EUROPEAN SCIENCE FOUNDATION
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EMBO

RESEARCH CONFERENCES

ESF-EMBO Symposium

Biological Surfaces and Interfaces

Hotel Eden Roc, Sant Feliu de Guixols (Costa Brava) • Spain
27 June – 2 July 2009

Chair: **Julie Gold**, Chalmers University of Technology, SE
Co-Chair: **Joachim P. Spatz**, Max-Planck-Institute for Metals Research, DE

Vice-Chairs:
Fredrik Höök, Chalmers University of Technology, SE
Janos Vörös, ETH Zürich, CH

ESF Rapporteur:
Kenneth Dawson, University College Dublin, IE

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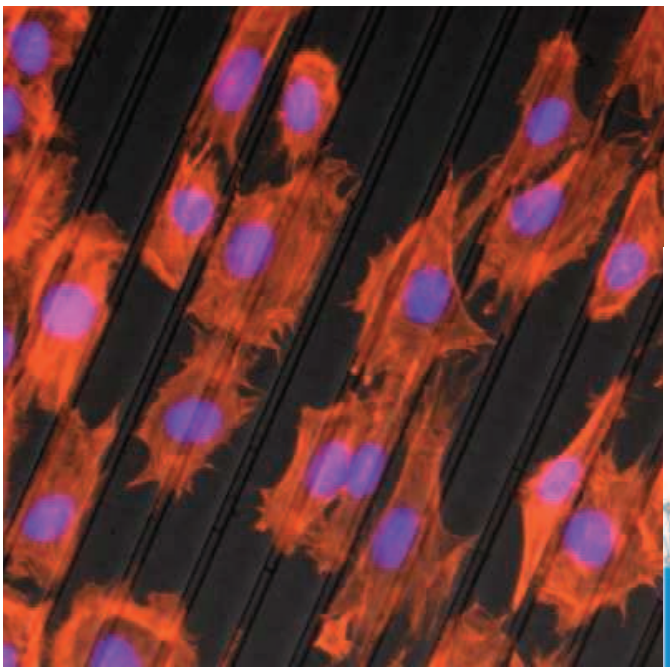

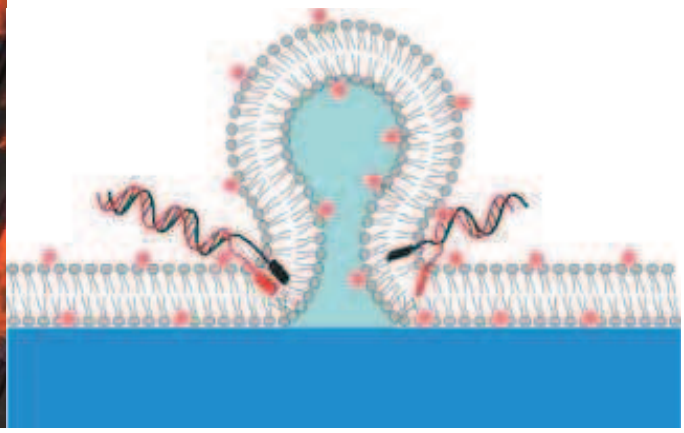

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Conference Highlights

Please provide a brief summary of the conference and its highlights in non-specialist terms (especially for highly technical subjects) for communication and publicity purposes. (ca. 400-500 words)

The “Biological Surfaces and Interfaces” conference in 2009 gathered together a highly multidisciplinary group of prominent scientists and engineers who study and design, from different perspectives, interfaces of scientific and technological interest that exist between biological entities (such as cell-cell or cell-biomolecular interfaces), as well as between synthetic materials that are in contact with biological systems and biological entities (such as medical devices, tissue engineering scaffolds and biosensors). There was a large focus on living cells and cell membrane mimics, and the interface between cells and their native surroundings in tissues, as well as interfaces between cells in vitro and other cells, biomolecules, organic molecules and engineered 2-D and 3-D material surfaces. The field is keen to understand, *at the molecular level*, how cells interact with and sense their natural 3-D environment, and subsequently how we can produce engineered systems that mimic key interactions, but in the laboratory, for a range of applications, such as tissue engineering, biosensing or smart / living feedback systems.

