Classification of Cell Fates with Support Vector Machine Learning

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Abstract. In human mesenchymal stem cells the envelope surrounding the nucleus, as visualized by the nuclear lamina, has a round and flat shape. The lamina structure is considerably deformed after activation of cell death (apoptosis). The spatial organization of the lamina is the initial structural change found after activation of the apoptotic pathway, therefore can be used as a marker to identify cells activated for apoptosis. Here we investigated whether the spatial changes in lamina spatial organization can be recognized by machine learning algorithms to classify normal and apoptotic cells. Classical machine learning algorithms were applied to classification of $3D$ image sections of nuclear lamina proteins, taken from normal and apoptotic cells. We found that the Evolutionary-optimized Support Vector Machine (SVM) algorithm succeeded in the classification of normal and apoptotic cells in a highly satisfying result.

This is the first time that cells are classified based on lamina spatial organization using the machine learning approach. We suggest that this approach can be used for diagnostic applications to classify normal and apoptotic cells.

1 Introduction

The nuclear envelope separates nuclear and cytoplasmic compartments in metazoan cells. The nuclear envelope is composed of outer and inner nuclear membranes and the nuclear lamina, which is connected to the inner nuclear membrane. The nuclear lamina is a filamentous protein network that gives the nucleus structure. Two major types of lamin proteins can be distinguished. B-type lamins are ubiquitously expressed and essential for cell viability. The expression of A-type lamins is developmentally regulated, and mutations in the human genes result in

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a variety of hereditary diseases with premature aging syndromes [1]. From the dynamic interactions between the lamina and chromatin domains, an active role of the nuclear lamina in gene regulation and chromatin organization was suggested [1][2][3]. Thus, the organization of the nuclear lamina can contribute to cellular function.

In *human mesenchemyal stem cells* (hMSCs) the nuclear lamina shows a round and flat shape after $3D$ image reconstruction. This distinct nuclear lamina shape is dramatically changed after caspase-8 activation and cell death. Activation of the caspase-8 pathway leads to an increase in intranuclear organization of the nuclear lamina, followed by massive degradation of the lamina proteins [4]. Intranuclear structures of the nuclear lamina were observed in interphase cells [5][6], and senescent cells [7], but the function of lamina reorganization is yet unclear. An increase in lamina intranuclear structures is one of the first events in nuclear remodeling after caspase-8 activation, and it precede the wholemarks of apoptosis, such as chromatin fragmentation and nuclear breakdown [4]. As the spatial organization of the nuclear lamina is initially changed when cells undergo deactivation, such as senescence or apoptosis, it can serve as a marker to distinguish between an active or non-active cells.

Here we considered classical machine-learning algorithms as a tool to classify nuclear lamina organization of normal and caspase-8-activated cells. The emphasis is on exploring the feasibility of the task, rather than comparing state-of-the-art classification algorithms. After the appropriate training, combined with an evolutionary optimization, we show that the Support Vector Machines (SVM) algorithm resulted in highly-satisfying classification.

Related Work. Machine learning algorithms have been widely used in biological applications for the tasks of pattern-recognition, classification, prediction and others. However, the application of machine learning techniques to the task of classifying $3D$ images has been very limited, as reported so far. A recent study [8], which originates in the field of brain imaging (fMRI), claimed to be the first research to apply machine learning techniques to a clinical diagnosis. This study reported successful classification of drug addicted human subjects and controls, based on $3D$ brain images, using state-of-art classifiers in combination with novel boosting algorithm. This study shows the use of image classification for clinical diagnosis.

The remainder of this paper is organized as follows: in section 2 we introduce the background for online learning and the algorithms in use. Section 3 provides the reader with technical details of the images acquisition and the data-instances construction. In section 4 the numerical results are presented and analyzed, and section 5 provides discussion and concludes this study.

2 Algorithms

We discuss briefly the basic concepts of *online learning* and provide an overview of the algorithms used. The reader should note that we limit ourselves, at this