SMART ELECTROCHEMICAL SENSING SYSTEM FOR THE REAL TIME DETECTION OF ENDOCRINE DISRUPTING COMPOUNDS AND HORMONES

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requirements for the degree of
Doctor of Philosophy
in
Electronics Engineering
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New Zealand

ASIF IQBAL ZIA

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Dedications

In the name of Allah the most beneficent and the most merciful

To my parents

Mr Sher Afzal Zia

Mrs Shamim Akhter

To my wife

Mrs Nazia Asif

&

To my boys

Muhammad Shaheryar Asif

Muhammad Asfandyar Asif

Muhammad Abdur-Rehman Bin Asif

Abstract

Presented research work has not only provided a real-time tool to perform week-long chemical and bio-chemical assays in minutes yet, it had been operating as a source of community awareness about the said chemicals that we keep ingesting knowing or unknowingly. Phthalates are the most ubiquitous chemicals that pose a grave danger to the human race due to their extraordinary use as plasticizer in consumer product industry. All contemporary detection methods require high level of skills, expensive equipment and long analysis time as compared to the technique presented in this research work that introduces a real time non-invasive assay. A novel type of silicon substrate based smart interdigital sensor fabricated by employing thin film micro-electromechanical system semiconductor device fabrication technology. Electrochemical Impedance Spectroscopy was used in conjunction with the fabricated sensor to detect hormones and phthalates in deionized water. Various concentrations of phthalates as low as 2 parts per billion to a higher level of 2 parts per million in deionized water were detected distinctively using new planar ID sensor based EIS sensing system. The sensor was functionalized by a self-assembled monolayer of 3-aminopropyltrietoxysilane with embedded molecular imprinted polymer to introduce selectivity for the phthalate molecule. Spectrum analysis algorithm interpreted the experimentally obtained impedance spectra by applying complex nonlinear least square curve fitting in order to obtain electrochemical equivalent circuit and corresponding circuit parameters describing the kinetics of the electrochemical cell. Principal component analysis was applied to deduce the effects of surface immobilized molecular imprinted polymer layer on the evaluated circuit parameters and its electrical response. The results obtained by the testing system were validated using commercially available high performance liquid chromatography diode array detector system.

Research Outputs

The research outputs which have been published are listed below. The research outputs are in conjunction with the author's PhD candidacy:

Journals

1. **<u>A. I. Zia</u>**, S. C. Mukhopadhyay, P.-L. Yu, I. Al-Bahadly, C. P. Gooneratne, and J. Kosel, "Rapid and molecular selective electrochemical sensing of phthalates in aqueous solution," ***Biosensors and Bioelectronics,*** **2014**. http://www.sciencedirect.com/science/article/pii/S0956566314006460

2. **<u>A. Zia</u>**, S. Mukhopadhyay, P. Yu, I. Al-Bahadly, C. Gooneratne, and J. Kosel, "Post Annealing Performance Evaluation of Printable Interdigital Capacitive Sensors by Principal Component Analysis," ***Sensors Journal, IEEE,*** vol. 67, pp. 342-349, **2014**.

3. **<u>A. I. Zia</u>**, M. S. A. Rahman, S. C. Mukhopadhyay, P.-L. Yu, I. Al-Bahadly, C. P. Gooneratne, J. Kosel, and T.-S. Liao, "Technique for rapid detection of phthalates in water and beverages," ***Journal of Food Engineering****,* vol. 116, pp. 515-523, **2013.**

4. **<u>A. I. Zia</u>**, A. M. Syaifudin, S. Mukhopadhyay, P. Yu, I. Al-Bahadly, C. P. Gooneratne, J. Kosel, and T.-S. Liao, "Electrochemical impedance spectroscopy based MEMS sensors for phthalates detection in water and juices," ***Journal of Physics****:* vol. 439, p. 012026, **2013**.

Proceedings and Conference Papers

1. **<u>A. I. Zia</u>**, S. C. M. P.L.Yu, I. H. Al Bahadly, "Development and evaluation of portable low cost testing system for phthalates ," in *eighth International Conference on Sensing Technology (ICST), 2014*, S2IS, vol. 7, pp. 385 – 391

2. **A. I. Zia**, S. C. Mukhopadhyay, P.-L. Yu, I. Al-Bahadly, C. P. Gooneratne, and J. Kosel, Poster presentation for "Rapid and molecular selective electrochemical sensing of phthalates in aqueous solution," 24th Anniversary World Congress on Biosensors, 27-30 May 2014, Melbourne, Australia.

