



# Calibration transfer of a Raman spectroscopic quantification method for the assessment of liquid detergent compositions from at-line laboratory to in-line industrial scale

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## ABSTRACT

Calibration transfer or standardisation aims at creating a uniform spectral response on different spectroscopic instruments or under varying conditions, without requiring a full recalibration for each situation. In the current study, this strategy is applied to construct at-line multivariate calibration models and consequently employ them in-line in a continuous industrial production line, using the same spectrometer.

Firstly, quantitative multivariate models are constructed at-line at laboratory scale for predicting the concentration of two main ingredients in hard surface cleaners. By regressing the Raman spectra of a set of small-scale calibration samples against their reference concentration values, partial least squares (PLS) models are developed to quantify the surfactant levels in the liquid detergent compositions under investigation. After evaluating the models performance with a set of independent validation samples, a univariate slope/bias correction is applied in view of transporting these at-line calibration models to an in-line manufacturing set-up. This standardisation technique allows a fast and easy transfer of the PLS regression models, by simply correcting the model predictions on the in-line set-up, without adjusting anything to the original multivariate calibration models.

An extensive statistical analysis is performed in order to assess the predictive quality of the transferred regression models. Before and after transfer, the  $R^2$  and RMSEP of both models is compared for evaluating if their magnitude is similar. T-tests are then performed to investigate whether the slope and intercept of the transferred regression line are not statistically different from 1 and 0, respectively. Furthermore, it is inspected whether no significant bias can be noted. F-tests are executed as well, for assessing the linearity of the transfer regression line and for investigating the statistical coincidence of the transfer and validation regression line. Finally, a paired *t*-test is performed to compare the original at-line model to the slope/bias corrected in-line model, using interval hypotheses.

It is shown that the calibration models of Surfactant 1 and Surfactant 2 yield satisfactory in-line predictions after slope/bias correction. While Surfactant 1 passes seven out of eight statistical tests, the recommended validation parameters are 100% successful for Surfactant 2. It is hence concluded that the proposed strategy for transferring at-line calibration models to an in-line industrial environment via a univariate slope/bias correction of the predicted values offers a successful standardisation approach.

## 1. Introduction

Calibration transfer or standardisation can be defined as the uniformisation of the spectral response on different spectroscopic instruments or under altered environmental conditions in view of eliminating the need for time-consuming recalibration procedures [1–4]. Such standardisation strategies are desirable on a number of occasions that result in the failure of the originally developed multivariate calibration

methods.

Firstly, drifts or nonlinearities in the instrumental response function of a spectrometer may be witnessed over time due to ageing of the equipment. Analogously, within one spectrometer, the instrumental response can alter due to a repair, causing a shift in the wavelength axis. Secondly, multivariate calibration models may become invalid when it is pursued to transport an existing chemometric model from one instrument to a second instrument. A variety of reasons may render

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erroneous results on this secondary or slave apparatus, as the measured intensity values from two spectrometers will generally be different, as may the wavelength axes and peak locations be. Thirdly, changes in the physical or chemical constitution of the samples between the calibration and prediction step may cause issues. When modifications to the viscosity, particle size or surface texture arise, the model predictions may become inaccurate. Likewise, when batch-to-batch variations occur due to modifications in raw materials or sample preparation, this may lead to incorrect prediction results. Furthermore, changes in the instruments environment exhibit another situation where a multivariate calibration model may become invalid. Fluctuations in temperature or humidity, for instance, may strongly influence the spectral outcome of the instrument [1–4].

As the construction of qualitative or quantitative multivariate models is often an elaborate process that requires quite a lot of effort and resources, it would negatively impact the business if full recalibrations would be required under all these circumstances, since they involve a lot of development costs and time delays. Therefore, a number of standardisation strategies has been developed with the objective of avoiding the need for a full recalibration. Generally, they can be divided into two main classes: strategies that can be applied prior to model implementation and instrument standardisation methods that can be of use after the model is already in operation.

Methodologies that can be performed before model implementation are instrument matching, global modelling, model updating and sensor selecting. These techniques aim at avoiding the need for data transformation by carefully controlling the experimental and environmental conditions and by selecting appropriate instrumental parameters [1–3].

