Review Article

Engineering Metal Nanostructure for SERS Application

Yanqin Cao,^{1,2} Dan Li,^{1,2} Fang Jiang,^{1,2} Yong Yang,¹ and Zhengren Huang¹

¹ State Key Laboratory of High Performance Ceramics and Superfine Microstructure, Shanghai Institute of Ceramics, Chinese Academy of Sciences, 1295 Dingxi Road, Shanghai 200050, China

² Graduate University of Chinese Academy of Sciences, Beijing 100049, China

Correspondence should be addressed to Yong Yang; yangyong@mail.sic.ac.cn

Received 4 October 2012; Accepted 10 December 2012

Academic Editor: Yongsheng Li

Copyright © 2013 Yanqin Cao et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Surface-enhanced Raman scattering (SERS) has attracted great attention due to its remarkable enhancement and excellent selectivity in the detection of various molecules. Noble metal nanomaterials have usually been employed for producing substrates that can be used in SERS because of their unique local plasma resonance. As the SERS enhancement of signals depends on parameters such as size, shape, morphology, arrangement, and dielectric environment of the nanostructure, there have been a number of studies on tunable nanofabrication and synthesis of noble metals. In this work, we will illustrate progress in engineering metallic nanostructures with various morphologies using versatile methods. We also discuss their SERS applications in different fields and the challenges.

1. Introduction

The physical phenomenon behind Raman spectroscopy is an inelastic scattering of a photon from a molecule in which the frequency changes precisely matching the difference in vibrational energy levels [1]. Raman spectroscopy offers rich information of molecules, such as molecular structures, surface information, interface reactions, and so forth [2]. The Raman signal is several orders of magnitude weaker than the fluorescence emission in most cases because of its very small scattering cross-section [3], thus preventing its applications in many fields. However, the discovery of the surface-enhanced Raman scattering (SERS) phenomenon renews interests in Raman scattering due to the improved signal intensity.

The first measurement of SERS was reported by Fleischmann et al. in 1974, who observed intense Raman signal from pyridine adsorbed onto a roughened silver electrode surface [4]. In 1977, Van Duyne and Jeanmaire reported that the enhanced Raman signal intensity was due to an increase of 10^5 - 10^6 times from the scattering cross-section compared to the signal intensity of the bulk pyridine [5]. The effect was later called surface-enhanced Raman scattering (SERS).

Generally, noble metals and some oxides [6] are used as SERS substrates, but the SERS enhancement originated from metal oxides is not strong [7]. In this paper, we mainly discuss noble metal nanoparticles and their SERS applications.

Following the discovery of SERS, there have been an extensive amount of fundamental researches and theoretical studies on the SERS effect. After much debate, the general consensus is achieved that there are two important mechanisms underlying SERS: the electromagnetic enhancement and chemical enhancement, and the former is responsible for the major portion of SERS enhancement [8]. We will discuss the theories in detail in the following part.

There have emerged a number of reports focusing on metal substrates with various morphologies for SERS applications, such as nanospheres, nanocubes, aggregate [9], as well as well-designed one-dimensional (1D), two-dimensional (2D), three-dimensional (3D) arrays and patterns [8, 10]. With those special structures, SERS has been used in various fields, such as trace detection of chemical and biological molecules and fast and effective detection of food additives, illicitly sold narcotics, and explosives. Although there are so many methods and different designs, it is still a challenge

to produce highly sensitive, greatly selective, stable, reproducible substrates using a facile, robust, low-cost, and high-yield method.

In this paper, we will briefly review the theoretical background of SERS firstly. Then some typical methods for metallic SERS substrates will be demonstrated. At last, we will report popular applications of SERS in different practical fields.

2. Theoretical Background

Since the discovery of SERS, researchers have devoted much effort to understand the mechanism for the enhancement. At present, the electromagnetic enhancement and chemical enhancement are regarded as the two predominant mechanisms. While electromagnetic enhancement arises from increasing the applied electric field, chemical enhancement derives from amplifying the molecular polarizability. For electromagnetic enhancement, the intensity of Raman spectrum is proportional to the square of the induced dipole moment, which is a product of the molecular polarizability and the applied electric field [1].

Electromagnetic (EM) enhancement is due to that the optical field is facilitated by localized surface plasmon resonance (LSPR) of metallic nanostructure, which results in the enhanced Raman signal intensity [1]. At a certain excitation frequency, collective oscillation of electrons in the conduction band of the metal will resonate with the incident light, resulting in a strong oscillation of the surface electrons, which commonly known as LSPR [11]. LSPR may appear only when dimensions of the structure are much smaller than the wavelength of the light. Besides, the shape, architecture, composition, and surrounding environment of metal nano-materials also affect the LSPR; thus, it is of great importance to design these parameters of nanomaterials for high SERS enhancement [1, 8, 12].

Chemical enhancement is considered to be relative to the direct interaction between the adsorbed molecule and the metal surface, which lead to an increased Raman cross-section for the adsorbed molecule [13]. The most attractive way is charge transfer between the adsorbed molecule and the metal surface [14]. Because of the chemisorptions of the molecules on the surface, new electronic states become accessible, which serves as resonant intermediate states resulting in the increase of the intensity. Ultimately, the chemical enhancement mechanism is a short-range effect due to the required direct adsorbate-surface interaction, which generally limits to only the first layer of adsorbed molecules [3, 14].

One of the important parameters to characterize SERS substrates is the enhancement factor (EF), which is especially true for the practical application of SERS and the comparison with the theoretical calculation [10, 15]. In fact, the most widely used definition of the enhancement factor is according to the following equation [1, 15, 16], which describes the overall enhancement in Raman scattering

$$EF = \frac{I_{\text{SERS}}/N_{\text{Surf}}}{I_{\text{RS}}/N_{\text{Vol}}} \quad (1)$$

In the above equation, while I_{SERS} denotes the intensity of the special band for the spectra of probe molecules which absorb

on the SERS substrate, I_{RS} denotes the intensity of the same band for the spectra of probe molecules in the Raman (non-SERS) measurement. N_{Surf} and N_{Vol} are the corresponding number of analyte molecules in the focal volume. Generally the magnitude of EF is in the range of 10^4 – 10^8 ; however, in the single molecule SERS detection, the EF can reach up to 10^{14} . A comprehensive study of enhancement factor was reported according to [15].

In general, the EM and chemical enhancement exist simultaneously, but the proportion of contributions is different, in which the former can give 10^4 – 10^6 enhancement and the latter usually provides 10–100 enhancement. At present, researchers focus on the EM enhancement because the EM enhancement is stronger than the chemical enhancement and more helpful for the practical applications of SERS substrates.

3. Noble Metallic Nanostructures Used as SERS Substrates

According to the theoretical background mentioned before for SERS, the EM enhancement provides the most contribution to the total enhancement of Raman signal. However, the EM enhancement is mainly due to LSPR, which is dependent on the shape, size, and structure of the material [17]. Hence, it is of great importance to design rational materials for achieving the strongest enhancement.

