

Recent progress in surface enhanced Raman spectroscopy for the detection of environmental pollutants

Da-Wei Li · Wen-Lei Zhai · Yuan-Ting Li · Yi-Tao Long

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Abstract Surface enhanced Raman spectroscopy (SERS) has emerged as one of the most promising analytical tools in recent years. Due to advantageous features such as sensitivity, specificity, ease of operation and rapidity, SERS is particularly well suited for environmental analysis. We summarize here some considerations with respect to the detection of pollutants by SERS and provide an overview on recent achievements in the determination of organic pollutants, heavy metal ions, and pathogens. Following an introduction into the topic and considering aspects of sensitivity, selectivity, reproducibility and portability, we are summarizing applications of SERS in the detection of pollutants, with sections on organic pollutants (pesticides, PAHs and PCBs, explosives), on heavy metal ions, and on pathogens. In addition, we discuss current challenges and give an outlook on applications of SERS in environmental analysis. Contains 174 references.

Keywords Surface-enhanced Raman spectroscopy (SERS) · Environmental pollutants · Detection techniques · Technological developments

Introduction

As a result of irrational human activities, environmental pollution has become an increasingly serious problem. Accordingly, there are growing demands for the development of corresponding analytical techniques for a variety of pollutants. Several techniques, such as chromatography, spectrophotometry, and electrochemical methods, are relatively

well established for environmental analysis [1–3]. However, most of these methods require sophisticated instruments and complex sampling processes or lack sufficient recognition capability for different pollutants, which limits their wider application [4, 5]. Recently, considerable efforts have been made to explore novel pollutant detection techniques such as microfluidics, biosensors, fluorescence probes, surface enhanced Raman spectroscopy (SERS), and so forth [4–9].

Among those emerging techniques, SERS is one of the most favorable methods for environmental analysis as it provides vibrational spectroscopic fingerprints for specific analytes with high detection sensitivity [10]. The original literature detailing the SERS phenomenon was reported in the 1970's by Fleischman and coworkers. They firstly observed a significant enhancement of the Raman scattering from a pyridine monolayer adsorbed on an electrochemically roughened silver electrode [11]. Subsequently, Van Duyne et al. systematically repeated the experiment and explained this unexpected enhancement as an electromagnetic effect [12], while other researchers proposed a chemical effect in the same period [13, 14]. Comparing with other techniques, SERS has a number of outstanding properties: (i) The ultrahigh sensitivity of SERS enables detection of very low concentrations of analytes, even at a single molecule level [15, 16]; (ii) SERS spectra are related to the inherent chemical structure of the target molecules thus yielding “fingerprint” information [16]; (iii) SERS is also a fast analytical technique which generally requires less than one minute for each measurement, illustrating its suitability for rapid detection [17]; (iv) Since water is a weak Raman scatterer, SERS can be directly applied in water sample analysis with negligible background signals [18]; (v) The validity for both chemical compounds and biological molecules render the SERS technique competitive for variable detection requirements [19]; (vi) SERS is a convenient and cost-effective process for the development of miniaturized Raman spectrometers and offers good practical utility for

D.-W. Li (✉) · W.-L. Zhai · Y.-T. Li · Y.-T. Long
Shanghai Key Laboratory of Functional Materials Chemistry,
State Key Laboratory of Bioreactor Engineering & Department
of Chemistry, East China University of Science and Technology,
130 Meilong Road, Shanghai 200237, People's Republic of China
e-mail: daweil@ecust.edu.cn

laboratory and field detection [20]. These remarkable advantages have led to the significant growth of SERS-based applications for the detection of environmental pollutants.

Therefore, the research effervescence in environmental analysis with SERS has motivated some recent review articles which cover various aspects of basic theory to specific applications [9, 21, 22]. This review is focused on some considerations in SERS detection of pollutants and the latest research developments of SERS in environmental analysis concerning pollutants such as organics, heavy metal ions, and pathogens over the past few years. Furthermore, this review covers current challenges and future prospects of SERS-based applications in pollutant detection.

Some considerations in SERS detection of pollutants

Routine environmental analysis often requires the accurate detection of extremely ultra low-level pollutant in complex samples, while some environmental accidents often involve a sudden release of chemical compounds which demand the field detection of pollutants in a convenient and expedient way. Therefore, the development of a suitable environmental analysis technique should consider requisite detection properties such as sensitivity, selectivity, reproducibility, and portability. SERS has excellent potential to meet these requirements because of its features described above. However, there are also drawbacks which may hinder it from becoming a more powerful and versatile method for pollutant detection. Recently, notable progresses were reported which address some of these challenges, which enable a broadening of the scope of applications of SERS for environmental analysis. Actually, these progresses on the properties such as sensitivity, selectivity, and reproducibility are also very important for SERS detection in other fields.

Sensitivity

Sensitivity is a major advantage of SERS which strongly depends on the enhancement property of SERS substrates and is closely related with their “hot spots” and surface areas [15, 16, 23, 24]. Thus, the high sensitivity of SERS detection can be achieved through fabricating novel SERS substrates with greater number “hot spots” and increased surface area. For example, the monodispers “flower-like” silver particles were prepared with a highly roughened morphology which could provide a mass of “hot spots” on a single particle which significantly improved the Raman enhancement [23]. Highly sensitive SERS substrates were also fabricated by constructing Ag nanoparticles (NPs) on the nanoporous surface instead of a conventional planar surface (Fig. 1a). The rendered SERS substrates have extremely large surface areas with abundant “hot spots” and yield greater Raman enhancement [24]. By

such means, ultrasensitive detection even at the single molecule level can be achieved using SERS under optimized conditions.

Coupling a pre-concentration process with the SERS technique is another strategy to improve the sensitivity of SERS detection without requiring elaborate fabrication of substrates with specialized nanostructure. As an example, a membrane filter with Au NPs coated on the surface was used to concentrate samples that were detected by SERS (Fig. 1b) [25]. This is a relatively simple method to improve the sensitivity of SERS for the detection of environmental pollutants at relatively low concentration. Furthermore, SERS detection of polar molecules such as anilines, phenols, and antibiotics, was recently developed by our group as an alternative novel method for improving the detection sensitivity by coupling SERS with electrokinetic pre-concentration [26, 27]. Polar organic pollutants can be pre-concentrated using this method and detected in a label-free way, with the sensitivity better than 1 nM.

The above-mentioned methods obviously enhance the sensitivity of SERS detection but these methods may not be sensitive to all kinds of environmental pollutants. Analytes which have strong affinity toward a substrate surface can yield strong SERS signals, whereas the analytes with low affinity to the substrate are challenging to directly detect with SERS [20, 28]. To overcome this limitation of SERS, many studies have been conducted to modify the SERS substrates with various functional molecules [29–34] such as alkylated-thiols, macrocyclic molecules, proteins, DNA fragments, graphene materials. The surface capture process brings analytes (e.g. polycyclic aromatic hydrocarbons (PAHs) and polychlorinated biphenyls (PCBs)) close to the zone of the enhanced electromagnetic field of substrates so that the SERS signals of those analytes can be highly enhanced (Fig. 1c). These recent studies significantly improve the sensitivity of SERS for diverse types of pollutants to meet their detection requirements. Continuous efforts are still required to extend the SERS-based application in environmental analysis.

Selectivity

The issue of selectivity of the detection method is also one of the most important aspects that should be considered for environmental analysis. Since the SERS method can provide information which ascertains chemical and molecular composition of a sample, it is usually regarded as a promising tool suitable for the selective detection of pollutants [9, 21, 22]. However, the environmental samples often contain multiple components which may generate many indistinguishable SERS signals thus rendering the qualitative detection of each component very challenging [35].

To improve the selectivity of SERS detection for complex samples, one can modify SERS substrates with specific

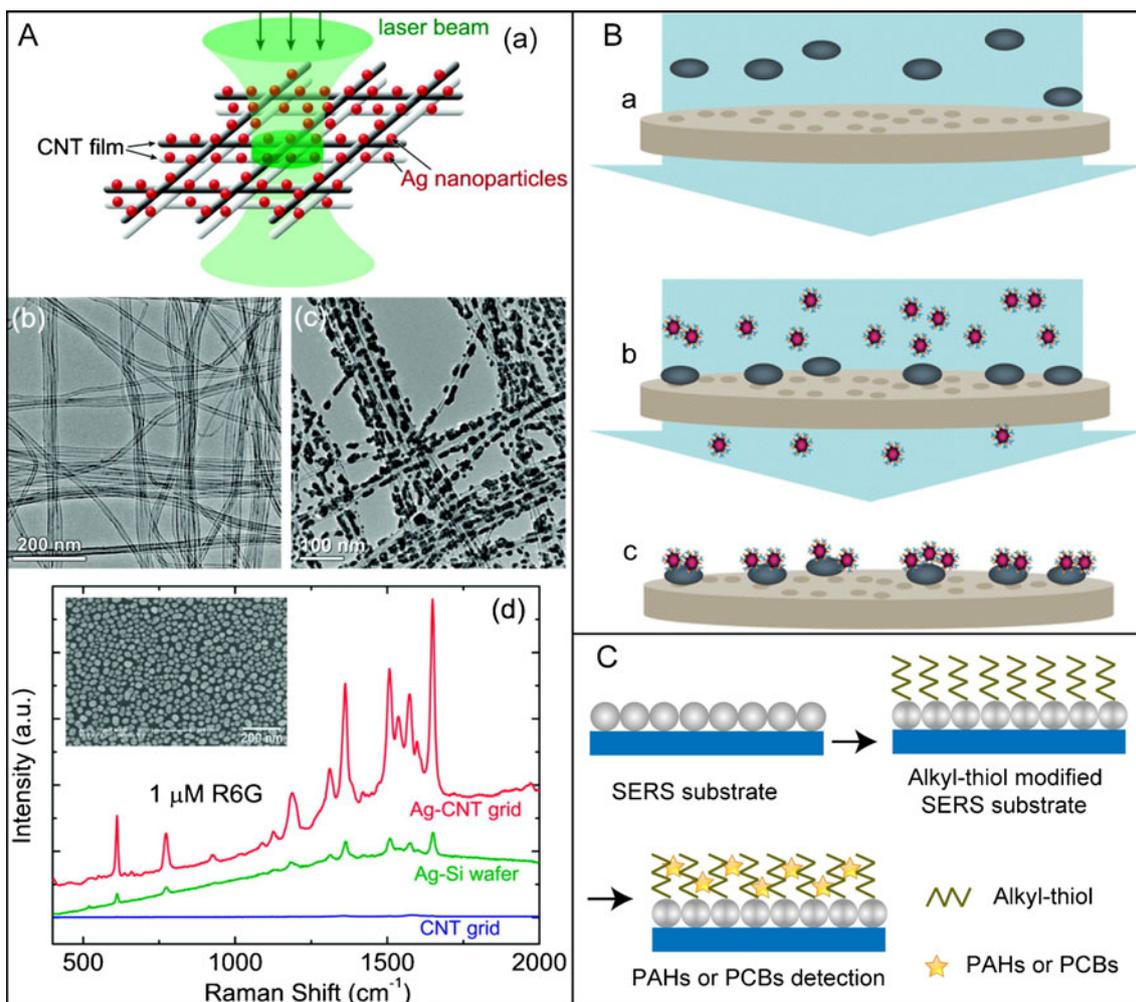


Fig. 1 Strategies for improving the sensitivity of SERS detection. **a** Highly sensitive SERS substrates made from carbon nanotube grids with silver nanoparticles and their SERS enhancement properties for rhodamine 6G, a SERS-active organic compound. **(a)** Schematic illustration of the nanoporous structure under a laser irradiation; **(b)** TEM image of a cross-stacking superaligned carbon nanotube (CNT); **(c)** TEM image of the Ag-CNT grid SERS substrate; **(d)** Raman spectra of R6G on Ag-CNT grid, Ag-Si wafer, and CNT grid. Reprinted with permission from ref. 24. Copyright

