DOI: 10.1002/anie.201204438

Sensing Using SERS

SERS Detection of Small Inorganic Molecules and Ions**

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inorganic chemistry · nanoparticles ·
Raman cross-section · SERS · ultradetection

Surface-enhanced Raman scattering (SERS) is one of the most straightforward applications of the so-called nanoplasmonics. This powerful molecular spectroscopy technique is based on the enhancement of the inelastic scattering from molecules located near nanostructured metallic surfaces when these are illuminated and surface plasmons are excited. The analytical applications of SERS are hindered when the Raman cross-section of the analyte is too low, which is often the case in inorganic molecular species. This problem is even more serious when atomic species are to be identified, since these cannot display a vibrational signal. Herein we discuss the recent advancements toward the SERS detection of small inorganic compounds, including both molecular and atomic species.

1. Introduction

Surface-enhanced Raman scattering (SERS) is a powerful molecular spectroscopy technique for ultradetection.[1] The simplicity of its application, together with its potential to detect minute amounts of organic molecules of potential interest even in complex media, has raised an increasing interest in this technique. In fact, during recent years a myriad of amazing applications involving SERS have been developed, especially in the fields of environmental monitoring,[2] diagnostics, biodetection, and bioimaging.[3] Notwithstanding, these applications usually involve the detection of organic molecular systems with high Raman cross-sections. In this scenario, the use of this technique for the detection of inorganic species has been very restricted, in part because of their small Raman scattering cross-section or even the absence of vibrational modes in atomic systems, but also because there is a set of established analytical methods that adequately fulfill this task. For example, metal cations are commonly detected and quantified by using atomic absorption or emission spectroscopy,[4] anions are detected by ion exclusion chromatography,[5] electrochemical methods,[6] electronic absorption or emission (colorimetry),[7] and resonance Raman scattering.[8] While these techniques provide detection limits ranging from the micro- to the pico-molar regime, most of them require a substantial amount of sample, are destructive, and cannot be applied remotely without direct interactions between sample and sensor. To solve this situation, a number of optical methods are being developed.[9] These methods rely on the measurement of fluorescence upon interaction of the inorganic species with a fluorophore,[10] plasmonic shifts or damping upon interaction of the inorganic species directly with the plasmonic surface (i.e. the case of Hg)[11] or upon interaction with a pre-adsorbed ligand.[12] SERS has also been applied, either by direct identification of the specific molecular vibrational fingerprint or by monitoring the spectral changes in a pre-adsorbed molecule upon interaction with the probe inorganic species.

We focused in this Minireview on the recent advances in SERS analysis of inorganic species, showing the potential of this technique for the remote and fast acquisition of information either from highly toxic sources or to study very fragile systems, such as living organisms under different conditions.

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[**] SERS = Surface-enhanced Raman scattering.

2. The SERS Activity

One of the most common questions in SERS relates to the activity of the studied molecular systems. The response should be clear: although all molecular systems can produce, in principle, SERS (and thus it can be safely stated that all molecular systems are SERS active), not all molecules are good SERS probes. The SERS activity depends essentially of three factors: 1) the electromagnetic field generated by the plasmonic nanostructure used as optical enhancer; 2) the intrinsic Raman properties of the molecule under study (the cross-section); and, 3) the affinity of the molecule for the plasmonic surface (adsorbent–adsorbate interaction).

The first factor, the electromagnetic field or localized surface plasmon resonance (LSPR) is the basis of SERS. The effects of the LSPR on the SERS intensity have been extensively studied[13] but the magnitude of this effect is the same regardless of the probe molecule, independent of its chemical nature, and therefore we chose not to discuss it herein.

2.1. Raman/SERS Cross-Section

As a general rule, a good Raman scatterer (a molecule with a high Raman cross-section) makes a good SERS scatterer. The cross-section of a molecule for a given linear optical process can be defined as the signal intensity produced by this process compared to the incident power density.[15] Rigorously, for each excitation wavelength a cross-section for each vibrational mode of the analyte should be provided for each molecular orientation. Notwithstanding, in Raman scattering, the geometry, polarization, and laser wavelength are often invariant and are determined by the instrument. Thus, an empirical cross-section for a given Raman band in that geometry is adequate for estimating the signal intensity. Table 1 shows the Raman cross-section for different molecular systems under excitation with a 514.5 nm laser line.

Table 1: Experimental Raman cross-sections for some representative probes. Values obtained from Ref. [14].

Molecular system	Raman cross-section (β)[a] [cm^2 molecule^{-1} sr^{-1}]
N_2	4.3×10^{-31}
O_2	5.8×10^{-31}
SO_4^{2-}	9.9×10^{-30}
ClO_4^{-}	1.3×10^{-29}
Cyclohexane	5.2×10^{-30}
Benzene	2.9×10^{-29}
Naphthalene	8.2×10^{-29}
Anthracene	5.4×10^{-28}

[a] Sample illuminated with a 514.5 nm laser line.

The comparison between the different molecules illustrates the factors controlling the cross-section and thus the expected intensity. Typically, small molecules without electron-rich atoms have small Raman cross-sections (β). However, β increases with size, and therefore with the presence of extended π–π systems and electron-rich atoms, which make the molecule more polarizable. In summary, although some oxyanions, may have Raman cross-sections similar to those of small organic molecules, most inorganic molecules are small, and do not contain electron rich-atoms. Thus, their Raman (and thus SERS) scattering intensity is small.

