Cell Classification Framework using U-Net: Convolutional Networks for Cervix Cell Segmentation

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ABSTRACT

With the technological advancements in machine learning, it has become more prevalent to use learning techniques for clinical decision-making based on medical images. One of the state-of-the-art methods used for this purpose is Convolutional Neural Networks (CNN) for medical image segmentation and deep learning models for disease detection and classification. In this paper, we propose a framework for image segmentation using hierarchical CNNs to classify different types of cells using small frame images. This paper aims to generalize the segmentation of cancer cells, starting with cervix cancer. The first step of the framework is to achieve automatic nucleus and cell masking of the images using U-Net. The images are then segmented into "satisfactory" and "unsatisfactory" categories to determine whether these images can be used in our classification model. Using the hierarchical CNN, the satisfactory images are clustered based on cell types since the cell features that need to be considered vary between different cell types. Lastly, our classification model is trained with automatically segmented images to classify different cancer types based on cell images using various features, such as the area of the nucleus, the ratio of the nucleus area and cytoplasm area and the visual morphology of chromatin strands in the nucleus. To demonstrate the performance of the proposed framework, a labeled dataset, taken from the Detay Pathology and Cytology Laboratory, with over 100 images were used.
Keywords: Hierarchical CNN, U-NET, PAP Smear cells, segmentation, generalization.

1. INTRODUCTION

As technology improved, it became apparent that technological means can be used to make professionals' jobs easier. One group of these professionals is pathologists. As the imaging and data processing technology improved, characterization and classification of images in the medical field become more popular. One of these medical fields is cytology. In our paper, we focus on cervical cell abnormality detection. Cancer is a disease that happens because of the changes in the make-up of cells and that make cells grow uncontrollably. By using deep learning techniques, it is possible to distinguish cell types, cancer types and stages of cancer[1]. Our aim in this paper is to determine cancerous cells in the cervical region by not good quality images. We aim to achieve this result by determining realistic parameters. Typically, when convolution neural networks are used on an image we get single labeled output, but in medical images this is a problem. In medical images, we want to localize the labels, which means that pixels are labeled not the whole image. U-net is a deep-learning approach for problems such as detection, shape measurement and cell counting that can be used for not so good quality images[2]. Even though these algorithms require huge datasets, they perform close to human expertise. However, these studies do not cover all possible variations of the problem such as overlapping cell boundary problem, division stage cells cannot be distinguished as only one cell and many more. One of the other problems of the algorithms is that they are too specific, like they are this or not. We do not have a middle ground. Our aim is to distinguish cells according to their tendency to become cancerous. And if they are cancerous. In this way we can detect possible risky patients and solve their problems earlier.

This paper is utilized U-Net to detect and classify cervical cancer cells and improve the diagnosis process's accuracy. To detect cancerous cells, clinics use specialists like pathologists to inspect the cells and determine the cell features. The expertise and experience of the pathologists and the image quality affect the results' accuracy. In recent years, deep learning techniques have started to be used to classify images with greater accuracy.

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2. MATERIALS AND METHODS

2.1 Slide Preparation and Microscope Imaging

After sample of cells are gathered with soft brush, PAP smear, liquid-based solution is centrifuged on to slide. Then stained with Harris Hematoxylin, Orange G-6, eosin EA50 sequentially, slides are prepared.

2.2 Dataset Preparation

Slides are examined under Nikon Eclipse E200 microscope with 400x magnification. Tucsen IS-1000 microscopic imaging camera is used to get images. As the magnification increases the light captured by the sensor decreases, to compensate for this effect, ISO is increased to 800 manually. To retain the full size of the sensor and image quality, images are captured with a resolution of 3664 x 2740. Captured images are then cropped with 2740 x 2740 frame and masks are created with this dimension.

Different approaches and various datasets are used to train models. In the images, cell count and overlaps are configured in different setups and tested.

2.3 Data Preprocessing and Augmentation

The cropped images are made grayscale and then resized to 512x512 pixels with the algorithm written by us that enables to maintain the ratio between nucleus and cytoplasm area. This algorithm is also applied to masked images so that our input and output dimensions are the same. To augment the input data, *ImageGenarator()* function of Tensorflow Keras library is used. This *ImageGenerator()* function includes rotation (range 0.2), zooming (range 0.05), width-height shift (range 0.05 - range 0.005), shearing (range 0.05) and flipping. Nearest fill mode in our augmentation is used to maintain the quality of the images.

