

Process Analytical Technologies: Products and Services

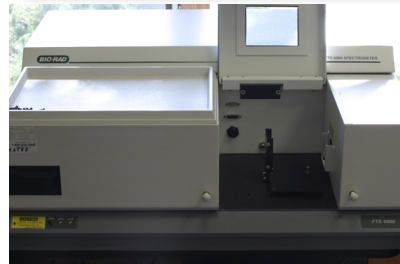
Process Analytical Technologies

Middleton Research is announcing its Process Analytical (PAT) and Quality by Design (QbD) services to help pharmaceutical quality control and manufacturing organizations outsource part of these development activities. We are focusing on non-destructive optical testing from visible to infrared, from machine vision projects to hyperspectral imaging. We develop special instruments, sampling devices and custom software as needed.

Laboratory and Analytical Services / Method Development



Middleton Research provides consulting and technical services for a wide range of applications. We work with customers to develop instrument systems, software solutions and analytical methods, or perform feasibility measurements that address specific challenges.

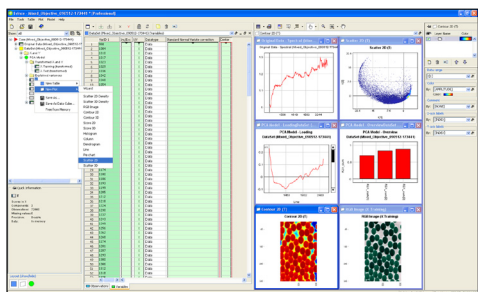


Process analytical problems are in search of the best methods that are sensitive, selective, cost effective to be transferred from the laboratory to the process environment. Our laboratory is equipped with sophisticated analytical equipment including high performance near-infrared Fourier transform instrument with fiber optics, integrating sphere diffuse reflectance, heated and temperature controlled transmission cells. In the mid-infrared we can provide FTIR in transmission, reflectance, ATR, photoacoustic and microscopic measurements. Our experienced scientists can help you create infrared and near-infrared analytical methods for use in your laboratory setting, or we can perform the actual laboratory measurements and data analysis for you in our laboratory as well as methods that can be transferred to chemical imaging and/or to process environment.



Chemical Imaging & Hyperspectral System Integration

In addition to traditional analytical equipment for infrared and near-infrared applications, Middleton Research is working with hyperspectral imaging (HSI) cameras that cover wavelength ranges from visible to short-wave infrared. For many near-infrared spectroscopy applications, hyperspectral imaging can extend sample measurement to an entire surface area. Each point on the sample surface has its individual spectrum measured and can be interpreted to determine chemical identity or chemical composition. The visual representation of such information is called chemical imaging. The samples can be small or large, stationary, or moving with a constant speed on a conveyor or other transport system. Middleton Research provides



feasibility studies, measurements, to test this new technology

For hyperspectral data analysis, Middleton Research offers Evince™ Image. Evince software was specially designed to process hyperspectral images. Common image formats such as Envi, Mat, SPF, JPG, PNG, DAT, and RAW are easily imported into and processed in Evince's graphical user interface. Many

visualization types of both raw and processed data are available as analysis tools. Extraction of desired information and exploration of data cube is facilitated with graphical interactions



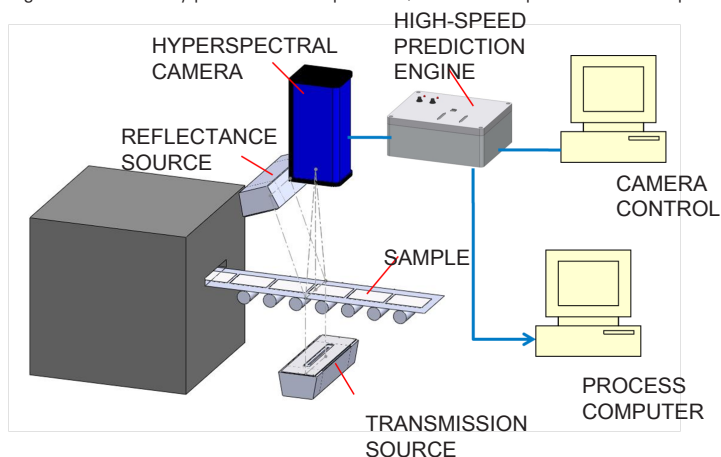
between data and plots. In addition, Evince provides many calculation and correction tools for multivariate image analysis.

