

Developments in Raman Spectromicroscopy for Strengthening Materials and Natural Science Research: Shaping the Future of Physical Chemistry

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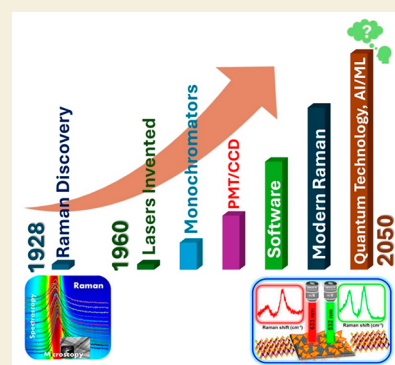
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ABSTRACT: Spectroscopic techniques, especially Raman spectroscopy, cover a large subset in the teaching and research domain of physical chemistry. Raman spectroscopy, and other Raman based techniques, establishes itself as a powerful analytical tool with diverse applications across scientific, industrial, and natural science (including biology and pharmacy) fields and helps in the progress of physical chemistry. Recent advancements and future prospects in Raman spectroscopy, focusing on key areas of innovation and potential directions for research and development, have been highlighted here along with some of the challenges that need to be addressed to prepare Raman based techniques for the future. Significant progress has been made in enhancing the sensitivity, spatial resolution, and time resolution of Raman spectroscopy techniques. Raman spectroscopy has applications in all areas of research but especially in biomedical applications, where Raman spectroscopy holds a great promise for noninvasive or minimally invasive diagnosis, tissue imaging, and drug monitoring. Improvements in instrumentation and laser technologies have enabled researchers to achieve higher sensitivity levels, investigate smaller sample areas with improved spatial resolution, and capture dynamic processes with high temporal resolution. These advancements have paved the way for a deeper understanding of molecular structure, chemical composition, and dynamic behavior in various materials and biological systems. It is high time that we consider whether Raman based techniques are ready to be improved based on the strength of the current era of AI/ML and quantum technology.

KEYWORDS: Raman Spectroscopy, Artificial Intelligence (AI), Data Interpretation, POC Device, Biomedical Applications, Physical Chemistry



1. INTRODUCTION

Historically, the term “physical chemistry”^{1,2} (along with its synonym “chemical physics”), one of the fields of study in chemistry, was initially termed by Mikhail Lomonosov in 1752. He tossed this term during one of his lectures to elucidate the underlying principles of physical experiments and to explain the reasons behind complex body phenomena through chemical operations.³ The main principles upon which it was elucidated and comprehended were associated with bulk characteristics rather than solely molecular or atomic structure. The progressive innovation of various characterization methods has been a crucial success factor in the field of physical chemistry. This success extends beyond the study of bulk materials, enabling researchers to gain insights into the mechanisms at molecular and atomic levels, including real-time responses.⁴ The interdisciplinary nature of this area makes it flexible to expand its domain and allows it to remain one of the major areas where scientists from research, academia, and

industry contribute. It is beyond doubt that physical chemistry has progressed and contributed significantly to the progress of scientific knowledge in different domains like materials, energy, spectroscopy, etc. Every generation experiences clear progress in scientific growth through physical chemistry methods where a school student grows to an independent researcher who later contributes to the growth of physical chemistry itself. It is time we take some time to discuss how we wish to see “physical chemistry” growing so that it touches upon a broader population so as to improve their overall intellect through

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scientific insight.⁵ Among all the spectroscopic techniques, Raman spectroscopy,^{6–9} a nondestructive method, stands out as a fingerprint characterization technique applicable to bulk, liquid, and thin film phases of materials.¹⁰ The spectroscopy¹¹ has been developed based on the basic principle of inelastic scattering discovered by C.V. Raman and K.S. Krishnan¹² from India and approximately around the same time by Mandelstam and Landsberg from Russia in 1928.¹³ Before the centenary year of this discovery in 2028, we can have a look at how Raman spectroscopy^{14,15} has developed and has improved the understanding in physical chemistry. It is well-known that the Raman effect explores the molecular vibrations/phonons in a molecule/material, resulting from a weak scattering process when incident radiation interacts with the molecular geometry and therefore offers a detailed molecular-level picture from the scattered radiations.^{6,16} It will be our privilege to witness and celebrate the 100th year of the success of the Raman effect in 2028. Consequently, the timeline of the Raman effect and spectroscopy in physical chemistry, from the past to the present, has been highlighted here from this perspective, which also helps us in chalking out our expectations and preparing a “To Do List” for the future. This can serve as a foundational guide to develop future outcomes in physical chemistry research using Raman spectroscopic techniques.^{17–20}

In contrast to Rayleigh scattering, Sir C.V. Raman identified new scattering phenomena of light from water molecules that therefore contribute to the blue color observed in the ocean, later defined as a Raman effect.^{21,22} The analysis of light scattering from water molecules involves detecting changes in the wavelength scattered from the molecules. This scattered light carries information about the molecular vibrational energy, generating a weak scattering pattern. This scattering phenomenon has proven to be highly valuable in comprehending the detailed molecular structure of unknown substances, essentially serving as a molecular fingerprint. As recognition of this groundbreaking work, Raman was honored with the Nobel Prize (Physics) in 1930. James Hibben quotes, “The Raman Effect became the adopted child of chemistry”, and undoubtedly, it has played a pivotal role in the advancement of physical chemistry.²³ It is also set to remain a high priority technique for future characterization.