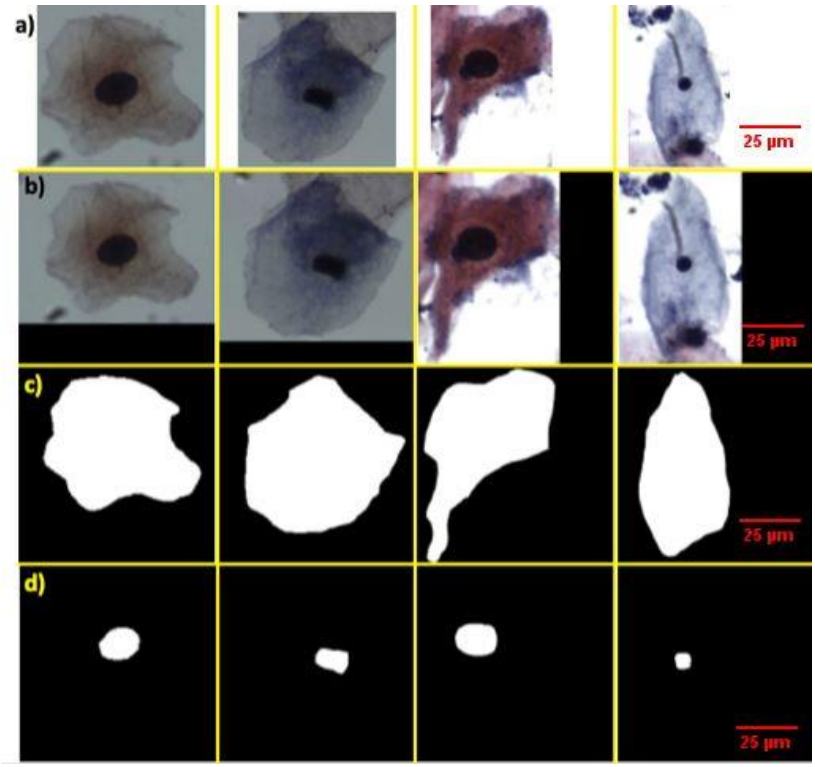

Figure 1. Image processing, a) cropped original images, b) resized images, c) cellular area, and d) area of their nucleus is presented. Scale bar is 25 micrometer long.

2.4 U-Net Model Training

Some changes are made to the previously implemented model to train the UNET model for segmentation. TIFF image format is used, and the software is run on a machine with Intel i7-7700HQ CPU, 16 GB RAM, NVIDIA GTX 1050 GPU. The operating system is Ubuntu 18.04, NVIDIA CUDA version 11.2 and cuDNN version 8.1.0 is used during model training.

2.5 Feature Extraction from Predicted Masks

To evaluate cell morphology, nucleus and cytoplasm dimensions are important metrics. Normal nucleus diameter is smaller compared to dysplasia occurred cell's nucleus. The ratio between the area of cytoplasm and nucleus is a determining factor of cell abnormality. After training the model, 50 images are used for prediction purposes. Algorithms for specific features like area and diameter are implemented since they are important metrics.

