PUBLISHABLE EXECUTIVE SUMMARY

(1/10/2006-30/09/2007)

Project overview

The detection of biological and chemical species is central to many areas of health care and the life sciences, ranging from uncovering and diagnosing disease, to the discovery and screening of new drug molecules. Neuroscience, especially diagnostics and therapies of neurological diseases, demand for development of new devices with a highly sensitive mechanism of transduction of the biological and chemical signals. Devices based on organic semiconductors emerge as a powerful and versatile class of ultra-sensitive electrical transducers for direct and dynamic detection of biological species. In fact, they can be fabricated and easily integrated with micro- and nanofluidics devices by the use of sustainable nanofabrication techniques, downscaled and endowed with specific recognition functionality by design and tailoring of the materials.

The vision of BIODOT is a hybrid bio-organic technology for transduction of dynamical phenomena of biosystems in-vitro. The device that will be developed is based on organic ultra thin film transistors integrated with microfluidics. It will respond to subtle changes of the electrostatic charge at the interface between the biosystem in the solution and the organic semiconductor. These changes are due, for instance, to the flow of ions, the adsorption and diffusion of charged or polarisable molecules, the motion of large biomolecules, the activity of cells grown on the organic semiconductor. Dynamical phenomena at multiple length scales govern the operations and the functionality of living systems. Signalling across neurons involves transport and diffusion of ions and molecules across membranes and synapses. Low frequency motions control the hierarchical organisation of proteins and membranes, which play a key role in the molecular pathology of many neurological diseases.

The transduction of the dynamical behaviour of a) *peptides involved in neurological functions,* b) *phospholipids and functional membranes*, c) *neurons and glia cells* will be demonstrated during the project. The signal will be correlated with dynamical data from fluorescence and scanning probe microscopy, computer simulations and structural techniques at the micro- and nano-scales. The integration of neural cells into this technology will extend the scope of the project towards long-term applications in biomedicine. These and other aspects make BIODOT a project aimed to achieve breakthroughs with respect to the state-of-the-art.

S&T Objectives

BIODOT aims to develop a hybrid technology and organic electronic devices that allow monitoring dynamical phenomena of biosystems at in-vitro conditions. This new experimental approach can be readily used in neuroscience, as well as being further developed in a variety of tools for different fields of research also in-vivo, from medical diagnostics, to pharmacological therapy, to interfacial phenomena in materials science employed in regenerative medicine. The objectives of BIODOT are:

- the development of a fluidics/bio-organic technology based on nanofabrication;
- the design and fabrication of the new device;
- the electrical transduction of dynamical phenomena of biomolecules;
- the scalability of the response down to the level of finite numbers of (bio)molecules;
- the quantification of the response of the device;
- the integration of functional membranes and neural cells in the device;
- the assessment of the technology towards development of new tools for research and therapy of neurological diseases;
- the evaluation of the societal issues in the context of neurological diseases.

Major Achievements to Date

During year 1, large part of the research activities have been targeted to achieve the proof of concept that the envisioned sensing scheme based on OFETs is viable and that the hybrid technology involving living cells and organic devices can be developed. This has involved a considerable joint effort, owing to the complexity of the problems and the requirement of diverse competences. Major achievements both in the fundamental knowledge and the technology of the hybrid bio-organic systems have been:

i) the demonstration of operation of organic field effect transistors under water environment;

ii) the demonstration of transduction of changes in pH and concentration of polyelectrolytes in water solutions with OFETs, also based on organic semiconductor ultra-thin films;

iii) the multiscale modelling of OFETs in water, and different device configurations in the presence of solutions;
iv) the fabrication of first generation microfluidics on the transistor test patterns;
v) the first experimental demonstration of a response to changes in peptide concentration of the transistor parameters;
vi) adhesion, growth, differentiation of neural stem cells on bare ultra-thin film organic semiconductors to form densely interconnected neural networks;
vii) the fine control of cell adhesion and growth of neuronal cells by the nanoscale morphology of the organic semiconductor layer;
viii) the patterning of glia cells on templates made of functional materials;
ix) the nanopatterning of adhesion proteins on the organic semiconductors by unconventional printing techniques;
x) the specific recognition of single antigen-antibody interactions on an organic semiconductor surface by means of functionalised AFM probes and TREC mode;
xi) the elucidation of the early stages of aggregation of peptide Aβ1-40 in microfluidics channels and its comparison with fibrillar aggregation in bulk solutions;
xii) the energy landscape of Aβ1-40 peptide conformations in oligomers.

