

Feasibility of applying NIR For Pharmaceutical Material Identification – Counterfeit Detection

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Abstract

Samples of over the counter antibiotics were purchased in Beijing and scanned using Axsun's NIR analyzer to determine if the system could discriminate different products apart with the intent of identifying counterfeit pharmaceuticals from legal product.

1. Experiment

1.1. Instrumentation

The instrument and accessories used for this study are listed in Table 1 and shown in figures 1 and 2.

Table 1: Spectrometer setup

Equipment	Source	Specification
Axsun OH-CH NIR Analyzer	Axsun Technologies	Wavelength Range: 1350 – 1800 nm. Resolution: 2 nm Number of scans: 32 scans averaged Data Collect time: 6 seconds
Sampling device	Axsun Technologies	Diffuse Reflectance Integrating Sphere sample system. Samples were scanned in vials, blister packs and neat. Only the neat pill data is presented here.
Fiber Optics	Axsun	1 M single mode PM fiber (9 micron) from source to integrating sphere assembly, electronically coupled to detector.
Chemometric Software	Infometrix	Pirouette Software – SIMCA Algorithm

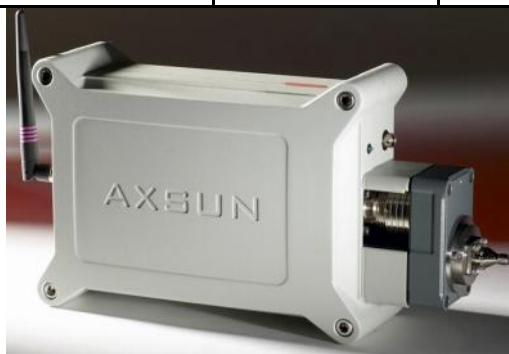


Figure 1: Axsun NIR analyzer

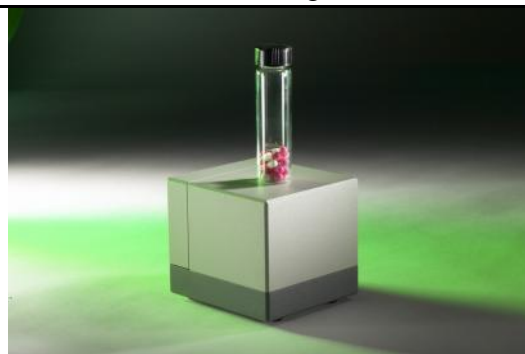


Figure 2: Axsun Lab study sampling system

1. Samples

Samples collected and scanned included:

1. HuYiHongMeiSu - AntiBiotics in Blister Pack

Total of 6 brand:

- a. LiZhu
- b. KangDiNi
- c. HuiRen
- d. XinMeiLuo
- e. HaoWaWa - Children's anti-biotics
- f. YanDi

2. HuYiHongMeiSu LiJunSha and ShiYao - Another kind of Anti-Biotics in Blister Pack

Total of 2 brand:

- a. LiJunSha
- b. ShiYao

3. FuFangGanChao - Non-anti-biotics drug within an opaque plastic bottle:

Total of 2 brand:

- a. GuoYao
- b. *Shuan He*

The samples were scanned in reflectance mode by placing the pill on top of the Axsun integrating sphere accessory. All samples were referenced to a spectralon reference plate. The samples were scanned over the range of 1350-1800 nm. This range is ideal for this type of measurement because it includes the CH, OH and NH overtone bands.

2. Data and discussion

The spectra were collected at 0.5 nm data point resolution, with a 2 nm smoothing function (boxcar) applied. Thirty two scans were averaged for each sample, and each sample was scanned three times. The scan time was approximately 6 seconds. The spectra of the samples are presented in figure 3. The spectra are color coded, (Yellow = FuFangGanChao, Red = HuYiHongMeiSu LiJunSha and ShiYao, Green = HuYiHongMeiSu) and major differences can be seen between the three classes of samples, allowing even visual product identification.

Baseline offsets due to sample particle size and compaction are observed. These are typically minimized by applying conventional NIR data processing techniques such as a SNV (Single Normal Variate), MSC (Multiplicative Scatter Correction), baseline correction or first and second derivatives. Figure 4 shows the calibration spectra after applying a SNV transform. The baseline offsets have been minimized, and the spectral differences between the three product types across the whole scanned spectral range can be more clearly seen.

