FINAL PUBLISHABLE SUMMARY REPORT

Grant Agreement number: NMP4-SL-2008-212533

Project acronym: BioElectricSurface

Project title: Electrically Modified Biomaterials' Surfaces: From Atoms to Applications

Funding Scheme: FP7 - Cooperation

Date of latest version of Annex I against which the assessment will be made: 18 June 2009

Periodic report: 1st 2nd Final Report

Period covered: from 1st October 2008 to 30th September 2011

Name, title and organisation of the scientific representative of the project's coordinator:

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Declaration by the scientific representative of the project coordinator

I, as scientific representative of the coordinator of this project and in line with the obligations as stated in Article II.2.3 of the Grant Agreement declare that:

- The attached 2nd Periodic Report represents an accurate description of the work carried out in this project for this reporting period;
- The project (tick as appropriate):

  ☐ has fully achieved its objectives and technical goals for the period;

  X has achieved most of its objectives and technical goals for the period with relatively minor deviations;

  ☐ has failed to achieve critical objectives and/or is not at all on schedule.

- The public website is up to date, if applicable.
- To my best knowledge, the financial statements which are being submitted as part of this report are in line with the actual work carried out and are consistent with the report on the resources used for the project (section 6) and if applicable with the certificate on financial statement.
- All beneficiaries, in particular non-profit public bodies, secondary and higher education establishments, research organisations and SMEs, have declared to have verified their legal status. Any changes have been reported under section 5 (Project Management) in accordance with Article II.3.f of the Grant Agreement.

Name of scientific representative of the Coordinator**Error! Bookmark not defined.**: .....
Syed TOFAIL.....

Date: .....30...../ ....November..../ ....**2011**....

Signature of scientific representative of the Coordinator**Error! Bookmark not defined.**: 
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BIO ELECTRIC SURFACE

MONTH 36
FINAL PUBLISHABLE SUMMARY REPORT

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Executive Summary

According to the World Health Organisation (WHO), cardiovascular diseases cause half the deaths in the EU. It is also the main cause of years of life lost (over 30 per cent) thus causing huge pressure on the labour force and family earnings. The problem is becoming more acute in Central and Eastern European countries. Due to the ageing population in the EU, osteoporosis related bone fractures have almost doubled in the last decade. It is estimated that 40 percent of women over 50 years in age will suffer from fractures due to low density bone. The European Commission considers the application of nanotechnology an important research strategy to address these problems. For this, design and control of biomaterial at the nanometer scale is set as a strategic research priority. Europe is, however, seriously underrepresented in the global market for nanotherapeutics, where the United States dominates with three-quarters of the market share. While the drive for nanoscale understanding of biological interaction can be high, the application of this knowledge in marketable devices should also be prioritised.

In this European Commission funded project, scientists from across Europe and Israel have carried out electrical modification of biomaterials' surfaces to manipulate surface charge that will mediate bio/non bio interactions *in vivo*. The project, coordinated by University of Limerick, has commenced in October 2008 and completed in September 2011. The project team has developed techniques to create localised areas (domains) of surface charge to probe biological interactions (e.g. proteins and cells) at biomaterials' surfaces at various length scales ranging from a few millimetres to hundreds of nanometres. Such an insight is important because the first reaction between biological species and a biomaterial takes place at the biomaterial surface. When a biomaterial is placed inside the body, a biological response is triggered almost instantaneously at the top few nanometres of the biomaterial. For devices that remain in the body for a medium to long term, biological interactions can cause encrustation, plaque formation and aseptic loosening in these device surfaces. These problems contribute to patient's trauma and even increase the risk of death.

The BioElectricSurface team has been working with the aim to decrease patients' trauma and the risk of death through a detailed understanding of nanoscale interactions of biological systems with biomaterials' surfaces. In addition to the enhancement of the knowledge of biological interactions with charged surfaces, the project has developed exploitable knowledge in modifying biomedical devices for improved performances. The project has developed a novel, patent-pending method of incorporation of nanoparticles into textiles, which are particularly effective against the hospital superbug MRSA when exposed to ultraviolet radiation available in day light. Between 80-100% killing of bacteria is possible even after 40 washes. In addition to this, the project has developed novel coatings that inhibits stone formation on urological stents and reduces the tendency blood clotting and plaque growth on cardiovascular stents

Further information on the outcome of this project can be found at www.bioelectricsurface.eu or by contacting the following address directly: Dr. Syed Ansar Md. Tofail, Project Coordinator, BioElectricSurface, MSG-016, Materials and Surface Science Institute (MSSI), University of Limerick, Ireland; Phone: +353-61-234132, Fax: +353-61-213529; email: tofail.syed@ul.ie

Bio Electric Surface
www.bioelectricsurface.eu

Context and Project Objectives

The Context:

Cardiovascular diseases account for half the deaths in the EU. They are the main causes of 30 per cent years of life lost in early deaths. Osteoporosis related bone fractures have almost doubled in the EU in the last decade. 40 percent of women over 50 years in age will suffer from bone fractures. 65 percent of urinary stents suffer from encrustation and forms stone in 13-24 weeks. In Southern and Western Europe over 40 per cent of hospitals showed prevalence of MRSA super bug. Medical devices and textiles are important products used in combatting such threats to our quality of life.

