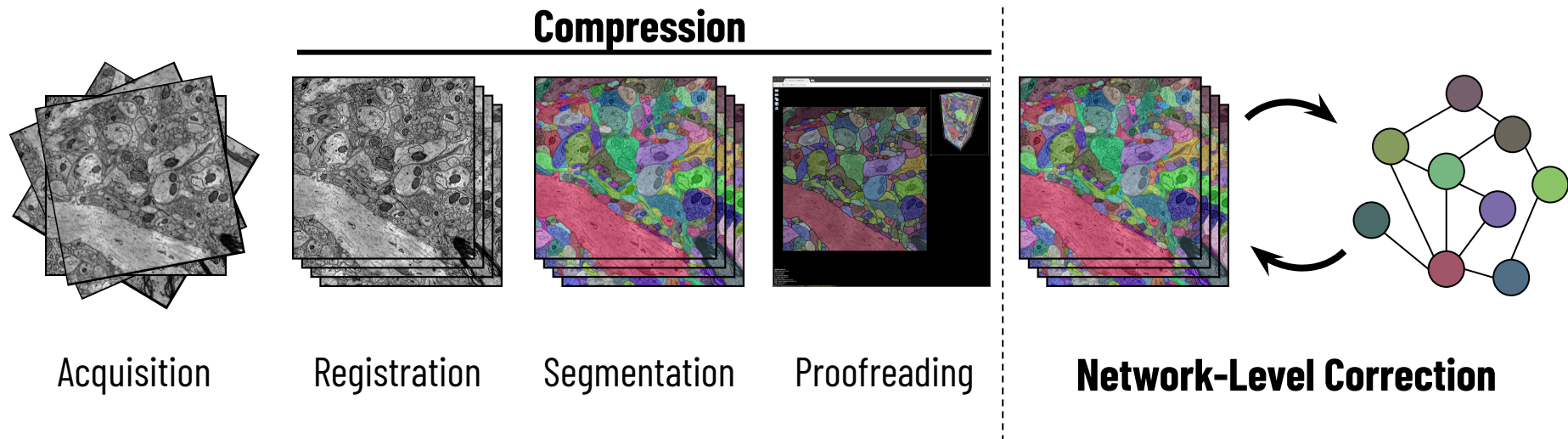
Specialized compression techniques for raw images (currently use JPEG 2000)

Use convolutional neural networks to improve compression of images

Add random access to Compresso for smoother real-time visual analysis of large datasets

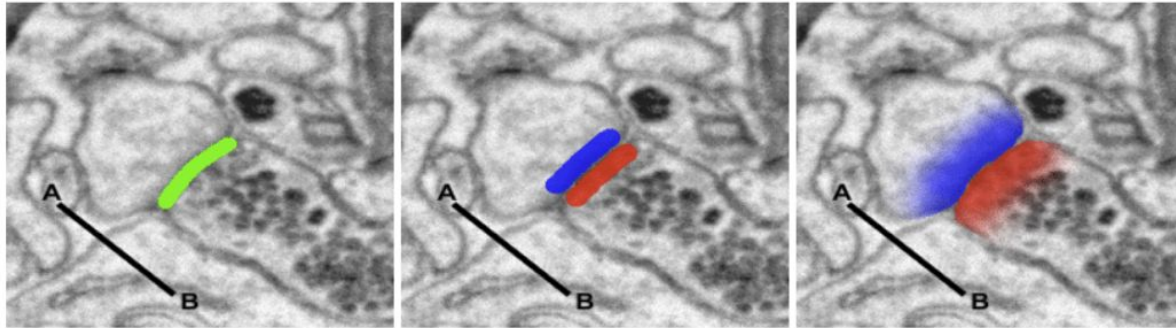


# Connectomics Pipeline



# Additional Biological-Constraints

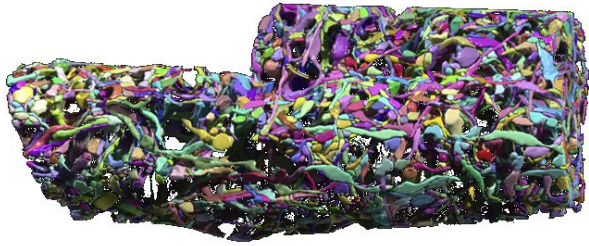
Use synaptic information to prevent dendrites and axons from merging



