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2-Mercaptoethanesulfonate (MES) anion-functionalized silver nanoparticles as an efficient SERS-based sensor of metal cations

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ABSTRACT

The first SERS (surface enhanced Raman scattering) sensor for detection of alkaline and alkaline earth metal cations is presented. System composed of silver nanoparticles functionalized with 2-mercaptoethanesulfonate (MES) anions exhibits high selectivity and sensitivity toward aforementioned cations thanks to high affinity of surface-attached MES monolayer to cations. This interaction results in formation of contact-ion pairs between MES sulfonate groups and metal cations. We demonstrate a big potential of the Ag nanoparticles functionalized with MES in quantitative detection of a great variety of cations, including alkaline and alkaline earth metal cations, down to 10^{-8} M in case of Ca^{2+} which is unmatched by analogous SERS sensors. We also prove simultaneous determination of calcium and magnesium in physiological concentrations with the nanosensor feasible.

1. Introduction

Ultrasensitive detection of monoatomic cations is an important task of analytical chemistry, mainly in bioanalytical, biomedical and environmental areas of applications. Despite significant progress in modern analytical techniques which offer very high sensitivity in quantitative analysis, there is still a need of developing non-destructive, small-size detectors whose work is based on the optical signal [1]. One of the most sensitive tool which is employed to a large family of optical sensors is surface-enhanced Raman scattering (SERS). By means of SERS we can reach sensitivity down to a single molecule level. Applications of this technique in detection of ions was recently reviewed by Alvarez-Puebla and Liz-Marzan [2].

Nanometric size of metal particles responsible for signal enhancement makes detection of ions inside biological cells possible. Good example of such use is detection and determination of a spatial distribution of Cr(VI) and Cr(III) species inside a living cell with the help of SERS signals enhanced by intracellularly reduced gold nanoislands [3].

Among SERS detectors of cations, sensors sensitive to pH value are studied the most extensively [4–11]. They have also been successfully employed in the intracellular investigations [4,6,8–10]. However, systems which enable detection of metal ions with the use of SERS nanosensors are still in the early stage of development.

Cation SERS nanosensors may be constructed in various ways. Monoatomic cations do not display any vibrational spectrum, therefore it is not possible to detect them directly by vibrational spectroscopy. The simplest way to overcome this problem is to monitor a cation-sensitive SERS spectrum of the so-called reporter molecule, which was previously attached to a plasmonic nanostructure [12–15].

Another approach to detection of monoatomic cations relies on measuring an increasing SERS intensity upon aggregation of plasmonic nanoparticles [16–18]. In these experiments, metal nanoparticles are functionalized with both, cation-receptor molecules and SERS reporter molecules, exhibiting a strong SERS spectrum. Appearance of the so-called hot spots due to ion-induced aggregation of nanoparticles causes a significant increase of the SERS spectrum of the reporter molecules.

The third strategy is based on monitoring a decreasing intensity of a very strong SERS signal which belongs to a reporter molecule (e.g. a dye). It is caused by displacement of these molecules by ions that have strong affinity to the metal (Ag or Au) nanoparticles. This approach was successfully applied to trace detection of Hg(II) cations in samples encapsulated within nanoliter droplets [19].

The first approach, based on direct monitoring of the ion-sensitive SERS signal of the reporter molecule, has several advantages over the other methods mentioned above. First, this method is potentially more quantitative, contrary to the approach based on colloid aggregation which is a hardly controllable process. Second, as opposed to the last mentioned strategy, this approach

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is not limited to the ions which have a strong affinity to Ag or Au. Moreover, simultaneous detection of various ions coexisting in the sample is possible, provided that the interaction of ions with the receptor molecules produces ion-specific changes in the SERS spectrum of the reporter.

In this report, we demonstrate the use of a system based on 2-mercaptoethanesulfonate (MES) anions attached to Ag nanoparticles. MES adsorbs easily on Ag surface, forming Ag–S chemical bonds. The monolayers are stable and exhibit strong SERS spectra [20,21]. As previously reported, the SERS band corresponding to symmetric stretching vibration of the SO_3^- group is split into two components [21]. The lower frequency component was ascribed to sulfonic groups interacting with water molecules and the higher frequency one to SO_3^- groups forming contact ion pairs with metal cations. Sensitivity of the SERS spectrum of MES to interactions with cations makes MES-functionalized Ag nanoparticles a promising candidate for ion sensing.

The choice of MES anions as reporter molecules brings several benefits. Important problem in designing SERS-based sensors which may be potentially used for biological samples (e.g. in intracellular sensing) is toxicity of the functionalized nanoparticles. MES molecules were proved to be almost completely non-toxic and were successfully used as an agent which detoxifies urotoxic metabolites in cancer chemotherapy [22,23]. It is also used as a mucolytic agent in acute or chronic pulmonary disease and sold as Mistabron. Moreover, 2-mercaptoethanesulfonate anions form complexes with various metal ions (Pd(II), Pt(II), Ag(I), Cd(II) and Zn(II)) and some of them (including Ag complexes) show negligible cytotoxicity and antiviral activity [24]. Thus, metal nanoparticles functionalized with MES are promising candidates in biological or biomedical applications. Another issue that needs to be considered while designing an efficient sensor is the concentration range within which the cations occur physiologically. For example, human blood or saliva samples can be expected to contain Mg^{2+} or Ca^{2+} in the order of 10^{-4}–10^{-3} M while the concentration of sodium cations reach the order of 10^{-1} M in the human body [25]. Sensor used to quantify ions in such samples has to exhibit sufficient sensitivity in the adequate working range in order to be able to efficiently detect the analyte.

