Wireless Hydrogel-Based Glucose Sensor For Future Implantable Applications

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***Abstract*—This paper presents a hydrogel-based glucose sensor for future implantable applications employing an inductive sensing technique. The prototype system is based on an ultra-low power tunnel diode oscillator employing a 2 mm-diameter/10-turn sensing coil enclosed in a 3D-printed sealed sensor package. A 3 mm x 3 mm x 80 µm metallic sensing plate embedded in a 3 mm x 3 mm x 400 µm glucose-sensitive hydrogel slab is positioned at 130 µm away from the sensing coil by using an adjustable platform in the prototype design. The small gap is critical for a high sensitivity. The oscillator achieves a 38 MHz nominal frequency while dissipating 40 µW. Under a stable DC power supply, the sensor demonstrates a sensing accuracy around 0.2 mM in human physiological glucose range.**

Keywords—inductive sensing; hydrogel-based glucose sensor; glucose-sensitive hydrogel, implantable sensor; tunnel diode oscillator; low power implant; biomedical implant.

I. INTRODUCTION

It is highly desirable to develop implantable hydrogel-based wireless sensing capability to capture *in vivo* biochemical parameters such as glucose, pH, and ionic strength. Advancement in MEMS technology has enabled the realization of cubic mm size complex systems [1]. However, energy sources, power dissipation, and reliable packaging impose severe challenges for realizing miniature long-term implantable sensors. This paper presents a proposed implantable wireless intraluminal glucose sensing architecture depicted in Figure 1, where a miniature sensor is implanted inside a major blood vessel and powered by an RF power source. Glucose concentration inside the vessel can be sensed by an inductive sensing technique employing a functionalized hydrogel embedding a miniature metallic sensing plate. Functionalized glucose-sensitive hydrogels can reversibly change in volume proportional to the change in glucose concentration [2], which causes a displacement of the embedded metallic sensing plate that can be detected by the inductance change of a sensing coil placed in a close proximity. This sensing method can potentially overcome several key limitations plaguing traditional enzymatic continuous glucose sensors as well as flexible membrane-based capacitive glucose sensors that are prone to leakage and hysteresis [3, 4]. Furthermore, the proposed sensing technique allows the sensing coil and associated electronics to be robustly encapsulated in a hermetically sealed glass package due to the sensing configuration that does not require a direct contact between the coil and hydrogel, attractive for long-term implantable applications. The implantable glucose sensor will be critical for future closed-loop insulin delivery system such as artificial pancreas for treatment of diabetes and prevention of diabetic related complications. The sensing coil employed as a part of an LC tank circuit can effectively modulate the frequency of an RF oscillator, thus wirelessly transmitting the sensor information to an external receiver. A tunnel diode oscillator architecture is chosen due to its ultra-low power dissipation [5], desirable for implant applications where power sources are highly constrained. As depicted in Figure 1, a non-glucose-sensitive reference hydrogel (without showing an embedded metallic sensing plate on top for illustration simplicity) and a reference coil inductor are proposed to be adjacently incorporated in the design, serving as a reference frequency for suppressing potential environmental effects.

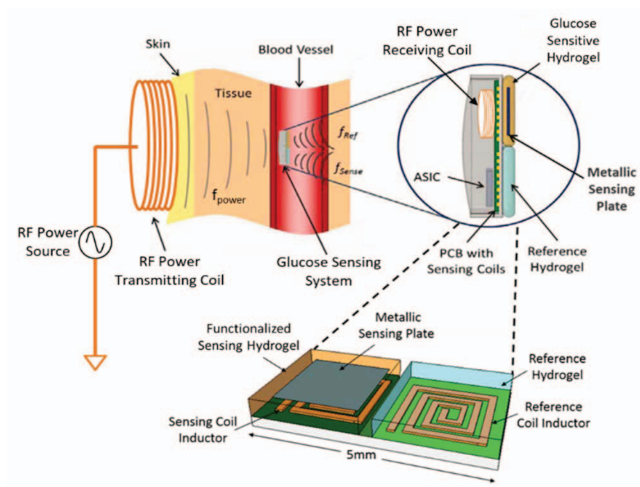

Fig. 1. Wireless implantable hydrogel-based glucose sensing architecture.