Optimal use of hyperspectral cameras requires effective choice and configuration of illumination, imaging optics, filters and data processing software. Middleton Research works closely with every customer to design an integrated hyperspectral system that meets the unique demands of each application.



Process Analytical Systems

Middleton Research provides custom systems development and integration for on-line monitoring applications including films and patches, blends, and tablets. Pharmaceutical products can be monitored during manufacturing using advanced hyperspectral imaging technology. 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, off-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. Hyperspectral imaging supports Process Analytical Technology (PAT) principles by helping to control for factors causing out-of-specification products.

Complete on-line hyperspectral installations include the need for fast prediction software to match the high-speed camera output. The resulting data is transformed into a format that interfaces with the customer's process control computer for on-line monitoring and process adjustment. Middleton Research works with each customer to create a complete system to match the data analysis and process interface needs for each application.

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

Optical Standards & Recertifications

Middleton Research offers a wide variety of optical standards to meet your spectroscopy needs. The optical standards include an extended range near infrared wavelength standard, diffuse and absolute specular reflectance standards, and ATR validation standards. Middleton Research also offers recertification services for all of these standards as well as for NIR and IR linearity standards and IR wavelength standards.



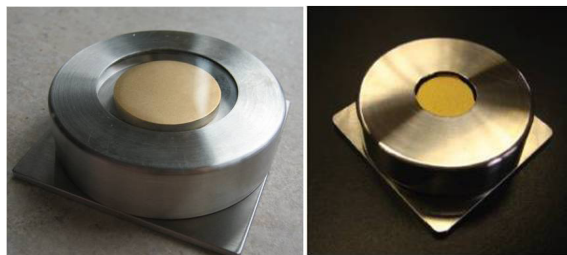
Special Sampling Devices

Middleton Research works with new unique patented FTIR photoacoustic gas, liquid and solid measurement systems and provides related applications and engineering services.

Among other sampling devices, Middleton Research has developed both a Transflectance



Liquid Cell and Paste Cell for easy sampling of viscous liquids on near infrared analyzers. Both cells offer reproducible optical pathlengths and quick application and cleanup. Should the analytical task require new sampling approaches, Middleton Research will select the best available analytical techniques and it is also able to develop new methods and sampling devices when necessary



Instrument Development / Custom Engineering

Middleton Research scientists and project managers collaborate with you and your engineering resources to develop product innovations in the areas of optical and analytical instrumentation and process analytical technologies (PAT).

Drawing on our extensive spectroscopic and industrial process analytical experience, Middleton Research provides contract engineering services to augment your in-house expertise. Our engineering staff can design new products or modify existing devices to optimally address your specific applications.

Our experienced staff is equipped with a variety of software tools, including SolidWorks for full 3-D modeling and mechanical design, Zemax optical design and simulation software for designing custom optical components and systems, Evince for hyperspectral image analysis, and numerous other spectroscopy and data analysis software programs. We are experienced in algorithm and user interface development for special software projects.

Quality System

Middleton Research has an internal quality system that follows ISO 17025 standards, and the facilities and the Quality System has been successfully audited by major pharmaceutical companies.

Personnel & Expertise

In addition to providing outstanding quality products, Middleton Research offers customers specific solutions by providing them access to our knowledgeable spectroscopic applications and engineering team. Our staff has a wide array of background and expertise, ranging from the fields of mechanical, optical, software, and computer engineering. By partnering with our customer's organization, we can work hand in hand with them to develop a clear understanding of their application needs and be there every step of the way to ensure the most comprehensive solution possible.

Publications

"Hyperspectral Monitoring of Continuous Pharmaceutical Manufacturing." *Transdermal Magazine*, July 2010.

"Comparative Performance Studies Between Tunable Filter and Push-broom Chemical Imaging Systems." *SPIE Proceedings*, March 2010.

"Novel Hyperspectral Prediction Method and Apparatus." *SPIE Proceedings*, March 2009.