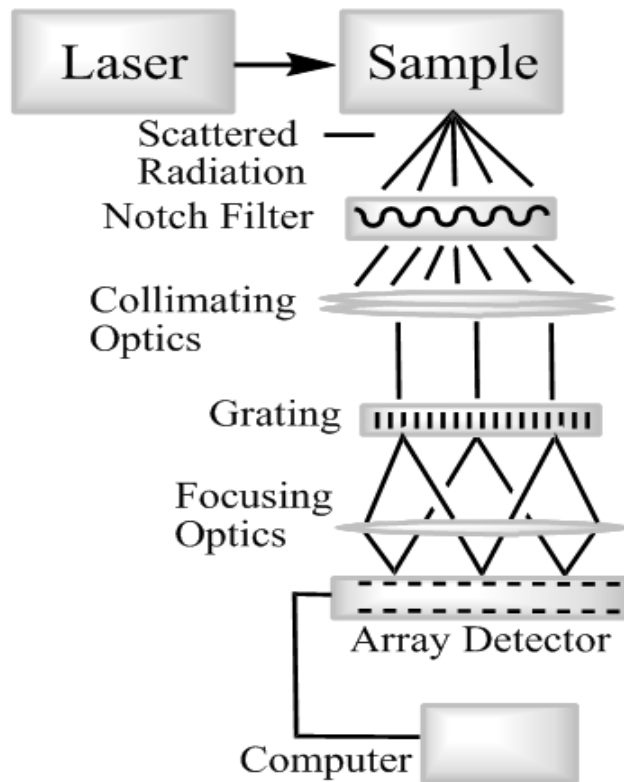


Raman Spectroscopy

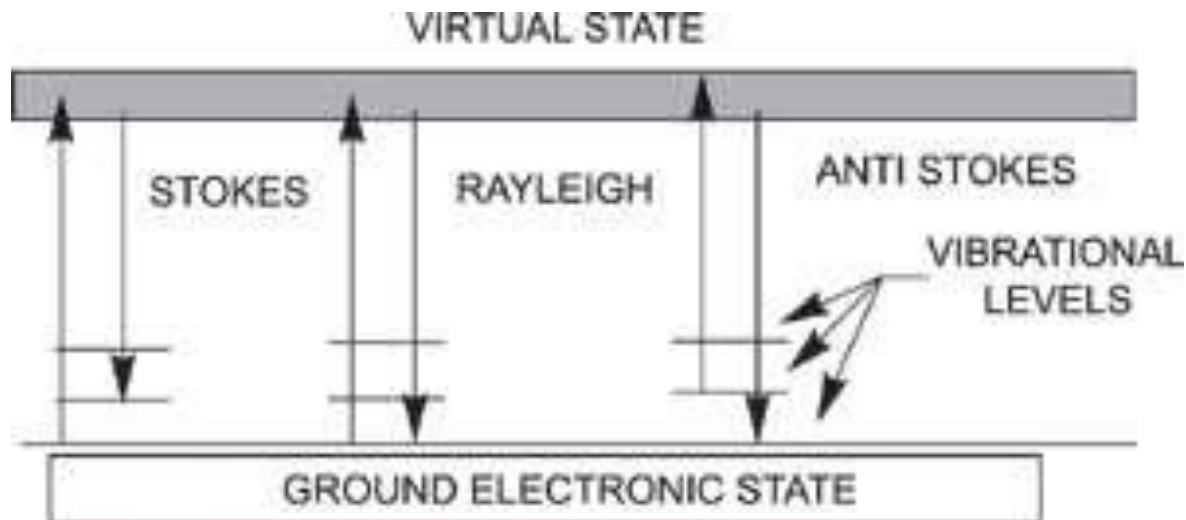
Raman spectroscopy has become an incredibly useful analytical technique for the identification of organic, inorganic, and biological samples. Raman spectra can generally be measured from solids, liquids, and gases, including thin films and powders.

Material characterization
Pharmaceutical analysis
Disease diagnostics
Forensics
Process control



Raman Spectroscopy

It is the shift in wavelength of the inelastically scattered radiation that provides the chemical and structural information. Raman shifted photons can be of either higher or lower energy, depending upon the vibrational state of the molecule under study. A simplified energy diagram that illustrates these concepts is shown below.

