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A SERS study of the molecular structure of alkanethiol monolayers on Ag nanocubes in the presence of aqueous glucose

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Abstract

We report progress towards the surface-enhanced Raman scattering (SERS) characterization of self-assembled monolayers (SAMs) on uniform Ag nanocubes. This study quantifies changes in the SAMs induced by the presence of aqueous glucose. The SAMs were prepared from dodecanethiol and they were representative of highly ordered monolayers as indicated by SERS analysis. We examined the SAMs response to glucose and observed conformational changes in the alkanethiolate SAMs. Analysis of the trans and gauche bands as well as the C-H stretching modes of the SAMs suggest that the analyte-SAM interactions were superficial and there was no penetration for the glucose molecules into the monolayers.

1. Introduction

As surface-enhanced Raman scattering (SERS) begins to mature in terms of reproducibility and understanding, issues relating to its application as a robust platform for sensing will become more important [1–3]. One of the most significant problems is the interaction of the analyte of interest to the enhancing metal surface. Spatially, the molecule of interest must be within an appropriate distance to the metal surface for enhancement to occur and, temporally, the molecule must be within the surface proximity for many seconds to minutes for spectral recording. Self-assembled monolayers (SAMs) have the potential to address these problems as they form readily on both silver and gold, two noble metals most commonly used for SERS; they are thin enough (0.5–2 nm) to allow for significant local-field enhancement; and their compositions, structural orders, and interfacial properties can be tailored for molecular retention [4,5]. The analyte-SAM interaction has been of notable interest as this subject is directly related to molecular recognition, chemical separations, and molecular electronics [6–8]. For proteins, this subject has been explored extensively, and an understanding of why proteins readily adsorb onto alkanethiolate SAMs but not oligo(ethylene glycol) SAMs has some experimental and theoretical evidence [9,10]. However, for smaller molecules, those that approach the size of the SAM component, there remains no rational design strategy for molecule/SAM interactions in the context of retention, partitioning, or exclusion.

Molecular retention at alkanethiolate SAM interfaces can be used to concentrate molecules for detection applications. In addition, SAMs on metal nanoparticles present a rich interface with

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many possibilities including the concentration of molecules on their surface for potential transportation and release applications [11]. However, this interface remains largely unexplored. In this study, uniform Ag nanocubes covered with alkanethiolate SAMs are used to demonstrate the detection of glucose by SERS, and to investigate the structural relationship of the SAM to the retention of glucose. SERS is gaining a strong presence in the analytical sciences for detection and quantification, but this technique is also primed to study how molecules and SAMs interact on a metal surface. An understanding of the interactions between small molecules and SAMs is vital for further engineering SAM-based nanoparticles in an effort to optimize SAM-based SERS platforms for chemical detection.

2. Experimental Section

2.1 Particle synthesis

The Ag nanocubes were synthesized using the polyol method where AgNO_3 was reduced to elemental silver and carefully grown to form nanocubes. Every effort has been made to advance the synthesis of Ag nanocubes [12]. The procedure for synthesizing Ag nanocubes in this study was reported elsewhere [13]. In brief, the Ag nanocubes were synthesized by reduction of AgNO_3 with ethylene glycol (EG) in the presence of poly(vinyl pyrrolidone) (PVP) and HCl. Following synthesis the Ag nanocubes were isolated by centrifugation, washed with water to remove EG and excess PVP and finally dispersed in deionized water for storage. The Ag nanocubes were characterized with scanning electron microscopy (SEM), and the samples were prepared by drying aqueous suspensions of Ag nanocubes on silicon wafers under ambient conditions. SEM images were obtained using an FEI Sirion SEM at 15 kV. Nanocube sizes were obtained from the SEM images using ImageJ (Wayne Rasband, NIH) software. Localized surface plasmon resonance (LSPR) spectra were recorded using a Varian Cary 50 UV-vis spectrophotometer equipped with tungsten lamp. Particle concentrations were estimated by determining the Ag concentration with an Agilent 7500 ce ICP-MS inductively coupled plasma spectrometer and using this knowledge with nanoparticle dimensions from the SEM. Ag nanocubes (7 nm) were dispersed into a 1 mM ethanolic solution of 1-dodecanethiol (1-DDT) to form the 1-DDT SAM. This mixture sat for ~18 h, followed by centrifugation and removal of supernatant. Neat ethanol was used to wash the sample several times before resuspending the sample in water to achieve a concentration of 1–2 nM of Ag nanocubes with the 1-DDT SAM (1-DDT nanocubes).

