2D materials coated plasmonic structures for SERS applications

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Abstract: Two-dimensional (2D) materials, such as graphene and hexagonal boron nitride, are new kind of materials that can serve as substrates for surface enhanced Raman spectroscopy (SERS). When combined with traditional metallic plasmonic structures, the hybrid 2D materials/metal SERS platform brings extra benefits, including higher SERS enhancement factors, oxidation protection of metal surface, and protection of molecules from photo-induced damage. This perspective gives an overview of recent progress in 2D materials coated plasmonic structure in SERS application. This review paper focuses on the fabrication of the hybrid 2D materials/metal SERS platform and their applications for Raman enhancement.

Keywords: Surface enhanced Raman spectroscopy, Two-dimensional materials, Plasmonic structure

1. Introduction

Raman spectroscopy is an optical analysis technique providing characteristic spectral information of analytes and has a wide variety of applications in chemistry, biology and medicine because of its capability of providing fingerprints of molecule vibration. One major drawback of Raman spectroscopy is the low yield of Raman scattering, leading to weak Raman signals in most cases, and thus normal Raman spectroscopy can hardly provide discernable signals of trace amount of analytes. Surface enhanced Raman spectroscopy (SERS) makes up this deficiency via plasmon resonance from metallic nanostructures. Molecules adsorbed at nanostructured metallic surface experience a large amplification of electromagnetic (EM) field due to local surface plasmon resonance, which leads to orders of magnitude increase in Raman yield and greatly enhanced Raman signal. SERS is capable of ultra-sensitive detection (single molecule detection) and allows for label-free detection with high degree of specificity. To achieve high SERS enhancement factors, many efforts have been devoted to develop various metallic (mainly Au and Ag) nanostructures to enhance the local EM field.

Two-dimensional (2D) materials, such as graphene and hexagonal boron nitride (h-BN), have unique electronic and optical properties, and attract wide interests for potential applications in electronic devices, sensors, and energy generation. In addition, 2D materials have been explored to enhance Raman signals. Since the discovery of graphene’s Raman enhancement capability, extensive researches have been done to reveal the enhancing mechanism of two-dimensional materials, as well as their application in Raman enhancement substrate. Unlike traditional SERS substrates, 2D materials provide a non-metallic surface to enhance Raman signal. Recently, combing 2D materials with metallic plasmonic structures to form a hybrid SERS platform becomes an emerging research field. 2D materials coated SERS platform offers synergetic Raman enhancement from both 2D materials and plasmon resonance, and other advantages such as metal oxidation protection and protection of molecules from photo-induced damages. This paper will first introduce the Raman enhancing mechanism of 2D materials, and then discuss the recent process of 2D materials coated plasmonic structures for SERS application, including their fabrication, sensitivity and stability.

2. Raman enhancement of 2D materials

This section will briefly introduce the Raman enhancement mechanism of 2D materials, including graphene, h-BN and molybdenum disulfide (MoS2). Unlike EM enhancement mechanism of most metallic SERS substrates, Raman enhancement of 2D materials is due to chemical enhancement mechanism. Chemical enhancement factor on metallic surface is usually low (~10 to 100) compared with EM enhancement factor (~10 to 1011). In a broad perspective, chemical enhancement can be considered as modification of the Raman polarizability tensor of molecule upon its adsorption, which in turn enhances or
quenches Raman signals of vibrational modes. 2D materials provide a superior platform to study the chemical enhancement mechanism because they have no dangling bonds in vertical direction and have atomically flat surface.

Graphene is the first one explored to enhance Raman signals of molecules. Raman enhancement of pristine graphene is ascribed to the ground state charge transfer mechanism. In ground state charge transfer, analyte molecules do not form chemical bond with SERS substrate necessarily. Graphene is chemically inert and the charge transfer between molecules and graphene causes change in analytes’ electronic distribution. Ground-state charge transfer can easily happen between graphene and molecules adsorbed on its surface because of graphene’s two unique features: abundant π electrons on its surface and continuous energy band. Figure 1 (a) shows the proposed ground state charge-transfer process in graphene enhanced Raman system. In normal Raman scattered process, molecule absorbs photon energy and electrons are excited to a higher-energy level. The electrons then relaxes down the vibrational sub-structure and Raman scattered photons are emitted. The graphene electrons involvement in the Raman scattered process can enhance the electron–phonon coupling, and thus induce the enhancement of the Raman signals. The vibrational mode involving the lone pair or π electrons, which has stronger coupling with graphene, has highest Raman enhancement.