II. WIRELESS HYDROGEL-BASED GLUCOSE SENSOR

Figure 2 depicts the *in vitro* experimental setup to characterize the proposed wireless glucose sensor, where an 8 mm-diameter oscillator PCB is placed inside a 3D-printed sensor package with a 2 mm-diameter/10-turn (226 nH with Q of 23 at 40 MHz) sensing coil sandwiched between the PCB and the sensor package bottom plate exhibiting a thickness of 80 µm. It should be noted that for the initial study the prototype design is powered by an external DC power supply to ensure a stable oscillator frequency. The sensor package is then filled with PDMS to seal the electronic components, followed by a 10 µm Parylene C coating serving as a biocompatible and moisture resistant layer. A 3 mm x 3 mm x 400 µm functionalized hydrogel slab embedded with a 3 mm x 3 mm x ~80 µm metallic sensing plate is adhered onto a 3D-printed adjustable platform via a gelbond film. The adjustable platform is then assembled to the 3D-printed sensor package by using screws, which can adjust the gap size between the metallic sensing plate and the package bottom plate to approximately 50 µm as shown in the figure. A small gap size is critical to achieve a high sensitivity. The assembled sensor is then immersed into 1xPBS solution with a controlled glucose level for characterization. The glucose concentration can alter the sensing coil inductance, which in turn modulates the oscillator frequency to be detected by a nearby receiver.

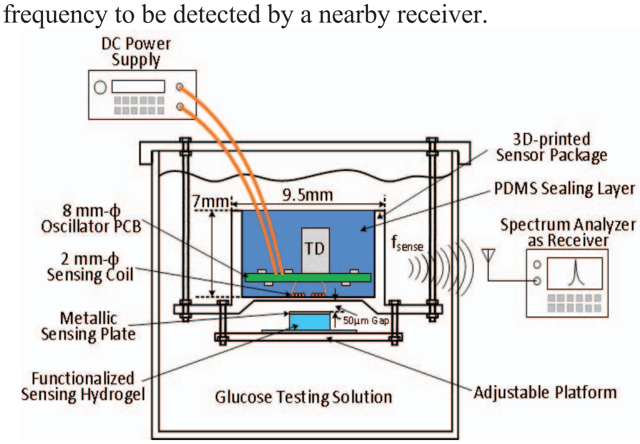

Fig. 2. DC-powered *In vitro* wireless glucose sensor test setup.

Figure 3 presents a tunnel diode oscillator-based sensor design topology, where a commercial silicon tunnel diode is employed for the prototype demonstration.

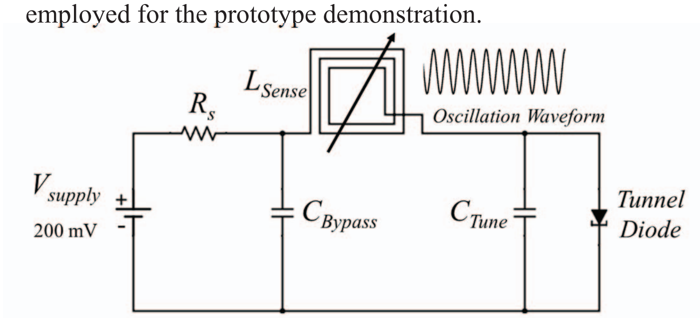

Fig. 3. DC-powered tunnel diode oscillator-based sensor topology.

The tunnel diode is biased at 200 mV to achieve a negative resistance of around -1200 Ω, sufficient to compensate the LC tank loss. The oscillator dissipates a low DC power of 40 µW while developing -19 dBm RF power. Figure 4 shows a typical oscillator output power spectrum, exhibiting a -78 dBm power at 37.96 MHz, received by a receiver positioned at approximately 4 cm away from the sensor module.

