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Review

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Exploration of Plasma-Enhanced Chemical Vapor Deposition as a Method for Thin-Film Fabrication with Biological Applications

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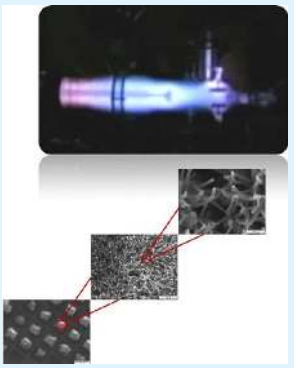
ABSTRACT: Chemical vapor deposition (CVD) has been used historically for the fabrication of thin films composed of inorganic materials. But the advent of specialized techniques such as plasma-enhanced chemical vapor deposition (PECVD) has extended this deposition technique to various monomers. More specifically, the deposition of polymers of responsive materials, biocompatible polymers, and biomaterials has made PECVD attractive for the integration of biotic and abiotic systems. This review focuses on the mechanisms of thin-film growth using low-pressure PECVD and current applications of classic PECVD thin films of organic and inorganic materials in biological environments. The last part of the review explores the novel application of low-pressure PECVD in the deposition of biological materials.



KEYWORDS: *PECVD, coating techniques, thin films, biological materials, cell culture, amino acids*

1. INTRODUCTION

Ultrathin films of polymeric and soft matter deposited via different coating techniques has been an area of increasing interest as these materials can be adapted for use in optical, electronic, biological, and sensing applications. Traditional techniques for the fabrication of thin films include simple solution and dip casting, spin-casting, spin-assisted layer-by-layer (LbL) assembly, self-assembled monolayer formation, Langmuir−Blodgett film formation, and vapor deposition. Chemical vapor deposition (CVD) is a versatile method for fabricating polymeric thin films using a vapor phase polymerization reaction that virtually eliminates the challenges associated with wet chemical synthesis of thin films on various surfaces.[1] CVD offers a facile method to overcome many of the issues associated with other surface coating methods while providing conformal, uniform coatings in a single, dry chemical fabrication step. CVD techniques have traditionally been applied to inorganic materials in the semiconductor industry and more recently to carbon-based structures such as carbon nanotubes and graphene.[2−4] The origins of polymeric CVD can be traced back to Gorham et al. where the polymerization of *p*-xylylene was investigated under heating in a vacuum.[5] Their work established the reaction mechanism in which two species react with others in a rapid step-growth type reaction.

Many CVD processes have been designed to allow monomers to undergo in situ polymerization during the deposition process resulting in a stable film of polymerized material on a variety of surfaces.[6−8] Hybrid techniques such as plasma-enhanced CVD (PECVD), initiated CVD (iCVD), oxidative CVD (oCVD), metal oxide CVD (MOCVD), atmospheric pressure CVD (APCVD), and low-pressure CVD (LPCVD), classified according to the deposition conditions, present a broad spectrum of possibilities in thin film deposition (Table 1).[9−13] These hybrid deposition methods provide a means of formation of soft matter thin films from a broad range of materials and each deposition method creates a polymerized film on a target substrate with variations in the morphology depending on the reaction mechanisms.[14] Each of the above fabrication techniques present a set of advantages and drawbacks, making them uniquely suited for specific thin-film production; although, one overarching technique that addresses all processing issues and is universally applicable is not currently feasible. A key advantage of these processes is the retention of specific chemical functionalities allowing the construction of chemically tailored surfaces and interfaces that can be designed for specific interactive, detection, or responsive applications. Control of the surface chemistry, chemical and physical cross-linking, and retention of functional groups allows the deposited films to be tailored for specific uses.

Plasma processes in the formation of thin films are generally used in three ways: plasma etching, plasma grafting of new functional groups, and finally, plasma-enhanced CVD.[15,16] PECVD, the main focus of this review, is a form of CVD

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Table 1. Compilation of Common Thin Film Fabrication Techniques

technique	description	attributes
physical vapor deposition (PVD)	Monomer is vaporized and adsorbed on surface and may require substrate modification for adhesion/growth.	• material is physically deposited on a surface • surface initiator may be needed to ensure grafting • post-deposition curing used
chemical vapor deposition (CVD)	The vaporized monomer undergoes a chemical reaction/interaction and is adsorbed on a surface in a chemically altered state.	• widely used in microelectronic fabrication for inorganic materials • readily adapted for use with organic monomers.
plasma enhanced CVD (PECVD)	Nonthermal RF plasma used to radicalize a monomer creating chemical reactive species for uniform coatings at low temperatures. Generally, depositions occur at low pressure but atmospheric pressure PECVD (AP-PECVD), which can use a dielectric barrier discharge (DBD), has also been explored recently.	• highly cross-linked, uniform, robust films with good surface adhesion • may suffer from high internal stresses, which can cause film delamination • compatible with solid, liquid, and gas monomers • AP-PECVD leads to higher deposition rates and high density of cross-linking
initiated CVD (iCVD)	Chemical initiator vaporized simultaneously with the monomer to initiate chemical reaction/chain formation via radicals. Activated by UV light or heat.	• films show high deposition rate and high functional group retention • chemical initiator begins polymerization and an additional cross-linking agent • limited to gas phase initiators
oxidative CVD (oCVD)	Oxidizing agent vaporized simultaneously with the monomer to induce reaction.	• used in the deposition of conductive monomers and show high conductivities • can only be used in case of monomers that are stable in the presence of strong oxidants
hot-wire CVD	Heated filament wire used to activate a monomer, usually through decomposition.	• lacks use of chemical initiator • heating of input gases decomposes them to a state where they become reactive

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which uses plasma to enhance/enable the reactivity of organic/inorganic chemical monomers for the deposition of thin films. This increased reactivity allows a broad range of materials to be used as precursors, including those that are typically considered inert. PECVD is a versatile fabrication method that is capable of utilizing precursors in either solid, liquid, or gas form for the facile, rapid and solvent free fabrication of thin coatings.[17,18] Plasma deposited films often have unique physiochemical and mechanical properties due to the controlled variation of process parameters in comparison to films deposited by other thermal deposition techniques. The PECVD process allows fabrication of pinhole free films while maintaining the substrate morphology and precise control over the thickness of the films. Typically, the PECVD deposited thin films are chemically inert, insoluble, mechanically tough, and thermally stable films because of highly branched and cross-linked architectures. Plasma-polymerized thin films exhibit excellent substrate adhesion, which offers resistance to solvent treatments; multiple exposures to heat, humidity, and atmosphere; and mechanical wear. The ability to deposit a monomer as a stable thin film on a substrate is complicated at times because of wet synthesis methods requiring complex chemistries, harsh solvents and extensive surface modifications for molecular attachment. Many of these issues are eliminated in PECVD because the plasma induces radicalization in the monomer and activates the substrate surface. PECVD facilitates not only thin film deposition and the chemical modification of surfaces but can also be used for the fabrication of nanostructures. Such a process has been adapted for use with soft matter and is compatible at low temperatures and low power. Most reports involve the use of monomers that are either in the gas or liquid phase since these are easily vaporized and induced into the plasma stream and are compatible with the majority of reactor constructs.[19−21] A limited number of studies report the use of direct sublimation of solid precursor monomers.[22−24] The use of sublimation for solid monomers deposition opens up PECVD to many atypical material systems and is worthy of further exploration. The two major constraints in the application of PECVD for the deposition of thin films are whether the monomer has the ability to be vaporized into the plasma stream via direct vaporization, heating, or sublimation, and second, the extent of dissociation of the monomer in the presence of applied plasma, which may cause significant damage to the monomer.