Figure 1. (a) Schematic of the Raman scattered process of graphene enhanced Raman spectroscopy. (b) Raman spectra of the CuPc molecule on the blank SiO2/Si substrate, on graphene, on h-BN, and on MoS2 substrates. The numbers marked on the peaks are the peak frequencies of the Raman signals from the CuPc molecule.

h-BN and MoS2 are other two kinds of 2D materials with different electronic and optical properties from graphene. h-BN is highly polarized and insulating with a large band gap of 5.9 eV. CuPc molecule Raman signal is found to be enhanced by h-BN substrate. One proposed Raman enhancement mechanism of h-BN is the interface dipole interaction with analyte molecules, which causes symmetry-related perturbation in the CuPc molecule. In addition, the Raman enhancement factor does not depend on the h-BN layer thickness, because the distribution of the intensity is uniform no matter how thick the h-BN flake is. Atomic layer thin MoS2 is semiconductor and also has a polar bond. For MoS2, both the charge transfer and interface dipole interaction are much weaker compared with graphene and h-BN respectively. The Raman enhancement of MoS2 is not as obvious as that of graphene and h-BN, as shown in Figure 1 (b).

3. Two dimensional materials coated plasmonic nanostructures

Traditional SERS analysis relies on metallic nanostructures that can generate strong local EM field. When combining 2D materials with metallic structure, the hybrid SERS substrate can provide even higher SERS enhancement factor due to the synergic effect of electromagnetic and chemical enhancement. 2D materials, like graphene and h-BN, could offer chemically inert and biocompatible surface, which is favorable in bio-detection. With 2D materials as shielding layer on metallic surface, metal SERS platform such as Ag could be protected from oxidation and have longer shelf life, which can improve the stability and repeatability of SERS analysis. The following discussion will focus on the fabrication, sensitivity, and stability of 2D materials/plasmonic structure for SERS application.

3.1 Fabrication

2D materials/plasmonic structures require incorporation of 2D materials and metallic plasmonic structures that can provide high local electric field upon laser excitation. Common fabrication methods of
2D materials include mechanical exfoliation, chemical exfoliation, and chemical vapor deposition (CVD). Summary of 2D materials synthesis\(^{33-35}\) and metallic SERS substrate\(^{36}\) fabrication can be found elsewhere. This section will focus on the incorporation of 2D materials with metallic plasmonic structure.

One simple way to incorporate 2D materials with metallic nanostructure is to transfer CVD grown 2D materials on metal surface. Graphene and MoS\(_2\) have been proven to be capable of overlapping on Au nanostructures and generating strong Raman signals of graphene and MoS\(_2\) \(^{37}\). Zhu et al.\(^{38}\) fabricated graphene-covered gold nanovoid arrays using CVD grown graphene and investigated the SERS performance of graphene/plasmonic structure. Figure 2 shows the graphene transfer process and the SEM images of graphene-covered gold nanovoid arrays. In this study graphene is actually suspended on Au nanovoid arrays instead of being conformally coated on Au surface. To achieve 2D material conformally coated SERS substrates, metallic structures need to have certain morphology. For instance, nanopyramid and nanocone structure can be conformally coated with 2D materials although some ripples are unavoidable. Figure 3 shows graphene coated Au nanopyramid \(^{16}\) and MoS\(_2\) coated SiO\(_2\) nanocone\(^{39}\), where 2D materials are transferred with the assistance of poly (methyl methacrylate) (PMMA). Metallic plasmonic structure with conformally coated 2D materials can be better isolated from air and thus has longer stability.

Figure 2. (a) Schematic illustrations of the graphene transfer process. (b) SEM image of a large-area nanovoid array integrated with the transferred monolayer graphene. The dark region is covered by graphene. The inset shows a SEM image of the cross-section of graphene-covered nanovoids\(^{38}\).

