Automated Segmentation of Epithelial Tissue Using Cycle-Consistent Generative Adversarial Networks

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Abstract

A central problem in biomedical imaging is the preparation of images for further quantitative analysis via automated image segmentation. Recently, fully convolutional neural networks, such as the U-Net were applied successfully in a variety segmentation tasks. A downside of this approach is the requirement for a large amount of well-prepared training samples, consisting of image - ground truth mask pairs. Since these have to be prepared for each experiment by hand this task can be very costly and time-consuming. Here, we present a segmentation method based on cycle consistent generative adversarial networks, which can be trained even in absence of prepared image - mask pairs. We show that it successfully performs image segmentation tasks on samples with substantial defects and even generalises well to different tissue types.

1 Introduction

Mechanically active tissues, force generating and proliferating cell groups, and topological tissue rearrangement play a critical role for a wide range of biomedical research challenges. Analyzing such dynamical tissues is of central importance to advance regenerative medicine and stem cell technologies, to understand cancer progression and treatment and for fundamental research into organogenesis and embryo development. Over the past decade, the rapid advancement of photonic imaging technologies has made it relatively easy to collect time lapse imaging data sets of massive size, recording tissue dynamics and rearrangement in vivo over extended periods of time. A prominent bottleneck in the computational analysis of such large-scale imaging datasets is the automated segmentation of cell shapes to quantify tissue topology, geometry and dynamics. Especially the segmentation of images with lower quality remains challenging.

Recently, deep convolutional neural networks were applied successfully in a vast variety of visual recognition tasks, including automatic biomedical image segmentation. In general, their performance is superior to rule-based methods. One drawback of these models, however, is the necessity to prepare a well-suited dataset on which the network can be trained. Generating hand-labeled datasets of image - ground truth mask pairs is time-consuming and thus represents an expensive bottleneck. Due to this training bottleneck many practitioners still use rule-based methods instead of machine learning techniques. Moreover, even if extensive training data is available, the performance of these systems degrades significantly when they are applied to test data that differ from the training data, for example, due to variations in experimental protocols. Furthermore, pixel by pixel classifiers based on deep convolutional architectures can perform poorly on image data with substantial defects that have been labeled incompletely due to bleaching and label failure.

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To overcome these problems we propose to employ a segmentation method based on cycle-consistent generative adversarial networks (Cycle-GANs) that can be trained even in absence of prepared image - mask pairs [1]. We show that this model performs competitively on standard segmentation tasks even when trained on just a few target samples. In addition, our model generalises well to test data differing from the training data and successfully performs image segmentation tasks on samples with substantial defects. Here, we focus on the segmentation of epithelial tissue from Drosophila Melanogaster (fruit fly) embryos. The specific cell tissue type is called Amnioserosa, an oval shaped tissue that appears by the end of gastrulation.

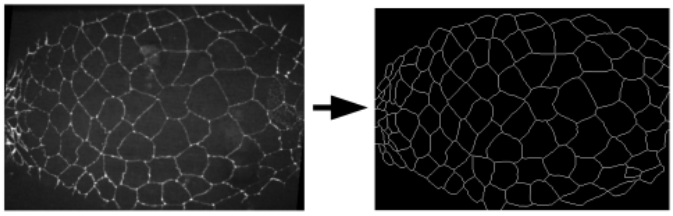


Figure 1: Sample segmentation of an epithelial tissue called Amnioserosa. To assess quantities like cell area or junction lengths a skeletonized version of the microscopy image, i.e. a segmentation, is needed that only contains the cell outlines.

2 Methods and Dataset

Our proposed segmentation method is based on the Cycle-GAN [1]. The model consists of two generators, one that maps from the image to the segmentation domain and a second that maps from the segmentation to the image domain, and two associated adversarial discriminators. A so-called cycle-consistency loss regularises the mapping and enforces a relationship between an image in the segmentation and the image domain.

The training dataset consisted of 112 unpaired images of Amnioserosa tissue and ground truth segmentation images, randomly chosen from a pool of ten Amnioserosa movies. For evaluation a movie with good contrast and high signal to noise ratio and a second movie with low contrast and discontinuously labeled cell contacts were excluded from the training data, see figure 2. The low contrast movie was chosen to represent a challenging example where rule-based methods might come to their limitations. Segmentation accuracy was measured in terms of the total number of i.) correctly identified cells (True Positives), ii.) cells that have been segmented although there is no corresponding cell in the ground truth (False Positives) and iii.) cells that appear in the ground truth but not in the segmentation (False Negatives)

