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# Application of orthogonal space regression to calibration transfer without standards

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**To transfer a calibration model in cases where the standardization samples are rare or unstable, a method based on orthogonal space regression (OSR) is proposed. It uses virtual standardization spectra to account for response changes between instruments or batches. A comparative study of the proposed OSR, piecewise direct standardization, finite impulse response, orthogonal signal correction, and model updating (MU) was conducted on both pharmaceutical tablet data and chlorogenic acid data. The results of these studies suggest that both the OSR and the MU are superior to the other transfer techniques in terms of root-mean-squared error of prediction and ratio of performance to interquartile distance. Moreover, OSR requires no identical standard samples, and it avoids re-optimizing the transfer models. In conclusion, both the differences among spectra measured on different spectrometers and the differences between different batches can be corrected successfully using the OSR method.**


**Keywords:** alcohol precipitation process; calibration transfer; piecewise direct standardization (PDS); model updating (MU); orthogonal space regression (OSR)

## 1. INTRODUCTION

The extraction of chemical information from rather featureless spectroscopic signals has been one of the notable successes of multivariate calibration approaches, and these tools have been applied to various analytical techniques including near-infrared (NIR) spectroscopy. With the aid of multivariate calibration methods such as partial least squares (PLS) and principal components regression (PCR), the quantitative information carried in the NIR spectra of analytes can be extracted and used to build models to predict the concentration and other properties of analytes.

These approaches are limited, however, when an elaborately developed model is used for the prediction of external samples. In this discussion, the external samples refer to any sample not included in the calibration model such as those collected at a different time, from different batch, measured using a different instrument, and so on. Because of instrument-to-instrument variations, inevitable long-term instrumental drift, or unexpected sample composition changes from batch to batch, a calibration model may become ineffective. Those variations in spectra make it difficult to construct calibration models that are robust across batches and instruments.

Various calibration transfer methods can be used to correct for those variations, and most of them have been comprehensively discussed in previous reviews [1,2]. These calibration transfers fall into three broad categories depending on the type of adjustment strategy. The most successfully used transfer techniques are the standardization methods. A transfer method proposed by Bouveresse *et al*. [3] corrects the predicted values by using a simple univariate slope and bias correction. Generally, it will work well only when the differences between instruments are simple and systematic. However, when the instrumental differences become more complex, approaches such as the direct standardization (DS) or the piecewise DS (PDS) developed by Wang *et al*. [4] may be more acceptable.

A standardization method modeling the relationships in the transformed wavelet domain between spectra was investigated by Walczak *et al*. [5]. The relationships between wavelet transform coefficients of a subset of carefully selected standard samples obtained on two instruments can be modeled through univariate linear regression. The corrected wavelet coefficients are converted back to the wavelength domain to make the spectra from the new instrument to resemble those from the original instrument. Fan *et al*. [6] proposed a method based on canonical correlation analysis (CCA) to correct for the differences among spectra measured on different spectrometers. Using a strategy similar to CCA, a method based on spectral regression successfully performed the transfer between instruments [7].

The second class of calibration transfer approaches includes signal preprocessing and other data transformations. In general, those methods do not require identical samples measured on both spectrometers. Common transforms include the multiplicative scatter correction [8–10], standard normal variate [10], orthogonal signal correction (OSC) [11–13], and finite impulse response (FIR) filtering [9,14]. These methods correct for changes in baselines and signal-to-noise ratios that invariably occur. However, in many situations, they cannot correct for changes in the instrument [11]. Thus, the third type of calibration transfer techniques, model updating (MU), is employed [11,15,16]. MU addresses the instrumental differences by incorporating the

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new instrumental information to rebuild the model. One limitation of MU is the increasing complexity of the model.

For analysis of intermediates, especially intermediates in pharmaceutical processes, the abovementioned methods present a dilemma because the intermediates are susceptible to environment and of high variations among batches; furthermore, the calibration samples must mimic these materials. Ideally, a range of standard intermediates could be used. However, maintaining the integrity of these standards over time and during transport is challenging because of contamination and component oxidization [17]. Even if the integrity of the standards is maintained, re-measuring the standard intermediates and replicating samples of such complexity in later batches are challenging.

To overcome this, a virtual standardization spectrum (VSS) was adopted to correct for the batch-wise variation without using actual standard samples and forms the core of the proposed orthogonal space regression (OSR) approach. The calibration transfer method was validated with three different batches of chlorogenic acid in an alcohol precipitation process monitored by Fourier transform NIR spectrometry. We show that OSR can successfully remove variations among batches. The application of OSR on the tablet data also indicates that it can be used to correct for differences among spectra measured on different spectrometers.

## 2. METHODS

### 2.1. Finite impulse response

The FIR may also be described as a moving window multiplicative signal correction [10] and is a transfer technique that reduces the instrumental variation in the presence of the desired, property-induced variation without standards.