When a biomaterial is placed inside the body, a biological response is triggered almost instantaneously at the top few nanometres of the biomaterial. For devices that remain in the body for a medium to long term, biological interactions can cause encrustation, plaque formation and aseptic loosening in these device surfaces. These problems contribute to patient's trauma and even increase the risk of death. The overall aim of the BioElectricSurface project was to decrease patients' trauma and the risk of death through a detailed understanding of nano scale interactions of biological systems with biomaterials' surfaces. In order to address this, we proposed electrical modification of biomaterials' surfaces, a novel innovative approach that will provide, for the first time, a quantitative insight into biological interactions (e.g. proteins and cells) at biomaterials' surfaces at the nanometre scale**.**

It is commonly understood that electrical properties such as local electrostatic charge distribution at biomaterial surfaces play a significant role in defining biological interactions [1,2,3]. Biomaterials that are currently used in such devices, e.g. in cardiovascular and urinary stents and coatings in hip prosthesis, do not specifically address this interfacial phenomenon in device designs. A detailed knowledge of such interactions at the nanometre scale, as proposed in the current project, will not only produce a **selective biological response** but also **pre-screen many inappropriate designs** of biomedical devices long before any expensive animal or potentially risky clinical trials. The project thus proposes a ground breaking concept that benefits from the convergence of nanomanipulation and biophysical, biochemical and materials characterisation and leads towards novel therapeutic devices in four specific biomedical applications: **cardiovascular stents, urological stents, orthopaedic implants and grafts, and anti-microbial fabrics**.

The key concepts pertaining to the BioElectricSurface project can be listed as follows:

- **The creation** of nanodomains of electrical charge to isolate the role of surface charge and the size and nature of these charged domains in biological interactions.
- **Up scaling** of the nanodomains creation to stimulate or inhibit biological response as desired
- **Application** of nanodomains to modify the surface of biomedical devices.
- **Exploitation** of nanodomains in biomedical devices: cardiovascular stents, urinary stents, orthopaedic implants and grafts and hospital gowns

The project addressed the strategic and priority areas set in the European Technology Platform on NanoMedicine [4], and aims for ambitious research and innovation in nanotechnology to strengthen Europe's competitive scientific and industrial position in the area

[1]. Zhang, P.C., Keleshian, A. M. and Sachs, F., *Nature*, **413**, 428, 2001.
[2]. Wang, Y., Gao, S., Ye, W-H., Yoon, H. S. and Yang, Y-Y., *Nature Materials*, **5**, 791, 2006.
[3]. Streimer, C.C., Gaborski, T.R., McGrath, J. L. and Fauchet, P. M., *Nature*, **445**, 749, 2007.
[4]. European Technology Platform: Strategic Research Agenda, Nanomedicine: Nanotechnology for Health, European Commission: Brussels, November 2006.

of nanomedicine and to improve the quality of life and healthcare. Clearly such objectives call for a multidisciplinary team with a European dimension, as no individual group has all the expertise needed to address the above issues. The objectives of the present project are given below:

Objective No.	Description
1	Benchmarking of electrically modified surfaces of hydroxyapatite (HA), titanium dioxide (TiO_2) and polyurethane (PU) with the help of atomistic modelling and innovative nanoscale experiments
2	Benchmarking of biomaterials/biological interactions through quantitative information at the nano-, micro- and macroscopic scale
3	Electrical modification of cardiovascular stent surfaces to demonstrate restenosis prevention
4	Electrical modification of urological stent surfaces to demonstrate encrustation prevention
	Proliferation of osteoblastic cells on electrically modified bone scaffolds/implants to increase bone growth stimulation by 30%.
6	Photosterilisation of nanoparticle-embedded fabric to make high performance reusable hospital gowns

The concept

We proposed to use a combination of atomistic modelling and nanoscale experimental techniques (fabrication and characterisation) to obtain a quantitative insight into bio/non bio interactions. We intended to modify conventional biomaterials' surface *electrically* to create discrete electrostatic domains of positive (cationic) or negative (anionic) charge. An array of such domains (nanodomains henceforth) and the variation of the size and nature of the array would, in turn, provide a benchmark for charge interactions between biomaterials' surfaces and water, proteins and cells so that the relationship between surface charge and biological interactions could be established more clearly.

Quantitative information is important to transform conventional biomaterials (HA, TiO_2 and PU) into *bioactive* forms in a controllable way and for scaling up for commercial applications and rapid prototyping. For example, electrically modified surfaces of a cardiovascular stent will immobilise proteins that can mask immunogenic responses to stent deployment. Such masking, in turn, will resist plaque formation and minimise the risk of renarrowing of the blood vessel (restenosis). An electrically modified urinary stent can inhibit biomineralisation to reduce the problem of encrustation, thereby reducing trauma and patient morbidity which will result in very significant socio-economic benefits.

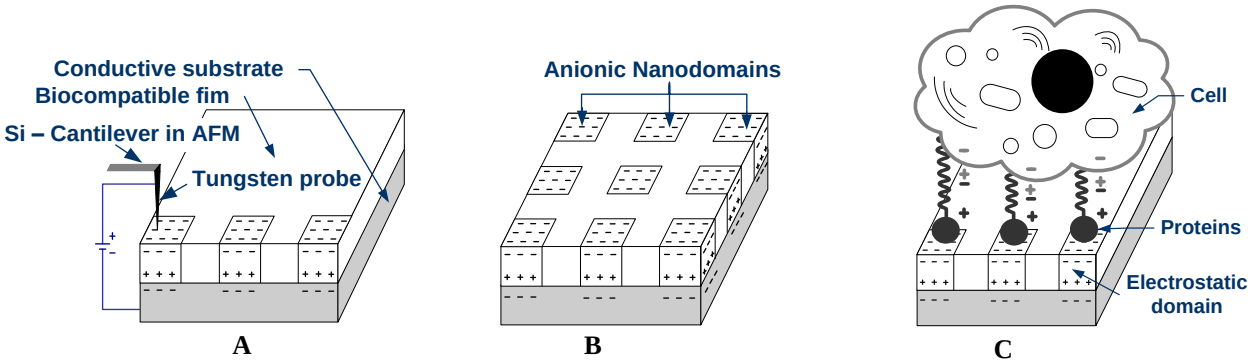

Figure 1.1 Schematic representations of electrical modification of conventional biomaterials' surfaces by using atomic force microscope (AFM): (A) The creation of electrostatic surface charge, (B) the creation of an array of nanodomains of electrostatic charge, (C) biological interactions with such nanodomains (not to scale).

