Surface enhanced Raman scattering analysis with filter-based enhancement substrates: A mini review

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Abstract: Surface enhanced Raman scattering is a powerful analytical tool with high sensitivity and unique specificity and promising applications in various branches of analytical chemistry. Despite the fabrication of ingenious enhancement substrates used in laboratory research, the development of simple, flexible, and cost-effective substrate is also great importance for promoting the application of SERS in practical analysis. Recently, paper and filter membrane as support to fabricate flexible SERS substrates received considerable attentions. Paper-based SERS substrate has been reviewed but no summary on filter-based SERS substrate is available. Compared with paper, filter membrane has unique advantage in robust mechanics, diverse component, and tunable pore size. These characteristics endow the filter-based substrates great advantages for practical SERS analysis including simple and low-cost substrate preparation, high efficiency in preconcentration, separation and detection procedure. Therefore, filter-based substrates have shown great promise in SERS analysis in environment monitoring, food safety with high sensitivity and efficiency. As more and more work has been emerged, it is necessary to summarize the state of such a research topic. Here, the research on filter involved SERS analysis in the past eight years is summarized. A short introduction was presented to understand the background, and then the brief history of filter-based substrate is introduced. After that, the preparation of filter-based substrate and the role of filter are summarized. Then, the application of filter involved SERS substrate in analysis is presented. Finally, the challenges and perspective on this topic is discussed.

Keywords: SERS, flexible substrate, food safety, environment monitoring, concentration, separation

1 Introduction

Surface-enhanced Raman spectroscopy (SERS) has become one of the most versatile and powerful analytical techniques due to its ultrahigh sensitivity (single molecule), unique “fingerprint” specificity and non-destructive analysis in molecule sensing [1]. These unique advantages make SERS a promising tool in various branches of analytical science, such as environment monitoring, food analysis, surface analysis, disease diagnosis and so on [1-3]. It is well known efficient enhancement SERS substrates play a vital role in achieving these advanced applications. Up to now, a mass of substrates with different components, structures and arrangements have been developed, and these studies continue. Searching new materials (semiconductor [4], graphene [5], metal organic framework [6], etc.) to achieve Raman signal enhancement is always an important topic in SERS research, and several excellent Reviews on this topic have been published [7-9]. Although many advanced Au/Ag micro-nano-structures or their hybrid with other materials have been developed for SERS analysis, most of them are only prototype used in lab analysis. The fabrication of these substrates often requires sophisticated equipment or elaborate skills, or high cost, which makes it hard to massive production, and thus not available for practical analysis.

In addition to explore new component material, the development of flexible and easy-prepared substrate becomes a new trend in recent years on the demand of practical analysis [10-12]. On this issue, paper- or filter-based SERS substrate have received considerable...
attentions. Gold or silver nanoparticles prepared by wet-chemical synthesis can adsorbed on or assembly on flexible matrix to form the flexible substrate. This substrate has good mechanical resistance, display high efficiency in target capture and detection on uneven surface, and can be cut into the desired size and shape, easily integrated with other structures or devices. That is why flexible substrates are important for advancing the real-world application of SERS technology. Currently, flexible SERS substrates are mainly based on fiber paper [13], filter membrane [14], flexible polymers [15], carbon nanotubes, and graphene materials [16]. Paper-based flexible SERS substrate have been widely reported, and their progress has been summarized by several good reviews published in recent years [10-12,17,18]. Compared with paper, filter is more versatile in component and structure, robust in mechanism, and more efficient for concentration by rapid and large-volume filtration [19]. In addition, filtration can be used to achieve the fast and uniform assembly of plasmonic particles on the filter or other matrix. These merits provide a guarantee to obtain a highly sensitive and reproducible SERS signal, which is important for practical quantitative analysis. Therefore, filter-based SERS substrate have been developed with great foresight and have attracted many researchers into the field, which shows great promise in environmental monitoring, food analysis, and so on [19].

At present, there is no review published on filter membrane-based substrates for SERS analysis, although nanofiber-based membrane for SERS analysis have been summarized in 2018 [20]. To better understand the origin and progress of filter-based SERS analysis, and further promote its research, we summarize the work on this topic in the past ten years here. We hope that it will play a positive role in promoting SERS to be a competitive tool in fast and accurate practical analysis. The main contents of the paper include: (1) origin and evolution of filter-based SERS substrates, (2) preparation of filter-based SERS substrates, (3) roles of filter in SERS analysis, (4) applications of filter-based substrates in SERS analysis, (5) challenges and perspective. The application is further divided into: (I) inorganic analysis, (II) organic analysis, (III) biomolecule analysis, and (IV) others depending on the type of analytes. About 50 related work on filter-based SERS analysis are cited.

2 Origin and evolution of filter-based SERS substrates

Previously, Au or Ag NPs suspension or exquisite Au/Ag nanoparticle assembly on hard matrix (such as glass or silicon slide) are often used as SERS substrate to incubate with target molecules for SERS analysis [21]. Directly using plasmonic particle suspension as substrate is simple, but the resulted SERS signal is poor in reproducibility. Therefore, Au/Ag assembly with order/periodic arrangement are developed to improve the reproducibility of SERS signal [22]. Nevertheless, the design and preparation of perfect Au/Ag assembly needs sophisticated skills. In addition, SERS analysis using both of these substrate needs a long-time incubation with target to improve the signal intensity, which leads to low detection efficiency. Considering these issues, a fast, simple method to prepare a highly active SERS substrate for sensitive and reproducible analysis is of great demand.

2.1 Origin

In 2012, Yu and White [19] developed the first filter-based SERS substrate, which is simple but highly efficient and fulfills all these requirements. They used syringe, Ag sol suspension and filter membrane to prepare the filter-based substrate as presented in Figure 1. The preparation is simple, economic, and fast. The subsequent detection is also simple and highly efficient as the filtration can not only concentration analyte, but also reduce the detection time (by avoiding long time incubation) and improve the signal reproducibility (by assembly AgNPs on filter under vacuum filtration). Thus, such substrate shows great promise in practical trace chemical analysis, and more and more work are published on this topic from then on [23-33].

