Stochastic Microsensors as New Tools for Fast Assay of Substances of Biological Importance

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Project Leader (PL):CSI Dr. Raluca-Ioana van Staden

PL's Project Laboratory: Laboratory of Eectrochemistry and PATLAB Bucharest

PL's Host Institution for the project: National Institute of Research and Development for Electrochemistry and Condensed Matter (INCDEMC), Timisoara

Project duration in months: 60 months (2011-2016)

Project budget: 1.500.000RON

Project Summary

Stochastic sensors and microsensors are well known for their capability of performing qualitative and quantitative analysis of one or more analytes in the same sample, at a very low concentration. The advantages of using this type of sensors for such analysis are the possibility of identifying and quantifying in one run different types of biomarkers – proteins type, DNA type as well as other substances of biological importance usually requested by medical doctors to be quantified, that can take the test from a fast screening method to a fast diagnostic method. The analysis is performed within minutes, this is very important for illnesses such as cancer that can develop fast in the body. The idea of the projects is the design of new stochastic microsensors based on new nanostructured materials. Modeling of electrochemical process and experimental study of the influence of different parameters will contribute to the theory of current development for this type of electrodes, The electrodes will be applied for

determination of substances of biological importance , and they will be part of a dedicated instrument – developed under the same project. A data base regarding values of toff will be constructed for the substances of biological importance. Integration in the research team of young researchers represents one of the main objectives of the project.

Team Members

Name	Role in the project
Raluca-Ioana van Staden, Dr habil., CSI	Director of Project
Jacobus Frederick van Staden, DSc, Prof., CSI	Principal Researcher
Bogdan Calenic, PhD	Postdoc
Iuliana Moldoveanu, MSc	PhD student
Livia Alexandra Gugoasa, MSc	PhD student
Ionela Raluca Comnea, MSc	PhD student
Ramona Georgescu, MSc	PhD student
Anita Elena Girbea, MSc	Young researcher
Radu Constantin Iacomin, MSc	Young researcher
Oana Elena Stoica, MSc	Technician

Objectives

The following are the main objectives of the project:

O1 To find the best nanostructured materials to be used in stochastic microsensors technology;

O2 Evaluation of different parameters which may affect the microsensors response characteristics, such as nature and material of microsensor matrix, pH of the solution, ionic strength, electrolytes;

O3 Application of new designed stochastic microsensors for determination of molecules of biological importance such as thyroid hormones, obesity biomarkers, etc.;

O4 Development of new instrumentation for screening of substances of biological importance;

O5 Creation of the data base for qualitative analysis using stochastic microsensors;

O6 Integration of young researchers in the laboratory team.

Methodology

Intermediate milestones:

- **December 2011 – data base of nanostructured materials for stochastic microsensor's design;**
- **December 2012 – new stochastic microsensors for obesity, hepatitis B and cancer diagnosis;**
- **December 2013 – new stochastic microsensors for thyroid hormones assay;**
- **September 2014 – protopype of a dedicated instrument containing the data bases and the sensor incorporated.**

The project is structured in the following work packages:

WP1 New nanostructured materials and matrices for stochastic microsensors development

WP2 Characterization of the stochastic microsensors

WP3 Development of dedicated instrumentation for screening

WP4 Dissemination

WP5 Management of the project

The core work packages (WP) comprised in the following tasks:

WP1

1.1– identification of nanostructured materials capable to be used in sensor design;

1.2– SEM, AFM and SPFM (Scanning Polarization Force Microscopy) characterization of the sensor materials;

1.3 – identification of possible matrices for sensor design, e.g., carbon paste based matrices, gold based matrix;

1.4 – AFM and SPFM characterization of the sensor surface topography and electrical and dielectrical characteristics;

1.5 – assembly of the sensor.

WP2

2.1 – Selection of different molecules of biological importance;

2.2 – Determination of t_{off} – the signature of the molecule;

2.3 – Determination of the response characteristics of the sensors;

2.4 – Determination of the influence of the pH, electrolyte, and ionic strength on the response of the sensors.

2.5 – Validation of the sensors.

WP3

3.1 – design of the prototype for the minielectrochemical cell containing the sensor;

3.2 – design of the electronic part of the instrument;

3.3 – integration of the data base in the "black box" of the instrument;

3.4 – validation of the instrument.

WP4

4.1 – website dedicated to the project;

4.2 – flyers dedicated to the project;

4.3 – dissemination through patents

4.4 – dissemination through published papers in ISI peer-reviewed journals;

4.5 – dissemination through papers presented at workshops, conferences, and seminars.

WP5

5.1 – evaluation of the results every quarter;

5.2 – writing reports;

5.3 – risk assessments – management of risk;

5.4 – integration of knowledge with training/education of students and young researchers.

