Appendix

A

**Aberration**  Aberration is a deviation from the normal.

**Amorphization**  It is the process of transforming a metallic or nonmetallic material from the crystalline state into the amorphous or glassy state.

**Anharmonicity**  Anharmonicity is the deviation of a system from being in a simple harmonic motion.

**Anharmonicity effects in nanocrystals**  Materials’ properties, especially the physical properties, are dependent on temperature. A change in the lattice parameters of crystalline materials is expected when population of the different levels for each normal mode is influenced by variation in temperatures. Therefore, any change of the lattice parameters with temperature is attributed to the anharmonicity of the lattice potential. Raman spectroscopy is a great tool to investigate these effects. The Raman spectra of various nanocrystals as well as other amorphous or crystalline materials show changes in line position and bandwidth with temperature. These changes manifest in shift of line position and a change in line width and intensity.

**Anisotropy**  While isotropy is homogeneity of a property (absorbance, refractive index, density, etc.) in all directions, anisotropy is the property of being directionally dependent.

**Anti-Stokes**  The atoms or molecules in excited state show special lines called anti-Stokes in the Raman spectra.

B

**Backscattering**  In physics, backscatter (or backscattering) is the reflection of waves, particles, or signals back to the direction they came from. It is a diffuse reflection due to scattering, as opposed to specular reflection like a mirror. Backscattering has important applications in astronomy, photography, and medical ultrasonography.

**Bimetallic nanomaterials**  Currently used monometallic SERS tags such as gold and silver NPs have a main drawback in that the metal surface is unprotected. The assays are therefore unreliable as components of the analyte can adsorb on the metal surface, leading to the possibility of replacing the label species. One way to overcome this problem is to encapsulate the metal particle/label molecule in a protective shell. Bimetallic nanostructures, with two different metals in a single particle, such as core-shell-type nanomaterials are gaining importance as Raman tags [1].
Bioanalysis Surface-enhanced Raman scattering (SERS) is seen in molecules that are in close proximity to nanostructured metal surfaces, primarily silver and gold, that are capable of supporting plasmon resonances in the visible spectral region where Raman scattering is excited. The phenomenon provides the basis for a powerful analytical technique offering both quantitative and qualitative molecular information about biological molecules. In contrast to IR spectroscopy, the Raman scattering cross section of water molecules is small, allowing vibrational information to be obtained from biological molecules in their native aqueous environment and their efficient detection and discrimination from the background. Low detection limits, narrow spectral bandwidths, the ability to quench fluorescence, and the capacity to be used with or without optical labels make SERS a good choice for DNA or RNA analysis, genetics and proteomics, medical diagnostics, and the detection of chemical warfare agents.

Biosensor SERS possesses many desirable characteristics as a tool for biosensing with high specificity, attomole to high zeptomole mass sensitivity, and to picomolar concentration sensitivity. Recently, SERS has been used in the quantitative detection and analysis of bio-related molecules [2].

Blackbody radiation Blackbody radiation, coming from all objects simply because of their temperature is greater than absolute zero, is a potential source of spectrally broad background signal.

C Cancer diagnosis Now it is well established that Raman spectroscopy has great potential in detection of tissue abnormalities and therefore is a promising new tool for noninvasive cancer diagnosis. Raman spectroscopy offers detailed information about tissue biochemistry (including conformations and concentrations of constituents). It particularly provides molecular specific information about tissues, which is necessary for cancer diagnosis. Surface-enhanced Raman spectroscopy (SERS) is an excellent technique that can detect molecular signatures in trace amounts. Similarly, near-infrared (NIR) dispersive Raman spectroscopy, in which NIR excitation minimizes fluorescence and absorption by tissue, has also proved to be a sensitive technique. Raman spectroscopy is particularly suited for diagnosing cancer because of its sensitivity in detecting small molecular changes that are associated with cancer, such as an increased nucleus-to-cytoplasm ratio, disordered chromatin, higher metabolic activity, and changes in lipid and protein levels. Thus, many researchers have applied NIR Raman spectroscopy in vitro, ex vivo, as well as in vivo for the diagnosis of cancer with varying degrees of success [4].