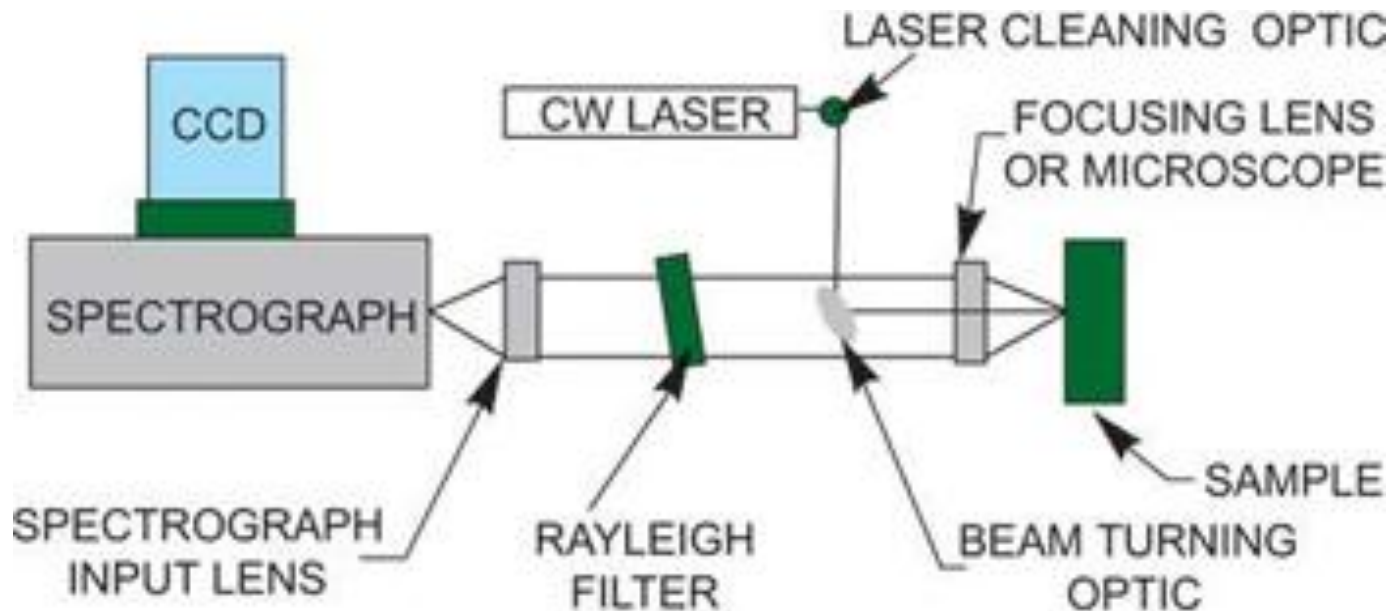


The energy increase or decrease from the excitation is related to the vibrational energy spacing in the ground electronic state of the molecule and therefore the wavenumber of the Stokes and anti-Stokes lines are a direct measure of the vibrational energies of the molecule.

Raman Spectroscopy

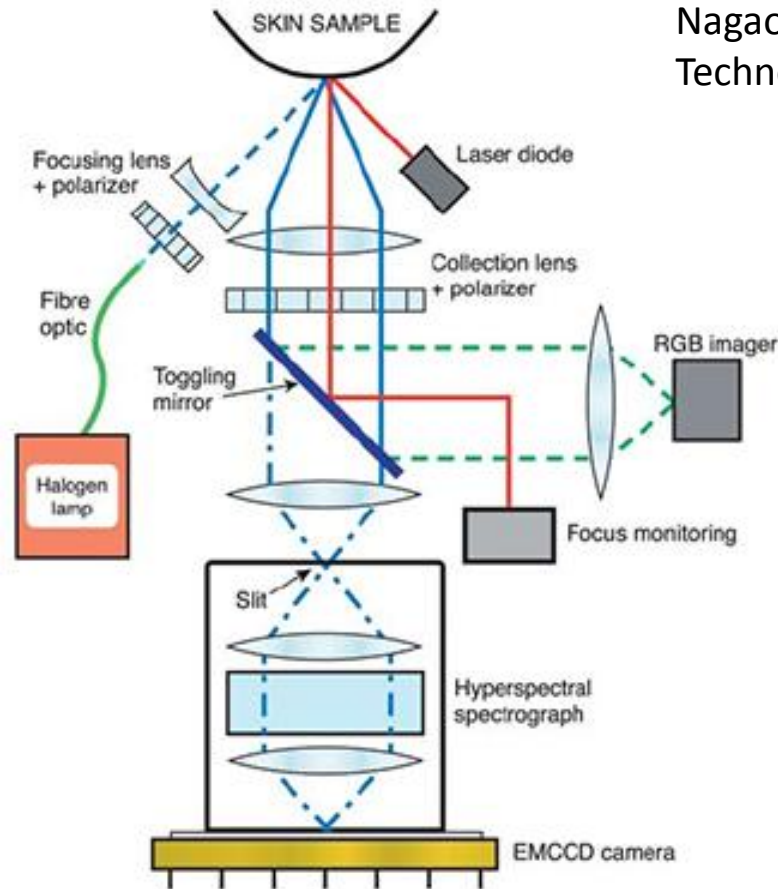
$$I_R \propto \frac{I_o \beta N \partial z}{\lambda^4}$$