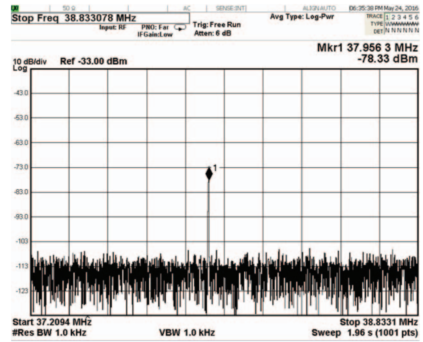

Fig. 4. Wirelessly received oscillator output power spectrum.

III. Glucose Characterization

The glucose characterization was performed using the test setup depicted in Figure 2. The sensor was first immersed in 1xPBS solution with a glucose concentration of 4 mM (close to that of human blood) to reach an equilibrium. The concentration was then dropped to 0 mM and remained unchanged for three days to exam the oscillator frequency stability, which exhibited a 5 kHz/day drift from the 24th to the 72nd hour. At this point, the glucose was ramped to 10 mM with a 2 mM step change every 24 hours. The measurement result is plotted in Figure 5.

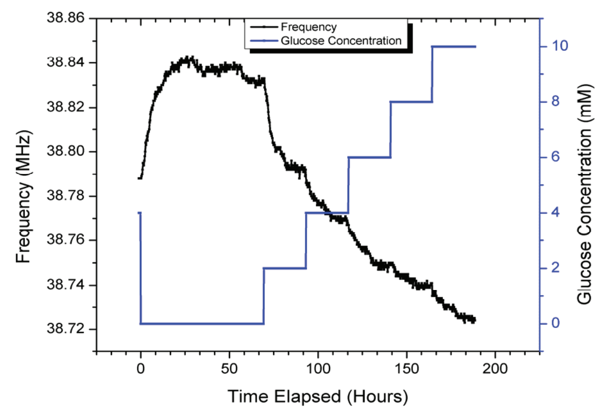

Fig. 5. Glucose test results using the DC-powered wireless sensor.

The sensor exhibited a sensitivity of 20 kHz/mM when the glucose concentration was below 2 mM. The sensitivity was reduced to 8.5 kHz/mM when the glucose concentration was increased to 10 mM, likely due to hydrogel saturation. Based on the measured frequency drift, a glucose sensing accuracy of approximately 0.2 mM at lower concentration and 0.6 mM at higher concentration, respectively, can be determined.

IV. RF-Powered Wireless Glucose Sensor Design

It is highly attractive to develop a fully wireless glucose sensor for future implantable applications. Consequently, the feasibility of an RF-powered wireless tunnel diode oscillator-based glucose sensor was explored. Figure 6 depicts the *in vitro* experimental setup for the proposed feasibility study, which leverages the design and packaging principle presented in Figure 2. Instead of powering the sensor module with a DC power supply, an RF powering scheme is employed, where a 2 cm-diameter/10-turn RF power transmitting coil (4.3 µH with

Q of 73 at 2 MHz) is positioned over an 8 mm-diameter/10-turn RF power receiving coil (1.3 μH with Q of 25 at 2 MHz) sealed inside the sensor package with a separation distance of approximately 2 cm.

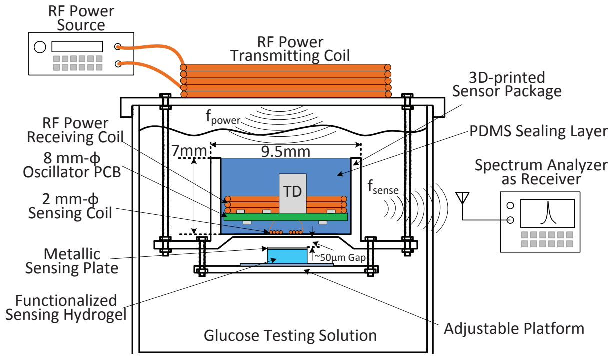

Fig. 6. RF-powered *In vitro* wireless glucose sensor test setup.

