## Confirming Product Consistency using Raman Microscopy

Determining the relative amounts or concentrations of components in a given system is critical to ensuring product quality and performance. Traditional methods to calculate the relative concentrations typically involve time and sample preparation intensive techniques such as HPLC or GCMS. Furthermore, any spatial information or solid structural information is lost due to the destructive nature of HPLC separation. Confocal Raman microscopy, however, is able to overcome many of the limitations presented by traditional methods, and quantitative Raman imaging can address the needs of industries ranging from pharmaceutical API determination to food and beverage characterization. Finally, throughput is high and sample turnaround can be achieved in a manner of minutes.

Raman spectroscopy has become an invaluable tool to analyze the spatial and chemical composition of materials. With a submicron laser spot size using a 532 nm laser source, surface area maps can be generated with a lateral resolution of 360 nm in minutes. Images can be generated with a pixel number limited only by the processing power of the computer. Since each pixel in the resulting image map corresponds to a unique spectrum, or mix of spectra, the number of pixels associated with a particular spectrum can be determined. From there, a weighted percent (based on the relative number of pixels) can be calculated for each species of interest.

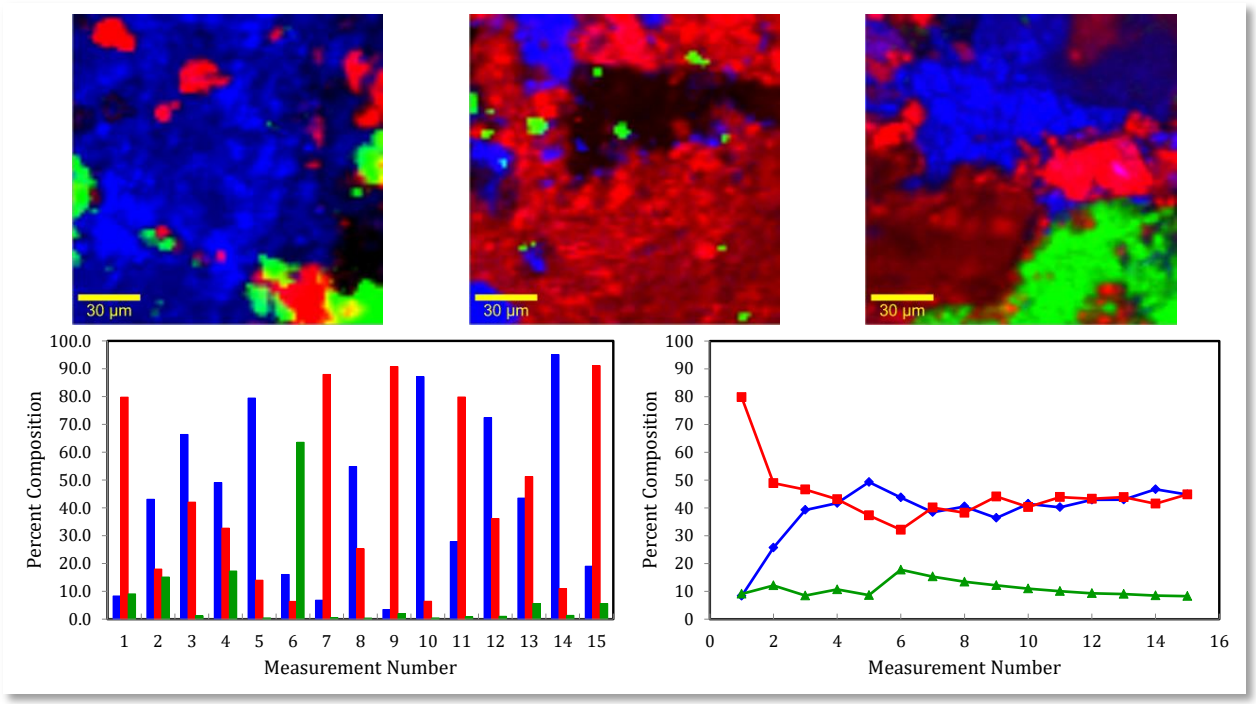


Figure 1. Representative Raman images of three different areas of a pain relief tablet (top), API compositions for each individual area (bottom, left), and the running averages of each API (bottom, right). Color code: red (acetaminophen), blue (aspirin), green (caffeine).

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To reach optimal and representative results, images may be continually obtained until the running average of each component stabilizes.

In this application note, a tablet is used to illustrate how Raman microscopy can be used to quantitate the amounts of substances present in a system. To determine the relative quantities of each of the active pharmaceutical ingredients (APIs: acetaminophen, aspirin, and caffeine) present in the pain relief tablet, 15 area maps were generated. Each area map covered an area of 150 µm x 150 µm at 75 pixels x 75 pixels (5625 total pixels each), and the integration time was 74 ms. Each scan took approximately 8 minutes, and the total acquisition time for all 15 scans was 120 minutes. The percentage of each API for each individual area map is shown in Figure 1 (bottom, left) along with the cumulative running average of each API (bottom, right). The relative amounts of acetaminophen, aspirin, and caffeine were determined to be 42 % ± 2 %, 45 % ± 2 %, 11 % ± 1 %, respectively. These values agree well with the packaging label, which indicated the relative amount of each API is 44 %, 44 %, 12 %, respectively.

Determining the relative amounts of components present in a system is critical to ensuring product quality and performance. Naturally, the above process could be repeated for almost any solid that is composed of a variety of constituents. Furthermore, not only can Raman spectroscopy determine the relative amounts of the individual components of copolymers, food ingredients, and tablets, but each image also captures the spatial arrangement of each component in the product.