



Strasbourg (France)

E-MRS 2005 Spring Meeting
May 31 – June 3, 2005

SYMPOSIUM H

Nano-structured and intelligent bioactive materials

Symposium Organizers :

Roberto Doddoli, BIOFUTURE Research Consortium
c/o University of Bari, Italy

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Papers to be published in Biomolecular Engineering

E-MRS 2005 Spring Meeting

SYMPOSIUM H

Tuesday, May 31, 2005
Mardi 31 mai 2005

Morning
Matin

9:00

WELCOME
by Roberto Doddoli

Session I

Session chair : **Dominique Muster**

H-I.01 9:10

NANOCOMPOSITES BASED ON POLY-D,L-LACTIDE AND MULTIWALL CARBON NANOTUBES

L.P. Krul,, A.I. Volozhyn, D.A. Belov, N.A. Poloiko, A.S. Artushkevich, Belarus State University, 14 Leningradskaja st., 220050 Minsk, Belarus, S.A. Zhdanok, Heat and Mass Transfer Institute, 15 Brovki st., 220072 Minsk, Belarus, A.P. Solntsev., A.V. Krauklis, I.A. Zhukova, Belarus

Preparation and properties of compositions of biodegradable polymer - poly-d,l-lactide with multiwall carbon nanotubes (MWCNT) are considered.

Poly-d,l-lactide is used in medicine as a biodegradable polymer. However due to low strength its usage is restricted. An attempt has been made to increase poly-d,l-lactide strength by incorporation of MWCNT into a polymer matrix. MWCNT were obtained from methane-air mixture upon atmospheric pressure without catalyst on high voltage atmospheric pressure discharge plasma set-up. MWCNT specimens were investigated by scanning (SEM) and transmission (ТЕМ) electronic microscope. According to ТЕМ and SEM data carbon nanotubes diameters are within 12-60 nm. Quantities of MWCNT incorporated did not exceed 0.5%. Nanocomposites were obtained by sonification of mixture of a poly-d,l-lactide solution in chloroform and MWCNT during 1 hour followed by film casting on glass substrates. Tensile strength and thermomechanical properties of the dried composite films were investigated. Distribution of MWCNT in polymeric matrix has been studied by electronic microscopy. An effect of concentration of carbon particles on properties of nanocomposites has been shown. An extreme dependence between mechanical properties of polymeric material and concentration of MWCNT has been established. A possibility of poly-d,l-lactide modifying by MWCNT has been shown. As a result of such modifying strength of nanocomposites obtained increases up to 30 %.

H-I.02 9:30

DEVELOPMENT OF POLYMER BASED SENSORS FOR INTEGRATION IN A WIRELESS DATA ACQUISITION SYSTEM SUITABLE FOR MONITORING ENVIRONMENTAL AND PHYSIOLOGICAL PROCESSES

K. Arshak(a), A. Arshak(b), D. Morris(b), O. Korostynska(a), E. Jafer(a), J. Harris(a), (a)Dept. of Electronics & Computer Engineering, University of Limerick, Limerick, Ireland, (b)Dept. of Physics, University of Limerick, Limerick, Ireland

In many professions and industries, the ability to make measurements in difficult to reach or dangerous environments without risking the health of an individual is now a necessity. In such systems, measurements are wirelessly transmitted from the area of interest to a receiver, which is remote from the sensor environment. Such systems can also be employed to make long-term measurements in biological environments, assisting in diagnosis and further understanding of disease and abnormalities. With this in mind a wireless data acquisition system, which is based on the principle of capacitance-frequency-voltage conversion and employs a phase locked loop as part of the interface circuit has been developed. This system has been developed with a view to measuring pressure. To minimize power consumption and maximize sensitivity, capacitive structures were formed using polyvinylidene fluoride (PVDF) and polyethylene for the sensing layer. These materials were chosen for their biocompatible properties. Also PVDF has shown itself as suitable for strain gauge applications. Each material was in the form of a film with thickness approximately 100 nm and electrodes were subsequently deposited by thermal evaporation or screen-printing. The materials sensitivity was tested up to 80 kPa and the change in capacitance with pressure was measured. It was found that polyethylene displayed a superior sensitivity. The sensors were then tested interfaced with the wireless system and measurements were taken in a liquid environment so that the devices were under hydrostatic pressure. Preliminary results obtained using this system showed good agreement with those previously obtained.

1.Arshak, K.I., et. al, (2000), Sensors and Actuators A, 79, p. 102-114

H-I.03 9:50

COMPETITIVE PROTEIN ADSORPTION ON MICRO PATTERNED POLYMERIC BIOMATERIALS, AND VISCOELASTIC PROPERTIES OF TAILOR MADE EXTRACELLULAR MATRICES

Alexander Welle, Institute for Biological Interfaces, Forschungszentrum Karlsruhe, P.O. Box 3640, 76021 Karlsruhe, Germany, Antonio Chiumiento, Rolando Barbucci, CRISMA Department of Chemical and Biosystem Sciences and Technologies, University of Siena, Via A. Moro 2, 53100 Siena, Italy

We have described modifications of polymers allowing the formation of cell patterns [Welle, et al., Biomed. Microdev. 4, 33, (2002)]. Masked UV irradiations opened a simple, fast, and economical route to obtain chemically patterned substrates for structured cell adhesion. It is possible to achieve structures of subcellular size and to produce immobilized gradients.

In order to examine the protein layer deposited on cell culture substrates, controlling cell adhesion, we applied a quartz micro balance (QCM-D) capable to extract viscoelastic data in addition to the mass uptake during plasma protein deposition: Quantity and viscosity of surface bound albumin is lowered when the surface is modified (patterned) by UV exposure altering the physico-chemical properties of the polymers. The UV modification promotes the competitive adsorption of cell adhesion proteins from the media or upon secretion by the cells and yields to the observed cell patterns. Another tissue engineering technique, using immobilized, modified and/or cross linked Hyaluronic Acid (HA), an important extra cellular matrix (ECM) component, is also examined by QCM-D. Our data demonstrate that HA can be modified by an activation with a carbodiimide, followed by the application of a bisamino polyethyleneglycol or similar compounds. Cross linking decreased the adsorbate thickness and caused an increase of the shear loss module and of the shear storage module. These findings can be interpreted as a stiffening of the HA layer combined with the release of hydration water and reduction of the mesh width and provide valuable inside into processes at the interface between man made carriers and living cells.

H-I.04 10:10

BIOMIMETIC IMPLANT COATINGS

E. Eisenbarth, D. Velten, J. Breme, Germany

One current trend in the research and development of biomaterials is to meet better the demands of the host system and tissue by a high degree of functionalization of the material surface. Bio-functional surfaces are most important for medical implants, tissue engineering scaffolds, biosensors and biochips. Biological recognition - as central property of living systems - must be used to enable biomimetic characteristics of an implant surface. The corresponding surface modifications designed to reach biomimetic properties can be divided into three classes, one aiming towards an optimized three-dimensional physical microarchitecture of the surface, the second one focusing on the (bio) chemical properties of the surface and the third one dealing with the physico-chemical properties of material surfaces. The surface is "recognized" by the biological system through the combined chemical and topographic pattern of the surface and by its surface energy. This is the reason why modification and patterning of biomaterial surfaces into sophisticated, topographic micro-architectures is required, on length scales from small biomolecules (nm) to cells (1-10 micrometers) (Kasemo) Responses of Bone building osteoblasts depend on topographical properties of the biomaterial at the nanometer scale. Niobiumoxide coatings with nanosized surface structures were produced by means of the sol-gel-process induced a range of desirable cellular responses.

H-I.05 10:30 -Invited-

MICRO-AND NANOSTRUCTURED MATERIALS FOR EXTRACORPOREAL BLOOD PURIFICATION

D. Falkenhagen(a), F. Loth(a), V. Weber(a), M. Sara(b), U. Sleytr(b), (a)Christian Doppler Laboratory for Specific Adsorption Technologies, Danube University Krems, (b)Centre for Nanobiotechnology, University of Natural Resources and Applied Life Sciences, Vienna, Austria

We aim at the development of adsorbent microparticles (1- 10 µm) for extracorporeal blood purification to be used in our newly developed Microspheres-Based Detoxification System (MDS). To target pathophysiological mediators of sepsis, adsorbents specific for endotoxin (LPS) were developed by immobilization of Polymyxin B (PMB) on cellulose microparticles. Adsorbents for TNF were obtained by functionalization of cellulose microparticles with a monoclonal antiTNF antibody (Mab) or with recombinant antibody fragments (Fab), respectively. As a treatment option for autoimmune diseases, nanostructured adsorbents for IgG were developed by crystallization of an Slayer fusion protein containing an IgG-binding domain onto cellulose microparticles.

In batch experiments in human plasma (1200 pg TNF/mL; 1 mg particles in 250 µL plasma; n=3), 258 ± 49 pg/mg of TNF were bound by cellulose-Mab as compared to 178 ± 9 pg/mg for cellulose-Fab. PMB-cellulose bound 940 ng/mL endotoxin (spiked plasma: 10 ng/mL; 1% v/v adsorbent). Particles functionalized with the IgG-binding S-layer fusion protein bound 620 µg/mg of IgG both in native form and after chemical cross-linking of the S-layer on the particles.

In conclusion, micro- and nanostructured materials have enormous potential for the specific elimination of pathophysiological important substances in sepsis as well as in autoimmune diseases due to excellent binding capacity and kinetics of adsorption.