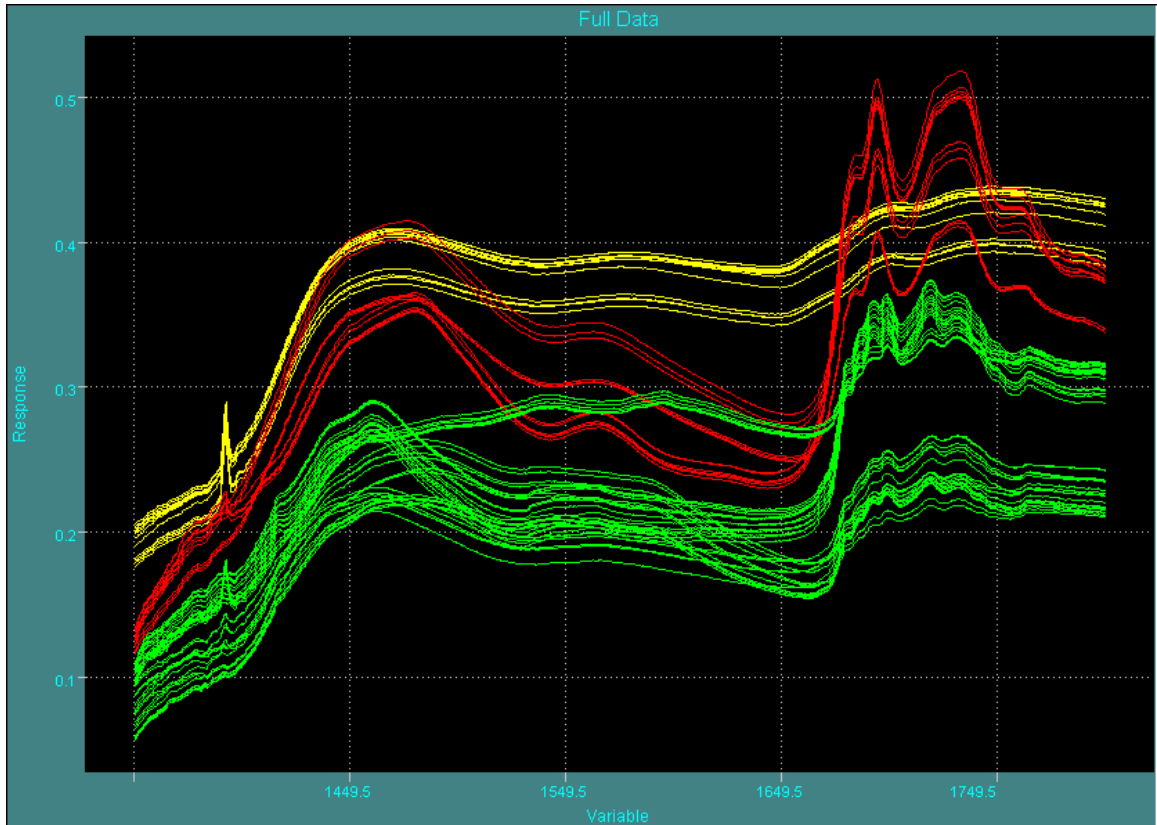


Figure 3: Chinese antibiotic Samples Absorbance– Yellow = FuFangGanChao, Red = HuYiHongMeiSu LiJunSha and ShiYaoGreen = HuYiHongMeiSu