![Figure 1: Schematic the pioneer work from Ian’s group on the fabrication, enrichment and SERS detection of filter-based substrate prepared by simple syringe filtering [19].](image-url)
2.2 Evolution

As the research continues, various filters were used to fabricate the active SERS substrate. The material of filter changes from paper [19,23] to organic polymer [19], glass fiber [24], AAO [25], or even use composite material itself as "filter" [26]. The loaded active materials also vary from spherical Au/Ag nanoparticles [19] to nanorod/nanowire [27,28], nanostar [23], or Au/Ag-based hybrid with SiO$_2$ [29], active carbon [30], cellulose nanofiber [31,32], etc. In most cases, commercial filter is used to support these materials as various substrate. However, in some cases, no typical filter paper or filter membrane was used, instead, Au/Ag particles with other functional materials (such as cellulose nanofiber) are mixed and filtrated to form an interlaced structure as a home-made filter [23,27]. These works are also included in this review.

3 Preparation of filter-based SERS substrate

Up to now, several approaches have been developed to prepare filter-based substrate or filtration involved SERS substrate. These approaches can be divided into four types according to their preparation or detection process as shown in Scheme 1.

1. Direct assembly of plasmonic particles suspension onto filter matrix by filtration [24,27,33]. This is the most widely used approach to prepare filter-based SERS substrate as it is fast and simple, and the particles can be uniformly arranged on the matrix. As particles are assembled onto filter by physical filtration, no surface treatment of the filter is needed, and the shape and size of Au/Ag can be easily tuned.

2. Adsorb or in situ growth of Au/Ag nanoparticles onto filter or other matrix [34,35]. These two approaches are widely employed to prepare paper-based substrate, and thus it is rational to transfer the methods to prepare filter-based substrate. Indeed, many filter-based substrates employed paper as filters [35]. Nevertheless, this method may not as convenient as the first one, as surface functionalization is required to achieve the high uniform loading particles onto the matrix. Besides, spherical particles are used in most cases, as other shape particles have low affinity to the filter or hard to achieve in-situ growth on filter matrix.

3. Transfer Au/Ag assembly or aggregate onto filter or other matrix by filtration [19,36,37]. To improve the reproducibility, Au/Ag was first assembled into ordered structures, and then coat them onto the filter [36]. Au/Ag assembly transfer to filter by filtration can improve its mechanical property, and thus provide more reproducible signals during multiple detection (RSD < 5.9 [36]). Sometimes, salt induced AgNPs aggregates suspension was passed through the filter to get the SERS substrate [19,37]. In this case, the filtration may improve the signal reproducibility.

4. Au or Ag nanoparticles first anchored Au/Ag onto porous matrix or fibers, and then engineered them into a filter [29]. Lin et al. [29] produced AuNPs onto porous silica, and then pressed them into filter like disc. Jia et al. [30] anchored Au/Ag onto porous SiO$_2$ and assembled them into column tube. Ankudze et al. [26] decorated cotton fiber with AuNPs and processed them into flexible pellet. In these cases, porous matrix such as active carbon, SiO$_2$, or cotton fiber are used as matrix to improve the adsorption ability and the Au/Ag loading efficiency. The processed product can be used as enhancement substrate and filter, and thus no commercial filter is needed.

4 Roles of filter or filtration in SERS analysis

The fabrication of filter-based SERS substrate is simple, but their performance is still desirable, especially for practical analysis. One of its features is the filtration operation, which bring it several advantages over other traditional substrate or ordinary paper-based substrate. Here, the role of filter or filtration are summarized (Scheme 2).
4.1 As support matrix to anchor Au/Ag NPs

Au/Ag nanoparticles can be directly grown onto filter surface or coated onto filter by filtration. Compared with in situ growth, filtration is simpler and versatile. In addition, filtration may improve the plasmonic particle loading on the matrix due to that filtration pressure can squeeze the Au/Ag nanoparticles into the inner layer of the matrix (such as the inner fiber of filter paper) [29,35], which produce more hot spots in Z direction [19,32]. The filtration can be achieved by manual pushing syringe [17,24,36] or by mechanical pump suction [24,33,38]. Au/Ag NPs with different morphology and dosage has been loaded onto filter to fabricate the SERS active substrate [33]. The effect of filtration procedure (For example: assembly 20 mL AgNPs onto filter by one (20 mL), two (10 mL/per), or four (5 mL/per) filtrations on the final SERS signal was also studied [33].

The flexible, transparent membrane makes it suitable for SERS analysis on real sample surface using both front and back excitation [28].

4.3 Concentrate analyte by filtration

This is one of the best merits for filter-based SERS analysis. During filtration, the analyte in sample can be captured by the filter-based SERS substrate to achieve fast concentration effect. In this aspect, the substrate also functions as a solid phase extraction material in addition to its SERS enhancement effect. So, filter-based SERS substrate displays great advantage for large volume sample analysis, such as environmental monitoring and food analysis. One typical example comes from Zhan’s group [27], who assembled AgNW on filter as solid phase extraction material to concentrate phorate and melamine and as SERS substrate to enhance Raman signal of targets.

4.2 Assembly Au/Ag nanoparticles with other material to form hybrid substrate

Usually, Au/Ag nanoparticles were mixed with other functional material, and then they were passed through a filter to form a hybrid membrane, which shows high SERS enhancement and other characteristics, such as flexibility, high surface area, high affinity/adsorption to analyte. For example, Kim et al. used filtration to assembly Au nanoparticles or Au nanowire with cellulose nanofiber to form a hybrid filter membrane for SERS analysis.

4.4 Separation non-target molecule by filtration

Separation is an intrinsic property of a filter. This function can be used to capture the target with large size, such as bacterial, or Au/Au nanoparticles coupled with target molecules, which also brings concentration effect. It also used to separate small molecules or uncoupled target probe to reduce the interferences from the complex sample matrix. For example: Wu et al. [40] developed a two-step filtration process to detect pathogenic bacteria Salmonella Poona from cantaloupe cubes. For determine E. coli O157:H7 from lettuce, a three-step filtration is needed, where an additional filtration is performed to separate interference chlorophyll from bacterial sample using a hydrophobic filter [40].

4.5 Combined merits

In most cases, filter-based SERS substrate often shows combined merits, such as assembly plasmonic particles, concentration, separation. For example, in the pioneer work by Yu and White, the filtration was used to assembly Ag sol to form the SERS substrate, and it also used to concentrate analyte onto this substrate for SERS detection. One representative work is from Cho et al. [41]. In their work, the filtration plays multiple roles. First, the bacteria-gold nanoparticle-magnetic bead complex was captured by the filter membrane. At the same time, non-coupled
gold nanoparticle or magnetic bead and sample matrix were passed through the filter, acting as a selection role to reduce the interference. During filtration, more and more bacteria-gold nanoparticle-magnetic bead complex was retained on the filter, which plays a concentration effect. By combining these effects, highly sensitive detection of target with good signal to noise ratio can be achieved, which is preferred for biosensing for complex sample [41].

