Voltage-Dependent Assembly of the Polysaccharide Chitosan onto an Electrode Surface

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We examined the assembly of the amine-rich polysaccharide chitosan from solution onto electrode surfaces as a result of voltage bias on the electrode. Chitosan is positively charged and water soluble under mildly acidic conditions and is uncharged and insoluble under basic conditions. We observed that chitosan is deposited from acidic solution onto the surface of a negative electrode and the thickness of the deposited layer is on the order of a micron. The thickness of the deposited layer was observed to be dependent upon the deposition time, the applied voltage, and the chitosan concentration. No deposition was observed on the positive electrode or on an "electrode" that had no applied voltage. Once deposited and neutralized, the chitosan layer can be retained on the electrode surface without the need for an applied voltage. Infrared (FT-IR) and electrospray mass spectrometry confirmed that the deposited material was chitosan. These results demonstrate that chitosan can be deposited and retained on electrode surfaces, and the potential advantages for applications in microfabricated devices are discussed.

Introduction

The ability to create devices (e.g., biosensors, microarrays, and microelectromechanical systems (MEMS)) requires facile methods to precisely control surfaces. A variety of patterning techniques can be used to produce desired structures, while various methods have been investigated to control surface chemistries. For instance, surface chemistries have been controlled by self-assembling monolayers using reactions between thiols and metal surfaces[1,2] or between alkyltrichlorosilanes and oxidized silicon.[3−5] An additional method to assemble macromolecules and particles is to exploit an applied voltage.[6] Applied voltages have been used to assemble colloidal particles,[7] proteins,[8−10] and cells[11] onto electrode surfaces. Here, we report the deposition of the polysaccharide chitosan onto the surface of a negative electrode.

Chitosan is an amine-rich polysaccharide derived by deacetylation of chitin. Chitin is the second most abundant polysaccharide in nature and is found in crustaceans, insects, and fungi. Chitosan is becoming an increasingly important biopolymer because it offers unique physicochemical properties.[12] Specifically, chitosan has primary amino groups that have pK_a values of about 6.3.[13,14] At pHs below the pK_a, most of the amino groups are protonated making chitosan a water-soluble, cationic polyelectrolyte. Chitosan's water solubility is unique as other β,(1→4)-linked polysaccharides (e.g., cellulose and chitin) are insoluble. At pHs above the pK_a, chitosan's amino groups are deprotonated, and this polymer becomes insoluble. Chitosan's pH-dependent solubility is attractive because it allows processing from aqueous solutions[15] while a modest increase in pH to neutrality enables chitosan to

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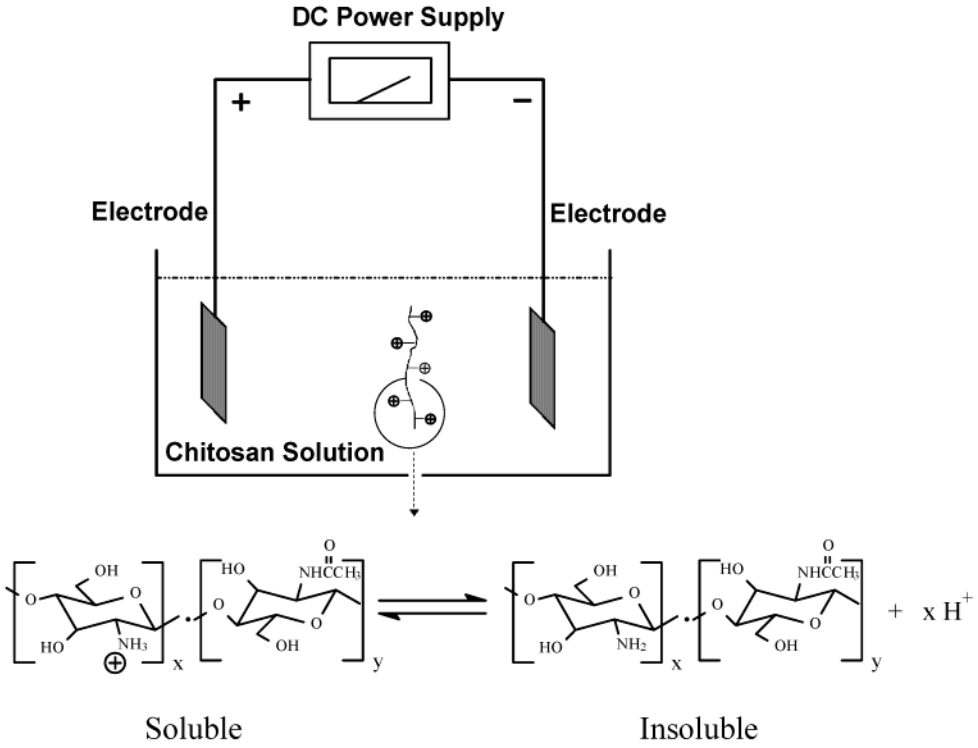
Scheme 1



