



Faculty of Electronics and Computer Engineering

**MODELING AND SIMULATION OF SINGLE AND DOUBLE GATES
ION SENSITIVE FIELD EFFECT TRANSISTOR FOR BIOMEDICAL
APPLICATIONS**

Ahmed Musa Dinar

Doctor of Philosophy

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**MODELING AND SIMULATION OF SINGLE AND DOUBLE GATES ION
SENSITIVE FIELD EFFECT TRANSISTOR FOR BIOMEDICAL
APPLICATIONS**

AHMED MUSA DINAR

**A thesis submitted
in fulfilment of the requirements for the degree of Doctor of Philosophy**

Faculty of Electronics and Computer Engineering

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2020

DECLARATION

I declare that this thesis entitled “Modeling and Simulation of Single and Double Gates Ion Sensitive Field Effect Transistor for BioMedical Applications” is the result of my own research except as cited in the references. The thesis has not been accepted for any degree and is not concurrently submitted in the candidature of any other degree.

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APPROVAL

I hereby declare that I have read this thesis and in my opinion this thesis is sufficient in terms of scope and quality for the award of Doctor of Philosophy.

Signature :

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Date :

DEDICATION

To our first teacher Rasulullah S.A.W

To my father

For earning an honest living for us and for supporting and encouraging me to believe in myself

To my mother

A strong and gentle soul who taught me to trust in Allah, and to believe in hard work

To my wife

Who has been a constant source of support and encouragement during the challenges of study and life

To the rose of my life, my daughter

To my brother, sisters, and friends

Thanks for all for your great support and continuous care

ABSTRACT

The modeling of Ion Sensitive Field Effect Transistor (ISFET) generally starts with its analogy to MOS devices and its threshold dependence on pH. Massobrio et al. proposed a macro-model plug in for SPICE. It was later modified to fit general SPICE based simulators without the need for a plug-in software. Then, different works followed the first modeling and simulation of ISFET by using widely available commercial CAD simulations. Unfortunately, the commercial TCAD is not supplied with model, material, and electrochemical packages to effectively manage the ISFET process and its operations. The main objective of this research is a comprehensive, accurate modeling and simulation of SG and DG ISFET devices. First, the adaptation of the Gouy-Chapman-Stern model mathematically and using TCAD to compensate for the roll-off non-ideality have been proposed. Performance analysis of conventional ISFET for six high-k materials as a Stern layer sensing membrane was also implemented. Moreover, a design and characterization of double-gate (DG) ISFET for SiO₂ and Six high-k sensing membrane toward beyond Nernst limit sensitivity was done. Finally, a model for the geometrical parameter's impact on DG ISFET sensitivity was proposed. To achieve these objectives, the parameters of the silicon semiconductor material (that is, energy bandgap, permittivity, affinity, and density of states) are reconstructed in the electrolyte solution utilizing user-defined statement offered by Silvaco ATLAS. The electrostatic solution of the electrolyte area can also be investigated by constructing a numerical solution for the semiconductor equation in this area. The devices were virtually fabricated using ATHENA module of TCAD software. The materials used as a sensing membrane in devices were normal silicon dioxide (SiO₂) and six high-k material (TiO₂, Ta₂O₅, ZrO₂, Al₂O₃, HfO₂, and Si₃N₄). Then, the developed TCAD is used with the design of experiments (DOE) to investigate the effect of geometrical parameters on the performance of DG ISFETs and enhance the classical model. Three and five geometrical parameters, namely, buried oxide, silicon body, top oxide, channel length, and electrolyte thickness, are considered as independent factors in the DOE. Validation results revealed that the developed TCAD model has an acceptable agreement with experimental results and theoretical models in SG and DG ISFET in terms of sensitivity and ideal amplification ratio. On the other hand, silicon body thickness does not only affect the sensitivity toward the ultra-thin body but also can achieve an ultra-thin-body-buried oxide (Box). Channel length and electrolyte thickness as new investigated parameters also showed a clear impact on ISFET sensing properties. Furthermore, the developed TCAD and RSM mathematical models agreed with real experimental results in terms of average sensitivity and amplification ratio. The final design that depends on the control model resulted in a sensitivity ~1250 mV/pH that is ~21 times higher than the Nernst limit. To sum up, this study can open new directions for further analysis and optimization. Besides, the small sensing area and the FDSOI ISFET-based technology of the device can make the sensors ideal for the biomedical and IoT devices market.