3. **A. I. Zia**, S. Mukhopadhyay, I. Al-Bahadly, P. Yu, C. P. Gooneratne, and J. Kosel, "Introducing molecular selectivity in rapid impedimetric sensing of phthalates," in *Instrumentation and Measurement Technology Conference (I2MTC) Proceedings, 2014 IEEE International*, 2014, pp. 838-843

4. **A. I. Zia**, A. R. Mohd Syaifudin, S. C. Mukhopadhyay, I. H. Al-Bahadly, P. L. Yu, C. P. Gooneratne, J. Kosel, and T.-S. Liao, "MEMS based impedimetric sensing of phthalates," in *Instrumentation and Measurement Technology Conference (I2MTC), 2013 IEEE International*, 2013, pp. 855-860.

5. **A. I. Zia**, S. C. M. P.L.Yu, I. H. Al Bahadly, "Ovarian Hormone Estrone Glucuronide (E1G) Quantification- Impedimetric Electrochemical Spectroscopy Approach," in *Seventh International Conference on Sensing Technology (ICST), 2013*, 2013, pp. 22 - 27.

6. A. Syaifudin, **A. I. Zia**, S. Mukhopadhyay, P. Yu, C. P. Gooneratne, and J. Kosel, "Improved detection limits of bacterial endotoxins using new type of planar interdigital sensors," in *Sensors, 2012 IEEE*, 2012, pp. 1-4.

7. **A. I. Zia**, A. Mohd Syaifudin, S. Mukhopadhyay, P. Yu, I. Al-Bahadly, J. Kosel, and C. Gooneratne, "Sensor and instrumentation for progesterone detection," in *Instrumentation and Measurement Technology Conference (I2MTC), 2012 IEEE International*, 2012, pp. 1220-1225.

8. **<u>Asif. I. Zia</u>**, A.R. Mohd Syaifudin, S.C. Mukhopdhyay, I. H. Al-Bahadly and P.L. Yu, C.P. Gooneratne and Jürgen Kosel. *"Development of Electrochemical Impedance Spectroscopy Based Sensing System for DEHP Detection"*. Proceeding of 5th International Conference on Sensing Technology (ICST 2011), Palmerston North, New Zealand. pp. 703 – 711. 28th Nov – 1st Dec 2011. IEEE Catalog Number: CFP1118E-CDR. ISBN: 978-1-4577-0167-2.

Seminars

1 "Real-time low-cost assay for the selective detection of endocrine disrupting compounds and hormones." Programme of Massey University Pakistani Students Association, Postgraduate Student Presentations, 28th – 29th October, 2014, Massey University, Palmerston North New Zealand.

2 "Development and evaluation of portable low cost testing system for the selective detection of endocrine disrupting compounds and hormones" Programme of IEEE Central Section, New Zealand Chapter IEEE Student Presentations, 18th September, 2014, Victoria University, Wellington, New Zealand.

3 "Post anneal performance evaluation of interdigital capacitive sensors for the selective detection of endocrine disrupting compounds and hormones" Electronics, Information and Communication System (EICS) Seminar, 30th July 2014. School of Engineering and Advanced Technology, Massey University, Palmerston North. New Zealand.

4 "Electrochemical Impedance Spectroscopy; a rapid detection tool for reproductive hormones and toxins" Electronics, Information and Communication System (EICS) Seminar, 15th September 2013. School of Engineering and Advanced Technology, Massey University, Palmerston North. New Zealand.

5 "Electrochemical capacitive sensing of alcohol in human breath " Programme of IEEE Instrumentation and Measurement Society New

Zealand Chapter Workshop on Smart Sensors, 18th -19th February, 2013, University of Waikato, Hamilton, New Zealand.

6 "Detection of Phthalates in water and beverages; interdigital sensors based electrochemical impedance spectroscopy approach" Programme of IEEE Central Section, New Zealand Chapter IEEE Student Presentations, 7th September, 2012, Massey University, Palmerston North New Zealand.

7 "Phthalates detection in using interdigital sensors based system" Electronics, Information and Communication System (EICS) Seminar, 2nd August 2012. School of Engineering and Advanced Technology, Massey University, Palmerston North. New Zealand.

8 "Improvements in detection limits for phthalates in aqua baverages " Programme of IEEE Instrumentation and Measurement Society New Zealand Chapter. Workshop on applications to agriculture and environment monitoring, 11th -12th April, 2012, Lincoln University, Christchurch, New Zealand.

9 "Smart sensing system for detection of reproductive hormones and toxins" PhD confirmation seminar. 20th October 2011. School of Engineering and Advanced Technology, Massey University, Palmerston North. New Zealand.

