

# Lighting Up the Raman Signal of Molecules in the Vicinity of Graphene Related Materials

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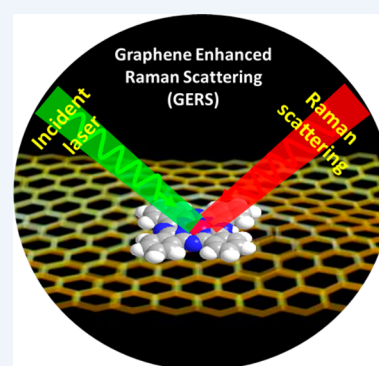
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**CONSPECTUS:** Surface enhanced Raman scattering (SERS) is a popular technique to detect the molecules with high selectivity and sensitivity. It has been developed for 40 years, and many reviews have been published to summarize the progress in SERS. Nevertheless, how to make the SERS signals repeatable and quantitative and how to have deeper understanding of the chemical enhancement mechanism are two big challenges. A strategy to target these issues is to develop a Raman enhancement substrate that is flat and nonmetal to replace the conventional rough and metal SERS substrate. At the same time, the newly developed substrate should have a strong interaction with the adsorbate molecules to guarantee strong chemical enhancement. The flatness of the surface allows better control of the molecular distribution and configuration, while the nonmetal surface avoids disturbance of the electromagnetic mechanism.

Recently, graphene and other two-dimensional (2D) materials, which have an ideal flat surface and strong chemical interaction with plenty of organic molecules, were developed to be used as Raman enhancement substrates, which can light up the Raman signals of the molecules, and these substrates were demonstrated to be a promising for microspecies or trace species detection. This effect was named “graphene enhanced Raman scattering (GERS)”. The GERS technique offers significant advantages for studying molecular vibrations due to the ultraflat and chemically inert 2D surfaces, which are newly available, especially in developing a quantitative and repeatable signal enhancement technique, complementary to SERS. Moreover, GERS is a chemical mechanism dominated effect, which offers a valuable model to study the details of the chemical mechanism.

In this Account, we summarize the systematic studies exploring the character of GERS. In addition, as a practical technique, the combination of GERS with a metal substrate incorporates the advantages from both conventional SERS and GERS. The introduction of graphene to the Raman enhancement substrate extended SERS applications in a more controllable and quantitative way. Looking to the future, we expect the combination of the SERS concept with the GERS technology to lead to the solution of some important issues in chemical dynamics and in biological processes monitoring.



## 1. INTRODUCTION

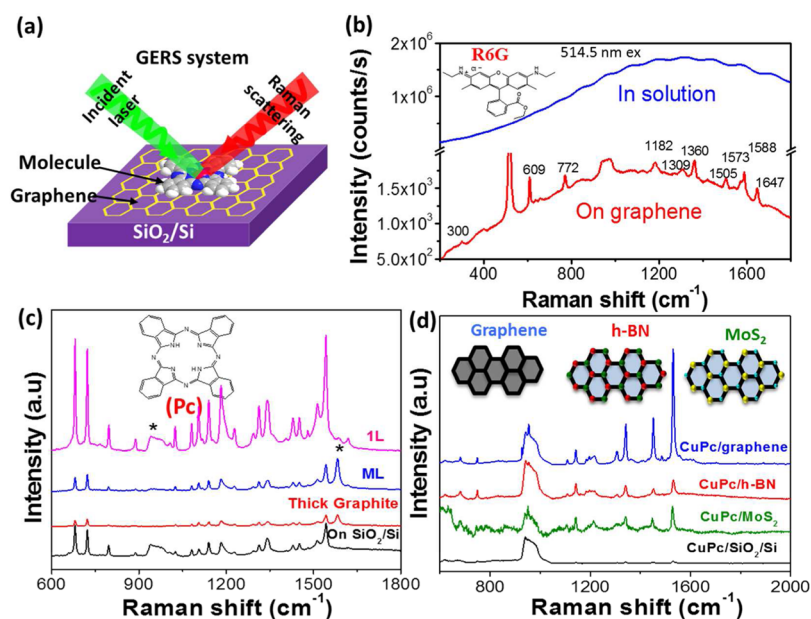
Microspecies or trace species detection is important in our everyday life, including food safety, environmental monitoring, medical quality, disease diagnosis, homeland security, and antique identification among others.<sup>1–3</sup> Raman spectroscopy has many advantages in species detection, such as having high selectivity, being nondestructive to the sample, providing quick response and convenience, and giving rich information about the species. Nevertheless, the application of Raman spectroscopy for microspecies or trace species detection is limited by the low scattering cross section, which results in a weak Raman signal intensity and low sensitivity of the normal Raman scattering spectral features. Therefore, how to light up the Raman signal of the molecule is an important topic and deserves further effort.