Raman spectroscopy, similar to various other chemical analysis methods, possesses the capability to detect, measure, and define a broad spectrum of substances. Nevertheless, it boasts a greater level of specialization compared to certain other techniques due to additional considerations necessitating prior understanding. The Raman spectrometer remains a potent instrument offering unique advantages absent in alternative methods, rendering it indispensable across diverse fields of research.²⁴ There are multiple uses for it, which makes it so special in material characterizations. This technique offers numerous advantages, particularly its widespread use as a noncontact method. It can consistently deliver excellent data quality for both solid and liquid samples with ease. Furthermore, it streamlines sample preparation and is adept at examining minute structures through its integrated resolution analysis via microscopy and imaging techniques.²⁵

Raman spectroscopy finds wide-ranging applications, encompassing quality control, failure analysis, sample identification, and characterization of materials, enabling the exploration of both physical and chemical properties. Moreover, when coupled with microscopy, it extends its utility to the examination of minute structures and virtually any

substance, enhancing its analytical capabilities significantly. Raman spectroscopy has become the mainstream technique for analyzing carbon containing materials (even inorganic hybrids with organics and polymers) like graphene and carbon nanotubes. It can also check for defects or precisely characterize the materials by determining the exact kind of chemical bonding and is helpful to study the degradation of the materials.²⁶ It is invaluable in the pharmaceutical sector, serving various stages of drug production, spanning from development to the verification of final products and the stability of components.²⁷ Additionally, in the biomedical field, this technique finds utility in investigating the structure of proteins and DNA too, elucidating their roles in diverse biological functions. Furthermore, in the exploration of materials for emerging technologies such as enhanced batteries and solar cells, and within the semiconductor industry, rapid material analysis is paramount, and Raman spectroscopy fulfills this role admirably.

This article highlights some of the key advantages of the Raman effect/spectroscopy,^{28–30} explaining why this characterization method is extremely valuable in understanding detailed molecular structures across different sample phases and geometries in different fields of science. It also highlights how “Raman” as a technique needs to equip itself in the evolving era of artificial intelligence and machine learning (AI/ML).³¹

2. RAMAN BASED TECHNIQUES IN DIFFERENT AREAS

2.1. Raman Spectroscopy and Microscopy in Device Physics

It has been established that Raman based techniques, Raman spectroscopy, Raman microscopy, surface enhanced and tip enhanced Raman spectroscopy, etc., play a significant role in the semiconductor industry, offering valuable insights into the composition, quality, and structural characteristics of semiconductor materials.³² It provides information about the vibrational modes of the materials, helping to identify and analyze different phases and crystal structures, along with the existing lattice defects and strain. This is vital for assessing the electrical properties of semiconductors and optimizing the performance of electronic devices. In an industrial point of view, Raman spectroscopy can be employed for real-time process monitoring during semiconductor fabrication, which ensures the consistency and quality of materials at various stages of production, allowing for immediate feedback and adjustments in manufacturing processes. Therefore, Raman spectroscopy is a versatile and nondestructive analytical technique that plays a crucial role everywhere in materials science and applications.²⁴ Recently, Raman spectroscopy has been widely used in the field of smart devices such as electrochromic (EC) smart windows, memory devices, etc., for live monitoring of the device performance.^{33,34}

Since the realm of electrochromics involves the utilization of materials that alter their color when subjected to an electric bias, when employing these materials for practical applications, Raman seems to be a great choice to monitor as it can identify between different molecular states of the EC materials in their different colored states. Researchers and engineers have identified new materials, fabrication methods, and applications to enhance the performance and efficiency of the EC devices. However, obtaining a comprehensive understanding of color