2. Materials and methods

2.1. Instrumentation

Raman spectra were collected on LabRAM HR800 (Horiba Jobin Ivon) Raman spectrometer with a charge-coupled device detector cooled by Peltier modulus. All the spectra were excited with a 532 nm Nd:YAG laser second harmonic line of a maximum light beam power (at the laser head) of about 100 mW. Holographic grating with 600 grooves/mm was used. The spectrometer was coupled with Olympus BX61 confocal microscope with a pinhole set to 200 μm. Backscattered light was collected through a 10× objective. Calibration of the system was performed with respect to 520 cm^{-1} silicon band.

2.2. Chemicals

Magnesium chloride (99%), potassium chloride (99.5%) and silver nitrate (99.9%) were purchased from POCH, the rest of the metal chlorides (99%) as well as hydroxylamine hydrochloride (99.9%) and sodium 2-mercaptoethanesulfonate (98%) were purchased from Sigma–Aldrich. Ultrapure water (18 $M\Omega\,cm^{-1}$) was used to prepare all solutions.

2.3. Sample preparation

Silver colloid which was exploited as a SERS substrate was synthesized according to Leopold and Lendl procedure [26]. Ten milliliters of 1×10^{-2} M silver nitrate was added dropwise to 90 ml of 1.66×10^{-3} M hydroxylamine hydrochloride while stirring. Required pH value was achieved by adding 300 μl of 1 M sodium hydroxide. The whole solution was then stirred for 10 min. Extinction spectra of the obtained colloids exhibited peaks in the range between 404 and 417 nm. Resulting nanoparticles had a mean diameter of 29 nm (based on the statistics from TEM images).

Functionalization of silver nanoparticles with sodium 2-mercaptoethanesulfonate (MESNa) was carried out by adding 1 ml of 1×10^{-2} M MESNa aqueous solution to 9 ml of the silver colloid. The mixture was subsequently centrifuged for 30 min and the supernatant was removed in order to get rid of the unattached MES molecules. The test tube with the precipitate was filled with 45 mM hydrochloric acid solution and the suspension was centrifuged once more. The precipitate of nanosensors was redispersed in water up to the initial volume of the sample.

Stock solutions of metal chlorides varying in the range between 5×10^{-9} M and 5 M with a step of one order were used for the ion-concentration-dependent measurements. They were performed on samples prepared by adding 100 μl of the aforementioned metal ion solution to 400 μl of the nanosensors suspension obtained in the procedure described above.

For simultaneous detection measurements, samples consisted of 400 μl of the nanosensor suspension, 90 μl of 5.56×10^{-4} M (for final concentration 1×10^{-4} M) or 5.56×10^{-2} M (for final concentration 1×10^{-2} M) Ca^{2+} and 10 μl of Mg^{2+} of the respective concentrations.

2.4. Raman measurements and data processing

All spectra were collected for five accumulations, 50 s each. Spectra were baseline-corrected before further processing. In order to calculate intensity ratio of the chosen bands, absolute intensities in respective peak positions were read out. Up to four measurements were performed for each series in order to obtain statistical data. Error bars on all the figures reflect standard deviations of the respective measurements. Boltzmann function was fitted and plotted in Figs. 7 and 8.

3. Results and discussion

Sodium 2-mercaptoethanesulfonate ($HSCH_2CH_2SO_3^-\ Na^+$) like other thiols has high affinity to the silver surface; it strongly binds to Ag nanoparticles through SH groups and forms a metal–sulfur bond [20,21]. Sulfonate groups are therefore left exposed to the surrounding solution and may interact with the solvent molecules and other species present in the solution. Negative charge of SO_3^- groups provokes strong electrostatic repulsion between adjacent MES anions in the monolayer, which may be diminished by attractive interaction with metal cations present in the solution. In the case of sodium 2-mercaptoethanesulfonate, used in functionalization of the Ag nanoparticles, saltlike structure of the MES monolayer on a surface is formed, resembling the structure of the MESNa crystal [20]. SERS spectrum of MES adsorbed on silver nanoparticles from 10^{-3} M solution of MESNa is shown in Fig. 1. As may be seen, new band at 290 cm^{-1} (not seen in the bulk spectrum of MES), which corresponds to the Ag–S stretching vibrations, appears. Among the rest of the bands present in the spectrum, there are two pairs worth pointing out, both sensitive to metal cations. The first one is made up of bands at 633 and 706 cm^{-1}. They are assigned to C–S (sulfur bound to the surface) stretching vibrations