engineering proceedings

MDPI

Proceeding Paper

Design and Characterization of a Passive Wireless DNA Sensor †

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† Presented at 8th International Electronic Conference on Sensors and Applications, 1–15 November 2021; Available online: https://ecsa-8.sciforum.net.

Abstract: This paper presents a concept of passive wireless DNA sensing platform that exploits a multidisciplinary area synthesizing the conventional DNA capacitive sensing mechanism and surface-based conformational characterization throughout DNA immobilization and hybridization. The resonant frequency shift caused by the change of capacitance throughout DNA immobilization and hybridization occurring on top of an interdigital capacitor is monitored by the means of impedance analyzer. 32 samples were measured throughout the experiment and the average capacitance measurements represented a variety of surface charges resulting from DNA molecule immobilization and hybridization. The capacitance changed from 11.58 pF to 114.5 pF when specific ssDNA was attached to electrodes and then increased to 218.6 pF once complementary strand DNA was involved and hybridized with existing DNA chains. In addition, using impedance analyzer measurements, the resonant frequency decreased from 2.01 MHz to 1.97 MHz in the presence of ssDNA and further down to 0.95 MHz after the complementary strand DNA was deposited.

Keywords: biosensor; DNA strand; interdigital capacity; LC circuit

Citation: Xu, H.; Jia, Y.; Cunci, L. Design and Characterization of a Passive Wireless DNA Sensor †. *Eng. Proc.* **2021**, *3*, x. https://doi.org/10.3390/xxxxx

Academic Editor: Firstname Lastname

Published: 1 November 2021

1. Introduction

The concept of biosensors, initially introduced by Millan and Mikkelson [1] in 1993, was discussed and numerous groups have carried out extensive studies in this area. A biosensor is generally defined as a device designed to detect or quantify a biochemical molecule such as a particular DNA sequence or particular protein [2]. Most molecular biosensors are affinity-based, meaning their role is to create an immobilized capture probe that binds the molecule being sensed, thus changing the problem of detecting the analyte in solution to detecting a change at a localized surface where the interaction of the analyte with the bio-receptor is designed to produce an effect measured by the transducer, which might be an electrochemical transducer, optical transducer, gravimetric transducer, Surface Plasmon Resonance (SPR) or electric transducer. An example of a biosensor can be our own body with its own biological recognition system demonstrated with every function of its complex yet efficient human body. This example can be related to the wireless DNA sensor transducer having the ability to detect DNA with different electrochemical detection methods. The immobilization and hybridization of the DNA can be quantified using specialized equipment that analyzes the data reading the sensitivity of the sensor. Impedance and capacitance analysis are the electrical measurements that indicate the sensitivity of the sensor when it is exposed to the DNA sample.

The detection of DNA hybridization has been possible with electro active molecules that monitor the electron transfer mechanism during the hybridization process which presents a potential application for the creation of biosensors. It has been shown that the

sensor performance (e.g., sensitivity, selectivity and stability) is highly dependent on properties of immobilized DNA probes such as orientation, conformation and surface density [3]. Generally, the sensitive element for a DNA biosensor is composed of single stranded DNA (ssDNA) molecules that allow the hybridization of complementary strands [4]. Different methods have been employed to convert these hybridization signals: (1) optical transducers that are based on fiber optics (reflection interference contrast microscopy [5], surface plasmon resonance [6] and Raman spectroscopy [7], (2) electrochemical transduction [8,9] or electrical transduction (i.e., integrated-circuit biochip [10]) and (3) piezoelectric transduction (measurement of changes in mass) [11]. The behavior of DNA attached onto metallic and semi-metallic surfaces has shown potential application in biomedical devices [12]. Because of this, the overall goal of this project is to provide a concept of a lab-on-chip biosensor using passive Wireless technology that can passively detect or identify different diseases that are characterized by a specific DNA sequence, such as Anthrax and Tuberculosis [13], in a more accurate and faster manner.

2. Principle and Design

2.1. Interdigital Capacitor Design

Interdigital capacitors (IDC) for technological applications have been studied by many authors since the early 1970s. An approximation schematic is briefly illustrated in Figure 1. The induction electrode is in the same plane as driving electrode and consists of two interpenetrating comb electrodes. The gaps (G), width (W). The thickness of electrodes height t and the thickness of the substrate hs is demonstrated. The permittivity constant of the substrate is εs. Each electrode is connected with opposite potential (either +V or -V). By symmetry due to system geometry, the whole system can be divided into a number of identical unit cells with dimension $\lambda/2$, from the center of electrode to the midpoint of adjacent pole. The perpendicular planes halfway between electrodes are equipotential planes. In common practice, this plane is considered as an electric ground and its voltage is set to zero.