Surface enhanced Raman scattering (SERS) is the most widely studied and promising Raman enhancement techni-

que.<sup>4,5</sup> The history of SERS can be traced back to 1974 when Fleischmann et al.<sup>6</sup> observed a strong Raman signal from pyridine on a rough surface of Ag electrode. In 1977,<sup>7,8</sup> SERS was defined as a Raman enhancement effect that is observed on a surface. However, there is still no complete picture to describe the SERS mechanism even though the electromagnetic mechanism (EM) has been successfully used to explain the major contribution for many situations.<sup>9,10</sup> Although a contribution from the chemical mechanism (CM) is widely accepted at the present time, the detailed study and understanding of the CM is incomplete because the CM is often overwhelmed by the EM. In the past 40 years, various metal nanostructures were explored as SERS substrates, and single molecule-level detection was achieved using SERS in

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**Figure 1.** (a) Schematic illustration of the GERS system. (b) Typical result of the photoluminescence suppression effect of R6G on graphene. The blue line is the spectrum of R6G in solution, and the red line is the spectrum of R6G on graphene. Adapted with permission from ref 18. Copyright 2009 American Chemical Society. (c) Typical result of the Raman spectra of Pc molecules on monolayer graphene (1L), multilayer graphene (ML), thick graphite, and a blank SiO<sub>2</sub>/Si substrate. (d) Typical result of the Raman spectra of the CuPc molecule on two-dimensional graphene, h-BN, MoS<sub>2</sub> and blank SiO<sub>2</sub>/Si substrates. Panels c and d are adapted with permission from ref 20. Copyright 2014 American Chemical Society.

1997.<sup>11,12</sup> SERS has been shown to have promising applications in many fields, including material science, environmental engineering, food science, and biological science.<sup>1,5,11,13</sup> So far, two of the biggest challenges still remain in SERS study: how to make SERS quantitative and repeatable and the detailed understanding of CM.

In a conventional SERS system, the rough and chemically active metal surface is the main impediment preventing the realization of quantifiability and repeatability.<sup>5</sup> Therefore, seeking a substrate with a flat surface offers a possible solution. To study the CM, a system without the contribution from the EM is needed, so avoiding the generation of the local surface plasmons under the incident laser excitation would be helpful. Graphene,<sup>14,15</sup> which is an ideal 2D ultraflat surface, was expected to address both challenges.<sup>16</sup> The graphene enhanced Raman scattering (GERS) effect was first reported in 2010,<sup>16</sup> which shows significant advantages over the conventional SERS effect to address the above challenges. In this Account, we will introduce this novel effect from the perspective of making SERS quantifiable and repeatable and of developing a model system to study the CM.

## 2. GERS

Many dye molecules are used as probe molecules to investigate whether they show a Raman enhancement effect on graphene.<sup>17</sup> The typical result is shown in Figure 1. Two significant effects are observed in the Raman spectra. First is the photoluminescence (PL) quenching effect by graphene.<sup>18</sup> Figure 1b shows that the PL of the rhodamine 6G (R6G) is quenched on graphene (red line) by a factor of 10<sup>3</sup> compared with that of R6G solution in water (blue line). Because of the quenched PL, we clearly observe the resonant Raman spectra of R6G. The suppression of the PL is attributed to both electron transfer and energy transfer interactions between graphene and the dye molecules.<sup>18</sup> Second is the Raman enhancement effect on graphene.<sup>16</sup> Figure 1c shows the GERS result for the

phthalocyanine (Pc) molecule. Pc molecules were equally deposited on the areas with and without graphene layers. However, the Raman intensities of the molecules are much stronger on graphene (pink line) than on the area without graphene (black line). This result gives direct evidence that a graphene substrate can enhance the Raman signal of certain molecules. We call this phenomena the “graphene enhanced Raman scattering (GERS) effect”. The enhancement is also observed to be depressed on multilayer graphene (blue line in Figure 1c) and on graphite (red line in Figure 1c) relative to that on monolayer graphene. The reduced contribution comes from the interference in the enhancement from the SiO<sub>2</sub>/Si substrate due to the light absorption of the graphene layers.<sup>19</sup>

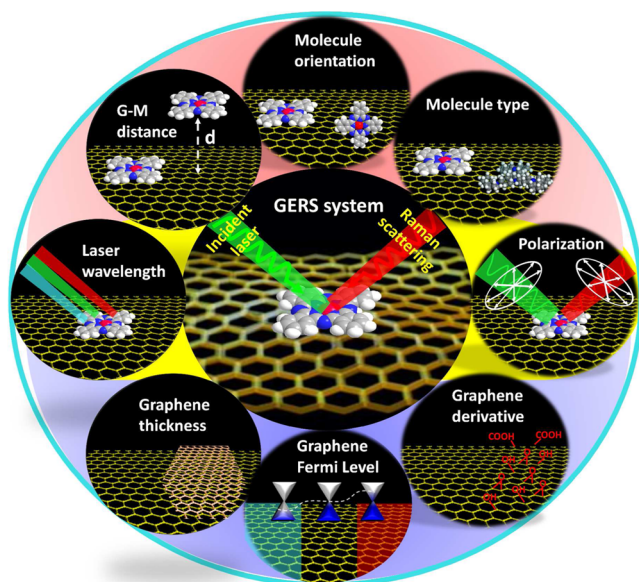
Similar experiments were implemented on other 2D materials, such as hexagonal boron nitride (h-BN) and monolayer MoS<sub>2</sub>.<sup>20</sup> As shown in Figure 1d, Raman enhancement effect was observed on all three 2D materials, compared with the blank SiO<sub>2</sub>/Si substrate. Stronger Raman enhancement effect was observed on graphene than on h-BN and MoS<sub>2</sub>. In addition, the relative intensity of the vibrational modes of the CuPc molecule is different on these substrates, which indicates a different enhancement mechanism and will be discussed later. For convenience, we call the Raman enhancement effect on the other 2D materials “GERS” as well.

