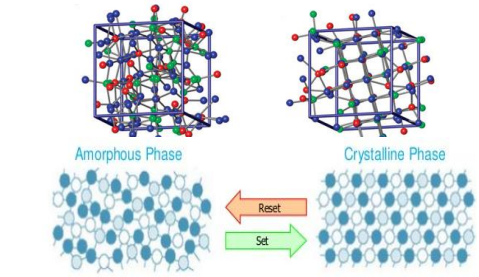
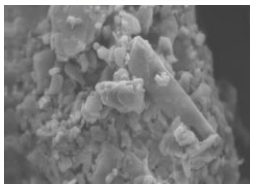
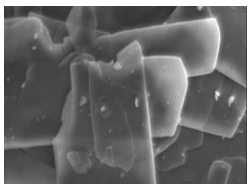
Crystallization and Reaction Monitoring

Challenge:

Measurement and control of reactions, crystallization rates and/or amorphous states is increasingly important across the chemical, pharmaceutical and electronics industries. Clear, unambiguous determination of material structure (such as polymorphs), crystallinity, and phase is essential to chemical process development, formulation, stability testing and material characterization. Most measurement modalities require special sample preparation for offline, destructive analysis and can't provide real-time feedback.





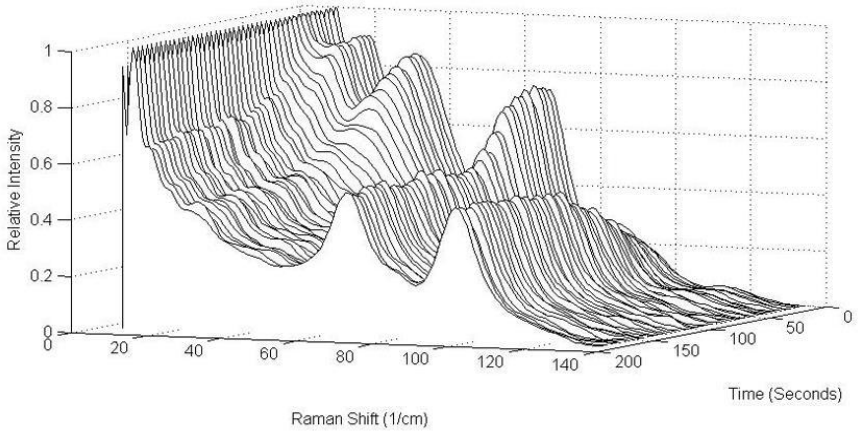


Traditional Solutions:

Observing structural or phase changes in a material can be accomplished several ways. ***Raman spectroscopy*** is used to observe small band shifts in the "fingerprint" region (200-1800 cm^{-1}), however these reflect subtle shifts in functional groups and are often difficult to detect during phase or polymorphic changes. ***X-ray diffraction (XRD)*** techniques yield extremely quantitative and conclusive analysis, but require expensive equipment and destructive off-line testing. ***Terahertz (THz) spectroscopy*** can easily differentiate structural shifts, as these signals correspond to large scale motions in the molecular and inter-molecular structure, however THz spectroscopy has limited spectroscopic range, is expensive, sensitive to moisture andrequires special sample preparation.

Ondax Solution:

Ondax ***THz-Raman®*** systems extend the range of traditional Raman spectroscopy to the terahertz/low frequency regime, where differentiation of inter- and intra-molecular structures that correlate to material structure and phase can be clearly seen. THz-Raman spectra can also be used to differentiate polymorphs, co-crystals, contaminants, synthetic pathways, crystal defects and as a real-time monitor of molecular structure. Anti-Stokes signals also add to Raman intensity and improve SNR. ***Ondax THz-Raman® systems provide fast, unambiguous real-time measurement of crystallization and phase characteristics, while preserving the complete Raman "fingerprint region" for chemical identification.***



Features / Benefits

- ***Fast, real-time monitoring of material structure and phase changes***
- ***In-situ, non-destructive and requires no sample preparation***
- ***Quantitative measurement of amorphous/crystalline mixtures***
- ***Simultaneous chemical AND structural analysis***
- ***Compatible with existing Raman spectrometers***
- ***Simple, compact, cost-effective***
- ***Available in probe , benchtop or microscope configurations at 532, 633, 785, 850, 976 &1064nm***

Low frequency spectra can be used to monitor transformation of polymorphs.

The waterfall plot at left[1] shows anhydrous theophylline before and after its transformation within a slurry into a monohydrate, over a period of approximately 100 seconds.

[1]Data courtesy Clairet Scientific, Ltd.

