Breakout Session 7: Track A

Developing Computational Tools to Analyze the Structure of Nerve Cells in the Bowel to Better Understand Digestive Disease

Dr. David Linden

Associate Professor of Physiology, Mayo Clinic

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Neurobiology of Intrinsic Afferent Neurons

Developing computational tools to analyze the structure of nerve cells in the bowel to better understand digestive disease

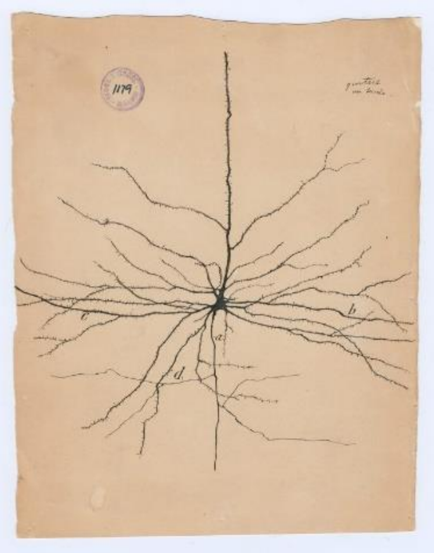
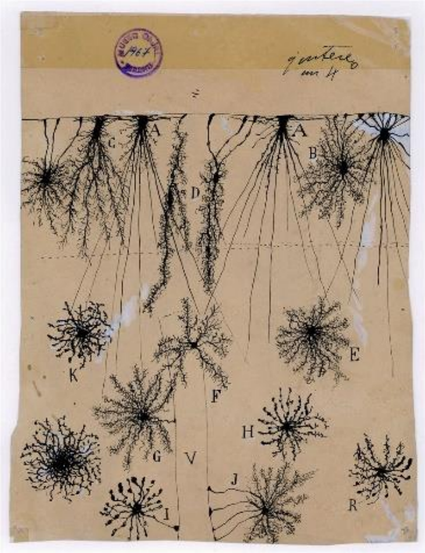
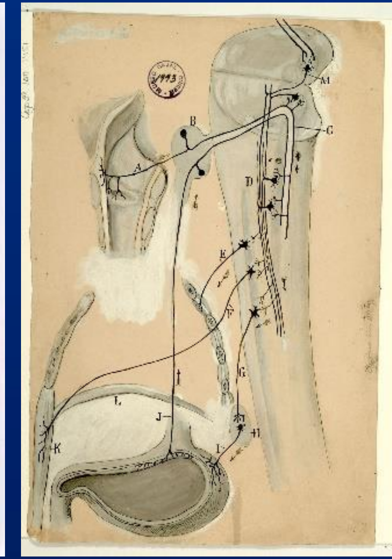
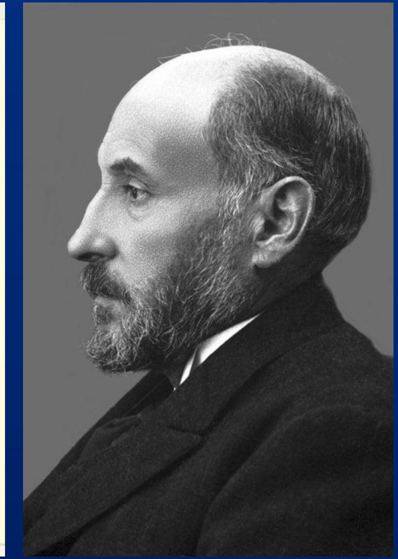
5R01DK129315-03

ENSP

David R. Linden

2024 NIH ODSS AI Supplement Program Virtual PI Meeting, March 28, 2024

Structure-Function in Neuroscience

Images Courtesy of the Cajal Institute, Spanish National Research Council and the Nobel Prize Museum, Stockholm

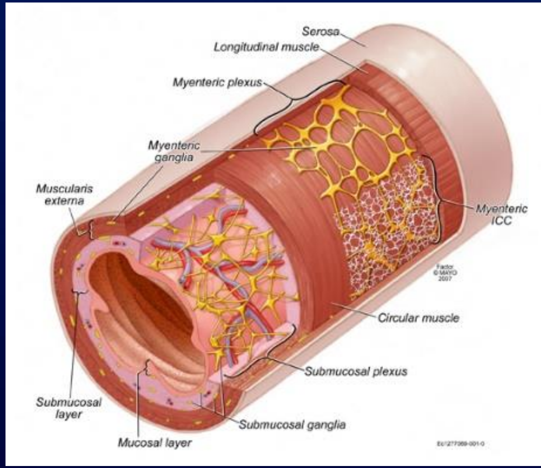
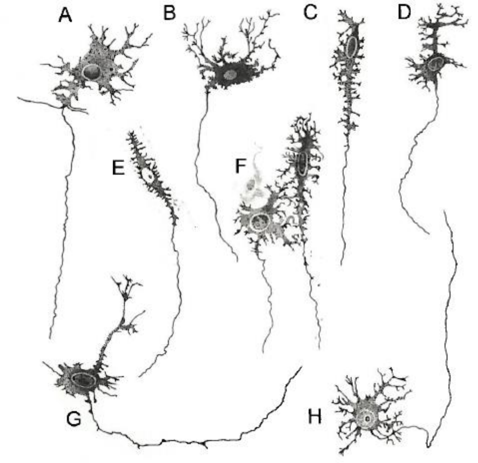
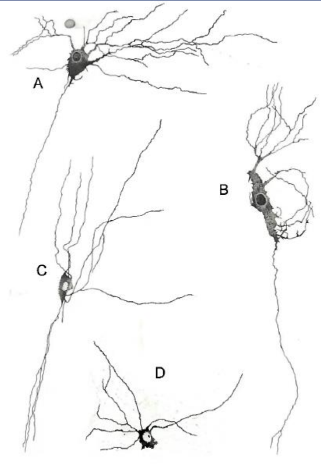
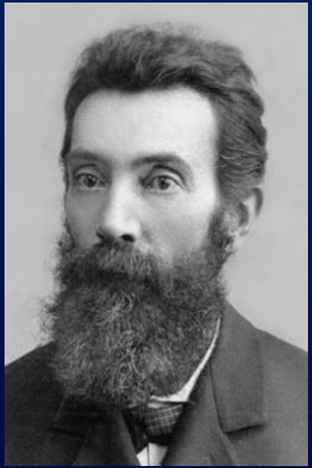


Figure From: Linden and Farrugia In: *Disorders of the Autonomic Nervous System 3rd Ed.*

