Real-time monitoring of powder blend composition using near infrared spectroscopy

Conference Paper · December 2017

DOI: 10.1109/ICSensT.2017.8304431

5 authors, including:

Niall O' Mahony
Munster Technological University
57 PUBLICATIONS **1,059** CITATIONS
SEE PROFILE

Trevor Murphy
Tricel Killarney
13 PUBLICATIONS **76** CITATIONS
SEE PROFILE

Krishna Kaushal Panduru
Institute of Technology, Tralee
15 PUBLICATIONS **190** CITATIONS
SEE PROFILE

Daniel Riordan
Munster Technological University
91 PUBLICATIONS **1,312** CITATIONS
SEE PROFILE

Real-time Monitoring of Powder Blend Composition using Near Infrared Spectroscopy

Niall O' Mahony, Trevor Murphy, Krishna Panduru, Daniel Riordan, Joseph Walsh
IMAR Technology Gateway,
Institute of Technology Tralee,
Tralee, Ireland
niall.omahony@research.ittralee.ie

***Abstract*— Near Infrared Spectroscopy (NIRS) is a very powerful utility in a Process Analytical Technology (PAT) system because it can be used to monitor a multitude of process parameters non-invasively, non-destructively in real time and in hazardous environments. A catch to the versatility of NIRS is the requirement for Multi-Variate Data Analysis (MVDA) to calibrate the measurement of the parameter of interest. This paper presents a NIRS based real time continuous monitoring of powder blend composition which has widespread applications such as the pharmaceutical industry. The proposed system design enables reduction of optical path length so that the sensors can be successfully installed into powder conveyance systems. Sensor signal processing techniques were developed in this work to improve accuracy while minimizing pre-processing steps.**

The paper presents the implementation of several parameter estimation methodologies applied to sensor data collected using MATLAB® software for a model powder blending process. Several techniques were examined for the development of chemometric models of the multi-sensor data, including Principal Component Analysis (PCA), Partial Least Squares Regression (PLSR), Support Vector Machines (SVM) and Artificial Neural Networks (ANN). The performances of each of the models were compared in terms of accuracy (MSE) in predicting blend composition. The results obtained show that machine learning-based approaches produce process models of similar accuracy and robustness compared to models developed by PLSR while requiring minimal pre-processing and also being more adaptable to new data.

Keywords— Sensors Signal Processing and Interfacing; On-line monitoring; Parameter Estimation; Machine Learning; Process Analytical Technology.

I. INTRODUCTION

This work describes experiments which aim to investigate the key elements to the implementation of Process Analytical Technology (PAT) in powder processing industries. PAT is concerned with the observation of the progress of reactions/processes (in batch or semi-continuous processes) as well as controlling process stability (in continuous processes), which requires real-time, in-line or on-line process measurements and the application of real-time data analytics.

The paper will examine the use of NIRS for the measurement of blend composition to control the critical rates of ingredients in powder mixtures (e.g. Active Pharmaceutical Ingredients (APIs) in the pharmaceutical industry). Blend homogeneity is a measure of how consistent the blend composition is throughout a mixture. It is a key CQA in pharmaceutical processes where doses of API must be carefully controlled to comply with FDA requirements and to minimise waste of expensive materials. This application is also of concern in other industries e.g. milling, mining and food processing industries. Section II will introduce NIRS and some of the considerations to be made with regards to the physical sampling of materials. Section III will give an overview of the traditional chemometric techniques used to develop process models from NIRS data and also review the use of machine learning algorithms to the application. Finally, the implementation and comparison of these data analysis approaches in a model blending process is detailed in Section IV.

