3rd URSI AT-AP-RASC, Gran Canaria, 29 May – 3 June 2022

Skeletal Muscle-Actuated Bio-Hybrid Implant and Wearable Reader Antenna System

Cagla Karabulut*[(1)], Ahmet Bilir[(1)], Macit Emre Lacin[(1)], Arda Deniz Yalcinkaya [(1)], Sema Dumanli[(1)]
(1) Electrical and Electronics Engineering, Bogazici University, Istanbul, Turkey

Abstract

Engineering living cells can open the gates for durable implants that constantly monitor patients' health without requiring any battery power. This work aims to develop a biohybrid implantable sensor that is capable of sensing and responding to a chemical stimulant within the medium. Structurally, the bio-hybrid device is composed of muscle tissue, a 3D-printed flexible scaffold, and a resonator. Mechanistically, muscle tissue, which is engineered to respond to particular stimulants, contracts in the presence of the stimulant and deforms the scaffold it is attached. This deformation results in a change in the resonance behavior. This change is tracked with a pair of wearable co-planar waveguide (CPW)-fed ultra-wideband (UWB) antennas. Thus, the proposed bio-hybrid device will enable monitoring chemicals within the medium owing to the biosensing and actuating capabilities of muscle tissue. The resonator, in turn, will allow reporting of this information to wearable readers. At 1 cm implant depth inside Dulbecco's Modified Eagle Medium (DMEM), more than 10 dB difference in $|S_{21}|$ between the reader antennas is observed when the engineered muscle contracts.

1 Introduction

The development of implantable sensors for monitoring biological measures can have a profound impact on the medical field. Early diagnosis has the potential to facilitate treatment, reduce costs, and improve patient prognosis. Compared to electro-mechanical counterparts, living cells hold several advantages as implantable sensors. First, cell-based sensors have higher energy efficiency and higher power-to-weight ratio [1]. Moreover, they use inexpensive and eco-friendly nutrients to thrive and are capable of self-healing [2]. Thus, they are particularly fit for use as implants in the human body.

Engineered living cells are emerging as novel means for sensing. So far living cells employed as biosensors include microbial cells such as bacteria, yeast, algae, and fungi; and animal cells such as rat and human cells derived from various tissues (e.g. epithelial, endothelial cells, etc.). Muscle tissue has previously been used to actuate biohybrid devices such as micro tweezers, walking, swimming robots, and pumps as demonstrated in [3]-[6]; however, has never been considered as a biosensor capable of detecting chemicals in the medium. Moreover, the most common outputs of biosensor cells utilized as a readout have either been of optical (fluorescent or luminescent signal) or electrochemical origin (redox-active species) [7]. Engineered skeletal muscle with its contractile response offers a novel cell type and output for biosensor systems.

In the current proposal, a novel biosensing mechanism is proposed which uses the contractile response of the skeletal muscle tissue. The proposed biosensing mechanism includes a bio-hybrid implant and a wearable reader antenna pair. The bio-hybrid implant consists of a resonator which is reconfigured with the contractile force generated by engineered skeletal muscle. The implant is a 3D printed setup accommodating a microwell studded with two compliant pillars, one of which has a conductive flat top that extends towards the split ring resonator and short circuits its gap, and a 3D muscle tissue grown within the microwell. When the muscle tissue contracts with a stimulant such as a disease bio-marker, the flat top deflects and open circuits the resonator's gap. This disrupts the closed loop and converts it into an split ring resonator. Figure 1 depicts the components of the bio-hybrid implant and the interaction between the muscle tissue and the resonator.

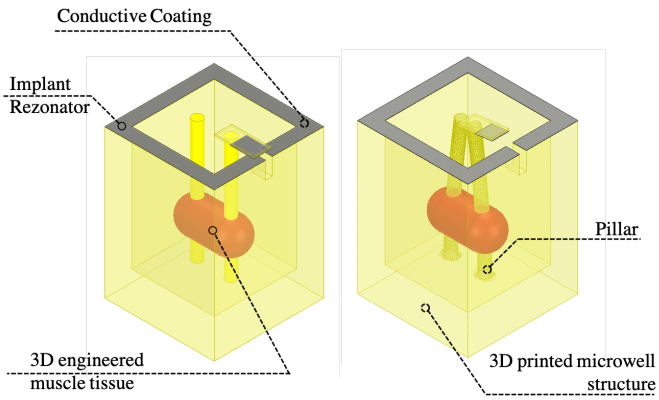

Figure 1. Figure depicts the components of the designed implant and muscle actuation.

This paper presents the initial simulations for the proof of concept for this novel sensing platform. Section 2 describes the reader antenna, while the bio-hybrid implant design is detailed in Section 3. The electromagnetic simulation results are presented in Section 4. Section 5 concludes the paper.