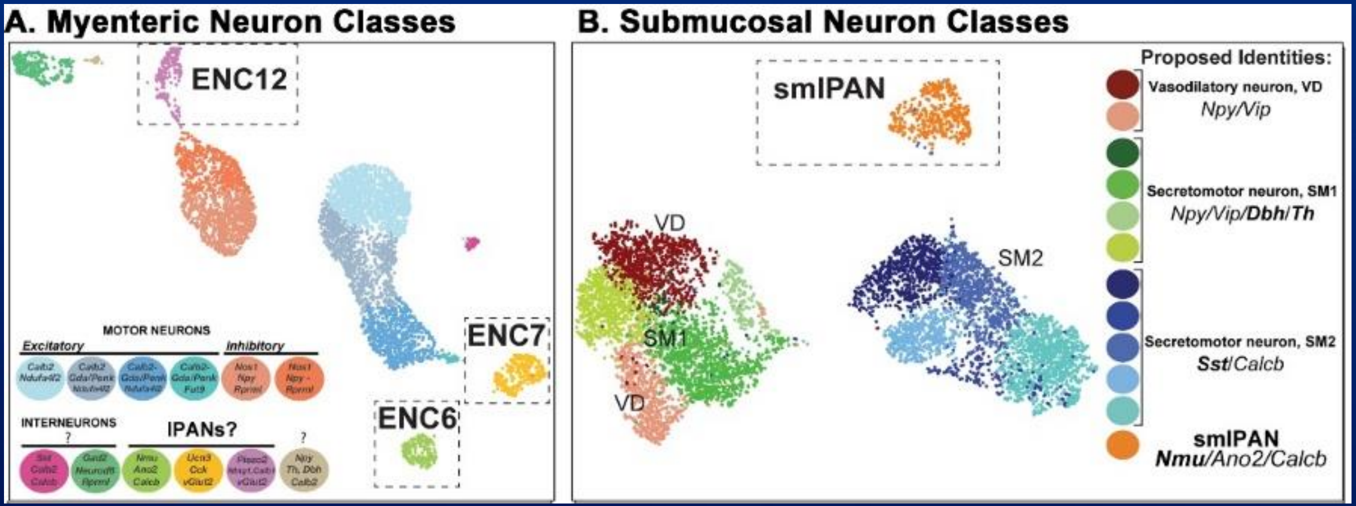




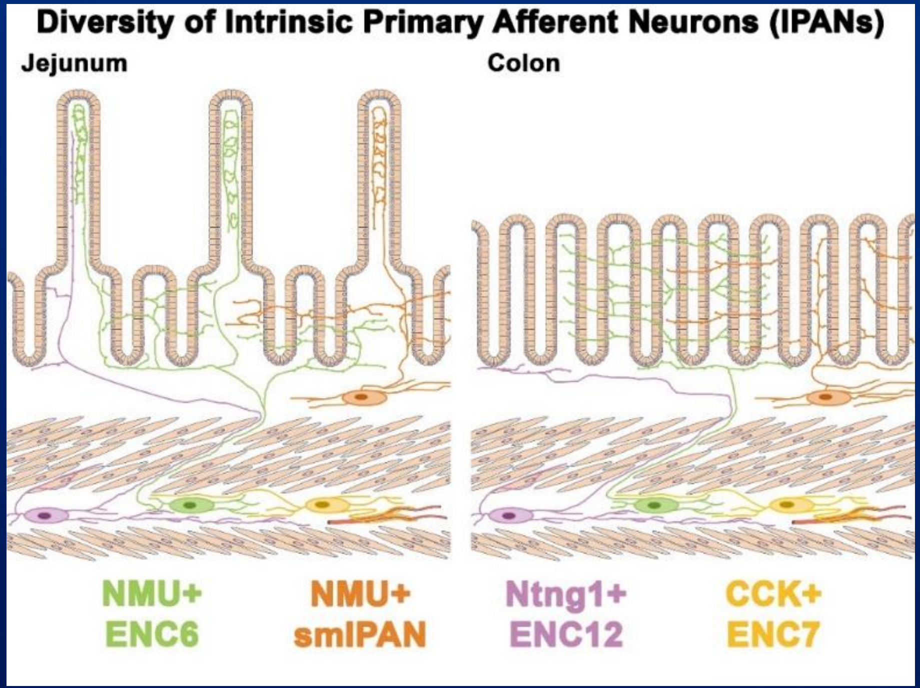


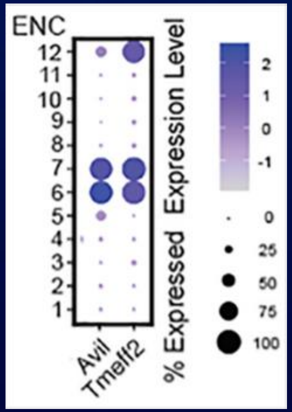
Images from Dogiel, 1899 Republished in Furness, 2004, *The Enteric Nervous System* and Courtesy of Tomsk State University

Single Cell Enteric Neuron Analysis



Morarach et al., 2021 *Nat. Neurosci.* **24**:34-46
Melo et al., 2020 *Neurogastroenterol Motil* **32**:e13989





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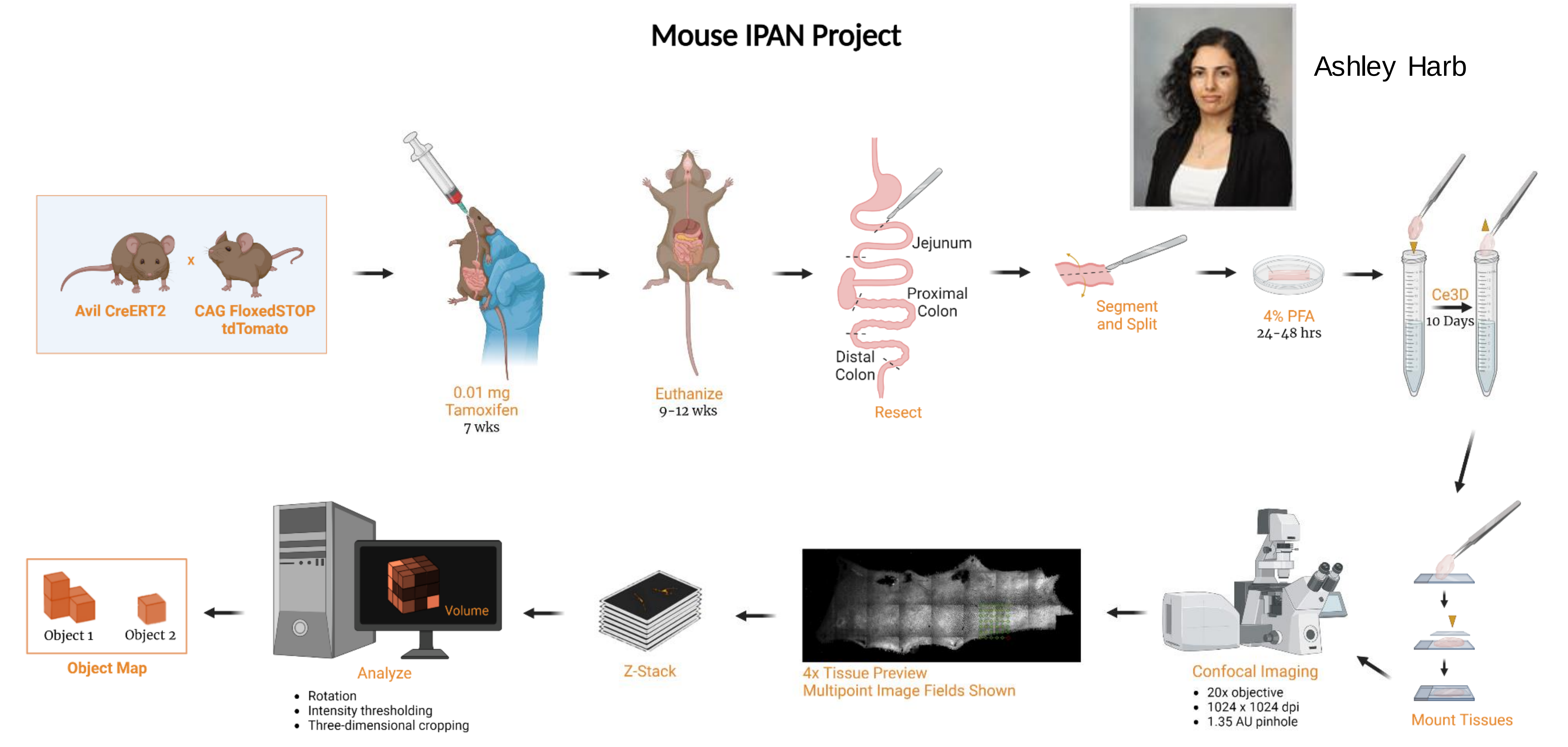
Ulrika Marklund

