Rapid Deposition of Uniform Polydopamine Coatings on Nanoparticle Surfaces with Controllable Thickness

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ABSTRACT: Polydopamine is a bioinspired, versatile material that can adhere to bulk and nanoscale surfaces made of disparate materials to improve their physical and chemical properties in many applications. The typical methods to coat polydopamine on the nanoparticle substrates usually take several hours to a day. This work successfully applies a dispersion method to form a controllable, uniform coating on a nanoparticle surface within minutes. Using plasmonic Ag nanoparticles as a substrate, the coating thickness can be monitored using a spectroscopic method based on the extinction peak shifts of the Ag nanoparticles. The deposition rate increases with dopamine concentration; however, too much excess dopamine leads to the formation of free dopamine particles. The optimized concentration of dopamine (i.e., ∼6 mM) can be applied to other nanoparticles by normalizing the number of particles to maintain a constant concentration of dopamine per unit surface area (i.e., 1.70 × 10^4 dopamine/nm^2). The molecular dynamics simulation reveals that the amount of hydrogen bonding increases with water content, suggesting that sufficient mixing using the dispersion tool facilitates the formation of hydrogen bonding, thus rapidly depositing PDA on the nanoparticle surface. The physical and chemical properties (e.g., pH response and thermal stability) can be tailored by varying the coating thickness due to the changes in the number of hydrogen bonds and the conformation of π−π interactions. This dispersion method provides a facile means to control the PDA coating thickness on nanoparticle surfaces and thus the surface properties of nanoparticles toward various applications.

INTRODUCTION

Polydopamine (PDA), a bioinspired macromolecule, has emerged as a versatile material that can find use in many applications ranging from surface coating to biomedicine, filtration, chemical sensing, and energy conversion and storage.1−3 PDA is an analogue to the naturally occurring pigment eumelanin, one type of melanin, and shares similar spectral characteristics with eumelanin; however, PDA is best known for its extraordinary adhesion capability comparable to that of the adhesion proteins secreted from the marine mussels. Since its first use as an adhesive material for diverse surfaces,4 PDA has been applied to numerous materials as a surface coating to fabricate multifunctional composites.5 PDA-coated surfaces can be further functionalized with different molecules through the catecholic and quinoid units to create desired functionality.5 It also has been demonstrated that PDA is biocompatible with negligible cytotoxicity, low acute toxicity, no detectable interference with hepatic function, and the physiological regulation of heme or immune response.6−8 The biodegradability of PDA is anticipated to be similar to its analogue melanin,9 which could be fully degraded in 8 weeks following its implantation in vivo.10

Owing to its strong adhesion, chemical reactivity, biocompatibility, and biodegradability, PDA has been extensively explored as a coating for inorganic nanoparticles to interface other materials or biological entities for various applications. For example, Fe_3O_4 nanoparticles coated with PDA shells of ∼20 nm in thickness were synthesized to serve as a platform for responsive drug delivery, recyclable catalyst support, and carbon adsorbent.11 Core−shell nanoparticles of Au−Ag were coated with a PDA layer of 4 nm and used as recyclable nanocatalysts.12 For biomedical applications, PDA-coated Au nanorods were demonstrated for targeted photothermal therapy and chemotherapy of cancer,13−15 while we reported that-PDA coated Au nanocages could be used as carriers for the controlled release of antibiotics, enabling therapeutic synergy of photothermal and antibiotic treatment of infections.16 In tribology, we demonstrated that PDA could serve as an interfacing layer between the Cu nanoparticles and Teflon to enhance the durability of the Teflon thin-film coating.17 Many of these applications require precise control of the PDA-coating...
thickness on the nanoparticles in order to optimize the performance of the hybrid materials for different purposes such as drug loading, chemical diffusion, thermal conductivity, and adhesion.

