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Imaging

Old Array, New Tricks

Imaging technique aids quality control for pharmaceuticals.

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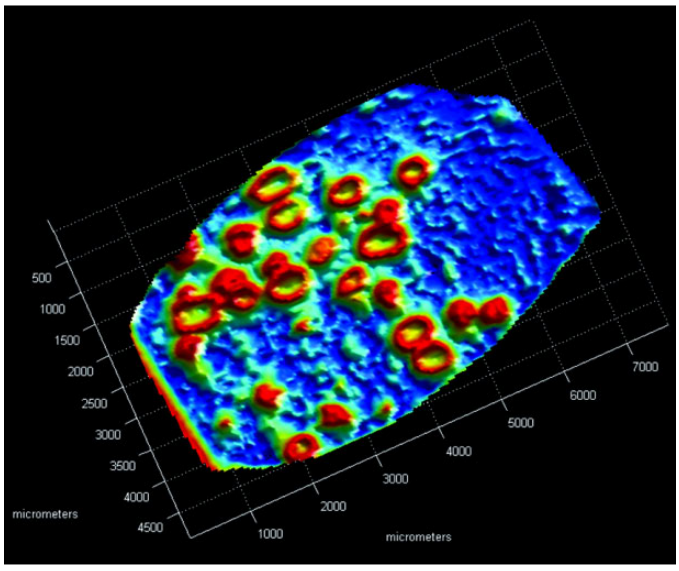
Once destined for MDA's Exoatmospheric Kill Vehicle, a focal plane array instead helped a scientist see farther into the infrared spectrum.

Because today's tablet formulations often have a timed-release component that is entirely dependent on how and where the active ingredient is distributed inside the tablet, it is critical for a pharmaceutical manufacturer to test its properties before packaging. Manufacturers perform dissolution testing, which requires destruction of the tablet in a series of complex experimental steps. In addition, this sort of "wet chemistry" analysis depends on sampling, with findings for a limited amount of product being extrapolated to other products in the same lot.

However, with spectral imaging, a drug manufacturer can visualize the heterogeneity profile of multiple tablets with confidence and accuracy, and without the limitations, time-consuming effort, and expense of destructive testing. The technology behind this imaging technique has had numerous progenitors, but one array in particular helped yield some insight into the problem.



▲ A near-infrared image of heartburn medication shows the architecture and spatial distribution of chemicals in a tablet, which would allow a manufacturer to evaluate its quality.

A new focus

"Dual-use" was still a popular buzzword when NIH researcher E. Neil Lewis picked up a mercury-cadmium-telluride (MCT) array from NIST colleague Ted Heilweil and placed it on the step-scanner of his infrared microscope. Lewis, a world-recognized expert in infrared imaging and recipient of numerous technology awards, used the array to extend the range of a microscope he had been refining for a number of years.

The MCT substrate had been meant for installation on a subsystem of the Exoatmospheric Kill Vehicle, but a few dead pixels disqualified it from use. For Dr. Lewis, it provided a better window into the infrared (to approximately 11,000 nanometers) through which his spectroscopic microscope could peer.

The subject of Lewis' interest at the time was to utilize the technology as a biodiagnostic tool for disease detection. The microscope could present this information in two ways: by location in an image plane and by wavelength in a spectrum, all contained in a three-dimensional space called a "hyper-cube." This allows pinpointing the location of a molecule of interest as well as the type of molecule present.

Dr. Lewis and his group developed highly specialized computer algorithms to decipher the large quantity of data in the hypercube, allowing the operator to locate a single pixel in the space of interest and view its spectral signature. With time and maturation of the focal-plane-array technology sector, arrays became larger, more robust, and affordable, leading the way to a new venture.

Assuring quality

In 1999, Dr. Lewis helped to found Spectral Dimensions, Inc. (Olney, MD), where this same chemical-imaging technology has now achieved a sophistication that has proven invaluable for the pharmaceutical industry. In a fine stroke of fortune for the company, the Food and Drug Administration recently rolled out an effort called the Process Analytical Technology (PAT) initiative, encouraging the pharmaceutical industry to use objective techniques wherever possible in the quality assurance sluice of the product pipeline. Spectral Dimension's rugged spectrometer, the Sapphire™ Near-

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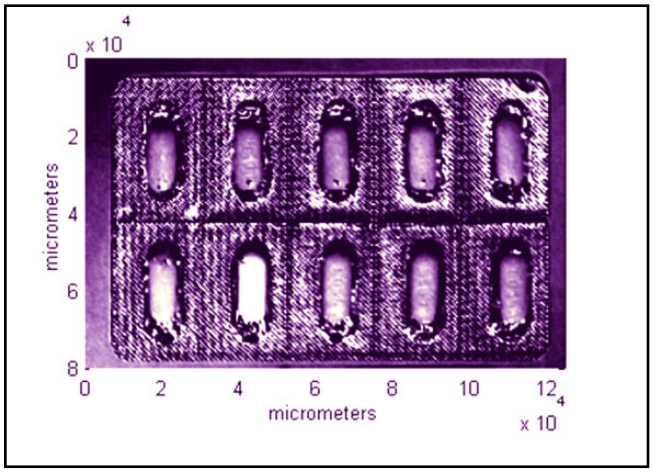

▲ Tablets in a blister pack would all look the same to the naked eye, but this near-infrared image shows that one tablet (the white tablet) has a different chemical composition from the others.

Infrared Chemical Imaging System, provides the high-fidelity, high-throughput spectral imaging that is just the ticket for the sort of testing the PAT initiative demands.

In major laboratories such as Johnson & Johnson, Merck, Pfizer, Astra-Zeneca, and Bristol-Myers Squibb, the Sapphire rapidly provides information about quality and performance parameters. Some industrial users of the technology advocate that it may ultimately replace the traditional dissolution analysis.

Spectral Dimensions' Sapphire NIR Chemical Imaging System operates on a cooled indium-antimonide-based focal plane array, with a wavelength range of 1,200 to 2,450 nanometers and a scan time of about two minutes. Sapphire features an open, accessible sample area and a variable field of view, from square millimeters to square inches. The unit is Spectral Dimensions' speediest system yet, and operates with ISys® hyperspectral data manipulation and visualization software. It is tailor-made for characterizing solid-dosage forms or, to use a less technical term, pills.

Where a larger field of view and greater depth of penetration is desired, Spectral Dimensions offers the MatrixNIR™ system, based on an indium-gallium-arsenide array. Whereas Sapphire is used primarily in pharmaceutical applications, the Matrix is often preferred for food and agricultural analyses, such as crop-seed viability.

Beyond these current applications, Spectral Dimensions is also in the process of pilot-testing its chemical-imaging system for the detection of animal protein in livestock feed. While the spread of bovine spongiform encephalopathy (mad cow disease) has largely been halted due to better industry oversight, the presence of nervous-system tissue in animal feed still represents a threat and is being monitored. Once again, spectrometry could provide a faster and possibly more accurate alternative to wet chemistry techniques. The company has units in Japan, Korea, and some European countries to test this concept.

Malvern Instruments acquired Spectral Dimensions in June 2006. It is a major instrumentation company with expertise in particle characterization, including imaging. Joining the strengths of the two companies will expedite the core mission of providing a complete suite of turnkey imaging systems, now including chemical imaging, for a variety of applications while helping clients maintain compliance with industry standards such as cGMP (current good manufacturing practices).

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