2.2 Data acquisition and processing

The Raman spectra were recorded from a solution phase using a Renishaw inVia confocal Raman spectrometer coupled to a Leica microscope with 50x objective in backscattering geometry. The 514 nm wavelength was generated with an argon laser and used with a holographic notch filter with a grating of 1200 lines per millimeter. The backscattered Raman signals were collected on a thermoelectrically cooled (-60°C) CCD detector. Samples of varying concentrations of aqueous glucose (pH ~7) were prepared with a fixed concentration of 1-DDT-covered nanocubes. The samples reacted for 1 h to ensure complete adsorption. There was no visual change to the solubility of the nanocubes with increasing glucose concentration. For temporal analysis, 1-DDT-covered nanocubes were incubated in a 250 mM solution of glucose 1 h, followed by centrifugation. The supernatant was pipetted off and an equal volume of water was added. The sample was sonicated to resuspend the nanocubes and immediately pipetted into the stage vessel for Raman-analysis. This step took 25 s. Data was taken continuously with $\lambda_{\text{ex}} = 785\text{ nm}$, $P_{\text{laser}} = 50\text{ mW}$, and $t = 15\text{ s}$. The short acquisition time necessitated the use of a more powerful laser. The 785 nm wavelength was generated with a diode laser and used with a holographic notch filter with a grating of 1200 lines per millimeter.

Preprocessing of the Raman spectra and all data analysis was done with IGOR Pro software (Portland, OR). All data was baseline corrected before normalization. For the baseline correction a fourth order polynomial was fitted to the raw Raman spectrum and subtracted. For glucose detection peak normalization was used. The SERS spectral intensities were normalized using the peak at 706 cm^{-1} from the 1-DDT SAM. The normalization factor for each spectrum was determined by subtracting the intensity of the peak at 706 cm^{-1} from the background of the spectrum. This absolute intensity was then divided by the average absolute intensity calculated for each experiment. This allowed for complete removal of the 1-DDT SAM spectrum. For determining the effect of glucose on the 1-DDT, vector normalization was done by calculating the sum of the squared intensity values of the spectrum and using the squared root of this sum as the normalization constant. We found that this normalization method was most agreeable to interpreting the structural changes in the 1-DDT SAM, as most of the Raman peaks varied and were not suitable for peak normalization. Furthermore, this preprocessing method has recently been investigated favorably [14]. For the temporal study the band intensities were obtained by fitting the data to the superposition of the Lorentzian amplitude line shapes after preprocessing.

3. Results and Discussion

3.1 Formation and stability of 1-DDT SAMs on Ag nanocubes

The formation of SAMs on extended metal surfaces and, to a lesser extent, metallic nanoparticles has been documented extensively [15]. Together, these studies have indicated that SAMs on nanoparticles exhibit a substantial difference in geometry, composition, packing density, and other physical properties as compared to SAMs on extended surfaces. These differences have been primarily found for small nanoparticles (5 to 20 nm), however, phase separation of mixed SAMs has also been observed for spherical particles 40 nm in diameter [16]. Figure 1A shows the Ag nanocubes used in this study; they have flat square faces characterized by {100} planes [13]. Figure 1B shows the effect of SAM formation on the LSPR of the Ag nanocubes. The broad LSPR peaks are common for large Ag nanocubes [17]. The dipole peak at 445 nm and the multipole peak at 400 nm are red-shifted by 22 nm after functionalization with 1-DDT due to a change in refractive index caused by thiol adsorption onto the Ag nanocube surface [18].