be formed into various shapes (e.g., beads, membranes, and films). An additional feature is that chitosan's amino groups confer nucleophilic properties to this polymer. Specifically, the deprotonated amino groups have an unshared electron pair that can undergo reaction with a variety of electrophiles. As a result, various chemistries can be exploited to cross-link chitosan and to graft substituents onto this polymer.[16−26]

In this study, we examined whether chitosan could be deposited onto the surface of a negative electrode in response to an applied voltage. Specifically, Scheme 1 shows that we contacted the electrodes with an acidic chitosan solution. As expected, we observed that a thin layer was deposited on the surface of the negative electrode. Using various techniques, we examined this deposition process and demonstrated that the material deposited was chitosan. No chitosan deposition was observed on the positive electrode.

Materials and Methods

Chitosan from crab shells (85% deacetylation as reported by the supplier) and the enzyme chitosanase were purchased from Sigma-Aldrich Chemicals. Chitosanase was reported by the manufacturer to have specific activities of 102.3 U/mg. Chitosan solutions were prepared by adding chitosan flakes to water and incrementally adding small amounts of HCl to the solution to maintain the pH near 3. After undissolved material was filtered, these chitosan solutions were diluted to various concentrations, and the pH was adjusted to 5.0 using NaOH (1 M).

Electrodes were prepared by depositing 90 Å thick chromium (Cr) and then 2000 Å thick gold (Au) films on 4 in. diameter silicon wafers already coated with 1 micron thick thermal oxide film. For chitosan deposition, the electrodes were dipped into a chitosan solution (pH = 5, 1% w/v) as shown in Scheme 1. In most experiments, three electrodes were examined. Two of the electrodes (positive and negative) were connected to a dc voltage supply using alligator clips. The third electrode was not connected to a power supply and is designated a "neutral" electrode. At specific times, the electrodes were removed from the solution and rinsed with distilled water, after which the voltage was removed. In some cases, electrodes were immediately oven-dried (60 °C for 3 h). In other cases, electrodes were neutralized by immersion in a basic solution (1 M NaOH) and then rinsed with distilled water prior to drying. After drying, the thickness of the deposited layers was measured by a profilometer (Alpha-step 500 Surface Profiler, TENCOR Instruments). Thicknesses were measured on different areas of the electrode surface, and the average values were calculated.

Scanning electron microscopy (SEM) was used to study the surface morphology of the deposited layer. SEM micrographs have been recorded using a Focused Ion Beam system (FIB/SEM workstation dual beam 620; FEI Co.). Samples on silicon substrates were placed in the chamber having a vacuum of about 10^{-6} Torr. Structural properties were examined at a 20 000-fold magnification.

For chemical analysis, deposition was obtained by placing electrodes in a chitosan bath (1% w/v, pH = 5) for 20 min with an applied voltage of 2.0 V. For IR analysis, the negative electrode was removed from the chitosan solution, rinsed, disconnected from the power supply, and then placed in 1 M NaOH overnight. When the electrode was soaked in base for such a long time, the deposited material was observed to detach from the electrode surface. This deposited material was then extensively washed with distilled water and dried overnight at 60 °C. After drying, it was ground with KBr powder and pressed into a pellet. IR spectra were collected using a Perkin-Elmer 2000 FT-IR system.

