

Hydrogel-Fractal Piezoelectric Bilayer Transducer for Wireless Biochemical Sensing

Sayemul Islam, Moonchul Park, Seung Hyun Song, and Albert Kim

Abstract— This paper reports on a novel transducer for wireless biochemical sensing. The bilayer transducer consists of a fractal piezoelectric membrane and pH-sensitive chemo-mechanical hydrogel, which overcomes many shortcomings in the chemical and biochemical sensing. The fractal design on the piezoelectric membrane enhances frequency response and linearity by employing periodically repeated pore architecture. As a basis of the pore, a Hilbert space-filling curve with modifications is used. On the surface of the fractal piezoelectric membrane, the hydrogel is laminated. When the bilayer transducer is introduced to a pH environment (e.g., pH = 4, 8, and 12), the hydrogel swells (or shrinks) and induces the curling of the bilayer transducer ($10.47^\circ/\text{pH}$). The curvature then exhibits various ultrasound responses when the bilayer transducer was excited. The measured voltage outputs using an ultrasonic receiver were 0.393, 0.341, 0.250 mV/cm² when curvature angles were 30°, 60°, and 120°, respectively. Overall pH sensitivity was 0.017 mV/cm²/pH. Ultimately, the biochemical sensing principle using a novel bilayer ultrasound transducer suggests a simple, low-cost, battery-less, and long-range wireless readout system as compared to traditional biochemical sensing.

Keywords – fractal, ultrasound transducer, pH, hydrogel

I. INTRODUCTION

In situ environmental sensing of temperature, pH, salinity, or specific molecular targets (e.g., glucose, heavy metal ions, protein, drugs, and their metabolites) is an important element in healthcare and environmental monitoring [1]–[3]. The emerging chemical and biochemical sensing pose unique challenges as it has a more complex mode of operation compared to a physical transducer. It is because chemical and biochemical sensing usually involve additional steps in the working principle. Briefly, traditional chemical or biochemical sensing consists of a sample analyte, a receptor, and a transducer [3]. Among them, a receptor is a component that makes chemical/biochemical sensing challenging. It converts the chemical information into a form of energy that can be measured by a transducer (chemical recognition). In spite of the advancements in chemical/biochemical sensing technology, a receptor always suffers from the co-existence of many interferences and target molecules, and it is often consumable [4].

More recently, there has been substantial interest in using hydrogel as a receptor [5], [6]. The hydrogel is a water-swollen

polymer network, engineered to contain chemical groups that are sensitive to specific environmental stimuli. Such smart hydrogels can exhibit reversible volume and shape change in response to small variations of stimulus such as temperature, pH, specific ions, antigens, or glucose [6]–[8]. It is an attractive choice as a receptor because it does not require an onboard power source, has a smaller form factor, and can be integrated into a simpler readout system. The hydrogels, coupled with rapidly advancing microelectromechanical system (MEMS) technology, have offered many novel chemical and biochemical sensing techniques [9]–[11]. For example, Lei et al. demonstrated a MEMS-based LC (inductor-capacitor) transponder in which the capacitance was modulated via osmotic swelling and shrinking of pH-sensitive hydrogel [9]. However, there are a few bottlenecks in the broader application of such sensors. One needs a cleanroom process to create a hermetically sealed MEMS transducer. Then, a wireless range is not sufficient if it is deeply implanted (e.g., bladder, gut, or arteries) due to higher operational frequency (~MHz) and tissue absorption [12].

In this paper, the new chemical/biochemical sensing technique is presented using a bilayer transducer that consists of pH-sensitive hydrogel and a fractal piezoelectric transducer. Figure 1 shows an example schematic of the bilayer

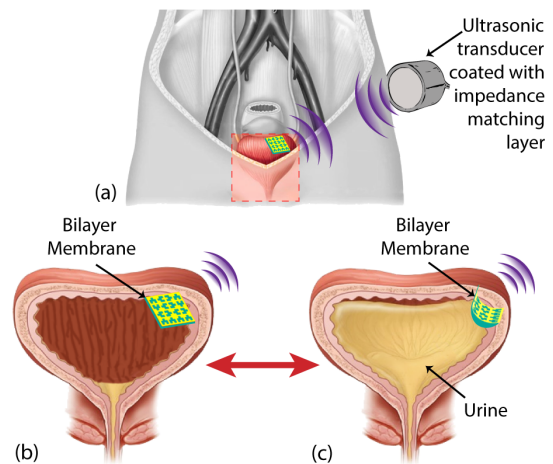


Figure 1: (a) Implanted hydrogel-fractal piezoelectric bilayer transducer in bladder sensing and radiating an ultrasonic wave that carries pH information; (b)-(c) detailed working principle of the transducer