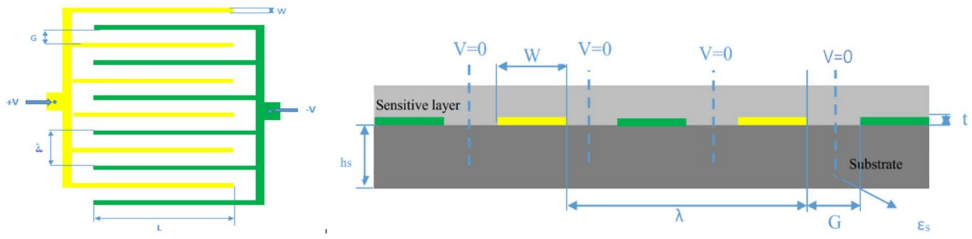

Figure 1. (**left**) Layout of electrode plane; (**right**) Cross-section of a periodic IDC-S.

The capacitance for a particular interdigital sensor configuration is a function of the dielectric permittivity of the materials, the fingers length, the number of electrodes comb and of two geometric dimensionless parameters r and η. i.e., C=C (η, r, εi, N, L, εs), where η represents the Metal ratio and can be calculated by η = W/(W+G). r is a geometric parameter defined as r = hi/ λ. hi is the thickness of each layer. N denotes the number of interdigital electrodes and L is the length of each electrode. εi and εs suggest the permittivity constant of i-th layer and the substrate, respectively.

In the previous work, we discussed the performance of these three configurations in different scenario to optimize the interdigital capacitor design [14, Unpublished]. It turned out the model with smaller gaps has the most sensitivity responding to the capacitance change and wider detectable area. However, the capacitors with inter spacing less than 10 um was practically hard to keep because it made about 50% of the electrodes to fail during our fabrication process. Through overall consideration, we decide to apply the configuration with 10 μm width and 10 μm gap for our design. Figure 2 shows the schematic of

suggested capacitor consisting of 130 fingers. The geometrical parameters are listed in Table 1.

Table 1. The geometrical parameters of the proposed capacitor.

PARAMETER	SYMBOL	VALUE
Finger Width	W_C	0.01 mm
Finger Gaps	G_C	0.01 mm
Finger Length	L_C	2 mm
Number of Fingers	N_C	130
The Thickness of Finger	t	0.002 mm

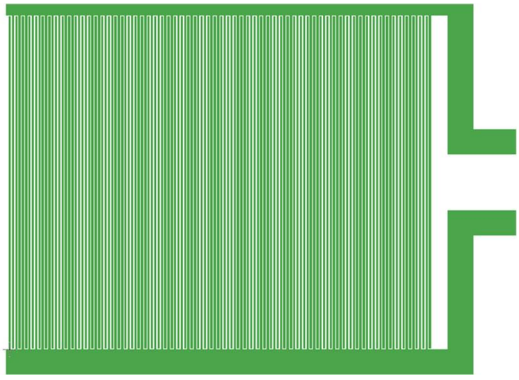

Figure 2. Layout of interdigital capacitor sensing element.

2.2. Spiral Inductor Design

Spiral inductors are utilized widely to make resonant circuit elements for capacitive sensors in the microelectronics field. Coupling the primary reader antenna, the spiral inductor acts as a transformer based on the principle of electromagnetic induction. When an oscillating current is executed on the antenna, a changing magnetic field to both the primary antenna and the spiral inductor is produced along the magnetic path in the air. An alternating voltage of the same frequency is induced in the spiral inductor. The DNA molecule behavior on the top of interdigital capacitor variations induce the frequency change, which can be detected from reader side by monitoring the impedance across the terminals of the wide bandwidth reader antenna. In other words, the electrical energy is transferred from the input antenna to the sensor and the DNA information can be detected by the reader from the coupled magnetic field. The spiral inductor with 5 turns was made of copper wire leads and connected to the electrodes of the capacitor. The diameter of the round copper ire was 0.674 mm and the radius of the inductor was 3.1 cm.

2.3. Electrical Model of Resonant Circuit

The planar inductor coil, together with the interdigital capacitor electrodes, forms a planar structure that has an integrated passive resonant circuit. Once the current with a varying frequency applied to the primary coil, a varying magnetic field generated around this coil. Based on Faraday's law, induced voltage is generated on the remotely placed sensor. The capacitance change due to Helmholtz ion plane displacement in the electrode-solution interface occurs corresponding to the reaction of DNA molecular with capacitors. When the gold electrode is clean, the equivalent capacitance is going to be relatively small. Once we introduced single strand DNA solution on the electrodes, the equivalent capacitance will increase. When the hybridization process occurs, the equivalent capacitance obtain is even higher.

