ACS OMEGA

http://pubs.acs.org/journal/acsodf

Editorial

Celebrating 50 Years of Surface Enhanced Spectroscopy

Published as part of ACS Omega special issue "Celebrating 50 Years of Surface Enhanced Spectroscopy".

Cite This: *ACS Omega* 2024, 9, 48867−48869

Read Online

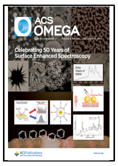
ACCESS | Metrics & More | Article Recommendations

Fifty years ago, the field of electrochemistry was experiencing a revolution. The advent of accessible spectroscopic methods was allowing electrochemists to actually "see" the chemical nature of processes at an electrode surface *in situ*, under applied potentials. However, one of the most informative of the spectroscopic methods, vibrational infrared spectroscopy, carried a serious limitation: the background contribution of the water completely overwhelmed the signal for experiments in aqueous solution. Scientists from Southampton, including Martin Fleischmann, a world-leading electrochemist at the time, Patrick Hendra, a well-established spectroscopist, and Jim McQuillan sought possible approaches to solve this problem. Although they were well aware that the Raman activity of water is much weaker than in infrared absorption experiments, the overall inefficiency of Raman scattering indicated that the detection of monolayer amounts of adsorbed species would be virtually impossible. In order to improve their odds of detection, they decided to "roughen" their silver electrode to increase the available surface area for adsorption, presumably which would lead to more molecules at the surface to be detected. Surprisingly, the results showed a very strong surface-sensitive and potential-dependent response for pyridine adsorption.[1]

This virtual special issue (VSI) celebrates the anniversary of those observations, which marked the first published surface-enhanced Raman scattering (SERS) experiments. It is important to point out that SERS was not recognized as a new physical phenomenon in that publication, and the authors simply thought that their approach to increase the surface area "worked". However, this exceptional result, i.e., detectable Raman scattering signal from such a small amount of adsorbed molecules, attracted a lot of attention. A short time later, the identification of SERS as a new effect was established by the works of Creighton,[2] van Duyne[3] and Moskovits.[4] SERS rapidly became an established field by the mid 1980s, but further discoveries, such as the observation of single molecule behavior in the 1990s[5,6] and the establishment of the role of hot electrons in plasmonic driven catalysis in the early 2000s,[7] have transformed surface-enhanced methods into one of the most active and interdisciplinary research areas in nanosciences and nanotechnology. Recent advances that include the discovery of atomic-sized hotspots,[8] the monitoring of ultra-high speed intensity fluctuations,[9] and the observation of submolecular resolution in "Tip-enhanced Raman Scattering" (TERS)[10] show that the field continues to thrive by revealing surprising new phenomena and effects. The work published in this VSI highlights how much the field has advanced over the 50 years since that serendipitous observation by the Southampton group. The breadth of the contributions to the VSI highlights the richness of the research interests related to the field of surface-enhanced spectroscopy. The variety of topics include fundamental mechanistic advances, the development of novel materials, and applications in photocatalysis, sensing, analytical chemistry, biomedicine, and electrochemistry.

The search for new types of enhancing surface platforms (fabricated surface-enhancing substrates) and their optimization has been a perennial research topic in SERS. Several methods, including wet chemistry synthesis of nanoparticles, bottom up self-assembly and nanofabrication top-down procedures, have been reported over the last 50 years.[11] This VSI introduces several contributions of new approaches for SERS substrate development. For instance, a laser-based approach for the generation of periodic metallic structures suitable for SERS (10.1021/acs.jpcc.4c00160) was introduced. The Bessel beam profile used for the fabrication has clear advantages over the generic Gaussian laser beams. Laser ablation combined with electrostatic mobility classification allowed the fabrication of silver nanostructures with controlled shape and size (10.1021/acsomega.4c03046). Examples of self-assembled SERS substrate included the deposition of gold nanorods onto Si surfaces previously smoothened with HF (10.1021/acs.jpcc.4c00930) and the deposition of Au nanoparticles on nanowrinkled polydimethylsiloxane (PDMS) (10.1021/acs.analchem.4c01212). The surface pretreatment drives the assemblies to improve SERS efficiency in both platforms. The synthesis of metallic nanoparticles suitable to SERS are represented in the VSI by a novel Au−Ag nanobox obtained through a relatively straightforward one pot synthesis (10.1021/acs.jpcc.4c03602). The nanoboxes possessed a large surface area and demonstrated efficient enhancement for both Raman scattering and fluorescence. Nanogap engineering refers to an approach to design specific metallic junctions that optimizes the performance of a SERS substrate (10.1021/acs.jpcc.4c04765). Branched dual-ring gold particles with engineered nanogaps led to an interesting additional contribution from external geometrical features (branches) to