Figure 3. (a) Graphene coated Au nanopyramid structure. Scale bare is 200 nm \(^{16}\). (b) Tilted false-colour SEM image of the 2D strained MoS\(_2\) crystal defined by the nanocone array. Scale bar is 500 nm \(^{39}\).

PMMA assisted transfer method has advantage to coat 2D materials for plasmonic structures with various morphology. However, the drawback is that PMMA residue left on the surface of 2D materials \(^{40}\) may generate noisy Raman peaks and prevent analyte molecules directly adsorbed on the surface of 2D materials. Therefore, special care needs to be paid to avoid large amount of PMMA residue. Another disadvantage of this transfer method is that the capillary force during the drying process of 2D materials may tear apart the 2D materials and expose the metallic surface. Xu et al\(^{13}\) developed a novel flexible graphene/plasmonic structure with PMMA as a carrying substrate for SERS application. In this study, PMMA was used to support a flat graphene surface instead of a sacrificing transfer layer. Figure 4 shows the fabrication process of the flexible graphene SERS tape.
Another way to incorporate 2D materials with metallic nanostructure is to use chemically exfoliated 2D materials to coat metallic nanoparticles. Kim et al. developed a method to sandwich Ag nanoparticles between layers of reduced graphene oxide (rGO) and graphene oxide (GO) in order to prevent Ag nanoparticle from oxidation and boost Raman signals of analytes. Compared with CVD grown 2D materials, chemically exfoliated 2D materials are cost effective and easily to be functionalized. Figure 5 shows the preparation of SERS substrates with chemically exfoliated graphene.

![Figure 5. Fabrication Process of GO/PAA-AgNP/PAA-RGO Films for Application as SERS Platform](image)

Besides ex-situ transferring 2D materials on metal surface, in-situ grown 2D materials, like graphene and MoS₂, on metal surface is another attracting approach to incorporate 2D materials with plasmonic structure. Liu et al. developed a CVD process to grow graphene shell with controllable thickness on the surface of metal NPs. In situ grown 2D materials on metal surface does not require 2D materials transfer process and has less chance to have polymer residue left on the surface of 2D materials. CVD in-situ grown 2D materials is a promising method to conformally coat 2D materials on metallic surface. However, due to the high temperature of CVD process, pre-designed metallic nanostructure may change their morphology during high temperature process and lose the pre-designed high local EM field. Low temperature plasma enhanced CVD method could be a potential choice to in-situ grow 2D materials on metal surface.

![Figure 6. Production process for the Metal@Graphene to serve as a SERS-active substrate](image)

### 3.2 Sensitivity

Among various 2D materials, graphene is the most widely explored one to incorporate with plasmonic structure. Graphene/metal hybrid SERS platform shows superior SERS performance compared with bare metal SERS substrates. As a result of chemical interaction between graphene and target molecules, certain SERS modes are enhanced or prohibited. Although the chemical enhancement factor of 2D materials is not as high as metallic nanostructure, several tens' times of Raman signal enhancement could be essential when detecting molecules at single molecular level. Several times enhancement determines whether the Raman peaks can be seen or not. Wang et al. developed a graphene/Au nanopyramid hybrid SERS platform, which shows single-molecule detection capability for analytes like R6G and lysozyme. Even for molecules with
small Raman cross-section, like dopamine and serotonin, graphene/Au hybrid platform can still achieve detection limit of $10^{-9}$ M in simulated body fluid\textsuperscript{46}. With graphene/Au nanopyramid hybrid SERS substrates, serotonin molecule Raman peak hot spots and graphene peak hot spots actually coincide as seen from the Raman intensity mapping of analytes peak with that of the graphene G peak (Figure 7). The results indicate that the intrinsic Raman signal of 2D materials in 2D materials/metal hybrid SERS platform can serve as a gauge of the near-field EM-field intensity to locate hot spots. This unique feature of hybrid platform offers an advantage for molecule detection in ultra-low concentration. Actual hot spots of SERS substrates are rare and random even for patterned nanostructure. For extremely diluted solution, the spatial coincidence of molecules and hotspots is rare, leading to long time of up to hours spent on searching for measurable signals. With 2D materials’ intrinsic Raman peak intensity as a SERS enhancement factor marker, the hot spots of the 2D materials/metal hybrid SERS platform could be located in advance and speed up the later detection of target molecules. For 2D materials used in hybrid SERS platform with patterned metallic SERS nanostructures, graphene is the ideal choice because graphene only has a few intrinsic Raman peaks and large-area high quality graphene is easily achievable. In addition, monolayer graphene has only 2.3% absorption of the incident laser, and its plasmon resonance frequency is the tetra Hz regime. Therefore, it has little effect on the EM field of underneath metallic SERS substrates.

