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RESEARCH PAPER

Microfluidic Chips for Preparation and Collection of Giant Vesicles

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Abstract: A microfluidic chip with preparation module and collection module for giant vesicles by microfluidic technology and microelectrode array was fabricated. First, lipid solution was loaded into the microelectrode array through microchannels to form lipid film, then an electric field was subsequently loaded on the microelectrode array, and giant vesicles with controlled diameter were formed efficiently. The ratio of formed stable giant spherical vesicles could reach up to 60%. Giant vesicles and other materials were flushed into the upper layer of the collection chamber by microchannel. 90% of the stable giant spherical vesicles with 10–50 μm diameter could be sorted in the upper layer of the collection chamber by using micropore filter and gravity depositing. This microfluidic chip could overcome some defects existing in the current preparation method such as low efficiency, wide distribution of diameters, as well as difficult for screening and collection.

Key Words: Giant vesicle; Microfluidic; Preparation; Collection

1 Introduction

Giant vesicles are the liposomes with a diameter of more than 1 μm[1]. Due to the large size, single giant vesicle can be directly observed under the light microscope. The membrane structure is similar to the cell membrane, so they can simulate the cell membrane or cell. In addition, giant vesicle has both hydrophilicity and hydrophobicity, which can carry water soluble and fat soluble substances. The physical properties of cytomembranes or cell were studied using giant vesicles[2–5]. For instance, they were used to simulate the cellular environment to study the proteins expression and cellular functions[6–8], used as carriers for the delivery of proteins, DNA and so on, to study gene transfer or drug delivery[9] and as biochemical reactor to observe rapid biochemical reactions within such small volumes[10]. Therefore, the giant vesicle can be applied in many fields such as molecular biology, cell biology, biochemistry, medicine and so on.

The formation ability and stability of micron sized giant vesicles are worse than nano liposomes. Therefore, the giant vesicles are more difficult to be prepared. Different methods were described to obtain giant vesicles, including gentle hydration method, solvent evaporation method, microfluidic jetting method, and electroform method[11,12]. In contrast, the electroform method for the preparation of giant vesicles by electric field get more and more attention due to its advantages such as fast speed, high controllability, mild reaction conditions and little environmental pollution[13]. However, the electroform method is not mature, especially the research on the preparation of micro electroform devices started relatively late, thus the method still has some defects such as low preparation efficiency, wide-spread diameters,

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and difficult for collection. Current collecting methods often require complex post processing operations, which results in the damage or lost to vesicles, thus greatly influence the actual production rate.

In this study, a microfluidic chip with the preparation module and collection module based on microelectrode array was presented. This chip used microelectrode array and multi microchannels structure to accurately control the formation of giant liposomes, and to improve the efficiency and size uniformity. This chip integrated the filter collection module, which provided a moderate and efficient collection of giant vesicles. Thus the chip made it possible to simply and efficiently prepare giant vesicles.

2 Experimental

2.1 Micro chip design and process

The microfluidic chip contained preparation part and sorting collected part, and the two parts were connected together by microchannels. A function signal generator provided electrical signal to the microelectrode array of the preparation part. Injection pumps were used to inject the lipid solution, buffer solutions, or draw waste liquid into the microchannels (Fig. 1A).

The preparation chamber contained two types of microelectrode arrays. One was interdigital electrode array (Fig.1B), whose opposite sidewalls were made of two chiasm comb shaped microelectrode arrays. Each comb ridge was distributed with a plurality of combing tooth, and a large number of microelectrodes were uniformly distributed on each combing tooth. The comb ridge width was 200 μm, the comb tooth width was 80 μm, and both the width and length of microelectrode on the comb were 20 μm. The distance between two adjacent or opposite protruding microelectrodes was 60 μm. For the design with interdigital electrode array, the electric field was spatially non-uniform, and the top of the microelectrode had the strongest electric field strength (Fig.1B). Another type was planar electrode array (Fig.1C), whose opposite sidewalls were also made of two chiasm comb shaped microelectrode arrays, but no microelectrodes on the combing tooth. So the electric field was uniform, and the intensity was weaker than the high electric field region of the interdigital electrode array (Fig.1C). The microchannels constituted of the opposite sidewalls of the microelectrode array with a depth of 42 μm.

