# Highly Sensitive Flexible SERS Substrates with a Sandwich Structure for Rapid Detection of Trace Pesticide Residues

Shenghui Yi<sup>a,#</sup>, Mingde Yang<sup>b,#</sup>, Yixin Yu<sup>b,#</sup>, Zebiao Li<sup>c</sup>, Deng Zhang<sup>d</sup>, Aleksei Grishko<sup>b</sup>, Qinghua Qin<sup>b,\*</sup>, Binbin Zhou<sup>e,\*</sup>

<sup>#</sup> These authors contribute equally: S.H. Yi, M.D. Yang, Y.X. Yu

\* Corresponding Authors: bb.zhou@siat.ac.cn (B.B. Zhou), qinghua.qin@smbu.edu.cn

<sup>a</sup> Faculty of Engineering, Shenzhen MSU-BIT University, 1 International University Park Road, Dayun New Town, Longgang District, Shenzhen 518100, China

<sup>b</sup> Faculty of Materials Science, Shenzhen MSU-BIT University, 1 International University Park Road, Dayun New Town, Longgang District, Shenzhen 518100, China

<sup>c</sup> PetroChina Shenzhen New Energy Research Institute Co., LTD, Nanshan District, Shenzhen , China

<sup>d</sup> School of Computer and Electronic Information, Nanjing Normal University, Nanjing 210023, China

<sup>e</sup> Shenzhen Institute of Advanced Electronic Materials, Shenzhen Institute of Advanced Technology,

Chinese Academy of Sciences, Shenzhen 518055, P. R. China

#### Abstract

Compared with rigid surface-enhanced Raman scatting (SERS) substrates, flexible SERS substrates are more attractive in detection of pesticide residues on vegetable and fruit surfaces due to the convenient sampling and short detection time. However, the enhancement effect of flexible substrates is usually too weak to meet practical requirements of trace detection of pesticides. To achieve high-performance flexible SERS substrates, a novel sandwich structure is proposed. Specifically, gold nanoparticles (AuNPs) are aggregated on expanded graphite (EG) under the chemical enhanced effect from LiCl. The EG is found to improve the adsorption capacity of the targeted molecules and to avoid the attenuation of the Raman signal by the filter paper. An appropriate aggregating agent of specific concentrations can efficiently increase the amounts of hot spots to provide a more significant enhancement effect. Furthermore, the developed flexible SERS substrates are applied to qualitatively and quantitatively detect pesticide residues, including Thiram, Nitrofural and Dinotefuran. High accuracy and robustness are obtained for the flexible SERS substrates, which can be easily stored and used for practical applications.

**Keywords:** SERS; Nanoparticles; Flexible substrates; Chemical enhancers; Pesticide residues

# **1.Introduction**

Surface-enhanced Raman scattering (SERS), as a spectroscopic technique that overcomes the weakness of the low Raman signal, is a useful approach for label-free and ultra-sensitive detection of chemical and biochemical analytes at low concentrations. [1-3] In recent years, SERS has been applied in various fields, such as biosensing and medical diagnosis[4,5], food safety[6,7] and environmental

protection[1,8]. SERS substrates can be divided into rigid and flexible substrates. Rigid SERS substrates are usually fabricated by depositing colloidal solutions on surfaces of rigid materials, such as glass, silicon, metals, etc. [9] Microstructures of abundant sub-10 nm gap structures can be fabricated on rigid substrates, which enable possible identification of single molecules.[10-12] Some rigid substrates are even made into different shapes for better detection purposes.[13] Furthermore, chemical enhancers, such as halogen salts, were used to provide additional SERS signal enhancement based on different mechanism for rigid and colloid substrates.[14] However, the rigid SERS surfaces have some drawbacks when performing practical applications. For example, rigid SERS substrates are not conducive to portability and are not suitable for direct and rapid detection of targets on irregularly shaped objects.[15] Therefore, flexible SERS substrates are proposed and have attracted world-widely interest due to various advantages, such as large surface area, excellent wicking characteristics, compatibility, biodegradability, and low cost [16,17], which have advantages over those with rigid SERS substrates.

Flexible materials including cellulose papers [18], PET films [19], polymers [20], and transparent adhesive tapes [21], have been used in flexible SERS substrates. The paper-based SERS substrate composed of silver nanowires (AgNWs) has been coupled with polymerase chain reaction (PCR), which can quantify the difference in dye embedding in the DNA structure through Raman spectroscopy to quickly verify the presence of the target gene. [22] A multifunctional plasmonic fabric composed of silver nanoparticles (AgNPs) and cotton gauze exhibited excellent flexibility and time stability, whose enhancement factor was close to  $10^5$ . [23] The silver nanoparticle-grafted wrinkled polydimethylsiloxane (AgNPs@W-PDMS) film prepared by surface-wrinkling technique and magnetron sputtering technology exhibited a low detection limit ( $10^{-7}$  M) and a high gain ( $6.11 \times 10^6$ ) in the detection of R6G. [24]

