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Fundamental Study of a BioMEMS to Detect Cells

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Abstract: Biological Micro-Electro-Mechanical System (BioMEMS) technology has increased tremendously in the last decade. Especially, surface stress-based BioMEMS have been investigated extensively in the recent years. In this paper, a surface stress-based BioMEMS based on microfluidics, membrane and optical detection method is proposed. The membrane as the crucial part of the biosystem consists of two layers, PDMS and gold. And a self-assembled monolayer is coated on the gold layer to improve biocompatibility and provide sufficient bending stiffness. To optimize the membrane and increase its sensitivity, a series of simulations have been done using ANSYS® software. And it can be known that the deflection of membrane is maximal when the ratio P_{Gold}/P_{PDMS} (P: size of PDMS and gold, length = width) is 0.85. Based on these fundamental studies, the BioMEMS can be designed and fabricated.

Keywords: BioMEMS, surface stress, membrane, simulation

Introduction

BioMEMS is a heavily researched area with a wide variety of important biomedical applications [1], such as area of research and application in cells. Detection of cells and biological molecules would facilitate inexpensive and high-throughput testing and diagnosis. Voldman and coworkers applied microfabrication technology to illuminate biological systems, especially at the cellular level [2]. In general, BioMEMS is made of microfluidic systems and sensors. Microfluidic systems provide a powerful platform for biological assays [3-5]. Examples of bioassays and biological procedures that have been miniaturized into a chip format include cell counting, cell sorting, cell culture, DNA sequencing, polymerase chain reaction (PCR), electrophoresis, DNA separation, enzymatic assays and immunoassays [6-8]. Manimaran *et al* designed a BioMEMS based microfluidic device as a deformation assay to study the deformability and growth capability of cells through microgaps [9]. To the sensor, surface stress-based biosensor as a relatively new class of sensor has been investigated extensively in recent years. These sensors use the change of free energy, the underlying concept in any binding reaction, and hence, offer a universal platform for chemical and biological sensing. Some researchers have demonstrated the capability of surface stress sensors in detecting a variety of reactions using microcantilever sensors, which include DNA hybridization [10-13] and antigen-antibody binding [14]. The value range of surface stress is reported to be 5 to 50 mJ/m^2 [15-17] or as high as 200 mJ/m^2 [18] and 900 mJ/m^2 [19] in such reactions.

Polydimethysiloxane (PDMS) is a biocompatible, transparent material and convenient for direct morphological observations of the cells under a microscope [20]. Also, it has high gas permeability suitable to the cell culture for the oxygen supply in closed microdevices [21]. Therefore, it has become the main researched material to be used in BioMEMS. Especially, the Young's modulus (E) of PDMS is lower than other materials, such as Si_xN_y and Si, so the sensitivity of the BioMEMS is very high if it is as the material of membrane, the sensitive part of sensor. In addition, the optical detection system is a full-blown technology [22-24] to be referred to measure the deflection of membrane resulting from surface stress. Thereamong, fiber optic interferometer [25, 26] has many advantages, better performance, low loss, high bandwidth, safety and relatively low cost, for example.

In this paper, the BioMEMS to detect cells is based on microfluidics, surface stress-based membrane and fiber optic interferometric technology. A series of simulations have been done using FE analysis software ANSYS® to optimize the parameters of membrane and to increase its sensitivity. Cells and solution are designed to manipulate in microchannels by means of pressure.

The structure

Microfluidics, membrane and fiber optic interferometer are the main parts of the BioMEMS (Figure 1). Microfluidics consists of inlet, microchannel and outlet. The membrane (Figure 2) as the crucial and sensitive part is made of two layers, PDMS (200 μm × 200 μm ×150 nm) and gold (30 nm thickness). The gold layer on the top of the membrane is essential for the fiber optic interferometer and forming self-assembled monolayer [15] to improve biocompatibility [15] and to provide sufficient bending stiffness [22]. The BioMEMS offers good biocompatibility and high sensitivity because its main material, especially for the membrane, is PDMS which is biocompatible, transparent and has small Young's modulus.

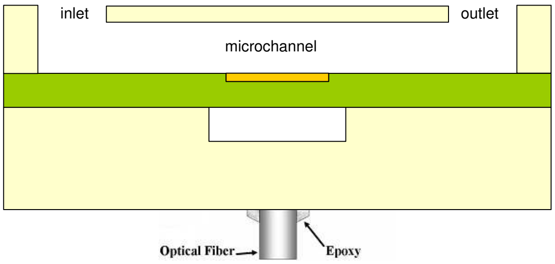

Figure 1: Schematic diagram of cross section of BioMEMS

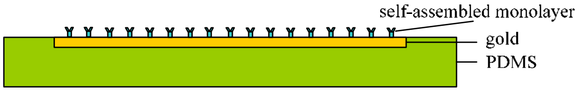

Figure 2: Schematic diagram of membrane

FE analysis

From basic membrane theory, it is well known that the deflection of a membrane is a function of the mechanical stiffness, here of the Au-PDMS composite membrane. Based on lots of prior simulations and the advice gotten from the technological fabrication workers, the thickness of PDMS and gold is 150 nm and 30 nm, respectively. Of course, the thickness of gold may be thinner (>10 nm) to increase sensitivity.

FE analysis software ANSYS® was used and the details of FE model are listed in Table 1. In general, there is no direct method to apply the surface stress load. Hence, a new method for applying surface stress load via an equivalent temperature load was proposed. The equivalent temperature load (ΔT) for a surface stress load (σ) was evaluated using Eq. (1) and the coefficient of thermal expansion (*CTE*) of all the material except the gold layer was set to zero for the analysis [27].

$$\Delta T = \frac{\sigma_s}{E_g \alpha_g T_g} \qquad (1)$$

E_g, α_g and T_g are the *E*, *CET* and thickness of gold, respectively.