receptors, such as molecular imprinted polymers (MIPs), antibodies, and aptamers, to selectively capture the target analytes, and then recognize specific components by measuring the SERS signals. In fact, this strategy has been successfully carried out for the detection of estrogens, explosives, heavy metal ions, and other analytes depending on the specific interaction between antigens and antibodies, metal ions and ligands, aptamers and their targets [36–40]. Moreover, magnetic NPs can also be used for the preparation of specifically modified SERS substrates to further improve their detection selectivity. Silver or gold coated magnetic probes are then capped with corresponding antibodies that have been successfully used for the separation and SERS-based immunoassay of analytes such as pathogens (Fig. 2a) [41–43].

2010 American Chemical Society. **b** Schematic representation of the gold-coated polycarbonate membrane filter for analyte concentration and SERS detection of pathogen which can be favorably captured on the filter surface. **(a)** Concentrating samples through a membrane filter; **(b)** Adding immunogold labels to the top of the filter; **(c)** Detecting analytes via SERS. Reprinted with permission from ref. 25. Copyright 2010 Royal Society of Chemistry. **c** Schematic representation of the SERS detection of PAHs (or PCBs), which are not SERS-active, with the alkyl-thiol modified substrate

Although the exploitation of specific receptor modified SERS substrates offer the selective detection of a wider number of pollutants, it is still difficult to recognize various components in a complex sample selectively by using one kind of modified substrate. Thus, researchers have tried to combine SERS with separation techniques such as capillary chromatography (CC), thin layer chromatography (TLC), capillary electrophoresis (CE), and ion-pair chromatography (IC) to distinguish different analyte components in sample mixtures [44–51]. For example, Carrillo-Carión et al. studied the coupling of CC and SERS detection using a microdispenser and Ag quantum dots as an at-line interface and an active substrate, respectively. This system yielded chromatographic detection with excellent analytical properties [45]. This type of strategy was a useful method for the qualitative and quantitative

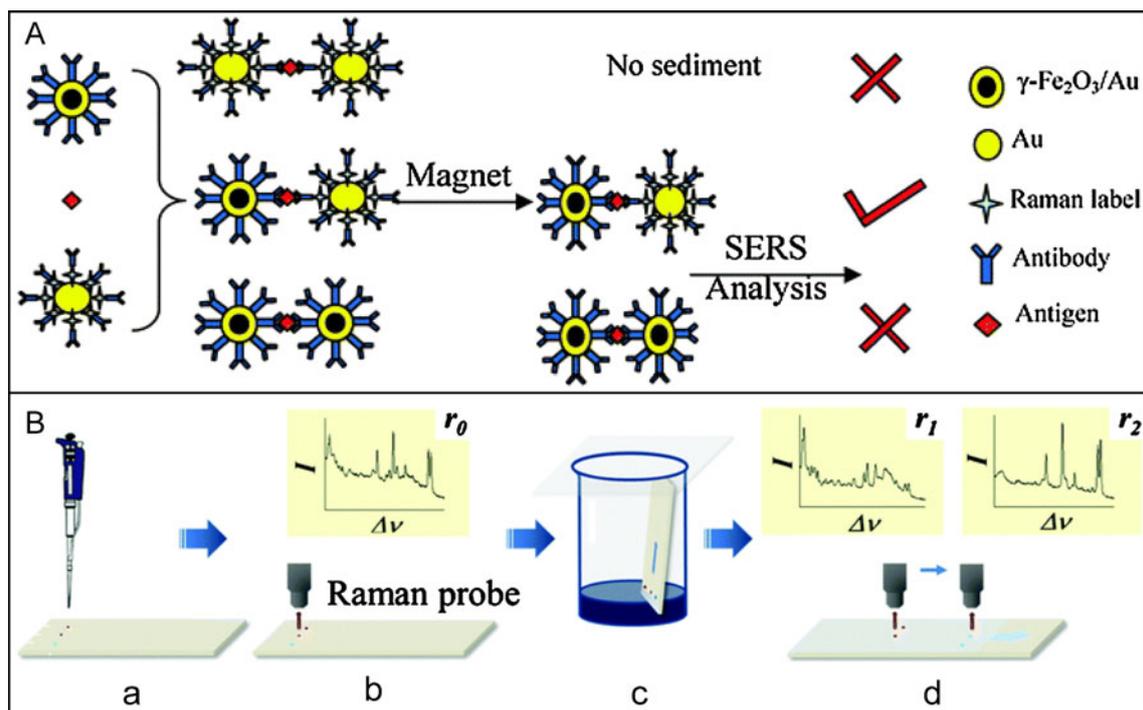


Fig. 2 **a** Schematic illustration of the SERS-based immunoassay of multi-antigen. Reprinted with permission from ref. 41. Copyright 2011 Royal Society of Chemistry. **b** Schematic illustration of TLC-SERS for the on-site detection of a mixture of different dyes including methyl orange, cresol red,

methylene violet 2B, and 2-bis(4-pyridyl)ethylene. **(a)** Loading samples onto the substrate; **(b)** Acquiring the SERS signal; **(c)** UTLC development; **(d)** Acquiring the SERS spectra along the development direction. Reprinted with permission from ref. 48. Copyright 2012 Royal Society of Chemistry

detection for complex pollutant samples. Furthermore, Leopold et al. developed an efficient approach for on-column SERS detection in CE, which presented time-dependent 3D CE-SERS with an on-column detection mode for the first time [50]. A highly sensitive SERS substrate was easily fabricated in situ within a few seconds in the column detection window by laser-induced growth of silver particles, enabling the collection of SERS spectra during the CE separation process. Thereby, accurate separation and high performance SERS detection was possible. By comparison, the coupling of TLC and SERS may be an alternative method that is more suitable for in-field detection application as it lessens the requirement of advanced instrumentation. Using this approach, a mixture of substituted aromatic compounds and dyes were successfully separated and detected in a convenient way (Fig. 2b) [35, 46–48].

Reproducibility

Reproducibility is also one of the basic requirements for any widely used analytical techniques to ensure that results are reliable and repeatable. In traditional SERS analysis, metal NPs colloids are extensively used as substrates due to their strong SERS activity and relatively simple preparation process. However, one of the main shortcomings of these substrates is that the aggregation of metal NPs in colloidal solutions is difficult to control and the SERS activity is less stable for a long time leading to poor SERS reproducibility.

The use of well-ordered metal nanostructures as SERS substrates is a promising tool for improving the reproducibility of SERS detection whilst maintaining high sensitivity. Therefore, many different kinds of nanofabrication techniques have been developed to produce uniform or periodic SERS substrates [52–57]. Among them, a well-known approach is electron beam lithography (EBL), which allows for both accurate control of fabrication and highly reproducible SERS performance [22, 53]. For instance, Materny et al. used an EBL technique to fabricate well-defined arrays of gold nanodots which serve as reproducible SERS substrates for quantitative SERS measurements [53]. In addition, many new approaches have been reported for the same purpose, such as optical lithography, vapor deposition, and other methods [54–57]. SERS substrates fabricated by these methods generally display excellent SERS reproducibility, but most of fabrication processes are laborious and expensive for batch production.

In particular, the laser spots of many Raman spectrometers generally cover a micron size range. Therefore, the preparation of substrates which are periodic at this scale affords highly reproducible SERS signals. Thereby, cost-effective fabrication methods involving assembly of NPs and printing technology may be promising alternatives to produce SERS substrates with good reproducibility for detection. In view of this, a facile method based on capillary-assisted assembly was used to fabricate highly reproducible SERS substrates that employed clean Au NPs. The spot-to-spot Raman intensity on the Au NPs

assembly coated with an rhodamine 6G molecule at 10^{-10} M demonstrated high reproducibility with less than 20 % RSD of the major vibrations (Fig. 3) [58]. In order to arrange metallic NPs in large arrays for SERS applications, a batch fabrication strategy based on screen printing was developed [59]. With these screen printed SERS arrays, the spot-to-spot SERS signals showed that the intensity variation is less than 10 %. In addition, surface organization processes based on the Langmuir-Blodgett (LB) technique represents a cost-efficient and simple strategy for mass production of SERS substrates with high reproducibility [60, 61]. Thus, the application of highly reproducible SERS substrates in environmental analysis has become possible with such type of emerging and cost-effective batch fabrication methods.

