

A New Approach to Near- and Mid-Infrared Process Analysis

Encoded photometric infrared technology has the ability to address the demands of modern process applications, including those of the PAT initiative.

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Infrared spectral measurements have been used for a broad range of applications from the composition of gas and liquid mixtures to the analysis of trace components for gas purity analysis. Examples include the measurement of combustion gases for carbon oxides and hydrocarbons, where simple filter-based instruments or nondispersive infrared (NDIR) photometers are used widely. Although such instruments are simple in concept, they are limited in application and moderately expensive to maintain. More complicated process measurements, involving multiple chemical species for on-line or environmental applications, require the use of more complex instrumentation such as FT-IR. These instruments provide good flexibility but often lack the robustness and reliability required for continuous operation within an industrial environment.

An alternative technology is proposed in this article, where an applications-specific analyzer based upon encoded photometric infrared (EP-IR) is introduced. Like a filter instrument the EP-IR instrument operates with a predefined set of wavelengths or wavelength regions with bandpasses optimized for the application. As many as 256 of these wavelength regions are available for a configured analytical system. Unlike a filter instrument, however, the EP-IR can be reconfigured easily for a different analysis by changing a single encoder disc. The operation of an EP-IR analyzer is similar to an FT-IR instrument, where the individual wavelength segments used for the analysis are uniquely modulated, and the final spectral intensities are computed via a Fourier transform. Multiple analytes are handled by the application of chemometrics.

Once developed and finalized, the method is recorded on a medium similar in appearance to a compact disk (CD). The configured disc can be distributed for multiple implementations of the method in a standardized and documented format — an important attribute for applications in regulated industries, including pharmaceutical and environmental process monitoring

EP-IR systems can be configured to accommodate measurements in all spectral regions, from the visible through the mid-IR. This is accomplished by implementing different source and detector combinations in conjunction with matched energy dispersion components (usually holographic diffraction gratings). More than one spectral measurement range can be han-

dled by a single EP-IR analyzer. For example, one system can handle both the NIR region with a lead sulfide detector, and the shortwave mid-IR region with a lead selenide detector. As such, the system is capable of addressing the needs of a range of applications based upon the nature of the sample and the type of sample handling interfaced to the instrument. Vapor monitoring is possible where the concentration ranges from percent levels down to parts-per-million levels. The need for long folded path gas cells often is eliminated, where the NIR can be used for measuring high concentrations; the mid-IR, in the 3–5 μm range, can be used for lower level concentrations.

As noted, the norm in process analysis has been the NDIR analyzer for simple, well-defined applications, which has competed with process gas chromatography (GC) systems for gas and vapor (volatile liquid) measurements. Since the early 1990s there has been a desire to shift toward spectrum-based analyzers, in which more complete spectral information is available to handle more complex analyses. Both standard FT-IR and NIR analyzer systems also come with a significant overhead in terms of method support — including chemometrics model development — especially for NIR-based applications.

The EP-IR Concept

An EP-IR analyzer is a photometrically simple system, where the infrared beam from the sample is transferred directly into holographic diffraction grating-based spectrograph. The dispersed radiation from the spectrograph is imaged through a slit aperture above the surface of a rotating encoder disk, as represented in Figure 1. The encoder disk features a series of unique reflective tracks which are spatially located to correspond to the specific wavelengths or wavelength regions required for the specific analysis. Each track is patterned to generate a reflected beam that is uniquely modulated for each individually reflected wavelength. The composite reflected beam is imaged on a single element detector, which generates a signal that forms a discrete interferogram (Figure 2). The intensity contribution for each wavelength or wavelength segment is obtained by applying a Fourier transform to this interferogram. The instrument's geometry allows for a dual measurement system, where two separate wavelength regions can be produced via two independent spectrographs.