Noble metallic nanostructures have been widely used in SERS because of their LSPR properties [11]. As a result, there have appeared many researches focusing on preparing ideal noble metallic nanostructures as SERS substrates [5]. Taking Ag and Au nanostructures as examples, various shapes have emerged [10], such as nanocubes [18, 19], nanorods [20, 21], nanocaps [16], nanochains [22, 23], nanoplates [24], honeycomb and hexagonally structured patterns [25], and nanoclusters [26]. Monodisperse nanoparticles show high SERS enhancement because of their special shapes and sizes. For example, a systematic study on Ag nanocubes with a size ranging from 60 to 200 nm, in which the intensity of SERS increased with the size and the particles with sharper curvature showed a high sensitivity in contrast to normal particles with the similar size [27]. The size of nanoparticles must be smaller than the wavelength of the light to produce LSPR, but it should not be too small, otherwise it may result in poor polarization of nanoparticles and hence poor plasmon resonance [8]. For the nanoclusters and nanopatterns, the shape of patterns and the size of gaps between particles may influence the interparticle coupling, which plays an important role in generating enhanced signals [28].

As a result, to achieve high sensitive SERS signals, fabrication of effective noble metallic nanostructures is crucial.

4. Fabrication of Metallic Nanostructures for SERS

With the development of nanotechnology, nanofabrication has improved for meeting simple, low-cost, large-scale, and green requirements. In this section, we will introduce several common methods, which have been used to generate noble metal nanostructures for SERS applications.

4.1. Solution-Phase Synthesis

4.1.1. Polyol Process. The polyol process is a simple and versatile method for preparing metal nanostructures with various shapes and sizes [11, 29–31], which show potential optical applications. The enhancement effect of SERS is dependent on the shape and size of materials; thus, the polyol process is a good choice for preparing SERS substrates.

In a typical polyol synthesis [32, 33], the salt precursor and polymeric capping agent are injected into a preheated polyol, especially ethylene glycol, which serves as both a solvent and a reducing agent. The nucleation and growth could be controlled through varying the reaction conditions, such as temperature, reagent concentration, and types of additive ions, thus controlling the final products.

The nucleation and growth mechanisms in the polyol process have been discussed in detail [11, 29]. In this section, we take the synthesis of Ag nanostructures as an example. Typically, to obtain Ag nanostructures, silver nitrate (AgNO_3) is used as metal salt precursor, ethylene glycol (EG) as the reductant and solvent, poly(vinyl pyrrolidone) (PVP) as the stabilizer and crystal-habit modifier [11, 30]. During the reaction process, initially formed small Ag clusters grow larger and become more stable which usually called seeds. The seeds may show three different structures: single crystalline, single twinned, and multiply twinned. By introducing additive chemical agents or ions, the growth speed of different crystalline faces can be changed, resulting in the formation of nanoparticles with different shapes by the selective growth of dominate crystalline faces. There are many works using different additive ions leading to different shapes with SERS applications. For example, Wiley et al. reported shape-controlled synthesis of various Ag nanostructures with this method [32] as shown in Figure 1. According to their study multiply twinned seeds grew into Ag pentagonal nanowires with addition of chloride and Fe^{3+} , in which chloride prevents seeds from aggregating and Fe^{3+} protects twinned seeds from etching by chloride and oxygen. Without adding Fe^{3+} , Cl^-/O_2 pair will dissolve both multiply twinned and singly twinned seeds, resulting in the products dominated by Ag cuboctahedrons or cubes. By adding Br^- into the solution, only single twinned seeds retained, ultimately resulting in the formation of Ag nanobars or right bipyramids. More recently, they produced large-scale Ag nanocubes by introducing argon into the NaHS-mediated synthesis [18]. However, in contrast to Ag synthesis, there is a notable difference in the mechanism for growing Au nanostructures: PVP preferentially promote the growth of {111} facets but not the {100} facets for Ag nanostructures, thus resulting in different shapes [29, 34, 35]. When using tetrachloroaurate trihydrate ($\text{HAuCl}_4 \cdot 3\text{H}_2\text{O}$) as precursor, diethylene glycol (DEG) or tetraethylene glycol (TEG) as reductant, PVP as capping agent, various polyhedral nanostructures have been prepared [34]. Moreover, adding Ag^+ into the solution, Au nanocubes with the size in the range of ~100 nm have been fabricated [35].

4.1.2. Seed-Mediated Growth. Another popular chemical synthesis method for preparing well-defined shapes and sizes is using preformed nanocrystals as seeds for further growth,

which is generally called seed-mediated growth [11, 36]. As a major advantage over conventional methods, the introduction of preformed seeds into a synthesis process allows nucleation and growth separately, thus making it easier to obtain a desired morphology by only manipulating the growth process. In general, metal atoms could deposit on seeds with the same composition or different composition, which are respectively called homogeneous or heterogeneous growth. The difference in lattice constant between the seed and the deposited metal will influence the final products. Besides, there are other influence factors [29, 36]: (1) the internal structure of the seed, for example, twin defects, stacking faults, and grain boundaries, which show a higher reactivity; (2) the presence and types of capping agents, such as surfactants, polymer stabilizers, ionic species, as well as unknown contaminants, which could bond selectively to different crystalline facets; and (3) the reduction or growth kinetics, which may influence the forming and dissolve of the seeds. Therefore, we can receive products with different shapes and morphologies through using different seeds and under different experimental conditions.

By using preformed spherical or cubic seeds, Ag nanocubes with uniform edge lengths controllable in the range of 30–200 nm have been prepared, in which the size was adjusted by varying the amount of AgNO_3 precursor added in the reaction solution [19]. In their study, the calculated EFs of Ag nanocubes did not vary much with the increase of size because I_{SERS} and N_{SERS} both became larger with increasing size of the cube. However, the enhancement factors have a relationship with the laser polarization. Recently by adding ionic or covalent bromides into the typical seed-mediated system, Ag nanobars with different aspect ratios were achieved [37], in which EFs showed anisotropy and were found to be dependent on the aspect ratios of nanobars, its orientation is relative to laser polarization, as well as the wavelength of excitation, as shown in Figure 2. A characteristic feature of anisotropic structures such as nanorods, nanowires is that its plasmonic band splits into two components, which corresponds to the longitudinal and transverse components of the localized surface plasmon resonance [20]. Faceted pentagonal Ag nanorods with tunable dimensions have also been reported by using photochemically synthesized decahedra seeds, in which the SERS enhancement dropped with the increase of the aspect ratio [21]. The report also suggests that interparticle cavities play a dominant role in SERS enhancement.

In addition, special Au nanostructures could be readily achieved by using different preformed seeds. For example, recently Au nanohexapods were prepared with single-crystal Au octahedral seeds, in which the seeds were also produced by seeded growth [38]. Core-shell nanostructure has also been prepared through an improved seed-mediated growth [39].