Benefiting from the atomic uniformity of graphene, the measurement of GERS enhancement factors (EFs) does not suffer from the nonuniformity on the traditional SERS substrate, which is most effective at “hot spots”. However, the GERS intensity depends on a series of parameters, such as incident laser wavelength, detection setup, adsorption of the analyte, and choice of substrate. Here, the EF of GERS is defined with respect to the non-GERS properties of the same molecule in the same environment used for the GERS experiment. Ling et al.<sup>20</sup> measured the EF of equivalent amounts of CuPc deposited on graphene, h-BN, and SiO<sub>2</sub>/Si. The results show that the EF varies from 5.5 to 63.5 for

different vibrational modes.<sup>20</sup> Deng et al.<sup>21</sup> reported the EF of R6G on graphene ranging between 1.7 and 5.6 for four Raman modes. In most cases, the EFs of GERS range between 0.3 and  $10^2$ .<sup>22,23</sup>

### 3. CHARACTERISTICS AND ENHANCEMENT MECHANISM OF GERS

As a distinct type of SERS, GERS shares some characteristics with traditional SERS while also having its unique ones. Figure 2 shows an overview of the factors investigated in the GERS



**Figure 2.** Overview of the factors investigated in the GERS system.

system.<sup>17,19–21,24–28</sup> These factors can be classified into three categories: molecule, graphene, and the excitation laser energy. The factors related to the molecule include molecule concentration,<sup>16</sup> molecule–graphene distance,<sup>24</sup> molecule orientation,<sup>25</sup> and the type of the molecule.<sup>17</sup> The factors related to graphene include graphene thickness,<sup>26</sup> graphene Fermi level,<sup>27</sup> and graphene derivative.<sup>20,29–31</sup> In addition, the dependences of the GERS effect on the laser wavelength and polarization are considered.<sup>21,28</sup>

Before discussing the characteristics of the GERS effect, it is worth mentioning that the interference effect from the SiO<sub>2</sub>/Si substrate, which we commonly used to support graphene, plays an important role in observing the Raman signal.<sup>19</sup> Strong interference enhancement occurs at 300 nm of SiO<sub>2</sub> layer, which is ideal to observe the Raman signal from both GERS and non-GERS systems and shows the EFs for some molecules. The characteristics of GERS are summarized as follows.

#### 3.1. High Sensitivity

The detection limit of GERS is down to  $8 \times 10^{-8}$  M for R6G and  $2 \times 10^{-8}$  M for PPP by the solution soaking method,<sup>16</sup> which is comparable to that of a classical SERS substrate. This is due to multiple reasons, including the  $\pi$ – $\pi$  interaction-induced enrichment of molecule and fluorescence quenching on graphene.

#### 3.2. Stabilization and Uniformity of Molecules on Graphene

The dye molecules we use as Raman probes in GERS are easy to photobleach normally.<sup>21</sup> The enhancement environment

becomes worse on a metal surface because of the catalytic effect of the metal, which is one of the crucial issues in traditional SERS systems.<sup>11,12,32</sup> However, graphene plays an important role in stabilizing the dye molecules and shows improved endurance to high laser power and stable Raman signals with exposure time.<sup>21</sup> Moreover, benefiting from the flatness of graphene, the distribution of the molecules on graphene can be very uniform,<sup>26</sup> which leads to a uniform lighting-up of the molecules.

#### 3.3. First Layer Effect

The EF of GERS strongly depends on the distance between the graphene and the probe molecule. In Ling and Zhang's work,<sup>24</sup> the first layer protoporphyrin IX (PPP) molecule closest to graphene was found to dominate the Raman intensity, while enhancement increase from the third PPP layer was unobservable, as shown in Figure 3a. The characteristics of the first layer effect reflect the dominant effect of the CM in GERS.

#### 3.4. Vibrational Mode and Molecular Orientation Dependence of GERS

Taking the Pc molecule as an example,<sup>16</sup> it is found that modes assigned as A<sub>g</sub> symmetry are most enhanced while B<sub>3g</sub> modes and macrocycle breathing modes are less enhanced. The EFs are also very sensitive to the molecule orientation. Larger EF values were found for the lying-down CuPc molecules than for the standing up configuration, as shown in Figure 3b. This is attributed to the different magnitudes of interaction between graphene and molecule in different molecular orientations.<sup>25</sup> Study of the molecular orientation dependence shows that one of the advantages of using graphene as a Raman enhancement substrate is the controllability of the molecular orientation, which benefits from the flat surface of graphene.

