Modeling and Optimal Design of High Sensitivity Piezoresistive Microcantilevers for Biosensing Applications

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ABSTRACT

The mechanical design and optimization of piezoresistive cantilevers for biosensing applications is studied via finite element analysis. Models are described for predicting the static behavior of cantilevers with elastic and piezoresistive layers. The silicon based cantilevers have thicknesses typically on the order of a few microns and are doped to introduce their piezoresistive characteristics. Parametric modeling based on the finite element method is used to help determine the optimum parameters of cantilever design. Chemo-mechanical binding forces have been analyzed to understand issues of saturation over the cantilever surface. Furthermore, the introduction of stress concentration regions during cantilever fabrication has been discussed which greatly enhances the detection sensitivity through increased surface stress. Finally, novel microcantilever assemblies are presented for the first time that can increase the deflection due to chemical reaction.

Keywords: piezoresistive cantilevers, chemo-mechanical stress, Finite element modeling.

1 INTRODUCTION

Fabrication Recent advances in integrated biosensing chips have shown that sensing methodologies based on the bending of micromachined cantilever beams have potential advantages over previously used detection methods. Biochips with mechanical detection systems use bi-material (e.g. Au-Si) cantilever beams as sensing elements. The Au side is usually coated with a certain receptor. Upon the binding of the analyte (e.g. biological molecules such as proteins or biological agents) with the receptor (each individual protein interacts with a unique receptor), the receptor surface is either tensioned or relieved. This causes the microcantilever to deflect and the deflection is proportional to the analyte concentration. Examples of bindings in biomolecular (receptor/analyte) applications are: antibody-antigen (receptor/analyte) bindings or DNA hybridization of a pair of DNA strands (receptor/analyte) having complementary sequences (Raiteri et. al. 1999). The deflection is usually in nanometers and is being conventionally measured using optical techniques. Biochips having microcantilevers as sensing elements do not require external power, labeling, external electronics or fluorescent molecules or signal transduction for their operation. These types of biochips can be used in screening certain diseases such as cancer and detecting specific chemical and biological warfare agents such as anthrax, and aflatoxin. Alcohol detection in gases has been demonstrated on polymer coated cantilevers by H.Jensenius et al. (2000). The detection of alkanethiol monolayer formation on gold coated surfaces over cantilevers in gases has been demonstrated by A. Hansen et al. (2001). Recent experiments by Ozkan et al. have shown that a measure of the shift in the resonance frequency of resonating cantilever beams can be used for biochemical detection.

The amount of bending of a cantilever beam can be detected by several read-out systems, including optical detection (Bauer P et al 1995), capacitive detection (Brugger J et al 1992), tunneling detection (Dragoman D et al 2001) and interferometric detection. The most commonly used methodology is based on optical detection, where a laser is beam focused on the end of a cantilever, and the position of the reflected beam is measured with a position sensitive photodetector. The displacement of the beam at the detector is equal to the deflection of the cantilever multiplied by the ratio between the distance of the detector from the cantilever and the length of the cantilever. Hence, one can measure very small cantilever deflections by placing the photodetector far from the cantilever. Disadvantages of these techniques are several folds: First of all, they require external devices for deflection measurements, in the form of lasers, optical fibers or capacitors. In addition, the alignment and calibration of these external elements are often periodically required. Furthermore, the overall dimensions and power requirements for such detection systems can exceed the requirements of field or aircraft deployable devices for biochemical detection purposes. Other difficulties involve the scanning of the whole conjugation area over a cantilever surface; the external detection devices are usually very bulky and do not have the flexibility for that purpose. These disadvantages can be avoided by integrating the detection elements or devices into the cantilever. When a piezoresistive material such as doped silicon is strained, its electrical conductivity is changed. The change in the resistivity can be most conveniently measured by using a Wheatstone bridge. Piezoresistive microcantilevers are ideal for detecting the changes in surface stress due to cantilever

deflection upon binding of biochemical agents; they do not require external detection devices, they do not require tedious alignment, and they can be made to fit in an integrated electromechanical system (Grabiec P et al).

The fractional change in resistance ($\Delta R/R$) of a piezoresistive cantilever is described by the following expression:

$$\frac{\Delta R}{R} = \beta \frac{3\pi_L(1-\upsilon)}{t}(\sigma_1 - \sigma_2) \quad (1)$$

where π_L is the piezoresistive coefficient of Silicon along the <110> axis, σ_1 is the longitudinal stress, σ_2 is the transverse stress, t is thickness of cantilever, υ is Poisson's ratio, and β is a factor that adjusts for the thickness of the piezoresistor (Harley and Kenny, 1999). From the above equation, the ratio ($\Delta R/R$) is proportional to differential stress ($\sigma_1 - \sigma_2$). Differential stress distribution over a cantilever surface depends on the geometric factors of the layers and the chemo-mechanical forces between the biomolecules and the capture or hybridization layers. Therefore, the deflection signal can be increased by maximizing differential stress ($\sigma_1 - \sigma_2$) in a way of changing the geometric factors. For a given geometry, β changes from a maximum value of 1.0 for extremely thin piezo layers to a minimum value of zero for piezo layers extending to the entire depth of a cantilever. To increase the cantilever detection signal, the piezo layer should be as thin as possible. The introduction of stress concentration regions (SCR) over the piezoresistive elements on a cantilever can be used to enhance the stress difference and hence the displacement and force sensitivities of the detection process. Furthermore, the thickness of the cantilever beam near the support area can be decreased which results in a further increase in the detection sensitivity (Bashir R et al 2000)

