Sensors & Transducers, Vol. 150, Issue 3, March 2013, pp. 120-124

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An Optical Fiber Read Out Method for a Reflective Microcantilever Biosensor

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Received: 27 February 2013 /Accepted: 19 March 2013 /Published: 29 March 2013

Abstract: An effective optical read out approach based on fiber reflective is presented to detect bends of a biomaterial microcantilever. The microcantilever was fabricated on single crystalline SOI wafer using a series of side definitions and backside wet/dry etchings. A Cr/Au layer with 30 nm Cr and 50 nm Au layer was deposited for the immobilized of bimolecular on the cantilever surface and for reflecting the light back into the fiber, the different light intensities means different bimolecular concentrations. The noncoherent light source is a super luminescent LED. Gradient index lens as a collimator and 50:50 optical coupler and signal modefiber was used to transmit light. Two PINFETs were used to convert the reflecting the light intensities and the light sources into electronic signals, two ADCs convert the signal into digital signals, a MPU was used to eliminate the fluctuation of the light source error. The method can has got high sensitivity is 6507.59 mV/um. Though the experiment, the cantilever biosensor can detect glucose, measurement results clearly demonstrate that the output voltage induced by the microcantilevers bending is proportional to the glucose concentrations and the sensitivity is up to 0.1V/mM, which is enough for glucose real-time trace detection. *Copyright © 2013 IFSA.*

Keywords: Optical fiber, Microcantilever, Biosensor, Reflective, GRIN collimator, SLED, PINFET, MEMS.

1. Introduction

During the past decades, a lot of new methods and technologies have been developed to improve the performance of biosensor. Among these new technologies, microcantilevers have been proved to be quite versatile and sensitive devices and have been used mainly in the trace detection of bio-chemical materials [1-2]. A microcantilever biosensor developed is a device that can act as a physical, chemical or biological sensor by detecting changes in micro cantilever bending (static operation mode) or resonance frequency shift (dynamic operation mode) [3-8]. Compared with conventional ELISA or immunofluorescent assay, the micro cantilever sensor has the advantages of label-free operation, fast detection, and low cost. They are tiny plates or leaf springs, which are connected on one end to an appropriate support for convenient handing. Micro cantilever beams can be used to detect bimolecular by defecting upon interaction with a specific bimolecular. The detection is normally achieved by modifying the

surface of the microcantilever with recognition molecules. The specific interaction between the recognition molecules and the target biomarkers generates surface stress in microcantilever and in turn the deflection of the microcantilever [9]. The deflections of the microcantilever biosensor are usually of the order of few tens to few hundreds of a nanometer. Such extremely low deflection require high advances instrument for accurately measuring the deflections. As a consequence, most of the applications of microcantilever biosensors are done in laboratories equipped with sophisticated deflection detection and readout techniques [10].

Now the deflections can be measured using optical, piezoresistive, piezoelectricity and other readout methods [11-13]. However, a great discrepancy was not been avoided by piezoresistive readout or piezoelectricity because the tolerances of electronic components, wiring and the temperature affect [15]. Optical lever is the commonly used method [16-22], optical fiber reflective intensity [23-24], interferometric and diffraction-type [23-26]. But in common used optical readout the bulky and expensive apparatus is not absent [27].

In this paper, a novel optical fiber reflective read out microcantilever biosensor was proposed. The read out method is simple, low cost and high performance. We use the 1310 nm super luminescent LED as lamp-house, single mode fiber with gradient index lens as a collimator and 3dB 50:50 optical coupler was used to transmit light, In GaAs PIN and GaAs IC (PINFET) was used to convert the reflecting the light intensities into electronic signal, two ADCs convert the signal into digital signals, a MPU was used to eliminate the fluctuation of the light source error, only if the appropriate distance of the cantilever to the collimator the method can get high sensitivity.