The sorting collected part consisted of collection chamber and waste chamber (Fig.1A), composed by PDMS (polydimethylsiloxane, PDMS). Diameters of the upper and lower parts of the collection chamber at different PDMS layers were 14 and 8 mm, respectively. A filter membrane (10.0 μm diameter filtration pores, 13 mm 100/pk, Whatman, Britain) was sandwiched between the two PDMS layers. The circular waste chamber with diameter of 14 mm was built with the two PDMS layers. Flow microchannels connected these chambers.

The micro electrode arrays part was fabricated by micro-electro-mechanical systems (MEMS) fabrication techniques. First, the silicon wafer was bonded with the glass wafer. Subsequently, a 20-nm thickness of Cr film was sprayed onto the silicon wafer, followed by spraying 2 μm thickness of Au onto the surface of the Cr film. The unwanted Cr-Au was etched away by KI etching solution. Finally, the microelectrode arrays were etched on the heavily doped silicon by inductively coupled plasma (ICP) etching technique.

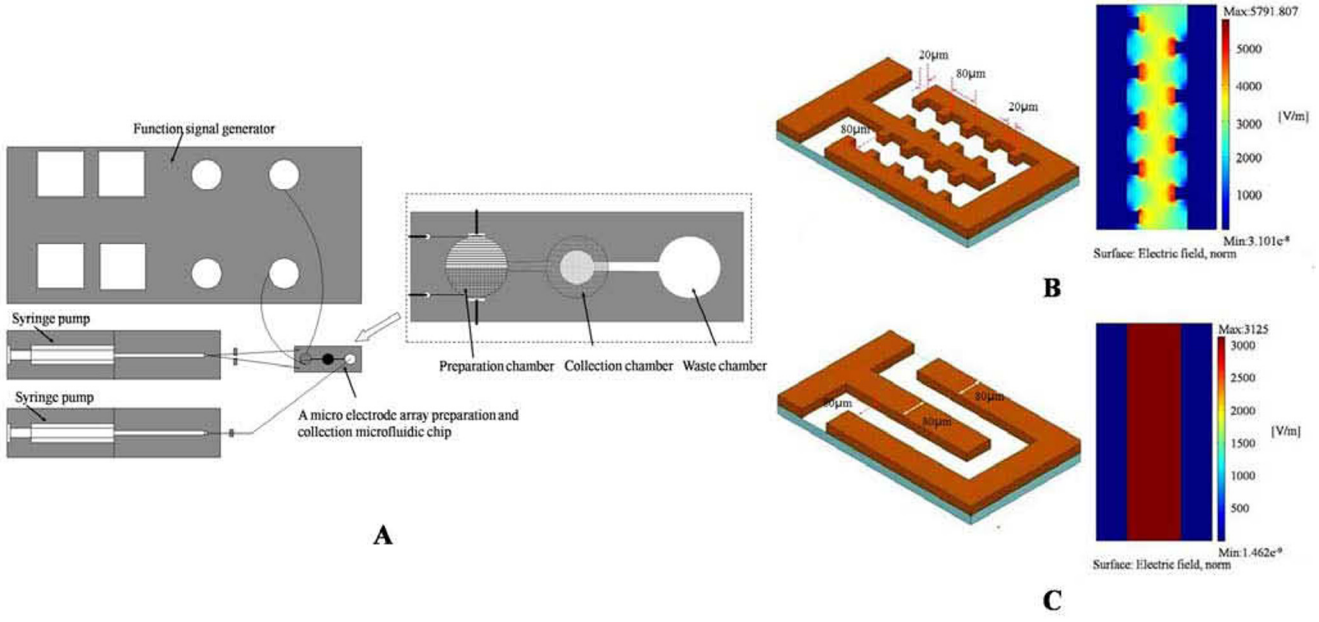

Fig.1 Chip design. (A) Chip structure and experimental platform, (B) interdigital electrode array and simulation of the electric field, (C) planar electrode array and simulation of the electric field