교육학석사 학위논문

Enhancement of Signal-to-Noise Ratio in Fiber-optics based Surface enhanced Raman scattering detection through Fiber-optics tip-shape modification

광섬유 끝단 모양 변화를 통한 광섬유 기반 표면 증강 라만 산란 신호 검출에서의 신호대 잡음비 개선

2023 년 2 월

서울대학교 대학원

과학교육과 화학전공

신 민 경

Enhancement of Signal-to-Noise Ratio in Fiber-optics based Surface enhanced Raman scattering detection through Fiber-optics tip-shape modification

지도 교수 정 대 홍

이 논문을 교육학석사 학위논문으로 제출함

2022 년 10 월

서울대학교 대학원

과학교육과 화학전공

신 민 경

신민경의 교육학석사 학위논문을 인준함

2022 년 12 월

위 원 장 ______________________ (인)

부위원장 ______________________ (인)

위 원 ______________________ (인)

Abstract

Enhancement of Signal-to-Noise Ratio in Fiber-optics based Surface enhanced Raman scattering detection through Fiber-optics tip-shape modification

Minkyung Shin
Department of Science Education
(Major in Chemistry)
The Graduate School
Seoul National University

Single fiber optics based surface-enhanced Raman scattering (FO-SERS) has the advantage of simple-alignment when

measuring the SERS signals. The sample fiber, which is chemically modified to capture the target on the end-tip of the optical fiber, is measured by connecting with the FO-SERS measurement system. FO-SERS measurement system is all fiber-based, so that it is necessary to consider the Raman signal of the optical fiber itself. This is because the optical fiber has a very strong Raman signal of the fused silica, which composes of the optical fiber and especially this signal increases as the length increases. Therefore, it is important to lower the Raman signal of the optical fiber itself in the FO-SERS measurement system to prevent from the Raman signal of the fiber itself overwhelming the Raman signal of the analytes. In addition, it can be possible to obtain high sensitivity in SERS measurements by lowering the Raman signal of the optical fiber itself, which is considered as the background signal of the SERS spectrum for analytes.

In this study, we modified the optical fiber end tip-shape to have an angular or rough surface to lower the Raman signal of the optical fiber itself and enhance the signal-to-noise ratio (SNR) for SERS detection. As the inclined angle of the tip increased, the Raman signal of the optical fiber itself decreased, especially in the case of the rough surface fiber, it decreased by 32 % compared to the case of the conventional flat surface fiber. To verify the feasibility as

SERS sensing platform using those fibers, silver nanoshells with a Raman label were loaded in those fibers. We obtained the SERS spectrum from each sample fiber and calculated the SNR value to compare the sensitivity for each tip-shape sample fiber. Through our study, it is expected that FO-SERS detection can be conducted with high sensitivity by using various types of the tip shape optical fibers.

Key words : Fiber-optics based SERS (FO-SERS), tip modification, fiber-optic with roughened surface, angled-tip fiber

Student number : 2021-27973

Contents

List of Figure

1. Introduction

Surface−enhanced Raman scattering (SERS) has been applied to various analysis based on the advantage of being a non−destructive and highly sensitive analytical technique tool[1−4]. In particular, fiber−optics based SERS (FO−SERS) has been spotlighted recently in that it has additional advantages such as flexible probe and remote sensing on targets[5−7]. In the case where optical fiber is used as probe fiber, metal nanoparticles, such as gold or silver, are conjugated at the end tip of the optical fiber to induce SERS from the analytes near the probe fiber[8, 9]. In other words, FO−SERS using probe fiber is somewhat limited for target−specific analysis.

As an alternative method, chemically modified optical fiber is proposed to capture the desired target and it needs to introduce additional probe particles[10, 11]. When the chemically modified optical fiber is reacted with target and probe particles, which is called sample fiber, most of the studies measure the sample fiber with the ‘optrode’ configuration[5, 12−14]. ‘Optrode’ configuration measurement is used the conventional microscope Raman system to focus the laser on the opposite side of the SERS modified tip, and then detect the backscattered signal via optical fiber[15]. However, measuring the sample fiber with the optrode configuration has the disadvantage of having to focus on the optical fiber and this is far from simple-alignment, which is the advantage of FO-SERS. Neverthelss, the optrode configuration is used widely because of the strong Raman signal of the optical fiber itself. Optical fiber is composed of fused silica and reacts with light to present a strong Raman signal[16, 17]. Therefore, it is important to lower the Raman signal of the optical fiber itself, which may overwhelm the signal of the analyte in FO-SERS detection.