The reflective optically encoded disk is fabricated from glass

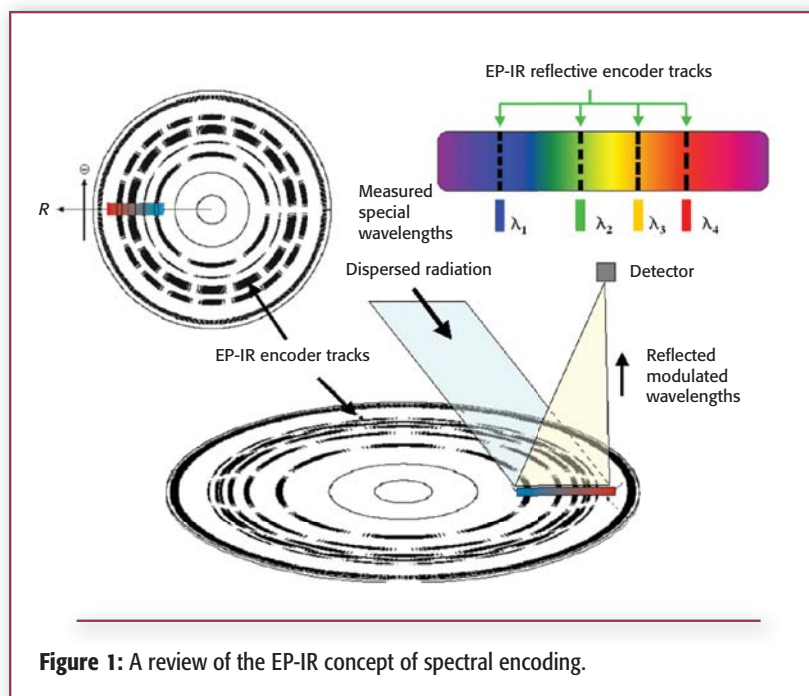


Figure 1: A review of the EP-IR concept of spectral encoding.

where the surface contains a series of concentric tracks made from deposited metal formed via a micro lithographic procedure (see Figure 3). The tracks are defined as “half-tone representations” of smooth orthogonal sinusoidal functions. These have the appearance of a

reflective bar code, which interacts with specific regions of the dispersed spectral image from the grating spectrograph. The center wavelength and bandpass are defined by the radial position and radial width of the reflective track, respectively. The reflective tracks serve the same pur-

pose as the optical bandpass filters in a filter instrument, but they are not fixed. Also, the EP-IR “filter sets” are identical from instrument to instrument due to the precision lithography used in creating the encoder disks.

In terms of implementation, the analytical method is defined in terms of the band centers and bandwidths required for a given analysis. Advanced Photometrics (Pleasanton, CA) has developed a proprietary encoder design software package that determines the radial positions and radial widths of the encoding tracks. These correspond to optimized spectral windows obtained from standard reference spectra by visual inspection or via statistical correlation methods (chemometrics). The encoding frequencies are selected to maximize the signal-to-noise performance of the instrument. The output of the design software is a DXF file, which is used by the fabricator to generate the photo-mask used for the production of the encoder disk. Figure 3 illustrates sample visual differences among encoder disks customized for different applications.

In its current configuration, the analyzer, when operating in the 3.0–5.0 μm range (lead selenide detector), has a baseline noise level of $>10^{-5}$ absorbance for the measurement of low levels of methane in a 15-cm cell (see Figure 4). The analyzer readily handles the analysis of mixed hydrocarbon gases containing methane, ethane, propane, butane, and certain higher hydrocarbons, with minimal cross talk — a major challenge for a filter instrument.

An EP-IR system can be configured into a relatively compact analyzer package, as indicated in the schematic rendering of the module shown in Figure 5. The final design and packaging of the analyzer is dependent upon the end-use application and its spectral requirements. Final configuration can range from a handheld analyzer to a fully packaged, on-line process analyzer.

Applications

The target applications for EP-IR analysis originally were gas and vapor measurements, with the intent to bridge the gap between NDIR and FT-IR. It is well suited to the analysis of prescribed gas

