Stochastic approach for early diagnosis of cancer

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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: 24 months (2012-2014)

Project budget: 1.500.000RON

Project Summary

The idea of the project is the design of new stochastic sensors for screening of patients, followed by coupling of this method with RAMAN. The new methodology based on stochastic sensors and RAMAN probes will be able to analyse more than one biomarker or substance of biological importance at a time increasing quality and reliability of the diagnosis process. 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. Therefore, we will use them to identify and quantify in one run the following types of biomarkers: usual biomarkers like CA153, CA125, CEA and specific biomarkers like: CA2729, NSE (Neuron specific enolase), EGFR, and CA72-4. The analysis is performed within minutes, this is very important for types of cancers that can develop fast in the body. Furthermore, coupling of the stochastic sensors with optical probes such as Raman can improve the certainty of the result and bring it more closed from a screening test to diagnosis. The new sensors and methods developed will help for early screening of cancer (e.g.,

breast, ovarian, lung). This approach can give a chance for life to the people that may develop the illness sooner or later, the final goal being its utilization as a fast mass screening as well as a screening tool at a very low cost.

Team Members

Name	Role in the project
Raluca-Ioana van Staden, PhD, CSI	Director of Project
Jacobus Frederick van Staden, DSc, Prof., CSI	Principal Researcher
Balcu Ionel, PhD, CSII	Principal Researcher
Bogdan Calenic, PhD	Postdoc
Oana Elena Stoica, MSc	Assistant Manager
Iuliana Moldoveanu, MSc	PhD student
Livia Alexandra Gugoasa, MSc	PhD student
Ionela Comnea, MSc	Young Researcher
Ingrid – Oana Mesinschi, Medical Doctor	Young Researcher

Objectives

The main objective of the project is the improvement of the statues of health of the population in the European Union by early detection of cancer, decreasing of the number of patients that can develop the illness and increasing their chance for life.

Specific objectives are:

1. **Mass screening of the population using low cost analysis based on stochastic sensors.**
2. **Fast diagnosis of cancer at the molecular level by using multianalytical platforms formed from stochastic sensors and RAMAN probes, at a low cost.**
3. **Creation of a data base regarding biomarkers specific to different types of cancer, and classical/standard methods used for their assay.**

4. **Development of new stochastic sensors with high sensitivity and that can assure excellent accuracy of the analysis.**
5. **Development of optical methods based on RAMAN to be integrated with stochastic sensors in multianalytical platforms.**

Methodology

The project can be structured in the following core work packages:

WP1 – identification of new substances and materials prone for stochastic behaviour;

WP2 – development of new stochastic sensors;

WP3 – development of RAMAN probes for biomarkers (usual biomarkers like CA153, CA125, CEA and specific biomarkers like: CA2729, NSE (Neuron specific enolase), EGFR, and CA72-4) detection;

WP4 – dissemination;

WP5 – management of the project.

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

WP1:

1.1 – identification of new substances with natural pores/channels that can be used in the design of the stochastic sensors;

1.2 – identification of classes of substances as well as materials from which one can develop engineered pores for the design of stochastic sensors;

1.3 – data base for classes of substances and materials used for the design of stochastic sensors.

WP2:

2.1– selection of the matrix for the design of the stochastic sensors;

2.2 – design of the stochastic sensors;

2.3 – determination of the signature of different biomarkers (CA153, CA125, CEA and specific biomarkers like: CA2729, NSE (Neuron specific enolase), EGFR, and CA72-4) (t_{off}) and design of dedicated data bases;

2.4 – creation of data bases with patterns for different biomarkers and substances of biological importance;

2.5 – quantitative evaluation of the response of the stochastic sensors, working concentration range, limit of detection, kinetic data;

2.6 – validation of the method against well established clinical methods using a drop of blood and/or saliva.

WP3:

3.1– determination of the pattern of substances to be analysed using RAMAN technique;

3.2 – validation of each pattern for real biological samples, e.g., blood, saliva vs well established clinical methods;

3.3 – creation of data bases for different patterns of the substances studied.

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 presentations 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

STOCAN – WORK PACKAGES	Year1/Q				Year2/Q				Year3/Q			
	1	2	3	4	1	2	3	4	1	2	3	4
WP1												
WP2												
WP3												
WP4												
WP5												

Dissemination

Papers published:

1. 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

2. Pattern recognition of HER-1 in biological fluids using stochastic sensing
   R.I. Stefan-van Staden, I. Moldoveanu, C. Stanciu-Gavan
   Journal of Enzyme Inhibition and Medicinal Chemistry, In Press

3. Screening tools for neuron specific enolase
   R.I. Stefan-van Staden, I.R. Comnea, J.F. van Staden, C. Stanciu Gavan
   RSC Advances, 4(50), 26383-26388, 2014

4. Platform based on amperometric microsensors used for the assay of HER-1 in peritoneal fluid
   I. Moldoveanu, R.I. Stefan-van Staden, J.F. van Staden, C. Stanciu-Gavan, C. Savlovschi
   J Electrochem Soc, In Press.

5. Molecular screening of HER-1 in whole blood samples
   I. Moldoveanu, C. Stanciu Gavan, R.I. Stefan-van Staden,
   J Molec Recogn, In Press

6. **Enantioanalysis of L-cysteine using enantioselective, potentiometric membrane electrodes**
   R.I. Stefan-van Staden, L. Holo
   Journal of Membrane and Separation Technology, 3(2), 86-90, 2014

7. **Challenges in Enantioanalysis of Fucose Using Stochastic and Potentiometric Microsensors**
   Moldoveanu, R.I. Stefan-van Staden, C.P. Kapnissi-Cristodoulou, J.F. van Staden, H.Y. Aboul-Enein
   Sensing and Biosensing Research, 1, 1-7, 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

Papers presented at conferences:

1. **New multimode sensors based on nanostrucured materials for simultaneous screening of biological fluids for specific breast cancer and hepatitis B biomarkers**
   RI Stefan-van Staden, et al.
   222nd Meeting of ECS, PRIME 2012 PACIFIC RIM MEETING ON ELECTROCHEMICAL AND SOLID-STATE SCIENCE, 7 - 12 October 2012, Honolulu, Hawai, USA. (Oral presentation)

2. **New trends in the technology of micro and nanosensors for biomedical analysis**
   RI Stefan-van Staden
   245th ACS Meeting, 7 - 11 April 2013, New Orleans, USA. (Oral presentation)

3. **Stochastic and multimode sensors based on porphyrins. New trends and applications in biomedical analysis.**
   R.I. Stefan-van Staden
   8th International Conference on Porphyrins and Phthalocyanines (ICPP-8), Istanbul, Turkey, June 22-27, 2014 (Keynote lecture)

4. **Stochastic sensors - new tools for screening in biomedical analysis**
   R.I. Stefan-van Staden
   The 3rd International Conference on Analytical and Nanoanalytical Methods for Biomedical and Environmental Sciences, "IC-ANMBES 2014", Brasov, Romania, June 13-15, 2014 (Keynote lecture)

5. Carbon nanostructures used for screening in biomedicine
RI Stefan-van Staden
225th ECS Meeting, May, Orlando, USA

7 lectures presented by PhD students: Iuliana Moldoveanu, Livia Alexandra Gugoasa, Ionela Raluca Comnea, Ramona Georgescu to National Conference.