5 Applications of filter-based SERS substrates in analysis

With the merits of simple preparation, high concentration, fast detection, filter-based SERS has shown great promise for practical analysis. The analytes have ranged from inorganic material to organic molecule and biomolecules as summarized in Table 1. The reproducibility, stability and selectivity of these substrates were summarized in Table 2. In this part, filter-based SERS for practical analysis is summarized and typical examples are discussed depending on the analyte type.

5.1 Inorganic analysis

Usually, SERS is not an excellent choice to determinate inorganic materials as most inorganic matters show extremely low Raman cross-section, which result in quite weak signal [42]. As an alternative, some specific indicator (usually organic dye) was introduced to achieve the indirect, sensitive detection of the inorganic material. Considering this, the concentration effect in filter-based SERS is a good compensation for improving sensitivity. For example, Guo et al. [37] designed an approach to detect the AgNPs in water by combining a filtration technique with surface-enhanced Raman spectroscopy (SERS). In their work, filtration was used to trap and enrich the target AgNPs from water samples, and then indicator ferbam was passed through the filter to complex with Ag to give SERS signal. The filtration shows unique advantage in processing large volume samples, which not only greatly improves the sensitivity of AgNP detection (LOD 5 mg/L, 20 folds lower than the centrifuge-based method), but also elevates the speed and precision of the detection [37]. In addition, filtration-SERS is also employed to analyze the heteroaggregation behavior of AgNPs with minerals, shows powerful performance in evaluation of the particle’s fate and transport behavior, and thus great promise for environment monitoring [37].

Compared with solid inorganic particles, gaseous inorganic analyte is hard to be captured, and thus its sensitive detection is more challenging. By combing Au/Ag with other functional materials, effective concentration gaseous analyte can be achieved. For example, Deng’s group developed a paper-based device (PAD) for colorimetric and SERS dual mode detection of SO$_2$ in wine samples [43]. The schematic illustration of the setup can be found in Figure 2. The novel PAD is fabricated by vacuum filtration of 4-mercaptopyridine (Mpy)-modified gold nanorods (GNRs), reduced graphene oxide (rGO) and SIC to form the hybrids (rGO/Mpy-GNRs/SIC). The PAD was used as a headspace sampling device to capture SO$_2$ and separate it from complex wine matrix. The presence of SO$_2$ could increase the SERS signal as SO$_2$ triggered conversion of Mpy to pyridine methyl sulfate on the GNRs. Such a PAD-based SERS method is effective for SO$_2$ detection with a wide range of 1 μM to 2000 μM, and a detection limit of 1 μM [43]. The substrate displays good reproducibility (RSD < 15) and high stability (no significant change in signal position or intensity was observed after 10 week storage). The combination of filtration with SERS makes the work is simpler, time-saving, high reliable and selective compared to commercial techniques or conventional methods, thus providing a promising method for rapid analysis of volatile compounds in complex matrix samples [43].

5.2 Organic analysis

SERS have been widely used in ultrasensitive detection of organic molecules, especially some environment pollutants such as aromatic dyes, pesticides, antibiotics. The large volume sample process ability of filtration indicates filter-/filtration-based SERS analysis is a good technique for environment monitoring. The following will list some representative work based on the categories of analyte.

5.2.1 Aromatic dye

Aromatic dyes such as crystal violet, Rodanmine 6G, and methylene blue are often used as probe to evaluate the enhancement ability of a new SERS substrate as they are easy to generate obvious Raman scattering signal due to their large cross section. So, detection one of these aromatic dyes is used to compare the performance of different SERS substrates. On the other hand, these aromatic dyes are also important environment pollutants, whose accurate detection is of importance for environment protection.
Table 1: Summaries of the filter-based SERS substrates and its detection performance in SERS analysis

| Analyte   | Filter substrate                                           | Linear range       | Detection limit | Ref.    |
|-----------|------------------------------------------------------------|--------------------|-----------------|---------|
| AgNPs     | AgNPs on PVDF Filter                                      | from 0.025 μg/L to 1 μg/L | 5 μg/L          | [37]    |
| SO₂       | rGO/Mpy-GNRs on cellulose filter paper                    | from 1 μM to 2000 μM | 1 μM            | [43]    |
| H₂O₂      | Ag triangular nanoplates on PVDF filter                   | from 10⁻⁴ to 10⁻⁹ M | 0.15 nM         | [55]    |
| R6G       | AgNPs on nylon filter                                     | N.A.               | 10 nM           | [19]    |
| R6G       | BPWHW/AgnW- GFFP on glass fiber filter                    | from 10 to 0.2 pmol/cm² | 0.2 pmol/cm² | [24]    |
| R6G       | TEMPO-CNfs- AuNPs on cellulose ester filter               | N.A.               | 10 nM           | [28]    |
| R6G       | AuNR-cellulose hydrogel filter                            | N.A.               | 10 pM           | [31]    |
| R6G       | AgNPs array-graphene on nylon filter                      | from 1×10⁻⁹ to 5×10⁻⁶ M | 0.2×10⁻¹² M     | [36]    |
| R6G       | AgNPs on filter membrane                                 | N.A.               | 1 pM            | [38]    |
| R6G       | PCNs/Ag-MFs@r-GO on PTFE filter                            | from 10⁻¹² to 10⁻¹⁵ M | 10⁻¹⁵ M        | [45]    |
| R6G particles | AgNPs on glass microfiber filter                        | N.A.               | from 0.6 to 3 mg/m³ | [46]    |
| R6G       | AgNPs on nylon filter                                     | N.A.               | 5×10⁻¹⁴ M       | [50]    |
| CV        | Ag/Au on polyamide filters                                | N.A.               | 100 aM or 10 fM | [33]    |
| CV        | AgNPs on filter membrane                                 | N.A.               | 10 pM           | [38]    |
| MG        | AgNPs on filter membrane                                 | N.A.               | 10 pM           | [38]    |
| Melamine  | AgNPs on nylon filter                                     | N.A.               | 6.3 ppb         | [19]    |
| Melamine  | AgNW on nylon filter                                      | from 1 to 100 μg mL⁻¹ | N.A.            | [27]    |
| Melamine  | AgNPs on nylon filter                                     | N.A.               | 5×10⁻⁸ M        | [50]    |
| Melamine  | AgNC@SiO₂ on filter paper                                 | from 0.063 to 1 mg/L | 0.17 mg/L      | [51]    |
| Melamine  | AuNPs-on home-made centrifuge filter                     | from 30 to 90 ppm  | 10 ppm in milk  | [52]    |
| Malathion | AgNPs on nylon filter                                     | N.A.               | 61.5 ppb        | [19]    |
| Paraquat  | BPWHW/AgnW-GFFP on glass fiber filter                     | from 20 to 2000 ng/cm² | 20 ng/cm²      | [24]    |
| Phorate   | AgNW on nylon filter                                      | from 2.5 to 10 μg mL⁻¹ | N.A.            | [27]    |
| Thiram    | TEMPO-CNfs-AuNPs on cellulose ester filter               | N.A.               | 100 nM          | [28]    |
| Thiram    | AuNR-Cellulose hydrogel filter                            | N.A.               | 100 fM          | [31]    |
Table 1: (continued)