PECVD was originally developed for the deposition of inorganic materials such as metal silicides, transition metals, different oxides and nitrides and has now been extended to organic molecules as well.[10,25] Industrially, amorphous silicon, silicon nitride, and silicon dioxide films have been deposited using high-power PECVD for flat panel displays and in antireflective coatings for solar cells.[26] PECVD is most widely used in the semiconductor industry for the deposition of silicon dioxide for temperature sensitive devices. PECVD has been recently adapted to successfully deposit a wide range of monomers, ranging from styrene, acrylonitrile, and benzene to responsive materials such as vinyl pyridine and N- isopropylacrylamide to biological materials including amino acids and peptides.[19,22,27,28] There is a growing interest in the deposition of biological molecules via PECVD, which can potentially be used to enhance surface functionalities and structures for cell viability and can bridge the interface between abiotic and biotic components in integrated systems.[3,29−31] Several plasma-deposited thin films are considered "biocompatible". The plasma-deposited thin films are cross-linked and therefore avoid leaching into the surrounding environment while providing the required functionality. Plasma-polymerized films have been used in various applications such as sensors, implant coatings, optical modifying agents, and biofunctional films.[29,32,33]

Most of the reported PECVD depositions occur at reduced pressure to stabilize the discharge plasma but there have been reports of deposition at atmospheric pressure.[13,34,35] The purpose of this paper is to review the current applications of low pressure PECVD in the deposition of biological materials as well as other inorganic precursors with potential applications in biology. The common mechanisms of the growth of the PECVD films will be discussed but it is not a full description of the PECVD process, which has been reported elsewhere.[36] Finally, the challenges facing the technology and the future direction will be presented as it relates to biologically relevant functional films.

2. REACTION CONDITIONS AND PROCEDURES

PECVD mainly uses radio frequency (RF) plasma, at room temperature, to induce radicalization of monomer species in the reaction chamber.[37,38] While several methods can be used to generate the plasma including electron cyclotron resonance, inductively-coupled or capacitively-coupled parallel plates, the most commonly employed one is the capacitive-coupled parallel plate configuration.[39] The plasma used in the PECVD process can have diverse characteristics such as ion density and temperature. Generally, the power supply used for the plasma generation process has a RF generator and a matching box in order to minimize reflected power. The power setting for soft matter deposition is much lower than for most industrial or inorganic depositions. As an example, thin films of silicon dioxide and silicon nitride used as antireflective coatings and passivating layers by companies such as Oxford Instruments and Manz have been deposited under a range of RF power varying from 200 W to 20 kW, whereas the deposition of soft material such as polymers occur under 20−100 W RF power.[26,40]

The characteristics and rate of deposition of the thin films produced are highly influenced by the modifiable deposition conditions such as temperature, length of deposition, pressure, inert gas flow rate, and RF power used for plasma generation. The substrates can be placed either directly in the plasma zone (i.e., between the parallel plates) or downstream from the plasma zone (in the flowing afterglow) to avoid plasma bombardment effects. The standard home-built PECVD chamber and setup is shown in Figure 1with the standard inlets for the monomer and argon gas used for the plasma generation as well as connections to a vacuum pump for low-pressure deposition purposes. The RF electrodes create plasma typically at 13.56 MHz for the PECVD process.

Plasma polymerization reactions appear to have elements of both a radical and step-growth growth with the reactive species reacting with each other, as opposed to a monomer, which is the case with many other types of polymerization. The process is truly unique and is used to form polymeric films under vacuum conditions. The plasma excitation and radicalization of the carrier gas and vapor phase monomer allows the excited species the opportunity to react with any surface in the plasma chamber, forming a film through two basic steps: formation of a free radical (R*) or reactive species, which initiates the process and propagation of the polymer chain via reaction with the monomers (M) as shown in the Figure 2.[41] The goal is to

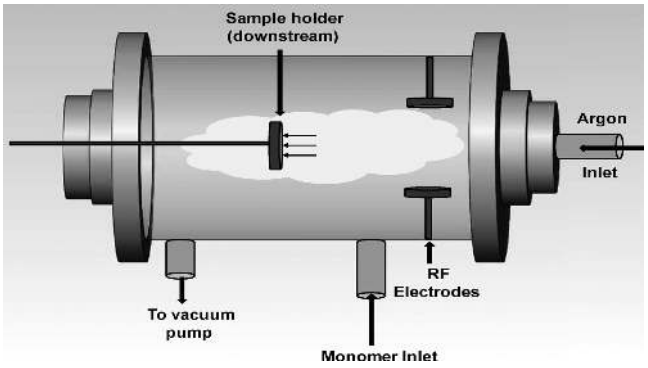

Figure 1. Schematic representation of a standard chamber used in the PECVD process.

$$R^{*} + M \longrightarrow R_1^{*} + M \longrightarrow R_2^{*} + M \longrightarrow R_3^{*} + M \longrightarrow \text{Uncross-linked polymer}$$
$$R_j^{*} + M \longrightarrow \text{Crosslinked Product}$$

Figure 2. Free radical propagation reaction and formation of cross-linked product.

induce radicalization causing the monomers to react while still retaining their original structure and functionality. A major concern is the integrity of the monomer when exposed to the plasma. Direct influx of the monomer into the plasma zone increases the probability of monomer destruction. By "softening" the radicalization, either through the use of pulsed plasma conditions or introducing the monomer downstream of the plasma zone (flowing afterglow), there can be excellent retention of the monomer chemistry and functionality.[42]

