CHAPTER 3

COMPACT SERS DETECTION INSTRUMENTATION

Present chapter illustrates the working principle of Raman spectrometer instrumentation that was used for detection and analysis of Raman and SERS signals. Also, a brief overview of few other compact Raman instruments which are used for rapid and portable SERS sensing applications have been discussed.

3.1 Raman spectrometer

The most important component in a SERS detection is the Raman spectrometer. From decades of research, the Raman spectrometers have advanced in many areas like- laser power, spectral resolution and sensitivity. In another way, the spectrometers have been reduced to compact size to enhance its application in various fields. The typical Raman spectrometer contains a number of components, like a laser source, excitation delivery optics, sample holder, collection optics, a wavelength separation device, detector and a recording device. Schematic representation of a modern Raman spectrometer is depicted in the figure 3.1(a). First, laser from the source travels through the excitation fiber, then a series of optical components- collimator, line filter, dichroic mirror, and lens which focuses the narrow band of light on the sample. The back-scattered light from the sample is collected and higher wavelength lights are reflected by the dichroic mirror, and then passes through the notch filter. The Collection fiber takes the Stokes shifted laser photons to a detector. Raman intensity is proportional to the fourth power of the frequency of the incident laser [1]. Short-wavelength laser provides intense Raman signals scattered from the sample. However, in this wavelength, sometimes the Raman analysis suffers due to high fluorescence emission and photodecomposition of the sample. To overcome these isssues, near infrared (NIR) laser sources often are utilized mainly for biological sample analysis.

