Low-frequency Raman spectroscopy

Raman spectroscopy is an analytical tool that permits measurement of the molecular structure and identification of materials based on the rotational and vibrational modes of a molecule. Most commercial laboratory Raman systems cover the fingerprint spectral region ranging from 200–3400 cm^{-1}.
The B&W Tek i-Raman Plus BAC102 probe can access lower-frequency modes down to 65 cm^{-1}, providing a cost-effective solution for fuller range measurements. Access to lower-frequency regions provides key information for applications in protein characterization [1], polymorph detection and identification [2], along with material phase and structure determination.

INTRODUCTION

The low-frequency region augments the information content from the fingerprint region of the Raman spectrum and broadens possible molecular applications, such as detection of hydrogen bonds. The result is increased detection sensitivity and differentiation of very similar materials.

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Amino acids

Raman spectroscopy is a modern way to study the structure and conformation of the building blocks of proteins—amino acids. Specifically, the vibrational information content in a Raman spectrum can help with interpretation of molecular interactions and biological processes [3].

Unlike many substances that do not exhibit peaks below ~400 cm^{-1}, the low-frequency portion of the Raman spectrum is a necessary source of information for a comprehensive study of amino acids. This is obvious in the full Raman spectrum of L-asparagine, from 65–3200 cm^{-1} (**Figure 1**).

Figure 1 shows both the fingerprint region (blue) as well as the low-frequency Raman region (red) for L-asparagine; note the three dominant bands below 200 cm^{-1}.
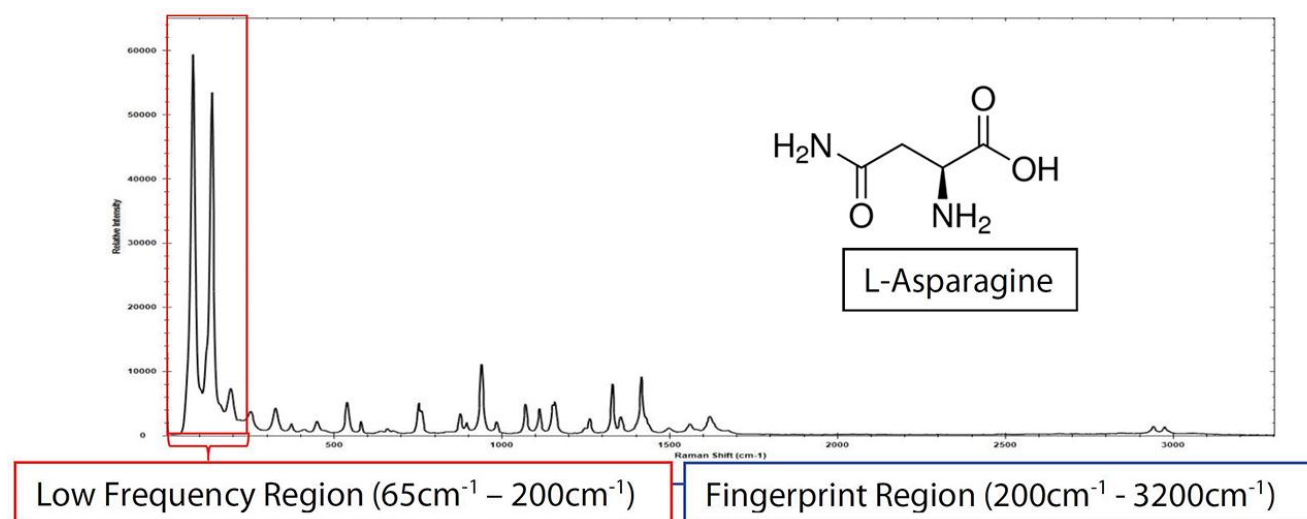
Figure 1. i-Raman Plus and a BAC102 E-grade probe were used to collect the low-frequency spectra of L-asparagine with a total integration time of 1.2 s.

EXPERIMENT

i-Raman Plus 785S, B&W Tek's laboratory Raman spectrometer that utilizes patented CleanLaze®, was used in this application. This instrument features 785 nm laser excitation with a linewidth of less than 0.2 nm and maximum power output of 300 mW.

i-Raman Plus is equipped with a sensitive, TE-cooled, back-thinned CCD. A BAC102 E-grade probe, utilizing proprietary technology, supports data collection within a full spectral range of 65–33500 cm^{-1} with a spectral resolution of 4.5 cm^{-1}.

Raman spectra were collected at room temperature using 300 mW laser power with integration times that ranged from 100 milliseconds to 10 seconds (**Table 1**).