Flexible SERS substrates are proposed for detecting pesticide residues [25,26], which are an important issue for human and animal lives. Pesticide residues can be metabolized, stored or bioaccumulated in body fat [27]. A wide range of health problems have been linked to pesticides used in agriculture fields, including cancer, skin allergies and poisoning deaths.[28] Pesticide overuse poses a risk to nature ecosystems [29]. Therefore, rapid and accurate detections of pesticide residues from food or ecosystems become an important public issue. Thiram, as a kind of pesticide, is widely used in agricultural production and seriously threatens human health. [30] The flexible SERS substrates prepared through silver mirror reaction with Ag

nanoparticles on filter papers have shown a detection limit of Thiram of 10<sup>-7</sup>M. [31] By using screen printing and graphene oxide, flexible SERS substrates with Ag nanoparticles/graphene oxide on papers are demonstrated with a detection limit of Thiram of 0.26 ng/cm<sup>2</sup>. [32] However, there are some issues that still need to be solved, e.g., further improving sensitivity, long-term stability, reducing cost. [33] Rapid and sensitive quantitative and qualitative detections of various pesticide residues need further development for practical applications.

This work proposes a convenient, low-cost flexible SERS substrate, which is suitable for various pesticide residues, demonstrated by Nitrofural, Dinotefuran and Thiram. As shown in Fig. 1, LiCl solution at an optimized concentration is selected as the chemical enhancer to aggregate gold nanoparticles (AuNPs) on expanded graphite (EG) and increase the number of "hot spots". EG is introduced as part of the substrate, which not only serves as a carrier for AuNPs, but also repairs the holes in filter papers. The usage of LiCl and EG prevents the flexible substrate from attenuating the Raman signal and enhances the adsorption capacity of the molecules to be measured. The solution using the developed flexible AuNPs-EG-filter paper sandwich substrates is fast, low-cost and efficient for SERS-based pesticide residue detection.

### 2.Experiments

#### 2.1 Materials and chemicals

All aqueous solutions were prepared using ultrapure water (Milli-Q, resistivity 18.2 M $\Omega$ -cm). Gold chloride solution (HAuCl<sub>4</sub>,  $\omega$ (Au) = 23.5-23.8% in dilute hydrochloric acid), Rhodamine 6G (R6G, C<sub>28</sub>H<sub>31</sub>ClN<sub>2</sub>O<sub>3</sub>, 95%), Lithium chloride (LiCl, 99%), Sodium chloride (NaCl, 99.5%), ascorbic acid (C<sub>6</sub>H<sub>8</sub>O<sub>6</sub>, 99%) and Crystalline flake graphite (99.9%) were obtained from Aladdin (Shanghai, China). Silver nitrate (AgNO<sub>3</sub>, 99%) and trisodium citrate dihydrate (Na<sub>3</sub>C<sub>6</sub>H<sub>5</sub>O<sub>7</sub>-2H<sub>2</sub>O, 98%) were taken from Innochem (Beijing, China).

#### 2.2 Synthesis of AuNPs and expanded graphite

The Frens method was employed to synthesize gold nanoparticle solutions. [34] 0.0449 g HAuCl<sub>4</sub> was dissolved in 150 ml ultrapure water before being heated to its boiling point while being stirred in a round-bottom flask. The quick inject of 6.25 mL sodium citrate solution led to a color change. After completing the reaction, gold nanoparticles were produced.

To achieve spherical nanoparticles with a large diameter, the nucleation growth method was employed. 0.062g HAuCl<sub>4</sub> and 0.4mL AgNO<sub>3</sub> were dissolved in 150mL ultrapure

water. The solution was subsequently poured into a three-necked flask. Then, 15mL previously obtained gold nanoparticle solution was added in the flask. Additionally, 61.58g ascorbic acid solid particles dissolved in 70mL ultrapure water was prepared. Then, 30mL mixed solution in the flask was transferred to a separatory funnel. The solution was stirred in another three-necked flask and twenty drops of the ascorbic acid solution were added uniformly (one drop takes 2.5 s). Finally, the AuNPs solution of larger diameters was synthesized.

# 2.3 Synthesis of expanded graphite

At ambient temperature, 2.5 mL CH<sub>3</sub>COOH was added gradually to 10 mL HNO<sub>3</sub> whilst stirring, followed by a slow addition of 5.0 g crystalline flake graphite. Then, 2.5 g KMnO<sub>4</sub> was introduced into the mixed system. The reaction was proceeded for 40 minutes with constant stirring. The resulting mixture was washed to neutrality, and subsequently dried at 60 °C. Finally, EG was produced by scorching the dried mixture with a spray gun for 15 seconds.