4.1.3. Self-Assembly. According to the two methods described above, they are usually used to prepare various monodisperse metal nanoparticles. While self-assembly is a typical process, in which metal nanoparticles spontaneously organize into special arrays or patterns with controllable size, structure,

FIGURE 1: Scanning electron microscopy (SEM) images of representative silver nanostructures: (A) nanobars, (B) truncated cubes, (C) cubes, and (D) wires, all at the same scale. Insets show TEM images of the nanowires. Reprinted with permission from [32]. Copyright 2007 American Chemical Society.

and composition. To date, different assembly approaches have been employed to assemble different dimensional metal nanoarchitectures based on corresponding metal nanoparticles [40, 41]. These typical assembly approaches include layer-by-layer (LBL) assembly [42, 43], solvent-induced evaporation [44], Langmuir-Blodgett assembly [45], external field-driven assembly [46], ion or small molecule or polymer induced assembly [22, 23, 47], liquid-liquid interface assembly [48], and so forth.

Chainlike 1D nanostructure has been widely fabricated through assembling nanoparticles [49–51]. For example, Yang et al. reported the assembly of Ag nanoparticles into nanochains under the inducing of cetyltrimethylammonium bromide (CTAB) and the assistance of 11-mercaptoundecanoic acid (MUA) [22] as shown in Figure 3. In their process, CTAB linked together the {100} facets of neighboring Ag nanoparticles and MUA prevented excess aggregations of nanoparticles. Their results show that the chain length could be easily controlled by adjusting the amount of CTAB and MUA. The maximum SERS enhancement factor around 2.6×10^8 was observed on the Ag monolayer mainly composing of four-particle nanochains, which was due to the enhancement of localized electromagnetic field. The localized surface plasmon coupling at the interstitial

sites of Ag nanochains resulted in the enhanced localized electromagnetic field. More Recently gold nanoparticle linear aggregates were generated by using a siloxane surfactant, in which the enhancement factor reached to 2.4×10^6 , that was about 5 times stronger than the isolated Au nanosphere [23]. In 2011, acid-directed self-assembly of Ag nanoparticles into special nanostructures has been achieved without using any polymer surfactant or capping agent [47]. In the process, ascorbic acid reduced the precursor solution, and with the assistance of citric acid perfect microspheres composing of nanosheets were produced. Helical nanochains were also prepared by self-assembly of spherical colloids in V-shaped grooves [52].

In addition, metal nanoparticles can be immobilized on solid substrates resulting in 2D structures through chemical attachment [53, 54], electrostatic interaction [55], capillary force driving [56], and direct transfer of pre-assembled nanoparticle film [45], focusing on which numerous works have been published [57]. Recently under the guiding of polystyrene-*b*-poly(4-vinylpyridine) (P4VP-*b*-PS) block copolymer, citrate-stabilized gold nanospheres assembled into arrays on the Si substrate driving by electrostatic interaction between the positively charged pyridinium groups on the substrate and the negatively charged surface ligands of

FIGURE 2: SERS spectra taken from a single Ag nanobar at two wavelengths and different orientations relative to the laser polarization. (a) SEM image of a typical Ag nanobar of 150 nm in length (l) and 75 nm in width (w) supported on a Si wafer. The 514 or 785 nm laser was propagating perpendicular to the Si substrate and the polarization angle (θ) with respect to the nanobar was varied from 0° to 180° . (b) SERS intensity as a function of θ , with the fit to $\cos^4(\theta)$. ((c), (d)) SERS spectra for 1, 4-BDT are plotted for 514 and 785 nm lasers at different polarization angles. The peak at $\sim 980 \text{ cm}^{-1}$ was from the Si substrate. The 1, 4-BDT peaks at 1562 cm^{-1} are highlighted in gray. ((e), (f)) Enhancement factors of individual nanobars calculated from the peaks of 1, 4-BDT for transverse (circles) and longitudinal (squares) polarizations, and with 514 nm (green) and 785 nm (red) excitations. Reprinted with permission from [37]. Copyright 2007 American Chemical Society.

the nanoparticles [55]. Their products showed a uniform response regardless of orientation and excellent reproducibility, which are very important for practical applications of SERS. Besides, nanoparticle cluster arrays were reported by using nanopatterns of poly(styrene-block-2-vinylpyridine) (PS-*b*-P2VP) [58].

Finally, the metal nanoparticle clusters have been obtained through controllable assembly. Different morphologies can be generated under usage of molecular linkers

[59], asymmetrically functionalized nanoparticles [60], and controlling the aggregation kinetics [61].

4.2. Template Technique. Template technique offers another way to prepare nanostructures with well-defined size and shape under the assistance of templates. By using different templates, different morphologies could be obtained. There are many approaches for preparing metal nanomaterial through hard templates, such as anodic alumina oxide

FIGURE 3: TEM images of Ag colloids: (a) sol-1, (b) sol-2, (c) sol-3, and (d) sol-4. All scale bars represent 50 nm. ((e)–(h)) Particle number distribution in Ag nanochains for related TEM images. The criterion to judge whether a group of Ag particles form a chain or not is that the distance between neighboring particles is less than the chain length of CTAB molecules. Reprinted with permission from [22]. Copyright 2007 American Chemical Society.

(AAO) [62, 63], polycarbonate membranes (PCM) [64], polymethylmethacrylate (PMMA) [65], monolayer colloidal crystal [66], and so forth, as well as soft templates, including micelles [67], reverse micelles, DNA, and so forth [11, 68]. In this section, we will describe some popular templates used to generate special noble metal nanostructures.

Anodic alumina oxide (AAO), also known as porous anodic alumina (PAA), is a very popular substrate for producing various metal nanostructures, such as nanowire, nanorod, nanopore, and nanodot arrays. Silver nanopores with abundant sub-5 nm gaps as SERS substrates were reported by electron beam deposition Ag on the porous side through controlling the temperature and the deposited Ag thickness, of which the EF reached to 10^7 using rhodamine 6G (R6G) as the probe molecule [62]. High ordered gold nanodots were also fabricated by using AAO template with the thickness of 750 nm [63], in which Raman signal of thin silicon membranes on polyethylene terephthalate (PET) substrates was enhanced and exhibited structure information.

Monolayer colloidal crystal (MCC) is another interested template for producing various metal nanopatterns, which is also widely used in fabricating SERS substrates. In general, there are two cases: metal materials depositing on the top of colloidal crystals and metal materials depositing on the interspaces of the colloidal crystal monolayer, which result in nanocaps, honeycomb, and hexagonal arrays. MCC could

be prepared by self-assembly process [68]. The target metal material can be deposited on the prepared MCC templates through plasma sputtering [69], magnetron sputtering [16], and so forth. In most cases, the templates finally need to be removed to produce ideal metal nanopatterns. For example, tunable Au nanoshell arrays were prepared by using pretreated uniform polystyrene (PS) monolayer colloidal crystals as template [69]. By varying the plasma sputtering deposition time, different nanopatterns with different spacing were generated, which showed different SPR intensity, thus tuning the SERS intensity. An order Ag nanocaps were also fabricated through magnetron sputtering Ag on the two-dimensional PS monolayer colloidal crystal template, which showed a high SERS intensity with an enhance factor $\sim 10^{12}$ using 4-mercaptopyridine (4-Mpy) as the probe molecule [16].