II. NEAR INFRARED SPECTOSCOPY (NIRS)

Near Infrared Spectroscopy is an analytical approach which records absorption, reflection, scattering or emission of light (with wavelengths from 800-2500nm), related to vibrational properties or the elemental composition of the material under test. NIR Spectroscopy is a favoured sensing method in industry as it provides non-contact measurement, does not require sample preparation and provides real-time data [1]. NIR can be used to measure many process parameters, primarily chemical composition, molecular weight [2] and particle size and also moisture, pH, temperature and other parameters relating to the molecular structure of the material under test. Such versatility come at the price of the need for calibration, however, the large amount of information an NIR sensor can collect makes it a valuable component in a process analytical platform. Recent reviews outline the versatility of and developments in the technology [3], [4].

A. Physical configuration

The physical integration of an NIR spectrometer into a process involves configuring a broadband light source (usually a tungsten-halogen or LED lamp) and the detector in one of the following modes: Transmittance, Transflectance, Diffuse Reflectance and Attenuated Total Reflectance (ATR).

The best configuration to use is dependent on the nature of the sample under test: for example, transmittance or transflectance is most suitable for liquids while reflectance is primarily used for powders [5]. The limited depth of penetration (in reflectance mode, depth of penetration is 0.5-2.5mm) can be a concern if the material under test is not homogenously distributed (Corredor, Bu and Both, 2011). This limitation can

be overcome with sampling procedures [6] or prediction algorithms [7], [8].

B. Applications

Due to complexity of analysis required NIRS was predominantly used in research and development in laboratories, however, this is now changing and the implementation of NIRS has moved out to the wider environment, e.g. testing in the Agri/food sector, surveillance applications involving unmanned Aerial Vehicles and indeed at-line process monitoring in the process industry. Motivation/drivers for this use of NIRS include greater precision, knowledge of data, power saving, improved quality, better efficiency and lower cost. NIRS was used in the completion of this research primarily for the on-line monitoring of blend composition of powder mixtures. This application is of particular concern in the pharmaceutical industry amongst other industries where the concentration of APIs and other ingredients must be carefully controlled. Monitoring deviations in real-time poses major cost reductions due to elimination of expensive waste material, time and labour.

III. Multi-Variate Data Analysis (MVDA)

Spectroscopic methods provide information on both physical and chemical characteristics specific to the sample being measured but data manipulation of the raw spectra is required. Supporting reference measurements are required for calibration of the multivariate data produced by NIRS. These references may come from offline laboratory methods or from online sensors in which case calibration can be updated continuously. The accuracy achievable by NIRS is limited by the accuracy of the reference measurements.

Chemometrics is an interdisciplinary science encompassing chemistry and computer science, where information is extracted from chemical data by data-driven means [9]. Real-time, in-line and cost-effective sensors for monitoring key strategic product parameters can be used for complementary sensor fusion with the NIR sensors for chemometrics to extract chemical and physical information about the material under test.

The analysis of spectroscopic data follows the steps of:

- pre-processing,
- data dimensionality reduction: reduces the no. of variables to speed up further analysis.
- model production by regression/classification,
- applying the model to perform prediction,
- (optionally) continuous updating of model parameters per new data.

A. Pre-processing

Pre-processing entails transforming the data to allow relationships to be more easily interpreted before performing regression or classification analytics.

NIR spectra have quite broad peaks at the fundamental overtones and combination bands of the materials it is used to test. This fact means that NIRS requires far less stringent sample preparation- a key feature which distinguishes it from other spectroscopic methods. Materials with strong interference bands need to be exactly calibrated and thus the wider combination and bands of NIR allow for greater flexibility. On the other hand, the overtones and combination bands are more easily hidden by noise and thus, NIRS requires MVDA with appropriate pre-processing. NIRS also suffers from scattering effects which further increases the requirement for pre-processing.

Additive baseline shift is due to scattering that is not wavelength dependent and can be caused by light attenuation due to variations in particle concentration. Solutions include normalisation and derivative processing. Note: 1st derivative processing can make spectra difficult to interpret, however, as the derivative of the spectral peaks (the slope tangential to the top of a curve) is zero and the 2nd derivative is preferred.