# 2.4 Assembling composite materials on flexible filter papers

The synthesized AuNPs solution was centrifuged to clear the supernatant. The obtained 0.01g expanded-graphite was added into 20ml pure water and evenly dispersed using an ultrasonicate. The two solutions were mixed with 0.1M XCl (X = Li, Na, K) and centrifuged to discard the supernatant. The remaining solution was added gradually onto filter papers of 1cm  $\times$  1cm size and dried in air to obtain the composite materials.

# 2.5 Characterization

All AuNPs solutions were examined using a UV-visible spectrophotometer (PGENERAL/T9) to evaluate the concentration and diameter of the nanoparticles. The microstructure, size and distribution of the nanoparticles were measured by the dynamic light scattering (DLS) and scanning electron microscopy (SEM) methods. DLS measurements were performed using a Litesizer (Anton Paar, Austria) and illuminated with a HeNe laser ( $\lambda = 658$  nm).

# 2.6 SERS measurements

The R6G stain was selected as a Raman molecular probe to assess the enhancement effect of SERS. 10  $\mu$ L R6G solution was added dropwise to the flexible sandwich substrates and dried in the air. Raman measurements were performed using a micro-Raman spectrometer (RENISHAW, USA) equipped with a 17 mW 632.8 nm HeNe laser. The laser power was fixed at 10%. Spectra were collected within the range from

600 to 1700 cm<sup>-1</sup>. The acquisition time was set as 20 s. To validate the detection of pesticide residues on fruits and vegetables using the developed flexible SERS substrates, cucumber and apple samples were selected. These samples were treated with solutions containing Dinotefuran, Nitrofural, or Thiram in different concentrations. The surfaces of the samples were wiped with the flexible SERS substrates and subsequent Raman measurements were conducted. At least five experiments were undertaken for each parameter and sample.



**Fig. 1** Fabrication and application of flexible SERS substrates based on aggregated gold particles-graphene-filter paper sandwich structures.

# 3. Results and discussion

#### 3.1 Preparation of flexible AuNPs/EG SERS substrates

High-performance flexible SERS substrates featuring AuNPs-EG on filter papers were fabricated through a series of steps. Initially, AuNPs were mixed with EG in a solution, and a chemical enhancer was added. This mixture was then dispersed onto filter papers, resulting in the creation of a flexible SERS substrate, as depicted schematically in Fig. 2a. The substrate exhibits a sandwich structure, with aggregated AuNPs combining with EG on the filter papers. The concept of controllable aggregation of gold nanoparticles on the surface of expanded graphite was utilized increase the density of hot spots . SEM images of AuNPs/EG with and without a chemical enhancer (0.1 M

LiCl) on filter papers are displayed in Fig. 2b and Fig. 2c. The images provide clear and objective evidence of the chemical enhancer's influence on AuNPs. Through comparison of Fig. 2b with Fig. 2c, it reveals that the AuNPs were uniformly and dispersedly distributed on the EG and filter paper without the addition of a chemical enhancer. With the addition of the chemical enhancer, there was a significant aggregation phenomenon observed in the nanoparticles. The aggregation of AuNPs creates stable hot spots, which in turn increases the signal enhancement of SERS. Fig. 2d and Fig. 2e display the EDS images of elements, including Au, Mn, O, C, in the substrates with and without the chemical enhancer. The Mn element originates from the KMnO<sub>4</sub> used in the synthesis of EG. The Mn, C and Au elements were evenly dispersed on the filter paper when no chemical enhancer was used. With the introduction of the chemical enhancer, the gold particles experienced a notable degree of aggregation, surpassing that of the Mn and C counterparts. The addition of the chemical enhancer is the key factor influencing the aggregation degree of AuNPs, whereas it has no effect on EG aggregation. Figs. 2f-h illustrate the particle diameter distributions and SEM images of AuNPs, AuNPs/EG and AuNPs/EG with 0.1 M LiCl as the chemical enhancer. The average diameter of AuNPs is 68 nm, as shown in Fig. 2f. When AuNPs are combined with EG, the average diameter reduces to 60 nm and the average diameter of EG is 1318 nm as shown in Fig. 2g. EG does not change the aggregation degree of AuNPs. With the addition of 0.1 M LiCl as the chemical enhancer, the average diameter of AuNPs becomes 122 nm as shown in Fig. 2h. Several AuNPs were aggregated together. The average diameter of EG increases to 1813 nm due to the attachment of AuNPs. The EG aggregation degree is considerably lower than that of AuNPs. SEM images in Figs. 2f-h directly show the enhanced aggregation of AuNPs due to the addition of the chemical enhancer.



**Fig 2** Material characteristics of flexible AuNPs/EG SERS substrates. (a) The fabricating schematic. The SEM images of AuNPs/EG on the flexible substrate (b) without and (c) with chemical enhancer. The EDS images of elements Au, Mn, O, C in flexible substrates (d) without and (e) with chemical enhancer (LiCl). The statistical size distributions and SEM images of (f) AuNPs, (g) AuNPs/EG and (h) AuNPs/EG with 0.1 M LiCl.