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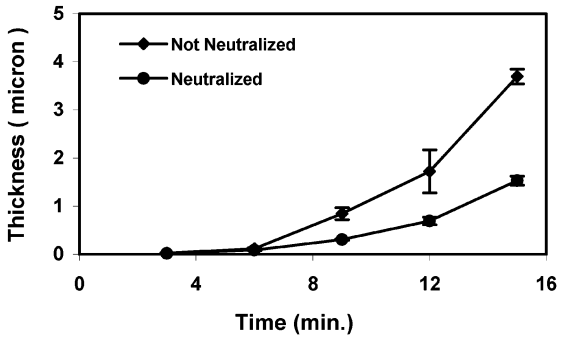


Figure 1. Deposition from chitosan solution onto the surface of a negative electrode. Deposition occurred from a 1% w/v chitosan solution using an applied voltage of 2.5 V. As discussed in the text, some electrodes were measured after being neutralized with 1 M NaOH.

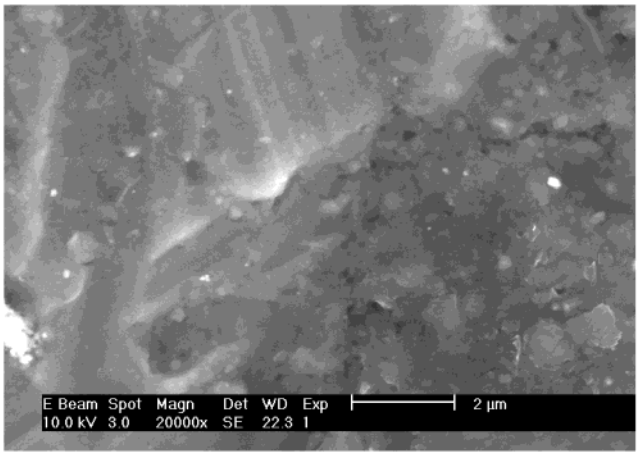
For analysis by electrospray mass spectrometry (ES-MS), the negative electrode was removed from the chitosan solution, rinsed, disconnected from the power supply, and then placed in a small volume of dilute acid (HCl, pH = 3) and held overnight to allow the deposited material to dissolve. This acid solution was recovered and diluted to approximately 0.08% w/v, and the pH was adjusted to 5.5. The sample was then incubated for 1 day at 37 °C with the enzyme chitosanase (0.2 U/mL). After incubation, the solution was filtered to remove precipitates and analyzed by ES-MS (Thermo Finnigan, San Jose, CA). All samples for ES-MS analysis were diluted in an aqueous solution containing 0.1% formic acid and analyzed in positive ion mode.[27]

Results and Discussion

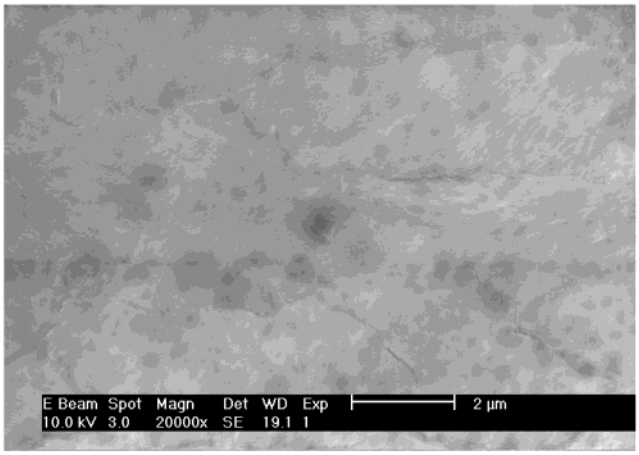
To examine deposition, we immersed electrodes in an acidic chitosan solution and applied a voltage of 2.5 V. After the voltage was applied for varying times, negative electrodes were removed from the solution and rinsed with distilled water, and the voltage was removed. In some cases, the electrodes were dried, while in other cases they were immersed in base, rinsed, and then dried. After drying, the thickness of the deposited layer was measured by profilometry. Figure 1 shows that the thickness of the deposited layer increases over time. Additionally, Figure 1 shows that the thickness of the deposited layer is less when the electrode was treated with base.

To examine the surface morphology of the negative electrodes, we used SEM. Figure 2a shows micrographs for electrodes that were dried without neutralization. As can be seen from Figure 2a, this sample has a nonuniform surface morphology. Possibly, the surface roughness of this electrode may be due to the presence of salts associated with the chitosan polyelectrolyte. Figure 2b shows the surface of a negative electrode that had been immersed in base and rinsed extensively before drying. As indicated in Figure 2b, the surface of this electrode is more uniform, presumably due to the neutralization of chitosan. The observation in Figure 1 that deposited layers are thinner after neutralization suggests that neutralization leads to a collapse of the polymer network and possibly also to the elimination of salts. In subsequent experiments, neutralization was performed prior to measuring the thickness of deposited layers.