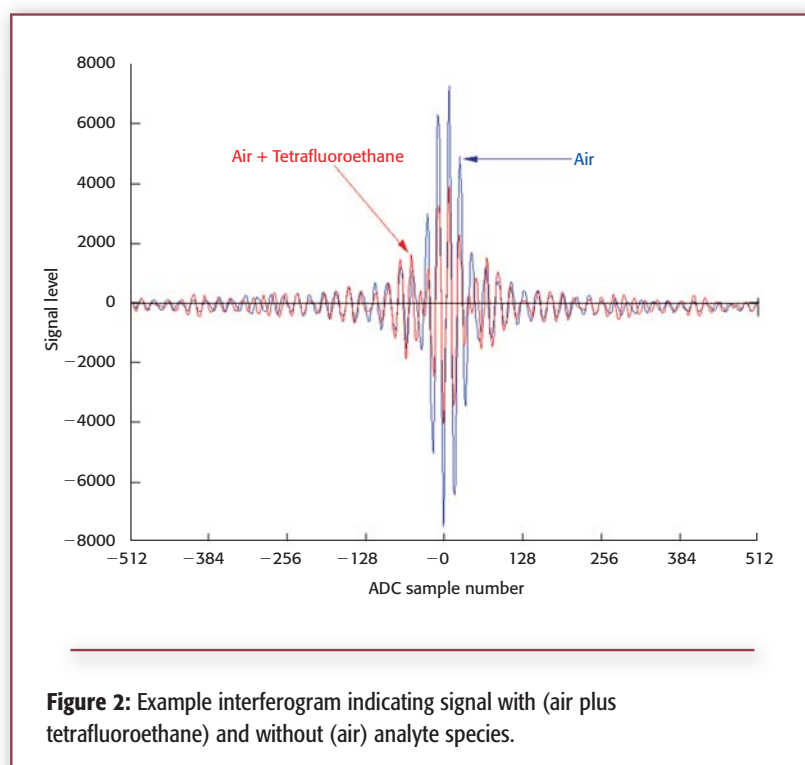


Figure 2: Example interferogram indicating signal with (air plus tetrafluoroethane) and without (air) analyte species.

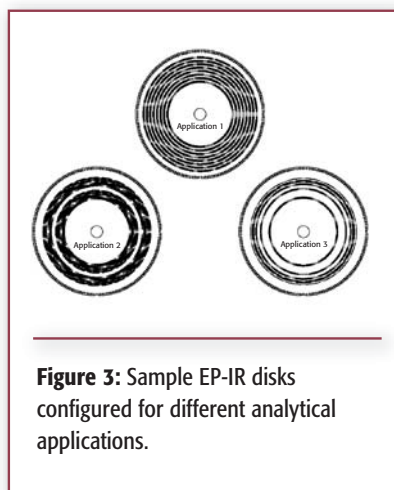


Figure 3: Sample EP-IR disks configured for different analytical applications.

mixture systems where specific analytes are well understood, and common interferences are known. EP-IR can differentiate adequately between components in mixtures with a high degree of spectral similarity or significant band overlap. Such a function requires a full spectrum analyzer normally and is out of the reach of a simple filter photometer. Figure 6 shows the spectral output of the analyzer with a 128-channel encoder disk for common gases at the part-per-million level, with a nominal spectral resolution of 9.7 cm^{-1} (15.7 nm) measured at 2500 cm^{-1} (4000 nm). In this example, the system is optimized for the 3–5 μm ($3333\text{--}2000\text{ cm}^{-1}$) region with a single-stage thermoelectrically cooled lead selenide detector. The system used for the data in Figure 6 was based upon a 15-cm, single-pass gas cell, capable of providing low levels of detection for the common hydrocarbons mixtures and common analyte gases.

A high signal-to-noise ratio is obtainable with the configuration described and can be extended to measure trace quantities of gases at parts-per-billion (ppb) levels by increasing the pathlength to 5 m (see Table II). Figure 7 provides an example of performance for carbon monoxide, where LODs of 100 ppb are obtained for 1-min sets of signal-averaged data.

Once an analytical system is defined, the best-fit wavelengths are determined with the aid of chemometrics. A disk design is created and prototype instruments are calibrated, and these calibrations subsequently are transferred to