H-I.06 10:50

SYNTHESIS OF POLYMER/CARBON NANOTUBE COMPOSITES FOR BIOMEDICAL APPLICATIONS

Ramesh babu.P(a), W. Blau(a), E. Titus(b), N. Ali(b), J. Gracio(b), G. Cabral(b), P. Pakonstantinou(c), J. McLaughlin(c) and D.S. Misra(d), (a)Materials Ireland Polymer Research Centre, Trinity College, Dublin-1, Ireland, (b)Department of Mechanical Engineering, University of Aveiro, 3810-193 Aveiro, Portugal, (c)NIBEC, University of Ulster, Newtownanney BT370QB, U.K., (d)Indian Institute of Technology, Bombay 400076, India

The use of carbon nanotube (CNT)/polymer composites has been exploited in many applications from biomedical devices to aerospace applications due to their exceptional mechanical, thermal, electrical and optical properties. In addition to their remarkable physical and electrical properties, CNTs have proven to be highly bio-compatible, a fact that has led CNTs to be used for medical applications, like tissue engineering, is poised to revolutionize modern medicine. Therefore, the combination of biocompatible polymers and carbon nanotubes can be expected as a step forward in biomedical technology research.

In this research, CNT composites were prepared with various water soluble polymers and were investigated using different analytical techniques. The analysis methods include, transmission electron microscopy (TEM), atomic force microscopy (AFM), X-ray diffraction (XRD), X-ray photon spectroscopy (XPS), UV-Visible, fourier transform infrared (FTIR), electron spectroscopy for chemical analysis (ESCA) and Raman spectroscopy. Hardness values and Young's modulus were obtained by nano-hardness tests (HNT) and tensile tests. Thermal properties were examined using differential thermal analysis (DTA) and thermo gravimetric analysis (TGA). Electro kinetic analyzer (EKA) for zeta potential measurement and surface tensiometry were used to characterize the bulk and surface properties of the biomaterials. High purity CNTs were used for this work and the purity was confirmed using TGA and FTIR analysis.

11:10

BREAK

Session II

Session chair : Andreas Lendlein

H-II.01 11:20

PH-RESPONSIVE VESICLES NANOCAPSULES BASED ON POLYPEPTIDE DIBLOCK COPOLYMERS

J. Rodríguez-Hernández(a), F. Chécot(a), J. Babin(a), Y. Gnanou(a), A. Brület(b), J. Oberdisse(c) and S. Lecommandoux(a), (a)Laboratoire de Chimie des Polymères Organiques (LCPO-UMR5629), ENSCPB, University Bordeaux 1, 16 Avenue Pey Berland, 33607 Pessac-Cedex, France, (b)Laboratoire Léon Brillouin (CEA-CNRS UMR12), CEA-Saclay, 91191 Gif sur Yvette Cedex, France, (c)Groupe de Dynamique des Phases Condensées (GDPC-UMR5581), Université Montpellier II, Place E. Bataillon, 34095 Montpellier Cedex 05, France

The self-assembly of well-defined polypeptide-based diblock copolymers into micelles and vesicles is presented. The stimuli-responsive behavior of polypeptides to pH and ionic strength is used to produce stimuli-responsive nanoparticles with a control size and shape. Results focusing on vesicles obtained from polypeptide-based diblock copolymers that are particularly promising for biomedical application will be detailed by means of static and dynamic light scattering analysis, UV circular dichroism, NMR and small angle neutron scattering experiments. We will also present systems that are able to form vesicles with a narrow size distribution at basic and acid pH going through and intermediate state of single molecule. These nanoparticles are particularly interesting for encapsulation and delivery purpose at a controlled pH. Finally, surface self-assembly of micelles and vesicles will be shown as model for biological surfaces such as mucosal surfaces. Here also, the stimuli-responsiveness of the polypeptide block used can lead to bio-active surfaces.

H-II.02 11:40

BIOADSORPTION STUDIES ON CARBON NITRIDE FILMS USING IN-SITU ELLIPSOMETRY

T. Berlind, M. Poksinski, L. Hultman, P. Tengvall and H. Arwin, Linköping University, 581 83 Linköping, Sweden

Carbon based materials have received considerable attention during the last decades due to their interesting tribological, electronic and optical properties. So far not much effort has been put into the investigation of the use of these materials in biotechnology. The objective with this study is to investigate the interaction of carbon and carbon nitride surfaces with biomolecules.

Carbon nitride (CN_x) and amorphous carbon (a-C) thin films were deposited by reactive sputtering. By changing sputtering parameters the microstructure can be controlled and amorphous, graphitic and fullerene-like films were grown to a thickness of 200 nm on silicon. The CN_x and a-C films were optically characterized by spectroscopic ellipsometry to determine their complex-valued refractive index $N=n+ik$ in the wavelength range 350-1700 nm. The films were exposed to human serum albumin (HSA) during in-situ measurements using dynamic ellipsometry. It is found that the changes of the ellipsometric angle Δ are larger for the amorphous films compared to the films with more ordered structure. The HSA adsorption effect is comparable to results obtained for silicon. These experiments could possibly render a versatile method to analyze and control the growth of monolayers and multilayers of different types of biomaterials. The measurements indicate that less protein adsorption take place on the films with more ordered structure compared to the amorphous films, but deeper analyzes is needed for further conclusions regarding thickness and structure of the biolayers.

H-II.03 12:00

ONE- AND MULTICOMPONENT LB FILMS BASED ON DPPC: PHASE TRANSITIONS AND FILM REORGANIZATION ONTO SOLID SURFACE

G. Zhavnerko, G. Marletta, Laboratory for Molecular Surfaces and Nanotechnology, Department of Chemical Sciences, University of Catania, Viale A.Doria 6, 95125 Catania, Italy

The phenomena involving molecular self-organization in confined domains are among the most promising processes for nano- and micropatterning of solid surface. Vesicles fusion from solution onto hydrophilic surface is a well-known example of such kind of phenomenon. The properties of molecular systems and the conditions provoking self-organization of molecular systems should be understood in details.

The present paper is aimed to construct and characterize lipid multicomponent domains onto solid surface. Dipalmitoylphosphatidylcholine (DPPC), Cholesterol (CHL), Sphingomyelin (SM), and Quercetin-3-O-Palmitate (Q3P) surfactants have been used to obtain monolayer films at water interface. Monolayer films were transferred on both mica and silicon substrates by modified LB method. Microcontact printing method (mCP) has been additionally used for cross-sectional surface patterning with lipid molecules. AFM was used to monitor the morphology and phase behavior of the transferred LB films and mCP composites. It was found that the thickness of DPPC monolayer films increase under water due to a swelling as well as molecular reorientation phenomenon. AFM results suggest that the molecular reorientation phenomena for DPPC monolayers on silicon is due to synchronous changing of molecular orientation from tilted to vertical position relatively substrate. The influence of CHL, SM, and Q3P additives on film morphology in monolayer mixtures with DPPC has also been studied. The addition of Q3P or SM to DPPC, as investigated by AFM phase measurements, showed that a marked phase separation occurs in DPPC/Q3P or DPPC/CHL/SM mixtures depending on the molar ratio of components. The effects are discussed in details, along with the complex structures deposited from the studied compounds.

H-II.04 12:20

ENHANCED ANTIBACTERIAL AND PHOTOCATALYTICAL PROPERTIES OF Fe+3 DOPED TiO2 SOL-GEL THIN FILMS DEPOSITED ON CARBON NANOTUBES

A.R. Phani, L. Lozzi and S. Santucci, INFN and Department of Physics, University of L'Aquila, via Vetoio, 67010 Coppito, L'Aquila, Italy

Fe+3 doped TiO2 based nanostructured thin films have been prepared by the sol-gel process and applied on to previously grown carbon nanotubes on quartz substrates. The carbon nanotubes were grown by plasma enhanced chemical vapor deposition technique. The as deposited films and annealed films have been characterized for structural and morphological properties by employing X-ray diffraction and field emission scanning electron microscopy techniques. The antibacterial activity against E-coli and S. aureus has been examined applying the so-called antibacterial drop test. The bactericidal activity for the above bacteria cells was estimated by relative number of bacteria survived calculated from the number of viable cells, which form colonies on the plates. The films exhibited enhanced antibacterial properties when compared to carbon nanotubes films filled with Fe+3 alone. The influences of Fe+3 dopant concentration, annealing temperature on the films structure, thickness of thin films, have been investigated.

H-II.05 12:40

FABRICATION OF A THREE-DIMENSIONAL NANO-STRUCTURED BIOMATERIAL FOR TISSUE ENGINEERING OF BONE

E. Garreta and D. Gasset, Institut Quimic de Sarria, Via Augusta 390, 08017 Barcelona, Spain, C. Semino, Center for Biomedical Engineering, NE47-383, Massachusetts Institute of Technology, Cambridge MA 02039, USA, S. Borros, Institut Quimic de Sarria, Via Augusta 390, 08017 Barcelona, Spain

Hydroxyapatite (HA), as a bioactive material, has a certain surface reactivity that allows its binding with bone tissue, thereby enhancing bone formation. Previous works done in our research group have developed a synthetic HA biomaterial with controlled properties. The aim of the present work is the development of a three-dimensional nano-structured biomaterial for its application in tissue engineering of bone. We have used hydroxyapatite powder combined with a self assembly peptide scaffold. This peptide forms a three-dimensional network of nanofibers in physiological conditions that resembles the natural extracellular matrices. We have modified the surface of the HA by polymerizing different monomers through a plasma polymerization technique and we have studied the dissolution, precipitation and ion exchange reactions of the modified HAs in simulated body fluid (SBF), obtaining different calcium and phosphate release rates depending on the interaction of the surface functionalities of the modified HAs with the SBF. Then, we have prepared different nano-structured composites by mixing the modified and non-modified HAs with the peptide in different proportions. The resultant composites were characterized by SEM and their rheological properties were also described. Finally, mouse embryonic stem cells were used to study the cell viability, proliferation and differentiation within the developed composites into bone-like structures.