Cell-based biosensors Sensing of toxic chemicals and biological toxins at relevant concentrations and in real time is the need of the day. Using living cells as the sensor elements offers a key advantage that they are not engineered to respond specifically to a single toxic agent but are free to react to many biologically active compounds. Of the many techniques to develop cell-based sensors, which can measure changes in cell behavior such as, cell-cell and cell-substrate contact, metabolism, or induction of cell death following exposure of
cells to toxic agents, optical method offers a significant advantage as it is a noninvasive tool. This is truer in the case of Raman spectroscopy as it has already been well established as a powerful analytical technique that can provide useful biochemical information regarding live cells, which can be related to the interaction with toxic agents or drugs, disease, cell death, and differentiation. Several different variants of Raman spectroscopy such as resonant Raman (RS) spectroscopy, surface-enhanced Raman spectroscopy (SERS), and coherent anti-Stokes Raman spectroscopy (CARS), in addition to conventional nonresonant Raman spectroscopy have been used for studying live cells and for developing sensors and biosensors. Of these, conventional nonresonant Raman spectroscopy has a great potential for interrogation of cells. Since different toxic chemicals have different effects on living cells and induce specific time-dependent biochemical changes related to cell death mechanisms, one can obtain comprehensive information of the overall biochemical composition of the cell using the Raman spectrum. It is expected that different toxic agents that initiate different cellular responses and biochemical changes should produce distinct changes in the Raman spectra. In addition, time-resolved Raman spectroscopy of living cells under real-time conditions can be obtained noninvasively. The information obtained will be purely based on intrinsic molecular composition of the cell without any alterations due to the use of labels or other contrast agents as is the case in other types of cell biosensors. The detection of time-dependent biochemical changes of cells has the potential to provide the additional level of information needed for quantification and discrimination of a wider range of toxic agents.

**Cellular imaging** Raman spectroscopy can be used for imaging of cells at the resolution of conventional microscopy based on the spectral signatures of cell’s components; Raman imaging of cellular organelles such as nucleus, chromatin, mitochondria or lipid bodies has been demonstrated. Particularly advantageous is the possibility to obtain the associated chemical information noninvasively. Raman imaging is also proving to be a useful tool to image uptake and distribution patterns of several drug delivery carriers and nanoparticle-based drug delivery systems.

**Charge-transfer resonance Raman (CT-RR) scattering** There is a chemical enhancement (CE) because of an increase in the static polarizability of a molecule due to adsorption on the metal and light-induced charge transfer between the molecule and the metal surface resulting in enhancement in the Raman cross section similar to molecular resonance Raman scattering. This effect is sometimes called charge-transfer resonance Raman (CT-RR) scattering.

**Chemical enhancement (CE)** The interaction of molecules with metallic surfaces may be behind an additional increase in the Raman scattering and this is called chemical enhancement (CE).

**Coherent anti-Stokes Raman spectroscopy (CARS)** Unlike spontaneous Raman emission, the magnitude of signal in CARS is number of orders stronger as multiple photons are employed to address the molecular vibrations, resulting in production of a signal in which the emitted waves are coherent with one
another. In this technique, which is a third-order nonlinear optical process, at least two different laser beams interact with the sample and generate a coherent optical signal at the anti-Stokes frequency. The Raman signal relies on a spontaneous transition, competes with other fluorescent processes and is detected on the red side of the incoming radiation. On the other hand, CARS signal relies on a coherently driven transition and is detected on the blue side, which is free from fluorescence. However, it comes with a nonresonant contribution.

**Coherent Raman spectroscopic imaging**  Coherent anti-Stokes Raman scattering (CARS) microscopy/microspectroscopy has become a powerful technique for three-dimensional vibrational imaging of chemical and biological systems. Recently, significant progress has been made in multiplex CARS micro-spectroscopy where a CARS spectrum covering $3,500 \text{ cm}^{-1}$ region was obtainable with the use of a white light laser source.

**Coherent Raman spectroscopy**  Coherent Raman spectroscopy is a term that refers to a series of closely related nonlinear Raman techniques in which the scattered Raman radiation emerges from the sample as a coherent beam – coherent meaning that the photons are all in phase with one another. The coherent techniques include Stimulated Raman Scattering (SRS), Coherent anti-Stokes Raman Spectroscopy (CARS), Coharent Stokes Raman Spectroscopy (CSRS), and Stimulated Raman Gain Spectroscopy (SRGS). Although most of the nonlinear Raman techniques are also coherent techniques, there is one incoherent nonlinear Raman process called Hyper Raman.

**Confocal microscopy**  It is an optical imaging technique to increase optical resolution and contrast. While in a conventional microscope, the entire specimen is flooded evenly in light from a light source resulting in detection of a large unfocused background part, the confocal microscope uses point illumination and a pinhole in an optically conjugate plane in front of the detector to eliminate out-of-focus signal – the name “confocal” stems from this configuration.

**D**

**Dark-field resonant Rayleigh scattering spectroscopy and imaging**  One approach to obtain excellent signal-to-noise ratio for both imaging and spectroscopy is by utilizing a dark field configuration. In this, a sample is obliquely illuminated through a dark-field condenser that partially blocks the incident light thereby resulting in the scattered light to be collected while providing a dark background. With this low background, it is now possible to carry out spectroscopy on a single nanoparticle or a nanostructure with the ability to make non-ensemble measurements so that individual LSPR spectra can be correlated either with nanostructure topography or surface-enhanced spectroscopic intensity depending on the secondary measurement method used.