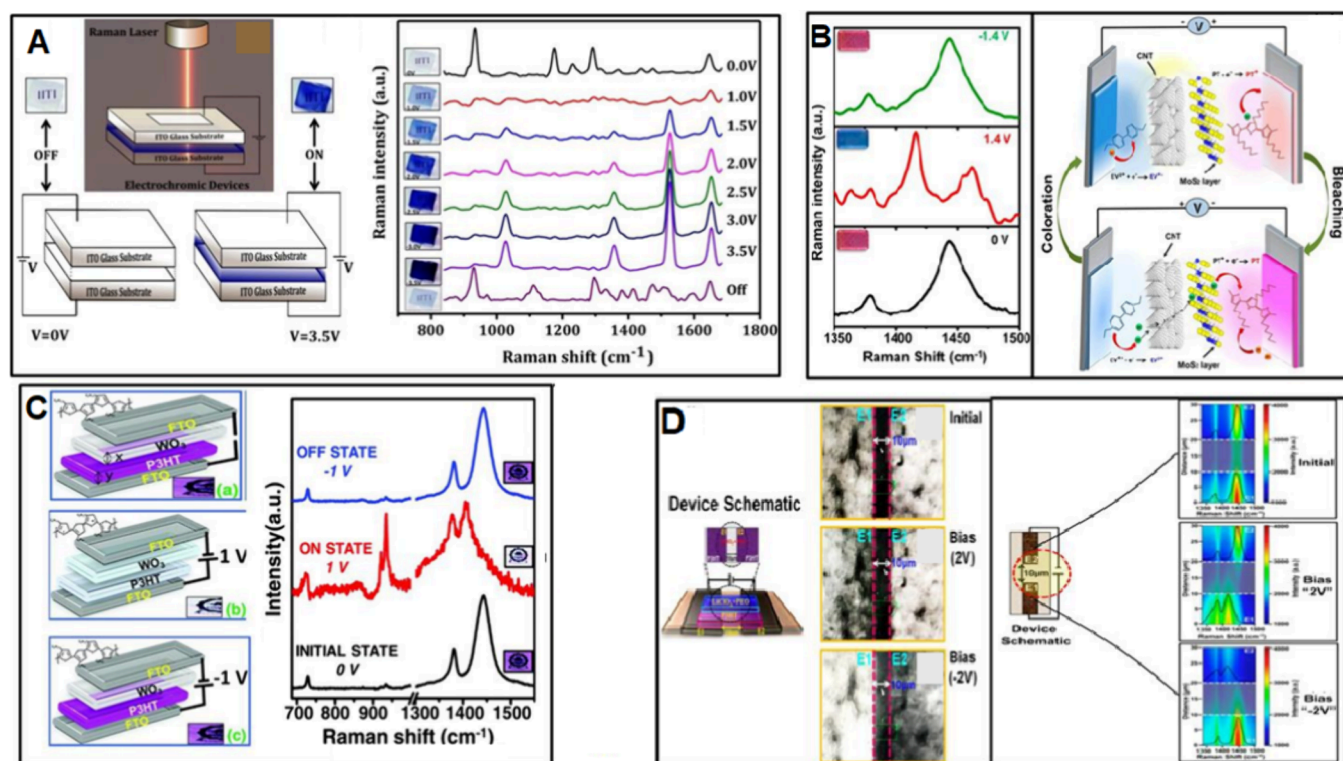


Figure 1. (A) Cross-bar geometry of the EC device under biased (ON) and unbiased (OFF) states along with in situ Raman operation and Raman spectra measured under different biasing potentials of various EC color states of the device from the transparent to the blue state. Reproduced with permission from ref 33. Copyright (2018) Springer Nature. (B) In situ Raman spectra of the solid-state device under ± 1.4 and 0 V along with its schematic device geometry for electron motion during the coloration and decoloration processes. Reprinted with permission under a Creative Commons CC BY-NC-ND 4.0 DEED license from ref 35. Copyright (2022) American Chemical Society. (C) In situ Raman spectra of the smart EC device with different potential states and cross-bar geometry of the device schematic with actual color images. Reproduced with permission from ref 36. Copyright (2020) Royal Society of Chemistry. (D) Open face geometry of the device schematic in three bias connections and its microscopic images and Raman maps in various states. Reproduced with permission from ref 37. Copyright (2021) American Chemical Society.

modulation in any material or device, along with real-time tracking of chromic species' characteristics, has proven to be a challenging endeavor. Nonetheless, the operando mode of Raman spectroscopy has been utilized to examine EC devices, providing insights into their molecular and structural change. This approach can assist in comprehending the refining device operational study.

The EC devices frequently entail redox (reduction–oxidation) reactions and experience alterations in their oxidation state. Raman spectroscopy can be employed to observe these redox reactions in real time either by a peak shift or by formation/suppression of other peaks. The dynamic doping of ions in response to applied voltage provides an enhanced understanding of color change transitions and color selectivity across different conditions, which can be deduced from the Raman spectra. Raman spectroscopy is renowned for being a nondestructive technique, and it does not typically impact molecular chemistry or cause any physical damage due to laser heating. However, as a precautionary measure, it is important to always use an optimal laser power to probe the molecular characteristics, especially in real-time measurements.