3. Experiment Procedure

3.1. Material and Preparation

For this proof-of-concept experiment, A specific ssDNA probes: Bacillus Anthracis CCG ACG AGG GTT GTC AGA GGA TGC GTC GG were used for indirect modifications, GGC TGC TCC CAA CAG TCT CCT ACG CAG CC for complementary target and TTA CTA CAA AGG AGT CAC AAC GAT AGT AA applied for non-complementary were obtained from Integrated DNA Technologies (IDT). Single strand of Poly G samples was diluted with 1 mL of nanopore water and modified with a disulfide for gold electrode immobilization.

Dr. Cunci fabricated the proposed microelectrodes at Conte Nanotechnology Cleanroom Lab at University of Massachusetts (UMass) at Amherst in collaboration with the Center for Hierarchical Manufacturing, an NSF Nanoscale Science and Engineering Center (NSEC). The fabricated sensors mush be treated properly and cleaned to be suitable for usage.

3.2. Experiment Setup and Procedure

- Setup and Calibration: The experiment setup is presented in Figure 3. Before introducing specimen, the 0 S, 0 Ω, and 50 Ω terminations in the calibration kit are required. In respect to LCR meter, the open and short circuit test were performed leaving an open or short connection between the IDC connection station docking terminals for eliminating stray capacitance.

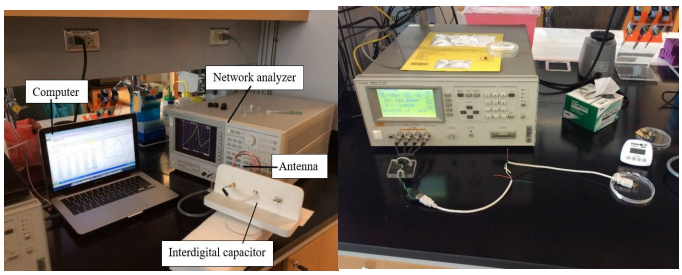

Figure 3. (**left**) Layout of interdigital capacitor sensing element and (**right**) LCR meter.

- Measure bare electrodes:
- Measurement of ssDNA: Drop of 5 mM ssDNA solution was deposited on the interdigital part enclosed by insulated rubber tape to prevent connection between two electrodes from presence of solution, then kept in a clean petri dish for 20 h. After of the period is complete, the electrode was rinsed with preparative buffer and dried with a nitrogen stream for eliminating the excess unattached to electrodes. The frequency peak was observed in network analyzer screen and the capacitance obtained by LCR meter.
- Measurement of 5 mM ssDNA with non-complementary target: non-complementary strand of DNA was introduced and remain 3 h. followed by the cleaning with buffer and nitrogen. measurement was taken. The measurement is aimed at being a contrast experiment for DNA hybridization process.
- Measurement of 5 mM ssDNA with complementary target: this step would also take 3 h and same cleaning task before measurement.

4. Results and Discuss

4.1. Bare IDC Capacitance Result

The bare IDC capacitance and impedance was measured as a reference (not shown). The average of the direct capacitance measurement is 11.58 pF with a resonant frequency 2.01MHz. The theoretical capacitance calculated is 11.76 pF.

4.2. Immobilization of ssDNA

After the specific DNA strand immobilization period concluded, a MES buffer was placed on the electrode array for removing the residual and Nitrogen stream was applied for drying, then the device capacitance and impedance were again tested as shown in Figure 4. The average capacitance resulted in 25.19 pF and 1.97 MHz. This presents a capacitance increase of 13.61 pF but a 0.04 MHz decrease of frequency peak over the clean dry IDC device.

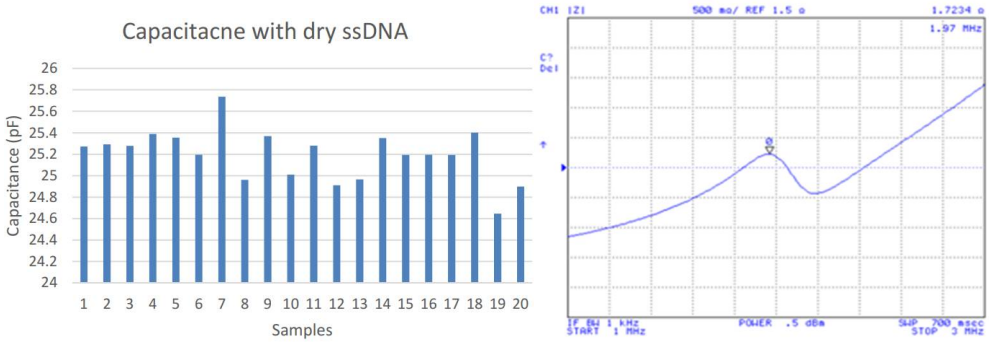

Figure 4. (**left**) Capacitances after ssDNA immobilization; (**right**) Impedance measurements.

