# CELL DETECTION FROM BRAIN HISTOLOGY USING ARTIFICIAL NEURAL NETWORK

*Mihovil Mladinov*[⋆] *Lea T. Grinberg*[⋆] *Daniela Ushizima*[†]

[⋆] Memory and Aging Center, UCSF, [†]Computational Research Division, LBNL

## ABSTRACT

Biomarkers for cell populations support investigation of mechanisms driving brain diseases, particularly at the early steps in the drug discovery process. A major challenge is to target key cells and quantify their concentration among batches of specimens. This paper describes preliminary steps in automating cell counts from brain tissue sections using artificial neural networks.

***Index Terms***— brain cells, detection, neural nets

## 1. INTRODUCTION

Validating biomarkers in cell populations provide critical insights into mechanisms driving disease, particularly at the early steps in the drug discovery process. Immunohistochemistry and immunofluorescence (IHC/IF) apply antibodies and other reagents to unlock information from cells into molecular cascades while preserving tissue integrity. IHC/IF often occurs in large batches resulting in high amounts of data, making manual analysis very time-consuming and prone to error. Despite a great deal of proposals to automate cell analyses, most of the methods for detecting and segmenting cells in IHC/IF images have been tailored to work with images derived from cell cultures or experimental animals, in which several parameters can be controlled to render IHC/IF images with a smooth, clean background and high contrast [1]. Contrary, IHC/IF images derived from postmortem human brain present considerable low signal-to-noise, inherent to human brain tissue because lipofuscin pigment accumulates with aging and uncontrollable periagonal factors affect tissue quality [2]. Moreover, state-of-the-art quantification requires stereological methods and the use of thicker tissue slides, increasing the amount of image artifacts. Here, we propose to create and test computer-based segmentation algorithms for segmenting cell in images from IHC/IF microscopy of thick postmortem human brain sections, aiming to reduce counting time and also reducing inter and intra-observer variability.

## 2. METHODS

Confocal microscopy often improves spatial resolution, but as the human brain cells are highly diverse, even regional analysis require a high amount of microscope time and data processing capabilities. Finally, as human brain histological sections usually have a much larger surface than thickness, artifacts such as folds and tears are common. As a result, available automated cell segmenting and counting algorithms perform poorly and require manual interaction, often subjected to low-throughput and prone to error, leading to low inter and intra-observer reproducibility.

Cell detection used an algorithm based on a neural network applied to 66 images, specifically 6 stereological stacks from human brain histology, each with 11 sections.

## 3. RESULTS CONCLUSIONS

Figure [**?**] shows preliminary results applied to IHC/IF stained microscopy image stacks. We tested both Extended Depth Focus (EDF) and Maximum Intensity Projections (MIP) for considering 3D information as well as improving image quality. Proposed algorithm detects IHC/IF cells, including neurons with approximately 90% accuracy.

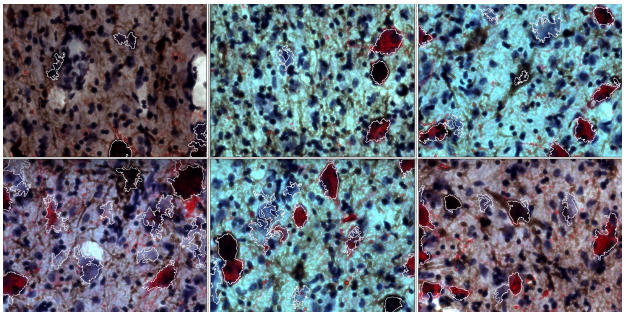

**Fig. 1**. Brain cytology.

## 4. REFERENCES

[1] Dzyubachyk et al, "Advanced level-set based multiple-cell segmentation and tracking in time-lapse fluorescence microscopy images," in *Proc. ISBI*, 2008, pp. 185–188.

[2] Alahmari et al., "Automated cell counts on tissue sections by deep learning and unbiased stereology," *Journal of Chemical Neuroanatomy*, vol. 96, 12 2018.