Chapter 1

INTRODUCTION

1.1 Ion sensitive field effect transistor and Enzyme field effect transistor

Remarkable progress has been witnessed in the past four and a half decades in the field of chemical sensing technology. Introduction of ion sensitive field effect transistor in the field of the chemical sensor has revolutionized the semiconductor sensor industry [1, 2]. It is based on the well-established MOS technology and hence it came with the advantage of being fast in response, smaller in size and low in cost. The first ISFETs were fabricated with silicon dioxide (SiO_2) as a sensing layer which was sensitive to hydrogen ions. Around the same time, Matsuo and Wise introduced silicon nitride, as sensing layer for ISFET device [3]. Use of silicon as a substrate for micro electrodes for electrophysiological measurements was introduced by Wise et al [4]. With these notable works, a rapid progress was witnessed in the family of FET devices based sensors since the inception of the ISFET [5].

ISFETs are similar to MOSFETs with the former devoid of the gate material. The gate insulator which is the sensing layer of an ISFET is in direct contact with the electrolyte and requires a reference electrode to complete the gate to source circuit. The working of an ISFET can be explained well by the site binding theory [6] and the electrical double layer theory [7, 8, 9, 10]. The ability of an ISFET device to be integrated with biologically active material helped it to venture into the field of biosensors. It was observed that ISFETs could be conveniently used in conjunction with enzymes and other biological membranes forming an Enzyme Field Effect Transistor (ENFET). The concept was proposed by Janata and Moss in 1976 [11] and the first ENFET were realized in 1980 by Caras and Janata which was penicillin based biosensor [12]. Since then several different enzymes are being used for different ENFETs. The enzymes are specific to a particular analyte. The enzyme Cytochrome P450 monooxygenase used in this work has the specificity of oxidizing n-hexadecane into n-hexadecanol [13, 14, 15]. This enzyme has the potential of bio-monitoring as it oxidizes hydrocarbon which is an effective tool in oil industry helping in monitoring environment degradation by the oil spill.

1.2 Motivation

Threshold voltage is an important parameter for any FET device as it indicates the onset of flow of drain current through the device. Any error in the measurement of the threshold voltage can lead to variation in other measuring parameters. The existing threshold voltage extraction methods involve parasitic components; slight changes in the parasitic components bring major changes in threshold voltage [16, 17, 18, 19, 20]. Also, the MOS structure cannot be considered as a normal capacitor. Its voltage is not only depended on gate capacitance but also on the surface potential. It is, therefore, a capacitor which comprises of the gate oxide and depletion capacitance. Appropriate modeling of the threshold voltage requires this factor to be taken into consideration.

Long exposure of ISFET devices in electrolyte witnesses an effect called drift which is a slow temporal change in the threshold voltage of the device. Researchers have indicated several reasons for drift but less information is provided on this secondary effect [21]. This effect can be attributed due to the additional charges which diffuse into the insulating layer which remains after reacting with compatible sites. This effect is more prominent in silicon dioxide gate pH ISFET. Therefore, the effects of these additional charges must be considered while modeling the long term drift for SiO_2 gate pH ISFET.

Ease in fabrication with a reduced number of steps has been possible with the introduction of Schottky MOSFET [22, 23]. This idea can also be extended to other FET devices. Therefore, Schottky based ISFET has been fabricated in this work. Further, the enzyme Cytochrome P450 monooxygenase is immobilized over the sensing layer. Cytochrome P450 enzyme has the property of oxidizing hydrocarbons. ISFET immobilized with this enzyme can be utilized for the development of a biosensor for detection of hydrocarbon. Hydrocarbon detection can prove to be an important tool in the oil industry for monitoring crude oil contamination into ecology and also in oil exploration [24, 25]. The chemicals present in crude oil and the related toxicities leads to changes in the physiochemical characteristics of the environment thus causing a hazardous impact on the local flora and fauna. The state of art involved in monitoring processes employed in oil industry is expensive and time-consuming. The hydrocarbon pollution by crude oil is one of the major problems faced by nature.

Both aliphatic and polycyclic aromatic hydrocarbons (PAHs) are present in the vicinity of oil fields. Also, its presence can be found in cases of oil spills while in transportation or at the refineries which adversely affect humans and everything around it. Available methods for detection of hydrocarbon involve various sensor types such as optical, electronic noses, chemical sensors etc. However, all these methods suffer from various disadvantages such as low detection limit, high temperature requirement, high power consumption, and complex fabrication processes. Therefore a biosensor capable of detecting hydrocarbon can make the detection process cheaper; less time consuming and low cost of analysis will be involved.

The constructional details of an ISFET clearly indicate the need of a reference electrode to complete the gate to source circuit. The complete potential profile of the diffused layer can be obtained only if the reference electrode is well positioned in the electrolyte. The effective interfacial oxide potential is not only dependent on the pH of the electrolyte but also on the positioning of the reference electrode from the sensing layer. A theoretical model proposed in 2009 indicated that the reference electrode should be placed at atleast three times of the Debye length from the sensing layer for each pH values so as to obtain unambiguous measurement [26]. Based on this work it can be extended to the modeling of the optimal positioning of the reference electrode for a Si_3N_4 gate pH ISFET. Further, the experimental validation of this theoretical model can prove to be vital in decreasing the overall device dimension.

