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Applications and Manipulation Method of Microbeads in Biological Field

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Abstract

In the fields of cell biology, such as biomolecular chemistry and genomics, microbeads play an important role as a powerful analysis tool. To realize above applications, manipulation of size selection of microbeads is required. Therefore, in this paper we summarized newest manipulation methods for size selection of microbeads and their applications. We believe our paper offers specific reference for those researchers intend to use microbeads in biological field.

Keywords: Microbeads; Manipulation; Application; Size Selection

Introduction

Currently, due to their availability in different aspects [1-4] microbeads are widely used for a variety of different laboratory procedures and protocols. Microbeads technology has great effect on biological assay in molecular and genomic researches [5,6], for example, bar-coded (encoded) microbeads have been used in bead-based arrays [7]. Also, microbeads are cost saving and have excellent mechanical and thermal stability. Microbeads can be coated with an assay specific reagent, thereby facilitating high-throughput affinity-based capturing and detection of target biological molecules from a small sample volume [8-10]. In addition, microbeads offer advantages when used to perform chemical tests in microfluidic chips: they could be introduced into the device at any time, can be easily functionalized off-chip with specific receptors for analytes, can have a very large surface area, enable absorption, reaction, and electrochemical assay formats, and can be packed for washing and signal reading steps [11]. Improved methods of tagging and handling microbeads have also allowed commercial products such as Luminex bead array technology to be used in applications of diagnostics and drug discovery [12]. Microbeads can also provide a suitable three-dimensional environment for cell growth and differentiation [13]. Therefore, separation and manipulation of microbeads has great importance in medical diagnostics, immunology, chemical and biological analyses. For example, microbead sorting and patterning technology would allow direct identification and mapping of analyte binding to size specific microbeads which are encoded with different target reagents [7,14,15]. Moreover, microbeads with an added physical dimension such as bead sizes, can be utilized for detecting cytokines and simultaneously measuring multiple analytes for immunoassay [16]. Hence, this paper briefly reviews recent advanced methods of manipulating and handling microbeads and their applications.

Methods of Microbeads Manipulation and its Application

Microfiltration: In general, microfiltration is recognized as one of the most widely used techniques in the separation of microbeads, as it depends on the size of microbeads. The basic method of microfiltration is to use the conventional membrane-based micro-filter. By employing membranes with different pore sizes, multi-component particle filtration can be achieved. With suitable pore size, this method can theoretically separate microbeads of any size. To increase the capture efficiency of smaller cells or particles, Sun et al. [17] developed a strategy employing modified microbeads to specifically bind onto target cells, which enlarged the size of target cells. Lin et al. [18] focused on the size amplification of cells by tagging them with 3μm microbeads. In addition, Wong et al. [19] designed a 3D micro-traps array to filter out smaller diameter beads while retaining larger ones, which would be useful in applications like bead microarray assays.

Inertia and Dean Flow Separation: Recently, inertial separation plays a significant role in the manipulation of microbeads, due to the feature of single-step, highly-selective [20]. Microbeads of different sizes achieve different lateral location inside the

channel due to the balance of inertial lift force and dean drag force [21]. This method is capable of manipulating the microbeads more than 1μm of diameter. Yoon et al. [22] reported a microscale benefit of a secondary flow obtained in a curved rectangular microchannel and achieved the separation and sorting of microbeads by their size using secondary flow. Wang et al. [23] exhibited a novel inertial microfluidic sorter that was compatible with the roll-to-roll hot embossing process for size-based sorting of microbeads. With optimized flow conditions and channel dimensions, the sorting efficiency of a mixture of 15μm and 10μm diameter microbeads was more than 97%.

Dielectrophoresis: Manipulation of microbeads can be achieved by using dielectrophoresis (DEP) and compact electrode layouts [24]. The magnitude and direction of the displacement caused by the DEP force are depended on the electric field and the feature of microbeads or solutions. Jaione et al. [25] presented an efficient and compact lateral displacement separation method for microbeads based on negative DEP forces employing a capillary-driven microfluidic chip and an optimized electrode layout, which achieved the efficient separation of 10μm and 5μm beads, with 98% of all concentrated beads sorted in two separate streams. Jaione's group also presented a highly efficient and reversible mechanism for manipulating microbeads by combining dielectrophoresis (DEP) with mechanical traps [26]. Khashayar et al. [27] designed a DEP system that utilized curved microelectrodes integrated into microfluidic system and applied microbeads of 1, 6 and 15μm to the system and their response to the DEP field was studied at different frequencies of 100, 200, and 20MHz. Finally, the separation of microbeads of different sizes was successfully achieved.

Magnetic Separation: Magnetic manipulation is a common technique used to obtain a highly pure population of microparticles/beads or cells from a mixed solution [28]. In biological analysis, to obtain the target cells, tag the cells with magnetic microbead conjugated antibodies and then place the mixed solution in a magnetic field. Under the action of magnetic field, the labeled cells with magnetic microbead are separated from the mixed solution [29]. Tomin et al. [30] has developed lectin-conjugated magnetic microbeads recognizing specific glycans of apoptotic cells and its use for detection and separation of dying cells. In addition, depending of the size of the magnetic microbeads, the behavior of different size microbeads in the magnetic field is different. Effect of the field is large on larger particle than on the smaller one, so the larger microbeads present in the sample are separated from the smaller microbeads [31].

Acoustic Separation: Acoustic-based method has emerged as a new and ideal technology for use in microbeads separation, and many applications of acoustic manipulation have been developed [32]. The acoustic radiation force acting on the microbeads is depended on the property of the microbeads, and one property that can be exploited for the separation of microbeads based on size [33]. Jonathan et al. [34] developed a tunable acoustic separation device which could sort microbeads or cells based on a range of sizes, and the device was capable of sorting an arbitrary range of microbead sizes between 3 and 10μm in diameter with high efficiency (98%). Jeonghun et al. [35] presented a method that used a standing surface acoustic wave to continuously separate microbeads in a size-gradient manner in a microchannel flow, and three microbeads with different diameters (1, 5 and 10μm) were successfully separated with high efficiency.

Microfiltration and Inertia and dean flow separation have simpler structure and do not employ external fields for the operation, but microfiltration method requires complicated fabrication procedure to assemble the device with filters and the inertial separation requires sophisticated channels that facilitate movement of the microbeads. DEP, magnetic or acoustic separation use various forms of external fields to generate external force to manipulate and separate particles with relatively better performance and shorter time.

Conclusion

In this paper, a brief review of methods of microbeads manipulation and their applications is discussed. Each method has its own characteristics and advantages. In the future, devices would make a combination of these methods to develop more suitable separation and manipulation techniques.

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