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Precision Target Guide Strategy for Applying SERS into Environmental Monitoring

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Abstract

Surface enhanced Raman spectroscopy (SERS) is a promising analytical technique that exhibits various applications in trace detection and identification. When it is applied into environmental monitoring, we should concern several key points to improve detection sensitivity and selectivity for the detection in complex matrix. In this tutorial review, we mainly focus on the strategies for improving the use of SERS into environmental application. The strategies are summarized for enhancing the ability of the substrate to selectively capture specific targets, and for achieving separation and concentration of the analytes from the matrix and the assembly structures for multiple phase detection. We have also introduced several newly developed detection systems using portable instruments and miniaturized devices that are more suitable for infield applications. In addition, we discuss the present challenges that hide it from wide real application and give the outlook for the future development in applying SERS in environmental monitoring.

Keywords: SERS, environmental monitoring, pollutant, target capture, concentration, separation, infield detection

1. Introduction

Tremendous achievements have been made in industrial, agricultural and medical fields in the last several decades, which also led much pressure on our living environment. The uncontrollable releasing of various toxic and potentially harmful chemicals and/or biological products into the environment results in serious damages to ourselves. The pollution in water, soil and air is becoming main threat to ecosystem and health, and the pollutants include inorganic gases, irons, pathogenic organisms and organic pollutants such as persistent organic pollutants (POPs),

antibiotics and pesticides [1, 2]. It is urgent to develop rapid and sensitive strategy to classify, quantify and assess them from the environment, which is the basic information to early warning for their threats and getting the precondition for solving these problems. Environmental monitoring requires the analysis of pollutants at (very) low concentrations since many of the pollutants have serious consequence at even extremely low levels. In addition, the methods to be used should also be simple and rapid for their operations in the real application.

Different techniques including chromatography, spectroscopy, mass-spectra methods are well established in environmental analysis [3–5], but most of these methods require sophisticated instruments and some of them are lack of sufficiently recognition capacity, which limit their wide applications for infield application. Recently, advanced nanomaterial-based methods have contributed a lot to this area, such as microfluidics, electrochemical sensor, surface plasmon resonance (SPR) method, single-molecule spectroscopy and hyperspectroscopy [6–8]. Among these methods, surface-enhanced Raman spectroscopy (SERS) is one of the most promising methods for environmental monitoring. As a molecular vibrational spectroscopy, SERS holds several outstanding advantages compared to the traditional techniques. Firstly, by making use of the SPR-induced strong electromagnetic field to enhance signals of the analytes, SERS has high sensitivity which enables detection at low concentrations, even as low as to single molecule level [9]. Secondly, the obtained Raman spectra contains abundant molecular information of the analytes, and the finger-print information is valuable for identification and classification [10]. Thirdly, the Raman character peaks have very narrow width, which enables multiple detection or complex identification. Unlike other vibrational spectroscopy such as infrared spectroscopy, SERS can be applied directly in solution since water has little background signal. SERS technique is also compatible with different sample conditions including aqueous, solidary and even gaseous state, and it needs less sample preparation and preoperation. This technique can get the character signal within seconds to minutes, which is suitable for rapid signal readout. SERS is also very convenient and cost-effective to be combined with miniaturized Raman spectrometers and offers good practical utility for real application, even for infield detection.

The above-mentioned remarkable advantages have led many significant achievements of SERS in the environmental detection [11]. Recently, several review articles have covered different considerations, such as facing various targets such as organics, [12] ions [13] or pathogens [14]. Considering the real condition when performing SERS in environmental application, we believe that special attention should be paid to the following aspect in order to fully realize the potential of SERS method. (1) SERS phenomenon only takes effect when the analyte is near the surface of the SERS substrate, which usually needs to be within several nanometers [15]. While for most of the environmental targets, their interaction with the bare substrate is not strong enough to get them close to the substrate; thus, it is important to shorten the distance between them. (2) The matrix of the environmental samples is complex, which will interrupt the effective interaction between the substrate and the analytes, and hence, the proposed method should have specific selectivity to the interested targets. (3) In many cases, the proposed method should have the ability to concentrate the target in order to meet the demands of sensitivity. (4) For most of infield detections, a strategy is required to be compatible

with portable instruments (or miniaturized devices). In this chapter, therefore, we mainly focus on the recent achievements with the goal of developing target-specific SERS-based methods for pollutant detection, the strategies for realizing selective target capture, concentration and separation. We also summarize detection systems that are compatible with specific complex matrix and newly proposed devices suitable for infield application. This review further covers the current challenge and future prospect for better application of SERS in environmental protection.

2. Strategies for selective target capture

The SERS effect is known to be a localized first-layer effect. The observed enhanced Raman signal comes from the analytes close to the metallic structures with a distance no longer than 5 nm, and the signal intensity exponentially decreases with increasing the distance [15]. The analytes may be divided into two groups. In the first group, the analytes have strong affinity to the bare surface of metallic structures due to their functional groups such as amino ($-\text{NH}_2$) and thiol ($-\text{SH}$) groups. These analytes are easily absorbed on the substrate, and their SERS responses are obtained directly if they are SERS active. As the second group of analytes, most of which are pollutants to be concerned, they have no strong affinity to the unmodified substrate, and hence, the distance between the analyte and the SERS substrate is too large to producing enough SERS-enhancing effect. Therefore, it is important to functionalize the surface of the substrate to capture such weakly affinitive targets. In addition, it should be noted that many SERS substrates are made with wet chemical synthesis methods. These wet chemically synthesized SERS substrates usually contain one or more surfactants and/or other organic species being used as the shape control reagents and/or reducing agents during the synthesis. The presence of these species may hinder the effective contact of analytes with the substrate surface, and hence, surface replacement of these capping species is needed to avoid the interference and further enhance the capture capacity of the substrate for the specific targets. Concerning targets with weak Raman response, surface functionalization can be used to increase the sensitivity by producing special interaction or generating specific complexes between analytes and modified molecules which could be used for the indirect detection [16, 17]. The detailed measures may aim at one or more of the following five types of interaction enhancement.