13:00

LUNCH

Session III

Session chair : Augustinus Bader

- H-III.01** 14:30 -Invited- NOVEL MEMBRANES AND SURFACE MODIFICATION ABLE TO ACTIVATE SPECIFIC CELLULAR RESPONSES
L. De Bartolo(a), S. Morelli(a), L. C. Lopez(b), L. Giorno(a), P. Favia(b), R.d'Agostino(b) and E.Drioli(a), (a)Institute on Membrane Technology, National Research Council of Italy, ITM-CNR, c/o University of Calabria, via P. Bucci cubo 17/C, 87030 Rende (CS) Italy, (b)Department of Chemistry, University of Bari, Bari, Italy
- H-III.02** 15:00 -Invited- THE CHALLENGE OF BIOLOGICAL TESTING OF INTELLIGENT BIOMATERIALS FOR REGENERATIVE MEDICINE
C.J. Kirkpatrick, REPAIR-Lab*, Institute of Pathology, Johannes Gutenberg University, Langenbeckstrasse 1, 55101 Mainz, Germany
The biomimetic concept involves the simulation of natural structures and functions. An holistic analysis of natural interfaces reveals two principal elements, namely cells, and their products, one important subgroup of which are matrix components. These considerations have led to different models for implant design, one of the exciting developments being that of a biodegradable matrix or scaffold which contains the essential bioactive signal molecules to elicit a physiological regenerative response. Natural and synthetic polymers offer great promise in achieving these goals. However, from a biological point of view much more knowledge is required on how such materials with different physical and chemical characteristics modulate the inflammatory and healing responses. Further focal points are the application of adult stem cell technologies as well as the need for deeper understanding of cell-matrix interactions and their signaling pathways. The presentation will show how in vitro methods play a major role in testing the efficacy of intelligent biomaterials. Due to our interest in vascularization, much of the experimentation involves endothelial cells (EC) from microvascular sources as well as endothelial progenitor cells (EPC) from human peripheral blood. One of the biopolymers of interest is the silk protein, fibroin, in combination with collagen type I. Phenotypic stability is an essential element in any cell type used in testing systems and demands investigation at gene transcript and protein expression level. Cell-biomaterial interactions can be readily observed using confocal laser scanning microscopy (CLSM) in a three-dimensional (3D) culture system [1]. Cytoskeletal organisation in EC also indicates the state of cellular activation and can therefore be used to monitor functional integrity [2]. ELISA and cell-EIA (enzyme immunoassays) permit determination of released and cell-associated gene products respectively, while RT-PCR methods can be used to monitor RNA transcripts. Co-culture systems, for example EC and osteoblasts, enable study of the suitability of the biopolymers for bone regeneration, and represent an in vitro system of higher complexity. Co-culture models of barrier systems in the body, for example the blood-brain barrier or the alveolo-capillary barrier are important in studying strategies for drug and gene delivery, using bioresorbable polymers in nanoparticulate form. An in vitro model of the human air-blood barrier has already been established by our group [3]. Further development of more sophisticated in vitro systems will be essential to make advances in regenerative medicine, especially to test the biofunctionality of new biomaterials.
[1] Unger RE et al. Biomaterials 2004; 25: 5137-5146
[2] Peters K et al. J Mater Sci Mater Med 2004; 15: 319-323
[3] Hermanns MI et al. Lab Invest 2004; 84: 736-752
* REPAIR-Lab : Laboratory for REgenerative PAtiology & Interface Research
- H-III.03** 15:20 EARLY STAGES OF HUMAN PLASMA PROTEINS ADSORPTION ON BIOCOMPATIBLE THIN FILMS PROBED BY ATOMIC FORCE MICROSCOPE
K. Mitsakakis, S. Lousinian, S. Logothetidis, Aristotle University of Thessaloniki, Department of Physics, 54124 Thessaloniki, Greece
Atomic Force Microscope (AFM) as a tool for surface characterization has offered a great impulse in the advance of biocompatible materials. In this study AFM was implemented to investigate the early stages of adsorption of two human plasma proteins on several titanium- and carbon-based (a-C and a-C:H) biocompatible thin films. The plasma proteins that were used for this purpose were Human Serum Albumin (HSA) and Fibrinogen, two of the most important proteins in human plasma. The significant interest on these proteins stems also from their controversial action, as fibrinogen tends to form thrombi, whereas HSA has the opposite action. The concentration of the protein solutions used was the same as that in human plasma. As the examined samples were soft, non-contact AFM mode was used to avoid their destruction. In order for the early stages of adsorption to be assessed, small incubation times were applied, from 10 minutes and less. AFM measurements in liquid buffer were also carried out, allowing us to probe the behaviour of the proteins in an environment much closer to their native one. Comparative conclusions between the different biomaterials and environments were extracted from the information acquired. In addition, there was an assessment of the adsorption mechanism of the proteins on the above mentioned biomaterials.

H-III.04 15:40

DISC CHONDROCYTE TRANSPLANTATION IN A CANINE MODEL: A TREATMENT FOR DEGENERATED OR DAMAGED INTERVERTEBRAL DISC

H.J. Meisel(a), T. Ganey(b), W. Hutton(c), (a)BG-Kliniken Bergmannstrost, Halle/Saale, Deutschland, (b)Tampa, FL, USA, (c)Emory Spine Center, Atlanta, GA, USA

Objective: As yet there are no effective therapies to retard or reverse disc degeneration. With this in mind, we designed a study (using the dog as our model) to investigate the hypothesis that 1) repair of the damaged disc is technically feasible, 2) autologous cells can be reproducibly cultured under defined and controlled conditions, 3) percutaneous delivery is possible, and that 4.) disc chondrocytes will integrate with the surrounding tissue, produce the appropriate intervertebral disc extracellular matrix, and provide a functional as well as formative solution to disc repair.

Results: In the context of degenerative changes in an injury model we were able to show the following: 1) Autologous disc chondrocytes could be expanded in culture and returned to the disc by a minimally-invasive procedure after 12 weeks. 2) Disc chondrocytes remained viable after transplantation as shown by BrdU incorporation and maintained a capacity for proliferation after transplantation as depicted by histology. 3) Transplanted disc chondrocytes produced an extracellular matrix that displayed elements similar in composition to normal intervertebral disc tissue. Positive evidence of proteoglycan content was supported by accepted histochemical staining techniques such as Safranin O-Fast Green. 4) Both Type II and Type I collagens were demonstrated in the regenerated intervertebral disc matrix by immunohistochemistry following chondrocyte transplantation. 5) When the disc heights were analyzed for variance according to treatment, a statistically significant correlation between transplanting cells and retention of disc height was achieved. Conclusions: In summary, autologous chondrocyte transplantation is technically feasible and biologically relevant to repairing disc damage and retarding disc degeneration.

16:00

BREAK

Session IV

Session chair : James C. Kirkpatrick

H-IV.01 16:20 -Invited-

IS THERE A NANOTECHNOLOGICAL NEED FOR BIOMATERIALS USED IN ORAL AND MAXILLOFACIAL SURGERY?

D. Muster, LEED Biomatériaux & Service de Stomatologie et Chirurgie Maxillo-faciale, CHRU, BP 426, 67091 Strasbourg Cedex, France

In oral and maxillo-facialsurgery, biomaterials are used to repair or reconstruct soft and hard tissues in the dento-maxillo-facial area. Their main applications (biodevices) concern the realisation of packing, augmentation or covering materials, dental implants, devices for crano-maxillo-facial fixation and prostheses for temporo-mandibular joint (TMJ). Even if numerous experimental studies have demonstrated a lot of potential clinical applications for various materials (metals, ceramics, polymers and natural materials), very few come to the industrial production step and to the current clinical use for the practitioner. In fact, it is not sufficient for a material to possess appropriate physico-chemical and mechanical characteristics together with a specific biocompatibility for introducing it in the current surgical practice. It must also satisfy to industrial feasibility criteria in acceptable economical conditions and to be of easy use for the surgeons. Moreover, its real interest has to be confirmed by multicentric clinical studies. With the advent of nanostructured materials it may be now possible i.e. to synthetize materials for hard tissue surgery which simulate the surface properties of physiological bone. The tailoring of nanostructures by the use of vapor deposition techniques opens up new opportunities to engineer innovative biomaterials and devices. Concerning tissue engineering, nice models are elaborated in various laboratories in the world but huge difficulties remain regarding the optimal molecular environment and the biomechanical functionality. In conclusion, for the daily clinical use in the next decade (and even the following), the traditional biomaterials (eventually optimized by surface treatment) will surely continue to keep the first place.

H-IV.02 16:50

INFRARED ELLIPSOMETRY STUDIES OF TEMPERATURE EFFECTS ON MULTILAYERS OF ANTI-HUMAN SERUM ALBUMIN AND ITS ANTIGEN

H. Arwin, A. Askendahl, T. Berlind, P. Tengvall, Linköping University, 581 83 Linköping, Sweden; T. Tiwald, J.A. Woollam Co., Inc, 645 M St., Suite 102, Lincoln NE 68508, USA; D.W. Thomson, J.A. Woollam, University of Nebraska, Lincoln NE 68588-0511, USA

Future bionanotechnology-based devices may contain self-assembled protein multilayers and temperature stability may be an issue. The objective is here to present methodology for detailed studies of effects of heating multilayers of human serum albumin (HSA) and anti-HSA. Multilayers equalling 10 monolayers of anti-HSA were prepared on silicon substrates and studied with infrared spectroscopic ellipsometry (IRSE) equipped with a heat stage. The complex-valued refractive index $N=n+ik$ and the layer thickness were determined and the amide bands analyzed. At room temperature (RT) the amide I band was observed at 1637 cm^{-1} (width 73 cm^{-1}), the amide II band at 1522 cm^{-1} (width 80 cm^{-1}) and the amide A band as two broader bands at 3259 and 2856 cm^{-1} , respectively. At 120 degrees C, n and k changed seen as changes in the amide band amplitudes. After cooling to RT, n and k returned to the original values. The thickness decreased from 42.4 nm at RT to 38.8 nm at 120 degrees C but increased to 41.4 nm upon cooling to RT. This may be due to temperature-induced densification/swelling but more likely to water desorption/uptake. Heating to 200 degrees C caused layer degradation observed as irreversible changes in n and k and a decrease in thickness of more than 40%. It is concluded that HSA/anti-HSA multilayers are stable for shorter times at temperatures above 100 degrees C, except for small thickness changes.

