

# PHARMACEUTICALS

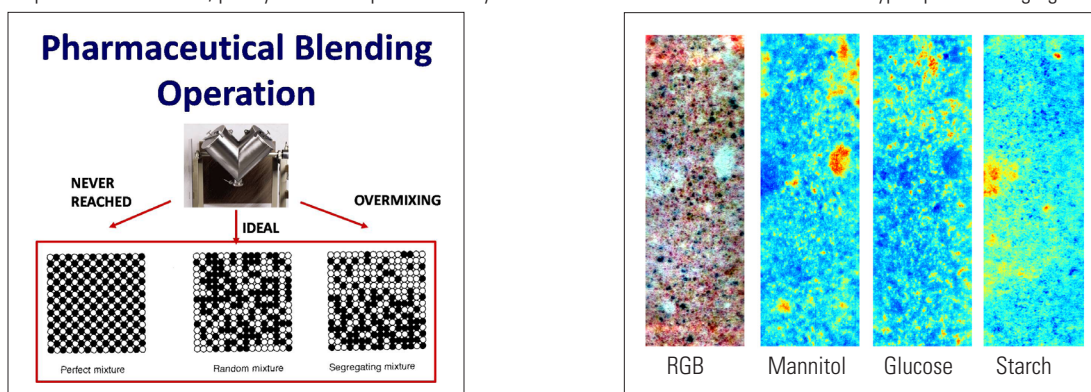
## Hyperspectral and Chemical Imaging

Chemical imaging is the application of hyperspectral imaging to identify and quantify chemical components of a sample or product and its dispersion or homogeneity. Chemical imaging typically uses the near-infrared (NIR) or short-wave (SWIR) infrared ranges, which contain information about chemical bonds, in contrast to hyperspectral imaging, which uses any wavelength range, from visible to long-wave infrared. Organic chemicals that comprise most pharmaceutical products have unique spectra in the NIR and SWIR ranges. Spectral information allows identification and quantification of chemical components within a sample. Chemical imaging is used in many areas of pharmaceutical research and industry, including blending, tablet production monitoring, and counterfeit product identification. Application examples are described below.

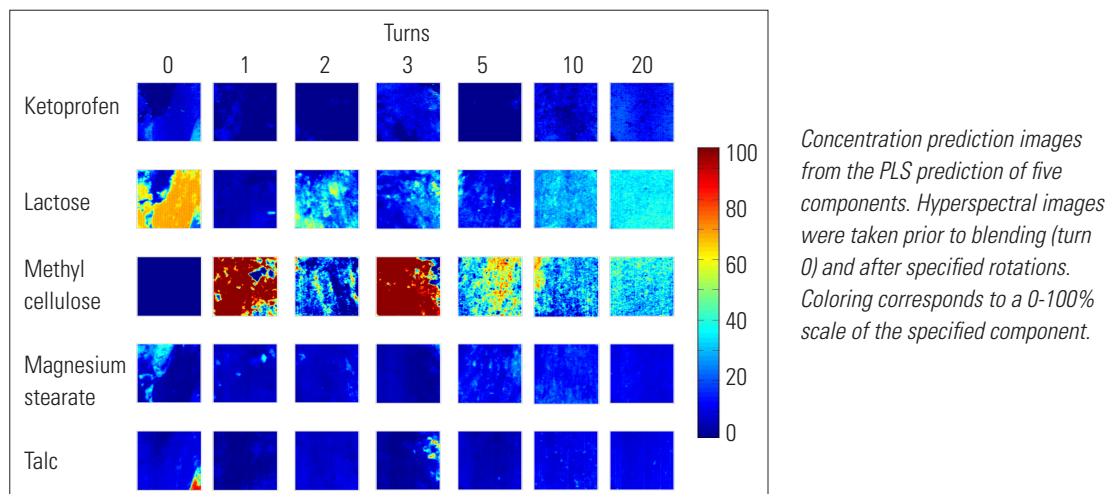
### Blending

Chemical imaging is used in the pharmaceutical industry for process validation. FDA regulations require control of the drug content at various stages of the manufacturing process, including granulation and final blending. Statistical sampling for content uniformity assessment is straightforward, but in practice, there is a potential for sampling bias when only a small sample volume is extracted (Berman, 2005). Pharmaceutical companies are discovering that chemical imaging is an effective and efficient way to detect problems in blending and tableting (El-Hagrasy, 2001, Lyon, 2002).