Generation of radicals due to the RF plasma enables polymerization to occur in a statistical fashion, driven by bond dissociation energies. Radical formation can occur both in the monomer in the gas phase and on the target substrate. Once radicalized, the modified monomer can either combine with another radicalized monomer or transfer its radical to a nonradicalized monomer during the reaction resulting in polymerization.[43] As long as the radical remains intact, propagation can continue. In the event that two radicalized monomers react to form a chain with no further radicals, termination occurs, ending the reaction. Because of the number of radicals in the system, there can be a significant amount entrapped in the final film if they do not react before being encapsulated. The surface adhesion is a result of the plasma process, which creates radicals not only of the monomer species but also on the substrate surface as well. These free radicals initiate grafting of the monomer to the surface and covalent binding, resulting in firm attachment of the thin film on the substrate. The amount of cross-linking in the deposited films is determined by the ratio of the radical concentration [R*] to the monomer concentration [M] where the monomer concentration is proportional to the chamber pressure.[41] There have been reports regarding the role of ions and gas phase reactions in the surface polymerization and the possible formation of charged oligomers in the gas phase prior to deposition on the surfaces.[37,44] Studies of hexamethyl disiloxane (HMDSO) have shown that under varying plasma deposition conditions, the flux of ions on the surface will vary and that as pressure increases, there is an increase in the film of radicals and neutral species as measured by mass spectrometry and time-of-flight secondary ion mass spectroscopy (ToF-SIMS).[45]

Thin films produced by PECVD thus consist of highly branched, cross-linked architectures in which a large variability can occur because of the reaction conditions. It has been observed that slower deposition rates produce better films and lower pressure allows higher density of charged particles.[6] At high rates of deposition, excessive polymerization can occur and lead to the formation of large particles before deposition.[46] Films produced at higher rates of deposition are physically weaker.[42] Some of the cross-linking and dangling bonds can be avoided by using pulsed PECVD method for deposition. It has also been observed that pulsed plasma deposition gives a measure of control over the chemical structure of the deposited films, in particular for depositions at low duty cycle. A pulse generator can be used for power modulation in the pulsed PECVD mode where the duty cycle is DC = $T_{on}/(T_{on} + T_{off})$.[42,47,48] The combination of low plasma power and low duty cycles during the deposition process helps the activation as well as the retention of chemical activity of the deposited molecule. The use of the pulsed mode PECVD provides versatility and makes it a "gentle" deposition technique since no solvents are used and the reactions are carried out at low applied powers and substrate temperatures.[49] Because species reactivity is increased due to plasma activation, this process is different from other deposition techniques, which may rely on a specific chemical initiator in the reaction, such as iCVD. But the iCVD method tends to produce more linear polymer chains in contrast to the PECVD films.[9,50]

Although most chemical characterization of plasma polymerized films has been limited to techniques such as FTIR, UV−vis, X-ray photoelectron (XPS) analysis, and atomic force microscopy (AFM), obtaining a better understanding of the structure of the films is necessary when studying their interactions and responses.[51−55] Other characterization methods such as X-ray and neutron reflectivity have been used to study the unique internal structure of plasma polymerized films.[52,56] For instance, films of benzene and octafluorocyclobutane showed structural variations at the polymer/substrate and polymer/air interfaces on the order of several nanometers in thickness. The bulk of the films were generally observed to be homogeneous, but depositions under different chamber pressure settings can affect the cross-linking density significantly. Typically, cross-linking density was lower in films deposited at higher pressure and the difference in cross-link density can be attributed to the change in radical concentration with pressure variations.[41] The surface roughness of copolymerized films was also probed and found to be very smooth, on the order of 3−6 Å and homogeneous in composition. This study offers excellent insight into the nature of the plasma polymerized films and the control of composition of films through the deposition parameters.

3. APPLICATIONS OF PECVD

PECVD of soft materials is being utilized in diverse fields from optical to biomedical applications. Most films for biological and biomedical applications typically are required to be stable in aqueous environments for extended periods of time. Good adhesion to the substrate and retention of functionality is critical in these cases. PECVD deposited soft material can be used for the surface treatment of implants or other biomaterials. By adjusting the plasma conditions, films can be tuned to exhibit the desired properties. There are two main applications of PECVD in the formation of biocompatible surfaces, one is the coating of surface-specific polymers and the second is the deposition of proteins, peptides, and amino acids directly on a substrate for protein binding, cell adhesion, antifouling,

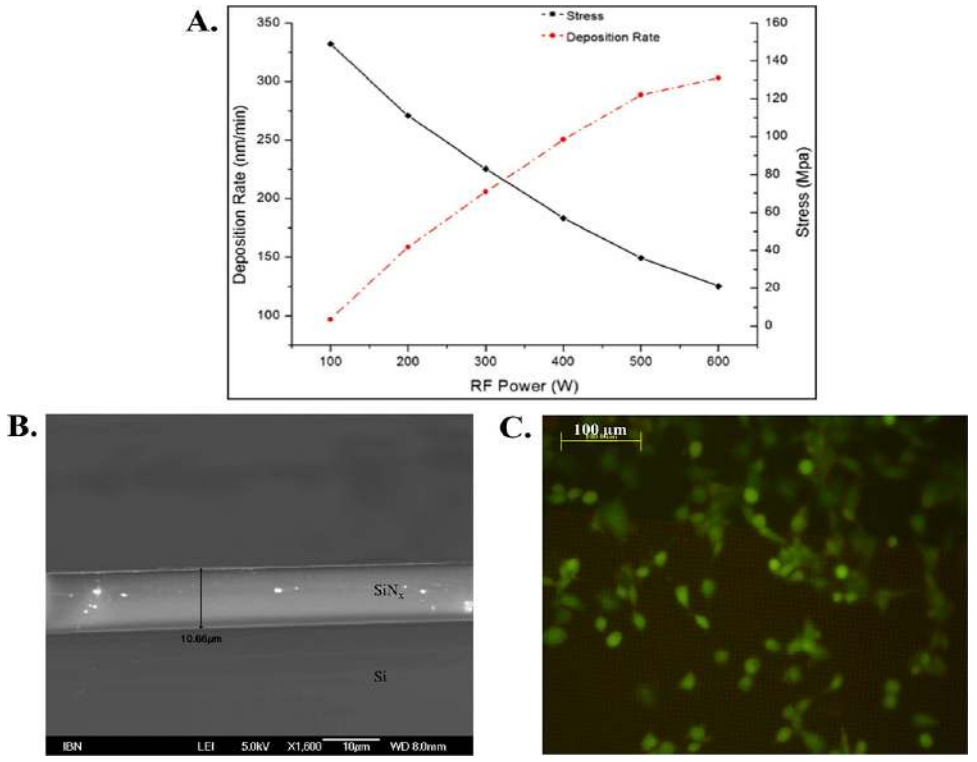

Figure 3. (a) Comparison of the deposition rate and stress in silicon nitride thin films deposited from silicon hydride precursor. (b) Secondary electron image of a low stress thick silicon nitride film deposited via PECVD. (c). Mouse mesenchymal stem cells cell cultured on the nanoporous SiN membrane to test their in vitro biocompatibility. Reprinted with permission from ref 64. Copyright 2008 Elsevier.

antibacterial, and biocompatibility applications. Deposition and attachment of biological moieties on surfaces are important in applications such as biosensors, where biological molecules need to be coupled with the surface of the sensor as well as retain their activity for sensing purposes. PECVD can be used as a method to functionalize surfaces with biomaterials which can then be implanted into a body or it can facilitate the integration of biotic and abiotic materials into a single integrated structure. PECVD allows surfaces to be tailored for specific molecular interactions, and provides a universal platform for device fabrication.