In this paper, we fabricated the different tip-shape optical fibers and compared the Raman signal of each optical fiber. Also, to confirm the feasibility as SERS sensing platform using modified tip-shape fibers, we used silver nanoshells labeled Raman molecule as probe particles and loaded them on each fiber. We obtained SERS spectra from each sample fiber and compared the sensitivity as calculating signal-to-noise ratio (SNR) value.

2. Experiments

2.1. Chemicals and materials.

Tetraethyl orthosilicate (TEOS), 3-mercaptopropyltrimethoxysilane (MPTS), ethylene glycol (EG), silver nitrate ($AgNO_3$), 4-fluorobenzenethiol (4-FBT), 11-mercaptoundecanoic acid (11-MUA) and hexadecylamine were purchased from Sigma Aldrich, Inc. (St. Louis, MO, USA). Ethanol (99.9%) and ammonium hydroxide (NH_4OH, 28-30%) were purchased from Daejung (Siheung, Korea). Multimode optical fibers with core/cladding diameter of 105/125 ㎛ were purchased from Thorlabs (Newton, NJ, USA).

2.2. Fabrication of fiber optics with different tip shapes.

The end of the optical fiber (FG105LCA, thorlabs, USA) is cut flat by commercial optical fiber cleaver (Fitel S326A, Furukawa Information Technologies and Telecommunications (Fitel), Japan). In the case of typical optical fiber cleaver, it is composed of mainbody and single fiber adapter part. The cutting blade located in the mainbody is placed perpendicular to the fiber adapter so that the end-facet of the optical fiber is always cut flat.

An angled-tip fiber was fabricated by using the commercial optical fiber cleaver that we modified. We removed the fiber adapter part, adjusted the fiber's height to the cutting blade using slide glass, and rotated the optical fiber to have a certain angle to cutting blade. In order to specify the angle of the angled-tip fiber, it was determined to be 0 degrees, when the fiber optic ends were flat. Since the maximum angle that could be placed while fixing the fiber to the fiber cutting blade was 20 degrees, only the tip up to 20 degrees could be fabricated.

In the case of the optical fiber with roughened surface, we used commercial optical fiber jacket stripper instead of a cleaver. the optical fiber with roughened surface could be fabricated in a simple way to cut the end of the optical fiber using optical fiber jacket stripper.

2.3. Synthesis of silver nanoshell labeled 4−FBT ($AgNS_{4-FBT}$) and preparation of sample fiber using various tip shape optical fibers.

To make a sample fiber simply, silver nanoshell labeled 4−FBT ($AgNS_{4-FBT}$), which can be used as a SERS probe particle, was synthesized and loaded on the optical fiber end tip. $AgNS_{4-FBT}$ was prepared with the previously reported method[18]. Briefly, using stöber method[19], we prepared silica nanoparticle as core with a diameter of about 150 nm. After modifying the silica core surface with a thiol group using MPTS, silver nanoshell (AgNS), which was composed of silica core covered with silver nanoparticle, was synthesized with adding $AgNO_3$, EG and hexadecylamine. Adding 4−FBT into AgNS dispersion, $AgNS_{4-FBT}$ was synthesized.

The sample fibers with different tip shapes were prepared by repeating the process of dropping and drying 1.5 μL of $AgNS_{4-FBT}$ dispersion on the end tip of each optical fiber 3 times.

2.4. All−fiber based SERS measurement.

As an all−fiber detection tool for FO−SERS measurement, we constructed customized fiber−type Raman measurement system with commercial optical system products. The 785−nm line of laser (Cobolt 08 NLD, Cobolt, Sweden) was used in all measurement as an excitation source. In the case of the laser power, we fixed the head power at a maximum output of 470 mW and the acquisition time at each measurement was 5 s. The laser and spectrometer (SR−303i−A, Andor Technology, UK) equipped with a CCD (DV401A−BV, Andor Technology, UK) and custom designed module (Dongwoo Optron, Korea) were connected by a 2 by 1 fiber coupler (BM Laser, Korea). The other end of the coupler was connected to the sample fiber, using splicing machine (A−80S, COMPTYCO, China). The custom designed module consists of xyz−axis holders, long pass filters and collimator, for simple alignment. In all configurations, multimode optical fiber (FG105LCA, Thorlabs, USA) was used.