Different classes of IPANs possess morphologies and physiology that uniquely contribute to intestinal function

Model and Methods



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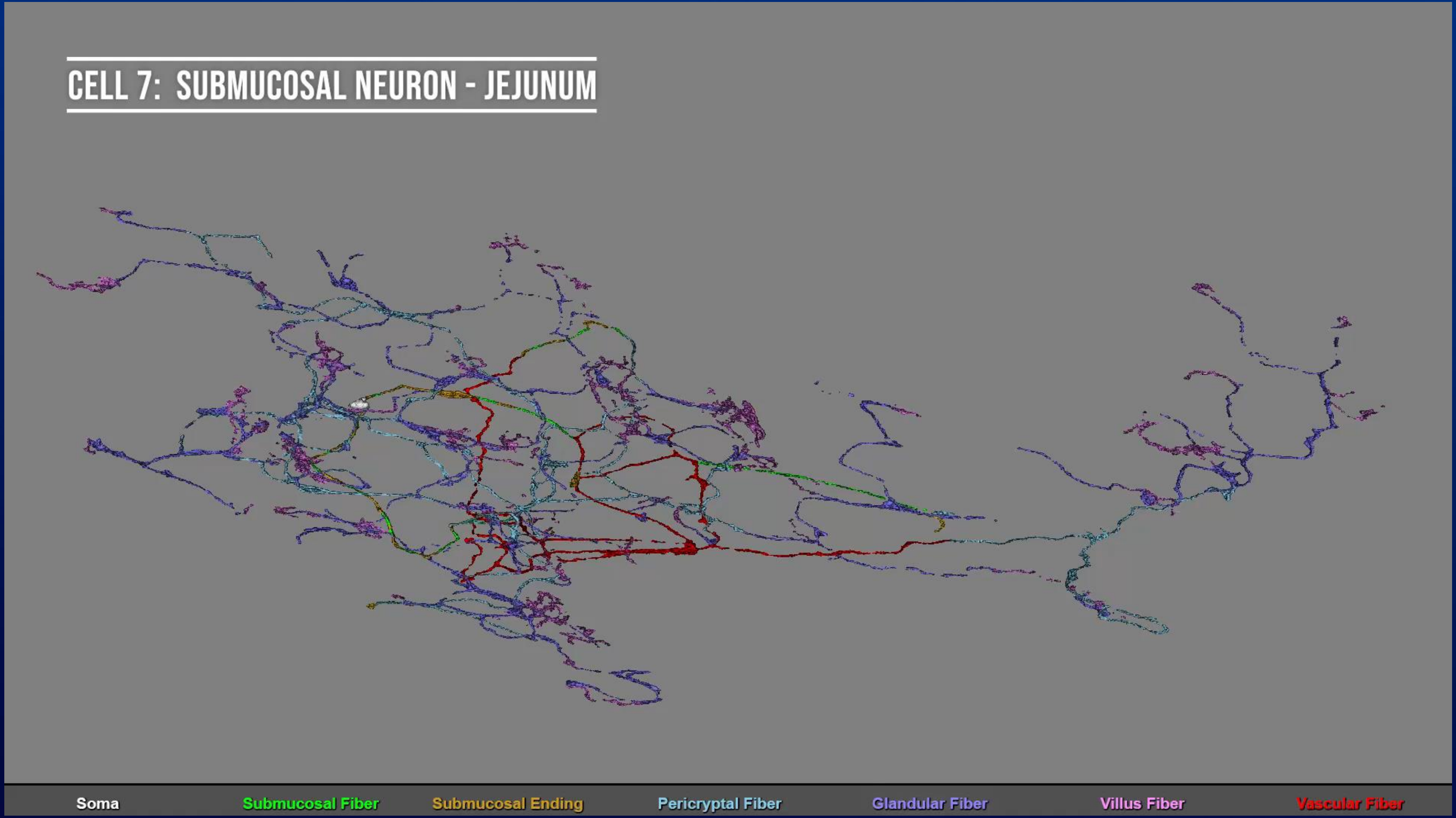
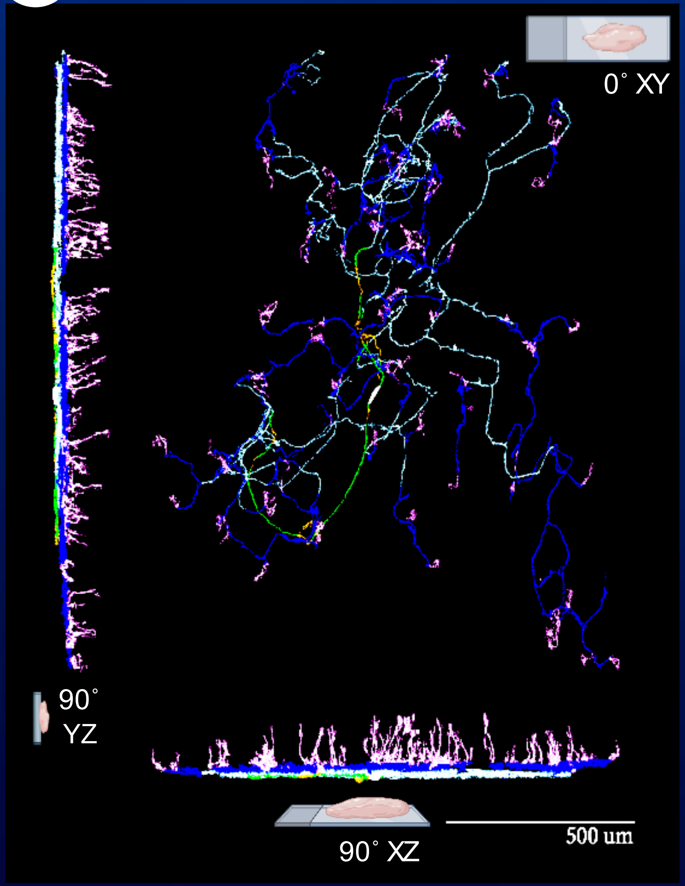
Single Cell 3D Reconstruction