**Dark-field spectroscopy (DFS)**  Dark-field spectroscopy, also known as resonant Rayleigh scattering spectroscopy (RRSS), is a technique that correlates the LSPR of single nanoparticles to enhancements in fluorescence and Raman scattering.
Deep-UV tip-enhanced Raman scattering  In order to analyze molecules using Raman spectroscopy with a nanoscale resolution beyond the diffraction limit, the technique of choice is tip-enhanced Raman spectroscopy (TERS). It has been successfully applied in the field of nanoscience and nanotechnology for the analysis and imaging of carbon nanotubes, organic dye molecules, DNA bases, various cellular components, and so on. In this technique, the localized surface plasmon resonance (LSPR) supported by a sharp metallic tip provides a strong and highly confined electromagnetic field at the tip apex, which is used to locally excite and enhance the Raman scattering of molecules under investigation. In TERS, the metal tips (e.g., in gold and silver) have an optical property that has negative real and minimal imaginary part in the dielectric function at the excitation wavelength. On the other hand, for deep ultraviolet (DUV) wavelengths there are some metal tips such as aluminum that show dielectric function with small imaginary part and negative real part. Therefore, the technique that utilizes tip-enhancement in the DUV region is called deep-UV tip-enhanced Raman scattering. This technique is proving to be an excellent one for imaging of proteins and nucleic acids as they exhibit electronic resonance in the DUV region. It is to be anticipated that DUV resonance Raman scattering technique along with the tip-enhancement technique will be invaluable for gathering information in the nanoscale for a number of biomedical applications [5].

Degenerate four-wave mixing (DFWM)  Degenerate four-wave mixing (DFWM) is another well-known nonlinear technique based on third-order nonlinear susceptibility similar to CARS

Density of states (DOS)  In statistical and condensed matter physics, the density of states (DOS) of a system is used to describe the number of states at each energy level that are available to be occupied. A high DOS at a specific energy level means that there are many states available for occupation. A DOS of zero means that no states can be occupied at that energy level.

Dispersive Raman spectroscopy  This spectroscopy technique uses grating and/or prism dispersing elements.

Double-resonant Raman scattering  In a double-resonant process, different wave vectors of phonons corresponding to different incident phonon energies scatter the excited electron across the band minimum. For phonons with dispersion, the different $k$-vectors correspond to different phonon energies, and hence the excitation-energy dependence of the phonon peak follows naturally. In order to fulfill momentum conservation (both incident and scattered photon momentums are very small), the electron has to be scattered back near to where it was excited. This process is usually ascribed to an elastically scattering defect ($D$-mode and high-energy mode) or a second phonon (second order mode scattering). Of course, in a full calculation of the Raman intensity in double resonance the single resonant process (only the photon is resonant) is automatically included; however, its contribution to the total signal is small. The process is shown schematically in Fig. 1. On the left, one can see double-resonant process for a metallic carbon nanotube with different incident phonon energies implying different phonon wave vectors in the double resonance. On the right, different
scattering vectors corresponding to different phonon frequencies are shown. One very well established process for describing a number of features of the Raman spectra of $sp^2$-bonded carbon compounds such as graphite or carbon nanotubes is the double-resonant Raman scattering [6].

E
ESM The elastic sphere model [7].

F
Far-from-resonance (FFR) limit The Raman scattering gets simplified dramatically where the exciting laser radiation is far from the lowest allowed excited electronic state of a molecule and this is called as Far-from-resonance (FFR) limit in Raman Spectroscopy. In this limit, the interaction of light with molecules is approximately same for both incident and scattered radiation.

Femtosecond stimulated Raman spectroscopy Femtosecond stimulated Raman spectroscopy (FSRS) is a tool for investigating real-time structural measurements of a chemical change through recording of vibrational structural information with high temporal (50-fs) and spectral (10-cm$^{-1}$) resolution. It, therefore, enables studies of chemical and biochemical reaction dynamics, giving previously unattainable insight into the structural dynamics of reactively evolving systems. In FSRS, the simultaneous interaction of a narrow-bandwidth picosecond Raman pulse and a broadband, femtosecond continuum probe pulse leads to the appearance of sharp vibrational gain features on top of the probe envelope [8]. Figure 2 shows a schematic of broadband vibrational probing employed in femtosecond stimulated Raman spectroscopy. In this figure, the Raman pulse is a narrow-bandwidth, picosecond pulse (green), whereas the probe is a broadband femtosecond continuum pulse (purple). When both pulses are overlapped spatially and temporally in a Raman-active medium, photons are transferred from the high-intensity Raman pulse to the weak probe pulse at the vibrational resonances of a sample. A typical spectrum obtained in a single laser shot for cyclohexane is depicted in Fig. 2. Division of probe spectra obtained in the presence (black) and absence (purple) of the Raman pulse produces a vibrational spectrum in the expanded trace (blue). Conceptually it is similar to femtosecond
dynamic electronic absorption spectroscopy where similar disentanglement of
time and energy resolution is exploited. However, the difference is that FSRS
drives vibrational rather than electronic coherence. Because vibrational
dephasing times are much longer (up to picoseconds) than their electronic
counterparts (<50 fs), the corresponding energy resolution is excellent
(<10 cm\(^{-1}\)) [8].

