Cell Segmentation Challenge - Project Report

CM2003 Deep Learning Methods for Medical Image Analysis.
A hands-on Course

October 22, 2019

By: Blanca Cabrera Gil & Laila Niazy

1 Introduction

Fluorescence microscopy is widely used for analyzing cellular processes due to the possibility of studying functional processes and morphological aspects of living cells. The need for accurate and efficient cell analysis has lead to the development of automated algorithms to accelerate the task of segmenting and analyzing the cells in microscopy images. Cell characterization in cell cultures is highly used in a wide variety of domains such as cancer research and drug discovery [7]. Since this task is of such high importance and is critical, there has been a lot of ongoing research for an automatic and reliable method to solve it.
Given the need to benchmark cell segmentation and tracking techniques, IEEE International Symposium on Biomedical Imaging (ISBI) launched in 2013 the first edition of Cell Tracking Challenge (CTC). The main goal of CTC is to objectively compare and evaluate state-of-the-art whole-cell and nucleus segmentation and tracking methods, using real and time-lapse microscopy videos of cells and nuclei moving in realistic environments [1]. Along this project the challenge of nuclei segmentation for the *Glioblastoma-astrocytoma U373 cells on a polyacrylamide substrate* is addressed. The database contains 34 images and its corresponding 34 ground truth masks.

2 Related Work

The challenge of biomedical image segmentation is approached in the original U-Net paper [4]. The authors present a U-shaped neural network architecture which relies heavily on data augmentation to use the available annotated samples in a more efficient manner. An improvement of U-net is presented in [5] under the name of Qip-Net. Qip-Net is a network constructed based on regions with convolutional neural networks. The architectures is proposed as an automated method to detect cell nucleus under varius conditions by using deep learning and stochastic processing method. Moreover, Qip-Net was proved to be much faster to compute in CPU than U-Net. Another improvement to the original U-Net has been published by [3]. Their work propose the R2U-Net regression model, which is a deep convolutional neural network approach that each cell is represented with a Gaussian density. The R2U-Net model estimates the Gaussian densities from the input samples instead of computing the class or pixel level probability. This method sowed a 3% better F1-score than existing models. A different network architecture is presented in [6], where the challenge of cell classification and segmentation is addressed simultaneously with the same network. Their architecture is based on three branches: 1) separates the nuclear pixels from the background, 2) regresses the horizontal and vertical distances of nuclear pixels to their centers of mass, and 3) determines the type of each nucleus. On the other hand, [2] proposes a method combining CNN with watershed to segment cell nuclei in cytological images. In the first part of their algorithm CNNs are employed to obtain a precise nuclei mask, while in the second part watershed is applied to separate overlapping nuclei.

3 Methods

To implement all the methods stated in this section, Python was used as programming language and Keras with Tensorflow backend was used as Deep Learning library to build the networks. In order to assess which network architecture would better fit our task, different experiments have been conducted. All of them are based on the original U-Net architecture. We tested the original U-Net, a weighted U-Net, a U-Net with LSTM convolution and a weighted U-Net with LSTM convolution. In all of our tests the accuracy score was the jaccard coefficient. For the weighted version of the networks, weighted binary cross-entropy was used as loss function, while for the not weighted versions regular binary cross-entropy is used.
The original U-Net configuration consists of a U-shaped structure. The first part of the architecture is the contracting path. This is the part in charge of producing the dimensionality reduction from input data and extracting the important features. The contracted path is then combined with an expanding path containing a large number of feature channels, allowing the network to propagate the context information to higher resolution layers. The symmetry between the contracting and the expansion path is what yields the U-shape to the network [4]. The second configuration was the same U-Net architecture but using weighted binary cross-entropy. For it, the weight maps of each image were extracted from the given ground truth masks. To obtain the weight maps the eroded and the dilated versions of ground truth masks were subtracted. By using the weight maps, the network pays more attention to where the contours of the cells are located, achieving better segmentation scores in theory. The third configuration consisted in using convolutional LSTM layers along the expansion path of the U-Net architecture. By using this modification, the architecture obtains certain memory of previous data samples and its corresponding predictions. This should help to increase the accuracy of future predictions. Finally, the fourth configuration consisted in a mixture of weighted U-Net with convolutional LSTM layers in the expansion path. To compare all the approaches, we used the same parameter configurations for all and they are stated in Table 1 are used.