| Analyte          | Filter substrate                                      | Linear range                      | Detection limit | Ref.   |
|------------------|-------------------------------------------------------|-----------------------------------|-----------------|--------|
| Methomyl         | AgNPs- bacterial nanocellulose on filter              | from $10^{-7}$ to $10^{-3}$ M     | 3.6$\times$10$^{-7}$ M | [32]   |
| Penicillin G     | AgNPs-AC on nylon filter                              | from $6.0\times10^{-8}$ to $4.0\times10^{-3}$ M | 2.5$\times$10$^{-9}$ M | [30]   |
| Ampicillin       | AgNPs-AC on nylon filter                              | from $8.0\times10^{-8}$ to $8.0\times10^{-3}$ M | 3.2$\times$10$^{-9}$ M | [30]   |
| Pyrene           | AuNPs-GMA-EDMA on filter                              | from $3\times10^{-10}$ to $1\times10^{-9}$ M | 2.1$\times$10$^{-10}$ | [54]   |
| Benzopyrene      | AuNPs-GMA-EDMA on filter                              | from $1 \times 10^{-9}$ to $2 \times 10^{-8}$ M | 3.8$\times$10$^{-10}$ M | [54]   |
| Phenanthrene     | AuNPs-GMA-EDMA on filter                              | N.A.                              | 8.3$\times$10$^{-10}$ M | [54]   |
| Benzofluoranthene| AuNPs-GMA-EDMA on filter                              | N.A.                              | 1.7$\times$10$^{-10}$ M | [54]   |
| Choline          | Ag triangular nanoplates on PVDF filter               | from $10^{-3}$ to $10^{-7}$ M     | 8.36 nM         | [55]   |
| 4-ATP            | AgNW-Cotton Pellet as filter                          | N.A.                              | 1$\times$10$^{-9}$ M | [26]   |
| 4-ATP            | AgNW on nylon filter                                  | from 0.001 to 0.1 μg mL$^{-1}$    | NA              | [27]   |
| E. coli          | AgNW-Cotton Pellet as filter                          | N.A.                              | N.A.            | [26]   |
| E. coli          | Ab-Au-Ag on nylon filter                              | N.A.                              | 1000 CFU/mL     | [41]   |
| E. coli          | Silver-nanorod on PEFE filter                         | N.A.                              | 10 CFU/mL       | [40]   |
| E. coli          | AuNP-on PVDF filter                                   | N.A.                              | 10 CFU/mL       | [58]   |
| Staphylococcus   | Au@meporous SiO$_2$ compressed into filter            | N.A.                              | N.A.            | [29]   |
| Salmonella       | Silver-nanorod on PEFE filter                         | N.A.                              | 100 CFU/mL      | [40]   |
| Salmonella       | AuNPs on nitrocellulose filter                        | from $4.7\times10^7$ to $1.4\times10^7$ CFU/mL | 10$^7$ CFU/mL | [57]   |
| Dimethyl disulfide| AuNSs-AAO filter                                     | from $1.0\times10^{-8}$ to $1.0\times10^{-3}$ M | 10 nM          | [25]   |
Table 2: Summaries of the repeatability, stability and selectivity of filter-based SERS substrates listed in Table 1

| Filter substrate                              | Repeatability/reproducibility                                      | Robustness/stability          | Selectivity | Ref. |
|-----------------------------------------------|-------------------------------------------------------------------|-------------------------------|-------------|------|
| AgNPs on PVDF Filter                         | RSD 2.2%–6.3% (spots to spots)                                   | N.A.                          | N.A.        | [37] |
| rGO/Mpy-GNRs on cellulose filter paper       | Below 15% (spots to spots)                                       | 10 weeks                      | good        | [43] |
| Ag triangular nanoplates on PVDF filter       | 6.89% (spots to spots), 5.05% (10 substrates)                    | N.A.                          | good        | [55] |
| BPWHW/AgNW-GFP on glass fiber filter         | Below 12% (spots to spots)                                       | N.A.                          | good        | [24] |
| TEMPO-CNfs-AuNPs on cellulose ester filter   | Below 9.6 (spots to spots)                                       | Anti-1000 bending             | N.A.        | [28] |
| AuNR-cellulose hydrogel filter               | 2.78% (50 spots)                                                 | Anti-500 bending              | N.A.        | [31] |
| AgNPs array-graphene on nylon filter         | 5.91% (50 spots)                                                 | Over 25 weeks                 | N.A.        | [36] |
| AgNPs on filter membrane                     | 11% (10 batches), 8% (50 spots)                                  | Anti-500 friction             | good        | [38] |
| PCNs/Ag-MFs@r-GO on PTFE filter              | 6.62% (144 spots), 10.24 (5 batches)                             | Reuse for 5 cycles            | N.A.        | [45] |
| AgNPs on nylon filter                        | 9%                                                                | Two months                    | N.A.        | [50] |
| AgNW on nylon filter                         | 4.1% (24 spots)                                                  | RSD 6.2% for 130 s continuous laser irradiation | N.A.       | [27] |
| AgNC@SiO$_2$ on filter paper                 | 10.29% (10 spots)                                                | RSD 9% for 2 months           | N.A.        | [51] |
| AuNPs on home-made centrifuge filter         | N.A.                                                             | N.A.                          | good        | [52] |
| Ag/LCP on polyamide filters                  | N.A.                                                             | N.A.                          | good        | [39] |
| AgNPs- bacterial nanocellulose on filter     | 10%                                                              | Stable for 3 months           | N.A.        | [32] |
| AgNPs-AC on nylon Filter                     | Less than 15%                                                   | Within 2 weeks                | N.A.        | [30] |
| AuNPs-GMA-EDMA on filter                     | 8.66% (spots to spots), 3.69% (batches)                          | N.A.                          | N.A.        | [54] |
| AgNW-cotton pellet as filter                 | 7.5% (10 spots)                                                 | N.A.                          | N.A.        | [26] |
| Silver-nanorod on PEFE filter                | N.A.                                                             | N.A.                          | good        | [40] |
| AuNP on PVDF Filter                          | N.A.                                                             | N.A.                          | good        | [58] |
| AuNSs-AAO filter                             | 10.11% (100 x 100 μm$^2$)                                        | Stable for 7 days             | good        | [25] |
5.2.1.1 Rhodamine 6G