PDA coatings are typically formed by self-polymerization of monomer dopamine under alkaline pH at ~8.5 in tris-(hydroxymethyl)aminomethane (tris) buffer at ambient temperature using a submerged stirring method. These methods usually take several hours (3–12 h) to deposit PDA coating on the nanoparticle surface, and thus it is hard to control the coating thickness efficiently. The reported PDA coating thickness varied from a few nanometers to tens of nanometers. Alternatively, the method using a sonication approach could speed up the coating process; however, it often results in inhomogeneous coating on the nanoparticle surface. Recently, an electrochemical method was reported to form PDA coating on magnetite nanoparticles in 30 min by adding the monomer during the electrochemical oxidation of Fe foils to magnetite nanoparticles. Nonetheless, this approach was only applicable for the PDA coating on oxide nanoparticles. Additionally, the controls over the size of nanoparticles and coating thickness of PDA remain challenging. In this work, we developed a rapid deposition method by the use of a dispersion tool to coat PDA onto a nanoparticle surface. Using Ag nanoparticles as an example, a uniform coating of PDA was formed on the nanoparticle surface, and the coating thickness increased with reaction time. Free PDA particles can be completely eliminated by adding the ratio of monomers to the total surface area of the nanoparticles added to the reaction. We further performed molecular dynamics simulations to elucidate the interaction among dopamine monomers/trimers and the stacking mechanisms of dopamine on a substrate. The results show that the π–π interactions vary depending on the existence of trimers/monomers, and the number of hydrogen bonds increases with increased PDA thickness and water content. This robust and facile approach to producing uniform PDA coatings on nanoparticle surfaces with controllable thickness provides the opportunity to maximize the performance of PDA-coated nanoparticles for various applications.

**EXPERIMENTAL AND SIMULATION METHODS**

**Chemicals and Materials.** Silver trifluoroacetate (AgTFA), sodium hydrogen sulfide (NaHS), hydrochloric acid (HCl, 99.999%), and nitric acid (HNO₃, 99.999%) were purchased from Alfa Aesar. Poly(vinylpyrrolidone) (PVP, MW = 55 000), tris-(hydroxymethyl)aminomethane (Trizma base, >99.0%), and dopamine hydrochloride were mixed in air at 50 °C. The concentration of Ag was determined using a flame atomic absorption (AA) spectrometer (GBC 932). UV–vis spectra were taken on a UV–vis spectrophotometer (Agilent Cary 50). Infrared (IR) spectra were obtained using a Fourier transform infrared (FTIR) spectrometer (Perkin Elmer). Thermogravimetric analysis (TGA) was performed using a TGA instrument (TA Q50).

**Simulation.** The deposition of dopamine on the substrate was studied using molecular dynamics simulations. Three different samples were created, where each sample consists of dopamine monomers, dopamine trimers, or a mixture of monomers and trimers. For the third sample, the monomer-to-trimer ratio is 1:1, to study the dopamine assembly process and the number of hydrogen bonds formed. Dopamine-coating thickness effects were studied by varying the coating thickness (h) from 5.5 to 24.2 Å. All models were equilibrated using the NVT canonical ensemble as implemented in large-scale atomic/molecular massively parallel simulator (LAMMPS) for 50 ps at 323 K. Periodic boundary conditions were used in the x and z directions, parallel to the substrate. The ReaxFF potential was used due to its quantum mechanical accuracy, as well as the ability to describe behavior of hydrocarbons. Visualizations were created using VMD and MATLAB.

**RESULTS AND DISCUSSION**

A dispersion method was developed to achieve controllable, rapid deposition of PDA coatings on nanoparticle surfaces. The disperser setup allows the reaction mixture to be automatically drawn circumferentially into the dispersion head and then forces out radially through the slots between the rotor and stator arrangement to provide optimal mixing of the suspension (Figure 1A). In a typical PDA-coating synthesis, 5.8 mM dopamine hydrochloride was mixed in air at 50 °C with 10 mM Trizma base dissolved in 200 mL of aqueous solution that contains a specific amount of nanoparticles (Figure 1B). The solution of 200 mL of 10 mM Trizma base alone had a pH of 10.02 at 25 °C. The pH of the solution decreased to 9.37 when the temperature was increased to 50 °C and further neutralized to 8.21 upon the addition of dopamine hydrochloride. The dissolved oxygen (DO) concentration of the reaction solution at 50 °C was 10.11 mg/L, which fell into the normal DO range of the marine water. To reduce the formation of free PDA particles in the reaction, nanoparticles were added to the tris-buffered solution prior to the addition of the dopamine monomer.