Figure 7. (a) Raman spectra of Serotonin molecules on graphene hybrid structure with 3 different concentrations ($10^{-4}$, $10^{-8}$, and $10^{-10}$ M). (b and C) Raman intensity mapping of graphene G band (green) and Raman intensity mapping of serotonin peak at 1546 cm\textsuperscript{-1} (red) of the same area, scale bar, 10 μm. (d) schematic of graphene/Au nanopyramid SERS substrate\textsuperscript{16}.

Besides graphene, h-BN also served as coating layer on plasmonic structure for SERS application. Kim et al\textsuperscript{43} reported h-BN layer wrapped Au nanoparticles as SERS substrate. h-BN coated Au SERS substrate can provide sensitive detection of aromatic hydrocarbon (PAC) molecules, such as B(α)P. PAC molecule Raman detection is very difficult using conventional metallic SERS because the weak interaction between polycyclic aromatic hydrocarbon (PAC) molecules and the metal surface prohibits their adsorption on the metal surface. With h-BN wrapped Au SERS substrates, noticeable and characteristic bands of B(α)P can be detected (Figure 8a), which is because the π−π interaction between B(α)P and h-BN enlarges the surface adsorption coverage (Figure 8b).

Figure 8. (a) SERS spectra benzo(α)pyrene on h-BN/Au/SiO\textsubscript{2} and Au/SiO\textsubscript{2} substrates. (b) Schematic mechanism to explain SERS of benzo(α)pyrene on h-BN/Au/SiO\textsubscript{2} and Au/SiO\textsubscript{2} substrates\textsuperscript{43}.

3.4 Stability
Ag nano-structure is known to have excellent SERS performance with wider plasmonic spectral window than other metallic structure made of Au or Al. However, one major weakness of Ag nanostructure is that it is easily to be oxidized in ambient environment. The degradation of Ag will lower the SERS performance and cause uncertainty of analysis. In addition, photo induced damage on analyte molecules is a well know side effect of metallic SERS substrates. This section will discuss recent process of using 2D materials as shielding layer to protect SERS metal substrates from oxidation and protect analyte molecules from photo-induced damages.

2D materials, like graphene and h-BN, are able to protect metal to be oxidized 44, 45. This feature of 2D materials can also be used in SERS substrate development 42, 46. When single layer graphene combines with Ag nanostructure, the hybrid SERS platform provides both better SERS performance and excellent stability in a harsh environment (sulfur) and at high temperatures (300 °C) 47. Liu et al. 46 combined CVD grown graphene with silver SERS substrates and demonstrated that with the graphene as protecting layer, the hybrid graphene/Ag SERS substrate could achieve large-area uniformity and long-term stability. Li et al. 48 compared the oxidation protection effect between CVD grown graphene and rGO coated Ag nanoparticles. They found out that CVD-grown monolayer graphene served as a better protecting layer than rGO to effectively suppress the oxidation of Ag nanoparticles. As seen from Figure 9, CVD grown graphene coated Ag SERS substrate can provide stable R6G SERS signals up to 28 days with ambient aerobic exposure, while rapidly decreasing Raman signals are seen from rGO coated and bare Ag nanoparticles. Worse performance of rGO protected Ag nanoparticle is because 1) the wide size distribution of rGO results an incoherent thin film; and 2) the cracks and holes on rGO film could act as a channel to allow air reach Ag surface, leading to the oxidation of Ag nanoparticles.