Multiplicative scatter effects are those which are wavelength dependent and can be caused by variations in particle size, sample packing and crystallinity of the powder. The effect must be removed if there is no interest in these parameters. Other causes include inconsistent path-length in diffuse transmission spectroscopy and variations in distance between particles and the probe in diffuse reflectance spectroscopy. These parameters must be kept constant as much as is possible by implementing procedures to ensure consistent sampling to achieve the best results. Solutions include Standard Normal Variate (SNV) and Multiplicative Scatter Correction (MSC).

Reference [10] analyses the effect of the pre-processing techniques used prior to the application of partial least squares and principal components regressions in the quality of the NIRS calibration models. The article's findings indicate that a certain combination of pre-processing methods together with orthogonal signal correction, prior to PLS and PCR regressions, allowed to decrease the number of latent variables and a slight decrease in RMSE. The work highlights the importance of trialling several pre-processing methods to find the optimal solution for the problem at hand. The reduction of the number of latent variables allows more parsimonious and hence more robust model to be developed. One should take care when applying pre-processing however so as not to lose important data due to averaging effects.

B. Data Dimensionality Reduction

The number of variables output by an NIR spectrometer is often in the range of hundreds or even thousands depending on the wavelength range and resolution of the spectrometer. Data dimensionality reduction is employed to simplify the interpretation of the data set. It is also employed to overcome the multi-collinearity problem where a high degree of correlation among the predictive variables (due to the broad peaks in NIRS data) increases the variance in estimates of the regression parameters [11].

Principal Component Analysis (PCA) looks for a few linear combinations of the variables that can be used to summarise the data without losing too much information in the process [11]. PCA is used when a linear reduction in dimensionality is required and produces a set of uncorrelated variables called Principal Components (PCs) which are simple orthogonal linear combinations of the original variables. The PCs are ordered according to the captured variance of the original data and therefore the more PCs you use the more process noise is being captured [12].

PCA gives no importance to the relationship between each predictive variable and the dependent or the target variable. Partial Least Squares (PLS) allows as much information in the raw predictive variables as well as in the relation between the predictive and target variables to be captured [11]. As discussed in Section III.C.1), the PLS technique works by successively extracting factors (rather than PCs) from both X and Y such that covariance between the extracted factors is maximised, thus it includes relationships between X and Y variables in its minimization.

C. Model Production

MVDA is implemented to identify patterns in NIRS data and apply regression/classification. Patterns are identified when there are similarities between groups of samples. Clustering effects and variable relationships can then be inferred, i.e. we can understand how different variables separate clusters of data and then control these variables to minimise variability between batches. Analysis can fall into two categories: regression and classification.

Regression analysis identifies the relationship between variables and allows us to predict process parameters (the output / response / dependent variables) based on process measurements (the input/predictor/independent variables from the NIR output/sensor array). Global models can be used or sometimes a separate model is required for each clustering effect. NIRS can also be used to classify raw materials. Classification is very similar to regression in that the output variables are discrete, categorical and unordered rather than continuous and ordered. Exploratory data analysis can also be used to identify which variables affect quality so as to eliminate the measurement of variables not affecting quality and hence reduce the cost of the measurement system.

1) Linear modelling

Multiple Linear Regression (MLR) tests the correlation of each of the original variables iteratively with the target property and includes only those whose regression coefficient is above some critical level in a regression equation. Variations of MLR algorithms (e.g. stepwise MLR) can repeat this process several times, alternating between selecting new variables based on their correlation with the existing fitted model and backward elimination of non-significant variables until no significant improvement of the model fit can be achieved by including more variables and all regression terms that are already selected are significant [13].

Principal Component Regression (PCR) compresses the variables to the most dominating dimensions rather than selecting the most important variables as in MLR above. PCR compression works to generate principal components (PCs) (linear combinations of the predictor variables) such that the variance between the components is maximised while having as few PCs as possible [12].

Partial least-squares (PLS) regression is a cross between Multiple Linear Regression and Principal Component Analysis that combines information about the variances of both the predictors and the responses, while also considering the correlations among them [14]. Once fitted, a model can be used to predict or simulate responses, assess the model fit using hypothesis tests, or use plots to visualise diagnostics, residuals, and interaction effects.