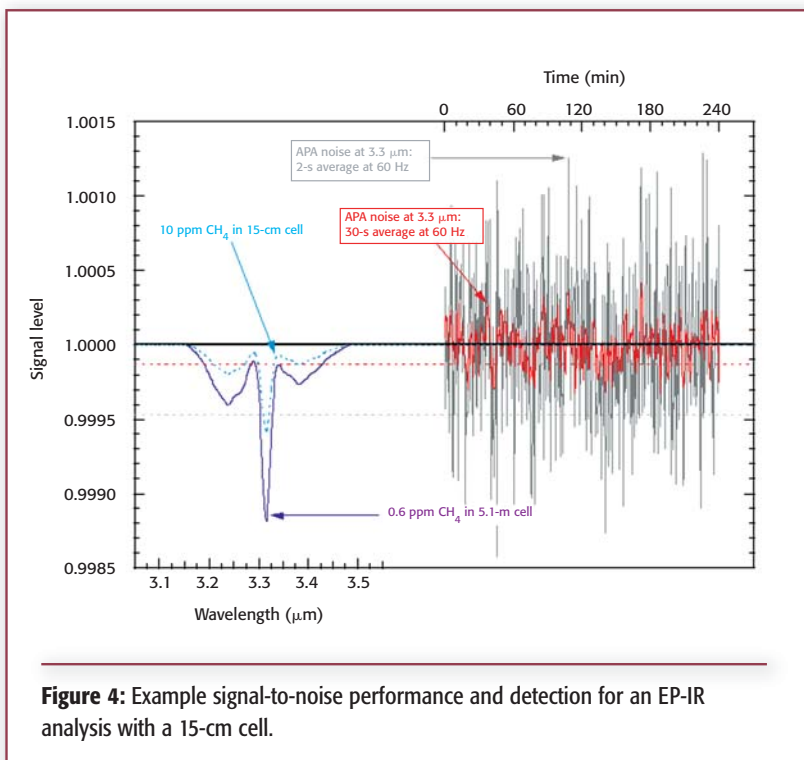


Figure 4: Example signal-to-noise performance and detection for an EP-IR analysis with a 15-cm cell.

production instruments. Following calibration, the analyzer is capable of providing quantitative measurements for all defined components. Figure 8 summa-

rizes the process for a formulated pharmaceutical product. In this case, a simple tertiary mixture of common excipients (magnesium stearate, povidone, and lac-

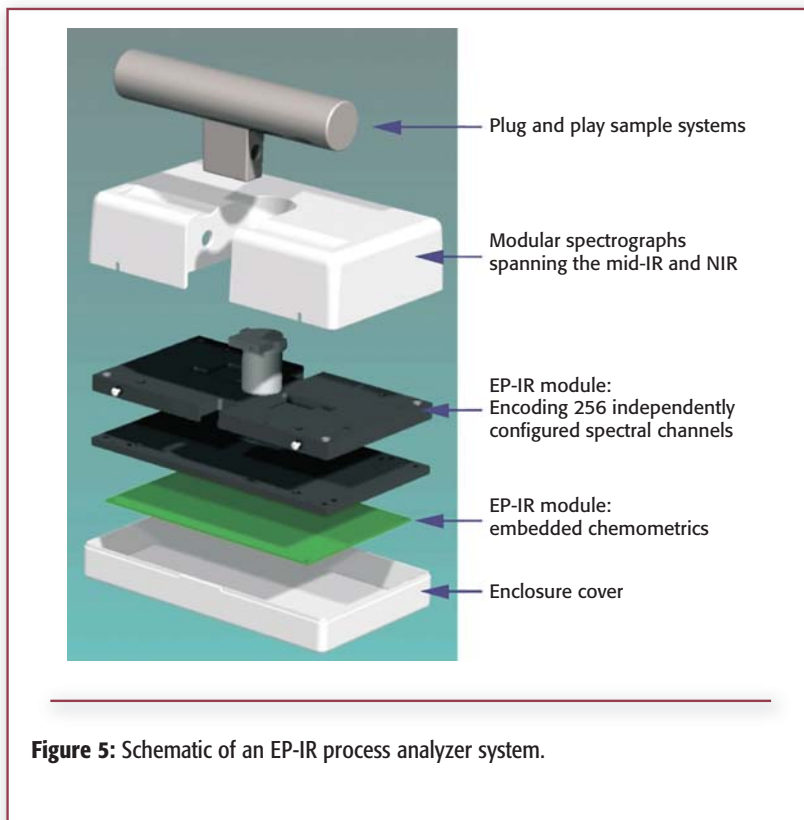


Figure 5: Schematic of an EP-IR process analyzer system.

tose) is shown as a composite spectrum, and as the separate components. In this particular case, the spectra were obtained in the mid-IR by an internal reflectance method. In practice, this could be either attenuated total reflectance (ATR) spectra as shown from a mid-IR measurement, or diffuse reflectance spectra in the NIR spectral region. The selection of the sampling and measurement method is dependent upon the desired implementation, as well as the location in the process where the measurement is to be made. As illustrated, regions of the spectrum are selected that are representative of the spectral contributions of key analytes, and also regions that are used as baseline reference points (where required). For some applications the regions can be defined by previously documented or published procedures. Alternatively, the spectral regions can be determined from one of several standard chemometric procedures. It is recognized that the product formulation might call for a variance in the ratio of the components in the form to be analyzed; a single encoded disk can be used in such cases, and the difference then resides in the final computation of results from the analyzer output from the disk. There are many industrial segments in which process analyzers can be used, ranging from traditional chemical and petrochemical manufacturing to fine-chemicals and specialized manufacturing, which includes pharmaceutical and consumer-oriented products (such as packaged goods and food products). Two overviews of EP-IR are provided below, one focused on general process analytical applications, and the other addressing key application areas in the pharmaceutical industry.