Published: December 5, 2024



Published 2024 by American Chemical Society

the near field enhancement. The branches acted as an antenna that intensified the field at the gap (10.1021/acs.jpcc.4c01170). The use of hybrid semiconductor−metal substrates have become popular in the SERS literature. The nanohybrid substrate can benefit from extra enhancement provided by charge transfer effects while being less susceptible to large spatial variations in SERS intensities (10.1021/acs.jpcc.4c03080). The use of supporting dispersants, such as graphene oxide, improves the stability of immobilized SERS-active metallic particles, leading to lower detection limits (10.1021/acsomega.3c08608). Conducting polymers, such as polyaniline (PANI), was shown to improve the SERS efficiency of silver nanostructures due to charge transfer effects (10.1021/acs.jpcc.4c00292). A high level of enhancement was also observed for nanostructures of GaN as supporting material for plasmonic structures; however, an interesting dependence of the SERS efficiency on the molecule size was observed in that case (10.1021/acs.jpcc.4c02206). Surface-enhancement can also be observed from nonplasmonic substrates, such as 2D materials (10.1021/acsomega.4c06398). The charge-transfer effect is considered to be the only contribution to the increased Raman efficiency in that case, leading to lower enhancement factors when compared to plasmonic materials. However, a contribution from Wang et al. in this VSI seems to reveal resonances within the 2D materials that can provide another enhancement channel for adsorbed species (10.1021/acs.analchem.4c01051). The observation of this mechanism should help rationalize multiple recent results involving 2D structures as SERS substrates. Another potential breakthrough reported in this VSI is the work of Li et al. related to a Sr-doped TiO_2 material that is capable of reaching limits of detection comparable with plasmonic SERS for nonresonant molecules (10.1021/acs.jpcc.3c07334). The doping-induced abundance of both surface oxygen vacancies and energy level defects of Ti seems to play a role in such large and unexpected enhancement. Both of these results potentially open up a new class of SERS substrate.

Applications of SERS in analytical chemistry requires reliable approaches for quantification. The exquisite sensitivity and efficiency of SERS is capable of detecting single molecules, relying on highly localized electromagnetic fields called hotspots. These hotspots, while confined individually within nanometric distances, have large spatial variations over the substrate that can lead to significant quantification uncertainties, particularly at low concentrations. Neumann et al. utilized a comprehensive combination of computational and experimental methods to demonstrate how the statistics of SERS intensities varies from the single molecule detection regime all the way up to the complete saturation of the hotspot (10.1021/acs.jpcc.4c00227). The understanding of the SERS intensity statistics at different concentrations is essential for quantification at low concentrations. Digital SERS is a very promising approach that deals with the SERS intensity variations at these low concentrations.[12] At the single molecule (or single particle) regime, each SERS event arises from individual entities. In that case, the average SERS intensity can be substituted by event counts for proper quantification. Zheng et al. introduced a plasmonic gold prism platform that yields strong SERS for each single molecule event (10.1021/acs.jpcc.4c04450). The high on/off contrast enabled by their platform allowed for a linear calibration curve down to the fM level.

The advent of novel statistical methods and machine learning techniques for both quantification and classification are revolutionizing SERS applications. Statistical implementations, such as cumulative distribution functions were reported in this VSI as an approach to quantify an antiviral drug (10.1021/acsomega.3c07641). Convolution neural network in combination with SERS was used to classify agricultural products (10.1021/acs.analchem.4c00064), bacteria (10.1021/acs.jpcc.4c00135), and breast cancer cell types decorated with magnetic plasmonic nanoprobes (10.1021/acs.analchem.4c01968). The models developed in those cases highlighted the power of SERS for rapid classification that can be useful in both food security and disease diagnostic. A random forest classifier was implemented in the SERS evaluation of impurities in opioids (10.1021/acs.analchem.4c01271). A very interesting aspect of that work is that authors developed a model and tested using real samples (street drugs).