2) Machine Learning

Machine Learning Algorithms such as Artificial Neural Networks (ANNs) reject the traditional programming paradigm where the given problem must be closely examined, considering every possible case, and represented as an algorithm to be implemented in the computer program. Instead, a more human-like approach to problem solving is used to find solutions: Problem analysis is replaced by a training framework where the system is fed a large number of training patterns (sets of inputs for which the desired outputs are known) which it learns and uses to compute new patterns. There is no need for a general rule as in classical programming, in fact, they are a by-product of the learning algorithm. Self-organisation and the exploitation of interactions between small units have proven to perform better than central control, particularly for complex non-linear process models in that better fault tolerance and adaptability to new data is achievable [15].

The use of machine learning techniques such as Kalman Filters, Support Vector Machines (SVMs), ANNs and Adaptive Neuro-Fuzzy Inference Systems (ANFIS) has been reviewed in previous papers relating to this research [16], [17]. In comparison with conventional statistical methods, machine learning algorithms are easier to use, can be used when the level of prior knowledge about the problem at hand is low, when the problem is highly non-linear or when there are too many variables to be simplified in a model. However, their black-box nature which allows them to be self-adaptive and easy to use also has the drawbacks of being non-parametric meaning the relationship between input and output variables cannot be interpreted or extrapolated, making it difficult to deal with uncertainties and requiring a large amount of data related to the input and output parameters to cover a wide range of possible scenarios. Therefore, machine learning algorithms should not be used when a simple mathematical model can describe a system.

IV. Implementation of a Powder Sampling System Using NIRS

In order to exploit the benefits of NIRS and associated data analytics the need exists for transmission-mode optical sensors to be installed onto powder conveyance systems. The typical diameter of the conduit used in the pharmaceutical and powder milling industries involved is 50mm minimum. This presents a challenge to implementing transmission mode optical measurement as an optical path-length of only 24-32mm is generally allowed. It was decided to build an apparatus which would reduce the optical path-length thus allowing the sensors to be integrated. The design and analysis of CFD flow