H-IV.03 17:10**THE IMMOBILIZATION OF NANO-STRUCTURED HYDROXYAPATITE SURFACE BY DNA MOLECULES FOR A STIMULATED MINERALIZATION**

O. Lysko(a), A. Veligura(a), I.Lysko(a), P. Lytvyn(b), V. Dubok(c), E. Buzaneva(a), (a)National Taras Shevchenko University of Kiev, The Scientific and Training Center "Physical and Chemical Material Science of Kiev National Taras Shevchenko University and NASU", 64 Vladimirska Str., 01033 Kiev, Ukraine, (b)Institute of Semiconductor NANU, Physiks 45, prospect Nauky, 03028 Kiev, Ukraine, (c)Institute for Problems of Material Science NANU, 3, Kryzhanovskogo Str., 03680 Kiev, Ukraine

Several aspects of a performance of nano-structured hydroxyapatite (HAP) surface by ds(ss)DNA attachments with aim to stimulate a mineralization process on a interface HAP implant/DNA coving in biological suspension have been studied.

We selected these molecules for the attachment to HAP surface, because the knowledge about the bioactivity of nano-structured HAP surface with adsorbed collagen, DNA [1] are far from optimum, and their interface chemistry remains poorly characterized, as also their applications in the tissue engineering for the regenerative medicine (use as bone-like implantes, in molecular cloning techniques). Chemical synthesized hydroxyapatite nanocrystals in sol-gel having -PO₄, -NH, -OH and other groups on the surface, which can be change at the synthesis, have been used.

The formation of the surface bonds between attached ds(ss)DNA with thiol groups and HAP before, after the mineralization under UV-vis irradiation, and formation of novel HAP structure by IR- and UV-vis spectroscopy, XPS, EPR have been confirmed.

For example, some changes in the spectra become more evident during staying of the nano-structured HAP in dsDNA hydrogel and the result of a increase of the time of an interactive. These changes by the regulation of HAP nanocrystals sizes and dsDNA chains were controlled.

It was revealed lateral sizes 20-60 nm of single hydroxyapatite nanopaticles in dsDNA hydrogel from AFM image. The models of DNA nanotechnology of nano-structured HAP surface formation were developed.

[1] World Technology Evaluation Centrer, Workshop Report on R&D Status and Trends in Nanoparticles, Nanostructured Materials, and Nanodevices in the United States, Proceedings of the May 8-9, 1997 Workshop Richard W. Siegel. http://wtcc.org/loyola/nano/us_r_n_d

H-IV.04 17:30**POLY(ETHYLENE OXIDE) HYDROGELS AS A TEMPLATE FOR THE CULTURE OF HEPATOCYTES**

E. Alexandre J. Cinqualbre(a), D. Jaeck(a), L. Richert(a), P.J. Lutz(b), (a)Fondation Transplantation, Laboratoire de Chirurgie Expérimentale, 5 Avenue Molière, 67200 Strasbourg, France, (b)Institut Charles Sadron, UPR 22, CNRS, 6 Rue Boussingault, 67083 Strasbourg, France

In the present work, such PEO hydrogels were tested with respect to their ability to serve as a template for the survival and the growth of hepatocytes. Two systems were considered: either the surface of existing hydrogels -of selected structural parameters- were seeded with isolated rat hepatocytes or the hepatocytes were dispersed in physiological medium containing the PEO macromonomer/initiator and heated to 37°C. In the first case, cells were examined at given times after spreading over two days. The effect of the structure of the surface of the hydrogel and its chemical nature on the extent of hepatocyte attachment and the morphology were investigated. Earlier studies confirmed that bifunctional PEO macromonomers can be homopolymerized at 37°C by a free radical process to hydrogels in less than one hour. However, the reaction has to be conducted in water and appropriate initiators have to be used. Preliminary experiments confirmed the survival of the hepatocytes in the presence of high concentrations of free radical polymerization initiators. This prompted us to proceed to crosslinking in the presence of isolated rat hepatocytes. Fresh hepatocytes were dispersed in physiological medium containing the macromonomer precursor and the redox initiator. Crosslinking occurs after 30 to 60 min. Phase contrast light micrographs confirmed that hepatocytes could be dispersed

H-IV.05 17:50

THE PATENT PROMOTED BY A UNIVERSITY AT THE CROSSROADS OF THE RESEARCH RESULTS AND THE IMMEDIATE UTILISATION BY THE INDUSTRY

R. Doddoli, BIOFUTURE Research Consortium in Regenerative Medicine, c/o Department of Chemistry, University of Bari, Italy

The departments, indeed the laboratories of the public research institutes no longer are satisfied with displaying a certain number of annual scientific publications meant to highlight their expertise and know-how. In fact, some years now, a new trend has been in vogue: stimulated by all the national and international public bodies, they are making increasing use of the “patent pending” solution to make optimum use of the results of specific research projects on the one hand and, on the other hand, to assert their excellence vis-à-vis the Ministry of Research of their country which is supposed to finance them.

However, caught up in the euphoria of the research results and lost in their formulae and practices, these researchers lose sight of the basis for a patent and its real reason for being (patent charter). A patent necessarily must be of service to the community, that is to say that essentially it must contribute to the improvement of the quality of life of the population. To achieve this goal, going through certain stages is a must, namely that to start with a patent must be absolutely profitable to industry in order that, subsequently, it be consistent with its being of service to the community. In this context, its validity is set at ten years renewable for another ten years based on specific parameters as stipulated by the national and international patent institutions, indeed by the EPO (European Patent Office) the headquarter of which is in Munich. Its use by industry ensures proceeds for then, even twenty years and must represent the material fruit of the applicant's effort. Beyond this period, the patent becomes public and therefore available to everyone. But the crucial problem is this: when can a patent really be used and how to do so as best as possible to guarantee profits for various parties involved and thus justify its reason for being?

The purpose of this work thus is to incite university researchers to think about the real usefulness of a patent on the one hand and, on the other hand, to ponder over the best way of using, in close cooperation with industry, the fruit of the research and the registering of the patent, both financed by public funds. For the latter, owing to their nature, demand that there be no wastage and cautious management thereof.

Keywords: a useful patent, negotiations with an industrial partner, know-how transfer.

H-IV.06 18:10 -Invited-

THE EUROPEAN FEDERATION FOR REGENERATIVE MEDICINE – THE VISION OF A EUROPEAN MERGER IN THIS FIELD

G. Knedlitschek, H.J. Meisel, Forschungszentrum Karlsruhe, Regenerative Medicine Programme, P.O. Box 3640, 76021 Karlsruhe, Germany

REGENERATE (Regenerative Medicine and TE = Tissue Engineering) aims at a strategic, collaborative merger of high level Tissue Engineering networks, scientific societies (covering various aspects relevant for the investigation and the establishment of regenerative therapies), scientific research institutions, clinicians and topic-related industries. Up to now in Europe there have been several initiatives to bring together researchers working in the various fields related to all aspects of Regenerative Medicine. They were, however, not fully effective so far to create a well interconnected research community in this field. This initiative is aiming at the consolidation of these activities and will give them a permanent platform.

International co-operation in science and technology is growing rapidly and innovation increasingly relies on cooperation between companies, universities, research institutes, regulatory authorities, financial partners and the public. The overall aim of REGENERATE is to create, share and exploit knowledge in the field of REGMED/TE on a European level in order to develop innovative solutions for the future utilisation of TE for Regenerative Medicine (REGMED). The network is intended to serve as a “European platform” for all groups being involved/interested in all aspects of Tissue Engineering and Regenerative Medicine (i.e. scientists, clinicians, industry, patients, patient associations etc.) to find the “best-fit” partners for their projects and to apply for funding.

This platform will foster the sharing and developing of joint research infrastructures, the education of the next generation of students, researchers, clinicians and technicians, the enhancement of social and political awareness and perception and in that way generate knowledge for the public. All research aspects as different as medicine, systems biology, post-genomic biological research, biotechnology, material sciences, engineering and bioinformatics etc. will be included to promote the interdisciplinary discussion and exchange. The common platform for TE will also help developing standardisation rules for precision and accuracy in this field and stimulate the economic exploitation of knowledge-based products and processes.

It is planned to structure the various activities and to give them a permanent spiritual home by founding a European Economic Interest Grouping (EEIG) based on Council Directive no. 2137/85 dated 25 July 1985 (“EEIG Directive”): the “European Federation for Regenerative Medicine”. Founding members will be national associations for the advancement of Regenerative Medicine, already established as in Germany or in the process of being founded. The presentation of paramount aims is intended to stimulate national initiatives to join our network.

Keywords: Regenerative Medicine; tissue engineering; European network involving scientists, clinicians, industry, patients, patient associations etc.

Session V

Session chair : Dieter Falkenhagen

H-V.01 14:30

HAEMOCOMPATIBILITY OF AMORPHOUS CARBON THIN FILMS, OPTICAL PROPERTIES AND ADSORPTION MECHANISMS OF BLOOD PLASMA PROTEINS

S. Lousinian, S. Logothetidis, A. Laskarakis, M. Gioti, Aristotle University of Thessaloniki, Department of Physics, 54124 Thessaloniki, Greece

Spectroscopic ellipsometry (SE) is a non-destructive technique, with high sensitivity, that can be applied both in air and in liquid environment. These advantages together with the use of advanced modeling procedures regarding SE can provide valuable information for the study of biological samples. The aim of this work is to explore the haemocompatibility properties of a-C:H thin films, grown with rf reactive magnetron sputtering on c-Si substrates, the optical properties and the adsorption mechanisms of two basic blood plasma proteins, which play an important role in preventing and causing thrombi formation, Human Serum Albumin (HSA) and Fibrinogen (Fib), respectively. This was performed by the use of SE from IR to Vis-UV spectral region and by supportive Atomic Force Microscopy (AFM) measurements.