Another benefit to combine 2D materials with metallic nanostructures is that 2D materials can help protect molecules from photo-induced damage, such as photobleaching 13, 42, 49, 50. The photobleaching (or photodegradation) of the Raman anlaytes induced by the laser is a well-known side effect in SERS experiments, especially for dye molecules. When combining graphene with metallic nanostructure, the hybrid SERS platform is more stable against photo-induced damage with an even higher enhancement factor. Liu at al. 42 fabricated graphene-encapsulated metal nanoparticles for molecule detection, and found out that AuNP/graphene hybrid substrate could significantly suppress photobleaching and fluorescence of cobalt phthalocyanine (CoPc) and R6G molecules. For instance, within the 160 s measurement period, the 1534 cm⁻¹ peak intensity of CoPc molecules decreases dramatically for Au NPs, while the same peak intensity almost keep constant for Au@Graphene, as shown in Figure 10 (a) and (b). Zhao et al. 50 also
demonstrated that graphene can enhance the photostability of R6G molecules with graphene coated Ag SERS substrates during continuous light illumination. Enhanced photostability of molecules provided by graphene during SERS detection is attributed to π−π interactions between graphene surface and molecules. Molecule π−π interaction with graphene allows the charge transfer between graphene and molecules, providing additional path for the molecules to relax from the excitation state to the ground state. This process reduces the number of molecules at excitation states and thus decreases photobleaching rate. Similar protection effect can be achieved by using h-BN layer as well. Kim et al. reported a h-BN film wrapped Au substrate showing extraordinary stability against photothermal and oxidative damages during laser excitation, as shown in Figure 10 (c) and (d). This outstanding stability against photothermal damage of h-BN wrapped Au SERS substrate is attributed to the ultrafast heat dissipation through the h-BN layer. With 2D materials as a shielding layer, hybrid SERS substrates will provide long-term stability.

Figure 10. Stability of SERS signals of monolayer CoPc LB films on (a) Au and (b) Au@G. Photothermal and chemical stability of 3L h-BN/Au/SiO2 substrate. SERS spectra of R6G on the Au/SiO2 substrate (c) without and (d) with h-BN protection at different time points (laser power = 0.1 mW, time interval = 15 min).

4. Conclusion and perspective

In summary, 2D materials’ Raman enhancement is due to chemical enhancement, which differentiates them from metallic SERS substrates. Coating 2D materials on metallic SERS substrates introduces extra benefits over bare metal substrates. First, adding 2D materials can further increase SERS enhancement factor due to the synergic effect of electromagnetic and chemical enhancement. Second, the atomic thin film of 2D materials can help map out the hot spots of metallic nanostructure without affecting the local EM field of metallic nanostructure underneath. For example, a Raman mapping of graphene G peak over the hybrid SERS substrates could give the precise position of hot spots. Finally, adding 2D materials as a shielding layer offers chemically inert surface and helps to reduce the fluctuation of SERS signal caused by degradation of the metallic nano-structures, photobleaching or metal-catalyzed site reactions, and thus improve the long-term stability and repeatability of SERS analysis.
References

1. Pillai, I. C.; Li, S.; Romay, M.; Lam, L.; Lu, Y.; Huang, J.; Dillard, N.; Zemanova, M.; Rubbi, L.; Wang, Y. Cardiac fibroblasts adopt osteogenic fates and can be targeted to attenuate pathological heart calcification. *Cell stem cell* 2017, 20, 218-232. e5.

2. Le Ru, E. C.; Etchegoin, P. G. Single-molecule surface-enhanced Raman spectroscopy. *Annual Review of Physical Chemistry* 2012, 63, 65-87.

3. Luo, S.-C.; Sivashanmugan, K.; Liao, J.-D.; Yao, C.-K.; Peng, H.-C. Nanofabricated SERS-active substrates for single-molecule to virus detection in vitro: A review. *Biosensors and Bioelectronics* 2014, 61, 232-240.

4. Blackie, E. J.; Ru, E. C. L.; Etchegoin, P. G. Single-molecule surface-enhanced Raman spectroscopy of nonresonant molecules. *Journal of the American Chemical Society* 2009, 131, 14466-14472.

5. Xia, M.; Zhang, P.; Qiao, K.; Bai, Y.; Xie, Y.-H. Coupling SPP with LSPR for Enhanced Field Confinement: A Simulation Study. *The Journal of Physical Chemistry C* 2015, 120, 527-533.

