A Biomedical Sensor Based on Resonant Absorption of Ultrasound Waves in Hydrogel-based Resonators

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ABSTRACT

Smart hydrogels can be tailored to undergo a volume change in response to an analyte. The potential biocompatibility of these materials has made them a very promising material for biomedical sensing applications. To fully exploit the benefits of these materials, a fast and reliable transduction mechanism is necessary. Here we report a new sensing method based on tracking the resonance absorption of ultrasound waves inside smart hydrogel pillars. This sensing mechanism enables a cost-effective and completely passive implantable sensing component with no need for transcutaneous connections. In addition, it is possible to employ a variety of different smart hydrogels with this sensing approach.

Keywords: biomedical sensor, smart hydrogel, ultrasound, mechanical resonator

1 INTRODUCTION

Smart Hydrogels are a cross-linked network of hydrophilic polymer that undergo a reversible volume change in response to an environmental change in concentration of a particular biomedical analyte [1–3].

The versatility of smart hydrogels and their potential biocompatibility has made them a promising candidate for many sensing schemes. A large variety of sensing mechanisms based on optical [4], mechanical [5–7], and conductimetric [8] principles have been reported. Beunger et al. [1], and Tavakoli and Tang [9] provide more comprehensive reviews of hydrogel-based sensors. A sensing scheme that enables the development of an entirely implantable sensing component could be very promising for a variety of biomedical real-time sensing applications. Most of the previously reported sensors either need a transcutaneous connection or active elements and electronics for *in vivo* operation.

Here we introduce a readout mechanism based on tracking the absorption of ultrasound waves in an array of hydrogel pillars, which act as mechanical resonators. The proposed sensor does not require the implantation of an active component inside the tissue and does not need any transcutaneous connection, which makes it a good candidate for *in vivo* sensing. Additionally, the readout is based on ultrasound which is generally considered safe and has the potential to be integrated with widely available medical ultrasound imaging equipment. Furthermore, the sensing principle applies to any smart hydrogel which makes it extremely versatile. The method used for fabricating the resonator pillars is also simple and cost-effective.

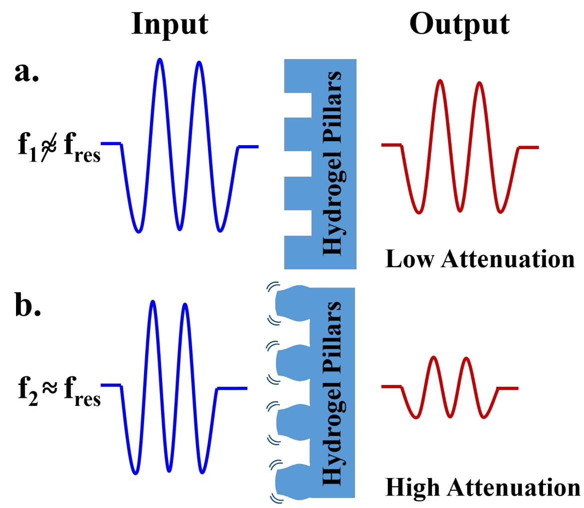

Figure 1: Hydrogel sheet with arrays of pillars formed on it. (a) At a frequency away from resonance frequencies of the smart hydrogel pillars ($f_1 \not\approx f_{res}$) the ultrasound waves pass through the structure with only very low attenuation. (b) If the ultrasound frequency matches one of the resonance frequencies of the pillars ($f_2 \approx f_{res}$), the resonators absorb and dissipate more energy and hence reduce the amount of the ultrasound transmission through the structure.

2 SENSOR CONCEPT

The sensor consists of a sheet of hydrogel with an array of smart hydrogel pillars formed on it as shown in figure 1. The ultrasound waves propagate by longitudinal compression and expansion motion of a medium. If the frequency of the ultrasound matches a mechanical resonance frequency of the smart hydrogel resonator pillars, the pillars excite to vibrations by absorbing energy from ultrasound. Since the resonance frequencies

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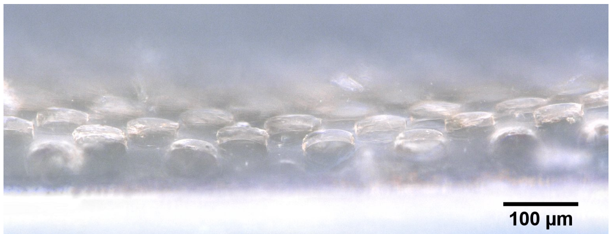

Figure 2: Optical image of a fabricated array of smart hydrogel resonator micropillars. The pillars are connected by a smart hydrogel backplane.

