Metasurface with metallic nanoantennas and graphene nanoslits for sensing of protein monolayers and sub-monolayers

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Abstract: Biomolecule sensing plays an important role in both fundamental biological studies and medical diagnostic applications. Infrared (IR) spectroscopy presents opportunities for sensing biomolecules as it allows their fingerprints to be determined by directly measuring their absorption spectra. However, the detection of biomolecules at low concentrations is difficult with conventional IR spectroscopy due to signal-to-noise considerations. This has led to recent interest on the use of nanostructured surfaces to boost the signals from biomolecules in a method termed surface enhanced infrared spectroscopy. So far, efforts have largely involved the use of metallic nanoantennas (which produce large field enhancement) or graphene nanostructures (which produce strong field confinement and provide electrical tunability). Here, we propose a nanostructured surface that combines the large field enhancement of metallic nanoantennas with the strong field confinement and electrical tunability of graphene plasmons. Our device consists of an array of plasmonic nanoantennas and graphene nanoslits on a resonant substrate. We perform systematic electromagnetic simulations to quantify the sensing performance of the proposed device and show that it outperforms designs in which only plasmons from metallic nanoantennas or plasmons from graphene are utilized. These investigations consider the model system of a representative protein-goat anti-mouse immunoglobulin G (IgG) – in monolayer or sub-monolayer form. Our findings provide guidance for future biosensors for the sensitive quantification and identification of biomolecules.

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1. Introduction

The identification of biomolecules and the monitoring of the binding processes they undergo are crucial for understanding the molecular mechanisms of cellular functions (e.g., for fundamental biological studies) and for medical diagnostic applications. Many techniques have thus been developed for the sensitive detection of biomolecules, including electro-chemical reactions [1,2], field effect transistors [3–7], surface plasmon resonances [8–14] and optical fibers [15]. In general, however, these methods suffer from lack of specificity in terms of what is being measured. On the other hand, infrared (IR) spectroscopy [16–22] is a highly specific sensing modality as it allows direct measurement of the vibrational fingerprints of molecules. It is also non-invasive, label-free, and has been used for a wide variety of biological samples, including proteins [16], lipids [23] and bacteria [24]. Nonetheless, conventional IR spectroscopy faces the challenge of low signal-to-noise for measurements of small quantities of biomolecules (e.g., monolayers), which originates from the large mismatch between the wavelength of light (~micrometers) and the size of biomolecules (<10 nm). This has led to the development of a method that leverages the large optical field enhancement that can occur in the vicinity of metallic nanostructures [25–29] that is known as surface-enhanced infrared absorption (SEIRA) [30–32].
The detection of small quantities of molecules has been demonstrated based on this method [9,33–39]. Metallic nanostructures have some drawbacks for SEIRA, however [28,40–42]. The spectral bandwidth over which they boost IR absorption is relatively narrow and generally fixed at the time of manufacturing. The field confinement of noble metal plasmons in the mid-infrared molecular fingerprint region is also relatively weak. Recently, graphene has emerged as an attractive candidate for biosensing as it supports mid-infrared plasmons that can be dynamically tuned by electrostatic gating [43,44]. In addition, graphene plasmons exhibit unprecedented spatial confinement [45,46]. These unique properties of graphene have been exploited for the quantification and identification of biomolecules down to monolayers, with key improvements over plasmonic sensing devices employing metallic nanostructures [47–49]. Despite these impressive features, one major disadvantage of biosensors based on graphene plasmons is the fact that the field enhancement that accompanies graphene plasmon is small compared to that occurring with plasmons on noble metals. For example, Rodrigo et al. [48] reported a tunable biosensor based on a graphene ribbon array, demonstrating the chemically-specific detection of protein monolayers by leveraging the tunability and spatial confinement of graphene plasmons. In that paper, the authors noted that the extinction change caused by the presence of proteins was an indicator of the sensitivity of their biosensor. This was reported to be below 1%, i.e. the extinction change was fairly modest due to the relatively small near-field enhancement of their device (∼30 times). One may anticipate that this approach would face challenges related to signal-to-noise ratio, especially for the detection of proteins in sub-monolayers. This leads to the question of whether one can realize a single device that exhibits both the large field enhancement of conventional metal plasmons and the strong field confinement of graphene plasmons. Here, we address this question by investigating a nanostructured surface, which we term a metasurface, that consists of an array of plasmonic nanoantennas and graphene nanoslits on a resonant substrate. In this device, the excitation of antenna plasmons and the subsequent coupling to graphene plasmons generate electric fields with both high intensity and strong spatial confinement near the graphene nanoslits. This results in strongly enhanced absorption by the adsorbed molecules, i.e. by the proteins that are being sensed, which improves the sensitivity of the device for sensing. We perform systematic electromagnetic simulations to quantitatively study the performance of our metasurface for protein quantification and identification of goat anti-mouse immunoglobulin G (IgG) down to sub-monolayer densities. For comparison, we also study the sensing performance of three other metasurfaces in which only plasmons from metallic nanoantennas or plasmons from graphene are employed. These consist of: a plasmonic nanoantenna array, a plasmonic nanoantenna array on a graphene sheet, and a graphene nanoribbon array. We find that among the metasurfaces investigated, the proposed metasurface exhibits the best performance for sub-monolayer protein detection due to the large field enhancement and strong field confinement. We also demonstrate that tuning the graphene Fermi level via external gate bias would allow our metasurface to achieve optimal sensing of different molecular fingerprints.