2.1. Electrostatic or hydrophobic interaction

Different function structures or molecules are used to enrich targets from the matrix, one of the functions is to modify the SERS substrate surface with improved electrostatic or hydrophobic interactions. For example, in most common colloidal systems (such as citrate reduced Ag or Au NPs), the substrate surface is negatively charged. To enhance the attractive interaction between the particle surface and the negatively charged target molecules, a substrate with controllable surface charge is favorable. By employing aliphatic amino acids as reductant and modifier, controllable surface charge range from -60 to $+30$ mV was obtained, which is favorable to smaller electrostatic repulsion and even attraction to increase analyte retention

[18]. Besides, the SERS substrate are often hydrophilic, but various toxic organic pollutants bearing aromatic structures are highly hydrophobic. Polycyclic aromatic hydrocarbons (PAHs) are a family of these pollutants, which consist of fused aromatic rings and contain no substituent that can absorb to the hydrophilic surface. The affinity between such hydrophobic analytes and the hydrophilic substrate may be enhanced by making use of the hydrophobic interaction. For example, Jing et al. reported thiol-functionalized magnetic nanoparticles (NPs) for the SERS detection of eight kinds of PAHs including benzene and naphthalene with limits of detection (LODs) down to 10^{-7} mol L⁻¹ [19]. Similarly, alkyl dithiol was modified onto the metal particles to enhance the affinity of pesticides to the substrate, and this greatly promoted adsorption constant and led to the LOD down 10^{-8} mol L⁻¹, proving a solid basis for identification and quantitative analysis of organochlorine pesticides [20]. For the detection of aromatic organics, π - π stacking could also be used, where the modifying molecules could be aromatic molecules and also special materials like graphene or carbon nitride with absorption ability [21, 22]. The capture strategies by making use of electrostatic or hydrophobic interaction could effectively enhance the detection activity to targets, but the selectivity is still weak due to the low selectivity of these interactions.

2.2. Forming surface complex

Surface modification with molecules that can selectively bond to the target by forming a complex is an effective method to enable selective detection. For example, mercury ion (Hg(II)) is one of the most toxic pollutants with bioaccumulative activity. It holds weak SERS response and weak interaction to the common SERS substrate, and thus, it is difficult to be detected by SERS directly. By modifying the gold nanomaterials with tryptophan (a SERS-active molecule that can interact with Hg(II) to form a complex with a weak SERS response), an easy and highly selective method was proposed to recognize Hg(II) with the LOD down to 5 ppb level [23]. By making use of the specific interaction between Hg(II) and single-stranded DNA to convert into a hairpin structure through forming of thymine–Hg(II)–thymine complex, Hg(II) ions at concentrations as low as to 0.2 ppt (1p mol L⁻¹) were readily discriminated, being much lower than conventional analytical methods (usually nanomolar level) [24]. Due to the high binding specificity of DNzyme to Pb²⁺ ions, a SERS DNzyme biosensor was developed to detection of Pb²⁺, such detection was further accomplished by SERS nanoprobe labeled with both DNA and Raman probe for signal amplification [25]. Another example of making use of the surface complex is the SERS detection of trinitrotoluene (TNT) with cysteine. Cysteine-modified gold nanoparticles (NPs) could selectively recognize of TNT molecules due to the formation of Meisenheimer complex, which underwent aggregation via electrostatic interaction to form hot spots and further enhanced the Raman signal of the complex by nine orders. High sensitivity (low to 2 pico molar level) and selectivity were observed for the detection of TNT without dye tagging [26]. Similarly, the surface-modified gold NPs with (aminomethyl)phosphoric acid were synthesized to selectively capture uranium(U) ions by making use of its phosphonic tails as terminal group. Without any pretreatment, the proposed method was performed directly for detection of uranium in contaminated water even under low pH and high salts conditions [27].

2.3. Host–guest interaction

The above-mentioned strategies for detection of targets by forming surface complex can greatly increase the sensitivity and selectivity, and the key point is to find a specific interaction between the analyte and the modifier; such analyte–receptor systems are not limited to the complex formation, but also many other interactions, such as host–guest interaction, molecular imprinting (MIP) recognition and antibody–antigen interaction. These interactions all have been successfully applied into promoting the selectivity of SERS-based method into specific target monitoring [28–31].

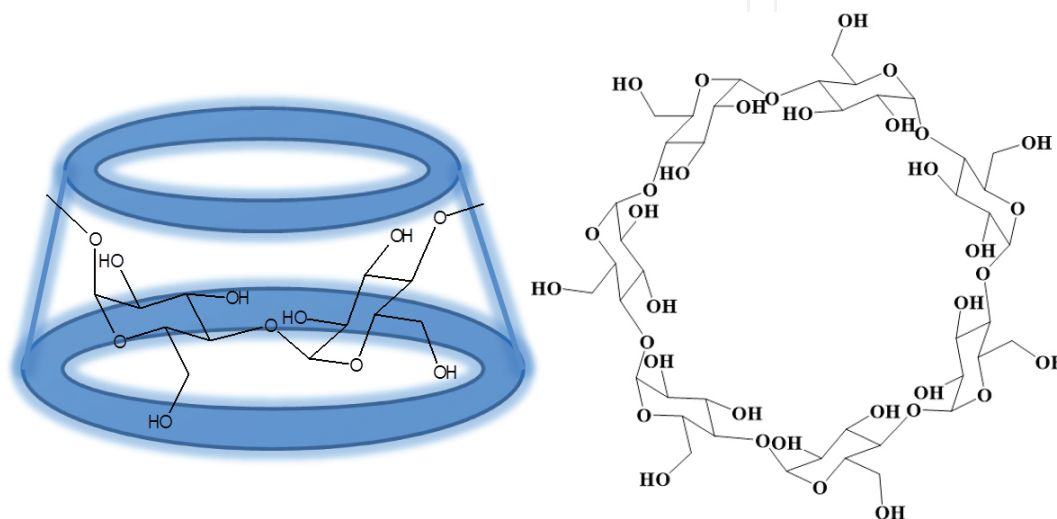


Figure 1. Molecular structure of β -CD.

