Segmenting Cell Mitochondria in 3D:

Biological research creates enormous quantities of image data. Often times, it requires experts to infer the boundaries of different cellular structures or anatomical features. The more computer vision can be harnessed to identify features in microscopy images, the faster data can be gleaned from scans. Since hand annotation can take much, much longer than the actual data collection, this would speed up data collection drastically, leading to more insights and discovery.

Specifically, this project will look at the identification within mitochondria within neuronal cells from Scanning Electron Microscope (SEM) images. A relatively new technique in this field is known as Focused Ion Beam - SEM, in which a three dimensional tissue sample is sequentially imaged by the SEM, and then a layer is ablated (vaporized) by a beam of focused ions, allowing the layer below to be imaged. This procedure was used to create a 5 micron x 5 micron x 5 micron volume of data representing neuronal cells.

Though there are many features of interest in a biological system the mitochondria are particularly important since they create the energy for the cell. Therefore, a group of researchers took the time to hand annotate 330 images to separate out mitochondria pixels from non-mitochondria pixels (CVLab SEM dataset). This dataset is notable in that the data is truly three dimensional, the data is given as an image stack in which each pixel is actually a 5 nanometer x 5 nanometer x 5 nanometer voxel.

In order to solve this problem, I will be making use of a deep convolutional neural net. Specifically, an architecture known as U-net (Ref). Convolutional nets have been shown to perform exceptionally well on image data since they attempt to find features that are localized in space. U-net is a specific architecture that both repeatedly applies convolutions and down-sampling (lowering resolution) operations as with most convolutional nets, and then applies convolutions and upsampling (raising resolution) which was an innovation when it was invented. This process first finds the features of interest (categorization problem), and then applies those features to the image to generate a map of which pixels correspond to which category. In the present problem the categories are "mitochondria" and "not mitochondria."

In applying this machine learning tool to the data, I will be looking at creating an accurate map of which pixels in the volume represent mitochondria. I will attempt to do this both by using two dimensional images and three dimensional volumes, and see which method gets better results. There will likely be a trade-off between using more layers to get 3D features vs having more training examples to get a more robust fit. It may be possible to achieve good results with a 3D model since this method can generate high

quality segmentation with remarkably small amounts of data. The original paper, for example, used 30 training images. Even at high resolution, this is remarkable when many computer vision algorithms require thousands or even millions of images.

The client for this product would be biotechnology laboratories, both public and private. Access to new techniques and greater computational power have led to rapid growth in the biological sciences, and especially neuroscience in recent decades. Automation of routine tasks would benefit both companies and academics to accelerate the pace of discovery. Discovery could have benefits ranging from pharmaceuticals, to new treatments, and greater understanding of the brain.

The deliverable will consist of all Jupyter notebooks I develop for this project, a final report detailing the work completed, and a presentation slide deck explaining the models and associated results.