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Development of microarray chip by Fluidic Self-assembly method and Application to biochip

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1. Introduction

We report here a new approach for the immobilization of many kinds of biomaterials on the particles to construct multifunctional DNA chip microarray. A high-density array of sensor probes was prepared by randomly distributing a mixture of particles immobilized with various biomaterials for DNA chip microarray applications[1-2] The process for immobilization of the biomaterials was separated from the assembly of the particles. The particles were arranged by RFSA (Random Fluidic Self Assembly) methods on the chip pattern, using hydrophobic interaction for the assembly because this method is very simple and stable[3]. Establishing the walls improved the arranging stability of the particles. Each DNA is able to distinguish using the tag written by the lithography process on the particles.

2. Experimentals

Fabrication of Particles. One side of the cover glass was spin-coated with CPFP (9.0wt-%, 0.5μm). The cover glass was baked at 115℃ for 4h. Cr (0.5~1.0Å/s, 200Å) and Au (5.0~10.0Å/s, 2,000Å) layers were evaporated on the other side. The negative photoresist (OMR83) was applied to give a tag to the particles using photo-lithography on Au by a spin coater (1st:500rpm/10s, slope:10s, 2nd:4000 rpm/20s, slope:5s, 3nd:5000 rpm/2s, slope:5s) and baked at 100℃ for 1min on hot-plate. A UV light was irradiated to the resist film for 4 sec through a photo-mask. It was developed by dip in OMR developer and OMR rinse for 30sec, and drying with N_2 gas. After post-baking at 100℃ for 1min on hot-plate, Au and Cr layers were etched in Au etchant and Cr etchant for 30sec, respectively. It was rinsed with filtrated water 2 times, and blown dry by N_2 gas. The sacrificial OMR layer was etched in clean strip, rinsed with strip rinse and acetone for 5min, and then blown dry by N_2 gas. Subsequently, exposing Au surface to oxygen plasma in 67Pa, 100SCCM, 200W for 5 min it turned hydrophilic. The particles were cut from the cover glass into particles of 100~400μm in length using dicing machine. Particles with a tag by this process were obtained.

Fabrication of Chip Pattern. One side of a slide glass was spin-coated with CPFP and the slide glass was baked at 115℃ for 4h. Cr/Au layers were evaporated onto the CPFP and baked to dry this surface at 200℃ for 15min on hot-plate. The negative photoresist (XP SU-8 50) was applied on the slide glass by a spin coater and baked at 100℃ for 30min on hot-plate. The slide glass was exposed to UV light through a photo-mask on the resist film for 20sec. It was baked at 100℃ for 30min on hot-plate, and cooled naturally. It was developed, by dip in SU-8 developer for 30min, rinsed with developer, and blown dry by N_2 gas. Subsequently, exposing SU-8 50 surface to oxygen plasma for 5 min it turned hydrophilic. The Au and Cr layer were etched in Au and Cr etchant for 30sec, rinsed with filtrated water 2 times, and blown dry by N_2 gas, respectively. The chip pattern was checkboard-like pattern with the wall of 25~30μm in thickness. The size is 100×100~500×500μm^2 in all sides. The chip pattern was divided by hydrophilic and hydrophobic site, respectively. Hydrophilic and hydrophobic sites of 10^3~10^4/cm^2 is obtained.

Arrangement of the Particles on the Chip Pattern. We loaded the chip pattern into suspension (Ethanol 90% + Distilled water 10%) of about 5,000 particles having of both various immobilized DNA and a tag. Then, particles group subsides to the chip pattern using RFSA by gravity and also hydrophobic interaction, and it were arranged in each hydrophobic sites randomly. An integration type DNA chip microarray was able to fabricate simple, stably, high-throughput and cost-effectively by this process.

Also, the ratio of the arranged particles was obtained for various rotating speeds of the spin coater after stirring at 100~900rpm for 6min with the apparatus. The adhesion strength between the particles and the chip pattern was measured from the force which detach the particles from the chip pattern by centrifugal force and the fluid flow in the flocculation medium.

3. Results and Discussion

Fabrication of Particles. Figure 1 (a) is the number that shows each bit of the tag that adopted to write the tag on the particle by using lithography process. It is able to show 0~255 with these 8 bits, when it makes the presence of a minute tile 1 bit. SP and EP are expressing starting point and ending point of the bit that are always written on the particle, respectively. Figure 1 (b) is the tag that is based in Figure 1 (a) and show 010110001 (digit numbers of 88) of binary system. Also, Figure 1 (c) is the SEM photograph of the particle that written `010110001`

of Figure 1 (b) on the particle by the lithography process and divided with the dicing machine. The size of the particle is $300\times300\mu m^2$. The particles of various sizes were also obtained using the dicing machine. In Figure 1 (c), it is seen the tag of $10\times10\mu m^2$/bit clearly. Even other tags wrote on the particles by this process.