6. Xia, M.; Zhang, P.; Leung, C.; Xie, Y. H. SERS optical fiber probe with plasmonic end facet. *Journal of Raman Spectroscopy* 2017, 48, 211-216.

7. Xia, M.; Qiao, K.; Cheng, Z.; Xie, Y.-H. Multiple layered metallic nanostructures for strong surface-enhanced Raman spectroscopy enhancement. *Applied Physics Express* 2016, 9, 065001.

8. Yan, Z.; Xia, M.; Wang, P.; Zhang, P.; Liang, O.; Xie, Y.-H. Selective manipulation of molecules by electrostatic force and detection of single molecules in aqueous solution. *The Journal of Physical Chemistry C* 2016, 120, 12765-12772.

9. Zhang, W.; Ma, R.; Chen, Q.; Xia, M.; Ng, J.; Wang, A.; Xie, Y.-H. The electro-mechanical responses of suspended graphene ribbons for electrostatic discharge applications. *Applied Physics Letters* 2016, 108, 153103.

10. Chen, Q.; Ma, R.; Lu, F.; Wang, C.; Liu, M.; Wang, A.; Zhang, W.; Xia, M.; Xie, Y.-H.; Cheng, Y. In Systematic transient characterization of graphene interconnects for on-chip ESD protection, Reliability Physics Symposium (IRPS), 2016 IEEE International, IEEE: 2016; pp 3B-6-1-3B-6-5.

11. Zhang, W.; Chen, Q.; Xia, M.; Ma, R.; Lu, F.; Wang, C.; Wang, A.; Xie, Y.-H. In TLP evaluation of ESD protection capability of graphene micro-ribbons for ICs, ASIC (ASICON), 2015 IEEE 11th International Conference on, IEEE: 2015; pp 1-4.

12. Ling, X.; Fang, W.; Lee, Y.-H.; Araujo, P. T.; Zhang, X.; Rodriguez-Nieva, J. F.; Lin, Y.; Zhang, J.; Kong, J.; Dresselhaus, M. S. Raman enhancement effect on two-dimensional layered materials: graphene, h-BN and MoS2. *Nano letters* 2014, 14, 3033-3040.

13. Xu, W.; Ling, X.; Xiao, J.; Dresselhaus, M. S.; Kong, J.; Xu, H.; Liu, Z.; Zhang, J. Surface enhanced Raman spectroscopy on a flat graphene surface. *Proceedings of the National Academy of Sciences* 2012, 109, 9281-9286.

14. Xu, W.; Mao, N.; Zhang, J. Graphene: A Platform for Surface Enhanced Raman Spectroscopy. *Small* 2013, 9, 1206-1224.

15. Wang, P.; Liang, O.; Zhang, W.; Schroeder, T.; Xie, Y. H. Ultra - Sensitive Graphene - Plasmonic Hybrid Platform for Label - Free Detection. *Advanced Materials* 2013, 25, 4918-4924.

16. Wang, P.; Xia, M.; Liang, O.; Sun, K.; Cipriano, A. F.; Schroeder, T.; Liu, H.; Xie, Y.-H. Label-free SERS selective detection of dopamine and serotonin using graphene-Au nanopyramid heterostructure. *Analytical chemistry* 2015, 87, 10255-10261.

17. Ling, X.; Xie, L.; Fang, Y.; Xu, H.; Zhang, H.; Kong, J.; Dresselhaus, M. S.; Zhang, J.; Liu, Z. Can graphene be used as a substrate for Raman enhancement? *Nano letters* 2009, 10, 553-561.

18. Xia, M. A Review on Applications of Two-Dimensional Materials in Surface-Enhanced Raman Spectroscopy. *International Journal of Spectroscopy* 2018, 2018.

19. Yan, Z.; Xia, M.; Zhang, P.; Xie, Y. H. Self - Aligned Trapping and Detecting Molecules Using a Plasmonic Tweezer with an Integrated Electrostatic Cell. *Advanced Optical Materials* 2017, 5.

20. Yan, Z.; Liu, Z.; Xia, M.; Efimov, A.; Xie, Y. H. Broadband surface - enhanced coherent anti - Stokes Raman spectroscopy with high spectral resolution. *Journal of Raman Spectroscopy* 2017, 48, 935-942.

