31st Annual International Conference of the IEEE EMBS
Minneapolis, Minnesota, USA, September 2-6, 2009

Wireless, Magnetic-based Sensors for Biomedical Applications

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Abstract – **Wireless magnetic sensor technologies are gaining popularity in biomedical community due to their remote query nature, which allows them to be used as long-term implantable sensors. Some of these sensors are also low cost so they are suitable for use on a disposable basis. In this paper, two wireless magnetic sensors are described: the magnetoelastic sensor and the magneto-harmonic sensor. Magnetoelastic sensors are made of magnetoelastic materials that when under an AC magnetic field excitation, vibrate and resonate at their resonant frequencies. Since the resonant frequency of a magnetoelastic sensor is proportional to the mass or viscosity of the surrounding material, it has been used to detect chemical and biological targets by incorporating coatings that change mass/elasticity in response to the parameters of interest. Conversely, magneto-harmonic sensors detect parameters of interest by monitoring the change in the pattern or amplitude of the magnetic higher-order harmonic fields. Typically, a magneto-harmonic sensor consists of a magnetically soft material (sensing element) and a permanent magnet (biasing element). When energized by an AC magnetic field, the sensing element generates higher-order magnetic fields that change with the biasing field from the biasing element. By designing the sensor so the separation distance between these two elements varies with the parameters of interest, the magneto-harmonic sensor has been used for remote measurement of pressure and stress. This paper presents the operating principles and biomedical applications of these sensors.**

I. Introduction

Wireless, passive sensors consist of two components: individual sensors placed in or near the target and detectors that remotely interrogate the sensor responses. These sensors have great potentials for various biomedical applications since they do not require internal power supply (all power generated by the detectors), and generally lower in cost compared to standard sensors. As a result, these sensors are actively being explored for use as long-term implantable sensors and disposable sensors.

One of the most common wireless, passive sensors is the inductive-coupling based sensor, such as the RFID (radio frequency identification) sensor [1]. Generally, this type of sensor consists of an inductor or magnetic coil that captures electromagnetic field and turns it into an electric voltage for power. Measurement data are then transmitted through the same coil or a different antenna. A separate device is used to generate the excitation electromagnetic field and capture the transmitted signal. A simpler version of this sensor connects a capacitor to the inductor, forming an inductor-capacitor resonant circuit [2]. Parameters of interest are detected by measuring the changes in the resonant frequency of the circuit. An example of the inductive-coupling based sensors for biomedical applications is the EnsdoSure™ aortic aneurysm pressure monitoring system (CardioMEMs Inc). EndoSure is a passive telemetry pressure sensor made of a pressure-sensitive capacitor and an inductor. As the capacitor changes its capacitance in response to the pressure, the resonant frequency of the circuit changes, allowing remote measurement of pressure. Another type of wireless, passive sensor uses piezoelectric material to receive energy from acoustic waves. An example of this sensor is the Impressure™ aortic aneurysm pressure monitoring system by Remon Medical Technology Inc. This sensor uses a piezoelectric membrane that charges a capacitor when actuated by an ultrasound waves generated by a remotely located probe. Once charged, the sensor measures the pressure and generates an ultrasound signal that is relayed back to the probe.

Magnetic materials are great candidates for construction of wireless, passive sensors as they can be remotely queried through magnetic fields. In addition, using magnetic fields for wireless data transmission is an attractive means because unlike electromagnetic fields and acoustic energy, magnetic fields have minimal attenuation in electrically and acoustically absorbing media such as human tissues. In this paper, the magnetoelastic sensor and the magneto-harmonic sensor are presented. Both technologies have the sensor components placed at or near the target, and their responses monitored by an external detection device.

Magnetoelastic sensors are typically made of amorphous ferromagnetic ribbons such as Metglas™ 2826MB (Metglas, Inc). Under an AC magnetic field excitation, these sensors vibrate and resonate at their resonant frequencies. Due to their small size, low cost, and passive and wireless nature, they have been used to monitor chemical concentrations such as glucose, ammonia, carbon dioxide, and pH by applying a mass- and/or elasticity-changing chemical-responsive layer [3]. Magnetoelastic sensors have also been used for detection of biological targets and biotoxins such as *Escherichia coli* O157:H7, staphylococcal enterotoxin B and ricin [4]. In addition, they have been used to monitor blood coagulation behavior [5].