**FRET: Förster resonance energy transfer** Förster resonance energy transfer,
named after German scientist Theodor Förster, is also known as fluorescence
resonance energy transfer, resonance energy transfer (RET), or electronic energy
transfer (EET). It is a process that describes energy transfer through nonradiative
dipole–dipole coupling between two chromophores: a donor chromophore and
an acceptor chromophore. When both chromophores are fluorescent, the term
“fluorescence resonance energy transfer” is often used in scientific literature.

**H**

**Hyper Raman** Hyper Raman is a nonlinear effect in which the vibrational modes
interact with the second harmonic of the excitation beam, thereby, allowing
observation of vibrational modes that are normally “silent.” It frequently relies
on SERS-type enhancement to boost the sensitivity.

**I**

**Impulsive stimulated Raman scattering (ISRS)** Impulsive stimulated Raman
scattering (ISRS) is the creation of coherent ground-state nuclear motion through
an impulsive force caused by the interaction of a Raman-active medium with an
ultrashort light pulse.

**Interferometric Raman spectroscopy** Interferometric Raman Spectroscopy is a
measurement technique that utilizes time-domain or space-domain measure-
ments of electromagnetic radiation or other type of radiation for collecting
Raman spectra based on the coherence of a radiative source. An example is a
Fourier transform (FT) Raman spectrometer.
Inverse Raman scattering  Inverse Raman scattering (IRS) is a coherent process involving stimulated loss at an anti-Stokes-shifted frequency. The term inverse Raman refers to the fact that, at resonance, the probe radiation is attenuated. In spontaneous Raman spectroscopy, on the other hand radiation at Raman-active frequencies would be generated in the course of the experiment. Inverse Raman scattering (IRS) and stimulated Raman gain (SRG) are closely related. While one involves stimulated gain at an anti-Stokes-shifted frequency, the other involves stimulated loss at a Stokes-shifted frequency.

Inverse Raman spectroscopy  The Inverse Raman effect is a form of Raman scattering, first noted by W.J. Jones and B.P. Stoicheff, wherein stokes scattering can exceed anti-Stokes scattering resulting in an absorption line (a dip in intensity) at the sum of irradiated monochromatic light and Raman frequency of the material. This phenomenon is referred to as the inverse Raman Effect, application of the phenomenon is referred to as inverse Raman spectroscopy, and a record of the continuum is referred to as an inverse Raman spectrum.

Inverse spatially offset Raman spectroscopy (SORS)  Inverse SORS is a useful sub-variant of SORS that improves certain measurements such as analysis of tissue in vivo. Rather than use spot collection geometry and a circular spot for illumination, the constant offset can be maintained by illuminating the sample with a ring of light centered on the collection region. This has several advantages, including lowering the total power density and allowing simple manipulation of offset distance.

L
Lattice vibrations (Phonons)  The vibrations of a crystal are classically described in terms of collective motions in the form of waves called lattice vibrations.

Localized surface plasmon (LSP)  The surface plasmon (SP) cannot propagate on the surface of metallic nanoparticles and therefore, is localized and hence known as “localized surface plasmon (LSP).” The LSP resonance of gold and silver NPs occurs in the visible range of the spectrum, which makes these two metals particularly useful for a number of applications ranging from ultrasensitive diagnostic tools to biosensing devices.

M
Michelson interferometer  The Michelson interferometer was invented by Albert Abraham Michelson. It is the most common configuration for optical interferometry in which an interference pattern is produced by splitting a beam of light into two paths, bouncing the beams back and recombining them. It is possible that different paths may be of different lengths or be composed of different materials to create alternating interference fringes on a back detector.

Microspectroscopy  Raman spectroscopy is a scattering technique and hence specimens do not need to be fixed or sectioned resulting in collecting spectra from a very small volume (<1 μm in diameter) leading to identification of species present in that volume. Raman spectroscopy, therefore, offers several advantages for microscopic analysis, particularly, suitable for microscopic
examination of minerals, materials such as polymers and ceramics, cells, and proteins. There are a number of approaches for Raman microspectroscopy. For example, it is possible to record the distribution of a molecule within a cell by selecting a wavenumber characteristic for that molecule from the scattering over a small range of wavenumbers (Raman shifts). This is called as direct imaging. In hyperspectral imaging or chemical imaging, one could see the distribution of any biomolecule ignoring the presence of water, culture media, buffers, and others that may interfere. Particularly, Raman confocal microscopy has a very high spatial resolution with the lateral and depth resolutions around 250 nm and 1.7 \mu m, respectively. It is also possible to obtain in vivo time- and space-resolved Raman spectra of microscopic regions of samples such as proteins, cells and organs. In addition, it has also been used in microscopic examination of inorganic specimens, such as rocks and ceramics and polymers.

