



Application Note 410000006-B

低周波ラマン分光装置

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 $\sim 400\text{ cm}^{-1}$, 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 $65\text{--}3200\text{ cm}^{-1}$ (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} .

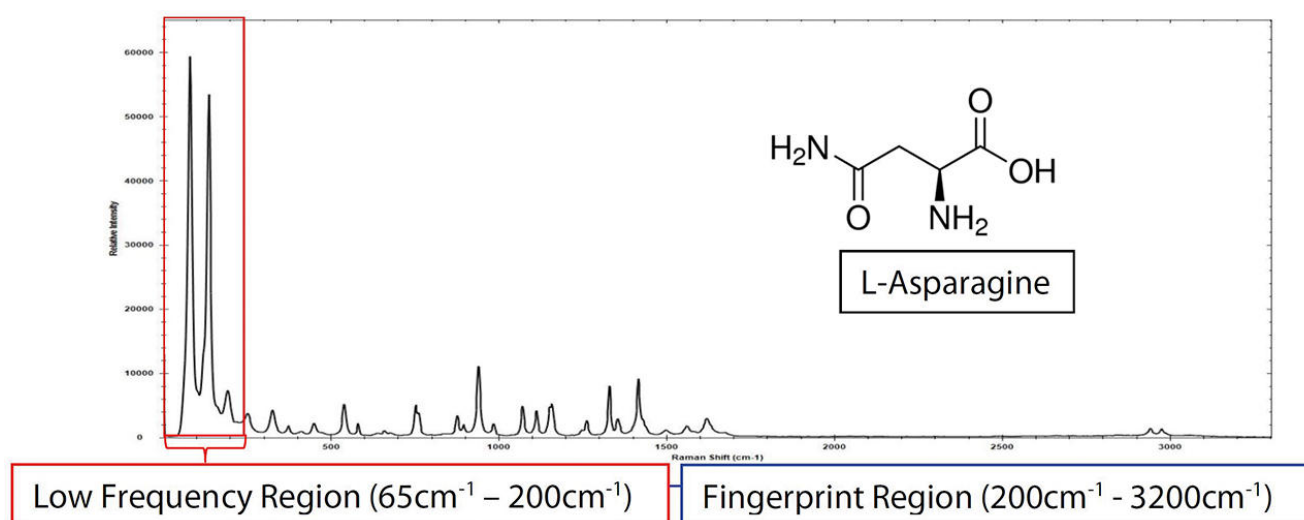


Figure 1. i-Raman Plus and a BAC102 E-grade probe were used to collect the low-frequency spectra of L-asparagine with a total integration time of 1.2 s.

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 $65\text{--}33500\text{ cm}^{-1}$ 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} .