As discussed above, the hotspot area is just a fraction of the total area available for adsorption of the analyte. The substrate can be designed to mechanically capture large viral particles to improve the probability for the species of interest "to find" the hotspot area (10.1021/acs.analchem.4c01117). The work by Dzhagan et al. introduces a self-organized SERS substrates that also drives preferential adsorption of the analyte molecules into the hotspot area (10.1021/acsomega.3c08393). An exciting strategy to concentrate species at a single hotspot was also reported (10.1021/acs.jpcc.4c03536). In this case, a single ∼20 nm TiO_2 nanoparticle was trapped at the hotspot by local optical forces. The plasmonic trapping method takes advantage of the enhanced field to localize single entities in the most enhanced regions of the substrate.

The early days of SERS were marked by a dispute about the dominant mechanism for the effect. A group of scientists, lead by Prof. Andreas Otto from Düsseldorf, defended the idea that chemical contributions, including charge transfer, played a major role in SERS,[13] while others were advocating that electromagnetic effects were dominant.[14] While the role of plasmonics on the overall SERS efficiency is now well-established, it is rewarding to observe that, in this VSI, after 50 years of SERS, the contributions of other types of mechanisms have also been established. SERS is indeed a complex phenomenon with multiple contributions from different origins. For instance, a new formalism to determine the effect of the chemical enhancement toward the overall mechanism was reported by Aizpurua (10.1021/acs.jpcc.4c03491). Systematic experiments at various excitation wavelengths (10.1021/acs.analchem.3c05189) and/or applied electrochemical potentials (10.1021/acs.jpcc.4c03084) reveal modulations in the SERS intensities of the various vibrational modes that can provide information about the bonding characteristics of the molecular−surface complex and the orientation of the functional groups relative to the surface.

Biomedical applications and biosensing development are among the most active areas of investigation in SERS. A comprehensive accounting of the state of the art in the development of SERS biosensors was provided by Jin et al. (10.1021/acs.jpcc.4c02011). Wearable devices and rapid disease diagnosis are among the most exciting current topics in the area of biosensor development. This VSI has contributions that highlight the potential for SERS to have a significant impact in those topics as well. Atta et al. reported on a wearable patch containing gold nanostars for the detection of sweat metabolites using a portable Raman instrument (10.1021/acsomega.4c05140), while Hassanain et al. developed a SERS based protocol coupled to an enzyme-linked oligonucleotide assay (ELONA) capable of detecting specific genes related to antimicrobial resistance (AMR) (10.1021/acs.analchem.4c02165). AMR is deemed one of the most relevant global public health and development threats and the SERS-based test is an excellent approach for fast point of care diagnosis.

The strong local fields produced by plasmonic surfaces are also efficient in catalyzing photochemical processes. The application of SERS to monitor these catalytic reactions is natural, since the same enhanced field that enables catalysis also increases the Raman scattering efficiency. Kopal et al. contributed a comprehensive investigation of the photochemistry of 4-aminobenzenethiol (4-ABT) in Au, Ag, and Cu plasmonic substrates (10.1021/acsomega.4c00121). The Cu surface was found to be the best at 532 nm excitation. Wang et al. showed that plasmonic catalysis can be further optimized by introducing a cocatalyst (10.1021/acs.jpcc.3c07887). The decarboxylation reaction of *p*-mercaptobenzoic acid (PMBA) on the surface of silver nanoparticles (AgNPs) was significantly accelerated by the coadsorption of *p*-hydroxythiophenol (PHTP). This contribution suggests a new avenue for the optimization of photocatalysis from plasmonic surfaces. The formation of hot electrons in plasmonic systems has also been shown to mediate catalysis in a variety of systems. Hot electron generation at various excitation wavelengths were induced in silver nanocubes and the contribution of the different plasmonic modes to hot electron generation was explored (10.1021/acs.jpcc.4c01903). The dipolar modes in the nanocubes yielded more hot electrons than the coupled modes. Plasmonic hot electrons were also used for the polymerization of polyacrylonitriles fibers (10.1021/acs.jpcc.4c00996). The SERS data were correlated to photothermal images to determine the relative contributions of heating and hot electron effects in the catalysis. Electrochemical catalysis continues to be a field that benefits tremendously from SERS. SERS can naturally be used for *in situ* and *in operando* measurements in aqueous electrochemical systems due to the weak contribution of the water scattering background. However, examples of application of electrochemical SERS from different solvents was also reported (10.1021/acs.jpcc.4c03621). The solvent bands from both methanol and acetonitrile were present but easily discernible from the vibrational contributions of the adsorbed species of interest. A mini-review in this VSI discussed how SERS can be used to study the oxygen evolution reaction from a variety of catalytic surfaces, including metals, single-atom catalysts, metal−organic frameworks, and other types of interfaces (10.1021/acs.jpcc.4c03607). Another review in this VSI (10.1021/acs.jpcc.4c03596) covers the application of SERS to investigate mechanistic details of the carbon dioxide reduction reaction (CO_2RR). Both reviews in electrocatalysis emphasizes the use of shell-isolated nanoparticles (SHINs) as Raman amplifiers.