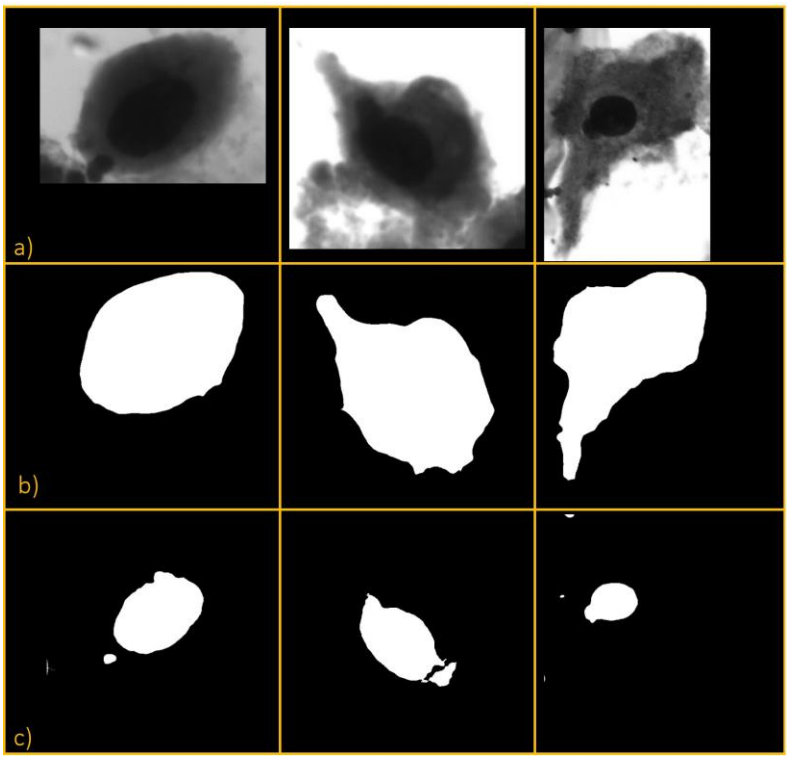

Figure 2. Prediction, a) cropped grayscale images, b) cellular area, and c) area of their nucleus is presented.

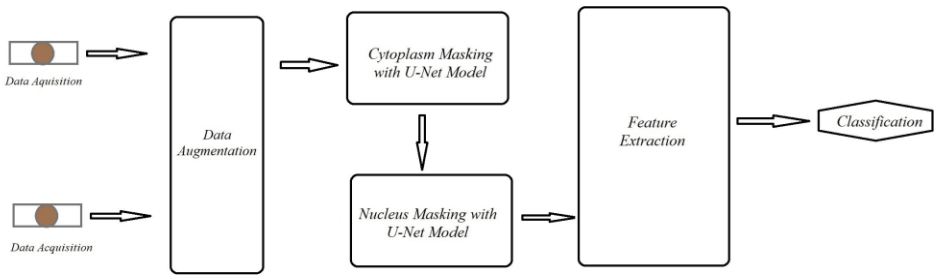

Figure 3. Process of the Paper

3. RESULTS

50 images are used in the testing for both cytoplasm and nucleus models. Images containing single cell and multiple nucleus can be found in an image. Hierarchical framework is used in this paper, Figure 3.