Host–guest interaction is an important phenomenon in supramolecular chemistry, which describes the special interaction between the host molecules with unique structure and the guest smaller molecules or ions. It encompasses the idea of molecular recognition and interaction through noncovalent bonding (such as hydrogen bonds, ionic binds, van der Waals forces and hydrophobic interactions) [32]. It has been widely used in the drug delivery, the removal of hazardous materials from the environment and for sensing called indicator–spacer–receptor approach [33]. It also can be used for the SERS detection of the specific guest molecules by making use of the host structures as a modifier. Several typical host molecules have been applied as functional modifiers, such as viologen host lucigenin for the selective detection of PAHs or pesticides [34–36], dithiocarbamate calix [4] arene derivatives for the capture and detection of organic pollutants such as pyrene and PAHs [28, 37], and cucurbit[n]uril for the SERS monitoring of diaminostilbene [38]. Cyclodextrins (CDs) are another class of host molecules in supramolecular chemistry, and they have cyclic oligosaccharide structures with hydrophobic internal cavities which can selectively capture suitable nanosized guest molecules [39]. The most widely used cyclodextrin is β -cyclodextrin (β -CD) with seven glucose units, which is a natural product of specific bacteria. As shown in **Figure 1**, the cavity diameter is 6.4 Å, which contributes to the interaction with guest molecules [39].

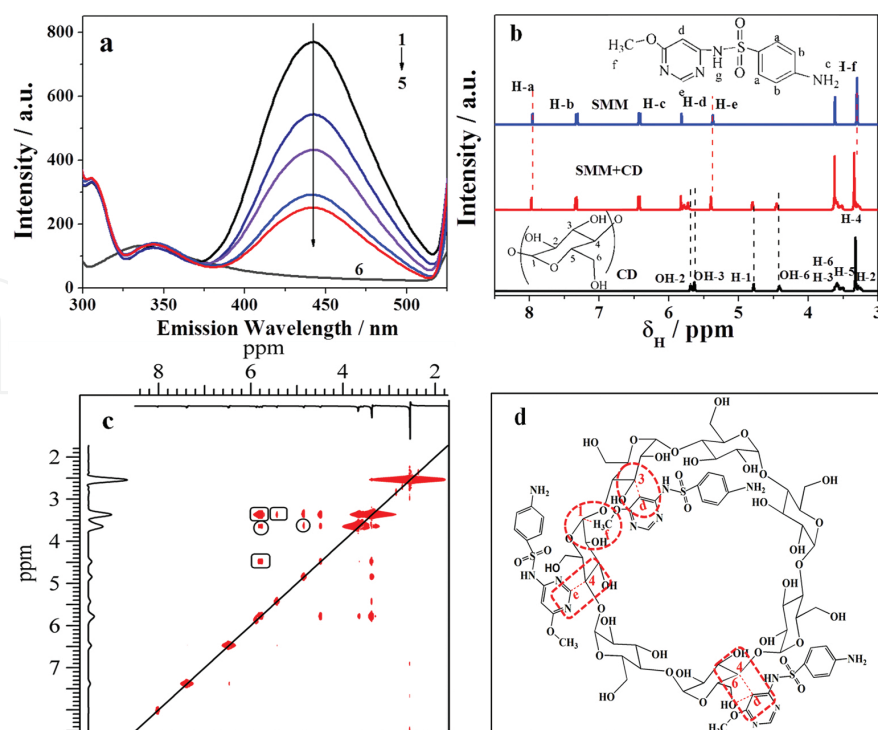


Figure 2. Molecular interaction between SMM and CD. Reproduced with permission from Ref. [45].

As a functional modifier, β -CD has been used for the SERS detection of both organic pollutants and inorganic ions, such as polychlorinated biphenyls (PCB-77, PCB-1) down to $3 \mu\text{M}$, [40] methyl parathion at picomolar level, [41] PAHs (anthracene, pyrene or anthracene) [39, 42] and micromolar Pb^{2+} ions [29]. In most of the reported works, thio-modified β -CD (such as per-6-deoxy-(6-thio)- β -CD) was used because of the weak modifying efficiency of natural β -CD onto the surface of the metal structure. In our earlier work, we proposed an in situ reduction strategy to synthesize β -CD modified Ag nanoparticles by making use of the reducing activity of the natural β -CD under heat and alkaline condition [43, 44]. The obtained substrate was successfully applied to detection of sulfonamide antibiotics with the LOD as low as 10 ng mL^{-1} [45]. Our results showed that by employing β -CD as both reductant and shape-controlling agent, the β -CD-modified Ag NPs could be easily obtained with controllable size and distribution, and much enhanced detection ability was observed with enhancement factor (EF factor) up to 1.97×10^6 . The mechanism for the promoted recognition ability was further studied by fluorescence and ^1H NMR methods. As shown in **Figure 2a**, the character fluorescence emission at 445 nm of sulfamonomethoxine (SMM) solution was significantly decreased with the addition of β -CD, and such a quenching effect suggests a considerably strong interaction between SMM and β -CD. More detailed information for the interaction from the molecular level was obtained from NMR analysis. **Figure 2b** shows the ^1H NMR spectra of SMM, β -CD and SMM- β -CD complex. After assigning the character chemical shift to each proton, obvious shift of several protons was observed, such as H-a, H-e and H-f of SMM by 0.01–0.03 ppm, and H-1, H-4, OH-2, OH-3 and OH-6 protons by 0.01–0.10 ppm. In order to get insight into the exact interaction sites, we further performed the 2D NMR characterization which could not

