Introduction
In the near-infrared (NIR) spectral region most materials develop characteristic and unique absorptions as in the mid-infrared. The specific absorbance of most bands is one-to-two orders of magnitude weaker than in the mid-infrared, thus permitting longer pathlength measurements. The relatively weaker absorption also allows materials to be sampled without dilution, which is a major advantage in most industrial and laboratory applications. Excellent light sources and highly sensitive detectors along with the use of rugged and non-hygroscopic optical materials also make NIR the method of choice for practical high throughput analyses.

The analytical NIR spectral range is considered to be between 10,000 cm⁻¹ to 4000 cm⁻¹ (1-2.5 μm). For long path liquid analysis sometimes the 700-1000 nm is also considered to be part of the NIR spectral region. Most of the absorbance bands in the NIR originate from the overtone and combination bands of the fundamental (mid-infrared) vibrations of the –CH, -OH and –NH moieties. This is why the spectral range between 7692-5263 cm⁻¹ (1300-1900 nm) is called the overtone region and the 5263-4000 cm⁻¹(1900-2500 nm) is called the combination region. Below 7692 cm⁻¹(1300 nm) the second overtones of the –CH, -OH and –NH vibrations dominate, thus it is called the second overtone region. Other bonds, such as those found in inorganic materials also have characteristic signatures, so this nomenclature and the limits of the regions is only tentative (Fig. 1).

There are many different geometries for NIR sampling optics and sample presentations. One of the useful, practical sampling devices in the NIR spectral region is the integrating sphere, such as the PIKE NIRT™ IntegratIR™. The advantages of the sphere for near-infrared sampling is that it allows an extended sample area, up to the size of the sample port size (in the case of the IntegratIR up to 12 mm), providing a uniform light collection independent of sample orientation. The integrating sphere collects light from all angles, thus the effects of particle size and other non homogeneities are minimized. It is also practical that the sphere is “upward looking”, with a window on top of the sphere. In this arrangement powdered and other samples can be easily placed on the window, or even kept in a glass container and placed on the top of the sphere. Sampling non-destructively, toxic or sensitive materials in sealed vials is one of the unique advantages of such an analysis system. Detectors are ideally an integral part of the sphere assembly. The proximity of a fixed position detector and its electronics also creates optimal conditions for a low-noise measurement system (Fig.2). In figure 2 the detector is located on the green mount directly at the sphere detector port.

Figure 1. NIR spectra of soil samples. From top to bottom; organic sandy loam, sandy clay loam, loam and silty loam.

Figure 2. NIR Integrating sphere based sampling system.
Near-Infrared Spectral Identification

According to Good Manufacturing Practice (cGMP) pharmaceutical production, all materials are quarantined upon arrival to a manufacturing site and have their identity checked before they are released to manufacturing. In Europe, for example, not only all materials but all individual containers of production materials have to be positively identified. This analytical burden and extended turnaround times are reduced by using NIR analysis for this task. Fig. 3 shows the spectra of a few selected tableting excipients placed in 19mm diameter sealed vials and placed on top of the integrating sphere. Even with small chemical differences, as seen in the 5500-6000 and 4000-4500 cm⁻¹ spectral regions, these very similar materials can be easily distinguished and positively identified [2, 3].

![Figure 3. NIR spectra of some pharmaceutical excipients.](image)

Identification of materials is done, in most cases, by representing the different spectra using principle component transformation of a training set and then developing mathematical models that most reliably separate and identify similar substances [4]. During incoming material inspection then, these models are used to predict into which groups the unknowns belong.

Composition Verification

Another application is predicting the concentration of materials, such as, the measurement of potency of active pharmaceutical ingredients. As an example, Fig. 4 shows the correlation of glucosamine in a formulation having six ingredients. Reliable, fast analysis of multi-component mixtures, especially in a solid mixture, is usually a difficult analytical task. Wide concentration ranges and mixtures of materials with different particle sizes tend to be optically nonlinear. The application in Fig. 4 done with the PIKE NIR IntegratIR, however, was linear with good accuracy and precision.

![Figure 4. Quantitative measurement of active ingredient in a varying composition mixture of magnesium stearate, lactose, calcium carbonate, Emco and Cab-O-Sil.](image)

Inhomogeneous Materials

Inhomogeneous materials benefit from presenting multiple sample aliquots to the integrating sphere and averaging the “snapshot” spectra taken off of the different parts of the sample. The sample spread out in a 90mm diameter Petri dish can be rotated in front of the window of the IntegratIR™ at the optically flat, clear part of the Petri dish. The illuminated spot is relatively small resulting in the best signal-to-noise measurement. By moving the sample slowly and continuously, repeated single scans are done on different parts of the sample surface around the Petri dish. The error of the measurement of an inhomogeneous sample is a result of the error from the measurement, such as instrument signal-to-noise, and the sampling error due to the variations across the area of the sample itself. When collecting multiple scans, the rotating cup averages out the sampling differences thus resulting in more reproducible spectral data. Fig. 5 shows multiple spectra of a candy sample with sampling individually placed stationary samples and the greatly reduced spectral variation when the same samples are measured with the rotating accessory, moving the same material and taking the same number of spectra.

Summary

The integrating sphere is a powerful and flexible sampling device in the near-infrared spectral region. In the form of a sample compartment mounted accessory, such as the PIKE IntegratIR™ with a built-in optimized detector, it can turn a general purpose FTIR (with near-infrared beamsplitter and source options) into a versatile near-infrared analyzer. Non-destructive qualitative and quantitative analysis of complex chemical and pharma-
ceutical samples becomes possible, even when samples are within sealed glass containers.

**Figure 5.** Effect of sample averaging using rotating stage on the PIKE NIR IntegratIR.

**References**

5. G.J. Kemeny: Chambersburg Conference on Diffuse Reflectance, Chambersburg, 2002