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| Equipment	Acquisition settings	
i-Raman Plus 785S	Laser Power	300 mW
BAC102 probe	Integration time	1.2 s
BWSpec software	Averages	1

RESULTS: POLYMORPH DETECTION

Determining the structural form of active pharmaceutical ingredients (APIs) is a primary concern for the pharmaceutical industry. This is especially true during drug development, manufacturing, and quality control.

APIs exhibit polymorphism—identical chemical composition but different solid-state structures. Polymorphs may affect bioavailability and therapeutic index. The efficacy of a drug can be compromised if the wrong form is used [2]. Pseudo-polymorphs include solvents suspended in a lattice structure.

Figure 2 is an example of the pseudo-polymorph D-glucose, demonstrating the ability of the E-grade probe to detect differences between the monohydrate and anhydrous forms at frequencies below 200 cm^{-1}.
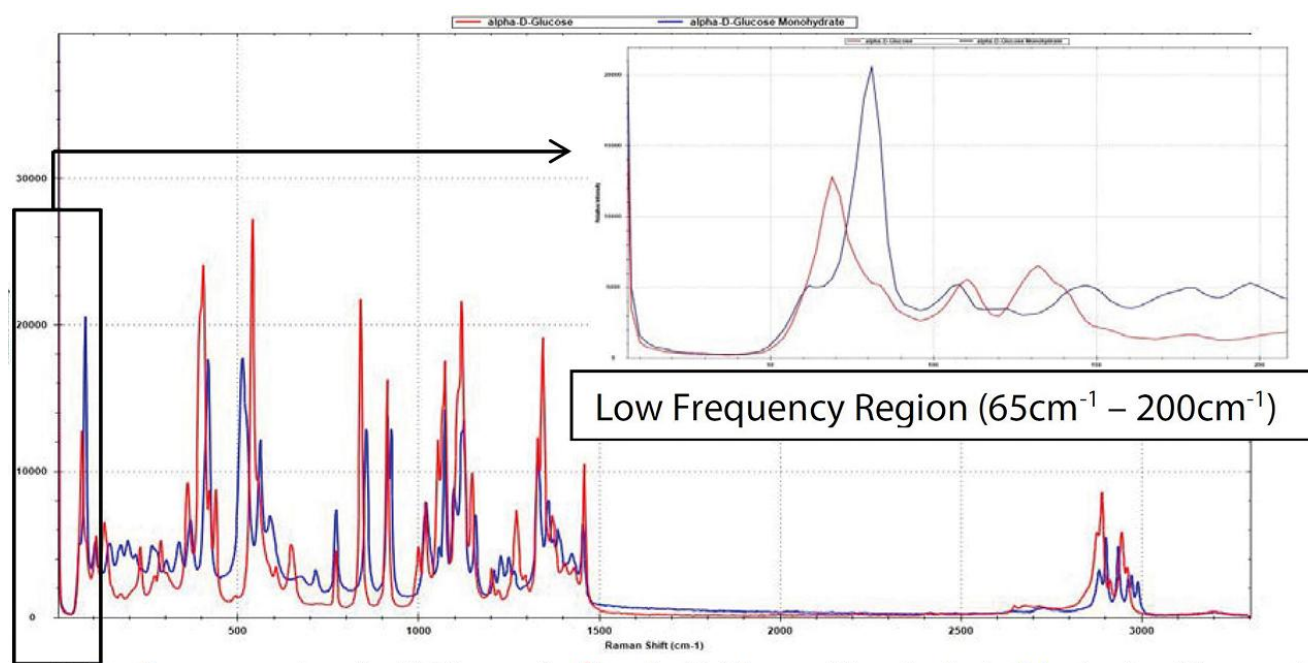
Figure 2. Raman spectra of α-D-glucose (red) and α-D-glucose monohydrate (blue), taken with 10 s integration time. Note the significant difference between the two pseudo-polymorphs within the low-frequency range (see inlay).

RESULTS: MONITORING PHASE CHANGE

Exceptional specificity is required to monitor phase changes like crystallization in chemical processes. The low-frequency E-grade probe can monitor such phase changes, as demonstrated for sulfur (**Figure 3**).