Chemical and Environmental Analysis

The petrochemical and chemical industries are extremely diverse, and offer many opportunities for process IR spectral measurements. Overall, they can be considered as segments of the hydrocarbon processing industry because natural gas and crude oil are considered to be the principal raw materials for a major part of these industries. From here, raw

materials such as ethylene and propylene are major building blocks. Products manufactured by the petrochemical and chemical industries range from commodity materials (basic chemicals and raw materials) to fully formulated or

compounded end-use products. Value-added products, which are manufactured from the back end of the refining process often require a flexible spectral analyzer system because of the range of materials and processes concerned.

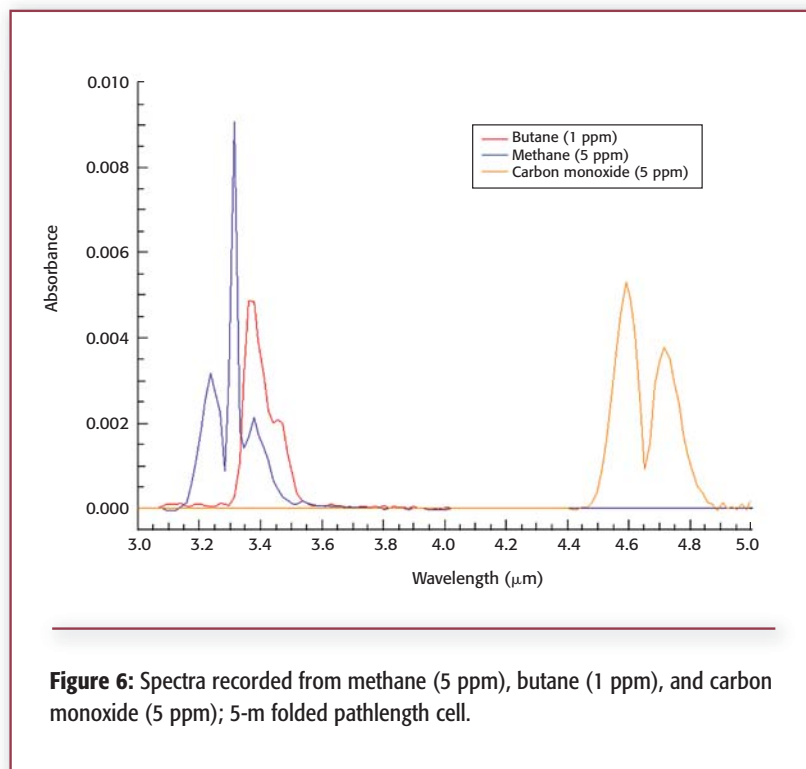


Figure 6: Spectra recorded from methane (5 ppm), butane (1 ppm), and carbon monoxide (5 ppm); 5-m folded pathlength cell.

