JVST B
Journal of Vacuum Science & Technology B

Clinical probe utilizing surface enhanced Raman scattering

Cite as: J. Vac. Sci. Technol. B **32**, 06FD02 (2014); https://doi.org/10.1116/1.4896479
Submitted: 17 June 2014 . Accepted: 12 September 2014 . Published Online: 26 September 2014

Jeonghwan Kim, Dooyoung Hah, Theda Daniels-Race, and Martin Feldman

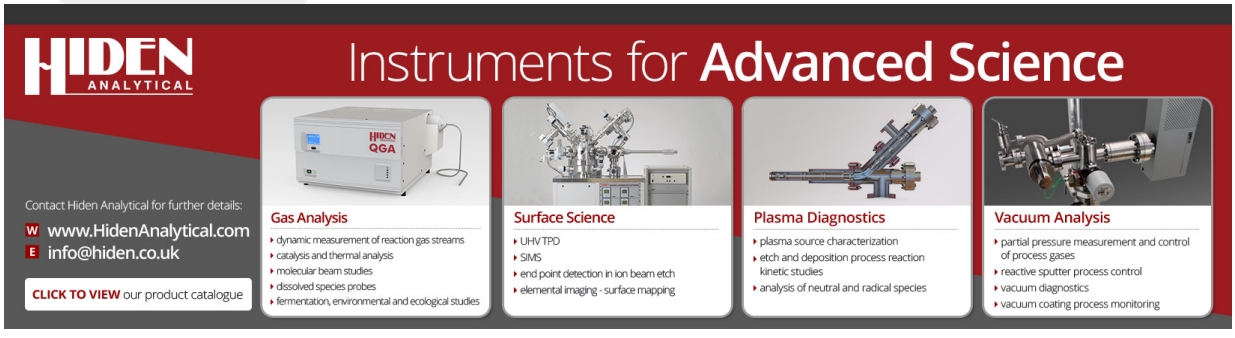
View Online Export Citation CrossMark

ARTICLES YOU MAY BE INTERESTED IN

A needle probe to detect surface enhanced Raman scattering (SERS) within solid specimen
Review of Scientific Instruments **88**, 023107 (2017); https://doi.org/10.1063/1.4975183

Single fiber surface enhanced Raman scattering probe
Journal of Vacuum Science & Technology B **35**, 06GF01 (2017); https://doi.org/10.1116/1.4990697

Nanorough gold for enhanced Raman scattering
Journal of Vacuum Science & Technology B **31**, 06FE02 (2013); https://doi.org/10.1116/1.4826701



© 2014 American Vacuum Society.

Clinical probe utilizing surface enhanced Raman scattering

Jeonghwan Kim
Division of Electrical and Computer Engineering, Louisiana State University, 3104-B Patrick Taylor Hall, Baton Rouge, Louisiana 70803

Dooyoung Hah
Electrical and Electronics Engineering Department, Abdullah Gul University, Kayseri, Turkey

Theda Daniels-Race
Electrical and Computer Engineering, 3104-B Patrick Taylor Hall, Louisiana State University, Baton Rouge, Louisiana, 70803 and Center for Computation and Technology, 3104-B Patrick Taylor Hall, Louisiana State University, Baton Rouge, Louisiana, 70803

Martin Feldman[a)]
Division of Electrical and Computer Engineering, Louisiana State University, 3104-B Patrick Taylor Hall, Baton Rouge, Louisiana 70803

(Received 17 June 2014; accepted 12 September 2014; published 26 September 2014)

Conventional Raman scattering is a well-known technique for detecting and identifying complex molecular samples. In surface enhanced Raman scattering, a nanorough metallic surface close to the sample enormously enhances the Raman signal. In previous work, the metallic surface was a thin layer of gold deposited on a rough transparent epoxy substrate. The advantage of the clear substrate was that the Raman signal could be obtained by passing light through the substrate, on to opaque samples simply placed against its surface. In this work, a commercially available Raman spectrometer was coupled to a distant probe. Raman signals were obtained from the surface, and from the interior, of a solid specimen located more than 1 m away from the spectrometer. The practical advantage of this arrangement is that it opens up surface enhanced Raman spectrometry to a clinical environment, with a patient simply sitting or lying near the spectrometer. © *2014 American Vacuum Society*. [http://dx.doi.org/10.1116/1.4896479]