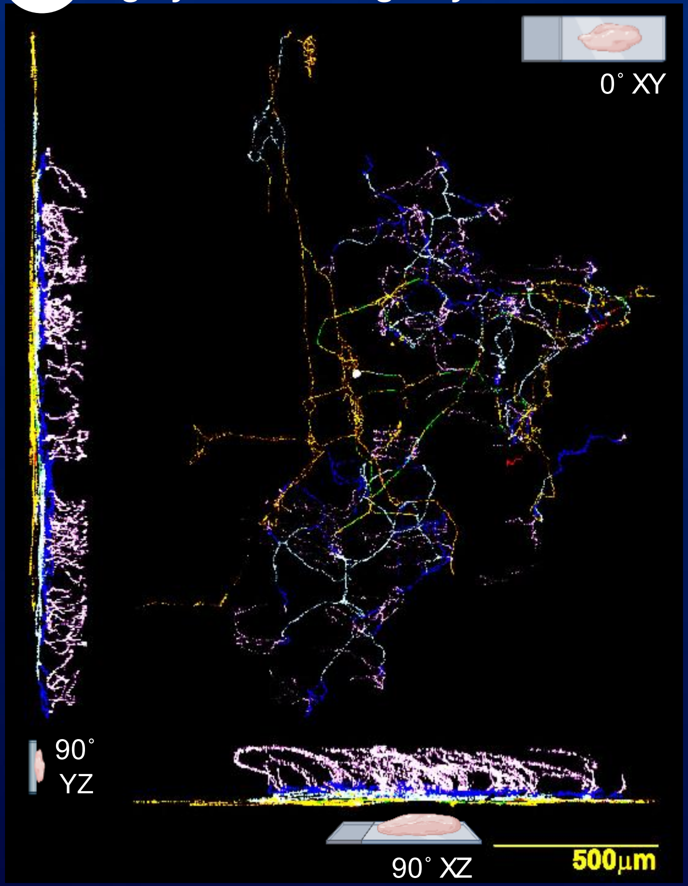


Three Cell Morphologies Based on Soma Location and Branching Pattern

1 Submucosal Cells



2 Highly-Branching Myenteric Cells



Myenteric Cells

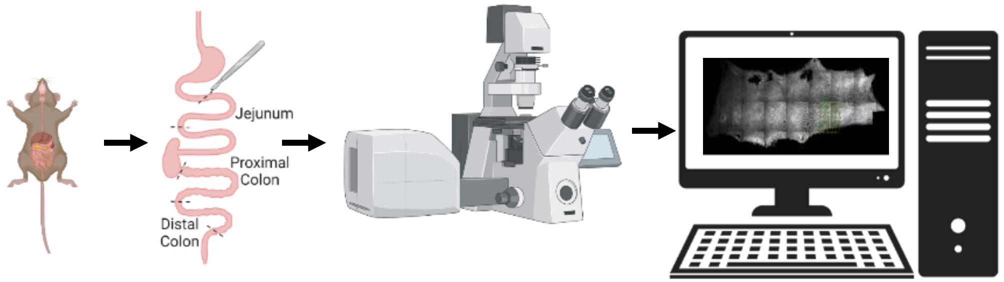
Ashley Harb

3 Long Descending Dogiel Type I Myenteric Cells