In addition, recently by sputtering deposition Ag and Au nanoneedles arrays were obtained, in which the firstly deposited carbon nanoneedles arrays serve as an template inducing the formation of final products [70, 71]. Rodríguez-Fernández fabricated Au semishells using Janus silica particles as templates [72].

4.3. Other Methods. Besides the methods mentioned before for fabricating SERS substrates, there have been other methods, such as combination of nanoparticles with special

structure or material [73, 74], screen printing [75], and sonochemical synthesis [76], and winkle-confined drying of collides [77].

For example, Ag nanoparticles deposited on the porous silicon in the AgNO_3 solution, in which Ag aggregates formed and the sizes could be controlled by varying the concentration of AgNO_3 solution [73]. The SERS performance was measured by detecting R6G and crystal violet (CV), which showed remarkable Raman signal enhancement. Besides, a facile and fast method was reported by chemically depositing Ag on polyaniline films treated by hydrazine in AgNO_3 solution, as well as adding lactic acid, which ultimately forming flower-like Ag nanostructure in less than one minute [74]. The prepared Ag nanostructure showed highly response to 4-mercaptobenzoic acid (4-MBA) up to ppb level. Large-scale fabrication was achieved through screen printing [75]. The printing ink consisted of Ag nanoparticles and sodium carboxymethylcellulose (CMC), in which the nanoparticles were reduced by sodium citrate and CMC was used to adjust the viscosity of the ink. The ink was placed on the woven mesh and forced into the image areas of the woven mesh as hard squeegee moving across the mesh. 3D Ag microflowers have been prepared by a simple and sonochemical method, which showed high sensitivity of SERS for R6G and 4-mercaptobenzoic acid (MBA) molecule [76]. In the procedure, AgNO_3 and L-ascorbic acid (AA) were mixed and sonicated using an ultrasonic generator at room temperature. The Ag nanoparticles of different sizes were achieved through controlling the ultrasonic time and power, as well as the reactant molar ratio. Gold nanoparticle arrays were produced through confining gold nanoparticle collides by wrinkled polydimethylsiloxane (PDMS) during drying [77].

5. Practical Applications of SERS

Raman spectrum can inherently imply rich information of analyte molecules, and SERS with higher signal intensity make it possible to detect analyte in very low concentration, which improves its practical applications. There have been a large number of works focusing on applications of SERS in various fields, including trace chemical detection, such as dye molecules [70, 78, 79], illicitly sold narcotics [70], food additives [47], and residual pesticide trace detection [20, 80, 81], as well as bioanalysis [82, 83] and explosives detection [84, 85].

5.1. Applications of SERS in Trace Chemical Detection. Dye molecules such as R6G and MG are reported to be used as SERS probe molecules. For example, Ag nanoneedles array substrates prepared by a simple Ar^+ ion sputtering technology were used to detect R6G at a very low concentration $\sim 10^{-11}$ M [70]. Besides, many bands are distinctly observed in the spectra even when the R6G concentration was down to 10^{-15} M, by using Ag nanosheets-assembled micro-hemispheres as SERS substrates [78]. There was another report showing that the detection concentration for R6G on the Ag microflower substrates was as low as 10^{-17} M [79]. Because of the low detection limit of R6G, it is useful for studies on single

FIGURE 4: Raman spectra of ketamine hydrochloride with different concentration of (A) 27 ppb, (B) 275 ppb, and (C) 2.7 ppm adsorbed on Ag nanoneedles (633 nm, 3s) [70]. Reproduced by the permission of the Royal Society of Chemistry.

molecule SERS. In addition, dyes can produce vibrant colors, thus make it treasured since antiquity [86]. The easy and facile detection of dye molecules may promote the historical and cultural research.

The detection of trace-level hazardous chemicals is also in high demand because of the increasing threat from harmful environments and unreliable food safety. For example, Yang et al. detected ketamine hydrochloride down to 27 ppb within 3 s, which offers significant applications in both biomedical diagnostics and forensics field [70] as shown in Figure 4.

Melamine, a chemical compound, has been widely used in milk, infant formula, and pet food as an additive to increase protein content because of its high nitrogen content (66% by mass). However, since 2007, melamine, with its contaminant cyanuric acid, has become prominent because of the milk scandal. As a facile and simple spectroscopy technique, SERS has been used to detect melamine content. For instance, Zhang et al. reported that melamine with a concentration of ~ 5 ppm could be readily detected by using the core-shell Ag nanostructure assembled by nanosheets [47]. In addition, pesticide residues have also been detected through SERS and using metal nanostructure substrates. For example, gold nanorods and silver nanocubes were used to detect three different herbicides: the organochlorine compound 2,4-D, the organophosphorus compound trichlorfon, and the triazinic compound ametryn, which were fabricated in solution phase [20]. Silver nanoparticles decorated silicon nanowires have been used to in situ detect pesticide residues on a cucumber surface with a high SERS intensity, which were prepared using CTAB as the soft template to induce nanoparticles absorbing on the nanowires [80]. Moreover, Li et al. in situ detected parathion residues on fresh orange using Au-SiO₂ core-shell nanostructure [81] as shown in Figure 5. And this provides an important potential to rapidly detect pesticide residue on the fruits and vegetables, which is crucial to diet safety.

(a)

(b)

FIGURE 5: In situ inspection of pesticide residues on food/fruit. (a) Normal Raman spectra on fresh citrus fruits. Curve I, with clean pericarps. Curve II, contaminated by parathion. Curve III, Shiners spectrum of contaminated orange modified by Au/SiO₂ nanoparticles. Curve IV, Raman spectrum of solid methyl parathion. Laser power on the sample was 0.5 mW, and the collected times were 30s. (b) Schematic of the Shiners experiment. Reprinted with permission from reference 81. Copyright 2010 Nature Publishing Group.

5.2. Applications of SERS in Biosensing. SERS has been widely used for bioanalysis [82], including detecting biomolecules [87, 88], pathogens sensing [89, 90], cancer diagnosis [91, 92], urine components detection [93], and in vivo molecular probing in live cells [94], which play an important role in the life science for health care or therapeutic treatment.