Magneto-harmonic sensors consist of a sensing element, made with a magnetically soft material, and a biasing element, which is a permanent magnet. When energized by a

Manuscript received April 22, 2009.

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low frequency magnetic field (<5 kHz) the sensing element of the sensor generates higher-order magnetic fields that can be independently detected. The biasing element is used to generate a DC magnetic field that alters the pattern and amplitude of the higher-order magnetic harmonic fields. By designing the sensor so the separation distance between these two elements varies with the parameters of interest, magneto-harmonic sensors have been used to measured pressure and stress by monitoring the changes in the pattern or amplitude of the higher-order harmonic fields [6-8].

II. Theoretical Description

A. Description of the Magnetoelastic Sensor

When subjected to a magnetic field, a magnetoelastic sensor vibrates at the frequency of the excitation field, and the magnitude of the vibration is greatest at the mechanical resonant frequency of the sensor. When the sensor vibrates, it also launches magnetic flux that can be remotely detected with a coil. Magnetoelastic sensors can be interrogated by performing a frequency sweep operation, which exposes the sensor to a frequency-changing, steady-state magnetic field and monitors the returned flux at every frequency. Alternatively, the sensor can be interrogated using a transient frequency-counting operation, which excites the sensor with a series of sinusoidal bursts and captures its transient response; sensor's resonant frequency is determined by measuring the frequency of the transient signal. The resonant frequency of the sensor decreases with a mass loading. Thus, wireless chemical sensors can be realized by combining the sensor with a mass or elasticity changing, chemically responsive layer (see Fig. 1).

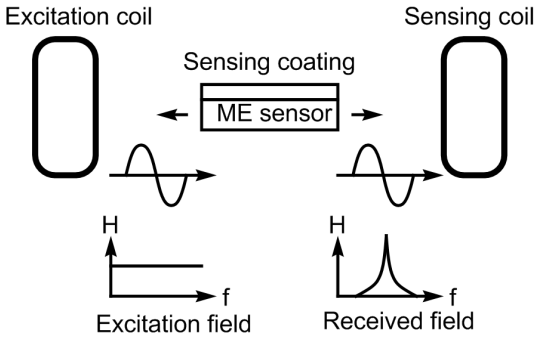

Fig. 1. Interrogation of the magnetoelastic sensor, where the excitation coil generates the excitation field and the sensing coil captures the received field.

B. Description of the Magneto-harmonic Sensor

The magneto-harmonic sensor consists of a soft magnetic material and a permanent magnet [6-8]. As illustrated in Fig. 2, the soft magnetic material (sensing element) generates secondary magnetic fields that also include the higher-order harmonic modes when exposed to a low frequency AC magnetic field. The pattern of the higher-order harmonic fields can be determined by measuring the field intensity as a function of an applied DC magnetic field. Generally, the 2nd order field is measured due to its larger field intensity compared to other modes. In the absence of a secondary DC magnetic field (besides the applied DC field), the 2nd order harmonic field pattern is symmetrical and has a null at zero biasing fields as shown in Fig. 2a. In the presence of a permanent magnet, the 2nd order harmonic field pattern shifted horizontally due to the introduction of the DC magnetic field (biasing field) generated by the permanent magnet (Fig. 2b). To quantify the shift, a variable, H_z, is defined as the null point between the two peaks of the 2nd harmonic. The sensor is designed so the separation distance between the sensing and biasing elements varies with the parameter of interest. As the separation distance decreases, the biasing field experienced by the sensing element increases. This increases H_z, allowing remote tracking of the parameter of interest (Fig. 2c).

