Targeted Range Analyses

APPLICATION NOTE

Introduction

A wide variety of instruments are used for near-infrared quantitative analyses, using quite different technologies[1]. These encompass techniques that cover the whole of the traditional near-infrared spectrum (scanning grating, Fourier transform, acousto-optical tunable filters), a portion of the spectrum (diode array grating polychromator), and specific wavelengths (interference filters and discrete-source light-emitting diodes). Although instruments with broad coverage are commonly employed in a research capacity, and to determine which region is best for an analysis, the targeted-range instruments are often those actually deployed in volume to perform the analysis. Thus, filter instruments are widely used in the food industry.

A typical interference filter has a resolving power of about one part in 100: at 1700 nm this translates to a bandwidth of around 17 nm. Using a dozen or more of these filters provides adequate information for applications like the measurements of moisture in natural products. However, analyses of mixtures of organic compounds – for example, alcohols that are typically used as solvents, and sugars and artificial sweeteners used in consumer products and as pharmaceutical excipients – are best studied with higher-resolution instruments, as the bands in these systems are much narrower. Process applications, which may deploy a series of instruments performing the same analysis, also need to ensure easy and consistent calibration from instrument to instrument – a tall order for traditional spectrometers.

Examples of limited range pharmaceutical analysis

A study of the hydrate form of a bulk drug used a PLS model based on the 1734 – 1772 nm region[2]; a study of surface and bound water in drug substances employed models using the 1822 – 1948 nm and 1890 – 1950 nm regions[3]; and a pan-dryer study just used the second derivative at the single wavelength of 1384 nm[4].

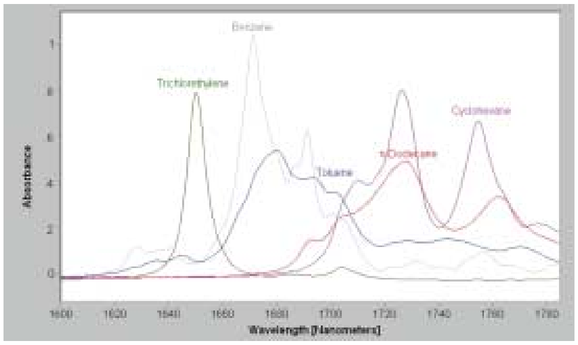
Axsun Spectrometers

Axsun spectrometers are based on semiconductor light sources and a Fabry-Perot tunable filter[5], and using a single source, they cover around 200 nm at a resolution of 2 nm or better. One of the key targeted ranges for these spectrometers is the first overtone of the carbon-hydrogen stretching band, which lies in the 1600 – 1800 nm region for virtually all organic compounds. Therefore, a spectrometer operating in this targeted range is capable of detecting and analyzing materials as diverse as cellulose and sugars, solvents and vapors, pharmaceutical excipients and active ingredients, etc.

Qualitative Analysis

Figure 1 shows the near-infrared spectra of some common organic solvents in the 1600 – 1800 nm region, showing that they are quite distinct. Indeed, the spectra are more distinct here, as compared to the second and third overtones in the shortwave near-infrared region, as spectra there tend to simplify, most likely due to 'local mode' as opposed to 'normal mode' behavior[6].

All Axsun's optics are contained in a single chip-sized module, which is thermostatted. This makes the optics immune to ambient temperature variations. In addition, Axsun's analyzers are portable amd more reliable than traditional instruments – qualified for 25-year lifetime. Readily configurable as rugged, low-cost systems, these powerful analyzers can be implemented throughout a process stream without extensive infrastructure or complex optical interfacing to help manufacturers in a wide range of industries realize dramatic improvements in productivity, throughput, yield, and quality.



Sucrose and lactose are disaccharides; xylitol is a five-carbon sugar alcohol. Sucrose and lactose have the same chemical formula ($C_{12}H_{22}O_{11}$) and are therefore structural isomers. Sucrose's component monosaccharides are glucose and fructose, while lactose's are galactose and glucose. Xylitol ($C_5H_{12}O_5$) is closely related to the pentose Xylose ($C_5H_{10}O_5$); xylose has a terminal aldehydic group (CHO), while xylitol has a terminal alcohol group (CH_2OH). Although xylitol tastes sweet, it is poorly absorbed by the body and is therefore used in low-calories candies, in many foods, soft drinks, in toothpaste, and as a pharmaceutical excipient, etc.