3. Results and Discussion

3.1. Characterization of the optical fibers with tip-shape modification.

As shown in **Figure 1**, the difference in tip-shape at the end of the optical fibers can be confirmed through the optical images. As we expected, the angled-tip fibers have a certain angle inclined tip and the rough-surface fiber shows uneven tip surface. With those fibers, we obtained the Raman spectra of each optical fiber. As shown in **Figure 2**, the Raman intensity of the inclined fibers was decreased as increasing the tip-inclined angle. Especially, on the basis of 1042 cm^{-1} peak intensity, which shows the highest peak in all spectra, the signal intensity of rough-surface fiber decreased by about 32% compared to that of flat-surface fiber. Also, in the range from 1300 to 1500 cm^{-1}, it can be observed that the plateau-shaped signal shown in flat-surface fiber and angled-tip fibers disappeared in rough-surface fiber. This shows the potential of using that region as an additional Raman detection window with using rough-surface fiber. The Raman signal of the optical fiber itself is related to the intensity of the specular reflection at the end of the optical fiber[20]. That's why tip-shape modification of the optical fiber makes the change of these signals.

The rough–surface fiber, from which we obtained the lowest Raman signal of the fiber itself, allows the tip to have random roughness by simple cutting. To verify the reproducibility of the reduction of the Raman signal by rough–surface fiber itself, we measured the Raman signals of the 8 different cutting fibers. As shown in **Figure 3**, it was confirmed that the Raman spectra of the optical fiber itself obtained from 8 different fibers were measured almost the same. Based on 1042 cm^{-1} peak intensity, we calculated the coefficient of variability (CV), which shows the degree of measured value accuracy, and it was confirmed to be 0.9%. This showed that reproducibility of the rough–surface fiber fabrication is guaranteed.

3.2. Characterization of $AgNS_{4-FBT}$ as SERS probe particle.

In order to enable analysis of the desired target material only, the end of the optical fiber is chemically modified to react with the target, which is called sample fiber. Additional probe particle need to be introduced into the sample fiber for target analysis. In our study, in order to simplify the fabrication of sample fibers, $AgNS_{4-FBT}$ as a probe particle was synthesized and loaded on the end of the optical fiber. $AgNS_{4-FBT}$ is labeled with 4-FBT on the surface of silver nanoparticles, so when irradiated with laser, it can detect SERS signals by 4-FBT. The TEM image of the $AgNS_{4-FBT}$ particles is shown in **Figure 4a**. Silver nanoparticles surround the silica core and 4-FBT is labeled on it, which is designed to cause SERS from the $AgNS_{4-FBT}$ particles themselves. Also, to confirm the SERS signal for the $AgNS_{4-FBT}$ particle itself, the SERS spectrum obtained by measuring it with a confocal microscope Raman system is presented in **Figure 4b**. The main peaks shown in the spectrum are the characteristic SERS bands of 4-FBT, which will be compared to the SERS peaks from the sample fiber.

3.3. Comparative analysis of SERS sensitivity for sample fibers using various tip shape fibers.

The sample fibers prepared from each different tip-shape fibers were measured by all fiber-optics based SERS measurement system for simple-alignment. As shown in **Figure 5**, all of optical equipment is connected only by optical fibers, which imply the possibility of increasing the Raman signal of the optical fiber itself due to increased interaction between light and optical fiber. **Figure 6a** shows the SERS spectra of the sample fibers using flat-surface fiber, angled-tip fibers and rough-surface fiber with the Raman signal of each optical fiber itself subtraction. All of the sample fiber was prepared by loading the $AgNS_{4-FBT}$ particles, so that we compared the SERS spectrum of sample fiber with that of 4-FBT (in **Figure 4b**). As shown in **Figure 6a**, SERS band appeared at 1072 cm^{-1} in all spectra, which is characteristic peak of 4-FBT. In the case of using rough-surface fiber and 20° angled-tip fiber, another characteristic peak of 4-FBT was also observed at 1486 and 1583 cm^{-1}. Based on 1072 cm^{-1} peak, which shows strong intensity in all of the spectra, the peak intensity increases as the optical fiber tip inclined angle increases and especially, rough-surface fiber gets by about 7 times higher intensity than flat-surface fiber. This includes the factors due to an increase in SERS signals as well as a decrease in the Raman signal of the optical fiber itself. Unlike the flat-surface fiber, rough-surface fiber has a valley-shaped area so that the particles can be aggregated there. Aggregated particles make more hot-spots, which enhanced the SERS intensity. To compare the sensitivity as SERS sensing platform, we calculated the SNR values of each sample fiber. SNR value is a good parameter of comparing sensitivity. It is defined as:

