Semester report

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Ph.D. Thesis title: Image-based single cell isolation with deep learning

Introduction

My current research at the Eötvös Loránd University has focused on single-cell isolation of yeast and unicellular parasites. In this project, one of the main objectives is to develop hardware and software tools to isolate *T brucei* cells for subsequent DNA/RNA sequencing. Further goal of the project is to establish different strategies to isolate cells by an automated micropipette from agar plates and, if possible, from microfluidic devices with the aim to maintain single-cell lineages separated for further downstream analysis (e.g. next generation sequencing). Therefore, it is important to have access to a fully automated micropipette with a precision of less than one nanoliter which improves the efficiency of the imaging-based single-cell isolation to above 90%. This improvement is crucial when sorting rare or precious cells, especially in medical applications.

Artificial Intelligence (AI) has had a significant impact on every research area. AI has been used to develop and advance numerous fields and industries including healthcare. Utilizing AI algorithms is a major objective of our project. Nowadays, many biological applications require the segmentation of the image of single-cells in microscopic images. Advances in deep learning have positioned neural networks as a powerful alternative to traditional approaches such as manual and algorithmic-based segmentation. In this project, we aim to develop a deep learning-based segmentation method which can precisely segment cells from a wide range of an image.

Description of my current research

My research in the CellSorter lab aims the robotic single-cell isolation of yeast and unicellular parasites. For the single cell image segmentation, I studied the recent deep learning-based approaches and publications such as Cellpose, nnU-Net, U-Net, Mask-RCNN that achieved state-of-the-art results.

I was introduced to fluorescent microscopes and learned how to work with them to be able to collect a large number of high-quality images for feeding the implemented neural network. I could capture more than 100 images in a single run to build a starting dataset using the provided Zeiss microscope.

Implementation and research results

I implemented the U-Net architecture from scratch. U-Net is a Convolutional Neural Network (CNN) for segmentation and classification tasks in biomedical imaging. U-Net provides a significant boost to segmentation performance and has now become the template for many modern segmentation models. The U-Net architecture consists of three sections: The contraction, The bottleneck, and the expansion section. The contraction section is made of many contraction blocks. Each block takes an input applies two 3X3 convolution layers followed by a 2X2 max pooling layer. The number of kernels or feature maps after each block doubles so that architecture can learn the complex structures effectively. The bottommost layer mediates between the contraction layer and the expansion layer. It uses two 3X3 CNN layers followed by a 2X2 up convolution layer. The general structure of the implemented U-Net is demonstrated bellow.

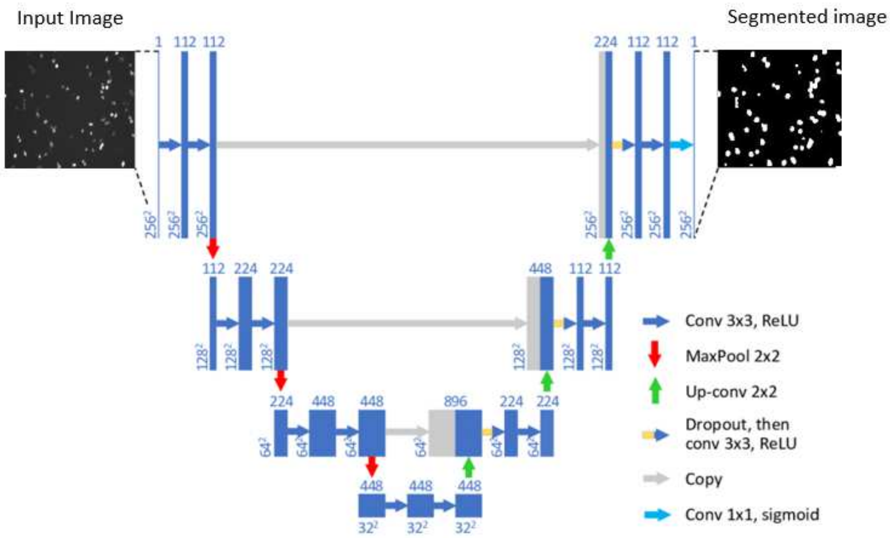

Figure 1. Architecture of the implemented U-Net neural network

One of the most important parts of our project is to generate mask images to help the neural networks to learn features. Therefore, I wrote a program to generate mask images based on the given images. Some of the provided masks are shown in Figure 2.

