

1.1. **Convolutional Neural Networks and analysis of Histology Images**

Development of techniques to perform automatic classification of histology images has become a fast growing research avenue in recent years¹⁻³. Traditional approaches require extraction of features from histology images, followed with a variety of machine learning methods for classification. Identification and extraction of features suffer from biases arising from user intervention and knowledge, variations in type of tissue, disease and dataset as well as the questions the final model is attempting to answer⁴. To this end, Convolutional neural networks (CNNs) have gained popularity as the technique to build automatic classifiers for histology images^{5,6}. CNNs employ a purely data driven approach to learn important morphological features from tiles of histology images and thus are generalizable to a variety of problems and datasets. Features of importance highly vary depending on disease and disease subtypes, and the use of CNNs removes the limitation of feature-based methods that may be limited by pre-defined or selective attributes. As CNNs require a large amount of training data to result in an effective classifier, histology images are usually tiled and utilized as input to CNN based methods. CNNs have proven to be successful in building classification models to answer a variety of questions from histology and morphology of cancer tissues^{1,4,7-9}.

References

1. Beck AH, Sangoi AR, Leung S, et al. Systematic Analysis of Breast Cancer Morphology Uncovers Stromal Features Associated with Survival. *Sci Transl Med*. 2011;3(108):108ra113-108ra113. doi:10.1126/scitranslmed.3002564.
2. Angel Arul Jothi J, Mary Anita Rajam V. Automatic classification of thyroid histopathology images using multi-classifier system. *Multimed Tools Appl*. 2017;76(18):18711-18730. doi:10.1007/s11042-017-4363-0.
3. Wang P, Hu X, Li Y, Liu Q, Zhu X. Automatic cell nuclei segmentation and classification of breast cancer histopathology images. *Signal Processing*. 2016;122:1-13. doi:10.1016/j.sigpro.2015.11.011.
4. Araújo T, Aresta G, Castro E, et al. Classification of breast cancer histology images using Convolutional Neural Networks. Sapino A, ed. *PLoS One*. 2017;12(6):e0177544. doi:10.1371/journal.pone.0177544.
5. Bayramoglu N, Heikkilä J. Transfer learning for cell nuclei classification in histopathology images. In: *Lecture Notes in Computer Science (Including Subseries Lecture Notes in Artificial Intelligence and Lecture Notes in Bioinformatics)*. Vol 9915 LNCS. ; 2016:532-539. doi:10.1007/978-3-319-49409-8_46.
6. Xu J, Luo X, Wang G, Gilmore H, Madabhushi A. A Deep Convolutional Neural Network for segmenting and classifying epithelial and stromal regions in histopathological images. *Neurocomputing*. 2016;191:214-223. doi:10.1016/j.neucom.2016.01.034.
7. Sirinukunwattana K, Raza SEA, Tsang YW, Snead DRJ, Cree IA, Rajpoot NM. Locality Sensitive Deep Learning for Detection and Classification of Nuclei in Routine Colon Cancer Histology Images. *IEEE Trans Med*

- Imaging*. 2016;35(5):1196-1206. doi:10.1109/TMI.2016.2525803.
8. Kashif MN, Raza SEA, Sirinukunwattana K, Arif M, Rajpoot N. Handcrafted features with convolutional neural networks for detection of tumor cells in histology images. In: *Proceedings - International Symposium on Biomedical Imaging*. Vol 2016-June. ; 2016:1029-1032. doi:10.1109/ISBI.2016.7493441.
 9. Ciresan DC, Giusti A, Gambardella LM, Schmidhuber J. Mitosis Detection in Breast Cancer Histology Images using Deep Neural Networks. *Proc Med Image Comput Comput Assist Interv*. 2013:411-418. doi:10.1007/978-3-642-40763-5_51.