To understand the EC color modulation of the viologen molecule, a device was constructed based on ethyl viologen in a cross-bar configuration, as depicted in Figure 1A (left panel), by sandwiching the EC layer between two transparent conducting ITO electrodes to investigate the origin of the perceived blue color under external negative biasing. Using bias dependent Raman spectroscopy with gradual bias (Figure 1A,

right panel), it could be established that viologen exists in its EV^{2+} in neutral form and $EV^{\bullet+}$ states, which are responsible for the transparent and colored (blue) states, respectively. It is this bias dependent switching in the oxidation state of viologen which makes the device switch color, hence it is the underlying mechanism of color switching. A detailed analysis helps in understanding the mechanism in almost all kinds of devices and is not restricted to viologen ones. Raman spectroscopy is useful not only for small viologen organic molecule based devices, where only one chromic species shows color modulation, but also to characterize devices based on inorganic/organic compounds to develop an overall color modulation analysis. This is done because the resulting color sometimes can arise from the combination of two colors. Therefore, to investigate the connection between the absorbing color wavelength and changes in molecular properties (by changing the redox nature), Raman spectroscopy is an easy and powerful technique. Researchers have established numerous combinations of EC devices using both inorganic and organic materials, such as P3HT/EV, P3HT/TiO₂, Co₃O₄/EV, WO₃/NiO, PPY/WO₃, NiO/PANI, etc.,³⁸ to demonstrate various color combinations and to emphasize their EC performance. Recently, Kandpal et al. proposed a type of EC device combining polythiophene (P3HT) predoped with multiwalled carbon nanotubes (MWCNTs) and MoS₂ based ethyl viologen gel.³⁵ In situ bias dependent Raman spectroscopy was conducted to comprehend the operational mechanism of the diode like characteristics of the EC device.

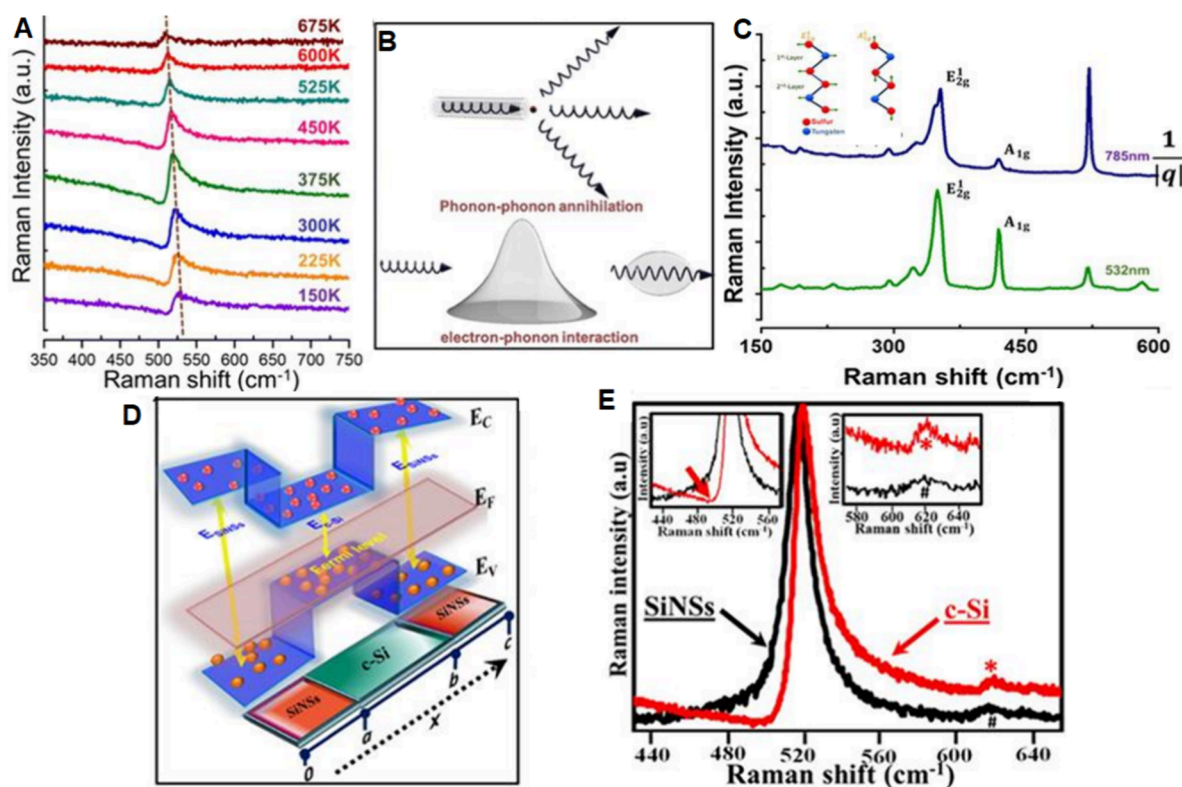


Figure 2. (A) Raman spectra of the heavily doped Si sample recorded under different temperature scales. (B) A schematic representation of possible pathways for the phonon decay in the system. Reproduced from ref 51 with permission from the PCCP Owner Societies. (C) Change in Raman spectra of WS₂ nanoflakes with different laser excitation. Reproduced with permission from ref 53. Copyright (2023) American Chemical Society. (D) Schematic illustration of the energy bands in the etched Si wafer and their relative Fermi energy levels. (E) Raman spectra from c-Si and Si NSs, showing the anti-resonance dip and signature of the boron dopant. Reproduced with permission from ref 54. Copyright (2020) American Chemical Society.