Base	Batch Size	Size	Epochs	BW	DA	BN	Optimizer
32	2	128x128	1000	False	True	True	Adam

Table 1: Parameter configuration for the tests. BW refers to the usage of balanced weights, DA means the usage of Data Augmentation during training and BN stands for Batch Normalization.

In an early stage of the project, cross-validation was used to improve the generalization capability of the model as the size of the dataset is quite small. However, considering the time-benefit trade-off of running several parameter configurations for each cross-validation fold, it was agreed on not to use it.
After obtaining the results from the first test, the architecture that gave the best jaccard coefficient was selected, which is the model using U-Net with weight maps. In order

to optimize its performance further tests were implemented. The different parameter configurations we tested are the ones described below:

- **Base**: 16, 32, 64
- **Batch Normalization**: True or False
- **Optimizers**: Adam, SGD, RMSprop, Adagrad, Adadelta
- **Epochs**: 1000 - 5000
- **Learning Rate**: 0.1, 0.01, 0.001, 0.0001, 0.00001
- **Class Weights**: Balanced or Automatic to account for the class imbalance problem

4 Results & Conclusion

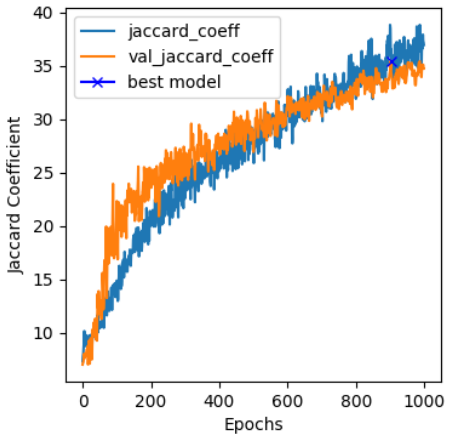
The best performing configuration for the cell segmentation task was given by the results obtained from running the 4 different architectures with the parameter configuration stated in Table 1. The resulting jaccard coefficient evolution and binary cross-entropy loss learning curves can be found in Fig. 1 and 2 respectively. In these figures it can be observed that the network that obtains the highest Jaccard coefficient is the Weighted U-Net. Even though its learning is a bit more unstable than the learning of the non-weighted versions, its final accuracy score after 1000 epochs is a 30% higher. When comparing the weighted U-Net accuracy score to the one of the weighted U-Net with LSTM, the first one obtained a jaccard coefficient which was 10% better than the one from the weighted LSTM architecture.

In the next step, we took the Weighted U-Net and tested the various configurations above to optimized it. The parameters that gave us the best results are listed in Table 2. Further, the highest jaccard accuracy and the lowest loss value that we obtained can be seen in Fig.1a and 3a.

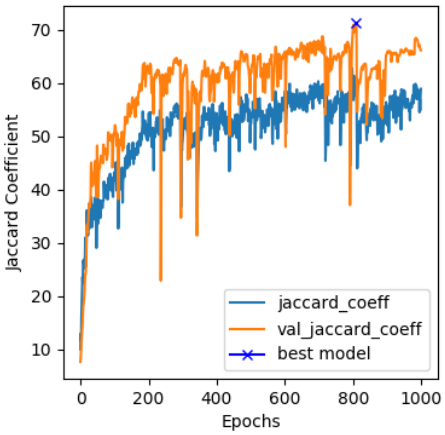
Base	Batch Size	Size	Epochs	BW	DA	BN	Optimizer
64	2	128x128	5000	True	True	False	RMSprop

Table 2: The best parameter configuration for the tests for the weighted U-Net

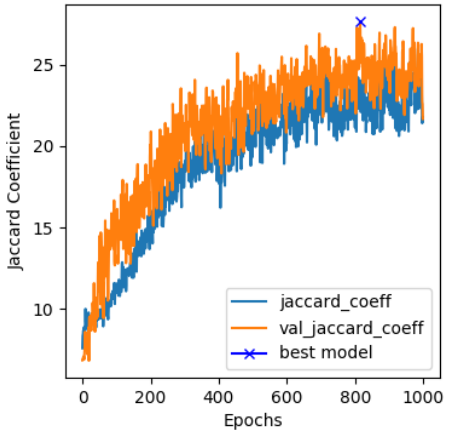
Moreover, we compared our results with the best results achieved in the challenge, thee best achieved jaccard accuracies and ours can be found in Table 3. The best results was achieved using also U-Net and loss-weight maps. However, they trained their algorithm for longer and used a higher resolution images, which we couldn't use due to the server capacity. The second best result used Markov chain Monte Carlo algorithm with temporal feedback, while the third one used again U-Net with maps. The biggest difference between our approach and the first and the third is the way of generating the weight maps. Overall we achieved a respectable result of 0.757.