2 Reader Antenna Design

A coplanar waveguide fed circular disc monopole antenna is designed on Rogers 3010 ($\varepsilon_r = 10.2$) as described in [8]. The antenna was modeled to operate on DMEM (ε_r= 76.73, σ= 1.71) in the shape of a rectangular prism of 150 mm x 150 mm x 25 mm. Figure 2 shows the antenna geometry and the optimized dimensions of the reader antennas are given in Table 1. As seen in Figure 3, the antenna operates in the frequency interval of 1-3 GHz.

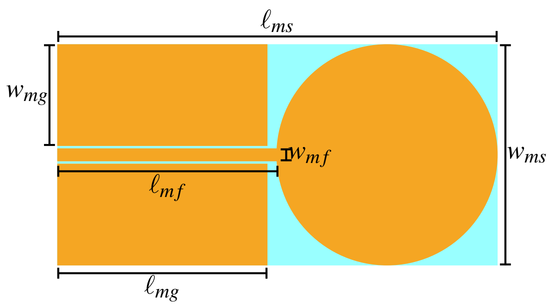

Figure 2. Antenna model and the parameterized dimensions.

Table 1. Dimensions of the CPW-fed UWB antennas in mm.

ℓ_{ms}	w_{ms}	ℓ_{mg}	w_{mg}	ℓ_{mf}	w_{mf}	t_m	t_{mr}
40	20	19	9.1	20	1	0.034	1.28

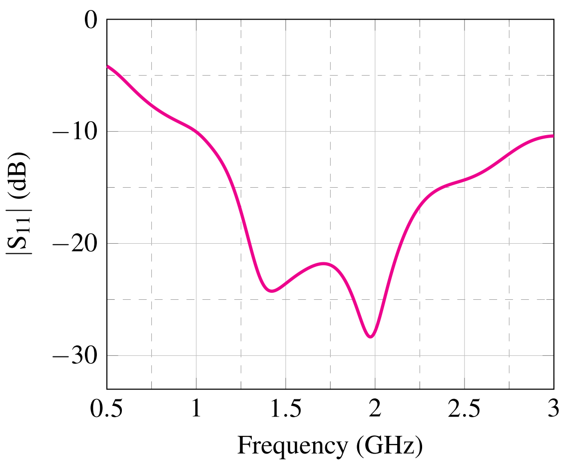

Figure 3. Reflection coefficient of the reader antennas.

3 Bio-hybrid Implant Design

The proposed biohybrid implant consists of a 3D printed rectangular micro-well, a square split ring resonator (SSRR) printed on the top surface of the well, and engineered muscle tissue as shown in Figure 1. The implant dimensions are 8.76 mm x 6.48 mm x 6.48 mm. The height and the radius of the pillars are 7.26 mm and 0.6 mm respectively. The bio-hybrid implant is designed to facilitate both the sensing and the actuating mechanisms. While chemical sensing is accomplished by the receptors on the individual cells, the actuation requires the joint activity of muscle fibers. To generate sufficient force to reconfigure the resonator, we employed two strategies. First, we embedded muscle cells in a hydrogel with an elastic modulus comparable to muscle tissue; and second, we engineered tendon-like interfaces (compliant pillar and beam structures) that mimic the tendon, bone, joint structures of the native musculoskeletal system. With this, we aimed to obtain better alignment of muscle fibers and improved transfer of contractile force to the reconfiguration of the resonator.

While pillars provide support for skeletal tissue to grow in 3D, they are also crucial to the actuation mechanism. Together with the conducting flat top of one of them, pillars are responsible for producing motion and structural deflection that reconfigures the resonance behavior of the system. The implant material is chosen to be Formlabs IBT resin. This resin is a suitable biocompatible and flexible material with an elastic modulus of 16 MPa [10].

The design of the 3D printed bio-hybrid implant structure was carried out using the ANSYS SpaceClaim tool. In addition, static structural analysis was conducted to simulate the structure's deflection against the net forces applied by the skeletal tissue in ANSYS Workbench tool. The previous studies on the skeletal muscle were able to demonstrate contractile forces measured up to 10μN to 2.5mN [11]. For a realistic approach, 500μN is assumed to be applied to both pillars in opposing x and -x directions.

Figure 5 and Figure 4 show the deflection of the flexible implant in z-direction and x-direction respectively. Initially, there is no stimulant present in the medium, thus zero net force is applied to the pillars and the pillars stand in an upright position. At t_1, the stimulant arrives, the tissue starts contracting, and once there is sufficient stimulant in the medium, the contraction force, and the deflection reach their maximum values. The closed-loop connection breaks at this point, open circuiting the gap to create a square split ring resonator. The maximum deflection of the flat top is observed as 614.4 μm and 179 μm in x and z directions respectively. The output of the ANSYS Workbench was fed into ANSYS HFSS for electromagnetic simulations.