For example, results presented at the conference included new imaging tools to observe the structure and topography of living cell surfaces with single molecule resolution, and the generation of cell surface mimics, such as synthetic, functionalized, supported lipid membranes, for use as in vitro models of real cell membranes, for biosensing interfaces, or as substrates for the artificial, in vitro synthesis of membrane protein receptors. In a similar fashion, new approaches to study the structure-function relationships as well as the mechanical properties of extracellular carbohydrates found on the cell surfaces were presented, followed by the production of synthetic carbohydrate arrays for screening interactions between cells, microorganisms, growth factors and potential drug targets of relevance in the field of glycobiology. A third main theme of the conference was the interface between living cells and proteins, located around the cells, that bind to receptors found in the cell membrane. Such binding events are key in determining cell attachment, shape, function and differentiation (maturation) – in general, cell fate. Results presented at the conference shed light on the binding interactions between small, active regions on the proteins and the cell receptors, and the mechanism by which such binding events activates the receptor to send a signal to the cell nucleus to turn on or off genes. Additional results shed light on the roles of multiple receptor bindings and the nanoscale spacing of receptor binding events on cell activation and cell fate. New surface modficiations were presented which are designed to control, in real time, such binding and un-binding events in order to turn “on” or “off” cells located at an engineered interface.

Conference participants, invited speakers and organizers had the opportunity to look into the future and discuss potential future applications of current research as well as point to new directions in biological surfaces and interface research and engineering. An overriding theme which emerged is the use biological processes, either in natural or synthetic, biomimetic forms, for production of energy – this being either pure energy, or energy sources needed to drive other biologically-relevant processes, such as implantable medical devices or biosensors.

☐ I hereby authorize ESF – and the conference partners to use the information contained in the above section on ‘Conference Highlights’ in their communication on the scheme.

Scientific Report

Executive Summary

(2 pages max)

The conference ran very smoothly, with almost no incidences, thanks to the great organization by, and collaboration with, ESF staff Anne Blondeel-Oman. It has been a pleasure and an asset to work with her. The conference consisted of 2 evening keynote speakers, 18 invited talks, 6 contributed talks selected from submitted abstracts, and 105 poster presentations. Corporate sponsors in attendance at the meeting were also given time to orally present their company and products to the general conference assembly. Selection for chairpersons and co-chairs for a continued meeting in 2011 was made by nomination to the positions of co-chairs and voting by all conference participants. Co-chairs at this conference are automatically designated as chairpersons for the next conference application. Chairpersons for the 2011 Biological Surfaces and Interfaces conference proposal are Fredrik Höök, Chalmers, Sweden and Janos Vörös, ETH, Switzerland. Elected Co-Chairs are Eva Sinner, MPI Polymer Research, Germany and Ralf Richter, CIC BiomaGUNE, Spain. One speaker cancelled on the first day of the conference due to the influenza, and his presentation was given in part by one of the Conference Chairs, and in part replaced by a presentation by one of the senior female participants, Dr Heike Hall, ETH.

Two committees, of three people each, were formed for evaluating posters and poster abstracts for Poster Sesions I and II, respectively. Committee members consisted of invited speakers and one journal representative. Balance between gender and country was carefully selected for the committees. The winners of Best Poster Prizes from sessions I and II received a free yearly subscription to either the EMBO journal, or to Nature Materials. We were very pleased to have this form of sponsorship for the conference, and to have one of the editors from Nature Materials in attendance for the entire duration of the meeting. The editor handed over the prize personally. Winners were Peter Jönsson, Chalmers, and Kislon Voitchovsky, MIT.

In addition to the Chairs, Co-Chairs and poster judges, there were several persons who assisted in organizing and running to the conference. These were thirteen doctoral students and post docs of the Chairs and Co-Chairs, who assisted in preparing the USB memory sticks with an electronic version of the conference book, controlling the audience microphones and helping speakers with their computer presentations and microphones.

We were very lucky to have an amateur photographer attending the meeting, complete with full-scale photography equipment. Jens Sobek, ETH, agreed to take the group photo of the meeting, but also took numerous photographs throughout the meeting. He compiled the best photos into a beautiful photoalbum, which was sent to the organizers, as well as a website which can be accessed by the participants (ESF-EMBO Biological Surfaces and Interfaces). In return he was reimbursed for his conference fees.

The overall budget for the conference was 56 000 €. Sponsorship raised by the chairpersons reached 22 000 € and was obtained from four corporate sponsors (Microvacuum, JPK Instruments, Leica Microsystems, QSense AB) as well as additional funds from ESF/EMBO and the local municipality. Poster awards were generously donated by EMBO and Nature Materials. Of the total budget, 28 950 € were spent speakers and organizers travel and conference fees, the abstract book and diverse running costs for the conference, while 25 445 € was given to particpants in the form of conference fee reimbursements and travel grants. There were 138 participants from 26 countries and 20 invited speakers from 9 different countries.

Scientific Content of the Conference

(1 page min.)