Gantt chart of WPs of the project

WORK PACKAGES	2011/Q	2012/Q				2013/Q				2014/Q		
	4	1	2	3	4	1	2	3	4	1	2	3
WP1												
WP2												
WP3												
WP4												
WP5												

Dissemination

Chapters in books:

Mechanism of potential development for potentiometric sensors, based on modeling of interaction between electrochemically active compounds from the membrane and analyte
R.I. Stefan-van Staden
Chapter 4, pp.131-154 in
Chemical Sensors Simulation and Modeling
Volume 5: Electrochemical Sensors (Ghenadii Korotcenkov, Ed)
Published in Sensors Technology Series (Joe Watson, Ed.)
Momentum Press, LLC, New York, 2013.

Papers published:

1. **Stochastic sensors based on nanostructured materials used in the screening of whole blood for hepatitis B**
   R.I. Stefan-van Staden, I. Moldoveanu
   Journal of Electrochemical Society, 161(2), B3001-B3005, 2014.
   DOI: 10.1149/2.026312jes

2. **Analysis of L-thyroxine and 3,3',5-triiodo-L-thyronine using potentiometric microsensors**
   Iuliana Moldoveanu, Raluca-Ioana Stefan-van Staden, Jacobus Frederick van Staden, Gabriel Lucian Radu
   U.P.B. Sci. Bull., 76(3), 3-10, 2014

3. **Amperometric microsensors based on inulins for the assay of L-T3 and L-T4**
   Livia Alexandra Gugoasa, Raluca-Ioana van Staden, Grzegorz Bazylak, Jacobus Frederick van Staden, Gabriel-Lucian Radu
   U.P.B. Sci. Bull., 76(3), 67-74, 2014

4. **New tool for screening of whole blood for early detection of breast cancer antigen (CA153)**
   R.I. Stefan-van Staden, J.F. van Staden
   J. Mod.Med.Chem., 1(2), 86-91, 2013

5. **Enantioselective Surface Plasmon Resonance Sensor Based on C_{60} Fullerene-Glutathione Self-Assembled Monolayer (SAM)**
   R.I. Stefan-van Staden
   Chirality, 26(3), 129-131, 2014

6. **New Multimode Sensors based on Nanostructured Materials for Simultaneous Screening of Biological Fluids for Specific Breast Cancer and Hepatitis B Biomarkers**
   R.I. Stefan-van Staden, I. Moldoveanu
   J Electrochem Soc, 161(4), B45-B48, 2014

7. **A genetic screening test for obesity based on stochastic sensing**
   R.I. Stefan-van Staden, L.A. Gugoasa, J.F. van Staden, O.C. Rusu
   J. Electrochem.Soc., 161(9), B167-B170, 2014

8. **Screening of children saliva samples for bisphenol A using stochastic, amperometric and multimode microsensors**
   R.I. Stefan-van Staden, L.A. Gugoasa, B. Calenic, J.F. van Staden, J Legler
   Analytical Chemistry Research, 1, 1-7, 2014

9. **Pattern recognition of estradiol, testosterone and dihydrotestosterone in children' s saliva samples using stochastic microsensors**
   R.I. Stefan-van Staden, L.A. Gugoasa, B. Calenic, J. Legler
   Scientific Reports 4, 5579; DOI:10.1038/srep05579, 2014

10. **Multimode sensors as new tools for molecular recognition of testosterone, dihydrotestosterone and estradiol in children's saliva**
    L.A. Gugoasa, R.I. Stefan-van Staden, B. Calenic, J. Legler
    J Molec Recogn, 28(1), 10-19, 2015.

11. **Pattern recognition of adipokines in whole blood samples using stochastic sensing**
    L.A. Gugoasa, R.I. Stefan-van Staden, O.C. Rusu
    Mycrosystem Technology, in pres

12. **Novel textile material based disposable sensors for biomedical analysis**
    R.I. Stefan-van Staden, L.A. Gugoasa, M. Badulescu, C. Surdu-Bob
    RSC Adv, 5(56), 45545-45550, 2015

13. **Multimode microsensors based on carbon matrices used for the assay of IL-6 in whole blood samples**
    L.A. Gugoasa, R.I. Stefan-van Staden
    ESC J Solid State Science & Technol, 4(10), S3006-S3010, 2015

14. **New stochastic microsensors based on inulines for the assay of thyroid hormones**
    G. Mitrofan, R.I. Stefan-van Staden, I.R. Comnea, J.F. van Staden, C.P. Kapnissi-Christodoulou, G. Bazylak, H.Y. Aboul-Enein
    Chirality, 27(12), 973-978, 2015

15. **New stochastic microsensors based on ionic liquids for the assay of thyroid hormones**
    R.I. Stefan-van Staden, G. Mitrofan, I.R. Comnea, J.F. van Staden, C.P. Kapnissi-Christodoulou, H.Y. Aboul-Enein
    RSC Adv, 5(92), 75451-75457, 2015

16. **Chitosan based diamond paste stochastic sensors modified with gold nanoparticles detect hepatitis C core antigen**
    I.Moldoveanu, R.I. Stefan-van Staden, J.F. van Staden
    Electroanalysis, 27(8), 1842-1846, 2015