The a-C:H films grown under floating conditions showed better haemocompatibility compared with those deposited under application of bias voltage. This is probably due to their different micro-structural characteristics, bonding structure, and charge transfer between the protein molecule and the surface, derived by their optical properties. Dielectric characteristics of the two proteins are rather featureless in Vis-UV range, but their bonding structure differences become distinct by SE measurements in IR energy range. Finally, complementary AFM measurements provide detailed information about adsorption mechanisms of the proteins on the a-C:H films.

H-V.02 14:50

SELF-SUPPORTED MULTILAYER FILMS OBTAINED BY DISINTEGRATION OF pH-RESPONSIVE LAYERS UNDER PHYSIOLOGICAL CONDITIONS

Shoko S. Ono(a,b), Gero Decher(a,c), (a)Institut Charles Sadron, 6 rue Baussingault, 67083 Strasbourg, France, (b)R&D Center, Mitsui Chemicals, Inc, 580-32, Nagaura, Sodegaura, Chiba 299-0265, Japan, (c)Université Louis Pasteur, Faculté de Chemie, 4 rue Blaise Pascal, 67000 Strasbourg, France

Thin films with multimaterials arranged with nanoscale precision have great potentials for facilitate integration, miniaturisation and multifunctionalisation of the devices. "Layer-by-layer deposition" permits to fabricate multilayer films consist of various materials arranged with nanoscale precision on almost any substrate. If the multimaterial film can be released from the substrate, the obtained self-supported multimaterial films open a wider field of applications, for example membrane separation, medical engineering with cell biology and so on. However, the methodology of releasing of those multimaterial films without damages of their properties has not yet established enough.

We developed a new system to obtain self-supported multimaterial films under physiological conditions. In this system, the pH responsive multilayer consists of biocompatible polymers formed via hydrogen-bonds which cover substrate surface releases the multimaterial films constructed onto the pH responsive multilayers. In the presentation, the main principle of the new system, the key factor for releasing the self-supported films and structural features of self-supported multimaterial films will be discussed..

H-V.03 15:10 -Invited-**DISC REPAIR WITH AUTOLOGOUS CHONDROCYTES: A PILOT CLINICAL STUDY**

Hans-Joerg Meisel(a), Olivera Alasevic(b), William Hutton(c), Timothy Ganey(d), (a)Bergmannstrost, Halle, Germany; (b)co.don AG, Berlin, Germany; (c)Emory Spine Center, Decatur, GA; (d)Tampa, Florida, USA

This pilot study was designed to assess whether autologous disc chondrocyte transplantation will prevent disc degeneration in patients that have undergone discectomy. Cultured autologous cells were transplanted into the nucleus pulposus by a closed procedure. While it has been shown previously that disc cells sustain a phenotype in culture and that transplantation into canine disc demonstrates appropriate integration, the fate of transplanted cells in a human population has not been reported.

Patients were actively recruited for this study from a population that was to be surgically treated for single level disc herniation. To be included in this study, patients could not have modic changes and must have failed previous conservative treatment. Patients were evaluated by VAS, Jenny neurological score, and an assessment of spine mobility was made. Intervertebral discs were also assessed qualitatively by MRI for disc height, degenerative changes (Modic), and fluid content. Disc material was removed by open microdiscectomy and intra-operative diagnosis of the disc (I-IV) was made. Cells were commercially expanded for transplantation under GMP conditions and maintained in culture with serum taken from individuals prior to their surgery. Transplantation occurred 3 months after the microdiscectomy procedure. Patients were hospitalized for 2 days following cell transplantation and required to wear a lumbar orthosis for the following 3 weeks. Follow-up occurred at 3, 6, 12, 24, and 36 months after the procedure.

MR images demonstrated changes at the surgical site that were characteristic of normal disc morphology. Introduction of cells had a positive affect on cell height, MRI signal, and matrix appearance. MRI changes were positive over time; showing enhanced central disc signal, and reduction in endplate effusion. All patients in the study showed improvement in the level of their low back pain and spine mobility was preserved or enhanced in 87.5% of the patients in this study. By 3 months, approximately 73% of the patients regained full motor sensation, and 82% of the patients achieved sensory recovery. Remaining symptoms were slight and in most cases not residual. Assessment on the VAS scale demonstrated a pre-operative mean of approximately 76mm that was reduced to 19mm in the final assessment. No secondary instability or degenerative change at adjacent levels was seen nor was progressive degenerative change at the treated intervertebral disc documented.

Autologous cells transplanted into a damaged intervertebral disc appear to retard degeneration. Evidence of matrix production and suppressed inflammation was evident by MRI, radiography, and by clinical assessment of pain. From these clinical results, autologous disc chondrocyte cell transplantation appears to offer the promise of retarding degeneration, maintaining intervertebral height, and stimulating matrix regeneration after micro-discectomy. Relief of pain, matrix production and integration, and no evidence of degeneration suggest autologous cell transplantation may be a valuable clinical tool for use in treating disc herniation.

H-V.04 15:40 -Invited-**SHAPE-MEMORY POLYMERS**

Andreas Lendlein, GKSS Research Centre Geesthacht, Kantstr. 55, 14513 Teltow, Germany

Shape-memory polymers are stimuli-responsive materials. Upon exposure to an external stimulus, they have the capability of changing their shape. A change in shape initiated by a change in temperature is called thermally induced shape-memory effect. The shape-memory effect results from the polymer's structure in combination with a certain processing and programming technology. Materials which obtain their functionality after a functionalization process as described for shape-memory polymers are called functionalized materials. An actual trend in polymer science is the design of materials which show multifunctionality meaning an unexpected combination of material functionalizations like the combination of biofunctionality, hydrolytic degradability, and shape-memory functionality. Substantial concepts in this context are polymer systems. These are families of polymers, in which macroscopic properties can be controlled by a systematic variation of molecular parameters. In this way shape-memory polymers having a specific combination of properties required for a certain application can be obtained by only slight variation of the molecular structure or chemical composition. Triggering of the shape-memory effect by other stimuli like light or electromagnetic fields will play a prominent role in future developments. [1, 2, 3]

Stimuli-sensitive implant materials have a high potential for applications in minimally invasive surgery. Degradable implants could be inserted into the human body in a compressed (temporary) shape through a small incision where they obtain their shape relevant for the specific application after warming up to body temperature. After a defined time period the implant is degraded. In this case subsequent surgery to remove the implant is not necessary. For applications in biomedicine, it is necessary to have tailor-made shape-memory polymers whose thermal, mechanical, or degradation properties can be varied over a wide range [4, 5, 6].

[1] A. Lendlein and S. Kelch: *Angew. Chem. Int. Ed.* Vol. 41 (2002), p. 2034-2057.

[2] A. Lendlein, S. Kelch: *Materials Science Forum* Vol. 492-493 (2005), p. 219-224.

[3] A. Lendlein and R. Langer: *Science* Vol. 296 (2002), p. 1673-1676.

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[5] D. Rickert, M. A. Moses, A. Lendlein, S. Kelch and R.P. Franke: *Clin. Hemorheol. Microcirc.* Vol. 28 (2003), p. 175-181.

[6] A. Altheld, Y. Feng, S. Kelch, A. Lendlein: *Angew. Chem. Int. Ed.* 44 (2005) p. 1188-1192.

H-V.05 16:00

AN AFM INVESTIGATION OF OLIGONUCLEOTIDES ANCHORED ON AN UNOXIDIZED CRYSTALLINE SILICON SURFACE

G. Longo, A. Cricenti, M. Girasole, P. Perfetti, Istituto di Struttura della Materia, C.N.R. Sezione di Tor Vergata Rome, Italy, F. Cattaruzza, A. Flamini, T. Prosperi, Istituto di Struttura della Materia, C.N.R. Sezione di Montelibretti Rome, Italy

Carboxylic terminated monolayers have been covalently attached on boron doped crystalline silicon (1,0,0) surfaces using a Cathodic Electro Grafting (CEG) technique. The functionalization concentration and efficiency have been evaluated through various surface analysis. In particular, topography images, performed with an Atomic Force Microscope (AFM), were used to optimise the protocol to obtain a most uniform monolayer.

Poli-thymine oligonucleotides (Poli-T) have been anchored on the functionalized surfaces to form a nano-bio sensing device, selectively reacting to a particular target molecule, the Poli-adenine (Poli-A). Characterization of these samples has been performed through surface imaging and quantitative fluorescence measurements. In particular, AFM images show that the DNA fragments self-assemble on the surface forming characteristic toroidal shapes.