In orthopaedic applications, electrical modification may make an orthopaedic implant surface bioactive to stimulate bone growth. This will substantially **reduce healing time** through better bonding at the tissue/implant interface resulting also in better long-term performance**.** The generation of surface charge in photocatalytic materials such as nanoscale titanium dioxide (TiO_2) can create free radicals on the fabric to **kill micro-organisms** and can be used in hospitals for external use. We, however, need to know how the surfaces modified this way will actually behave in a biological environment in a predictable way [5]. We would also require to scale up [6] electrical modification to industrially exploitable processes.

[5]. Nanotechnology Task Force, *Nanotechnology: A Report of the U.S. Food and Drug Administration*, July 25, 2007.
[6]. BCC Research, *HLC049A –Medical Device Coatings*, 2006.

Description of the main S&T results/foreground

In relation to the Objective No.1, the following results have been obtained:

- *More than 5000 samples of HA, TiO_2 and PU have been prepared, electrically modified and transferred between partners for compositional, structural, electrical, mechanical and biological tests*
- *Surface charge has been benchmarked on these modified samples at nano, micro and macroscopic scales by techniques such as piezo-response, Kelvin Force and electrostatic force microscopy, Kelvin Probe Method, thermally stimulated depolarisation current (TSDC) method*
- *Techniques such as Laser Intensity Modulation Method (LIMM) has been employed to measure depth and spatial distribution of surface charge in these bimaterials*
- *Innovative techniques such as apertureless Scanning Near Optical Microscope (s-SNOM) has been constructed with capability of testing biological species at a very high resolution; compact architecture shows potential for commercialisation.*
- *Industrial scale stainless steel masks with 5 μm diameter holes to create micro-arrays on a large area (15 mm^2); 500 nm size features can be created over large area using Si Mask. Reactive ion etching can produce mask with features below 100 nm.*
- *Capability demonstrated to pattern charge down to 2.5 μm diameter by electron beam poling*
- *Direct poling by electron beam has created domains with lower than 250 nm width over large area (> 4 μm^2) in a reasonable amount of time. This technique can further be extended to create electrostatic domains smaller than 100 nm in size.*
- *Finite element modelling showed that domain stability is a function of domain size and spacing. For HA thin films, the critical ratio of domain spacing to domain size has been calculated to be approximately 1.5.*
- *Kelvin probe method and Kelvin Probe Force method applied on an Aluminium (Al) /Gold (Au) interface have benchmarked the surface potential at macroscopic and microscopic length scale. Similar voltages have been measured by these two methods at the Al/Au interface.*
- *Establishing optimal poling conditions for HA/βTCP and PU*

In relation to the Objective No.2, the following results have been obtained:

- *More than 2300 samples of electrically modified HA/bTCP, TiO_2, PU, and PVDF have been tested for benchmarking biological interactions*
- *Stability of charge in electrically modified surfaces has been studied under physiological condition and after a commercial gamma sterilization process*
- *Extensive data on protein interactions with charged surfaces are obtained*
- *Modified protein adsorption as well as cell adhesion on HA/bTCP indicates the effect of poling treatment.*
- *Better understanding of the impact of different sub-processes of poling*
- *Correlations between preparation, composition (mainly Ag-content) and property profiles of TiO_2-coatings produced on different substrates especially with respect to cell and bacteria adhesion after various types of illumination*

In relation to the Objective No.3, the following results have been obtained:

- *Over 1130 PU and TiO_2 coated stainless steel (SS) samples have been transferred between partners for surface charge measurement and in vitro studies before and after photoexcitation*
- *~ 300 of such samples were microarrays*
- *The cardiovascular stent repeatable thin film titanium coating meeting real stent surface conditions was produced and fully characterized.*
- *Cardiovascular bare metal SS 316L sized 3.0x15 mm and 3.5x15 mm were successfully coated with new coating and benchmark tests were performed.*
- *Serum proteins binding to sterilized and photoexcited titanium coatings was measured showing increased fibronectin binding facilitating HUVEC adhesion to Ti surfaces comparing to SS 316L.*
- *HUVEC and SMC adhesion and proliferation on sterilized and photoexcited titanium coatings were evaluated showing promoted HUVEC long term proliferation on new coating along with decreased SMC proliferation comparing to SS 316L.*
- *Wettability studies on titanium stent coating showed high hydrophilicity which meets the criteria of good biocompatibility of an cardiovascular implant surface.*
- *Statistical analysis and correlation of the data obtained was performed .*
- *Road map for prototype demonstration has been worked out based on mechanical trials, KPM, XPS and SEM analysis and in vitro cell toxicology study and protein adhesion assessment.*

In relation to the Objective No.4, the following results have been obtained:

- *900 samples of industry quality PU disks, tubes and stents have been transferred between partners*
- *An 'encrustation model' that mimics the flow of urine from kidney to bladder has been successfully designed, constructed and validated for in vitro tests.*
- *Membrane protein responsible for biofilm formation by P. mirabilis identified*
- *Polar fluoropolymers have found to possess favourable anti-encrustation properties. Three invention disclosures have been filed to capture this invention.*

