

DEEP LEARNING-BASED SEMANTIC SEGMENTATION OF CELLS IN FLUORESCENCE MICROSCOPY IMAGES FOR CYTOTOXICITY ANALYSIS

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ABSTRACT

Accurate segmentation of cellular structures is essential for the automated investigation of drug-induced alterations in cytotoxicity analysis. The morphological variations in healthy and toxic images pose a significant challenge in segmenting cell structures. In this study, a semantic segmentation network is used to effectively delineate the structure of cell nuclei in healthy and toxic conditions. For this, fluorescence microscopic images of healthy (drug-untreated) and toxic (drug-treated) HL1 cells are considered. Input images are preprocessed and are fed as input to a customized Convolutional Neural Network to generate pixel labels. The model is trained using underlying semantics-based pixel labels for healthy, toxic, and combined images. The performance of the network in segmenting healthy and toxic cell structures is evaluated using Mean Intersection Over Union and Boundary F1 scores for respective class labels. Results indicate that the proposed approach is able to segment cell structures. The network model yields a Mean IOU of greater than 90% and BF1 scores greater than 95% for healthy, toxic, and combined classes. The model performance metrics are found to be higher for toxic conditions as compared to the healthy class. This study could be employed as a cell localization method for analyzing the cytotoxic effects of different drugs during their development process.

Keywords: Fluorescence microscopy, Deep learning, Semantic segmentation, Cytotoxicity, Drug, Cell structures.

INTRODUCTION

Cytotoxicity is defined as toxic effects that are caused by materials such as drugs, immune cells, pathogens, and stress factors causing cell damage or death of living cells. The affected cells undergo morphological changes which include fragmentation of nuclei, shrinkage of cellular structures, loss of membrane integrity, leakage of cell content, membrane blebbing, and swollen nuclei [1]. Cytotoxicity testing is the main requirement of all important standards for the biological evaluation of medical devices and helps in characterizing the cellular dynamics in normal and toxic conditions [2]. High throughput cytotoxicity and proliferation assays are used in drug discovery, as toxicity is the major cause of failure in that process [3]. Primarily, to analyze cytotoxicity, cell imaging techniques such as fluorescence microscopy with conventional cytotoxicity are used as it aids in visualizing cell structures [4].

Individual cells in different stages of the cell cycle and the influence of certain drugs were reported to induce variations in intensity, morphology, and texture [5-6]. Normal cells appear to have lower intensity with higher confluence, regular shape with intact membranes, and normal adherent morphology [7].