The transfer of the spectrum $\boldsymbol{s}_j$, the $j$th spectrum of the set $\boldsymbol{S}$, is achieved by the following sequence of operations [14]. First, a window size of $2p+1$ is predefined. Next, both the spectra $\boldsymbol{s}_j$ and $\boldsymbol{r}$, the later of which is the mean of spectra obtained on the target instrument (primary instrument in this study), are mean centered in the processing window. According to usual least squares, a regression coefficient $b_{ij}$ is obtained by regressing the mean-centered spectrum $\bar{s}_j$ on the mean-centered target spectrum $\bar{r}$. Finally, the $i$th point of the $j$th transferred spectrum is generated by the equation

$$\bar{s}_{ij}^{*} = \bar{s}_{ij}/b_{ij} + mean(\mathbf{r}) \tag{1}$$

where $mean(\mathbf{r})$ refers to the average value of the sequence of numbers in $\boldsymbol{r}$ within the $2p+1$ point window.

The processing window is moved one point forward, and the centering, regression, and projection procedures described earlier are repeated until all points in $\boldsymbol{s}_j$ are transferred. It is notable that the ends of the spectrum specifically the first and last $p$ points are untreated. These end points can be processed using multiplicative scatter correction (MSC) [9] or by duplicating the first and last $p$ points to augment the spectrum on both ends, separately. In this work, the later procedure is used.

### 2.2. Orthogonal space regression

Orthogonal space regression is proposed to make the response obtained on a secondary batch (the batch to be transferred) appear as if it has been measured on the primary batch that was used to form the calibration set. The OSR algorithm corrects the variation among batches using a VSS, which is defined as the OSC-corrected spectrum divided by its corresponding property value. The primary assumption here is that the spectrum–property relationship is linear. Although this assumption is not always correct, it is reasonable in that there are lots of successful applications of partial least squares (PLS) for NIR data [18]. Below gives an overview and brief explanation of the proposed OSR procedure. The details of it are given in the appendix.

First, both groups of spectra (to be transferred or not) are corrected using Westerhuis's direct OSC algorithm (DOSC) [19]. Unlike many other versions reported in the literature, it will always find the components that are orthogonal to the property $\mathbf{Y}$ and describe the largest variation of the spectra $\mathbf{X}$:

$$\mathbf{X}corr = \mathbf{X} - \mathbf{t}\mathbf{p}^{\mathbf{T}} = \mathbf{X}\mathbf{r}\mathbf{p}^{\mathbf{T}} \tag{2}$$

where,

$$\mathbf{r} = \mathbf{X}^{+}\mathbf{t}$$
$$\mathbf{p} = \mathbf{X}^{\mathbf{T}}\mathbf{t}(\mathbf{t}^{\mathbf{T}}\mathbf{t})^{-1}$$

and $X^{+}$ is the Moore–Penrose inverse of $\mathbf{X}$. It is interesting to note that the generalized inverse $\mathbf{X}^{-}$, the substitute for $\mathbf{X}^{+}$, can be used to loosen the rigid orthogonality constraint. By doing so, the prediction performance could be improved. The principal component $\boldsymbol{t}$ denotes the largest singular value using principal component analysis (PCA) on the orthogonal subspace $\mathbf{A}_{\hat{\mathbf{Y}}}\mathbf{X}$ [19]. If more DOSC components are required, more principal components can be extracted. Note that $\boldsymbol{t}$ is not only the one-dimensional subspace of $\mathbf{X}$ orthogonal to $\mathbf{Y}$ but also accounts for the maximum variance of $\mathbf{A}_{\hat{\mathbf{Y}}}\mathbf{X}$ and $\mathbf{X}$. Here, cross-validation is used to estimate the number of DOSC components.

Next, the virtual standardization spectra for both the primary batch and the secondary batch (the batch to be transferred) are estimated. As described earlier, the virtual spectrum is defined as the OSC-corrected spectrum divided by its corresponding property value and can be calculated with

$$\mathbf{v}_i = \mathbf{x}^{\mathbf{corr}}{}_i./y_i \tag{3}$$

where, $\mathbf{x}^{\mathbf{corr}}{}_i$ is the OSC-corrected spectrum of the $i$th sample, $y_i$ is the reference property value for the $i$th samples, and $\mathbf{v}_i$ denotes the $i$th sample's VSS. After the quantity-related information is removed, the main variation retained in the spectra can be attributed to batch differences.

Then, for any DOSC-corrected secondary spectrum, the batch-wise variation can be further removed by using least squares and VSS:

$$\mathbf{x}^{\mathbf{tran}}{}_i = bias + slope \cdot \mathbf{x}^{\mathbf{corr}}{}_i \tag{4}$$

where *bias* and *slope* are obtained by regressing $\mathbf{v}_{primary}$ on $\mathbf{v}_{transferred}$, $v_{primary}$ stands for the mean of primary VSS, and $v_{transferred}$ denotes the median (or mean) of the selected VSS to be transferred.

The multivariate calibration model built under the initial calibration conditions, that is, on the DOSC-corrected primary spectra, can then be used to predict the concentrations of the target constituents in the test samples from the transformed spectrum $\mathbf{x}^{tran}$.