I_o = laser power, β = scattering cross section
 N = number of scatters in probe volume, ∂z = path length, λ = excitation light wavelength



Imaging for Clinical Diagnosis of Melanoma

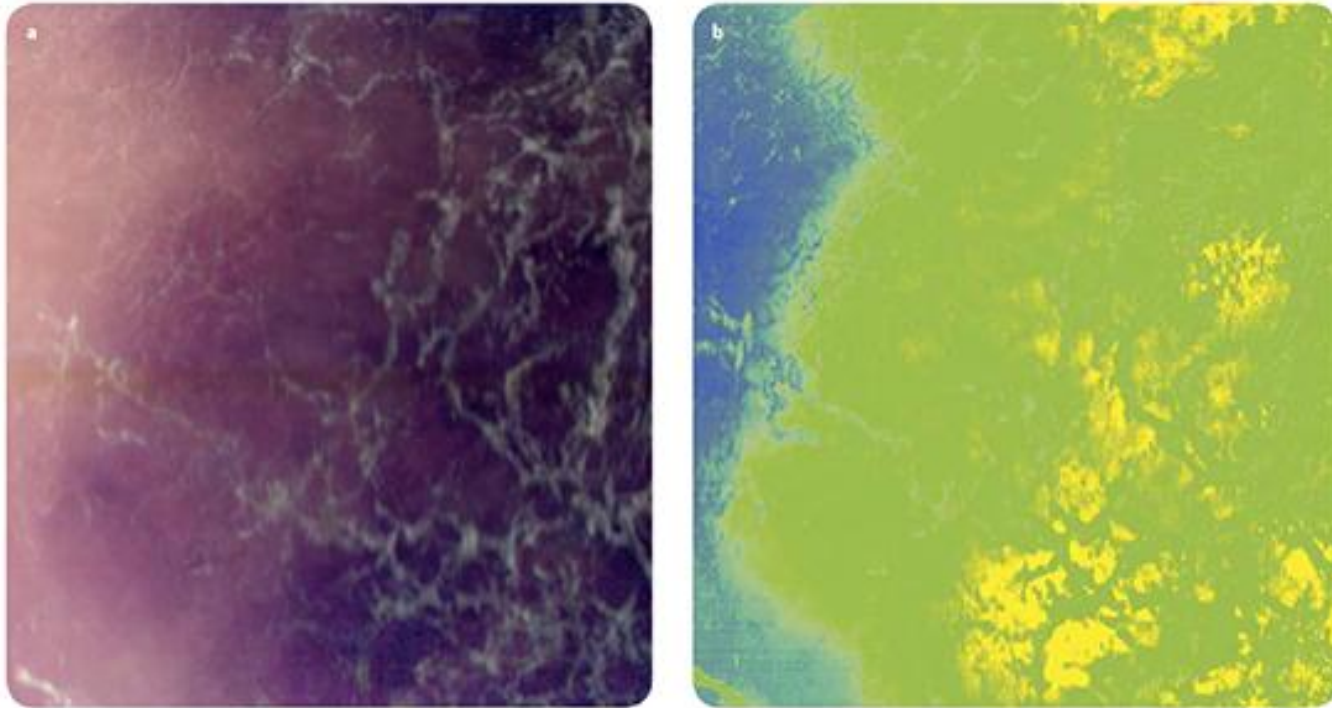
Nagaoka T. et al.: Skin Research and Technology, 0:1–10 (2011)



The high resolution spectrometer dispersed the light on to the EMCCD sensor so that spectral data corresponding to each spatial point along the length of the slit was displayed across the sensor, giving spectral information in one dimension and spatial in the other.

