Modified multicapillary glass structure for SERS application

N E Markina¹, A V Markin¹,², A M Zakharevich², Y S Skibina³, I Yu Goryacheva¹
¹ Institute of Chemistry, Saratov State University, Saratov 410012, Russia
² Education and Research Institute of Nanostructures and Biosystems, Saratov State University, Saratov 410012, Russia
³ SPE Nanostructured Glass Technology Ltd, Saratov, 410033, Russia

Abstract. The aim of the work is the fabrication and analytical testing of SERS substrate by modification of inner surface of multicapillary glass structure (MCGS). Silica based composite with embedded silver nanoparticles (AgNPs) was used for MCGS modification. The testing was carried out by performing solid phase extraction of the analyte (rhodamine 6G) with further its SERS registration. The results showed that modified MCGS possesses superior Raman enhancement compare to pure AgNPs and provides 12 times larger SERS signal. The growth of SERS efficiency was explained by improved sorption characteristics.

1. Introduction
Currently, investigations dedicated to surface-enhanced Raman scattering (SERS) are shifted from the fields of fundamental physics, physical chemistry, and materials science to solving practical problems. For example, application of SERS was proposed for study of corrosion [1], catalysis [2], and chemical analysis [3]. Because SERS has high sensitivity and enables identification of target analytes via analysis their vibration spectra, it is widely tested for biochemical analysis, e.g., detection of cancer cells [4], therapeutical drug monitoring of antibiotics in urine [5], saliva [6], and blood [7], etc. SERS-active composites with high specific surface area are of particular interest because they enable extraction of the target molecules that additionally improves effectiveness (sensitivity and selectivity) and reliability of SERS based analysis. This approach was recently realized by combination of SERS with solid phase extraction (SPE) using SERS-active sorbents based on inorganic (silica [8], calcium carbonate [9], etc.) and organic matrices (polysaccharides [10]). Various micro- and nanostructured glass fibres and multicapillary glass structures (MCGS) with high specific surface area were also proposed as support for fabrication of SERS platforms [11,12] or luminescent sensors [13]; however only their unique optical properties were accounted while sorption capability was not used for improvement of SERS efficiency yet.

Therefore, the aim of this study is the fabrication of SERS-active MCGS (SERS-MCGS) and estimation of its potential for SERS-based analysis. SERS-activity was achieved by modification of MCGS with silver nanoparticles (AgNPs) embedded to silica sol. Besides of strong binding of AgNPs to the MCGS, silica also plays an important role because of following advantages: (i) physical and chemical protection of AgNPs from aggregation, fusion, and oxidation during the preparation and application, (ii) transparency for probing laser light and negligible Raman cross-section, i.e. low background signal, and (iii) excellent sorption properties and facilitation of analyte adsorption (improvement of extraction efficiency).
2. Experimental part

2.1. Materials
Silver nitrate, sodium citrate (Na$_3$C$_6$H$_5$O$_7$·2H$_2$O), tetraethyl orthosilicate (TEOS), rhodamine 6G (R6G) were purchased from Sigma-Aldrich and have chemical grade purity. Ammonia solution (25 wt%), sulphuric acid (98 wt%), and ethanol (96 wt%) were purchased from ZAO “Vekton” (Russia). Borosilicate MCGS consisted of 4293 capillaries was kindly provided by SPC Nanostructured Glass Technology Ltd. Deionized water was used for preparation of all solutions.

2.2. Methods of characterization
SERS-active composite and MCGS before and after modification were characterized by scanning electron microscopy (SEM; Mira II LMU, Tescan, Czechia). Registration of hydrodynamic (HD) diameter and surface charge (zeta potential) of AgNPs and modifying solution were performed by dynamic light scattering (DLS) method using Zetasizer Nano (Malvern, UK). UV-visible absorbance and fluorescence measurements were performed with hybrid reader Synergy H1 (BioTek, USA).

SERS spectra were recorded using probing nanolaboratory Ntegra Spectra (NT-MDT, Russia) with integrated Raman spectrometer (Solar) using 473 nm laser and registration scheme 180°. Raman spectrometer was calibrated before SERS measurement using silicon wafer (Raman band at 520 cm$^{-1}$). All SERS spectra were normalized to laser power and acquisition time (counts per 1 mW and 1 sec).

2.3. Preparation of MCGS-SERS composite and SERS testing
The preparation of solution for MCGS modification includes synthesis of AgNPs and their embedding into silica sol. The synthesis of SERS-active AgNPs was performed by well known procedure based on reduction of silver nitrate with citrate ions in aqueous environment [14]. The suspension of as-prepared AgNPs was 100 times concentrated before further application using centrifugation at 10$^3$ g for 10 min. Solution of silica sol with embedded AgNPs was prepared by mixing of 2 ml of ethanol, 20 µl of AgNPs, and 20 µl of TEOS and further sonication of the mixture for 15 min. The silica sol with embedded AgNPs was 10 times diluted by water for DLS measurements in order diminish influence of ethanol on the DLS results.

The modification of MCGS was performed by passing of the modifying solution through MCGS with further rinsing by water and drying at 50°C. MCGS was cut before modification to the short pieces (~2 cm length) and fixed by glue in a tip for micropipette in order to facilitate operation with it.

Testing of SERS-MCGS was performed by R6G as the model analyte with the well known spectrum. The SERS analysis procedure includes passing of 25 µl of R6G solution (10$^{-6}$ M) through SERS-MCGS with further SERS measurements. The effectiveness of SERS-MCGS was estimated by control experiment with pure AgNPs which was performed by mixing of equivalent portions (10 µl) of AgNPs, R6G, and NaCl (1M) solutions with further SERS measurements.