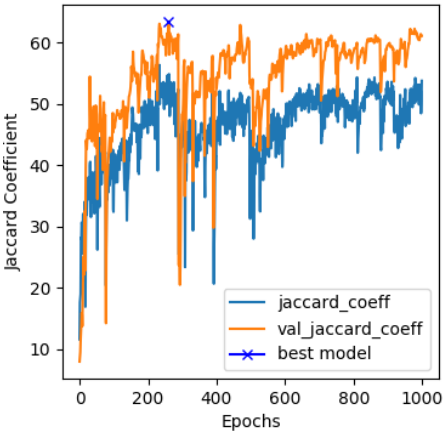
(a) original U-Net.



(b) Weighted U-Net.



(c) LSTM U-Net.

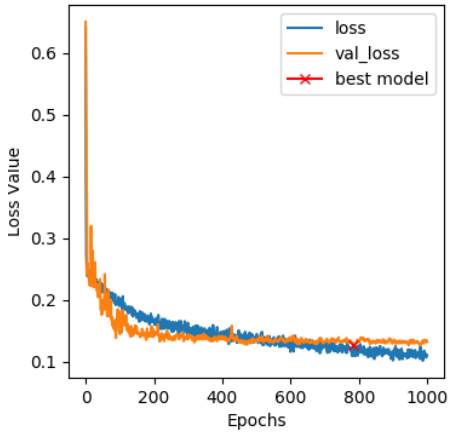


(d) Weighted LSTM U-Net

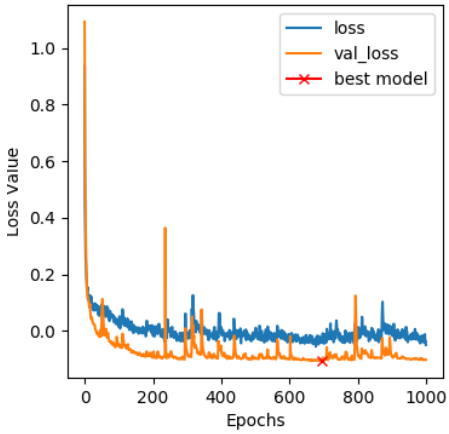
Figure 1: Comparison of Jaccard accuracy score for the different architectures

5 Future Work

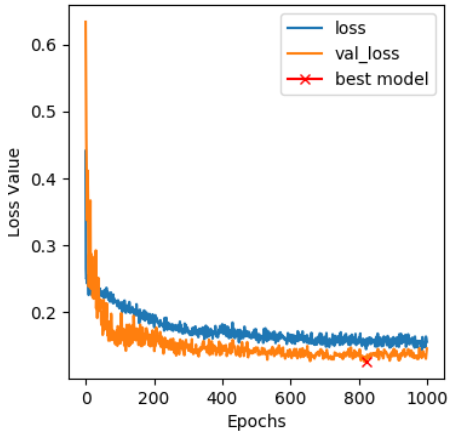
The main focus of this project was to reproduce the same or similar results to the ones obtained by the team (FR-Fa-GE), which was the winner of the Cell Segmentation Challenge for *Glioblastoma-astrocytoma U373 cells* database. However, the team that obtained the second position, CUVT-CZ, used a model defined implicitly in terms of a Markov chain Monte Carlo algorithm that contained temporal feedback allowing the detector to correct errors from the information obtained from neighboring frames. This method is very different from the weighted U-Net used by FR-Fa-GE, yet, the final jaccard score was very similar. A way to improve the obtained results would be to explore the possibility of merging the methods used by FR-Fa-GE and CUVT-CZ.