S. Islam is with the Department of Electrical and Computer Engineering, Temple University, Philadelphia, PA, USA (email: sayemul@temple.edu).

M. Park is with the Department of Electrical and Computer Engineering, Temple University, Philadelphia, PA, USA (email: moonpark@temple.edu).

S. H. Song is an Assistant Professor in the Department of Electronics Engineering, Sookmyung Women's University, Seoul, Korea (email: shsong.ee@sookmyung.ac.kr).

A. Kim is a member of IEEE and currently an Assistant Professor at the Department of Electrical and Computer Engineering, Temple University, Philadelphia, PA 19122 USA (phone: 215-204-3222; e-mail: albertkim@temple.edu).

transducer, which senses the pH of urine to detect urinary tract infection (UTI). The normal urine pH is in a slightly acidic range of 4.5 to 8 [13]. However, the pH value in the bladder can shift to the alkaline range due to the existence of urea-splitting organisms (e.g., *Proteus*, *Klebsiella*, or *Ureaplasma urealyticum*) [14]. Therefore, ambulatory pH monitoring may allow prevention for UTI. The sensing strategy is shown in Figure 1(b) and (c). The proposed bilayer transducer can be rolled and deployed into the bladder through the urethra. When urine fills the bladder, higher pH induces curvatures of the bilayer transducer, which in turn generates different ultrasound responses, such as varying amplitude, frequency, and focal points. In this transduction, the pore architectures defined in a fractal membrane play important roles: 1) enhancing power output by increased plate mobility [15], 2) widening bandwidth by increased vibrational modes [16], and 3) increasing curvature ratio by providing void space to fill with hydrogel. It is expected to overcome many of the aforementioned shortcomings by using ultrasonic energy to interrogate the pH information. Use of ultrasound as a mean of wireless interrogation also addresses deep implantation needs and provide a simple readout system. Additionally, fabrication can be carried out without a cleanroom process.

II. DESIGN AND OPERATION

B. Hydrogel- Fractal Piezoelectric Bilayer

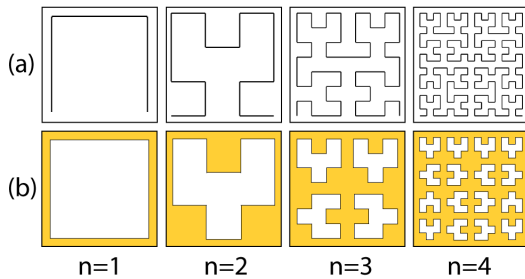


Figure 2: (a) Hilbert curves; (b) Modified Hilbert curves (n indicates iteration order)

Previously, our group reported a fractal ultrasound transducer that enhanced frequency response and acoustic intensity response [16]. Herein, we also implemented the Hilbert curve in the hydrogel-fractal bilayer ultrasound transducer. With slight modification, the Hilbert curve can be a closed shape, defining periodic pore architectures. Figure 2 illustrates both the original Hilbert curves and the modified Hilbert curves. The iteration order, n , denotes the number of segments that are repeated to fill more in the two-dimensional area. In each iteration, the Hilbert curve was modified by relocating one or two segments to form a closed shape. Such fractal design is then implemented onto a piezoelectric membrane. Finally, a novel hydrogel-fractal transducer can be created by depositing a pH-sensitive chemo-mechanical hydrogel, such as poly(methacrylic acid-co-acrylamide) to coat and fill the fractal transducer.

