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Low Frequency Raman Spectroscopy

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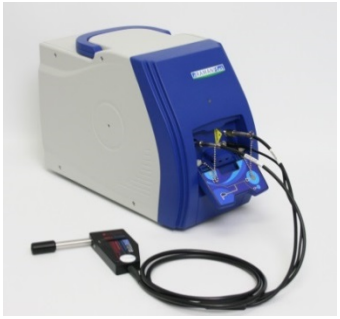
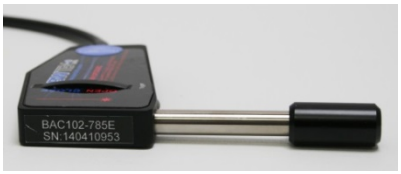
Introduction

Raman Spectroscopy is an advantageous analytical tool that allows for the measurement of molecular structure and identifying chemical composition of materials based on the rotational and vibrational modes of a molecule. The spectral range of the standard probe for the i-Raman Plus series focuses on the fingerprint region ranging from 176cm^{-1}-4000cm^{-1}. With advanced technology and an optimized optical design, the B&W Tek BAC102 series E-grade probe can access lower frequency modes down to 65cm^{-1}, providing a cost effective solution for fuller range measurements. Figure 1 shows both the fingerprint region as well as the low frequency Stokes transitions for L-asparagine; note the three dominant bands below 200 cm^{-1}. 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.



i-Raman Plus



BAC 102 series E-Grade Probe

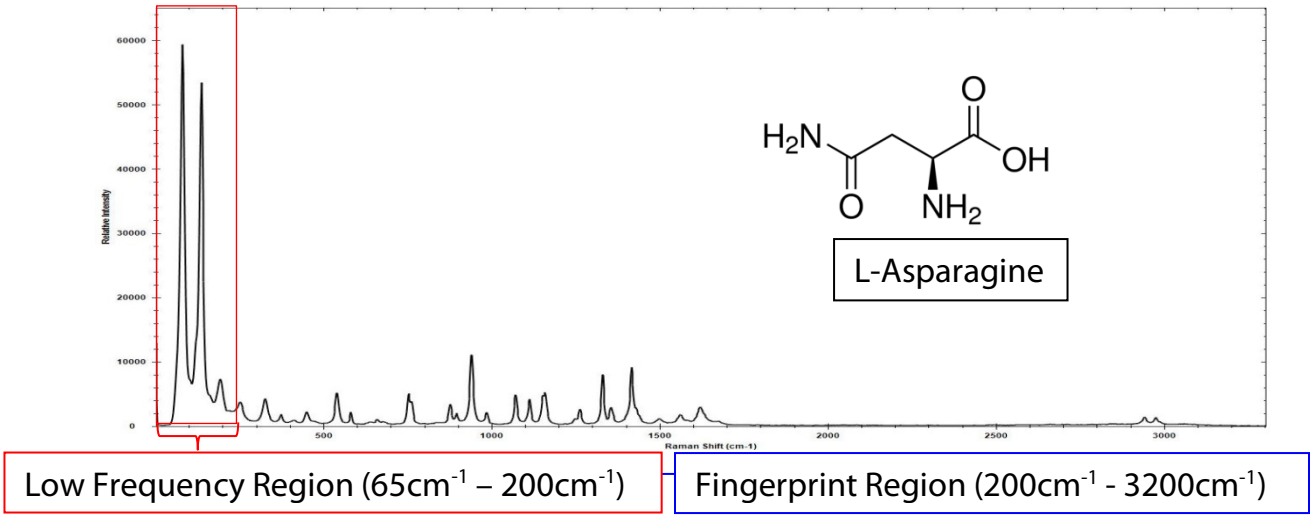


***Figure 1:** The i-Raman Plus 785nm system using an E-grade probe was used to collect the low frequency spectra of L- Asparagine with a total integration time of 1200ms.*

Experiment

Low Frequency Raman Instrumentation

The instrument used to measure the samples was B&W Tek's i-Raman Plus portable Raman spectrometer that utilizes a patented CleanLaze® 785nm laser excitation with a linewidth of less than 0.2nm and maximum power output of 300mW. The system is also equipped with a sensitive TE cooled back-thinned CCD. The system is connected to a BAC 102 E-grade probe utilizing proprietary technology enabling coverage between the spectral range of 65cm^{-1} – 3200cm^{-1} with a spectral resolution of 4.5cm^{-1}. The Raman spectra were collected at room temperature and the integration times ranged from 100 milliseconds to 10 seconds using 300mW laser power.