Biomolecules, such as DNA, can be detected using SERS. There have been reports focusing on detecting the sequence of DNA molecule by SERS technique, which based on the mixed DNA-functionalized silver nanoparticles probe [87] or using gold nanoparticle aggregates [88]. Bacteria, one

of the pathogens, have been identified using SERS through internally or externally depositing Ag and Au colloids on bacteria [89]. The applications of SERS on cells for detecting pathogens have also been studied, as well as the SERS-based immunoassay. Binding the antibody and the metal nanoparticles can be used to detect the special antigen, which serves as biomarker of corresponding cancer [91]. Moreover, recently there has been a study focusing on the detection of β -agonist in urine, in which the chemometric method was introduced for high sensitivity [93]. Their work provided a potential use of SERS in drug test and clinic detection.

Much effort to meet reliable, fast, and high specific detection requirements remains to be proceeded.

5.3. Applications of SERS in Explosives Detection. The detection and analysis of explosives are important to homeland security, environment cleaning, military issues, and land mine detection. For instance, Ni–Au nanocarpet (NCs) were prepared through a galvanic replacement reaction, starting from prefabricated Ni NCs, which showed high activity and reproducibility as SERS substrates for detecting explosives with a low concentration about 10^{-7} M [84]. Silver-gold bimetallic nanostructures were achieved by sunlight inducing and DNA template assisting [85]. By varying the molar ratio of silver to gold, the morphologies of products could be controlled. The prepared Ag–Au nanostructure showed a very low detection concentration of TNT down to 10^{-15} M through SERS technology. Stable and reproducible substrates for detecting explosives are still challenging.

6. Conclusion

In this paper, we mainly discuss the theoretical background of SERS, some synthesis methods of SERS substrates, and their applications in different fields. Although there have been many studies focusing on the theories, some issues remain unclear and unsure, such as the attribution of chemical mechanism. With the development of designing various nanostructures, it is possible to further understand the enhancement theories and the factors influencing the enhancement. Different dimensional nanostructures have been prepared through various methods, such as polyol process, seed-mediated synthesis, self-assembly and template technique. Using these noble metal nanostructures, SERS has been used in detecting various molecules and thus has been applied into different real fields. However, it is still a challenge to produce highly sensible, reproducible, and stable substrates using a simple, low-cost, large-scale, and rapid method. Further works should be continued to generate high-performance SERS substrates for wider applications.

Acknowledgments

Y. Yang thanks the Century Program (One-Hundred-Talent Program) of the Chinese Academy of Sciences for special funding support. This study was also supported in part by Funds from the National Natural Science Foundation of China (no. 51071167, 51102266), the Instrument Developing Project of the Chinese Academy of Sciences (no. YZ200939), the Shanghai Yangtze River Delta Science Project (no. 11495810100), and the Shanghai Pujiang Program (10PJ1410700). Y. Yang is also thankful for the support by Fund from Key Laboratory of Nanodevices and Applications, Suzhou Institute of Nano-Tech and Nano-Bionics, Chinese Academy of Sciences (no. 12CS01).

References

- [1] P. L. Stiles, J. A. Dieringer, N. C. Shah, and R. P. Van Duyne, "Surface-enhanced Raman spectroscopy," *Annual Review of Analytical Chemistry*, vol. 1, no. 1, pp. 601–626, 2008.
- [2] T. Vo-Dinh, "Surface-enhanced Raman spectroscopy using metallic nanostructures," *Trends in Analytical Chemistry*, vol. 17, no. 8–9, pp. 557–582, 1998.
- [3] C. L. Haynes, A. D. McFarland, and R. P. Van Duyne, "Surface-enhanced: Raman spectroscopy," *Analytical Chemistry*, vol. 77, no. 17, pp. 338A–346A, 2005.
- [4] M. Moskovits, "Surface-enhanced spectroscopy," *Reviews of Modern Physics*, vol. 57, no. 3, pp. 783–826, 1985.
- [5] Z. Q. Tian, B. Ren, and D. Y. Wu, "Surface-enhanced Raman scattering: from noble to transition metals and from rough surfaces to ordered nanostructures," *Journal of Physical Chemistry B*, vol. 106, no. 37, pp. 9463–9483, 2002.
- [6] X. Wang, W. Shi, G. She, and L. Mu, "Surface-Enhanced Raman Scattering (SERS) on transition metal and semiconductor nanostructures," *Physical Chemistry Chemical Physics*, vol. 14, no. 17, pp. 5891–5901, 2012.
- [7] Y. Wang, W. Ruan, J. Zhang et al., "Direct observation of surface-enhanced Raman scattering in ZnO nanocrystals," *Journal of Raman Spectroscopy*, vol. 40, no. 8, pp. 1072–1077, 2009.
- [8] H. Ko, S. Singamaneni, and V. V. Tsukruk, "Nanostructured surfaces and assemblies as SERS media," *Small*, vol. 4, no. 10, pp. 1576–1599, 2008.
- [9] Y. Yang, S. Matsubara, L. Xiong, T. Hayakawa, and M. Nogami, "Solvothermal synthesis of multiple shapes of silver nanoparticles and their SERS properties," *Journal of Physical Chemistry C*, vol. 111, no. 26, pp. 9095–9104, 2007.
- [10] G. V. P. Kumar, "Plasmonic nano-architectures for surface enhanced Raman scattering: a review," *Journal of Nanophotonics*, vol. 6, no. 1, Article ID 064503, 2012.
- [11] M. Rycenga, C. M. Cobley, J. Zeng et al., "Controlling the synthesis and assembly of silver nanostructures for plasmonic applications," *Chemical Reviews*, vol. 111, no. 6, pp. 3669–3712, 2011.
- [12] R. J. C. Brown, J. Wang, and M. J. T. Milton, "Electromagnetic modelling of Raman enhancement from nanoscale structures as a means to predict the efficacy of SERS substrates," *Journal of Nanomaterials*, vol. 2007, Article ID 12086, 10 pages, 2007.
- [13] A. Campion, J. E. Ivanecky III, C. M. Child, and M. Foster, "On the mechanism of chemical enhancement in surface-enhanced Raman scattering," *Journal of the American Chemical Society*, vol. 117, no. 47, pp. 11807–11808, 1995.
- [14] A. Campion and P. Kambhampati, "Surface-enhanced Raman scattering," *Chemical Society Reviews*, vol. 27, no. 4, pp. 241–250, 1998.
- [15] E. C. Le Ru, E. Blackie, M. Meyer, and P. G. Etchegoin, "Surface enhanced Raman scattering enhancement factors: a comprehensive study," *Journal of Physical Chemistry C*, vol. 111, no. 37, pp. 13794–13803, 2007.
- [16] Y. X. Wang, S. S. Liu, W. T. Gao, W. Li, Y. J. Zhang, and J. H. Yang, "Surface-enhanced Raman spectroscopy based on ordered nanocap arrays," *Superlattices and Microstructures*, vol. 52, no. 4, pp. 750–758, 2012.
- [17] K. A. Willets and R. P. Van Duyne, "Localized surface plasmon resonance spectroscopy and sensing," *Annual Review of Physical Chemistry*, vol. 58, pp. 267–297, 2007.
- [18] Q. Zhang, C. Cobley, L. Au et al., "Production of Ag nanocubes on a scale of 0.1 g per batch by protecting the NaHS-mediated polyol synthesis with argon," *ACS Applied Materials & Interfaces*, vol. 1, no. 9, pp. 2044–2048, 2009.
- [19] Q. Zhang, W. Li, C. Moran et al., "Seed-mediated synthesis of Ag nanocubes with controllable edge lengths in the range of 30–200 nm and comparison of their optical properties," *Journal of*

