SUSPENDED MICROCHANNEL RESONATORS WITH INTEGRATED ELECTRONIC READOUT FOR BIOMOLECULAR AND SINGLE CELL ANALYSIS

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1. ABSTRACT

We describe the fabrication and electrical testing of Suspended Microchannel Resonators (SMRs) with integrated piezoresistive readout. The SMR incorporates fluidic channels inside a resonant cantilever thereby eliminating viscous damping from the solution. Previously, this concept has been used to measure mass in fluid with a resolution of 1 femtogram (1 Hz bandwidth) [1]. Piezoresistive readout eliminates the need for external optics, and we anticipate that the integrated device can be used in a variety of biomolecular and cell-based assays for point-of-use applications.

Keywords: piezoresistor, cantilever, biosensor

2. INTRODUCTION

Suspended microchannel resonators with integrated readout can measure the mass density of solutions with high precision [2,3,4]. We have recently designed SMRs with low intrinsic mass and a very high quality factor [4]. This has enabled the weighing of biomolecules and single cells with a million-fold higher sensitivity than the quartz crystal microbalance [1,5]. So far, the frequency measurement of our device has relied on measuring the deflection of a laser beam that is focused onto the tip of the resonator. The optics used in our lab do not scale favorably for large arrays and are not suitable for point-of-use applications.

3. DESIGN AND FABRICATION

The resonators are vacuum packaged on the wafer scale and integrated with glass microfluidics to provide the fluidic control necessary for biological measurements ([1], Figure 1a). Piezoresistors can be implemented by standard silicon micromachining [6] and are highly robust. For our SMR biosensors, there are two design constraints that must be addressed when piezoresistors are incorporated: i) The doping profile is constrained by the depth of the cantilever lid (3μm) and should be shallow for high sensitivity. The resistor must not penetrate the 0.5μm oxide layer which is between and electrically isolates fluid inside the cantilever from the silicon surface. ii) Power dissipation must be controlled as heating the cantilever may denature or damage biological substrates inside.

We have fabricated SMR piezoresistors with n-type phosphorous dopants at the surface of the cantilever along the <110> direction. Ion implantation is used to achieve a peak dopant concentration of $10^{18}/cm^3$ in a p-type silicon substrate characterized by a resistivity of 10-20 Ωcm. The resistor implant junction depth is 1.6μm. Limiting the resistor to the bottom portion of the cantilever beam (Figure 1b) increases the average stress within the implanted area. A glass layer is anodically bonded to the silicon surface to create a high

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vacuum chamber. Instead of bonding over metal traces which may compromise the seal, highly doped conductive traces connect the resistor to metal bond pads on the chip edge.

4. RESULTS AND FUTURE

Readout of the resistance change is amplified through a Wheatstone bridge (Figure 2). Potentiometers are incorporated in order to balance the amplifier as well as compensate for capacitive coupling of the electrostatic drive signal. Figure 3 shows the frequency response which corresponds to superposition of the signal from the resistor and the drive signal feed-through. Measurements of resistance change as the entire device is heated in a convection oven suggest that a reasonable bias voltage of 1V on the bridge will result in biocompatible temperatures of less than 40°C. We are currently optimizing the readout signal and developing a variety of biomolecular and cell-based assays for point-of-use applications.