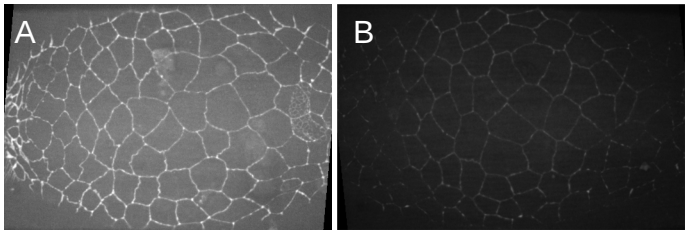
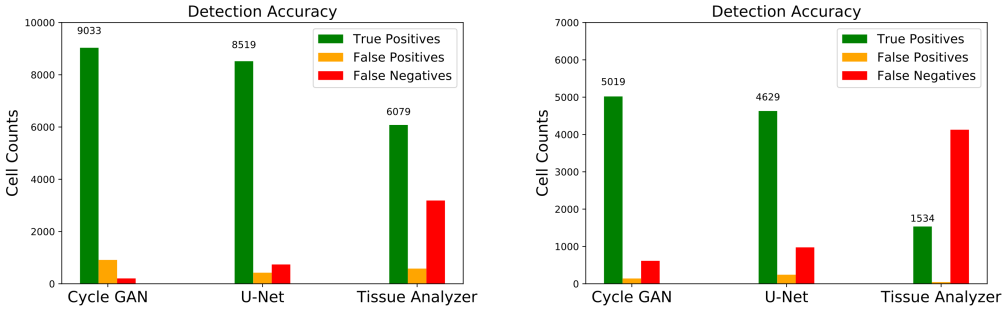


Figure 2: Two movies of differing image quality were chosen to evaluate the segmentation accuracy of the different approaches.

3 Results

For the evaluation, we have compared the performances of the Cycle-GAN, the U-Net, a well-established method based on a fully convolutional network with pixel by pixel classification [2] and the Tissue Analyzer, a method based on the watershed algorithm [3], see figure 3. While the deep learning based methods clearly outperform the rule-based approach in both examples, it is noteworthy

that the accuracy of the Cycle-GAN is at least comparable to the U-Net, which has to be trained on image-mask pairs.



high quality movie low quality movie

Figure 3: Segmentation accuracy for the two Amnioserosa movies. Both deep learning methods outperform the rule-based approach. The Cycle-GAN approach achieves an accuracy that is at least comparable to the U-Net but without the need for hand-labeled image-ground truth pairs. The watershed approach clearly breaks down for the low quality movie.

To show the domain adaptation capabilities of the Cycle-GAN framework, we have tested its segmentation performance on different tissue types that are qualitatively different from the tissue on which the network was trained, see figure 4.

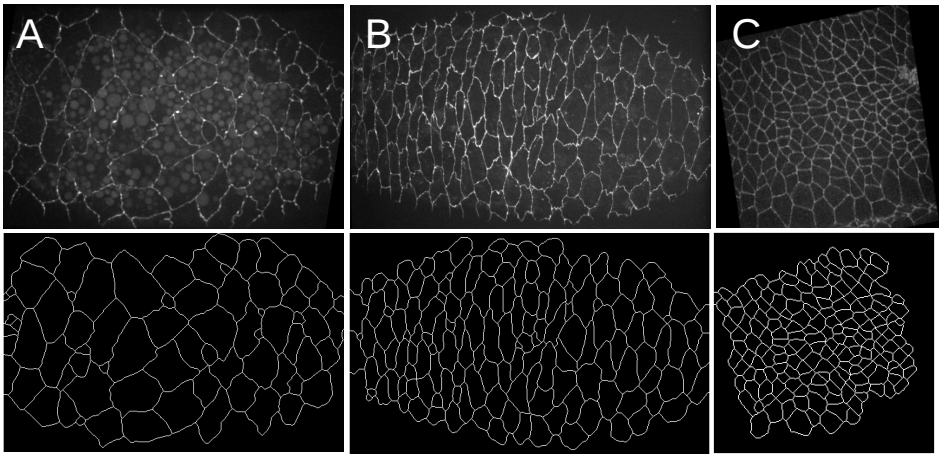


Figure 4: Cycle-GAN segmentations of sample tissues that are qualitatively different than the training data. **A)** TMC Amnioserosa mutant, where cells are bigger and many yolk granules wandered into focus that can make segmenation very challenging. **B)** Xit Amnioserosa mutant, which shows a different phenotype with longer stretched cells. **C)** Epithelial tissue from germband, which exemplifies a completely different tissue type.

References

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[2] Ronneberger O., Fischer P., Brox T. (2015) U-net: Convolutional networks for biomedical image segmentation. *International Conference on Medical Image Computing and Computer-Assisted Intervention, pp. 234-241* Springer

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