Portability

For environmental analysis, especially for the analysis of pollution accidents, field detection is an important application so the portability of SERS detection should also be considered. The miniaturization of Raman spectrometers and the development of fiber optic-based techniques facilitate the development of portable SERS-based techniques, particularly for field-based application. However, the conventional colloidal substrates are not suitable for SERS detection in the field. In contrast, devices which employ solid SERS substrates may work well for this purpose due to its good portability. Optical fiber-based SERS sensors are devices which have generated steady interest as a versatile means of extending SERS for portable field applications. Since a number of research achievements on fiber-based SERS sensors have already been previously reviewed [62, 63], the

most recent literature are discussed herein. For instance, a bidirectional fiber SERS sensor was fabricated by the EBL technique, which produced two-dimensional arrays with well-defined geometry which allows the optical response of the sensor to be tuned and the density of the “hot spots” to be controlled (Fig. 4a) [64]. Yap et al. reported another kind of fiber SERS sensor which was fabricated by template-guided self-assembly of Au NPs into ordered arrays of uniform clusters enabling high-performance SERS detection on an optical fiber facet. This approach provides a batch method for production of 3D configured surfaces for remote sensing applications [65]. In addition, some other fiber SERS sensors were developed using a tip-coated multimode fiber, a liquid core photonic crystal fiber, and so on [66–68]. Obviously, fiber SERS sensors offer a promising tool for the field-based analysis. However, the limited reuse of the fiber sensor may hinder the high throughput detection and the contribution of fiber material as a background signal may be an issue limiting precise detection.

Besides fiber SERS sensors, there is currently growing interest in the fabrication of paper-based SERS sensors which exhibit excellent SERS performance at relatively low cost, facile fabrication, ease of operation, and disposal [69]. The application of paper-based SERS sensors was reported by Vo-Dinh et al. for the detection of trace amounts of organic compounds [70]. These sensors were prepared by spin-coating polystyrene latex particles on the surface of filter paper, followed by the thermal evaporation of Ag NPs. Since then, paper-based SERS sensors have been prepared rapidly and simply using elegant approaches such as physical vapor deposition, pulse-laser sputtering, dip coating, and printing technology. These methods have been introduced in other

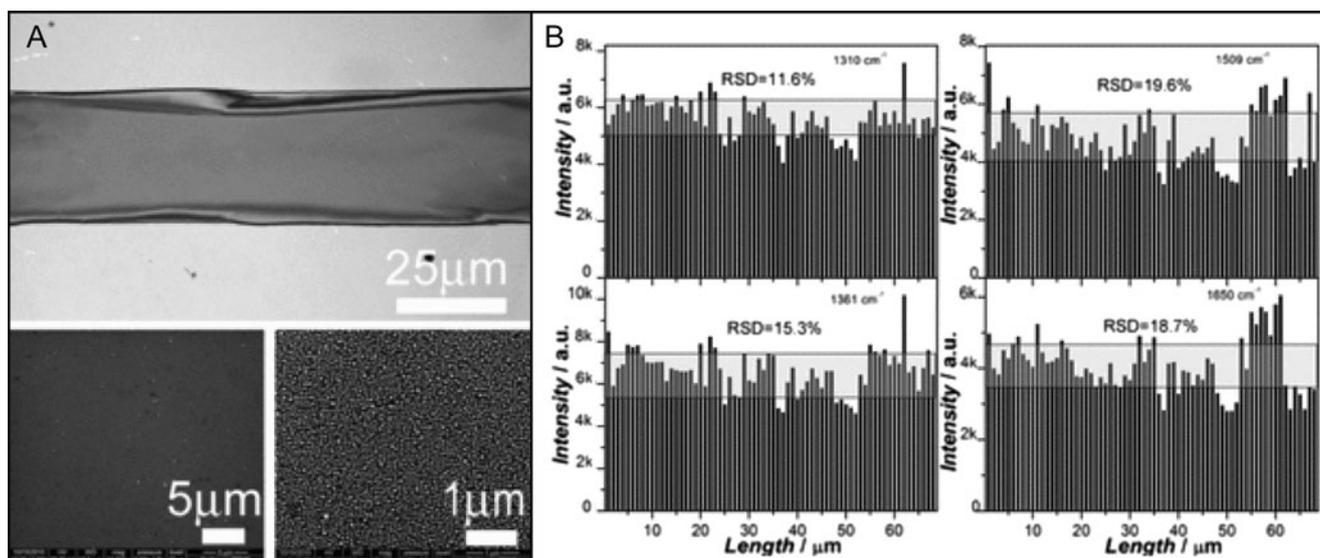


Fig. 3 **a** Optical photograph and SEM images of the highly reproducible SERS substrates fabricated by capillarity-assisted assembly showing the large-scale and uniform Au NP assembly. **b** The intensities of the main

Raman vibrations of R6G (at 1×10^{-10} M) in the 68 spots of the reproducible SERS substrates. Reprinted with permission from ref. 58. Copyright 2011 American Chemical Society

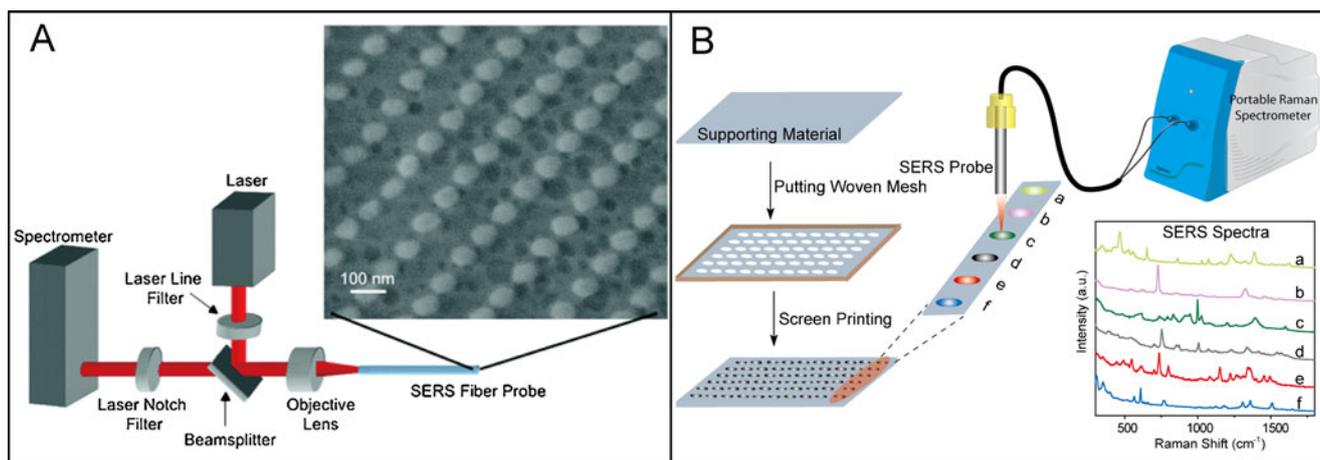


Fig. 4 **a** Schematic depiction of the configuration used to characterize the SERS fiber optic probe and a scanning electron micrograph of an array of gold optical antennas on the facet of a fiber. Reprinted with permission from ref. 64. Copyright 2009 American Chemical Society. **b** Schematic illustration of the processes for screen printing of SERS arrays

reviews [69, 71–74]. Recently, a facile method was developed to fabricate a low-cost disposable paper-based SERS sensor by printing SERS active NPs arrays onto filter paper using a screen printing technique (Fig. 4b) [59]. The screen printed SERS arrays may offer portable high-throughput evaluation of multiple samples with a single sensor. These paper-based sensors fabricated by different methods dramatically improve the portability and feasibility of SERS detection for pollutants as a promising technique for both laboratory and field-based detection. The metal NPs exposed on the paper for these sensors may undergo oxidation to lose some SERS activity. Therefore, more efforts are required to improve the stability of such sensors for demanding field applications.

Applications of SERS in pollutant detection

SERS has become more and more attractive for pollutant detection because of its unique advantages in analysis. Although there are several reviews detail the progress of the SERS application in environmental analysis [9, 21, 22], many new achievements have been reported in the past few years. Therefore, these achievements will be described herein including the application of SERS for the detection of organic pollutants, heavy metal ions, and pathogens.

Organic pollutant detection

Since the SERS spectrum can directly reveal molecular-vibration energies, the technique is widely used for the detection of many organic pollutants, such as pesticides, PAHs, PCBs, explosives, and so on, through developing suitable substrates or coupling with other techniques (Table 1).

and their application in the detection of different analytes (such as rhodamine 6G, flavin mononucleotide, L-tryptophan, L-phenylalanine, and adenosine) using a portable Raman spectrometer. Reprinted with permission from ref. 59. Copyright 2012 Royal Society of Chemistry.

Pesticides Sanchez-Cortes et al. performed the initial research about the absorption of pesticides such as dithiocarbamate and cyromazine on gold and silver surfaces using SERS [75, 76]. Thereafter, more attention was drawn to the usage of SERS detection for pesticide pollutants as reported during the past several years [77–88]. By utilizing traditional colloidal silver and gold NPs as active substrates, the direct SERS detection of pesticides such as fonofos, dimethoate, omethoate, and methamidophos have been successfully achieved [77–79]. Furthermore, to further increase the detection sensitivity, many elaborate metal substrates with specialized geometries have been developed for the SERS detection of pesticides [80–83]. For instance, Yuan et al. fabricated self-assembled clusters based on thousands of Ag NPs, which bear numerous “hot spots” and demonstrated good performance for sensing thiram where the limit of detection (LOD) was as low as 0.024 mg/L (Table 1) [80]. Recently, with gold nanorods and nanodogbone served as active substrates, Narayanan et al. explored quantitative solution-based and direct readout SERS methods for enhanced sensitive detection of thiram, ferbam, and ziram [81, 82].