2.2. Adsorbent–Adsorbate Interaction

It is important to note that although a high Raman cross-section is necessary to produce intense SERS, it is not a sufficient condition. SERS is a first-layer effect, meaning that, for a given probe, the highest intensity is obtained when the target molecule is very close to the plasmonic surface (which is optimized by chemical bonding), and the intensity decreases exponentially with distance.[16] This situation is mainly due to the exponentially decay of the electromagnetic field generated upon excitation of the LSPR, which is responsible for the electromagnetic enhancement,[17] with the distance from the surface.[18] In addition, the chemical enhancement mechanism[19] requires the analyte to be directly bonded to the plasmonic surface, so as to allow charge transfer. Small inorganic species, including oxyanions and most other molecular and atomic species, have a limited affinity for gold and silver. Thus, even though some species such as sulfate or perchlorate may have a moderate Raman cross-section (see Table 1) their SERS signal is very low,

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almost negligible, even at relatively high concentrations. In fact, silver salts of these two oxyanions are sometimes used to produce plasmonic nanoparticles for SERS enhancement, without relevant interferences.[20] An exception occurs with halogens and pseudohalogens, which will be discussed in detail in the corresponding Sections of this Minireview.

3. Molecular Inorganic Species

The use of several inorganic probes can be tracked to the origins of SERS. The use of pseudohalogens (cyanide and thiocyanate)[21] in SERS was recursive in the early 1980s. These simple species display two interesting features, namely a very simple vibrational spectrum with characteristic bands arising from the C≡N bond and a high affinity towards noble-metal surfaces. However, these early works were devoted either to the proof of concept of detection or to carry out fundamental research on the concept of SERS itself. In more recent times, however, the use of SERS with an analytical perspective has dramatically increased.

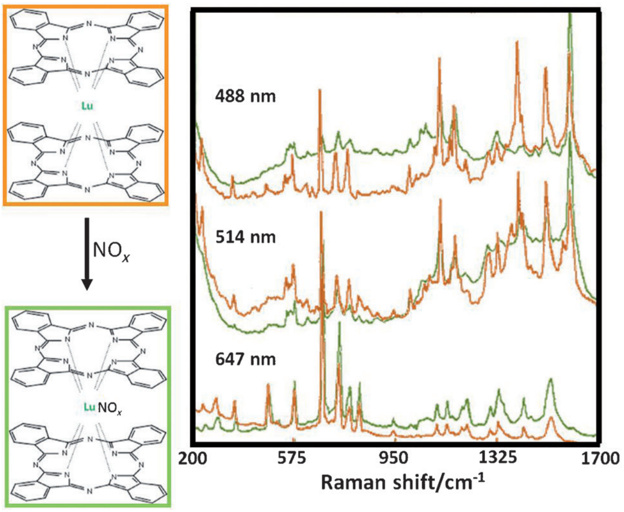

Figure 1. SERS spectra of a lutetium bisphthalocyanine Langmuir–Blodgett monolayer on a plasmonic island film before (yellow) and after (green) exposure to NO_x gas. Adapted with permission from Ref. [25]. Copyright 1992 American Chemical Society.

3.1. SERS Detection of Inorganic Gases

The trace sensing of inorganic gaseous species is required for atmospheric monitoring (climate and pollution studies), industrial process monitoring, and medical diagnostics. Owing to their spectral simplicity, SERS can be used to monitor not only one target but a set of probes in a multiplexed fashion. One of the first reports related to this application studied the composition of mixed atmospheres of CO, NO, and O_2.[22] In this study, the plasmonic enhancer was gold partially coated with Pt, Rh, or Ru. The choice of this material as the optical platform was based on the low affinity for pure gold by all three gases studied, as reported in earlier SERS studies, so adsorption on the other (catalytic) metal could be exploited for SERS analysis.[23] This approach of using a different metal (such as Cu) either as a plasmonic platform or as a coating to increase the affinity for gas targets has been popular and is still employed today.[24] Nevertheless, inorganic molecular gases are small and usually contain electron-rich atoms. Thus, their Raman cross-sections are small (see Table 1) and so is the intensity that can be obtained by applying this direct method. The solution to this problem was indirectly proposed in 1992.[25] In this work the SERS evolution of a lutetium bisphthalocyanine Langmuir–Blodgett monolayer deposited on a plasmonic island film was studied before and after exposure to NO_x gas. As shown in Figure 1, the complexation of the gas to the metallic core of the phthalocyanin completely changes the electronic distribution of the resulting complex, with the subsequent change in the SERS signal. This seminal experiment demonstrated the possibility of using a highly active SERS probe for the indirect detection of the target analyte. Unfortunately, the authors did not realize the analytical possibilities of their findings and, neither this group nor others ever continued exploiting these systems for detection. Notwithstanding we anticipate this approach to be central in the development of new SERS-based optical sensors for the trace detection of inorganic molecules in the gas phase. Analogously, a similar approach using metal-organic frameworks (MOFs) for the capture of gases such as H_2 and their detection by IR spectroscopy has been reported.[26] This method presents a great potential to be used in conjunction with SERS[27] and thereby extended to the ultrasensitive analysis of other inorganic gases.[28]