10 "A review of Smart materials and sensors for energy harvesting applications" Programme of IEEE Instrumentation and Measurement Society New Zealand Chapter Workshop on Sensors and Instrumentation in Environmental Health and Agriculture Applications, 1st ,2nd September, 2010, Massey University, Wellington.

Awards

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Table of Contents

Table of Figures

List of Tables

Abbreviated Terms

AC	Alternating Current
AFM	Atomic Force Microscope
Alumina-Al_2O_3	Aluminium Oxide
APTES	3-aminopropyltrietoxysilane
Au	Gold
BBP	Butylbenyl phthalate
Bode	Data presentation as a function of frequency
BSA	Bovine serum albumin
C	Capacitance
C_{ad}	Adsoption capacitance
C_{dl}	Double-layer capacitance
CNLS	Complex Non-linear Least Square
CPE	Constant Phase-Element
Cr	Chromium
D	The electric displacement
DBP	Di-*n*-butyl phthalate
DEHP	Di-(2-ethylhexyl) phthalate
DEP	Di-ethyl phthalate
dH_2O	Distilled water
DINP	Di-isononyl phthalate
DMF	dimethyl formamide
DMP	Di-methyl phthalate
DNA	Deoxyribonucleic Acid
DOP	Di-*n*-octyl phthalate
DUT	Device Under Test
E	The electric field intensity
EC	Electrolyte Conductivity
EDCs	Endocrine Disrupting Compounds
EDs	Endocrine Disruptors
EIS	Electrochemical Impedance Spectroscopy
ELISA	Enzyme Linked Immunosorbent Assays
EtOH	Ehanol
EU	Endotoxin Unit
f	Frequency
FDA	United States Food and Drug Administration
FR4	Fiberglass reinforced epoxy laminates for PCB fabrication
FTIR	Fourier Transform Infrared Spectroscopy

GND	Electrical ground
H^+	Hydrogen ions
H_{CUR}	Carries the signal current source.
HPLC	High performance liquid Chromatography
HPLC	High Performance Liquid Chromatography
H_{POT}	Monitors the excitation potential, V.
I	Current
IDAM	Interdigitated Array Microelectrode
IDES	Interdigitated Electrode Structures
IDTs	Interdigital Transducers
IS	Impedance Spectroscopy
ISE	Ion-Selective Electrodes
ISFET	Ion-Sensitive Field Effect Transistors
LCR3522-50	Measuring instrument for impedance (inductance, capacitance and resistance) (1mHz to 100kHz)
LCR3532-50	Measuring instrument for impedance (inductance, capacitance and resistance) (42Hz to 5MHz)
L_{CUR}	Accepts the signal current return.
LOD	Limit of Detection
LOD	Limit of Detection
L_{POT}	Connected to the sensor's sensing electrodes
MEMS	Micro-electromechanical Systems
MilliQ	Ultra-pure water which undergo the proses filtration and deionisation that has been characterised in terms of resistivity (typically 18.2 MΩ·cm)
MRL	Minimal Risk Level
MUT	Material Under Test
NaCl	Sodium Chloride
NMR	Nuclear Magnetic Resonance
Nyquist	Data presentation in complex impedance plot
OH^-	Hydroxide ions
PC	Principal Component
PCA	Principal Component Analysis
PCB	Printed Circuit Board
PCR	Polymerase Chain Reaction
PDEs	Partial differential equations

PECVD	Plasma enhanced chemical vapour deposition
PETE	Polyethylene Terephthalate
pH	Potential of Hydrogen
PPB	Parts per billion
PPM	Parts per million
PR	Photo Resist
PVC	Polyvinyl chloride
Q	Charge
θ	Phase Angle, theta
QCM	Quartz Crystal Microbalance
R	Resistance
$\mathbf{r^2}$	Residual mean squares
R_{ct}	Charge/electron transfer resistance
RIE	Reactive ion etching
R_s	Solution resistance
RS232	Serial communication port
SAW	Surface Acoustic Wave
SEAT	School of Engineering and Advanced Technology
SEM	Scanning Electron Microscope
Si	Silicon
Si_3N_4	Silicon Nitride
SiO_2	Silicon Dioxide
SNR	Signal to Noise Ratio
SPR	Surface Plasmon Resonance
SPSS	IBM Statistical Analysis software
σ_ω	Warburg coefficient
TDI	Tolerable Daily Intake
TEOS	Tetraethylorthosilicate
TMAH	Tetra-Methyl Ammonium Hydroxide
UV	Ultra-violet
V	Voltage
W_e	The electrostatic energy density
Z	Impedance
Z_W	Warburg impedance
ω	The angular frequency
ε_0	The permittivity of vacuum which sets to be 8.854×10^{-2} F/m
ε_r	The relative permittivity
ε	The permittivity