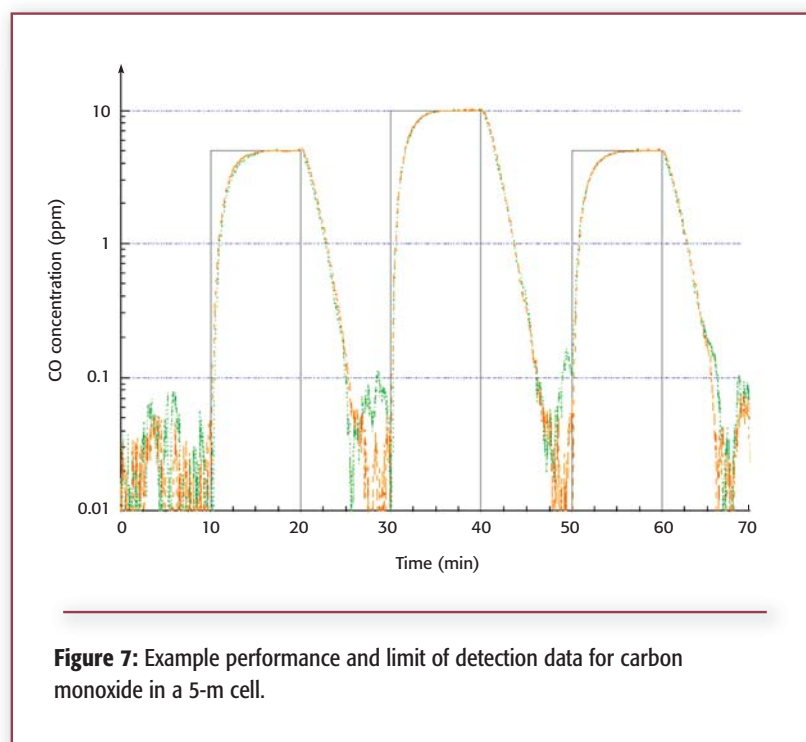


Figure 7: Example performance and limit of detection data for carbon monoxide in a 5-m cell.

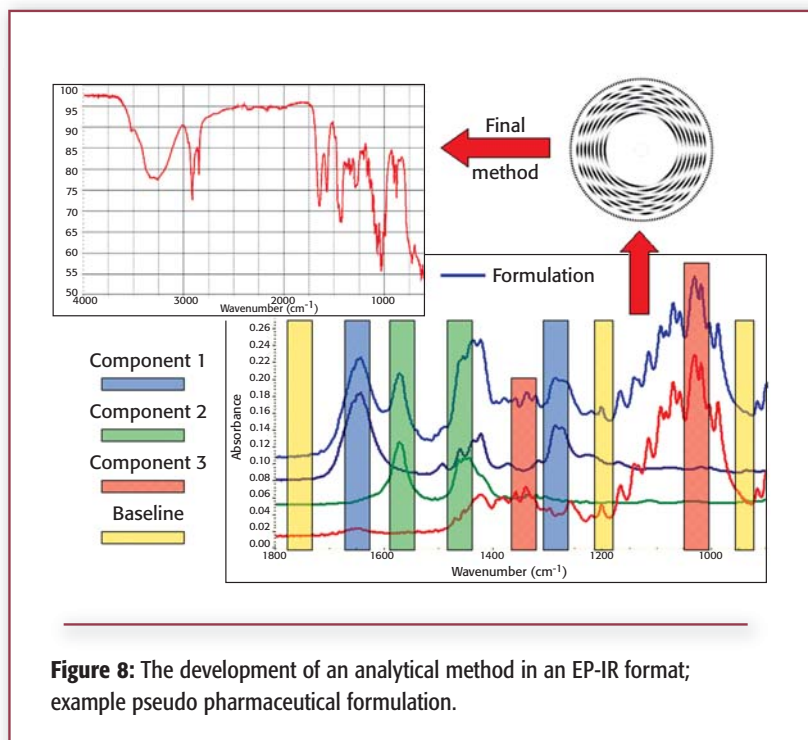


Figure 8: The development of an analytical method in an EP-IR format; example pseudo pharmaceutical formulation.

Beyond the obvious applications for gases, such as fuel gases, combustion gases, and production gases, there are several other, sometimes less obvious applications. For example, the semiconductor industry is well served by IR spectroscopy at the production level for purity measurements on refined silicon, and for critical compositional analysis of processed silicon, such as BPSG measurement. However, in addition to these traditional applications, infrared spectroscopy can be used to monitor process gases such as the various hydrides (arsine, diborane, phosphine, and so forth) that are used in processes for composition and purity. Other applications include the monitoring of plasma and ion implantation chambers.

Many industries use drying processes, where water and organic solvents are removed either in an airflow or under vacuum. Analogous examples include solvent recovery units, important in many industries on environmental and process economy grounds. Practical examples include the pharmaceutical industry, various coatings industries, and consumer product industries. The measurement of residual vapors in some industries is regulated, so there are good opportunities for instruments that typi-

cally provide measurements of vapors at from 1 to 100 ppm levels. Other areas involving solvent removal are more for product quality and stability reasons. Drying processes also are prominent in the food industry, where an analogous application, roasting, is equally important for product quality. Infrared spectral measurements have been used for applications such as coffee roasting, where the end point of the roasting process is determined, which in turn

defines the ultimate flavor of the coffee. Other food products featuring roasting and or other forms of heat treatment also lend themselves to quality and process monitoring.