The study revealed the formation of (bi)polarons as a result of dynamic doping, ultimately leading to a color change. The device operates through the EC-enabled electrolyte medium, which provides the viologen molecule in the polymer matrix, as depicted in Figure 1B (right panel). In situ Raman spectroscopy was performed on the device under various bias conditions. The Raman spectrum of the as-fabricated device along with the ON and OFF state devices (Figure 1B, left panel) help in revealing that the formation of polaron and bipolarons as a result of the redox process is responsible for the color switching in the devices.³⁶ Here, again, Raman spectroscopy proved to be a great technique to understand this mechanism.

Smart devices, constructed from a combination of various material classes based on their individual electrical and optical properties, serve as effective electrodes in one combined geometrical device. Among their numerous applications, energy savings stand out as a common and currently in-demand feature from an industrial perspective. Such a device combination was fabricated using the inorganic material WO₃ and the conducting polymer P3HT, with the addition of a mobile Li-ion electrolyte medium (schematic in Figure 1C, left panel). Under the application of external biasing, dynamic doping of Li⁺ occurs at the electrode from the bulk of the electrolyte. As a result, the device exhibits its combined EC color in dual bands (magenta and blue), with their characteristic features easily measurable by optical spectroscopy and characterized by in situ Raman spectroscopy (Figure 1C, right panel). The bias induced Raman spectroscopy of the device in

cool and warm states helped in establishing the device operation mechanism of this energy saving device.

Furthermore, to monitor dynamic doping in solid-state EC devices, Raman mapping is an essential concept. Therefore, Chaudhary et al. mapped real-time color dynamics in polythiophene based solid-state EC devices to comprehend and validate the mechanism of bias induced redox-driven color switching. The schematic shows the device's top view along with its close-up section for Raman microscopy (Figure 1D, left panel). It shows E1 and E2 as gold film electrodes separated by ~10 μm on a Si/SiO₂ substrate along with the actual images in Figure 1D. Once a bias of 2 V is applied across the device, a noticeable change in color contrast between the electrodes is observed. Continuing with the aforementioned bias induced redox dynamic doping, applying a positive bias to the E1 electrode oxidizes P3HT, resulting in polaron formation, and consequently alters its optical properties. The same phenomenon occurs on the opposite electrode when the bias is reversed. The whole formation of the polaron as a result of dynamic doping and its distribution over the whole device can be mapped using Raman microscopy (Figure 1D, right panel). In this experiment, it could be established that Raman mapping proves to be an advantageous tool for identifying dynamic doping compared to traditional Raman spectroscopy, as it enables the visualization of bias induced polaron formation and dynamics.^{37,39,40}

2.2. Raman Spectroscopy to Inspect Microscopic Processes

Raman spectroscopy offers a quick and convenient way to examine the vibrational characteristics of crystalline and

amorphous semiconductors. As mentioned earlier, the physics of Raman scattering in semiconductor crystals relies on the inelastic interaction between incident photons and lattice vibrations, known as phonons, which are sensitive to internal or external disturbances. In bulk crystalline materials, Raman scattering is constrained to near-zone-centered phonons because of spectroscopic selection rules.^{41–45} However, in nanostructures, this selection rule relaxes, allowing phonons other than the zone-centered ones to contribute due to the phonon confinement within a crystallite of finite dimensions.^{46,47} Due to its immense application, significant research has been conducted on Si, and phenomena such as the Fano effect,^{48–50} harmonics behavior, and more have been identified, both with and without the influence of doping. This research has contributed to a deeper understanding of the behavior and properties of silicon based materials. Rani et al.⁵¹ elucidated that their study illustrates how thermal effects can be employed to explain wavelength dependent Fano interactions using Raman spectroscopy, which in principle is an excitation wavelength independent process.⁵² This approach aids in comprehending the dispersion of the Fano interaction and the bonding of Fano interferons across varying wavelengths. The Fano interaction in heavily doped p-type Si, excited by a 785 nm wavelength (Figure 2A), shows a distinct temperature profile. A systematic Raman analysis helped in discovering different temperature dependent phonon decay pathways, namely single phonon decay, multiple phonon decay, or phonon decay to Fano interferons, as illustrated schematically in Figure 2B.⁵¹