$$SNR = I_{analyte\ signal} / I_{noise}$$

SERS signal based on the 1072 cm^{-1} peak of 4-FBT as shown in **Figure 6a** was used as a SERS signal standard for calculating the SNR values and the noise was calculated as standard deviation at the range from 1515 to 1535 cm^{-1}, which is a flat section in all sample fiber spectra. As shown in **Figure 6b**, SNR value increases as the tip angle increases, especially when the optical fiber has a rough surface, the SNR value increases by about 27 times compared to the flat-surface fiber. This shows that the rough-surface fiber as FO-SERS sensing platform can be obtained high sensitivity.

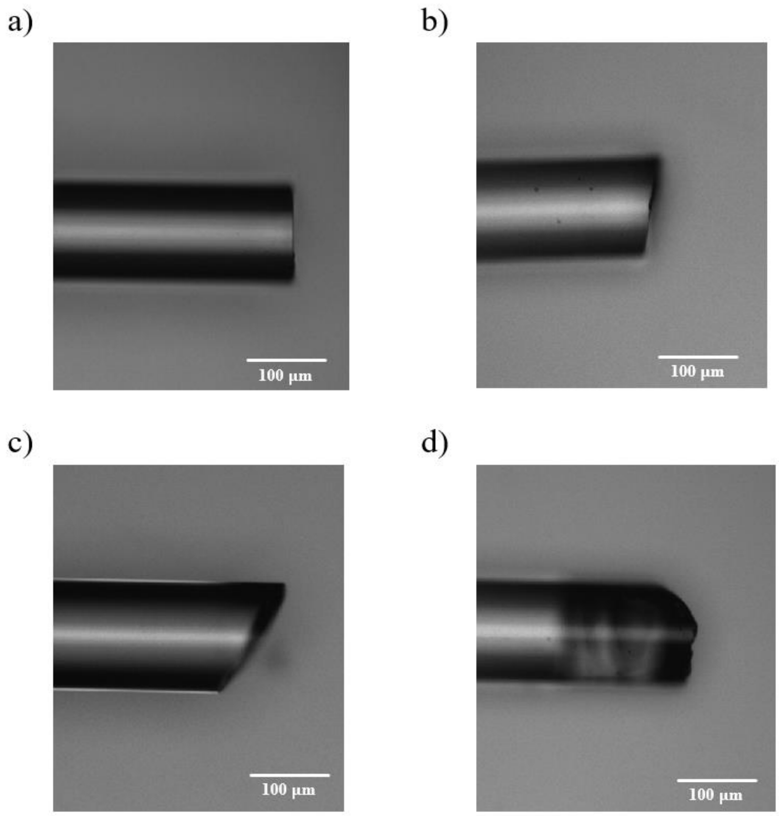

Figure 1. Optical image comparison for fiber optics end tip−shape modification. Optical image of (a) flat surface fiber, (b) 10° angled−tip fiber, (c) 20° angled−tip fiber, and (d) rough surface fiber.

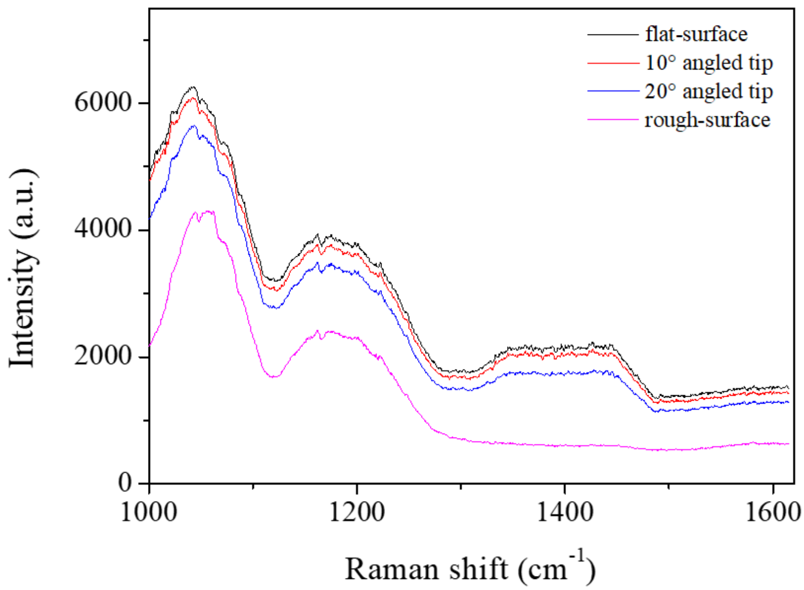

Figure 2. Raman spectra of optical fiber itself with different tip-shape.