In relation to the Objective No.5, the following results have been obtained:

- *Established techniques to mass produce high density HA/β-TCP pellets that can provide required surface for poling and cell proliferation studies*
- *Transfer of 1200 electrically modified samples were sent to partners for biological testing*
- *Contact angle measurements have been carried out on high density HA/βTCP using micro- and pico-litre droplets*
- *Cell biological tests carried out on electrically modified samples revealed evidence of reduced inflammatory reactions that could be ascribed to the required heat treatment as an essential part of the poling process. Some trends were observed for additional effects of pure charge but could not be verified with statistical significance.*
- *Animal studies were performed with HA/βTCP applying a defect model due to general constraints of the poling technique that require parallel surfaces for the charge implementation. Under these conditions of diminished initial mechanical integrity of the implants no indication for an increase in bone formation could be found for electrically modified samples. For titanium implants, due to the possibilities of other poling and treatment possibilities that can be realized, a more advanced animal model was used. In this*

case the defect (hole) was located within the implants thereby ensuring optimal initial mechanical integrity of the implants.

In relation to the Objective No.6, the following results have been obtained:

- *Novel hot spray technique for nanoparticle incorporation; 2 invention disclosures submitted, 1 patent application filed in March 2011. Received widespread national and internation media coverage*
- Sonochemical method of covering both sides of fabrics with nanoparticles.
- *Minimum Inhibitory Concentration determined for nanotitania*
- *~100 gms of textiles incorporated with nano-TiO_2 and transferred between partners for photoexcitation and microbial activity tests.*
- *Design, construction and operation of aset up capable of in situ photoexcitation during microbial test.*
- *Prototype rig for incorporating nanoparticles in textiles*
- Prototype rig for photosterilisation
- Prototype clean room garments successfully embedded with nanoparticles using the patent pending process. Microbial test confirmed efficacy against MRSA retained even after 40 washes.

The overall targets of the work that has been carried out are as follows:

1. Mastering preparation of biomaterials to enable supply of sufficient samples required for meaningful biological experiments
2. Electrical modification of biomaterials, surface charge measurements, and data on charge stability
3. Feasibility study and establishment of charge patterning at macro, micro and nano scale
4. Investigating biological interactions with charged surface: continuous and patterned (i.e. with domains) and isolating the effects of surface charge
5. Selection of materials, forms of materials and methods of electrical modifications to be carried out at a device level with a focus on applicability to an industrial scale production, and
6. Assimilation of data to enable decision for application and prototype development
7. Proof of concepts in specific application areas within the targeted application areas and developing technology to a realistic device application
8. Prototype demonstration

The main focus of the work remained on the creation of knowledge, innovative processes and know-how that will be useful for screening out unsuitable techniques and processes for industrial applications.

T**hese targets were achieved** despite *a number of both anticipated and unforeseen challenges* that the project faced: These challenges can be listed as follows:

1. The stability of surface charge in physiological conditions. The stability of charge of PU and HA in physiological condition. This problem was overcome by discontinuing work with PU and changing poling parameters for HA. PU was replaced by ferroelectric polymers.
2. Identifying suitable methods for electrical polarisation and the creation of nanodomains: so as to obtain strong evidence from biological studies that endeavouring into the nanodomain creation is actually worthwhile. While the best charge stability in HA, PU and PVDF has been achieved through contact poling on a macroscopic scale, a rendering of such success into a nanometer scale through contact poling was complicated by surface roughness and contact pressure issues. Non contact poling by using a pre-patterned mask and electron beam, plasma and corona provided varying level of success, but the charge stability and morphological changes remained problematic. The overall conclusions was that nanodomains are important to understand biological interactions but such investigations should be restricted to model systems on a laboratory scale rather than applying on an industrial scale.
3. The number of samples needed for meaningful biological tests, process optimisation to obtain reliable and repetitive surface composition, morphology and roughness. This was a significant barrier and was overcome through a strong collaborative effort and careful experiment designs.

The main conclusions that can be drawn from the fundamental research in the BioElectricSurface project are given below:

1. To define the role of surface charge in biological interactions, it is critical that electrical modification (polarisation) is carried out on biomaterials that undergo minimum or no change in surface chemistry, possess reasonable reasonable flatness; can be produced in tens to hundreds in number with repeatable quality of surface chemistry and roughness. Without this data interpretation can be tricky and often misleading.
2. Common method of poling thus needs to be employed with caution, as they are usually associated with heating. Low temperature or ambient poling methods need to be developed for polymeric biomaterials.
3. HA suffered minimal surface chemistry and roughness change as a result of polarisation. While HA pellets could be polarised by thermoelectric poling, nanodomain creation was difficult: noncontact method such as e-beam poling could not create localised domains due to the predominance of global charging, whereas contact poling by conductive grids or nanowire arrays were not satisfactory due to roughening of the surface.
4. Contrary to the literature on polarised HA pellets (and also HA/β-TCP pellets), but expectedly due to the capacitive behaviour of such non-ferroelectric insulators, we have found that charge in HA decays with time. This instability of charge is even more prominent when dipped in water.
5. Similar observation was made on PU pellets, which, even though successfully poled for the first time ever, lost charge much quicker than HA. This loss was regained after soaking in PBS but only due to the soaking by PU of a highly ionic fluid which in a TSDC experiment gave rise to ionic currents.
6. Any probe based process was discarded early in the project and known knowledge/skills in morphological patterning was used to build up expertise. Contact method, while suitable for macroscopic polarisation and industrial applications, not suitable for nano or submicron

scale poling and was not recommended for application WPs. Stability of charge will be higher in polar and ferroelectric materials and these will be suitable for further studies of surface charge effect on biological processes.