# 3.2 Characterizations of flexible AuNPs/EG SERS substrates

To assess the effect of chemical enhancers on SERS detection performance, the sensitivity, uniformity, and reproducibility of flexible AuNPs/EG SERS substrates were investigated. The SERS performance of a substrate is reliant on the augmentation of the local EM near-field of nanostructures. To gain a better understanding of the distribution of "hot spots" on nanoparticle monolayer arrays, numerical simulations of the electromagnetic field between two nanoparticles of different gaps were conducted using Finite Difference Time Domain solutions (FDTD). The separation distance of the interparticle gap was set to 21 nm, and the nanostructure was exposed to incident light in the form of a 633 nm electromagnetic wave with a vertical incidence direction. The

electromagnetic field distributions simulated for the monolayer array of core-shell AuNPs, AuNPs/EG, aggregated AuNPs/EG are compared in Figs. 3a-c. The numerical results demonstrate a significant increase in the electromagnetic near-field within the interstitial region of adjacent nanoparticles. This is attributed to the strong local surface plasmon resonance between them. Fig. 3c indicates that the electromagnetic field is amplified upon the aggregation of AuNPs due to the addition of the chemical enhancer. More "hot spots" are generated from the enhanced aggregation. As shown in Figs. 2b, c and Figs 3a, b, the usage of EG does not result in the aggregation of gold nanoparticles, nor does it influence the amplification of the electromagnetic field among AuNPs. However, the electromagnetic field between the nanoparticles and the substrates is considerably increased, which results in a tighter attachment. The AuNPs aggregation further increases the attachment.

To assess the function of each component in the sandwich substrates, several tests were conducted for the R6G stain to compare and evaluate the SERS performance of different substances. Fig. 3d shows that R6G at concentration of 10<sup>-5</sup> M does not result in a significant SERS signal enhancement on either AuNPs or EG substrates independently. In contrast, a substantial increase in SERS enhancement appears using AuNPs/EG substrates for the R6G stain. This is attributed to the existence of graphene layers in EG's layered structures, providing SERS enhancement through the dual mechanisms of charge transfer and electromagnetic enhancement upon combining with AuNPs. [35,36]

To identify the chemical enhancers that offer the most efficient SERS detection performance, three chemical enhancers, including KCl, NaCl and LiCl, were prepared with concentrations ranging from 0.01 M to 1 M. The spectra in Fig. 3e display the SERS detecting results for R6G at a concentration of 10<sup>-7</sup> M. When the concentration of chemical enhancers exceeds certain thresholds (0.1 M for LiCl and NaCl, and 0.01 M for KCl), crystallization of these chloride salts arises, impeding SERS detection. As shown in Fig. 3e, the type and concentration of chemical enhancers affect the SERS signals. LiCl solution with a concentration of 0.1 M was proven to provide the best SERS enhancement in this work. Fig. 3f presents a histogram exhibiting the highest intensity of the R6G stain at 1362 cm<sup>-1</sup> or 1372 cm<sup>-1</sup> using different substrates. The most robust peaks using the AuNPs/EG substrate were shown with the addition of 0.1 M LiCl solution as a chemical enhancer, which are significantly greater in comparison to those obtained with other substrates.

To study the sensitivity of the flexible AuNPs/EG/filter paper substrate with chemical

enhancer LiCl, SERS detection tests were conducted with R6G solutions of different concentrations. Fig. 3g displays the acquired SERS spectra. Characteristics peaks were identified at R6G concentrations as low as  $10^{-9}$  M. A linear calibration curve correlating between the Raman intensity at 611 cm<sup>-1</sup> and the logarithmic R6G concentration, is shown in Fig. 3g. The correlation coefficient is 0.99, indicating a good correlation. The detection limit was up to  $3.16 \times 10^{-10}$  M, presenting a high sensitivity for the flexible sandwich SERS substrate. Therefore, the flexible sandwich-structured AuNPs/EG/filter paper substrate shows good promise as a high-sensitivity SERS substrate for tracking minute levels of contaminants.

Moreover, stability is an important and critical factor for SERS-based detections in practical applications, as the sensitivity of SERS substrates may degrade with time and temperature change. [32] The thermal stability of this flexible SERS substrate was proven to be good through experiment. In the experiment, the substrate was subjected to thermal treatment in an oven for 30 minutes with increasing temperatures from room temperature (20°C) to 50°C and 80°C before being used to test the R6G solution. As illustrated in Fig. 3h, the flexible AuNPs/EG substrate remained stable, even demonstrated a noticeable improvement at 80°C, which was shown by the intensity histograms at 611 cm<sup>-1</sup> and 1362 cm<sup>-1</sup> in Fig. 3h, depicting the intensities of R6G Raman peaks at three temperature measurements. This enhancement was believed attributed to the good thermal conductivity and chemical stability of EG within the substrate. No significant decrease was observed in the peak intensities using the flexible substrates treated with different temperatures. The time stability of the flexible AuNPs/EG/filter paper substrates were checked at room temperature and air conditions for 30 days. The SERS spectra of R6G stains of 10<sup>-5</sup> M concentration in Fig. 3i were collected by the developed substrates stored after different days. The flexible SERS substrates still provide good SERS signal enhancement after one month, indicating good reproducibility and stability of the substrate for practical applications.