Polymorph Detection

A primary concern for the pharmaceutical industry during drug development, manufacturing and quality control is determining the structural form of their Active Pharmaceutical Ingredients (API). APIs exhibit polymorphism, which is characterized as having identical chemical compositions but different solid state structures that may affect the bioavailability and therapeutic index, which could lead to compromised efficacy of any final drug product[2] if the wrong form is used. There are also pseudo-polymorphs that involve solvents suspended in a lattice structure. Figure 2 is an example of the pseudo-polymorph D-glucose and demonstrates the ability for the E-grade probe to detect the differences between the crystalline structures and hydrate form at frequencies below 200cm^{-1}. The addition of the low frequency region increases the detection sensitivity and expands the ability to differentiate between very similar materials.

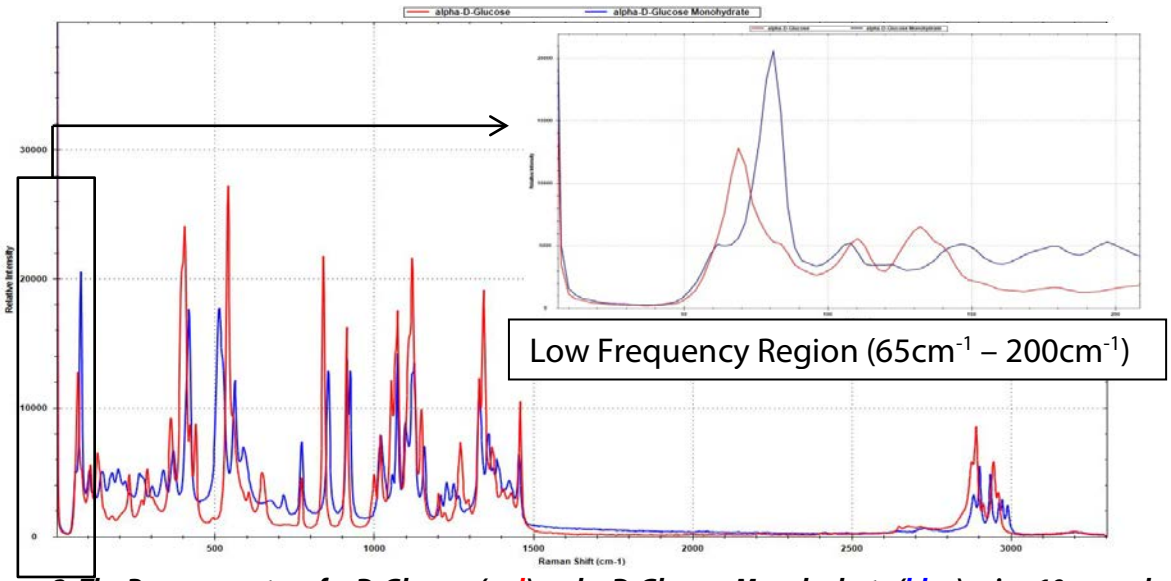


Figure 2: The Raman spectra of α-D-Glucose (red) and α-D-Glucose Monohydrate (blue) using 10 second integration time. Note the significant difference between the two pseudo-polymorphs within the low frequency range of 65cm^{-1} - 200cm^{-1}.

Monitoring Phase Change

Another important application in the industry is the ability to monitor phase changes or crystallization of chemical processes. An example that demonstrates the ability for the E-grade probe to monitor phase changes can be shown below using Sulfur. A sample of solid α- Sulfur was deposited onto an aluminum tray and heated with a hot plate while the Raman spectra was collected using the low frequency E-grade probe couple to the i-Raman Plus, using 100% laser power (~300mW) and 100 milliseconds integration time for both the solid and liquid phase. After the sample was heated above its melting point at 115.2C°, the low frequency peak at 83.6cm^{-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.

