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Deep learning enabled neurite segmentation and circuit analysis in retina development

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Abstract

The human brain is composed of approximately 100 billion neurons that collaborate to interpret our senses and control our thoughts and actions. Neurons are known to form circuits with specific functions, yet the brain's wiring diagram remains largely unknown which greatly limits our ability to determine how degenerative diseases affect it and thus impedes the development of targeted therapies. Recently, the complete brain of the fruitfly was imaged using state of the art electron microscopy and parts of its connectome were mapped manually [1]. However, on average each neuron took 11 hours to be traced. Tracing all 100 billion neurons in the human brain would take about 550 million years. To solve the problem, deep learning-based approaches to automate neuron detection and tracing in brain samples have been proposed before. In this work we create an efficient pipeline using a 3D fully convolutional network that quickly and accurately detects neurons and traces circuits present in the mouse retina.

Training and deploying the trained DL model

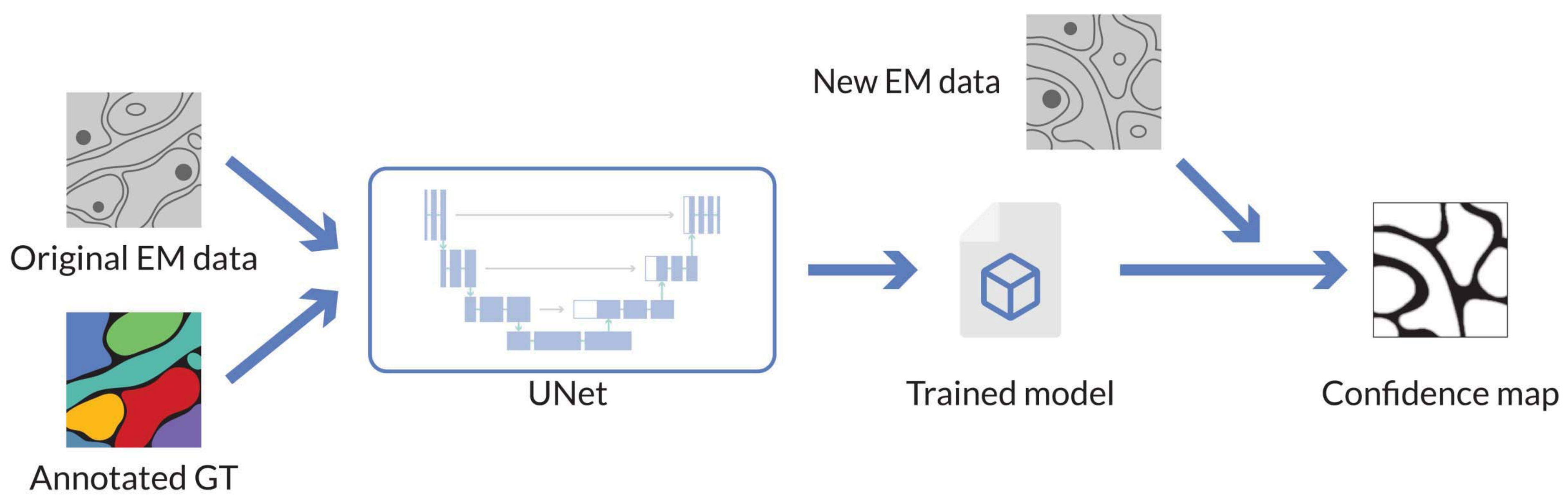

Figure 1. Deep learning model training workflow diagram. The training takes pairs of EM images with corresponding annotated ground truth (GT images). The model generated by UNet [2] can be applied to new datasets to generate confidence map image for object segmentation.