2. Biosensor structure and optical properties

The biosensor we proposed is shown schematically as Fig. 1. It consists of a rectangular array of Ti/Au (5 nm/45 nm) linear antennas on a monolayer of graphene over a resonant substrate comprising an alumina film (300 nm thick) on aluminum (100 nm). The graphene within the antenna gaps is removed, forming an array of graphene nanoslits [Fig. 1(a)] for the excitation of graphene plasmons upon illumination. Here, the alumina layer acts both as a gate dielectric for electrical tuning of the graphene Fermi level and a low-loss spacer for the optical cavity. For all the simulations performed in this work, the antenna gap G, antenna width W, period P, and width of graphene nanoslit Ws are fixed as G = 30 nm, W = 240 nm, P = 2 μm, Ws = 22 nm.

In this work, we also investigate three other metasurfaces and compare their sensing performance to the proposed metasurface [metasurface I, Fig. 2(a)]. These are schematically shown as
Fig. 1. (a) Schematic of biosensor structure that consists of an array of Ti /Au ($h_3 = 5 \text{ nm}/h_4 = 45 \text{ nm}$) linear antennas and graphene slits on top of alumina ($h_2 = 300 \text{ nm}$) and aluminum ($h_1 = 100 \text{ nm}$) films. Antenna gap $G$, antenna width $W$, period $P_y$ and width of graphene slit $W_s$ are fixed as $G = 30 \text{ nm}$, $W = 240 \text{ nm}$, $P_y = 2 \mu\text{m}$, $W_s = 22 \text{ nm}$. (b) Side-view of structure.

Figs. 2(b)–2(c) and consist of: plasmonic nanoantenna array [metasurface II, Fig. 2(b)]; plasmonic nanoantenna array on graphene sheet [metasurface III, Fig. 2(c)]; and graphene ribbon array [metasurface IV, Fig. 2(d)]. All metasurfaces are on the same substrate.

Fig. 2. Schematic of the four metasurface structures. (a) Metasurface I: plasmonic nanoantenna array with graphene slits, (b) Metasurface II: plasmonic nanoantenna array, (c) Metasurface III: plasmonic nanoantenna array on graphene sheet, (d) Metasurface IV: graphene ribbon array.

We first investigate the optical field enhancement in the mid-infrared region where most biomolecules have their vibrational fingerprints. Electromagnetic simulations are conducted using the finite difference time domain method implemented in a commercial package (Lumerical FDTD). The computational domain consists of a single unit cell of the structure. Periodic boundaries are used at the x- and y- boundaries. Perfectly matched layers (PMLs) are used at the
z- boundaries to avoid unwanted backscattering of the electromagnetic fields. Illumination is from a plane wave linearly polarized along the x axis at normal incidence. In the simulations, graphene is modelled as a two-dimensional surface with a surface conductivity given by the Kubo formula [50,51]:

\[
\sigma(\omega, \mu_c, \Gamma, T) = \sigma_{\text{int}}(\omega, \mu_c, \Gamma, T) + \sigma_{\text{inter}}(\omega, \mu_c, \Gamma, T) \\
= \frac{i e^2 (\omega - i 2 \Gamma)}{\pi \hbar^2} \left[ \frac{1}{(\omega - i 2 \Gamma)^2} \int_0^\infty \epsilon (\frac{\partial f_\epsilon(\epsilon)}{\partial \epsilon} - \frac{\partial f_{-\epsilon}(\epsilon)}{\partial \epsilon}) d\epsilon \\
- \int_0^\infty \frac{f_{-\epsilon}(\epsilon) - f_\epsilon(\epsilon)}{(\omega - i 2 \Gamma)^2 - 4(\epsilon/\hbar)^2} d\epsilon \right] \\
\]  

(1)

where \( \omega \) is angular frequency, \( \mu_c \) is chemical potential, \( \Gamma \) is scattering rate, \( T \) is temperature, \( e \) is the electron charge, \( \hbar = h/2\pi \) is the reduced Planck’s constant, \( f_\epsilon(\epsilon) = (e^{(\epsilon-\mu_c)/k_B T} + 1)^{-1} \) is the Fermi-Dirac distribution, and \( k_B \) is Boltzmann’s constant. The values for \( \mu_c, \Gamma \) and \( T \) are set to be 0.3 eV, 0.022 eV and 300 K, unless otherwise stated.