PEMODELAN DAN SIMULASI BAGI TRANSISTOR KESAN MEDAN SENSITIF ION SATU-GET DAN DUA-GET UNTUK APLIKASI BIOPERUBATAN

ABSTRAK

Pemodelan Ion Sensitif Field Effect Transistor (ISFET) umumnya bermula dengan analoginya dengan alat-alat MOS dan ketergantungan ambangnya keatas pH. Plag-plag makro model untuk SPICE telah disarankan oleh Massobrio et al. Ia kemudiannya diubahsuai untuk dipadankan dengan simulator berasaskan SPICE umum tanpa bantuan perisian yang telah sedia dipasang. Kemudian, kajian-kajian berbeza mengikut pemodelan pertama dan simulasi ISFET dengan menggunakan simulasi CAD komersial yang sedia ada. Malangnya, TCAD komersial tersebut tidak dibekalkan dengan model, bahan dan pakej elektrokimia untuk mengawal proses dan operasi ISFET dengan berkesan. Objektif utama kajian ini adalah pemodelan dan simulasi alat-alat SG dan ISFET yang tepat dan komprehensif. Seterusnya, pengadaptasian model Gouy-Chapman-Stern secara matematik dan menggunakan TCAD untuk mengimbangi roll-off non-ideality telah dicadangkan. Analisis prestasi ISFET konvensional untuk enam bahan k yang tinggi oleh kerana membran pengesan lapisan Stern juga telah dilaksanakan. Tambahan pula, satu rekabentuk dan pencirian dua pagar (DG) ISFET untuk SiO₂ dan enam membran pengesan k-tinggi yang boleh menandingi sensitivity batasan Nernst limit sensitiviti telah dilakukan. Akhir sekali, satu model untuk impak parameter geometri keatas sensitiviti DG ISFET sensitiviti telah dicadangkan. Untuk mencapai objektif-objektif ini, parameter bahan semi-konduktor material silikon (iaitu, energy bandgap, permitiviti, afiniti, dan ketumpatan) dibangunkan semula dalam larutan elektrolit menggunakan pernyataan mengikut pengguna yang disediakan oleh SILVACO ATLAS. Larutan elektrostatik kawasan elektrolit boleh juga dikaji dengan membina satu solusi bernombor untuk persamaan semikonduktor. Alat-alat tersebut telah difabrikasi secara maya menggunakan modul ATHENA dari persisian TCAD. Bahan-bahan yang digunakan sebagai membran pengesan dalam alat adalah silikon dioksida biasa (SiO₂) enam bahan k-tinggi (TiO₂, Ta₂O₅, ZrO₂, Al₂O₃, HfO₂, and Si₃N₄). Kemudian, TCAD yang dibangunkan, digunakan dengan rekabentuk eksperimen (DOE) untuk mengkaji kesan parameter geometri keatas prestasi DG ISFETs dan meningkatkan lagi model yang klasik. Keputusan pengesanan menunjukkan bahawa model TCA yang dibangunkan selaras dengan keputusan eksperimen dan model teoretikal dalam SG dan DG ISFET dari aspek sensitiviti dan nisbah amplifikasi yang ideal. Sebaliknya, ketebalan tubuh silikon tidak hanya menjejaskan sensitiviti terhadap tubuh yang sangat nipis tetapi ia juga mampu mencapai oksida tertanam ultra-nipis (Kotak). Panjang saluran dan ketebalan elektrolit sebagai parameter yang baru dikaji juga menunjukkan impak yang jelas keatas ciri-ciri pengesan ISFET. Seterusnya, model-model matematik TCAD and RSM selari dengan keputusan eksperimen sebenar dari aspek sensitiviti secara purata dan nisbah amplifikasi. Rekabentuk akhir yang bergantung kepada model kawalan membawa kepada sensitiviti ~1250 mV/pH iaitu ~21 lebih tinggi dari had Nernst. Kesimpulannya, kajian ini boleh membuka satu halatuju untuk analisis dan optimisasi selanjutnya. Di samping itu, kawasan pengesan yang kecil dan teknologi berasaskan FDSOI ISFET alat boleh menjadikan pengesan itu ideal untuk pasaran alat-alat bioperubatan dan IoT.

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LIST OF ABBREVIATIONS

ANOVA	-	Analysis of Variance
BioFET	-	Field Effect Transistor based Biosensor
BOX	-	Buried Oxide
CCD	-	Central Composite Design
CMOS	-	Complementary Metal-Oxide-Semiconductor
CoV	-	Coefficient of Variation
DG	-	Double Gate
DL	-	Double Layer
DNA	-	Deoxyribonucleic Acid
DOE	-	Design of Experiment
EIS	-	Electrolyte Insulator Semiconductor
FD	-	Fully Depleted
IC	-	Integrated Circuit
ISFET	-	Ion sensitive field effect transistor
MOS	-	Metal Oxide Semiconductor
MOSFET	-	Metal Oxide Semiconductor field-effect transistor
pH	-	Potential of Hydrogen
RNA	-	Ribonucleic Acid
RSM	-	Response surface methodology
SD	-	Standard Deviation
SG	-	Single Gate

SOI	-	Silicon on Insulator
SPICE	-	Simulation Program with Integrated Circuit Emphasis
TCAD	-	Technology Computer-Aided Design
TFT	-	Thin Film Transistor
T _{si}	-	Top Silicon
UHS	-	Ultra High Sensitive
UTB	-	Ultra Thin Body
UTBB	-	Ultra Thin Body and Buried-box

LIST OF PUBLICATIONS

Dinar, A.M., Zain, A.S.M., and Salehuddin, F., 2019. Beyond Nernst Sensitivity of Ion Sensitive Field Effect Transistor based on Ultra-Thin Body Box FDSOI. *Journal of Physics: Conference Series*. (Accepted will Published in Scopus / WoS).

