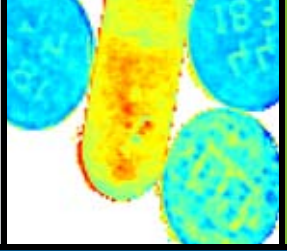
middleton research

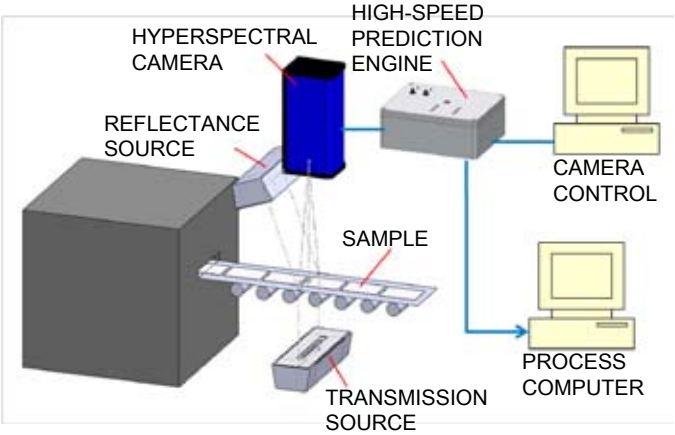


APPLICATION NOTE

Monitoring of Continuous Manufacturing

Hyperspectral Imaging for Pharmaceutical Products

Pharmaceutical products can be monitored during manufacturing using advanced hyperspectral imaging technology (HSI). HSI technology is ideal for non-contact/non-destructive, on-line analysis of mass-produced pharmaceutical products such as transdermal patches or films, tablets and blends. A push-broom camera focused on the manufacturing line images the moving product during production. By capturing both spatial and spectral information simultaneously, out-of-specification chemical composition, poor dispersion of ingredients and other nonconformances can be identified from spectral signatures. For many pharmaceutical products, the correct spatial location or pattern of the active ingredient within a formulation is crucial to achieve the desired effect. Immediate analysis of nonconformances during continuous manufacturing can reduce costs of manufacture compared to batch manufacturing and off-line analysis. HSI supports Process analytical technology (PAT) principles by controlling for factors causing out-of-specification products.



Basic components and setup of hyperspectral imaging on-line monitoring system, customized for specific applications

Applications

Middleton Research develops complete HSI monitoring systems for numerous industrial and pharmaceutical applications, such as the examples below.

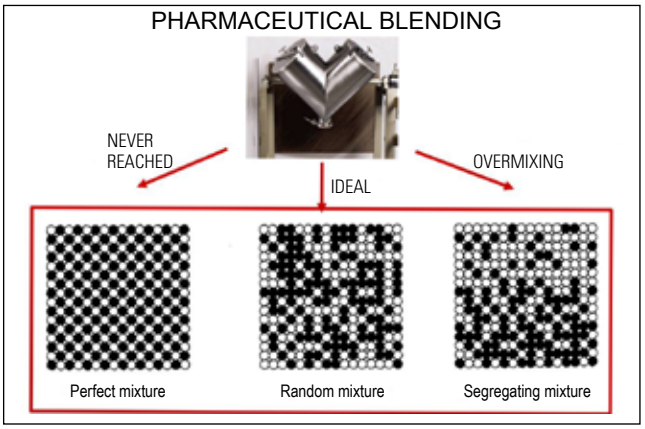
Films

Hyperspectral imaging systems can monitor films, transdermal patches, single or multi-layer webs, and wound dressings during production to ensure a uniform or correctly patterned API/excipient concentration distribution across the width of the material. HSI allows real-time, non-destructive full coverage compositional analysis. Transmission and/or diffuse reflectance can be applied, depending on the spectral characteristics of the product.

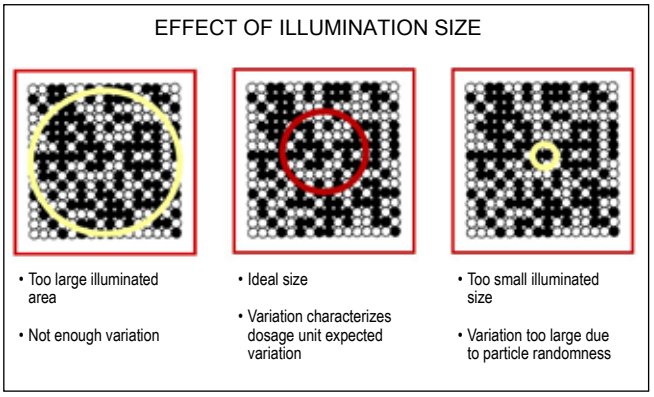
Films such as trans-dermal patches can be analyzed using on-line hyperspectral imaging

Blend Monitoring

Blending of pharmaceutical powders and mixtures is an important step in many manufacturing processes. Optimal blending can benefit from on-line/at-line uniformity monitoring. The diagrams below illustrate ideal blending and the dependence of the measurement of variation on the size of the illuminated sample. Historically, blending has been monitored using near-infrared spectroscopy. One of the difficulties of this method is the matching of the illuminated sample size to the unit dose. Another challenge is that when measuring only one point at a time, the ingredients' distributions are not revealed.