The electric field intensity enhancement distributions are provided as Fig. 3 for all four metasurfaces. For metasurfaces I-III, the antenna length is the same, i.e. \( L = 1.25 \mu m \). For

![Simulated electric field intensity enhancement distributions on XZ cross-section for structures with (a) metasurface I, plasmonic nanoantenna array with graphene slits, (b) metasurface II, plasmonic nanoantenna array, (c) metasurface III, plasmonic nanoantenna array on graphene sheet and (d) metasurface IV, graphene ribbon array, with ribbon width \( W_g = 24 \text{ nm} \) and period \( P = 80 \text{ nm} \). Antenna length (\( L = 1.25 \mu m \)) is same for (a-c). Each structure is illuminated at its resonant wavelength, i.e. \( \lambda = 6531 \text{ nm}, 6540 \text{ nm}, 6014 \text{ nm} \) and \( 6180 \text{ nm} \), for panels a-d, respectively. White dotted lines indicate antenna boundaries and/or substrate surface. Dark red solid lines represent graphene.](image-url)
metasurface IV, graphene ribbon width is \( W_g = 24 \text{ nm} \) and period is \( P = 80 \text{ nm} \). Each structure is illuminated at its resonant wavelength. It can be seen that for the proposed metasurface [metasurface I, Fig. 3(a)], the electric field is strongly enhanced and confined in the vicinity of the graphene slit, with a maximum intensity enhancement factor of \( 6.1 \times 10^5 \). Note that the colorbar is set to have a maximum value of \( 1 \times 10^5 \) in Figs. 3(a)–3(c) to enable intuitive comparison. The enhancement results from the resonant excitation of antenna surface plasmon polaritons and subsequent coupling to graphene plasmons. In comparison, the maximum electric field intensity enhancement factors are \( 4.1 \times 10^5 \), \( 1.4 \times 10^5 \) and 104 for metasurfaces II [Fig. 3(b)], III [Fig. 3(c)] and IV [Fig. 3(d)] respectively. The field intensity enhancement provided by our proposed metasurface that combines graphene plasmons with antenna plasmons is more than three orders of magnitude greater than that generated by metasurface IV in which only graphene plasmons are excited, and is comparable to that of the device (metasurface II) in which only antenna plasmons are excited. We note that the ratio between field intensity at the bottom of the antenna (where it meets the substrate) to the top of the antenna is greater for our proposed metasurface than that for the antenna-only structure (metasurface II, Fig. 3(b)). We also note that with the addition of the graphene sheet underneath the antennas (i.e., metasurface III), the maximum field intensity enhancement [Fig. 3(c)] is markedly reduced, taking a value that is less than one quarter of that of the proposed metasurface.

3. Sensing performance for protein monolayers

To study the sensing performance of the proposed metasurface, goat anti-mouse immunoglobulin G (IgG) is employed as a representative target protein to be sensed. We furthermore assume that sensing is performed by measuring the reflection spectrum of the metasurface. We thus simulate the reflection spectrum from our metasurface with an adsorbed protein monolayer (or sub-monolayer). The protein permittivity is modelled as a Lorentz series with two oscillating terms that account for amide I and II bands [48]:

\[
\varepsilon_{\text{protein}}(\omega) = n_{\text{re}}^2 + S_1^2 / (\omega_1^2 - \omega^2 - i\omega\gamma_1) + S_2^2 / (\omega_2^2 - \omega^2 - i\omega\gamma_2)
\]

where \( n_{\text{re}}^2 = 2.08 \) is the permittivity at infinite frequency; \( \omega_1 = 1668 \text{ cm}^{-1} \), \( \omega_2 = 1532 \text{ cm}^{-1} \), \( \gamma_1 = 78.1 \text{ cm}^{-1} \), \( \gamma_2 = 101 \text{ cm}^{-1} \), \( S_1 = 213 \text{ cm}^{-1} \), \( S_2 = 200 \text{ cm}^{-1} \) are the resonant frequencies, damping rates and oscillation strengths for the amide I and II bands respectively.

Figures 4(a)–4(d) show the simulated reflection spectra for metasurfaces I, II, III and IV respectively, including a coating that comprises a monolayer of protein IgG. The antenna lengths and graphene ribbon widths are chosen so that the resonance wavelengths of the four metasurfaces span approximately the same spectral range. In the simulation, the protein monolayer is modelled as a 8-nm thick film whose permittivity is as given by Eq. (2) that conformally coats each metasurface [48]. It can be seen that each spectrum exhibits a reflection dip in the spectral range \( \lambda \approx 7 \) to 9 \( \mu \text{m} \). This corresponds to the antenna and/or graphene plasmon resonant wavelength. In addition, the reflection spectra exhibit dips that originate from plasmonically enhanced light absorption by the protein. We indicate these features via green and orange shaded regions in Figs. 4(a)–4(d). These are at wavelengths near the amide I (~6 \( \mu \text{m} \)) and II bands (~6.5 \( \mu \text{m} \)) of the protein IgG, and thus represent its spectroscopic fingerprint. It can be seen that these dips become weaker as the antenna resonance shifts away from the protein absorption bands as a result of the weaker coupling between the plasmonic resonance modes and the protein vibration modes [38]. In addition, dips caused by protein absorption of metasurface IV [Fig. 4(d)] are much weaker than those of metasurface I, II and III [Figs. 4(a)–4(c)], due to the much weaker field enhancement of pure graphene plasmons.