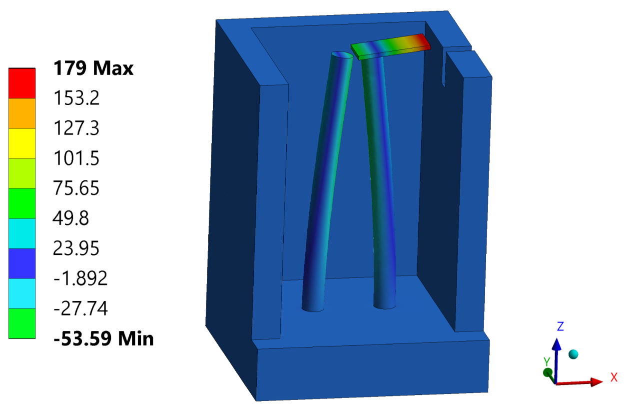

Figure 4. Figure depicts the mechanical activity of the implant at z-direction.

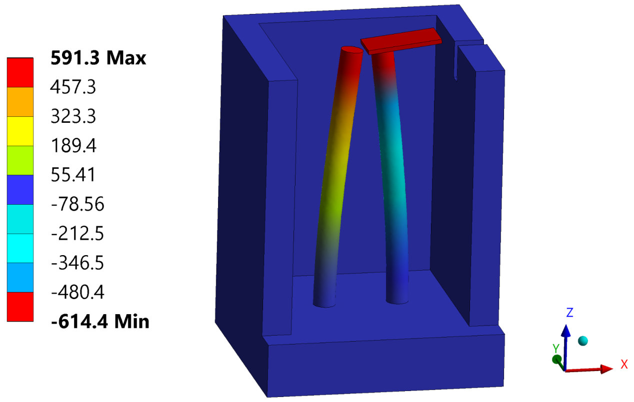

Figure 5. Figure depicts the mechanical activity of the implant at x-direction.

The square split ring resonator (SSRR) is formed by coating the top surface of the microwell walls with a conductive material and has a thickness of 0.1 mm. One of the pillars has a flat top that extends towards the split ring resonator. When the muscle is relaxed, the flat top short circuits the SSRR. As the concentration of stimulants in the medium increases, the force generated by the tissue increases up to a threshold. Due to the high flexibility of the resin, the deflection of the pillars increases, and the flat top is disconnected from the walls open circuiting the gap of the SSRR.

The resonance frequency of the SSRR is calculated by equation (1) where L_{eq} and C_{eq} are equivalent inductance and equivalent capacitance, respectively.

$$\omega_0 = \frac{1}{\sqrt{L_{eq} \times C_{eq}}} \tag{1}$$

L_{eq} is equal to the difference between the sum of the self inductances of each segment and the mutual inductance between the parallel conductors [12]. C_{eq} is equal to the sum of the gap capacitance, C_{gap}, and the surface capacitance, C_{surf}. The resonant frequency is analytically calculated to be 1.03 GHz.

4 Results

The wireless tracking of tissue activity is modeled and analyzed in ANSYS HFSS as seen in Fig 6. The in-body biohybrid device is implanted inside a DMEM serum block at a depth of 1 cm. Wearable CPW-fed UWB reader antennas are directly located on the serum block.

The change in transmission behavior $|S_{21}|$ of the wearable readers in response to resonator's geometry transformation is shown in Fig 7. As can be seen from the figure, the resonance of the SSRR is visible in the transmission coefficient at 1.1 GHz. More than 10 dB difference is observed between the contracted and relaxed muscle cases.

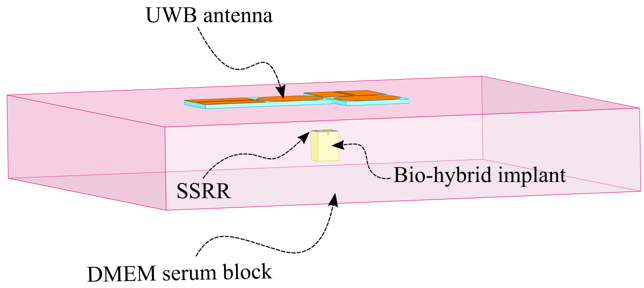

Figure 6. HFSS model of the system.