The results I-V show that the BIODOT approach is viable, and there are no major fundamental technological or chemical-physical barriers for OFETs used as biosensors.
The results VI-IX show that living cells can be integrated in the OFET by a variety of approaches. The results X-XII build the fundamental knowledge for the interpretation of the electronic transduction experiments that will be carried out in year II.

The project has been producing already papers and a patent is in preparation. Overall, the project is developing nicely, with a very high level of cooperation among academic partners and industries, with a substantial networking and open flow of information. The expected jargon barriers, which have been experienced within the first six months of the project, seem now to have been abated, or at least do not constitute a major obstacle to the flow of information and experiment planning. It should be noted that the project has prompted some groups to acquire young researchers with competences that were traditionally outside their field of expertise, thus increasing the multidisciplinarity of the environment. In this sense BIODOT is, so far, a successful example of project of converging technology.

Potential impact in terms of socio-economic development perspectives

BIODOT preludes to the development of low-cost portable devices in the long term. Sustainable products for diagnostics, to be used in mass screening for a variety of pathologies, imply enormous benefit to health care programs and improvement of the quality of life. Early screening is even more compelling for neurodegenerative diseases that are becoming more and more relevant as life expectancy increases. We mention that BIODOT has stimulated one of the partners to consider the foundation of a spin-off company to develop hybrid technology and “smart” substrates for in vitro cell cultures. The envisioned company stems from a majoritary group of women scientists and professionals, with different backgrounds.

BIODOT merges enabling technological platforms, such as bio- and nanotechnology, in which EU has invested substantial resources. It opens broad market segments to multifunctional materials and organic electronics, beyond consumer electronics and displays. The scope of the project and its long-term objectives are consistent with the concepts of ERA and the development of a knowledge-based economy as stated in the Lisbon conference.

Consortium

The consortium has brought together several centres of excellence of European research operating on nanoscience, processing and nanofabrication, organic electronics, biophysics, neuromedicine and neuroscience. Partnership includes a major electronics industry research centre at the forefront of innovation, and a spin-off company developing products based on unconventional nanofabrication. The complementary expertise is carefully balanced management according to the objectives.

List of Participants

Participant name	Participant short name	Country
Consiglio Nazionale delle Ricerche-ISMN Bologna	CNR	I
University of Groningen	RuG	NL
Università di Bologna	UNIBO	I
Ludwig Maximilians Universitaet, Munich	LMU	D
Consejo Superior de Investigacíones Cientificas - IMM Madrid	CSIC	E
Philips Research Laboratories, Eindhoven	Philips	NL
SCRIBA Nanotecnologie Srl, Bologna	Scriba	I
Institute of Experimental Medicine, Hungarian Academy of Sciences, Budapest	IEM-HAS	HU

Dissemination of knowledge

Publications

1. Teobaldi Gilberto; Zerbetto Francesco. **Adsorption of Organic Molecules on Gold Electrodes.** Journal of Physical Chemistry C (2007), 111(37), 13879-13885.

2. Cramer Tobias; Garcia Ricardo; Zerbetto Francesco. **The Molecular Mechanism of Water Bridge Build up: Field-induced Formation of Nanoscale Menisci,** submitted

3. Eva Bystrenova, Marta Jelitai, Ilaria Tonazzini, Adina Lazar, Martin Huth, Pablo Stoliar, Chiara Dionigi, Marcello G. Cacace, Bert Nickel, Emilia Madarasz and Fabio Biscarini. **Neural Networks Grown on Organic Semiconductors,** submitted

4. A. Lazar, P. Greco, C. Dionigi, E. Bystrenova, M.G. Cacace, F. Biscarini. **Self-assembling of amyloid peptide in a confined fluidic environment,** in preparation

Presentations

-Invited talk at "Structure and Stability of Biomacromolecules" SSB 2007, Kosice, Slovakia, 05-08 September 2007.

- "Study of neural cells on ultra thin organic semiconductors" E. Bystrenova, I.Tonazzini, S.Dutta, P. Stoliar, A. Lazar, P. Greco, C. Dionigi, M.G. Cacace, C. Martini, M. Jelitai, E. Madarasz and F. Biscarini

-Oral presentation at "Advances in Single Molecule Research for Biology & Nanoscience" meeting, Linz, Austria, 02-05 February 2007.

- "Immobilization of neuronal cells using ultra thin organic film", Bystrenová E, Stoliar P, Lazar A, Greco P, Tonazzini I, Martini C, Jelitai M, Madarasz E,. Cacace MG, Biscarini F.

