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High-Efficiency Cellular Separation Method Utilizing Optically-Induced Dielectrophoretic (ODEP) Force-based Microfluidic Platform

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Abstract

This study reports an optically-induced dielectrophoretic (ODEP) force-based microfluidic platform for live and dead cell separation and collection. Combining the flow control in a microfluidic system and their opposite responses to an ODEP force, the live and dead cells can be separated and subsequently collected in an efficient and effective manner. Results of separation experiments showed that the recovery rate and purity of the isolated live cells was as high as 78.3±6.8 % and 96.4 ±2.2 %, respectively. Overall, the proposed method is found to be particularly valuable for biological research which requires the isolation of highly pure live or dead cells.

1. Introduction

With the recent progress in micro electro-mechanical system (MEMS) or microfluidic technology, several micro-scale devices based on cellular size- [1], fluorescence- [2], and magnetic- [3] have been actively pursued to perform cell separation from limited biological or clinical sample. Among them, dielectrophoretic (DEP) force-based cell manipulation technique has attracted considerable interest in various cell separations [4]. However, due to the costly and technically-demanding microfabrication process of the unique metal electrode layout, the optically induced dielectrophoretic (ODEP) schemes, in which light images are utilized as a virtual electrodes to induce DEP force, have been actively proposed to manipulate biological cells for various applications [13-19]. However, these studies did not provide an efficient cell separation scheme and cell collection method. Hence, to address the above issues, this study proposed a combination of a new microfluidic-based flow control and an ODEP-based cell manipulation to achieve both efficient and effective live and dead cell separation and collection. Overall, the proposed cell separation method is found particularly valuable for the biological researches in which the isolation of highly pure live or dead cells is important.

2. Materials and methods

The operation scheme of ODEP force-based live and dead cell separation by using the T-shaped microfluidic platform is illustrated in Fig. 1(a). In the platform, it comprises microchannels for sucrose solution flow and cell mixture flow. In addition, the two reservoirs are used to collect the separated live and dead cells.

The working mechanism is schematically shown in Fig. 1. Briefly, a sucrose solution was firstly loaded in to the microchannel, and followed by the cell mixture sample. After that, a negative pneumatic pressure was applied to drive the cell mixture to distribute in the microchannel (Fig. 1 (b)). After that, a dynamic rectangular light bar was illuminated on the microchannel to exert ODEP force on the loaded cells (Fig. 1 (c)), by which the dynamic shrinkage of light bar only attracted the live cells to the shrinking direction of light bar and simultaneously repelled and excluded the dead cells. This was followed by illuminating another dynamic light bar moving toward the opposite direction to repel and collect the dead cells (Fig. 1 (d)). After the two cell populations partitioned, the sucrose solution was again delivered into the T-shaped microchannel to drive the separated live and dead cells to the live and dead cell collection reservoirs. Simply based on the operations, the live and dead cells in the sample can be effectively and efficiently separated. To generate the ODEP force, a function generator was used to apply an alternating-current (AC) voltage between top and bottom indium-tin-oxide (ITO) layers. A commercial digital projector coupled with a computer was used to display controllable optical images onto the photoconductive material on top of an ITO layer to generate the ODEP force (Fig. 2).

2. Results and discussions

In this study, the operating conditions for generating ODEP force to separate the live and dead cells (primary steer chondrocytes) were first investigated. Figure 3 showed the maximum velocity that the moving light bar can manipulate the cells under different operating conditions. Based on the differences between the live and dead cells, the control of the velocity of dynamic light patterns can be used to separate these two populations at a given operating condition. Figure 4 showed the sequential microscopic images of the all procedures for live and dead chondrocytes separation and collection based on the processes of Fig. 1. By the processes, therefore, the two cell populations can be efficiently and effectively separated as shown in Fig. 4 (i). Figure 5 showed that the recovery rate and purity of the isolated live cells are as high as 78.3±6.8 % and 96.4 ±2.2 %, respectively. This could suggest that the proposed method was able to achieve high recovery rate and purity live and dead cell separation.