7. Optimal spacing of nanodomains have been calculated to be over 1,5 times the diameter of the domains.
8. Current models of surface charge and interactions have been found inadequate and soon de-prioritised in the project altogether. Some correlations have been found between protein probe analyses and FE models. The work is still preliminary and will be continued after the project through collaboration between partner
9. The stability of charged domains on HA thin films created by e-beam raster poling was even shorter, only a few minutes. Even such a short stability period was enough to establish electrostatic nature of model proteins. Semi-quantitative insights have been obtained for surface charge interactions with protein. More in depth study should be pursued in future.

Overall, the BioElectricSurface project has achieved its deliverables and milestones in the best possible way. A self assessment of the key successes and limitations of the BioElectricSurface is given below:

Successes

- *4 US patent applications & 1 Polish patent application*
- *Quality publications in prestigious journals and conferences*
- *High level of commercial and public interest*
- *Pushed forward the state of the art understanding of bio-non bio interactions*

Limitations

Despite the best effort, not all questions could be answered due to the complex nature of the problems investigated and due to a high priority given in producing data and knowledge that are relevant to industrial partners

Potential Impact

The outcome of research conducted in the BioElectricSurface project will have the following impacts:

A. Solutions going well beyond state of the art

- The creation of nanodomains of electrostatic charge that have isolated the role of surface charge in biological interactions. Two peer reviewed journal articles that elucidate this role are currently in press. These articles describes methodologies to converge nano and micro manipulation with biophysical characterisation
- Combination of modelling, nanoscale manipulation and biological interactions to develop industrial applications and prototypes
- Techniques such as LIMM were employed to measure the depth of electrical charge penetration in biomaterials. This technique provided valuable insights and can probably be developed further to be able to measure interfacial charge.
- A compact and portable aperture-less s-SNOM has been developed. This can be used for biological characterisation with very high resolution.
- A better insight has been obtained on electrically modified surfaces that will enable in future tailoring biomaterial surfaces to stop or stimulate biomineralisation

B. Innovation for new products with high added value

- Urinary stents that prevent stone formation on the surface to significantly reduce trauma and revision surgery
- Self-sterilising anti-microbial fabric that will kill microbes thus reducing the spread of antibiotic resistant micro-organisms in hospitals

C. Medium to long term innovation •

- Cardiovascular stent that stops renarrowing of blood vessels and reduces the risk of thrombosis

D. Overall Impact:

- Better health, quality of life and safety of European citizens
- Reduction in patient morbidity, trauma and patient care expenditure through the reduction in occurrence of diseases and hospitalisation time.
- Extension to new application areas such as biosensors, biodiagnostics, localised drug delivery
- Higher level of profit for, and competitiveness of, European companies
- Six High quality journal publications and 5 patent applications.

Main Dissemination Activity

- *Development of the Project website*

The project website is accessible by visiting www.bioelectricsurface.eu. Currently the public area of the website gives a brief introduction to the project, the thematic area of the project, the participants are listed and contact details are provided.

The private/internal Partner area of the website is the method by which reports are submitted to Task leaders, Work Package leaders and the Coordinator. It is routinely used by partners for internal communication and results dissemination. It acts as a repository for guidelines and other project related documents.

- *Use of foreground and dissemination activities.*

An Exploitation Strategy Seminar was held to identify foreground intellectual property that can be potentially exploited for commercial value. A report of this seminar has now been submitted to the Project Officer by the Animator of the Seminar.

- *Public dissemination of Results:*

Books/Chapters

1. Tofail, S.A.M. (ed.), Surface Charge in Biomaterials, Cambridge: RSC Publishing, 2011. DOI: 10.1039/9781849733366.

Partners have contributed in 16 out of 17 Chapters in this book as given below:

I. S. A. M. Tofail and A. A. Gandhi, Electrical Modifications of Biomaterials' Surfaces: Beyond Hydrophobicity and Hydrophilicity
II. M. Kopaczyńska, M. Vargová, K. Wysocka-Król, G. Plesch and H. Podbielska, Photocatalytic Effects in Doped and Undoped Titania
III. M. Gregor, T. Plecenik, A. Plecenik, C. Wolf-Brandstetter, D. Scharnweber and S.A.M. Tofail, Surface charge measurements on biomaterials in dry and wet conditions
IV. S. B. Lang, G. A. Stanciu, S. G. Stanciu, Nonlinear characterizations of surface charge and interfacial morphology.
V. P. Periyat and E. Magner, Immobilisation of Enzymes on Porous Surfaces,
VI. C. Wolf-Brandstetter and D. Scharnweber, Fibrous Proteins Interactions with Modified Surfaces of Biomaterials.
VII. X. Hu, I. B. O'Connor and J. G. Wall, Antibody immobilisation on solid surfaces: methods and applications
VIII. U. Hempel, C. Wolf-Brandstetter and D. Scharnweber, Interactions of bone forming cells with electrostatic charge at biomaterials surface.
IX. S. Robin, T. Soulimane and S. Lavelle, Interactions of biofilm-forming bacteria with abiotic surfaces.
X. M. Wawrzyńska, B. Sobieszczańska, D. Biały, J. Arkowski, Endothelial cells and smooth muscle cells interactions at biomaterials' surfaces.
XI. E.Dworniczek, R.Franiczek, U.Nawrot, G.Gościniak, Interactions of Bacteria and Fungi at the Surface,
XII. B. Sobieszczańska, M. Wawrzyńska and D. Biały, Immunological response of electrostatic charge at the surface of biomaterials.
XIII. R. Thornton and J.Cooney, Community and hospital acquired Staphylococcal infections.