The breadth of the contributions to this historical VSI celebrating the 50th anniversary of the first observation of enhanced spectroscopy highlights how far the field has advanced and has branched into unexpected directions. The state of the art involves novel optical and photocatalytic materials, new fundamental insights, and a large number of interdisciplinary applications ranging from food security to biomedical devices. The increased understanding of the role of hotspots allied to the advent of modern statistical methods and machine learning indicate that SERS will continue to play a major role in analytical devices and applications. It is clear that SERS will be among the most important nanotechnology tools shaping our future. It certainly makes us wonder how far the field will be on the celebration of its centenary, 50 years from now.

Alexandre G. Brolo orcid.org/0000-0002-3162-0881
Nathan C. Lindquist orcid.org/0000-0002-1226-5212

AUTHOR INFORMATION

Complete contact information is available at:
https://pubs.acs.org/10.1021/acsomega.4c10071

Notes

Views expressed in this editorial are those of the authors and not necessarily the views of the ACS.
This editorial is jointly published in *The Journal of Physical Chemistry C*, *Analytical Chemistry*, and *ACS Omega*.

REFERENCES

(1) Fleischmann, M.; Hendra, P. J.; Mcquillan, A. J. *Chem. Phys. Lett.* **1974**, *26*, 163−166.
(2) Albrecht, M. G.; Creighton, J. A. *J. Am. Chem. Soc.* **1977**, *99*, 5215−5217.
(3) Jeanmaire, D. L.; Van Duyne, R. P. *J. Electroanal. Chem.* **1977**, *84*, 1−20.
(4) Moskovits, M. *J. Chem. Phys.* **1978**, *69*, 4159−4161.
(5) Nie, S.; Emory, S. R. *Science* **1997**, *275*, 1102−1106.
(6) Kneipp, K.; Wang, Y.; Kneipp, H.; Perelman, L. T.; Itzkan, I.; Dasari, R.; Feld, M. S. *Phys. Rev. Lett.* **1997**, *78*, 1667−1670.
(7) Brongersma, M. L.; Halas, N. J.; Nordlander, P. *Nat. Nanotechnol* **2015**, *10*, 25−34.
(8) Benz, F.; Schmidt, M. K.; Dreismann, A.; Chikkaraddy, R.; Zhang, Y.; Demetriadou, A.; Carnegie, C.; Ohadi, H.; de Nijs, B.; Esteban, R.; Aizpurua, J.; Baumberg, J. J. *Science* **2016**, *354*, 726−729.
(9) Lindquist, N. C.; de Albuquerque, C. D. L.; Sobral-Filho, R. G.; Paci, I.; Brolo, A. G. *Nature Nanotechnology* **2019**, *14*, 981−987.
(10) Lee, J.; Crampton, K. T.; Tallarida, N.; Apkarian, V. A. *Nature* **2019**, *568*, 78−82.
(11) Fan, M. K.; Andrade, G. F. S.; Brolo, A. G. *Anal. Chim. Acta* **2011**, *693*, 7−25.
(12) de Albuquerque, C. D. L.; Sobral-Filho, R. G.; Poppi, R. J.; Brolo, A. G. *Anal. Chem.* **2018**, *90*, 1248−1254.
(13) Otto, A; Mrozek, I; Grabhorn, H; Akemann, W *Journal of Physics-Condensed Matter* **1992**, *4*, 1143−1212.
(14) Moskovits, M. *Reviews of Modern Physics* **1985**, *57*, 783−826.