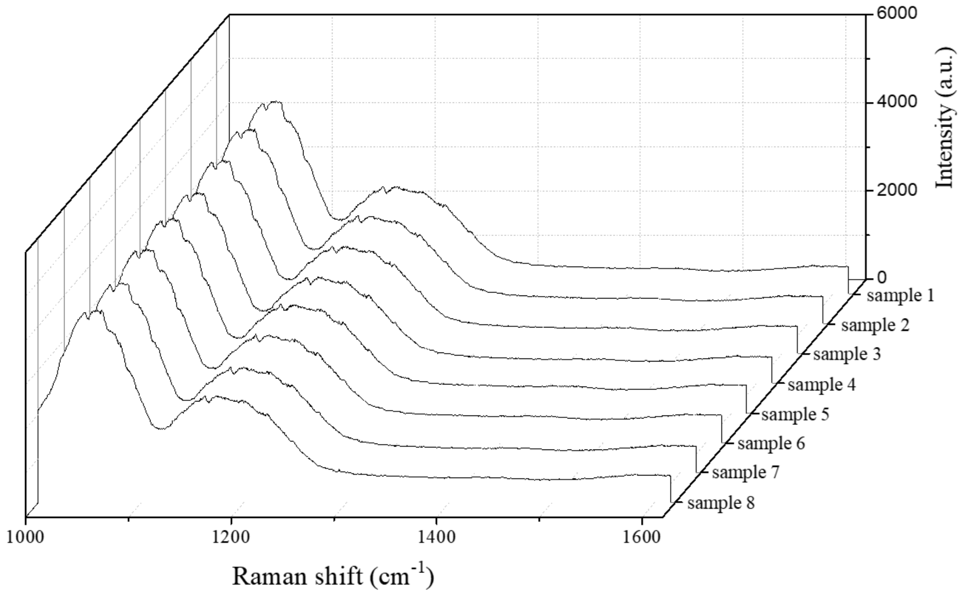

Figure 3. Raman spectra of 8 different rough-surface fibers.

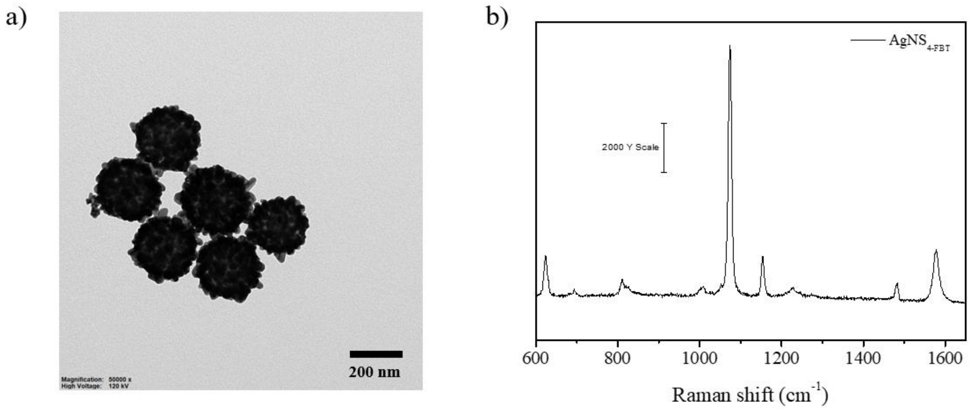

Figure 4. Characterization of $AgNS_{4-FBT}$ particles as SERS probe particle. (a) TEM image of $AgNS_{4-FBT}$. (b) SERS spectrum of $AgNS_{4-FBT}$ using as SERS probe particle (measured by confocal microscope Raman system with 785 nm line of laser of 2 mW, acquisition time of 3 seconds and 10X lens.)