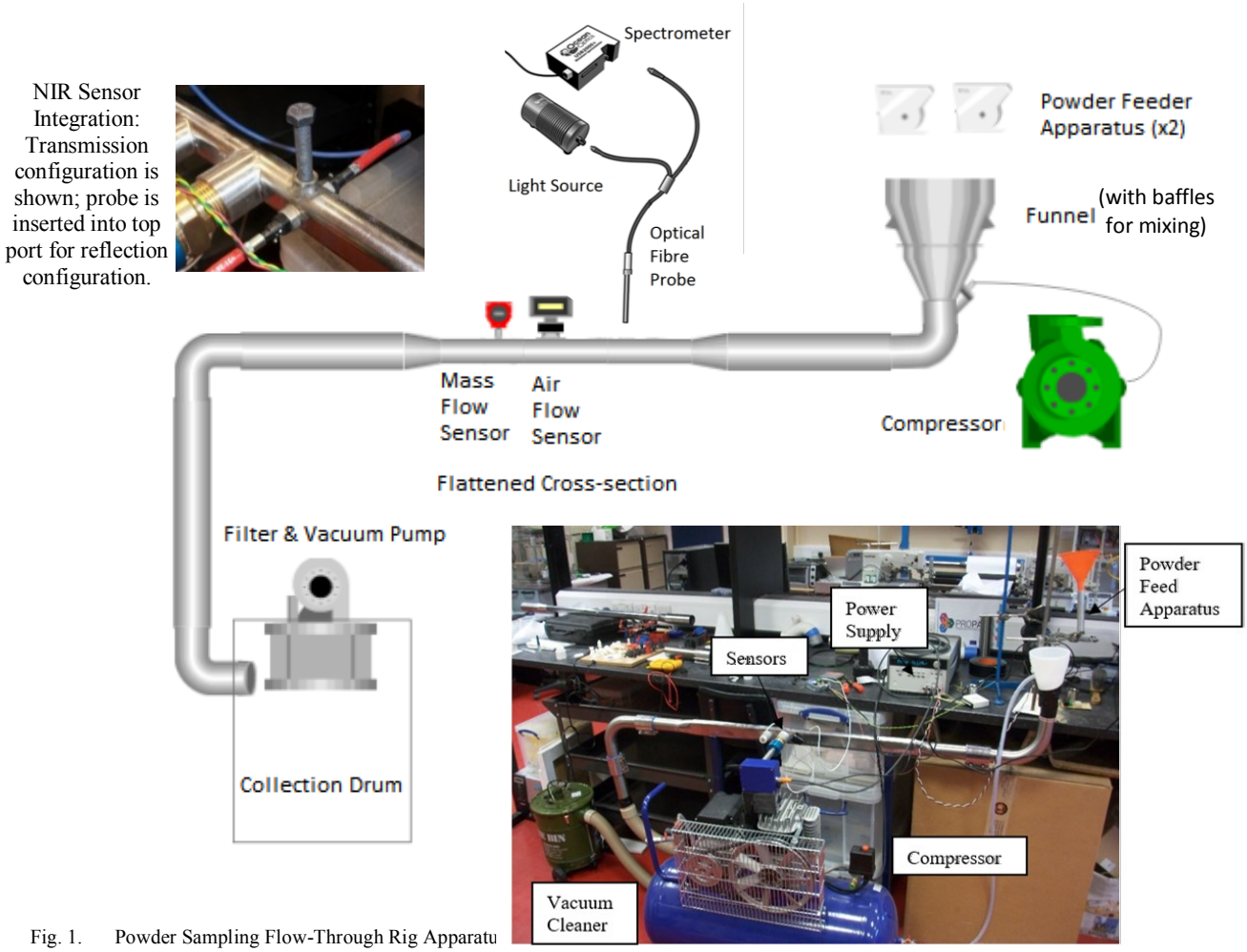

Fig. 1. Powder Sampling Flow-Through Rig Apparatu

simulations is detailed in [18]. Prototypes of the design were tested with the aid of 3D printing and the final system was fabricated from 304 stainless steel with the transition pieces being fabricated by 3D Metal printing [19].

A. Apparatus Setup

An NIR Spectrometer (Ocean Optics NIRQuest512 with wavelength range from 900 – 1700 nm) lies at the heart of the measurement system. A number of univariate smart sensors were also integrated into the designs to provide additional variables to be combined with the NIR spectra in complementary data fusion. These sensors include a microwave mass flowmeter, a thermal dispersion airflow sensor, a differential pressure sensor and an infrared temperature sensor. These sensors were not exploited in the data analysis presented in this paper, however.

Transmission and reflection optical configurations (shown in Fig. 1) were tested. Generally, NIR reflection is generally used for powder samples, however NIR Transmission was deemed more appropriate in this situation as higher signal to noise ratio was achievable with this method and a more representative sample of the powder stream is obtained (The entire diameter of the pipe inside the focus of the collimating lens is sampled compared to the 1 cm sensing envelope of the Ocean Optics QR400 reflection probe). Transmission NIR is also less effected by sampling issues such as the proximity of powder particles to lens. Collimating lens were used which ensure that light passes through the sample in parallel lines thus path-length is kept constant and absorbance measurements from transmittance readings can be calculated.

It was decided to use powders of similar particle size and density as the powder blend constituents to avoid gravimetric separation during conveyance through the test rig. Coffee (Constituent A) and sugar (Constituent B) were selected - both being organic compounds to which NIRS is suited. To collect calibration data, the powder mixture was passed through the apparatus several times, incrementing the ratio between constituents A and B each time. The constituents were mixed as they passed through a series of baffles in the entry funnel.