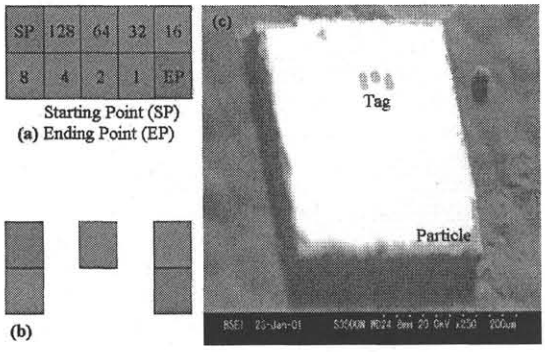

Figure 1. (a) It is the number that each bit of the tag shows and able to express 0~255 with 8 bit. (b) The tag that shows `010110001` of binary system. (c) The SEM photograph of the particle that the tag of (b) was written on it.

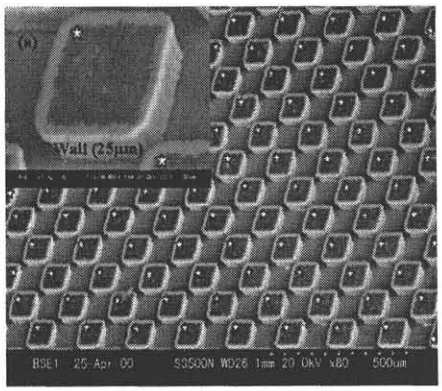

Figure 2. The SEM photograph of hydrophilic and hydrophobic chip pattern. Figure (a) is the photograph of the expanded aspect of the hydrophilic face.

Fabrication of Chip Pattern. Figure 2 shows the chip pattern that was established by the lithography process and also oxygen plasma processing. The area of asterisk marks shows the hydrophilic part and the remainder is the hydrophobic part. This chip pattern is $100\times100\mu m^2$ (10000 sites/cm^2), the wall of 25~30μm in height is established in all sides regularly, and the stability of the particles after the arrangement is expected. Besides, we were also able to fabricate the chip patterns of $500\times500\mu m^2$. Figure 2 (a) is the photograph of the expanded aspect of the established wall, where it is shown that the etching between the hydrophilic part and the wall are skillful. The wall could be seen clearly. Besides, the hydrophobic sites of various sizes were also obtained using the photolithography process.

Arrangement of the Particles on the Chip Pattern. Figure 3 shows the SEM photograph of the integration type DNA chip microarray that the particles with the tag are arranged on the hydrophobic sites of the chip pattern using RFSA by hydrophobic interaction with water-chip pattern site for assembly in a suspension. Each asterisk and square parts show the hydrophilic and hydrophobic site, respectively. The probability that the particles arrange in the hydrophobic sites on the chip pattern was about 75~85%. In Figure 3, the thickness of the particle is about 50μm and the particles were arranged firmly and 3-dimensionally due to surrounding wall (25~30μm). Because each particle is able to distinguish by the tag (for example, the tag that `01011000` (digit numbers of 88) and `01100011` (digit numbers of 99) of binary numbers are writing), each DNA is able to recognize when many kind of DNA is immobilized on the particles.

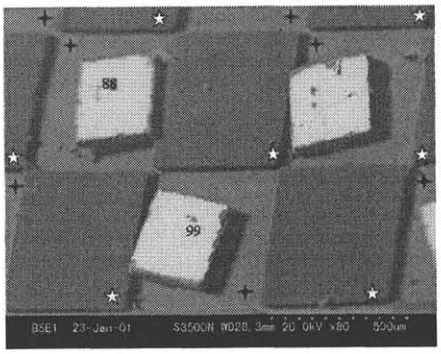

Figure 3. SEM image of DNA chip microarray. The particles that the various kinds of DNA were immobilized are arranged on the hydrophobic sites using RFSA by hydrophobic interaction.

4. Conclusion

We have used the RFSA technique based on the chip pattern of hydrophobic self-assembly layers to assemble microfabricated particles onto the chip pattern. Advantages of this method are process simplicity, wide applicability and stability. This method can be applicable as a new fabrication technology to develop an integration type biosensor microarray. We are presently extending this work to various biosensor microarray. Finally, DNA chip microarray offers the ultimate flexibility-as new assays come along, new microspheres simply can be added to the existing microsphere mixture at virtually no setup or time cost.

Acknowledgments

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