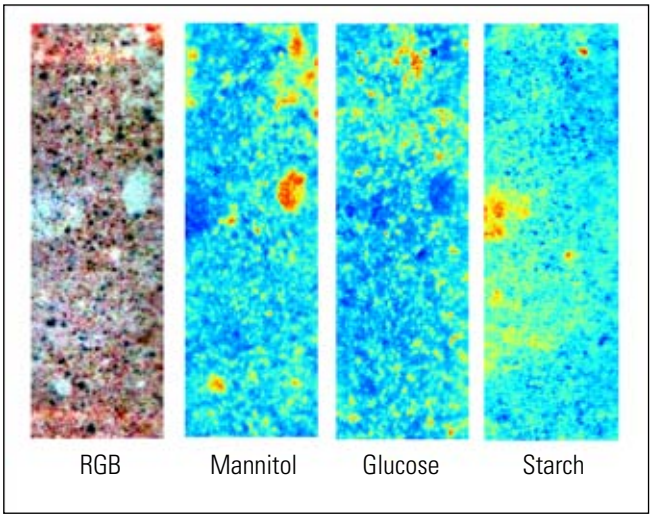


Hyperspectral imaging helps to achieve optimal blending



Limitations of single point measurement to determine blend quality

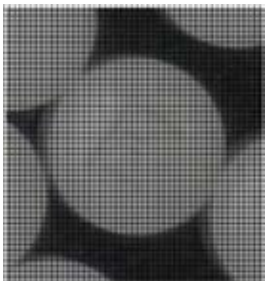
Hyperspectral imaging adds spatial information beyond traditional NIR spectroscopy, and allows simultaneous measurement of multiple unit doses. It is also possible to calculate the average concentration across a unit dose and compare the maximum concentration range of equivalent areas. The following images are calculated concentration maps of three different, poorly mixed components. One hyperspectral snapshot allows detection of areas of poor blending, the location of high concentration pockets of particular constituents, as well as the progression of the blending.



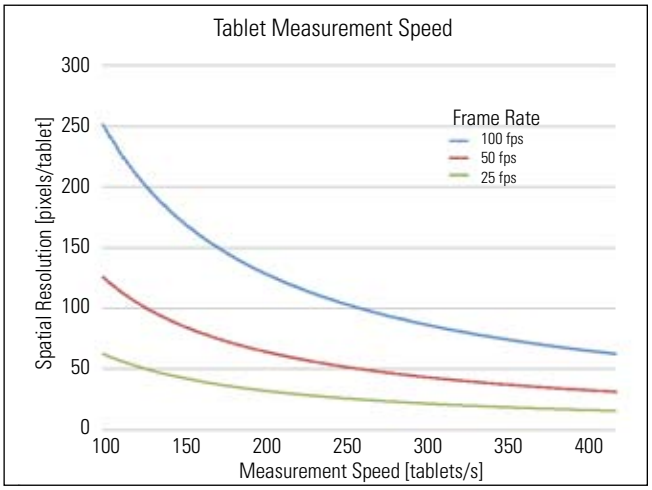
Spectral images and RGB of a three-component sample showing uneven blending

Tablets

High-speed quality monitoring can be performed on-line to evaluate tablet uniformity and coating thickness. To quantify spatial coverage at manufacturing speeds, the relationship between the speed of tablets measured and the resolution of the image is depicted in the graph below for a Specim SWIR push-broom camera collecting one line of sample data in each frame, 320 pixels per line. For this calculation, tablets are assumed to be of uniform diameter and arranged in a square pattern. For example, at 100 frames per second, 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). With fewer measurement points on each tablet, the number of tablets covered could be increased even further.



Spatial resolution on tablet imaged with SWIR hyperspectral camera



Relationship between resolution of tablet image (points/tablet) and monitoring speed (tablets/second) using a Specim SWIR camera with 320 spatial pixels per line

Complete custom hyperspectral systems

Middleton Research staff works with you to address your unique quality monitoring challenges and design requirements. We develop a customized system that works best for your specific application. We create integrated systems including:

- Cameras optimized to the appropriate wavelength range, measurement speed and sensitivity
- Illumination systems, hyperspectral lenses and other optical elements
- Integrated software for data collection, processing, display, and process computer interface
- Mechanical components for referencing and camera mounting adapted to your current manufacturing system

Please contact Middleton Research or visit our website for further information. www.middletonresearch.com