To study the coating process, Ag nanoparticles were chosen as an example because they are readily available in large quantity through a scale-up synthesis, and the sharp and intense localized surface plasmon resonance (LSPR) peak of Ag nanoparticles can be used to monitor the coating process.
Figure 2A shows the TEM image of the Ag nanoparticles, indicating that nanoparticles were cubic in shape with an average edge length of $47.6 \pm 6.0$ nm. These nanoparticles at a final concentration of 48 pM or $2.9 \times 10^{10}$ particles/mL were added to the reaction as described in Figure 1B, yielding a uniform coating of PDA on the surface of each nanoparticle in 15 min (Figure 2B). On the basis of analysis of the TEM images (Figure 2B–E), the PDA-coating thickness increased with the reaction time, from $12.0 \pm 2.1$, to $18.0 \pm 1.9$, 22.5 ± 2.9, and $28.4 \pm 3.2$ nm, corresponding to the reaction times of 15, 30, 45, and 60 min, respectively. We plotted the PDA-coating thickness as a function of reaction time. Interestingly, the data points agreed well with a linear fit within the time period of 15–60 min. The slope of the fitting curve was steeper than the connected line between 0 and 15 min, suggesting that the initial rate of the PDA deposition on nanoparticle surfaces was faster than that of the later stage of the reaction, that is, after the coating process had proceeded for 15 min. The coating rate was estimated to decrease by half, from $\sim 0.8$ to $\sim 0.4$ nm/min.

The reaction progress was monitored by the shift of the LSPR peak of the Ag nanoparticles. Figure 3A shows the extinction spectra of Ag nanoparticles at different time points during the PDA coating process. The shape of the LSPR peaks remains unchanged, indicating that the nanoparticles are well-dispersed after coating with PDA. The hydrodynamic diameter of the PDA-coated Ag nanoparticles was measured to be 195.5 ± 3.2 nm with narrow size distribution, which also confirmed a good dispersion of the composite nanoparticles. A progressive red-shift of the LSPR peak of the Ag nanoparticles was observed as the reaction proceeded. The LSPR of metal nanoparticles is sensitive to the refractive index of the media surrounding individual particles. The LSPR shift as a function of the coating/adsorbate thickness follows the relationship described in eq 1:

$$\Delta \lambda_{\text{max}} = m \Delta n \left[ 1 - \exp \left( -2d/L_0 \right) \right]$$

where $\Delta \lambda_{\text{max}}$ is the shift of the LSPR peak, $m$ is the coating molar absorptivity, $\Delta n$ is the change in the refractive index of the coating layer, $d$ is the coating thickness, and $L_0$ is the LSPR length of the nanoparticles.
Therefore, the LSPR shift and the calculated PDA-coating thickness of the nanoparticle(s) are linearly shift to the red as the PDA shell becomes thicker according to the relationship described in eq 2. We plotted the LSPR peak shift of Ag nanoparticles as a function of the PDA-coating thickness (Figure 3B). A linear fit of the data was only found within the coating-thickness range from 0 up to ~25 nm, suggesting that the linear relationship in eq 2 could no longer be applied to predict the LSPR shift for the coating thickness > 25 nm. It is implied that the LSPR shift is not sensitive to the change of coating thickness beyond 25 nm due to the exponential decay of the EM field. Nonetheless, the LSPR sensing method could be useful for monitoring the coating progression on plasmonic nanoparticles such as Ag, especially at the early stage when the coating is thin.

After the reaction, the product was collected and the functionality was analyzed by FTIR spectroscopy. Figure 3C shows the IR spectrum of the PDA-coated Ag nanoparticles that were compressed with KBr powder as a transparent pellet. The peak at 1611 cm$^{-1}$ can be assigned to C–C stretching of indole or indoline structures, while the peaks at 1729, 2846/2916, and 3600 cm$^{-1}$ can be attributed to C=O, C–H, and N–H stretching on the heterocyclic molecules.27 Combined with the TEM observation, the results confirmed the PDA coating on the Ag nanoparticles. The product was further characterized by TGA. The TGA was performed under N$_2$ flow at a rate of 60 mL/min with temperature ramping from 30 to 800 °C at a rate of 10.0 °C/min (solid black curve of Figure 3D). The thermal degradation underwent multiple steps beginning at ~350 °C. After the temperature reached 800 °C, 60 wt % residue remained in the sample, which may contain both Ag and char. The TGA was also carried out under air flow at a rate of 60 mL/min with temperature ramping from 30 to 800 °C at a rate of 10.00 °C/min (solid red curve of Figure 3D). The oxidative environment led to an increase in the weight loss of the sample to 64% at 800 °C. The control experiments indicated the PDA alone without Ag nanoparticles completely degraded in air when temperature reached ~550 °C (dashed red curve of Figure 3D). On the basis of the complete degradation of PDA in air above 550 °C, it is suggested that the 36 wt % residue left from the TGA data of PDA-coated Ag nanoparticle sample in air is composed of Ag only. Thus, the 60 wt % residue left from the TGA data of PDA-coated Ag nanoparticle sample under N$_2$ is composed of 36 wt % Ag and 24 wt % char. This result agreed well with the control experiment in which PDA alone was thermally decomposed under N$_2$, leaving 22 wt % char residue at 800 °C (dashed black curve of Figure 3D). It is suggested that the charring process generates a thermal insulation barrier to prevent PDA from complete thermal degradation. This finding is supported by the previous study on the flame-retardant properties of PDA.28 For
comparison, the pristine Ag nanoparticles before the PDA-coating process were characterized by FTIR spectroscopy and TGA (Figure S2). Because the weight percent of PVP in the sample was <5%, no detectable peaks of PVP were observed in the IR spectrum of the pristine Ag nanoparticles.