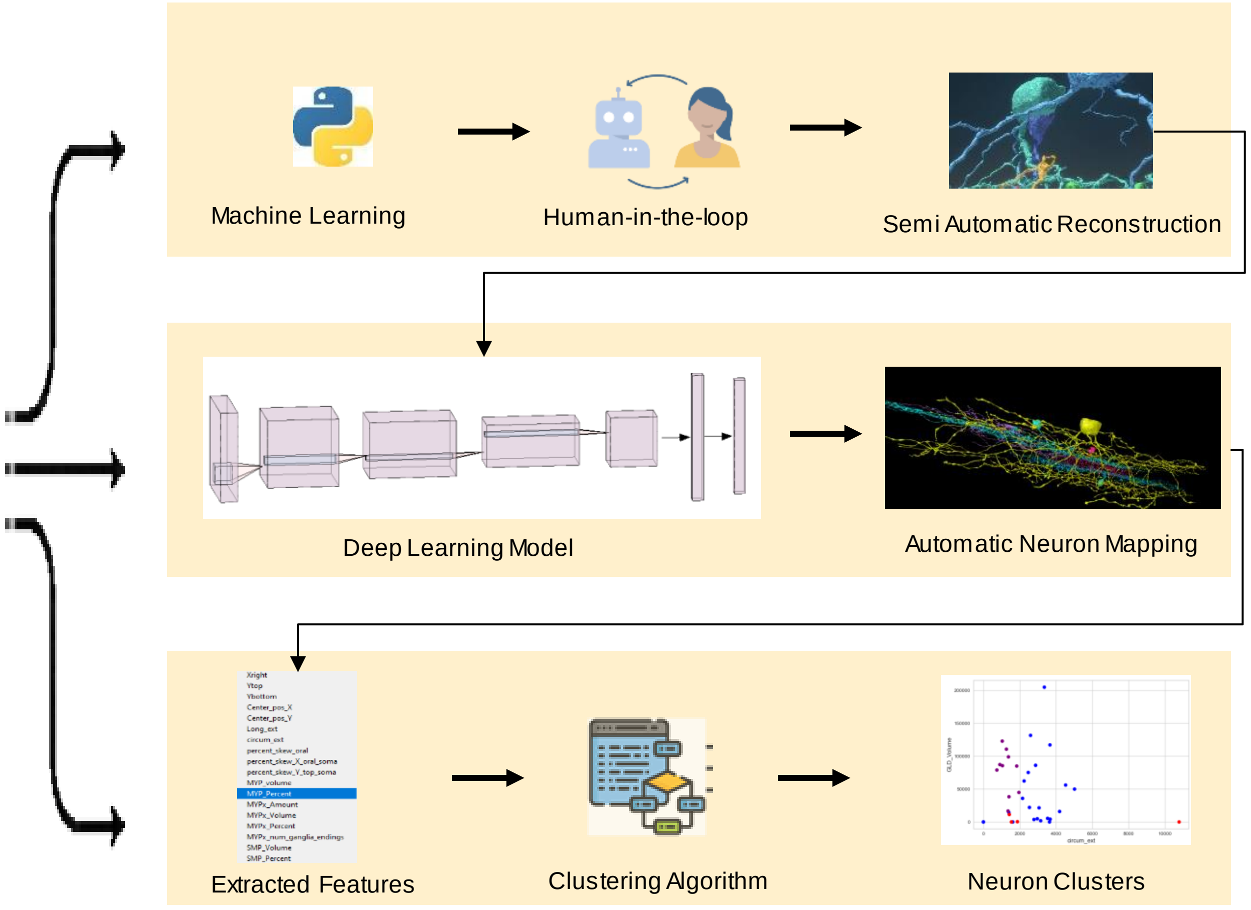
AI/ML Collaboration


Shivaram Poigai Arunachalam


Kamrul Foysal



Data Acquisition



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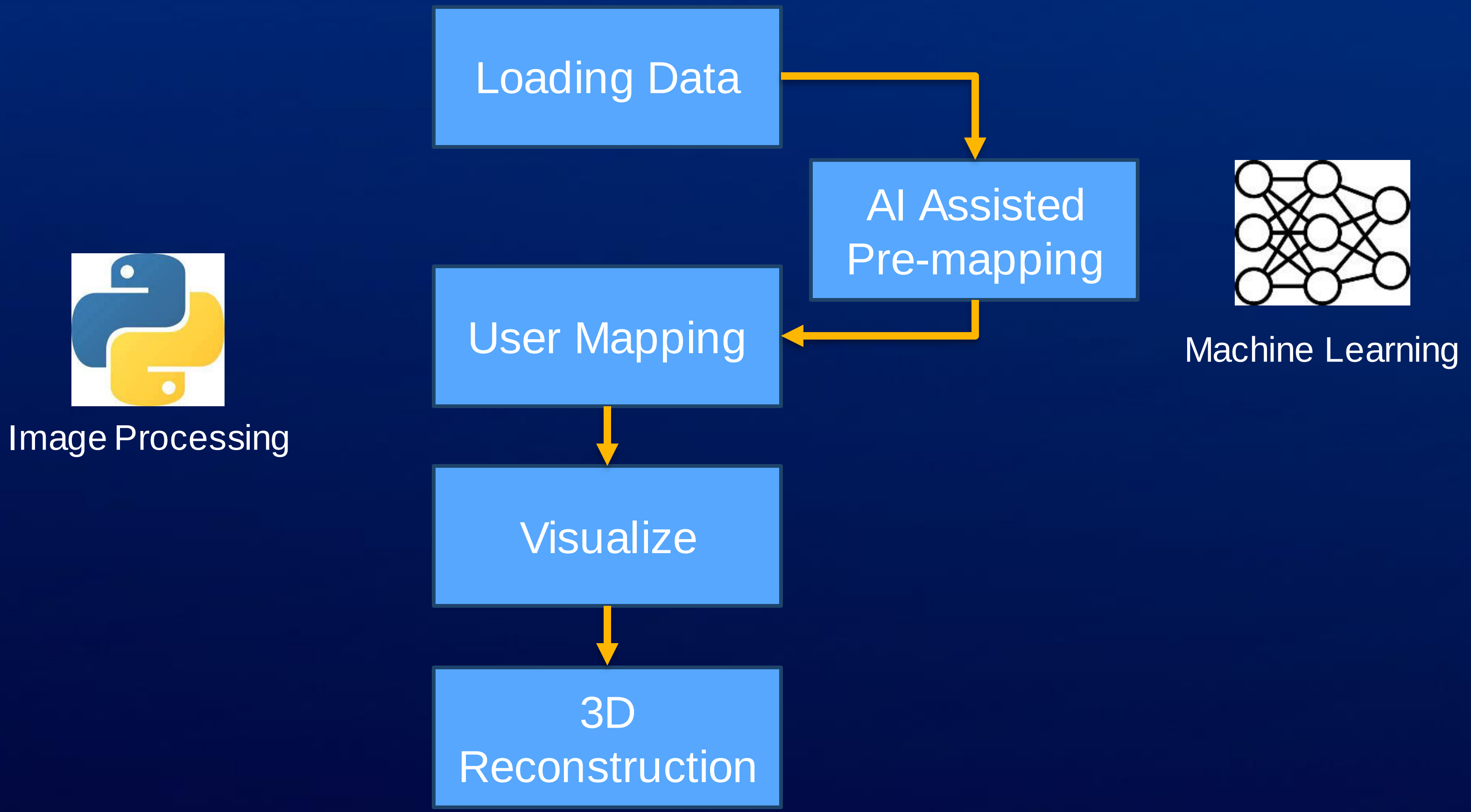
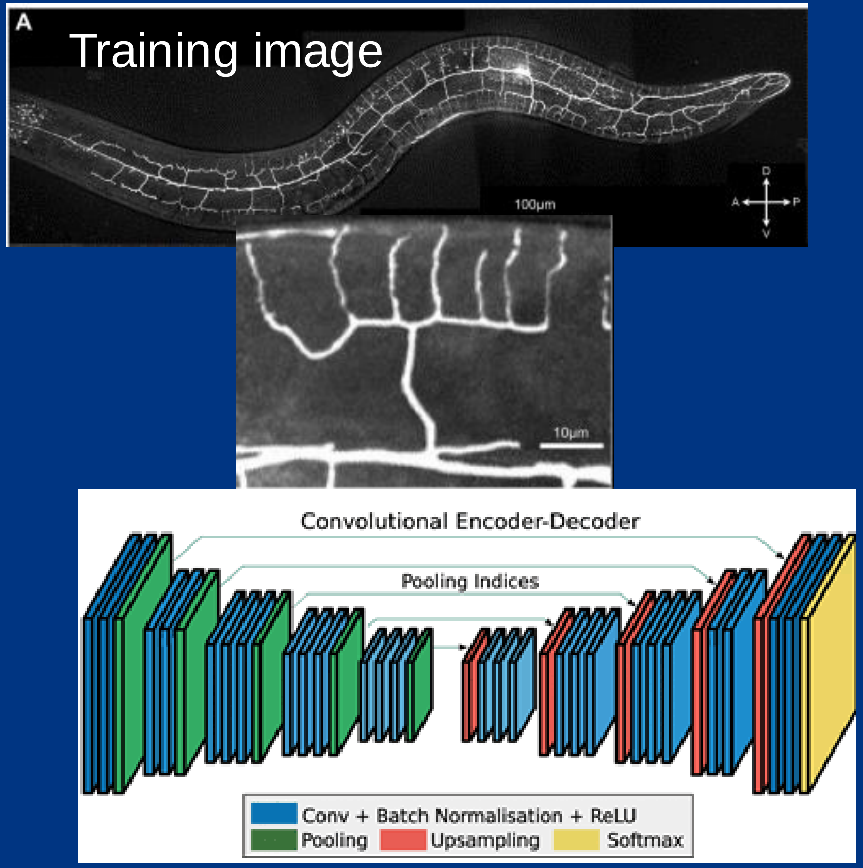
Semi-Automated Human-in-the-Loop AI Assisted Mapping