3.2. Oxyanions and Oxycations

As a general rule, it is worth mentioning that if the aim of the research is the detection of a particular oxyanion, that particular species should be avoided during the synthesis of the enhancing material. In fact, to avoid competition with the target oxyanion,[29] it is advisable to employ synthetic methods such as physical vapor deposition,[30] which avoid the use of metallic salts. Although in principle, direct SERS may allow the detection of oxyanions, especially those with moderate Raman cross-sections (for example phosphate or perchlorate),[31] their remarkably low affinity for gold or silver made this strategy not viable. Thus, during recent years several other approaches have been developed. Most of the SERS detection methods rely on the surface functionalization of the plasmonic material with positively charged agents that improve the retention of the oxyanion close to the particle surface and allow direct identification of the oxyanion characteristic vibrational bands. For example, perchlorate has been detected by using cationic trapping agents, such as cystamine,[32] 2-dimethyl-aminoethanethiol,[33] or poly(ethyleneimine).[34] These methods yield detection limits ranging from the millimolar to the nanomolar regimes, which are competitive with those obtained when using ion exclusion chromatography[5] or ion-selective electrodes.[6b]

Direct SERS has also been applied to the detection of arsenate in drinking water, aided by polymers as trapping

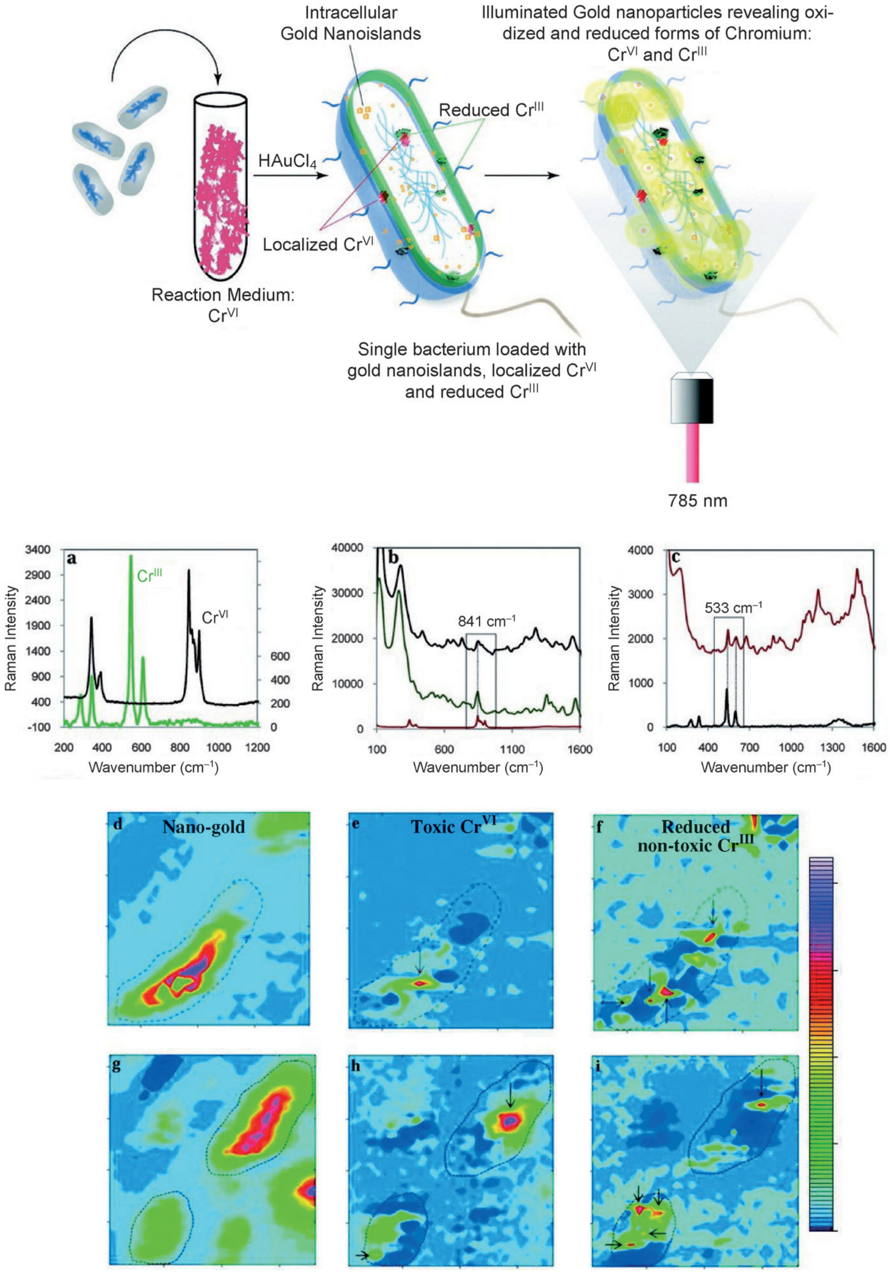

Figure 2. *S. oneidensis* MR-1, a versatile metal reducer, is exposed to hexavalent chromium, Cr^{VI}, then treated with Au^{III}, which results in the formation of numerous metal nanoislands within the cells. Single-cell Raman chemical imaging driven by intracellularly grown gold nanoislands allows detailed chemical localization and oxidation state information to be obtained for Cr^{VI} and Cr^{III} in living cells. a) Raman signatures obtained from chemical controls for Cr^{VI} and Cr^{III} display distinctive differences in their chemical spectra. b) SERS spectra obtained from *S. oneidensis* MR-1 loaded with intracellularly reduced gold nanoislands indicate the presence of Cr^{VI} signals within the cells (black and green spectra, acquired from two different cells). The signals from the chemical control (red) at 841 cm^{-1} perfectly align with the Cr^{VI} signals detected from within the cell. c) Bacterial SERS spectrum (red) indicates the presence of Cr^{III} signals, which are aligned with those of the chemical control, Cr^{III} (black spectrum). The two peaks of Cr^{III} present around 533 cm^{-1} are perfectly aligned with the intracellularly reduced Cr^{III}. Raman intensity maps: d)–f) aerobic reduction, g)–i) anaerobic reduction, averaged over the phonon-plasmon peak (ca. 230 cm^{-1}) depicting the presence of intracellular pockets of gold nanoislands (d and g), localization of toxic hexavalent chromium, Cr^{VI} (e and h), and reduced nontoxic chromium, Cr^{III} (f and i), within a single cell. Adapted with permission from Ref. [41]. Copyright 2011 American Chemical Society.