21. Ling, X.; Moura, L.; Pimenta, M. A.; Zhang, J. Charge-transfer mechanism in graphene-enhanced Raman scattering. *The Journal of Physical Chemistry C* 2012, 116, 25112-25118.

22. Ling, X.; Zhang, J. First - Layer Effect in Graphene - Enhanced Raman Scattering. *Small* 2010, 6, 2020-2025.
23. Liang, E.; Kiefer, W. Chemical effect of SERS with near-infrared excitation. *Journal of Raman spectroscopy* 1996, 27, 879-886.

24. Kneipp, K.; Wang, Y.; Kneipp, H.; Perelman, L. T.; Itzkan, I.; Dasari, R. R.; Feld, M. S. Single molecule detection using surface-enhanced Raman scattering (SERS). *Physical review letters* 1997, 78, 1667.

25. Xu, H.; Aizpurua, J.; Käll, M.; Apell, P. Electromagnetic contributions to single-molecule sensitivity in surface-enhanced Raman scattering. *Physical Review E* 2000, 62, 4318.

26. Le Ru, E.; Etchegoin, P. *Principles of Surface-Enhanced Raman Spectroscopy: and related plasmonic effects*. Elsevier: 2008.

27. Moskovits, M. Surface-enhanced spectroscopy. *Reviews of modern physics* 1985, 57, 783.

28. Ling, X.; Wu, J.; Xu, W.; Zhang, J. Probing the Effect of Molecular Orientation on the Intensity of Chemical Enhancement Using Graphene - Enhanced Raman Spectroscopy. *Small* 2012, 8, 1365-1372.

29. Dean, C. R.; Young, A. F.; Meric, I.; Lee, C.; Wang, L.; Sorgenfrei, S.; Watanabe, K.; Taniguchi, T.; Kim, P.; Shepard, K. L. Boron nitride substrates for high-quality graphene electronics. *Nature nanotechnology* 2010, 5, 722.

30. Splendiani, A.; Sun, L.; Zhang, Y.; Li, T.; Kim, J.; Chim, C.-Y.; Galli, G.; Wang, F. Emerging photoluminescence in monolayer MoS2. *Nano letters* 2010, 10, 1271-1275.

31. Liu, Y.; Yu, D.; Zeng, C.; Miao, Z.; Dai, L. Biocompatible graphene oxide-based glucose biosensors. *Langmuir* 2010, 26, 6158-6160.

32. Li, N.; Zhang, Q.; Gao, S.; Song, Q.; Huang, R.; Wang, L.; Liu, L.; Dai, J.; Tang, M.; Cheng, G. Three-dimensional graphene foam as a biocompatible and conductive scaffold for neural stem cells. *Scientific reports* 2013, 3, 1604.

33. Zhu, Y.; Murali, S.; Cai, W.; Li, X.; Suk, J. W.; Potts, J. R.; Ruoff, R. S. Graphene and graphene oxide: synthesis, properties, and applications. *Advanced materials* 2010, 22, 3906-3924.

34. Li, X.; Zhu, H. Two-dimensional MoS 2: Properties, preparation, and applications. *Journal of Materiomics* 2015, 1, 33-44.

35. Zhang, K.; Feng, Y.; Wang, F.; Yang, Z.; Wang, J. Two dimensional hexagonal boron nitride (2D-hBN): synthesis, properties and applications. *Journal of Materials Chemistry C* 2017, 5, 11992-12022.

36. Fan, M.; Andrade, G. F.; Brolo, A. G. A review on the fabrication of substrates for surface enhanced Raman spectroscopy and their applications in analytical chemistry. *Analytica chimica acta* 2011, 693, 7-25.

37. Xia, M.; Li, B.; Yin, K.; Capellini, G.; Niu, G.; Gong, Y.; Zhou, W.; Ajayan, P. M.; Xie, Y.-H. Spectroscopic signatures of AA’ and AB stacking of chemical vapor deposited bilayer MoS2. *ACS nano* 2015, 9, 12246-12254.

38. Zhu, X.; Shi, L.; Schmidt, M. S.; Boisen, A.; Hansen, O.; Zi, J.; Xiao, S.; Mortensen, N. A. Enhanced light–matter interactions in graphene-covered gold nanovoid arrays. *Nano letters* 2013, 13, 4690-4696.