17. **Pattern recognition of HER-2 in whole blood samples using stochastic microsensors**
    I.Moldoveanu, R.I. Stefan-van Staden
    ESC J Solid State Science & Technol, 4(10), S3067-S3070, 2015

18. **Nanostructured materials detect epidermal growth factor receptor, neuron specific enolase, and carcynoembrionic antigen**
    R.I. Stefan-van Staden, I. Comnea, CC Surdu-Bob, M Badulescu
    Nanoscale, 7(38), 15689-15694, 2015

19. **Pattern recognition of monocyte chemoattractant protein-1 (MCP-1) in whole blood samples using new platforms based on nanostructured materials**
    R.I. Stefan-van Staden, L.A. Gugoasa, A.R. Biris
    Nanoscale, 7(36), 14848-14853, 2015 & Cover

20. **A new graphene stochastic sensor for the molecular screening of TNF-α**
    I.R. Comnea-Stancu, R.I. Stefan-van Staden, A.R. Biris
    J.Electrochem.Soc., 162(9), B245-B247, 2015

21. **New nanocomposite-graphene pastes based stochastic microsensors**
    R.I. Stefan-van Staden, L.A. Gugoasa, C.A. Socaci, A.R. Biris
    RSC Advances, 5(81), 66185-66191, 2015

22. **Fast screening of biological fluids for cytokines and adipokines using stochastic sensing**
    L.A. Gugoasa, R.I. Stefan-van Staden, A. Dima, C.A. Visan, A. Streinu-Cercel, A.r. Biris, B. Calenic
    Microelectronic Engineering, 148, 64-69, 2015

23. **New platforms for fast assessment of levels of testosterone, dihydrotestosterone and estradiol in children's saliva**
    L.A. Gugoasa, R.I. Stefan-van Staden, J.F. van Staden, B. Calenic, J.F. van Staden, J. Legler
    Anal.Lett., In Press.

Papers submitted to ISI journals:

24. **New stochastic sensors based on inulins for the early detection of cancer biomarkers**
    RI Stefan-van Staden, G Bazylak
    Submitted to ISI journal

25. **Recent Methods Proposed for the Detection of Hepatitis C Virus**
    I. Moldoveanu, R.I. Stefan-van Staden, J.F. van Staden, G.L. Radu, H.Y. Aboul-Enein
    Submitted to ISI journal

Papers presented at conferences:

1. **New Stochastic Sensors for Biomedical Applications**
   Raluca-Ioana Stefan-van Staden, Iuliana Moldoveanu, Jacobus Frederick van Staden
   IMCS 2012 The 14th International Meeting on Chemical Sensors, May 20 – 23, 2012 Nuremberg, Germany (Oral presentation)

2. **Simultaneous neurotransmitters analysis using microelectrodes based on porphyrins**
   Raluca-Ioana Stefan-van Staden, iuliana Moldoveanu, Jacobus Frederick van Staden
   4th EuCheMS Chemistry Congress (EuCheMS 2012) 26-30 August 2012, Prague, Czech Republic (Oral presentation)

3. **Multimode Sensors - A New Concept in Sensors' Technology**
   Raluca-Ioana Stefan-van Staden
   221st ECS Meeting, May 6-11, 2012, Seattle, WA, USA (Oral presentation)

4. **Enantioselective sensors for biomedical analysis**
   Raluca-Ioana Stefan-van Staden
   Chirality 2012, June 10-13, 2012, Dallas, TX, USA (Oral presentation)

5. **Single Molecule Detection in Molecular Diagnosis of Hepatitis B**
   Raluca-Ioana Stefan-van Staden, Iuliana Moldoveanu, Marius Enachescu
   XIV. Linz Winter Workshop. Advances in Single-Molecule Research for Biology & Nanoscience, February 3-7, 2012, Linz, Austria (Oral presentation)

6. **Stochastic Sensors for Single Molecule Detection**
   Raluca-Ioana Stefan-van Staden
   1st International Conference on Analytical Chemistry. Analytical Chemistry for a Better Life, September 18-21, 2012, Targoviste, Romania, (Oral presentation)

7. **Stochastic Sensors – New Tools for the Screening for Obesity**
   Raluca-Ioana Stefan-van Staden, Livia Alexandra Gugoasa, Jacobus Frederick van Staden
   223rd ECS Meeting, May 12-16, 2013, Toronto, Canada (Oral presentation)

8. **Stochastic sensors based on nanostructured materials used in the screening of whole blood for hepatitis B**
   R.I. Stefan-van Staden, I. Moldoveanu
   224th Meeting of ECS, 27 October – 1 November, 2013, San Francisco, CA, USA (Invited keynote)

9. **Multimode microsensors based on carbon matrices for the screening of whole blood for IL-6**
   Raluca-Ioana Stefan-van Staden, Livia Alexandra Gugoasa
   227th ESC Meeting, Chicago, May, 2015

Posters were presented by RI Stefan-van Staden and LA Gugoasa at EUROANALYSIS 2015, Bordeaux, Franta.