3.1. Thin Films of Inorganic Monomers for Biological Applications. *3.1.1. Applications in Implants and Cell Culture.* PECVD-grown films have received a lot of attention for applications in medical devices such as implants, stents, and intraocular lenses because of their chemical inertness, corrosion, and wear resistance. Diamondlike carbon (DLC) films, carbon alloys such as carbon nitride (CN), silicon carbide (SiC) films, and 316L stainless steel with silicalike coatings have all been demonstrated as good surfaces for use in such medical devices.[57−60] Silicon has been used increasingly as a part of implants and other devices both in vivo and in vitro. But the biocompatibility of silicon is not very well established. Bayliss et al. demonstrated that cell growth on polycrystalline silicon synthesized by PECVD followed by annealing demonstrates higher cell adherence and viability as compared to bulk silicon without requiring polylysine coating for cell adhesion. The thin film not only influences cell adhesion but also can act as cues for changes in cell morphology. Such surfaces can be further modified by PECVD to have functional groups for the attachment of specific cells.[61] Gandhiraman et al. have demonstrated the deposition of hexamethyl disiloxane (HMDSO) in two different forms, polymerlike and silicalike, on 316L steel and studied the effects under physiological conditions. In particular, the interaction with fibrinogen which is an important protein in the inflammatory reaction was studied. The changes in deposition conditions such as oxygen content results in the formation of two different types of thin films and also influences the properties such as wettability and surface roughness. Though the adhesion of the silicalike film was higher than the polymerlike film, the polymer film showed higher retention of fibrinogen as well as increased cell proliferation. The hydrophobic nature of the polymerlike film leads to the higher adhesion of fibrinogen and cell proliferation.[59,60]

Silicon nitride and silicon carbide films have been used for culturing of cell lines such as mesenchymal and fibroblast cells, which indicates that such films have potential applications in BioMEMS. Thin α-SiC films obtained via PECVD deposition have been shown to be optically transparent and therefore conducive for optical imaging. PECVD films of silicon carbide (α-SiC), and silicon nitride (SiN), produced via alternate high- and low-frequency RF methods in order to form low-stress films are important in applications where intrinsic stress affects the performance of the devices.[62] By alternating between high- and low-frequency RF and using low power, the tensile and compressive stresses are compensated in the two cycles and the resultant film has low residual stress.[62−64] The RF power applied during the reaction chamber affects both the deposition rate as well as the residual stress in the deposited film and increased RF power implies high rate of deposition and lower residual stress (as shown in Figure 3). Szili et al. demonstrated the use of PECVD for the formation of strongly adherent silicon dioxide films on titanium followed by silanization to form amino groups on the SiO_x surface. The investigation showed that the percentage of amine groups on the PECVD

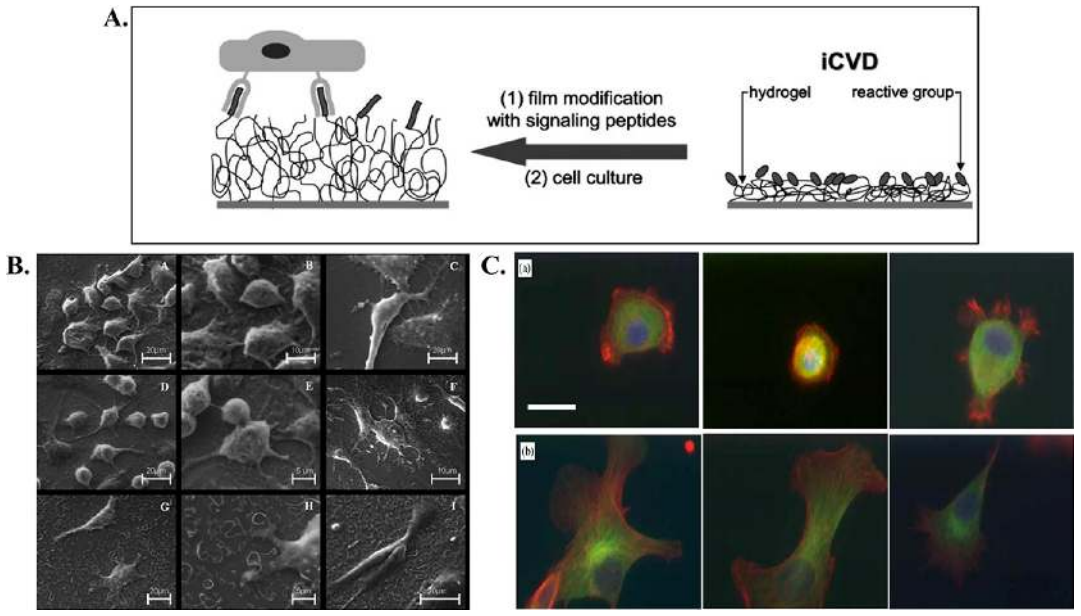

Figure 4. (a) iCVD polymerization of a biomimetic surface (combination of a hydrogel and a monomer that allows attachment of aminated molecules). Reprinted with permission from ref 31. Copyright 2009 Wiley-Blackwell. (b) ESEM images showing 3T3 Swiss Albino mouse fibroblasts morphologies. (A, B) Cells seeded on PET surfaces. (D, E) Cells seeded on FLAT surfaces. (G, H) Cells seeded on ROUGH surfaces. (C, F, I) Cells after 24 h of seeding on PET, FLAT, and ROUGH surfaces, respectively. Reprinted with permission from ref [68]. Copyright 2006 Wiley Periodicals Inc. (c) Fluorescence images of cells on (i) polystyrene (PS), (ii) l-pdAA-coated PS after 24 h of incubation (tubulin filaments in green, actin in red). Bar (50 mm). Reprinted with permission from ref 69. Copyright 2005 Elsevier.

SiO_2 surface was high and constant through this process.[65] Mandracci et al. showed that the use of the silicon oxide deposition on dental composites improved biocompatibility and reduced the cytotoxicity associated with traditional dental implant materials. The use of PECVD films helps to improve the biocompatibility of the dental prosthetics as well as the aesthetic value due to the optical properties.[21] PECVD has been established as a good process for deposition of SiO_x films because the silicon and oxygen content can be tuned easily and the contamination level in the material can be controlled. Pulsed PECVD was also used to obtain a conformal coating of siloxanes on materials used in neural probes, where the power supply was pulsed on and off in order to reduce the presence of dangling bonds and cross-linking.[48] Multiple tests under physiological conditions showed that the PECVD films were robust and adhered well to the surface.