Additional studies were performed to characterize deposition and to compare deposition onto the negative and positive electrodes. Figure 3a shows that the thickness of the deposited layer on the negative electrode increased over time. No material was observed to deposit on the positive electrode under the conditions studied. An additional control was an electrode in which no voltage was applied (designated as the neutral electrode). As shown in Figure 3a, no deposition was observed on the surface of this neutral electrode. Figure 3b shows that when the concentration of chitosan in the solution was increased, there was increased deposition on the surface of the negative electrode. Again, no deposition was observed on the positive electrode or on the control electrode in which no voltage was applied. Figure 3c shows that deposition on the negative electrode also increased with increasing voltage.



(a)



(b)

Figure 2. SEM micrograph of a deposited layer on a negative electrode (a) without neutralization and (b) with neutralization. See the text for details.

In summary, Figures 1−3 demonstrate that an applied voltage can be used to deposit a thin layer onto a negative electrode when the electrode is immersed in a chitosan solution. Additionally, the thickness of the deposited layer can be controlled by the deposition conditions. Finally, once the deposited layer is neutralized, it can be retained on the electrode surface even in the absence of an applied voltage (i.e., the electrode can be extensively rinsed). This latter observation is consistent with the fact that chitosan is insoluble under neutral and basic conditions.

We used two independent techniques to provide chemical evidence that the material deposited on the negative electrode is chitosan. For IR analysis, we recovered the "neutralized" material from the electrode surface, rinsed it extensively, dried it overnight, and incorporated the material into a KBr pellet. Figure 4 compares the IR spectrum for the KBr pellet of the deposited material with

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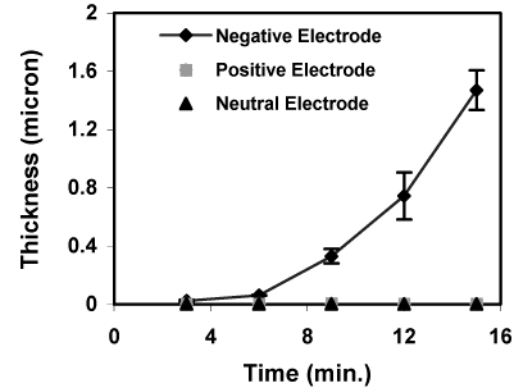

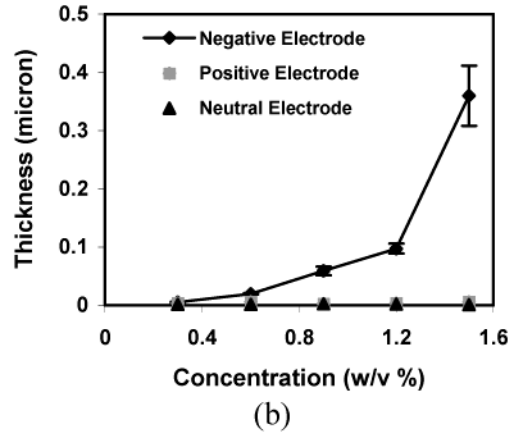

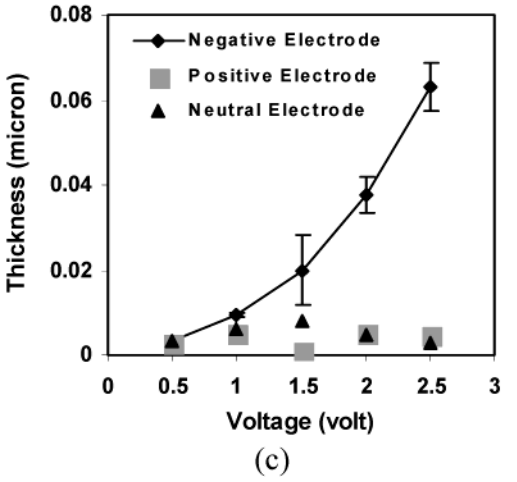

Figure 3. Deposition under varying conditions. (a) Deposition occurred from a 1% w/v chitosan solution using an applied voltage of 2.5 V. (b) Deposition was measured after 6 min using chitosan solutions of varying concentrations and an applied voltage of 2.5 V. (c) Deposition was measured after 6 min from a 1% w/v chitosan solution using varying voltages. In all cases, the electrode was immersed in caustic, rinsed extensively, and dried prior to measuring thickness.