III. FABRICATION

Figure 3 shows the fabrication process for a prototype hydrogel-fractal bilayer transducer. It starts with a selection of fractal designs. For the demonstration, the third and fourth-

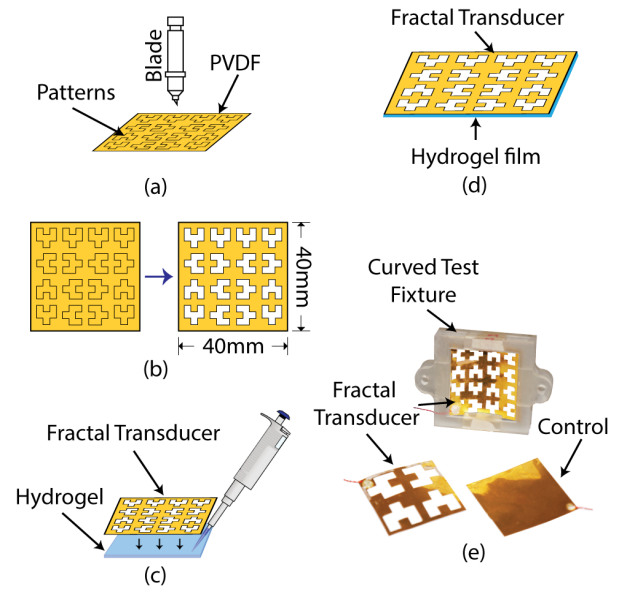


Figure 3: Fabrication process: (a)-(b) fractal design was cut from PVDF membrane, (c) placing fractal membrane on pre-cured hydrogel, (d) completed bilayer transducer, and (e) pictures of prototypes

order Hilbert curves were selected, which generates higher vibration amplitudes than the first and second orders [16]. First, modified third and fourth-order Hilbert curves, as described above (Figure 2(b)), were drawn using a CAD program. Using a cutter plotter (CAMEO[®] 3, Silhouette America, Inc.), the polyvinylidene fluoride (PVDF) sheet was cut (Figure 3(a)-(b)). Total three different types of transducers were prepared: two bilayer transducer (3rd and 4th iterations) and a control sample (one without fractal cutouts). 30-gauge (0.25 mm diameter) polyimide insulated copper wires were attached to the corner of the samples by applying conductive silver epoxy (8331-14G, MG Chemicals). The pH-sensitive hydrogel was prepared separately. The pre-gel solution A and B could be prepared as follows. The solution A was prepared with 334.5mg of acrylamide base (AAM, Sigma-Aldrich), 100.8μL of methacrylic acid (MAA, Sigma-Aldrich), 100μL of N,N,N',N'-tetramethylethylenediamine (TEMED, Sigma-Aldrich), 16.35mg of N,N'-methylenebisacrylamide (crosslinker, Sigma-Aldrich) with 1.2mL of deionized (DI) water. The solution B was a mixture of 80 mg/mL ammonium persulfate (Sigma-Aldrich) in DI water. A pH-sensitive hydrogel was then synthesized by mixing solutions A and B in a 5.9:1 ratio. To laminate pH-sensitive hydrogel on the surface of the fractal transducer, the aforementioned pre-gel solution A and B were added to a beaker and mixed by a vortex mixer. The pre-gel solution was transferred to a petri dish, and the fractal transducer was placed on top while the petri dish was gently shaken. Gravity allowed to create a 1-mm thickness gel layer (Figure 3(c)-(d)), as described in [17]. The polymerization allows the hydrogel film to attach to the fractal transducer, completing hydrogel-fractal bilayer transducer (Figure 3(d)). Figure 3(e) shows fabricated bilayer transducers (an experimental apparatus with a fourth-order fractal bilayer transducer is shown at the back).

IV. EXPERIMENTAL RESULTS

The experiments were conducted to characterize hydrogel-fractal piezoelectric bilayer transducer for wireless biochemical sensing. First, pH-mediated curvature tunability was investigated. Then, natural mechanical frequency (i.e., eigenfrequency) of the bilayer transducer was studied. Lastly, ultrasound amplitude in terms of the received output voltage (mV/mm²) was characterized.

