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Electromagnetically controlled microfluidic chip for DNA extraction

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ABSTRACT

A microfluidic chip for DNA extraction by using solid phase extraction method was demonstrated in this paper. The microfluidic chip features three PDMS layers with microchannels, and a silica bead well with a thin PCTE membrane sandwiched between two PDMS layers. The height difference between the microchannels in the top PDMS layer and the bottom PDMS layer generates a gravity-based pressure difference to transport the regent and washing buffer solutions. Since the DNA extraction process based on solid phase extraction involves multiple sequential steps (i.e., loading, washing, and elution), an automated electromagnetically controlled valve-array was designed and used to control the flow sequence of the required reagents and washing buffer. It was demonstrated that by using this chip and HindIII-digested λ-phage DNA as the sample, the DNA extraction process can be completed within 15 min and the DNA extraction efficiency is approximately 50%. Such a simple and automatic microfluidic chip system eliminates many complicated hardware and human intervention, and can perform the DNA extraction with relatively high efficiency.

1. Introduction

Sample preparation is one of the major challenges in lab-on-a-chip devices. For DNA analysis of clinical and forensic samples, as the first step, it is essential to extract DNA from cellular or extracellular components for downstream processes, such as polymerase chain reaction (PCR) [1]. Usually using sophisticated instruments and many manual processes operated by a well-trained technician are required for the preparation of DNA samples, a critical step affecting the process from sample to result. Among these various ways for DNA sample preparation, solid phase extraction (SPE) is one of the most important and useful methods. Christel et al. published the first microchip-based SPE in 1999 [2]. Since then, with the development of micro/nanofabrication technologies, various microfluidic devices [3–11] have been developed to perform DNA extraction from biological samples. Most of these approaches packed solid phases such as silica beads, sol–gels, or ion exchange resins to create a SPE bed or column in the microfluidic chips [3,12–14]. This type of SPE bead bed or column in microchannels usually suffers from the requirement of large driving pressure, limited sample capacity, and low flow-rates. Membrane based extraction methods [4,15] typically have a much larger cross-sectional area for flow, in comparison with the packed beads bed or column in microchannels, and can reduce the pressure drop. However, the disadvantages of

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these membrane-based methods include the difficulty of integrating the membrane into a microfluidic system, and the limited adsorption capability of the membrane.

This paper presents a new microfluidic chip for DNA extraction using a combination of a well of silica beads and a membrane. In comparison with the microchannel filled with micro-beads as reported in the literature, the bead well designed in this work has a shorter depth and a larger diameter of a few millimeters and hence allows for larger flow rates and lower pressure drop for the flow. A PCTE membrane is placed at the bottom of the bead well to hold the micro-beads and also provides the same function for DNA extraction as the beads. Three PDMS layers were utilized to realize this goal: the top layer with microchannels for loading reagents and washing buffer, the middle layer with a well for holding the silica beads where the DNA molecules are trapped and eluted, the bottom layer with microchannels for collecting DNA and storing waste. In order to achieve automatic control of the sequential processes of the solid phase extraction, an electromagnetic valve-array was used to control the reagent flow on the chip. When actuated by an electrical signal, one permanent magnet in the electromagnetic valve is pulled downwards to press the thin PDMS membrane and thereby close the microchannel sandwiched between two PDMS layers; thus the liquid flow is stopped. When a reversed electrical current is applied, this permanent magnet will be pushed upwards, and then the microchannel is open again. The objective of this work is to examine the efficiency of this simple microfluidic chip for DNA extraction. Experiments were conducted with HindIII-digested λ-phage DNA as the sample. The result of the DNA extraction efficiency was found to be comparable with other existing extraction methods.

2. System design and fabrication

2.1. System design and working principle

The solid phase extraction of DNA requires three processing steps. The first step is the binding of the target DNA molecules to silica beads in GuHCl Loading buffer. The second step is to wash off impurities and other undesirable molecules. The last step is to release the DNA from the silica beads with TE elution buffer. In the microfluidic chip designed in this work, as shown in Fig. 1, there are three PDMS layers. The top layer has wells for washing buffer and elution buffer and microchannels connecting these wells to the bead well. The middle layer has hole as a section of the bead well. The bottom chip has wells for DNA collection and for waste storage, and microchannels connecting these wells to the bead well. The bead well is a hole from the top layer through the middle layer. A PCTE membrane is placed under the hole between the middle layer and the bottom layer, and holds the silica beads above it in the bead well. The height difference between the microchannels in the top PDMS layer and the bottom PDMS layer generates a gravity-based pressure difference to drive the flow of the regent and washing buffer solutions from the top layer through the bead well to the microchannels in the bottom layer.

In the operation, the first step is to load the DNA sample with the binding buffer solution to the well of silica beads, while all the channels are closed. The second step is to open the channel of washing buffer to wash away the undesired components from the bead well to the waste well, while the channel from elution buffer well and the channel to the DNA collection well are closed. The last step is to close the channel of washing buffer and open the channel of elution buffer and the channel to the DNA collection well, releasing the trapped DNA from the silica beads and collecting the DNA in the collection well. To accomplish these sequential steps, four electromagnetically controlled valves were used. Such a valve works on the basis of the attractive or repulsive force between a permanent magnet and an electromagnet. The permanent magnet can be pulled down when the electromagnet is powered on, pushing the thin PDMS layer down and thus closing the microchannel sandwiched between two PDMS layers. When a reversed electrical current is applied to the electromagnet, a repulsive force is generated between the permanent magnet and the electromagnet; and the

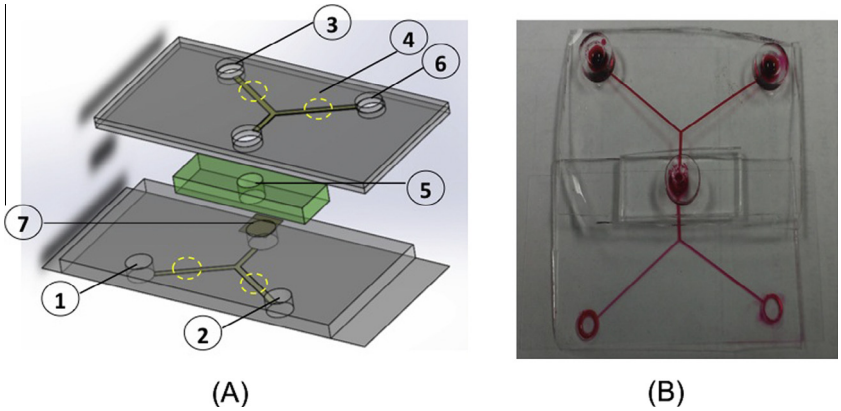

Fig. 1. The schematic and the photograph of the microfluidic chip developed in this study for DNA extraction. 1. The waste well in the bottom layer. 2. The DNA collection well in the bottom layer. 3. Elution buffer well in the top layer. 4. Electromagnetically controlled valve-array. 5. Bead well. 6. Washing buffer well in the top layer. 7. PCTE membrane between the bottom layer and the middle layer.