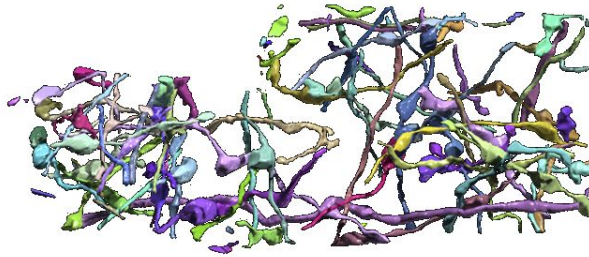
# Additional Biological-Constraints

Use synaptic information to prevent dendrites and axons from merging

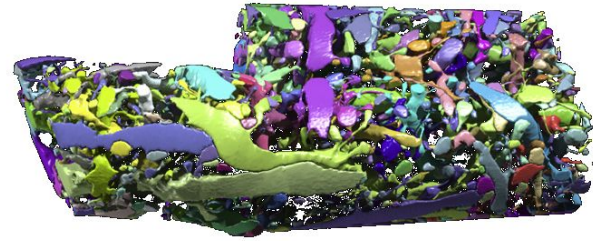
Classify neuron types to prevent inhibitory and excitatory neurons from merging



Excitatory Axons



Inhibitory Axons



Dendrites

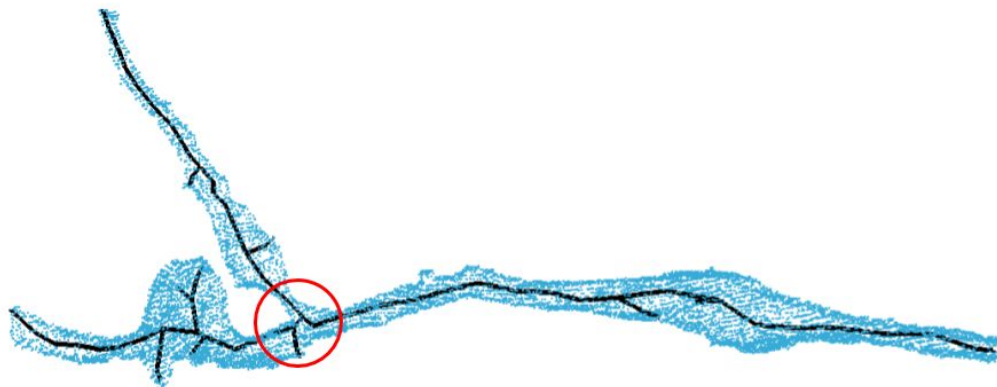
# Address Merge Errors

Currently difficult because the number of potential split candidates grows quickly

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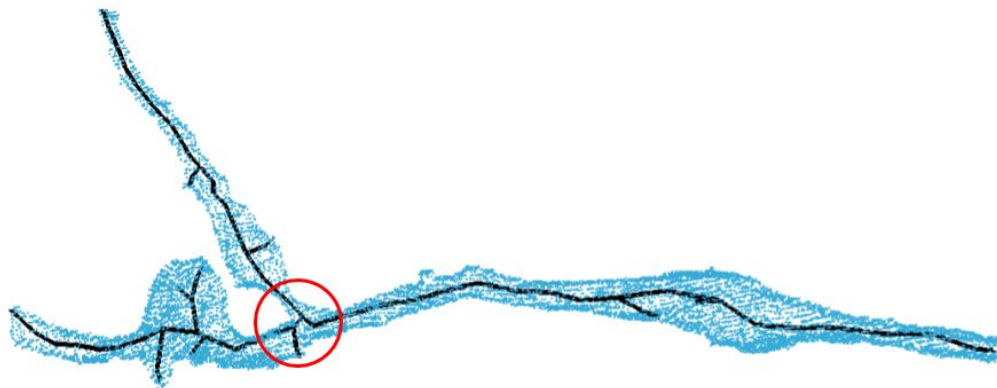


# Address Merge Errors

Currently difficult because the number of potential split candidates grows quickly

Use skeletons to quickly locate potential merge errors

Divide segments with a watershed algorithm and use existing CNN



Thank you!



Questions?