Application Note 410000006-B

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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.

### 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 $cm^{-1}$.

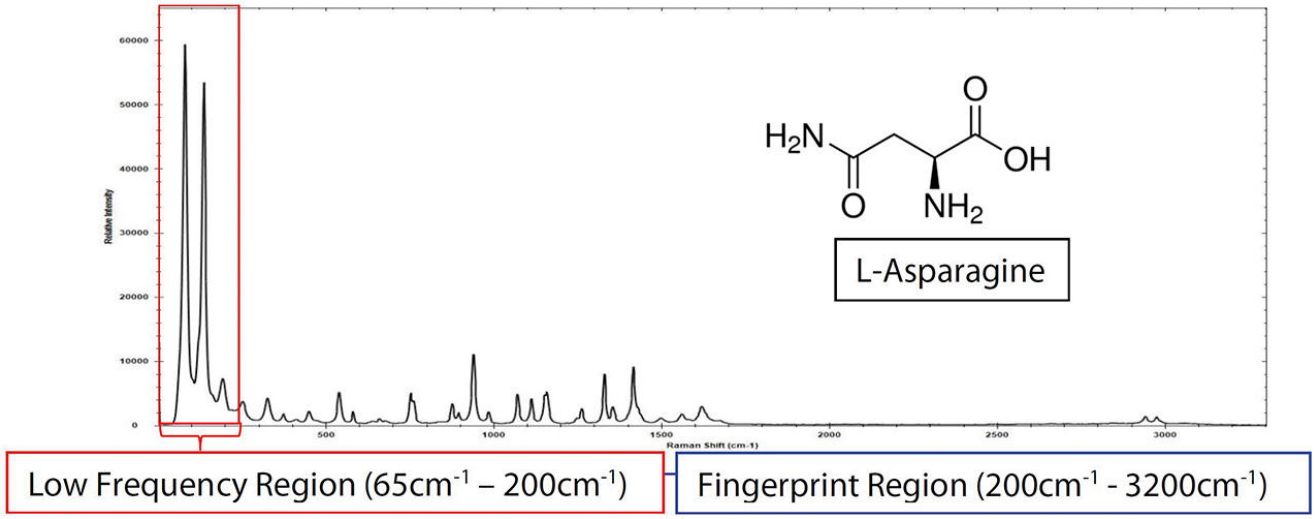


**Figure 1.** i-Raman Plus and a BAC102 E-grade probe were used to collect the low-frequency spectra of L-asparagine with a total integration time of 1.2 s.

## 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).

**Table 1.** Experimental parameters.

| 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 $cm^{-1}$.

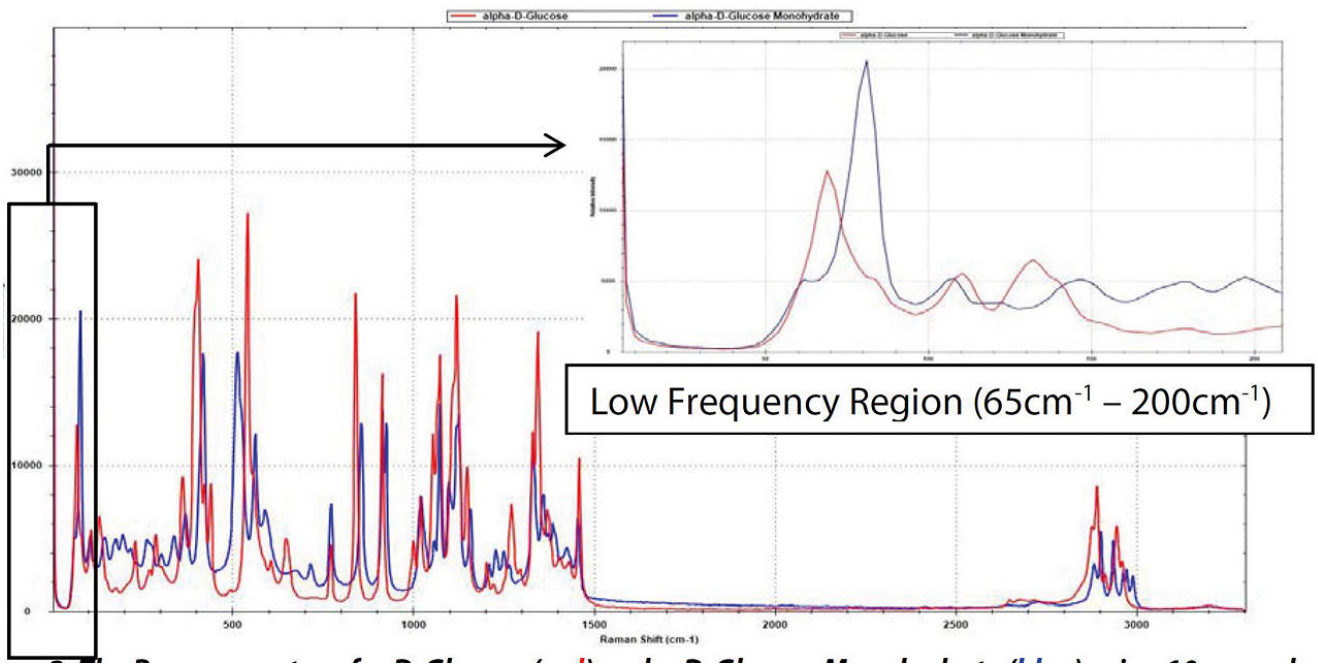


**Figure 2.** Raman spectra of α-D-glucose (red) and α-D-glucose monohydrate (blue), taken with 10 s integration time. Note the significant difference between the two pseudo-polymorphs within the low-frequency range (see inlay).