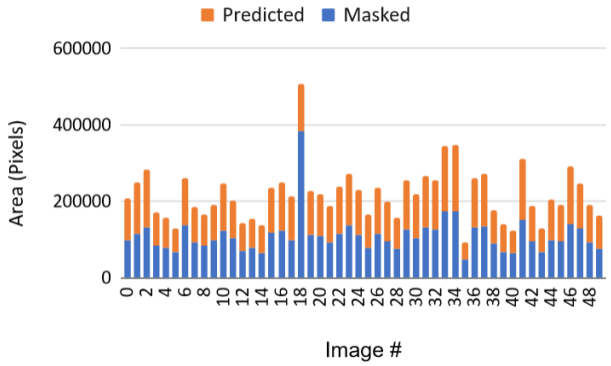

Figure 4. *Comparison of cell areas measured and masked*

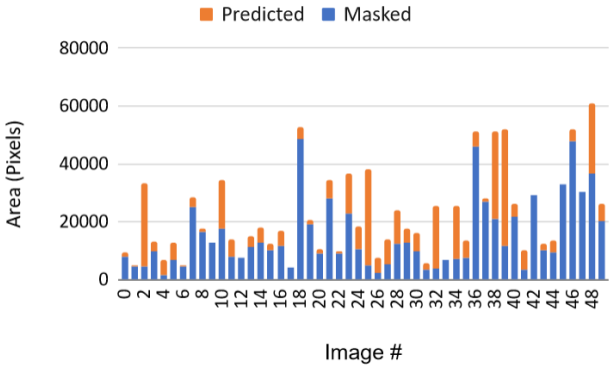

Figure 5. Comparison of nucleus areas measured and masked

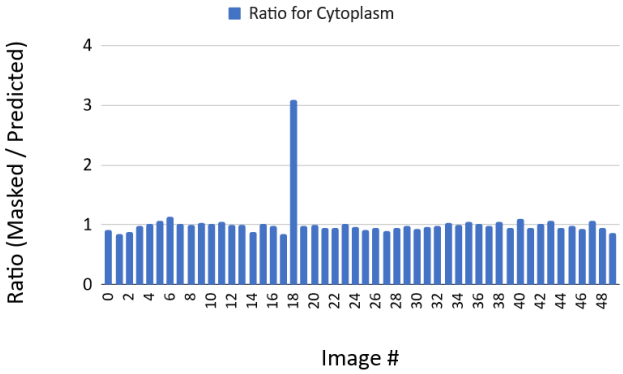

Figure 6. *Comparison of cytoplasm areas measured and masked, ratio*

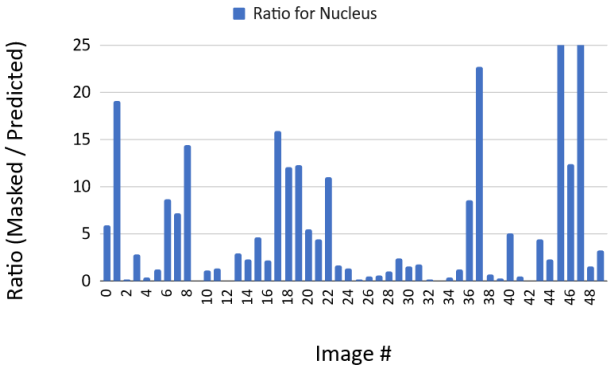

Figure 7. Comparison of nucleus areas measured and masked, ratio

The model for cytoplasm is trained with 26 images with multiple cells in it. Overlapping areas of different cells are masked as a part of only 1 cell, the cell they included is chosen by their color and border lines otherwise arbitrarily. Therefore, every cytoplasm in a mask image is segmented to establish no overlaps. It is trained with 410 step size for 9 epochs. Training accuracy is 0.974 and the loss is 0.026. The standard deviation of the area measurements is 0.3. The predictions of the model, by a rate of 98%, the area of a cytoplasm is lying within the ± 0.13 boundary, as depicted in Figure 6.

For the nucleus segmentation model, the training dataset contains 42 images, it is running with 60 step size for 1 epoch. The trained model has an accuracy of 0.9 and loss is considerably higher than the cytoplasm model with a value of 0.1. Dataset contains images that have both single and multiple nucleus. This increases variety for scale factor and reliability. Confidence intervals are exceeded for the measurements on predicted nucleus area, Figure 7.

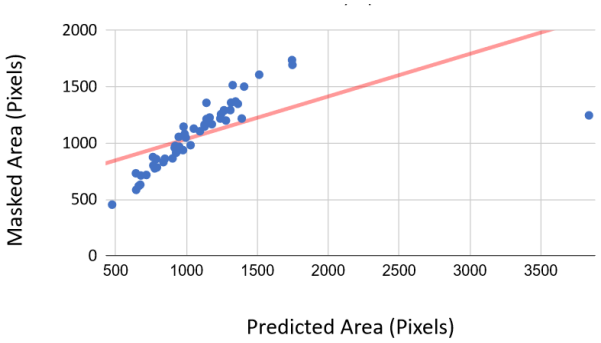

Figure 8. *Cytoplasm area predicted vs. masked, Regression Analysis*

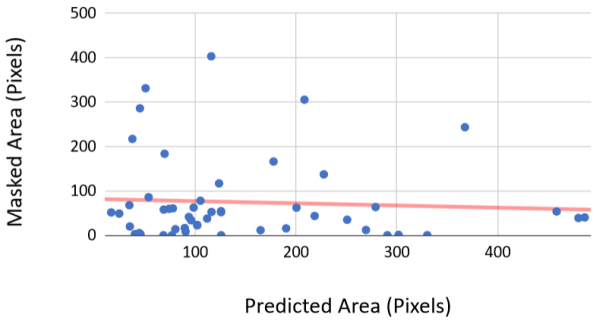

Figure 9. Nucleus area predicted vs. masked, Regression Analysis

Figure 8 and 9 and shows the correlation between predicted and actual area size of cytoplasm and nucleus, respectively. In the conducted regression analysis, R^2 is 0.398 for cytoplasm model and 0.004 for nucleus model. Cytoplasm segmenting model is far better than the nucleus model. The low accuracy of the nucleus prevents a solid classification for cervical cells. Columnar Epithelial cells are confusing, the reason being they are very similar cytoplasm/nucleus ratios. The approach lacks the precision needed when segmenting the nucleus.

4. CONCLUSION

In this paper, a method of classification and segmentation of cervical cells is implemented utilizing the U-Net deep learning model. 98% and 15% accuracies were reached for cytoplasm and nucleus respectively. The future work of the team is to enhance the performance of training model for nucleus segmentation with additional pre-processing methods and to enlarge the dataset and most importantly to adjust the optimal training values such as step size and epoch. Success for these steps will be followed by other tissues and samples to provide aid for pathologists on different diagnosis processes.

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