DETERMINATION OF SENSITIVITY
TSI ASSURx®
HANDHELD RAMAN ANALYZER

Abstract

In this application note, the method to determine -CO_3 limit of detection and measurement sensitivity is applied to our pharmaceutical handheld system, the ASSURx G7 Raman Handheld Analyzer. Hardware performance characteristics are then compared to those of the TSI ChemLogix® ProRaman-L desktop system.

Introduction

As discussed in the previously mentioned application note, sensitivity of Raman spectroscopy is a hard factor to pin down. It is a function of laser wavelength, excitation cross section of the analyte, laser power on target and acquisition time. By holding some of these variables constant (laser excitation wavelength and power, acquisition time, analyte), we can determine differences in sensitivity of various hardware sets.

In this brief application note, we compare the previously documented results on the desktop instrument with those acquired on the newly-released ASSURx G7 analyzer. The ASSURx analyzer, as a handheld instrument is functionally different from the ProRaman-L, with slightly lower maximum laser output and a shorter spectral range. The detector is also not cooled as deeply as the one in the ProRaman-L.

Figure 1. Prepared samples of $CaCO_3$ in NaCl.

Here we will describe our method for comparing measurement characteristics of different Raman systems applied to a TSI ChemLogix handheld instrument. This method uses five samples from 0 to 4.5% $CaCO_3$ in finely ground NaCl powder to acquire spectra dominated by the carbonate v_1 stretching feature at 1082 cm^{-1}. The background subtracted peak height of this feature is plotted against concentration to generate a calibration curve that is used to establish both sensitivity (counts per %$CaCO_3$ in NaCl) and the limit of detection of the carbonate peak (LOD).

Sample Preparation

Acros Organic $CaCO_3$ (calcium carbonate, CAS 471-24-1) was used without additional preparation. Sigma-Aldrich ACS grade NaCl (sodium chloride, CAS 7647-14-5)) was ground with a mortar and pestle to a fine powder that was used as a non-Raman active support for the $CaCO_3$. Both components were weighed on an analytical balance and combined, then mixed again thoroughly with the mortar and pestle. Generating similar particle sizes in both of the mixture components is critical if they are to remain mixed.

These samples were then introduced to small glass chromatographic vials and submitted to Raman analysis.

Experimental Conditions and Calculations

This work was performed using a TSI ChemLogix ProRaman-L and an ASSURx G7 instrument, both with excitation lasers operating at 785 nm. 10 spectra of each sample were collected. The ASSURx analyzer was operated on the high power setting (240 mW), the ProRaman-L applied 290 mW of laser power on sample. The data from the ProRaman-L instrument was collected with an acquisition time of 60 seconds. The ASSURx analyzer automatically selects an optimized acquisition time, which was about 15 seconds for most of these samples, but varied slightly from sample to sample. To enable comparison

Figure 2. Raman spectra of 4.48 wt% $CaCO_3$ in NaCl collected with ASSURx G7 analyzer.

with the ProRaman-L, signal levels were mathematically scaled to 60 seconds. No averaging was performed during data acquisition.
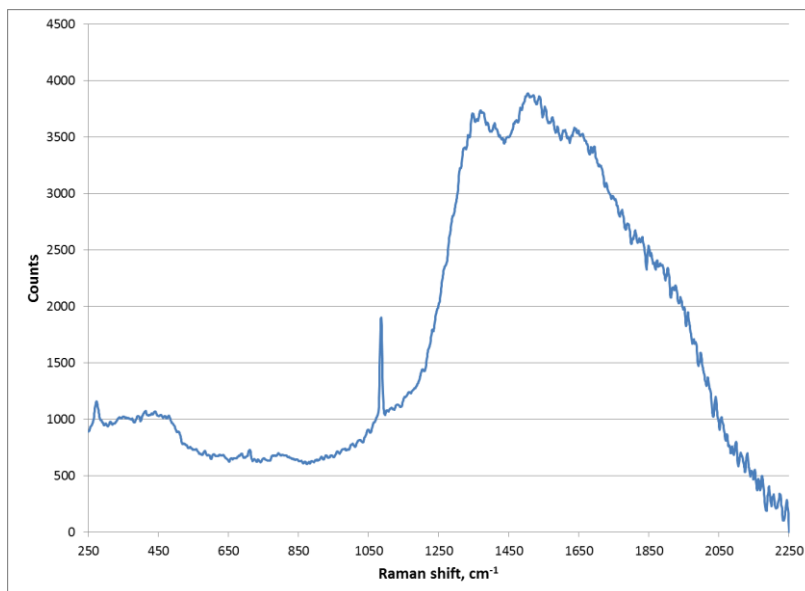
An example raw spectrum (4.48% $CaCO_3$ in NaCl) is shown in Figure 2. This data was taken off the handheld instrument in the form of an .ept file which also contains HQI information when the device is used in material identification. The .ept file is read into the ASSURx Reporter software and a .txt file of the spectrum saved for import into Microsoft® Excel®. In this data, the background (including broad features from the glass vial used to contain the samples) was not corrected, as in the ProRaman-L data. Peak heights of the spectra with the background removed were used to create a calibration curve (counts vs. $CaCO_3$ wt% in NaCl) that was fit to a line (R^2=0.9968). These features are shown in Figure 3.
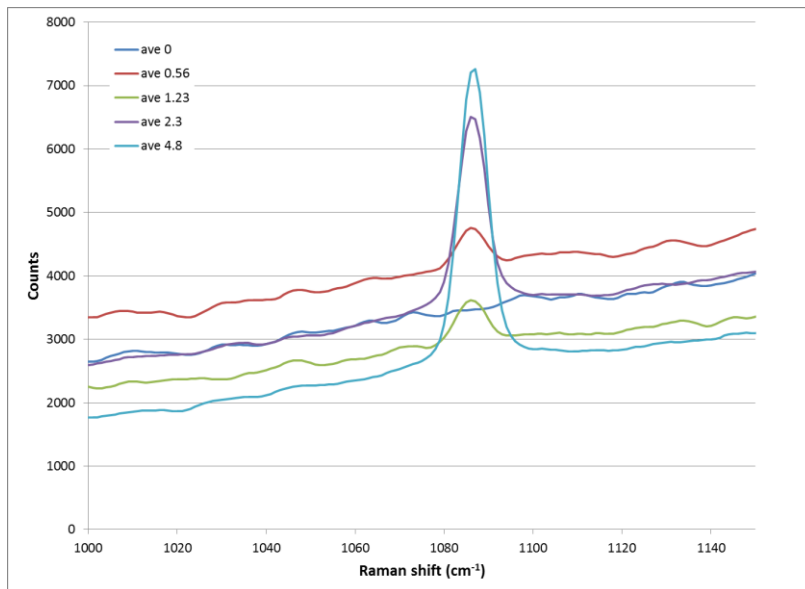