only give the chemical shifts similar to ^1H NMR, but also reveals the correlation between the interacted protons. The obtained 2D NOESY NMR spectra of the SMM- β -CD complex are shown in **Figure 2c**. As indicated in the spectra, these cross-peaks indicate a close interaction of β -CD with SMM, since such cross-peaks could only be observed when the distance of relative molecules is shorter than 0.5 nm, such as H-3 with H-d, H-1 with H-f, these cross-peaks comes from the protons of SMM and interior cavity of β -CD, as marked by elliptic circles. Besides that, cross-peak from the SMM with the outside face of β -CD cavity was also obtained, as marked by rectangles in **Figure 2c**. These results provide us the interaction pattern of β -CD with SMM: It could not only set SMM into its cavity by host-guest interaction, but it also acts as a scaffold or a bridge to pull the SMM close to the out-surface of the cavity which yield greatly enhanced activity in SERS detection of SMM. The strategy of using native β -CD as scaffold for analytes with low affinity to the substrate shows wide application prospect in selectively capture and sense other concerning pollutants.

2.4. Antibody-antigen interaction

Antibody-antigen interaction is the most specific and useful recognition interaction that has been widely used in clinical diagnose. The highly specific binding is due to the specific chemical constitution of each antibody. The antigenic determinant or epitope is recognized by the paratope of antibody, situated at variable regions of polypeptide chain which also has unique hypervariable regions in each antibody [46]. The strategy of using antibody as modifier for selective SERS detection of antigens is commonly applied in the biological detection and imaging, and also for environmental monitoring, and it is widely used for the detection of pathogen organisms with both label and label-free methods [47, 48]. There are several reviews that summarized the achievement of such strategy in the pathogen detection [49–51]. Beside the common antibody modification, other interactions that base on immunological recognition has also been applied into the detection of specific pollutants recently. For example, aptamer is made of single-stranded DNA oligomer that can be selected against specific target (biological macromolecule or small organic molecule) come from systematic evolution of ligands by exponential enrichment (SELEX) [31]. On the basis of capture and enrichment by the PCB-77 specific aptamer, the improved detection of PCB77 was accomplished with a LOD down to $1 \times 10^{-8} \text{ mol L}^{-1}$ [52]. The aptamer-based strategy was used to detect bisphenol A, one of the most important endocrine disrupting chemicals, with a LOD as low as 3.9 pg/mL with excellent recovery for real sample detection [53]. Aptamer-based SERS sensor has also been developed for the selective detection of Hg^{2+} by employing the structure-switching aptamer in the presence of spermine [54]. These antibody, aptamer or other recognition structures such as phage that making use of the immunological reaction have the advantage of high selectivity, but also have some limitations that need further study, due to their low stability under harsh conditions.

2.5. Artificial antibody-antigen interaction (molecular imprinting effect)

Molecular imprinting (MIP) is a powerful technique to create specific recognition site in polymer by employing target molecules or molecules with similar structures as templates. The

recognition cavities after removing the templates provide the capability and functionality to selectively rebind specific targets without interference from other molecules. The surface MIP technique has been used for selective detection and removing of organic pollutants from the complex matrix [30, 55]. Such a strategy could be performed to functionalize the surface of the substrate to promote the recognition ability of the SERS method. Zhang et al. proposed a ligand replacement approach to rapid determination of penicilloic acid in the penicillin by using a molecularly imprinted monolayer as recognition surface, which efficiently excluded the interference of penicillin and provided a selective determination down to 0.1‰ (w/w) [56]. Similarly, thiol-terminated MIP microspheres which have been immobilized on a gold-coated substrate were used for the selective capture of nicotine, showing good capture efficiency and SERS response [57]. In considering of using MIPs techniques for selective SERS detection, two key points should be kept in mind. The first is that the imprinted layer should be thin thick because a thick layer will interfere the enhancement from the under layer metal structure. The second is that the polymer film should have clear background signal to prevent any interference to the detection of target molecules.

3. Strategies for target concentration and separation

In order to get satisfactory result, the strategy for target concentration and separation after selectively capture is also important. In various environmental cases, the concentrations of the interested targets are usually rather low and the matrix is complex. Therefore, preconcentrating the targets is required to increase the sensitivity. The combination of SERS-active structures with magnetic materials is an effective method to endow the substrate with facile recycle property, many different magnetic structures were applied into the SERS detection of pollutant, the improved ability of recycle and separation benefits a lot to the fast and convenient observation [17, 48, 58, 59]. In addition to the magnetic field-assisted separation strategy, some other techniques were also performed for effectively separating the substrates captured with targets from the matrix, by using such as a membrane filter, [60] filter paper [61] and even commercial tap-based substrates [61]. Besides the mentioned traditional methods for sample concentration and separation, there are several other typical strategies that have been applied effectively, such as electrochemical concentration, hydrophobic concentration, paper-based substrate for separation and hydrogel-based structure for target gathering. The integrated SERS detecting, preconcentrating and separating make the whole SERS method have the promoted ability for fast and facile application.