2. Method

2.1. Microcantilever Fabrication

The microcantilever was fabricated from a SOI wafer using a series of bulk silicon process. The main steps of the process flow were depicted in Fig. 1 and described as follows. Firstly, a SOI wafer was papered and cleaned (Fig. 1a), all the device layer was removed by isotropic etching using ASE system (Fig. 1b). In order to get reflective layer and bio-sensing layer, a Cr/Au layer with 30nm Cr and 50nm Au was evaporated on the buried oxide layer using the ion sputtering system. (Fig. 1c). Lithography, defined metal shape and formed structure by stripping (Fig. 1 d). Then, definition of cantilever beam shape and release window of the mask pattern, RIE SiO2 down to the silicon substrate (Fig. 1e). At last, ASE system was employed to anisotropy etching Si 10um and then isotropy etching Si 25um to release the cantilever (Fig. 1f). Fig. 2 gives the SEM image of the reflective microcantilever which was fabricated, the typical dimensions of 200 um length, 60 um width and 1 um thickness in these experiments.

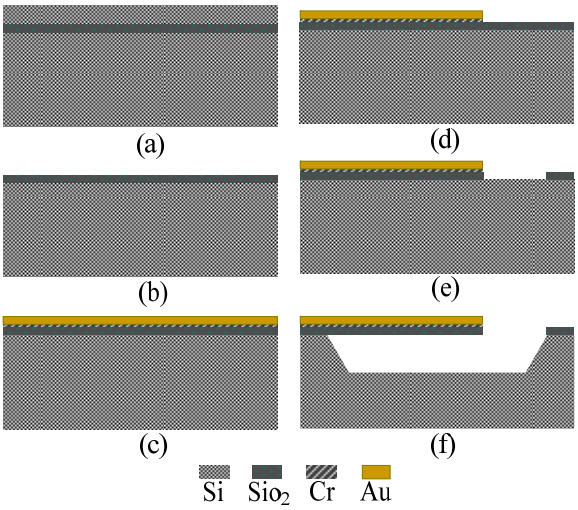

Fig. 1. Fabrication process of the reflective microcantilever.

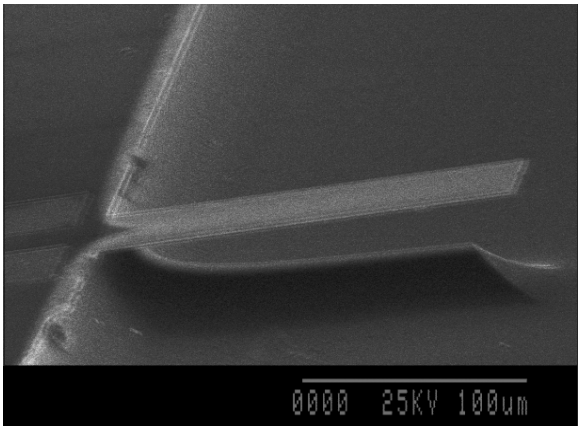

Fig. 2. The SEM image of the reflective microcantilever

2.2. Immobilized

Microcantilever beam can be used to detect bimolecular with a specific bimolecular. For detecting the glucose, the microcantilever must be functionalized, a self-assembled monolayer of 4-mercaptophenylboronic acid (4-MPBA) was immobilized on the surface of each sensing microcantilevers as the capturer of the molecules. The 4-MPBA is a type of synthetic chemical with two specially designed terminal groups. One of the groups is sulfhydryl, which has a strong binding with gold atoms, and the other is a hydroxyl group which can react specifically with glucose molecules. These two terminal groups make 4-MPBA is the ideal modification agent for microcantilever-based glucose biosensing. Fig. 3 shows the schematic of the sensing modification.

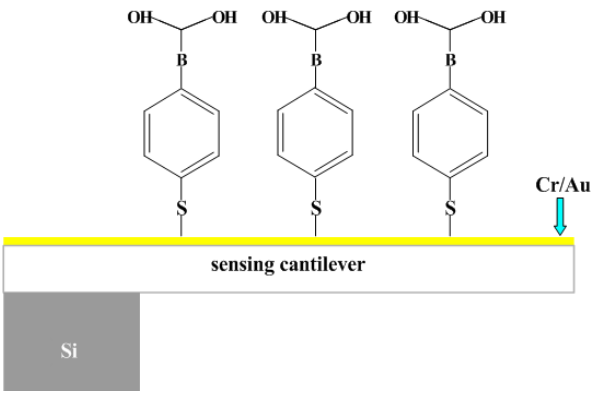

Fig. 3. Schematics of the 4-MPBA SAM modification on the sensing cantilever.