To quantify the intensity of the amide band features of the reflection spectra, we calculate the second derivatives of these spectra. It can be seen that this results in spectral peaks (Fig. 5) that can be readily compared. Indeed, the peak second derivative is positively correlated with...
Fig. 4. Simulated reflection spectra for metasurfaces I (a), II (b), III (c) and IV (d). Antenna lengths are \( L = 1.25 \mu m \sim 1.95 \mu m \) for (a-b), and \( L = 1.5 \mu m \sim 2.2 \mu m \) for (c). For metasurface IV, graphene ribbon widths are \( W_g = 32 nm \sim 42 nm \) and period is 80 nm. For all cases, a monolayer of protein IgG is coated on the metasurface. Green and orange shaded areas indicate the amide I and II bands of the protein.

the protein absorption as can be seen in Fig. 6 for metasurface I. This means that larger peak value in the second derivative curves corresponds to larger total protein absorption, providing the opportunity to quantify the amount of proteins.

Figures 5(a)–5(d) show the second derivatives calculated from the curves of Figs. 4(a)–4(d), respectively. Note that only positive values have been shown to facilitate interpretation of these curves. Positive values of the second derivative correspond to the regions of upward concavity in the reflection spectra and thus include the features associated with protein absorption. Peaks in the second derivative spectra of Fig. 5 can be seen to occur at wavelengths corresponding to the amide I and amide II bands of the protein. It can be seen that these peaks decrease in strength as the antenna resonance shifts away from the absorption bands of the protein. It can also be seen that metasurface I [Fig. 5(a)] has a second derivative spectrum whose peaks are larger than metasurface III [Fig. 5(c)] but smaller than metasurface II [Fig. 5(b)]. However, we show later on that the electrical tunability of metasurface I allows the device to be optimized and produces second derivatives greater than that of metasurface II. More importantly, the electrical tunability of metasurface I by gate voltage allows us to generate distinctive characterization spectra, i.e. reflectance spectra measured at different gate voltages, that would be very advantageous for sensing and identification. Here, the smaller second derivatives of metasurface I than that
Fig. 5. Second derivatives calculated for the reflection spectra from Fig. 4 for metasurface (a) I, (b) II, (c) III and (d) IV. Note that only positive values are presented in all figures for brevity.

Fig. 6. Peak second derivative (red) and the corresponding protein absorption (blue) as a function of antenna length at the amide I band. Results obtained from metasurface I.

of metasurface II is probably due to the fact that the plasmonic mode volume is smaller for metasurface I than metasurface II, leading to weaker interplay between plasmonic polaritons and phonon-polaritons in IgG thin film. This can be further understood by examination of the
intensity distributions of Figs. 3(a) and 3(b). It can also be seen that the maximum values of the second derivative peaks for metasurface IV [Fig. 5(d)] are about two orders of magnitude smaller than those of metasurface I. This indicates that this metasurface, which employs graphene plasmons only, would have much lower sensitivity in a protein sensing application.

4. Sensing performance for protein sub-monolayers

Fig. 7. Sensing performance for protein sub-monolayers. (a-c) Reflection spectra simulated for metasurface I, II and III coated with protein with varying surface percentage coverage. Antenna lengths are $L = 1.25 \ \mu m$, $1.25 \ \mu m$ and $1.5 \ \mu m$ for metasurface I, II and III respectively. Green and orange shaded regions indicate the amide I and II bands of the protein. (d-f) Second derivatives calculated from the simulated reflection spectra in (a-c) respectively.
We next compare the sensing limitations of metasurface I, II and III by considering proteins in sub-monolayer form. We note that metasurface IV is not considered here since it already shows much lower sensitivity for the sensing of protein monolayers. We model each (single) IgG protein as a cuboid with dimensions of 4 nm (width) $\times$ 14 nm (length) $\times$ 8 nm (height) [52]. The proteins are positioned within the antenna gaps in the vicinity of antenna/graphene slit edges where the electric field is maximum. Figures 7(a)–7(c) show the simulated reflection spectra for metasurfaces I, II and III respectively, with varying protein surface percentage coverage. The green and orange shaded regions indicate the amide I and II bands of the protein. To enable a fair comparison to be made, the lengths of the antennas of the three metasurfaces are chosen so they have the same resonant wavelengths.

We calculate the second derivatives of the spectra in Figs. 7(a)–7(c) for quantitative comparison. The results are shown as Figs. 7(d)–7(e). The amide I peak (centered around 6 $\mu$m) can be seen for all three metasurfaces and decreases as the protein density decreases [Figs. 7(d),7(e)]. For the same protein density, metasurface I shows the largest amide I peak value. We can also see a weaker feature corresponding to the absorption of the protein amide II band for metasurface I [Fig. 7(d), indicated by the blue arrow]. Furthermore, all three metasurfaces show large peaks associated with the antenna resonances that redshift as the protein density increases. The shift of antenna resonance can also be used to detect the presence of proteins. In Figs. 8(a)–8(b), we show the antenna resonance wavelength shift [Fig. 8(a)] and the amide I peak values [Fig. 8(b)] as a function of protein density. The antenna resonance wavelength shift is calculated with respect to the resonance wavelength that occurs in the absence of the protein coating. It can be clearly seen that metasurface I shows the greatest antenna resonance shift and amide I peak values for all values of protein density, indicating the highest device sensitivity among the three metasurfaces. One can also compare the metasurfaces in terms of the minimum protein density (surface percentage coverage) needed for the second derivative to be non-zero. From Fig. 8(b), it can be seen that for metasurface I this takes a value of 0.11%, compared to 0.12% for metasurface II and 0.18% for metasurface III.

