Estimating the Proliferation Indices from Microscopic Images

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Introduction

Every year there are an estimated 367,000 new cancer cases in the UK, this is about 1,000 every day [1]. A method in estimating the growth rate of a tumour is the proliferation index or the mitotic index, this involves staining a sample of patient's tumour cells and having clinicians count the amount of cells going under mitosis (cell division), this is then compared to the total number of cells under the microscope to give a proliferation index of the tumour growth rate.

This project is to develop a deep learning technique to aid the clinicians in the analyse of microscopic images of the tumour cells by producing a density estimate of cells going under mitosis and other cells. These will be used to help make treatment decisions of the patient.

Aim and Objectives

The main aim of this project is to develop a machine learning algorithm capable of counting the number of cells undergoing proliferation through the use of integrating density heatmaps to produce an estimation, similarly to the FCRN [2].

Objectives:

- Annotate and add dot point positions of stained cells undergoing proliferation
- Use annotated dot point positions to create density heatmaps by applying a gaussian filter
- Produce and develop a machine learning algorithm capable of estimating the number of proliferating cells
- Evaluate the model by integrating the predicted density heatmaps and comparing to the ground truth

Methodology

Toolsets Used

The machine environment used to achieve this project was python, with the main use of two libraries; TensorFlow and Keras. These Libraries allowed python to create and develop Neural Networks with ease for quick experimentation.

Evaluation Metrics

The metric used to evaluate the model where Mean Absolute Error (MAE) and Mean Squared Error (MSE). MAE is used to see the average number of cell difference between the ground truth and predicted. MSE is a measure of the quality of an estimator in a machine learning algorithm.

MAE:

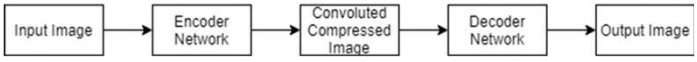
$$\varepsilon_{abs} = \frac{1}{N}\sum_{n=1}^{N}|y_n - \widehat{y_n}|$$

MSE:

$$\varepsilon_{sqr} = \frac{1}{N}\sum_{n=1}^{N}(y_n - \widehat{y_n})^2$$

Machine Learning Design

The model used to achieve the projects goal is a Convolutional Neural Network Autoencoder



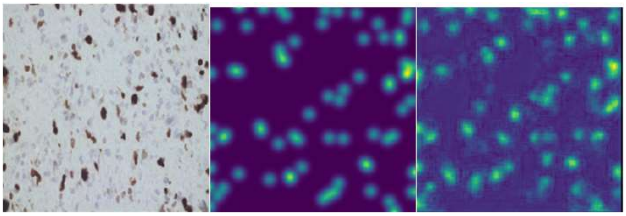
The Architecture of the model consist of an encoder block made up of three blocks of Convolution and Max pooling with increasing number of filters, from 32, 64, 128 then 512 filters. After this the compressed convoluted image is decoded by up sampling and convoluting back from 512 to 128, 64 then 32 filters, lastly the finally output is convoluted to generate a density heatmap of the inputted image.

Results

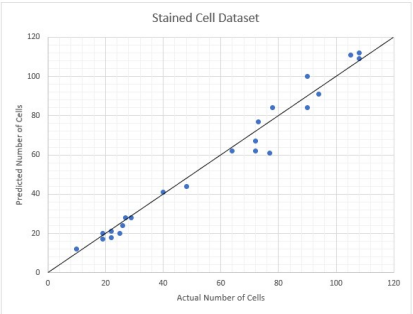
The results of the model are as follows

Mean Absolute Error	Mean Squared Error
4.217391	30.82609

The mean absolute error shows that on average it overestimates the number of cells in an image by 4 cells.



From left to right is the original input image, middle the ground truth of the density heat map and lastly the predicted heatmap. A problem with the predicted heatmaps is the noisy background which affects the integration of to produce an estimation.



The Graph shows the predicted estimations against the ground truth.

Conclusion

The project has developed a machine learning algorithm capable of estimating the number of proliferating cells in a microscopic image. Though there is room for improvement, it is a good foundation and start for further improvement with the use of more and better annotated datasets.

References

[1] (2020) Cancer Research UK website. [Online]. Available: https://www.cancerresearchuk.org/health-professional/cancer-statistics-for-the-uk#heading-Zero

[2] Weidi, X., Noble, J. A., & Zisserman, A. (2015). Microscopy cell counting with fully convolutional regression networks. In 1st Deep Learning Workshop, Medical Image Computing and Computer-Assisted Intervention (MICCAI).