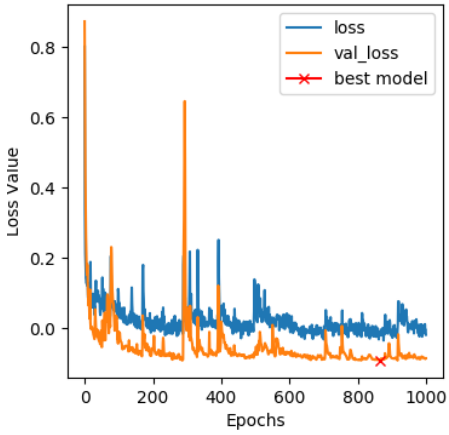
(a) original U-Net.



(b) Weighted U-Net.

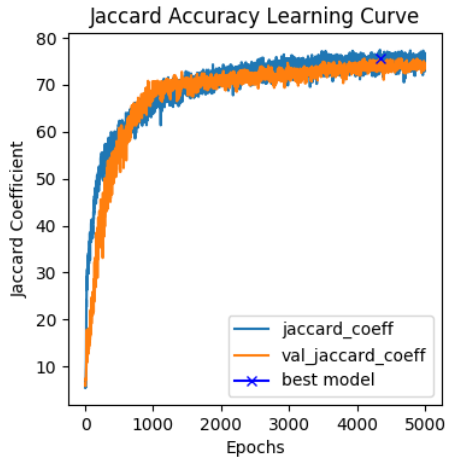


(c) LSTM U-Net.

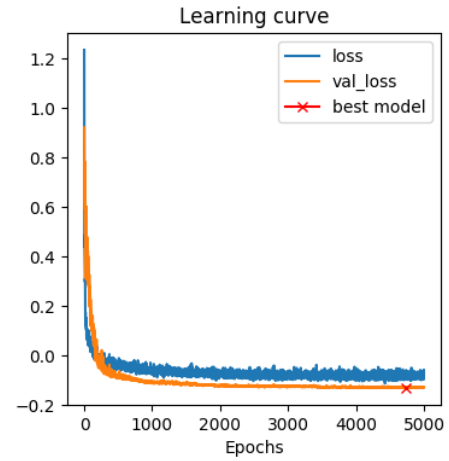


(d) Weighted LSTM U-Net

Figure 2: Comparison of binary cross-entropy loss score for the different architectures



(a) The jaccard accuracy for the best weighted U-Net configuration



(b) The loss function for the best weighted U-Net configuration

Team	Jaccard Coefficient
FR-Fa-GE	0.924
CVUT-CZ	0.922
FR-Ro-GE	0.920
Us	0.757

Table 3: Benchmark table with the best scores of the state-of-the-art techniques from the Cell Segmentation Challenge.

Bibliography

[1] Cell tracking challenge, Oct 2019. URL: http://celltrackingchallenge.net/.

[2] Marcin Skobel Józef Korbicz Roman Monczak Marek Kowal, Michał Żejmo. Cell nuclei segmentation in cytological images using convolutional neural network and seeded watershed algorithm. *Journal of Digital Imaging*, page 1–12, June 2019.

[3] Tarek M. Taha Md Zahangir Alom, Chris Yakopcic and Vijayan K. Asari. Microscopic nuclei classification, segmentation and detection with improved deep convolutional neural network (dcnn) approaches. *Medical Imaging 2019: Digital Pathology;*, March 2019.

[4] Philipp Fischer Thomas Brox Olaf Ronneberger. U-net: Convolutional networks for biomedical image segmentation. *International Conference on Medical Image Computing and Computer-Assisted Intervention*, pages 234–241, Nov 2015.

[5] Hui Zhang Xuyang Shi Qing Wu, Shiyu Xu. Cell nuclei segmentation in divergent images using deep learning and stochastic processing. *Medical Imaging 2019: Digital Pathology;*, March 2019.

[6] Shan E Ahmed Raza Ayesha Azam Yee Wah Tsang Jin Tae Kwak Simon Graham, Quoc Dang Vu and Nasir Rajpoo. Hover-net: Simultaneous segmentation and classification of nuclei in multi-tissue histology images. June 2019.

[7] Robert Graves Will Marshall Mirabela Rusu Yousef Al-Kofahi, Alla Zaltsman. A deep learning-based algorithm for 2-d cell segmentation in microscopy images. *BMC Bioinformatics volume*, 19(365), 2018.