3.1. Electrochemical and hydrophobic concentration

Electrochemical techniques such as electrostatic concentration offer a reliable and convenient way of concentration target from the matrix. It is an effective way to draw charged analytes toward the substrates through electrostatic forces and hence increase the concentration of the analytes to the required levels. Dan et al. proposed silver-electrode-positing screen-printed electrodes for concentrating aniline and phenol derivatives (as shown in **Figure 3a**, and realized both the qualification and quantification of these pollutants in the concentration range

of 1 nM–1 μ M [62]. Li and co-workers reported a disposable Ag-graphene sensor for concentrating antibiotics, and found that under optimized conditions (applied potential and preconcentration time), their proposed SERS detection method displayed a significant performance for rapid and sensitive analysis of low concentration polar antibiotics without prepreparation step [63]. Another promising way is to use superhydrophobic surfaces to concentrate the analytes. For commonly used hydrophilic surface, the samples randomly spread over the substrate when they are dipped, but the surface with superhydrophobic activity can overcome the “diffusion limit” of analytes in highly diluted aqueous solutions by concentrating analytes into a small area arising from the small superhydrophobic substrate–water interface, thereby further improving SERS detection sensitivity (typical illustration of such phenomenon is shown in **Figure 3b**). Xu et al. fabricated a superhydrophobic Ag-coated ZnO array SERS platform for the highly diluted and small volume target detection [64]. This emphasized the synergistic effect of both intense electromagnetic field and superhydrophobic surface with target concentrating effect, which were also used for the ultrasensitive trace detection of rhodamine 6G with a LOD as low as to 10^{-16} M by employing superhydrophobic Ag nanocubes as substrate [65]. Recently, a universal SERS substrate called “slippery liquid-infused porous substrate” that enables the enrichment and delivery of targets originating from various phases into the SERS-active sites was proposed with using superhydrophobic surface. By the aid of this universal substrate, the detection of various chemicals, biologicals and environmental contaminates was obtained with sensitivity down to subfemtomolar level [66].

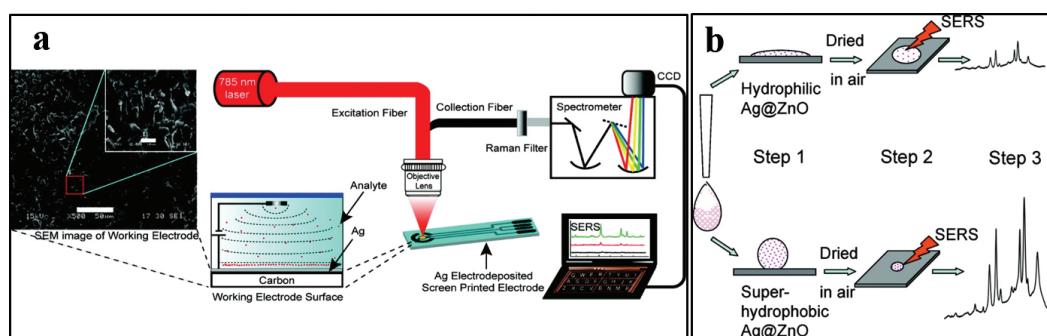


Figure 3. (a) Schematic representation of the portable SERS sensor used for detection of polar molecules in solution with the contribution from electronic concentration. Reproduced with the permission from Ref. [62]. (b) Principle of Superhydrophobic condensation for amplifying SERS Signal. Reproduced with the permission from Ref. [64].

3.2. Paper-based substrate for both concentrating and separating

Paper has been widely used as a flexible supporting material in electronic devices and also in the SERS substrate. There is growing interest in fabricating of low-cost flexible substrates by making use of cellulose paper impregnated with SERS-active structures for SERS application [67]. Besides the advantages of flexible and low cost, paper-based substrates also hold the ability for concentrating and separating analytes, which is rather useful for environmental application. For example, a starlike shape paper-based SERS device was fabricated for the subattomolar detection [68]. The complex samples are separated by a surface chemical gradient

created by polyelectrolyte coated paper, and the designed starlike shape generates a rapid capillary driven flow capable of dragging targets and SERS-active nanoparticles into a single cellulose microfiber, providing an concentrated and optically active observation spot. An important but often overlooked consideration for the developed substrates for real application is the efficiency of the target collection. Conventional designs based on rigid materials such as silicon and alumina resist effective contact to the interested surface, leading to inefficient target collection. However, the paper-based structure is flexible and allows conformal contact to real-world surfaces, which dramatically enhances the sample collection efficiency. The successfully detection of trace analytes (140 pg spread over 4 cm²) was realized by simply swabbing the surface with the paper-based substrate [69]. The hierarchical structure of the paper contributes to easy uptake and concentration the target into the SERS hot spots and leads to excellent performance. Similarly, Ag NPs-decorated filter paper was synthesized as a “dynamic SERS” substrate for the rapid and accurate identification of pesticide residues at various peels [70].

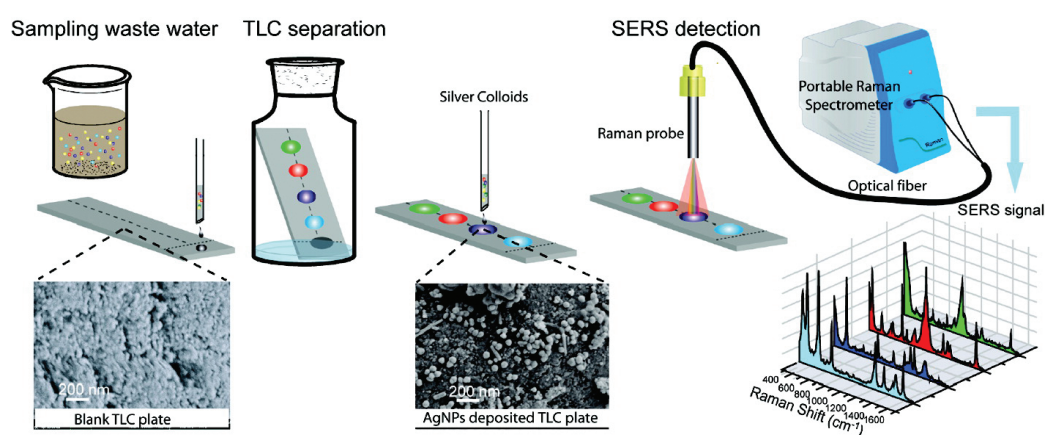


Figure 4. Schematic illustration of TLC-SERS for on-site detection of substitute aromatic pollutants in waste water. Reproduced with the permission from Ref. [77].

