Deep Detection and Classification of Mitotic Figures

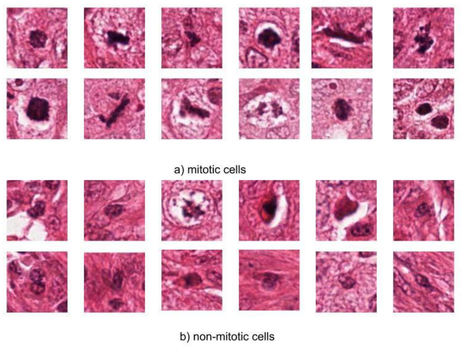
Balamurali Murugesan[a,b], Sakthivel Selvaraj[b], Kaushik Sarveswaran[b], Keerthi Ram[b], Jayaraj Joseph[b] and Mohanasankar Sivaprakasam[a,b]

[a]Indian Institute of Technology Madras (IITM), India

[b]Healthcare Technology Innovation Centre, (IITM), India

INTRODUCTION

According to the World Health Organization (WHO), breast cancer is the most common cancer among women worldwide. The WHO recommends the Nottingham Grading System (NGS) for tumor grading. It is a modification of Scarff, Bloom and Richardson grading system. It is obtained from the assessment of three morphological features: tubule formation, nuclear pleomorphism, and mitotic count. Among these, the mitotic count is an important indicator of invasive ductal carcinoma. During a biopsy, the tissue samples are stained with Haematoxylin and Eosin (H&E) stain which is the standardized technique for visualizing the tissue components. The Haematoxylin stain enhances the nuclei with purple/blue color while the eosin enhances the cytoplasm with pink color. To grade the tumor, the pathologist visually inspects the microscopic slides usually with 40x magnification images known as High Power fields (HPF). In NGS, a score is given by counting the number of mitotic cells in 10 consecutive HPFs. The scores given for the range of mitotic count are as follows 1:0-9, 2:10-19 and 3:>19. The lack of consistency in identifying mitotic cells between pathologists will affect the diagnosis. And also, identifying mitotic cells in a whole slide can be time-consuming for a pathologist. This makes it necessary to have a computer-aided diagnosis (CAD) which can assist pathologists. Recent advancement of whole slide scanner technology has made this CAD possible.



a) mitotic cells

b) non-mitotic cells

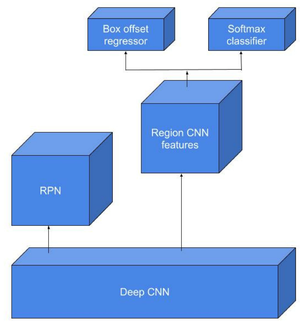
The mitosis detection is a challenging problem due to the following reasons:

- The mitotic cells are a rare event compared to non-mitotic cells.
- It has a similar appearance to other structures such as apoptotic nuclei, lymphocyte nuclei, and dust particles.
- There is a high variation in shape and texture, as the mitotic cell division is a complex biological process which undergoes various morphological transformations.

Therefore, the main aim of our work is focused on automatic detection of mitotic cells from histopathology image which will assist the pathologist.

METHODS

Faster R-CNN[1] is state of the art in object localization and classification. It consists of two stages: A Region proposal network (RPN) and an object detection network (Fast R-CNN detector). The RPN takes a H&E image patch as input and outputs a set of rectangular object proposals, each with an objectness score. The object detection network then takes the region proposals and performs a region of interest (ROI) pooling operation and subsequently non-maximum suppression (NMS) with a chosen threshold to select only proposals with confidence greater than the chosen threshold. The object detection network contains regressor and classifier to regress the bounding box and classify the object in the bounding box. A multi-task loss function is used - cross entropy loss for classification and smooth L2 loss for regression.

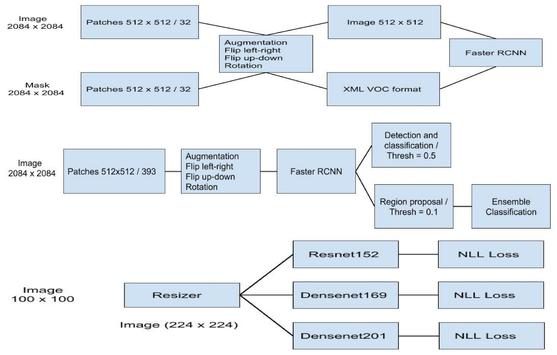


We have made use of Faster RCNN in two ways:

- Selecting the confidence threshold at which the F1-score is maximum.
- Keeping the confidence threshold to a minimum at which Recall is maximum.

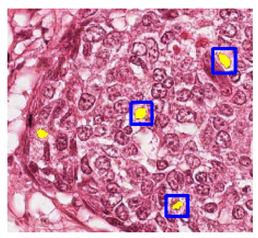
The former is a Faster RCNN-only pipeline, where the final outputs are predicted by the Faster RCNN Network, constrained by a chosen confidence threshold hyperparameter. The latter method is a two-stage pipeline - Faster RCNN Network constrained by a low confidence threshold, followed by an ensemble of state-of-the-art ImageNet classifiers like ResNet152, DenseNet169 and DenseNet201[2], which have additional residual and dense connections on top of a convolutional neural network. DenseNets have skip connections from any layer to every other layer, while a ResNet architecture contains a skip connection between each pair of successive layers. These auxiliary connections alleviate the vanishing gradient problem, strengthening feature reuse. The classifiers are initialized with ImageNet pre-trained weights, which are subsequently fine tuned using gradients obtained from negative log-likelihood loss.

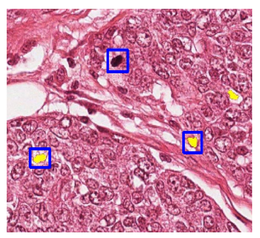
The dataset[3] is used from 2012 ICPR MITOSIS detection contest. The images in the dataset are taken from Aperio XT scanner, resolution of the scanner is 0.2456 µm per pixel. The HPF image has an area of 512 x 512 μm^2.The dataset consists of 35 train and 15 test images. The images are of dimension 2084 x 2084. Each image contains a random number of mitotic cells. The total number of mitotic cells in train, test images are 226 and 101 respectively.



RESULTS

Method	Precision	Recall	F1-Score
DeepDet	0.854	0.812	0.832
RRF	0.835	0.811	0.823
Our Model (Th = 0.5)	0.856	0.735	0.790
CasNN	0.804	0.772	0.788
HC + CNN	0.84	0.652	0.735
Our Model (RPN) (Th = 0.1) + Classifier	0.761	0.732	0.746
IPAL	0.698	0.74	0.718
SUTECH	0.70	0.72	0.709
NEC	0.75	0.59	0.659
Our Model (RPN) (Th = 0.1)	0.213	0.92	0.341





CONCLUSION

In this work, we have studied how state of the art classifiers and object detectors can be used in mitotic cell detection. In the future, we have planned to perform joint segmentation and classification task to get a better F1-score and also to extend the procedures to other publicly available datasets.

REFERENCES

1. *Ren, S et al. "Faster r-cnn:Towards real-time object detection with region proposal networks", IEEE TPAMI, June 2017.*
2. *Huang, G et al. "Densely connected convolutional networks", IEEE CVPR, July 2017.*
3. *Roux, L et al. "Mitosis detection in breast cancer histological images an icpr 2012 contest", JPI 2013.*