The immobilization of the self-assembled monolayer of 4-MPBA on sensing cantilevers was implemented by immersing the cantilever array into a 4-MPBA solution. However, in order to obtain the best immobilization effect, several preparations were finished in advance. Firstly, the cantilever array was cleaned for 10 minutes with Piranha Solution which contains sulphuric acid and hydrogen peroxide in a 4:1 volume ratio. Then the chip was rinsed using deionized water several times and dried by a nitrogen gun. Next, the microcantilevers were ready for self-assembled monolayer immobilization on the gold surface. The immobilization of 4-MPBA SAM was achieved by the immersion of the cleaned, gold-coated cantilever into a 5 mM of 4-MPBA in ethanol for 16 hours. Finally, the functionalized cantilevers were rinsed with ethanol again to remove any loosely bound thiol compound. After being dried with nitrogen, the cantilever sensor was ready for glucose trace detection.

2.3. Read out Method

A read out system was set up as in Fig. 4.The light source is a broadband SLED that operates in a true inherent superluminescent mode. This superluminescent property generates broader band at higher drive currents in contrast to other conventional SLEDS which are ASE-based. Its low coherence reduces Rayleigh backscattering noise. Coupled with high power and large spectral width, it offsets photoreceiver noise and improves measurand sensitivity for sensors. The light is passed through a signal mode fiber which is one branch of a 50:50 coupler, the light is split into two beams by the coupler, one is travel into a low noise and high sensitivity PINFET2 which is used to detect the light source fluctuation as a reference for the result of cantilever deflection, the other is travel into a min fiber GRIN collimator which is fixed vertically to the cantilever beam. The light travel back into the collimator through when incident light is reflected by the reflective microcantilever, at last the reflecting light is detected by PINFET1 which convert the light intensity into voltage signal. The final signal is processed by MPU (microprocessor). It is relevant to the microcantilever deflection angle.

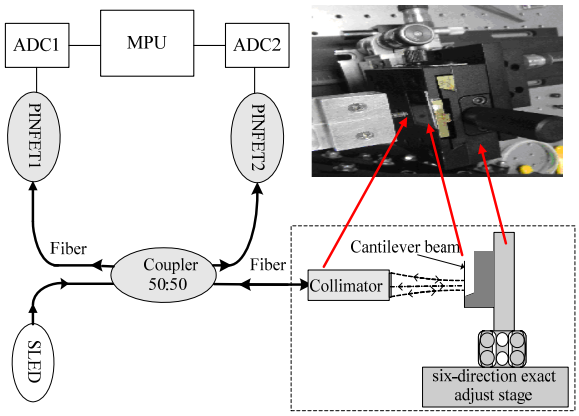

Fig. 4. The sketch map of the test system.

The min fiber GRIN collimator was at first by one of the other side of the coupler. The cantilever biosensor was fixed on a six- direction high precisions adjust stage. We adjust the bracket make the PINFET1 output is maximum , then we adjust the bracket subtle angle from 0 degree to 0.2 degree by 0.005 degree each step, the output of the PINFET1 is also changed with the cantilever beam angle changing. The sensitivity can be measured by this way, the measured results was shown in Fig. 5.

For detecting the glucose solution concentration, the functionalized cantilever array was firstly immersed in a well with a pure phosphate buffer solution (PBS). Next, by adjusting the stage make the output signal at zero stable stage. It was injected with a glucose solution which has a concentration of 5 mM. Finally, when the reaction was finished, a glucose solution with a concentration of 15 mM was injected into another well. The output signal was measured by the ADC1, ADC2 and MPU. The final measured result was shown in Fig. 6.

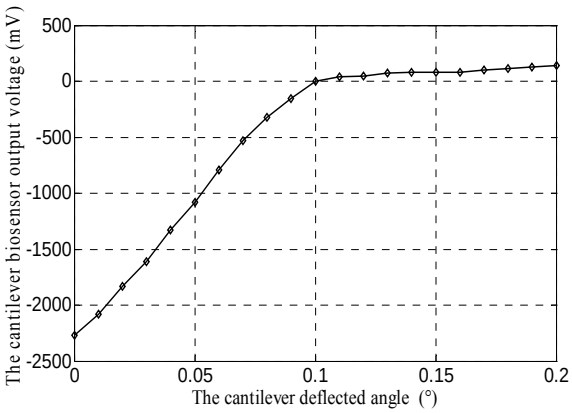

Fig. 5. The output voltage signal changes as a function of cantilever deflecting angle.