From Figure 1A it is clear the particles used in this study are not spherical and are relatively large as compared to other studies that suggest SAMs formed on small nanoparticles have loose packing densities. Figure 2 presents the SERS spectrum of the 1-DDT SAMs on Ag nanocubes that are suspended in water. The binding of 1-DDT to the surface of Ag nanocubes proceeds by losing its hydrogen to form a thiolate and chemisorption of the sulfur head group to Ag [19]. This is readily observed in the SERS spectrum of the SAMs on Ag nanocubes. Alkanethiols exhibit a strong $\nu(\text{S-H})$ vibration at 2575 cm^{-1} which is absent in the spectra taken with the 1-DDT-covered nanocubes. The vibrational contributions of the gauche (G) and trans (T) intensities in the $\nu(\text{C-S})$ region is indicative of the extent of order and crystallinity in the SAMs [20,21]. The ratio between the intensities of the 706 cm^{-1} $\nu(\text{C-S})_{\text{T}}$ and the 632 cm^{-1} $\nu(\text{C-S})_{\text{G}}$ for the 1-DDT SAMs on Ag nanocubes differs by a factor of >10 , indicating that the monolayer is highly ordered which in turn signifies a dense SAM coverage on the Ag nanocube. The 1080 cm^{-1} $\nu(\text{C-C})_{\text{G}}$ band is a third less intense as the 1125 cm^{-1} $\nu(\text{C-C})_{\text{T}}$ band, which is a characteristic of 1-DDT SAMs. Table 1 summarizes the Raman modes observed in our study in comparison to values reported for 1-DDT SAMs formed on extended Ag surfaces. The agreement between peak frequencies also supports the formation of highly ordered SAMs.

3.2 Detection of glucose

Glucose has been shown to interact with a C8 hydrophobic stationary phase in reverse-phase chromatography (RPC) [22], and also various alkanethiolate SAMs over extended surfaces [22,24]. Attempts to detect glucose with metal surfaces and also, specific to this study, unfunctionalized Ag nanocubes have been unsuccessful. The mechanism elucidating the retention of an analyte to a hydrophobic surface in an aqueous environment remains unsettled and is experimentally dependent on a number of factors related to the analyte, stationary phase, and mobile phase [25,26]. For RPC silica beads modified by C4-C18 alkyl chains, a reversible adsorption-partition model has been used to explain the retention mechanism for polar and neutral analytes [27], and has been evoked to explain the interaction of glucose with various SAMs formed on metal surfaces [23,24]. While spectroscopic studies on RPC columns reveal significant differences in the packing structure for alkyl chains as compared with alkanethiolate SAMs on metal surfaces [28], RPC retention mechanisms can be helpful in understanding the analyte-SAM interactions for both metal nanoparticles and extended metal surfaces. Figure 3, A–D, shows the SERS spectra taken from 1-DDT SAMs on Ag nanocubes in the presence of glucose at different concentrations. There was a direct correlation between the intensity of the resolved glucose bands and the concentration. This data indicates that the glucose was within an appropriate distance to the metal surface to facilitate signal enhancement. No Raman signal was detectable with our acquisition parameters for the highest pertinent concentration of glucose used in this study (250 mM) in the absence of 1-DDT nanocubes.

Figure 3F shows the Raman spectrum of a saturated (~5 M) solution of glucose. The Raman bands at 1465 cm^{-1} for $\nu(\text{CH})$; 1365 and 1267 cm^{-1} for $\delta(\text{C-C-H})$, $\delta(\text{O-C-H})$, and $\delta(\text{C-O-H})$; 1125 cm^{-1} for $\nu(\text{C-C})$; 1065 cm^{-1} for $\nu(\text{C-H})$; 915 and 847 cm^{-1} for $\nu(\text{C-O})$ and $\nu(\text{C-C})$; and 519 cm^{-1} for $\delta(\text{C2-C1-O1})$ correspond to aqueous glucose [29]. The spectra in Figure 3, G–J, show the SERS spectra obtained by subtracting the spectrum in (E) from the spectra displayed in (A–D), clearly demonstrating the presence of glucose.