Solid α-sulfur was deposited onto an aluminum tray and heated with a hot plate while the Raman spectra were collected with an E-grade probe and i-Raman Plus, using 100% laser power (~300 mW) and 0.1 s integration time for both the solid and liquid phase. After the sample was heated above its melting point at 115.2 °C, the low-frequency peak at 83.6 cm^{-1} broadened and shifted, indicating the change from the α- to the λ-form. Note that there are no observable changes within the fingerprint region (**Figure 3**).
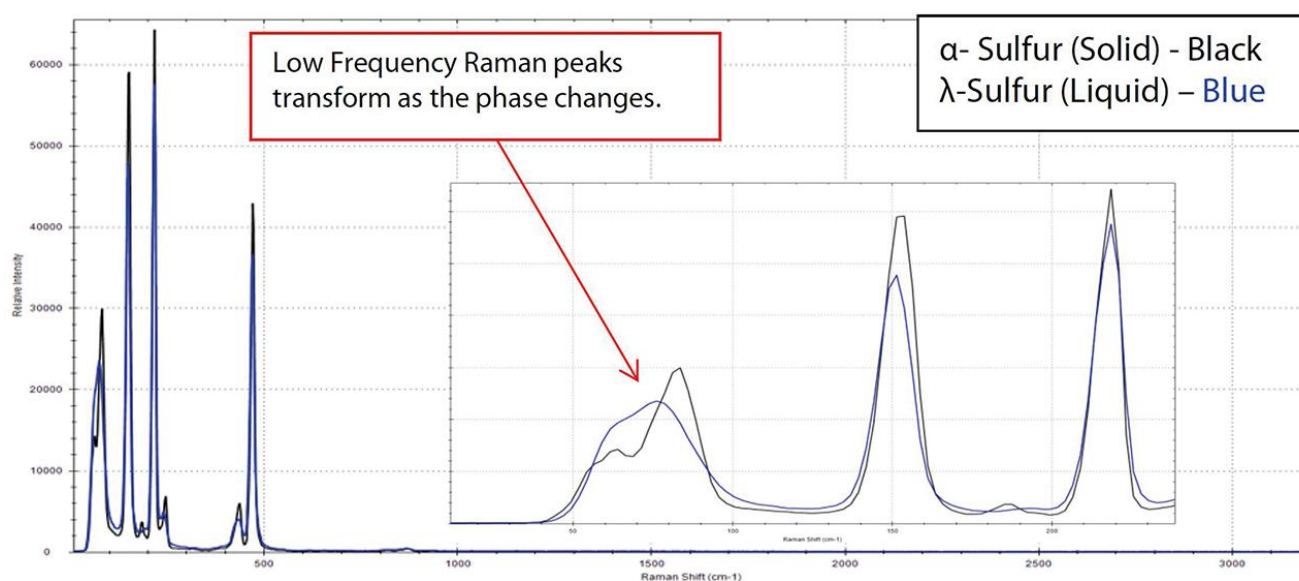
Figure 3. Raman spectra of sulfur transitioning from the α-crystalline form to the λ-liquid form, taken with 0.1 s integration time. Note significant broadening in the peaks located in the low-frequency region (see inlay).

CONCLUSION

i-Raman Plus 785S Raman spectrometer, coupled with the low-frequency E-grade probe, can be a valuable tool for applications requiring low-frequency detection down to 65 cm^{-1}. The ability to characterize polymorphs and solvated forms supports manufacturing and formulation processes in the pharmaceutical and biological industries.

Along with protein, polymorph, and phase characterization, low-frequency Raman spectroscopy can also be used to study semiconductor lattices [4], carbon nanotubes [5], solar cells, and an assortment of minerals, pigments and gemstones.

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CONTACT

Metrohm Vietnam
Phan Dinh Giot
70000 Herisau

info@metrohm.vn

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CONFIGURATION

i-Raman Plus 785S Portable Raman Spectrometer

The i-Raman® Plus 785S is part of our award-winning series of i-Raman portable Raman spectrometers powered by our innovative intelligent spectrometer technology. Using a high-quantum-efficiency CCD array detector with TE cooling and high dynamic range, this portable Raman spectrometer delivers excellent performance with low noise, even at integration times of up to 30 minutes, making it possible to measure weak Raman signals.

The i-Raman Plus 785S features the unique combination of wide spectral range and high resolution with configurations which allow measurements from 65 cm^{-1} to 3,350 cm^{-1}. The system's small footprint, lightweight design, and low power consumption ensure research-grade Raman analysis capabilities at any location. The i-Raman Plus is equipped with a fiber probe for easy sampling, and can be used with a cuvette holder, a video microscope, an XYZ positioning stage with a probe holder, as well as our proprietary BWIQ® multivariate analysis software and BWID® identification software. With the i-Raman Plus, you always have a high precision Raman solution for qualitative and quantitative analysis.

E-Grade Raman Trigger Probe (785 nm)

Lab grade fiber optic Raman probe assembly for cut-on start from 65 cm^{-1} with hand trigger; 105 μm diameter, 0.22 NA fiber for 785 nm excitation, 200 μm diameter, 0.22 NA for Raman pickup. Optical density >6; 1.5 m fiber length terminated in SMA905 on the spectrometer end and FC/PC on the laser end. Adhesive sealed quartz window for non-contact sampling. 5.4 mm working distance. Not for immersive use.

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