the spectrum of a chitosan film. The absorption spectra are similar for the two samples, providing evidence that the material deposited on the negative electrode is chitosan. Some differences in the spectra are observed in the amine and amide regions (1500−1700 cm^{-1}),[28−30] suggesting the possibility that chitosan chains that are more highly deacetylated (and therefore more highly charged) may be preferentially deposited onto the negative electrode.

Table 1. Expected and Observed *m/z* Values for Enzymatically Hydrolyzed Chitosan[a]

	monomer	dimer	trimer	tetramer	pentamer
$(Gln)_x-3H_2O$	126	287	448	609	770
	(126)	(288)	(448)	(609)	(769)
$(Gln)_x-2H_2O$	144	305	466	627	788
	(144)	(306)	(467)	(625)	(789)
$(Gln)_x-H_2O$	162	323	484	645	806
	(162)	(324)	(484)	(644)	(805)
$(Gln)_x$	180	341	502	663	824
	(180)	(342)	(503)	(663)	(821)
$[GlcNAc\cdot(Gln)_{x-1}]-H_2O$	204	365	526	687	848
	(205)	(364)	(525)	(686)	(847)
$[GlcNAc\cdot(Gln)_{x-1}]$	222	383	544	705	866
			(545)	(705)	(864)

[a] Observed values from Figure 5 appear in parentheses. Gln, glucosamine; GlcNAc, *N*-acetylglucosamine.

The second technique to provide chemical evidence that the deposited material is chitosan was provided by ES-MS. Because chitosan's molecular weight (>300 000 g/mol) exceeds the limit for analysis, we enzymatically hydrolyzed the deposited material and analyzed the hydrolysate. For this analysis, the deposited layer was dissolved from the electrode surface into an acidic solution. After dilution, the solution was incubated with the chitosan-hydrolyzing enzyme, chitosanase.[31] Figure 5 shows the ES-MS results for this hydrolyzate.

To examine the results in Figure 5, it is necessary to consider the peaks expected for the enzymatic hydrolysis of chitosan.[27] Enzymatic hydrolysis of chitosan is known to result in the formation of various species (monomers, dimers, etc.).[32] Additionally, chitosan is a copolymer of glucosamine and *N*-acetylglucosamine, and the predominant oligomeric species are expected to consist of either glucosamine units or both glucosamine and *N*-acetylglucosamine units. Because the degree of acetylation is low (15%), we do not expect significant amounts of oligomers that contain more than a single *N*-acetylglucosamine residue. Finally, it is known that MS spectra of glucosamine and glucosamine trimers contain product ions resulting from the loss of H_2O.[33] Table 1 lists a series of peaks expected for the hydrolysis of chitosan (e.g., various monomers, dimers, trimers, tetramers, and pentamers). By comparison of these expectations with results in Figure 5 (listed in parentheses in Table 1), it is clear that the ES-MS provides strong evidence that the deposited material is chitosan.

A control in the ES-MS study was provided by a sample that was incubated in the absence of chitosanase. The ES-MS analysis of this control showed weak signals with a low signal-to-noise ratio (not shown). This is consistent with the expectation that unhydrolyzed chitosan will be too large (300 000 g/mol) to be measured by ES-MS. The highest signals in this control appeared at *m/z* of 220 and 299, and the latter signal does not even appear in Figure 5. Thus, chitosanase-catalyzed hydrolysis of the deposited material was necessary to attain strong signals in the ES-MS.