During these tests, it was found that lens fouling caused the output to be attenuated across the spectrum as powder built up on the lens. The preferential build-up of one material over another could prohibit accurate measurement of blend composition and may require remedying actions such as a periodic air purge or other methods. An additional port above the NIR transmission optical configuration (shown to be plugged by a bolt in Fig. 1) was used to insert an air gun to clean the optical lenses periodically.

B. System Modelling

The raw spectral data for each test (shown in Fig. 2) was pre-processed using MATLAB® software with Eigenvector Research PLS_Toolbox [20]. The models were validated by cross-validation with random sampling of the test data. Mean Centering (MC) pre-processing was applied for the most part for the comparison of the data analysis approaches. Several statistical regression analysis techniques were then performed which identified a number of principal component/latent factors from which the blend concentration could be inferred. The PLS model produced was tested by cross-validation with the test data. Machine learning algorithms (feedforward ANN using backpropagation training [21] and epsilon-support vector regression [22]) were also trained on the data.

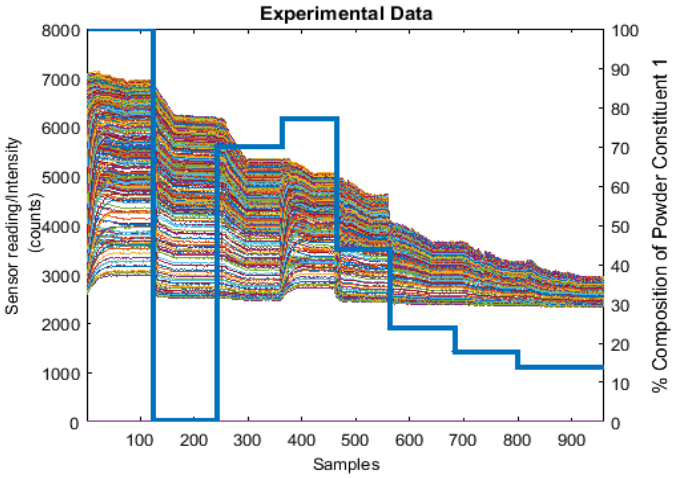

Fig. 2. NIR Data collected from model blending process for various powder mixtures.

TABLE I. COMPARISON OF CHEMOMETRIC/MACHINE LEARNING MODELS TESTED.

Description	X-block preprocess- ing	Y-block preprocess- ing	X-block compression	Layer 1 Nodes	Layer 2 Nodes	RMSEC	RMSECV	Bias	R^2 Cal
ANN Preprocessed	*	MC	PCA with 1 component(s)	2	0	22.415	22.475	0	0.549
ANN raw data	None	None	PCA with 1 component(s)	2	0	21.166	21.195	0.023	0.598
ANN Mean Centred	MC	MC	PCA with 1 component(s)	2	0	21.18	21.209	0.024	0.597
ANN PLS Reduction	*	MC	PLS with 6 component(s)	2	0	2.602	2.934	-0.016	0.994
ANN PLS Reduction 2 Layers	*	MC	PLS with 6 component(s)	1	1	5.777	8.221	0.03	0.97
ANN PLS Reduction+MC	MC	MC	PLS with 6 component(s)	2	0	3.283	3.547	-0.001	0.99
ANN PLS Reduction 2 LV	MC	MC	PLS with 2 component(s)	2	0	10.604	12.237	-0.957	0.902
PLSR 2 LV	MC	MC	2 LV	N/A	N/A	20.792	0	0	0.612
PLSR 6 LV	MC	MC	6 LV	N/A	N/A	3.573	0	0.015	0.987
PLSR 6 LV Preprocessed	*	MC	6 LV	N/A	N/A	6.563	0.232	0.259	0.959
PCR	MC	MC	4 PC	N/A	N/A	17.379	17.394	0.006	0.729
MLR	MC	MC	N/A	N/A	N/A	1.49	3.458	0	0.998
SVM	MC	MC	PLS with 2 component(s)	N/A	N/A	8.103	9.788	-0.897	0.942

* Transmission to Absorbance (log(1/T)), Baseline (Automatic Weighted Least Squares), 2nd Derivative (Savitzky–Golay, order 2, window 41 pt, include only, tails)

C. Results

The RMSE and goodness of fit (R^2 value) for the output of each of the algorithms were recorded in TABLE I. to allow comparisons to be made and determine the effectiveness of pre-processing techniques and identify the best model produced. Note that RMSECV (Root Mean Square Cross Validation) was taken as the most important measure of performance.