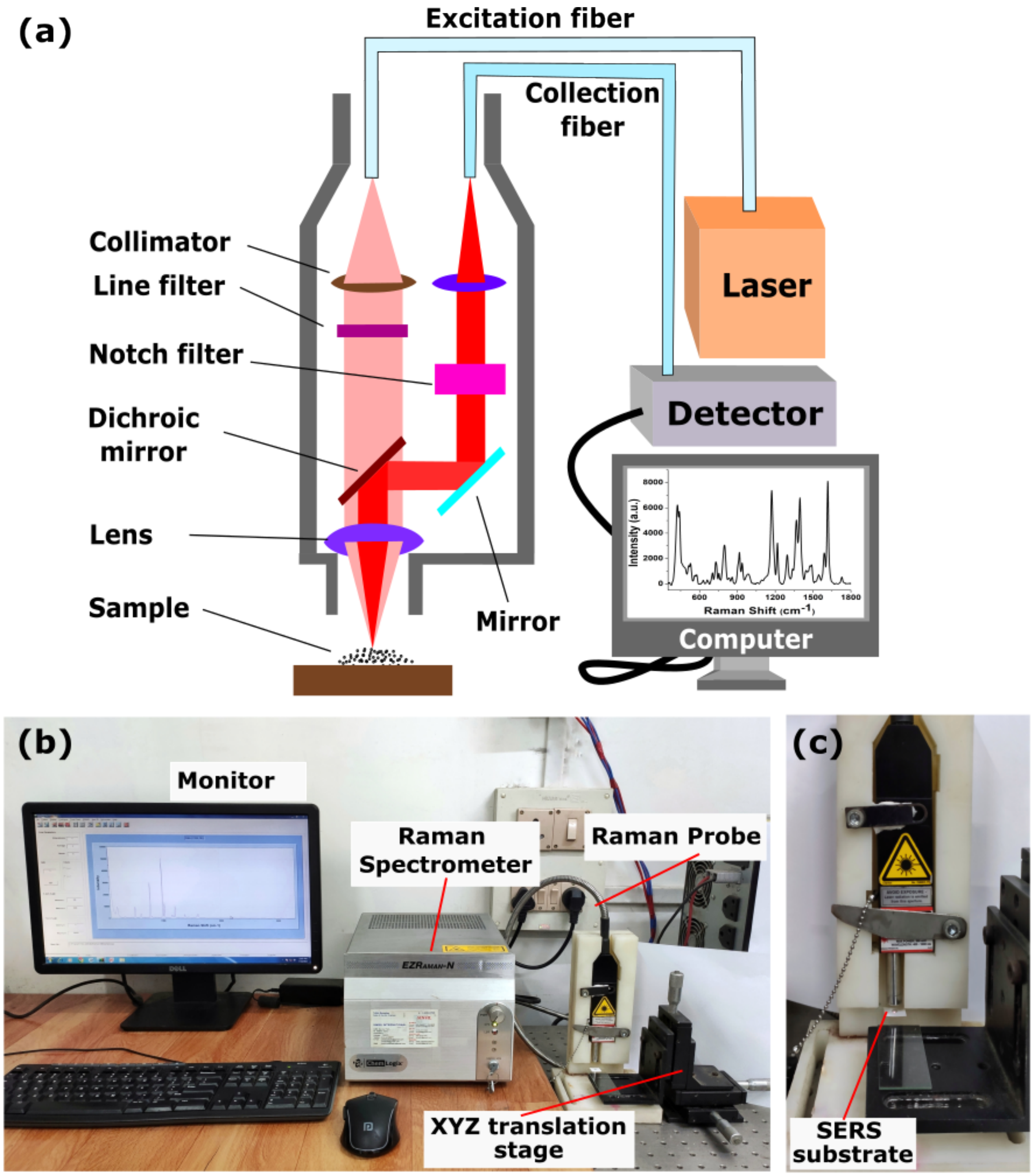

Figure 3.1: (a) Schematic representation of a Raman spectrometer. (b) Laboratory setup for Raman and SERS signal collection. (c) Raman signal collection from the paper-based SERS substrate.

3.2 Compact Raman spectrometers

The compact Raman spectrometers can be classified into two categories: modular and handheld spectrometer [2]. Here, by the term modular means the portable spectrometers which has one or more components are exeternally coupled with the main body of the spectrometer. In handheld spectrometers, all the components are contained in a single and miniaturized form, and can be operated being held.

3.2.1 Modular Raman instruments

The modular Raman instruments have several advantages, like- powerful laser, high sensitivity, high resolution, broad spectral range, flexibility. These make the modular instruments very polpular for Raman and SERS-based sensing applications.

In this thesis, all the Raman and SERS signals have been recorded using a NIR Raman spectrometer developed by Enwave Optronics, USA (Model No: EZRaman-N-785-B1S) [3]. In this instrument, a laser signal of wavelength 785 nm from a diode laser is guided using a fiber optic probe, and the same probe is used to collect the back-scattered Raman signals from the sample. The spectrometer is equiped with a thermoelectrically cooled charge-coupled device (CCD) detector and a f/1.6 NIR optimized spectrograph having a pixel resolution of 1.45 cm^{-1} per pixel. During the signal collection, Raman probe was first attached to the holder as shown in the figure 3.1(b). The analyte sample or the SERS substrate is placed on a glass slide. With a linear XYZ translation stage, laser from the probe is focused on the analyte surface and scanned over the sensing region of the SERS substrate as shown in the figure 3.1(c).

A highly sensitive and high throughput modular Raman spectrometer iRaman from B&W Tek have been used several point-of-care diagnostic applications. Tudor et al. have developed a SERS strategy to detect bladder cancer from human urine sample [4].

Lee et al. have integrated polymerase chain reaction (PCR) and SERS to detect *Mycoplasma pneumoniae* with a NS220 personal Raman spectrometer (Nanoscope Systems) paired with a 633 nm laser to collect SERS data [5].

A modular Tec5USA Raman spectroscopy system (Tec5USA Inc.), with a 785 nm excitation wavelength have been employed by Yanjun et al. for the rapid sensing of SARS-CoV-2 RNA in human nasopharyngeal swab specimens [6].

3.2.2 Handheld Raman instruments

Handheld Raman instuments have gained attentions in recent years due to their versatility in medical point-of-care diagnosis, forensic science, food safety and pharmaceutical analysis. These small and low-cost spectrometers enables the operation and transportation in different environmental conditions. The Raman spectra could be displayed on the same hanheld unit, a coupled smartphone or a digital tablet.

SERS-based detection of ultra-low concentration of SERS-CoV-2 has been performed using a MIRA DS handheld Raman spectrometer (Metrohm, 785 nm, 50 mW, 1s collection times) within 30 minutes [7]. In another work, same spectrometer have been used to detect SERS-CoV-2 spike protein in saliva using a SERS-based lateral flow test strip [8].

Gahlaut et al. have used a handheld Raman device (the ASSURx model from TSI Inc., USA, operating at 785 nm, 50 mW) for the detection and identification of Dengue NS1 antigen in clinical blood samples [9].

