Institute for Bioengineering of Catalonia

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IBEC
BIOENGINEERING AND NANOMEDICINE SYMPOSIUM '07

Barcelona - 7 November 2007

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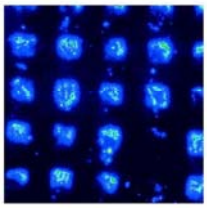
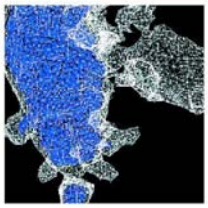
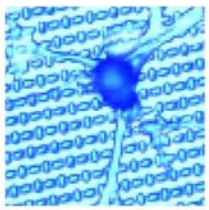

Book of abstracts

Amb el suport de
Generalitat de Catalunya
UNIVERSITAT DE BARCELONA
UNIVERSITAT POLITÈCNICA DE CATALUNYA

Programme

09:30 - 10:00	**Registration**
10:00 - 10:40	Welcome address
10:40 - 11:15	***Health technology assessment as a mean for translating research into clinical practice*** Dra. Marta Aymerich Agència d'Avaluació de Tecnologia i Recerca Mèdiques (Spain)
11:15 - 11:50	***Bioactive Polymer Based Materials for Tissue Reconstruction*** Prof. Luigi Ambrosio Institute for Composite and Biomedical Materials. National Research Council (Italy)
11:50 - 12:15	**Coffee break**
12:15 -12:50	***A hard day in the life of a soft cell*** Prof. Jeffrey Fredberg Harvard School of Public Health (USA)
12:50 - 13:25	***New Trends In Computational Mechanobiology*** Dr. Manuel Doblaré CIBER-BBN (Spain)
13:25 - 14:00	***The Challenges of Managing Innovation*** Léonard Aucoin, M.Ps., M.P.H. InfoVeille Santé Itée (Canada)
14:00 - 15:00	**Lunch**
15:00 - 16:30	**Poster session** (flash presentations)
16:30 - 17:05	***When medicine goes "nano": the use of engineered nanodevices and nanostructures in biomedical applications*** Prof. Josep Samitier Institut de Bioenginyeria de Catalunya – Universitat de Barcelona (Spain)
17:05 - 17:40	***Optical nanotools to investigate the spatio-temporal organization of the cell membrane at the nm scale*** Prof. Maria F. Garcia-Parajo Institut de Bioenginyeria de Catalunya (Spain)
17:40 - 18:15	***Biomedical Engineering Strategy: Capturing the Future*** Prof. Jean Louis Coatrieux Laboratoire de Traitement du Signal et de l'Image. University of Rennes (France)
18:15 - 18:30	Closing remarks

Lectures

Health Technology Assessment as a Mean for Translating Research into Clinical Practice

Marta Aymerich, MD, MPH, PhD
Director of the Catalan Agency for Health Technology Assessment and Research

Health Technology Assessment (HTA) seeks to inform health policy makers by using the best available scientific evidence on the medical, social, economic and ethical implications of investments in health care. Health technology is broadly defined to include the drugs, devices, medical and surgical procedures used in health care, as well as measures for prevention and rehabilitation of disease, and the organisational and support systems in which health care is provided. Thus, the HTA researcher task is to retrieve, analyze and synthesize the available scientific evidence, preparing it in a way that is useful for decision-makers. To some extent, scientific evidence synthesis can be seen as a bridge linking the world of research and the world of decision-making, either at the clinical level or at the health policy making level.

On the other hand, healthcare systems in Europe face many competing priorities: accessibility, affordability, quality and progress, as well as solidarity in financing and responsibility. Moreover, the healthcare system is not isolated from the rest of society: it interacts with other factors such as education, employment, and social insurance. In that context, it is possible for universities, governments and industry to work together without forgetting the pursuit of sustainable healthcare development? Actually, a successful patient oriented healthcare system needs an outstanding research structure as well as a successful R&D industry to supply innovative products.