The PDA-coating rate highly depends on the concentration of the dopamine monomer. With other reaction conditions fixed, the dopamine concentration was reduced by 5-fold. The reaction was monitored by UV–vis spectroscopy, as shown in Figure 4A. Using the linear relationship of LSPR shift and coating thickness derived from Figure 3B, the coating thickness was calculated and plotted as a function of reaction time (Figure 4B). The rate of the coating process was estimated to be 0.06 nm/min. After the reaction proceeded for 60 min, the coating thickness was calculated to be 3.6 nm, which matched the value of 0.06 nm/min. After the reaction proceeded for 60 min with the coating thickness measured to be 29.2 ± 3.8 nm, which is surprisingly similar to that of the previous reaction in Figure 2. Compared to the “bare” Ag nanoparticles, the LSPR peaks were shifted by ~42 nm after the coating process. These results suggest that the PDA-coating method described in this work can be easily applied to other nanoparticle surface through simple normalization of the dopamine amount to surface area.

A number of models have been proposed to elucidate the PDA structures based on the different pieces of spectroscopic evidence; however, the reaction pathways remain to be unclear because there exist several oxidative forms of dopamine and all of them can undergo covalent polymerization and/or noncovalent self-assembly. The predominate intermediate monomers and oligomers depend on the reaction conditions such as initial dopamine concentration, pH, type of buffer, O2 concentration, and temperature. When all other conditions are fixed, the change of dopamine concentration evidently influences the ratio of uncyclized catecholamine to cyclized 5,6-dihydroxyindole (DHI). At a high concentration of dopamine (e.g., 10 mM), the reaction favors the formation of catecholamine-based oligomers, while a low concentration (e.g., 0.5 mM) promotes the intramolecular cyclization to DHI for polymerization. In both cases, the reaction was followed by self-assembly of the monomers/oligomers. On the other hand, only noncovalent assembly predominated by trimers of uncyclized catecholamine to DHI (2:1) was found in solution during the synthesis. On the basis of this evidence, because a high concentration of dopamine (~6 mM) was used in our case, we therefore hypothesize that the catecholamine-based pathway is favored.

To study the self-assembled behavior of the monomers and oligomers in our synthesis, computational models of dopamine monomers, trimers, and 1:1 ratio of monomers to trimers were generated, as shown in Figure 6. Trimers are visualized by a mauve color, while monomers are represented by green. We studied the self-assembled behavior for four thicknesses of dopamine trimers with h values of 5.5, 11.3, 19.2, and 21.5 Å, three thicknesses of dopamine monomers with h values of 11.6, 13.6, and 15.9 Å, and four thicknesses of monomer–trimer 1:1 mixture with h values of 10.3, 14.0, 21.1, and 24.2 Å. Six models were also created for dopamine trimers with a constant h value of 21.5 Å, while allowing the amount of water content to vary from 0%, 4%, 7%, 9%, 12%, to 14% weight of the sample. The samples were generated by depositing the monomers and trimers on a metal substrate and equilibrated using molecular dynamics method. We note that the objective of the computational models is not to predict the reaction rate but to understand the deposition process of monomers and trimers.