However, when it is impossible to foresee all future sources of variation or these instrumental and experimental design techniques offer insufficiently accurate results, standardisation techniques are required to deal with non-calibrated variations that are observed after the model is already in use. Herein, a distinction can be made between transfer strategies that standardise either the model coefficients, the spectral responses or the predicted values. Modification of the spectral responses is the most popularly applied approach for diminishing the observed dissimilarities in model outcome. Univariate procedures such as the Shenk and Westerhaus standardisation or single wavelength standardisation (SWS), for example, allow to correct simple wavelength shifts or linear intensity differences in spectra. In case the transfer issue is more complex and involves the correction of peak broadening or effects in the data where the covariance between separate channels cannot be neglected, multivariate standardisation methods are employed. Among the most commonly suggested standardisation strategies in this category are direct standardisation (DS) and piece-wise direct standardisation (PDS) [1–4]. In view of correcting the predicted values rather than the spectral responses, only one standardisation approach is widely used, namely the slope/bias correction (SBC). In this univariate method, a linear relationship is assumed between the predictions from the secondary instrument or conditions and the corresponding predictions that would have been obtained on the primary instrument or conditions. This standardisation approach allows to rapidly compensate for simple and systematic differences and has proven valuable on a number of occasions [1,2,5–10].

In this study, it is aimed to transfer PLS regression quantification models from an at-line to an in-line set-up within one spectrometer. Firstly, quantitative calibration models are constructed for predicting the concentration levels of two surfactants in a liquid detergent composition based on Raman spectra. In order to allow the preparation of calibration samples with deviating compositions at a small scale, these multivariate regression models need to be developed at-line. Secondly, once it is validated that the model can adequately predict the concentration of unknown samples, a transfer of these at-line calibration models to an in-line manufacturing environment at industrial scale is pursued. Running the constructed quantification models in a production line would allow to evaluate the quality of the fabricated liquid

detergent compositions in real-time. This would offer the opportunity of quickly observing trends and regulating the process when products tend to go out of specification. Such fast interventions could result in decreased manufacturing costs and increased product quality, while requiring less manpower [11].

The calibration transfer challenge in this specific case lies in overcoming the differences in spectral response that are witnessed between the at-line and the in-line set-up. As only one Raman instrument is employed, it is a change in environmental factors and sample presentation that defines the observed variation between the primary (at-line) and secondary (in-line) conditions. It is expected that this alteration in sampling strategy affects the response of the Raman spectrometer. Previously, Karande et al. have illustrated that shifting from static to dynamic sampling influences the acquired spectral data and hence has an impact on the quality of the resulting multivariate models [12]. This study on near-infrared spectroscopy stresses the importance of appropriate sampling and shows the negative consequences of dissimilar sampling strategies between the calibration and the prediction step.

Furthermore, previous work by the authors has revealed that such dissimilarities in spectral outcome between static and dynamic sampling are to be expected in Raman spectroscopy as well [10]. As this experimental work, which served as a proof of concept for this standardisation strategy, has illustrated that a univariate slope/bias correction allows to transfer calibration models from an at-line to an in-line set-up at laboratory scale, the same approach is addressed here [10]. Slope/bias corrections are hence employed to achieve a transfer of the two PLS calibration models between the stationary at-line and dynamic in-line conditions. This univariate standardisation of the predicted values offers the benefit of being simple, practical and straightforward, without requiring sophisticated software packages or complex calculations [1–3,13,14].

A handful of studies are described in literature, which value the use of univariate slope/bias correction in achieving a successful standardisation [5–9]. A first series of investigations aimed to transfer quantitative multivariate calibrations between different near-infrared spectrometers [5–7]. Comparing several standardisation strategies to achieve their goal, the authors have witnessed that a simple slope/bias correction could successfully be applied and yielded small prediction errors. Analogously, Sales et al. have investigated both univariate and multivariate standardisation techniques for extending the lifetime of a PLS calibration model based on UV–VIS spectra [8]. Herein, the authors highlight the preference of slope/bias correction over multivariate PDS due to the simplicity of the univariate method. More recently, Brito et al. evaluated the feasibility of instrument standardisation to transfer calibration models between a bench scanning and a submersible diode array spectrophotometer [9]. It was concluded that slope/bias correction yielded the most adequate results in comparison to other univariate transfer approaches.

To the best of our knowledge, only one study has previously been performed on the calibration transfer of multivariate calibration models from an at-line to an in-line measurement set-up via Raman spectroscopy [10]. Since the results of this small-scale investigation showed promising perspectives for in-line quantification based on at-line calibration, the proposed strategy is expanded in this study to a continuous manufacturing process at industrial scale.

## 2. Materials and methods

### 2.1. Liquid detergent composition

The liquid detergent compositions under investigation are hard surface cleaners (HSC), consisting of fourteen ingredients in a largely water-based carrier. These constituents are a combination of surfactants, builders, polymers, solvents, dyes, perfumes, preservatives, viscosity modifiers and pH-adjustment agents. As the proprietary

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