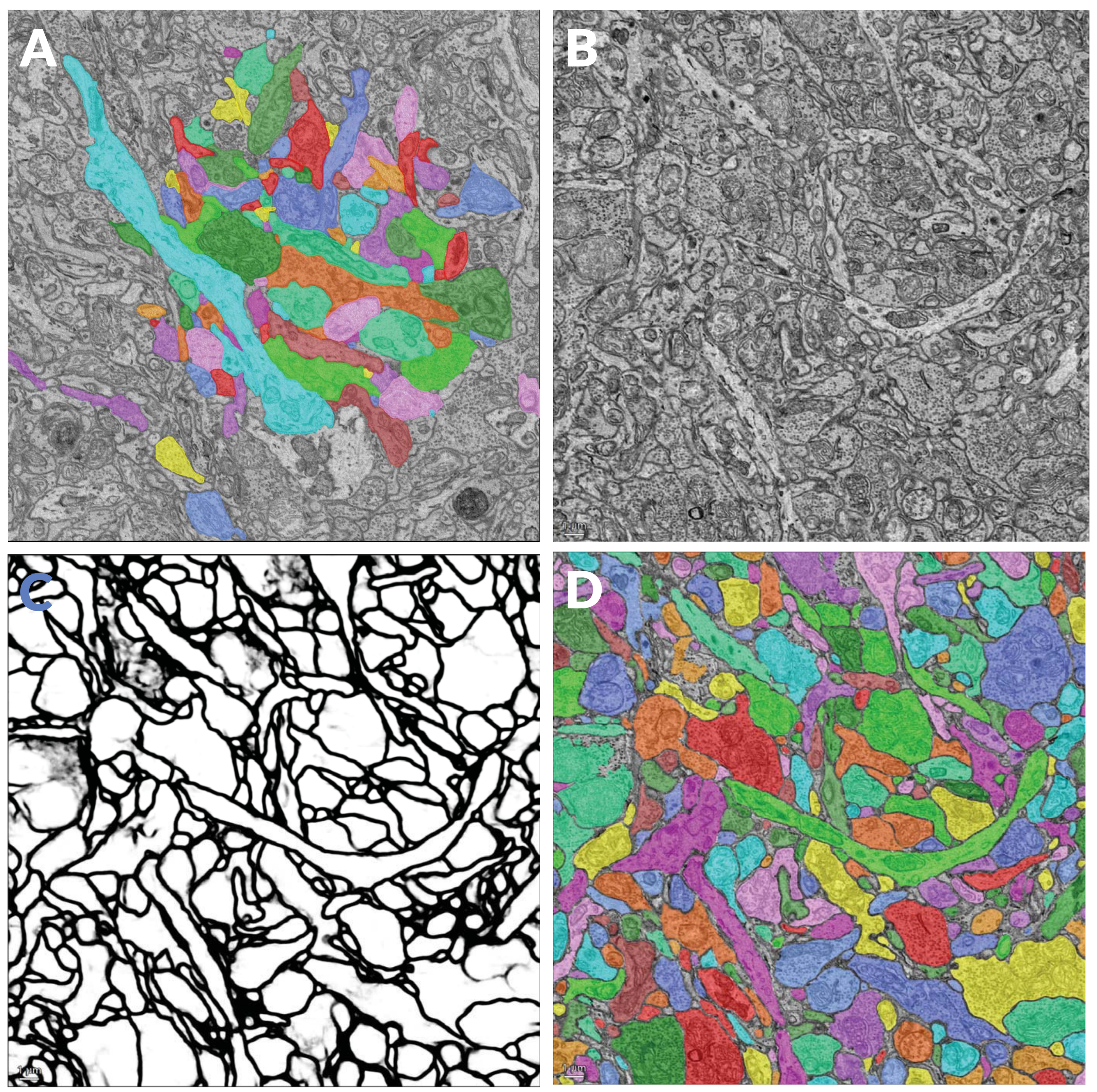

Figure 2. Training with partial GT and applying DL model to new data. (A) Our model was trained using a novel (patent-pending) approach which only requires a partially labeled image. The serial block face scanning electron microscopy (SBEM) stack used for training was composed of 1,500 x 1,500 x 75 voxels of which approximately 30% was annotated manually. Random rotations of 90, 180 and 270 degrees in the XY plane and flips in X and Z dimensions augments the existing data. Each Z slice was randomly shifted along X and Y directions to simulate misalignment. Our model was trained by Adam optimizer with a base learning rate of 10^{-3} for 300 epochs, which took 10 hours on two NVIDIA GeForce GTX 1080Ti GPUs. The trained model was applied to a new image stack (B) of 1500x1500x100 pixels (i.e. 225 million voxels) taking 4.5 minutes to complete the process on a single NVIDIA GeForce GTX 1080Ti GPU. This represents a throughput of 50 million voxels per minute. The network generated confidence map (C) was then segmented using a seeded watershed algorithm to identify each neurite segment (D).