4.3. Hybridization of the Complementary Strand

Before measuring the hybridization of complementary strand, a series of blank tests involving non-complementary strand were performed. As expected, the impedance peak was stable in 1.97 MHz (not shown). Then a MES buffer solution including 5 μM of the complementary strand was placed on the same electrode array, capacitance measurements were taken three hours after the deposition procedure to ensure greater strand hybridization. Figure 5 shows the IDC capacitance and impedance measurement after the hybridization process that yielded an average capacitance of 218.6 pF and an average resonant frequency of 1.95 MHz. It presents a capacitance increase of 104.1 pF while frequency decreased by 0.02 MHz for the hybridization process.

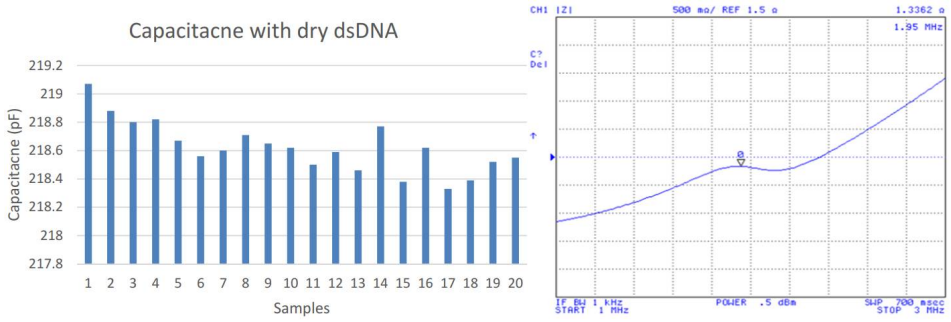

Figure 5. (**left**) Capacitances after dsDNA hybridization; (**right**) Impedance measurements.

4.4. Result Discussion

Figure 6 left panel shows the capacitance increase after the immobilization and hybridization stage and the frequency peak decrease meanwhile as presented in right panel. It is noticeable that each sample is measured and performed an arithmetic average of 32 subsamples. The capacitance of bare electrodes is relatively small. Once the ssDNA is immobilized, the related capacitance increased significantly resulted from free charge interfacial transfer between the ssDNA which carries the negative charge inherently and the electrodes surface. The DNA hybridization occurred in the presence of complementary target strand is deposited on the preceding electrodes. It is indicated that the capacitance obtained rise drastically up to 104.1 pF since more free charge and energy is presented.

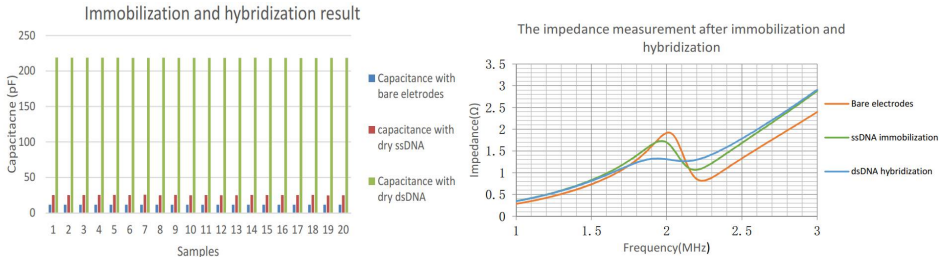

Figure 6. (**left**) capacitance measurements after each experiment stage; (**right**) Impedance measurements.

For impedance measurement, the frequency peak changes in response to the presence of DNA as demonstrated in Figure 6 right panel. Initially, the frequency point of abrupt change is stable at 2.01 MHz, then the ssDNA is used to modify IDC surface, which cause the resonant frequency of the related circuit decreased to 1.97 Mz. The measurement following hybridization shows the abrupt point dropped to 1.95 MHz. The variations were not as significant as the ones in direct capacitance measurement. However, the contrast experiment regrading the non-complementary DNA strands suggested the impedance variations subject to the hybridization were sensitive enough.

Author Contributions: Conceptualization, Y.J.; methodology, H.X. and L.C.; investigation, H.X. and L.C.; resources, H.X. and L.C.; writing—original draft preparation, H.X.; writing—review and editing, Y.J.; supervision, Y.J. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by National Science Foundation, grant number 1152940.

Institutional Review Board Statement:

Informed Consent Statement:

Data Availability Statement:

Acknowledgments: I would like to thank Carlos R. Cabrera and his group from UPRRP, in charge of preparing DNA molecule and arranging chemical experiments for the study of the capacitive label-free detection of DNA immobilization and hybridization process. This project would not have been possible without the kind help of my co-workers Hong Li and Orlando J Lopez Vazquez.

Conflicts of Interest: The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

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