- the American Chemical Society*, vol. 132, no. 32, pp. 11372–11378, 2010.
- [20] J. C. Santos Costa, R. A. Ando, A. C. Sant'ana et al., "High performance gold nanorods and silver nanocubes in surface-enhanced Raman spectroscopy of pesticides," *Physical Chemistry Chemical Physics*, vol. 11, no. 34, pp. 7491–7498, 2009.
 - [21] B. Pietrobon, M. McEachran, and V. Kitaev, "Synthesis of size-controlled faceted pentagonal silver nanorods with tunable plasmonic properties and self-assembly of these nanorods," *ACS Nano*, vol. 3, no. 1, pp. 21–26, 2009.
 - [22] Y. Yang, J. Shi, T. Tanaka, and M. Nogami, "Self-assembled silver nanochains for surface-enhanced Raman scattering," *Langmuir*, vol. 23, no. 24, pp. 12042–12047, 2007.
 - [23] H. Jia, X. Bai, N. Li, L. Yu, and L. Zheng, "Siloxane surfactant induced self-assembly of gold nanoparticles and their application to SERS," *CrystEngComm*, vol. 13, no. 20, pp. 6179–6184, 2011.
 - [24] I. Pastoriza-Santos and L. M. Liz-Marzán, "Colloidal silver nanoplates. State of the art and future challenges," *Journal of Materials Chemistry*, vol. 18, no. 15, pp. 1724–1737, 2008.
 - [25] C. L. Haynes and R. P. Van Duyne, "Nanosphere lithography: a versatile nanofabrication tool for studies of size-dependent nanoparticle optics," *Journal of Physical Chemistry B*, vol. 105, no. 24, pp. 5599–5611, 2001.
 - [26] P. H. C. Camargo, L. Au, M. Rycenga, W. Li, and Y. Xia, "Measuring the SERS enhancement factors of dimers with different structures constructed from silver nanocubes," *Chemical Physics Letters*, vol. 484, no. 4–6, pp. 304–308, 2010.
 - [27] J. M. McLellan, A. Siekkinen, J. Chen, and Y. Xia, "Comparison of the surface-enhanced Raman scattering on sharp and truncated silver nanocubes," *Chemical Physics Letters*, vol. 427, no. 1–3, pp. 122–126, 2006.
 - [28] S. K. Ghosh and T. Pal, "Interparticle coupling effect on the surface plasmon resonance of gold nanoparticles: from theory to applications," *Chemical Reviews*, vol. 107, no. 11, pp. 4797–4862, 2007.
 - [29] Y. Xia, Y. Xiong, B. Lim, and S. E. Skrabalak, "Shape-controlled synthesis of metal nanocrystals: simple chemistry meets complex physics?" *Angewandte Chemie*, vol. 48, no. 1, pp. 60–103, 2009.
 - [30] A. R. Tao, S. Habas, and P. Yang, "Shape control of colloidal metal nanocrystals," *Small*, vol. 4, no. 3, pp. 310–325, 2008.
 - [31] C. M. Copley, S. E. Skrabalak, D. J. Campbell, and Y. Xia, "Shape-controlled synthesis of silver nanoparticles for plasmonic and sensing applications," *Plasmonics*, vol. 4, no. 2, pp. 171–179, 2009.
 - [32] B. Wiley, Y. Sun, and Y. Xia, "Synthesis of silver nanostructures with controlled shapes and properties," *Accounts of Chemical Research*, vol. 40, no. 10, pp. 1067–1076, 2007.
 - [33] A. Tao, P. Sinsermsuksakul, and P. Yang, "Polyhedral silver nanocrystals with distinct scattering signatures," *Angewandte Chemie*, vol. 45, no. 28, pp. 4597–4601, 2006.
 - [34] D. Seo, C. I. Yoo, I. S. Chung, S. M. Park, S. Ryu, and H. Song, "Shape adjustment between multiply twinned and single-crystalline polyhedral gold nanocrystals: decahedra, icosahedra, and truncated tetrahedra," *Journal of Physical Chemistry C*, vol. 112, no. 7, pp. 2469–2475, 2008.
 - [35] D. Seo, C. P. Ji, and H. Song, "Polyhedral gold nanocrystals with Oh symmetry: from octahedra to cubes," *Journal of the American Chemical Society*, vol. 128, no. 46, pp. 14863–14870, 2006.
 - [36] J. Zeng, X. Xia, M. Rycenga, P. Henneghan, Q. Li, and Y. Xia, "Successive deposition of silver on silver nanoplates: lateral versus vertical growth," *Angewandte Chemie*, vol. 50, no. 1, pp. 244–249, 2011.
 - [37] Q. Zhang, C. H. Moran, X. Xia, M. Rycenga, N. Li, and Y. Xia, "Synthesis of Ag nanobars in the presence of single-crystal seeds and a bromide compound, and their surface-enhanced Raman scattering (SERS) properties," *Langmuir*, vol. 28, no. 24, pp. 9047–9054, 2012.
 - [38] D. Y. Kim, T. Yu, E. C. Cho, Y. Ma, O. O. Park, and Y. Xia, "Synthesis of gold nano-hexapods with controllable arm lengths and their tunable optical properties," *Angewandte Chemie*, vol. 50, no. 28, pp. 6328–6331, 2011.
 - [39] T. Liu, D. Li, D. Yang, and M. Jiang, "An improved seed-mediated growth method to coat complete silver shells onto silica spheres for surface-enhanced Raman scattering," *Colloids and Surfaces A*, vol. 387, no. 1–3, pp. 17–22, 2011.
 - [40] S. Guo and S. Dong, "Metal nanomaterial-based self-assembly: development, electrochemical sensing and SERS applications," *Journal of Materials Chemistry*, vol. 21, no. 42, pp. 16704–16716, 2011.
 - [41] J. M. Romo-Herrera, R. A. Alvarez-Puebla, and L. M. Liz-Marzan, "Controlled assembly of plasmonic colloidal nanoparticle clusters," *Nanoscale*, vol. 3, no. 4, pp. 1304–1315, 2011.
 - [42] X. Zhang, H. Chen, and H. Zhang, "Layer-by-layer assembly: from conventional to unconventional methods," *Chemical Communications*, no. 14, pp. 1395–1405, 2007.
 - [43] Y. Huang, Y. Yang, Z. Chen, X. Li, and M. Nogami, "Fabricating Au-Ag core-shell composite films for surface-enhanced Raman scattering," *Journal of Materials Science*, vol. 43, no. 15, pp. 5390–5393, 2008.
 - [44] S. Peng, Y. Lee, C. Wang, H. Yin, S. Dai, and S. Sun, "A facile synthesis of monodisperse Au nanoparticles and their catalysis of CO oxidation," *Nano Research*, vol. 1, no. 3, pp. 229–234, 2008.
 - [45] A. R. Tao, J. Huang, and A. P. Yang, "Langmuir–blodgett of nanocrystals and nanowires," *Accounts of Chemical Research*, vol. 41, pp. 1662–1673, 2008.
 - [46] H. Wu, F. Bai, Z. Sun et al., "Nanostructured gold architectures formed through high pressure-driven sintering of spherical nanoparticle arrays," *Journal of the American Chemical Society*, vol. 132, no. 37, pp. 12826–12828, 2010.
 - [47] B. Zhang, P. Xu, X. Xie et al., "Acid-directed synthesis of SERS-active hierarchical assemblies of silver nanostructures," *Journal of Materials Chemistry*, vol. 21, no. 8, pp. 2495–2501, 2011.
 - [48] H. Duan, D. Wang, D. G. Kurth, and H. Möhwald, "Directing self-assembly of nanoparticles at water/oil interfaces," *Angewandte Chemie*, vol. 43, no. 42, pp. 5639–5642, 2004.
 - [49] Y. Yang, M. Nogami, J. Shi, H. Chen, G. Ma, and S. Tang, "Controlled surface-plasmon coupling in SiO₂-coated gold nanochains for tunable nonlinear optical properties," *Applied Physics Letters*, vol. 88, no. 8, Article ID 081110, 2006.
 - [50] Y. Yang, S. Matsubara, M. Nogami, J. Shi, and W. Huang, "One-dimensional self-assembly of gold nanoparticles for tunable surface plasmon resonance properties," *Nanotechnology*, vol. 17, no. 11, pp. 2821–2827, 2006.
 - [51] G. Kawamura, Y. Yang, and M. Nogami, "End-to-end assembly of CTAB-stabilized gold nanorods by citrate anions," *Journal of Physical Chemistry C*, vol. 112, no. 29, pp. 10632–10636, 2008.
 - [52] Y. Yin and Y. Xia, "Self-assembly of spherical colloids into helical chains with well-controlled handedness," *Journal of the American Chemical Society*, vol. 125, no. 8, pp. 2048–2049, 2003.