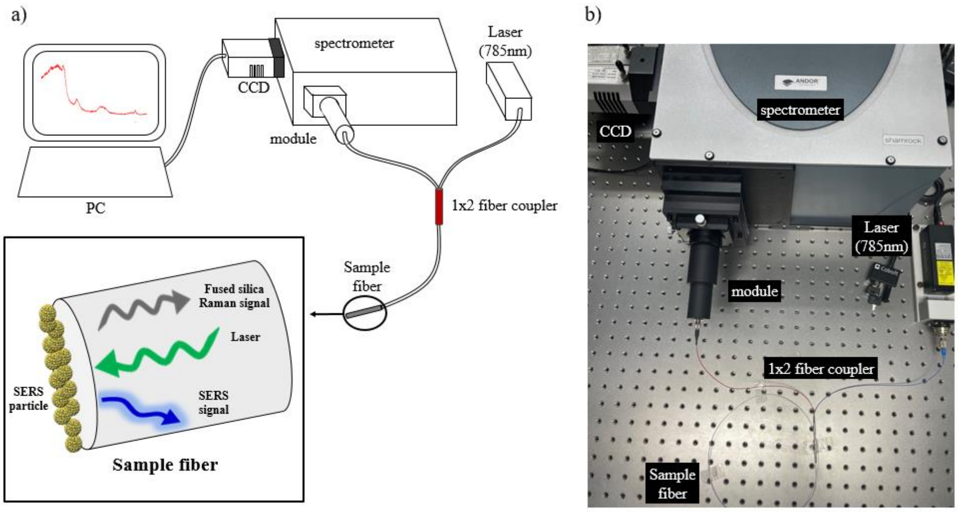

Figure 5. Optical system configuration for measuring FO-SERS composed of all as optical fiber. (a) Sketch diagram and (b) photo of SERS measurement system based on fiber-optics.

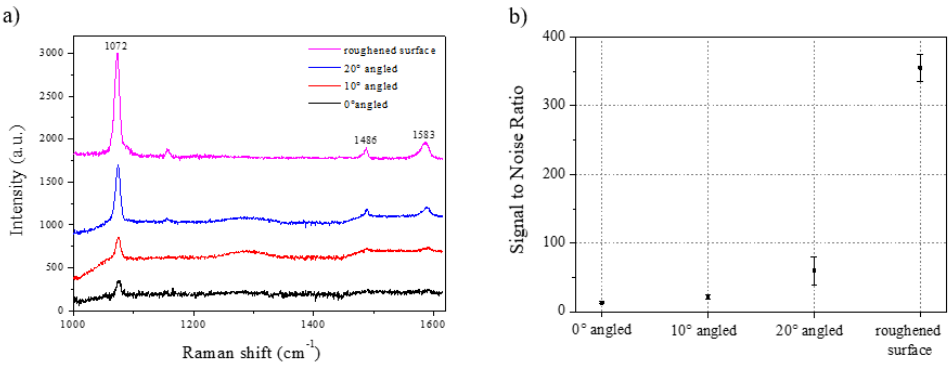

Figure 6. Comparative analysis of sensitivity as SERS sensing platform. (a) SERS spectra of $AgNS_{4-FBT}$ loaded on different tip−shape optical fibers with bare fused silica Raman signal subtraction. (b) Scatter plot of signal−to−noise ratio (SNR) values of different tip−shape optical fibers. (SERS signal based on the 1072 cm^{-1} peak of 4−FBT as shown in Figure. 6a and the noise was calculated as standard deviation at the range from 1515 to 1535 cm^{-1}, which is a flat section in all samples in Figure. 6a)

4. Conclusion

We enhanced the SNR value in FO−SERS system, using simple modified optical fiber. As tip of the optical fiber inclined more, the Raman signal of the optical fiber itself decreased and especially in the case of the optical fiber with roughened surface, the Raman signal of the rough−surface fiber itself got the lowest signal, which was reduced by about 32 % compared to the flat surface fiber. In the case of a sample fibers using different tip shape fibers as a SERS sensing platform, the SNR value was increased as the tip inclined angle increases. Especially, SNR value from rough−surface fiber can obtain about 27 times higher than that from the flat−surface fiber. This is because not only reduced Raman signal of the optical fiber itself, also enhanced Raman signal of $AgNS_{4-FBT}s$ loaded on the fiber end tip. Through our research, it is expected that all−fiber based SERS detection can conduct with high sensitivity.