**Multiplexing** Multiplexing is the ability to send multiple signals at the same time using a single carrier in the form of a single complex signal and then recovering the separate signals at the receiving end.

N  

**Nanoparticle-enhanced backscattering Raman imaging**

**Nanotags – Raman spectroscopy** Surface-enhanced Raman spectroscopy (SERS) is gaining in its popularity due to several unique advantages. However, current bottleneck in its utility is the lack of signal reproducibility due to variation in nanoparticle size and shape or aggregation and quantification. Overcoming this is especially important in the case of in vitro or in vivo imaging applications. While aggregation substantially enhances SERS, it is undesirable from an imaging or sensing application standpoint of view since aggregation cannot be controlled and hence results in SERS signal fluctuation. An alternate approach is to encapsulate organic dyes as signature reporter dyes between metallic nanoparticles and a layer of silica or polyethylene glycol (PEG) which prevents agglomeration of the nanoparticles. These are called nanotags, each with a unique Raman spectrum (color). They can be utilized as beacons for imaging with target ligands attached to the PEG or silica surface with well-established bioconjugation chemistries [9].

**Near-infrared surface-enhanced Raman spectroscopy** Some of the major irritants in Raman measurements are sample fluorescence and photochemistry. However, with the help of Fourier transform (FT) Raman instruments, near-infrared (near-IR) Raman spectroscopy has become an excellent technique for eliminating sample fluorescence and photochemistry in Raman measurements. As demonstrated recently, the range of near-IR Raman techniques can be extended to include near-IR SERS. Near-IR SERS reduces the magnitude of the fluorescence problem because near-IR excitation eliminates most sources of luminescence. Potential applications of near-IR SERS are in environmental monitoring and ultrasensitive detection of highly luminescent molecules [11].

**Nonlinear Raman spectroscopy** The nonlinear techniques include stimulated Raman scattering (SRS), hyper Raman, stimulated Raman gain (SRG), inverse...
Raman scattering (IRS), coherent anti-Stokes Raman spectroscopy (CARS), and coherent Stokes Raman spectroscopy (CSRS). Figure 3 shows Quantum diagrams of the nonlinear Raman processes, with spontaneous Raman included as a reference [10]. The Levels shown are virtual states (——) and ground and excited vibrational levels (-) in the ground electronic state of a molecule. Ground vibrational levels are marked “G.” For each Raman process shown, arrows entering at left are incident photons, up arrows represent photon absorption, down arrows represent photon generation, and arrows at right are output photons. Note the conservation in the number of photons created and lost in each process (each photon is represented as an arrow); vI = laser frequency, $\omega_s$ = Stokes frequency, $\omega_Y$ = anti-Stokes frequency, $\omega_v$ = vibrational frequency.

Nyquist frequency The Nyquist frequency is also sometimes known as the folding frequency of a sampling system. Originally discovered by the Swedish-American engineer Harry Nyquist, it is defined as half the sampling frequency of a discrete signal processing system.

P

Partial least squares (PLS) Partial Least Squares (PLS) is a chemometric technique that enables identification and utilization of the regions of complex overlapping Raman spectra.

Photoacoustic Raman spectroscopy (PARS) Photoacoustic Raman spectroscopy (PARS) is again a nonlinear spectroscopic technique. In this technique, selective population of a given energy state of a system (transitions must involve change in polarizability) is amplified using coherent Raman amplification (also known as stimulated Raman scattering). In this process, it is also important that the frequency difference of the two incident laser beams must be adjusted to equal the frequency of Raman-active transition.

Polarizability Polarizability is defined as the measure of the ability to move the electron cloud in a chemical bond using an external electric field. Since electron cloud in a chemical bond changes with the change in the position of atoms held together by the bond, measurement of polarizability, especially the polarization of Raman scattered light, is important. For a particular molecular vibration, it will be in the same direction as the changing polarizability of the electron cloud.

Polarized analysis There is useful spectral information arising from the analysis of polarization of Raman scattered light. This, typically called as polarized analysis, provides an insight into molecular orientation, molecular shape, and vibrational symmetry. One can also calculate the depolarization ratio. Overall, this technique enables correlation between group theory, symmetry, Raman activity, and peaks in the corresponding Raman spectra. It has been applied successful for solving problems in synthetic chemistry; understanding macromolecular orientation in crystal lattices, liquid crystals or polymer samples and in polymorph analysis.