Figure 7 presents the RF-powered wireless tunnel diode oscillator-based sensor design, where a pair of tuned LC tank circuits is used to couple an external RF power source to energize the sensor module. The RF powering frequency is chosen at 2 MHz so that the circuit achieves a highest/optimal power transfer efficiency. A clamping diode is introduced after the rectifier diode with an objective to achieve a stable output DC voltage around 200 mV to bias the tunnel diode. The clamping diode dissipates a DC power of 60 μW, thus resulting in an overall oscillator power dissipation of 100 μW. An external RF power of 41 mW is required to operate the wireless sensor module.

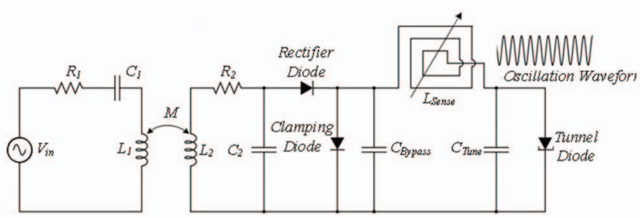

Fig. 7. RF-powered tunnel diode oscillator design topology.

The RF-powered wireless glucose sensor assembly process and test setup are illustrated in Figure 8. A similar procedure was employed for the sensor package and glucose characterization described in Section II. It should be noted that the current system form factor can be greatly minimized by employing integrated electronics and optimizing the sensor package housing the functionalized hydrogel slab. Long-term oscillator frequency stability under RF powering was investigated over 65 hours. The measured result shows that the oscillator frequency exhibits a significant drift over time, which was not observed from the previous stability test using a DC power supply. A further analysis reveals the frequency drift exhibits a periodicity of approximately 24 hours, which could be caused by environment changes such as temperature and electric load conditions. A robust voltage regulator is, therefore, planned to replace the clamping diode to achieve a more stable DC output bias voltage for the tunnel diode, thus expecting an improved frequency stability. Other techniques employing FSK modulation and reference oscillator will also be explored for a robust data communication.

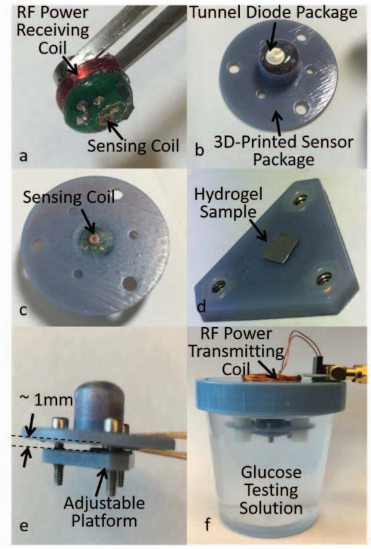

Fig. 8. Photos of RF-powered wireless glucose sensor assembly and test setup. (a) Tunnel diode oscillator PCB with RF power receiving coil; (b) Oscillator PCB placed inside 3D-printed sensor package sealed with PDMS; (c) Bottom view of the 3D-printed sensor package showing the sensing coil; (d) 3D-printed adjustable platform holding the functionalized hydrogel sample embedded with a metallic sensing plate; (e) Assembled wireless glucose sensor module; (f) Assemble sensor module in glucose testing container.

V. CONCLUSIONS

A wireless hydrogel-based glucose sensor employing an inductive sensing technique has been demonstrated for future implantable applications. The prototype system under a stable DC supply is capable of sensing and wirelessly transmitting glucose information within the human physiological range. Future research effort will be devoted to improving frequency stability under RF-powering condition as well as shortening the response time of the glucose-sensitive hydrogel.

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P. Tathireddy has commercial interest in Applied Biosensors, LLC.

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