#### 3.5. Molecule Selectivity of GERS

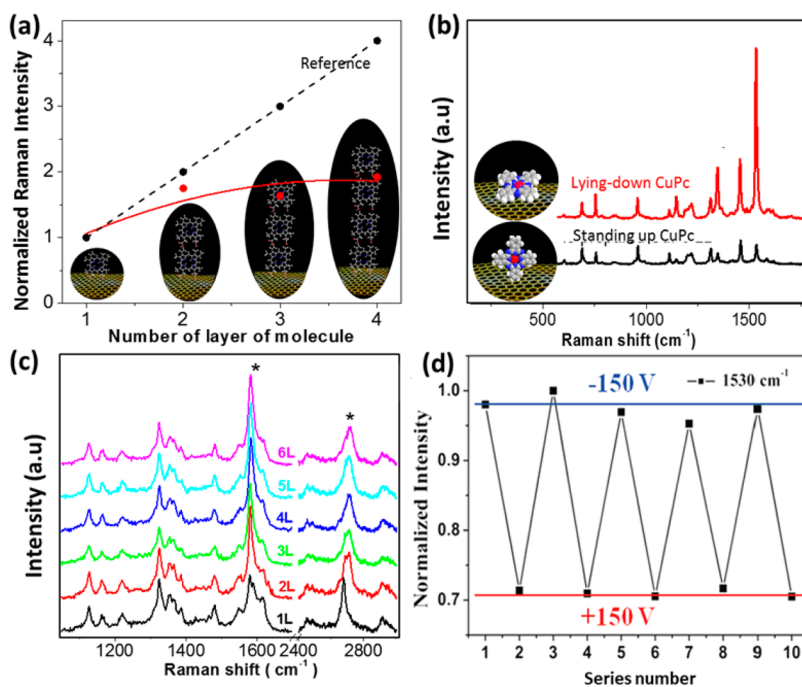
Due to the different energy level and molecular structure, the interaction between the molecule and graphene is much different for different molecules, resulting in different EFs. It is found that the GERS effect follows the two molecular selectivity rules as follows.<sup>17</sup> (i) Energy level rule, GERS enhancement requires the appropriate HOMO/LUMO energy levels of the molecules with a certain energy laser excitation. (ii) Structure rule, molecular structure with D<sub>nh</sub> symmetry is favorable for GERS enhancement because D<sub>nh</sub> symmetry favors structural compatibility with graphene.

#### 3.6. Available GERS Effect on Few-Layer Graphene

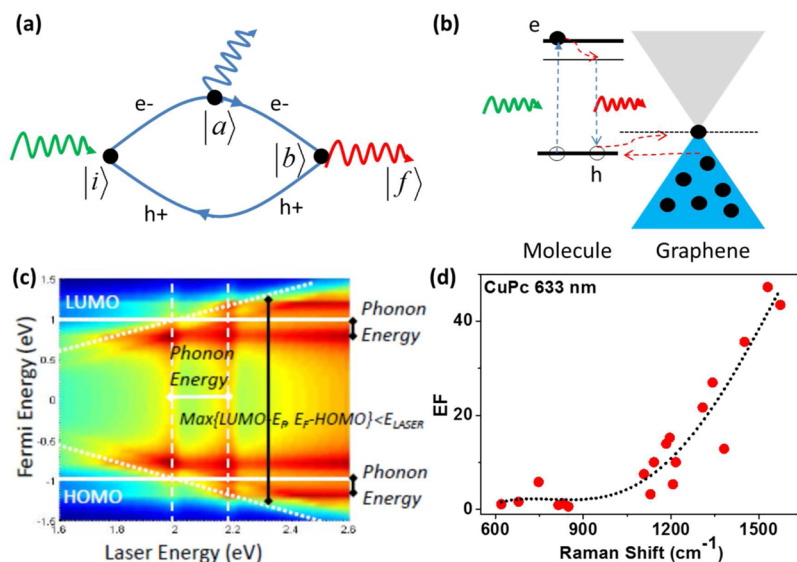
Not only monolayer graphene but also few-layer graphene shows remarkable GERS effects. As shown in Figure 3c, the GERS signal was the same for one to six graphene layers when equal numbers of molecules are deposited on them.<sup>26</sup> The results suggested that future applications of GERS will not be limited to monolayer graphene. This gives more flexibility to the material, including the graphene derivatives, which will be discussed in the next section.