Titanium dioxide is commonly used in orthopedic implants due to its biocompatibility and mechanical robustness but has issues with inflammatory reactions. The traditional methods of generating bioactive coatings on titanium include sol−gel, plasma spraying, and enameling but these methods have not shown good adhesion to the surface of titanium.[43,66] This adhesion can be controlled by the deposition conditions during the PECVD process. PECVD has also been used for the incorporation of metals such as Ti into the DLC matrix, which shows an increased differentiation of bone marrow cells into osteoblasts in rats.[43] This can lead to enhanced bone growth on the implants and reduced bone resorption, which is required in good implant materials.[66]

Viable cell culture substrates should promote the attachment of cells and allow for cell proliferation. Cell attachment, morphology, and phenotype are all greatly influenced by the topographical features of substrate used for cell culture. PECVD can be an essential tool for this process specifically if the topography and features of the substrate are to be maintained and functional groups on the surface are required. Pfluger et al. showed that PECVD-deposited pHEMA replicates the topography of intestinal basement membrane. Though pHEMA is not considered an ideal substrate for cell culture, it has been shown that the highly cross-linked form of pHEMA deposited via PECVD allows for the attachment and culture of certain cell lines. The conformality of the coatings on the intestinal basement membrane was verified using high-resolution SEM images.[67] Rosso et al. used PECVD as a method to deposit fluorocarbon coatings on polyethylenethereflalate (PET) substrates. Fluorocarbon films are attractive due to their high chemical inertness and biocompatibility. Pulsed PECVD was used to change surface roughness by controlling the shape and size distribution of the fluorocarbon nanostructures but maintain the common chemical compositions of the surface used for the proliferation of mouse fibroblast cells (as shown in Figure 4b).[68] Allylamine is another material that has been investigated through plasma deposition as a means of fabricating surfaces for cellular adhesion.[69] The morphology of polymerized allylamine films have not been well characterized for biological applications. Detomaso et al. have investigated the effects of plasma processing conditions on the carboxyl content in the allylamine films formed on various substrates such as polystyrene (PS) and silicon. Lower density of surface carboxyl groups in allylamine films was found at continuous high RF power (100 W) conditions and was conducive to the growth of fibroblast cells (as shown in Figure 4c) . Favia et al. investigated the use of PECVD for patterned deposition of both poly(acrylic acid) (PAA) and polyethylene oxide (PEO) films on polystyrene using masks for making substrates with cell culture applications. PEO films are resistant to the attachment of proteins and bacteria and are known to be antibiofouling in nature. PAA films promote cell adhesion and the carboxylic groups on the PAA films were retained through pulsed PECVD deposition, which promoted the attachment of cells and

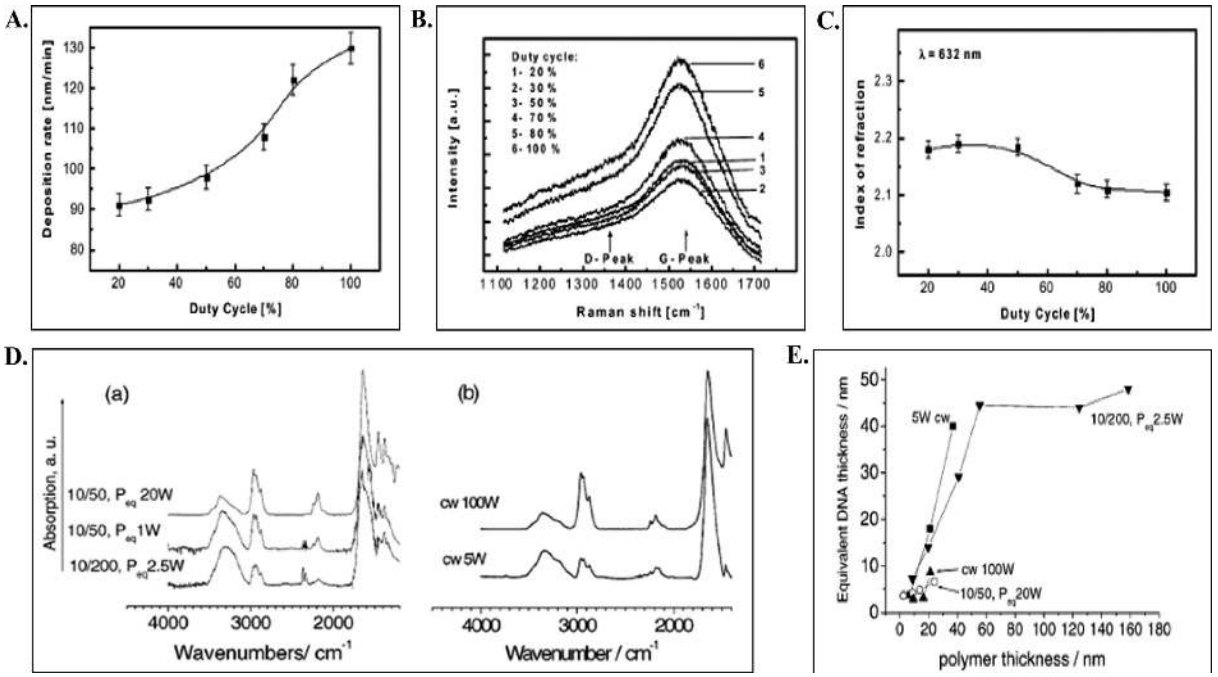

Figure 5. (a) Variations in the deposition rate of DLC films deposited from acetylene with increasing duty cycle. (b) MicroRaman spectra of the films deposited at varying duty cycles. (c) Change in the refractive indices of the DLC films based on varying duty cycles. Reprinted with permission from ref 74. Copyright 2002 Elsevier. (d) FTIR Analysis of the allylamine film deposited via (a) pulsed mode PECVD and (b) continuous mode PECVD. (e) Thickness variation of the DNA films formed on PECVD deposited allylamine films at low and high duty cycles. Reprinted with permission from ref 79. Copyright 2003 The American Chemical Society.

proteins. The patterned surfaces demonstrate that the cells attach preferentially to the PAA coated surface and in contrast, the PEO sections did not support cell growth.[70] These plasma-polymerized surfaces were observed to be robust through autoclaving and stable enough to be used for several cell culture cycles. Allylamine films were highly effective in promoting the growth and adhesion of neuronal cells in the study by Harsch et al.[47]

3.1.2. Antibiofouling Coatings. Biofouling occurs when proteins, bacteria or cells grow on engineered surfaces and cause degradation of the material properties. Uncontrolled and irreversible attachment of such biomolecules can have a detrimental effect on materials used in several technological areas including medical devices such as implants and lenses, surfaces of ships and water filtration systems. Biosensors in physiological conditions face an issue with the nonspecific adhesion of proteins. But the selective adhesion of proteins or other biomolecules is important since they can encourage the growth of cells and accelerate the wound healing process and reduce the "foreign body" reaction when implants or other biomaterials are used in vivo applications. Protein adhesion is an important aspect of biosensors and improves both the specificity and sensitivity.