5. Electrical tuning of sensitivity for the proposed metasurface

Lastly, we show that varying the graphene Fermi level presents a means for further improving the performance of the device for detecting protein adsorption. This would be achieved by electrostatic gating. To exploit the tunability of graphene plasmon and achieve tuning of the resonance across the absorption bands of the protein, we tune the graphene plasmon closer to
the protein absorption bands by changing the width of the graphene slits. Figure 9(a) shows the reflectance spectra of metasurface I coated with protein IgG monolayer, with the width of graphene slits $W_s$ varied from 19 nm to 5 nm. It can be seen that both the graphene plasmon resonance (indicated by red arrow) and the plasmonic resonance of the nanoantennas (indicated by yellow arrow) undergo redshift as $W_s$ decreases. In particular, when $W_s = 5$ nm (dark blue curve), the graphene plasmon resonance locates in-between the two absorption bands. The corresponding second derivatives are shown in Fig. 9(b). As the graphene slit width decreases

Fig. 9. Tuning of plasmonic resonance and device sensitivity via graphene slits for metasurface I. (a-b) Simulated reflectance spectra of metasurface I coated with protein IgG monolayer (a) and corresponding second derivatives (b), with width of graphene slits $W_s$ varied from 19 nm to 5 nm. Antenna length $L = 1.25 \mu$m. (c-d) Simulated reflectance spectra of metasurface I coated with protein IgG monolayer (c) and corresponding second derivatives (d), with Fermi level of graphene $E_F$ varied from 0.1 eV to 1 eV. Antenna length $L = 1.25 \mu$m. Graphene slit width $W_s = 5$ nm. Graphene plasmon resonance and antenna resonance are indicated by the red and yellow arrows respectively. Figure 9. Tuning of plasmonic resonance and device sensitivity via graphene slits for metasurface I. (a-b) Simulated reflectance spectra of metasurface I coated with protein IgG monolayer (a) and corresponding second derivatives (b), with width of graphene slits $W_s$ varied from 19 nm to 5 nm. Antenna length $L = 1.25 \mu$m. (c-d) Simulated reflectance spectra of metasurface I coated with protein IgG monolayer (c) and corresponding second derivatives (d), with Fermi level of graphene $E_F$ varied from 0.1 eV to 1 eV. Antenna length $L = 1.25 \mu$m. Graphene slit width $W_s = 5$ nm. Graphene plasmon resonance and antenna resonance are indicated by the red and yellow arrows respectively.
from 19 nm to 5 nm, the two peaks corresponding to amide I and II bands of the protein first decrease and then increase. This is due to the fact that as the plasmonic resonances undergo redshift, the coupling between the graphene plasmon mode and the protein film becomes stronger while the coupling between the antenna resonance mode and the protein film becomes weaker. Consequently, there exists a value of $W_s$ for which the overall protein absorption is lowest and the corresponding second derivative value reaches minimum. We also note that in order to obtain a distinct protein signature, it is desirable to design the plasmonic resonances away from the protein fingerprints region so that the reflectance dips caused by the protein absorption could be readily distinguished from that caused by the plasmonic resonances.

Based on these simulations, we choose the width of the graphene slits $W_s$ to be 5 nm for the demonstration of electrical tuning of plasmonic resonances and device sensitivity, because it corresponds to graphene plasmon resonance closest to the protein absorption bands. Figure 9(c) shows the simulated reflectance spectra of metasurface I with the Fermi level of graphene varied from 0.1 eV to 1 eV. The graphene slit width and antenna length are fixed at $W_s = 5$ nm and $L = 1.25 \mu m$ respectively. It can be seen that both the graphene plasmon resonance and antenna resonance undergo blueshift as the Fermi level of graphene increases from 0.1 eV to 1 eV. Specifically, the wavelengths of graphene plasmon resonance and antenna resonance are shifted from 7.01 $\mu m$ to 4.43 $\mu m$ and from 8.95 $\mu m$ to 7.51 $\mu m$, corresponding to a tuning range of 2.58 $\mu m$ and 1.44 $\mu m$, respectively. Notably, the graphene plasmon resonance is tuned across the two absorption bands of IgG protein, allowing active control of device sensitivity for detecting different protein fingerprints. Figure 9(d) shows the corresponding calculated second derivatives from Fig. 9(c). It can be seen that, as the graphene plasmon resonance is shifted toward the protein absorption bands, the peak values corresponding to amide I (grey dashed lines) and amide II (grey dotted lines) bands of the IgG protein becomes larger. In particular, the peak second derivative corresponding to amide I reaches a maximum value of 9.41 when the Fermi level is tuned to 0.3 eV. Similarly, the peak corresponding to amide II reaches a maximum value of 4.74 when the Fermi level is tuned to 0.2 eV. This means that by fine tuning the graphene Fermi level to the appropriate values, the metasurface could be configured to be optimal for the detection of different molecular fingerprints. The distinctive pattern of the second derivative spectrum vs Fermi level is advantageous for the accurate detection of protein fingerprints in sensing experiments as one can tune the Fermi level of graphene and see whether the obtained second derivative pattern matches that of simulation. This approach would not be possible for metasurface II, for which only metallic antennas are used for sensing. It should be noted that the two peaks corresponding to amide I and II bands undergo slight red (blue) shift as the graphene plasmon resonance moves closer to the absorption bands from shorter (longer) wavelength. This phenomenon is more evident in the region near $E_f = 0.3$ eV, at which the graphene plasmon resonance is in-between the two protein absorption bands.

