Magnetization-induced self-assembly method: Micro-needle array fabrication

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ABSTRACT

Magnetization-induced self-assembly method (MSM) was proposed to fabricate micro-needle array (MA). Curable magnetic fluid droplet array was extruded from the holes of perforated mask and meanwhile drawn to form the MA shape by magnetic force. MA was heated and cross linking solidified. The formation mechanism of magnetization-induced self-assembly micro-needle was analyzed and its process was divided into three stages: powders magnetizing, chain and aggregation, formation of micro-needle tip, and formation of micro-needle. The formation process was observed by high-speed camera. It was found that the formation process was consistent with the theoretical analysis. The effects of mask-hole diameter, powder-to-volume ratio and magnetic field intensity on MA fabrication were investigated by experiments. The results showed that the sharpness of micro-needle decreased with the decrement of mask-hole diameter and the increment of magnetic field intensity. The height of micro-needle increased with magnetic field intensity and powder-to-volume ratio. We anticipate that MSM will be suitable to fabricate MA-substrate for biomedical engineering fields such as biosensor, bio-electrode and transdermal drug delivery.

1. Introduction

The micro-needle array (MA) has been widely applied in various fields, such as collection of micron-size oil droplets from water (Li et al., 2013), temperature monitoring for electroporation (Wilke et al., 2005), transdermal drug delivery (McCrudden et al., 2014), cutaneous delivery of vaccine (Kim et al., 2014), fast drug detection (Vazquez et al., 2014), biochemical sensor (Valdés-Ramírez et al., 2014), MA dry electrodes for bio-potential monitoring (Forvi et al., 2012), trace amount blood collection (Aoyagi et al., 2008), treatment of hydrocephalus (Oh et al., 2014), etc. Therefore, research on MA fabrication is worthy.

Several methods have been reported to fabricate MA. The photolithography and etching was always adopted to fabricate MA from silicon. O'Mahony et al. (2011) fabricated MA on the front side of wafer, and a through-silicon via backside by photolithography and etching. It was applied for ECG and EMG bio-signal recording. Yu et al. (2009) utilized deep reactive ion etching and

photolithography to fabricate a hollow MA from silicon wafer for ECG measurement. However, photolithography and etching has disadvantages: (1) photolithography or etching requires sophisticated equipment located in clean rooms and produces toxic waste. It is inconvenient, expensive and eco-unfriendly; (2) silicon needles may break off and stay behind in the skin due to the fragile property of silicon (van der Maaden et al., 2012). Micromoulding was proposed to fabricate MA due to its potential of up-scaling production. Park et al. (2010) fabricated polymer MA roller for transdermal drug delivery based on micromoulding method. Bystrova and Luttge (2011) employed micromoulding and ceramic sintering to fabricate ceramic MA for transdermal drug delivery. However, micro-mould is the key element and fabricated by photolithography and etching technique. Micromoulding process is also complex. Laser machining was suggested to fabricate MA due to its high machining efficiency and resolution. Pearton et al. (2012) employed infrared laser to fabricate planar MA on 75 μm thick stainless steel sheets for the delivery of plasmid DNA to human skin. The resultant stainless steel micro-needles should be electro-polished firstly before application. Zhou et al. (2013) used laser micromachining process to fabricate MA electrode on pure copper substrate for human electrical impedance test. However, the surface of MA was usually

too rough to use directly due to the thermal effect during material removal. Drawing technique, including drawing lithography and droplet-born air blowing, was also proposed to fabricate polymer MA. Lee et al. (2011) fabricated dissolving MA from maltose by stepwise controlled drawing technique for transdermal drug administration. Several research teams, Lee et al. (2014) and Choi et al. (2013) also from Yonsei University, Korea reported similar work about MA fabrication by drawing lithography. Kim et al. (2013) employed droplet-born air blowing method to fabricate dissolving MA for transdermal drug delivery. However, the fabrication process was time-consuming and difficult to operate. So, significant challenges still remain for fabricating MA conveniently and low-costly. Furthermore, above researches mainly focused on MA application but little concerned on its fabrication process.

In this paper, a novel magnetization-induced self-assembly method (MSM) was proposed to fabricate MA. Droplet array of curable magnetic fluid was drawn into MA shape due to the magnetic force in self-developed uniform magnetic equipment. This fabrication process was simple and effective. MA formation process was analyzed theoretically and observed by high-speed camera. Three effect factors such as mask-hole diameter, magnetic field intensity and powder-to-volume ratio would be investigated by experiments.

2. Theory analysis

The magnetic powders are dispersed in curable polymer fluid uniformly as magnetic fluid. Magnetic fluid droplets are extruded from holes of perforated mask. Powders in droplet are magnetized by uniform magnetic field. And a gradient magnetic field is induced due to magnetized powders. Thus, the magnetized powders aggregate and form chains and nets. The magnetic force between powder aggregations can overcome the surface tension of droplets and drive the aggregations breaking through fluid surface to form the tip of micro-needle. More powders aggregate and micro-needles grow up with the continuous extrusion of magnetic fluid. Finally, formation of micro-needles reaches a steady state, and the micro-needles are heated for cross linking solidification. The interrelationship between micro-needles can be ignored, so the formation process of one micro-needle is taken as an example to understand the formation mechanism of MA. The formation process of micro-needle can be divided into three stages: powders magnetizing, chain and aggregation, formation of micro-needle tip and formation of micro-needle. The schematic diagram of micro-needle formation process is shown in Fig. 1.