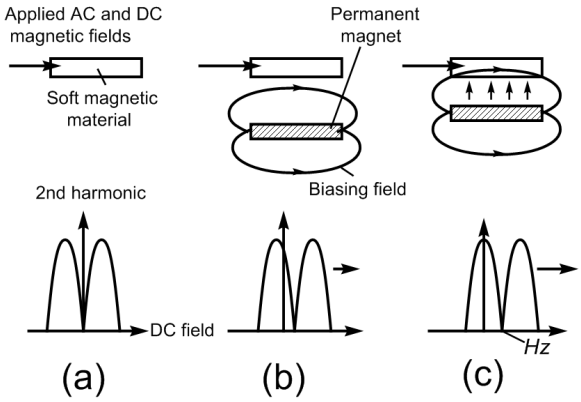

Fig. 2. Interrogation of the magneto-harmonic sensor. (a) The sensing element is alone. (b) The biasing element (permanent magnet) is placed next to the sensing element. (c) The distance between the sensing and biasing elements decreases.

III. Magnetoelastic Sensor Applications

A. pH Monitoring

A magnetoelastic sensor made of 8 mm × 0.5 mm × 26 μm Metglas 2826MB ribbon was first dip-coated with 0.4 μg polyurethane and cured at 80 °C for 4 hours to form a moisture resistant film that protected the sensor from rusting and improved adhesion of the polymer. The pH responsive polymer was then applied by dip-coating the sensor in a 1:1 ethanol and ethyl ether mixture solution at a concentration of 5 w%. The polymer-coated sensor was dried in a vacuum oven at 80 °C under 10 torr overnight to remove the solvent. Copolymer poly(acrylic acid-co-isooctylacrylate) was used as the pH responsive coating. The copolymer was synthesized at 70 °C by free radical copolymerization of acrylic acid and isooctylacrylate with an initial mole ratio of acrylic acid to isooctylacrylate of 1:1. When exposed the sensor to test solutions from pH 4 to pH 7.5, the sensor showed a resonant frequency shift of ~0.6%/pH [4]. The response time to reach 90% of the steady-state value was found to be less than 3 minutes [4].

B. Bacteria and Biotoxin Detection

Magnetoelastic sensors were used to detect biotoxin such as *Staphylococcal enterotoxin B* (SEB), ricin (Ricinus

communis), and bacteria such as *Escherichia coli* O157:H7 [4]. To fabricate the SEB detecting sensor, affinity-purified rabbit anti-SEB antibody was covalently immobilized. The affinity reaction of biotin/avidin and biocatalytic precipitations was used to amplify antigen-antibody binding events on the sensor surface so a small change in SEB concentration can cause a large change in sensor response. Similarly, *E. coli* O157:H7 sensor was mobilized with alkaline phosphatase as a labeled enzyme to the anti-*E. coli* O157:H7 antibody, and the mass change associated with the antibody-antigen binding reaction was amplified by biocatalytic precipitation of 5-bromo-4-chloro-3-indolyl phosphate (BCIP). To detect ricin, the magnetoelastic sensor was coated with a ricin-sensitive assay consisted of a sandwich complex of anti-ricinus antibody-ricin-alkaline phosphatase conjugated rabbit anti-ricinus antibody on the sensor surface, with biocatalytic precipitation of BCIP to amplify the mass change associated with antigen-antibody binding events on the sensor surface.

In all experiments, the resonant frequencies of the sensors decreased with increasing analyte concentrations. Results indicate changes in resonant frequency were linearly proportional to the logarithmic value of *E. coli* O157:H7 concentration, with a detection limit of 10^2 CFU/ml [4]. Similarly, the resonant frequency of the SEB sensor decreased with increasing SEB concentration. The 1 hr-change in resonant frequency was determined to have a linear response towards SEB concentration, and the detection limit was 0.5 ng/ml [4]. The same response was also observed for the ricin sensor, where the 1-hr resonant frequency change was found to be linear to the logarithmic value of ricin concentrations from 10 ng/ml to 100 μg/ml [4]. The lowest concentration of ricin that could be detected with an incubation time of 1 hr is 10 ng/ml.