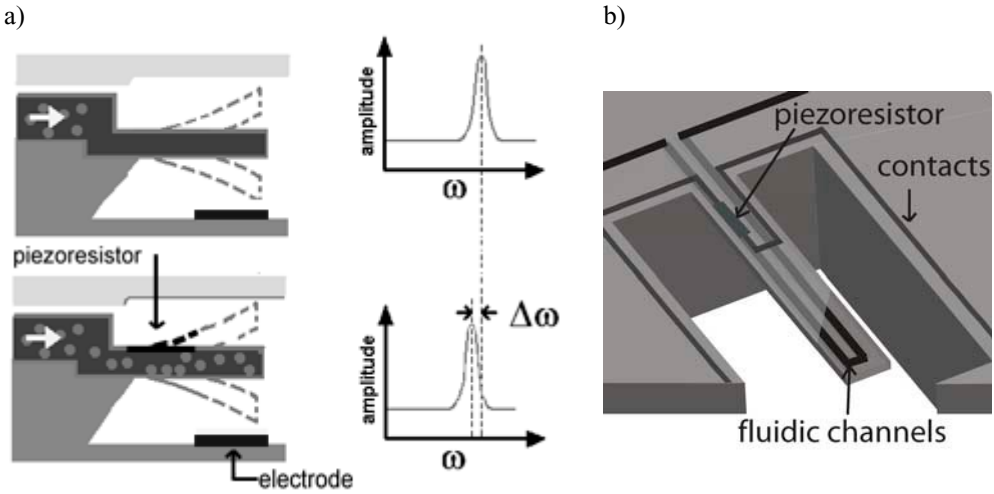

Figure 1: a) Resonant frequency of the SMR shifts upon entrance of biomolecules in the channel. The drive signal is electrostatically applied via an electrode. 1b) 3D-representation of the cantilever. Silicon at the tip is cut away to show the fluidic channels.

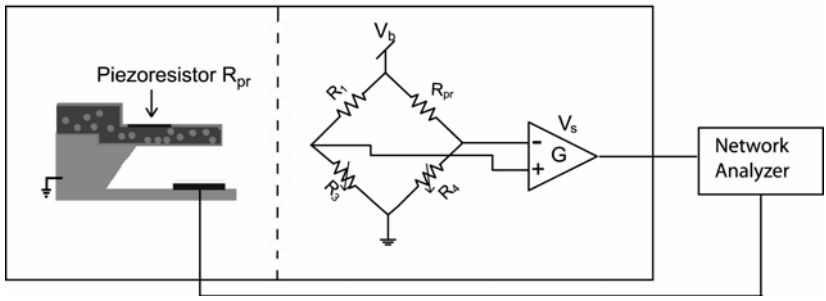

Figure 2: Measurement setup for AC drive of the cantilever and readout from the piezoresistor. The drive signal contains 50VDC and 200mVAC components.

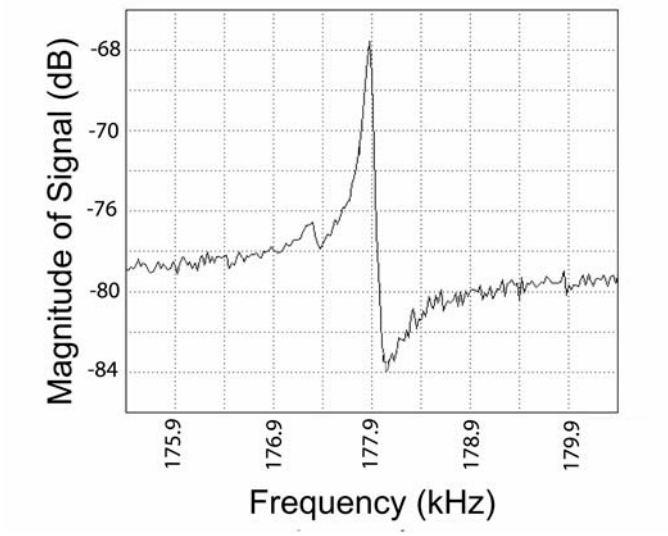

Figure 3: Output spectrum: superposition of the resonant signal from the cantilever and capacitive coupling of the drive signal.

REFERENCES

[1] T.P. Burg, M. Godin, S.M. Knudsen, W. Shen, G. Carlson, J.S. Foster, K. Babcock, S.R. Manalis, "Weighing of biomolecules, single cells and single nanoparticles in fluid", Nature 446 (2007).
[2] D. Westberg, O. Paul, G.I. Andersson, H. Baltes, "A CMOS-compatible device for fluid density measurements fabricated by sacrificial aluminium etching" Sens. Act. A 73 (1999).
[3] P.Enoksson, G.Stemme, E.Stemme, "Fluid density sensor based on resonance vibration," Sens. Act. A, 47 (1995).
[4] D. Sparks, R. Smith, R. Schneider, J. Cripe, S. Massoud-Ansari, A. Chimbayo, N. Najafi,"A variable temperature, resonant density sensor made using an improved chip-level vacuum package" Sens. Act. A 107 (2003).
[5] S. J. Martin, V. E. Granstaff, G.C. Frye, "Characterization of a Quartz Crystal Microbalance with Simultaneous Mass and Liquid Loading", Anal. Chem. 63 (1991).
[6] M. Tortonese, H. Yamada, R. C. Barret, C. F. Quate: Proc. 2nd Int. Conf. on Solid-State Sensors and Actuators (Transducers'91) (1991).