**Fig. 3** Data analysis of flexible AuNPs/EG SERS substrates. Electromagnetic field distribution surrounding AuNPs from FDTD simulations: (a) AuNPs, (b) AuNPs/EG, and (c) Aggregated AuNPs/EG. These were subjected to a 633 nm laser. (d) SERS spectra of 10<sup>-5</sup> M R6G molecules absorbed on AuNPs, EG and AuNPs/EG substrates. (e) SERS spectra of 10<sup>-7</sup> M R6G molecules absorbed on AuNPs/EG substrates using different chemical enhancers. (f) The histogram of the highest intensity of the R6G stain at 1362 cm<sup>-1</sup> or 1372 cm<sup>-1</sup> absorbed on the substrates with different chemical enhancers. (g) SERS spectra collected from R6G at different concentrations absorbed on the flexible AuNPs/EG substrate with 0.1 M LiCl. (h) SERS spectra of R6G absorbed the on AuNPs/EG substrate with 0.1 M LiCl after thermal treatment at 20 °C, 50 °C and 80 °C. (i) SERS spectra of the R6G stain using the substrates freshly fabricated and stored after one day, 7 days, 21 days and 30 days.

#### 3.3 Applications for detecting pesticide residues.

The developed flexible AuNPs/EG/filter paper substrate is of practical application features. As a flexible substrate, the developed sandwich composite material is friendly to store and carry (Fig. 4a.). The most attractive feature is that the flexible substrate is easy to use for detecting various contaminants, such as pesticide and insecticide residues on fruits and vegetables. The residues can be accurately detected via Raman spectroscopy using the flexible substrate to simply wipe the pesticide-containing surface of the fruits and vegetables, as shown in Fig. 4a. Here, three different pesticides

and three different samples were selected for demonstration. Fig. 4b presents the SERS spectra using the flexible substrate to detect Nitrofural in the collected water sample from an artificial lake. Different concentrations of Nitrofural were prepared. Three Nitrofural characteristic peaks, including 777 cm<sup>-1</sup>, 1108 cm<sup>-1</sup>, and 1449 cm<sup>-1</sup>, in SERS spectra were easy to be observed. Taking the characteristic peak of 1108cm<sup>-1</sup> as reference data, the characteristic peak appeared when the Nitrofural concentration was  $6.3 \times 10^{-9}$  M, which increased considerably with the increase of the Nitrofural concentration. The linear calibration curve using the flexible substrate detecting nitrofural is shown in Fig. 4c. A good linear correlation was found between the Raman intensity at 1108 cm<sup>-1</sup> and the logarithm of Nitrofural concentration.

For detecting pesticide Dinotefuran, the contaminant solution was first sprayed onto the cucumber sample, which was wiped in an air-dried state by the flexible substrate. The collected SERS spectra were shown in Fig. 4d. The characteristic peak at 1448cm<sup>-1</sup> appeared when the concentration was  $6.3 \times 10^{-8}$  M which became obvious when the concentration increased into  $3.2 \times 10^{-7}$  M. The linear calibration curve in Fig. 4e showed an excellent correlation between the Raman intensity at 1448cm<sup>-1</sup> and the logarithm of Dinotefuran concentration.

For pesticide Thiram detection, the operation was similar to Dinotefuran. The apple sample was sprayed by the prepared Thiram solutions of different concentrations and wept in an air-dried state by the flexible SERS substate. The detection results were shown in Fig. 4f. The characteristic peak 1381cm<sup>-1</sup> appeared obviously when the concentration was  $4.2 \times 10^{-9}$  M. The linear calibration curve in Fig. 4g also present a good correlation between the Raman intensity at 1381cm<sup>-1</sup> and the logarithm of Thiram concentration.



**Fig 4** Applying the developed SERS substrates to trace pesticide residues. (a) Operation process using the SERS substrates to detect pesticide residues. (b-g) SERS spectra obtained and linear calibrations from the flexible SERS substrate for in-site detection of water from an artificial lake with Nitrofural(b, c), cucumbers with Dinotefuran(d, e) and apples with Thiram (f,g) of different concentration.