2 FINITE ELEMENT MODELING

2.1 Chemo-Mechanical Binding Analysis

We have developed a finite element computational model for simulating the chemo-mechanical binding of analytes to specific binding molecules on fucntionalized surfaces using CFDRC™. We have conducted simulations using a model where a substrate functionalized with the binding molecules is inserted in a thin plate-shaped flow cell. The simulation system is schematically illustrated in Figure 1. A liquid solution containing the analyte passes through an orifice with a circular inlet port connecting to the flow cell. A functionalized substrate surface (such as a gold-coated glass-slide) on which the binding molecules are attached is located in the bottom of the flow cell. For the simulations, we have assumed an arbitrary set of analyte and binding molecules that have a strong binding affinity. The initial analyte concentration in the bulk solution was taken to be 5E-6M, and the inlet volumetric flow rate was 300µl/min.

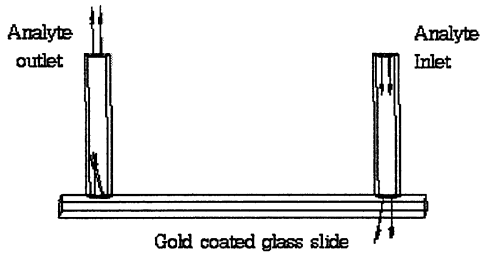

Figure 1. Schematic illustration of the model system used for the analysis of analyte-receptor binding.

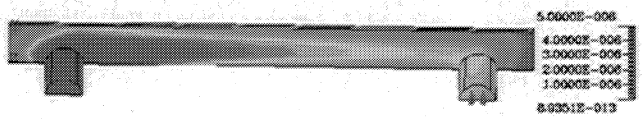

Figure 2. Distribution of analyte concentration at t=5 s

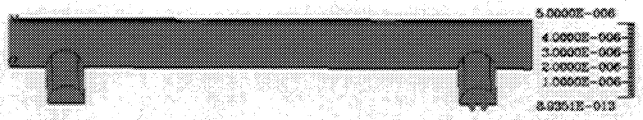

Figure 3.Distribution of analyte concentration at t=60 s

Analyte-receptor binding is a very common biological process in nature, which include protein, DNA and protein-DNA interactions. Depending on the chemistry, the binding reaction can be reversible or irreversible. The extent of the binding process depends on the affinity of the analyte to the receptor for chemical reaction, or to the chemical potential of the system. In the presence of multiple analytes and receptors, the binding process can be competitive (different analytes compete for the same receptor) or non-competitive (each analyte binds to a different receptor). The affinity between each individual analyte-receptor complex determines the partitioning of total receptor sites in a competitive binding environment. For the modeling problem considered here, the analyte binds to its receptor forming a reversible analyte-receptor complex indicated with an association rate constant Ka. This complex subsequently dissociates with a rate constant, K_d. This complex again can further form an immobilized complex with a rate constant (Kr):

$$A + B \underset{K_d}{\overset{K_A}{\rightleftarrows}} AB \xrightarrow{K_r} AB^* \quad (2)$$

The distribution of analyte concentration over the reaction surface as a function of time is illustrated in Figures 2 and 3. After a certain time, when the analyte concentration reaches a saturated level (Figure 3), the process of binding will reach a state of dynamic

equilibrium. The analyte concentration is uniformly distributed over the reaction surface. This means that the stable chemo-mechanical binding stress gives rise to a uniform distribution for surface stress which can be utilized for bio-sensing using a cantilevered detection system.

2.2 Geometrical Analysis

In general, the adsorption of molecules to a binding surface causes a change in the surface free energy, which is also called the surface tension. The mechanical response of a biosensing cantilever is caused by a change in the surface stress upon binding and hybridization of biomolecules. The change of relative resistivity is proportional to the differential stress, so the sensitivity of the cantilever can be enhanced by maximizing this differential stress.

We developed a finite element model to simulate the mechanical and electrical properties of piezoresistive cantilevers using CFDRC™. The cantilever beam is 30 μm wide and 120 μm long and has a depth of 1 μm. The piezoresistive layer has a depth of 0.1μm, which can make the β factor close to 1. The length of the piezoresistive layer is 80 μm, which covers the most area near the support. The capture area is located at the top surface of the cantilever.