16:20

BREAK

Session VI

Session chair : Gudrun Knedlitschek

H-VI.01 16:40

METAL-POLYMER SMART BIO-ACTIVE NANOCOMPOSITES

Nicola Cioffi, Nicoletta Ditaranto, Luisa Torsi, Luigia Sabbatini, P. Giorgio Zambonin, Dipartimento di Chimica, Università degli Studi di Bari, 4 via Orabona, 70126 Bari, Italy, Lucia Novello, Giuseppina Tantillo, Dipartimento di Sanità e Benessere degli Animali, Università degli Studi di Bari, Strada Provinciale per Casamassima Km 3, 70010 Valenzano, Bari, Italy, Lina Ghibelli, Maria D'Alessio, Dipartimento di Biologia, Università di Roma Tor Vergata, 1, Via della Ricerca Scientifica, 00133 Roma, Italy, Teresa Bleve-Zacheo, Istituto per la Protezione delle Piante, Sezione di Bari, C.N.R., 165/A via Amendola, 70126 Bari, Italy, Enrico Traversa, Dipartimento di Scienze e Tecnologie Chimiche, Università di Roma Tor Vergata 1, Via della Ricerca Scientifica, 00133 Roma, Italy

A spinnable coating capable to release metal species to a broth of living organisms in a controlled manner is an extremely interesting material for a number of biotechnological applications. Polymer/metal nanocomposites are a viable choice but very little is known on their biological properties. Here a polymer based nanocomposite loading stabilized copper or silver nanoparticles as a smart biostatic coating is proposed and systematic correlations between material properties and biological effects are established. Experimental proves of the nanocomposite capability to release metal species in a controlled manner and eventually to slow down or even inhibit the growth of living organisms, such as fungi and other pathogen micro organisms, are provided. The biostatic activity is correlated to the nanoparticles loading that controls the release of metal ions, independently evaluated by means of Electro-Thermal Atomic Absorption Spectroscopy. Insights into the understanding of the controlled releasing process, involving metal oxides dissolution through the nanoclusters stabilizing layer, is also proposed.

H-VI.02 17:00

2004 BIOACTIVE COATINGS BASED ON POLYELECTROLYTE MULTILAYER ARCHITECTURES FUNCTIONALIZED BY EMBEDDED PROTEINS, PEPTIDES OR DRUGS

Nadia Jessel(a), Joelle Ogier(a), Gero Decher(b), Pierre Schaaf(b), Jean-Claude Voegel(a), (a)INSERM Unité 595, Université Louis Pasteur, 11 rue Humann, 67085 Strasbourg Cedex, France, (b)Institut Charles Sadron (CNRS/ULP), 6 rue Boussingault, 67083 Strasbourg Cedex, France

The layer-by-layer adsorption technique is a general and versatile tool for the controlled fabrication of multimaterial surface coatings on a large variety of surfaces[1,2]). Self assembled multilayer architectures can be build using materials as different as synthetic or natural polyelectrolytes, a large variety of proteins, inorganic complexes and clusters, clay platelets or colloidal particles, ..., all adsorbed from aqueous solutions or suspensions. Never before it was possible to combine such a diversity of components in single architectures whose layer structure can moreover be controlled on the nanoscale. We and others have shown how protein adsorption or cell adhesion can be controlled by using multilayer films especially how complex multilayer architectures can be used to control the access of cells to embedded bioactive protein[3], bioactive peptide[4], bioactive lipopolysaccharide[5] or drugs[6].

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[2]G. Decher, (eds. G. Decher & J. B. Schlenoff), WILEY-VCH, Weinheim, 2003

[3]N. Jessel et al. Adv. Mater. 2003, 15(9), 692

[4]N. Jessel et al Adv. Mater. 2004, 16(17), 1506

[5]N. Jessel, Adv. Funct. Mater., 2004, 14(10), 962

[6]N. Jessel, Adv. Funct. Mater., 2004, 14, 174

H-VI.03 17:20

INTELLIGENT MULTILAYERS IN BIOMEDICAL APPLICATIONS

B. Saulnier(a), O. Félix(a) and G. Decher(a,b), (a)Institut Charles Sadron (CNRS, UPR 22), 6 rue Boussingault, 67083 Strasbourg Cedex, France, (b)Université Louis Pasteur, 4 rue Blaise Pascal, 67000 Strasbourg, France

During the last three to four decades, considerable efforts have been devoted to the development of surface functionalization techniques. Research in this domain is driven by both challenges on the fundamental level and by numerous potential applications in life science and in materials science. Few years ago, our group has developed a technique called "layer by layer" that allows the modification of a wide variety of surface (metals, glass, polymers, ...) with a large number of materials (polymers, colloids, proteins, lipids, ...). The layer-by-layer adsorption from solution offers an easy structural control in preparation of multicomposites materials by immobilizing functional components consecutively on a single surface. Interactions involved in the deposition are non-covalent bonds (hydrogen, electrostatic and hydrophobic interactions) or of covalent nature.

Here we report on a project where the layer by layer technology is involved for the development of a bioartificial pancreas for type I diabetes therapy. Our aim consists on the preparation of new multilayers intelligent membranes in order to control the transport of bioactive molecules across the membrane. The first step of our study was to optimise the multilayers construction under these conditions and to check the survival and the biofunctionality of cells.

H-VI.04 17:40

PHOTOCHEMICAL CONTROL OF CdS NANOPARTICLES SIZE

M. Marandi, N. Taghavinia, A. Irajizad and S.M. Mahdavi, Physics Department, Sharif University of Technology, Tehran 14588, Iran

Optical and electrical properties of semiconductor nanoparticles are strongly dependent on their size. Here a photochemical method is used to synthesize and controlling the sizes of CdS nanoparticles. Na₂S₂O₃ and CdSO₄ were used as initial materials, while the former is sensitive to the UV light. CdS nanoparticles were formed via a photo induced reaction between precursors. The effect of illumination time on the size of the CdS nanoparticles was investigated. Optical spectroscopy was mainly used for the characterization. Larger nanoparticles formed by increasing the illumination times from 5 min to 30 min and particles sizes were in the range of 5.5 nm to 11 nm. To achieve smaller sizes for the particles mercaptoethanol was used as a capping agent to prevent further growth. Capping agent concentration, illumination time and illumination intensity were investigated as the main parameters that influenced the size of the particles. Capping agent concentration of 0.005 Mol/lit to 0.5 Mol/lit were used at different illumination times between 1min to 10 min. Band gaps between 3.4 eV to 2.75 eV were obtained by changing the concentration of capping agent and illumination time. These correspond to the sizes between 3.2 to 6 nm. Lower UV intensity also resulted in smaller particles for a constant illumination time. TEM images also confirm the optical data and electron diffraction pattern showed crystalline particles. We demonstrated that by adjusting these parameters we can cover all of the sizes between 3.2 nm to 11 nm.

19:00

AWARD CEREMONY

The symposium organizers and the candidates to the graduate student award are requested to attend.

CONFERENCE RECEPTION

9:00 – 13:00 **POSTER SESSION**

11:00 – 11:20 **BREAK**

12:30 **LUNCH**

POSTER SESSION

Session chair : **Roberto Doddoli**

H/P01

HYDROGEN PLASMA SURFACE ACTIVATION OF SILICON FOR BIMEDICAL APPLICATIONS

Ricky K.Y. Fu, Xuanyong Liu, Paul K. Chu, Department of Physics & Materials Science, City University of Hong Kong, Tat Chee Avenue, Kowloon, Hong Kong, Chuanxian Ding, Shanghai Institute of Ceramics, Chinese Academy of Sciences, Shanghai 200050, China

Silicon has gradually been recognized to be an essential trace element in the normal metabolism of higher animals, and the role of silicon in the human body has aroused interest in the biomedical community. In fact, the interaction between silicon-based devices and the human body is not well understood and silicon-based biosensors and MEMS often suffer from poor biocompatibility. In this work, hydrogen plasma immersion ion implantation (H-PIII) was conducted to improve the bioactivity or bone conductivity of silicon. High energy ion bombardment rendered the silicon surface amorphous and gave rise to surface Si-H bonds. After immersion the implanted samples into a simulated body fluid, a negatively-charged surface containing the functional group (Si-O^-) as produced and bone-like apatite was observed to nucleate and grow on the surface. A good understanding of the formation mechanism of apatite on hydrogen implanted silicon is not only important from the viewpoint of biophysics but also vital to the actual use of silicon-based microchips and MEMS inside a human body.

H/P02

CARBON NANOMATERIALS PRODUCTION IN THE ELECTRIC DISCHARGE AND THEIR UTILIZATION IN THE POLYMER COMPOSITES

A.E. Shashkov, S.A. Zhdanok, A.P. Solntsev, I.F. Buyakov, A.V. Krauklis, I.A. Zhukova, Heat- and Mass Transfer Institute, Brovki st. 15, Minsk, Belarus

New carbon materials such as fullerenes, nanotubes, nanofibers attracts attention of researchers, technologists and practical persons during last decade. Unique physical properties of this new form of carbon is known very well at the present time, and they stipulate wide range of their possible practical utilization. Alongside with a study of carbon nanostructures production processes, simultaneously are conducted studies of possibility of its usage as additives in different sort of polymeric composites. In this work we presented the results of investigation of possibility of using carbon nanomaterials (CNM) in polyethylene and polyamide nanocomposites. Nanostructures were obtained from methane-air mixture upon atmospheric pressure without catalyst in high voltage atmospheric pressure discharge plasma (HVAPD). Carbon material specimens were investigated on scanning (SEM) and transmission (TEM) electronic microscope. Also their thermogravimetric and X-ray structural analyses were done. The data obtained reveals about complex deposit composition which consist of multiwalled nanotubes, and carbon nanofibers. Investigations of polymer composites obtained have shown the importance of CNM incorporation in polymer matrix method.

H/P03

TRANSLOCATION OF BIOMOLECULES ACROSS CELL MEMBRANES BY SINGLE-WALL CARBON NANOTUBES

F. Torrens, Institut Universitari de Ciència Molecular, Universitat de València, Dr. Moliner 50, 46100 Burjassot (València), Spain

A simple and general approach is reported to non-covalent functionalization of the sidewalls of single-wall carbon nanotubes (SWNT), and subsequent immobilization of various biomolecules onto SWNTs with a high degree of control and specificity. The functionalization involves a bifunctional molecule, 1-pyrenebutanoic acid, succinimidyl ester (PBASE), adsorbed onto the surfaces of SWNTs in a solvent. The pyrenyl group interacts with SWNTs, providing a fixation point for PBASE. The anchored molecules of PBASE on SWNTs are stable against desorption in water. This leads to the functionalization of SWNTs with succinimidyl ester groups, which are reactive to substitution by amines that exist on the surface of proteins. Functionalized SWNTs are able to cross the cell membrane. SWNTs are a carrier system for applications in drug delivery. The use of SWNTs as nanovehicles is explored, and the functions of the linked molecules are evaluated after cellular uptake. The absence of immunogenicity of SWNTs will increase the efficacy of the therapeutics. SWNTs can be derivatized to enable attachment of proteins. The functionalized SWNTs enter cells and are not toxic. Streptavidin enters cells when complexed to a SWNT-biotin transporter. The biocompatibility, unique physical, electrical, optical and mechanical properties of SWNTs provide the basis for new classes of materials for drug, protein and gene-delivery applications.