In addition, a strategy of coating metal nanostructures with functional molecules can also be used to fabricate active substrates to improve the property of SERS detection for pesticides. For example, Liu et al. performed trace SERS analysis of methyl parathion insecticide by mono-6-thio- β -cyclodextrin coated Au NPs, formed via the strong interaction between Au and thiol [84]. Based on the host-guest interaction, the cyclodextrin coating favors inclusion binding of target guest molecules according to the cavity size of cyclodextrin. This results in the location of the target molecule close to the SERS substrate so that greater sensitivity at ppt level can be obtained. This strategy can also prevent the detection from interference by other pollutants with a molecular size greater than the

Table 1 Samples for SERS application in organic pollutant detection

Analytes	SERS substrate	Sensitivity (LOD)	Ref.	
Pesticides	Fonofos	Ag NPs in form of dried films	10 ppm [77]	
	Omethoate	Aggregated Ag NPs	2 ppm [78]	
	Methamidophos	Ag NPs ^a	0.1 mg·L ⁻¹ [79]	
	Thiram	Single clusters of self-assembled Ag NPs	0.024 ppm [80]	
	Thiram	Gold nanorods	~34 nM [81]	
	Ferbam		~26 nM	
	Ziram		~13 nM	
	Methyl parathion	CD-SH ^b modified Au NPs	ppt level [84]	
	Parathion	Silica shell-isolated Au NPs	— [90]	
	Paraquat	Ag NPs ^c	2 nM [86]	
	Methyl parathion		5 ppm [87]	
	Malachite green	Ag NPs ^d	0.1 ppb	
	Thiram		5 ppb	
	Chlortoluron	Ag-Quantum dots “sponge” nanocomposite ^e	0.2 mg·L ⁻¹ [91]	
	Atrazine		0.2 mg·L ⁻¹	
	Diuron		0.1 mg·L ⁻¹	
	Terbutylazine		0.1 mg·L ⁻¹	
	PAHs & PCBs	Fluoranthene	1-Hexanethiol functionalized Ag NPs	5 µg·L ⁻¹ [97]
		Fluorine	aggregates on copper foil	10 µg·L ⁻¹
		Acenaphthene		500 µg·L ⁻¹
Naphthalene			500 µg·L ⁻¹	
Pyrene		Viologen functionalized Ag NPs	1 nM [100]	
		SWCNTs assemblies on Ag NPs	1 nM [103]	
Anthracene		CD-SH functionalized AuNPs	100 nM [102]	
Pyrene		Au NPs-modified alginate gel network	10 nM [105]	
Chrysene			100 nM	
Triphenylene			1,000 nM	
Benzo[a]pyrene			0.365 nM	
Explosives		2,2',4,4'-tetrachlorobiphenyl	Decanethiol assembled silver film over NPs	50 pM [107]
	3,3',4,4'-tetrachlorobiphenyl	Ag nanosheet-assembled hemispheres modified with CD-SH	0.1 µM [110]	
		Cone-shaped ZnO nanorods/Ag NPs	0.01 nM [112]	
	2,4,6-trinitrotoluene	Cysteine modified Au NPs	2 pM [113]	
		<i>p</i> -Aminothiophenol-functionalized Ag NPs on Ag ₂ MoO ₄ nanowires	1 pM [39]	
		Popcorn-shaped Au NPs/SWCNT ^f hybrid	100 fM [117]	
		Fe ₃ O ₄ /AuNPs/Lignin modified microspheres	1 pM [118]	
	2,4-dinitrotoluene	CD-SH functionalized gold nanoprisms	sub-ppb [120]	
	2,4-dinitroanisole	Ag NPs modified by L-cysteine methyl ester hydrochloride	20 µg·L ^{-1h} [121]	
			100 µg·L ⁻¹ⁱ	
Other organic pollutants	Ciprofloxacin	Dendritic silver nanosubstrates	20 ppb [124]	
	Phosphorus triphenyl	Metal nanostructured film/graphene oxide	1 nM [125]	
	Tetracycline	Micro-scale Au hollow spheres	0.1 µg·L ⁻¹ [127]	
	Furadantin		5 ppm	
	Furaltadone	Au NPs ^a	5 ppm [128]	
	Endosulfan	Bis-acridinium lucigenin functionalized Ag NPs	20 ppb [129]	
	Pentachlorophenol	Silver-coated magnetite-carbon core-shell microspheres	0.1 nM [131]	
	Diethylhexyl phthalate		pM	
	Melamine	Filter membranes trapping Ag NPs	6.3 ppb [132]	
	4-chlorophenol	Au-coated TiO ₂ nanotube arrays	nM [133]	
Rhodamine 6G	Ag NPs-decorated reduced graphene oxide	10 nM [33]		

Table 1 (continued)

Analytes	SERS substrate	Sensitivity (LOD)	Ref.
Rhodamine B	Silver-electrodeposited screen printed electrodes ^g	1 nM	[26]
Methyl violet		10 nM	
Methylene blue		1 nM	
Phenol		0.19 nM	
<i>l</i> -Naphthol		0.15 nM	
Hydroquinonecarboxylic acid		0.095 nM	
<i>p</i> -Phenylenediamine		0.13 nM	
<i>p</i> -Nitroaniline		0.16 nM	
Aniline		0.11 nM	

^{a, c, d, e, g} By the method coupling SERS with density functional theory, microfluidic technique, optofluidic technique, capillary chromatography, and electrostatic preconcentration

^b Mono-6-thio- β -cyclodextrin, ^f Single-wall carbon nanotubes; ^h For deionized water; ⁱ For aged tap water

cyclodextrin cavity size. Tian et al. reported a novel method named as shell-isolated nanoparticle-enhanced Raman spectroscopy (SHINERS) and its application on the detection of parathion as a model pesticide analyte (Fig. 5) [89, 90]. In this method, the ultrahigh Raman signal enhancement is provided by Au NPs coated with an ultrathin silica or alumina shell. Compared with bare metal substrates, the coating prevents nanoparticles from agglomerating and allows for good versatility of SERS for different types of samples.

Although, the above-mentioned substrates can provide sensitive detection of pesticides, the portability and the expected precision of the SERS method is often poor under ordinary sampling conditions. A highly precise and portable measurement may be achieved if a continuous flow and homogeneous mixing condition between the analytes and colloidal SERS substrates are maintained. For this reason, a

polydimethylsiloxane (PDMS) microfluidic channel coupled with SERS was applied to the detection of methyl parathion pesticides [85]. As well, an approach combining microfluidic channel with SERS-based microdroplet sensor was used for the analysis of paraquat [86]. More recently, an optofluidic SERS device optimized for on-site analysis was investigated for the multiplexed detection of three fungicides (e.g. methyl parathion, malachite green, and thiram) [87]. Such optofluidic SERS microsystem offers good portability for on-site (or online) analysis of water samples without requiring a bulky pump for sample loading. However, in order to guarantee high precision of detection, the stability of the colloidal SERS substrates requires further enhancement. Furthermore, the integration of CC with SERS may be another promising method for the separation, identification, and quantification of multiple pesticide pollutants [91].

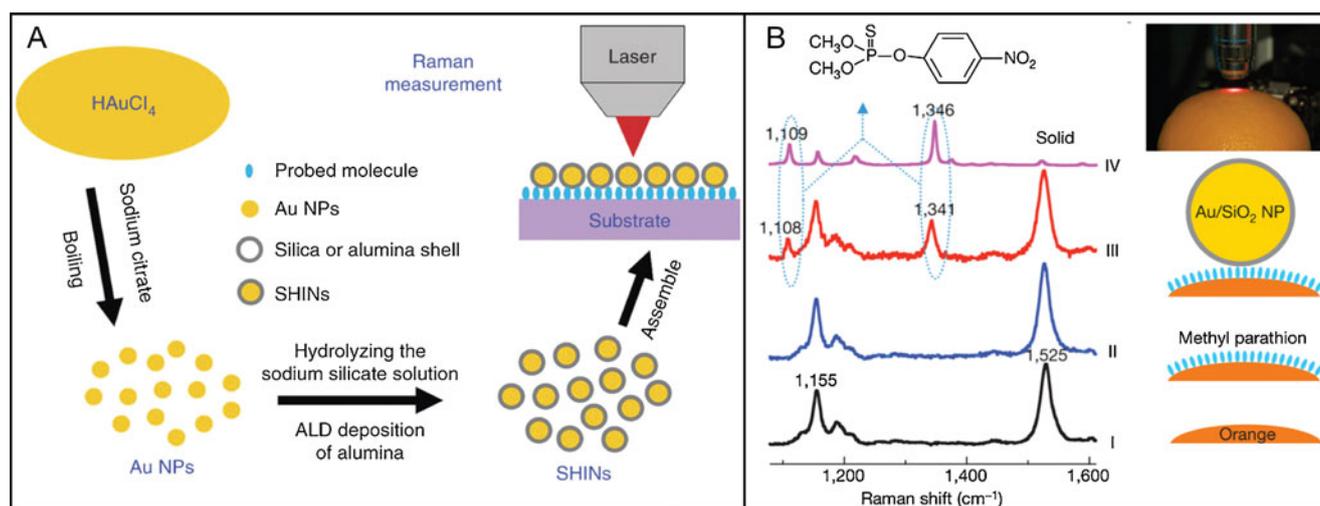


Fig. 5 **a** Schematic illustration of shell-isolated nanoparticle-enhanced Raman spectroscopy (SHINERS). Reprinted with permission from ref. 90. Copyright 2013 Nature America Inc. **b** In situ detection of pesticide pollutants with SHINERS. Curve I, with clean pericarps; curve II,

contaminated by parathion. Curve III, SHINERS spectrum of contaminated orange modified by Au/SiO_2 nanoparticles. Curve IV, Raman spectrum of solid methyl parathion. Reprinted with permission from ref. 89. Copyright 2010 Nature America Inc

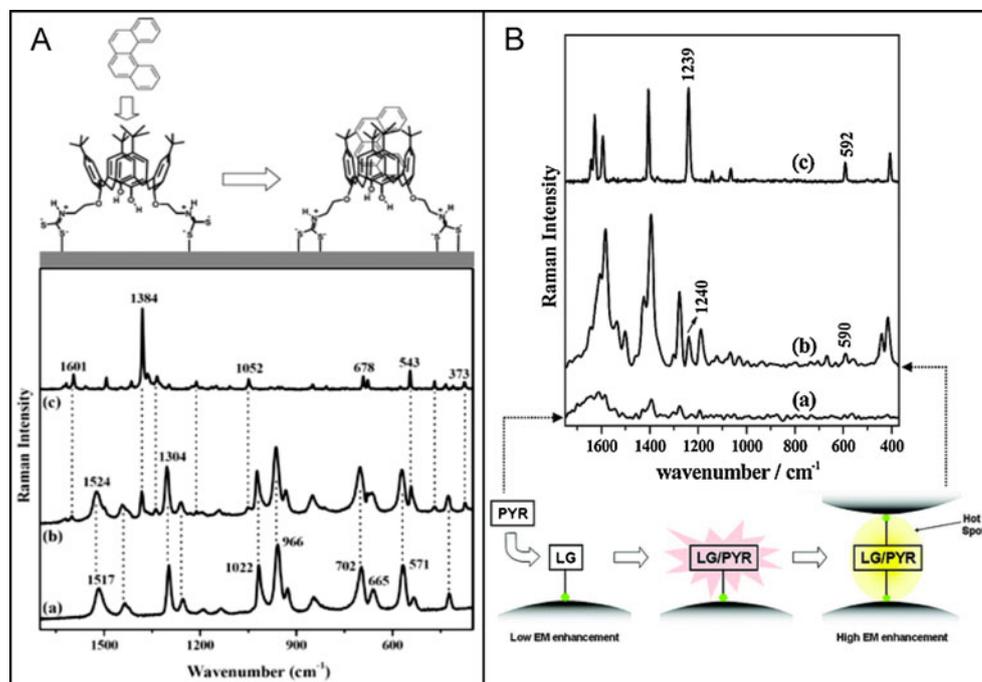
PAHs & PCBs PAHs represent an important group of persistent organic pollutants (POPs) which generally consist of two or more conjoined aromatic rings and show very poor affinity to metallic surfaces, limiting their SERS detection with conventional substrates [21]. In order to overcome this limit, new approaches to increase the surface/solution partition coefficient of PAHs can be developed through the chemical modification of metal SERS substrates [21, 92–108]. Octadecylthiol-coated silver substrates were initially applied to detect naphthalene by SERS, illustrating the great potential for SERS detection of PAHs [92]. A number of alkyl-thiols and alkyl-silanes, such as propanethiol [93], decanethiol [29], pentanethiol [94], C18 silane [95], (3-mercaptopropyl) trimethoxysilane [96], and hexanethiol [97], have been used to modify SERS substrates to increase their surface hydrophobicity to enable adsorption of PAHs for detection by SERS. It was found that the alkyl coated metal SERS substrate produced a system which could partition the PAHs out of solution onto the strongly Raman-enhanced region of the substrate, allowing the analysis of PAHs at trace concentration levels.