6. Conclusions

In conclusion, we propose a biosensor metasurface that consists of an array of plasmonic nanoantennas and graphene nanoslits on a resonant substrate. Systematic simulations are carried out to study the performance of the proposed metasurface for sensing the protein goat anti-mouse immunoglobulin G (IgG). Three other metasurface designs are also investigated for comparison. These consist of a plasmonic nanoantenna array, a plasmonic nanoantenna array on a graphene sheet, and a graphene ribbon array. The proposed metasurface combines the large electric field enhancement of metal plasmons with the strong spatial confinement of graphene plasmons, providing an opportunity for the sensitive quantification and identification of biomolecules down to sub-monolayer densities. We show by simulation that in the sensing of a monolayer of protein IgG, the proposed metasurface exhibits a sensitivity (strength of reflection dips associated with protein absorption) that is higher than that of the other metasurfaces. Indeed, the sensitivity
is in excess of two orders of magnitude greater than that of the metasurface with graphene ribbon array. For the sensing of sub-monolayer of IgG, the proposed metasurface shows the highest sensitivity and best specificity among the four different metasurfaces, enabling fingerprint detection of proteins with densities down to a surface percentage coverage of 0.11%. The use of graphene nanoslits also allows an active tuning of the structure’s resonance by electrostatic gating and provides a degree of freedom to configure the metasurface to be optimal for the detection of different molecular fingerprints, which is not possible for metasurface with plasmonic nanoantenna array. We believe the sensing strategy we propose in this paper, in which metal plasmons and graphene plasmons are combined synergistically, provides guidance for the future development of biosensors with ultra-high sensitivity and specificity.

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Disclosures
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References
1. H. Lee, T. K. Choi, Y. B. Lee, H. R. Cho, R. Ghaffari, L. Wang, H. J. Choi, T. D. Chung, N. Lu, and T. Hyeon, “A graphene-based electrochemical device with thermoresponsive microneedles for diabetes monitoring and therapy,” Nat. Nanotechnol. 11(6), 566–572 (2016).
2. J. A. Hansen, J. Wang, A.-N. Kawde, Y. Xiang, K. V. Gothelf, and G. Collins, “Quantum-dot/aptamer-based ultrasensitive multi-analyte electrochemical biosensor,” J. Am. Chem. Soc. 128(7), 2228–2229 (2006).
3. Y. Cui, Q. Wei, H. Park, and C. M. Lieber, “Nanowire nanosensors for highly sensitive and selective detection of biological and chemical species,” Science 293(5533), 1289–1292 (2001).
4. X. Duan, Y. Li, N. K. Rajan, D. A. Routenberg, Y. Modis, and M. A. Reed, “Quantification of the affinities and kinetics of protein interactions using silicon nanowire biosensors,” Nat. Nanotechnol. 7(6), 401–407 (2012).
5. N. Gao, T. Gao, X. Yang, X. Dai, W. Zhou, A. Zhang, and C. M. Lieber, “Specific detection of biomolecules in physiological solutions using graphene transistor biosensors,” Proc. Natl. Acad. Sci. 113(51), 14633–14638 (2016).
6. F. Schedin, A. Geim, S. Morozov, E. Hill, P. Blake, M. Katsnelson, and K. Novoselov, “Detection of individual gas molecules adsorbed on graphene,” Nat. Mater. 6(9), 652–655 (2007).
7. S. X. Xu, J. Zhan, B. Mao, S. Jiang, W. Yue, S. Gao, C. Guo, H. Liu, Z. Li, and J. Wang, “Real-time reliable determination of binding kinetics of DNA hybridization using a multi-channel graphene biosensor,” Nat. Commun. 8(1), 14902 (2017).
8. J. N. Anker, W. P. Hall, O. Lyandres, N. C. Shah, J. Zhao, and R. P. Van Duyne, “Biosensing with plasmonic nanosensors,” in Nanoscience and Technology: A Collection of Reviews from Nature Journals (World Scientific, 2010), pp. 308–319.
9. A. E. Cetin, D. Etezadi, B. C. Galarreta, M. P. Busson, Y. Eksioglu, and H. Altug, “Plasmonic nanohole arrays on a robust hybrid substrate for highly sensitive label-free biosensing,” ACS Photonics 2(8), 1167–1174 (2015).
10. J. Homola, “Present and future of surface plasmon resonance biosensors,” Anal. Bioanal. Chem. 377(3), 528–539 (2003).
11. A. Kabashin, P. Evans, S. Pastkovsky, W. Hendren, G. Wurtz, R. Atkinson, R. Pollard, V. Podolskiy, and A. Zayats, “Plasmonic nanorod metamaterials for biosensing,” Nat. Mater. 8(11), 867–871 (2009).
12. K. S. Phillips, “Jiri Homola (Ed.): Surface plasmon resonance-based sensors,” Anal. Bioanal. Chem. 390(5), 1221–1222 (2008).
13. N. Ramachandran, D. N. Larson, P. R. Stark, E. Hainsworth, and J. LaBaer, “Emerging tools for real-time label-free detection of interactions on functional protein microarrays,” FEBS J. 272(21), 5412–5425 (2005).
14. S. Zeng, K. V. Sreekanth, J. Shang, T. Yu, C. K. Chen, F. Yin, D. Baillargeat, P. Coquet, H. P. Ho, and A. V. Kabashin, “Graphene–gold metasurface architectures for ultrasensitive plasmonic biosensing,” Adv. Mater. 27(40), 6163–6169 (2015).
15. A. Leung, P. M. Shankar, and R. Mutharasan, “A review of fiber-optic biosensors,” Sens. Actuators, B 125(2), 688–703 (2007).
16. A. Barth, “Infrared spectroscopy of proteins,” Biochim. Biophys. Acta, Bioenerg. 1767(9), 1073–1101 (2007).
17. L. P. DeFlores, Z. Ganim, R. A. Nicodemus, and A. Tokmakoff, “Amide I’– II’ 2D IR spectroscopy provides enhanced protein secondary structural sensitivity,” J. Am. Chem. Soc. 131(9), 3385–3391 (2009).
18. A. Dong, P. Huang, and W. S. Caughey, “Protein secondary structures in water from second-derivative amide I infrared spectra,” Biochemistry 29(13), 3303–3308 (1990).
19. N. M. Iverson, P. W. Barone, M. Shandell, L. J. Trudel, Sen, F. Sen, V. Ivanov, E. Atolia, E. Farias, and T. P. McNicholas, “In vivo biosensing via tissue-localizable near-infrared-fluorescent single-walled carbon nanotubes,” Nat. Nanotechnol. 8(11), 873–880 (2013).

