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Investigation of a Biosensor for DNA Detection

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To my wife

Laya

My daughters

Elena & Erica

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Abstract

The aim of this project was to design a fully electronic sensor to detect hybridized DNA. In this study an integrated circuit for measuring capacitance of the sensor has been designed, which uses DNA as dielectric between the fingers of the sensor.

Nowadays, bio-sensors are widely used in electrical sensing where, most of these sensors use the conversion of capacitance for sensing. Some of the benefits of capacitive sensors are: high resolution, high sensitivity, low power dissipation, the ability to be integrated with other circuits, good stability and near zero thermal factors in heat exposure. Capacitive sensors are not affected by magnetic disturbances from electrical fields.

The first challenge in this study was bonding Single-strand DNA (ssDNA) to the sensor, which has been explained in chapter 2. After bonding ssDNA, the sample ssDNA will connect to their pairs on the sensor in the process called hybridization and the bonded addition then changes the capacitance of the sensor. To measure the change of the sensor's capacitance it is necessary to use interface circuits called "readout circuits". These circuits convert every change in the capacitive value to electrical changes such as current, voltage, frequency or pulse bandwidth to make the processing easier. Changes in the signal are very small, making factors such as noise and offset very important.

There are different methods available in measuring the changes in capacitance, which are discussed in this thesis and their advantages and disadvantages are described. After considering the best choice in DNA sensor, a suitable circuit for measuring the capacitance changes has been designed and simulated. Considerations for reducing noise and offset is also built in to the design of the circuit, Correlated Double Sampling (CDS) and Chopper Stabilisation (CHS) methods are used. Also, to achieve optimum results, these two methods are combined in this thesis. From the results of simulations, it is concluded that CDS and CDS&CHS methods are best suited for our design.

In chapter four, at first, two methods for detection of the capacitance in the sensors are demonstrated in the form of block diagrams, and then the advantages and disadvantages of these methods are discussed. After choosing the better method, every part of that method was implemented separately, as an integrated circuit. After linking the different parts, an analogue integrated circuit was designed that turned the capacitive variations to time period variations. Then a digital circuit was designed in order to turn the period time variations to a digital output. The analogue part of the circuit was simulated using 0.25 μ m technology parameters

in Tanner software and the digital part was simulated with VHDL software. The results of these simulations are presented in chapter five. This study succeeded in reaching an accuracy of $0.7fF$ (Femto Farad, 10^{-15}) capacitor variations. In the summary some suggestions for further research in this field were given.

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Glossary:

A/D: Analogue to digital
ASV: Anodic Stripping Voltammetry
C/F: Capacitor-to-Frequency
CDS: Correlated Double Sampling
CHS: Chopper Stabilisation
CMOS: Complementary metal–oxide–semiconductor
CSA: Charge Sensitive Amplifier
DNA: Deoxyribonucleic acid
DIAPOPS: Detection of Immobilized Amplified Products in a One Phase System
EDC: Ethyl-dimethylaminopropyl-carbodiimide
GBM: Gain Bandwidth
HPR: Horseradish Peroxidase
LPF: Low Pass Filter
LSI: Large Scale Integration
MEMS: Micro Electromechanical System
MOSFET: Metal–oxide–semiconductor field-effect transistor
OLEDs: Organic light emitting diodes
OpAmp: Operational amplifier
PCR: Polymerase chain reaction
PLL: Phase Locked Loop
PSD: power spectral density
PM: Phase-Margins
QCM: Quartz Crystal Microbalances
RNA: Ribonucleic acid
SAM: Self-Assembled Monolayer
SC: switched capacitors
SNP: Single Nucleotide Polymorphism
SNR: Signal-to-Noise Ratio
SPR: Surface Plasmon Resonance
ssDNA: Single strand of denatured DNA
TIA: Transimpedance Amplifier
TLC: Thin-layer chromatography