C. Monitoring of Blood Coagulation

Magnetoelastic sensors have been used to record Thromboelestograph (TEG) of whole blood. TEG provides a global assessment of the hemostatic function. TEG measures defects in coagulation, abnormalities in platelet function, and enhanced clot lysis (fibrinolysis). It can be performed rapidly with native blood at the point of care or after recalcification of citrated anticoagulated blood in the clinical laboratory. TEG consists of two horizontal lines, and the separation distance between these two lines represents the blood clotting strength. When blood is liquid, these two lines join together. However, as blood begins to clot, the lines split and gradually trace a 'C' shaped curve.

Magnetoelastic sensors captured the clot profile of a blood sample by determining the changes in the resonant amplitude of the sensor. Fig. 3 plots the TEG of a bovine blood sample captured by a magnetoelastic sensor. The blood sample was originally mixed with sodium citrate to prevent coagulation. At the beginning of the experiment, calcium carbonate was added to initiate the clotting process. The change in resonant amplitude of the sensor was found to decrease with blood clot formation. To construct a TEG plot, another curve was created by mirroring the measured curve.

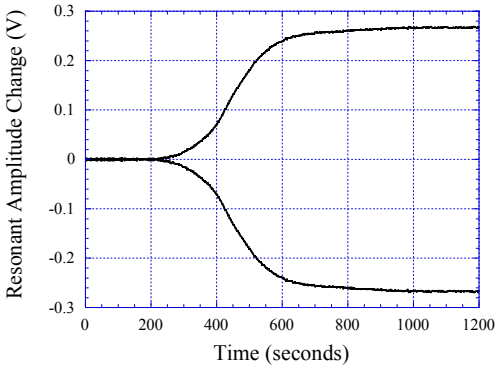

Fig. 3. The clot profile obtained by the magnetoelastic sensor when converted into a TEG curve by vertically mirroring the curve.

IV. Applications of Magneto-harmonic Sensors

A magneto-harmonic stress/strain sensor and a pressure sensor were developed and characterized. Fig. 4 illustrates the design of the sensors. For the stress/strain sensor, the biasing and sensing elements were separated by a flexible substrate. Compressive and tensile forces flexed the substrate, changing the separation distance between the two elements and hence the higher-order harmonic fields. Similarly, for the pressure sensor, the biasing element was placed at the membrane of an airtight chamber. Changes in the ambient pressure deflected the membrane, altering the separation distance between the two magnetic elements and thus the higher-order harmonic fields. The wireless and passive nature of the presented sensor allows long-term implantation in human bodies without worrying about battery lifetime issues. In addition, the sensor is simple in design compared to wireless, passive sensors that are based on microelectronic circuits.

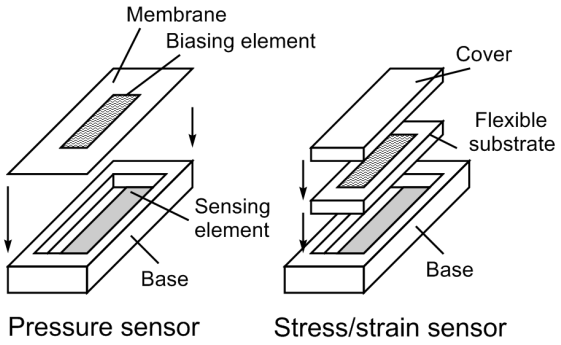

Fig. 4. The design of the magneto-harmonic pressure sensor and strain/stress sensor.

The sensing elements of both sensors were made of Metglas 2826MB, which generated a large magnetic higher-order harmonic field upon excitation by a low-frequency magnetic field. Conversely, the biasing elements were made of Arnokrome III (Arnold Magnetic Technologies, Marengo, IL) strips. The pressure sensor, shown in Fig. 4, was machined from a polycarbonate block with a CNC milling machine. The dimensions of the sensor were 30 mm

× 12 mm × 6 mm. The sensing element was applied to the rigid bottom of the well. The flexible membrane, made of a10 μm thick Mylar sheet, was glued onto the well to form an airtight seal. The dimension of the sensing element was 25 mm × 6.5 mm × 26 μm, and the dimension of the biasing element was 20 mm × 2.5 mm × 30 μm.