#### 4. Conclusion

A high-performance flexible SERS substrate based on the sandwich structure of aggregated AuNPs combined with EG on filter papers is proposed and developed, which is friendly to store, carry and use. Chemical enhancers are adopted to increase the AuNPs aggregation degree for better electromagnetic near-field within the interstitial region of adjacent nanoparticles, which results in more "hot spots" for better SERS performance. 0.1 M LiCl solution is selected as the optimal chemical enhancer for the most outstanding SERS signal enhancement. The developed flexible substrate is proven to possess good stabilities under thermal treatment and excellent reproducibility. The substrate provides excellent SERS signal enhancement even after a thermal treatment under temperature of 80  $^{\circ}$ C and functions well at room temperature after 30 days in the air. The fabricated flexible substrate is applied to detect three

pesticide residues, including Nitrofural in lake water, Dinotefuran on cucumber surface and Thiram on apple surface. The detectable concentrations are lower than the values in governmental standards and good correlations are found between the Raman intensity at characteristics peaks and the logarithm of the concentration of contaminants. The developed flexible AuNPs/EG/filter paper substrate is promising for practical applications.

# Acknowledgement

The work is supported by the Natural Science Foundation of China [grant number 12102376 and 52303092]; and the Guangdong Basic and Applied Basic Research Foundation [grant number 2023A1515011592].

#### **Declaration of interests**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

#### References

- [1] J. Langer, D. Jimenez de Aberasturi, J. Aizpurua, R.A. Alvarez-Puebla, B. Auguié, J.J. Baumberg, G.C. Bazan, S.E.J. Bell, A. Boisen, A.G. Brolo, J. Choo, D. Cialla-May, V. Deckert, L. Fabris, K. Faulds, F.J. García de Abajo, R. Goodacre, D. Graham, A.J. Haes, C.L. Haynes, C. Huck, T. Itoh, M. Käll, J. Kneipp, N.A. Kotov, H. Kuang, E.C. Le Ru, H.K. Lee, J.-F. Li, X.Y. Ling, S.A. Maier, T. Mayerhöfer, M. Moskovits, K. Murakoshi, J.-M. Nam, S. Nie, Y. Ozaki, I. Pastoriza-Santos, J. Perez-Juste, J. Popp, A. Pucci, S. Reich, B. Ren, G.C. Schatz, T. Shegai, S. Schlücker, L.-L. Tay, K.G. Thomas, Z.-Q. Tian, R.P. Van Duyne, T. Vo-Dinh, Y. Wang, K.A. Willets, C. Xu, H. Xu, Y. Xu, Y.S. Yamamoto, B. Zhao, L.M. Liz-Marzán, Present and Future of Surface-Enhanced Raman Scattering, ACS Nano 14 (1) (2020) 28–117. https://doi.org/10.1021/acsnano.9b04224.
- [2] A. Shumskaya, E. Kozhina, S. Bedin, S. Andreev, E. Kulesh, A. Rogachev, M. Yarmolenko, I. Korolkov, A. Kozlovskiy, M. Zdorovets, V. Belyaev, V. Rodionova, L. Panina, Detection of polynitro compounds at low concentrations by sers using Ni@Au Nanotubes, Chemosensors 10 (8) (2022) 306. https://doi.org/10.3390/chemosensors10080306.
- [3] N. Chauhan, K. Saxena, R. Rawal, L. Yadav, U. Jain, Advances in surfaceenhanced Raman spectroscopy-based sensors for detection of various biomarkers, Progress in Biophysics and Molecular Biology 184 (2023) 32–41. https://doi.org/10.1016/j.pbiomolbio.2023.08.003.
- [4] M. Haroon, M. Tahir, H. Nawaz, M.I. Majeed, A.A. Al-Saadi, Surface-enhanced Raman scattering (SERS) spectroscopy for prostate cancer diagnosis: A review, Photodiagnosis and Photodynamic Therapy 37 (2022) 102690.

https://doi.org/10.1016/j.pdpdt.2021.102690.