A. Experimental Setup

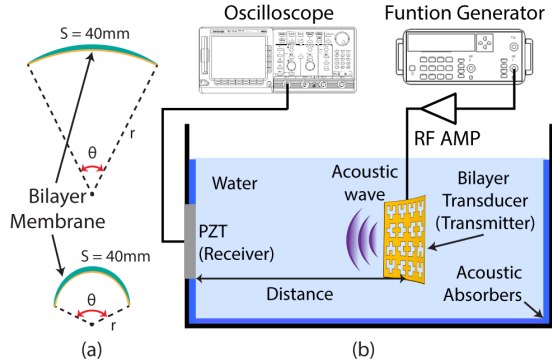


Figure 4: Experimental setup: (a) curved bilayer and (b) water tank setup

Figure 4 illustrates the experimental setup. For the ultrasound amplitude measurement, a custom-designed frame to hold a prototype was designed (Figure 3(e)). The frames could hold a prototype in specific angles. (θ). The specific angles refer to the curvature angle when a bilayer transducer is curled due to the change in pH (Figure 4(a)). The angle was determined by $\theta = S/r$, where S is the length of the curvature, and r is the radius of curvature. In our case, $S = 40$ mm, $\theta = 0^\circ, 30^\circ, 60^\circ$, and 120° .

As water has similar acoustic properties as soft tissue [18], all characterizations were performed in a water tank (60 cm $\times$ 30 cm $\times$ 20 cm) (Figure 4(b)). The bilayer transducer was driven by pulsed signals ($V_{in} = 225$ mV, frequency = 5kHz, pulse width = 250 ns) using a signal generator (MSOX3024T, Keysight Technologies). The bilayer transducer generates a segment of ultrasound whose amplitude varies depends on the curvature angles; thus, a specific pH level. A PZT transducer (PZT5H, Piezo Inc.) mounted on the side of the water tank is used as a receiver. The distance between the bilayer transducer and the PZT receiver was varied from 20 mm to 90 mm. Note that this method was implemented to mimic the sensing application and to simplify the experiment. In real cases, an external ultrasound transducer will be used to apply the ultrasound to the bilayer transducer, followed by reading the reflected ultrasonic waves.

B. pH Tunability of Bilayer Transducer

Three different pH solutions (pH 4, 8, and 12) were prepared to observe how the hydrogel can bend the transducer. Figure 5 shows time-lapse pictures of the bilayer transducer at different pH levels. As soon as the pH solution was introduced, the bilayer transducer started to curl and showed dramatic curvature. The hydrogel swells at a higher pH level

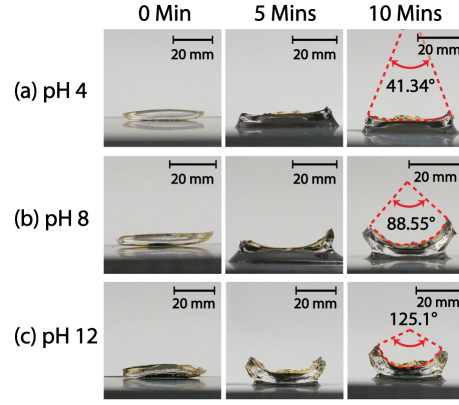


Figure 5: pH tunability of the bilayer transducer

(alkalic) and shrinks at a lower pH level (reversible action). Thus, the angle of the curvature was greater in the higher pH environment. After 10 min, the measured angles of the curved bilayer transducer were 41.3° , 88.6° , and 125.1° at pH 4, 8, and 12, respectively. The sensitivity was $10.47^\circ/\text{pH}$. The angle of the bilayer transducers remained stable after 10 minutes.

C. Frequency Response of Bilayer Transducer

The frequency response of the fractal transducer is shown in Figure 6. The resonance frequencies of all bilayer transducers were recorded around 11.6 MHz. The 3 dB bandwidths, marked with '+' on the plot were 1.87, and 2.08 MHz for iteration order three and four, respectively. The positive trends of bandwidth with the increase in the iteration order corresponds to the finding that the plate mobility is higher at the vicinity of the hole [16].

The increased topological complexity introduced by the fractal design iteration order allows the transducer to vibrate in more than one vibrational mode. Additional features on the surface of the sample introduce different lengths and shapes compared to samples with less complexity. These features will naturally vibrate in different directions and at different amplitudes due to their inherent physical structure.