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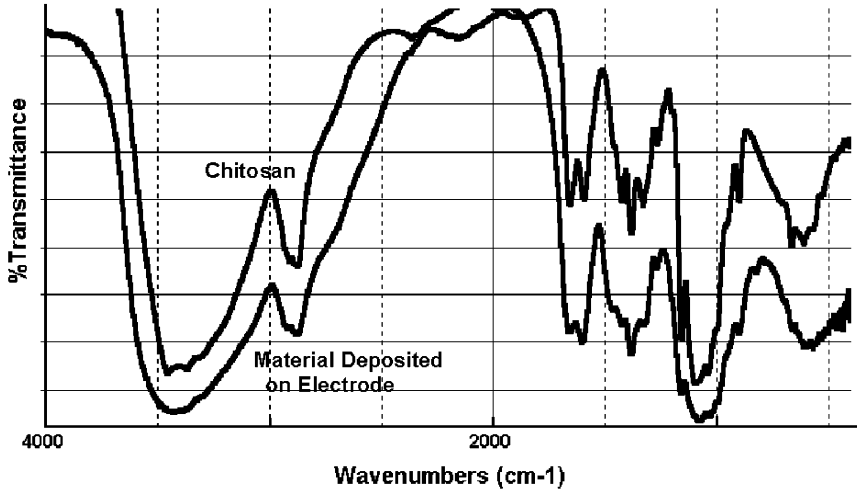

Figure 4. IR spectrum of deposited material and chitosan. Material deposited on the negative electrode was neutralized in base, extensively washed with distilled water, and dried. The IR spectrum was collected using a KBr pellet. The control spectrum was collected using a chitosan film.

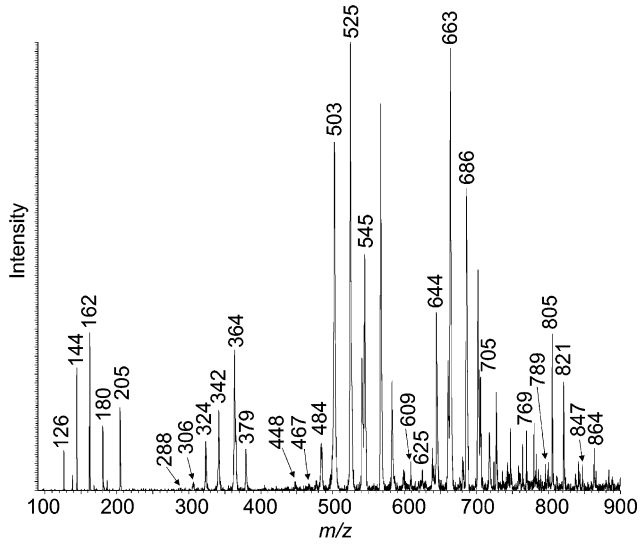

Figure 5. ES-MS spectrum of deposited material after incubation with chitosanase. See the text and Table 1 for details.

In summary, two independent techniques were used to provide chemical evidence that the deposited material was chitosan. Standard IR analysis shows that the spectrum for the deposited material is similar to the spectrum for chitosan. Further, the deposited material was susceptible to hydrolysis by the enzyme chitosanase while the hydrolysate shows a family of peaks consistent with glucosamine and *N*-acetylglucosamine residues, the repeating units of chitosan.

Conclusions

Chitosan is a unique biopolymer that we believe offers interesting possibilities for controlling the surface chemistry of devices. First, chitosan is an amine-rich polysaccharide that is positively charged under mildly acidic conditions. This characteristic allows a thin chitosan layer to be deposited (i.e., "self-assembled") onto a negative electrode in response to an applied voltage. The results reported here demonstrate that the thickness of the deposited layer can be controlled by the conditions used. Second, chitosan's pK_a is rather low (p$K_a \approx 6.3$) compared to those of other amine-containing biopolymers (e.g., polylysine's pK_a is 10.5), and above its pK_a chitosan is insoluble. As a result of this pH-dependent solubility, a simple neutralization step is sufficient to convert chitosan to an insoluble form that can be retained on the surface of the electrode (i.e., the applied voltage is required only for deposition and not to retain the chitosan layer). Third, the high content of primary amine groups allows a chitosan coating to be used for controlling surface properties and for subsequent modification steps. The utility of amine groups is illustrated by the current interest in creating amine-terminated monolayers.[2,34−38] The amine groups also enable biologically active molecules (e.g., peptides and proteins) to be coupled onto chitosan surfaces using standard coupling chemistries (e.g., glutaraldehyde- or carbodiimide-based chemistries)[39−42] or using enzymatic methods.[43,44] Finally, chitosan is gaining increasing attention as a biomaterial for applications ranging from enzyme immobilization[45−49] to the creation of biocompatible surfaces.[50−53] Thus, chitosan may provide an ap-

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propriate interface between biological systems and microelectronic devices.

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