SERS detection of PAHs that utilize host-guest interactions is another widely-adopted approach. In this respect, Sanchez-Cortes and coworkers have performed a series of systematic studies [98–100]. They successfully applied calixarene (CX) with carboxy group on the SERS detection of PAHs with CX-functionalized Ag nanoparticles (Ag NPs) as active substrates [99]. They synthesized a dithiocarbamate (DT) functionalized CX aimed to improve the affinity of the

calixarene host toward the metal nanoparticle surface. The combination of the favorable host properties of CXs and the high affinity of the DT group in the same molecule afforded a self-assembled complex on a metal nanostructure. This design strategy is sensitive and selective at surfaces for the SERS detection of PAHs (Fig. 6a) [30]. Recently, they expanded their research on the functionalization of Ag NPs with lucigenin (LG) and applications for the SERS detection of PAHs. As indicated in Fig. 6b, LG can form intermolecular cavities at interparticle junctions where PAHs can be located with greater intensification of the SERS signals [100]. Using this method, the LODs of 1 nM could be achieved for model analytes, pyrene and benzo[c]phenanthrene (Table 1). Based on such host-guest molecular recognition, Yukihiro Ozaki et al. performed similar studies by using Ag NPs or Au NPs functionalized with per-6-deoxy-(6-thio)- β -cyclodextrin (CD-SH). Their results indicated that CD-SH functionalized metal NPs may also serve as platforms for the selective and sensitive SERS detection of PAHs [101, 102]. In addition, SERS detection of PAHs were studied by using other functioned substrates such as carbon nanotube-deposited silver structure [103], humic acid-decorated Ag NPs [104], Au NPs-modified alginate gel networks [105], Au NPs-modified TiO₂ nanotube arrays [106].

PCBs are another important class of POPs with properties similar to PAHs such as solubility in water and affinity to metallic surfaces. Thus, some of the strategies suitable for PAHs can be applied for SERS detection of PCBs. Haynes et al. carried out the early research on the SERS detection of PCBs with a silver film over nanospheres (AgFON) modified

Fig. 6 **a** SERS spectra of DTCX (10^{-4} M) and DTCX/benzo[c]phenanthrene. Top scheme: structural change induced by the interaction of benzo[c]phenanthrene with DTCX, as deduced from the SERS spectra. Reprinted with permission from ref. 30. Copyright 2009 American Chemical Society. **b** SERS spectra of LG 10^{-9} M (a), SERS spectra of LG/pyrene (10^{-9} M/ 10^{-6} M) (b), and Raman spectrum of pyrene in the solid state. Reprinted with permission from ref. 100. Copyright 2009 American Chemical Society



by a layer of decanethiol [107]. Their research revealed detection of 50 pM PCBs without further substrate or instrumental optimization and the measured SERS spectra allow easy recognition between PCB-47 (2,2,4,4-tetrachlorobiphenyl) and PCB-77 (2,2,3,3-tetrachlorobiphenyl) through the C-Cl and aromatic peak signatures. Using decanethiol as a modifier, Meng et al. performed further study on SERS substrates for detection of PCBs [108]. They fabricated a vertically aligned Ag nanoplate-assembled film modified by a DT layer and employed it as a robust and reproducible SERS substrate for detection of PCBs. Additionally, HS-CD was also used to modify various silver surfaces, such as Ag film on copper foil [109], large-scale well-separated Ag nanosheet-assembled micro-hemispheres [110], and large-area Ag nanorod array [111], to serve as substrates for detection of PCBs using the host-guest recognition method. It was shown that modifying substrates with HS-CD which contain a suitable hydrophobic cavity matching the size of PCB molecules facilitates efficient capture of PCB congeners to improve their SERS sensitivity. More recently, a highly sensitive and uniform three-dimensional SERS substrate was fabricated through assembling Ag NPs on the side surface and the upper region of vertically aligned array of ZnO nanorods [112]. This three-dimensional hybrid substrate provided reproducible detection with a LOD for PCB-77 as low as 10^{-11} M (Table 1).

In short, these recent studies together demonstrate that sensitive and reproducible SERS detection of PAHs or PCBs can be achieved by using chemical-modified and well-controlled nanostructures as SERS substrates and that individual PAH or PCB molecules in simple mixtures can be distinguished. However, environmental field samples generally contain trace levels of PAHs or PCBs that coexist with many other SERS active pollutants. The detection demands of such samples are beyond the capability of most developed SERS substrates in sensitivity and selectivity. Although these achievements offer favorable features for expanding the SERS technique to PAHs and PCBs, significant efforts are still required to further develop more sensitive and specific SERS substrates for these types of pollutants.

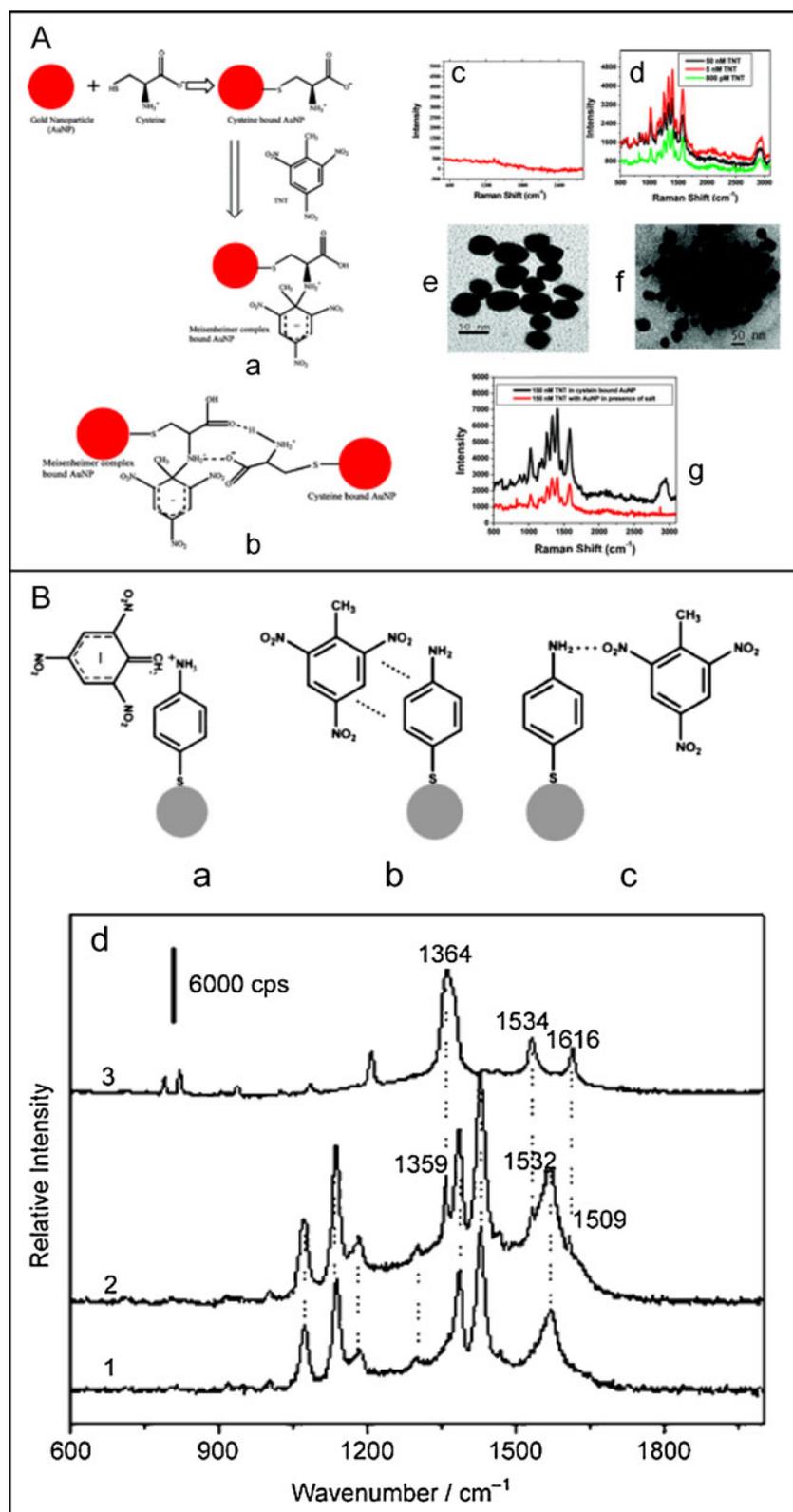
Explosives Explosives are often classified into nitro aromatic compounds, and their pollution to soil and water is a concern because of the related detrimental effects to human and ecosystem health. Apart from the environmental pollution, explosives are also closely related with national security. The efficient SERS detection of explosives has therefore attracted a great deal of attention. Dasary et al. firstly demonstrated a label-free, highly selective and ultra sensitive SERS sensor for trinitrotoluene (TNT) using cysteine-modified Au NPs (Fig. 7a) [113]. They found that Au NPs undergo aggregation in the presence of TNT due to the formation of Meisenheimer complex between TNT and

cysteine. Therefore, TNT was quickly and accurately detected at the 2 pM level without interference from other nitro aromatic compounds and heavy metals (Table 1). Similar Meisenheimer complex based methods were also developed for TNT detection by Yang et al. [114, 115]. Additionally, a novel strategy of imprinting molecular recognition can be developed for the ultra-trace detection of TNT using the *p*-aminothiophenol (PATP) based complexation and SERS on Ag NPs which were attached to silver molybdate nanowires (SMN). The π -donor-acceptor interactions between TNT and π -donor *p,p'*-dimercaptoazobenzene (DMAB) produced by a catalytic coupling reaction of PATP molecules adsorbed on Ag NPs results in an optimal imprint molecule contours for highly selective and sensitive SERS detection of TNT (Fig. 7b) [39]. Recently, SERS detection of TNT was further performed by using the active substrates such as molecularly imprinted polymers deposited onto AuNPs [116], popcorn-shaped gold nanoparticle-functionalized SWCNT hybrid [117], Fe₃O₄/Au nanoparticles/lignin modified microspheres [118], and silver-gold bimetallic nanostructures on DNA [119].

