UNIVERSITY OF SOUTH FLORIDA

Defense of a Doctoral Dissertation

A Multiple Input Multiple Output Framework for The Automatic Optical Fractionator-based Cell Counting in Z-Stacks Using Deep Learning

by

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For the Ph.D. degree in Computer Science and Engineering

Unbiased stereology is the state-of-the-art method for quantifying stained cells in biological tissue. The majority of the previously available automatic stereology cell count methods were developed for single immuno-stained tissue sections. As the first contribution, this dissertation proposes an adaptive stain separation method to extend the previous methods to counterstained tissue sections. The proposed method is demonstrated on two counterstained datasets. The previous methods performed counting on 2D Extended Depth of Field images instead of z-stacks leading to under-counting bias due to overlapping and masked cells in different z-planes. The next contribution of this dissertation is a disector-based Multiple Input Multiple Output (MIMO) framework which resolves the overlap by using z-separation between the cells. The framework obtained comparable to manual counts on three different datasets. A MIMO U-Net architecture introduced as part of the MIMO framework enables a 2D U-Net to exploit inter-image features without the shortcomings of known methods like RNNs. The inter-image feature learning capability of the MIMO U-Net for microscopy image sequences was also demonstrated using a publicly available dataset and results comparable to a method equipped with memory units dedicated to inter-image feature learning were obtained.

Examining Committee

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Publications

1) **Dave, P.**, Kolinko, Y., Morera, H., Allen, K., Alahmari, S., Goldgof, D., Hall, L.O., & Mouton, P. R.. MIMO U-Net: efficient cell segmentation and counting in microscopy image sequences. In Medical Imaging 2023: Digital and Computational Pathology. SPIE. (Accepted)
2) **Dave, P.**, Goldgof, D., Hall, L. O., Kolinko, Y., Allen, K., Alahmari, S., & Mouton, P. R. (2022). A disector-based framework for the automatic optical fractionator. Journal of Chemical Neuroanatomy, 124, 102134.
3) Morera, H., **Dave, P.**, Kolinko, Y., Allen, K., Alahmari, S., Goldgof, D., Hall, L.O., & Mouton, P. R. (2022, April). Classification of global microglia proliferation based on deep learning with local images. In Medical Imaging 2022: Image Processing (Vol. 12032, pp. 682-687). SPIE.
4) **Dave, P.**, Alahmari, S., Goldgof, D., Hall, L. O., Morera, H., & Mouton, P. R. (2021). An adaptive digital stain separation method for deep learning-based automatic cell profile counts. Journal of Neuroscience Methods, 354, 109102.
5) Alahmari, S., Goldgof, D., Hall, L., **Dave, P.**, Phoulady, H. A., & Mouton, P. (2018, December). Iterative deep learning based unbiased stereology with human-in-the-loop. In 2018 17th IEEE International Conference on Machine Learning and Applications (ICMLA) (pp. 665-670). IEEE.

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