#### 3.7. Graphene Fermi-Level Dependence

Using an electrical field modification method, Xu et al. studied the variation of the Raman intensities of molecules on graphene with the shift of the Fermi level of graphene.<sup>27</sup> For a series of metal phthalocyanine (M-Pc) molecules, the Raman intensities become weaker when the graphene Fermi level is up-shifted, while the intensities become stronger when the graphene Fermi level is down-shifted, as shown in Figure 3d. The modulation of



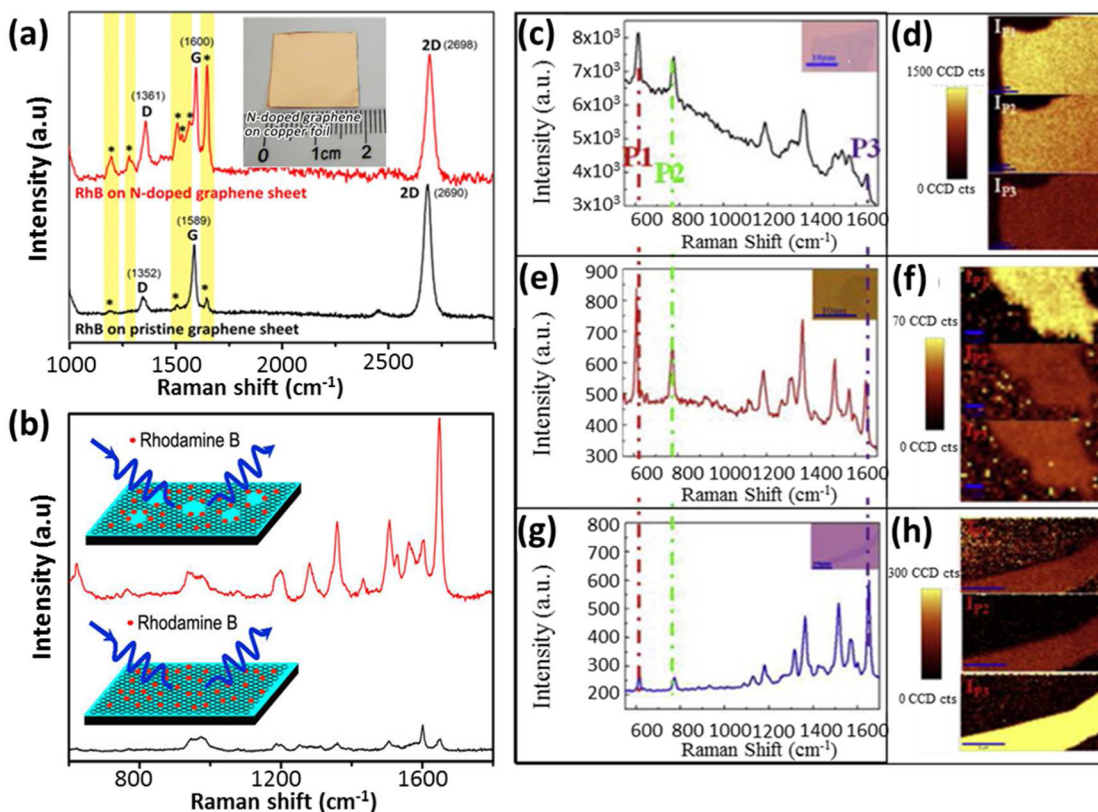
**Figure 3.** (a) Relative intensities of the  $1360\text{ cm}^{-1}$  Raman mode from PPP as a function of the layer number of the LB film of PPP (red dots). Red line is the corresponding polynomial fit. The black dotted line is a reference considering that the different numbers of layers of PPP contribute equally. Inset shows schematic diagrams of 1–4 layer PPP LB films on graphene. Adapted with permission from ref 24. Copyright 2010 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim. (b) Comparison of Raman spectra of an as-prepared CuPc LB film (standing up, black line) and that after annealing at  $300\text{ }^{\circ}\text{C}$  (lying down, red line) on a  $\text{SiO}_2/\text{Si}$  substrate with graphene. Inset shows schematic diagrams of standing up and lying down CuPc molecules on graphene. Adapted with permission from ref 25. Copyright 2012 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim. (c) Raman spectra of the PPP molecules collected on different graphene layers. The peaks labeled with \* are from graphene. All other peaks are from the PPP molecule. Adapted with permission from ref 26. Copyright 2013 American Chemical Society. (d) Raman intensity variations of the  $1530\text{ cm}^{-1}$  mode of CuPc molecules with the gate voltage change between  $-150$  and  $+150\text{ V}$ . Adapted with permission from ref 27. Copyright 2011 American Chemical Society.



**Figure 4.** (a) Feynman figure of the Raman scattering process. (b) Schematic analysis of the Raman scattering process of GERS. Adapted with permission from ref 28. Copyright 2012 American Chemical Society. (c) Calculation result of the GERS EFs by considering the energy level matching between graphene and the molecule. Adapted with permission from ref 35. Copyright 2014 American Physical Society. (d) Experimental result of EFs of the vibrational modes of CuPc in GERS system under  $633\text{ nm}$  excitation. Adapted with permission from ref 17. Copyright 2015 American Chemical Society.

the GERS effect with the Fermi level of graphene is the result of the change of the interaction between graphene and the molecule, consistent with the discussion of the molecule selection rules in terms of the energy level rule.