Polarized Raman spectroscopy Polarized Raman spectroscopy is utilized to investigate molecular orientation and has special significance in the study of polymer systems.
Fig. 3  Quantum diagrams of different nonlinear Raman processes [10]
PRET: Plasmon resonance energy transfer  Similar to SERS, plasmon resonance energy transfer (PRET) between biomolecules and the plasmonic nanoparticles that they are adsorbed to allows for detection of biomolecules without appending a fluorophore. This approach yields a considerably higher sensitivity than previously known techniques in addition to spatial resolution amenable for in vivo assays.

Q
Quantitative Raman analysis  The intensity of Raman band of an analyte is linearly proportional to the analyte concentration. A plot of analyte band area (integrated intensity) vs. analyte concentration is used to create an equation that predicts analyte concentration from Raman band area. This is an example of quantitative Raman analysis.

R
Raman effect  The change in the wavelength of light that occurs when a light beam is deflected by molecules is called Raman Effect. When a beam of light traverses dust-free through a transparent sample of a chemical compound, a small fraction of the light emerges in directions other than that of the incident (incoming) beam. Most of this scattered light is of unchanged wavelength. A small part, however, has wavelengths different from that of the incident light; its presence is a result of the Raman Effect. The phenomenon, discovered in 1929 by Chandrasekhar Venkata Raman, was named after the discoverer.

Raman intensity invariants  Rayleigh scattering is an elastic scattering of light or other electromagnetic radiation by particles much smaller than the wavelength of the light, which may be individual atoms or molecules. Named after the British physicist Lord Rayleigh, it can occur when light travels in transparent solids and liquids, but is most prominently seen in gases. It is a function of the electric polarizability of the particles.

Raman near-field scanning optical microscopy (RNSOM)  Tip-enhanced Raman spectroscopy (TERS) came originally as an implementation of Raman near-field scanning optical microscopy (RNSOM). In RNSOM, the optical field is confined to a small aperture at the tip of a metal-coated optical fiber brought extremely close to the sample. This allowed overcoming resolution-limiting diffraction phenomena but only a faint signal could be collected owing to the fiber cutoff. In TERS, the optical fiber is replaced with an apertureless metallic tip, which favors surface enhancement of the Raman signal (the so-called SERS effect).

Raman optical activity (ROA)  Due to molecular chirality there is a difference in the intensity of Raman scattered right and left circularly polarized light. Raman optical activity (ROA) is a vibrational spectroscopic technique that is reliant on this difference and the spectrum of intensity differences recorded over a range of wavenumbers reveals information about chiral centers within a sample molecule. It is a useful probe to study biomolecular structures and their behavior in aqueous solution especially those of proteins, nucleic acids, carbohydrates, and viruses. The information obtained is in realistic conditions
complementing the data from crystallographic approaches in static conditions. Depending on the polarization of the incident and the scattered light, ROA can be observed in a number of forms. When the incident light is linearly polarized and the differences in circular polarization of the scattered light are measured, it is called as the scattered circular polarization (SCP). However, when both the incident and the scattered light are circularly polarized, either in phase (DCPI) or out of phase (DCPII), it is called the dual circular polarization (DCP).

**Raman tensors** The Raman scattering of a molecule is generated by the interaction of its electrons with an incident light. The electric vector of the scattered light is related to the electric vector of the incident light through a characteristic Raman tensor. A unique Raman tensor exists for each Raman-active molecular vibrational mode [12].

**Raman-induced Kerr effect spectroscopy (RIKES)** There is an intensity-dependent birefringence induced in a material through its interaction with applied laser fields. This effect is called as the Raman-induced Kerr effect (RIKE). Generally, a media containing ellipsoidal molecules which are free to reorient themselves under the influence of an external electric field show a large optical Kerr effect. The field tends to orient the molecules so that their polarizabilities are largest in the direction of the field. RIKES offers a relatively easy method for suppressing the nonlinear background signal when there are several Raman modes in addition to a nonresonant Kerr susceptibility [13].

**Scattering** The scattering of light is defined as the redirection of light that takes place when an incident light encounters a scattering material. The light can be an electromagnetic (EM) wave. When the light or EM wave interacts with molecules, it results in perturbation of the electron cloud leading to a periodic separation of charge within the molecules, which is called an induced dipole moment. The oscillating induced dipole moment manifests as a source of EM radiation, thereby, resulting in scattered light. The scattering is of two types: elastic and inelastic. In elastic scattering, majority of the light scattered is emitted at the identical frequency of the incident light. However, in inelastic scattering, additional light is scattered at different frequencies and Raman scattering is one such example of inelastic scattering. If the scattered frequency corresponds to the incident frequency, it is elastic scattering (e.g., Mie or Rayleigh). If the frequencies are shifted to lower or higher frequencies, these are therefore inelastic processes with the down-shifted frequency (longer wavelength) referred to as Stokes scattering, and the up-shifted frequency (shorter wavelength) referred to as anti-Stokes scattering.