- [53] T. Makiabadi, A. Bouvrée, V. Le Nader, H. Terrisse, and G. Louarn, "Preparation, optimization, and characterization of SERS sensor substrates based on two-dimensional structures of gold colloid," *Plasmonics*, vol. 5, no. 1, pp. 21–29, 2010.
- [54] J. L. Seung, M. B. Jeong, and M. Moskovits, "Polarization-dependent surface-enhanced Raman scattering from a silver-nanoparticle-decorated single silver nanowire," *Nano Letters*, vol. 8, no. 10, pp. 3244–3247, 2008.
- [55] W. Lee, S. Y. Lee, R. M. Briber, and O. Rabin, "Self-assembled SERS substrates with tunable surface plasmon resonances," *Advanced Functional Materials*, vol. 21, no. 18, pp. 3424–3429, 2011.
- [56] A. Cerf, G. Molnár, and C. Vieu, "Novel approach for the assembly of highly efficient SERS substrates," *ACS Applied Materials and Interfaces*, vol. 1, no. 11, pp. 2544–2550, 2009.
- [57] M. Fan, G. F. S. Andrade, and A. G. Brolo, "A review on the fabrication of substrates for surface enhanced Raman spectroscopy and their applications in analytical chemistry," *Analytica Chimica Acta*, vol. 693, no. 1–2, pp. 7–25, 2011.
- [58] F. L. Yap, P. Thoniyot, S. Krishnan, and S. Krishnamoorthy, "Nanoparticle Cluster Arrays for SERS through direct self-assemble," *Acs Nano*, vol. 6, pp. 2056–2070, 2012.
- [59] M. A. Olson, A. Coskun, R. Klajn et al., "Assembly of polygonal nanoparticle clusters directed by reversible noncovalent bonding interactions," *Nano Letters*, vol. 9, no. 9, pp. 3185–3190, 2009.
- [60] R. Sardar and J. S. Shumaker-Parry, "Asymmetrically functionalized gold nanoparticles organized in one-dimensional chains," *Nano Letters*, vol. 8, no. 2, pp. 731–736, 2008.
- [61] G. Chen, Y. Wang, L. H. Tan et al., "High-purity separation of gold nanoparticle dimers and trimers," *Journal of the American Chemical Society*, vol. 131, no. 12, pp. 4218–4219, 2009.
- [62] J. Wang, L. Huang, L. Yuan et al., "Silver nanostructure arrays abundant in sub-5nm gaps as highly Raman-enhancing substrates," *Applied Surface Science*, vol. 258, no. 8, pp. 3519–3523, 2012.
- [63] L. Nataraj and S. G. Cloutier, "Highly ordered periodic array of metallic nanodots fabricated through template-assisted nanopatterning and its use for surface-enhanced Raman scattering spectroscopy of flexible crystalline-silicon nanomembranes," *Journal of Raman Spectroscopy*, vol. 42, no. 6, pp. 1294–1297, 2011.
- [64] E. A. Batista, D. R. D. Santos, G. F. S. Andrade, A. C. Sant'Ana, A. G. Brolo, and M. L. A. Temperin, "Using polycarbonate membranes as templates for the preparation of Au nanostructures for surface-enhanced Raman scattering," *Journal of Nanoscience and Nanotechnology*, vol. 9, no. 5, pp. 3233–3238, 2009.
- [65] C. Tian, Z. Liu, J. Jin et al., "Gold mesoflower arrays with sub-10 nm intraparticle gaps for highly sensitive and repeatable surface enhanced Raman spectroscopy," *Nanotechnology*, vol. 23, no. 16, Article ID 165604, 2012.
- [66] S. Yang and Y. Lei, "Recent progress on surface pattern fabrications based on monolayer colloidal crystal templates and related applications," *Nanoscale*, vol. 3, no. 7, pp. 2768–2782, 2011.
- [67] W. Zhang, X. Qiao, and J. Chen, "Synthesis of silver nanoparticles—effects of concerned parameters in water/oil micro-emulsion," *Materials Science and Engineering B*, vol. 142, no. 1, pp. 1–15, 2007.
- [68] J. Zhang, Y. Li, X. Zhang, and B. Yang, "Colloidal self-assembly meets nanofabrication: from two-dimensional colloidal crystals to nanostructure arrays," *Advanced Materials*, vol. 22, no. 38, pp. 4249–4269, 2010.
- [69] G. Liu, Y. Li, G. Duan et al., "Tunable surface plasmon resonance and strong SERS performances of Au opening-nanoshell ordered arrays," *ACS Applied Materials & Interfaces*, vol. 4, no. 1, pp. 1–5, 2011.
- [70] Y. Yang, Z. Y. Li, K. Yamaguchi et al., "Controlled fabrication of silver nanoneedles array for SERS and their application in rapid detection of narcotics," *Nanoscale*, vol. 4, no. 8, pp. 2663–2669, 2012.
- [71] Y. Yang, M. Tanemura, Z. Huang et al., "Aligned gold nanoneedle arrays for surface-enhanced Raman scattering," *Nanotechnology*, vol. 21, no. 32, Article ID 325701, 2010.
- [72] D. Rodríguez-Fernández, J. Pérez-Juste, I. Pastoriza-Santos, and L. M. Liz-Marzán, "Colloidal synthesis of gold semishells," *ChemistryOpen*, vol. 1, no. 2, pp. 90–95, 2012.
- [73] J. C. Yang, C. H. Chen, and R. J. Wu, "Facile growth of silver crystals with greatly varied morphologies by PEO-PPO-PEO tri-block copolymers," *CrystEngComm*, vol. 14, pp. 2871–2878, 2012.
- [74] J. He, X. Han, J. Yan et al., "Fast fabrication of homogeneous silver nanostructures on hydrazine treated polyaniline films for SERS applications," *CrystEngComm*, vol. 14, no. 15, pp. 4952–4954, 2012.
- [75] L. L. Qu, D. W. Li, J. Q. Xue, W. L. Zhai, J. S. Fossey, and Y. T. Long, "Batch fabrication of disposable screen printed SERS arrays," *Lab on a Chip*, vol. 12, no. 5, pp. 876–881, 2012.
- [76] X. Hong, D. Wang, and Y. Li, "Kinked gold nanowires and their SPR/SERS properties," *Chemical Communications*, vol. 47, no. 35, pp. 9909–9911, 2011.
- [77] N. Pazos-Pérez, W. Ni, A. Schweikart, R. A. Alvarez-Puebla, A. Fery, and L. M. Liz-Marzán, "Highly uniform SERS substrates formed by wrinkle-confined drying of gold colloids," *Chemical Science*, vol. 1, no. 2, pp. 174–178, 2010.
- [78] C. Zhu, G. Meng, Q. Huang et al., "Ag nanosheet-assembled micro-hemispheres as effective SERS substrates," *Chemical Communications*, vol. 47, no. 9, pp. 2709–2711, 2011.
- [79] M. F. Zhang, A. W. Zhao, H. H. Sun et al., "Rapid, large-scale, sonochemical synthesis of 3D nanotextured silver microflowers as highly efficient SERS substrates," *Journal of Materials Chemistry*, vol. 21, no. 46, pp. 18817–18824, 2011.
- [80] X. Han, H. Wang, X. Ou, and X. Zhang, "Highly sensitive, reproducible, and stable SERS sensors based on well-controlled silver nanoparticle-decorated silicon nanowire building blocks," *Journal of Materials Chemistry*, vol. 22, no. 28, pp. 14127–14132, 2012.
- [81] J. F. Li, Y. F. Huang, Y. Ding et al., "Shell-isolated nanoparticle-enhanced Raman spectroscopy," *Nature*, vol. 464, no. 7287, pp. 392–395, 2010.
- [82] S. Pahlow, A. März, B. Seise et al., "Bioanalytical application of surface- and tip-enhanced Raman spectroscopy," *Engineering in Life Sciences*, vol. 12, no. 2, pp. 131–143, 2012.
- [83] J. Kneipp, H. Kneipp, and K. Kneipp, "SERS—a single-molecule and nanoscale tool for bioanalytics," *Chemical Society Reviews*, vol. 37, no. 5, pp. 1052–1060, 2008.
- [84] P. R. Sajanal and T. Pradeep, "Functional hybrid nickel nanostructures as recyclable SERS substrates: detection of explosives and biowarfare agents," *Nanoscale*, vol. 4, no. 11, pp. 3427–3437, 2012.
- [85] L.-B. Yang, G.-Y. Chen, J. Wang, T.-T. Wang, M.-Q. Li, and J.-H. Liu, "Sunlight-induced formation of silver-gold bimetallic nanostructures on DNA template for highly active surface enhanced Raman scattering substrates and application in