Neuron segmentation and 3D reconstruction

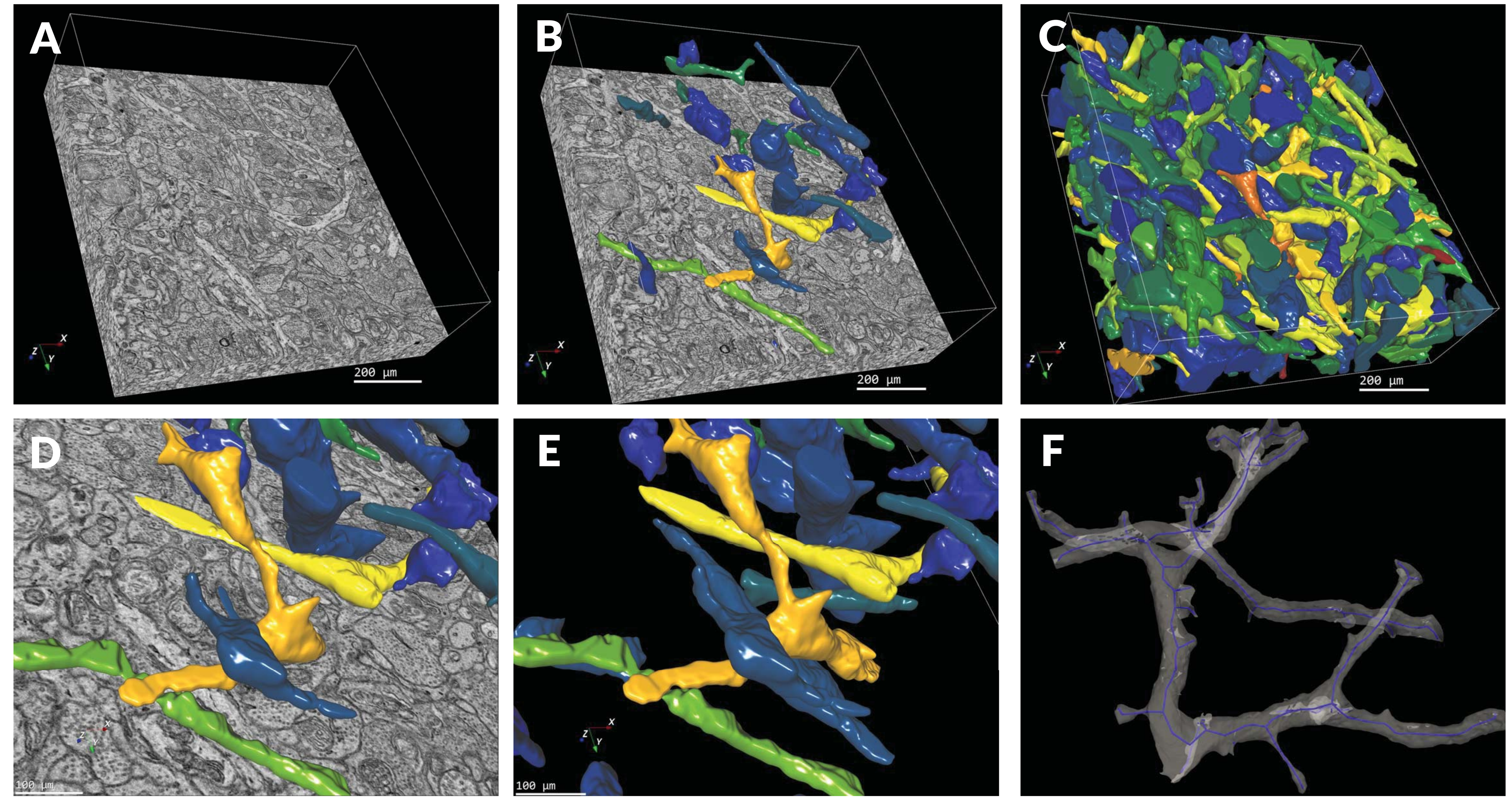

Figure 3. Neurite 3D segmentation and circuit detection. The processed raw data set (A) included 989 neuron segments. To greatly increase throughput, we have deployed the trained deep learning model using Aivia Cloud, which currently makes uses of eight NVIDIA V100 GPUs. With this set up we can process approximately 4 billion voxels per minute – taking a total of 60 minutes on the tested dataset. B) shows a subset of the reconstructed neurites and part of the 3D EM volume – a clipping plane was used to reveal the reconstructed neurites present on the upper part of the data set. C) shows a 3D representation of the larger (by volume) 50% of all neurites detected. Color coded for volume. Editing of individual neuron boundaries is possible with a range of semi-automated tools in Aivia. D) and E) illustrates a close-up view of a small subset of neurites that are in contact with each other. F) Partial neuron circuits were automatically created.

Summary and acknowledgement

Here we describe a novel machine learning enabled pipeline to greatly expedite the processing and segmentation of neurites imaged by serial block face electron microscopy. Future work includes training a DL model to recognize post synaptic densities which will subsequently be used to validate neuron circuits. This approach has the potential to greatly accelerate the field of regional connectomics.

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References

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2. O Ronneberger, P Fischer, T Brox. (2015) U-Net: Convolution networks for biomedical image segmentation. MICCAI 2015. Lecture notes in computer science, vol. 9351.