Rhodamine 6G (R6G) is one of the most used probes to test the SERS enhancement ability of new developed substrate. The pioneer work of filter-based SERS analysis from White’s group also used R6G to compare the performance of filter-based substrate and traditional drop-coated substrate [19]. Their filter SERS achieved a detection limit of 10 nM for R6G, which is at least 1-2 orders of magnitude better than the traditional substrate due to the concentration effect induced by filtration. Besides, high signal reproducibility is achieved on the filter-based substrate, which shows great potential in field-based quantitative analysis. Another work from Zhang et al. used AuNR to coat cellulose nanofiber by filtration as substrate to achieve the SERS detection of R6G with a LOD below 10 pM [44]. The high sensitivity can be ascribed to the low fluorescence and Raman background of the CNF matrix, and the concentration effect of filtration.

To improve the affinity of analyte to the substrate, new functional materials are used to integrate with Au/Ag to fabricate hybrid substrate. Qiu et al. [45] developed a ternary flexible membranes as sensitive and reusable SERS substrate for the detection of dye R6G. The ternary hybrid was fabricated by assembling reduced graphene oxide (r-GO), Ag meso-flowers (Ag-MFs) and phenyl modified carbon nitride nanosheets (PCNs) onto a filter using vacuum filtration. The mesoflowers provide high density of hotspot, and rGO is helpful to capture the dye R6G, while the PCN endows the flexible substrate self-cleaning characteristics. The produced PCNs/Ag-MFs@r-GO membrane shown a detection limit of $10^{-15}$ M for rhodamine 6G (R6G) molecules, and this membrane could be reused at least five times without obvious signal attenuation (95% retained) [45]. In addition, the PCNs/Ag-MFs@r-GO membrane can be also used as a high-efficiency filter membrane for simultaneous detection and purification in wastewater treatment using 10 mg/mL imidacloprid solution as the example [45].

Another interesting work comes from Yuan et al. [46]. Instead of determination of dye molecules in solution, they detected the R6G particles in air as a prototype of hazardous material in air. A home-made vacuum filtration paper chromatography-SERS (VF-PC-SERS) system was developed to achieve the sensitive detection of R6G powder, where glass fiber coated with AgNPs plays a central role for capture, separation, and identification of R6G particles with the help of vacuum pump. The detection can achieve a 100% accuracy (true positive rate) at R6G levels as low as 0.6 mg/m$^3$. 99% of R6G particles can be retained by this filter substrate. Selective detection of R6G at quite low content in powder mixture was also achieved. Such a VF-PC-SERS system may have great potential for on-site identification of hazardous material.

5.2.1.2 Crystal violet

Fateixia’s group [33] prepared a series of substrates by loading metal NPs onto polyamide (NL16, PA) filter membranes using reduced-pressure filtration. They used SERS analysis assisted with Raman imaging to optimize the fabrication parameter (chemical and morphological distinct plasmonic NPs (Ag, Au), NPs load and order of addition of analyte) of the filter type substrate. The interlaced microfibers of PA filter form a network to support the metal NPs. Thanks to the filtration operation, metal NPs not only
attached to the PA fibers at the surface but also migrated and are retained within the interior of the PA membranes, achieving a high density of SERS-active NPs [33]. Using crystal violet as probe, the substrate can achieve a detection limit for CV as low as 100 aM in ultrapure water and 10 fM in real samples, which is one of the lowest detection limits in reference.

5.2.1.3 Methylene blue
A simple AgNPs decorated filter paper was prepared by Meng et al. [47] for detection of methylene blue and 6-thioguanine. AgNPs were in-situ reduced via hydroxyl groups in cellulose under alkaline conditions. Using this filter substrate with a flow-through detection procedure, the detection limit is 0.374 μg/L and 10 μg/L for methylene blue trihydrate (MB) and 6-thioguanine (6-TG), which improves by 1-2 orders of magnitude compared to the common immersion method. Quantitative determination of MB and 6-TG were also achieved on this simple filter paper substrate by the flow-through method [47]. Thus, substrates fabricated by this simple and low-cost method have potential application in the monitoring of dyes, drugs, and pollutants.

5.2.1.4 Rhodamine 6G, crystal violet, and malachite green
Zeng et al. [38] used vacuum filtration to fabricate a silver nanoparticles (AgNPs) embedded nylon filter membrane (ANFM) as flexible paper-based SERS chips for point-of-care detection of dyes. The flexible ANFM can be cut into various size and shape depending on the practical analysis. The porous filter membrane as supporting matrix endows the ANFM-based SERS chips a high efficiency in separation of small molecules from complex mixture, resulting in “purified” SERS signals of targeted molecules. The filtration fabrication is simple and endows the substrate several merits such as high mechanical stability, low cost, and high signal reproducibility. The ANFM can be used to pre-concentrate target contaminants by multiple swapping on sample surface or paper chromatography separation. Therefore, ultrasensitive detection of dyes is achieved at concentration of 1 pmol for Rhodamine 6G (RH6G) and 10 pmol for both crystal violet (CV) and malachite green (MG), respectively [38].

5.2.2 Pesticide
Organic pesticides are widely used in modern agriculture; however, the overuse also pose great danger to human being and ecological system. Therefore, fast and sensitive identification of pesticide in various samples is of great importance. SERS has merit in identification of pesticides due to its high sensitivity and fingerprint specific response [48]. The filter type substrate with flexible property of filter makes it suitable to capture and concentrate pesticide on various sample surface. Some examples are presented here.

5.2.2.1 Malathion
The first work on filter-based SERS analysis from White’s group [19] also reported the detection of toxic illegal additive melamine and pesticide malathion in addition to probe R6G. In their work, common filter membranes can transfer into a SERS-active surface by trapping and concentrating nanoparticles from a colloid solution through a simple filtration using syringe. Concentration of analyte was also achieved by simple filtration. The fabrication of substrate and detection process is quite simple and rapid, while the sensing performance is encouraging in sensitivity, reproducibility, and time- and cost- efficiency. The detection limit for melamine and malathion is 6.3 ppb and 61.5 ppb, respectively, improving 200-fold than conventional approach [19].