The intermolecular interactions among the monomers, trimers, and water molecules were studied in the simulations. Figure 7A shows that the number of hydrogen bonds formed between hydrogen atoms in dopamine molecules and oxygen atoms in water increases as the percentage of water increases. The molecule stacking of (i) and (ii) labeled in Figure 7A is
shown in Figure 7B. Similar trends were found for all layer thicknesses in all three cases, i.e., monomers alone, trimers alone, and a mixture of 1:1 monomer-to-trimer ratio. This observation implies that good accessibility to water during the reaction can promote the formation of hydrogen bonding in the PDA structure. Because the backbones of dopamine oligomers or polymers repel water, agitating the reaction solution vigorously can increase the contact between water molecules and PDA, thus promoting the formation of hydrogen bonding. The number of hydrogen bonds increases as the dopamine-coating thickness increases, as plotted in Figure 7C. Figure 7D shows the visualization of the front view for the selected conditions indicated as (a−d) in Figure 7C. It is worth noting that the hydrogen bonding in the PDA structures is responsive for the controlled release of the trapped molecules in response to pH changes.\(^{34,35}\) The dispersion method can effectively mix the solution and facilitate the formation of hydrogen bonding, resulting in the PDA coating on nanoparticles having a better pH response for controlled release\(^7\) and a more stable layer against thermal degradation.\(^{28}\)
Because each dopamine contains a benzene ring, π−π interactions were observed in all samples. For monomers, π−π interactions cause the monomer stacking to be either parallel to each other or in a pinwheel arrangement, as shown in Figure 8A. As the layer thickness of the monomer models increases, the amount of parallel stacking and pinwheel stacking increases proportionally. In the mixture of 1:1 monomers and trimers, the monomers were observed to create predominately parallel stacking to trimers. Interestingly, we observed the conformation changes of π−π interactions as the coating thickness increases (Figure 8B). With a thin coating (e.g., 10.3 Å), the trimers and monomers would separate and attempt to from π−π bonds with their corresponding counterparts. As the thickness increases to 14.0 Å, the trimers and monomers mix homogeneously. At a thickness of 21.1 Å, the trimers are beginning to form π−π interactions with multiple trimer molecules. This observation suggests that the monomers form intermittent π−π interactions with trimers, leaving the trimers with one less spot for another π−π interaction, which leads to uneven alignment among multiple trimers. Thus, the uniformity of the π−π interactions decreases as the layer thickness increases in the mixed samples. In the case of trimers alone, the samples contain π−π interactions by stacking parallel to each other, similar to benzene ring π−π interactions, as shown in Figure 7B(i) and (ii), for the trimers samples containing 4 and 14 wt % water content, respectively. These observations suggest that morphology of the PDA structures could be tuned by the π−π interactions. The simulation results can be used to explain the thermal stability difference between PDA coating on nanoparticles and the PDA particles. As shown in Figures 3D and S1, the decomposition of PDA coating on nanoparticles shows substantial weight loss at 352 °C, but the PDA particles display a much slower degradation process starting from 350 to 550 °C. This increase in the thermal stability for PDA particles compared to the PDA coating is due to the thickness difference of the PDA. Increasing the thickness from PDA coating (~30 nm) to PDA particles with a radius of 50 nm increases the number of hydrogen-bonding and strength of π−π interactions, thus improving the stability of the PDA layer. Thus, being able to experimentally control the PDA thickness provides a means to tailor the PDA properties.

**CONCLUSION**

A dispersion method was successfully employed to effectively deposit uniform coating of polydopamine on a nanoparticle surface. The coating thickness can be controlled up to ~30 nm by simply varying the reaction time. Using plasmonic nanoparticles such as Ag, the reaction progression can be monitored based on the LSPR linear shift for the coating thickness within the range of tens of nanometers. At a fixed particle concentration, the deposition rate increases with increased dopamine concentration; however, too much excess dopamine concentration led to the increased formation of free dopamine particles. The optimized condition can be applied to other nanoparticles based on the normalized dopamine per unit surface area (i.e., 1.70 × 10^4 dopamine/nm^2). Compared to the typical PDA formation at a rate of ~0.06 nm/min, the deposition rate in this work was improved by an order of magnitude at a rate of ~0.6 nm/min. The molecular dynamics simulation reveals intermolecular interactions such as hydrogen bonding and π−π interactions among the monomers, oligomers (e.g., trimers), and water molecules. The simulation shows that the number of hydrogen bonds increases with water content, suggesting that sufficient mixing using the dispersion tool facilitates the formation of hydrogen bonding, thus rapidly depositing PDA on the nanoparticle surfaces. The physical and chemical properties (e.g., pH response and thermal stability) can be tailored by the coating thickness because the amount of hydrogen bonding increases with coating thickness and the conformation of π−π interactions varies with the ratio of monomers to trimers. This study developed a robust means to tailor the PDA thickness on nanoparticle surfaces and provided some insight and guideline to optimize the PDA structures and properties for various applications such as drug delivery and tribology.

**ASSOCIATED CONTENT**

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.langmuir.7b00671.

First derivative analysis of TGA data; IR spectra and TGA curves of pristine Ag nanoparticles (PDF)

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Notes

The authors declare no competing financial interest.

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