- *Summary of the conference sessions focusing on the scientific highlights*
- *Assessment of the results and their potential impact on future research or applications*

The conference was organized into a number of sessions covering various aspects of the interface between materials that are in contact with biological systems (eg medical devices, tissue engineering scaffolds, biosensors), as well as key interfaces of scientific and technological interest that exist between biological entities (eg cell-cell or cell-biomolecular interfaces). The largest contribution in terms of volume of scientific findings was from the two poster sessions, and the two contributed presentation sessions, that covered all the subtopics of the meeting. The oral sessions of invited talks focused on nanomanipulation and characterization of surfaces and bioentities, engineering surfaces and bioactive interfaces, cell-surface interactions, tissue engineering, biosensing interfaces and microfluidics. The scientific topics ranged from methods for production and characterization of material and biological surfaces, to the use of these surfaces in controlling or mimicking molecular and cellular interactions. Hence focus was placed on “both sides” of the biointerfaces scenario.

Highlights from Session 1 – Nanomanipulation and characterization of surfaces and bioentities – included a new and improved method for imaging the surface of living cells in media based on scanning ion conductance microscopy, with resolution down to 20nm. This method, published during the first half of this year in Nature Methods, allows monitoring of real time responses of cells to a number of ligands or changes in the cell environment. With such capabilities, we are able to study mechanisms of for example, cell-cell and cell-molecular interactions, as well as the uptake of nanoparticles used in drug delivery. Another highlight focused on new ways to probe and characterize the organization and mechanical properties and the glycocalyx, or pericellular coat, surrounding cells. These are based on microrheology and optical force probe microscopy. A relative talk described approaches to produce in vitro mimics of these hyaluronen-rich layers at solid-liquid interfaces, and use them to study their structure-biological function relationships, especially in their interaction with other native biomolecules, eg proteins.

Session 2- Engineering surfaces and bioactive interfaces: A new application of nanoimprint lithography to produce nanoridged surfaces in optically transparent materials was presented for studying cell interactions with nanoscale structure mimics of the extracellular matrix environment. It is well known that cells align and exhibit contact guidance to nanoridges, but what was now presented was a possible explanation as to why this occurs, and why no new cell protrusions form in directions orthogonal to the ridge orientation - due to lack of focal contact formation in these directions. In fact, cells having bipolar morphology in general were found to form fewer and smaller focal contacts than cells having isotropic morphology. Another highlight was the presentation on dynamic substrate surfaces that can alter their presentation of ligands to adherent cells, in real time, and thus change the behavior of the cells. Such surface modifications are based on self-assembling molecular systems functionalized with bioactive ligands, and which can be switched by changing electrical potential the surface. In addition to allowing studies into cell-extracellular matrix interactions, these surface functionalizations will have great application in biotechnology.

Clearly one of the highlights of the conference overall were the keynote lectures on a) the discovery of proteins in their role as mechano-chemical switches (V Vogel), and the implications that this mechanical force sensing mechanism has in normal cell signaling and hemostasis, as well as how we can exploit this in applications of eg tissue engineering; and b) interfaces between cells and electrodes used in applications from cell-chip biosensors to electrodes for characterizing neural signaling in the brain (P Fromhertz).

Session 3- Cell-surface interactions: Although this topic was most prevalent throughout the conference, highlights from this session were based on the single molecular-level understanding of events taking place at cell-cell and cell-extracellular matrix interfaces, and the consequences fo them. Firstly, the use of functionalized, supported phospholipid bilayers in cell culture as cell membrane mimics which are used to study cell-cell interactions with resolution down to single receptor-ligand binding events by clever design of lateral surface patterning. For example, the role of Tcell receptor organization (clustering) and the need for only two foreign antigens in signaling

activation of the cell and inititation of an immune response. Similary results were presented on the precisely defined nanometer-scale spacing (ca 60 nm) of integrin-binding ligands needed to promote cell attachment and signal transduction via focal contact formation, and the specific protein molecules within the focal contact which are responsible for this detailed level of control / spacing of extracellular binding sites.
In the more applications-oriented sessions of Tissue Engineering (Session 5) and Biosensing interfaces and lab-on-a chip (Session 6), fantastic results from the Fraunhofer Institute on the generation of several different types of vascularized tissues grown in vitro using decellularized tissue scaffolds together with mechanical stimulation (perfusion systems) show a pathway to overcoming the main bottleneck of vascularizing laboratory-grown tissues. Applications include in vitro tissue models as well as tissue engineering.
Another highlight was clearly the synthetic synthesis of cell membrane receptors in vitro, starting with cDNA and ending with membrane-bound proteins (synthetic biology). Membrane proteins are notoriously difficult to isolate and handle, and their synthesis directly in vitro is one way of getting hold of these molecules in their native configuration/environment for use in biosensing applications. Additional highlights included smart and highly sensitive microfluidic devices that allow for on-line single cell analysis; and automated synthesis of oligosaccharides that makes possible the design and use of large scale, combinatorial screening arrays for carbohydrate-carbohydrate, carbohydrate-cell, carbohydrate-protein and carbohydrate-nucleic acid interactions. Such array-based libraries are just emerging in the field of glycobiology and will be key in future vaccine designs, as it is possible to sense pathogen binding to carbohydrates found on cell surfaces, as well as modifications of the carbohydrate moities to eg prevent binding.