Similar to traditional semiconductors, Raman spectroscopy also can be used to investigate the Fano effect in 2D WS₂ nanosheets.⁵³ A typical asymmetric Raman line shape characteristic under red wavelength excitation was observed, giving a hint about the presence of the Fano effect. The Raman spectrum of WS₂ nanoflakes comprises two vibration modes, namely, E_{2g}¹ and A_{1g}¹, at 350 and 420 cm⁻¹, respectively (Figure 2C). The E_{2g}¹ Raman mode originates from the in-plane vibrations, where two sulfur atoms vibrate in one direction, and one tungsten (W) atom vibrates in the opposite direction. The E_{2g}¹ Raman mode (350 cm⁻¹) exhibits asymmetry with greater spectral line width on the lower-frequency side compared with the higher-energy side. In contrast, the A_{1g}¹ Raman mode (420 cm⁻¹) appears to be completely symmetric. The E_{2g}¹ Raman mode in the Raman spectra obtained by using a 785 nm excitation wavelength displays significant asymmetry. It is worth noting that the vibrations of the multilayered WS₂ sample are influenced by the excitation wavelength, leading to variations in the Raman spectra from multilayered to monolayer configurations.

Raman spectrum from crystalline Si is significantly different from its nanocrystalline counterpart, hence giving Raman the capability to distinguish between these two phases.⁵⁴ Apart from this, Raman spectroscopy can also probe other processes taking place at a subtler level, as can be seen using the following example. During the fabrication of porous Si using chemical etching techniques, variations in the concentration of doped elements was observed to occur, leading to changes in the net charge or modifications to the Fermi energy band near the edges and bulk of the nanowires.⁵⁴ Raman spectroscopy was used to identify the unintentional deviation of the Fermi level from its inherent position during the etching process (Figure 2D) as established by Tanwar et al. For this, Raman spectroscopy was utilized by comparing the Raman spectra

obtained from the Si NSs and c-Si (Figure 2E). These spectra reveal two distinct peaks: one near 520 cm⁻¹, representing the typical optical phonon mode, and the other near 620 cm⁻¹, corresponding to the presence of boron in the sample. Observing the low-intensity boron peak compared to that in the c-Si wafer directly indicates a relatively lower dopant concentration in the Si NSs. Other Fano resonance markers were also analyzed to establish the above-mentioned facts.

2.3. Raman Spectroscopy in Life Sciences

Raman spectroscopy has proven to be immensely valuable in the biological and medical fields due to its ability to provide detailed molecular information without the need for exogenous labels. It can identify specific biomolecules such as proteins, lipids, nucleic acids, and carbohydrates within biological samples and helps disease diagnosis by detecting subtle changes in molecular composition associated with various medical conditions. For example, Raman spectroscopy has been employed in the identification of cancerous tissues, distinguishing between healthy and diseased states based on unique spectral signatures. By capturing real-time molecular information, Raman spectroscopy aids in studying cellular dynamics and processes. It can also provide insights into cellular responses to stimuli such as drug treatments or environmental changes. In neuroscience, Raman spectroscopy has been employed to study brain tissues and to understand molecular changes associated with neurological disorders. It contributes to research on neurodegenerative diseases, providing valuable information about protein aggregation and structural alterations. Advancements in Raman spectroscopy techniques, such as surface-enhanced Raman scattering (SERS) and coherent anti-Stokes Raman scattering (CARS), have enabled in vivo imaging. This allows for real-time, noninvasive monitoring of biological processes, making it a promising tool for clinical applications.

Raman spectroscopy serves as a highly sensitive tool capable of capturing the distinctive bond vibrations of molecules. In clinical research, this technique is frequently paired with other experimental methods to integrate it and enhance its capabilities. Raman spectroscopic imaging is occasionally employed to spatially map the Raman signals within cells.⁵⁵ By utilization of automated translation stages, Raman spectra are gathered through the movement of the sample to reveal various locations. Additionally, confocal microscopy boasts impressive spatial resolution and signal quality; however, it proves to be a slow process for Raman imaging. This is because the sample must be scanned point by point, often requiring relatively long dwell times owing to the weak Raman signals, and therefore employing a high-quality imaging spectrometer enables the acquisition of spectra from all probed regions in a single measurement.⁵⁶ Additionally, it proves invaluable as a tool for studying virus entry and pathogen induced alterations within the host organism with remarkable efficiency. The mechanisms underlying Epstein–Barr virus (EBV) entry and the subsequent changes in the biochemistry of glial cells upon infection were not studied. Tiwari et al. detected biomolecular changes in human glial cells, specifically HMC-3 (microglia) and U-87 MG (astrocytes), at two distinct cellular locations (nucleus and periphery) using Raman spectroscopy following EBV infection at various time points.⁵⁷ The Raman signals originating from both the nucleus and periphery of the cell exhibited variations, suggesting distinct biochemistry and signaling processes implicated in the progression of infection

at these locations, as observed through *in vitro* Raman scattering analysis.⁵⁸ These changes in biomolecules also resulted in modifications of the associated signaling pathways (Figure 3). The temporal (infection progression over time)