- TNT/tumor marker detection,” *Journal of Materials Chemistry*, vol. 19, no. 37, pp. 6849–6856, 2009.
- [86] K. L. Wustholz, C. L. Brosseau, F. Casadio, and R. P. Van Duyne, “Surface-enhanced Raman spectroscopy of dyes: from single molecules to the artists’ canvas,” *Physical Chemistry Chemical Physics*, vol. 11, no. 34, pp. 7350–7359, 2009.
- [87] Z. Zhang, Y. Wen, Y. Ma, J. Luo, L. Jiang, and Y. Song, “Mixed DNA-functionalized nanoparticle probes for surface-enhanced Raman scattering-based multiplex DNA detection,” *Chemical Communications*, vol. 47, no. 26, pp. 7407–7409, 2011.
- [88] N. T. B. Thuy, R. Yokogawa, Y. Yoshimura, K. Fujimoto, M. Koyano, and S. Maenosono, “Surface-enhanced Raman spectroscopy for facile DNA detection using gold nanoparticle aggregates formed via photoligation,” *Analyst*, vol. 135, no. 3, pp. 595–602, 2010.
- [89] S. Efrima and L. Zeiri, “Understanding SERS of bacteria,” *Journal of Raman Spectroscopy*, vol. 40, no. 3, pp. 277–288, 2009.
- [90] L. Yang, B. Yan, W. R. Premasiri, L. D. Ziegler, L. D. Negro, and B. M. Reinhard, “Engineering nanoparticle cluster arrays for bacterial biosensing: the role of the building block in multiscale SERS substrates,” *Advanced Functional Materials*, vol. 20, no. 16, pp. 2619–2628, 2010.
- [91] A. Samanta, K. K. Maiti, K. S. Soh et al., “Ultrasensitive near-infrared Raman reporters for SERS-based in vivo cancer detection,” *Angewandte Chemie*, vol. 50, no. 27, pp. 6089–6092, 2011.
- [92] A. Kumar, B. M. Boruah, and X. Liang, “Gold nanoparticles: promising nanomaterials for the diagnosis of cancer and HIV/AIDS,” *Journal of Nanomaterials*, vol. 2011, pp. 1–17, 2011.
- [93] F. Zhai, Y. Huang, X. Wang, and K. Lai, “Surface-enhanced Raman spectroscopy for rapid determination of β -agonists in swine urine,” *Chinese Journal of Analytical Chemistry*, vol. 40, no. 5, pp. 718–723, 2012.
- [94] J. Kneipp, H. Kneipp, M. McLaughlin, D. Brown, and K. Kneipp, “In vivo molecular probing of cellular compartments with gold nanoparticles and nanoaggregates,” *Nano Letters*, vol. 6, no. 10, pp. 2225–2231, 2006.