Diamondlike carbon (DLC) and silver-DLC coated surfaces have shown good antibacterial properties and can be used as coatings for the antibiofouling applications.[71−74] DLC films were synthesized by plasma decomposition of a hydrocarbon-rich atmosphere, such as methane or butane with an intermediate silicon hydride layer grown from silane to improve adhesion on substrates such as 316L steel or borosilicate glass. Cell viability studies show no significant difference between the DLC films and uncoated glass slides.[72] Silver nanoparticles were incorporated between PECVD-grown layers of DLC. Silver nanoparticles are known for their antimicrobial properties and in combination with DLC have demonstrated a 3-fold increase in bactericidal activity in comparison to DLC films.[71] Fedosenko et al. have demonstrated the pulsed plasma deposition of DLC films from acetylene monomer with helium and argon carrier gases. The duty cycle was varied for a constant RF power and the effects on the deposition rate and optical properties such as refractive indices was studied (as shown in Figure 5a).[74] PEG-coated surfaces have shown good antibiofouling properties because of their resistance to nonspecific protein adhesion. Martin et al. used plasma polymerized amine monolayers for the covalent binding of PEG on various surfaces. Heptylamine monomer was deposited in a home-built reactor with the substrate placed on the lower electrode for the formation of reactive amine groups on the surface.[75] Lopez et al. demonstrated the growth of thin layers of pHEMA by RF PECVD whose performance was compared with spin-cast pHEMA films, radiation grafted pHEMA films and bulk pHEMA. The films produced by the other methods have certain disadvantages such as radiation damage of the substrate and surface roughness.[20] These were overcome by the use of PECVD thin films because bulk material properties are not affected by the plasma polymerization process.

Belegrinou et al. compared the interactions of common proteins such as BSA and fibronectin with PECVD grown films of PAA, which are protein-adherent, and PEO-like films, which are essentially protein-resistant. The depositions were done in a custom built PECVD chamber, where the samples were placed on the lower electrode and the plasma power was applied in a combination of continuous and pulsed modes. The protein interaction with the two surfaces was monitored using a quartz crystal microbalance and the influence of the pH on their interactions was studied. The protein solutions at lower pH were generally found to adhere quicker to the PAA surface and reach equilibrium. Most of the proteins did not adhere to PEO-

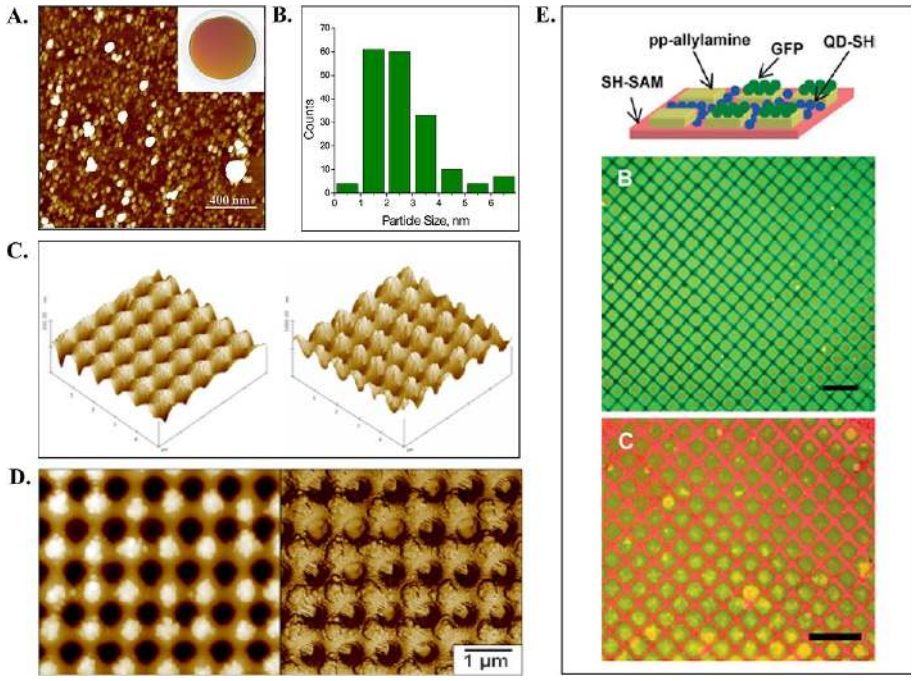

Figure 6. (a) AFM Analysis of gold nanoparticles after reduction on PECVD tyrosine film (z = 15) (b) Histogram of particle size distribution. (c) 3D AFM image showing (left) pristine periodic porous pattern at z = 600 nm height and (right) the same structure after titania nanoparticle formation on lattice nodes, z = 1000 nm height. (d) 2D AFM image of conformal titania coating on a periodic porous patterned structure. Reprinted with permission from ref 23. Copyright 2010 American Chemical Society. (e) Coupling to the SH-SAM/pp-allylamine multiple functionality surfaces. (A) Illustration depicts composition and selective binding of GFP and QDs. (B) Fluorescence of coupled GFP to pp-allylamine patterns by EDC. (C) Dual-color fluorescence of GFP coupled to the amine groups on the patterned pp-allylamine and quantum dots coupled to the SH-SAM. Scale bars in B, C: 100 μm. Reprinted with permission from ref 33. Copyright 2006 John Wiley & Sons.

like films except for fibronectin, which showed slight attachment confirming that the PEO-like films deposited via PECVD are useful in antibiofouling applications.[76]

3.2. Thin Films with Functional groups. Producing functional groups such as amines and carboxyls commonly used in biological applications is an important aspect of the thin film deposition. Such functional groups are used for the selective immobilization of proteins, or cell adhesion on various substrates. Monomers such as amino silanes and allylamine have been commonly used for the deposition of thin films with reactive amine groups. Volcke et al. demonstrated the formation of reactive amine groups on surfaces using aminosilanes.[77] One of the aspects in the deposition process was the control of RF power in order to maintain the reactivity of the amino species, while also activating and breaking down the monomer for deposition. The immunoassay performed to verify the functionality demonstrated a 2-fold improvement in the detection limit in comparison to amine groups produced by standard methods. Another example is the plasma coating of simple amine, hydroxyl, and fluorinated compounds onto the poly (ethylene terephthalate) (PET) substrate to significantly alter the surface chemistry and monitor the influence on fibrinogen adsorption.[42] The adsorption and retention of fibrinogen were observed to be influenced by the surface functionality. The highest adsorption of fibrinogen was observed on fluorinated surfaces whereas the adsorption was significantly lower with hydroxyl and allylamine groups. In addition, the study also indicated that the surface interactions were more important than functionality in protein interaction. They have demonstrated that such surfaces could be both antifouling and adhesion promoters in nature, which could be important in future applications. A related study investigated the adsorption of IgG on plasma polymerized hexamethyldisiloxane (HMDSO), which is a hydrophobic surface and acrylic acid (AA), which is highly hydrophilic.[78] The deposition of HMDSO and AA was done in a home-built reactor at low pressure (5 mTorr) and the monomers were stabilized by hydroquinone monoethyl ether. The HMDSO film showed good adsorption of the IgG, but failed to retain it upon rinsing. The retention of IgG on the surface was observed to be much higher with the AA films upon rinsing because of the covalent coupling with a PEG-PEI copolymer, making these films of interest in immunoassays.