Dinar, A.M., Zain, A.S.M., and Salehuddin, F., 2019. Influence of Channel Length on Sensing Properties of FDSOI Ion Sensitive Field Effect Transistor. *Journal of Physics: Conference Series*. (Accepted will Published in Scopus / WoS).

Dinar, A.M., Mohd Zain, A.S., and Salehuddin, F., 2019. Comprehensive identification of sensitive and stable isfet sensing layer high-k gate based on isfet/electrolyte models. *International Journal of Electrical and Computer Engineering*, 9 (2), pp.926–933. (Published in Scopus).

Dinar, A.M., Mohd Zain, A.S., Salehuddin, F., Attiah, M.L., Abdulhameed, M.K., and Mohsen, M.K., 2019. Modeling and simulation of electrolyte pH change in conventional ISFET using commercial Silvaco TCAD. In: *IOP Conference Series: Materials Science and Engineering*. Institute of Physics Publishing. (Published in Scopus / WoS).

Dinar, A.M., Suhaila, A., Zain, M., Salehuddin, F., and Abdulhameed, M.K., 2019c. Impact of Gouy-Chapman-Stern model on conventional ISFET sensitivity and stability. *Telkomnika*,

17 (December). (Published in Scopus).

Dinar, A.M., Suhaila, A., Zain, M., Salehuddin, F., and Mohsen, M.K., 2019d. Performance analysis of high-k materials as stern layer in ion-sensitive field effect transistor using commercial TCAD. *Telkomnika*, 17 (December). (Published in Scopus).

Dinar, A.M., Zain, A.S.M., and Salehuddin, F., 2019. Performance analysis of capacitive coupling model for Dual-Gate ISFET Using TCAD. *Journal of Computational Electronics, Springer*. (Under review Scopus / WoS).

Dinar, A.M., Zain, A.S.M., and Salehuddin, F., 2019. Influence of Geometrical Parameters on DG ISFET Sensitivity using Developed TCAD and Design of Experiments. *International Journal of Circuit Theory and Applications*. Wiley (reviewer assigned Scopus / WoS).

Dinar, A.M., Zain, A.S.M., and Salehuddin, F., 2018. Utilizing of CMOS ISFET sensors in DNA applications detection: A systematic review. *Journal of Advanced Research in Dynamical and Control Systems*. (Published in Scopus).

Dinar, A.M., Zain, A.S.M., Salehuddin, F., 2018. Insight of Research on CMOS Image Sensor in Molecular Diagnostics / Detection: A Systematic Review. *Opción*, 34, pp.2737–2753. (Published in Scopus).

Dinar, A.M., Zain, A.S.M., and Salehuddin, F., 2017. CMOS ISFET device for DNA Sequencing: Device compensation, application requirements and recommendations. *International Journal of Applied Engineering Research*, 12 (21), pp.11015–11028.

CHAPTER 1

INTRODUCTION

1.1 Motivation and background

Over the past few years, bio-inspired technology combined with the integration of semiconductors in biomedical applications has created a fertile ground for the development of methods that offers novel solutions to these applications. These include nanofabrication of electrode-based systems for neural recording with interfacing capabilities to the brain periphery (Jackson and Zimmermann, 2012), significant advances in the field of genetic technology (Garner et al., 2010), point-of-care diagnostics and (on-the-spot) testing to be the future of drastically effective monitoring of critical biological markers and personalized application of therapeutic schemes. These examples reveal that such technologies have been engineered according to the demands of therapy and diagnosis of disease.

Lately, a vast convergence in Complementary Metal-Oxide-Semiconductor (CMOS) based microtechnology has been playing a crucial role in chemical sensing applications. This trend is allowed using solid-state sensors that can be fabricated using CMOS technology and in a consistent manner by integrated on a single chip (Pullano et al., 2018). Chemical sensors can exploit this on semiconductor CMOS technology to provide more miniaturization, scalability, and integration with intelligent instrumentation advantages. The ion-sensitive field-effect transistor (ISFET) is the most sensor that provides all these advantages. Utilizing ISFET as a chemical sensor grants a low cost, high productivity, simple interface, and high integration ability (Kaisti, 2017).

Real-time monitoring of electrolytes calls for attention as necessary in healthcare and