-Oral presentation at EMRS meeting, Strasbourg, France, 28 May-01 June 2007.

- "Controled self-assemblies of proteins at a sub-micrometric scale", Adina N. Lazar, Chiara Dionigi, Eva Bystrenova, Pablo Stoliar and Fabio Biscarini

-Oral presentation at International Conference on Organic Electronics 2007, Philips High Tech Campus, Eindhoven, The Netherlands, 04 – 07 June 2007.

- "Growth of neural cells on ultra thin organic semiconductors" E. Bystrenova, P. Stoliar, A. Lazar, P. Greco, C. Dionigi, M.G. Cacace and F. Biscarini, I.Tonazzini, C. Martini, M. Jelitai, E. Madarasz

-Oral presentation at XXXVI Congresso Nazionale di Chimica Fisica, Gallipoli, Italy, 17 – 22 June 2007.

- "Growth of neural cells on ultra thin organic semiconductors" E. Bystrenova, P. Stoliar, A. Lazar, P. Greco, C. Dionigi, M.G. Cacace and F. Biscarini, I.Tonazzini, C. Martini, M. Jelitai, E. Madarasz

-Oral presentation P. Greco, E. Bystrenova, I. Tonazzini, A. Lazar, P.Stoliar, M. Jelitai, C. Dionigi, M. Cacace, E. Madrasz , C. Martini and F. Biscarini, *Growth of neural cells on organic semiconductor thin film*
given at "VI Convegno Nazionale per sulla Scienza e Tecnologia dei Materiali", Perugia 13 June 2007

-Oral presentation at EUROMAT meeting of Federation of European Materials Societies, Nürnberg, Germany, 10 – 12 September 2007.

- "Growth of neural cells on ultra thin organic semiconductors" E. Bystrenova, P. Stoliar, A. Lazar, P. Greco, C. Dionigi, M.G. Cacace and F. Biscarini, I.Tonazzini, C. Martini, M. Jelitai, E. Madarasz

-Poster presentation at AFM BioMED conference, Barcelona, Spain, 19-21 April 2007.

- "Evolution of amyloid-peptides self-assembly – from thin films to fibrillary structures", Adina N. Lazar, Chiara Dionigi, Eva Bystrenova, Paolo Greco, Pablo Stoliar, Soumya Dutta and Fabio Biscarini

- Poster presentation at 3rd Biological Surfaces and Interfaces Conference, San Feliu de Guixols, Spain, 01-06 July 2007.

- "Influence of roughness of organic semiconductor film on viability of human central nervous system cells". Tonazzini I, Bystrenova E, Greco P, Lazar A, Stoliar P, Dutta S, Dionigi C, Cacace MG, Martini C and Biscarini F.
- "Growth of astroglial and neuronal cells on organic semiconductor films". Bystrenova E, Tonazzini I, Greco P, Lazar A, Stoliar P, Dutta S, Dionigi C, Cacace MG, Jelitai M, Madarasz E, Martini C and Biscarini F.
- **Evaluation of the kinetics of amyloidogenic protein self-assenbling in crowded/confined environments,** A. N. Lazar, E Bystrenova, C. Dionigi, P. Greco, S. Dutta, P. Stoliar, M.G. Cacace and F. Biscarini

-Poster presentation at "Bionanotechnology: From self-assembly to cell biology", Cambridge, Great Britain, 03-05 January 2007.

- "Controled aggregation of amyloids in confined environment", Adina N. Lazar, Chiara Dionigi, Eva Bystrenova and Fabio Biscarini

-Poster contribution was presented at CeNS workshop in Irsee.
-Poster contribution was presented at CeNS winter school in Mauterndorf, Austria.

Dr. Fabio Biscarini (coordinator) presented seminars including BIODOT results at :

- Symposium on Nanotechnology and Regenerative Medicine at R2B exhibition, Bologna (4 May 2007)
- Department of Chemistry, Berkeley, California (13 April 2007)
- Nano Spain, Seville, 16 March 2007
- Primavera Italiana in Giappone (Rome, 31 January 2007)
- MESA + Colloquium, Technical Univeriteit Twente, the Netherlands, (12 December 2006)

Exhibition

-Scriba has organised a stand in “Research-to-Business” (R2B) from May 3-4, 2007. R2B is the largest fair in Italy dedicated to knowledge-based industry, technology transfer and spin-off companies. During R2B the CEO has been interviewed by “Il Sole 24ore”, the major economic daily newspaper of Italy. He has highlighted the participation of Scriba in BIODOT project.

Logo of the project

Contact details

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