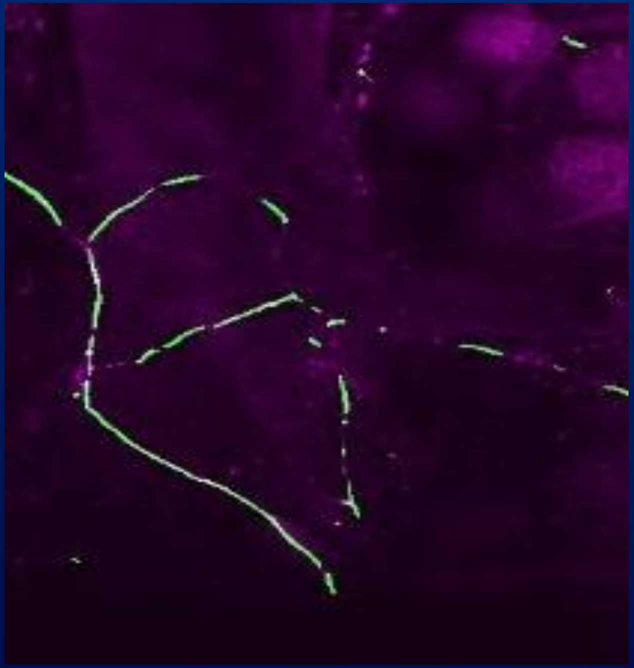


AI Assisted Pre-Mapping

- Dataset Trained on *C. elegans* neuron
- Connect 3D Shapes, Cleans Data
- Suppress Background

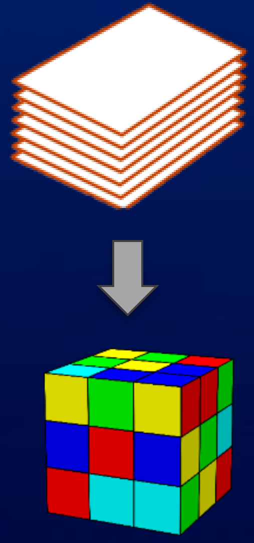


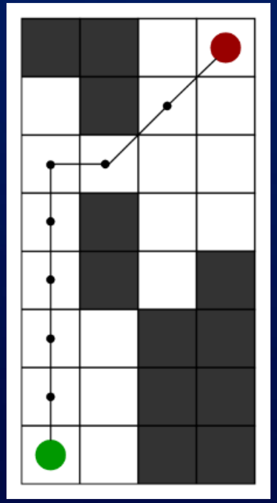
CNN Model

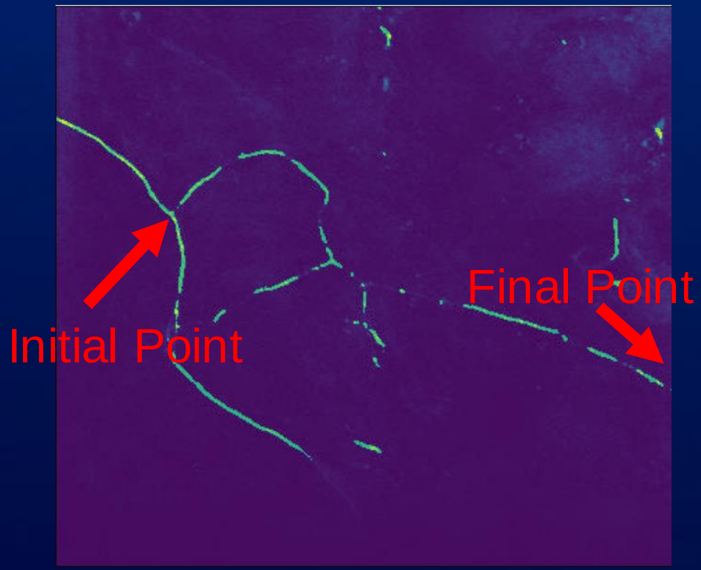


User Mapping Function

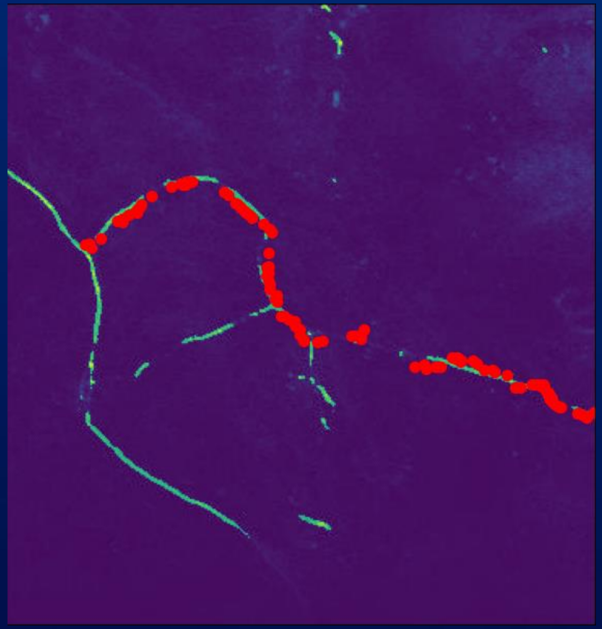
- 3D Graph Search
  - Dijkstra's Algorithm
  - A Star Search Algorithm