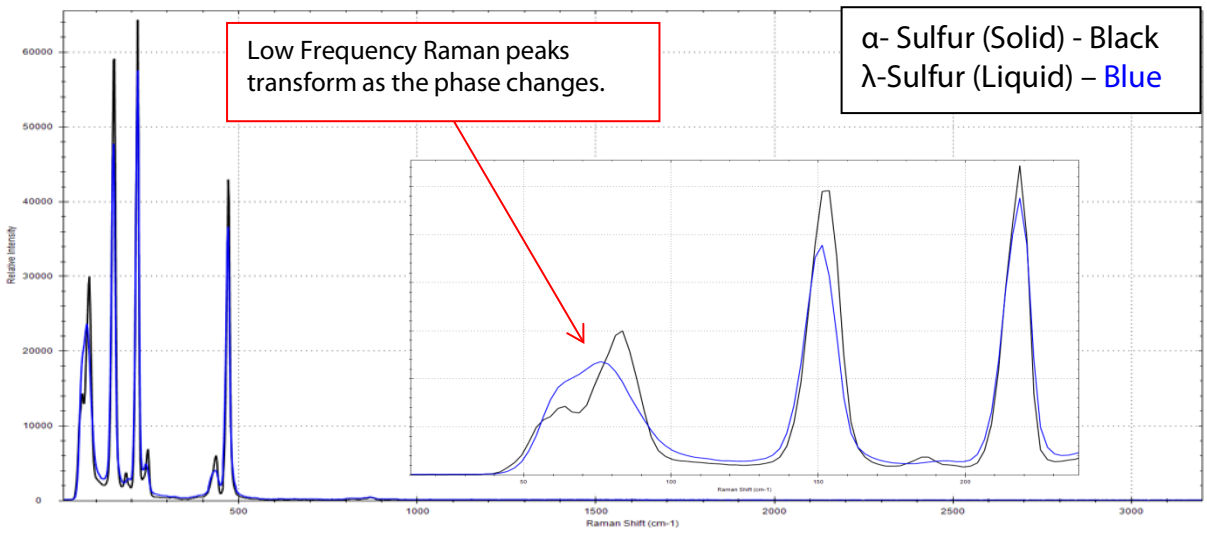


Figure 3: The Raman spectra of Sulfur transitioning from the α-crystalline form to the λ- liquid form using 100 milliseconds integration time. Note the significant broadening in the peaks located in the low frequency region between 65cm^{-1} - 200cm^{-1}.

Conclusions

The i-Raman Plus 785nm Raman spectrometer coupled with the low frequency E-grade probe can be a valuable tool in applications requiring low frequency detection down to 65cm^{-1}. The ability to characterize polymorphs and solvate forms will allow better control in the 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[3], carbon nanotubes[4], solar cells and an assortment of minerals, pigments and gemstones.

References

1. A.M.R. Teixeira, P.T.C. Freire, A.J.D. Moreno, J.M. Sasaki, A.P. Ayala, J. Mendes Filho, F.E.A. Melo. "High-pressure Raman study of L-Alanine Crystal". Solid State Communications. 2000. 116 (7): 405-409.
2. P.J. Larkin, et al. "Polymorph Characterization of Active Pharmaceutical Ingredients (APIs) Using Low-Frequency Raman Spectroscopy". Applied Spectroscopy. 2014. 68 (7):758-776.
3. E. Smith, G. Dent, Modern Raman Spectroscopy-A Practical Approach. Hoboken, NJ. John Wiley and Sons. 2005.
4. M.J. Pelletier. Analytical Applications of Raman Spectroscopy. Oxford, UK: Blackwell Science Ltd. 1999.

Additional Resources

i-Raman Plus datasheet
BAC102 datasheet
Further reading: in-situ Monitoring of Moisture-Induced Polymorphic Transition Using Raman

If you have any questions about the application or would like to know how Raman would work for your application, please contact us at appnote@bwtek.com or call us at +1 (855) 297-2626 to speak with an expert.