In addition to TNT, other explosives, such as dinitrotoluene (DNT), dinitroanisole (DNAN), cyclotrimethylenetrinitramine (RDX), trinitrobenzene (TNB), and their mixtures have been successfully detected by SERS or the coupling of the SERS method with other techniques [120–123]. For instance, Liu et al. expanded their analysis strategy for pesticides to the SERS detection of DNT using HS-CD modified triangular gold nanoprisms [120], while Xu et al. conducted the SERS analysis of DNAN using Ag NPs modified by L-cysteine methyl ester hydrochloride [121]. Furthermore, to facilitate the SERS detection of explosives, a low-cost and facile paper-based SERS sensor was fabricated by depositing Au NPs on common lab filter paper [122]. This paper-based sensor combines the advantages of other elaborate SERS sensors with the flexible property of paper, suitable for routine applications in the lab and the field. Although these introductory strategies can be applied to the SERS analysis of individual explosives and their mixtures in environmental samples based on their fingerprint Raman peaks, challenges remain for the analysis of complex field samples. The combination of SERS with other separation approaches such as capillary liquid chromatography may have potential for both good quantitative results and additional qualitative information [46].

Other organic pollutants The SERS technique can also be applied for the detection of a number of other types of organic pollutants such as antibiotics, pigments, estrogens, and substituted aromatics [124–134]. For example, using dendritic silver nanosubstrates, He et al. carried out the SERS detection of three antibiotics (enrofloxacin, ciprofloxacin, and chloramphenicol) illustrating the feasibility of accurate and

Fig. 7 **a** Cysteine modified gold nanoparticle based label-free SERSprobe for TNT recognition. **(a)** Schematic representation of the formation of Meisenheimer complex between cysteine modified gold nanoparticle and TNT; **(b)** schematic representation for the possible cross-linking between gold nanoparticle bound Meisenheimer complex with gold nanoparticle bound cysteine; **(c)** SERS spectra from gold nanoparticle+TNT (50×10^{-7} M); **(d)** SERS spectra from cysteine modified gold nanoparticle+TNT (50 nM - 800 pM TNT); **(e)** TEM image of cysteine modified gold nanoparticle; **(f)** TEM image demonstrating aggregation of gold nanoparticle in the presence of TNT; **(g)** SERS spectra from gold nanoparticle+TNT (150×10^{-9} M) in presence of 0.2 M NaCl and SERS spectra from cysteine modified gold nanoparticle+TNT (150 nM). Reprinted with permission from ref. 113. Copyright 2009 American Chemical Society. **b** Schematic representation of the possible interactions between TNT and PATP: **(a)** through the anion-cation pair, **(b)** π -donor-acceptor interactions, **(c)** possible hydrogen-bonding interaction); **(d)** SERS spectra of 1) DMAB-modified Ag-SMNs complex, 2) DMAB-modified Ag-SMNs complex in the presence of TNT, and 3) Raman spectrum of TNT in the solid state. Reprinted with permission from ref. 39. Copyright 2009 Wiley



rapid detection of antibiotics with the LOD at the ppb level (Table 1) [124]. The fabrication of a metal-graphene oxide

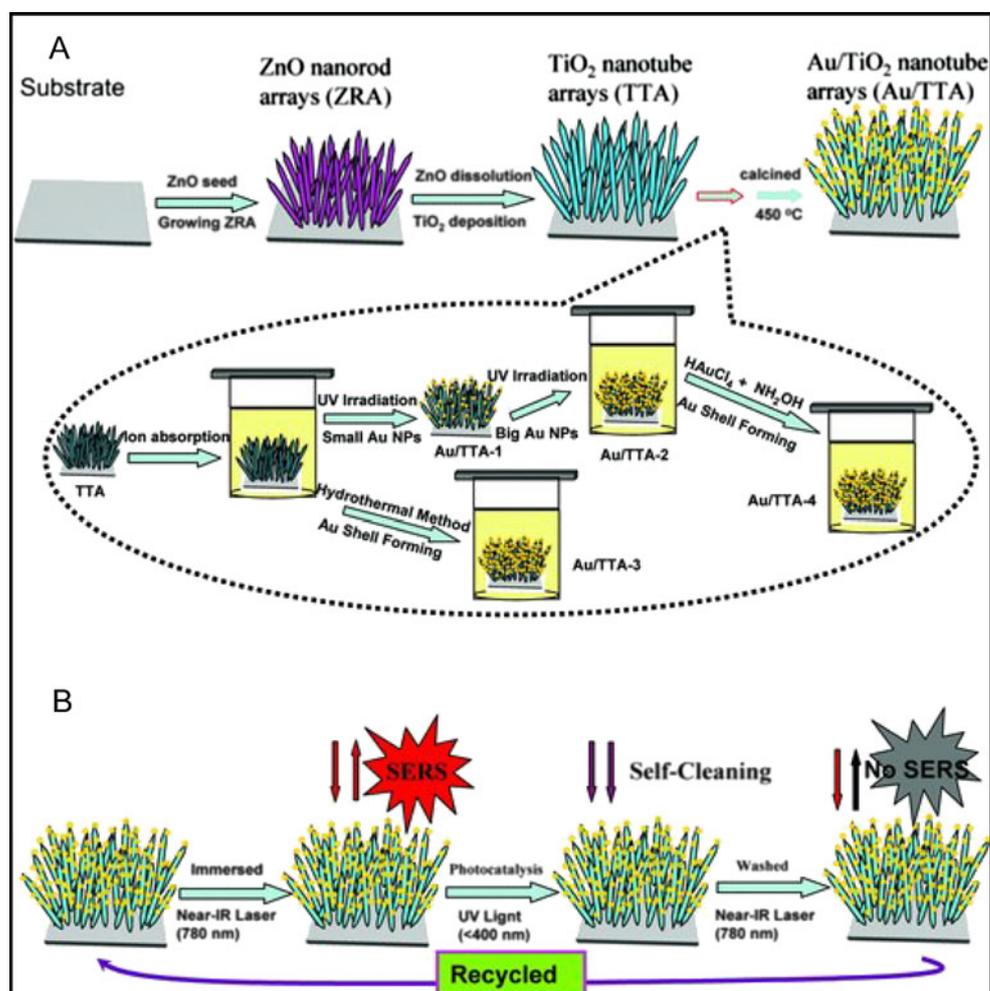
nanostructured film by Liu et al. and Lu et al. provided the SERS detection of diverse aromatic compounds (e.g., crystal

violet, methylene blue, and neutral phosphorus triphenyl). The results showed that graphene oxide in the proposed substrates stimulated analyte enrichment and SERS effect on the substrate surface [33, 125]. Moreover, SERS substrates, such as conventional silver or gold colloids, bis-acridinium dication LG assembled Ag NPs, Ag NPs embedded mesoporous silicon, Ag NPs modified Fe_3O_4 @carbon core-shell microspheres, surface-imprinted core-shell Au NPs, have been used for the detection of organic pollutants including phthalic acid [130], tetracycline [131], nitrofurans [128], endosulfan [129], cyanine dye [130], pentachlorophenol and diethylhexyl phthalate [131], and bisphenol A [37]. To further improve the analysis sensitivity and portability, simple Ag NPs coated filter membranes were developed as SERS substrates for the trace detection of various organic compounds (e.g., melamine, 4-aminobenzoic, mitoxanthrone dihydrochloride, and flavonoids) [132].

In addition, recyclable active substrates of Au (or Ag) coated TiO_2 (or ZnO) were constructed with the multifunctional behavior for both SERS detection and photocatalytic

degradation of organic pollutants (Fig. 8) [133, 134]. Besides SERS detection, these substrates can be cleaned for reuse by photocatalytic degradation of the organic pollutants absorbed on their surfaces. The unique recyclable property of such substrates represents a promising application in organic pollutant detection as online sensors. It is still difficult to provide reliable qualitative detection of complex sample mixtures. To overcome such difficulties, our group has carried out the simultaneous multi-component detection of organic pollutants in a sample mixture by coupling SERS with pre-concentration and separation techniques. For polar organic pollutants such as anilines, phenols, and antibiotics, we established an analysis method which combines SERS with electrostatic pre-concentration (EP) through a portable SERS sensor [26]. Using this method, the polar molecules were selectively adsorbed for pre-concentration by controlling the applied potential and sensitive detection using SERS. For pollutants of substituted aromatics, we explored a facile on-site detection method by combing SERS with TLC [35]. In this way, various substituted aromatic pollutants can be separated using a facile TLC process and then detected by a portable Raman spectrometer with silver colloids

Fig. 8 **a** Scheme of the fabrication process of the gold-coated TiO_2 nanotube arrays (Au/TTA). **b** Scheme of reversible SERS behavior of a multifunctional SERS substrate. Reprinted with permission from ref. 133. Copyright 2010 Wiley



as SERS substrates. It is shown that such EP-SERS and TLC-SERS methods represent excellent candidates for the in-field detection for the emergency monitoring of pollution accidents involved with polar organic compounds and substituted aromatics.

