Surface Modification of Materials by Plasmas for Medical Purposes Focus Topic
Room: 211D - Session SM+AS+BI+PS-ThA

Plasma Processing of Biomaterials and Biological Systems
Moderator: David Graves, University of California, Berkeley, Jean-Michel Pouvesle, GREMI CNRS/Université d'Orléans

2:20pm **SM+AS+BI+PS-ThA1 Matching Plasma Sources with Intended Biomedical Outcomes: Open Questions in Modeling of Plasma Surface Interactions**, *W. Tian*, University of Michigan, *S.A. Norberg*, US Military Academy - West Point, *A.M. Lietz*, University of Michigan, *N.Yu. Babaeva*, Joint Institute for High Temperatures, ***Mark Kushner***, University of Michigan **INVITED**

Plasma surface modification of materials for biomedical applications typically involves atmospheric pressure plasmas in the form of dielectric barrier discharges (DBDs) or atmospheric pressure plasma jets (APPJs). In many cases, APPJs operate similarly to DBDs with an ionization wave (IW) propagating through a rare-gas dominated gas channel. The intersection of the IW with the surface being treated, for example tissue, in both DBDs and APPJ produces locally large fluxes of ions, UV/VUV photons and electric fields onto the surface. These fluxes are collectively *hard fluxes* due to the higher levels of activation energy they represent. Remote DBDs and APPJs where the plasma plume does not intersect the surface produce *soft fluxes*, dominated by neutral reactants. The character and ratios of *hard-to-soft fluxes* and their compositions are functions of flow dynamics, ambient conditions (e.g., humidity) and pulse power waveforms. In many biomedical applications, the tissue is covered by a liquid (or the intended surface is liquid as in plasma activated water). In these cases, plasma produced activation energy, radicals and ions must penetrate through the plasma-liquid interface, where liquid phase mechanisms then determine the reactants to the tissue. From one perspective, significant advances have been made in modeling these processes and furthering our understanding. From another perspective, there are still significant open questions that models need to address, including the manner of coupling of the gas phase plasma and liquid, gas induced fluid dynamics, long term evolution of the liquid chemistry, reactions at the surface of the tissue and control schemes to minimize variability. A brief overview of progress in modeling plasma modification of biomaterials will be provided followed by examples of the authors' modeling works for APPJs and DBDs intersecting with model tissues and liquids.

3:00pm **SM+AS+BI+PS-ThA3 Plasma Processing of Biomimetic and Sintered Calcium Phosphates for Bone Regeneration and Repair**, ***Cristina Canal***, Technical University of Catalonia, Spain **INVITED**

Large bone defects caused by trauma, osteoporotic fractures, infection and tumour or cysts resection pose a great clinical and socio economic problem. Bone grafting materials respond to the need generated by over 2 million bone grafting procedures that are performed every year worldwide. As an alternative to autografts or xenografts, different biomaterials have been proposed, yet with partial success since different aspects remain yet to be improved.

In this context, the use of low pressure (LP) and atmospheric pressure (AP) plasmas opens new opportunities in the field of bone biomaterials. It is the aim of this talk to provide an overview on the strategies undertaken in our group to enhance diverse features of bone biomaterials and to enhance bone therapies.

The examples discussed here include biomimetic hydroxyapatite (HA) and β-tricalcium phosphate (β -TCP) as the most clinically used calcium phosphate (CaP) ceramics for bone regeneration. Some of the points of improvement include increasing their mechanical strength, or using them as local dosage forms for the delivery of drugs, to aid in different therapies, such as combating infection or fighting cancer.

For instance, we have investigated LP plasmas with the aim of expanding the use of biomimetic CaPs to load-bearing sites. Although composites have been defined, their performance is not yet optimal, possibly due to insufficient adhesion between the matrix and the reinforcing agent. Oxygen and argon plasmas have been employed in the surface modification of polylactide fibers to improve the adhesion at the interface between them and biomimetic CaPs with interesting results.

In a different approach we have focused on modulating drug delivery from bone biomaterials. Both AP and LP plasmas are of interest with views on different medical applications and in the design of advanced biomaterials with controlled drug release properties. Different strategies are considered with that aim, such as using either plasma functionalization with AP plasma jet to modulate the interactions of the drug with the CaP surface or employing LP plasma polymerization on CaP scaffolds as a strategy to control the drug release. Lastly, AP plasmas are in the limelight due to their wide potential in the medical field, and here we will discuss some recent findings for application in bone therapies and regeneration.

Acknowledgements

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4:00pm **SM+AS+BI+PS-ThA6 Plasma Processing of Biomaterials and Biomedical Devices**, *H.J. Griesser, T.D. Michl, S.S. Griesser, M. Jasieniak, H.H. Mon*, ***Bryan Coad***, University of South Australia **INVITED**

Gas plasmas have attracted considerable attention over more than 40 years as a convenient method for changing the surface chemical composition of biomaterials and thereby alter and control the interfacial interactions between biomedical devices and contacting "biology" such as protein solutions, blood, cells and tissue, and bacterial biofilm growth. Plasma technologies are already in use on a large industrial scale in several biomedical device companies; for example 30-day contact lenses use a thin plasma coating to confer wettability and low fouling to silicone-based contact lens materials. Bio-interfacial interactions are very short range, and hence it is sufficient to apply ultrathin coatings (< 20 nm thick). Plasma techniques are ideally suited because process control is straightforward and the resultant surface modifications or coatings tend to have a high degree of uniformity and reproducibility compared with other, solution based coating methods. On the other hand, the complex chemical composition of plasma gas phases prevents fine control of chemistry to the extent achievable by conventional chemical approaches. Detailed surface analysis is essential.