**Scattering cross section** The scattering cross section, $\sigma_{\text{scat}}$, is a hypothetical area which describes the likelihood of light (or other radiation) being scattered by a particle. In general, the scattering cross section is different from the geometrical cross section of a particle, and it depends on the wavelength of the light and the permittivity, shape, and size of the particle. The total amount of scattering in
a sparse medium is determined by the product of scattering cross section and the number of particles present.

**Shell-isolated nanoparticle-enhanced Raman spectroscopy (SHINERS)**

Traditionally, tip-enhanced Raman spectroscopy (TERS) studies have been largely limited to molecules having large Raman cross sections. The reason is that the total Raman scattering signal from the tip area (about 20–50 nm in diameter) is rather weak. Adding to this is its high cost and complexity. Therefore, TERS is impractical for many applications. It has been recently demonstrated that if the Au tip is replaced by a monolayer of Au nanoparticles, each coated with an ultrathin shell of silica or alumina (here denoted Au/SiO$_2$ or Au/Al$_2$O$_3$ nanoparticles), with each nanoparticle acting as an Au tip in the TERS system, it is possible to simultaneously bring thousands of TERS tips to the substrate surface to be probed. With this approach one can obtain combined enhanced Raman signal contributed by all of these nanoparticles; which is a two to three orders of magnitude higher than that obtained with a single TERS tip. This new technique is called as shell-isolated nanoparticle-enhanced Raman spectroscopy (SHINERS). Since a chemically inert shell coating is around the Au nanoparticle, it protects the SERS-active nanostructure from contact with whatever is being probed. The main virtue of such a shell-isolated mode is its much higher detection sensitivity and vast number of practical applications utilizing various materials with diverse morphologies [14].

**Shifted excitation Raman difference spectroscopy (SERDS)**

One way to remove the fluorescent background in traditional Raman Spectroscopy is to take advantage of the shift response of the Raman Effect to excitation wavelength shifts. In SERDS, two spectra of a sample are acquired with slightly different excitation wavelengths, and are then subtracted to estimate the Raman spectrum of a sample. This difference will impact the Raman spectra where the entire spectrum will shift in energy by the amount of excitation shift [16].

**SIERA: Surface-enhanced infrared absorption**

As in the case of surface-enhanced Raman scattering (SERS), molecules adsorbed on metal island films or particles exhibit intense infrared absorption several folds higher than what one would expect from conventional measurements without the metal. This effect is referred to as surface-enhanced infrared absorption (SEIRA).

**Single-electronic-state (SES) limit**

The Raman spectroscopy in SES limit is where the incident photon energy is very close to, or falls within, the absorption band of an excited electronic state of a molecule, and the resulting Resonance Raman (RR) scattering is dominated by the properties of this resonant electronic state.

**Spatially offset Raman spectroscopy (SORS)**

Conventional Raman Spectroscopy is limited to the near-surface of diffusely scattering objects and to the first few hundred micrometers depth of surface material. Spatially Offset Raman Spectroscopy (SORS) is a variant of Raman Spectroscopy that allows highly accurate chemical analysis of objects beneath obscuring surfaces. This is done by making at least two Raman measurements; one at the surface and one at an offset position of typically a few millimeters away. To do this without using an offset measurement would be severely restricted by photon shot noise generated
by Raman and fluorescence signals originating from the surface layer. It is possible to extend this to multilevel systems requiring multivariate analysis. Accurate chemical analysis of bone beneath skin, tablets inside plastic bottles, explosives inside containers, and counterfeit tablets inside blister packs have been previously carried out. It is also used to discover counterfeit drugs without opening their internal packaging, and for noninvasive monitoring of biological tissue. In inverse SORS, rather than use spot collection geometry and a circular spot for illumination, the constant offset can be maintained by illuminating the sample with a ring of light centered on the collection region.

**Stimulated Raman gain** Stimulated Raman gain (SRG) and inverse Raman scattering (IRS) are closely related. While one involves stimulated gain at a Stokes-shifted frequency, the other involves stimulated loss at an anti-Stokes-shifted frequency. SRG can be viewed as an induced emission process at the Stokes frequency. Both SRG and IRS are coherent processes.