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More info at www.ondax.com

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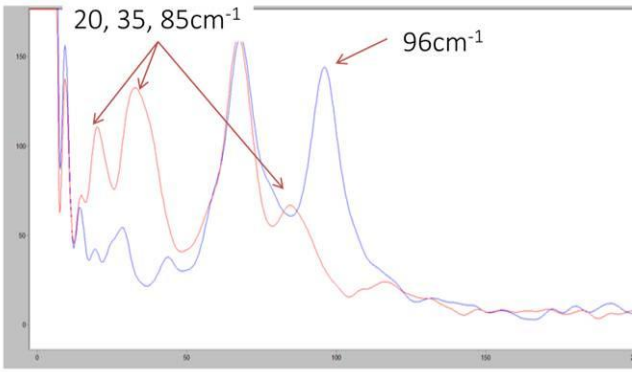
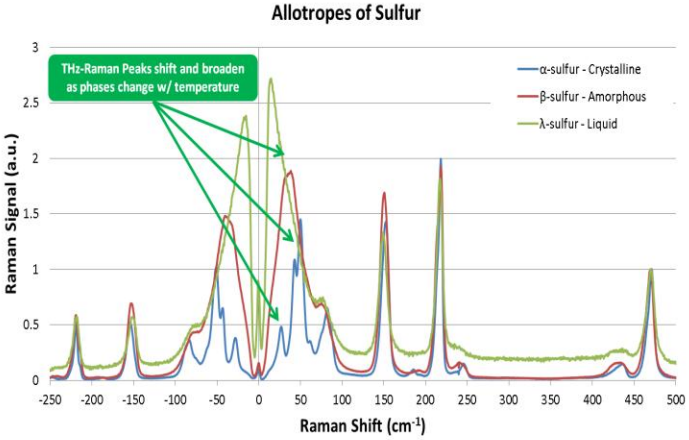
Structural PLUS chemical composition measurements with the same system

Low frequency/THz-Raman measurements are a clear indicator of material structure. The figure below left shows low frequency spectra of anhydrous theophylline (Form II) in a slurry, before and after its transformation into a monohydrate (Form M). Spectra collected at the start and finish (t=2s red and t=200s blue) show the disappearance of peaks at 20, 35 and 85 cm^{-1} in the anhydrous spectrum, and the appearance of a new peak at 96 cm^{-1} in the spectrum of the monohydrate.

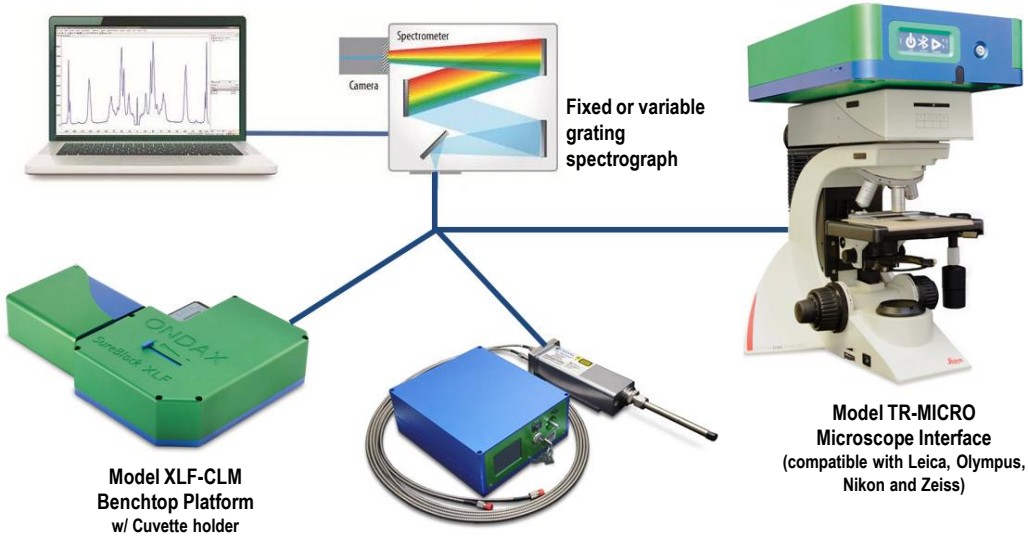
Phase changes in sulfur are shown below right. The crystalline phase exhibits sharp peaks, indicating a high degree of order in the structure, whereas the the amorphous and liquid phases become increasingly disordered, leading to a broadening and ultimate disappearance of the distinctive peaks.





Ondax's patented[2] **THz-Raman® Spectroscopy Systems** extend the range of traditional Raman spectroscopy into the terahertz/low-frequency regime, exploring the same range of energy transitions as terahertz spectroscopy – without limiting the ability to measure the fingerprint region. This enables ***simultaneous analysis*** of both molecular structure and chemical composition for advanced materials characterization.

All **THz-Raman®** systems are compact, robust, plug-and-play platforms that deliver incredible speed, throughput and ease of use, all at an extremely affordable price. With a broad selection of excitation wavelengths from 488nm to 1064nm, optional polarization control and a wide variety of sample interfaces, there is a THz-Raman® solution for any application.



[2] *US Patents 8,184,285 and 9,986,407*

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