Although HTA is not an exact science, there is value in developing a tool to help health systems evaluate whether it is worth investing in a health technology innovation. In other words, scientific evidence synthesis can provide evidence-based information to decision-makers regarding health technology innovations. However, HTA can only provide part of the answer because not always there is enough evidence-based knowledge. In that context, research has to be promoted. To do so, ex-ante research assessment is important (to select the best and needed research proposals) but also ex-post research assessment must be carried out. The latter could be defined as an assessment that measures the return on investment or "payback" from the research and by means of this assessment it is possible to measure the return on investment in quantifiable terms such as, for instance, improvements in the medical practice.

Bioactive Polymer Based Materials for Tissue Reconstruction

Prof. Luigi Ambrosio
Institute of Composite and Biomedical Materials, National Research Council (IMCB-CNR),
Piazzale Tecchio 80, 80125 Naples, Italy

One of the principal goals of the biomedical engineering is to design of biomaterials capable to replace, substitute, repair and regenerate natural tissues. Over the past twenty years the research in this field has led to the formulation of novel highly biocompatible materials and new methods to obtain structures able to better interact with biological tissues. In order to mimic the behaviour of natural tissue, the optimal approach for designing novel biomaterials has to be inspired to *nature* guidelines. Following this approach it is possible to design prosthesis for dental implant, bone substitutes, intervertebral disc, ligaments, and scaffolds for tissue engineering. To prove this concept, results on the design of novel intervertebral disc prostheses and scaffolds for tissue engineering (bone, meniscus, nucleus) will be discussed.

Intervertebral disc degeneration, is one of the major causes of low back pain, which is one of the most common medical cases in the western world. Currently, the two major surgical interventions for treating conditions related to the degenerated disc, discectomy and fusion, provide a relatively good short-term clinical results. Thus, the ideal solution to a degenerated disc seems to be an artificial disc substitute. However, the artificial disc prostheses on the market have been reported to frequently undergo failure due to wear and degeneration of the materials, and, the mismatch between the mechanical properties of the devices and the natural tissue. The aim is to design a novel composite intervertebral disc prosthesis with appropriate bio-mechanical and transport properties.

In tissue engineering applications, an ideal scaffolds should be biocompatible and biodegradable in medium-long term; it should initially maintain its structural behaviours, allow cellular in-growth and diffusion of nutrient, and used as carrier of growth factors and drugs. Actually many synthetic, natural and semi-synthetic organic and inorganic materials have been used, and even if they posses appropriate biological and biodegradable properties, their structural performances are not completely adequate. In order to satisfy all the complex requirement, composites materials technology can be implemented to designed an appropriate scaffolds.

For connective tissue regeneration (bone, ligaments, meniscus) composite scaffolds are obtained by phase inversion, salt leaching and RP technique to modulate mechanical properties and cell interactions. These techniques permits to obtain scaffold with controlled micro and macro porosity.

Ester of Hyaluronic Acid reinforced with degradable fibres were processed by composite technology, phase inversion and salt leaching technique to obtain scaffolds for meniscus regeneration. In vivo results demonstrated the possibility to regenerate the meniscus by using an appropriate scaffolds loaded with chondrocytes and without, as reported in the following figures.

Injectable gel-like scaffolds were prepared by using Esters of Hyaluronic Acid, to engineer an nucleus pulposus (NP) substitute able to reproduce the viscoelastic properties of NP as well as to guide and promote bone marrow stem cells to adhere and differentiate according to a tissue engineering approach.

A Hard Day in the Life of a Soft Cell

Prof. Jeffrey Fredberg
Harvard School of Public Health, USA

Cytoskeletal (CSK) dynamics are surprising and strange. As an empirical rule the single best predictor of CSK stiffness is traction force that the cell exerts upon its substrate as in a tensed cable network, and yet the CSK fluidizes promptly in response to stretch and exhibits slow structural relaxation1-3 as do colloids, pastes, clays, and foams. In biology both traction and stretch are ubiquitous and their importance far-reaching, but their relationship has remained inaccessible and unquantified. We plated the isolated cell on an elastic substrate, imposed biaxial stretch with a ring-shaped punch-indenter, and measured cell tractions with dynamic traction microscopy. Prompt CSK fluidization and slow resolidification changed in parallel with cell tractions, suggesting a primitive fact of evolutionary biology: eukaryotes harbor collections of molecular conformations in energy wells just deep enough to avoid thermal insult but shallow enough to be selectively responsive to physical forcing.