XIV. J. Bauer1, K. Kowal, S.A.M. Tofail and H. Podbielska, MRSA resistant textiles.
XV. S. Robin, T. Soulimane1 and S. Lavelle, Inhibition of encrustation in urological devices,
XVI. J. Arkowski, M. Wawrzyńska, D. Biały, B. Sobieszczańska and W. Mazurek, The Reduction of Restenosis in Cardiovascular Stents.

2. Kowal, K., Tofail, S.A.M., Podbielska H., How to prevent patients from nosocomial activity?, Nutraceutics, Biomedical remedies and physiotherapeutic methods for prevention of civilization-related diseases, vol.4/2011, Acta Biomedical Engineering,Halina Podbielska, Tadeusz Trziszka (eds). Wroclaw: Indygo Zahir Media, 2011, 255-262.

- *List of journal papers*

.Submitted

1. Kopaczyńsk, M., Sobieszczańska, B., Ulatowska-Jarża, A., Hołowacz, I., Buzalewicz, I., Sitarek, P., Wasyluk, L., Tofail, S.A.M., Wawrzyńska, M. and Podbielska, H., Cellular response to photoactivated titania-based coatings for potential cardiovascular stents (submitted to Biomaterials in November 2011).
2. Truchly, M., Plecenik, T., Secianska,K., Gregor, M., Zahoran,M., Vargova, M., Mikula, M., Grancic, B., Plesch, G., Tofail, S.A.M., Kus, P. and Plecenik, A., Limits of minimal size of surface potential patterns created on hydroxyapatite films by focused electron beam (submitted September 2011)

<u>Accepted/Published (6)</u>

1. Robin S.; Gandhi A A.; Gregor M., Laffir F., Plecenik, T.; Plecenik, A., Soulimane T.; and Tofail, S.A. M., Charge specific protein placement at submicron and nanometer scale by direct modification of surface potential by electron beam, Langmuir, 2011 (in press).
2. Plecenik, T, Robin S., Gregor M., Truchly, M., Lang S.B., Gandhi, AA, Zahoran M., Laffir F., Soulimane T., Vargova, M., Plesch, G., Kus, P., Plecenik, A. and Tofail, S.A.M., Directly created electrostatic micro-domains on hydroxyapatite: probing with a Kelvin Force probe and a protein, J. Materials: Materials for Medicine, 2011 (in press)
3. Periyat P., Laffir, F., Tofail, S.A.M., and Magner, E., A facile aqueous sol–gel method for high surface area nanocrystalline CeO2, RSC Advances, 1, 2011, pp.1794–1798
4. Kowal K., Wysocka-Król, K. Kopaczyńska, M., Franiczek, R., Dworniczek E., Wawrzyńska M., Vargová, M., Zahoran M., Rakovský, E., Kuš, P., Plesch, G., Plecenik, A., Laffir, F., Tofail, S.A.M., Podbielska, H., In situ photoexcitation of silver doped titania nanopowders for activity against methicillin resistant Staphylococus aureus (MRSA), J. Colloids and Interface Science, 362, October 2011, pp. 50-57..
5. Lang, S.B., Tofail, S.A.M., Gandhi, A. A., Gregor, M., Wolf-Brandstetter, C., Kost, J., Bauer, S., and Krause, M., Pyroelectric, piezoelectric, and photoeffects in hydroxyapatite thin films on silicon, Applied Physics Letters, 98, March 2011, pp. 123703-5.
6. Plecenik, T., Tofail, S. A. M., Gregor, M, Zahoran, M., Truchly, M., Laffir, F., Roch, T., Durina, P., Vargova M., Plesch G., Kus P., Plecenik, A., Direct creation of micro-domains with positive and negative surface potential on hydroxyapatite coatings, Applied Physics Letters, 98, March 2011, pp. 113701-3.

List of conference presentations (22)

Gandhi, AA, Robin, S., Soulimane, T. and Tofail, SAM., Detection of submicron and nano scale electric charge patterning on biomaterials using KPFM, Investigating Electrical Properties at the Nanoscale Using AFM & STM: Scientific Symposium sponsored by Agilent Technologies and CRANN, Trinity College Dublin, Ireland, 6 December 2011.

Lang, S.B., et al, Hydroxyapatite Thin Films on Silicon: Biomaterials with Pyroelectric, Piezoelectric and Photoeffect Properties, IUPAC 7th International Conference on Novel Materials and their Synthesis (NMS-VII) & 21st International Symposium on Fine Chemistry and Functional Polymers (FCFP-XXI), which are held in Shanghai, China, 16-21 October, 2011

Robin, S., Gandhi, A.A., Soulimane, T. and Tofail, S.A.M., Nanoscale Protein Placement by Electrical Modification of Hydroxyapatite, ESB2011, 24th European Conference on Biomaterials, September 4-9, 2011, Dublin, Ireland.

Kopaczyńska, M., Sobieszczańska, B., Ulatowska-Jarża, A., Hołowacz, I., Buzalewicz, I., Tofail, S.A.M., Wawrzyńska, M. and Podbielska, H., Surface charge, wettability and biological examinations of titania coated stainless steel, ESB2011, 24th European Conference on Biomaterials, September 4-9, 2011, Dublin, Ireland.

Wysocka-Król, K., Pucińska, J., Kopaczyńska, M., Bauer, J., Tofail, S.A.M. and Podbielska, H. Photoluminescence examination of TiO2 nanoparticles doped by Europium, ESB2011, 24th European Conference on Biomaterials, September 4-9, 2011, Dublin, Ireland.