5.2.2.2 Methomyl
Attasith et al. [32] developed a flexible SERS substrate-based on bacterial nanocellulose (BNCP)-AgNPs composite using vacuum-filtration method for rapid detection of pesticide on fruit peel. Due to the filtration pressure, AgNPs are firmly adhered onto both outer and inner fibrous scaffold of BNCP, resulting in good 3D SERS substrate with high activity and signal uniformity (RSD < 10%) as evaluated by 4-ATP molecule. The optical transparency of BNCP makes it suitable to achieve a direct and rapid detection of methomyl (from $10^{-3}$ to $10^{-7}$ M) on fruit peels using a simple and effective ‘paste-and-read’ SERS approach. The signals from two detection configure “top-side up” or “bottom-side up” are almost identical in intensity using 14 mW laser power. BNCP as scaffold also brings it good stability, which produces comparable signal to that of the freshly prepared one after 3 months storage time.

5.2.2.3 Thiram
Fateixa et al. [39] developed a SERS active Ag/LCP/PA filter membranes for detection of pesticide thiram in standard solution and real samples. They used filtration to fabricate liquid polymer crystal (LCP) textile fibers network,
and then adsorbed AgNPs onto it to form the substrate. The capture and concentration of target molecules are achieved by simply filtering the sample solution by Ag/LCP/PA filter. The prepared substrate Ag/LCP/PA provided enhancement factors of $1.67 \times 10^7$ and $3.86 \times 10^5$ for SERS analysis of thiram dissolved in river water and in fruit juices, respectively. The detection limit (0.024 ppm) achieved in fruit juices is lower than the maximal residue limit (MRL) of 5 ppm in fruit, as prescribed by European regulations (EU) 2016/1, indicating a great potential in vestigial analysis, environmental monitoring, and biological detection. Interesting, the in-situ prepared substrate shows better selectivity for thiram as compared to the other pesticides analysed while Ag/LCP substrate prepared by LBL method shows sensitivity to all pesticides.

5.2.2.4 Phorate

By using a typical flow-through method, Shi et al. [27] assembled silver nanowires on filter to form a dual function membrane combing solid-phase extraction (SPE) with surface-enhanced Raman spectroscopy (SERS) for the rapid collection and detection of food contaminants. Silver nanowires are uniformed assembled on the filter membrane to provide reproducible signal for quantitative analysis. A good linear relationship was established between the characteristic SERS intensity of phorate and melamine against their concentrations in the concentration range of $2.5 \times 10^{-10}$ mg mL$^{-1}$ (phorate) and $2.5 \times 10^{-10}$ mg mL$^{-1}$ (melamine). The simple flow-through operation not only makes it simple to prepare efficient, stable, reproducible SERS substrate (RSD 4.1%), but also greatly improve the detection efficiency in sensitivity, operation time and quantitation [27]. It is believed the application of silver nanowire also contributes to the improvement of sensing performance compared to their previous similar work using spherical AgNPs coated filter [47].

5.2.3 Antibiotic

The development of antibiotics great advance human’s health. Nevertheless, the abuse of antibiotic or overtake of antibiotic also cause serious problem such as organ damage and drug resistance. SERS has been proved an efficient tool for screening antibiotics in various samples [49], however, detection of antibiotic by filter-based SERS is rarely reported. An excellent work comes from Jia et al. [30]. As shown in Figure 3, they fabricated a solid-phase extraction (SPE) membrane by filtration of the activated carbon modified with silver nanoparticles (AgNPs/AC). The high adsorption properties of AC endow the SPE membrane outstanding preconcentration ability, while the embedded AgNPs show excellent ability to enhance Raman signal. Due to their synergy, a low detection limit (LOD) of $5.0 \times 10^{-11}$ M and $1.6 \times 10^{-10}$ M was achieved for detection of probe R6G and p-aminothiophenol. The SERS active membrane with outstanding SPE effect was used for in-situ detection of antibiotics, penicillin G sodium and ampicillin in wastewater. The LODs of penicillin G sodium and ampicillin were calculated to be $2.5 \times 10^{-9}$ M and $3.2 \times 10^{-9}$ M, respectively [30].

Figure 3: Scheme of the fabrication of the Ag NPs/AC nanocomposites and its application to preconcentration and SERS detection of analytes in water. Reproduced with permission from Ref. [30]. Copyright: 2018 Springer.
Such a SERS active SPE membrane with simple preparation, fast operation, high-efficient preconcentration, high reproducibility (RSD < 15%) and significant enhancement shows great potential for on-site detection of various pollutants in real sample.

5.2.4 Melamine

Illegal adulteration of melamine in dairy-related food poses great threat to human health. Fast and accurate identification of melamine plays an important role in food safety control, and SERS is a powerful tool as it can directly distinguish melamine using its intrinsic Raman scattering signal. Filter-based SERS also employed to achieve the screening of melamine in various samples. For example, several work in above section have reported detection of melamine in solution or real sample [19,27].

Wang et al. [50] developed a filter-based approach for sensitive and reproducible detection of R6G and melamine. By simple filtration, large particle AgNPs are densely and homogeneously coated onto the filter, while the analyte was highly concentrated. The RSD of SERS signal is <10%, and the detection limit is 5×10^{-8} M for R6G, and 10^{-8} M for melamine. The substrates are hardly oxidized and are stable for about two months.

A similar work was reported by Su et al. [51]. They filtered Ag nanocube@SiO2 to fabricate active substrate for detection of melamine in milk. The used SiO2 shell was used to capsule AgNC to increase its stability and control the interparticle distance to increase sensitivity. The substrate achieved a quantitative detection of melamine quantification in the range of 0.063 mg/L to 1 mg/L, with a good linearity (R² = 0.9948) and a detection limit of 0.06 mg/L. For practical detection of melamine, the detection limit increases to 0.17 mg/L, which is still below the permissible residue limit. The SiO2 shell endowed it with good chemical stability and showed nearly the same performance (RSD = 9%) after two months storage at ambient condition.

Another work comes from Durucan and coworkers [52]. They developed home-made microfluidic nanopillar filters to extract and detect melamine in milk by combines centrifugal force and wetting properties of the SERS substrate. The SERS-microfluidics platform can automatically perform the sample handling, where both capillary and inertial forces are exploited for a precise and facile wicking-filtration of a sample solution. Interestingly, AuNPs not only as enhancement substrate, but also as filter to block macromolecules in milk to purify the SERS signal. As a result, high quality of SERS signal from melamine was obtained and the detection limit is down to 10 ppm.