Plasma approaches are useful to produce coatings designed to combat the problem of bacterial and fungal biofilm growth on biomedical devices, which leads to infections and delayed healing. One approach is the use of organochlorine plasma polymer coatings, which are highly effective at contact killing. Other, cytocompatible approaches comprise the use of plasma polymer coatings that release NO or available antibiotics such as levofloxacin. A different approach entails the covalent immobilization of a monolayer of antimicrobial molecules onto a thin plasma polymer interlayer whose function is to provide good adhesion and reactive surface chemical groups that can be used to attach antibiotics. Such covalently grafted monolayers have given excellent deterrence of attachment and biofilm formation of bacteria and pathogenic fungi.

4:40pm **SM+AS+BI+PS-ThA8 Organs on a Chip – Biointerfaces in Stem Cell Research**, ***Kevin Healy***, University of California at Berkeley **INVITED**

Highly regulated signals in the stem cell microenvironment such as ligand adhesion density, matrix stiffness and architecture, and growth factor presentation and concentration have been implicated in modulating stem cell differentiation, maturation, tissue formation, and ultimately function. My group has developed a range of materials systems and devices to study and control stem cell function and their self-organization into three-dimensional microtissues (e.g., 'organs on a chip'). These systems are being developed for screening molecular therapies and patient specific medicine via *in vitro* disease specific tissue models. Examples of how biointerface science is important in these applications will be highlighted. The benefits of our approach include: 1) robust and reproducible platform embodies precision microengineering to create better microtissue environments; 2) precise delivery of molecules (e.g., drugs) in a computationally predictable manner; 3) ability to model human cardiomyopathy; and, 4) cost efficient and high content characterization of cardiac tissue drug response.

5:20pm **SM+AS+BI+PS-ThA10 Effect of the Radical Species for Gene Transfection by Discharge Plasma Irradiation**, ***Yoshihisa Ikeda***, *M. Jinno*, Ehime University, Japan

Gene transfection is a technique of deliberately introducing nucleic acids into cells in order to give them specific characteristics. In practice, this can be achieved in three different ways: chemical method, physical method and the viral vector method.

One of the physical methods that uses discharge plasma irradiation was invented by Satoh, who is one of the authors, and his group in 2002. Since this technique is free from adverse effect associated with viruses, there are no risks as the others mentioned above. The plasma irradiation on genes and cells induces the transfection process in which the genes and cells are exposed to discharge current, charged particles and chemically reactive species.

The authors investigated the factors for plasma gene transfection by changing protocols and looked at the time periods the factors become effective. The results is that transfection rate drops to 1/10 of the standard protocol when the charged particles and chemically reactive species genes are washed out from the wells by PBS solution 60s after plasma irradiation. Since the life times of the charged particles delivered from plasma to the plasmid solution is less than 60s, the direct effect of the charged particles causing transfection finishes before wash out process. This means that nearly 1/10 of transfections occur during plasma irradiation and that the last 9/10 of transfections occur after plasma irradiation is stopped. This second stage transfection is mainly caused by the residual chemically reactive species, however, plasma irradiation stress to cells and plasmids also induces transfection., i.e. possibly charging effect and oxidation stress induce bio-chemical process of the cells in addition to the chemical reactions on the cell membrane and plasmid induced by chemically reactive species such as radicals.

5:40pm **SM+AS+BI+PS-ThA11 Nonlinear Optical Spectroscopic Observation of Plasma-Treated Bio-Specimen**, ***Kenji Ishikawa***, *R. Furuta, K. Takeda,* Nagoya University, Japan, *T. Nomura, T. Ohta,* Meijo University, Japan, *H. Hashizume, H. Kondo,* Nagoya University, Japan, *M. Ito,* Meijo University, Japan, *M. Sekine, M. Hori*, Nagoya University, Japan

Applications of nonequilibrium atmospheric pressure plasma (NEAPP) to the medical field have been reported in recent years. However, a mechanism of interactions between NEAPP and living cells has not been yet elucidated comprehensively. Our strategy for elucidation of plasma-biomaterial interactions is to observe reactions *in situ* at real time. By applying nonlinear optical spectroscopic techniques, the vibrational sum-frequency-generation (SFG) and multiplex coherent anti-Stokes Raman scattering (CARS) microscopy, which are a beneficial tool for addressing best sensitivity at surface and interface, have been used in this study. By using SFG, we have explored topmost surface modification after the interaction between plasma and biopolymeric materials. For the NEAPP-induced reactions on budding yeasts as an eukaryotic cell model, a two-dimensional mapping of budding yeasts treated by the plasma using the CARS microscopy was observed with fluorescence label-free contrasts of chemical vibrational nature. The biomedical imaging of cell membranes, intracellular organelles, nucleus and so forth, was revealed to decompose intracellular membrane by exposure of plasma-generated chemically reactive species, especially for induction of lipid peroxidation. These results will be useful for understanding the plasma induced reactions in the plasma medicine.

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