The results presented at this conference have clear anchoring in basic research and the studies of mechanisms of interactions and function, yet also are clearly directed towards applications in biosensing, cell- and tissue-engineering. By understanding binding events in biological systems at the molecular level, and the consequences of such events, we can build biomimetic systems for model studies, as well as engineer applications ranging from smart, bioresponsive medical devices and new vaccine development, to far reaching ideas such as molecular or cell based computers, cell robotics, or new sources for bioenergy.

Forward Look

(1 page min.)

- *Assessment of the results*
- *Contribution to the future direction of the field – identification of issues in the 5-10 years & timeframe*
- *Identification of emerging topics*

The Foward Look session was introduced at the opening of the conference, when ESF Rapporteur Kenneth Dawson made a brief presentation about the ”Forward Look” session and how to prepare for it. He challenged us to discuss under the coming days and identify the open questions in the field. In addition, he also requested us to suggest topics for broad area/ blue sky research projects representing future directions of the field, but which could also be eligible for a large multinational initiative.

The following ideas took form during the conference days and were presented by participants during the Forward Look session as open questions or challenges that are on the horizon in the Biointerface field:

• Biopowered implantable devices / self-powered prostheses: Where the implant device field will move in the coming years. Takes advantage of the bodies’ own active dyanmic processes to generate energy to run eg pacemakers. Examples of such processes include electron transfer in cells. If succeed, could find applications in other fields.

• Living interfaces: Design of interfaces that are alive, where mixed biofilms or complex biomimetic architectures on the surface receive commands from the underlying device to produce what is desired by the host.
• 2D-3D structural organization of molecules: investigations into how molecules in biology are organized spatially in 3D units. Involves surface topography, protein responses to mechanical forces, and temporal aspects. A biomimetic approach to control spatial organization of molecules in engineered materials that are build via bottom-up approach, such as in soft matter and liquids. A long term goal is to synthetically control the spatial organization of molecules in biology.
• In situ/in vitro synthesis of transmembrane proteins and complex biomimetic membranes: By using synthetic molecular machines, it is possible to study and understand interactions between biocomplexes. Synthesis of proteins at surfaces, which is currently being attempted, could be expanded to more complex model systems (eg synthetic compartments of cells) that could provide a solution to energy sources for self powered prostheses mentioned above.
• Logistical interfaces – cells as machines: This idea involves the ability to communicate with cells and to make them do what we want them to do. It includes the development of a dynamic feedback system, eg. control over gene transduction, with processes that can control transduction in situ/in real time. Will need logical device/sensors for control of feedback loops.
• Bioenergy: using interfaces to harvest energy. Piezoelectric cells generating charge or voltage drop in response to mechanical strain – grow cells eg. on sea surface, where the mechanical strain induced by tides/waves will stimulate cells to generate energy. Another alternative is to use the process of photosynthesis on solar panels as a bioenergy source. Interfaces will be necessary in order to harvest energy produced in such systems

An overriding theme which emerged is the use biological processes, either in natural or synthetic biomimetic forms, for production of energy – this being either pure energy, or energy sources needed to drive other processes, eg implantable medical devices. The driving force for these ideas are the need to better understand basic mechanisms involved in each of the processes described above, but also the need for new, renewable energy sources for applications within the human body but also in the world at large.

▪ Is there a need for a foresight-type initiative?

Not applicable

Atmosphere and Infrastructure

▪ *The reaction of the participants to the location and the organization, including networking, and any other relevant comments*

As organizer, I was very surprised by the overwhelming amount of positive feedback and thanks I received for organizing this conference. This is highly rewarding, and is also the result of the excellent organization and opportunities made available by the ESF and its staff. The Eden Roc location is fantastic, the food and service is excellent. The infrastructure of the hotel still has its problems, however people appear to be very pleased with the venue.

Results of the evaluation questionnaire (completed by 77 of the 138 participants, and 6 speakers) show an overriding positive response to the conference, with 99% of those responding feel the conference should be repeated. It is also rewarding to learn that benefits from the conference include new collaborations established with another lab (35%), an exchange with another lab (37%), a new employee (2%) and a new employer (2%). The participants felt that the management/organization of the conference was excellent (84%) or good (16%). The atmosphere of the conference was very positively evaluated, with the conference being more than “just a

meeting" (82% agreed completely, 12% mild agreement), conducive to easy exchange of information (82%, 16%), and ample time for informal discussions (80%, 18%). Concerning the age distribution, 93% found the balance between young and senior scientists was appropriate.