5. References

1. Yoon, J.; Choi, N.; Ko, J.; Kim, K.; Lee, S.; Choo, J., Highly sensitive detection of thrombin using SERS-based magnetic aptasensors. Biosensors and Bioelectronics **2013,** 47, 62-67.

2. Song, C.; Wang, Y.; Lei, Y.; Zhao, J., SERS-Enabled Sensitive Detection of Plant Volatile Biomarker Methyl Salicylate. The Journal of Physical Chemistry C **2022,** 126 (1), 772-778.

3. Shanmukh, S.; Jones, L.; Driskell, J.; Zhao, Y.; Dluhy, R.; Tripp, R. A., Rapid and Sensitive Detection of Respiratory Virus Molecular Signatures Using a Silver Nanorod Array SERS Substrate. Nano Letters **2006,** 6 (11), 2630-2636.

4. Khlebtsov, B. N.; Khanadeev, V. A.; Panfilova, E. V.; Bratashov, D. N.; Khlebtsov, N. G., Gold Nanoisland Films as Reproducible SERS Substrates for Highly Sensitive Detection of Fungicides. Acs Appl Mater Inter **2015,** 7 (12), 6518-6529.

5. Zhang, J.; Chen, S.; Gong, T.; Zhang, X.; Zhu, Y., Tapered Fiber Probe Modified by Ag Nanoparticles for SERS Detection. Plasmonics **2015,** 11 (3), 743-751.

6. Li, L.; Deng, S.; Wang, H.; Zhang, R.; Zhu, K.; Lu, Y.; Wang, Z.; Zong, S.; Wang, Z.; Cui, Y., A SERS fiber probe fabricated by layer-by-layer assembly of silver sphere

nanoparticles and nanorods with a greatly enhanced sensitivity for remote sensing. Nanotechnology **2019,** 30 (25).

7. Chen, Z.; Dai, Z.; Chen, N.; Liu, S.; Pang, F.; Lu, B.; Wang, T., Gold Nanoparticles-Modified Tapered Fiber Nanoprobe for Remote SERS Detection. IEEE Photonics Technology Letters **2014,** 26 (8), 777-780.

8. Long, Y.; Li, H.; Yang, X.; Yuan, Y.; Zheng, M., Controlling silver morphology on a cramped optical fiber facet via a PVP-assisted silver mirror reaction for SERS fiber probe fabrication. New Journal of Chemistry **2021,** 45 (8), 4004-4015.

9. Geßner, R.; Rösch, P.; Petry, R.; Schmitt, M.; Strehle, M. A.; Kiefer, W.; Popp, J., The application of a SERS fiber probe for the investigation of sensitive biological samples. The Analyst **2004,** 129 (12), 1193-1199.

10. Zheng, D.; Wang, Z.; Wu, J.; Li, S.; Li, W.; Zhang, H.; Xia, L., A Raman immunosensor based on SERS and microfluidic chip for all-fiber detection of brain natriuretic peptide. Infrared Physics & Technology **2022,** 125.

11. Li, X.; Zhang, Y.; Xue, B.; Kong, X.; Liu, X.; Tu, L.; Chang, Y.; Zhang, H., A SERS nano-tag-based fiber-optic strategy for in situ immunoassay in unprocessed whole blood. Biosensors and Bioelectronics **2017,** 92, 517-522.

12. Cao, J.; Zhao, D.; Qin, Y., Novel strategy for fabrication of sensing layer on thiol-functionalized fiber-optic tapers and their application as SERS probes. Talanta **2019,** 194, 895-902.

13. Meng, L.; Shang, L.; Feng, S.; Tang, Z.; Bi, C.; Zhao, H.; Liu, G., Fabrication of a three-dimensional (3D) SERS fiber probe and application of in situ detection. Opt Express **2022,** 30 (2), 2353-2363.

14. Long, Y.; Li, H.; Du, Z.; Geng, M.; Liu, Z., Confined Gaussian-distributed electromagnetic field of tin(II) chloride-sensitized surface-enhanced Raman scattering (SERS) optical fiber probe: From localized surface plasmon resonance (LSPR) to waveguide propagation. J Colloid Interface Sci **2021,** 581 (Pt B), 698-708.

15. Viets, C.; Hill, W., Single-fibre surface-enhanced Raman sensors with angled tips. Journal of Raman Spectroscopy **2000,** 31 (7), 625-631.