New Trends in Computational Mechanobiology

Prof. Manuel Doblaré
Aragon Institute of Engineering Research (I3A), University of Zaragoza
Networking Centre on Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN)
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It is well-known that tissue structure develops by a complex interaction between cells and surrounding environment controlled by genetic instructions. One of the main factors that influences on this process is the mechanical environment, and thus, structural tissues are optimized in terms of their specific mechanical function [1]. Normally, these processes are classified according to their specific target into: remodelling, growth, differentiation, damage or healing models [2].

Remodelling describes the adaptive process by which the tissue modifies its microstructure and hence its mechanical properties according to the mechanical environment that it supports [3]. *Growth* involves the addition or loss of mass, shaping the organs and adjusting their final dimensions [1,2]. Tissue *differentiation* describes the differentiation to the various cell types from a non-specialized cell source [1,2]. Finally, partial or total tissue *damage* is quite common. It can be caused by the sudden appearance of an overload that exceeds tissue strength, or by cyclic loads that gradually accumulate damage at a rate that cannot be repaired by tissue remodelling [4]. After global tissue disruption *healing* is activated, involving many different cellular events like simultaneous differentiation, growth and remodelling in a combined way [4].

This has motivated the appearance in the last years of some numerical models to better understand the interaction between mechanical and biological processes in developmental biology [1,2,4,5,6]. Most of them have been only focused on particular aspects or specific biological processes, while their combined analysis requires formulating more general models. In these formulations tissues are described from a macroscopic point of view as a continuum mixture of cells and different types of extracellular matrices (ECMs) composed by fluid and several solid aggregates. In this work, we present a general continuum formulation for tissue growth, differentiation and damage, controlled by the mechanical environment that includes the biological processes associated to each specialized cell population [7]. Finally, several applications are presented related to tissue remodelling and bone fracture healing.

References:

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[2] L.A. Taber. Biomechanics of growth, remodelling and morphogenesis. *Appl Mech Rev.* 48(8):487–545, 1995.
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[5] Marjolein C.H. van der Meulen, R. Huiskes. Why mechanobiology? A survey article. *J Biomech.* 35:401–414, 2002.
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The Challenges of Managing Innovation

Léonard Aucoin, MPs, MPH
InfoVeille Santé Ltée, Canada

From a business and management standpoint, innovation occurs when someone uses an invention to develop it into a product or a service and deliver it to the market. How can a research centre, like IBEC, cultivate an environment that is conducive to innovation? What kind of vision, strategy and processes does it need to put in place, in order to facilitate innovation, i.e. the development of ideas from mind to market? Delving into management literature, Mr. Aucoin will first present the characteristics of innovation, in the context of a research centre. He will then identify drivers and barriers to innovation. Finally, he will suggest an organizational framework for innovation.

When Medicine Goes "Nano": the Use of Engineered Nanodevices and Nanostructures in Biomedical Applications

Prof. Josep Samitier
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IN2-Universitat de Barcelona, Spain
Networking Centre on Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN)

The term nanomedicine was used in a research publication in the year 2000, according to the Science Citation Index. However, the definition of nanomedicine is ambiguous and includes two main concepts. Some authors define nanomedicine very broadly as a technology that uses molecular tools and knowledge of the human body for medical diagnosis and treatment. Others emphasize the physical effects occurring in nanoscale objects that exist at the interface between the molecular and macroscopic world.

In this sense the document produced by the European Science Foundation about the Nanomedicine, includes the definition of 'Nanomedicine' as the science and technology of diagnosing, treating and preventing diseases and traumatic injuries, of relieving pain, and of preserving and improving human health, using molecular tools and molecular knowledge of the human body.