Lang, S.B., Tofail, S.A.M., Gandhi, A. A., Gregor, M., Wolf-Brandstetter, C., Kost, J., Bauer, S and Krause, M., Hydroxyapatite Thin Films on Silicon: Biomaterials with Pyroelectric, Piezoelectric and Photoeffect Properties, ESB2011, 24th European Conference on Biomaterials, September 4-9, 2011, Dublin, Ireland.

Kowal, K., Żegliński, J., Cronin, P., Tiernan, P., Tofail, S.A.M. and Podbielska, H., Nanopowders immobilization on textiles by modified dip-coating method, ESB2011, 24th European Conference on Biomaterials, September 4-9, 2011, Dublin, Ireland.

Wolf-Brandstetter, C., Hempel, U., Clyens, S., Korostynska, O., Gandhi, A.A., Theilgaard, N., Tofail, S.A.M. and Scharnweber, D., Impact of Heat Treatment on Biological Interactions with Contact-Poled Hydroxyapatite based Materials, ESB2011, 24th European Conference on Biomaterials, September 4-9, 2011, Dublin, Ireland.

Plecenik, T., Robin, S., Gregor, M., Gandhi, A.A., Zahoran, M., Lang, S.B., Laffir, F., Soulimane, T., Roch, T., Vargova, M., Plesch, G., Kus, P., Plecenik, A. and Tofail, S. A. M., Directly created electrostatic micro-domains on hydroxyapatite: probing with a Kelvin Force probe and proteins, ESB2011, 24th European Conference on Biomaterials, September 4-9, 2011, Dublin, Ireland.

Lang,S.B., Abuhatzira, Y., Kost, J., Gandhi, A.A., S.A.M. Tofail, Olga Korostynska, Poled PVDF-TrFE Coatings on Quartz Microbalance Sensors: A New Technique For Study of Proteins In Solution, The 14th International Symposium on Electrtets (ISE14), 28th-31st August 2011, Montpellier, France.

Kowal K., Tofail S.A.M, Podbielska H., How to prevent patients from nosocomial infections? Nutraceutics, Biomedical remedies and physiotherapeutic methods for prevention of civilization-related diseases, Humboldt Kolleg, 26-29.05.2011 Wroclaw, Poland

Kowal K., Wysocka-Król K Dworniczek, E., Franiczek, R., Kopaczyńska, M., Buzalewicz, I., Wawrzyńska, M., Plesch, G., Vargova, M. Laffir, F., Tofail, SAM and Podbielska, H. Minimal inhibitory concentration of nanoparticles-impregnated photosterilisable textiles against Escherichia coli and MRSA, International Conference on Antimicrobial Research 2010 ICAR2010, November 3-5, 2010, Valladolid, Spain.

Wysocka-Król K., Kowal K. Dworniczek, E., Franiczek, R., Kopaczyńska, M., Buzalewicz, I., Wawrzyńska, M., Plesch, G., Vargova, M. Laffir, F., Tofail, SAM and Podbielska, H., ntimicrobial activity of silver doped silica and titania based nanoparticles: an in situ study of photosterilization performance, International Conference on Antimicrobial Research 2010 ICAR2010, November 3-5, 2010, Valladolid, Spain.

Wolf-Brandstetter, C., Gregor, M., Tofail, S.A.M., Clyens, S., Theilgaard, N., Lang, S. and Scharnweber, D., Cell adhesion to charged hydroxyapatite surfaces, ESB2010, 23rd European Conference on Biomaterials, September 11-15, 2010, Tampere, Finland.

Lang, S. B. Tofail, S.A.M., Gandhi, A.A., Gregor, M., Wolf-Brandstetter, C. and Clyens, S. Pyroelectric Effect In Nano-Layers Of Hydroxyapatite, ISAF-ECAPD-2010 (19th International Symposium on Applications of Ferroelectrics and 10th European Conference on Applications of Polar Dielectrics, 9-12 August, 2010, Edinburgh, Scotland.

Lang, S. B. Tofail, S.A.M., Gandhi, A.A., Gregor, M., Wolf-Brandstetter, C. and Clyens, S., Hydroxyapatite – A New Pyroelectric Material, AMF-AMEC-2010, 7th Asian Meeting on Ferroelectricity and 7th Asian Meeting on ElectroCeramics, 28 June – 01 July, 2010, Jezu, Korea.

Kowal, K., Tofail, S.A.M., and Podbielska, H., Nanomaterials doped textiles, Biomedical Engineering in Poland, 29 April, 2010, Warsaw, Poland.

Jamal, M., Gregor, M., Zhang, Y., Gandhi, A.A., Redington,W., and Tofail, S.A.M., Heterogenous nucleation and bone-like texture evolution in synthetic hydroxyapatite films, ESB2009, 22nd European Conference on Biomaterials, September 7-11, 2009, Lausanne, Switzerland.

Gregor, M., Jamal, M., Gandhi, A.A., Zhang, Y., Redington, W. and Tofail, S.A.M., Stress relief Patterns in bone like apatite films prepared by a solgel technique, E-MRS 2009 Spring Meeting, June 8 - 12, 2009, Strasbourg, France

Tofail, S.A.M., Ecological considerations in designing nanoparticle-loaded textiles, EuroNanoForum2009, 2-6 June, 2009, Prague, Czech Republic

Tofail, S.A.M., Opportunities and Challenges in the Application of Nanoparticles in MRSA-resistant Medical Textiles, CleanRooms Europe 2009, 24 -26 March 2009, Neue Messe Stuttgart, Stuttgart, Germany.