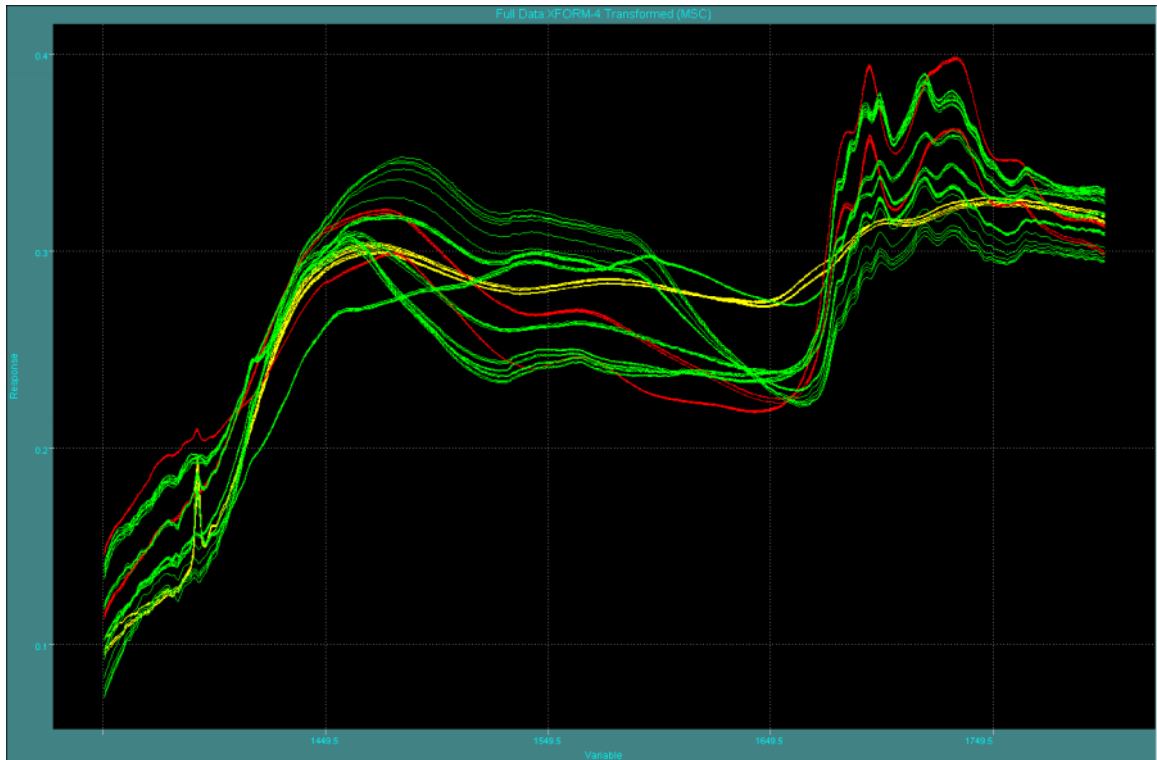


Figure4: Chinese antibiotic Samples –Multiplicative Scatter Correction. Yellow = FuFangGanChao, Red = HuYiHongMeiSu LiJunSha and ShiYaoGreen = HuYiHongMeiSu

Figure 5 shows the spectra after applying a second derivative transformation was applied to the SNV corrected spectra. Figures 6 and 7 show the second derivative spectra zoomed in to highlight the region containing various C-H bands (figure 6) and the region containing various O-H and N-H bands (figure 8). Clear differences can be seen between the three product types in both spectral ranges.