16. Santos, L. F.; Wolthuis, R.; Koljenović, S.; Almeida, R. M.; Puppels, G. J., Fiber-Optic Probes for in Vivo Raman Spectroscopy in the High-Wavenumber Region. Analytical Chemistry **2005,** 77 (20), 6747-6752.

17. May, J.; Li, Y.-S., Fiber Raman background study and its application in setting up optical fiber Raman probes. Appl. Opt. **1996,**

35 (15), 2527−2533.

18. Kang, H.; Kang, T.; Kim, S.; Kim, J.−H.; Jun, B.−H.; Chae, J.; Park, J.; Jeong, D.−H.; Lee, Y.−S., Base Effects on Fabrication of Silver Nanoparticles Embedded Silica Nanocomposite for Surface−Enhanced Raman Scattering (SERS). J Nanosci Nanotechno **2011,** 11 (1), 579−583.

19. Stöber, W.; Fink, A.; Bohn, E., Controlled growth of monodisperse silica spheres in the micron size range. Journal of Colloid and Interface Science **1968,** 26 (1), 62−69.

20. Bennett, H. E.; Porteus, J. O., Relation Between Surface Roughness and Specular Reflectance at Normal Incidence. J. Opt. Soc. Am. **1961,** 51 (2), 123−129.

국문 초록

단일 광섬유 기반의 표면 증강 라만 산란 연구 (fiber optics based SERS, FO-SERS)는 SERS 신호를 측정하기 위한 광학 장비들의 세팅을 보다 간결하게 할 수 있다는 장점을 갖고 있다. 분석을 원하는 타겟 물질과 반응할 수 있도록, 광섬유 끝단을 적절한 작용기로 화학적으로 변형하여 만든 광섬유 샘플은 FO-SERS 측정 시스템에 연결되어 SERS 신호가 측정될 수 있다. FO-SERS 측정 시스템은 간단한 광학 장비 정렬을 위해 전체가 광섬유로 연결되어 있는데, 이로 인해 광섬유 자체에 의한 Raman 신호에 대한 고려가 불가피하다. 왜냐하면, 광섬유를 구성하고 있는 용융 실리카는 빛과 반응하여 강한 Raman 신호를 낼 수 있는데 특히 이것은 광섬유의 길이가 증가함에 따라 그 신호의 세기가 증가하기 때문이다. 그러므로 FO-SERS 측정 시스템을 이용하여 원하는 광섬유 샘플의 분석 신호를 얻기 위해서는 강한 광섬유 자체 Raman 신호로 인해 분석물의 신호가 가려지지 않도록 광섬유 자체 Raman 신호를 낮추는 것이 중요하다. 또한 광섬유 샘플의 SERS 측정에서 배경 신호로 여겨질 수 있는 광섬유 자체 Raman 신호를 낮춤으로써 보다 높은 감도의 FO-SERS 측정 결과를 얻을 수도 있다.

본 연구에서는 광섬유 끝단의 모양이 특정한 각을 갖도록 기울어지거나 무질서하게 거친 표면을 갖도록 변형하여 광섬유 자체 Raman 신호

의 세기를 낮추었다. 광섬유 끝단이 기울어진 정도가 증가함에 따라 광섬유 자체 Raman 신호는 감소하였으며, 특히 거친 표면을 갖는 광섬유의 경우 기존의 평평한 광섬유 대비 자체 Raman 신호가 32 % 가량 감소하였다. 또한, 다른 형태의 끝단을 갖는 광섬유들을 사용하여 이것이 광섬유 기반의 SERS 측정에서 적합한지 확인하였다. 이를 위해 Raman 신호를 내는 물질을 표지한 SERS 탐지 입자를 합성하고, 각 광섬유 끝단에 흡착시켜 광섬유 샘플을 준비하였다. 각 광섬유 샘플로부터 SERS spectrum을 얻고, 그로부터 신호대 잡음비 값을 계산하여 감도를 비교하였다. 우리의 연구를 통하여, 다양한 형태의 끝단 모양을 갖는 광섬유를 이용하여 광섬유 기반 SERS 측정이 높은 감도로 이루어질 것으로 기대되어진다.

주요어 : 광섬유 기반 표면 증강 라만 산란 (SERS), 광섬유 끝단 변형, 거친 표면 광섬유, 각진 광섬유

학번 : 2021-27973