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Review of PhD thesis: Cell segmentation from wide-field light microscopy images using CNNs presented by Ali Ghaznavi

Digital image processing has become increasingly widespread in biological research as high throughput and high-content microscopy and screening generate significant quantities of complex fine-grained cellular images. In clinical applications of imaging techniques computer-aided digital pathology plays an increasingly important role in interpreting results from imaging techniques and thus understanding, diagnosing and treating various diseases. In light microscopy image processing made a dramatic increase in resolution and detection sensitivity of even single molecules in cellular processes possible. But these methods referred mainly to fluorescence microscopy and is based on specific staining of selected molecules or molecular structures. So specific staining of the cell membrane facilitated segmentation procedures as recognizing the different cells in an image. This is, however, not possible in wide-field optical microscopy, although this simple form of light microscopy is of widespread use in biology and medicine. The availability of efficient and reliable outcome of segmentation and detection is particularly important for any computer assisted interpretation of biological or medical images. The need of such fast and reliable methods initiated considerable research mainly based on traditional image processing or on more modern basic machine learning concepts mainly based on neural networks. Nevertheless, the outcome of any of these attempts was far from satisfactory, especially assuming that it could be used as base for a medical diagnosis.

With the development of novel artificial intelligence methods some 10 years ago also program architectures became available specific to resolve these problems. That is for instance U-NET implementing a convolutional neural network CNN that was developed for biomedical image segmentation. These methods were shown to gain reliable results but only for high computational costs and high expenses for selecting data and training of the models mostly not available in average laboratories.

On this background the main objectives of the thesis are clearly defined: on the one hand side a most accurate and computationally reasonable approach based on such deep learning methods should be implemented and on the other hand side a specific application of multi-class cell segmentation to classify living cells according to the life cycle phases should demonstrate the successful applicability of the concept. These are important questions and this research is thus best suited for a dissertation work.

It seems to me, that the experimental setup especially the use of a telecentric optics in the microscope, is crucial for the success of the mathematical methods applied. It remains unclear to me, if this experimental and technological issue is also one point within the developments reached within the thesis or it was already purported by the specially designed instrument used.

The experimental setup of the used cell line and their observation is straight forward and appropriate for a basic initial research. The selection of different computational models for comparison is clearly described and motivated and transparent. This also refers to the description of image calibration, training systems and the presentation of the segmentation results. Positive and less successful outcome is clearly visualized and thus understandable for the reader. The comparison of the results for the use of the different computational models is clearly compared and transparent.

Implementation and results of the work are clearly summarized and lead to a significant gain of knowledge. This positive evaluation of the work is also supported by the list of three scientific papers already presented to the scientific community.

In total, I rate the presented work as an important contribution to the use of AI based cell segmentation concepts in optical microscopy which promotes their use in biological and medical research.

Based on this I recommend the thesis with the title ***Cell segmentation from wide-field light microscopy images using CNNs*** presented by ***Ali Ghaznavi*** to be defended.

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