5.2.5 Polycyclic aromatic hydrocarbon

Polycyclic aromatic hydrocarbons (PAHs) are hazardous pollutant in environment and food. SERS detection of PAHs suffers from poor signal as these PAHs often have low affinity to the enhancement substrate. Consequently, surface modification is required to improve the affinity to PAH and therefore the sensitivity [53], which is complicated and low efficiency. Recently, Shi et al. [54] developed a novel filter-based 3D SERS substrate to achieve the sensitive, reproducible detection of PAHs in sea water. They first prepared a porous polymer glycidyl methacrylate-ethylene dimethacrylate (GMA-EDMA) and then smashed it and loaded it into syringe filter. For the detection of PAH, mixture of AuNPs, PAH and NaOH (pH = 13) was added onto the syringe filter for SERS measurement. The authors found tuning pH of AuNPs solution to 13 bring 12-fold increase in SERS signal as the ions of OH− promote the aggregation of AuNPs and make the molecules of pyrene easier to connect with AuNPs. Another 8-fold increase of SERS signal are obtained using porous GMA-EDMA instead of bare filter as support as GMA-EDMA material can adjust the distribution of AuNPs to generate more ‘hot spots’ with the help of syringe filtration [54]. The substrate displays good reproducibility with RSD of signals from intra-substrate is less than 10% and that from inter-substrate is less than 4%. A linear range was found for detection of pyrene (from 3×10^{-10} to 1×10^{-8} mol L^{-1}) and benzo(a)pyrene (from 1×10^{-9} to 2×10^{-8} mol L^{-1}). The detection limits of phenanthrene, pyrene, benzo(a)pyrene, and benzo(k)fluoranthene are 3×10^{-10} (phenanthrene), 2.1×10^{-10} (pyrene), 3.8×10^{-10} (benzo(a)pyrene), and 1.7×10^{-9} mol L^{-1} (benzo(k) fluoranthene), respectively. Their mixture at 10^{-8} M was also successfully distinguished. The sensitivity is 3 orders of magnitude better than reference work and comparable or even better than fluorescence method [54].

5.2.6 Other organic molecules

Besides the detection of dyes, pesticides, and antibiotics, filter-based SERS substrate also employed to detect other organic molecules in food and environment samples.

Recently, Weng et al. [52] developed a simple and sensitive surface-enhanced Raman scattering (SERS) technique for the detection of choline in infant formulas based on a filter-based flexible substrate. The flexible substrate
with excellent SERS activity and reproducibility was fabricated using a syringe filter and Ag triangular nanoplates. The detection ranges of this method for H₂O₂ and choline were 10⁻⁴–10⁻⁹ M and 10⁻³–10⁻⁷ M, and the detection limits were 0.15 and 8.36 nM, respectively.

Very recently, Kim et al. [31] presented a SERS active array film for detection of multiplex hazardous materials. The SERS active array film was fabricated by deposition of AuNR on regenerated cellulose hydrogels covered with silicon rubber mask using vacuum filtration. After removing the silicon mask, AuNRs array on cellulose hydrogels were formed. The AuNRs loaded onto 3D porous hydrogel matrix form an effective 3D substrate, while interparticle nanogap can be tuned by the deformation of hydrogel induced by drying. These factors contribute to the high enhancement of this substrate (detection limit of 10 pM for R6G and 100 fM for thiram), good stability, and excellent reproducibility. Simultaneous detection of nine different organic compounds were achieved on this AuNRs array decorated cellulose hydrogel film [31]. The substrate also displayed good reproducibility, high flexibility, and excellent robustness: signal fluctuation was smaller than 2.78% after 500 cycles 90% strain bending, demonstrating a great potential for practical SERS analysis.

5.3 Bacterial

Besides pollutant, the concern on food safety and human health is of great significance. Fast and sensitive identification of food borne pathogen and bacterial caused serious diseases receive considerable attention. SERS has been widely used in bacterial identification [56], and filter-based substrate with simple operation, the high efficient concentration also shows promising applications.

5.3.1 E. coli from urine

Bright Ankudze et al. [26] presented a silver nanowire-cotton fiber membrane for effective filtering and detection of E. coli from urine. Silver nanowires were decorated onto APTES modified cotton fiber, and then this composite was processed into a robust and porous SERS active “filter” sheet by hydraulic press. The filter sheet achieved a detection limit of 1×10⁻⁹ M (a 100% urine sample) and the enhanced factor is 1×10⁶ for detection of 4-aminothiophenol with good reproducibility. Then, the filter substrate was used to trap E. coli bacteria from urine, and identification of E. coli bacteria using silver nanowire in the filter as SERS substrate. Further enhanced SERS signal can be obtained by loading another layer silver nanowire onto the trapped bacterial. A good signal reproducibility with RSD of 7.5% was obtained on this substrate.

5.3.2 E. coli O157:H7

The Irudayaraj team [41] proposed a simple and rapid technique to detect low levels of E. coli O157:H7 from ground beef by comprising immunomagnetic separation, centrifugal membrane filtration, and silver intensification followed by SERS measurement (Figure 4). Filter membrane combined with magnetic separation was employed to capture, separate, and concentrate the immunomagnetic nanoparticle-coated bacteria from the complex sample, greatly reducing the interference from unbound components and background flora, indicating good specificity and no significant cross-reactivity. The total assay time was less than 1 h, and the detection limit was less than 10 CFU/mL after silver intensification.

Figure 4: Schematic of the proposed membrane filter-assisted SERS for rapid detection of E. coli O157:H7 in ground beef. Reproduced with permission from Ref. [41]. Copyright 2015 Elsevier.
5.3.3 *Staphylococcus aureus*

Lin et al. [29] demonstrated the fabrication and application of a filter-like bioactive SERS substrate made of gold nanoparticles@mesoporous silica (AuNPs@MS) to detect *Staphylococcus aureus* from water. Au NPs embedded in mesoporous silica was prepared by combination of wet-chemical reaction and subsequent calcination, and then pressed into filter-like SERS active disk. Silanol groups (Si–OH) on the AuNPs@MS surface have strong hydrogen-bonding interaction with bacterial, and thus bacterial can be very close to the AuNPs. Together with the significant concentration induced by filtration, the as-prepared filter like AuNPs@MS provides much reproducible SERS signal with a 900 times increased SERS signal compared to the planar rigid Au/Cr-coated substrate. The effect of Au content in the AuNPs@MS was also discussed, which shows 16 wt% displays the best performance.