Table 1 Material and FE model properties

Parameters material	*E* (GPa)	Poisson ratio	Length×Width (µm)	Thickness (nm)	Element type
PDMS	0.5	0.48	200×200	150	Solid186
Gold	780	0.44	variable	30	Shell93

A typical value (10 mJ/m^2) of surface stress [17] was used in the FE analysis. Once the compressive surface stress is loaded on the model geometry, the new deformed shape of the membrane can be gotten. The surface stress causes the membrane to deflect as shown in Figure 3, which is the simulation result when the parameters of gold is 200 µm × 200 µm (length × width).

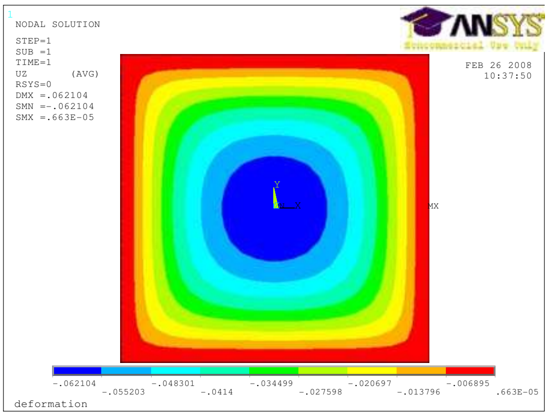

Figure 3: Simulation diagram of the deflection of membrane due to surface stress

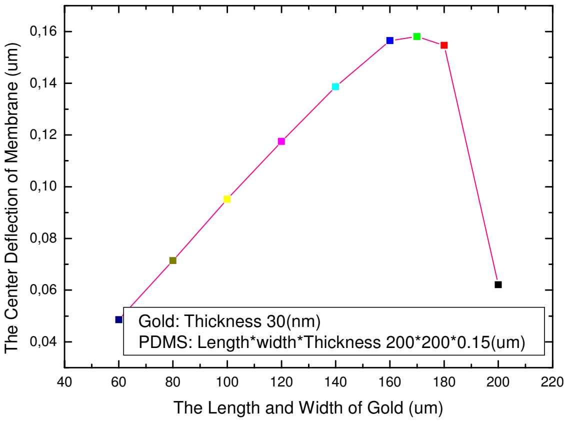

Figure 4: Deflection of membrane as a function of coating gold geometry

Figure 4 gives a series of simulation results when the PDMS layer of membrane is fixed value (200 µm × 200 µm × 150 nm), and the size of gold changes. It can be seen that the center deflection of membrane is the function of coating gold geometry. And it will reach the maximum when the ratio P_{Gold}/P_{PDMS} is 0.85, which gives us a good reference to design the parameters of membrane for getting the best sensitivity.

The optical detection method

In the optical detection methods, fiber optic interferometer is a full-blown technology and has many advantages just like explanation in the introduction. And it can measure the deflection in range of 10^{-11} to 10^{-13} m, which is suitable for our BioMEMS, just like the deflection of membrane in Figure 4. The principle schematic diagram is as Figure 5, the interference is formed inside an optical fiber. When the laser diode light arrives at the fiber end-face, a portion is reflected off the fiber/air interface (R_1) and the remaining light propagates through the air gap (L) with a second reflection occurring at the air/membrane interface (R_2). R_1 is the reference reflection called the reference signal (I_1) and R_2 is the sensing reflection or sensing signal (I_2). These reflective signals interfere constructively or destructively based on the optical path length difference between the reference and sensing signals which is called the interference signal. Therefore, small deflection of the membrane causes a change in the air gap (L), which changes the phase difference between the sensing and reference signals producing fringes.

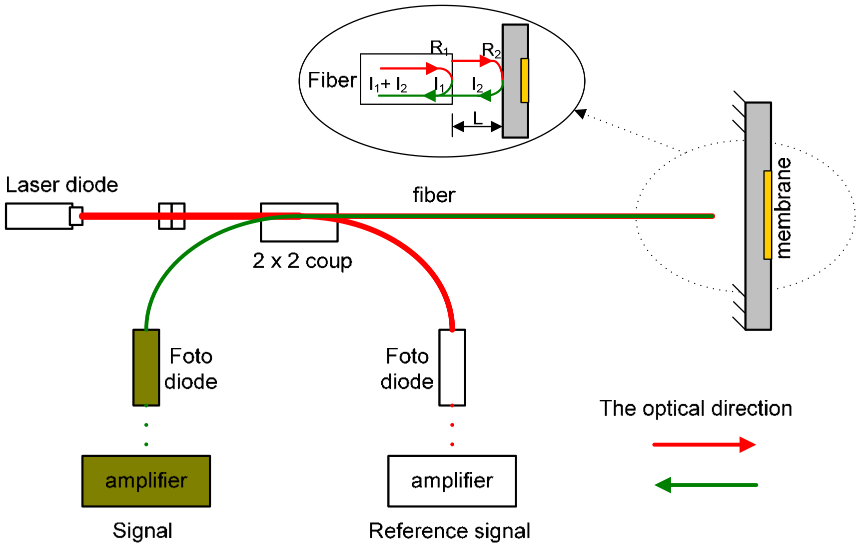

Figure 5: The principle schematic diagram of fiber interferometer

Conclusion

The new BioMEMS based on the microfluidics is feasible to detect and diagnose the cells by measuring the deflection of surface stress-based PDMS membrane using the fibre optic interferometer. And the best sensitivity can be gotten if the ratio P_{Gold}/P_{PDMS} is 0.85.

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