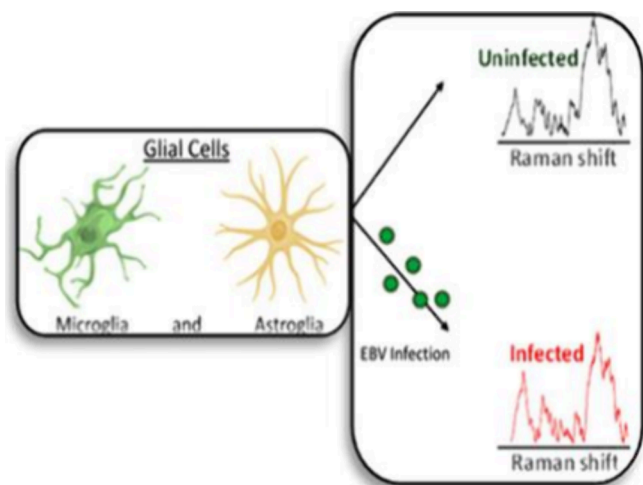


Figure 3. A schematic illustration of glial cells and their temporal *in vitro* Raman spectra measured under EBV infection. Reproduced with permission from ref 57. Copyright (2021) American Chemical Society.

and spatial (infection conditions at different cell locations) Raman analysis offers a comprehensive investigation into the dynamics of EBV infection. A comparison between the pre- and postinfection Raman spectra may enable one to identify the detection of infection as well as in many cases to diagnose and stage the malignancies in various cells. As a result of infection of any other cellular level perturbation, the Raman line shape can manifest through only limited parameters like peak position, width, intensity, and symmetry. On the other hand, the reasons to assign changes in these parameters are plenty, which makes it difficult to exclusively assign the exact reason for changes in these parameters. Even though it can be done in principle, there lies some ambiguity in exact diagnosis of diseases using Raman spectroscopy along with instrumentation related constraints.

Raman spectroscopy, renowned for its remarkable sensitivity to molecular packing, including subtle structural variations such as bond length, dihedral angles, and hydrogen bonding patterns, proves to be an invaluable tool for characterization in the pharmaceutical field.⁵⁹ In addition, *in situ* Raman spectroscopy finds applications in studying crystal nucleation processes, such as those observed in glycine, with the objective of elucidating the nature of intermediate clusters and their evolution into the definitive crystalline structure. In a study, Wang et al.⁶⁰ has demonstrated that micro-Raman spectroscopy, even without the use of optical trapping, can offer crucial insights into molecular rearrangements occurring during the transition from liquid to solid states while also providing valuable information on crystal growth. To identify the molecular arrangement associated with nucleation or crystal growth, the same measurements were repeated by the same research group at the center of the droplet, where nucleation is less likely to occur, and the Raman spectrum of the CH region over time was recorded.⁶¹ The changes in fwhm and peak position of $\nu_s(\text{CH})$ and $\nu_{as}(\text{CH})$ corresponding to 2971 and

3007 cm^{-1} , respectively, indicated that α -glycine is forming,⁶² which is in agreement with the results obtained from crystallization of H_2O at the edge region of the droplet. This leads to the crystal growth through a nucleation process rather than molecular rearrangements.

Various spectroscopic and scattering methods have been applied to examine how solute molecules interact in solution both broadly and specifically during nucleation. While these methods have achieved some success, they struggled to offer detailed molecular-level insights into the supersaturated state preceding nucleation. A nonresonant X-ray scattering approach, i.e., X-ray Raman scattering (XRS), provides an alternative way for probing the unoccupied valence density of states. The XRS probes not only dipole transitions but also higher-order transitions, which depend on the momentum transfer engagement. This dependence is associated with the angle between the incident beam and the detection angle of the scattered photon, making this technique bulk-sensitive. Additionally, XRS offers the added benefit of self-absorption corrections to spectra distortions. Therefore, this technique is used to study the molecular structure in the bulk of liquid water and aqueous solutions.⁶³ It is obviously more useful for exploring the effect of isotope substitution on local structure.⁶⁴ Al-Madhagi et al. proposed that XRS of the C and N K-edge spectra was employed to track the structural changes of aqueous imidazole in real time during cooling crystallization.⁶⁵ The comparison of the C and N K-edge XRS spectra of imidazole in solution and in the solid phase highlighted the near-edges' sensitivity to alterations in the local bonding of the imidazole molecules.

