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Electro-magnetic templates with magnetic nanoparticles for cell-based assays

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Abstract

We discuss the possibility of a specially designed electro-magnetic template with magnetic nanoparticles for cell-based-assays. There is an urgent need for a special type of hardware allowing for biological cell manipulation. We have developed an original technique of using electro-magnetic templates with magnetic nanoparticles for biological cell manipulation. The essence of this approach is to generate a non-uniform magnetic field profile using a system of electric current carrying wires. The gradient of the magnetic field results in the movement of the nanoparticles towards the magnetic energy minima. In turn, the flow of magnetic nanoparticles drags biological cells in the same direction. We present experimental data on biological cells (erythrocytes) manipulations by magnetite (Fe_3O_4) on specially designed templates The results show controlled biological cell motion and destruction via haemolysis. This technique allows us to capture and to move cells located in the vicinity (10-20 microns) of the current-carrying wires. One of the most interesting results shows a periodic motion of erythrocytes between the two conducting contours, which frequency is controlled by the electric circuit. The obtained results demonstrate the feasibility of cell manipulation which can be utilized in cell-based assays.

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1. Introduction

Cell-based assays are emerging as the preferred tools for screening potential drug compounds. The global market for cell-based assays for drug discovery was valued at $6.2 billion in 2010. This sector is projected to increase at an 11.6% compound annual growth rate (CAGR) to reach nearly $10.8 billion in 2015 (2011). Growth in the market for

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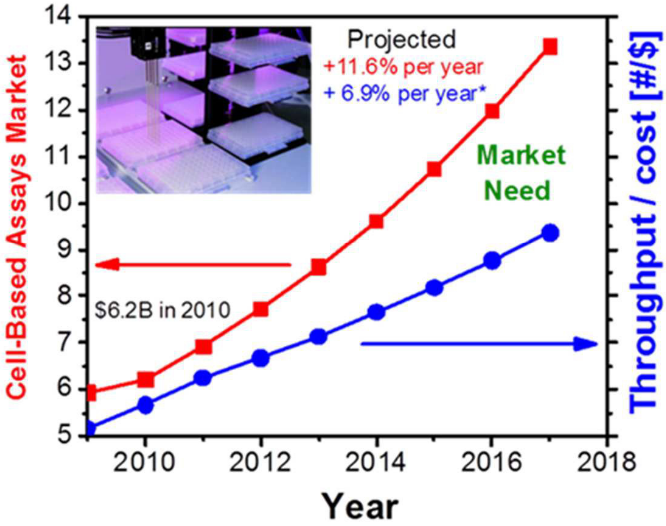

Fig.1 General trends in the cell-based assays market. The red curve depicts the permanent market growth and AGGR of 11.6%, and the blue curve shows the increase in the throughput to cost with the annual rate of 6.9%. The data are compiled from the Cell Based Assays Market - Global Industry Analysis, Share, Size, Growth, Trends, And Forecast 2012 – 2018; Transparency and Market Research, 2012; BCC research report: Global Markets and Technologies for Cell and Tissue Analysis, 2013; Frost and Sullivan, North America; New Product Innovation Award - Cell-based Assays, 2013.

cell-based assays is driven primarily by the increasing number of drug targets being screened through genomics and proteomics applications. This, in turn, is driving the increasing use of cell-based assays and the related expenditure by companies in the pharmaceutical and biotechnology sectors. Surge in demand for cell-based assays is attributed to the increasing need for efficient and economical release of new drug products into the market. While a major proportion of research activities are centered on drug discovery, cell-based assays are also expected to find applications in various other fields, such as toxicology studies, diagnostics, molecular biology, genetics, biochemistry, and neuroscience. Pharmaceutical and biotechnology companies are willing to employ cell-based assays in place of other in-vitro and biochemical assays in drug discovery. Numerous applications of cell-based assays include target identification and validation, screening of compounds for biosafety and efficacy, and monitoring of cellular events. Emergence of revolutionary branches in science such as synthetic biology and its dependence on accurate cell testing and the emergence of new technologies such as microfluidics are some of the factors that will ensure a healthy future growth of the cell based assay market. At the same time, there is a much slower progress (+6.9% annual rate) in increasing the efficiency of cell-based assays. These two general trends on the cell-based assay market are illustrated in Fig.1. The disparity among the fast growing market and the slow efficiency enhancement creates an urgent need for developing novel and efficient techniques for cell-based assays.

High-throughput at lower cost is the critical need for the majority of customers using cell-based assays. Conventional cell-based assay systems are very laborious, time consuming, and usually require an expensive system. We are addressing this need by proposing a novel, low-cost and high throughput multi-functional instrument for a variety of cell-based assays, which is based on the use of micro electro-magnetic templates with magnetic nanoparticles. The technology has been successfully tested on red blood cells (Gertz et al., 2012). The results of preliminary experiments have demonstrated the unique capabilities of this approach including a *micrometer-scale spatial resolution* and the ability to carry out procedures on *a large number of cells simultaneously*. The rest of the paper is organized as follows. In Section II, we describe the material structure of the micro-electromagnet and present the results of numerical modeling on the magnetic field profile. Next, we present experimental data on RBCs manipulation by magnetic nanoparticles in Section III. The obtained results are discussed in Section IV.

2. Experimental Setup

The schematics of the device are shown in Fig.2. The template from the bottom to the top consists of a silicon or glass substrate, multiple layers of conducting contours, an insulating cover layer of silicon dioxide, and metallic contacts on the sides of the template for individual electric biasing of each of the contours. The work place is the