For the stress/strain sensor, the sensing element and biasing element were separately embedded in the cover and base of the sensor package. The dimensions of the cover and base were 26 mm × 8 mm × 2 and 30 mm × 12 mm × 5 mm, respectively. The base also had a 26 mm × 10 mm × 6 mm well. Deformable rubber pads with tensile strength of 0.66 MPa and 6.21 MPa were used to separate these two elements. The cover and base of the sensor were sealed with silicone glue. The dimensions of the sensing and biasing elements were 25 mm × 6.5 mm × 26 μm and 20 mm × 2.5 mm × 30 μm, respectively.

During the experiment, the sensors were placed inside the excitation coil, consisted of two sets of superimposed AC coil and a DC coil in Helmholtz configuration. The AC coil was connected to a function generator (Fluke 271 10MHz) and an amplifier (Tapco J1400), and the DC coil was connected to a DC power supply (Kepco MBT 36-10M). The detection coil was made of two oppositely wound square coils. To determine the shift in the 2nd harmonic field spectrum, the AC field frequency was set at 200 Hz, and the DC field was varied from 0 to 140 A/m to determine H_z.

For pressure measurements, the sensor was placed inside a pressure chamber. The static pressure inside the chamber was measured with a digital pressure gage, and the chamber was pressurized with an air pump. On the other hand, a vice was used to provide the desired stress on the stress/strain sensor. The stress on the sensor was measured with a digital load cell.

The pressure sensor was exposed to varying pressures from 0 to 69 kPa, and the shift in harmonic spectrum H_z was recorded. Fig. 5 plots the responses of the sensors, determined by averaging three measurements at each pressure setting. The harmonic shift of the sensor increased with increasing pressure. There was no drift for this sensor, and the hysteresis was less than 5%.

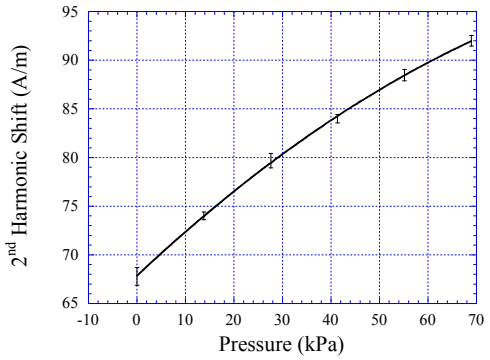

Fig. 5. The 2nd order harmonic shift of the sensors at varying pressures from 0 to 69 kPa.

Fig. 6 plots the harmonic field shift of the stress/strain sensors as a function of the applied force. As shown, the applied compressive force is linearly proportional to the harmonic shift H_z. As shown in the plot, the harder the rubber material, the lower the sensor sensitivity but the larger the dynamic range. The drift of the stress/strain sensors was also investigated, and there was no visible drift in the sensor response.

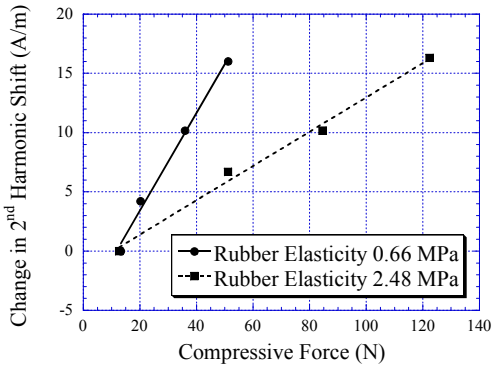

Fig. 6. The relationship of compressive stress and changes in the 2nd order harmonic shift exhibited by sensor with rubber elasticity of 0.66 MPa and with rubber elasticity of 2.48 MPa.

V. Conclusion

The design and application of the magnetoelastic sensors and magneto-harmonic sensors were reported. While both technologies show promising future in biomedical area, future work will be conducted to address issues such as biocompatibility, sensor miniaturization, and long-term reliability.

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