Zhang et al. investigated plasma-polymerized allylamine films on the surface of gold-coated glass slides for DNA probe immobilization. Allylamine was deposited in a RF chamber using both pulsed and continuous modes of deposition. FTIR spectroscopy of the allylamine films deposited at lower duty cycles revealed that the films retained the amine groups and had low cross-linking (as shown in Figure 5d). DNA absorption was also highest on the low duty cycle coated allylamine films (as shown in Figure 5e).[79] Patterned deposition of allylamine has been demonstrated by Slocik et al. on a silicon wafer substrate modified with a −SH-terminated self-assembled monolayer. A TEM grid was used for the patterning and selective binding was demonstrated by using cysteamine conjugated quantum dots bound to the −SH region and GFP protein bound to the allylamine region via EDC coupling (as shown in Figure 6e).[33] Poly(4-aminostyrene) (PAS) thin films were deposited by Xu et al. on several different substrates such as PDMS, polyethylene, and polycarbonate for applications in microfluidic devices. Initiated CVD (iCVD) was used for deposition and the precursor and initiator used were 4-aminostyrene and tert-butyl peroxide, respectively. The iCVD grown films were compared

to PECVD grown polyallylamine films and better conformal coverage and chemical functionality retention was observed in the iCVD grown films. But the chemical functionality was also retained in PECVD films grown under low plasma power conditions and slow deposition rates. The conformal coverage of amine groups on the surface was confirmed using SEM imaging and the functionality was confirmed by surface-immobilized CdSe/ZnS quantum dots with carboxyl groups.[50]

3.3. Thin Films of Biological Monomers. Although many different polymeric thin films can be fabricated with PECVD, the deposition of biological molecules via PECVD and their interface with different material systems is one which provides a significant area for development. Biomaterials of interest are often in a powdery solid form, presenting unique challenges for plasma deposition. Some solid monomers can be deposited through sublimation methods wherein the monomers are preheated under vacuum in the plasma chamber and vaporized into a gas phase. Physical vapor deposition based on monomer heating has been studied with some amino acids but these demonstrations typically require a surface modification of the substrate with an initiator or a specific substrate to be used to allow the reaction to occur. The example developed by Lee and Frank uses a heating method under vacuum to deposit a range of polyamino acids which were firmly grafted to a substrate and preserved their composition and functionalities.[80,81] These films were limited to ~80 nm in thickness because of the surface modification required for adhesion to the substrate. The major disadvantage of this deposition method is that the substrate requires modification with an initiator to allow the grafting of amino acid on the surface. The use of PECVD can effectively eliminate the need for initiator surface modification and can also provide the possibility of coating a wide range of different and in many cases, nonideal substrates. Heyse et al. have demonstrated the deposition of enzymes on glass and PET substrates using PECVD at atmospheric pressure. The bioactivity of enzymes such as glucose oxidase and lipases have been retained by atomizing the enzymes and depositing them simultaneously with an organic precursor such as acetylene and pyrrole.[82] A home-built atomizer has been used in conjunction with a PECVD chamber at atmospheric pressure in which the electrodes were coated with a glass dielectric. The atomization process provides a watery shell which protects the enzyme in the plasma environment and the enzyme molecules get trapped in the polymer chains of pyrrole and acetylene. This also leads to a homogeneous distribution of the enzymes in comparison to other immobilization techniques, which can cause aggregation and clustering.

Single amino acids or simple peptides can be deposited in the same way as any other monomer via low-pressure PECVD because they are in many respects similar to other chemical monomers, with a specific chemical structure and an ability to form long chains of amino acids under the appropriate conditions. The use of a uniform coating technique such as PECVD has not been explored previously to assess the retention of functionality in thin films of amino acids or peptides for applications as biomineralization and surface modification agents. Biomolecules, such as amino acids, peptides, and proteins can be used to precipitate inorganic materials directly from a precursor solution onto a surface for biomineralization.[83] Amino acids contain side groups that interact with the inorganic precursors to induce nucleation and growth of the inorganic nanoparticles. By employing PECVD as a means of depositing dry amino acid or peptide monomers, a viable method of surface modification is available by which the film is bound to the surface while still maintaining the necessary functionality to induce mineralization of inorganic particles from solution.

Anderson et al. have deposited amino acids such as tyrosine and histidine to form polytyrosine and polyhistidine thin films for the fabrication of gold and titanium dioxide nanoparticles (as shown in Figure 6a).[22,23,84] Micropatterned templates have been used to create tyrosine rich areas for the biotemplating process (as shown in Figure 6d). The authors observed that optimal pressure conditions were required to obtain robust thin films which did not delaminate and were resistant to mechanical wear. The PECVD deposited films are exposed to an inorganic precursor solution containing ions in a dilute solution of the material to be deposited. Copolymerization of amino acids and other organic and inorganic monomers has also been demonstrated by Anderson et al.[22,85] Copolymerized films of L-tyrosine with materials such as HEMA and acrylonitrile have been produced. This technique has the potential for producing enhanced biological interfaces. Selective coatings of microparticles with a variety of precursors have been used to create robust Janus microparticles (shown in Figure 7).[86] Physical vapor deposition of short peptide sequence heated under vacuum to undergo polymerization into various ordered structures such as nanotubes on surfaces has been