3. Results and discussions

3.1. SERS-MCGS: preparation and characterization
Citrate stabilized AgNPs were used as SERS-active material due to simplicity of their preparation and strong Raman enhancement. We have widely used this SERS substrate earlier for detection of pharmaceuticals in water and urine [5,9]. The successfullness of the synthesis and quality of as-prepared AgNPs were verified by DLS measurements of the size and zeta potential (Figure 1a,b) the average values of which were found as ~65 nm and ~45 mV. UV-visible spectrum of AgNPs solution (Figure 1c) demonstrates the presence of pronounced plasmon band at ~400 nm which is responsible for colour of modified MCGS (Figure 2a). DLS study also showed that the size and charge of silica sol with embedded AgNPs are different from these parameters of pure AgNPs. Modification of AgNPs by silica led to growth of the size of the detected particles and improvement of the size distribution (more homogeneous) (Figure 1a). We associate changing of surface charge with high contribution of OH-
groups which are poorly dissociated compare to citrate ions used for stabilization of as-prepared AgNPs (Figure 1b).

![Graphs and images](image)

**Figure 1(a-e).** Size (a) and zeta potential (b) of initial citrate stabilized AgNPs and SiO$_2$-AgNPs composite (according to DLS measurements). (c) UV-visible spectrum of the suspension of as-prepared AgNPs. (d) SEM image of SiO$_2$-AgNPs composite and (e) size distribution of AgNPs inside the composite.

SEM studies of the dried silica sol with embedded AgNPs demonstrated that AgNPs inside silica matrix are partially aggregated (Figure 1d), while their size is in appropriate agreement with one determined by DLS (Figure 1e). However, the partial aggregation is an advantage in the case of SERS because aggregated AgNPs possess stronger Raman enhancement due to presence of “hot spots” (the space between aggregated AgNPs) [15]. SEM measurements of MCGS before and after modification (Figure 2a) demonstrate uniform distribution of AgNPs and SiO$_2$ inside MCGS and negligible influence of modification on inner diameter of a single capillary (~20 µm) (Figure 2b-d). Although the modification coating is not dense, the colour of modified MCGS is significantly changed (Figure 2a) due to remarkable plasmonic properties of AgNPs.

### 3.2. SERS detection of model analyte

The results of SERS testing demonstrate 12 times larger SERS signal for SERS-MCGS compare to pure AgNPs (Figure 2a). We explain this by better sorption properties which were improved by (i) contribution of specific surface area of MCGS and (ii) application of silica as the matrix for AgNPs. Additionally, sorption capacity was estimated by fluorescence measurements of R6G solution before and after passing through SERS-MCGS (Figure 3b). The results support our guess about improvement of sorption capacity and SERS efficiency and demonstrate almost complete extraction of R6G molecules (the sorption is ~98%).
4. Conclusions
Summing the results we can conclude that modified MCGS enables significant improvement of SERS sensitivity due to increased sorption characteristics. Moreover, SERS-MCGS can be used as SPE column which enables speed-up of SERS analysis due to direct detection of the adsorbed analytes in the column immediately after extraction. Finally, the analysis requires 25 µl of the analyte only that is comparable with sample amount required for the most advanced analytical techniques such as HPLC and LC-MS.
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References
[1] Cao P G, Yao J L, Zheng J W, Gu R A, Tian Z Q 2002 Langmuir 18 100
[2] Li J, Liu J, Yang Y, Qin D 2015 J. Am. Chem. Soc. 137 7039
[3] Fan M, Andrade G F S, Brolo A G 2011 Anal. Chim. Acta 693 7
[4] Vendrell M, Maiti K K, Dhaliwal K, Chang Y T 2013 Trends Biotechnol. 31 249
[5] Markina N E, Markin A V, Goryacheva I Y 2018 Anal. Bioanal. Chem. 410 2221
[6] Hernández-Arteaga A, Nava J J Z, Kolosovas-Machuca E S, Velázquez-Salazar J J, Vinogradova E, José-Yacamán M, Navarro-Contreras H R 2017 Nano Research 10 3662
[7] Bonifacio A, Dalla Marta S, Spizzo R, Cervo S, Steffan A, Colombatti A, Sergei V 2014 Anal. Bioanal Chem. 406 2355
[8] Markina N E, Markin A V, Zakharevich A M, Gorin D A, Rusanova T Y, Goryacheva I Y 2016 J. Nanopart. Res. 18 353
[9] Markina N E, Markin A V, Zakharevich A M, Goryacheva I Yu 2017 Microchim. Acta 184 3937
[10] Abalde-Cela S, Auguie B, Fischlechner M, Huck W T S, Alvarez-Puebla R A, Liz-Marzan L M, Abell C 2011 Soft Matter 7 1321
[11] White I M, Yazdi S H, Yu W W 2012 Microfluid. Nanofluid. 13 205
[12] Markin A V, Markina N E, Goryacheva I Yu 2017 Trends Anal. Chem. 88 185
[13] Pidenko S A, Burmistrova N A, Shuvalov A A, Chibrova A A, Skibina Y S, Goryacheva I Y 2018 Anal. Chim. Acta 1019 14
[14] Lee P C, Meisel D 1982 J. Phys. Chem. 86 3391
[15] Camden J P, Dieringer J A, Wang Y, Masiello D J, Marks L D, Schatz G C, Van Duyne R P 2008 J. Am. Chem. Soc. 130 12616