Figure 1. The spectra of trichlorethylene, benxene, toluene, n-dodecane and cyclohexane in the first C-H overtone region

Many organic compounds contain O-H groups, and important classes of these are alcohols (often used as solvents), sugars and sugar alcohols (often used as pharmaceutical excipients). Although condensed-phase O-H bands are often broad, due to hydrogen bonding, Figure 2 shows the spectra of liquid-phase methanol, ethanol, and iso-propanol in the 1600 – 1800 nm range, and illustrates the narrower and more-distinct bands in this first C-H overtone region. Figure 3 shows the spectra of some solid-phase, hydrogen-bonded, compounds, and even for these species, their spectra in the C-H overtone region are again very distinct.

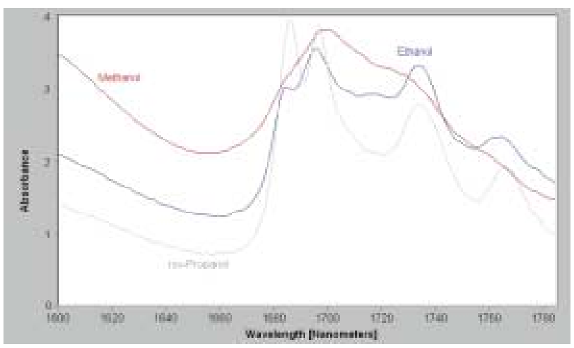


Figure 2. The near-infrared spectra of methanol, ethanol and iso-propanol in the first C-H overtone region

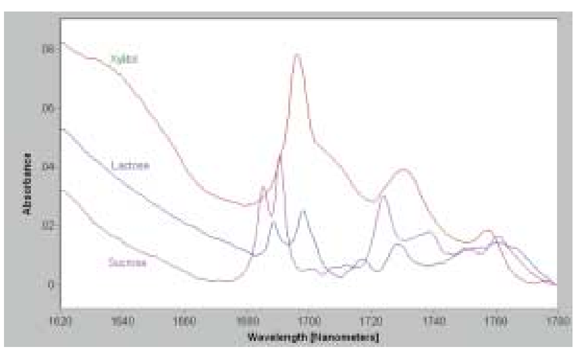


Figure 3. The near-infrared spectra of solid sucrose, lactose and xylitol in the first C-H overtone region

The alcohol bands have a "PQR" structure with a sharp Q-branch. Some fine structure is visible for methanol, but this is not resolved at the resolutions and pressures used in this experiment. Water is a very light, low-symmetry molecule, and has exceedingly broad and complex bands, both in the mid-IR and near-IR.

The second overtone of the oxygen-hydrogen stretch lies around 1400 nm. In condensed phases, the O-H band is very broad, due to hydrogen bonding. However, in the vapor phase, there is no association, and the different alcohols display characteristic band profiles, enabling easy identification and quantitation. Figure 4 shows the spectra of methanol, ethanol, and iso-propanol in the 1400 nm region, with the spectrum of water vapor also included. These spectra were obtained with an Axsun NIR Analyzer OH spectrometer, operating at about 0.1 nm resolution.

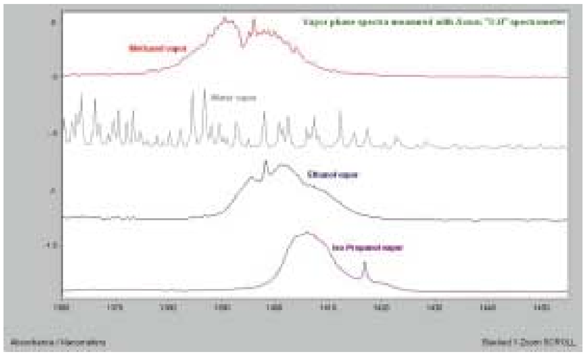


Figure 4. Vapor phase near-infrared spectra of methanol, ethanol, iso-propanol and water

Quantitative analysis

The ability to transfer models developed on one analyzer to additional analyzers without performing exhaustive model or spectral mapping functions is essential for wide-scale implementation of NIR analyzers. To insure successful model or data transfer, the spectal response from instruments must be nearly identical in wavelength accuracy, photometric linearity, and band shape. As an example of a targeted spectral range quantitative analysis and calibration transfer from one spectrometer to another, a set of standards were prepared, based on a system described in the literature[7]. Typical spectra from this set are shown in Figure 5.