- H/P04** SYNTHESIS AND CHARACTERIZATION OF AMPHIPHILIC POLY(LACTIC ACID)-GRAFTED CHONDROITIN SULFATE COPOLYMER FOR BIOMEDICAL APPLICATIONS
Chih-Ta Lee, Ching-Ping Huang, Yu-Der Lee, Taiwan
In this study, new biodegradable brush-like amphiphilic copolymers were synthesized by ring opening polymerization. Poly(lactic acid) (PLA) was grafted onto chondroitin sulfate (CS), which is one of the specific glycosaminoglycans (GAGs) with physiological significance, using a tin octanoate [Sn(Oct)₂] catalyst in DMSO. The hydroxyl groups of the chondroitin sulfate in the grafted copolymer were used as the initiating groups. These functional groups enable specific mucoadhesion or receptor recognition. The degree of substitution (DS), the degree of polymerization (DP), and the chondroitin sulfate content were analyzed by ¹H-NMR. Characteristics of these grafted copolymers, such as the structure, thermal properties, and others, were investigated with respect to CS content. Meanwhile, amphiphilic core (PLA)-corona (CS) nanoparticles, with size less than 200 nm, were also prepared by solvent evaporation method. The critical aggregation concentration (CAC) was measured using the fluorescence technique and the morphologies of the nanoparticles were observed via field-emission scanning electron microscopy (FE-SEM) and atomic force microscopy (AFM). Furthermore, considering its possible application in oral protein delivery, the cytotoxicity of the graft copolymer toward Caco-2 cells in culture was examined.
- H/P05** STUDY OF LASER CREATED ZrO₂ AND HYDROXYAPATITE/ ZrO₂ FILMS FOR IMPLANTOLOGY
M. Jelínek(a,b), T. Dostálová(c), Z. Teubrová(a), M. Seydlova T.(a), P. Mašínová(a), T. Kocourek(a), W. Mróz (d), K. Smetana(e), (a)Institute of Physics AS CR, 182 21 Prague 8, Na Slovance 2, Czech Republic, (b)Institute of Biomedical Research of CTU, nám. Sítňá 3105, 27201 Kladno, Czech Republic, (c)1st Medical Faculty, Charles University, Department of Stomatology, Katerinská 32, Prague 2, Czech Republic, (d)Institute of Optoelectronics, MIT, 01-489 Warsaw 49, 2 Kaliski Str. Poland, (e)Institute of Anatomy, 1st Medical Faculty, Charles University, U nemocnice 3, 128 00 Prague 2, Czech Republic
Thin films of ZrO₂ and hydroxyapatite/ZrO₂ were created by excimer laser ablation on Ti6Al4V substrates. The ZrO₂ layers were fabricated in vacuum by KrF laser at various substrate temperatures (up to 700 °C) and HA layers were fabricated in water vapor ambient (50 Pa) by ArF laser ablation.
Film properties were evaluated by XRD, SEM and WDX methods. The test of adhesion was proceeded on ZrO₂ films. The HA/ZrO₂ and ZrO₂ samples were tested in vitro for cytotoxicity, adhesion and proliferation. The XRD analysis proved the presence of the crystalline HA in the deposited films. The SEM demonstrated smooth HA surface covered by droplets with the diameters of 5 - 20 μm. The Ca/P ratio of the films is higher than that of the natural HA and is within the range of 2.2 - 2.4. The best results were received by the HA + ZrO₂ samples. After 24 hours the test of attachment showed that 53% of cells have attached on the surface of the sample and 47% of cells in the surroundings. The test of spreading showed the 47 % growth of the cells on the surface of the sample and the 53 % growth of the cells in the surroundings. The fibroblasts created subconfluent and confluent growth and showed fibronectin homogeneously. The comparison of results of in vitro study on HA /ZrO₂ films and in vitro study of ZrO₂ films will be also presented.
- H/P06** NANOSTRUCTURED LAYERS FROM DNA, DNA:AU, DNA:C60 CLUSTERS
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The aim of the article is to present the results of an investigation of functional properties DNA, DNA:Au, DNA:C60 clusters from water solution for building biochip.
Our investigations were included directly quantifying DNA, DNA:Au, and DNA:C60 samples for use in sequencing or polymerize chain reactions, or pharmaceutical testing and quality control. Besides, we also performed the study caused by quantum effects features of these phenomena at low temperatures. These results could be applied to producing credit card-sized sensor arrays for clinical applications such as detection of pathogenic bacteria, tumors, and genetic disease, or for forensics. The variety of alive organisms has appeared, evolutionary and now exists due to persistent interaction with various factors of environment. The majority of these factors has electromagnetic nature. The most interesting frequency range is from the superhigh frequencies to infralow frequencies. We measured the resistance versus temperature curve. The behavior of the resistance of the layer from DNA polymerised molecules networks on Si or Al₂O₃ under the temperature increase is typical for a semiconductor. The rectified type of I-V characteristic for the structure metal (Pt/Ir or Cu) - the layer from DNA polymerised molecules networks on Si also has been measured. Both the resistance of this layer of and its change were less than known from literature.
- H/P07** SAR IS THE ESTIMATION CRITERIA OF THE INFLUENCE OF AN ELECTROMAGNETIC FIELD ON BIOLOGICAL OBJECTS
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Nowadays, a great significance has been given to the ecological problems of a human being due to many problems of such type in the modern microwave electronics. The main task, has not been studied yet, is the problem of an influence of the microwave electromagnetic fields on the health of human. But the investigations in this way have blocked by a human factor. We propose a method, which can eliminate this limitation. It is based on the computer experiment realized with a CAD system.
We use HFSS and Serenade to simulate the influence of a microwave electromagnetic field on the human head. The primary parameter is used to characterize such systems is the specific absorption rate (SAR). We propose to use the SAR parameter as primary parameter of an interaction between microwave electromagnetic field and a biological object. For instance we can say about dangerous zones in a human head, which highly depends on an external electromagnetic field. SAR is the universally recognized parameter for this field of research, so this is the another reason to use it.

H/P08**MICRO-PLASMA TEXTURED TI-IMPLANT SURFACES**

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The surface state of titanium implants modulates bone response and im-plant anchorage. This evidence brought implant manufacturers to switch from the standard surface refinements and implement new surface treat-ments for more bone apposition and enhanced interfacial strength meas-ured by removal torque or push-out tests. Anodic plasma-chemical treat-ment of implant surfaces is a cost-effective process to modify surface top-ography and chemistry. This technique is used for structuring connected with a coating of implant surfaces. The aim of our investigations here is to texture the implant surface in the nanoscale without coating.

Different structured cp Ti disks were used as a substrate. Micro-plasma texturing was carried out in an aqueous electrolyte. By applying a pulsed DC voltage to the specimen, micro-plasma discharge was generated in the steam gas thin gap between immersed specimen and electrolyte. To modify the texture formed by the micro-plasma the initial structure of the Ti disks (by polishing, blasting with glass balls, grinding) and the elec-trical and chemical parameters of the plasma process were changed. The textured Ti surfaces were characterised optically by SEM and electro-chemically by CV- (for testing the corrosion parameters), CA- (to give the enlargement of the real surface) and EIS-measurement in range of 100kHz to 100μHz.

H/P09**THE APPLICATION OF NUCLEATION EXPLOSION MODEL FOR CALCIUM-PHOSPHATE COATING FORMATION IN BIOMIMETIC PROCESS**

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Biomimetic synthesis is successfully employed in technology of obtaining of calcium-phosphate coatings such as calcium hydroxyapatite (HAP) and octacalcium phosphate (OCP) on metal implants. In order to obtain calcium-phosphate coatings by biomimetic method it is necessary to define the conditions of heterogeneous formation of certain calcium-phosphate phase, the quantitative ratio of the forming phases and the values characterizing the processes of nucleation and crystal growth of calcium phosphates from aqueous solutions. As a rule, optimal growth conditions of this process are very difficult to define from the experiment. Thus development of method of calculation of named values is a relevant task.

In this work critical supersaturation (value below which heterogeneous crystallization is dominant) of nucleation of HAP, OCP, tricalcium phosphate (TCP) and dicalcium phosphate dihydrate (DCPD) in temperature interval 20-50 C was calculated using nucleation explosion model. Plots of induction time of nucleation and amount of nuclei versus temperature and supersaturation are obtained taking into account the value of interface (calcium-phosphate nucleus-solution) surface energy. The probabilities of formation of HA, OCP, TCP and DCPD nuclei in this system are estimated. The interface surface energy and supersaturation values at which heterogeneous nucleation is predominant in solution during the biomimetic process was determined. The calculated values of the critical supersaturation in an approach of nucleation explosion model for the biomimetic process are agree with experimental data.