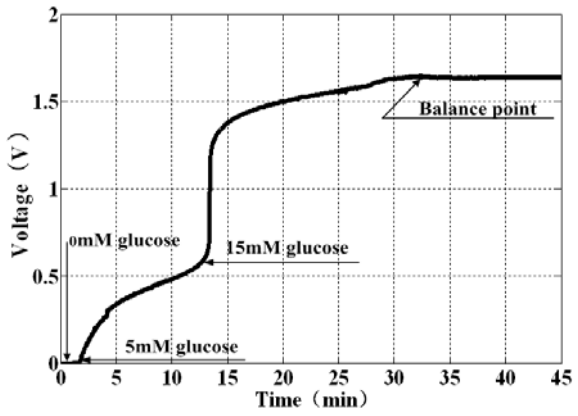

Fig. 6. The response of a 4-MPBA SAM-functionalized microcantilevers for glucose concentration change.

4. Results and Discussion

The relation of the cantilever deflecting angle between with PINFET1 output is very important because this determine sensitivity of the biosensor. The relation was measured as in Fig. 5. From Fig. 5, the PINFET1 output voltage is linear change from -2270 mill volt to 1.15 mill volt when the cantilever deflecting from 0 degree to 0.1 degree, but output is almost unchanged when deflect over 0.1 degree, that is to say when the cantilever deflecting over 0.1 degree the light can not reflect into the collimator. The immobilization microcantilever bend down displacement is very small when interaction with a specific bimolecular. The cantilever beam which used in the experiment length is 200 um, the cantilever beam tip displacement is only 0.349 um when deflecting 0.1 degree. The results demonstrate that microcantilever biosensor has very high sensitivity is 6507.59 mV/um by this read out method. The full range is 0.1 degree, so first adjust the cantilever to the collimator vertically is very important.

The following three steps are used to get the minimum detectable deflection δ min of the microcantilever: 1) get the minimum distinguishable light intensity I_{min} of the PINFET; 2) Calculate the spectrum distance Xu according to the minimum distinguishable light intensity I min; 3) Calculate the minimum detectable deflection δ min corresponding to the spectrum distance Xu. In addition, the minimum detectable deflection angle θ min ≈ arcsin(δ min /Lm)

It's known that PINFET sensitivity is -42 dBm and saturated light power is -3 dBm. The spectrum distance Xu according to the minimum distinguishable light intensity can be expressed as (1):

$$X_u = D \times (1 - \frac{I_{\min}}{I_{\max}}), \tag{1}$$

where D stands for the diameter of the fiber, Imax represents the light intensity when the microcantilever does not deflect. Next, the relationship between microcantilever deflection δ and its spectrum shift distance Xu can be deduced by Fraunhofer diffraction theory and the formula can be expressed as (2)

$$\arcsin(\frac{X_u}{f}) = 2 \times \arcsin(\frac{\delta}{L_m}) \tag{2}$$

Here, f represents the focal length of the self-focusing lens and Lm stands for the length of the microcantilever.

Fig. 6 shows the measured glucose solution concentration results. The output was first stabilized in the pure phosphate buffer solution at 0 V. The output voltage started to increase rapidly 2 minutes later after the glucose solution with a concentration of 5 mM was injected. After 12 minutes of reaction, the output voltage slowly rose to about 0.544 V and kept stable again until the second glucose solution of 15 mM. At the first stage, the out put increased rapidly. After 17 minutes of reaction, output reached 1.632 V and remained stable until the experiment ended. The experiment measurement result clearly demonstrate that the output voltage induced by the microcantilevers bending is proportional to the glucose concentrations and the sensitivity is up to 0.1 V/mM, which is enough for glucose real-time trace detection.

5. Conclusions

This work described a reflective microcantilever biosensor designed and fabricated process. A novel optical read out method based on optical fiber reflective was proposed. The practical measurement sensitivity is up to 6507.59 mV/um. The detecting the glucose solution concentration experiment measurement result clearly demonstrates that the output voltage induced by the microcantilevers bending is proportional to the glucose concentrations and the sensitivity is up to 0.1 V/mM, which is enough for glucose real-time trace detection. This biosensor is suit for using much biochemical detection in the further research.

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