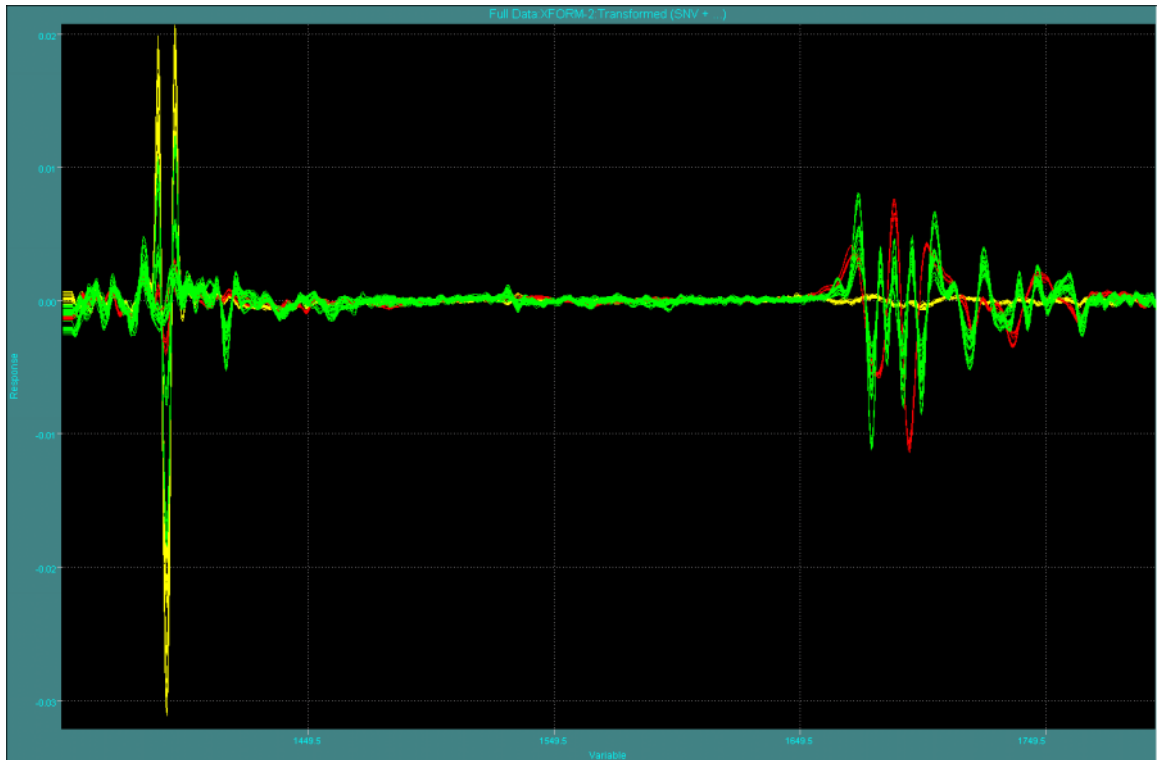


Figure 5: Chinese Antibiotics spectra after applying SNV transform and a second derivative.

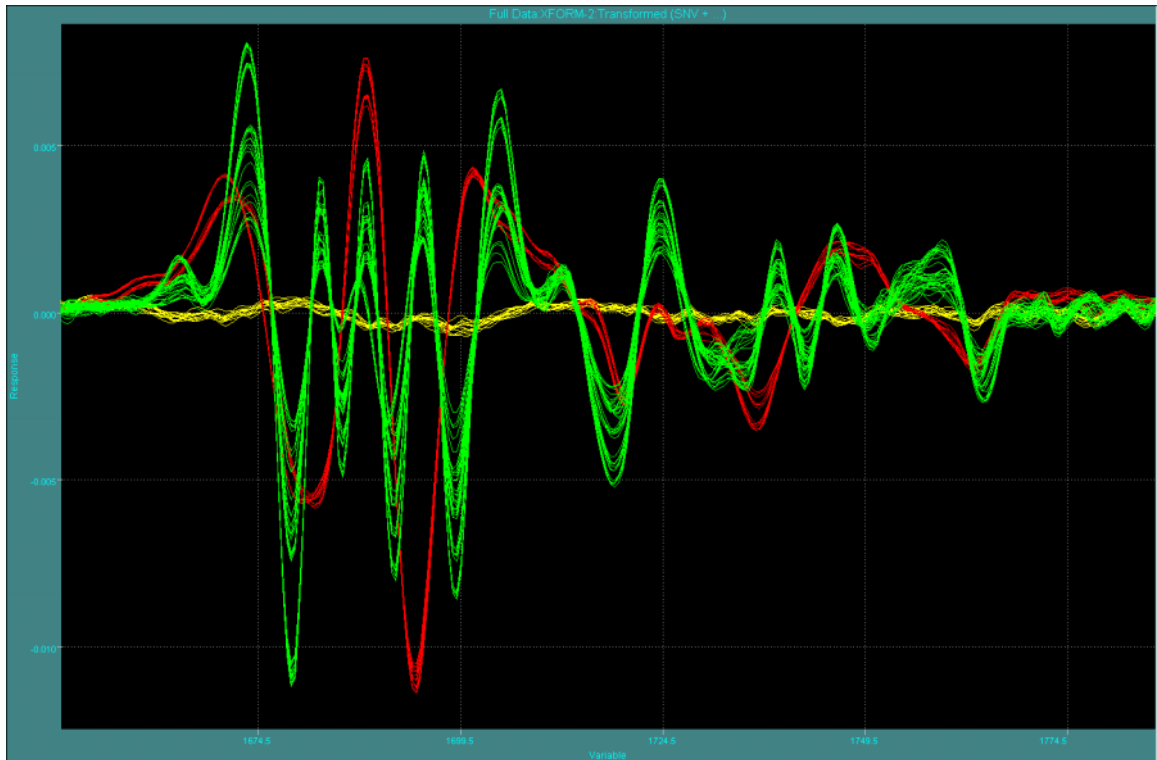


Figure 6: Chinese Antibiotics spectra after applying SNV transform and a second derivative – zoomed in region of various C-H absorption bands.