H/P10**MICROWAVE-HYDROTHERMAL SYNTHESIS OF HYDRANGEA-LIKE CALCIUM PHOSPHATE**

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Hydroxyapatite (HAp, Ca₁₀(PO₄)₆(OH)₂) has been widely used as a bone substitute due to its structure similarity and biocompatibility with biological hard tissues such as bone and tooth enamel. Recently, crystals of calcium phosphate have received a good deal of attention as a delivery system, the artificial hematocyte, transfection of cells or gene because of their physical and chemical properties, and high surface interaction properties. In this study, the hydrangea-like calcium phosphate was precipitated from dilute calcium nitrate and ammonium dihydrogenphosphate by novel microwave-hydrothermal processing. The final products were characterized by x-ray powder diffraction (XRD), Fourier transform infrared spectroscopy (FTIR), and thermogravimetric analysis (TGA), and specific surface (BET). The XRD pattern of final precipitate in the reaction medium shows characteristic peaks pertaining to HAp phase with poor crystallinity. The hydrangea-like calcium phosphate has higher surface areas than the commercial powder.

H/P11**STUDY OF MICRO AND NANO SURFACE STRUCTURES FROM UV IRRADIATED URETHANE/UREA ELASTOMERS**

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In this work we address new results obtained with a thin free standing flexible film (120 m) of a urethane/urea copolymer related to the formation of micro and nano size structures. The copolymer was synthesized from a polypropylene oxide-based prepolymer with three isocyanate terminal groups (PU) and polybutadienediol (PBDO) with PBDO content of 40% wt. After casting and curing the film was cut into different samples and each exposed to UV radiation for different periods of time; 23h, 25h, 26h, 31h and 49h (=254 nm) and later extracted with toluene. The dried films were then studied by Polarising Optical Microscopy (POM), Small Angle Light Scattering (SALS) and the surfaces exposed to UV radiation analyzed by means of Atomic Force Microscopy (AFM). Before extraction with toluene a nanometer-flat surface, characterized by a mean roughness value Ra=0.59 nm, was obtained. Depending on exposure time to UV radiation and after extraction with toluene a corrugated surface, with features m-sized in all axes, resulting in a dramatic increase of the overall mean roughness value to Ra=105.4nm, starts to develop for a critical exposure time of 25h. As the exposure time increases the exposed surfaces show an increasing density of the structures observed and also an increasing characteristic peak-to-valley height. The peak-to-valley height measured for samples exposed for 23h, 25h, 26h, 31h and 49h is respectively 193, 383, 381, 1550 and 2039 nm and the corresponding mean roughness values are Ra=50.7nm, Ra=105.4nm, Ra=116.8nm, Ra=438.3nm and Ra=515.4 nm respectively.

The irradiation time dependence of the results will be analyzed in order to establish the relation between the molecular structure and the visco-elastic properties of the elastomer.

H/P12 USE OF SILVER CONTAINING HYDROXYAPATITE GRANULES IN THE RECOVERY OF INFLAMED BONE DEFECTS

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In vitro and in vivo tests were carried out with hydroxyapatite (HAp) granules incorporated with 0.15, 1.5, and 4.3 mol% of silver (Ag) to explore their potential application as a bone filler with antibacterial properties. According to the in vitro test, the degree of cytotoxicity was dependent on the amount of Ag. With 0.15 mol% of Ag, mild cytotoxicity was observed, while cytotoxicity increased to a moderate level with the increase of Ag to 1.5% and 4.3% in the standard agar overlay assay. The in vivo test was carried out by implanting Ag-HAp granules in artificial bone defects of rats and no remarkable cytotoxicity was found unlike what was observed in the in vitro data. All of the implanted Ag-doped HAp granules, regardless of Ag contents, allowed appropriate cellular proliferation and favorable bone repair without remarkable inflammatory reaction during 3 weeks of healing periods except for the mild delay in organization of fibrin and inflammatory reaction with the 4.3% Ag doped HAp at the early healing phase. New bone formation with osteointegrative and osteoconductive properties were successfully supported by the granules. The results suggest that HAp doped with Ag up to 4.3% of total cations can be applied for repair of infection-associated bony defects.

H/P13 SOME ASPECTS RELATED TO HYDROXYAPATITE FORMATION FROM NATURAL RESOURCES

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This work is focusing on preparation processes of hydroxyapatite and other calcium phosphates from biogenic materials that are available in large quantities in nature. Hydroxyapatite (HAP) is known as a highly bioactive inorganic material. Therefore, it presents widespread applications in tissue engineering and bone replacement. In this study calcium phosphate-based bioceramics have been synthesized by using eggshell-derived raw materials and phosphoric acid at different molar ratios. In order to get the full use of the benefits provided by high percentages of calcium carbonate in eggshell, it is crucial to optimize the entire synthesis process. Development of the elaboration processes has been conducted to gain mono-phase HAP. Because of unfavorable mechanical properties of porous HAP and calcium phosphate-based ceramics, importance should be given to composite processing. Morphological, structural observations, as well as characterization of mechanical properties will be presented.

H/P14 OPTICAL PROPERTIES OF PORPHYRINE MOLECULES IMMOBILIZED IN NANO-POROUS SILICON MATRIX

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Nano-porous silicon (pSi) has found recent application in controllable and targeted drug delivery. For this purpose its bio-degradability is mainly explored - while being dissolved in corporal fluids pSi releases into the environment the substances preliminarily introduced into the pores.

We have studied the possibilities for bio-medical implementation of non-linear optical properties of pSi. In this research we studied optical properties of porphyrine deposited into pSi matrix. Porphyrines are known for their efficient photo-generation of singlet oxygen (excited oxygen molecule with anti-parallel spins of electrons), very strong oxidant of organic molecules and living cells. Combination of photo-chemical activity of porphyrine with non-linear optical properties of pSi and its bio-degradability can be very perspective for design of new methods of therapy. We have concentrated on 1) methods of immobilizing the porphyrine molecules on the walls of porous silicon and 2) optical response of absorbed porphyrine. Obtained results show unambiguously that by using pSi in combination with post-growth treatments, on the one hand, and cationic forms of porphyrines, it is possible to achieve very good optical response of the system and open perspectives its application for singlet oxygen generation.

H/P15 KINETIC MEASUREMENTS OF ACETYSALICYLIC ACID RELEASE FROM MG-AL LAYERED DOUBLE HYDROXIDES

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Development of the drugs with pre-defined regime of an active component release is a very important problem of modern pharmacology. One of the ways to control drug release is an encapsulation of active substance into neutral non-toxic matrix. Promising matrices for the preparation of depot pharmaceuticals are anion-substituted layered double hydroxides (LDHs). The structure of LDH consists of positively charged hydroxide layers, which enable to intercalate any biologically active anions into the interlayer space.

In the present work the release of acetylsalicylic acid (AA) from $Mg_3Al(OH)_6[(AA)_x(CO_3)_{2-x}] \cdot nH_2O$ LDH was studied by UV-VIS spectroscopy and using radioactive tritium label. It was shown, that the increase of LDH synthesis pH from 8 to 12 results in the increase of drug release time and the decrease of total amount of AA intercalated into the interlayer space. The optimal pH of synthesis was found to be 11 with corresponding half-release time of 40 minutes. Kinetics of acetylsalicylic acid release in hydrochloric acid media with pH from 1 to 7 was studied. Release of AA from commercially available acetylsalicylic acid-containing drugs (Aspirin®) was compared with the release of AA from powder LDH and pellets pressed at $P = 7500, 22600, 37700, 52700$ kPa.

H/P16**POLYURETHANE CATHETER WITH SUSTAINED ANTIMICROBIAL EFFECT**

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Interventional radiology enabled the minimally invasive diagnostics and therapeutic procedures. With the use of catheter based technology, vascular and non-vascular conditions can be treated with minimally invasive techniques under guidance with various imaging tools. The catheter-associated infection is usually assumed to be rare and asymptomatic. But it may be associated with significant morbidity, fever, chronic renal failure. Therefore lasting care should be taken to avoid infection. In this work, catheter comprising antimicrobial agent was developed to reduce the concern of infection. Hydroxyapatite (HAp) is a well known biocompatible material. It can also incorporate antibiotic ion such as silver to control bacterial infections. In this work, Ag doped HAp was synthesized through co-precipitation route and introduced in the preparation of catheter aiming sustained antimicrobial effect. As a matrix, medical grade polyurethane was hybridized with co-precipitated Ag-HAp. In the preparation of HAp from $\text{Ca}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$ and $(\text{NH}_4)_2\text{HPO}_4$, washing is known to be essential to remove NO_3^- and NH_4^+ radicals that are detrimental to phase stability. However, in the synthesis of Ag-HAp through co-precipitation, washing needs to be avoided to conserve the introduced Ag ion. Microscopic observation on the synthesized composite showed that degree of the powder agglomeration was dependent on the sequence of mixing. Due to the low viscosity of pure DMF compared with polyurethane dissolved DMF, Ag-HAp powder dispersed in pure DMF led to the homogenous distribution after preparation of hybrids. The antimicrobial test showed that co-precipitated Ag-HAp effectively suppressed the reproduction of E.Coli. until 1000 h contrary to ion exchanged Ag-HAp.

H/P17**HEXAKIS-[b-(5-METHOXY-3-INDOLYL)-ETHYLAMINO] CYCLOTRIPHOSPHAZENE: SYNTHESIS AND QUANTUM-CHEMICAL CALCULATION**

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We have synthesized the hexakis-[b-(5-methoxy-3-indolyl)-ethylamino] cyclotriphosphazene and its complexes with the neutral metallocontaining molecules CuCl_2 , CoCl_2 and ion $[\text{PtCl}_6]^{2-}$. These compounds are of potential interest as pharmacological active ingredients. The quantum-chemical calculations have permitted to establish geometrical structure and to study their electronic properties. Molecular electrostatic potential was calculated (Figure 1.) for a finding of reactionary centres. The data will assist to construct possible molecular architectures for different hexasubstituted cyclotriphosphazene complexes with neutral molecules and ions.

This research was supported by Russian Foundation of Basic Research, Project #8470; 03-03-33157 and Russian Ministry of Education and Science "Leading R&E Teams". 3D graph of the molecular electrostatic potential of the hexakis-[b-(5-methoxy-3-indolyl)-ethylamino] cyclotriphosphazene. zene.

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