- [5] H. Chen, A. Das, L. Bi, N. Choi, J. Il Moon, Y. Wu, S. Park, J. Choo, Recent advances in surface-enhanced Raman scattering-based microdevices for point-ofcare diagnosis of viruses and bacteria, Nanoscale 12 (42) (2020) 21560–21570. https://doi.org/10.1039/d0nr06340a.
- [6] L. Jiang, M.M. Hassan, S. Ali, H. Li, R. Sheng, Q. Chen, Evolving trends in SERSbased techniques for food quality and safety: A review, Trends in Food Science & Technology 112 (2021) 225–240. https://doi.org/10.1016/j.tifs.2021.04.006.
- B. Hu, H. Pu, D.W. Sun, Multifunctional cellulose based substrates for SERS smart sensing: Principles, applications and emerging trends for food safety detection, Trends in Food Science & Technology 110 (2021) 304–320. https://doi.org/10.1016/j.tifs.2021.02.005.
- [8] L. Zhou, J. Yang, X. Wang, G. Song, F. Lu, L. You, J. Li, Ag nanoparticles decorated Ag@ZrO<sub>2</sub> composite nanospheres as highly active SERS substrates for quantitative detection of hexavalent chromium in waste water, Journal of Molecular Liquids 319 (2020) 114158. https://doi.org/10.1016/j.molliq.2020.114158.
- [9] R. Gaur, P. Manikandan, D. Manikandan, S. Umapathy, H.M. Padhy, M. Maaza, M. Elayaperumal, Noble metal ion embedded nanocomposite glass materials for optical functionality of UV-visible surface plasmon resonance (SPR) surfaceenhanced Raman scattering (SERS) X-ray and Electron Microscopic Studies: An Overview, Plasmonics 16 (2021) 1461–1493. https://doi.org/10.1007/s11468-021-01413-w.
- [10] Y. Mao, B. Yu, H. Zhang, Y. Ma, F. Han, B. Zhou, L. Yang, Z. Han, Surfactantfree preparation expanded graphite coupled with Ag nanoparticles as SERS high sensor via optimizing electromagnetic enhancement and adsorption behavior, Applied Surface Science 592 (2022) 153264. https://doi.org/10.1016/j.apsusc.2022.153264.
- [11] Y. Zhan, G. Zhang, J. Shen, B. Zhou, C. Zhao, J. Guo, M. Wen, Z. Tan, L. Zheng, J. Lu, Y.Y. Li, Facile electrochemical surface-alloying and etching of Au wires to enable high-performance substrates for surface enhanced Raman scattering, Nano Materials Science (2023). https://doi.org/10.1016/j.nanoms.2023.05.002.
- [12] W. Li, X. Lu, R. Yang, F. Liang, W. Chen, Z. Xie, J. Zheng, J. Zhu, Y. Huang, W. Yue, L. Li, Y. Su, Highly sensitive and reproducible SERS substrates with binary colloidal crystals (bCCs) based on MIM structures, Applied Surface Science 597 (2022) 153654. https://doi.org/10.1016/j.apsusc.2022.153654.
- [13] Y. Liu, B. Zhou, W. Wang, J. Shen, W. Kou, Z. Li, D. Zhang, L. Guo, C. Lau, J. Lu, Insertable, Scabbarded, and Nanoetched Silver Needle Sensor for Hazardous Element Depth Profiling by Laser-Induced Breakdown Spectroscopy, ACS Sensors 7 (5) (2022) 1381–1389.
- [14] C.Y. Yu, D.Y. Lin, C.K. Chung, Novel dipole-enhancement mechanism and detection of high-sensitivity trace environmental hormone bisphenol A with LiCl as co-adsorbates using simple metal-nanoparticle-free solid SERS substrates, Sensors and Actuators B: Chemical 398 (2024) 134735.

https://doi.org/10.1016/j.snb.2023.134735.

- [15] B. Yu, C. Cao, P. Li, M. Mao, Q. Xie, L. Yang, Sensitive and simple determination of zwitterionic morphine in human urine based on liquid-liquid micro-extraction coupled with surface-enhanced Raman spectroscopy, Talanta 186 (2018) 427–432. https://doi.org/10.1016/j.talanta.2018.04.094.
- [16]L. Tay, S. Poirier, A. Ghaemi, J. Hulse, S. Wang, Paper-based surface-enhanced Raman spectroscopy sensors for field applications, Journal of Raman Spectroscopy 52 (2) (2021) 563–572. https://doi.org/10.1002/jrs.6017.
- [17] C. Wang, B. Liu, X. Dou, Silver nanotriangles-loaded filter paper for ultrasensitive SERS detection application benefited by interspacing of sharp edges, Sensors and Actuators B: Chemical 231 (2016) 357–364. https://doi.org/10.1016/j.snb.2016.03.030.
- [18] T.N. Quynh Trang, N.T. Phuong Trinh, N.T. Gia Bao, V.T.H. Thu, Hotspot-type silver-polymers grafted nanocellulose paper with analyte enrichment as flexible plasmonic sensors for highly sensitive SERS sensing, Journal of Science: Advanced Materials and Devices 8 (2023) 100597. https://doi.org/10.1016/j.jsamd.2023.100597.
- [19]K. Wang, D.W. Sun, H. Pu, Q. Wei, L. Huang, Stable, Flexible, and High-Performance SERS Chip Enabled by a Ternary Film-Packaged Plasmonic Nanoparticle Array, ACS Applied Materials & Interfaces 11 (32) (2019) 29177–29186. https://doi.org/10.1021/acsami.9b09746.
- [20] N. Chamuah, N. Bhuyan, P.P. Das, N. Ojah, A.J. Choudhary, T. Medhi, P. Nath, Gold-coated electrospun PVA nanofibers as SERS substrate for detection of pesticides, Sensors and Actuators B: Chemical 273 (2018) 710–717. https://doi.org/10.1016/j.snb.2018.06.079.
- [21] J. Jiang, S. Zou, L. Ma, S. Wang, J. Liao, Z. Zhang, Surface-Enhanced Raman Scattering Detection of Pesticide Residues Using Transparent Adhesive Tapes and Coated Silver Nanorods, ACS Applied Materials & Interfaces 10 (10) (2018) 9129–9135. https://doi.org/10.1021/acsami.7b18039.
- [22] H.G. Lee, W. Choi, S.Y. Yang, D.H. Kim, S.G. Park, M.Y. Lee, H.S. Jung, PCR-coupled Paper-based Surface-enhanced Raman Scattering (SERS) Sensor for Rapid and Sensitive Detection of Respiratory Bacterial DNA, Sensors and Actuators B: Chemical 326 (2021) 128802. https://doi.org/10.1016/j.snb.2020.128802.
- [23] S. Liu, X. Tian, J. Guo, X. Kong, L. Xu, Q. Yu, A.X. Wang, Multi-functional plasmonic fabrics: A flexible SERS substrate and anti-counterfeiting security labels with tunable encoding information, Applied Surface Science 567 (2021) 150861. https://doi.org/10.1016/j.apsusc.2021.150861.
- [24] H. Zhang, N. Zhao, H. Li, M. Wang, X. Hao, M. Sun, X. Li, Z. Yang, H. Yu, C. Tian, C. Wang, 3D Flexible SERS Substrates Integrated with a Portable Raman Analyzer and Wireless Communication for Point-of-Care Application, ACS Applied Materials & Interfaces 14 (45) (2022) 51253–51264. https://doi.org/10.1021/acsami.2c12201.
- [25] T. Gong, H. Li, G. Wang, F. Guan, W. Huang, X. Zhang, An anti-scratch flexible

