Transfer of diffuse reflectance spectral libraries

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Introduction

There is an increasing awareness in the pharmaceutical industry of the importance of incoming inspection, as both a manufacturing and a safety issue. Global trade patterns and regulatory harmonisation is putting pharmaceutical manufacturers on the path of 100% inspection. In September, 2009, the Pharmaceutical Inspection Cooperation Scheme (PIC/S) recommended 100% inspection for pharmaceutical raw materials used for the manufacture of active pharmaceutical ingredients (APIs). Transferability of spectra generated on one instrument to another is of increasing concern for instrumentation users. New instruments often represent new capabilities and significant differences in sampling. These differences can cause significant scaling and distortion of the spectra. There have been only a few descriptions of transfer of NIR diffuse reflectance libraries of materials in open cups and glass vials.[1–4]

NIR spectroscopy has distinct advantages as a release method, in particular its rapid acquisition and analysis time. Process-ready and handheld instrumentation allow release in the loading dock. It also has a history as a release method, and is supported by both EMEA and USP as a release method for pharmaceutical ingredients.[5,6] Specificity, despite the appearance of a relatively featureless spectrum when compared to MIR and Raman, remains high. Good signal to noise ratios and sensitivity to crystal forms allow the extraction of significant details. A majority of the effort for spectral library transfer has been focused on mid-infrared libraries. While mid-infrared library transfer is useful in guiding NIR library transfer, the variety of instrumentation and diffuse reflectance accessories are much broader than in the mid-infrared. Continued study on library specificity and the effects on transfer are warranted.

Experimental

Pharmaceutical (USP, EP and JP) grade materials were used as supplied by pharmaceutical distributors, Farma International, Mutchler, Sigma-Aldrich and Thermo-Fisher Scientific. The containers were opened, and the contents placed in 50 µm thick polyethylene reclosable zipper lock bags.

Test 1: Destination instrument stability

Archived data from multiple instruments and a single grade of material, and single type of presentation were gathered.

Test 2: Bruker MATRIX-F → PHAZIR 1624

Spectra were taken in triplicate using a MATRIX-F, using an 8 mm fibre-optic probe with a 16 fibre bundle. The 8 emission fibres are arranged at random at the probe tip. The 8 cm^{-1} spectra were taken using the default data acquisition parameters. Spectra were taken with a PHAZIR 1624, with an independent test set. The PHAZIR uses a 45°/0° diffuse reflectance geometry, and the typical "Collect" acquisition parameters.

Test 3: Thermo-Nicolet Antaris → PHAZIR 1624

A single reference spectrum was provided for caffeine taken in a glass vial, using a Thermo-Nicolet Antaris at 32 cm^{-1} resolution with a diffuse reflectance sphere. Ten reference spectra were taken from a different lot of caffeine using a PHAZIR 1624 under standard conditions.

A common platform was needed for data manipulation. Built in functions from MATLAB 7.5 and PLS_Toolbox 4.0.2 were used.

Results and discussion

Traditional libraries are built using a single spectrum to represent a class of material. The difference between a reference spectrum and a measured, or test, spectrum is expressed as a measure. Euclidean distance and wavelength correlation are frequently used as a measure. More sophisticated libraries incorporate statistical descriptors of the variation from a synthetic average of each material. In the pharmaceutical industry, these libraries are extremely valuable. Commonplace raw materials are not easily accessible to quality control or research and development groups, due to internal controls. The ideal material, used during formulation development, is long gone or has degraded during storage. The administrative effort for collecting new material is significant. API may be shipped rarely, or may be dangerous to handle. Libraries should be conserved and transferred when possible.

In the following tests, harmless excipients are used as a model. The transfer process is identical, and equally successful with most precursors and APIs.

Test 1: Destination instrument stability

When libraries are constructed with a single reference spectrum, instrument stability is generally not reported. It is generally true that for identification purposes, most instruments are stable between re-qualifications. Presentation and material variability are the dominant sources of variability. If the library spectrum is an average, then the effect of short term variability is reduced. However, for predictions, we are subject to all sources of variability.

To determine stability, data were collected on several PHAZIRs and subjected to visual comparison. Correlation scores are better than 0.99, indicating that performance is material limited.

Test 2: Bruker MATRIX-F → **PHAZIR 1624**

The spectra were taken on the parent (Bruker Matrix) and the child (PHAZIR) of a set of 14 pharmaceutical white powders in 50 µm thick bags. Sampling locations were varied while taking replicates. The spectra were matched between instruments using scaling, Finite Impulse Response [FIR],[7] Direct Standardisation [DS].[8]

All methods of transfer produced acceptable results. The advantage of scaling is the need to collect data on a single polystyrene standard on the two instruments. FIR and DS require that a single spectrum of each material is taken on both instruments to build a material-specific transformation. The quality of the transfer was assessed using a separate validation set. Quality of identification improves from scaled to DS. In this particular example, DS provided results that were similar to a PHAZIR-native library. The materials are summarised in Table 1.

Test 3: Thermo-Nicolet Antaris → **PHAZIR 1624**

In this test, the Antaris is equipped with a diffuse reflectance sphere. The propagation of photons through the material is very different than the PHAZIR. This results in different scales of absorption features in the spectra. Because there is only 1 reference spectrum, the PHAZIR spectra were transformed using first derivatives and scaled.

Because the Antaris spectra are acquired at 32 cm^{-1}, the post-processing spectrum of caffeine is at a slightly lower resolution than the equivalent PHAZIR spectra. This results in a scale mismatch in the first derivative for sharp bands. The correlation scores for all spectra are better than

Table 1. Results from different methods of library transfer from a Bruker Matrix-F to a PHAZIR. "Bruker native" indicates library matching using Bruker software and hardware.

Material	PHAZIR Native	Scaled	FIR	DS	Bruker Native
1-phenyl–1,2-ethane diol	+	+	+	+	+
4-aminobenzoic acid	+	+	+	+	+
Acetaminophen	+	+	+	+	+
Caffeine	+	+	+	+	+
Cinnamic acid	+	+	+	+	+
Creatine monohydrate	+	+	+	+	+
Ethyl cellulose	+	+	+	+	+
Inositol	+	+	+	+	+
Lactose hydrate	+	+	+	+	+
Mannitol	+	+	+	+	+
Microcrystalline cellulose	+	+	+	+	+
Ethyl cellulose	+	+	+	+	+
Polystyrene	+	+	+	+	+
Quinine	+	+	+	+	+

0.96, which corresponds to a wavelength correlation of 0.98. This exceeds 0.95 EMEA recommendations for identity confirmation.

Conclusions

Transfer of NIR libraries between different instruments and sampling arrangements is possible and minimises the need to collect new reference spectra. Even the simplest methods of instrument standardisation, wavelength and intensity scaling provide excellent results for similar optical arrangements.

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