agents, either by using Langmuir–Blodgett[35] or layer-by-layer[36] plasmonic films. Notably, in both cases a linear response was obtained with detection limits ranging from the nanomolar to the picomolar regimes, which were unprecedented results for the direct sensing of inorganic molecules.

Analogously, direct SERS detection of oxyanions and cations of metals has been reported including CrO$_4^{2-}$, MoO$_4^{2-}$ and WO$_4^{2-}$,[37] UO^{2+} and NpO^{2+},[38] or TcO^{4-}.[39] In such cases, SERS not only provides information regarding the presence of the chemical element but also of its chemical form, oxidation state, or complexation,[40] which are critical aspects in the toxicological evaluation of heavy metals. This feature has also made it possible to map and characterize the chromium content in a living cell (Figure 2).[41]

4. Atomic Inorganic Species

4.1. Atomic Species that Form Surface Complexes with the Optical Enhancers

As a molecular spectroscopy technique, SERS cannot be used to detect/recognize atomic species directly. However the strong interaction of noble metals with the heavier halogens (Cl, Br, and I) and chalcogens (S, Se, Te) is well established.[42] In such cases, when present in the medium, these species form a strong covalent bond with gold or silver. Thus, instead of being considered single atomic ions they become molecules and can then be analyzed by SERS. In fact, their moderate SERS activity is due to both their electron-rich nature and their close distance to the optical enhancer. The SERS vibrational signatures and activities of the halogens were described in detail for silver and gold.[43] To our knowledge, no similar study has been carried out for chalcogens, but their SERS patterns are well known through the multiple studies of small molecules containing S, Se, or Te atoms.[44] Both families of compounds show characteristic bands below 250 cm^{-1} arising from the M−X (X = halogen or chalcogen) covalent interaction. These vibrational characteristics of M−X have been exploited, for example, for studying the role of different halogens during the growth of nanoparticles (Figure 3).[45] However, the simplicity of their spectrum (usually one single peak) and the close positions of their respective characteristic bands, make band assignment difficult when present in solutions containing several species (including amines, pseudohalogens, carboxylic acids).