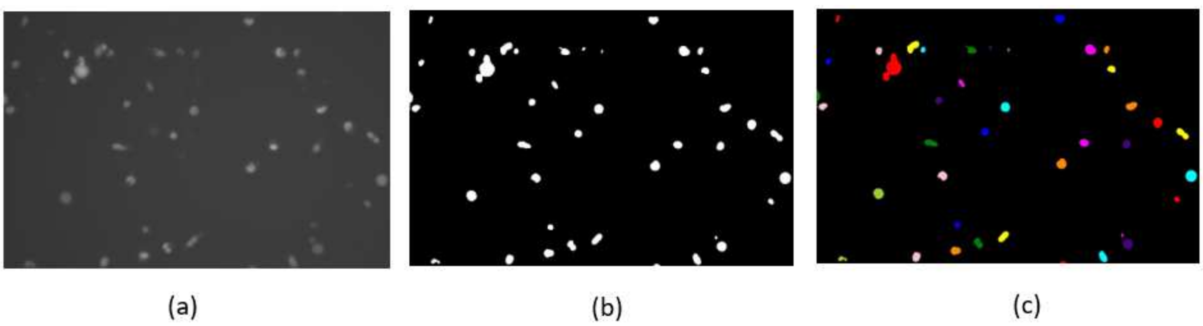

Figure 2. Generated mask images to feed the network. (a) an input image to the program to create mask image, (b) a generated gray scale mask image (c) a generated colorful mask image.

We aim to improve the precision and the accuracy of segmenting of cell images. Thus, we are going to develop a software to achieve better segmentation results. So far, the output of our network for cell image segmentation is illustrated in Figure 3.

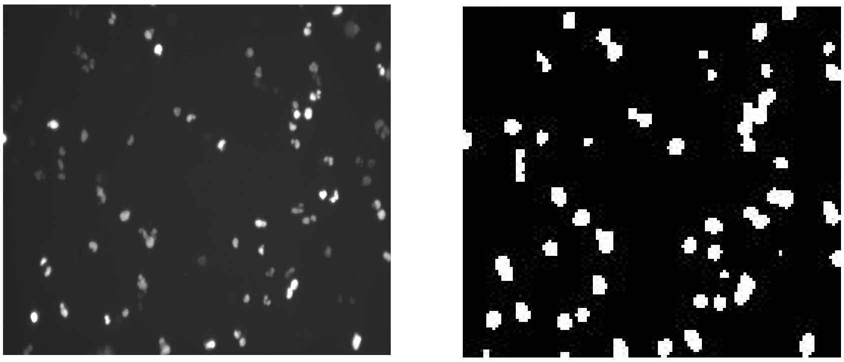

Figure 3. Result of cell image segmentation by implementing the U-Net neural network.

Study activities

I completed the course with the title "Adatbányászat és gépi tanulás" Data mining and machine learning (Neptun code: FIZ/3/084). My grade was: 'Good'.

During the semester, I participated in weekly lectures organized by the Ludwig Maximilian University of Munich in the cell2cell ITN: https://cell2cell.eu

In these thirteen lectures professors from different universities including Oxford, LMU, Radboud University gave presentations of their current research and state of the art in single cell science. Moreover, I participated in a virtual lecture about recent advances in single-cell omics organized by SCOG MANAGEMENT TEAM: https://www.singlecell.de/index.php/events/scog-vls-emmanuel-saliba/