

# THE USE OF NET ANALYTE SIGNAL ORTHOGONALIZATION IN THE SEPARATION OF MULTI-COMPONENT DIFFRACTION PATTERNS OBTAINED FROM X-RAY POWDER DIFFRACTION OF INTACT COMPACTS

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**Purpose.** Demonstrate the use of net analyte signal (NAS) orthogonalization as a means to accurately separate multi-component diffraction patterns thereby permitting the calculation of multivariate figures of merit (FOM) to evaluate the suitability of transmission and reflectance modes of quantitative X-ray powder diffraction (XRPD) on intact consolidated samples.

**Methods.** A four-component system consisting of two crystalline materials (anhydrous theophylline and lactose monohydrate), and two disordered materials (microcrystalline cellulose (MCC) and starch) was employed. Powder mixtures of varying composition were compressed into 13 mm cylindrical compacts varying in compression. The compacts were analyzed by XRPD in both reflectance and transmission geometries, using a PANalytical X'Pert Pro MPD with Cu K $\alpha$  radiation ( $\lambda = 1.5406 \text{ \AA}$ ). Quantitative models of composition were estimated using partial least squares regression and classical least squares regression. FOM were used to compare geometrical modes of analysis.

**Results.** Quantitative models were successfully generated for each individual component using whole pattern analysis. The R<sup>2</sup> values for theophylline, lactose, MCC and starch were 0.97, 0.98, 0.96, and 0.97 for the transmission data, and 0.92, 0.95, 0.95, and 0.95 for reflectance data, respectively. Though the transmission geometry showed superiority in specificity and accuracy, the reflectance geometry showed increased angular resolution.

**Conclusions.** The use of XRPD in the analysis of intact compacts remains an important mainstay in the characterization of solid state phenomena. Accurate separation of multi-component diffraction patterns with respect to the covariance structure enables direct observation of changes to material structure without compromising the intensity of correlated angular variables. Multivariate FOM provide additional descriptors for model performance permitting a direct comparison between reflectance and transmission mode analyses. Transmission provides an enhancement in signal-to-noise, sensitivity and precision, albeit somewhat attributable to decreased effects from sample displacement. The ability of multivariate FOM to discriminate model performance from data collected via two separate modes of analysis provides impetus for the increasing use of chemometric tools in PXRD applications.