From the above GERS characteristics, it is realized that the GERS effect matches the characteristics of the chemical mechanism very well. The coupling strength between graphene and the molecule is very important to the GERS effect.<sup>33</sup> The



**Figure 5.** Enhanced Raman scattering effect of diverse graphene derivatives. (a) SERS of RhB molecules on pristine and N-doped graphene. The Raman bands of RhB are marked with \*. Adapted with permission from ref 36. Copyright 2012 Macmillan Publishers Limited. Inset shows photograph of an N-doped graphene sample on Cu foil. (b) SERS of RhB molecules on exfoliated graphene (bottom) and on a graphene nanomesh (top). Adapted with permission from ref 39. Copyright 2012 American Chemical Society. (c, e, g) Typical SERS spectra of R6G on single layer GO, rGO, and exfoliated graphene, respectively. P1, P2, and P3 are three characteristic bands of R6G. (d, f, h) Raman mapping images of these three bands on monolayer GO, rGO, and exfoliated graphene samples. Adapted with permission from ref 30. Copyright 2013 Elsevier Ltd.

energy level matching between graphene and molecule, which influences the charge transfer efficiency, and the molecular structure, which influences the distance between graphene and the molecule and consequently the charge transfer efficiency, are two crucial factors influencing the coupling strength between graphene and molecule. Based on the description of the Raman scattering process in the Feynman figure,<sup>34</sup> the normal Raman scattered processes are shown in Figure 4a. The Raman intensity can be expressed as

$$I(E_L) = K \left| \frac{\langle i|H_{e-r}|a\rangle\langle a|H_{e-ph}|b\rangle\langle b|H_{e-r}|f\rangle}{(E_L - E_g - i\Gamma_a)(E_L - E_{ph} - E_g - i\Gamma_b)} \right|^2 \quad (1)$$

where  $|i\rangle$  is the initial state,  $|a\rangle$  and  $|b\rangle$  are two intermediate states,  $|f\rangle$  is the final state;  $H_{e-r}$ ,  $H_{e-ph}$  are the matrix elements of the Hamiltonians of the radiation of the light and the electron–phonon coupling, respectively;  $E_L$  is the energy of the incident light;  $E_g$  is the energy of the electron transition;  $E_{ph}$  is the energy of the phonon (or vibrational mode);  $\Gamma_a$  and  $\Gamma_b$  are the damping constants, which are related to the lifetimes of the two intermediate states  $|a\rangle$  and  $|b\rangle$ .

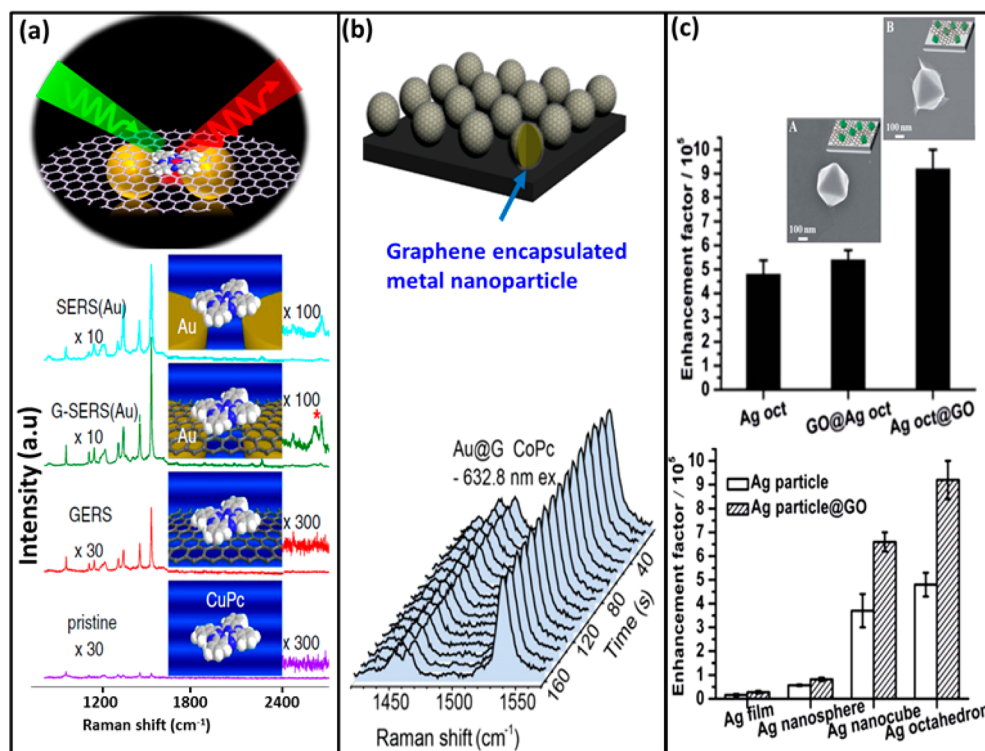
In the GERS system, the electrons in graphene can be involved in the Raman scattered process of CuPc molecules and enhance the process of electron–phonon coupling (Figure 4b), and then  $H_{e-ph}$  is larger than the normal Raman scattering process. This induces the enhancement of the Raman signals as eq 1. This is supported by a theoretical model based on the