From the results of the chemo-mechanical analysis, we know the stress is uniformly distributed in the saturated situation. However, for the difference of geometry in longitudinal and transverse directions, i.e. the difference between the width and the length of the cantilever, there is a stress difference between the two directions. In our simulations, it is assumed that the piezoresistor is of p-type. The device sensitivity is defined by (Marc Madou, Fundamentals of microfabrication CRC 1997)

$$S = \frac{\Delta R}{Rg} = \frac{\Pi_{44}}{2g}(\sigma_1 - \sigma_2) \qquad (3)$$

where Π_{44} is the piezoresistive coefficient and g is the unit load.

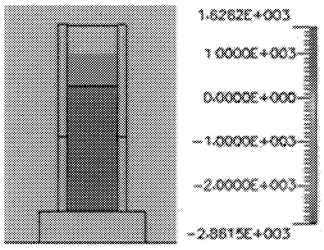

Figure 4. Distribution of stress difference ($\sigma_1 - \sigma_2$) in a piezoresistive cantilever beam

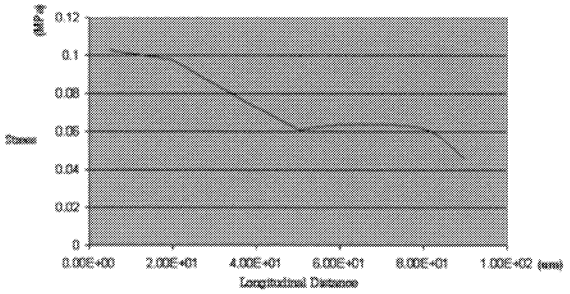

Figure 5 Integrated stress difference along the longitudinal axis of the cantilever beam.

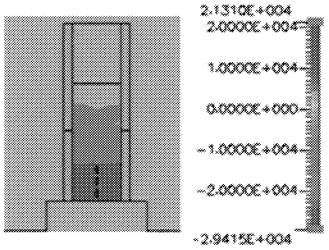

Figure 6. Distribution of stress difference in a piezoresistive cantilever with SCR's.

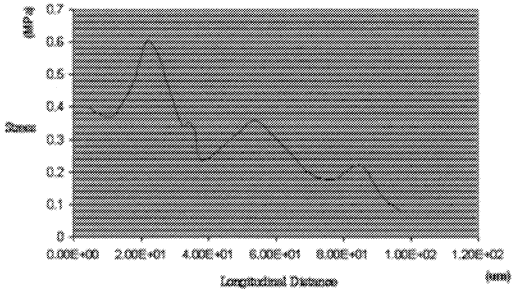

Figure 7 Integrated stress difference along the longitudinal axis of the cantilevers with SCR's.

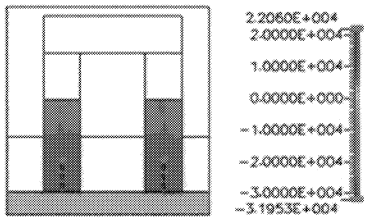

Figure 8 Distribution of stress difference for the double piezocantilever arrangement

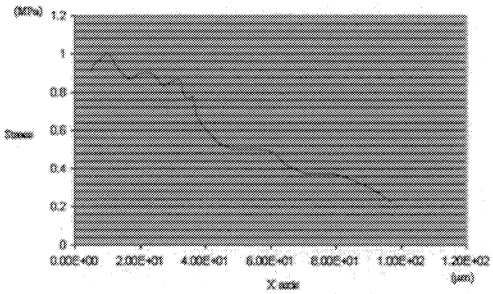

Figure 9 Integrated stress difference along the longitudinal axis for the "C" piezocantilever arrangement.

All three simulations were conducted with the same conditions of analyte concentration and the same analyte capturing area. For the double cantilever beam arrangement, the capture area was designed to be the whole area of the connection beam. For the regular piezoresistive cantilever as shown in Figure4 and Figure 5, the quantity of stress difference $(\sigma_1 - \sigma_2)$ is maximized near the cantilever beam support area as expected. Figure 6 and Figure 7 shows the integrated value of $(\sigma_1 - \sigma_2)$ over the length of the cantilever where over the capture area, the value of $(\sigma_1 - \sigma_2)$ is constant around 0.06 MPa. Towards the beam support area, the value of $(\sigma_1 - \sigma_2)$ increases to around 0.1 MPa. For the case of a single piezoresistive cantilever with stress concentration regions (SCR) as shown in Figure 8 , The value of $(\sigma_1 - \sigma_2)$ further increases near the support area reaching a maximum value of 0.6 MPa over a plateau that is 30 microns in length (Figure 9). This would be the optimum region for placing the piezoelectric layer to collect sufficiently large displacement signals.

3 CONCLUSION

We have developed a finite element computational model for simulating the chemo-mechanical binding of analytes to specific binding molecules on fucntionalized surfaces. The analyte concentration is uniformly distributed over the reaction surface when the analyte concentration reaches a saturated level. This means that the stable chemo-mechanical binding stress gives rise to a uniform distribution for surface stress which can be utilized for bio-sensing using a cantilevered detection system. Finally, several novel cantilevers such as SCR modified "C" cantilevers are designed for high piezoresistive sensitivity.

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