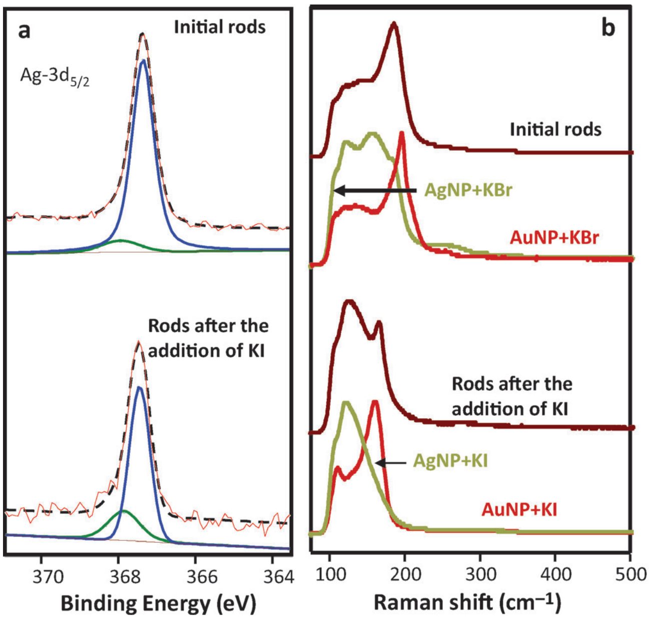

Figure 3. a) High-resolution X-ray photoelectron spectroscopy (XPS), characteristic bands of Ag-3d$_{5/2}$ (broken line) and their deconvoluted contributions (green and blue), and b) SERS spectra of gold nanorods (containing Br^- ions) before and after KI addition. The characteristic XPS peaks from silver (Ag–3d$_{5/2}$) shift toward lower energies, from 368 eV to 367.34 and 367.49 eV for Ag–Br and Ag–I, respectively. These Ag-3d$_{5/2}$ bands also comprise two contributions: one at 368 eV, with lower intensity and a binding energy common to both samples, which is ascribed to metallic silver; whereas the second contribution, with higher intensity, is located at 367.34 eV for Ag–Br and 367.54 eV for Ag–I components. SERS measurements were performed on the different rod samples and on citrate-reduced gold and silver colloids, which were previously exposed to 10^{-3} M solutions of KBr or KI. SERS spectra of Au nanoparticles display broad and intense peaks at 196 and 160 cm^{-1} which are attributed to Au–Br and Au–I stretching vibrations. In the case of silver, both SERS spectra show complex peaks at 152 and 121 cm^{-1}, assigned to Ag–Br and Ag–I. In both cases, the SERS results show that the halides are coordinated to the metallic surface. Spectra for both nanorod samples (before and after KI addition) show patterns corresponding to the combination of the corresponding halides. Additionally, after KI addition, no Br signals remain. Adapted with permission from Ref. [45].

4.2. Detection of Atomic Species by Indirect Methods

As previously stated, SERS is a molecular technique and cannot be used to analyze atomic species. However, several recent reports have been published describing the use of indirect methods based on different approaches. Although all these methods may rely on the use of secondary probes, they are of different nature. The high affinity of Hg^{II} for gold surfaces has been exploited not only in the plasmonic detection[11] of this metal but also by using SERS.[46] This approach is based on the displacement of a pre-assembled molecule with a high SERS activity (rhodamine B, RB) from the nanoparticle gold surface as they amalgam mercury, with the subsequent decrease in the SERS signal (Figure 4). This approach is powerful, with detection limits below the nanomolar regime, and can be implemented into microfluidic devices for the online detection of Hg^{II}, for example in tap or waste water. Notwithstanding, the method can again be applied only to identify cations (or anions) with strong affinity for the plasmonic surface.

An alternative to this method comprises the immobilization of a DNA fragment on a surface. Then, plasmonic particles, functionalized with the complementary DNA sequence and a Raman reporter, are assembled onto the surface. When a given ion is present, it forces the DNA to disassemble and thus the SERS intensity decreases. This approach has been demonstrated for the detection of Pb^{II} in the presence of other metallic ions, with detection limits around the nanomolar regime.[47]

Another method for the detection of ionic atoms is based on the aggregation of particles induced by the presence of a certain cation. To achieve this goal, the plasmonic particles are functionalized with a specific ion receptor and a highly active Raman reporter. When the ion is present in solution, it reacts with the receptor and reduces the colloidal stability of the system. As a consequence, the particles aggregate forming