Raman scattering theory.<sup>35</sup> As shown in Figure 4c, the largest enhancement happened when  $E_L = \text{HOMO (or LUMO)} \pm E_{ph}$ .<sup>35</sup> This theory is supported by the vibration dependence of CuPc molecule in GERS (Figure 4d, where the higher frequency vibration modes show stronger enhancement factor (for the phonon energy  $< 0.2$  eV)).<sup>17</sup> Furthermore, the excitation wavelength dependence of GERS indicates that GERS is mainly based on ground state charge transfer.<sup>28</sup> In the case of h-BN and MoS<sub>2</sub>,<sup>20</sup> which are insulator and semiconductor, respectively, the charge transfer with molecules is hard to execute. However, the polar environment of these surfaces induces a strong dipole–dipole interaction with the molecule and breaks the symmetry of the molecule, which increases the matrix element  $H'_{kl}$ . From Fermi's golden rule, the electron transition probability rate can be expressed as

$$w_{lk} = \frac{2\pi}{\hbar} g(E_k) |H'_{kl}|^2 \dots \dots \dots \quad (2)$$

where the  $g(E_k)$  is the density of states and  $H'_{kl}$  is the matrix element for the LUMO–HOMO transition. The increase of the matrix element  $H'_{kl}$  leads to the increase of the transition probability and thus an increase of the Raman intensity occurs.

Since GERS (including the Raman enhancement effect on both graphene and its derivatives) shows strong characteristics of the chemical mechanism, GERS offers one of the ideal models for CM study. So far, the understanding of the enhancement mechanism in the GERS system is mainly based



**Figure 6.** (a) Raman spectra of CuPc in different systems, including pristine CuPc, GERS system, G-SERS system, and SERS system. Inset shows schematic illustration of Raman scattering with SERS substrates combining graphene and metal nanostructures. (b) Few-layer graphene encapsulated metal nanoparticles for SERS.<sup>47</sup> (top) Schematic illustration of the structure of the graphene-encapsulated metal nanoparticle. (bottom) Stability comparison of CoPc LB film on Au@G substrates. Adapted with permission from ref 47. Copyright 2014 American Chemical Society. (c) SERS of Ag nanostructures and GO.<sup>51</sup> Inset shows the corresponding SEM images of octahedral Ag on GO (GO@Ag oct) and GO on octahedral Ag (Ag oct@GO), respectively. (top) Average SERS EFs of these three structures, Ag oct, GO@Ag oct, and Ag oct@GO. (bottom) Average SERS EFs of 4-MBT on an Ag film, Ag nanosphere, Ag nanocube, and Ag octahedron with and without GO. Adapted with permission from ref 51. Copyright 2014 Royal Society of Chemistry.

on experimental results. A theoretical model considering both the charge transfer effect and the dipole interaction effect is needed to investigate the chemical mechanism in GERS system in detail. This is one of the important directions for future research.

#### 4. RAMAN ENHANCEMENT EFFECT ON THE GRAPHENE DERIVATIVES

Besides mechanically exfoliated graphene, the GERS effect can be applied to various kinds of graphene-based materials, such as graphene synthesized by different methods (CVD, oxidation–reduction), doped graphene, graphene oxide (GO), and graphene quantum dots. Most of them show much larger Raman EFs than exfoliated graphene. These materials not only allow fast detection of molecules and push the detection limit to the nanomole level but also supply researchers with alternative options to explore the true fact of the GERS effect.

Using CVD graphene as a GERS substrate, Lv et al.<sup>36</sup> discovered that bands at 1650 cm<sup>-1</sup> of RhB were stronger when on N-doped graphene (NG) than on pristine CVD graphene, as shown in Figure 5a. This phenomenon is ascribed to the enhanced charge transfer between RhB molecules and the NG substrate. As mentioned before, the change of the Fermi level of graphene influences the GERS effect. Here, the lattice doping of graphene by N or B atoms also modifies the Fermi level of graphene and subsequently influences the GERS EF.

Another commonly used derivative of graphene is GO. Yu et al.<sup>37</sup> found that mildly reduced GO exhibited high EF values up

to 10<sup>3</sup>. By introduction of fluorine atoms to rGO with CF<sub>4</sub> plasma treatment, the EF increased with the fluoride percentage, benefiting from the local dipoles of the C–F bond, which generated a significant local electric field. In this regard, the graphene surface modification with functional groups of strong dipoles acts as a way to tune the Raman enhancement.<sup>29,38</sup> Yu's group<sup>30</sup> thoroughly compared the GERS effect on graphene, GO, and rGO. As in Figure 5c–h, they showed selective enhancement of vibrational modes because of the different species and number of functional groups. Graphene and rGO show relatively larger enhancement activities for the aromatic stretching vibrational mode located at 1648 cm<sup>-1</sup> (labeled as P3).

For graphene with different morphologies and dimensions, such as graphene quantum dots (GQDs),<sup>31</sup> graphene nanomesh,<sup>39</sup> and nanocolloids,<sup>40</sup> the GERS effect also works. As shown in Figure 5b, a graphene nanomesh<sup>39</sup> shows remarkable Raman enhancement, with the edges acting as molecule-trapping sites, where the GERS effect can be tuned by changing the size, density, and the edge length of the nanomesh.