Heavy metal ion detection

Heavy metal ions are an important class of inorganic pollutants which usually exist in the environment as oxy-metal ions or monatomic metal ions. In general, oxy-metal ions can be detected directly with SERS by identifying their specific spectral fingerprints. In contrast, direct SERS detection of monatomic metal ions is more challenging since they generally do not display vibrational spectra due to their small scattering cross section [135]. Consequently, a number of modified substrates have been invented and used for their SERS detection by monitoring the spectral changes of the modifier upon its interaction with the target ions. In this section, we focus on the recent achievements involving SERS detection of heavy metal ions, showing its potential application in environmental analysis.

Oxy-metal ions Arsenic species are considered as a kind of common oxy-metal ions which are generally found in environment in the form of arsenate (As^{5+}) and arsenite (As^{3+}). Since SERS of As^{5+} from silver colloids has been demonstrated successfully, a number of studies for the detection of arsenic species were performed with SERS [40, 136–138]. Yang et al. fabricated close-packed arrays of polymer-coated Ag nanocrystals using LB technique and applied them to the direct SERS detection of arsenic species by indentifying their SERS spectra [136]. Aided by a trapping agent poly(vinyl pyrrolidone), this close-packed arrays of nanooctahedra presented the most intensive activity for arsenic detection with sensitivity at ppb level. Thereafter, Meng et al. also conducted the SERS detection of arsenic species with Ag nanofilm prepared by a modified mirror reaction and an electroless deposition process, respectively [138]. They found that As^{5+} and As^{3+} species can be discriminated with the prepared SERS substrates and a good linear relationship could be obtained with LODs that ranged from 5 ppb to 10 ppb. In addition, a highly sensitive and selective method was developed for SERS detection of As^{3+} with a glutathione (GSH)/4-mercaptopyridine (4-MPY)-modified Ag NPs [40]. In this system, GSH conjugated onto the surface of Ag NPs was used for specific binding of As^{3+} through the As-O linkage, while 4-MPY was used as a Raman reporter. With this method, As^{3+} could be detected quickly and accurately with sub-ppb sensitivity.

Uranium is another common oxy-metal ions mainly existing in the environment as a state of UO_2^{2+} , which is

SERS active and produces typical symmetric stretching vibration peaks at near 700 cm^{-1} and 800 cm^{-1} [139–142]. However, ordinary SERS substrates can hardly generate SERS enhancements sufficient for uranium detection. Using a silver-doped sol-gel film prepared with a base-catalyzed process, Dai et al., reported the first observation of SERS signals from UO_2^{2+} . The SERS active film was prepared by an acid-catalyzed procedure and applied it to uranyl detection with a LOD of $8.5 \times 10^{-8}\text{ M}$ [139]. In order to further improve the detection sensitivity, new SERS substrates based on the modified metal NPs were developed and used for the SERS detection of uranyl ions [140–143]. For example, Teiten and Burneau fabricated SERS substrates through modifying the colloidal Ag NPs with 2-(5-bromo-2-pyridylazo)-5-diethylaminophenol and N-(2-mercaptopropionyl)glycine, which may form complexes with uranyl ions in solution [140]. These modified substrates revealed a uranium LOD of $10^{-8}\sim 10^{-9}\text{ M}$. In addition, SERS detection of uranium was also carried out by using (aminomethyl)-phosphonic acid modified Au NPs, which allowed uranium analysis at low concentrations with improved reproducibility [142]. More recently, Leverette et al. reported the trace detection and differentiation of uranyl ions with aligned Ag nanorod SERS substrates and Partial Least Squares Discriminant Analysis (PLSDA) approach [141]. As well, Bhandari et al., using silver modified polypropylene filter (PPF) substrates, achieved the detection of uranyl ion at concentration of 20 ng/mL without any surface modifications [143].

Monatomic metal ions The monoatomic mercury ion (Hg^{2+}) is considered to be one of the most toxic metal pollutants and it is challenging to detect directly with SERS. Thus, the “turn off” or “turn on” mechanisms are indirect methods for SERS detection of Hg^{2+} developed recently [144–152]. For example, Wang et al. demonstrated the highly sensitive detection of Hg^{2+} in water using SERS combined with droplet-based microfluidics [144]. In their work, aqueous droplets containing Hg^{2+} and SERS substrates of the reporter molecule (rhodamine B) adsorbed onto Au NPs served as individual reaction vessels. With this method, an initial SERS signal was recorded for rhodamine B adsorbed on Au NPs. The SERS signal decreased in presence of Hg^{2+} ions because of the stronger affinity with Au NPs and displacement of rhodamine B molecules. Through monitoring this “turn off” change in SERS signal, quantitative analysis of Hg^{2+} could be accomplished with the LOD at about 100 ppt. Taking advantage of this “turn off” mechanism, SERS substrates such as, 4-mercaptopyridine conjugated Ag NPs [145], *para*-aminothiophenol coupled Au NPs [146], mesna-modified Ag NPs [147], aptamer-modified Au/Ag core-shell NPs [148], and Au-Ag alloy NPs adsorbed by aminated ring-close structure of rhodamine 6 G [149] were also developed and applied to the highly efficient detection of Hg^{2+} . Despite

these advances, SERS detection based on the “turn on” mechanism represents a better alternative method to further improve the detection selectivity for Hg^{2+} ions. By exploiting the selective and strong binding of Hg^{2+} to thymine-thymine base pairs (T-Hg²⁺-T), Chung et al. demonstrated a “turn on” SERS probe for the detection of Hg^{2+} with a single DNA-modified gold microshell [32]. This strategy was further developed with a single Au nanowire-on-film SERS platform by Kim et al., which showed that the LOD of Hg^{2+} was 100 pM and the sensor was stable for storage. Similar with the “turn on” sensing of Hg^{2+} , other monatomic metal ions such as Pb^{2+} , Cu^{2+} , Cd^{2+} , Cr^{3+} , etc. can also be detected in an indirect way using SERS aided by different specific ligands including DNAzyme, 2-mercaptobenzimidazole, trimercaptotriazine, citrate, etc. [150–153]. The detected SERS signals correspond to the specific interaction between the metal ions and the ligands (also serve as Raman reporters). This method can reduce the potential background signals from other species in the sample with the use of ligands as internal standards.

Metal ions often coexist in one sample, their multiplex detection is highly desirable. To achieve this goal, powerful ligands which can both serve as SERS reporter and bind to various metal ions to generate different Raman spectroscopic shifts were functionalized onto (or mixed with) the silver or gold SERS substrates. These were used to simultaneously immobilize and identify metal ion analytes [154–156]. For instance, Chiş et al. have demonstrated the potential of 1-(2-pyridylazo)-2-naphthol and Eriochrome Black T in the multiplex detection of metal ions such as Al^{3+} , Mn^{2+} , Fe^{3+} , Cu^{2+} , Zn^{2+} and Pb^{2+} using SERS spectroscopy coupled with quantum chemical calculations to characterized the vibrational spectra of their chelating complexes [155]. In order to improve the capability of determining the relative contributions of

various metal ions in a mixture, a SERS active separation medium was prepared by anchoring 4-mercaptobenzoic acid-modified Au NPs on the inner wall surface of the glass capillary. The fabricated capillary could be used to identify the metal ions according to the different equilibrium constants of the coexisting metal carboxylate ion complexes (Fig. 9a) [157]. Although these assays are effective, it is still challenging to achieve portable metal ion detection for field applications. Accordingly, Kim et al., using metal ion-specific dsDNAs, developed an Au nanowire (NW)-on-chip SERS sensor for rapid, sensitive, and multiplex detection of metal ions (Fig. 9b) [158]. In this work, Hg^{2+} , Ag^{2+} , and Pb^{2+} could be detected simultaneously and selectively in a sample mixture with a LOD lower than 50 nM.

As introduced herein, numerous studies have focused on SERS detection of heavy metal ions and progress has been achieved in this field with these existing SERS methods, while only a limited number of metal ions can be detected. Moreover, problems including nanoparticle aggregation, nonspecific binding, and biomolecule denaturation may readily lead to false results. For this reason, more emphasis should be placed on developing novel SERS substrates or methods to expand the applicable scope of SERS detection for additional metal ions and improving their selectivity, reproducibility, and feasibility for the detection of real samples.

Pathogens detection

The applications of the SERS technique in environmental analysis are not limited to the detection of organic compounds and metal ions. Due to the capability of obtaining sensitive fingerprint spectra rapidly, SERS represents a promising technique for the detection and identification of pathogens in

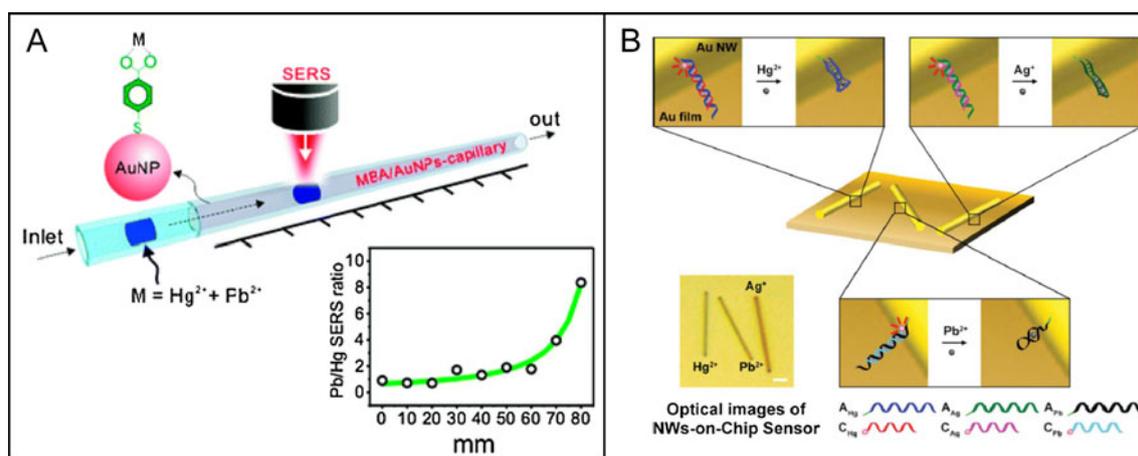


Fig. 9 a Schematic representation of the visualization of the chromatographic separation and SERS analysis of heavy metals. Reprinted with permission from ref. 157. Copyright 2011 American Chemical Society. b Schematic representation of the alignment-addressed

Au NWs on-chip sensor. The dsDNAs-modified single Au NW works as a specific metal ion sensor, integration of which enables multiplex detection of toxic metal ions. Reprinted with permission from ref. 158. Copyright 2012 Royal Society of Chemistry

environmental samples [9, 21]. Actually, SERS has been utilized for the detection of various pathogens [159], e.g., *Giardia* [24], *Enterococcus faecalis* [160], *Streptococcus pyogenes* [160], *Acinetobacter baumannii* [160], *Klebsiella pneumonia* [160], *Salmonella typhimurium* [161–163], *Pseudomonas aeruginosa* [163], *Bacillus megaterium* [164], *Staphylococcus cohnii* [164], *Helicobacter pylori* [165], *Listeria monocytogenes* [166], *Erwinia amylovora* [167], and *Escherichia coli* [168, 169].