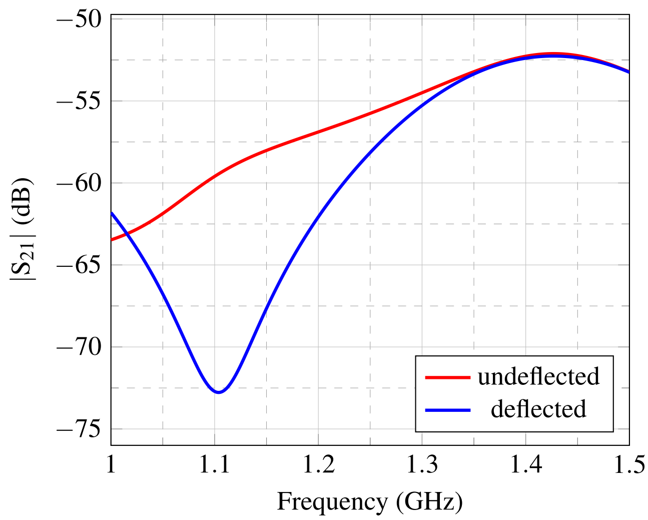

Figure 7. The change in the transmission behavior between the reader antennas in dBs, vs. frequency

5 Conclusions

While engineered muscle tissue has previously been used to develop various microdevices ranging from pumps to walking robots, it has never been considered as a biosensor capable of detecting chemicals. Moreover, in previous biohybrid designs, the contractile output of the muscle tissue has either been used to propel the robot forward, pick objects or pump fluid but has never been employed to reconfigure an implant resonator or antenna capable of sensing. We believe the current design holds potential for developing more sophisticated biohybrid devices capable of detecting specific molecular targets while communicating to remote readers.

6 Acknowledgements

This work was supported in part by Bogazici University Scientific Research Fund (BAP) under project number BAP-M 19081 and the Scientific and Technical Research Council of Turkey (TUBITAK) under Grant 120C131.

References

[1] L. Ricotti et al., "Biohybrid actuators for robotics: A review of devices actuated by living cells,"

Sci Robot, vol. 2, no. 12, Nov 29 2017, doi: 10.1126/scirobotics.aaq0495.

[2] L. Gao et al., "Recent progress in engineering functional biohybrid robots actuated by living cells," Acta Biomater, vol. 121, pp. 29-40, Feb 2021, doi: 10.1016/j.actbio.2020.12.002.

[3] Y. Sun, R. Duffy, A. Lee, and A. W. Feinberg, "Optimizing the structure and contractility of engineered skeletal muscle thin films," Acta biomaterialia, vol. 9, no. 8, pp. 7885-7894, 2013.

[4] Y. Morimoto, H. Onoe, and S. Takeuchi, "Biohybrid robot powered by an antagonistic pair of skeletal muscle tissues," Science Robotics, vol. 3, no. 18, 2018.

[5] C. Cvetkovic et al., "Three-dimensionally printed biological machines powered by skeletal muscle," Proceedings of the National Academy of Sciences, vol. 111, no. 28, pp. 10125-10130, 2014.

[6] Z. Lin, T. Jiang, and J. Shang, "The emerging technology of biohybrid micro-robots: a review," Bio-Design and Manufacturing, pp. 1-26, 2021.

[7] N. Gupta, V. Renugopalakrishnan, D. Liepmann, R. Paulmurugan, and B. D. Malhotra, "Cell-based biosensors: Recent trends, challenges and future perspectives," Biosens Bioelectron, vol. 141, p. 111435, Sep 15 2019, doi: 10.1016/j.bios.2019.111435.

[8] Jianxin Liang, Lu Guo, C. C. Chiau and Xiaodong Chen, "CPW-fed circular disc monopole antenna for UWB applications," IWAT 2005. IEEE International Workshop on Antenna Technology: Small Antennas and Novel Metamaterials, 2005., 2005, pp. 505-508, doi: 10.1109/IWAT.2005.1461127.

[9] L. Vannozzi et al., "Self-assembly of polydimethylsiloxane structures from 2D to 3D for bio-hybrid actuation," Bioinspiration biomimetics, vol. 10, no. 5, p. 056001, 2015.

[10] Formlabs, “IBT Resin.” [Online]. Available: https://dental-media.formlabs.com/datasheets/2102519-TDS-ENUS-0.pdf,

[11] Yoshitake Akiyama, Akemi Nakayama, Shota Nakano, Ryuichiro Amiya, Jun Hirose, "An Electrical Stimulation Culture System for Daily Maintenance-Free Muscle Tissue Production", Cyborg and Bionic Systems, vol. 2021, Article ID 9820505, 12 pages, 2021.

[12] H. Greenhouse, "Design of Planar Rectangular Microelectronic Inductors," in IEEE Transactions on Parts, Hybrids, and Packaging, vol. 10, no. 2, pp. 101-109, June 1974, doi: 10.1109/TPHP.1974.1134841.