20. E. Kauffmann, N. C. Durton, R. H. Austin, C. Batt, and K. Gerwert, “Lifetimes of intermediates in the β-sheet to α-helix transition of β-lactoglobulin by using a directional IR mixer,” Proc. Natl. Acad. Sci. 98(12), 6646–6649 (2001).

21. K. J. Rothschild, “FTIR difference spectroscopy of bacteriorhodopsin: toward a molecular model,” J. Bioenerg. Biomembr. 24(2), 147–167 (1992).

22. C. Zscherp and J. Heberle, “Infrared difference spectra of the intermediates L, M, N, and O of the bacteriorhodopsin photocycle resolved by time-resolved attenuated total reflection spectroscopy,” J. Phys. Chem. B 101(49), 10542–10547 (1997).

23. M. D. Guillen and N. Cabo, “Infrared spectroscopy in the study of edible oils and fats,” J. Sci. Food Agric. 75(1), 1–11 (1997).

24. X. Lu, H. M. Al-Qadiri, M. Lin, and B. A. Rasco, “Application of mid-infrared and Raman spectroscopy to the study of bacteria,” Food Bioprocess Technol. 4(6), 919–935 (2011).

25. L. Novotny and N. Van Hulst, “Antennas for light,” Nat. Photonics 1(1), 69–75 (2012).

26. C. Zscherp and J. Heberle, “Thinner, smaller, faster: IR techniques to probe the functionality of biological and biomimetic systems,” Angew. Chem., Int. Ed. 49(32), 5416–5424 (2010).

27. R. Adato, A. A. Yanik, R. Adato, N. Arju, A. A. Yanik, H. Altug, and G. Shvets, “Fano-resonant asymmetric metal nanoparticles for ultrasensitive spectral and identification of molecular monolayers,” Nat. Mater. 11(1), 69–75 (2012).

28. A. A. Yanik, A. E. Cetin, M. Huang, A. Artar, S. H. Mousavi, A. Khanikaev, J. H. Connor, G. Shvets, and H. Altug, “Seeing protein monolayers with plasmonic nanoantennas,” Nat. Commun. 4(1), 2154 (2013).

29. F. Neubrech, M. Pucci, T. W. Cornelius, S. Karim, A. García-Etxarri, and J. Aizpurua, “Resonant plasmonic and vibrational coupling in a tailored nanoantenna for infrared detection,” Phys. Rev. Lett. 101(15), 157403 (2008).

30. K. Crozier, A. Sundaramurthy, G. Kino, and C. Qute, “Optical antennas: Resonators for local field enhancement,” J. Appl. Phys. 94(7), 4632–4642 (2003).

31. M. Osawa, K.-I. Ataka, K. Yoshii, and Y. Nishikawa, “Surface-enhanced infrared spectroscopy: the origin of the absorption enhancement and band selection rule in the infrared spectra of molecules adsorbed on fine metal particles,” Appl. Spectrosc. 47(9), 1497–1502 (1993).

32. M. Moskovits, “Surface-enhanced spectroscopy,” Rev. Mod. Phys. 57(3), 783–826 (1985).

33. K. Ataka, T. Kotike, and J. Heberle, “Thinner, smaller, faster: IR techniques to probe the functionality of biological and biomimetic systems,” Angew. Chem., Int. Ed. 49(32), 5416–5424 (2010).