By using the separation ability of paper-based strip, the paper-based substrate is possibly applied for trace detection from the complex sample containing multiple components. Lateral flow assay (LFA) strip biosensor has been extensively used in point-of-care (POC) test, infectious disease diagnosis and field detection for hazardous materials in environmental samples [71]. In a typical detection procedure, the mobile phase is first pulled through the stationary phase capillary action, then passes through capture zone, and the labeled probes are then captured and detected. When combined with SERS technique, the sensitivity and quantification capability are enhanced. From the view point of SERS methods, the selectivity and anti-interference ability are also improved. Such a SERS-based LFA strip was proposed for the sensitive quantitative evaluation of staphylococcal enterotoxin B (SEB) down to 0.001 ng mL⁻¹ [72]. Concerning to environmental real-life samples with complex constituents, the multiple rendering detection of each component is a challenge, even for finger-print spectrum-based SERS method. Accordingly, separation techniques such as thin-layer chromatography (TLC) and capillary electrophoresis (CE) could be combined with SERS to realize separation and detection of multiple analytes [73, 74]. TLC as a traditional separation techni-

que is very suitable to be combined with SERS because of the facile operation, no need of special instruments, and effective target concentration and separation ability. It has been successfully applied into SERS detection of various analytes, such as carotenoids, medicinal herbs and dyes in textiles [75, 76]. Recently, the TLC-SERS technique has also been used for the on-site detection of substituted aromatic pollutants in water (the whole detection process is shown in **Figure 4**) [77]. Various pollutants in the water were separated by a convenient TLC platform and detected by a portable Raman spectrometer, which was successfully applied to the detection of aniline <0.1 ppm [77]. These results reveal the ability of the proposed method for effective separation and concentration of substituted pollutants in site from environmental samples, and the shortened overall analysis time is appreciated for both emergency and routine detection of pollutants.

3.3. Hydrogel-based substrate for target gathering

As mentioned above, paper-based substrates can collect sample effectively from different surfaces by simply wiping or dipping. Hydrogel with a flexible polymer structure also holds such ability for facile target collection, which has been used as SERS substrate for the nondestructive identification of organic colorants from an ancient painting [78]. The self-standing hydrogel-based substrate also shows good prospects with advantages of fast target gathering and easy to recycle from the matrix for detection [79]. Because of the fast mass transfer between the matrix and the hydrogel network, the hydrogel substrate can act as a scaffold for target capture and concentration [80]. Le et al. prepared a gold NPs-embedded alginate gel for the detection of PAHs and found that the targets were captured by the three-dimensional network and brought close to the hot spots generated by the nanoparticles embedded in the gel, leading to significant SERS enhancement [80]. Using this substrate, quantitative analysis of four PAHs such as benzo(a)pyrene was realized with LODs as low as to 0.365 nmol L⁻¹ [81]. By making use of the collapse and recover ability of the hydrogel upon drying and rehydrated, the hydrogel-based substrate can also act as excellent mechanical molecular trap for the SERS detection. More importantly, when the hydrogel is loaded with SERS-active nanoparticles, the network volume decrease will give rise to dynamic hot spots because the particles are driven close to each other, thereby generating promoted enhancing effect. This method was successfully applied to the detection of dichlorodiphenyltrichloroethane and pesticides down to 10⁻⁸ and 10⁻⁹ mol L⁻¹, respectively [82, 83].

Besides the gathering and trapping effect for targets, the hydrogel is a bulk structure with three-dimensional network. When loaded with nanoparticles, the nanoparticles are distributed in a three-dimensional manner, and hence, the formed hot spots were not only limited on a plane but also in three-dimensional volumes which would give rise to better enhancement. In our earlier work, a polyvinyl alcohol (PVA) hydrogel substrate decorated with Ag nanoparticles was fabricated for trace SERS detection [84]. The in situ reducing process offered the hydrogel substrate with tunable, easily-operational properties with extremely homogeneous hot spot distribution. Due to its good light penetration, more than 100 mm of effective depth was confirmed by both slice observation and depth scanning techniques (the illustration for the structure and the effective depth is shown in **Figure 5**). The effective harvesting plasmonic

effects between active Ag particle couplings in all the x , y and z directions lead to a great average field within the whole substrate region, which results in excellent SERS performance [84]. Because of the large effective depth, the substrate is more tolerant toward an out-of-focus laser position, being favorable to the analysis operation on portable Raman instrument. After modified with specific capture scaffold, the hydrogel-based substrate has been successfully applied for the identification and trace detection of pollutants (such as sulfonamides, and 2,2-dipydy) in real-world samples [45, 84].

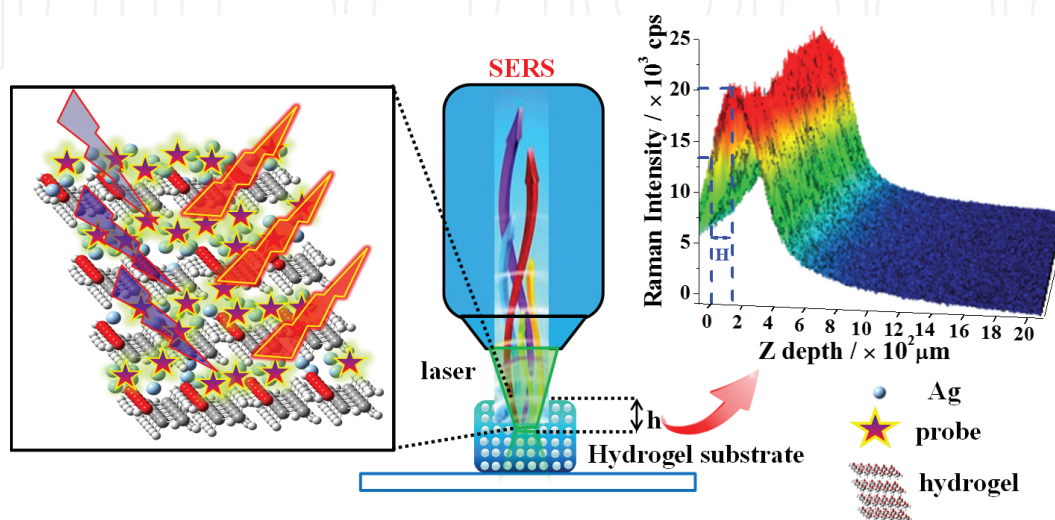


Figure 5. PVA-Ag hydrogel substrate with macroscale effective depth for trace detection. Reproduced with the permission from Ref. [84].

