Mitotic Instance Detection in Stain Normalized Histopathological Images

Anand H
Computer Science and Engineering
Amrita Vishwa Vdyapeetham
Trivandrum, India
anand.h1729@gmail.com

Anoop K Rajan
Computer Science and Engineering
Amrita Vishwa Vdyapeetham
Pathanamthitta, India
anoopkrajan7@gmail.com

Gautham Santhosh
Computer Science and Engineering
Amrita Vishwa Vdyapeetham
Trivandrum, India
gautham18sks@gmail.com

Mrs. Lekha S Nair
Computer Science and Engineering
Amrita Vishwa Vdyapeetham
Kollam, India
lekhas@am.amrita.edu

***Abstract*—Our paper aims to detect and identify the possibility of malignancy based on abnormal mitotic cell division using Artificial Intelligence. In tumour grading, the mitotic activity index is an important prognostic factor. The conventional approach involves skilled pathologists manually observing H&E stained histopathology sections on glass slides through a microscope which is tedious and error-prone, thereby a need for automation. Automated mitotic nuclei detection poses several challenges due to the lack of pixel-level annotations, presence of mitotic nuclei in various morphological configurations, their sparse representation, and close resemblance with other cellular and nuclear bodies. Hence an efficient and accurate automated approach is necessary for early prognosis. This early detection helps the pathologists to find the mitotic cells considerably faster. We will be using a Faster RCNN model to classify the mitotic and non-mitotic nuclei..**

***Index Terms*—Mitosis Detection, Faster RCNN, Detetron 2**

I. Introduction

Cancer is a disease that needs an efficient and accurate diagnosis during early prognosis to provide better treatment. The conventional approach involves skilled pathologists manually observing HE stained histopathology sections on glass slides through a microscope for cancer grading. This process is time-consuming and error-prone where the accuracy depends highly on the skill and experience of the professional. For detections, we will be using HE stained histopathological sections in which the interaction between hematoxylin and the nucleus makes the nucleus blue, while eosin makes the cytoplasm and connective tissue this helps in better distinguishing the nuclear body from the surrounding cytoplasmic body. The number of mitotic cells present in histologically stained cancer tissue sections is an important criterion for tumour prognosis. The Nottingham grading system (NGS) is a breast cancer grading criterion in which pathologists examine the pleomorphism of the nucleus and the number of cells undergoing mitosis in the tissue section, and assign scores. Thus, the mitotic activity index is the most important determinant in assessing the size, proliferation rate, and aggressiveness of a tumour. With the emergence of digital pathology, automated mitosis detection systems were developed to detect mitotic cells automatically. Our paper proposes an end-to-end Mitotic Instance Detection in HE stained histopathological images using a Faster RCNN model.

We will be training and evaluating our model using three datasets Mitos Atypia 2014, Mitos 2012 and Midog dataset. These datasets consist of images of breast cancer biopsy slides which were annotated by skilled pathologists. Here, we must estimate the bounding box annotations of mitotic cells before training the detector since it only annotates the centroid of mitosis. Initially, we conduct stain normalisation which is an important preprocessing step for normalising the stain variations in the histopathological sections. There are various stain normalisation techniques like Macenko, Reinhard, and Vahadane stain normalisation. We compared these stain normalising methods and selected an appropriate one for each of the dataset in our project to pass the resulting image to the Mitosis detection module. The Mitosis detection module primarily consists of 2 parts: Annotation parsing Faster RCNN model for mitotic cell identification. The pre-processed images are then passed to Faster-RCNN. The RPN network generates potential mitotic cell locations. These generated proposals are then ROI pooled and sent to the classifier network of Faster-RCNN which performs the bounding box regression and classification.

II. Related Work

In[2], the paper proposes a system for CRC (Colorectal) tissue classification based on convolutional networks (ConvNets). It investigates the importance of stain normalisation in tissue classification of CRC tissue samples in H&E-stained images. They also report the performance of ConvNets on a cohort of rectal cancer samples and an independent publicly available dataset of colorectal HE images. In this paper, the performance of ConvNets was evaluated and compared between the one which used stain

normalisation and one without, to emphasise the need for stain normalisation. An easy way to comply with the conference paper formatting requirements is to use this document as a template and simply type your text into it.

In[4], the paper proposes a transfer learning-based object-detection technique for mitosis detection. They adopt a ResNet101 combined with a feature pyramid network (FPN) as the backbone architecture in Mask R-CNN. The performance of the proposed scheme suggests that in the future, Mask R-CNN can be exploited for the detection and segmentation of other weakly annotated nuclear bodies in histopathological images. Yet, the proposed method has a rather long training and evaluation time, so its scalability is limited by hardware performance.

In[5], the paper proposes a multi-stream version of the Faster R-CNN object detection network adapted to classify regions of interest having mitosis, instead of classifying actual physical objects. It proposed a unique pipeline where one stream takes an input of the segmented image map while the other takes an input of the original RGB image. Original images with all three colour channels are used again in Faster R-CNN as input to the RGB stream. The purpose of the segmentation stream is to provide additional evidence of mitosis locations by emphasising the segmented features picked up by U-net. Finally, a Region Proposal Network is used for classification and bounding box regression.

REFERENCES

[1] S. Ren, K. He, R. Girshick and J. Sun, "Faster R-CNN: Towards Real-Time Object Detection with Region Proposal Networks", arXiv.org, 2021. https://arxiv.org/abs/1506.01497.

[2] F. Ciompi et al., "The importance of stain normalization in colorectal tissue classification with convolutional networks", arXiv.org, 2021. [Online]. Available: http://arxiv.org/abs/1702.05931.

[3] Pan, Xipeng Lu, Yinghua Lan, Rushi Liu, Zhenbing Qin, Zujun Wang, Huadeng Liu, Zaiyi. (2021). Mitosis detection techniques in HE stained breast cancer pathological images: A comprehensive review. Computers Electrical Engineering. 91. 107038. 10.1016/j.compeleceng.2021.107038.

[4] A. Sohail, M. Mukhtar, A. Khan, M. Zafar, A. Zameer and S. Khan, "Deep Object Detection based Mitosis Analysis in Breast Cancer Histopathological Images", arXiv.org, 2021. [Online]. Available: https://arxiv.org/abs/2003.08803.

[5] R. Yancey, "Multi-stream Faster RCNN for Mitosis Counting in Breast Cancer Images", arXiv.org, 2021. [Online]. Available: https://arxiv.org/abs/2002.03781

[6] Ciompi, Francesco Geessink, Oscar Ehteshami Bejnordi, Babak Souza, Gabriel Baidoshvili, Alexi Litjens, Geert Ginneken, Bram Nagtegaal, Iris van der Laak, Jeroen. (2017). The importance of stain normalization in colorectal tissue classification with convolutional networks. 160-163. 10.1109/ISBI.2017.7950492

[7] A. Vahadane et al., "Structure-Preserving Color Normalization and Sparse Stain Separation for Histological Images", 2021.

[8] Macenko M, Niethammer M, Marron JS, Borland D, Woosley JT, Xiaojun Guan, Schmitt C, Thomas NE. "A method for normalizing histology slides for quantitative analysis". in 2009 IEEE StainNet 14 International Symposium on Biomedical Imaging: From Nano to Macro, 1107–1110. doi:10.1109/ISBI.2009.5193250.

[9] E. Reinhard; M. Adhikhmin; B. Gooch; P. Shirley. "Colour transfer between images", 2001.DOI: 10.1109/38.946629