SERS detection of pathogens is achieved mainly through obtaining representative spectra of the chemical composition of the pathogen membrane. The related studies were performed by simply mixing or coating pathogen samples with colloidal Au NPs or Ag NPs and then directly collecting their SERS spectra on a glass slide or in a cuvette [21, 159]. This strategy is straightforward and simple to carry out, whereas, the reproducibility of the detection is hard to control because metal NPs often distribute randomly on the surface of pathogen cells. To address this challenge, periodic nanoparticles cluster arrays and quasi-3D Au plasmonic nanostructure arrays were fabricated with the EBL technique [169]. These arrays have regular structures and excellent plasmonic properties, thus allowing for the quantitative and reproducible detection of pathogen species with SERS. In addition, the detections of pathogen samples whose concentrations are too low to be directly detected by SERS require pre-concentration processes to improve the limit of detection. For example, Vikeslan et al. developed a SERS-based concentration method for the sensitive detection of *Giardia lamblia* cysts in water, wherein the cysts were pre-concentrated with a membrane filter and labeled with immunogold SERS labels and quantified *via* SERS [25]. After optimizing the detection conditions, the LOD <10 cysts per L could be achieved with this method. In addition, multifunctional magnetic-plasmonic Fe₃O₄-Au core-shell nanoparticles (Au-MNPs) can also be used for fast pre-concentration and sensitive detection of bacteria by SERS [170]. By applying an external magnetic field, bacterial cells can be concentrated 60-fold prior to SERS detection.

Although such approaches work well, it is still difficult to discriminate microorganisms solely by SERS since the chemical components of the membranes of many microorganisms are similar, especially for different strains of the same species. Thus, statistical methods, such as principal component analysis (PCA) and hierarchical cluster analysis (HCA), are introduced into SERS detection to resolve this problem [21, 159]. By this means, the identification of pathogens at the strain level can be accomplished. Moreover, combining SERS with immunoassay is attractive because of its high sensitivity and selectivity, representing another potential method for the detection and identification of pathogens. For instance, Porter et al. developed the early SERS-based immunoassay method for the low-level detection

of viral pathogens by using Au NPs conjugated with antibodies and Raman reporters (Fig. 10a) [171]. After incubation with the antibody modified Au NPs, the model target feline calicivirus was easily differentiated according to the signals from the reporters. A series of other methods combining SERS with this sandwich immunoassay were also developed for the selective and sensitive detection of various pathogens by functionalizing specific pathogen antibodies on SERS substrates such as gold nanorods, silica-coated magnetic nanoparticles (MNPs), gold-coated MNPs, etc. [41–43, 172].

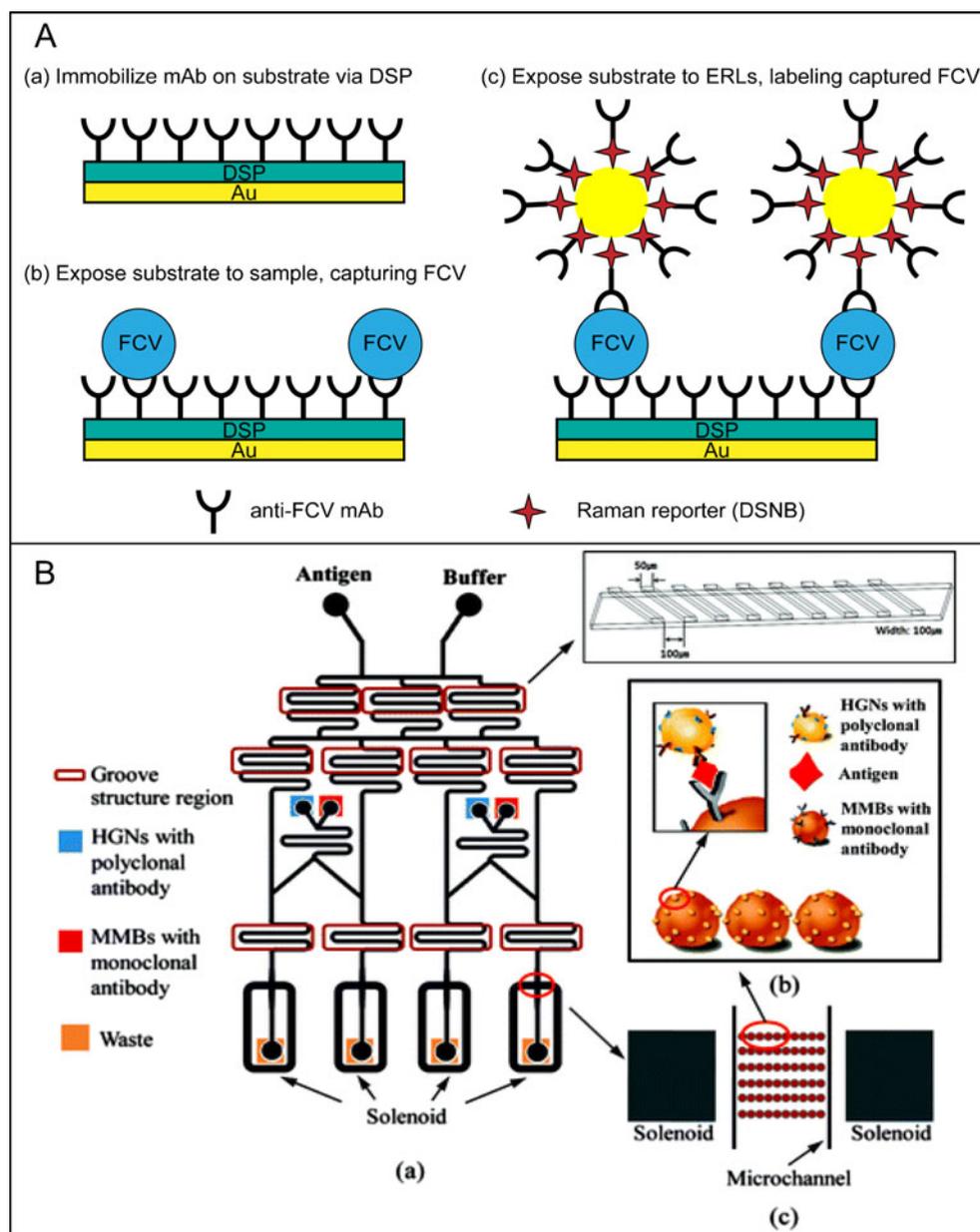
These achievements demonstrate that a large number of notorious pathogens can be successfully identified using the SERS technique without cell culture or DNA extraction. However, further efforts are required to improve the operability of the processes to bring SERS methods as a routine application in pathogen detection. In this regard, the combination of SERS with immunoassay and fluidic devices might be a promising candidate due to its potential for meeting the high efficiency requirements and automation requirements of microorganism detection. For example, a novel microfluidic sensor with functional internal structures was developed for the on-chip immunoassay using SERS. Since almost all of the detection conditions are automatically disposed inside the exquisitely designed microfluidic channel, less than 30 min is required to perform the assay from serial dilution to SERS detection (Fig. 10b) [173, 174].

Conclusions and outlook

Since the first observation in the 1970's, SERS has illustrated its potential as an excellent analytical approach for a wide range of research and applications due to its capability of achieving highly sensitive detection of analytes and providing related structural information. In this review, we summarized the latest published research in the past few years on SERS-based methods and their application in environmental analysis. It has been demonstrated here that various environmental pollutants such as organic compounds, heavy metal ions, and pathogens can be detected with SERS by rationally designing the active substrates and skillfully combination with other techniques. We hope the introduction and discussion of these achievements will provide the appropriate background for developing novel analysis methods for the detection of diverse environment pollutants with SERS.

Like any other burgeoning analytical technique, SERS also has its own challenges for the real implementation in environmental analysis. Although tremendous efforts have been made to improve the sensitivity and reproducibility of SERS substrates, certain pollutants at trace concentration are still difficult to detect and the reliable analysis of real samples still poses challenges. Furthermore, due to the operational

Fig. 10 **a** Schematic illustration of the steps in the SERS-based immunoassay of feline calicivirus (FCV). Reprinted with permission from ref. 171. Copyright 2009 American Chemical Society. **b** Layout of SERS-based gradient optofluidic sensor integrated with solenoids (**a**), formation of sandwich immunocomplex between hollow gold nanospheres and magnetic beads (**b**), and trapping of sandwich immunocomplexes in a microfluidic channel (**c**). Reprinted with permission from ref. 173. Copyright 2010 American Chemical Society



inconvenience and limitations on batch fabrication, a great number of SERS substrates or methods reported in literatures are not suitable for large batch of tests which are often required for the environmental analysis both in lab and in field. The tested samples are often complex that multiple spectral peaks are generated during SERS detection, thus making it very difficult to identify each component from the SERS spectra.

In order to address such challenges, we believe the future growth of pollutant detection with SERS should be focused on the following issues: Firstly, sensitivity and reproducibility of active substrates are still one of the major concerns in SERS detection. Higher sensitivity and reproducibility of SERS substrates will be helpful to provide more precise quantitative detection of environmental pollutants. In addition, to further

improve the operability of detection process, efforts should be directed to the development of novel multi-channel SERS-active devices enabling larger batch production, more facile operation, greater cost efficiency, and better portability. When coupled with a portable Raman spectrometer, this robust approach can be easily extended to in-field detection. Another encouraging aspect in SERS detection of pollutants, especially for complex samples, is the coupling of SERS and separation techniques (e.g. such as CC, CE, and TLC) [44–50]. We anticipate that this trend will continue though the future design of a portable integrated system, where separation functions are coupled with SERS detection. On the other hand, chemometrics methods could also be combined with powerful SERS substrates to improve the

resolution capability for various components. It is expected that the continued studies and achievements in this field will significantly advance the practical application of the SERS technique for environmental analysis.

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