4. Strategies for multiple phase detection

Environmental samples frequently contain multiple analytes dispersed in various phases including aqueous phase, gaseous phase and even that dissolved in organic solvents at the same time. Therefore, the demands of multiple phases (or states) detection and identification are still a great challenge for the analytical methods. It is easy to fabricate substrate that suitable for SERS detection in a single phase such as aqueous and even organic phase, but the substrate or system that could be applied for the multiple phase detection is rather rare. Recently, a SERS sensor assembled at the liquid–liquid interface capable of multiple-phase, multiple-analyte detection was proposed, and such a liquid/liquid system allows the SERS-active particles to access either hydrophilic, hydrophobic or amphiphilic molecules at the same time [85]. The method for airborne analyte detection was also realized by simple conversion of a liquid–liquid interface to liquid–air interface. The interface assembled structure was further modified for the trace detection of Hg^{2+} . The functional polyaromatic ligands are soluble in organic phase, while the Hg^{2+} ion is soluble in aqueous phase. The interface self-assembly realizes the effective interaction between them and enables the sensitive detection down to 10 p mol level, and the airborne mercury detection was proved to be possible within 5 min of exposure [86]. Such

interface assembly strategy provides us a facile way to build a structure that has the access of multiple phases, but for such assembled film, the interacted surface is limited and the mass transfer is rather slow. Other surface assembled structure such as Pickering emulsion can further overcome these limits. Pickering emulsion is a promising way of producing ordered NP assemblies in three-dimensions that building blocks (such as nanoparticles) were assembled on the interface of different phases. It has been proven to be versatile immobilization techniques that provide efficient encapsulation in structures, which shows promising application in biphasic reactions [87]. By employing SERS-active particles with suitable wettability as the building block, it is possible to fabricate plasmonic Pickering emulsions as the SERS observation platform for multiphase detection. For example, surface-modified Ag nanocubes were used for constructing plasmonic colloidsomes as three-dimensional multiplex sensing platforms for ultratrace detection of both aqueous and organic soluble toxins low to sub-femtomole level [88]. Because of the emulsion-based structure, only sub-microliter sample volume is needed.

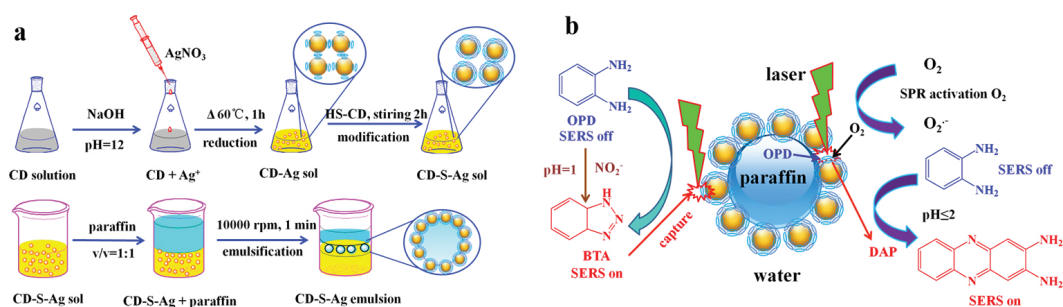


Figure 6. (a) Schematic illustration of the preparation of CD-S-Ag NPs and its emulsions. (b) The application of the proposed plasmonic Pickering emulsion system for the multiple phase pollutant detection. Reproduced with the permission from Ref. [89].

In our earlier work, we applied mercapto- β -cyclodextrin (HS-CD) as both emulsifier and functional host molecule to fabricate a Pickering emulsion-based SERS sensing system to selective detection of targets from both aqueous and organic phases (the synthesis process and the basic principle for quantify detection are shown in **Figure 6**) [89]. The HS-CD-modified Ag NPs were emulsified to assemble stable Pickering emulsion with paraffin, which shows much promoted SERS performance with dense hot spots and enables them accessible for multiple targets at the same time. Two special interface reactions on the emulsion surface were investigated and then used for detection of common pollutants NO₂⁻ and o-phenylenediamine (OPD). For water-soluble ionic pollutant NO₂⁻, it was emulsified and reacted with the CD-captured SERS-inactive OPD to form SERS-active benzotriazole, and then, the indirect quantification of its concentration was realized with the LOD down to 1 $\mu\text{mol L}^{-1}$. For the oil-soluble OPD, its trace detection was also achieved by using the surface catalyzed oxidation to form a SERS-active 2,3-diaminophenazine (DAP) under acidic conditions. The detection limit was as low as 1 nmol L⁻¹. From the *in situ* SERS monitoring, the kinetic data of the reaction(s) were obtained and the reaction mechanism was also proposed.

5. Special measures for practical on-site application

SERS is a promising trace analytical technique. However, we have noted that among thousands of the reported SERS researches, most are limited on conceptual or laboratorial uses. The out-room or on-site SERS analysis that required special instruments such as portable SERS device is also important to make such ideas into real application. In this part, we mainly focus on special measures for real application, including specially designed SERS substrates and the newly reported SERS-based devices that are designed with the goal of real application with facile sample preparation, fast signal readout and also ability for online sensitive quantification.