5.3.4 *Salmonella* cells

Gao et al. [57] used filter-based SERS detection procedure combined with specific aptamers to accomplish the selective detection of bacterial. A label (FAM) attached on aptamer was used to provide SERS signal. As a result, the approach can be used to quantitative detection of *Salmonella* cells with a sensitivity goes down to 10^3 CFU/mL for 1 mL sample, and a quantitative range from 4.7×10^3 to 1.4×10^7 CFU/mL. The application of specific aptamer endows the method a high selectivity, which also successfully used to detect *S. Enteritidis* directly from rinsed water of spinach leaves without any additional sample pre-treatment.

5.3.5 *Salmonella Poona* and *E. coli O157:H7*

Wu et al. [40] developed a direct SERS method for identification of *Salmonella Poona* from cantaloupe cubes and *E. coli O157:H7* from lettuce. The key to achieve the direct SERS analysis is the utilization of filtration to separate matrix particle or interference and capture, concentrate the target bacterial. Using vancomycin-functionalized silver nanorod (AgNR) array as substrate, detection of *Salmonella Poona* from cantaloupe cubes was achieved by two step-filtration before SERS signal acquisition. For determine *E. coli O157:H7* from lettuce, an additional filtration is needed to separate interference chlorophyll from bacterial sample using a hydrophobic filter. The limits of detection are as low as 100 CFU/mL for *Salmonella Poona* from cantaloupe cube, and 100 CFU/mL for *E. coli O157:H7* from lettuce.

5.3.6 *Escherichia coli, Salmonella enterica*, and *Listeria monocytogenes*

Gao et al. [58] developed a simple flow-through-based SERS method for sensitive detection of several food-born pathogen bacterial in water. The total routes include several filtration operation: (1) Bacterial cells are first captured and concentrated on the filter membrane; (2) 4-mercaptophenylboronic acid (4-mpba), an indicator molecule specifically binds to the surface of bacteria through diol group was incubated with bacterial cell for 30 min and then passed through the membrane by filtration; (3) NH_4HCO_3 was used to wash the filter to remove potential interference like organic acids, sugars and colorants in juice sample provide high-quality SERS signal; (4) AuNPs are loaded onto the filter by filtration to enhance the SERS signal of 4-mpba for indirect detection of bacterial. This approach can achieve nonselective detection of *Escherichia coli, Salmonella enterica*, and *Listeria monocytogenes* within 80 min without pretreatment. Later, they used aptamer to replace 4-mpba to improve the selectivity of the SERS detection as presented above [57].

5.3.7 Metabolites of bacteria

In addition to the direct detection of bacteria in/on samples, identification of their gaseous metabolites is another approach to evaluate their contamination, which is more challenging despite of its advantage of noninvasive measurement and elimination of interference from sample matrix. Recently, Guo et al. [25] developed an interesting SERS “nose” to identify gaseous metabolites of bacteria to trace the spoiled degree of food. This SERS nose was fabricated by loading gold nanostars (AuNSs, 66 nm) on a flat AAO filter support with vacuum filtration as shown in Figure 5. The small pore size (20 nm) of the AAO filter is vital to achieve the dense and uniform assembly of AuNSs, otherwise uneven substrates and lower SERS signal were produced using AAO filter or cellulose ester filter membranes with 200 nm pore. The setup for the capture and identification of metabolite of bacteria is shown in Figure 5. The SERS nose distinguished bacteria based on their different SERS spectra of from the gaseous metabolites (some volatile organic compounds such as methyl sulfide, alkane, ketone, aldehyde, and
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aromatic compounds) of bacteria. Using dimethyl disulfide as a biomarker of pork spoil degree, the SERS nose can be used to monitor the spoiled degree based on the signal change. The SERS nose showed good quantitative response to DMDS from $1.0 \times 10^{-8}$ to $1.0 \times 10^{-3}$ M with a limit of detection of 10 nM. That makes it more sensitive than human eye and FTIR to distinguish spoiled food to fresh food at early stage. The substrate also displayed a good signal uniformity with RSD of 10.11% in 100 μm × 100 μm area. Considering its simple preparation and miniaturized setup, such SERS nose holds great promise in point-of-care monitoring.

6 Conclusions and prospects

The exploration of new SERS substrate is always a hot topic in SERS research. Beside the elaborately tailing their component and assembly structure, the development of flexible SERS substrate with multiple function is a new trend in recent years. Filter-based SERS substrates display several attractive features such as simple preparation, easy operation, low cost, high efficiency in concentration and separation, and short detection time. All these merits make the filter-based substrate a competitive candidate in fast and sensitive SERS detection, especially in real sample analysis. By using different filters, altering the enhancement active materials, a variety of filter-based SERS substrates have been fabricated and shown great value in practical SERS detection of inorganic molecule or particles, organic pollutant, biomolecules, or bacteria.

Although filter-based SERS substrates display plenty of merits and show tremendous potential in SERS analysis, its development still faces great challenges. (1) Highly sensitive detection with less sample volume. The concentration effect of filtration is obvious for large volume sample solution. So, for sample with limited volume, how to guarantee the detection sensitivity must be considered. (2) The extend application in biosensing. SERS has displayed powerful performance in biosensing and imaging. However, most application of filter-based SERS substrate focus on determination small organic molecules in relatively simple sample matrix, such as pollutant water. The application of filter-based SERS substrate in biosensing is still quite limit, although some good example has been published. (3) Developing new multifunctional filter-based substrate. Recently, multifunctional substrate has become a new trend in SERS research. By integrating Au/Ag with other functional material, the resulted hybrid not only shows great improvement in enhancement ability, but also displays attractive features like magnetic separation, good reusability, selective capture, and concentration and so on. While filter-based SERS substrate

Figure 5: Schematic illustration of Fabrication of SERS “nose” and its application in point-of-care SERS monitoring of gaseous metabolites from contaminated sample. Reproduced with permission from Ref. [25]. Copyright: 2020 American Chemical Society.
has intrinsic advantage in concentration and separation, its combination with new functional material should bring more appealing properties for advanced analysis. The address of these issues will greatly accelerate the development of filter-based SERS substrate for practical analysis in a larger scope.

The fast development of nanomaterial and nanotechnology may shed a light on the future of filter-based SERS. Using advanced technique, micro- or even nano-filter with high efficiency in capture or concentration can be created. Fantastic materials are emerging in SERS analysis, their combination with filter/filtration will further improve the function and performance of filter-based SERS substrate and bring it more possibility. With the efforts of researchers and development of modern nanotechnology, filter-based SERS substrate is believed to show great promise and bright future in trace analysis and other analytical fields.

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