Having achieved significant success in Raman spectroscopy since its discovery is a significant milestone for the scientific community at this point. However, it would be unfair to overlook the limitations of Raman spectroscopy and the challenges associated with troubleshooting the Raman spectrometer and analyzing data with precision. Given the rapid pace of advancements and innovations in science and technology today, it is essential to integrate any necessary improvements or advancements into Raman spectrometry for future development.

3. FUTURE PROSPECTS OF RAMAN SPECTROSCOPY IN PHYSICAL CHEMISTRY

As discussed above and looking at the growth of Raman mostly in the last 50 years after the invention of a laser, Raman spectroscopy has become a very powerful technique in almost all the areas of science and has become the first choice of scientists when it comes to probing subtler dimensions of physics without perturbing the system. There has been exponential advancement in Raman spectroscopy over time due to constant technological developments related to sources (lasers), detectors (CCD), interfacing (software), etc. There exists a lot of scope to make this technique more advanced, making it a universal technique not only in research but also in our daily life. There are some potential directions and advancements for the future of Raman spectroscopy in which we can work:

1. Portable and point-of-care (POC) devices: Portable and POC Raman spectroscopy devices hold great promise for enabling real-time, on-site analysis in various fields, revolutionizing the way samples are analyzed and monitored outside traditional laboratory settings and

facilitating rapid decision-making and problem-solving in diverse applications. Therefore, in order to make Raman spectroscopy a more accessible analytical tool, it is important to make it a hand-held technique. Portable and POC Raman spectroscopy devices are becoming increasingly significant due to their potential to provide rapid, on-site analysis in various fields including healthcare, pharmaceuticals, food safety, environmental monitoring, and security. As of now it appears that this is possible in areas where spectral resolution is of less importance, otherwise high-resolution Raman spectrometers need to be designed with small sizes.

- Artificial intelligence (AI) and machine learning (ML) compatibility: Data analysis commonly utilizes artificial intelligence (AI) techniques to automate the process of analyzing data. In the realm of data science, AI refers to the utilization of a computational system that employs a meticulously crafted mathematical model, often coded directly by the user by the capability of machine learning (ML). In the 1990s, it was recognized that machine learning methods could effectively distinguish between spectra of various molecules.⁶⁶ In the field of analytical sciences, ML/AI offers an unparalleled opportunity to extract insights from complex or large data sets in chromatography, mass spectrometry, NMR, spectroscopy, and other related areas. Among them, Raman spectra has a lot of information about the sample, but it is difficult to extract all the information manually from the data. Therefore, if by advanced data analysis techniques, including chemometric techniques, AI and ML algorithms can be added to the interpretation of the Raman spectra, then it will be easy to get all the meaningful information about the sample. The addition of these techniques can improve spectral interpretation and enable automated classification and identification of samples. The best utilization of AI/ML in Raman techniques will extend its reach to non- and semitechnical users as it will remove the tedious job of Raman data interpretation. Another technique related to Raman spectroscopy is SERS, which involves acquiring vibrational spectra of intricate chemical mixtures as extensive data sets for the analysis or imaging of chemical systems.
- Materials and instrumentation innovation: Ongoing research in materials science and engineering leads to the development of novel Raman-active materials, substrates, and optical components with improved properties, as well as innovative Raman spectroscopy instrumentation with enhanced performance, stability, and versatility. Apart from this, the integration of additional analytical techniques or detection modalities, such as fluorescence spectroscopy, near-infrared spectroscopy, and SERS, into portable Raman devices expands their analytical capabilities and enables more comprehensive sample analysis. As part of instrumentation innovation, numerous supervised learning algorithms could be utilized in Raman spectrometer data analysis programs to conduct real-time analysis of spectra, which can be separated into distinct submethods such as methods based on discriminate analysis, or discriminant function analysis, artificial neural network based models or support vector machines, regression analysis like multiple linear regression based models, and evolutionary based algorithms such as genetic algo-

gorithms, genetic programming and computing, evolutionary algorithms, and evolutionary programming in new functional materials.^{67,68}

4. SUMMARY

Raman spectroscopy is one of the most sensitive techniques that is now used in all areas of research. Raman based techniques are not limited to basic sciences, but they are now popular in all branches of engineering such as civil (to check the quality of bricks), mechanical, electrical engineering, etc. In the last few decades, the use of Raman spectroscopy widely increased in the area of biology because of its insensitivity toward water, and the most important advantage of Raman spectroscopy is that it does not damage cells, which is the first requirement in the biological area. Therefore, considering the growth, usage, and benefits of Raman spectroscopy, it is required to make some advancements in this technique, which will be helpful in research. Utilizing the potentials of AI and ML in data interpretation can bring a revolution in this research area as only from one technique can all the information be obtained. The future of Raman spectroscopy appears promising, with continued advancements driving its widespread adoption across various scientific disciplines and applications as well as opening up new possibilities for scientific discovery, technological innovation, and societal impact to assist the overall development of physical chemistry and chemical physics.

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Notes

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