5.1. Special SERS substrates matching with miniaturized (portable) Raman instrument

Concerning to infield detection or fast signal readout, portable Raman instrument is no doubt more favorable, but unfortunately, most commonly used nanoparticle-based substrates are not suitable on portable Raman instrument because of the high demands of focus position (partly due to low reproducibility from Brownian movement and uncontrollable aggregation). The assembled or encapsulated substrates have been successfully applied in developing SERS detection system combined with portable instruments. For example, the PVA hydrogel-based substrate was applied into the trace antibiotics detection from the real polluted water with portable Raman spectrometer [45]. Recently, a portable SERS kit was demonstrated for rapid and reliable detection of trace drugs from environmental samples [90]. The whole detection procedure included a 3-min pretreatment for target extraction and a handheld Raman detection with highly reproducible assembled gold nanorod array as substrate (the sample preparation and detection process are shown in **Figure 7a**). The portable kit was successfully used for detecting methamphetamine, 3,4-methylenedioxymethamphetamine and methcathinone from real urine samples, showing great prospective toward public safety and healthcare [90].

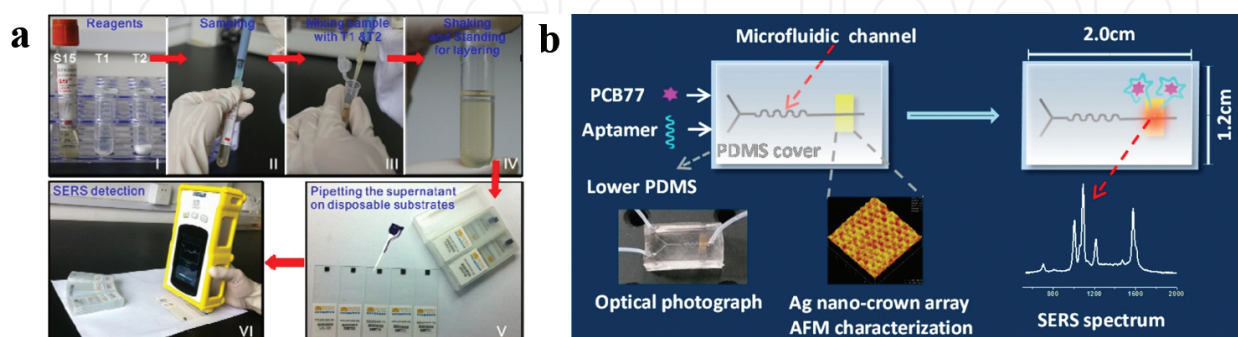


Figure 7. (a) Illustration of a portable kit for rapid SERS detection of drugs in real human urine. Reproduced with the permission from Ref. [90]. (b) Schematic diagram of the fabrication of the aptamer-based SERS microfluidic sensor for the detection of PCB77. Reproduced with the permission from Ref. [52].

5.2. Microfluidic SERS device

In recent years, applications of microfluidic system (or lab-on-a-chip) to environmental analysis have attracted much attention because of the notable advantages such as low sample consumption, rapid analysis, online analysis and incorporation of separation, concentration and quantification process [6]. The combination of microfluidic device with SERS technique not only makes use of these advantages, but also benefits a lot for the sensitive and fast online or infield detection. A microfluidic chip was developed for the trace detection of polychlorinated biphenyls [52]. The targets were selectively captured into the detection zone in the channel with aptamer functionalization, and then detected with Ag nanocrown array as enhancing substrate (illustration for the microchip is shown in **Figure 7b**). The detection concentration down to 1.0×10^{-8} mol L⁻¹ demonstrates such smart chip can be utilized for sensitive detection of pollutants in the environment [52]. Similarly, by mixing the confluent streams of Ag colloids and trace analytes in the channel through triangular structure, the trace detection of cyanide was accomplished in an alligator teeth-shaped microfluidic channel [91]. An integrated real-time sensing system by making use of a portable Raman spectrometer and a micropillar array chip was developed for the field analysis of two pollutants dipicolinic acid and malachite green, and the observed LOD was estimated to be 200 and 500 ppb, respectively, and further exhibited the capability of microfluidic-SERS ship for environmental detection in the field [92].

6. Challenges and outlook

As a promising advanced analytical technique, SERS has illustrated its potential for a wide range of applications due to its capability of achieving high sensitivity and providing molecular information. In this review, we mainly summarized the achievements in the selective target trace detection for the environmental application. For a given target, an appropriate strategy should be chosen according to the nature of the target and the sample matrix. Even though a great achievement has been made in this area, there still are some challenges for the real implementation in environmental analysis.

Surface functionalization strategies may be applied to enhance the detection sensitivity and selectivity, but the high cost of the capture element such as antibody and their low stability under harsh analysis conditions are not favorable in the large-scale practical applications, which need to be improved by further studying. In addition to the sensitivity, for the developing of SERS-based methods for environmental detection, the attention should also be paid to the guarantee of good accuracy and reproducibility. The highly sensitive SERS response can lead to signal deviation, while reliable quantification becomes difficult due to the relatively poorer reproducibility. Fabrication of substrates with high selectivity, enough sensitivity and reliable reproducibility are the basic demands for real application. On the other hand, advanced data analysis technique such as chemometrics methods can also be applied to further get into the abundant spectrum information for

multiplex component analysis. By the way, most of the reported SERS substrates are still based on results obtained in laboratory, and commercial products are still rare. Therefore, more concerning should be paid onto developing substrate that can be manufactured on large scale and used easily during the on-site analysis. Concerning to large batch production, the cheap, robust and stable substrate such as hydrogel or paper-based substrate would find more applications.

Detection systems that can be directly applied for infield SERS detection are still rare. For the practical application, the followings are required: (1) the preoperation for the sample preparation should be easy and fast. (2) the target capture, concentration and separation should also be accomplished without additional complex procedures. (3) the detection system should be portable and can be easily extended to the infield detection. In order to meet the demands for real sample which also contains complex matrix, we believe that the future development of SERS-based detection strategy will be combined with advanced separation or concentration techniques such as fluidic chip devices and test strip techniques. This trend will continue through the future designing of portable integrated systems.

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