39. Li, H.; Contrryman, A. W.; Qian, X.; Arakani, S. M.; Gong, Y.; Wang, X.; Weisse, J. M.; Lee, C. H.; Zhao, J.; Ajayan, P. M. Optoelectronic crystal of artificial atoms in strain-textured molybdenum disulphide. *Nature communications* 2015, 6, 7381.

40. Pirkle, A.; Chan, J.; Venugopal, A.; Hinojos, D.; Magnuson, C.; McDonnell, S.; Colombo, L.; Vogel, E.; Ruoff, R.; Wallace, R. The effect of chemical residues on the physical and electrical properties of chemical vapor deposited graphene transferred to SiO2. *Applied Physics Letters* 2011, 99, 122108.

41. Kim, Y.-K.; Han, S. W.; Min, D.-H. Graphene oxide sheath on Ag nanoparticle/graphene hybrid films as an antioxidative coating and enhancer of surface-enhanced Raman scattering. *ACS applied materials & interfaces* 2012, 4, 6545-6551.

42. Liu, Y.; Hu, Y.; Zhang, J. Few-layer graphene-encapsulated metal nanoparticles for surface-enhanced Raman spectroscopy. *The Journal of Physical Chemistry C* 2014, 118, 8993-8998.

43. Kim, G.; Kim, M.; Hyun, C.; Hong, S.; Ma, K. Y.; Shin, H. S.; Lim, H. Hexagonal Boron Nitride/Au Substrate for Manipulating Surface Plasmon and Enhancing Capability of Surface-Enhanced Raman Spectroscopy. *ACS nano* 2016, 10, 11156-11162.

44. Liu, Z.; Gong, Y.; Zhou, W.; Ma, L.; Yu, J.; Idrobo, J. C.; Jung, J.; MacDonald, A. H.; Vajtai, R.; Lou, J. Ultrathin high-temperature oxidation-resistant coatings of hexagonal boron nitride. *Nature communications* 2013, 4, 2541.

45. Chen, S.; Brown, L.; Levendof, M.; Cai, W.; Ju, S.-Y.; Edgeworth, J.; Li, X.; Magnuson, C. W.; Velamakanni, A.; Piner, R. D. Oxidation resistance of graphene-coated Cu and Cu/Ni alloy. *ACS nano* 2011, 5, 1321-1327.
46. Liu, X.; Wang, J.; Wu, Y.; Fan, T.; Xu, Y.; Tang, L.; Ying, Y. Compact shielding of graphene monolayer leads to extraordinary SERS-active substrate with large-area uniformity and long-term stability. *Scientific reports* 2015, 5, 17167.

47. Hu, Y.; Kumar, P.; Xuan, Y.; Deng, B.; Qi, M.; Cheng, G. J. Controlled and Stabilized Light–Matter Interaction in Graphene: Plasmonic Film with Large Scale 10-nm Lithography. *Advanced Optical Materials* 2016, 4, 1811-1823.

48. Li, X.; Li, J.; Zhou, X.; Ma, Y.; Zheng, Z.; Duan, X.; Qu, Y. Silver nanoparticles protected by monolayer graphene as a stabilized substrate for surface enhanced Raman spectroscopy. *Carbon* 2014, 66, 713-719.

49. Du, Y.; Zhao, Y.; Qu, Y.; Chen, C.-H.; Chen, C.-M.; Chuang, C.-H.; Zhu, Y. Enhanced light–matter interaction of graphene–gold nanoparticle hybrid films for high-performance SERS detection. *Journal of Materials Chemistry C* 2014, 2, 4683-4691.

50. Zhao, Y.; Xie, Y.; Bao, Z.; Tsang, Y. H.; Xie, L.; Chai, Y. Enhanced SERS stability of R6G molecules with monolayer graphene. *The Journal of Physical Chemistry C* 2014, 118, 11827-11832.

51. Xie, L.; Ling, X.; Fang, Y.; Zhang, J.; Liu, Z. Graphene as a substrate to suppress fluorescence in resonance Raman spectroscopy. *Journal of the American Chemical Society* 2009, 131, 9890-9891.