Partial Least Squares (PLS) models were developed for each of the three components using Pirouette chemometric software (Infometrix Inc., Bothell, WA, USA). Models were developed for each instrument ("1", "2" and "3"), and those models were used to estimate the concentration of the components in the data sets collected on the other instruments (i.e., independent validation). Figure 6 shows the fit attained (actual vs. estimated concentration) across the instruments. The SEP presented in Table 1 summarizes these results. The SEP did not change significantly when models from different instruments were used to estimate the concentration on an independent system. Similar results were obtained for the weight % chlorobenzene and toluene. If model transfer were unsuccessful, the SEP would have increased across instruments.

We can draw two significant points from these data: first, quantitative analysis using this high-resolution, limited-range data works very well; and second, these spectrometers are essentially identical, allowing direct calibration transfer from spectrometer to spectrometer.

Data from spectrometer	Model from spectrometer	Standard error of prediction (SEP)
1	1	0.213
2	1	0.223
3	1	0.243
2	3	0.162

Table 1. **Standard error of prediction for different models and spectrometers**

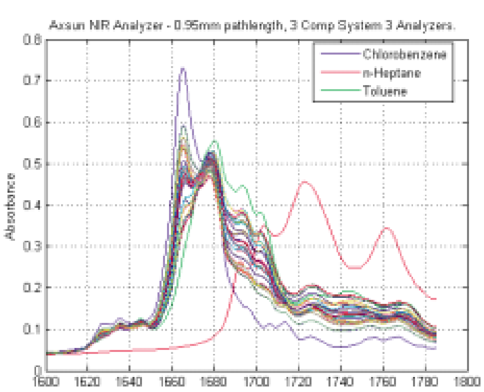


Figure 5. Near-infrared spectra of mixtures of chlorobenzene, n-heptane and toluene

Experimental

20 Standards were prepared gravimetrically containing chlorobenzene, varying from 20.74 – 75.48%, toluene from 21.59 - 77.02%, and heptane from 2.07 - 10.74%. The spectra were run on three different Axsun spectrometers, with the samples held in a conventional slide-mounted 0.95 mm pathlength transmission cell with quartz windows (Harrick Scientific), placed in Axsun's sampling accessory. Light was delivered to the sample via a single-mode fiber and 5.5 mm diameter collimator, and returned to the single-element InGaAs detector via a second collimator and 600 micron diameter multimode fiber. The spectral resolution was 2 nm, and data collection time 7 seconds per spectrum.

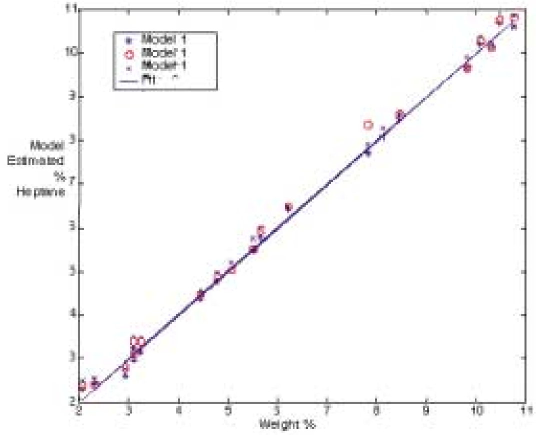


Figure 6. **Actual vs. estimated concentration for heptane in the three-component mixture**

Conclusions

Using Axsun's high-resolution NIR Analyzer, we can target specific portions of the spectrum for use in qualitative and quantitative analyses. The first overtone regions of the carbon-hydrogen stretching and the oxygen-hydrogen stretching modes are well-suited for this purpose, because all organic compounds (aliphatic and aromatic), in all phases (gas, liquid, and solid) have specific and distinct bands in this region. Axsun spectrometers are also essentially identical, allowing direct transfer of quantitative analysis models from spectrometer to spectrometer.

Compact, rugged, and reliable, Axsun's micro-optic spectrometer technology has immediate application in industrial vibrational spectroscopy, especially in the emerging field of distributed process analytical spectroscopy in the chemical and pharmaceutical industries. A very small size is achieved, without loss of either signal-to-noise or resolution. Small size and ruggedness of these devices allow their deployment in harsh temperature and vibration environments, where traditional-design instruments, derived from laboratory systems, are not suitable. This technology represents a paradigm shift for industrial spectroscopy, and enables a variety of new industrial applications for these spectroscopic sensors.

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