D. Discussion of Results

MLR was found to perform the best giving a RMSE of 1.49 percentage composition. This was followed closely by ANN modelling in conjunction with PLS dimensionality reduction (2.6% RMSE). The reduction in performance between "PLSR 6 LV" and "PLSR 6 LV Preprocessed" highlights the importance of understanding the effects of pre-processing operations. In this instance, the application of Savitsky-Golay filtering had averaging effects on the data which slightly reduced the accuracy of the PLSR model. For some models however, preprocessing was beneficial (compare "ANN PLS Reduction"

and "ANN PLS Reduction+MC" in TABLE I.). Therefore, trial and error must be exercised when applying pre-processing as the results are highly dependent on the nature of the input data. In agreement with existing research [10], the effect of the pre-processing methods on model performance was found to be minimal for a given number of latent variables.

PCR was less accurate than PLSR (also PCA compression for ANN modelling was less effective than PLS compression). This is because PCA gives no importance to the relationship between each input variable (the NIRS measurements for each wavelength) and the output variable (blend composition). It should be noted that these experiments were carried out in laboratory conditions and the reliability of the models can only be determined when they are applied to the actual process.

V. Conclusion

In conclusion, the chemometric algorithms applied were extremely effective in extracting information about the constituent concentration of the powder blends in non-ideal sampling conditions. This paper has detailed the setup of a demonstration unit of PAT where a flow-through sampling pipeline has been equipped with a suite of smart sensors and an NIR spectrometer. The multi-sensor data was analysed to extract information on the percentage composition of powder blend constituents in a model blending process.

The project results will yield a process model tailored specifically to the processes they are calibrated on which can easily be implemented on an embedded platform. The research has successfully implemented transmission spectroscopy on a disperse powder flow under pneumatic conveyance in a pipeline. Such an implementation is unprecedented as usually at-line or offline sampling procedures using diffuse spectroscopy are used. The developed system offers totally inline, non-invasive monitoring empowered by advanced data processing algorithms for sensor fusion, system modelling and parameter estimation.

The project provides a proof of concept for the real-time monitoring and control of powder blend composition using NIRS, supporting smart sensors and data analytics and also tackles many issues which have arisen in the course of the project including for example sensor placement for optimum sampling, overcoming lens-fouling and the development of robust data analysis algorithms to compensate for non-ideal sampling conditions. Such real-time adaptive modelling and control in response to parameters such as chemical composition is made more accessible by decreasing sensor cost and advancing data processing algorithms which allow features to be extracted and patterns to be recognised in challenging conditions.

REFERENCES

[1] C. C. Corredor, D. Bu, and D. Both, "Comparison of near infrared and microwave resonance sensors for at-line moisture determination in powders and tablets," *Anal. Chim. Acta*, vol. 696, no. 1–2, pp. 84–93, Jun. 2011.

[2] W. Li, *Process Monitoring of Polymer Systems by using Near-Infrared Spectroscopy*. INTECH Open Access Publisher, 2011.

[3] Y. Ozaki, "Near-infrared spectroscopy--its versatility in analytical chemistry," *Anal. Sci. Int. J. Jpn. Soc. Anal. Chem.*, vol. 28, no. 6, pp. 545–563, 2012.

[4] J. Rantanen and J. Khinast, "The Future of Pharmaceutical Manufacturing Sciences," *J. Pharm. Sci.*, vol. 104, no. 11, pp. 3612–3638, Nov. 2015.

[5] A. Sánchez-Paternina, A. D. Román-Ospino, M. Martínez, J. Mercado, C. Alonso, and R. J. Romañach, "Near infrared spectroscopic transmittance measurements for pharmaceutical powder mixtures," *J. Pharm. Biomed. Anal.*, vol. 123, pp. 120–127, May 2016.