Objectives: Modeling of the threshold voltage considering the MOS capacitance as a variable capacitor will help to overcome the drawback of conventional extraction methods. MOS capacitance is not merely the ratio of charge and voltage rather under the ideal condition it is the summation of bulk potential and surface potential. Appropriate modeling of the threshold voltage is required for the MOS devices. Diffusion of hydrogen ion into the insulator results into the drift. This effect has to be considered for modeling the threshold voltage of the device. Expensive and complex machinery involved in bio-monitoring can be substituted with the introduction of biosensors capable of hydrocarbon detection which are cheaper, easy to fabricate and convenient. Possibility of minimization of the overall device dimension can be made futile by the proper positioning of the reference electrode. Based on these problems the objectives of this work have been set as

1. Modeling of the threshold voltage of MOSFET using Capacitance Voltage characteristics and its extension for ISFET
2. Modeling of long term drift in SiO_2 gate pH ISFET's
3. a. Design, fabricate and characterization of Schottky based ISFET

   b. Immobilization of the bare ISFET with Cytochrome P450 enzyme and characterization of the ENFET device
4. Modeling for the detection of optimal positioning of the reference electrode for Si_3N_4 gate pH ISFET and validation of this rule using a hardware setup developed for this purpose

1.3 Thesis outline

The second chapter titled "**Overview on Ion Sensitive Field Effect Transistor and Enzyme FET**" discusses the basics of ISFET, the fundamentals of insulator/electrolyte interface encompassing the site binding theory, electrical double layer thus explaining the physico-chemical modeling of the device. Silicon dioxide has been used as the sensing layer in particular to explain a generalized model for the planar ISFET based on the site binding theory and electrical double layer. Silicon dioxide has single surface site which is used as pH sensing surface. Further, an ENFET operation has been explained with the reaction kinetics associated with the biological recognition process and the mass theory. The simulation results presented at the end of the chapter gives an idea about the ISFET and ENFET.

In the third chapter titled "**Threshold voltage modeling using capacitance voltage characteristics**" mathematical modeling and simulations have been carried out to calculate the threshold voltage of a MOSFET. Threshold voltage is an important parameter for any FET devices as it is the minimum voltage to be applied at the gate terminal to initialize the flow of current. In this chapter, the model is based on the MOS capacitance property. A change in the space charge width in the depletion region results in a change in the voltage across the depleted layer and also the input capacitance. Segregation of the whole space charge region into smaller sections and the summation of individual voltages across each section at the maximum width give the threshold voltage of the MOSFET. The ISFET is similar to MOSFET except for the absence of gate over layer in the former; therefore this model has been further extended to ISFET device. Simulation has been carried out in MATLAB and the proposed model is compared with the values obtained using Shockley's model. The results obtained from the proposed model and the well-established model closely resemble each other.

In the fourth chapter titled "**Long term drift in ISFET due to Hydrogen ion diffusion**", the secondary effect called drift found in ISFET has been discussed. This effect cannot be overlooked especially when these devices are employed for ambulatory pH measurements or continuous monitoring and detection processes which are vital in industrial applications. Hydrogen ion diffusion into the insulating layer can lead to long term drift in ISFET devices. In this chapter, a mathematical model has been formulated describing the long term drift in SiO_2 surface under the effect of diffusion of protons. Also, it incorporates the electric field created due to this diffusion. This field has some influence on the threshold voltage of the device especially at lower pH values. Hence, a final equation for long term drift in threshold voltage has been formulated considering the SiO_2 as the sensing surface. Validation of this mathematical model has been done by the comparison with the experimental data obtained from the ISFET device; fabrication details of which are stated in the fifth chapter. The resultant curves obtained from the mathematical model and experimental data show similar trend.

In the fifth chapter titled "**Fabrication of a Schottky based ISFET immobilized with enzyme CYP450**", process and steps involved during the fabrication of a Schottky based ion sensitive field effect transistor have been discussed. Further the fabricated device was immobilized using an enzyme

(Cytochrome P450 monooxygenase) for detection of hydrocarbon. SiO_2 was used as the sensing layer because of its biocompatibility. Therefore, an ENFET was fabricated by immobilizing the bare ISFET device with the enzyme Cytochrome P450 monooxygenase system obtained from *Bacillus stratosphericus sp*., an extremophile. The enzyme was partially purified and immobilized in an agarose layer (5%w/v) on the sensing surface of the ISFET device. The analyte which the enzyme catalyzes is n-hexadecane, and in presence of nicotinamide adenine dinucleotide phosphate (NADPH) forms a product called n-hexadecanol. The correlation of the sensor output indicates its potential to be used as a biosensor for hydrocarbon detection. The sensitivity of the ISFET sensor is found to be about 50.65 mV/pH and that of the Cytochrome enzyme based ENFET is about 54.34 mV/molar.

In the sixth chapter titled "**Modeling and experimental validation of the optimal positioning of reference electrode for a Silicon nitride gate pH-ISFET**" modeling and validation for the proper positioning of the reference electrode for a Si_3N_4 gate pH ISFET has been done. The modeling is based on a theory which was proposed for SiO_2 as the sensing layer. In this chapter, the modeling has been extended to silicon nitride surface and the theoretical data was validated by a precise mechanical set up with data acquisition system. The experimental data conform to that of the theoretical data suggesting the optimal position of reference electrode. Validation of this rule will be helpful in determining the complete dimension of the pH measuring system using ISFET. This could very well be extended to ENFET and other bioFETs requiring a reference electrode.

Finally, seventh chapter titled "**Conclusion**" summarizes the dissertation and future prospects of the work have been put forward.

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