For several years, blending has been monitored using the near-infrared region to non-invasively determine the concentration of an active ingredient in a sample (Ma, 2007). The challenge is that by taking one single-point measurement at a time (for example during one rotation of the blender), the distributions of the ingredients are not revealed. The image (below left) illustrates ideal blending. Multiple components can be predicted from the same hypercube of data. The images (below right) are calculated concentration maps of three different, poorly mixed components. They demonstrate the rich detail available from hyperspectral imaging.

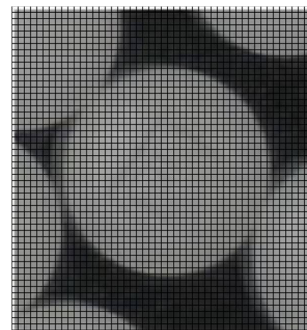
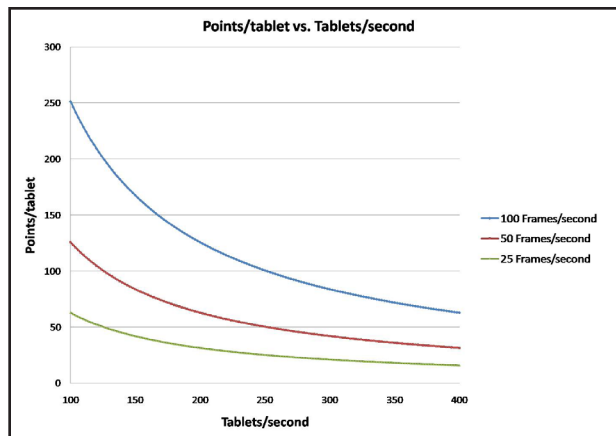


One hyperspectral image datacube can detect areas of poor blending, the location of high concentration pockets of particular constituents, as well as the progression of the blending. The predicted images for the first few turns of an experimental blend, taken after each rotation of the blender, are shown below (Kemeny, 2010).



## Tablets

Pharmaceutical tablets can be monitored on the production line with hyperspectral imaging. To establish the possible optical coverage at real production speeds, the relationship between the speed of tablets measured and the resolution of the image is plotted below in a SWIR camera example (320 pixels per sample width). For this calculation, it is assumed that the tablets are of uniform diameter and arranged in a square pattern. The hyperspectral camera operates with the push-broom method, collecting one line of sample data in each frame. At 100 frames per second, for example, it is possible to image 200 tablets per second with a spatial resolution of 125 pixels per tablet. An approximation of the image points per tablet is shown below. With fewer measurement points on each tablet, the number of tablets covered can be increased even further. As a screening tool, uncoated tablets can be measured to detect uneven distribution of ingredients, whereas coated tablets can be measured to check for potentially uncoated or unevenly coated areas.



Spatial resolution on tablet imaged with SWIR hyperspectral camera

## Counterfeit Identification

Identifying counterfeit products is extremely important in the pharmaceutical industry, as the number of counterfeit drug products has grown exponentially in recent years. Counterfeit drugs have serious potential health risks to the consumer, and can also jeopardize the reputations of pharmaceutical companies. (Puchert, 2009) Hyperspectral imaging combined with chemometric data analysis is a useful method for identifying off-specification products. Hyperspectral cameras can be placed over a moving line of products to efficiently scan and report counterfeits in real-time, or products can be measured individually off-line.

Chemical imaging provides several advantages over older methods of identifying counterfeit pharmaceuticals. In contrast to chromatographic assays and dissolution testing, chemical imaging is fast and non-destructive. (Dubois, 2007) Researchers at the Institute of Pharmacy and Molecular Biotechnology in Germany demonstrated that near-infrared chemical imaging is an innovative, effective and non-destructive way to detect counterfeit tablets by discovering differences between amount and spatial distribution of ingredients within a genuine or counterfeit tablet. (Puchert, 2010)

## References

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