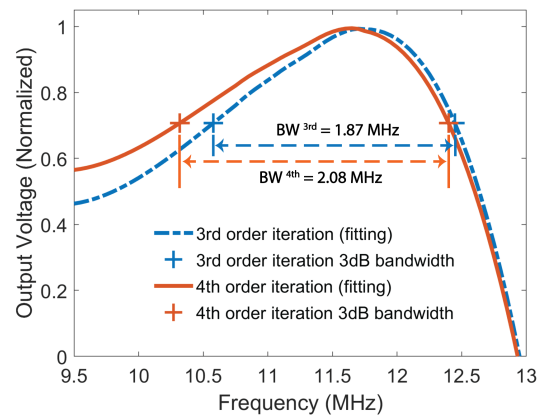


Figure 6: Frequency response of bilayer transducers.

D. Wireless pH Sensing

As mentioned in the working principle and pH tunability results, it is expected that the curvature will induce different

ultrasound response. In our case, the received ultrasonic intensity in terms of voltage was measured. The trend of the output voltage from the PZT receiver was monitored when a bilayer transducer was bent and fixed at specific angles such as 0°, 30°, 60°, and 120°. Those angles were chosen arbitrarily for the convenience of the experiments as well as based on the pH tunability results (41.34° to 125.1°). A custom-made apparatus was used, as shown in Figure 3(e).

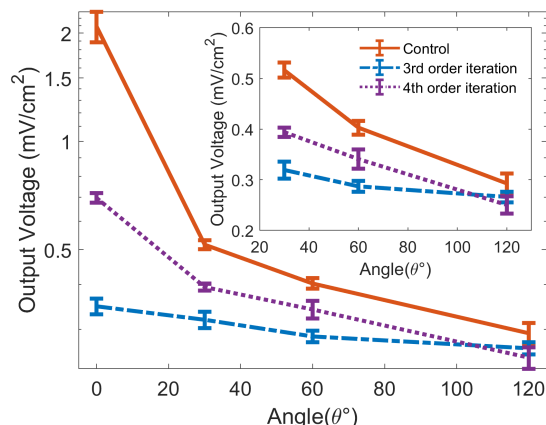


Figure 7: Received voltage output vs. specific angle of curvature of bilayer transducers

The output voltages were measured from 20 mm to 90 mm between the bilayer transducer and the PZT receiver every 3 mm in resolution. The corresponding ultrasound time delay was 14 μ s to 62 μ s with 2 μ s resolution (the acoustic velocity in water is 1,496 m/s at 25 °C). Then, the total voltage outputs were averaged. It was to account for the dynamic ultrasound propagation caused by the fractal transducer. The trend in ultrasound response improved as the iteration order increased. Figure 7 shows the received output voltage on a logarithmic scale as a function of the curvature angle of the bilayer transducer. The control sample (one without fractal cutouts) showed an exponential voltage drop as the curvature increases. On the contrary, the third-order bilayer transducer showed an improvement in terms of linearity (0.0006 mV/cm²/degree, $R^2=0.90$). Lastly, the fourth-order bilayer transducer exhibited 0.0016 mV/cm²/degree, $R^2=0.99$. From the subset in Figure 7, the improvements in both linearity and sensitivity could be observed. Overall, the sensitivity of the wirelessly received voltage was 0.006 mV/cm²/pH for third-order bilayer transducer, and 0.017 mV/cm²/pH for the fourth-order bilayer transducer.

Overall, we demonstrated a new class of wireless electrochemical sensing by combining hydrogel and ultrasonic transducer. To implement it in medical application, however, the proposed sensor will need to incorporate a protective layer on the hydrogel to prevent potent complications, such as septic cystitis [19]. Furthermore, the sensitivity can be improved to match with that of the commercial sensors. Further research and long-term study are required to be adopted to the clinic.

V. CONCLUSION

A novel wireless chemical/biochemical sensing scheme

using a hydrogel-fractal piezoelectric bilayer transducer was presented. The transducer included two important components: a hydrogel as a receptor and a fractal transducer as an improved ultrasound transducer. By combining these two components, the hydrogel translated the pH level to the curvature of the fractal transducer, which enhanced frequency response as well as sensing linearity. This simple, low-cost, battery-less, and long-range wireless chemical/biochemical sensing is expected to address many shortcomings in a traditional chemical/biochemical sensing.

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