The reversible nature of the glucose/1-DDT SAM interaction was verified by first allowing the 1-DDT-covered Ag nanocubes to equilibrate with a 250 mM solution of glucose, followed by centrifugation and resuspension in pure water. The glucose $\delta(\text{C-C-H})$ vibration at 1365 cm^{-1} , which is not overlapped with a band from the monolayer, was monitored after the Ag nanocubes were dispersed in pure water, and its intensity as a function of time is shown in Figure 4A. Figure 4B shows a plot of the Lorentzian fitted amplitude changes of the 1365 cm^{-1} band at different times. The steady decrease in the glucose Raman intensity implies that the glucose/SAM interaction is reversible and comparatively transient. The driving force for glucose adsorption onto the 1-DDT SAM/water interface is most likely related to the high surface energy of the hydrophobic nanocubes. Glucose adsorption can reduce the solvation energy of the 1-DDT-coated Ag nanocubes in water [30], while the relative solubility of glucose in water, and to a lesser extent, the loss of translational freedom upon adsorption make this interaction reversible.

3.3 Interaction of glucose with the 1-DDT SAMs

1-DDT was chosen because the SAM of this alkanethiol is a relatively disordered [20,31]. This is reflected by the 1125 cm^{-1} $\nu(\text{C-C})_{\text{T}}$ and 1081 cm^{-1} $\nu(\text{C-C})_{\text{G}}$ band intensities. In addition, the thickness (~1.5 nm) [32] of 1-DDT SAMs is appropriate considering the decay length of SERS enhancement. It has been suggested that a disordered SAM will have greater permeability for or adsorption affinity to analyte molecules [33–35]. Several 1-DDT SAM Raman bands were investigated to establish evidence for the partition mechanism, by which the glucose is assumed to penetrate into the 1-DDT SAMs. We argue that if partitioning occurs this will disrupt the crystallinity of the 1-DDT SAMs and increase gauche vibrational modes. To this end, several Raman bands of the 1-DDT nanocubes were analyzed in the presence of

glucose at varying concentrations. The SERS spectra of the C-H region (Figure 5A) and the C-C region (Figure 5B) in the presence of 250 mM and 0 mM aqueous glucose are plotted together to highlight the differences introduced by glucose. Note that we have to limit this study to the SERS bands of 1-DDT SAMs that do not overlap with those of glucose. Otherwise, Raman bands will increase in intensity with glucose concentration and thus will not be able to provide information on the structural rearrangement of 1-DDT SAMs.

While the influence of glucose on the Raman bands of 1-DDT SAMs can be quantified, the relationship between the changes in the spectra and the structure of the monolayer is more difficult to determine. From the C-C spectral region, the structural integrity of the broad feature centered at 1440 cm^{-1} , with the CH_2 scissor deformation at 1433 cm^{-1} and the CH_3 symmetric deformation band at 1454 cm^{-1} , suggests that in the presence of glucose there was little to no gauche bond formation. An increase in gauche bond formation would result in the split-peak pattern to degrade towards a single peak, which was not observed [36,37]. Furthermore, while both the $\nu(\text{S-C})_{\text{T}}$ and $\nu(\text{C-C})_{\text{G}}$ bands were attenuated in the presence of glucose the ratio between the peaks, $I[\nu(\text{S-C})_{\text{T}}]/I[\nu(\text{C-C})_{\text{G}}]$, was constant, indicating that the gauche bond population near the inner monolayer did not change due to adsorbed glucose.

The C-H region is more sensitive to conformation changes, but analysis of the C-H region is complex due to the overlap of several Fermi resonance bands of both symmetric and antisymmetric methylene and methyl modes. Peak intensity ratios from this region are used to determine the conformation of the alkyl chains. These ratios have long served as empirical indicators of the conformational structure of biological membranes [38], alkanes [39], and, more recently, alkanethiolate SAMs [40]. The $\nu_{\text{as}}(\text{CH}_2)$ 2904 cm^{-1} , $\nu_{\text{s}}(\text{CH}_2)$ 2850 cm^{-1} , and the $\nu_{\text{s}}(\text{CH}_3, \text{FR})$ 2936 cm^{-1} are the three bands used to determine changes in conformation or rotational disorder of alkyl chain assemblies. Table 2 lists the various empirical ratios used in this study.