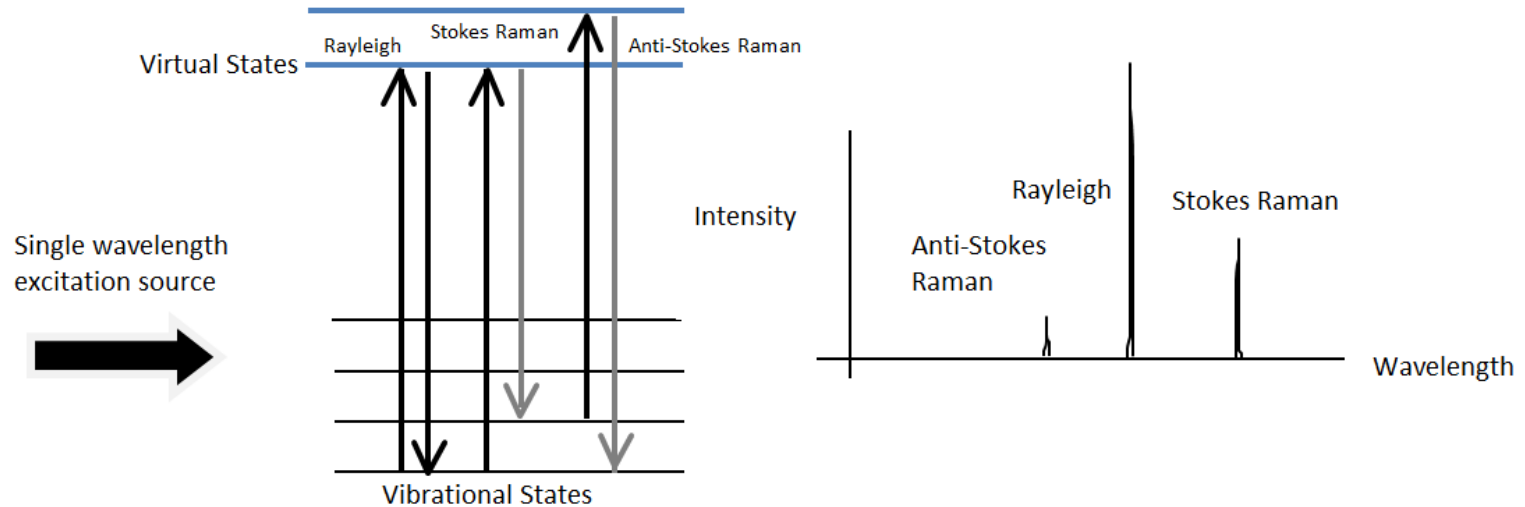
Imaging for Clinical Diagnosis of Melanoma

The figure shows a standard dermoscopy image of a malignant melanoma (a) and the derived 2D “spectral angle map” (b).



The key advantages of hyperspectral imaging compared with conventional dermoscopy are i) a lot more information can be acquired (compared to RGB images), ii) the potential for real-time diagnostics and iii) reduction of unnecessary surgical biopsies and associated costs.

Raman Spectroscopy



Rayleigh and Raman scattering (Stokes and anti-Stokes) as seen on energy level diagram. An associated spectrum is included, note the Raman lines intensity are greatly exaggerated. Raman spectra are usually shown in wavenumbers as a shift from the Rayleigh scattered line.

Selection Rules

Roughly speaking the primary selection rule for a Raman transition is that the *molecular polarizability must change during the molecular vibration*.

The polarizability of the molecule, α , tells us about how hard or how easy it is for an electric field to change or distort the electron cloud in an atom or molecule. An atom in which the electron cloud is further away from the nucleus has a larger polarizability than an atom where the electron cloud is closer to the nucleus.

There are several useful *generalities* we can make concerning Raman & IR spectroscopy:

- **symmetric vibrations lead to relatively strong Raman signals and no IR signals.**
- **asymmetric vibrations lead to much weaker Raman signals and are often quite strong in IR spectroscopy.**
- **bending vibrational modes lead to much weaker Raman signals and are often quite strong in IR spectroscopy.**
- **a molecule can have both IR and Raman signals at the same frequency, though if the Raman signal is strong, the corresponding IR peak will be weak and vice versa.**

Raman Spectroscopy

Electric polarizability is the relative tendency of a charge distribution, like the [electron cloud](#) of an [atom](#) or [molecule](#), to be distorted from its normal shape by an external [electric field](#) (electromagnetic radiation).