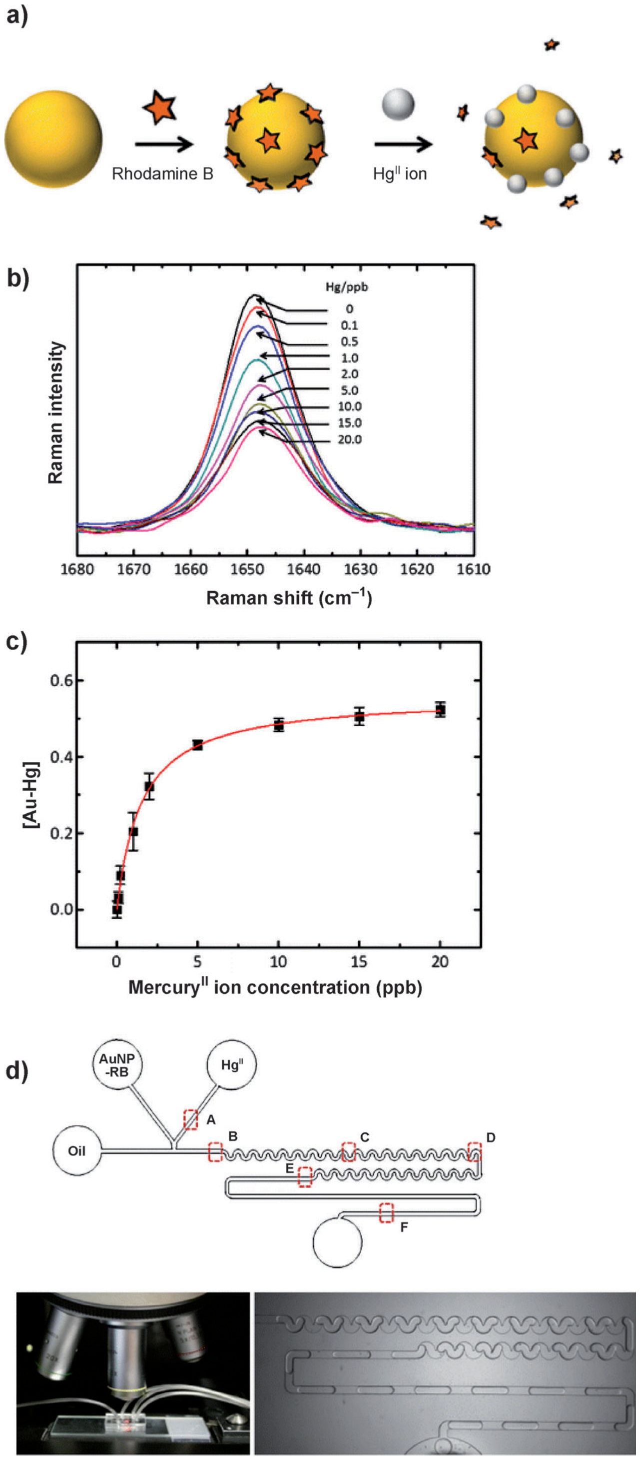

Figure 4. a) Schematic representation of the mercury(II) ion sensing mechanism based on the removal of Rhodamine B dye molecules through the reduction of mercury(II) ions on the surface of Au nanoparticles (AuNPs). b) Variation of the Raman intensity of Rhodamine 6GB (between 1680 and 1610 cm^{-1}) as a function of Hg^{2+} ion concentration. All spectra were measured at position F of the microfluidic device shown in (d). c) Variation of the peak area as a function of Hg^{II} ion concentration. Error bars denote the standard deviation resulting from three measurements. d) Schematic representation of the microfluidic channel pattern used for the online detection; optical arrangement for focusing the excitation beam into the microchannel network; and photograph of the assembled device in operation. Adapted with permission from Ref. [46]. Copyright 2009 Springer-Verlag.

the so-called electromagnetic hot-spots, consequently increasing the SERS signal of the system (Figure 5). Examples of this approach can be found in the detection of Cd^{II} with a Cd^{II}-chelating polymer,[48] As^{III} with glutathione,[49] Hg^{II} with a DNA aptamer,[50] or Hg^{II} with Bismuthiol II.[51]

The selective detection of atomic ions through the induced aggregation of colloidal nanoparticles restricts the use of the method to a single target. In addition, the aggregation is uncontrolled, giving rise to aggregates of different sizes and within different interparticle distances, which translates into a different number and activity of such hot spots in each aggregate formed.[13a] This, together with the fact that the SERS signal is due to an external reporter that is not related to the recognition event, may yield rather different SERS intensities for assays carried out under similar conditions. In such a scenario, these methods can be considered as qualitative or perhaps semiquantitative. Another possible constraint is also related to the aggregation event, which cannot be safely induced inside biological systems, so that the applicability of these methods is limited to environmental or industrial samples.

As an alternative, it is possible to use a molecular probe with high SERS cross-section that is directly adsorbed onto the plasmonic surface. This agent is required to undergo a recognizable change, usually geometrical or electronic, upon exposure to the desired analyte. In fact, this strategy has been successfully employed in biosensors, using antibodies[52] or nucleic acid aptamers[53] as the active interlayer for the indirect detection of proteins and other analytes. Regarding atomic ions, the first report in the literature described the use of gold nanoshells for the measurement of protons (pH value) upon ionization/deionization of the carboxylic group of 4-mercaptobenzoic acid (MBA) when exposed to solutions with different pH values.[54] In fact, similar sensors based on MBA-capped nanoparticles have been widely used for internal monitoring of the pH value in living cells.[55] Other reports were subsequently published, describing the use of different organic ligands for the indirect SERS determination of atomic cations, such as Zn^{II} with 4-(*N*-piperazinyl)terpyridine dithiocarbamate,[56] Cu^{II}, Zn^{II}, Hg^{II}, and Pb^{II} with MBA,[57] Hg^{II} and Cd^{II} with trimercaptotriazine,[58] Cu^{II} with 2-mercaptobenzimidazole,[59] or Cl^{-} with 2-(2-(6-methoxyquinoliniumchloride)ethoxy)ethanamine hydrochloride (amino-MQAE).[60] The detection limits of this method depend essentially on those of the molecular probe used to interact with the ionic atom. Thus, it is not unusual to find reported detections below the picomolar regime.

Contrary to the other methods, the detected signal directly corresponds in this case to the interaction event between the inorganic ion and the Raman reporter. This offers several advantages over the other alternatives. First, as the ligand protects the plasmonic surface and interacts specifically with one or more atomic ions, the potential background signal from other molecular species present in the sample, a recursive problem in direct SERS, is reduced. Further, quantitative detection of the target analyte is possible by using the ligand receptor also as an internal standard. For example, in the case of chloride it is possible to obtain a linear response by plotting the ratio between band