Handheld Raman spectrometers have also been used for the detection of bacteria. Dryden et al. used an ID Raman mini 2.0 (Ocean Insight, 785 nm, 50 mW) for the multiplexed detection of urinary tract infections commonly caused by three different pathogens (*Escherichia coli, Enterococcus faecalis, Klebsiella pneumonia*) [10].

Handheld Raman has also been employed in the detection of small nucleic acid biomarkers such as microRNA (miRNA). Mabbott et al. detected cardiac stress biomarker miR-29a using handheld Raman by Snowy Range Instruments (638 nm, 40 mW) in combination with 3D paper fluidics [11].

3.3 Summary

The present chapter introduces compact Raman instruments utilized for rapid and sensitive detection analyte samples. The brief working principle of the Raman instrument and the photograph of Raman setup have been included.

Bibliography

[1] Ferraro, J. R. *Introductory raman spectroscopy.* Elsevier, 2003.

[2] Tripathy, S., Chavva, S., Coté, G. L., and Mabbott, S. Modular and handheld raman systems for sers-based point-of-care diagnostics. *Current Opinion in Biomedical Engineering*, page 100488, 2023.

[3] Biswas, S., Devi, Y. D., Sarma, D., Namsa, N. D., and Nath, P. Gold nanoparticle decorated blu-ray digital versatile disc as a highly reproducible surface-enhanced raman scattering substrate for detection and analysis of rotavirus rna in laboratory environment. *Journal of Biophotonics*, 15(11):e202200138, 2022.

[4] Moisoiu, T., Dragomir, M. P., Iancu, S. D., Schallenberg, S., Birolo, G., Ferrero, G., Burghelea, D., Stefancu, A., Cozan, R. G., Licarete, E., et al. Combined

mirna and sers urine liquid biopsy for the point-of-care diagnosis and molecular stratification of bladder cancer. *Molecular Medicine*, 28(1):39, 2022.

[5] Lee, H. G., Choi, W., Yang, S. Y., Kim, D.-H., Park, S.-G., Lee, M.-Y., and Jung, H. S. Pcr-coupled paper-based surface-enhanced raman scattering (sers) sensor for rapid and sensitive detection of respiratory bacterial dna. *Sensors and Actuators B: Chemical*, 326:128802, 2021.

[6] Yang, Y., Li, H., Jones, L., Murray, J., Haverstick, J., Naikare, H. K., Mosley, Y.-Y. C., Tripp, R. A., Ai, B., and Zhao, Y. Rapid detection of sars-cov-2 rna in human nasopharyngeal specimens using surface-enhanced raman spectroscopy and deep learning algorithms. *Acs Sensors*, 8(1):297–307, 2022.

[7] Leong, S. X., Leong, Y. X., Tan, E. X., Sim, H. Y. F., Koh, C. S. L., Lee, Y. H., Chong, C., Ng, L. S., Chen, J. R. T., Pang, D. W. C., et al. Noninvasive and point-of-care surface-enhanced raman scattering (sers)-based breathalyzer for mass screening of coronavirus disease 2019 (covid-19) under 5 min. *ACS nano*, 16 (2):2629–2639, 2022.

[8] Mohammadi, M., Antoine, D., Vitt, M., Dickie, J. M., Jyoti, S. S., Wall, J. G., Johnson, P. A., and Wawrousek, K. E. A fast, ultrasensitive sers immunoassay to detect sars-cov-2 in saliva. *Analytica chimica acta*, 1229:340290, 2022.

[9] Gahlaut, S., Savargaonkar, D., Sharan, C., Yadav, S., Mishra, P., and Singh, J. Sers platform for dengue diagnosis from clinical samples employing a hand held raman spectrometer. *Analytical chemistry*, 92(3):2527–2534, 2020.

[10] Dryden, S. D., Anastasova, S., Satta, G., Thompson, A. J., Leff, D. R., and Darzi, A. Rapid uropathogen identification using surface enhanced raman spectroscopy active filters. *Scientific Reports*, 11(1):8802, 2021.

[11] Mabbott, S., Fernandes, S. C., Schechinger, M., Cote, G. L., Faulds, K., Mace, C. R., and Graham, D. Detection of cardiovascular disease associated mir-29a using paper-based microfluidics and surface enhanced raman scattering. *Analyst*, 145(3):983–991, 2020.