I. INTRODUCTION

Raman spectra have been used to identify substances for many years. The generally weak Raman signal levels are enormously enhanced when the specimens are in contact with a rough metallic surface.[1–5] There is considerable interest in extending this surface enhanced Raman (SER) capability to endoscopic probes, so that samples may be studied *in vivo*,[6] rather than removed and placed on a microscope stage. In previous work,[7] the authors obtained SER spectra through a rough gold film on a transparent epoxy substrate, so that access was needed to only one side of an opaque sample. In the present work, instead of viewing a specimen placed on its stage, a LabRAM Raman spectrometer (HORIBA Scientific, 3880 Park Avenue, Edison, New Jersey) is optically coupled to remote probes. The probes contain 2 mm diameter graded index (GRIN) lenses, which replace one of the spectrometer's microscope objectives. Raman spectra were obtained with probes both on the surface, as well as inserted into, solid specimens. The small diameter of the remotely positioned probes allows them to be minimally invasive in a clinical environment, so that surface enhanced raman scattering (SERS) may be performed on a patient simply sitting or lying near the spectrometer.

II. EXPERIMENT

A. Probe

The LabRAM spectrometer uses a 1 mW He–Ne laser at a wavelength of 633 nm. When a microscope objective is removed the light exits as a nearly parallel beam. Within a GRIN lens, this beam follows a sinusoidal path. GRIN lenses are specified by their length, in radians, of the sinusoidal path. Initially, 2 mm diameter $\pi/4$ GRIN lenses (NSG Group, 134 East Main Avenue SEPZ, Laguna Technopark, Binan, Laguna, Philippines) were used, resulting in focusing the laser beam about 2 mm past the back surfaces of the lenses. The GRIN lenses focused the beam to about 20 μm, the same as the 10× microscope objective in the spectrometer, and produced a reasonably long working distance [Fig. 1(a)].

Later, work used $\pi/2$ GRIN lenses, which focus incident parallel beams onto their back surfaces. The transparent epoxy substrates carrying the 20 nm thick rough gold film were bonded directly to the back surfaces of these lenses and had negligible effect on the SERS. For the thickness of the substrates used, about 0.4 mm, the optical conjugate to the gold surface was approximately 1.5 cm upstream of the lenses [Fig. 1(b)].

The light was focused on the gold surface by varying the distance between the lens and the intermediate focus at the conjugate [Fig. 2(a)]. The large axial magnification simplified precise focusing on the gold while providing the robust structure needed to support a probe to be inserted into solid specimens. The focusing range was limited, but well within the variation in thickness of the epoxy substrate (Fig. 3). In addition, locating the focusing mechanism behind the probe tip minimized the diameter of the probe. A photograph of the completed probe is shown in Fig. 2(b).

B. Arm

In previous attempts to couple a Raman spectrometer to a remote probe, an optical fiber was inserted between the

[a)]Electronic mail: mfeldm1@lsu.edu

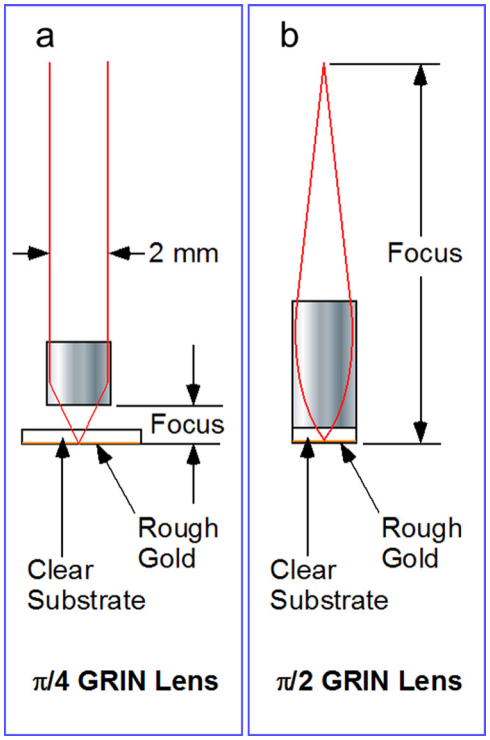


FIG. 1. (Color online) (a) Initial probe utilizing an air gap between the GRIN lens and the rough gold surface in contact with the specimen. (b) Advanced probe, with the rough gold surface bonded via the clear substrate spacer directly to a longer GRIN lens.

spectrometer and the probe. We have found, as did previous workers,[8,9] that Raman spectra arising from the fiber material produced a large background to the signal from the probe. It is possible that photonic bandgap or hollow core fibers will generate less Raman background; however, they were not yet available in the 633–735 nm bandwidth required for our application.

Consequently, an articulated arm was constructed to couple the Raman spectrometer to the probe (Fig. 4). The spectrometer was converted from conventional to remote operation by removing an objective and placing the adjustable mirror M1 on its microscope stage. This mirror centered the beam on the entrance to a long articulated arm. A second adjustable mirror, M2, directed the beam along the optical axis of the arm. A long focal length lens, L1, slightly converged the beam to fill the 2 mm diameter probe at the end of the arm.