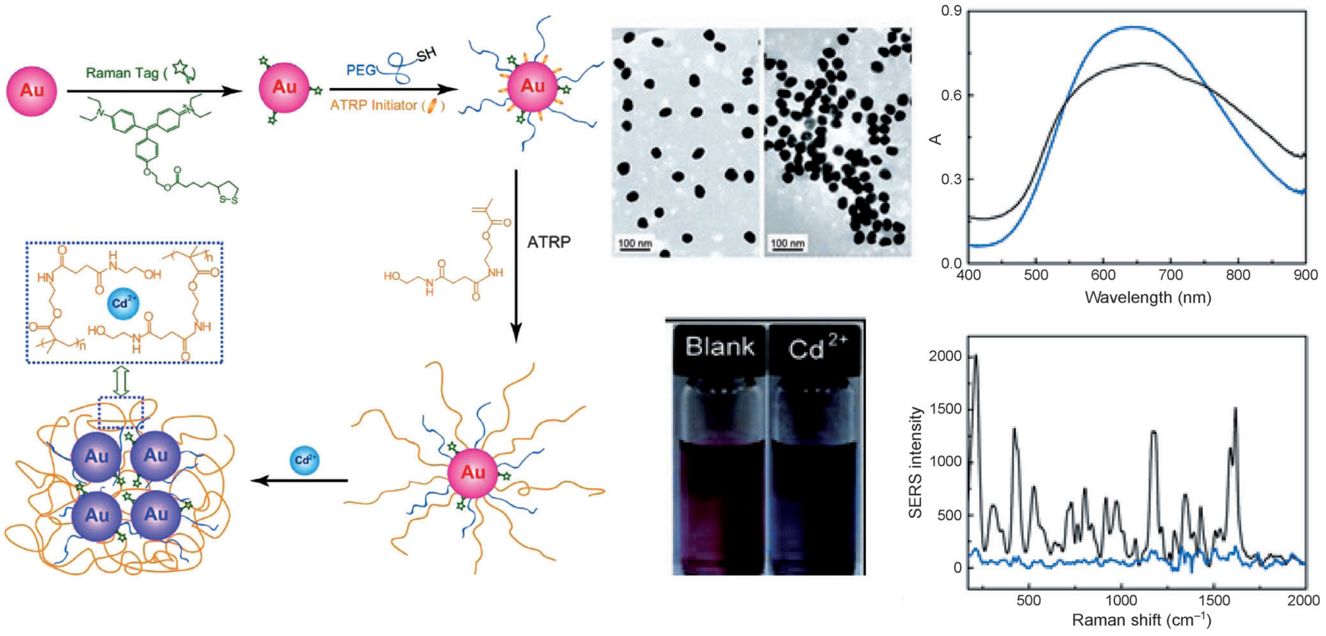

Figure 5. Schematic illustration of the procedure employed for the selective recognition of Cd^{II} by induced aggregation of a nanoparticle dispersion. TEM and optical images, UV/Vis and SERS spectra of the nanoparticles in the absence (blue lines) and presence (black lines) of 8 μM Cd^{II} ions. ATRP = atom transfer radical polymerization. Adapted with permission from Ref. [48]. Copyright 2011 American Chemical Society.

areas at 1497 and 1472 cm^{-1} (Figure 6) versus chloride concentration. It is interesting to note that, with these sensors, the detection range depends on the amount of receptor molecules deposited on the surface of the plasmonic material. Thus, this detection scheme permits the selection of ranges of about two orders of magnitude from the micro to the picomolar regimes. The use of specific receptors also allows for the multiplex detection of several targets if the receptor forms complexes with more than one atomic ion. In line with this, the SERS spectra of several metallic complexes with mercaptobenzoate were recently recorded (M: Cd^{2+}, Pb^{2+}, Pd^{2+}, Hg^{2+}, Zn^{2+}, Fe^{2+}, Cu^{2+}, or Ag^{+}) all showing characteristic shifts for the bands associated with the COO^{-} functional group, among others. Proof of concept of multiplex detection was achieved through the simultaneous detection and quantification of mercury and lead in a chromatographic capillary (Figure 7).[57a]

The main drawback of this approach relies on the nature of most specific receptors, which are organic ligands with low polarity, thereby compromising the colloidal stability of the nanoparticle dispersion when these ligands are assembled on their surfaces. This usually induces aggregation, thereby hindering the contact and interaction/complexation of the ionic atoms with the sensing nanoparticle interlayer. Most of the above mentioned reports were demonstrated on nanostructured thin films, which are adequate for monitoring environmental processes but not for the fabrication of miniaturized sensors. A suitable alternative comprises the fabrication of plasmonic surfaces on submicron or micromaterials used as supports, thus generating a stable platform containing a dense collection of hot spots.[60,61]

5. Conclusions and Outlook

We have summarized in this Minireview the problems involved in the application of SERS as a technique for analysis of molecular and atomic inorganic species (ions). Although much work has been carried out in this direction during the last few years, many and important challenges remain before SERS can be efficiently used in practice. These include improvements in the detection capability and sensitivity, multiplexing, and performance. For example, SERS detection of molecular gases or oxycations/anions is now successfully performed directly on nanostructured surfaces aided by trapping functionalities; however, the evolution of this sensing technique toward the use of high Raman cross-section ligand probes will dramatically improve its detection limits. Further, proof of concept of the multiplex detection of atomic ions has also been recently demonstrated, but this powerful detection method is still in its infancy.

Although many sensors have been developed at the laboratory level, their transformation into robust practical tools is, to date, a challenge. Nanostructures for sensor fabrication must be prepared in a way that ensures signal reproducibility. Also, the nanoparticles must be stable against aggregation and, in the case of in vivo applications, biocompatible. Additionally, the inherent complexity associated to the analysis of complex real life samples including natural and waste waters would require some form of sample preparation, even in the case of indirect sensing. These samples may require sedimentation and/or filtration prior to analysis to ensure the separation of their larger constituents that may destabilize the colloidal system, in addition to providing vibrational and fluorescence contamination.