**Stimulated Raman spectroscopy** Conventional Raman Spectroscopy is insensitive to be useful in sub cellular imaging [10, 15]. An extension of that technique is Coherent anti-Stokes Raman scattering (CARS) in which two lasers (a pump beam and a Stokes beam) interact with a sample, causing identical molecules to vibrate in phase, generating an enhanced anti-Stokes signal. Thus CARS increases the sensitivity of detection several folds over conventional Raman microscopy. However, the problem with CARS is that the resulting spectrum’s strong background makes assigning all but well-isolated bond frequencies very difficult. One approach to eliminate the strong background is to amplify the Raman signal only when the difference in laser frequencies matches a particular molecular frequency and generate no signal if the difference frequencies do not match any molecular frequency. This new approach called stimulated Raman spectroscopy (SRS) trains a pump beam and a Stokes beam on the sample; when the difference in laser frequencies matches a particular molecular frequency, the Raman signal is amplified. When the difference frequency does not match any molecular frequency, no signal is generated, thereby eliminating the spectral background. Thus the SRS spectrum is essentially identical to a conventional Raman spectrum, making spectral assignment much easier than in CARS. Also, SRS microscopy allows three-dimensional imaging of specific molecular species to a depth of about 0.3 mm making it particularly useful for imaging lipids and small molecules such as drugs. It is to be noted that stimulated Raman scattering, unlike stimulated Raman gain (SRG) is a nonlinear technique in which the spontaneous Raman radiation is amplified and the amplified radiation emerges as a coherent beam coincident with the direction of the incident laser radiation.

**Stokes and anti-Stokes scattering** There are two types of Raman scattering, Stokes scattering and anti-Stokes scattering. In Stokes scattering, molecules absorb energy and the resulting photon of lower energy generates a Stokes line on the red side of the incident spectrum. On the other hand, in anti-Stokes scattering, molecules lose energy because the incident photons are shifted to the blue side of the spectrum, thus generating an anti-Stokes line. Since lower
energy states will have more molecules in them than in the case of higher (excited) energy states, the Stokes spectrum will be more intense than the anti-Stokes spectrum.

Surface plasmons Surface plasmons (SPs) are collective excitations of the electrons within the conduction band of a metal.

Thermo-Raman spectroscopy Raman spectroscopy is a useful technique to extract information during dynamic thermal processes and this specific application is termed as thermo-Raman spectroscopy (TRS). It is possible to investigate thermally induced changes in Raman band positions, band intensities, and bandwidths and correlate with corresponding structural changes in samples. TRS can also provide quantitative information related to the dynamics thermal processes. Unlike techniques such as thermogravimetric analysis (TGA) and differential thermal analysis (DTA) which can only provide bulk information associated with thermal properties of a solid sample, TRS can be used to study thermally induced structural transformation in solids [17].

Time-resolved Raman spectroscopy (TRRAS) Time-resolved Raman spectroscopy (TRRAS) is used to analyze low energy excitation on ultrafast timescale. While it is not directly sensitive with respect to the atomic positions, it is possible to extract information related to structural, magnetic, and electronic properties. In this technique, by monitoring the Stokes to anti-Stokes ratio, one can obtain information about the thermodynamics of different excitations measuring directly the temperature of the excitation investigated, and thereby to disentangle. A unique aspect of TRRAS is that one can measure the “strength” of the crystalline potential in real time. Since it is inexpensive to carry out TRRAS, this is one of the most sought after tools for studying electronic dynamics. It is also a power tool for investigating structural and magnetic dynamics.

Tomography-Raman Even though the Raman Effect is weaker than fluorescence, algorithms developed for fluorescence imaging can be applied to Raman signals. Using the waves of energy one can image section by section of an object, thereby creating what is known as tomography. Since Raman signals are used for imaging, the tomography is called Raman Tomography.

Transmission Raman spectroscopy (TRS) Raman spectroscopy has several variants and Transmission Raman Spectroscopy (TRS) is one such. In a conventional back-scattering Raman spectroscopy the signal tends to be a representative of the surface and near-surface composition. In TRS Raman photons can be created at all points such that the light passing through the total scrambled Raman signal can be measured on the opposite face of an object. Therefore, Transmission Raman Spectroscopy (TRS) is highly representative of the bulk of the material and a large thickness can be measured in the absence of photon absorption. This produces an analysis representative of the entire mixture and is typically insensitive to coatings, or thin containers. The technique is also somewhat similar to Spatially Offset Raman Spectroscopy, where the light in a diffusely scattering sample spreads through the object randomly. Therefore,
TRS can be regarded as an extreme example of SORS. Most importantly, Transmission Raman is rapid as it requires no sample preparation and involves no phase change.

**Waveguide Raman spectroscopy (WRS)** Waveguide Raman spectroscopy (WRS), in which the pump laser beam in traditional Raman spectroscopy is coupled into a planar dielectric waveguide in order to probe the Raman-active vibrations of the waveguiding material, is used to study thin films, surfaces, and interfaces. Since micrometer dimensions of a waveguide can generate large electric field strengths resulting in high intensities, WRS signals are three to four orders of magnitude higher compared to those from conventional Raman scattering [18].

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