The arm has five rotating joints, equipped with 45° mirrors, to deflect the beam by 90° angles. Rotation of the joint at A positions B on a circle of radius 34 cm. Simultaneous rotation of the two closely spaced joints at B positions C roughly in a sphere of radius 14 cm centered at B. Rotation of all three joints positions C at a point anywhere within a torus of major radius 34 cm and minor radius 14 cm. The last two joints, at C, point the probe at any direction from that point. The clinically useful working volume is a fraction of the torus, roughly a cylinder 34 cm tall by 28 cm diameter, centered about 60 cm from the spectrometer. The measured transmission of the arm is about 50% and is relatively independent of polarization and wavelength.

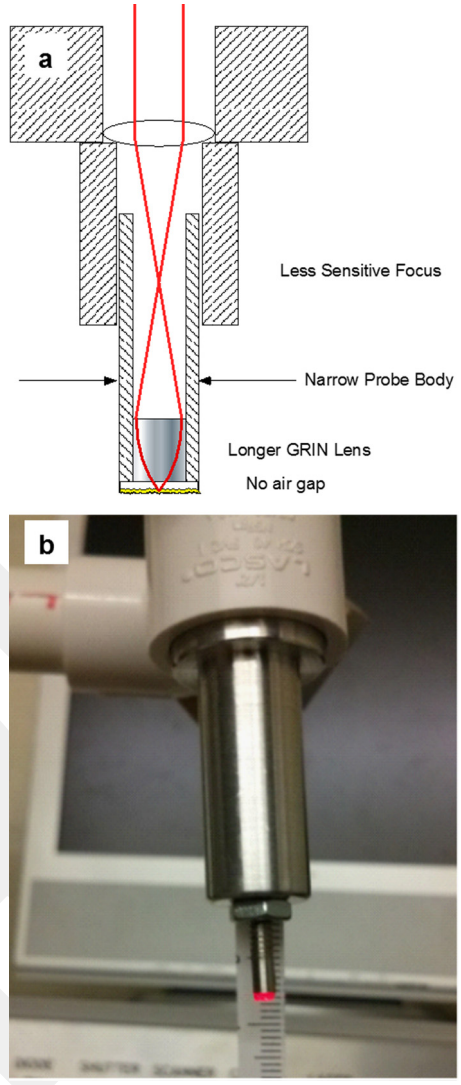


FIG. 2. (Color online) (a) Sketch of the advanced probe indicating the focusing to the intermediate conjugate. (b) Photograph of the probe with light exiting through the rough gold surface. The scale indicates 1 mm divisions.

C. Test specimen

Test specimens were prepared from a gelatin powder widely available as a food ingredient in grocery stores

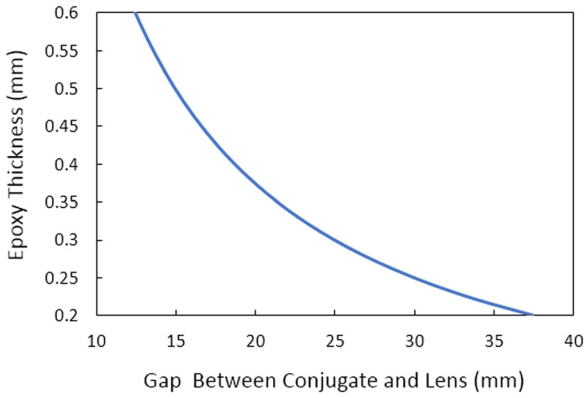


FIG. 3. (Color online) Focusing of the π/2 GRIN lens. The depth of the epoxy substrate through which the light is focused is plotted as a function of the distance from the back conjugate to the lens.

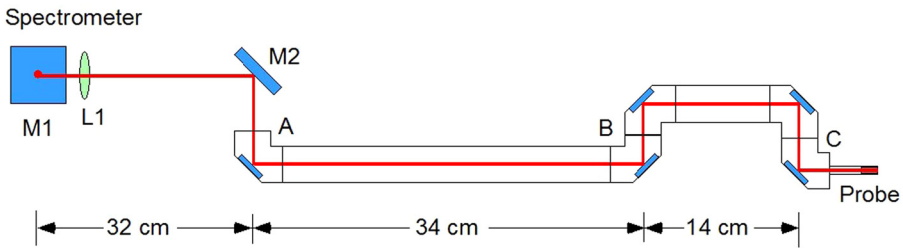


FIG. 4. (Color online) Layout of the fully extended articulated arm connecting the spectrometer to a remote probe. The probe can be pointed in any direction at any point within a large working volume.