The European Nanomedicine platform in the strategic research agenda defines Nanomedicine as the application to achieve breakthroughs in healthcare. It exploits the improved and often novel physical, chemical and biological properties of materials at the nanometer scale. In this sense, Nanomedicine has the potential to enable early detection and prevention, and to essentially improve diagnosis, treatment and follow-up of diseases.

In any case, Nanomedicine research has increased worldwide very quickly in the last years. A comparison of numbers of publications in nanomedicine with nanotechnology shows that the first one represents about 4% of nanotechnology research. Nanomedicine is in process to establish itself, although at present there are numerous applications under consideration. In this sense, recent advances in nanotechnology- related drug delivery, diagnosis and tissue engineering beginning to change the landscape of medicine.

Although it is very difficult to predict whether nanomedicine will make small but valuable contributions to healthcare or whether it will act as a catalyst for a vast medical revolution.

In this presentation, I will limit the nanomedicine analysis and two main examples to the detection and controlled manipulation of human biological systems at the molecular level via engineered nanostructures and/or devices. The first example concerns the miniaturization of biomedical sensors for diagnostics using G-protein coupled receptors existing in the olfactory neurons. The second example illustrates very well the interactions between biomaterials and cells at nanoscale level, analyzing the effects on cells cultured over two-dimensional nanostructured surfaces.

Optical Nanotools to Investigate the Spatio-temporal Organization of the Cell Membrane at the nm Scale

Prof. Maria F. Garcia-Parajo
Institut de Bioenginyeria de Catalunya (IBEC), Josep Samitier 1-5, 08028 Barcelona, Spain

The ability to study the structure and function of cell membranes and membrane components is fundamental to understanding cellular processes. This requires the use of methods capable of resolving structures with nanometer-scale resolution in intact or living cells. Although fluorescence microscopy has proven to be an extremely versatile tool in cell biology, its diffraction-limited resolution prevents the investigation of membrane compartmentalization at the nanometer scale. In our group we are applying a combination of near-and far-field optical techniques equipped with single molecule detection sensitivity to gain deeper insight on the spatio-temporal organization of the cell membrane at the nm scale. On the one hand, near-field scanning optical microscopy (NSOM) combines both enhanced spatial resolution and simultaneous measurement of topographic and optical signals. Because of the very small near-field excitation volume, background fluorescence from the cytoplasm is effectively reduced, enabling the visualization of nano-scale domains on the cell membrane at physiologically relevant packing densities. On the other hand, epi/TIRF microscopy can provide exquisite temporal information of the cell membrane at the level of single molecules.

In this contribution I will show our current efforts towards the investigation of "lipid rafts" as local organizers of the cell membrane using NSOM imaging in aqueous conditions on intact cells. Lipid rafts (domains within the membrane enriched in cholesterol and glycosphingolipids) are believed to play a key role in many membrane related processes like immune cell signaling and viral entry. Their existence is however rather controversial, since evidence for the presence of lipid rafts in native cell membranes can only be obtained via indirect methods. We have used single molecule NSOM to investigate the nano-scale organization of both lipid and protein domains on cells of the immune system. Most recent results will be presented and discussed on the basis on distinct nano-scale compartmentalization.

Furthermore, I will show most recent results concerning the spatio-temporal organization of the adhesion receptor LFA-1 on living monocyte cells. Using epi/TIRF microscopy in combination with micro-fabricated biofunctionalized patterned surfaces we have discovered that the dynamics and functional binding of LFA-1 to its ligand ICAM-1 is determined by both the conformation sate of LFA-1 and its spatial distribution on the cell membrane. These studies will shed light on the role of affinity vs. avidity of LFA-1 to its ligand ICAM-1 on a single molecule basis.