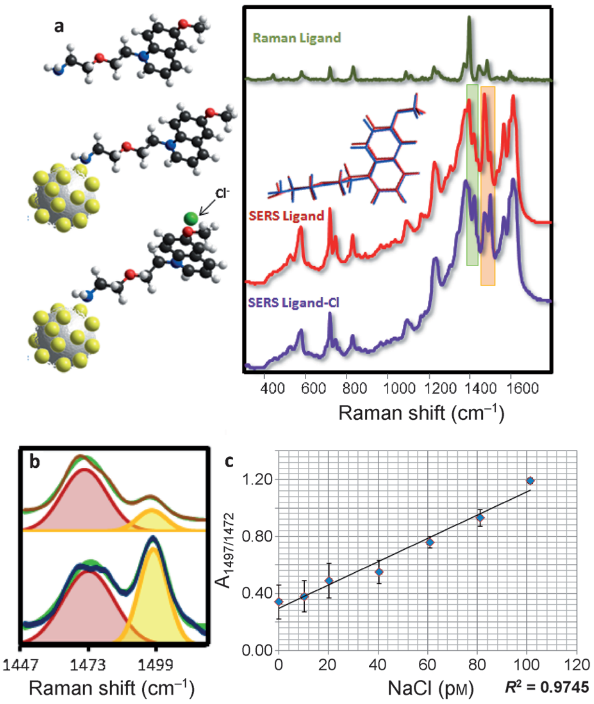

Figure 6. a) Left: Schematic representation of the detection of Cl^- ions with amino-MQAE. Right: Raman and SERS spectra of amino-MQAE and SERS spectrum of amino-MQAE in the presence of an equimolar concentration of chloride (10^{-6} M). Samples were excited with a 532 nm laser line. Inset: Optimized molecular geometry of amino-MQAE (at the M052X; 6-31þG* theory level) in the presence (blue) and absence (red) of Cl^- ions. b) Band deconvolution of the SERS spectra of amino-MQAE (10^{-10} M) without (top) and with (bottom) chloride (10^{-10} M): brown and blue are experimental spectra; green is the spectrum resulting from summing peak 1 (red), and 2 (yellow). c) Linear plot of the ratio between the areas of the peaks at 1472 and 1497 cm^{-1}, as a function of chloride concentration. Error bars represent the standard deviations of five replicated experiments. Adapted with permission from Ref. [60]. Copyright 2011 American Chemical Society.

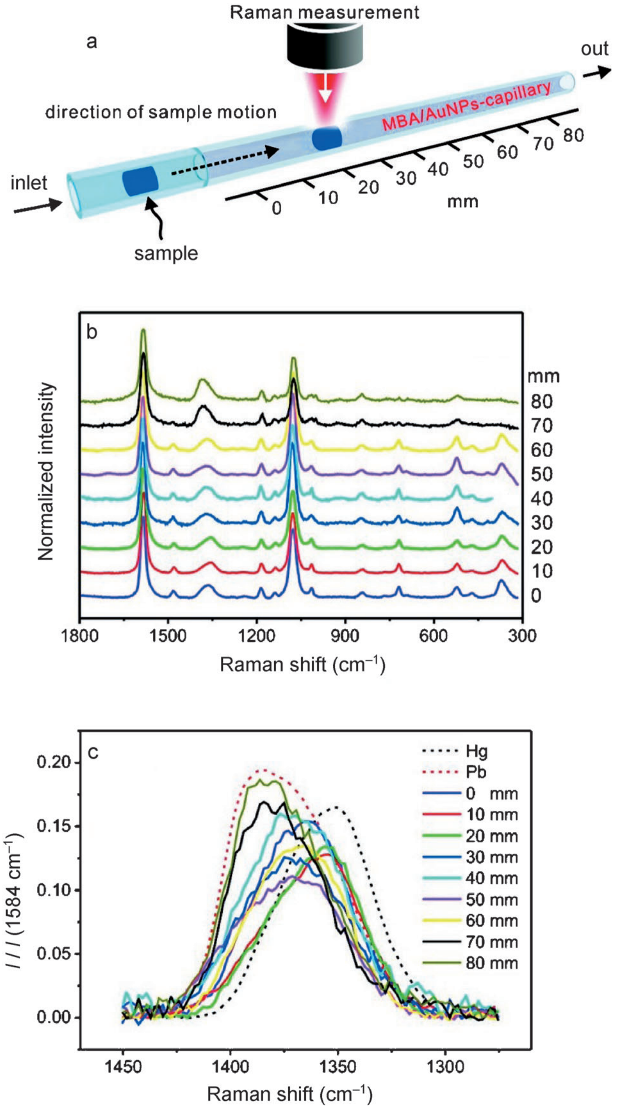

Figure 7. a) Schematic drawing of the capillary system used to separate Hg^{II} and Pb^{II} ions from an equimolar solution of the two ions, detecting their relative concentrations along the length of the capillary at the positions indicated, which are separated by approximately 10 mm. b) SERS spectra recorded at the indicated locations. c) Carboxylate stretching region. Intensities in both panels (b) and (c) were normalized to that of the 1584 cm^{-1} band, which was used as an internal standard. Adapted with permission from Ref. [57a]. Copyright 2011 American Chemical Society.

In conclusion, SERS sensing offers many promising features and potential applications in the case of these inorganic species. However, a combined multidisciplinary research effort is still necessary to extract and gather all these features to develop highly sensitive and reliable platforms that could compete with current commercially available sensor devices and applications.

R.A.A.-P. acknowledges funding from the Spanish Ministerio de Economia y Competitividad (CTQ2011–23167). L.M.L.-M. acknowledges funding from the Spanish Ministerio de Ciencia e Innovacion (MAT2010–15374), the Xunta de Galicia (09TMT011314PR), and the ERC (Advanced Grant 267867, PLASMAQUO).

Received: June 7, 2012
Published online: October 16, 2012

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