Refrigerants usually are chlorofluorohydrocarbons; note that perhalogenated materials are environmentally prohibited because of links to the depletion of the ozone layer. However, some refrigeration systems still contain these prohibited materials, and it is important that these materials are not intermixed with the current accepted materials. Analyzers based on mid-IR measurements have been used for monitoring of these materials. This includes both large industrial refrigeration units as well as automotive applications. Environmental monitoring around refrigeration units also is important because the current materials are considered to be toxic as well.

Measurement of contaminants in high purity gases is a natural application for EP-IR analysis. One of the most important areas of application for high purity gas analysis concerns compressed breathing gases — air, helium (deep sea diving) and oxygen. Infrared spectral measurements already are standard for these measurements for military (all armed forces), commercial aviation, industrial and medical applications. The sensitivity and method standardization of EP-IR adds a new dimension to the analysis, making it an

Table I. Comparison of EP-IR versus NDIR analyzers and FTIR spectrometers.

	NDIR	EP-IR	FTIR
Spectral range	NIR–Mid IR (bandpass filters)	Visible–Mid IR (configurable)	NIR–Mid IR (configurable)
Res. at 4 $\mu\text{m}/$ 12 μm (mid-IR)	25 $\text{cm}^{-1}/9 \text{cm}^{-1}$	9 $\text{cm}^{-1}/4 \text{cm}^{-1}$	0.5–8 cm^{-1}
Spectral channels	10	256	850
S/N	10,000	100,000	100,000
Drift (8 h)	10^{-3}	10^{-5}	10^{-5}
Size	100 in^3	180 in^3	2000 in^3
Weight	3 lb	5 lb	40 lb

Table II. Limits of Detection for common hydrocarbons and carbon monoxide; 5-m folded pathlength cell.

Species	1 s	1 min	5 min
Methane	775 ppb	100 ppb	45 ppb
Ethane	465 ppb	60 ppb	27 ppb
Propane	310 ppb	40 ppb	18 ppb
Butane	194 ppb	25 ppb	12 ppb
Carbon monoxide	775 ppb	100 ppb	45 ppb

important addition to existing measurement regimes for gas purity measurement.

Pharmaceutical Production

Applications of NIR and mid-IR span a broad range of areas in the production of pharmaceutical products, ranging from the screening of incoming raw materials to the composition and quality of final produced dosage forms. These include, as indicated, raw materials characterization, active material synthesis, dosage measurement, blenders, granulation, product drying, coating, and the production of final dosage forms. Three approaches can be used with EP-IR. The first is a broad overview system configured with multiple channels for broad-based materials characterization. This is an ideal approach to raw material screening, where a universal “mask” effectively is produced to provide a go/no-go on raw materials. Again, as stressed earlier, the benefits here are standardization, where every system can be configured to provide identical spectral and analytical performance.

In the second approach, the EP-IR encoder disk can be optimized for formulations used in specific dosage forms. Such a system can be used for granulation, blenders and the final dosage form production. Again, a highly uniform, and easily regulated rigorous procedure of measurement can be adopted.

For the final approach, there is the ability to configure the analyzer for two very different spectral regions. This can include color and NIR, where the color of a final dosage form or pharmaceutical preparation can be as important to the product preparation as the final composition. Both can be monitored by the same EP-IR analyzer system. Likewise, for some applications, UV absorption and possibly UV fluorescence could be combined with NIR to provide a sensitive readout for low levels of active ingredients, while monitoring the overall composition of the excipients.

Conclusion

A large number of traditional instruments are sold into industry for both process and QC applications. Today, there is a large push in the highly regulated pharmaceutical industry to inject new methods and new technology to provide better methods for the process control and production of formulated products. These include applications ranging from raw material screening to final packaged product manufacture. EP-IR is a new concept providing benefits of simplicity of design and method standardization, along with the ability to operate in multiple spectral ranges. EP-IR analysis has the potential to comprise a wide range of configurations, from handheld devices to fixed process analyzers. From a traditional point of view, EP-IR offers the benefits of a fully functional spectrometric analyzer with the cost and simplicity of a simple filter device — an important attribute for any process analyzer. ■

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