[6] Jérôme Mantanus, "New pharmaceutical applications involving Near Infrared spectroscopy as a PAT compliant process analyzer," Doctoral thesis in Biomedical and Pharmaceutical Sciences, University of Liege, Liege, 2012.

[7] Metrohm AG, "NIR Spectroscopy - A guide to near-infrared spectroscopic analysis of industrial manufaturing processes." Metrohm AG, 2013.

[8] N. O. Mahony, T. Murphy, K. Panduru, D. Riordan, and J. Walsh, "Fibre-optic sensors for Process Analytical Technology," in *33rd International Manufacturing Conference (IMC33) 2016*, University of Limerick, Ireland, 2016.

[9] J. Workman Jr, "Chemometrics and PAT: What Does it all Mean?," *Role Spectrosc. Process Anal. Technol.*, pp. 18–23, 2005.

[10] P. Felizardo, P. Baptista, J. C. Menezes, and M. J. N. Correia, "Multivariate near infrared spectroscopy models for predicting methanol and water content in biodiesel," *Anal. Chim. Acta*, vol. 595, no. 1–2, pp. 107–113, Jul. 2007.

[11] S. Maitra and J. Yan, "Principle component analysis and partial least squares: Two dimension reduction techniques for regression," *Appl. Multivar. Stat. Models*, vol. 79, 2008.

[12] I. V. Kovalenko, G. R. Rippke, and C. R. Hurburgh, "Dimensionality reduction of near infrared spectral data using global and local implementations of principal component analysis for neural network calibrations," *J. Infrared Spectrosc.*, vol. 15, no. 1, pp. 21–28, Feb. 2007.

[13] R. M. Balabin and S. V. Smirnov, "Variable selection in near-infrared spectroscopy: benchmarking of feature selection methods on biodiesel data," *Anal. Chim. Acta*, vol. 692, no. 1–2, pp. 63–72, Apr. 2011.

[14] MathWorks, Inc, "Partial Least Squares - MATLAB & Simulink - MathWorks United Kingdom." [Online]. Available: http://uk.mathworks.com/help/stats/partial-least-squares.html. [Accessed: 07-Oct-2016].

[15] P. Koehn, "Combining genetic algorithms and neural networks: The encoding problem," University of Tennessee, Knoxville, 1994.

[16] N. O. Mahony, T. Murphy, K. Panduru, D. Riordan, and J. Walsh, "Machine Learning Algorithms for Process Analytical Technology," in *World Congress on Industrial Control Systems Security*, London, UK, 2016, pp. 20–26.

[17] N. O. Mahony, T. Murphy, K. Panduru, D. Riordan, and J. Walsh, "Adaptive process control and sensor fusion for process analytical technology," in *2016 27th Irish Signals and Systems Conference (ISSC)*, 2016, pp. 1–6.

[18] T. Murphy, N. O' Mahony, K. Panduru, D. Riordan, and J. Walsh, "Computational Fluid Dynamics, Rapid Prototyping and Design of Materials Sampling Processes for PAT," in *33rd International Manufacturing Conference (IMC33) 2016*, University of Limerick, Ireland, 2016.

[19] U3D, "U3D » Equipment." [Online]. Available: https://umg.ucd.ie/u3d/?page_id=6. [Accessed: 27-Feb-2017].

[20] "Eigenvector Research: Chemometrics Software, Consulting and Training." [Online]. Available: http://www.eigenvector.com/. [Accessed: 27-Jun-2017].

[21] "Ann - Eigenvector Documentation Wiki." [Online]. Available: http://wiki.eigenvector.com/index.php?title=Ann. [Accessed: 27-Jun-2017].

[22] "Svm - Eigenvector Documentation Wiki." [Online]. Available: http://wiki.eigenvector.com/index.php?title=Svm. [Accessed: 27-Jun-2017].