(Knox unflavored gelatin, Kraft Foods Global, Inc., Northfield, IL). The gelatin was prepared with a 1 mM of Rhodamine 6G solution[10,11] in place of the customary water. The result was a soft somewhat transparent solid that was readily penetrated by the probe [Fig. 5(a)].

III. RESULTS AND DISCUSSION

Raman spectra were obtained of the Rhodamine 6G in the gelatin specimen with the probe at the end of the articulated arm and either in contact with the specimen or inserted into it as shown in Fig. 5(a). The integration time in the spectrometer was 5 s. Essentially, identical spectra were obtained both on the surface and at ten locations within the specimen [Fig. 5(b)]. Due to a variety of losses in the articulated arm and the probe the signal strength at 1 mM concentration was only about 1% that of previous results,[7] which had an enhancement factor of 10^6.

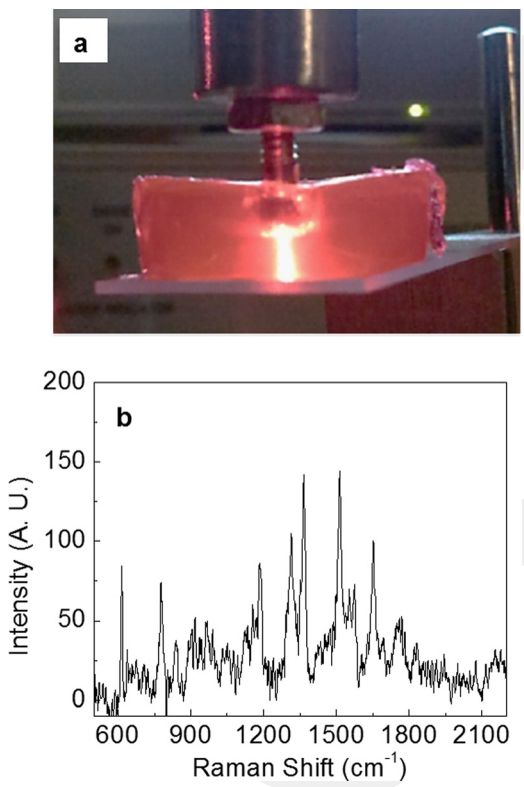


FIG. 5. (Color online) (a) Photograph of the probe inserted into a solid block of gelatin prepared with a 1 mM solution of Rhodamine 6G. (b) Rhodamine spectrum obtained with the probe operated as in (a).

What has been demonstrated is that LabRAM Raman spectrometers are readily converted to remote operation. Our spectrometer was coupled to a remote probe that could be oriented in any direction within a relatively large working volume. The overall diameter of the probe was less than 3 mm to minimize its invasiveness in a clinical environment.

High signal to noise ratio surface enhanced Raman spectra were obtained with the remote probe at multiple locations both on and within a solid specimen far removed from the spectrometer. This demonstrates the usefulness of this technique in a clinical environment, with a patient potentially sitting or lying near the spectrometer.

ACKNOWLEDGMENT

This work was supported in part by the National Institutes of Health Grant No. 1R03EB012519-01A1.

[1]M. Fleischmann, P. J. Hendra, and A. McQuillan, Chem. Phys. Lett. **26**, 163 (1974).
[2]R. P. Van Duyne, J. Phys. Colloques **38**, C5-239 (1977).
[3]G. L. Liu and L. P. Lee, Appl. Phys. Lett. **87**, 074101 (2005).
[4]J. I. Gersten, J. Chem. Phys. **72**, 5779 (1980).
[5]S. M. Nie and S. R. Emory, Science **275**, 1102 (1997).
[6]S. Keren, C. Zavaleta, Z. Cheng, A. de la Zerda, O. Gheysens, and S. S. Gambhir, Proc. Natl. Acad. Sci. U. S. A. **105**, 5844 (2008).
[7]J. Kim, K.-N. Kang, A. Sarkar, P. Malempati, D. Hah, T. Daniels-Race, and M. Feldman, J. Vac. Sci. Technol., B **31**, 06FE02 (2013).
[8]G.-L. Lan, P. K. Banerjee, and S. S. Mitra, J. Raman Spectrosc. **11**, 416 (1981).
[9]L. F. Santos, R. Wolthuis, S. Koljenović, R. M. Almeida, and G. J. Puppels, Anal. Chem. **77**, 6747 (2005).
[10]P. Hildebrandt and M. Stockburger, J. Phys. Chem. **88**, 5935 (1984).
[11]A. Weiss and G. Haran, J. Phys. Chem. B **105**, 12348 (2001).