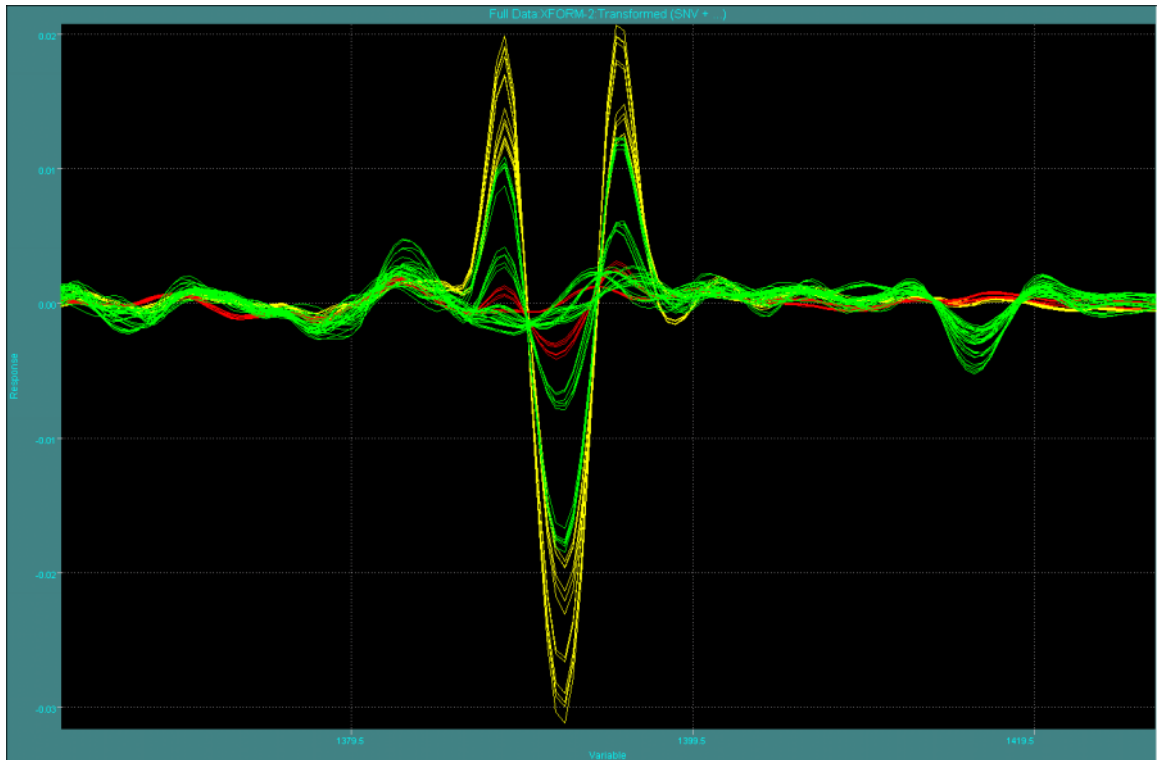


Figure 7: Chinese Antibiotics spectra after applying SNV transform and a second derivative – zoomed in region of various O-H and N-H absorption bands.

There are numerous algorithms that have been applied to product classification using NIR and FTIR spectra. We used commercially available software (Pirouette by Infometrix, Woodinville, WA) for data analysis.