Figure 3. ASSURx analyzer spectra of a range $CaCO_3$ concentrations in NaCl. These peak heights were used to generate the calibration curve in Figure 4.

The error bars shown on Figure 3 are 2σ bars. It is clear from experiments with calibration material that is not well mixed that their extent is caused more by the difficulty of fully homogenizing the sample material and keeping it mixed than by instrument instability.

The calibration curve is shown in Figure 4. The linear fit provided by Microsoft® Excel® spreadsheet program was used to model each data point, and then residuals, squared residuals and root mean square error (RMSE) were calculated (*see Calculation Details*). The limit of detection is defined for these purposes as 3.3*RMSE/slope, and for this method described above, LOD=0.3 wt % $CaCO_3$ in NaCl. The sensitivity of this analysis is then 605 background corrected counts per 1 wt % $CaCO_3$ in NaCl.

Calculation Details

In this example, the line of best fit has been calculated by Excel® program and is displayed on the graph (y=604.62x - 8.0852). This equation is used to calculate the y values associated with the model (given the known concentration, x, values). The residuals are found by subtracting the real data from the modeled set. The root mean square of the error (RMSE) is found by squaring the residuals, adding them together, dividing by the number of measurements and then taking the square root of the sum. The Excel® command line for this

Figure 4. Calibration curve of $CaCO_3$ in NaCl with ASSURx G7 Analyzer

process is =SQRT(SUM(range)/N). RMSE is then used to finally calculate the LOD by multiplying it by 3.3 and dividing the result by the slope of the best fit line.
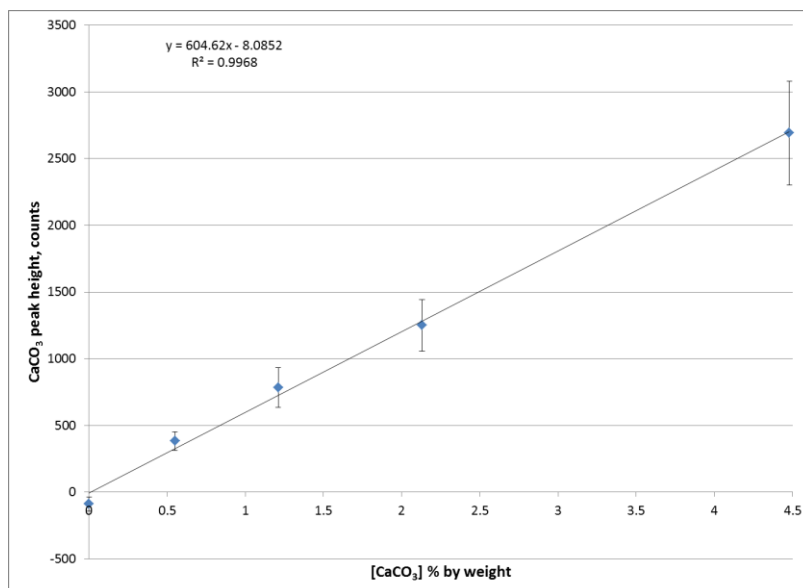
The measurement characteristics of the ASSURx analyzer can now be compared with the desktop unit, the ProRaman-L.

Instrument	Limit of Detection	Sensitivity
ProRaman-L	0.07 wt % $CaCO_3$ in NaCl	757 counts per 1% $CaCO_3$ in NaCl
ASSURx G7	0.3 wt % $CaCO_3$ in NaCl	605 counts per 1% $CaCO_3$ in NaCl

This table contains quantified performance comparison between the desk-top system and the newest of the ChemLogix handheld Raman instruments.

The differences in the hardware configuration are doubtless responsible for the differences in the LOD and the sensitivity. Below is a table describing the measurement conditions. The detector temperature (and; therefore, dark current) probably drives the limit of detection difference. The ProRaman-L detector is cooled thermoelectrically to -60 C°; the ASSURx analyzer is not as deeply cooled.

Instrument	Laser Power	Spectral Range	Nominal Resolution
ProRaman-L	290 mW (max)	100 to 3300 cm^{-1}	8 to 10 cm^{-1}
ASSURx G7	240 mW (max)	250 to 2350 cm^{-1}	6 cm^{-1}

Conclusion

This simple, safe and convenient technique can be used to compare sensitivities of Raman instruments, especially useful in helping decide in the process of purchasing new hardware. Use of this technique should make clear the measurement performance differences between similar instruments, and enable the purchaser to make informed decisions. No more guessing about relative performance in Raman spectrometers is needed.