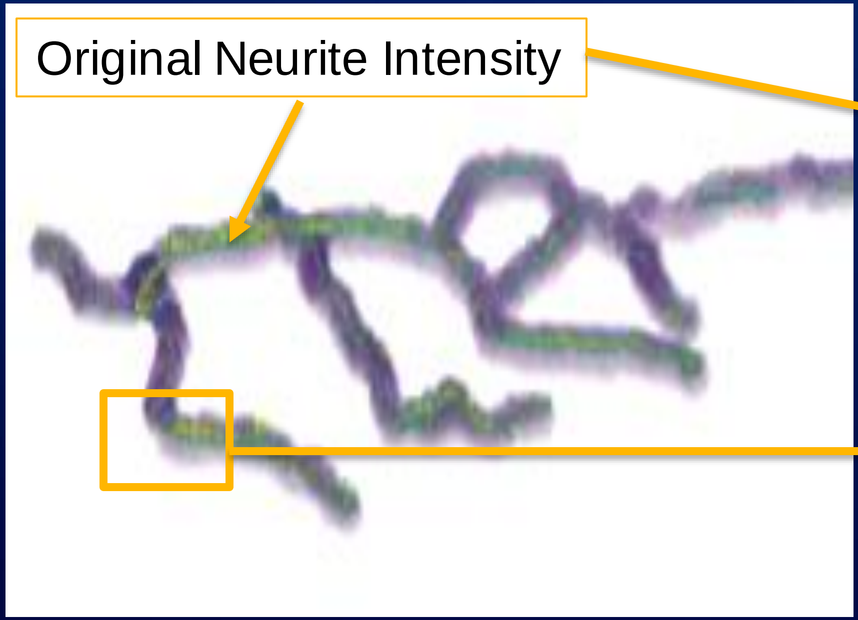
- Broken paths can be connected.
- User defines the Start and the End of the Neurite Branch.
- The mapping is performed in 3D.

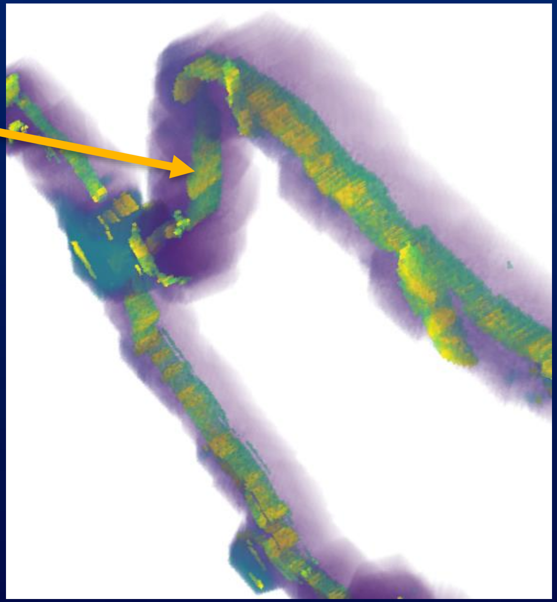


Mapping Function: Neurite Extraction

3D Volumetric Mask

- Traced 3D Voxels act as 3D Volumetric Mask
- Intensity Variation is captured within mask
- Adaptive histogram equalization extracts the neuron structure
- The whole neuron is one single connected object





Neurite Strand

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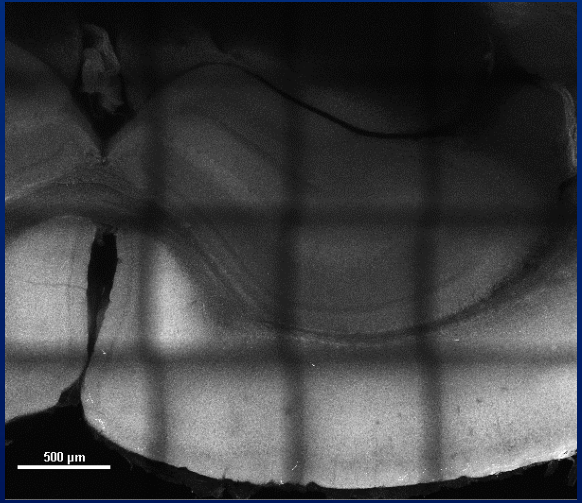
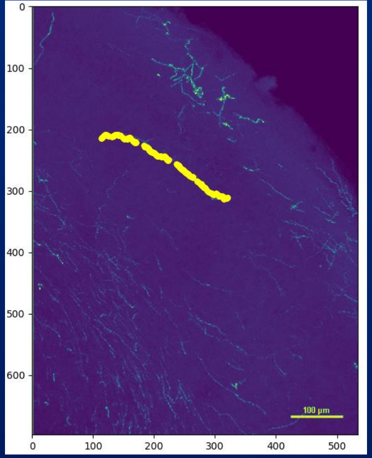
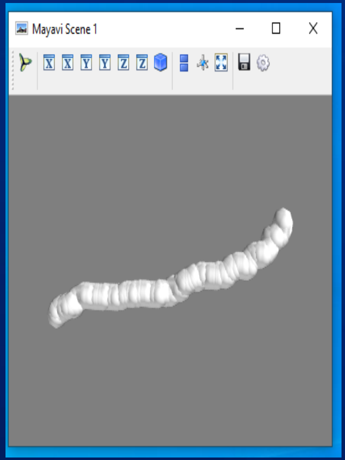
Application to Broad Neuroscience Field

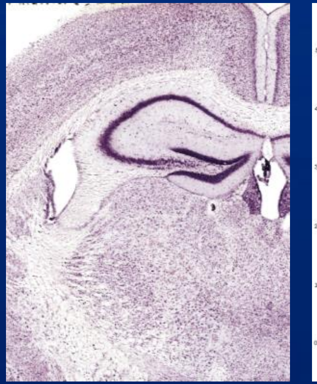


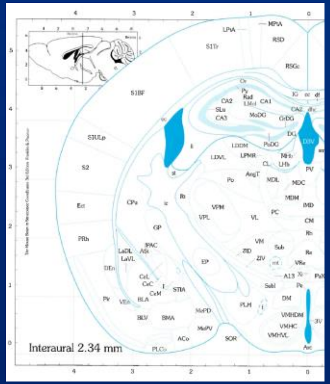
Mapped Neuron



Neuron Mask in 3D







Franklin and Paxinos *The Mouse Brain In Stereotaxic Coordinates* 3rd *Ed.* 2008.

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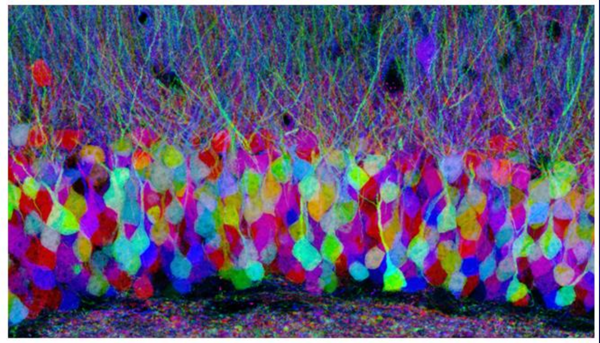