A calibration model for the samples was developed using the SIMCA (Soft Independent Modeling of Class Analogy¹) algorithm. This develops a Principal Components Analysis model for each class (product type), and new samples are compared against each of these models to determine if it is similar to that product type. An “interclass distance” is calculated to indicate separation between classes, this is a unit-less number, and in general an interclass distance of 3 or greater indicates very clear separation of groups. Table 3 shows the interclass distances obtained on calibration, the values shown indicate very clear class separation, for example the Class 1 is 48.63 “interclass distances” from Class 2. These large separations indicated that products will be correctly identified into the right class. Samples from a class are analyzed and have very small distances from their correct class and very large distances from other classes indicating that they belong to the class. Samples different from each class will be classified with a high distance from all classes, so a counterfeit product, particularly an incorrectly formulated one would have a large distance from legal samples of the type identified by the label, and fail the confidence test of belonging to the product type.

Table 2: SIMCA Interclass Distances for model

Product	Class 1	Class 2	Class 3
Class1	0.000000	48.626801	12.470956
Class2	48.626797	0.000000	13.162300
Class3	12.470956	13.162300	0.000000

Figure 8 shows the class distances for the three product types examined, with clear segregation by product type. The spread of the data for each type may be due to legitimate product variations or sampling variations. It may also be that some of the products that we examined were counterfeit, without additional sample testing and information we cannot say. For example, perhaps the green samples circled are truly counterfeit.

Figure 7 shows the calibration spectra plotted in scores space (reference 1), the different classes (product types) are color-coded and large separations can be seen between the three classes. Unknown or test samples are transformed into scores space using the models in SIMCA, and if it maps into a cluster it is classified as being of the same product type.

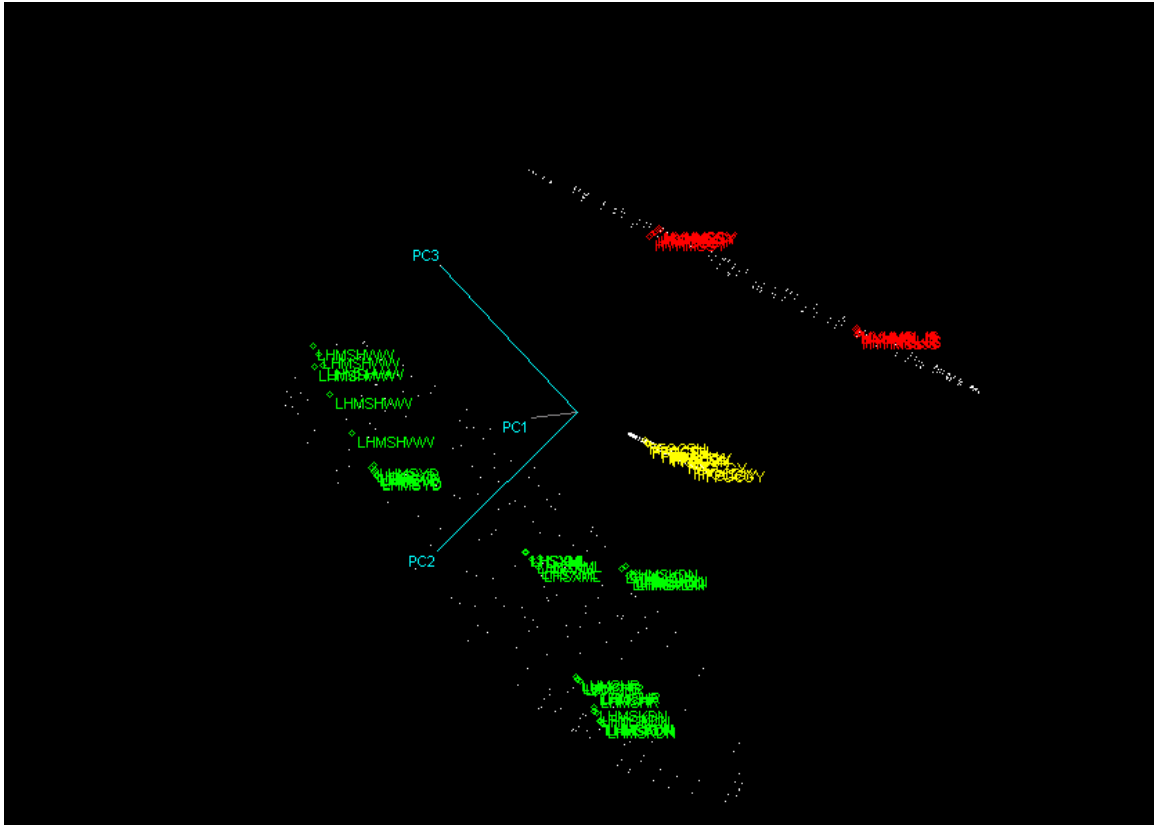


Figure 7: Presentation of calibration set in scores space showing the three classes.