The polarizability, α , is defined as the ratio of the induced [dipole moment](#), ρ , of an atom to the electric field, E , that produces this dipole moment.

$$P = \alpha E$$

Generally, polarizability increases as volume occupied by electrons increases.

Though water is a very [polar](#) molecule, [alkanes](#) and other [hydrophobic](#) molecules are more polarizable. Alkanes are the most polarizable molecules.

Raman Imaging

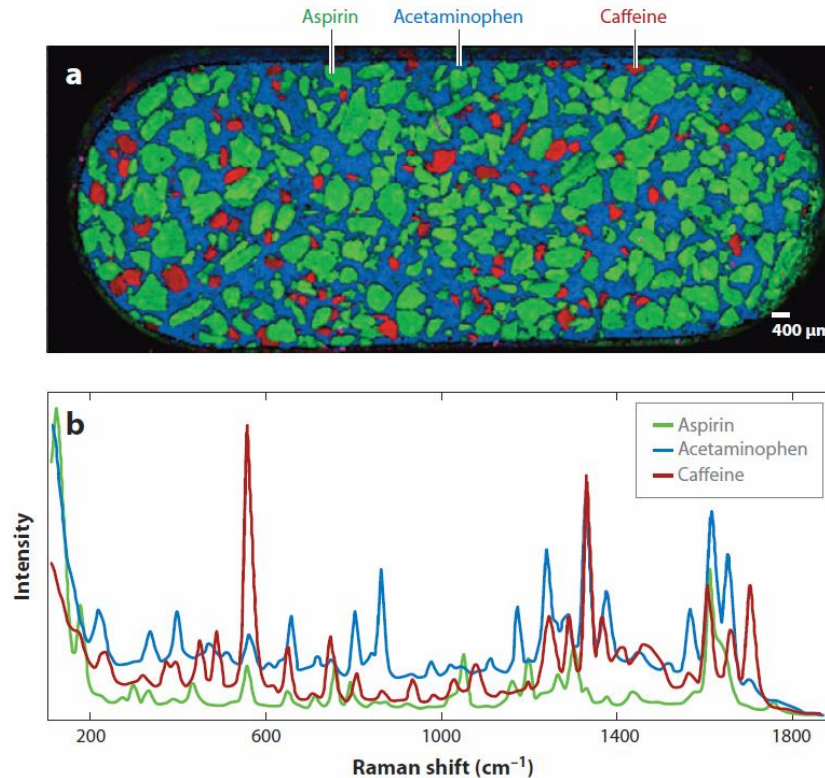
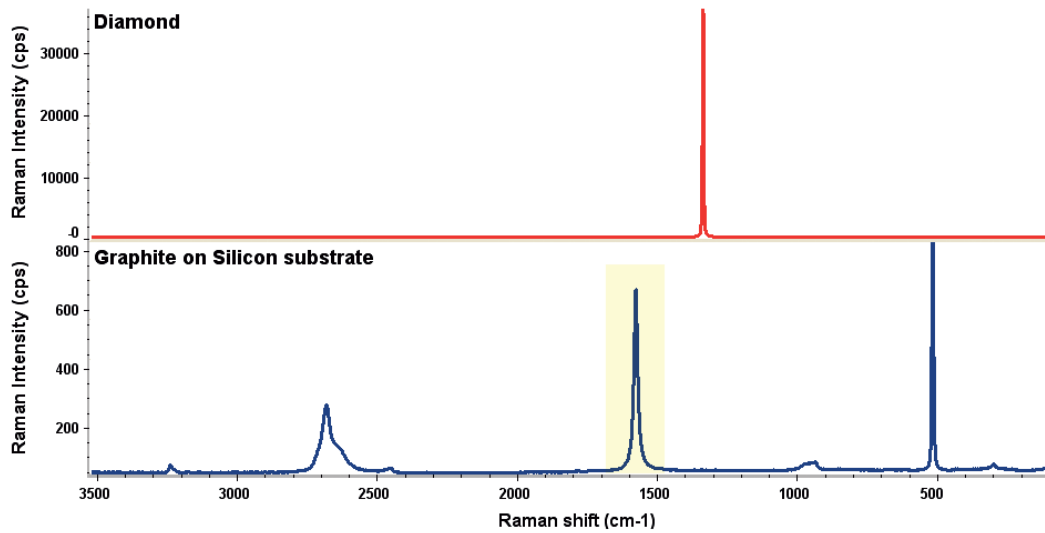
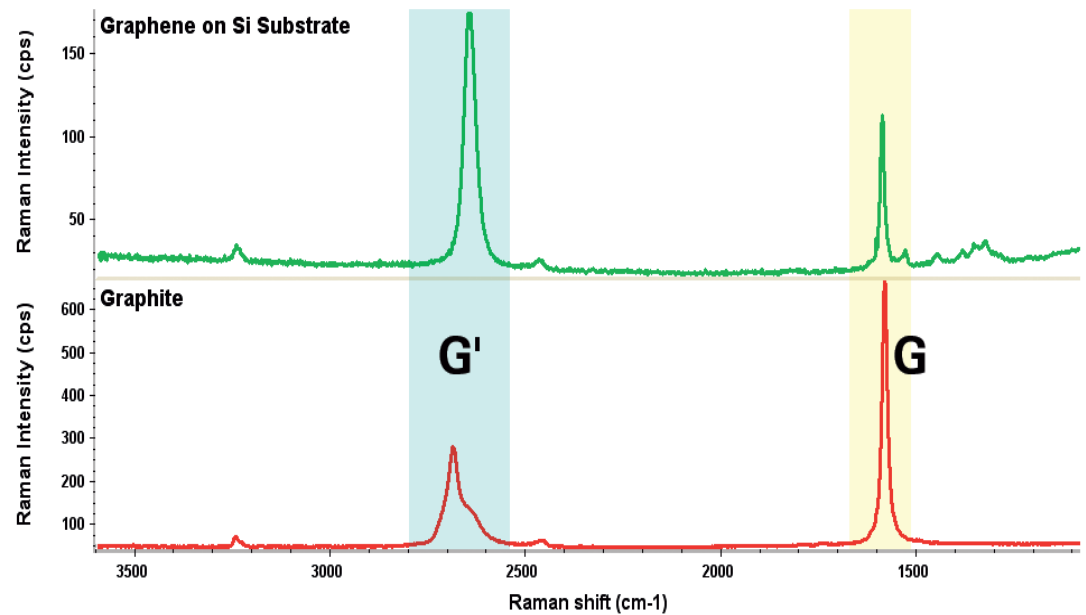