34. S. Cataldo, J. Zhao, F. Neubrech, B. Frank, C. Zhang, P. V. Braun, and H. Giessen, “Hole-mask colloidal nanolithography for large-area low-cost metamaterials and antenna-assisted surface-enhanced infrared absorption substrates,” ACS Nano 6(1), 979–985 (2012).

35. F. Neubrech and A. Pucci, “Plasmonic enhancement of vibrational excitations in the infrared,” IEEE J. Sel. Top. Quantum Electron. 19(3), 4600809 (2013).

36. A. A. Yanik, A. E. Cetin, M. Huang, A. Artar, S. H. Mousavi, A. Khanikaev, J. H. Connor, G. Shvets, and H. Altug, “Seeing protein monolayers with naked eye through plasmonic Fano resonances,” Proc. Natl. Acad. Sci. 108(29), 11784–11789 (2011).

37. E. Cubukcu, S. Zhang, Y.-S. Park, G. Bartal, and X. Zhang, “Split ring resonator sensors for infrared detection of single molecular monolayers,” Appl. Phys. Lett. 95(4), 043113 (2009).

38. J. Kundu, F. Le, P. Nordlander, and N. J. Halas, “Surface enhanced infrared absorption (SEIRA) spectroscopy on nanoshell aggregate substrates,” Chem. Phys. Lett. 452(1-3), 115–119 (2008).

39. Z. Li, Y. Zhu, Y. Hao, M. Gao, M. Lu, A. Stein, A.-H. A. Park, J. C. Hone, Q. Lin, and N. Yu, “Hybrid Metasurface-Based Mid-Infrared Biosensor for Simultaneous Quantification and Identification of Monolayer Protein,” ACS Photonics 6(2), 501–509 (2019).

40. Y. Zhu, Z. Li, M. Hao, C. DiMarco, P. Maturavongsadit, Y. Hao, M. Lu, A. Stein, Q. Wang, and J. Hone, “Optical conductivity-based ultrasensitive mid-infrared biosensing on a hybrid metasurface,” Light: Sci. Appl. 7(1), 67 (2018).

41. B. Stuart, “Infrared spectroscopy: fundamentals and applications,” John Wiley and Sons, Ltd., West Sussex, England. DOI 10.0470011149 (2004).

42. O. Selig, R. Siffels, and Y. Rezus, “Ultrasensitive ultrafast vibrational spectroscopy employing the near field of gold nanoantennas,” Phys. Rev. Lett. 114(23), 233004 (2015).

43. R. Adato, A. A. Yanik, J. J. Amsden, D. L. Kaplan, F. G. Omenetto, M. K. Hong, S. Erramilli, and H. Altug, “Ultra-sensitive vibrational spectroscopy of protein monolayers with plasmonic nanoantenna arrays,” Proc. Natl. Acad. Sci. 106(46), 19227–19232 (2009).

44. Z. Fang, Y. Wang, A. E. Schlather, Z. Liu, P. M. Ajayan, F. Javier García de Abajo, P. Nordlander, X. Zhu, and N. J. Halas, “Active tunable absorption enhancement with graphene nanodisk arrays,” Nano Lett. 14(1), 299–304 (2014).

45. V. W. Brat, M. S. Jang, M. Sherrott, J. J. Lopez, and H. A. Atwater, “Highly confined tunable mid-infrared plasmonics in graphene nanoresonators,” Nano Lett. 13(6), 2541–2547 (2013).

46. T. Low and P. Avouris, “Graphene plasmonics for terahertz to mid-infrared applications,” ACS Nano 8(2), 1086–1101 (2014).

47. F. Javier García de Abajo, “Graphene plasmonics: challenges and opportunities,” ACS Photonics 1(3), 135–152 (2014).
47. H. Hu, X. Yang, F. Zhai, D. Hu, R. Liu, K. Liu, Z. Sun, and Q. Dai, “Far-field nanoscale infrared spectroscopy of vibrational fingerprints of molecules with graphene plasmons,” Nat. Commun. 7(1), 12334 (2016).
48. D. Rodrigo, O. Limaj, D. Janner, D. Etezadi, F. J. G. De Abajo, V. Pruneri, and H. Altug, “Mid-infrared plasmonic biosensing with graphene,” Science 349(6244), 165–168 (2015).
49. A. Marini, I. N. Silveiro, and F. J. García de Abajo, “Molecular sensing with tunable graphene plasmons,” ACS Photonics 2(7), 876–882 (2015).
50. G. W. Hanson, “Dyadic Green’s functions and guided surface waves for a surface conductivity model of graphene,” J. Appl. Phys. 103(6), 064302 (2008).
51. V. Gusynin, S. Sharapov, and J. Carbotte, “Magneto-optical conductivity in graphene,” J. Phys.: Condens. Matter 19(2), 026222 (2007).
52. Y. H. Tan, M. Liu, B. Nolting, J. G. Go, J. Gervay-Hague, and G.-Y. Liu, “A nanoengineering approach for investigation and regulation of protein immobilization,” ACS Nano 2(11), 2374–2384 (2008).
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