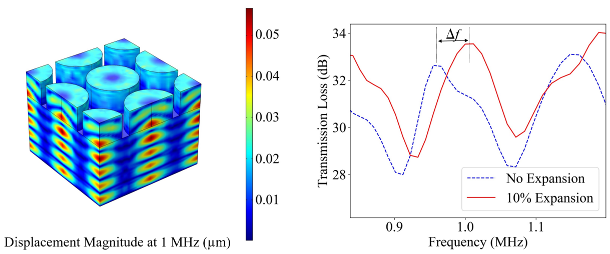

Figure 3: Exemplary, three-dimensional finite element simulation of the hydrogel resonator arrays. (a) Shows a building block from an infinite sheet of resonators at a mechanical resonance in which the color scale shows the maximal displacement amplitude. (b) The ultrasound transmission loss spectrum of the resonators in two different swelling states indicating a shift in the peak.

of the pillars depend on the swelling state of the smart hydrogel, tracking the frequencies at which a absorption maximum is found can give information about the changes in the environmental concentration of the target biomedical analyte.

3 SENSOR FABRICATION

The hydrogel pillars were made using a molding-based approach. A negative mold structure of the hydrogel pillars was created using lithography on SU8 photoresist. The structure was then coated with Parylene-C to avoid adhesion of the hydrogels during the molding process. The hydrogel pre-gel solution was prepared as described by Horkay et al. [2] and Leu et al. [10]. This pre-gel solution was then put in the mold using vacuum to facilitate the filling of the mold structure. The pre-gel solution was then polymerized using UV light with 365 nm wavelength. Figure 2 shows the hydrogel pillars after their release from the mold.

4 PRELIMINARY RESULTS

The sensing concept was first investigated for an exemplary design of 100 um diameter pillars in finite element simulations. Figure 3(a) shows a building block that was used together with Floquet periodic boundary conditions to simulate an infinite sheet with mechanical resonators in COMSOL Multiphysics.

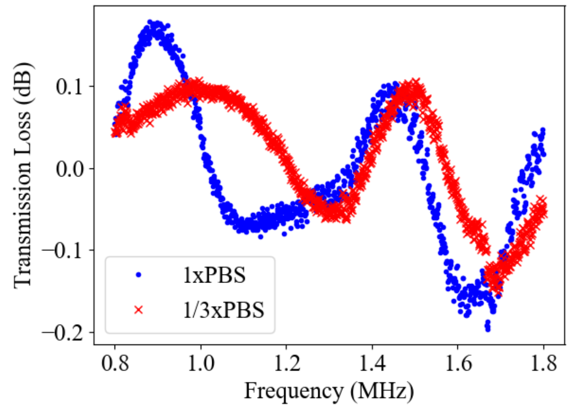

Figure 4: Experimental transmission loss spectrum from a sample array of smart hydrogel micropillars indicating a shift in resonance peaks as a result of a change in concentration of the phosphate buffer saline (PBS) which induces a change in the swelling state of the pillars with 100 um diameter.

As the hydrogel expands, the resonance frequency of the pillars undergoes a frequency shift. This is depicted in Figure 3(b) in terms of the transmission loss which is defined as $20log\frac{|p_i|}{|p_t|}$, where p_i and p_t are the incident and transmitted pressures of ultrasound waves, respectively.

Several designs were fabricated and tested in two different salt concentrations to validate the concept. The response from the resonator sheets was tested with a pulser-receiver setup inside a water tank, which measures the transmission of ultrasound through smart hydrogel resonator sheets by sending burst signals of different frequencies through them and recording the transmitted signals. Transmission loss is calculated from comparing the amplitude of the transmitted burst signals to the background. The results indicate a frequency shift in two different swelling states of the hydrogel, as shown in figure 4. The promising preliminary results obtained from finite element simulations and transmission experiments indicate a high potential of this sensing principle for implantable applications. Further work is needed to optimize the pillars for faster and stronger response at specific medical ultrasound frequencies as well as to test different hydrogels tailored for a variety of analytes with this sensing scheme.

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6 Conflict of interest statement

Florian Solzbacher declares financial interest in Blackrock Microsystems LLC and Sentiomed, Inc.; Jules Magda declares financial interest in Applied Biosensors LLC.

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