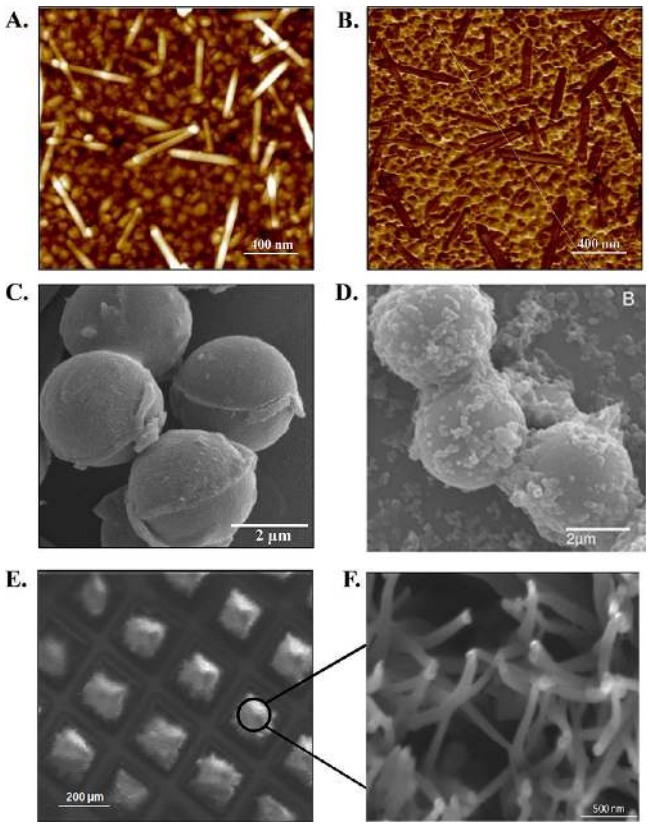

Figure 7. High-resolution AFM images of composite films PP-Tyr/TTIP. (a) Topography (z = 24 nm). (b) Surface adhesion (arb.). Reprinted with permission from ref 22. Copyright 2012 American Chemical Society. (c, d) Microparticles coated with plasma polymerized amino acids of histidine and tyrosine. Reprinted with permission from ref 86. Copyright 2010 American Chemical Society. (e, f) Patterned deposition of peptide nanotubes on silicon substrates (unpublished results).

demonstrated previously.[80,87] We have used PECVD to deposit uniform forests of self-assembled nanotubular structures composed of diphenylalanine peptide on various substrates. The deposition of the peptides using PECVD can produce nanostructures of large aspect ratios and features up to tens of micrometers in size and this affects the surface properties such as wettability (shown in Figure 7). The deposition conditions such as power and duty cycles can be varied to produce nanostructures with different morphologies. Since the substrate was not subjected to higher temperatures and held downstream from the plasma zone, several different materials including polymers such as PDMS, PMMA and graphene have been used as substrates for the peptide nanotubes formation.

Further testing of plasma-polymerized amino acids and peptides are required in order to evaluate their use in cell culture and biosensors applications. Studies must be undertaken to fully characterize the structure of these films as well as in-depth studies investigating all amino acids and short peptide sequences. Detailed analysis of the nature of the bonding between multiple amino acids and how peptides are formed is also essential to understanding the limitations faced in future applications. Future experiments with these material systems should focus on further characterization of the cross-linking and internal structure of films by techniques such as TOF SIMS, X-ray, and neutron reflectivity, as well as real time monitoring. Additional compositional studies by NMR, especially in the case of copolymerized films, would more accurately determine the nature of the monomer mixing and determine if truly random mixing occurs and evaluate the degree of mixing. Currently, NMR measurements face challenges such as sample preparation. Although some studies are able to report these data, it remains a more obscure feature, especially when compared to more accessible techniques such as FTIR and XPS.[88−91]

4. SIGNIFICANCE, BROADER IMPACT, AND FUTURE DIRECTIONS

PECVD holds an advantage as a deposition technique over many traditional wet chemical methods in several areas. PECVD is dry, making the process cleaner and greener without excess chemical waste since the only chemicals required are the monomers themselves and eliminates the need for complex chemical synthesis procedures for attaching polymers to surfaces. Because of the nonselective nature of the plasma, the monomer can be coated onto any substrate in the plasma chamber producing an infinite combination of monomer−substrate systems, which may be difficult to fabricate otherwise. Each year, reports of novel monomers for thin film fabrication via PECVD, along with other CVD methods, have become more common. The various coatings produced reflect the tremendous progress made in the past decade. They provide researchers with an array of options that can be employed for developing thin films of specific surface functionality. The advent of a broadly applicable deposition method for biomaterials such as amino acids and peptides that can be used on many different substrates to establish stable, uniform, robust, and functional coatings provides a unique opportunity to expand the application of these materials. Plasma-polymerized biomaterials address issues of surface compatibility and substrate adhesion while allowing direct modification of surfaces with no pre- or postdeposition treatments. The use of PECVD with biomaterials is highly relevant to many biocoating applications since it provides a facile means of uniformly coating a surface with materials capable of supporting functionalization as well as providing a platform for chemical modification of biological monomers with other inorganic materials during the plasma reaction for tailored surface compositions. Some of the potential engineering applications of this coating technology include use in implant coatings, biosensors, and as agents to facilitate surface enhancement and biocompatibility. Such a deposition method can be used in the development of substrates for microfluidic devices which may swell or degrade in the presence of solvents when precursors are insoluble or soluble in harsh solvents. Plasma grown thin films have been shown to be conformal and produce biocompatible surface functional groups and their use as substrates for cell culture has been demonstrated. Cell attachment, morphology, and phenotype are all greatly influenced by the topographical features of substrate used for cell culture. Future applications can include the development of PECVD coated substrates with different topographical features to induce the mechanical differentiation of stem cells. Further testing of plasma-polymerized amino acids and peptides are required in order to evaluate their use in cell culture and biosensors applications. The PECVD process lends itself to simultaneous deposition and copolymerization of monomers leading to the formation of complex and stable functionalized coatings. Copolymerization PECVD as a method of depositing multiple monomers (biological and synthetic materials) has the potential for many future developments with varying surface characteristics. Copolymerization is expected to help facilitate integration of inorganic systems with host bodies in the form of compatible coatings for implants, bioactive surfaces, and materials that support the facile integration between two dissimilar systems. Nonetheless, the PECVD method of producing synthetic substrates or functionalities has some limitations. Some issues include the highly cross-linked network and limitation of monomers used for deposition.

5. CONCLUSIONS

There is a broad range of materials and applications enabled by PECVD deposition. The distinct advantages of these processes will become a major factor in their growing use, both in research and in industrial applications since the processes are simple, robust single-step, solvent-free, green, readily scalable especially through the use of off-the-shelf commercial monomers, and can be applied equally well to many different kinds of surfaces on a larger scale without the need to change the deposition process significantly. The use of PECVD in relation to biomaterials and anisotropic coatings are young fields that are starting to develop as the technical details of the deposition methods are being developed. PECVD holds tremendous potential for the coating of many different biomaterials directly onto surfaces using a process free from any wet chemistry and substrate adhesion difficulties. The challenges present in these types of deposition require interdisciplinary knowledge in materials science, bioengineering, and plasma coatings to appropriately determine not only the processing conditions for unique materials, but also the motivation behind choosing materials to be investigated for deposition.

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Notes

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