Figure: (a) Colored coded distribution of aspirin, acetaminophen and caffeine within a tablet. (b) Raman spectra of aspirin, acetaminophen and caffeine.

Raman Spectroscopy of Carbon Materials



Distinct spectra for the different allotropes of carbon!



FTIR vs. Raman

Table 12.2: Side by Side comparison of Raman and FTIR spectroscopy

Raman	FTIR
Symmetric stretches are strong. Asymmetric stretches and bends are weak.	Asymmetric stretches and bends are strong. Symmetric stretches are not seen.
Standard sample holders can be used- glass, plastic, etc.	IR transparent materials (salts) are generally used for sample holders. However ATR eliminates the need for a sample holder in many cases.
Samples can be in water/water can be the solvent	FTIR in water is a challenge do to IR absorption and some IR optics are water soluble.
Essentially no preparation of sample needed	Sample preparation can be challenging, however IR variants such as ATR-FTIR and Diffuse Reflectance Infrared Fourier Transform Spectroscopy (DRIFTS) allow for little to no sample prep.
Optics for systems can be glass	Custom optics required
Can be used to image small scale structures via micro Raman	Tunable ATR-FTIR can be used to probe sample composition as a function of depth.
Can measure vibrations of homonuclear species (ex. N ₂ , O ₂ , C ₆₀ , P ₄ etc.)	More readily lends itself to application of group theory for the identification of molecular isomers (i.e. cis vs. trans).
Requires a laser source	Requires broadband IR source
Raman selection rules require changing polarizability	IR selection rules require changing dipole moment
Can use high sensitivity UV-Vis detectors	Uses thermal or piezoelectric IR detectors
Wavelength discrimination is accomplished using a grating.	Wavelength discrimination is accomplished using a Michelson's Interferometer.

Factors Controlling Magnitude of β

- β is larger for molecules with extended π electron systems as they are more easily polarized.
- Molecules with single C-H, C-O and C-C bonds have small cross sections.
- Molecules with large, electron-rich atoms, such as S or I, have large cross sections.
- Multiple bond stretches generally have high cross sections.

$$I_R \propto \frac{I_o \beta N \partial z}{\lambda^4}$$