In the presence of glucose the $I[\nu_{\text{as}}(\text{CH}_2)]/I[\nu_{\text{s}}(\text{CH}_3, \text{FR})]$ ratio increased. The increase of this ratio has been observed in alkanethiolate SAMs that have become more ordered [40]. Furthermore, these bands are sensitive to intermolecular interactions and with an increase in interchain disorder the $\nu_{\text{as}}(\text{CH}_2)$ band decreases and the $\nu_{\text{s}}(\text{CH}_3, \text{FR})$ band increases [39,41]. Our data shows an opposite trend and suggests that in the presence of glucose there is a decrease in the intramolecular motion of the alkyl chains and an increase in interchain coupling. Similarly, the $I[\nu_{\text{s}}(\text{CH}_3, \text{FR})]/I[\nu_{\text{s}}(\text{CH}_2)]$ ratio is sensitive to chain coupling related to terminal methyl rotations, and also the effects of the solvent [42]. This ratio is observed to decrease with an increase in disorder in alkanes [39]. In our study, this ratio increased in the presence of glucose, also suggesting that the 1-DDT SAMs became more ordered.

The $I[\nu_{\text{as}}(\text{CH}_2)]/I[\nu_{\text{s}}(\text{CH}_2)]$ ratio is sensitive to small changes associated with both conformation and rotational order. For alkanes and alkylsilane stationary phases this ratio is observed to decrease with disorder [39,43]. In our study this ratio was observed to increase in the presence of glucose, which is interpreted as an increase in the order of the 1-DDT SAMs. The observed increase in order can be further attributed to a decrease in rotational disorder or a decrease in gauche bond population [42]. For the 1-DDT SAMs, because they are already highly ordered the observed increase in order can be attributed to a decrease in rotational freedom of the terminal methyl groups, which in turn promotes intermolecular coupling of alkyl chains. This argument fits well with the lack of conformational change observed for the inner monolayer, the $\nu(\text{S-C})$ bands, and the bands centered at 1440 cm^{-1} which are primarily sensitive to gross conformation changes. If adsorption of glucose occurs, the terminal methyl groups of the 1-DDT SAMs would be affected, and indeed the data supports a decrease in terminal methyl rotation and concomitant ordering. The interaction of glucose and 1-DDT can therefore best be thought of as a van der Waals interaction between glucose and the terminal

methyl groups of the 1-DDT SAM after glucose adsorbs to the SAM surface. This weak attraction may contribute to the observed decrease in terminal methyl rotation, however, the ordering of the 1-DDT SAM is most likely a result of adsorbed glucose excluding water from the 1-DDT SAM interface.

4. Summary and conclusion

The data from individual line shapes and intensities suggests that the 1-DDT SAMs, in the presence of glucose, did not increase its gauche bond population, but instead, gained order. Taken together, these spectral attributes lead us to conclude that glucose adsorbs to the 1-DDT SAMs superficially in an effort to reduce the high surface energy of the SAM/water interface. The adsorbed glucose reduces this high-energy interface provisionally, attenuates the terminal methyl rotation, and promotes the chain-chain coupling of the 1-DDT SAMs. These results are not without precedent. There are several examples of alkane SAMs and RPC phases altering to more ordered states with the presence of various analytes [31,40,44]. Further studies concerning the transformation of alkanethioate SAMs at the water-analyte interface are needed to fully understand the observed changes. However, the present work strongly supports a superficial interaction of glucose at a 1-DDT SAM interface.

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Fig. 1. (A) Scanning electron microscopy image of the Ag nanocubes. The average edge length was 111 ± 10 nm. The scale bar corresponds to 200 nm. (B) UV-visible absorption spectra of the Ag nanocubes before (—) and after (----) functionalization with 1-dodecanethiol (1-DDT). The LSPR dipole and multipole bands (peak 1 and peak 2 respectively) red shifted after the derivatization with 1-DDT SAMs.

Fig. 2. SERS spectrum of 1-DDT SAMs on Ag nanocubes suspended in water. $\lambda_{\text{ex}} = 514 \text{ nm}$, $P_{\text{laser}} = 5 \text{ mW}$, $t = 2 \text{ min}$.