Figure 8 shows the unknown/test samples plotted in scores space. The white dots encompass the “sphere” of the calibration models, if an unknown/test sample falls within the sphere of the product type it is classified as being that type of product. Most of the unknown samples submitted fall neatly into the 3 calibration clusters, but some can be seen outside the space of the models.

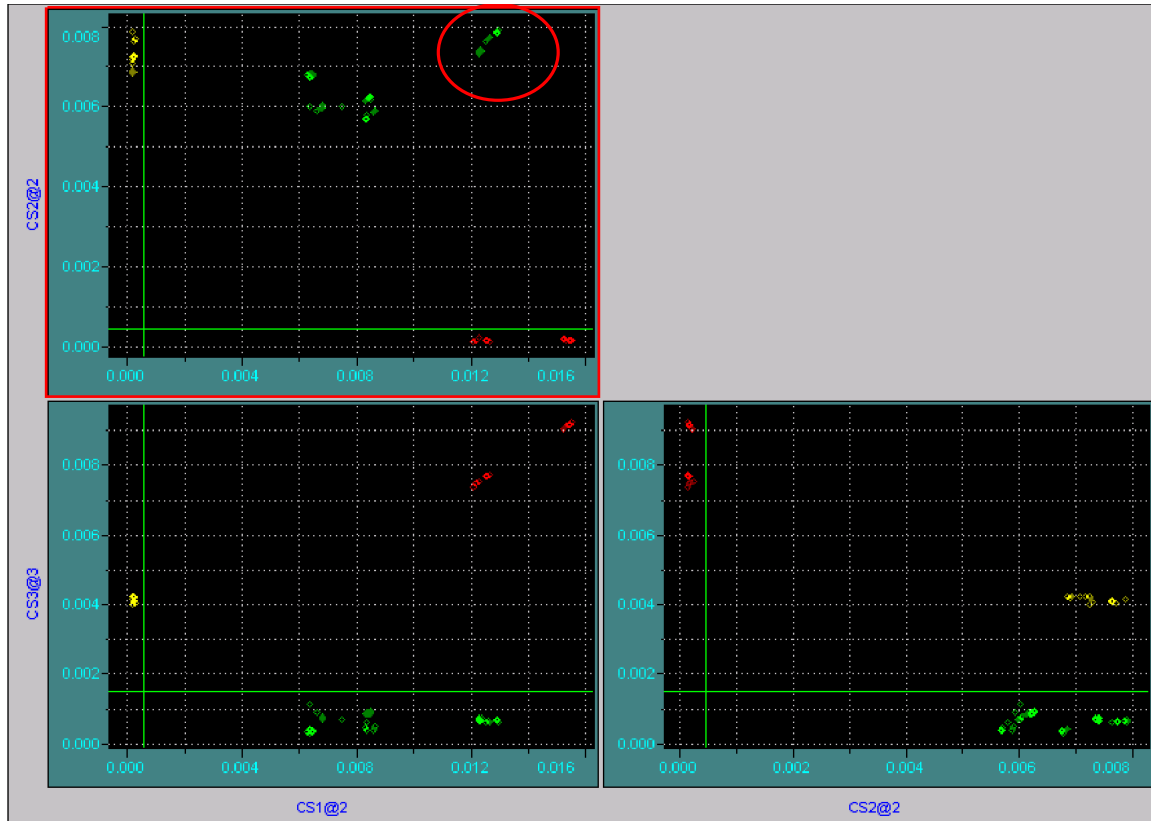


Figure 8: Class distances showing clear separation of 3 products. Circled group may be different from balance of the green coded (*HuYiHongMeiSu*) product group.