## 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).

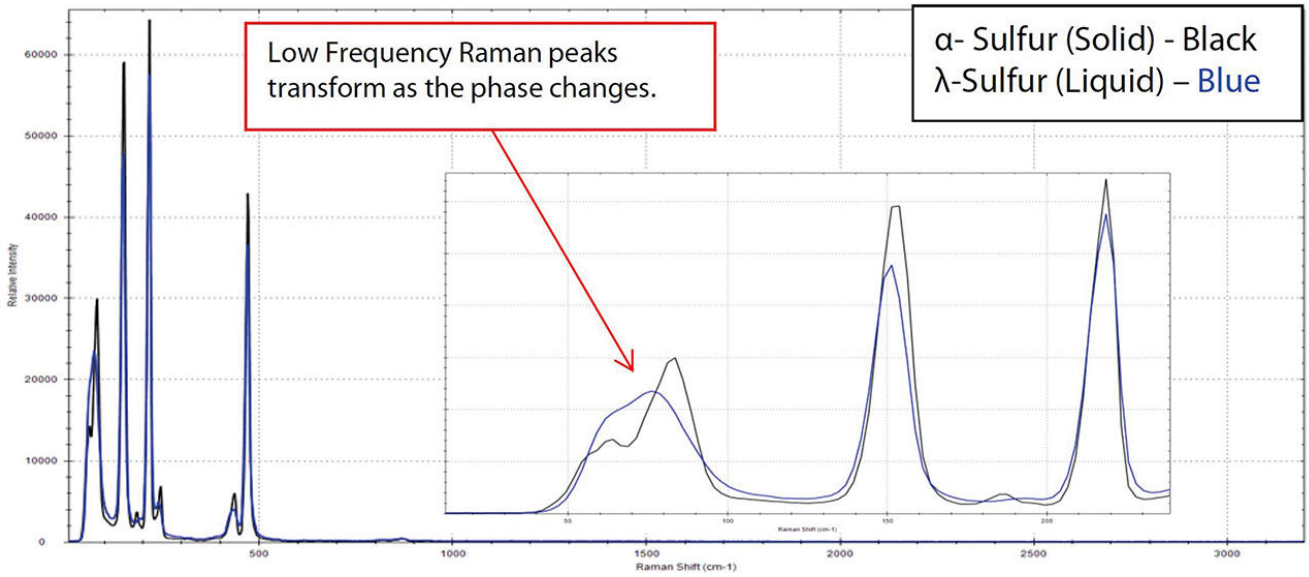


**Figure 3.** Raman spectra of sulfur transitioning from the α-crystalline form to the λ-liquid form, taken with 0.1 s integration time. Note significant broadening in the peaks located in the low-frequency region (see inlay).

## 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.

## REFERENCES


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4. Smith, E.; Dent, G. *Modern Raman Spectroscopy: A Practical Approach*, 2nd ed.; John Wiley & Sons, 2019.
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## CONFIGURATION

**i-Raman Plus 785S**

i-Raman® Plus 785S 是我屡殊的 i-Raman 便携式拉曼光系列的一部分,其采用我新的智能光技。款便携式拉曼光使用了具有高量子效率、TE 冷却功能和高范的 CCD 列器,即使集成 30 分,也能提供出色的低噪声性能。因此,可以量弱的拉曼信号。

i-Raman Plus 785S 具有光范和高分辨率的特点,其配置允在 65 $cm^{-1}$ 至 3350 $cm^{-1}$ 之行量。 系基面小,形式巧并且能耗低,故此可随随地行研究的拉曼分析。i-Raman Plus 配有便于采的光探,并可以与一个比色皿支架、一个微、一个探支架的 XYZ 平移台、我公司内部的 BWIQ® 多量分析件和定件 BWID® 搭配使用。有了 i-Raman Plus,始可以使用高精度拉曼解决方案行定性和定量分析。


(785 nm)

室量的光拉曼探的模,用于 65 $cm^{-1}$ 以上的 Cut-on-Start,包括手触器,直径 105 µm,0.22 NA 光,用于在 785 nm 激,200 µm 直径,0.22 NA 用于拉曼拍。光密度 > 6;1.5 m 光度,光端 SMA905 接口,激光器端 FC/算机接口。用于非接触式取的粘合密封石英玻璃窗。5.4 mm 工作距。不合用于浸入。