Biomedical Engineering Strategy: Capturing the Future

Prof. Jean Louis Coatrieux
Inserm, University of Rennes 1, Campus de Beaulieu, 35042 Rennes Cedex, France

This short talk is aimed at opening a debate through the review of some basic features of the medical technology area. Although of major importance in the worldwide economy and in Europe (employment, market, budget, etc.) and despite the recurrent emphasis put on the role of science interface, its position remains fragile. The reasons for this situation are multiple: its fragmentation in subfields sometimes far from each other, the size of the research groups and companies, the limited capability in capturing the major evolutions (nano- and micro-technologies, molecular imaging, information technology, system biology, etc.). Other critical aspects concern the difficulties in setting an efficient lobbying and the lack of operational organizations. We will discuss these issues through examples going from some recent European projects such as STEP, SYMBIOMATICS, ELIXIR, etc., up to the recent Call on Virtual Physiological Human. The role of ERC and ESFRI will also be highlighted to show that major initiatives have to be undertaken in the next future.

Posters

List of posters

1 Eduard Torrents
Structure and function of bacterial proteins that modulate virulence expression

2 Alexandre Perera Lluna
Clustering of individuals given SNPs similarity based on normalized mutual information: F7 SNPs in the GAIT sample

3 Xavier Fernandez Busquets
The Biomolecular Interactions Team (BIT): Nanotechnological Approaches to Biomedicine

4 Romen Rodríguez
High speed particle detection in a micro-Coulter counter with two-dimensional adaptable aperture

5 Chris Mills
Nanoimprint assisted contact printing of proteins

6 J.-Pablo Salvador
A Localized Plasmon Resonance Nanoscale Optical Immunosensor for Stanozolol

7 Ramon Eritja
Use of synthetic DNA for the assembly of nanostructures

8 Daniel González Pinacho
Development of a Class Selective Indirect Competitive Enzyme-Linked Immunosorbent Assay (ELISA) for Detection of Fluoroquinolone Antibiotics

9 Elisa Elizondo Sáez de Vicuña
Precipitation of antibiotic/polymer composites from CO2-expanded solvents

10 Joan Comenge Farré
Exploring interactions between nanoparticles and biological systems

11 Ivan Marcos
Dendritic cell uptake of iron-based magnetic nanoparticles

12 Thomas van Zanten
Mapping nano-landscape of pathogen recognition receptor DC-SIGN and lipid rafts on dendritic cells

13 Ruth Díez Ahedo
Biofunctional Micropatterned Surfaces to Study Individual LFA-1&ICAM-1 Interactions in Living Cells

14 Laura Fumagalli
Electrical characterization of biological samples at the nanoscale by atomic force microscopy

15 Irene Acerbi
Cell mechanics probed by atomic force microscopy during indentation and pulling

16 Isaac Almendros López
Intratracheal negative pressure triggers upper airway inflammation in a rat model of sleep apnea

17 Jose Muñoz
Gradient decomposition method for the mechanical analysis of morphogenesis

18 Eduardo Soudah Prieto
One-dimensional numerical model for the simulation of blood flow on arteries

19 Aitor Aguirre Cano
Obtention and Characterization of EPCs for Neovascularization in Bone Tissue Engineering

20 Elisabeth Ángel
Protein Adsorption on Calcium Phosphate Cements

21 Eduard Vergés Garcia
3D Reconstruction of Bone Implants Porous Space

22 Marc Elias Edo
Turning Cholinergic Nerve Terminals Into Functional Dopaminergic Nerve Terminal

23 Michael Riss
Star-shaped polymer-on-Multielectrode (PoM) arrays for interfacing with neurons

24 Ivan Montoliu Roura
Study of Olfactory Bulb time response by using Multivariate Image Analysis tools

25 Agustín Gutiérrez
Exploratory Analysis of the Rat Olfactory Bulb Activity

26 Benjamin Sánchez
Fast EIS using a multisine burst for time varying biological system characterization

27 Judith Gallego Blanco
Quantification of DAT SPECT Imaging with 123I: Evaluation of the Degrading Phenomena

28 Francisco Pino
Development and characterization of a small animal SPECT system based on a small gamma camera

29 Nuria Roé
Comparison between a gamma probe and a portable gamma camera for SLN intraoperative detection: first image guided SLN resection