Chuck Howe

Ben Clarkson

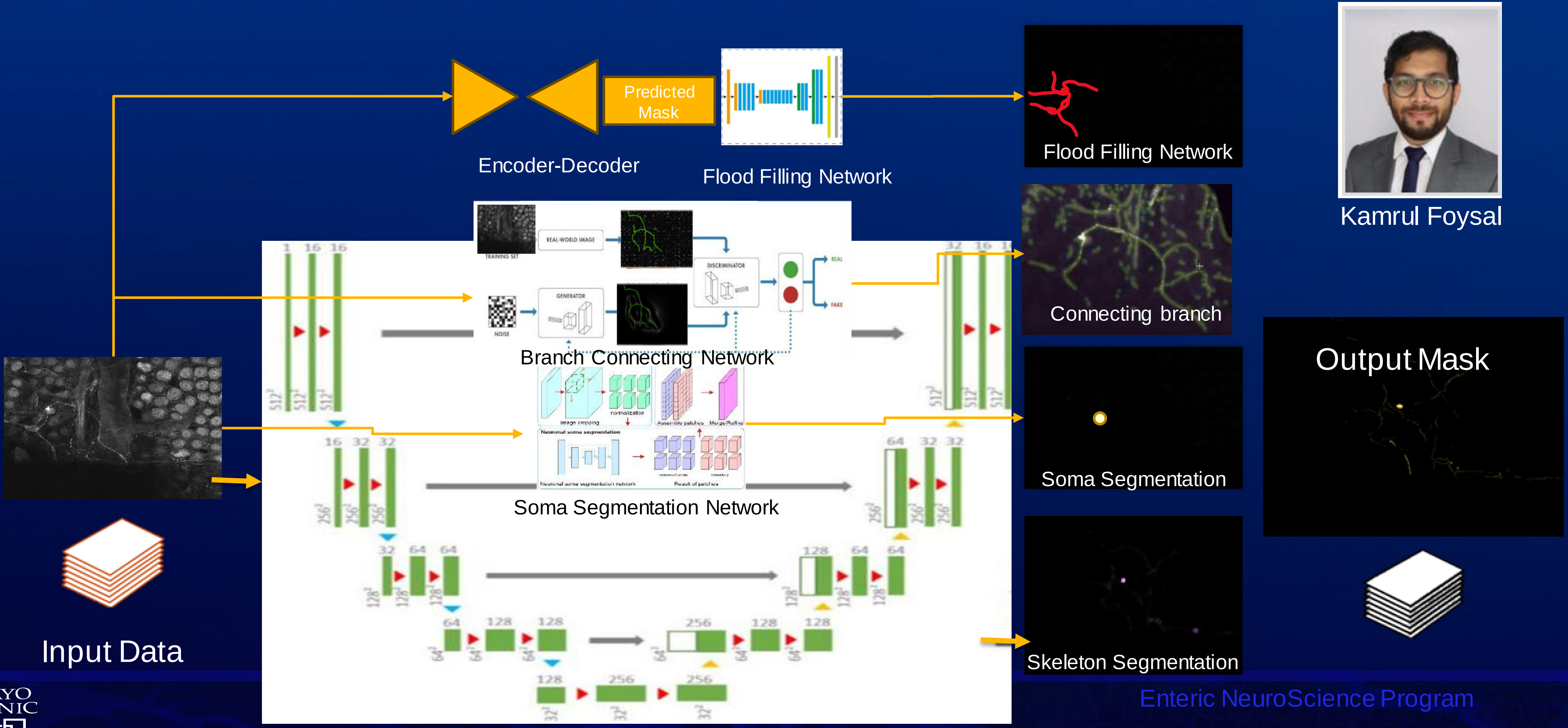
Maria Westphal

Kamrul Foysal

Tim Kline

George Cao

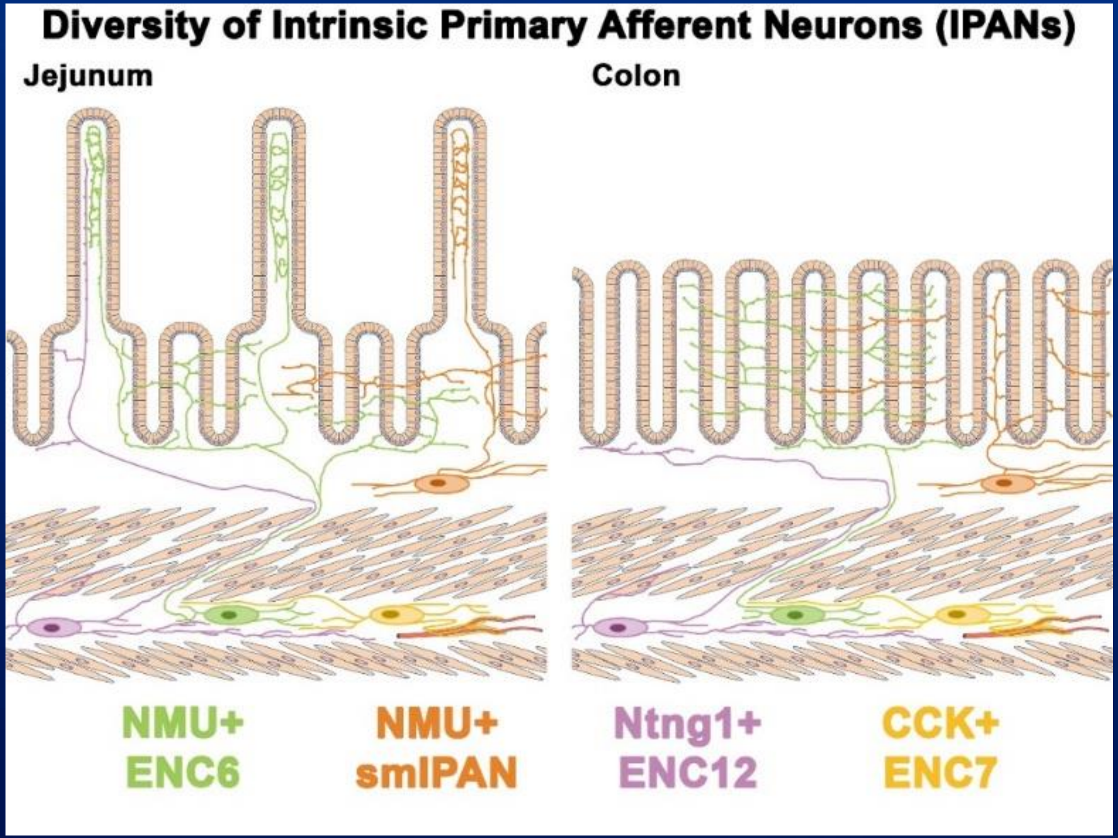
Hybrid Automated Enteric Neuron Mapping Model



Skeleton U-Net Model

Conclusions

- AI / ML Supports Aims of Parent R01
  - Enhanced Throughput
  - Enhanced Objectivity
- Creation of Neuron Morphology Datasets for Future AI / ML
  - Ground Truth to Improve Fully Automated AI/ML Models
  - Applicability to Broad Neuroscience Community



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