Overall, the study of the GERS effect on the graphene derivatives reveals that the GERS EF is strongly related to the  $\pi$ – $\pi$  interaction, doping level, local dipole moment and energy levels of graphene and the probe molecule. The characteristics of CM are strongly reflected in these materials. If we can control and determine the structure and morphology of the graphene derivative, as well as develop a method to control the

number of molecules on their surfaces, more intrinsic properties of the CM are expected to be revealed.

## 5. GERS MEETS WITH THE METAL SUBSTRATE

GERS has many advantages, especially in obtaining clean background, repeatable, and quantitative spectra. However, toward to some practical applications, larger enhancement factor is expected. Combining GERS and conventional SERS is expected to maintain the advantages from both. A graphene-media SERS (G-SERS) system is developed, where graphene is covered on metal to separate the adsorbate and metal, as shown in Figure 6a.<sup>32</sup> A typical comparison of the Raman spectra in different systems is shown in Figure 6a. There are several significant advantages of combining graphene or graphene derivatives with conventional metal SERS substrates. First, graphene and graphene derivatives separate the metal and the molecules, which avoids the side reaction of the molecules. Second, graphene or a graphene derivative protects the surface of the metal, which reduces the laser-induced carbonization on the metal surface. In addition, the flat and inert surface of graphene makes the density and the orientation of the molecules more controllable. All these conditions help to obtain clean, reproducible, and strong SERS signals. In addition, the results show that the G-SERS keeps the advantages from GERS and has even higher enhancement factor.<sup>32</sup>

When the graphene and metal are in contact, different plasmonic effects from either the metal or graphene are expected due to the charge transfer between them.<sup>41–43</sup> This effect depends on several factors, such as the type of metal, the metal surface morphology, graphene thickness,<sup>42,44</sup> etc. Graphene has been integrated with various shapes of gold nanoparticles for SERS enhancement, such as arrays of gold nanodisks,<sup>41</sup> photonic-crystal nanocavities,<sup>45</sup> gold nanorods,<sup>46</sup> and silver, copper, or gold nanospheres.<sup>47</sup> The effectiveness of graphene in stabilizing the SERS system of thermally grown Au and Ag nanoparticles and achieving strong enhancement has been proven,<sup>32,47</sup> as shown in Figure 6a,b. These studies showed that the detection limit is  $\sim 100$ -fold larger with graphene coupled with the SERS system.<sup>48,49</sup> Besides graphene, SERS substrates using graphene derivative covered Au or Ag films were also studied.<sup>28,50</sup> Figure 6c<sup>51</sup> shows that octahedral Ag @ GO gives the strongest enhancement of  $9.5 \times 10^5$ , stronger than  $6.9 \times 10^5$  for a Ag nanocube on GO and  $1.0 \times 10^5$  for a Ag nanosphere on GO. In future research, more promising structures are expected for specific applications.

## 6. APPLICATIONS OF GERS IN CHEMICAL AND BIOANALYSIS

In the past five years, utilizing the advantages of GERS, as well as its hybrid configurations with metals, has been reported as applied in diverse species sensing devices, including chemical sensors and biological sensors.<sup>46,52–54</sup> Qi et al. monitored the charge transfer induced chemical reaction between TCNQ and graphene.<sup>54</sup> Lu et al. reported the sensitive and selective detection of DNA and proteins.<sup>55</sup> Some important biomolecules, such as metalloprophyrins,<sup>53</sup> and more complex systems, such as bacteria<sup>52</sup> and stem cells,<sup>56</sup> are successfully lit up under the GERS effect due to their strong interaction with graphene. Xu et al.<sup>57</sup> designed a G-SERS tape constructed with a PMMA/metal/graphene structure, which was used to analyze trace amounts of molecules in an aqueous solution, on a flat surface,

and on a cauliflower vegetable surface. The advanced application of G-SERS benefits from the substrate being flexible, transparent, compatible in solution and biosystems, and able to give uniform and stable signals. In the future, we foresee that the complex and multicomponent structures between diverse metals and 2D materials could be soon developed for highly active SERS technological platforms. This could lead to the effective detection of both chemicals in the environment and possible life-threatening diseases.

## 7. IN SUMMARY

In this Account, we introduced a newly developed technique for Raman enhancement, named “graphene enhanced Raman Scattering (GERS)”. It is a novel branch of SERS, which uses graphene, as well as other 2D materials, as an active substrate. Different from the conventional SERS substrate, which is based on the rough surface of metal and is EM dominated, GERS shows its superiority in lighting up molecules uniformly, repeatability, and quantifiably, due to the flat and chemically inert surface of 2D materials. In particular, it is an available model to study the CM, since there is no disturbance from the EM, which opens a window to see the CM in more detail and gives a chance to realize the complete picture for the SERS mechanism. In addition, great progress has been made to extend this effect to other graphene derivatives, and more diverse molecules with particular functions. It offers potential stages to study this effect more deeply and reveal the CM. In the future, from the fundamental study side, more detailed theoretical models are expected based on this system to understand the principle of CM. From the applications side, more promising applications are expected in process monitoring in chemical and biological systems, utilizing the ability of graphene in lighting up the molecule.

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### Notes

The authors declare no competing financial interest.

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