As a demonstration, the circled samples were removed from the *HuYiHongMeiSu* class and assigned as a separate class. A SIMCA model was calculated and it appears that these samples can be separated reliably from the balance of the *HuYiHongMeiSu* data set. This may be due to true, actual product variation, or they may be counterfeit. The scores plot for this model is shown in figure 9,

Table 3: SIMCA Interclass Distances for model with fourth group assigned based on prior plots.

CS1@3	CS1@3	CS2@3	CS3@3	CS4@3
Class 1	0.000000	20.622231	6.110181	19.958830
Class 2	20.622231	0.000000	10.500333	18.731913
Class 3	6.110181	10.500333	0.000000	3.609535
Class 4	19.958828	18.731913	3.609535	0.000000

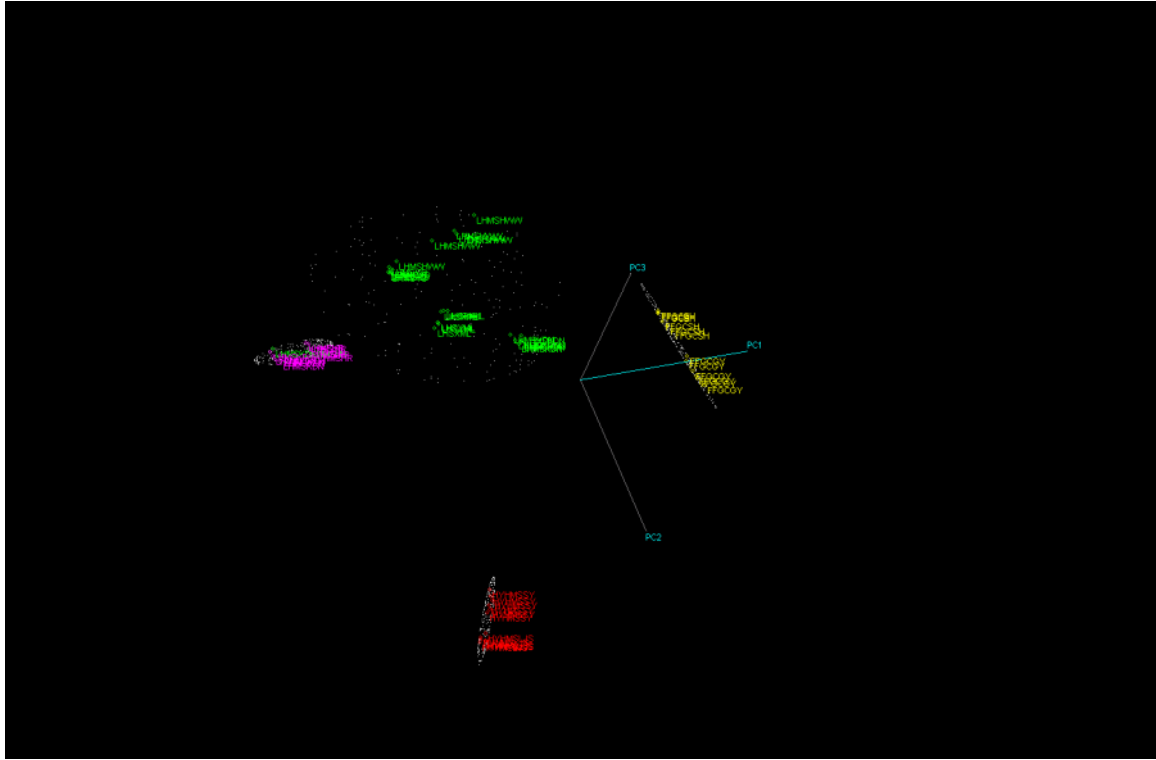


Figure 9: Presentation of calibration set in scores space showing the three classes.

3. Conclusions and recommendations

Axsun's NIR analyzer with diffuse reflectance sampling can be effectively used for rapid, routine product identification. The system can be automated so that an operator simple has to press button to run and analyze a sample. The high resolution attainable (1 nm) with the Axsun spectrometer will allow enhanced product classification if compared to low resolution grating based systems. The small size, utility requirement and solid state nature of the Axsun spectrometer make it an ideal solution for industrial NIR applications such as loading dock product identification.



References:

1) Wold, S.; "Pattern Recognition by Means of Disjoint Principal Components Models", Pattern Recognition, (1976) 8: 127-129.