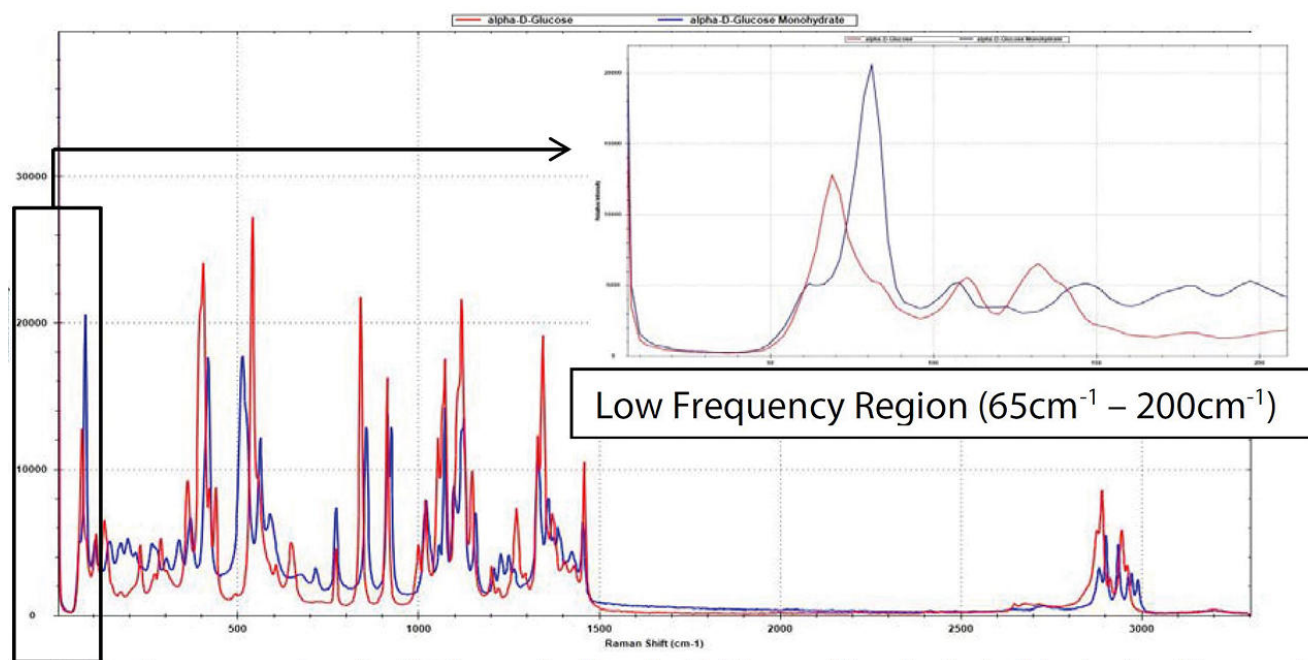


Figure 2. Raman spectra of α -D-glucose (red) and α -D-glucose monohydrate (blue), taken with 10 s integration time. Note the significant difference between the two pseudo-polymorphs within the low-frequency range (see inset).

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).

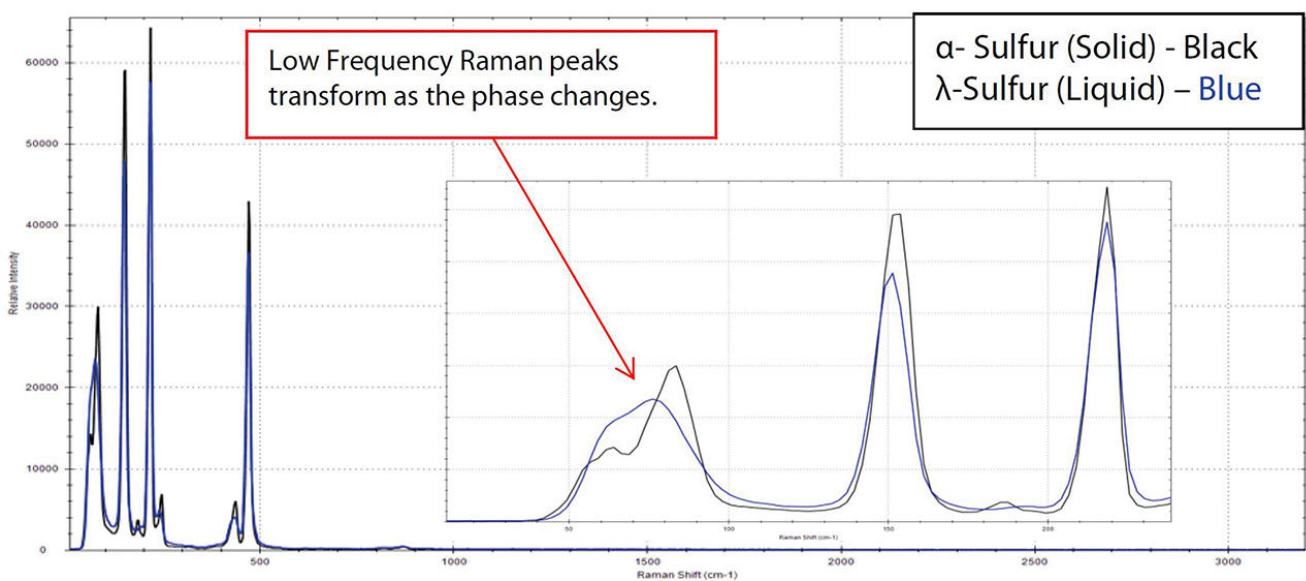


Figure 3. Raman spectra of sulfur transitioning from the α -crystalline form to the λ -liquid form, taken with 0.1 s integration time. Note significant broadening in the peaks located in the low-frequency region (see inlay).