Fig. 3. SERS spectra taken from the 1-DDT-modified Ag nanocubes after they had been mixed with aqueous glucose solutions of different concentrations: (A) 250 mM, (B) 175 mM, (C) 100 mM, (D) 30 mM and (E) 0 mM. (F) Raman spectrum of a saturated aqueous solution of glucose. (G–J) Subtraction spectra displaying the presence of glucose in each sample. $\lambda_{\text{ex}} = 514 \text{ nm}$, $P_{\text{laser}} = 5 \text{ mW}$, $t = 2 \text{ min}$.

Fig. 4. Temporal study of glucose desorption from the 1-DDT-coated Ag nanocubes. (A) Real-time SERS intensity change indicating desorption of glucose; (B) SERS spectra of the 1-DDT SAMs and glucose at different times. The peak at 1365 cm⁻¹ is indicative of glucose. The peaks at 1335 cm⁻¹ and 1297 cm⁻¹ correspond to the 1-DDT SAMs. $\lambda_{\text{ex}} = 785$ nm, $P_{\text{laser}} = 15$ mW, $t = 15$ sec.

Fig. 5. Structural changes in the 1-DDT SAM upon adsorption of glucose. (A) The C-H region and (B) the C-C region. (----) represents the 1-DDT SAMs on Ag nanocubes in contact with 250 mM aqueous glucose and (—) represents the 1-DDT SAMs on Ag nanocubes in contact with pure water. $\lambda_{\text{ex}} = 514 \text{ nm}$, $P_{\text{laser}} = 5 \text{ mW}$, $t = 2 \text{ min}$.

Table 1

Raman band assignments and comparison of peak frequencies (cm^{-1}) for 1-DDT SAM functionalized Ag nanocubes and a smooth Ag surface.

Assignment ^a	Adsorbed Ag nanocubes	Adsorbed Ag surface ^a
$\nu(\text{C-S})_{\text{G}}$	632	632
$\nu(\text{C-S})_{\text{T}}$	706	706
CH_2 rock	866	869
CH_2 rock	875	870
CH_3 rock	890	894
CH_3 rock	1012	-
$\nu(\text{C-C})_{\text{T}}$	1066	1065
$\nu(\text{C-C})_{\text{G}}$	1080	1081
$\nu(\text{C-C})_{\text{T}}$	1125	1126
$\nu(\text{C-C})_{\text{T}}$	1162	1162
$\nu(\text{C-C})_{\text{T}}$	1185	1189
$\nu(\text{C-C})_{\text{T}}$	1214	1216
CH_2 wag	1297	1299
CH_2 wag	1335	1329
CH_2 deform ^b	1434	-
CH_3 deform ^b	1454	-
$\nu_2(\text{H}_2\text{O})^c$	1640	-
$\nu(\text{CH}_3)^d$	2733	-
$\nu_{\text{s}}(\text{CH}_2)$	2850	2853
$\nu_{\text{s}}(\text{CH}_3)$	2875	2878
$\nu_{\text{as}}(\text{CH}_2)$	2904	2900
$\nu_{\text{as}}(\text{CH}_2, \text{FR})$	2922	2921
$\nu_{\text{s}}(\text{CH}_3, \text{FR})$	2936	2936
$\nu_{\text{as}}(\text{CH}_3, \text{jp})$	2965	2966

^a Assignments and frequencies taken from [20] unless noted.

^b Taken from [45]

^c [46]

^d [47].

Table 2

SERS intensity ratios for 1-DDT SAM with glucose (250 mM) and without glucose (0 mM).

Mode	Ratio ^a	1-DDT SAM	1-DDT SAM/glucose
$\frac{\nu_{\text{as}}(\text{CH}_2)}{\nu_{\text{s}}(\text{CH}_3, \text{FR})}$	I_{2904}/I_{2936}	0.59 ± 0.06	0.94 ± 0.07
$\frac{\nu_{\text{s}}(\text{CH}_3, \text{FR})}{\nu_{\text{s}}(\text{CH}_2)}$	I_{2936}/I_{2850}	2.61 ± 0.05	5.37 ± 0.66
$\frac{\nu_{\text{as}}(\text{CH}_2)}{\nu_{\text{s}}(\text{CH}_2)}$	I_{2904}/I_{2850}	1.54 ± 0.05	5.05 ± 0.66

^a Subscripts indicate frequency shifts in cm^{-1} .