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), degree of 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 "chemical fingerprint" region (200 to 1800 cm^{-1}), however these reflect subtle shifts in functional groups and it is often difficult to detect phase or polymorphic form changes. X-ray diffraction (XRD) techniques have been the industry standard, but require expensive equipment and destructive off-line testing. Terahertz (THz) spectroscopy can differentiate structural changes but is expensive, sensitive to moisture and requires special sample preparation.

Coherent Solution

Coherent's THz-Raman® systems extend the range of traditional Raman spectroscopy to the "structural fingerprint" (also referred to as low frequency, see Fig. 1) region very close to the laser line (5 to 200 cm^{-1}) that corresponds to terahertz vibrational energies while simultaneously collecting "chemical fingerprint" signals. Like ordinary Raman, the process is non-destructive and can be used for real time, in situ process monitoring. As materials change from disordered to highly ordered (e.g. amorphous to crystalline), the low frequency bands shift and become sharper. When changes in polymorphic form, co-crystalline bonds are created or broken, or the degree of hydration is changed, the low wavenumber bands change as well. With up to 10X stronger signals than standard Raman, THz-Raman systems provide fast, unambiguous real-time measurement of crystallization and phase characteristics.

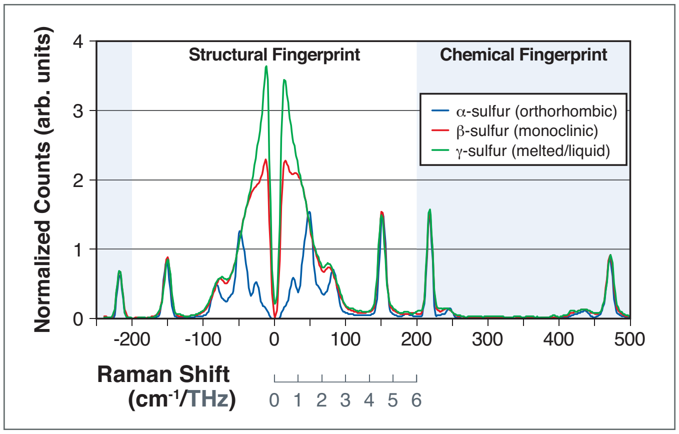

Figure 1. Phase changes in sulfur: The orthorhombic crystalline phase exhibits sharp peaks, indicating a high degree of order in the structure, whereas the the monoclinic form and liquid phases become increasingly disordered, leading to a broadening and ultimate disappearance of the distinctive peaks.

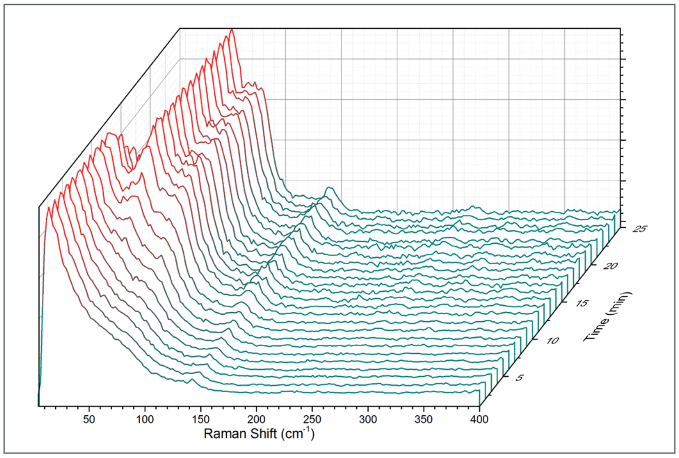

Figure 2. To simulate dynamic process measurements, a commercial Advil tablet was heated then cooled at room temperature while monitoring the THz-Raman spectra. The active ingredient was initially in an amorphous state, then transitioned to the stable crystalline form after ~15 minutes.

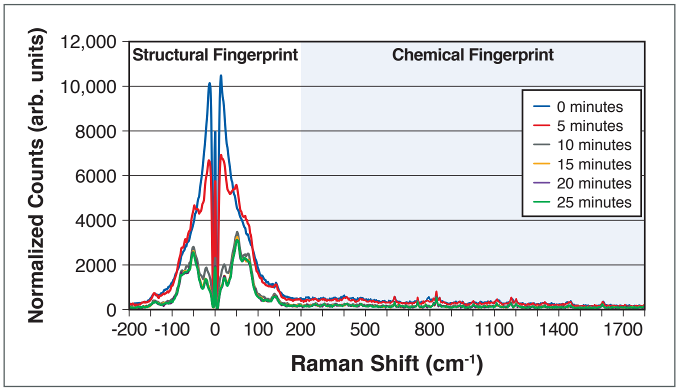

Figure 3. Individual spectra plotted in 5 minute increments for the dynamic process in Figure 2 showing the spectral transition as the tablet cools.

Application Field

Crystallization, polymorphism, phase monitoring, degree of crystallinity, polymorphic transformation, real-time non-destructive structural analysis, low-frequency THz-Raman spectroscopy.

Contact

Email: tech.sales@coherent.com
For more information, visit: http://www.thz-raman.com