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

1. Teixeira, A. M. R.; Freire, P. T. C.; Moreno, A. J. D.; et al. High-Pressure Raman Study of L-Alanine Crystal. *Solid State Communications* **2000**, *116* (7), 405–409. [https://doi.org/10.1016/S0038-1098\(00\)00342-2](https://doi.org/10.1016/S0038-1098(00)00342-2).
2. Larkin, P. J.; Dabros, M.; Sarsfield, B.; et al. Polymorph Characterization of Active Pharmaceutical Ingredients (APIs) Using Low-Frequency Raman Spectroscopy. *Appl Spectrosc* **2014**, *68* (7), 758–776. <https://doi.org/10.1366/13-07329>.
3. Golichenko, B. O.; Naseka, V. M.; Strelchuk, V. V.; et al. Raman Study of L-Asparagine and L-Glutamine Molecules Adsorbed on Aluminum Films in a Wide Frequency Range. *Semicond. Phys. Quantum Electron. Optoelectron.* **2017**, *20* (3), 297–304. <https://doi.org/10.15407/spqeo20.03.297>.
4. Smith, E.; Dent, G. *Modern Raman Spectroscopy: A Practical Approach*, 2nd ed.; John Wiley & Sons, 2019.
5. Pelletier, M. J. *Analytical Applications of Raman Spectroscopy*, 1st ed.; Blackwell Science: Oxford, 1999.

CONTACT

メトロームジャパン株式会社
143-0006 東京都大田区平
和島6-1-1
null 東京流通センター アネ
ックス9階

metrohm.jp@metrohm.jp

CONFIGURATION



i-Raman Plus 785S

i-Raman® Plus 785S は、弊社の革新的かつインテリジェントなスペクトロメーターテクノロジーを備えた i-Raman ホータフル型ラマンスペクトロメーターの受賞歴のあるシリーズの構成要素です。このホータフル型ラマンスペクトロメーターは、高い量子効率、TE 冷却、ならびに高いダイナミックレンジを備えた CCD アレイ検出器を用い、積分時間でさえ最長30分、低ノイズの傑出した性能を提供します。こうして、弱いラマン信号も測定することかてきます。

i-Raman Plus 785S は、 65 cm^{-1} から 3350 cm^{-1} までの測定を可能にするコンフィグレーションを有する幅広いスペクトル範囲と高分解能のユニークな組み合わせを特徴としています。システムの小さな底面、軽量構造、そして低消費電力により、とこてもラマン分析を研究レベルで実施することかてきます。i-Raman Plus には、サンプル採取を簡単にする光ファイバーフローフが装備されており、キューベットホルター、ヒテオマイクروسコーフ、フローフホルター付き XYZ スライドテーブル、ならびに弊社独自の多変量解析ソフトウェア BWIQ® および同定ソフトウェア BWID® と共に使用することかてきます。i-Raman Plus により、品質分析および定量分析のための高精度のラマンソリューションを常に使用することかてきます。

(785 nm)

ハントトリカー付き 65 cm^{-1} 以上のカットオンスタート用のラホ品質のラマン光ファイバーフローフ付きのモジュール、直径 $105\text{ }\mu\text{m}$ 、785 nm 励起のための 0.22 NA 光ファイバー、直径 $200\text{ }\mu\text{m}$ 、ラマン記録のための 0.22 NA 。光学密度 > 6 ; ファイバー長 1.5 m 、スペクトロメーター末端に SMA905 コネクタ、レーザー末端に FC/PC コネクタ付き。非接触式サンプル採取のための、接着剤で密封された石英カラスウィントウ。作動距離 5.4 mm 。浸漬には適していません。

