ACS APPLIED MATERIALS & INTERFACES

Editorial

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Preface: Forum on Frontiers and Challenges in Biomaterials

This *ACS Applied Materials & Interfaces* special Forum is focused on new frontiers and challenges in biomaterials and their analysis. In a recent meeting with colleagues discussing new directions for a multidisciplinary biomaterials proposal, we were asked "What is the "Holy Grail" in biomaterials research?" Alternatively, "What are the grand challenges in biomaterials research?" poses the same question using language recently adopted by the National Science Foundation in its report on the 2012 NSF Workshop entitled "Biomaterials: Important Areas for Future Investment" (http://nsfbiomatworkshop2012.caltech.edu/report/index.html). Either way the question is asked, the answer for many biomaterials researchers usually entails topics relevant to "biocompatibility." Beyond that, creation of complex multiscale functional materials that are responsive to their environment, development of experimental analysis techniques capable of accurately reflecting materials properties as well as material-biomolecule interactions, and creation of theoretical models to predict function−structure properties are all challenges that need to be addressed in the field of biomaterials.

The notion of overcoming one of the prevailing challenges in materials research, namely the so-called "biocompatibility" problem that arises when synthetic materials come in contact with cells and tissue, provides an ideal platform for introducing this Forum. Notably, biocompatibility issues can be addressed by (i) better understanding biological events that occur at the interface between the synthetic surface and blood or tissue and (ii) designing advanced materials that can direct biological events at the biointerface. The articles included here, based on content presented in a Colloids and Surface Division symposium at the 2013 Spring National ACS Meeting, broadly span both of these approaches and provide a useful starting point for highlighting various aspects across the entire spectrum of the field.

Understanding biological events at biointerfaces often requires new analysis and probe techniques, tailored surface chemistries and topographies, and creative surface modification strategies. Advancements in surface techniques such as scanning probe microscopies (Raigoza et al.) and femtosecond laser desorption mass spectrometry (fs-LDPI-MS) allow for better understanding of the material interactions in biologically relevant media. For example, conductance-based sizing methods provide accurate tuning of nanopore dimensions for single molecule sensing elements to examine biological nanoscale environments (Frament et al.). Likewise, fs-LDPI-MS measurements of *E. coli* cocultures and 3D multispecies biofilms allow for spatially resolved images of biofilm formation at interfaces without sample damage and without using a complicating matrix (Cui et al.). Surface modifications such as nanopatterning to produce smart polymers and spatial immobilization of multiple biomolecules can direct biological events at surfaces (Yu et al.). Precise control over surface structure into brushes and placement of active groups using multiple click strategies yields a level of control previously not attained by other methods (Bally et al.). Furthermore, these new methods are more straightforward and provide superior processing conditions than were available with initial generations of biomaterials. Plasma-treatment also offers advantages in tailoring surface properties without causing damage, while achieving even and stable coatings (Fisher). Still, critical analytical challenges remain in characterizing plasma-treated materials for 3D constructs, including distinguishing between material−cell interaction effects arising from changes in chemistry and/or topography induced by plasma treatment. (Are improved biomolecule interactions caused by surface functional groups or by the physical properties of the surface?) Finally, a super resolution method (mbPAINT) was developed to elucidate the positions of a particular sequence within a longer single-stranded DNA that has been immobilized on a substrate (Chen et al.). Given the importance of DNA as biomaterials, this technique afforded a an order improvement in the resolution compared with traditional optical methods

New materials design efforts have focused on overcoming biofouling on surfaces by preventing bacterial adhesion and blood interactions without introducing tissue toxicity. The size, shape and surface features of nitric oxide (NO) releasing nanoparticles play an important role in the kill efficiency when NO release levels are maintained (Slomberg et al.). Furthermore, the size and shape of the particles influence gram positive and negative bacteria differently, with the latter exhibiting the greatest susceptibility to NO with limited antimicrobial resistance. For composite-based NO materials used to prepare blood-contacting devices, it is important to determine whether the NO is released from the bulk material, the surface of the material, or in the buffer (Joslin et al.). This information is valuable for determining critical thresholds of NO to mediate clotting, but also for understanding the NO donor behavior in complex polymeric microdomains. Three-dimensional collagen−hyaluronan composite materials with tunable mechanical and chemical properties are being developed to understand cell migration in glioblastoma multiformed tumors in the central nervous system (Rao et al.). Combining microscopy with cell morphology and spreading techniques, these studies will influence treatment options for cancer patients and offer a model to investigate the migration capacity of other cancer types. An overarching challenge in all of these systems is the need to detangle the material data as it relates to cell behavior because the material properties and the biological microenvironments are inherently intertwined. Indeed, the ability to develop overarching guiding principles from promising results related to a single attribute (e.g., cell type, bacterial type, antimicrobial mechanism, material architecture, or chemistry) remains both a new frontier as well as a grand challenge in biomaterials research. As editors, we were delighted to see that many of the articles in this Forum seek to draw larger picture conclusions that at a minimum begin to take the first steps at focusing on the entire system as

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opposed to just one aspect of what are, by their very definition, very complex systems.

Notably, from an applications viewpoint in the world of biomaterials, all material–cell interactions must maintain the delicate balance between cytotoxic and protective effects. For synthetic materials to be effective therapeutics, they must exhibit therapeutic action over the requisite time domain, but must also maintain the function of normal cells over that same time domain. Without the ability to create and sustain the balance between cytotoxic and protective effects, a truly therapeutic surface will never be realized. Furthermore, appropriate cell conditions such as serum-free media and appropriate concentrations for the application are necessary to control materials behavior. An example of such an approach was demonstrated recently for polymers (e.g., conjugated phenlylene ethynylene-based polymers and oligomers) that are known antimicrobials (Wilde et al.). Investigations examining the cytotoxic behavior of the materials in both tissue and bacterial cultures truly provide a more comprehensive picture of the anticipated outcomes of specific materials of potential use in biomedical devices.

Despite significant advances on both the scientific and practical aspects of biomaterials research, much remains to be explored. Notably, as the outcomes of the NSF workshop on biomaterials research highlighted, the next generation of advances in biomaterials will have an enormous economic impact on the world's population from human and animal health care to creation of new sources of energy to environmental protection. The field of biomaterials will also undoubtedly impact our approach to truly multidisciplinary education as chemists, physicists, biologists, and engineers are all important to the development of revolutionary materials and devices. Remarkably, articles in this Forum provide a genuinely panoramic view of the range of diverse challenges that must be addressed as well as the wide open frontiers that are accessible to the next generation of biomaterials researchers.

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Notes

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