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Original Research Article

Full-automatic computer aided system for stem cell clustering using Content-based Microscopic Image Analysis

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ABSTRACT

Stem cells are very original cells that can differentiate into other cells, tissues and organs, which play a very important role in biomedical treatments. Because of the importance of stem cells, in this paper we propose a full-automatic computer aided clustering system to assist scientists to explore potential co-occurrence relations between the cell differentiation and their morphological information in phenotype. In this proposed system, a multi-stage *Content-based Microscopic Image Analysis* (CBMIA) framework is applied, including image segmentation, feature extraction, feature selection, feature fusion and clustering techniques. First, an *Improved Supervised Normalized Cuts* (ISNC) segmentation algorithm is newly introduced to partition multiple stem cells into individual regions in an original microscopic image, which is the most important contribution in this paper. Then, based on the segmented stem cells, 11 different feature extraction approaches are applied to represent the morphological characteristics of them. Thirdly, by analysing the robustness and stability of the extracted features, *Hu* and *Zernike* moments are selected. Fourthly, these two selected features are combined by an early fusion approach to further enhance the properties of the feature representation of stem cells. Finally, *k*-means clustering algorithm is chosen to classify stem cells into different categories using the fused feature. Furthermore, in order to prove the effectiveness and usefulness of this proposed system, we carry out a series of experiments to evaluate our methods. Especially, our ISNC segmentation obtains 92.4% similarity, 96.0% specificity and 107.8% ration of accuracy, showing the potential of our work.

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1. Introduction

By image analysis of cells treated in *vitro*, a large amount of toxicological data can be acquired. After stimulation by chemical agents in lab and then long-term cultivation, the stem cells are fissioned to translate into tissue stem cells of different properties. No matter in terms of external or internal characteristics, these stem cells tend to possess varying styles. To explore potential co-occurrence relations between the differentiated cells and their morphological information in phenotype, there are great technical demands in both bioinformatics and biomedical applications [1]. Traditionally, manual image analysis methods, such as [2], are not only costly, low correctness, but also cannot deal with a large amounts of data. In contrast, current *Content-based Microscopic Image Analysis* (CBMIA) [3] approaches have following advantages:

- Cost saving: Cells are analyzed through automated CBMIA approaches by computers to reduce manpower and equipment input.
- High efficiency: Computer aided systems are more rapid and efficient than manual image analysis. They are easy to employ the idea of big data and statistical learning, which can analyze multiple cells and many images effectively.
- Intelligentization: Pattern recognition and machine learning algorithms are used to establish an intelligent CBMIA framework, which can be easily extended to deal with other related tasks.

Since CBMIA approaches have many advantages as mentioned above, they are selected and applied to the stem cell analysis task in this paper. First, we propose a novel image segmentation approach, namely *Improved Supervised Normalized Cuts* (ISNC) segmentation, to explore single stem cells, where the ISNC method is the most important technological contribution of this paper. Then, the segmented stem cells are represented by different shape features for further morphological analysis. In this step, we can monitor the cell differentiation process and collect the morphological information for an intuitive analysis, which is significant to investigate the mechanism of how stem cells change into different cell tissues. Finally, feature selection, fusion and clustering methods are applied to classify cells into different categories. Fig. 1 shows a work flow of the proposed computer aided system.

This paper is structured as follows: Relate works are first introduced in Section 2, then the newly proposed ISNC segmentation method is presented in Section 3, thirdly the most effective feature extraction techniques are selected and explained in Section 4, next Section 5 introduces the clustering approach, and then Section 6 evaluates the effectiveness and usefulness of the system by a multi-stage experiment, finally Section 7 closes the paper by a conclusion.

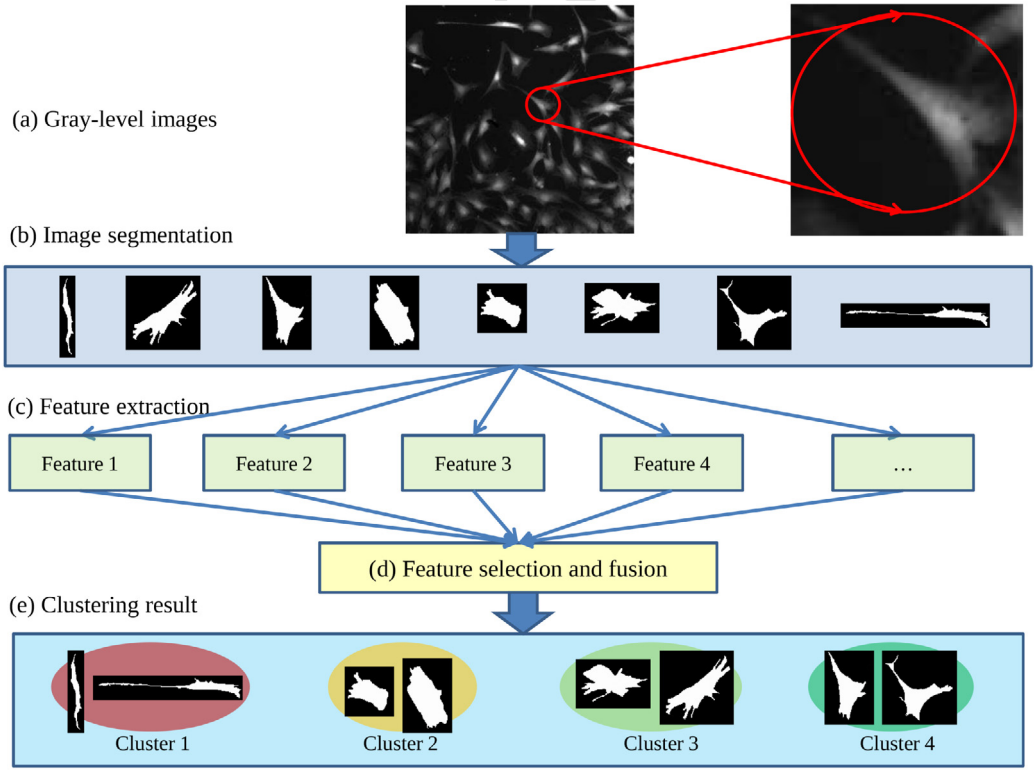

Fig. 1 – Workflow of the stem cell clustering system using CBMIA approaches. (a) shows an original image of stem cells and a partial enlarged drawing of a single cell. (b) represents the segmentation results of stem cells image using ISNC method. In (c), multiple shape features are extracted to represent the morphological properties of cells. (d) supplies a post-processing step to enhance the performance of the extracted features, where feature selection and fusion methods are applied. (e) obtains the final clustering result of stem cells by a *k*-means clustering algorithm.

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