DEVELOPMENT OF A POLYMER BASED FORCE AMPLIFIED CAPACITIVE TYPE IMMUNOSENSOR
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ABSTRACT
Cantilevers have been the frontrunners for label-free detection of wide range of analytes. But position dependent mass sensitivity has limited their usage to qualitative sensors. In this work we report the design and analysis of a SU8 based capacitive type mass sensor with a four beam proof mass structure where receptor analyte binding would occur on the separate thicker proof mass. A sandwich ELISA chemistry is used via which we amplify the mass of an analyte of interest (10^-23 kg) by non-covalently attaching them to functionalized microparticles (10^-15 kg) thereby circumventing the problem of reduced sensitivity due to four beams.

KEYWORDS: label-free, position dependent mass sensitivity, sandwich ELISA.

INTRODUCTION
Although high sensitivity has been achieved in case of MEMS sensors using different schemes (resonant and piezoresistive cantilever sensors), but accurate quantification of analytes has been a challenging task. Two major drawbacks of cantilever sensors include dependence of deflection of the cantilevers on position of immobilized analyte from the free end of the cantilever [1] which has limited their usage to qualitative type measurements applications and also the lack of proper modelling of surface stress [2] due to analyte immobilization. We have developed a SU8 based quad beam type sensor in order over to overcome these problems. Firstly the four beams provide a uniform mass sensitivity towards analyte binding which is established through extensive mechanical and electromechanical and mechanical testing. And since receptor-analyte interaction would occur on a centrally designed microchamber of a separate thicker proof mass leaving the beams unaffected, we circumvent the modelling complexities due to surface stress on thin micro-beams. But due to the four beams the device sensitivity is affected. This tradeoff between device sensitivity and device design is addressed using a unique sensing chemistry known as force amplified biosensing (FABS) [3]. Here the analyte mass is enhanced through a functionalized microbeads coupled ELISA technique.

THEORY

![Figure 1](a) Schematic view of complete device (b) figure showing device operation using FABS mechanism

Figure 1(a) shows the schematic conceptual view of complete device which consist of four bilayer composite beams with central seismic or proof mass as top electrode which is anchored to gold patterned glass substrate which serves as the bottom electrode. The flexures were of length \( l \) and width \( w \) and square proof was of side length \( L \) and \( h_b \), \( h_p \) are thickness of SU8 layers of beam and proof mass respectively and \( h_b \) is thickness of gold of both beam and proof mass.
Table 1. Device dimensions

<table>
<thead>
<tr>
<th>w (µm)</th>
<th>l (µm)</th>
<th>L (µm)</th>
<th>h_p (µm)</th>
<th>h_t (µm)</th>
<th>h_b (nm)</th>
<th>a (µm)</th>
<th>b (µm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>500</td>
<td>3000</td>
<td>4000</td>
<td>60</td>
<td>4</td>
<td>150</td>
<td>800</td>
<td>600</td>
</tr>
</tbody>
</table>

The central microchamber was of dimensions a and perforation in the structure made for successful releasing of device was of side length b. A vital part of sensor design was accurate modelling of bilayer composite flexures. The device dimensions shown in Table 1 are calculated on the basis of required effective spring constant $k_{eff}$ which can be expressed as a function of the effective flexural rigidity $(EI)_{eff}$ [4] of the composite beam given by

$$k_{eff} = 48 \frac{(EI)_{eff}}{l^3}$$

where

$$(EI)_{eff} = \frac{E_2}{12} \frac{w^2 h_b^3}{(1+pr)[(1 + pr)(1 + p^3 r) + 3pr(1 + p)^2]}$$

where

$$p = \frac{h_t}{h_b} \quad r = \frac{E_1}{E_2}$$

Simulations results using Coventerware© indicate parallel bending of proof mass (figure 2(a)) and uniform mass sensitivity studies was carried out using discrete load points distributed over a central area of 1000 x 1000 µm to study the bending uniformity towards static deflections. Results shown in type form contour plot (figure 2(b)) indicate larger uniformity over an area of 800 x 800 µm with maximum variations of 3.2% which could be considered as negligible as it is beyond detection limit of our device.

![Coventerware© simulations showing parallel bending of proof mas](image1)

![Contour plot showing uniform deflection](image2)

**Figure 2:** (a) Coventerware© simulations showing parallel bending of proof mass (b) Contour plot showing uniform deflection

**EXPERIMENTAL**

The devices were fabricated using standard lithography techniques with SU8 as structural material and gold for metallization. The top (figure 3(a)) and bottom electrodes were fabricated separately and bonded together using adhesive bonding [5] to construct a fully fabricated device (figure 3(b)).

![Released top electrode](image3)

![Fully fabricated device](image4)

![Schematic of setup](image5)

**Figure 3:** (a) Released top electrode (b) Fully fabricated device (c) Schematic of setup

In order to test the bending uniformity of top electrode a further indentation analysis was carried out with point load of 0 to 10 nN applied on five different points on hanging top electrode. A sandwich ELISA
chemistry (figure 1(b)) was adapted to couple anti prostrate specific antibody coated magnetite microbead to prostate specific antigen (PSA) trapped on mixed monolayer thiol (PEG and Biotinylated thiol) functionalized surface. Neuteravidin-biotin chemistry was adopted to immobilize antibody on sensor surface and EDC-NHS chemistry to attach antibody to amine functionalized microbeads. Fluid dispensing was carried out using surface patterning tool (SPT) of Nanoenabler© system by Bioforce Instruments which operates via capillary action and unbound samples were removed using a micro-syringe (Figure 3(c)).

RESULTS AND DISCUSSION

The nanoindentation test results (figure4 (a-b)) show very small variation (7%) between middle and lateral indentation plots. The spring constant was calculated from the slope of the indentation profile was 0.0561N/m which was close to calculated value 0.0488N/m. The normalized capacitance to analyte binding curve (figure4(c)) indicate successful FABS assay with mass sensitivity of $32 \text{ pN}^{-1}$.

CONCLUSION

We have successfully fabricated polymer-glass based capacitive type uniaxial force sensor for biosensing applications. The characterization results reveal good bending uniformity of device with only 7% variation between middle and lateral indents. The FABS assay results indicate successful immobilization of microparticles on device surface with a device mass sensitivity of $32 \text{ pN}^{-1}$. The results however doesn’t show good linearity and need to be calibrated properly for clinical trials. The issues regarding steric hindrance between microparticles in assay also need to be investigated in greater detail in future.

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REFERENCES


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