

BIOLOGICAL APPLICATIONS OF POLYMER BRUSHES

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Polymer brushes are polymer coatings in which polymer chains are tethered on one end to a surface at sufficiently high grafting density such that steric repulsion between the chains causes chain stretching. The polymer coating thickness is typically dictated by both the polymer chain length and surface graft density, and ranges from a few nanometers to several hundred nanometers. Thus, polymer brushes occupy a unique interfacial niche between self-assembled monolayers that are typically only a few nanometers thick and spin-cast polymer films that are typically thicker than several hundred nanometers. The synthesis of ultrathin, dense polymeric films and structures on surfaces has been a long standing challenge in interface science because packing polymer chains at high density onto a surface is difficult to achieve via methods that involve grafting polymers from the vapor or solution phase on to a surface, due to the intrinsic thermodynamic penalty for additional surface grafting that arises from size exclusion. The recent development of highly controlled polymer synthesis techniques largely based on controlled radical polymerizations that can be carried out from surface-tethered polymerization initiators, has allowed this thermodynamic constraint to be circumvented, and enables the facile, surface-initiated synthesis of polymer brushes with a broad range of chemical and structural properties.

In reviewing the field, we have come to the conclusion and one that may excite raucous debate that the most promising technical advances in using polymer brushes have been associated with their biointerfacial applications, as defined by the interaction of these brushes with biological macromolecules, supramolecular assemblies, and cells. This In-Focus section contains a set of papers that provides the reader with an idea of the breadth of the field associated with polymer brushes at biointerfaces, ranging from robust methods of brush synthesis and patterning, their use for protein imprinting, to the design of sophisticated macromolecular architectures to control protein and cell adhesion.

Surprisingly, despite the wealth of approaches for polymer brush synthesis that are now available, the substrates used to grow polymer brushes have been largely confined to glass and gold. Similarly, methods to pattern polymer brushes over large, e.g., wafer-scale, areas are also scant. Hucknall *et al.* address these challenges, and demonstrate the synthesis of protein and cell-resistant poly(oligo(ethylene glycol) methyl methacrylate) (POEGMA) brushes over large areas on a range of substrate materials via simple and versatile methods. Furthermore, they present complementary ap-

proaches to pattern these polymer brushes with high fidelity and reliability on the wafer-scale for device production.

There has been a proliferation of methods to grow stimulus-responsive polymer brush coatings that can be suitably functionalized to regulate biological function in response to an external stimulus. These methods enable the design of polymeric interfaces that can dynamically control the presentation of regulatory signals with applications that span the modulation of biomolecule activity, coatings that dynamically control drug permeation through nanoporous membranes, and substrates that control cell and protein adhesion. Here, Ionov *et al.* report on a novel approach that uses mixed polymer brushes with gradually changing charge composition to fabricate pH-sensitive surfaces that produce reversible gradients in protein adsorption. The paper by Arifuzzaman *et al.* describes amphiphilic polymer brush coatings whose chemistry and stimulus responsiveness can be tailored to protect against marine biofouling—a particularly vexing biointerfacial problem and one for which a solution has so far proved elusive. Their innovative approach, using amphiphilic copolymers comprising EG and fluorinated groups, stemmed from the crucial insight that a polymer brush that presents only a single chemical moiety was likely to be insufficient to prevent marine fouling. Control over cell adhesion is an important goal in the design of biomedical implants to improve their biocompatibility and integration with surrounding tissue. Raynor *et al.* show that titanium implants, modified with POEGMA brushes that present a bioactive peptide, promote osteoblast differentiation and enhance osseointegration.

The function of bioanalytical devices, such as biosensors, heterogeneous immunoassays and microarrays, depends critically on generating a sufficiently large signal-to-noise ratio in response to the presence of an analyte of interest, so that minimizing nonspecific binding to reduce noise and maximizing specific binding between the analyte and a capture agent on the surface the receptor is a critical requirement. The immobilization of poly(ethylene glycol) (PEG) is the most commonly employed approach to render surfaces resistant to the adventitious and undesirable adsorption of proteins, cells and other biological components. However, synthetic polymer brushes, such as POEGMA as described by Hucknall *et al.*, or polypeptoid brushes, such as described by Statz *et al.*, have marked advantages over simple PEG coatings. In comparison with linear or branched PEGs that are grafted to a surface either by physisorption or covalent attachment and whose surface density cannot be increased

beyond a relatively low surface coverage, the thickness and surface density of oligoethylene glycol functionalized polymer chains in polymer and polypeptoid brushes can be significantly greater, which is critical to eliminating protein adsorption and cell adhesion on their surface. The paper by Statz *et al.* also provides a nice example of the use of molecular theory for the rational design of nonfouling polymer and polypeptoid brush coatings.

In bioanalytical devices such as diagnostics and sensors, it is not only necessary to reduce background noise resulting from nonspecific binding interactions, but it is also important to increase the signal by imparting molecular recognition to the substrate, to preferentially capture the desired molecule—the analyte—from a complex soup of biomolecules. Although biomolecules are typically used as the receptor in

these applications, synthetic polymer structures can be directly used as the receptor through biomolecular imprinting. Here, Zdyrko *et al.* show how synthetic polymer brushes, using solvent assisted polymer grafting, can be harnessed for the fabrication of synthetic materials that are capable of recognizing a specific protein.

From this brief synopsis, we hope, it is evident that polymer brushes provide exciting platforms for the design of precision molecular interfaces for biological applications. Although this is a nascent field, the diverse set of papers in this In-Focus edition suggests that the biointerfacial applications of surface tethered polymer brushes are likely to yield a wealth of new physico-chemical properties and applications in the decades to come.