2.1. Magnetizing, chain and aggregation of magnetic powders

The ferromagnetic powders are dispersed in the polymer solvent fluid uniformly as shown in Fig. 1a. The powders are magnetized due to the external uniform magnetic field. The induced magnetic field $\mathbf{B}_p$ can be expressed by Eq. (1) (Morimoto and Maekawa, 2000).

$$\mathbf{B}_p = \frac{\mu_0}{4\pi}\left[\frac{3(\mathbf{m}\times\mathbf{r})\mathbf{r}}{r^5} - \frac{\mathbf{m}}{r^3}\right](r > R) \tag{1}$$

where μ_0 is the permeability of vacuum; R is powder radius; $\mathbf{r}$ is displacement vector; $\mathbf{m}$ is magnetic moment which can be expressed by Eq. (2)

$$\mathbf{m} = \frac{4}{3}\pi R^3 \mathbf{M} \tag{2}$$

where $\mathbf{M}$ is magnetization intensity. It can be calculated from the magnetization curve of ferromagnetic powder. The induced magnetic field is shown in Fig. 1b. The magnetic interaction between magnetized powders is shown in Fig. 1d. And the force on a powder

due to magnetic interaction by the other powders can be expressed by Eq. (3)

$$\mathbf{F}_{mp} = -\frac{\mu_0}{4\pi}\sum_{j=1\&j\neq i}^{n}\frac{\partial}{\partial r_{ij}}\left[\frac{\mathbf{m}_i\times\mathbf{m}_j}{r_{ij}^3} - \frac{3}{r_{ij}^5}(\mathbf{m}_i\times\mathbf{r}_{ij})(\mathbf{m}_j\times\mathbf{r}_{ij})\right] \tag{3}$$

The adjacent powders form chains by head-to-tail connection due to the magnetic interaction. The adjacent chains also connect by head-to-tail to form the larger chains. The joints will form between the chains due to the lower potential energy of powders near the end of chain. As chains coarsening and aggregation proceeds, net structure aggregations of magnetic powders form (Fang et al., 2007), as shown in Fig. 1c.

2.2. Formation of micro-needle tip

2.2.1. Initial status

Before the formation of micro-needle tip, the position of powders aggregations in droplet is shown in Fig. 1e. The shape of aggregation can be assumed as cylinder and its bottom area is s, height is h. Due to the curved surface of droplet, the position of aggregation a is higher than aggregation b and c as shown in Fig. 1e. The force analysis of aggregation a is shown in Fig. 1g. $\mathbf{F}_{mb}$ and $\mathbf{F}_{mc}$ are the magnetic force from aggregation b and c respectively. The resultant magnetic force $\mathbf{F}_m$ is expressed as

$$\mathbf{F}_m = C_m hs \tag{4}$$

Buoyancy $\mathbf{F}_b$ is

$$\mathbf{F}_b = \frac{C_g hs\rho g^2}{\rho_m} \tag{5}$$

The gravity of aggregation $\mathbf{G}$ is

$$\mathbf{G} = C_g ghs \tag{6}$$

Surface tension $\mathbf{F}_{st}$ is

$$\mathbf{F}_{st} = \sigma k \tag{7}$$

where k is the top curvature of droplet. C_m and C_g are the variables of external magnetic field intensity. According to Eqs. (2) and (3), the magnetic interaction increases with external magnetic field intensity and the structure of aggregation also becomes more compact. Thus, C_m and C_g increase with external magnetic field intensity. The resultant force of aggregation a $\mathbf{F}_{res}$ is expressed by Eq. (8) and it is in the opposite direction of gravity.

$$\mathbf{F}_{res} = \mathbf{F}_m + \mathbf{F}_b - \mathbf{G} - \mathbf{F}_{st} \tag{8}$$

2.2.2. Breaking through

At the beginning of micro-needle tip breaking through, the position of top aggregation a in droplet is shown in Fig. 1f. The aggregation will carry polymer and form a hemispherical droplet above the top of aggregation due to the viscosity of polymer. The hemispherical droplet is the tip of micro-needle and it mainly determines the sharpness of micro-needle. The force situation of aggregation a is similar to that described in Section 2.2.1. In this stage, the gravity keeps invariant. Buoyancy $\mathbf{F}'_b$ and magnetic force $\mathbf{F}'_m$ vary little and are approximately equal to $\mathbf{F}_b$ and $\mathbf{F}_m$, respectively. However, surface tension $\mathbf{F}'_{st}$ increases rapidly due to the decrease of micro-needle tip radius. It can be expressed as

$$\mathbf{F}'_{st} = \sigma\sqrt{\frac{\pi}{s}} \tag{9}$$