Tofail, S.A.M., Nanoparticles in Medical Textiles: Opportunities and Challenges, Innovations in Textiles 2009. Smart, Nano and Technical Textiles for Medical, Industrial and Clothing Applications, 18th – 19th March 2009. Royal College of Physicians, London, UK

Patent Applications

S. B. Lang, Encrustation Resistant Stent, 22 November 2011, US Provisional Application No., 61/562,451

S.A.M Tofail, S. Robin and Tewfik Soulimane, A Urological Implant Coating, 06 September 2011, Ireland 2011/0392, US Provisional Application No.61/531,322; 03 October 2011, EPO 11394016.7

S. Lavelle, Electrically Charged Medical Device, 06 September 2011, US Provisional Application No.61/531,178.

Płowiecki, E., Ł. Wasyluk, M. Truszewska- Raczyńska H. Podbielska, M. Kopaczyńska, A. Ulatowska – Jarża, M. Wawrzyńska, B. Sobieszczańska, D. Biały, Colloidal material for coating the medical device, medical device and method of coating medical devices, 05 August 2011, Polish patent application, WIPO ST 10/C PL395888.

Tofail, S.A.M, Zeglinski, J., Cronin, P., Podbielska, H. Dworniczek, E., Tiernan, P., Franiczek, R. Buzalewicz, I., Wawrzyńska, M., Embedding Nanoparticles in Thermoplastic Polymers, 18 March 2011, US Provisional Application No., 61/454,252.

- *Other disseminations*

Dr. Gerard Wall (Partner 13) Radio Interview on Galway Bay FM, Ireland 2 October 2008.
John Mulcahy (Partner 1) Radio Interview on Limerick's Live 95FM, Ireland 6 October 2008.
Irish TV News report on the Project [http://www.tv3.ie/videos.php?video=1162] 2 October 2008
Press release on CORDIS News [Record control number (RCN):30105] 17 November 2008

Widespread Irish national newspaper and online coverage of the project launch including:
Clare Champion, Page 20, 10-Oct-2008
Kerrys Eye, Page 90, 09-Oct-2008
Irish Daily Mirror, Page 20, 03-Oct-2008
Irish Examiner, Page 10, 03-Oct-2008
Irish Independent, Page 11, 03-Oct-2008
The Sun, Page 2, 03-Oct-2008
Irish Medical News, Page 14, 13-Oct-2008

John Mulcahy made a Presentation of the BioElectricSurface Project at the Enterprise Ireland FP7 National Conference on 30 June 2009, at The Royal College of Physicians, Dublin, Ireland.
The event was viewed by over 800 people many from across Europe through the webcasting of the event.

BES meeting in Wrocław in 2011 included a press conference, devoted to BES achievements on emphasis of successfully elaborated in WP6 antibacterial textiles and photosterilization possibilities. Partners were interviewed by Polish press, radio and TV. Several information were publicized after the meeting.
The spots from interviews and reports in TV and radio are available at the Press Office at WrUT (Partner 2).
Some reports:
Gazeta Wyborcza from 18.04.2011
http://wyborcza.pl/1,75476,9458483,Fartuchy_kontra_mikroby.html

http://naukawpolsce.pap.pl/palio/html.run?_Instance=cms_naukapl.pap.pl&_PageID=1&s=szablon.depesza&dz=stronaGlowna&dep=380661&data=&lang=PL&_CheckSum=-1515833107
Opracowano nanomateriały niszczące bakterie

http://wroclaw.gazeta.pl/wroclaw/1,88047,9283354,O_fartuchach_lekarskich__co_sie_bakteriom_nie_klaniaja.html
O fartuchach lekarskich, co się bakteriom nie kłaniają
http://www.prw.pl/articles/view/13094/naukowcy-kontra-szpitalne-zarazki
Naukowcy kontra szpitalne zarazki

http://dobrylekarz.info/artykul/nanomaterialy-niszczace-bakterie-opracowane-we-wroclawiu.htm
Nanomateriały niszczące bakterie opracowane we Wrocławiu

http://www.rynekaptek.pl/doniesienia-medyczne/nanomaterialy-z-wroclawia-zabojcze-dla-bakterii,2417.html
Nanomateriały z Wrocławia zabójcze dla bakterii

http://wiadomosci.onet.pl/regionalne/wroclaw/odkrycie-naukowcow-material-niszczy-bakterie,1,4214877,region-wiadomosc.html
Odkrycie naukowców: materiał niszczy bakterie

http://tvp.info/informacje/technologie/nanotkanina-zniszczy-bakterie/4162689
Nanotkanina zniszczy bakterie

- *Exploitation of Key results beyond the project:*

Nanodomains and test data: Public Dissemination (Conferences/Journal publications)

Reports on Nanodomains, Process parameters for electrical modification
and Surface charge benchmark: Public dissemination (Monograph/lecture notes/Conferences and Journal publications)

Biological interaction at electrically modified surface and data: Public Disemination (Conferences/Journal publications)

Electrically modified cardiovascular stents, process parameters, in vitro test data, factual data for prototyping and regulatory roadmap: Exploitable know-how for Balton.

Data on electrically modified urinary stents and in vitro test: Exploitable IP, potential exploitation by COOK.Report on the in vitro test of urological stents: Commercial Dissemination (Specification for “CE” mark and COOK marketing literature to urologists)

Data on electrical stimulation of bone growth in vivo: Public Dissemination (Conferences/Journal publications)

Reports on systemic response of nanodomains *in vivo* and inflammatory response: Public Dissemination (Conferences/journal publications). Allergogenic and immunogenic response Biocompatibility data: Public dissemination (Conferences/Journal publications).
Design specifications for scaling up antimicrobial textiles: Commercial exploitation through licensing, Public Dissemination (trade show and publications).