SERS substrate for pesticide residue detection on the surface of fruits and vegetables, Nanotechnology 33 (40) (2022) 405501. https://doi.org/10.1088/1361-6528/ac7cf3.

- [26] T. Xie, Z. Cao, Y. Li, Z. Li, F.-L. Zhang, Y. Gu, C. Han, G. Yang, L. Qu, Highly sensitive SERS substrates with multi-hot spots for on-site detection of pesticide residues, Food Chemistry 381 (2022) 132208. https://doi.org/10.1016/j.foodchem.2022.132208.
- [27] Alewu B., Nosiri C., Pesticides and human health, in: Dr. Margarita Stoytcheva (Eds.), Pesticides in the modern world–effects of pesticides exposure, InTech ,2011, pp. 231-250.
- [28]L. Rani, K. Thapa, N. Kanojia, N. Sharma, S. Singh, A.S. Grewal, A.L. Srivastav, J. Kaushal, An extensive review on the consequences of chemical pesticides on human health and environment, Journal of Cleaner Production 283 (2021) 124657. https://doi.org/10.1016/j.jclepro.2020.124657.
- [29] R. Zamora-Sequeira, R. Starbird-Pérez, O. Rojas-Carillo, S. Vargas-Villalobos, What are the main sensor methods for quantifying pesticides in agricultural activities? A review, Molecules 24 (14) (2019) 2659. https://doi.org/10.3390/molecules24142659.
- [30] K. Liu, Y. Li, M. Iqbal, Z. Tang, H. Zhang, Thiram exposure in environment: A critical review on cytotoxicity, Chemosphere 295 (2022) 133928. https://doi.org/10.1016/j.chemosphere.2022.133928.
- [31] Y. Zhu, M. Li, D. Yu, L. Yang, A novel paper rag as 'D-SERS' substrate for detection of pesticide residues at various peels, Talanta 128 (2014) 117–124. https://doi.org/10.1016/j.talanta.2014.04.066.
- [32] Y. Ma, Y. Wang, Y. Luo, H. Duan, D. Li, E. Kouadio, Rapid and sensitive on-site detection of pesticide residues in fruits and vegetables using screen- printed paperbased SERS swabs, Analytical Methods 10 (38) (2018) 4655–4664. https://doi.org/10.1039/c8ay01698d.
- [33] M.S.S. Bharati, V.R. Soma, Flexible SERS substrates for hazardous materials detection: recent advances, Opto-Electronic Advances 4 (2021) 210048. https://doi.org/10.29026/oea.2021.210048.
- [34]G. Frens, Controlled Nucleation for the Regulation of the Particle Size in Monodisperse Gold Suspensions, Nature Physical Science 241 (1973) 20–22. https://doi.org/10.1038/physci241020a0.
- [35]F.L. Article, Three dimensional porous Expanded Graphite/Silver Nanoparticles nanocomposite platform as a SERS substrate, Applied Surface Science 568 (2021) 150946. https://doi.org/10.1016/j.apsusc.2021.150946.
- [36] X. Ling, L. Xie, Y. Fang, H. Xu, H. Zhang, J. Kong, M.S. Dresselhaus, J. Zhang,
  Z. Liu, Can Graphene be used as a Substrate for Raman Enhancement?, Nano Letter 10 (2) (2010) 553–561. https://doi.org/10.1021/nl903414x.