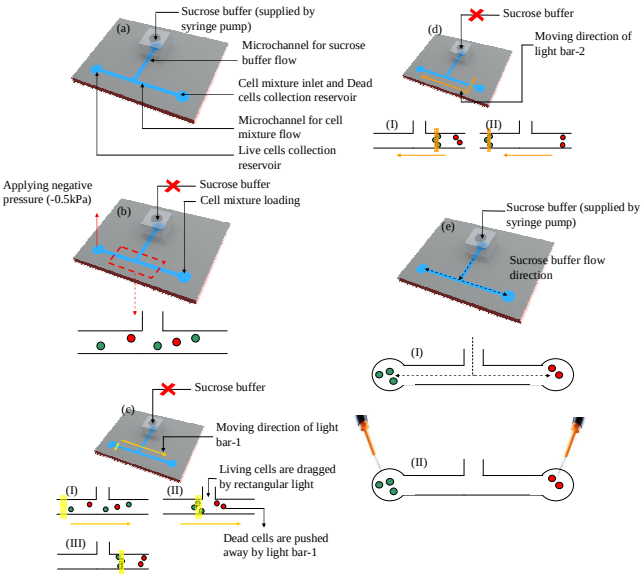

Fig. 1 The top view layout of the platform and the working mechanism for live and dead cell separation

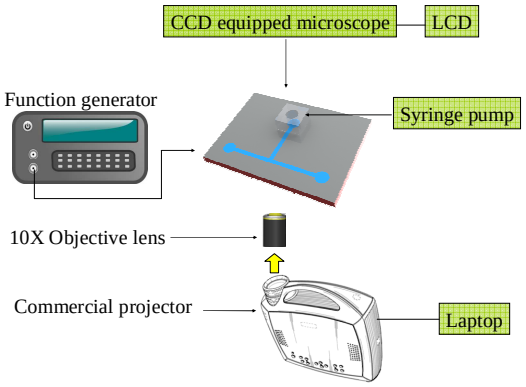

Fig. 2 The overall experimental setup of the ODEP based microfluidic platform

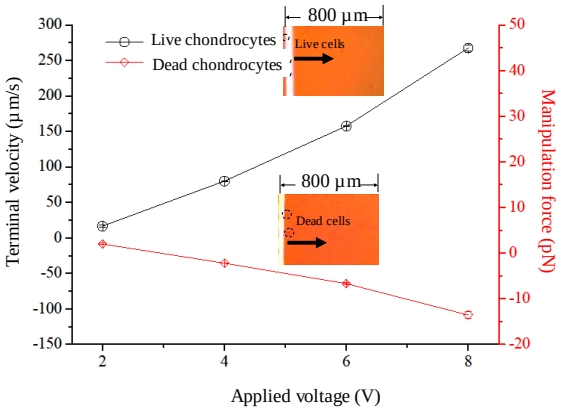

Fig. 3 The evaluation of the terminal velocity and the manipulation force of the live and dead chondrocytes under different magnitude of applied voltage (2, 4, 6, and 8 V)

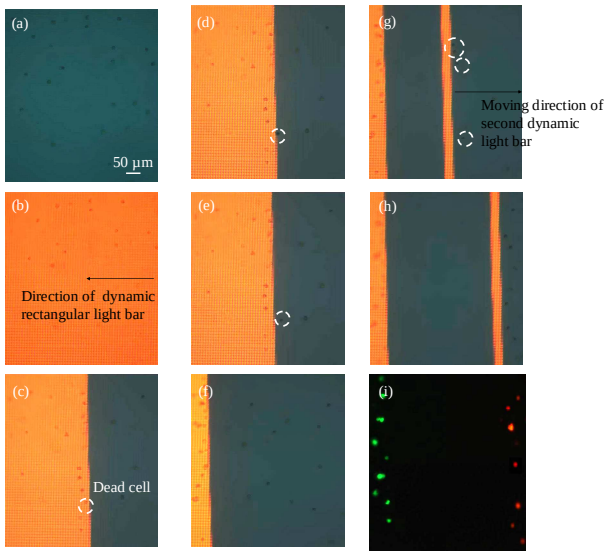

Fig. 4 Microscopic observation of the sequential actions for live and dead cell separation: (a) the original state, (b) the illumination of rectangular light bar on the microchannel to generate ODEP force on cells, (c)-(f) the dynamic shrinkage of light bar so as to gather the live cells to one side, (g)-(h) the illumination of another dynamic light bar to collect the dead cells, and (i) the fluorescent microscopic images of the separated cells, in which the green, and red dots represent the live and dead cells, respectively.

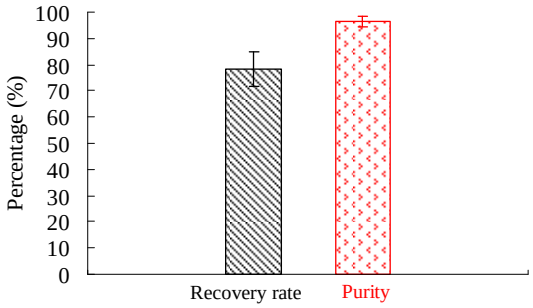

Fig. 5 The evaluation of recovery rate and purity of the isolated live cells by using the ODEP based microfluidic platform.

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