As illustrated in the aforementioned calculations, the proposed method decomposes the spectra variation into three main parts, that orthogonal to $\mathbf{Y}$, that beneficial to predict $\mathbf{Y}$, and that harmful to the estimate of $\mathbf{Y}$. It eliminates the spectral differences induced by the changes in batches. This is because

  

the novel method transforms two spectral spaces spanned by the corresponding virtual standardization spectra of two subsets of samples collected on two different batches. For the convenience of description, the proposed method is therefore named OSR. Please note that OSR does not require standardization samples measured on two instruments or under two sets of experimental conditions. It can therefore be applied to any case, especially those in which standardization samples are rare or unstable.

### 2.3. Model updating

Model updating can correct for variations by adding samples collected on the secondary situations (situations to be transferred) to the training set and rebuilding the calibration model [10,20–22]. To fully span all possible situations, it is necessary to choose an appropriate number of samples obtained across secondary situations. Not surprisingly, the optimal number of chosen samples varies with the amount of correction required to make the prediction useful on the secondary spectra. The part of samples used to update the calibration model can be selected by Kennard–Stone algorithm (KS) [23–25].

To evaluate the accuracy of these various methods, each was used in conjunction with calibration models based on PLS regression. These models were then applied to predict the transferred data in a validation set.

## 3. EXPERIMENTAL

### 3.1. Data

Two datasets were employed to investigate the performance of the calibration transfer methods described earlier. One study is a publicly available pharmaceutical dataset [26]. The dataset consists of 1308 spectra of 655 pharmaceutical tablet samples measured on two spectrometers (Foss NIR systems, Silver Spring, MD). The transmittance spectra covering the range 600–1898 nm at 2 nm interval are used to estimate the assay value of the active ingredient in each individual tablet. Spectra between 780 and 1638 nm are selected for the subsequent data analysis because the region between 600 and 780 nm extends the NIR region suggested by International Union of Pure and Applied Chemistry. The samples with number 19,122, 126, and 127 of the calibration set and number 11, 145, 267, 295, 294, 342, 313, 341, and 343 of the test set were considered as potential outliers and were excluded [27]. No extra preprocessing is performed on the spectra mentioned earlier. The original spectra of the same pharmaceutical tablet obtained with both spectrometers are shown in Figure 1.

The second study monitors the chlorogenic acid concentration in the alcohol precipitation process of the *Flos Lonicerae japonicae* water extractions. Three batches of extractions concentrated to known densities were considered. Sixty samples collected every 30 s in a 30 min alcohol precipitation process were prepared for each batch. The chlorogenic acid contents of these samples were determined according to the Chinese Pharmacopoeia (2010 edition, volume I) by using an Agilent 1100 high-performance liquid chromatography system (Agilent Technologies, USA) equipped with an autosampler and a diode array detector. The NIR spectra of these samples were collected in transmittance mode on an Antaris Nicolet FT-NIR system (Thermo Scientific, Madison, USA). Each spectrum was recorded from 4000 to 10,000 $cm^{-1}$ with digitization interval of 8 $cm^{-1}$. An overlay of the spectra for each batch is given in Figure 2.

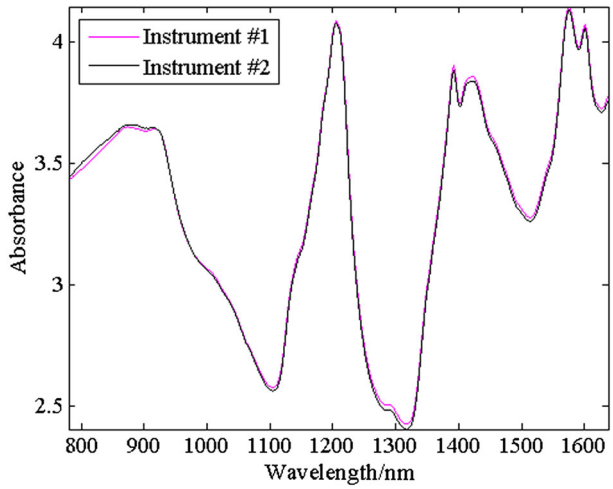


**Figure 1**. NIR spectra of the fifth pharmaceutical tablet measured with the primary (spectrometer #1, blue) and the secondary (spectrometer #2, green) instrument.

### 3.2. Software

The calculations were performed on a personal computer i7 880 processor with 6 GB RAM running Windows 7 Professional operating system using Matlab 7.9 (Mathworks, Inc., Natick, MA). The PLS, MU, and FIR routines were obtained from or modifications of functions in the PLS_Toolbox 2.1 (Eigenvector Research, Inc., Manson, WA). The DOSC and Kennard–Stone routines were implementations of well-established algorithms.

## 4. RESULTS AND DISCUSSION

### 4.1. The pharmaceutical tablet data

The optimal number of latent variables (LVs) was determined by a multiple venetian blind cross-validation procedure for the primary PLS model built on spectrometer #1. The model that resulted in the minimum root-mean-squared error (RMSE) of

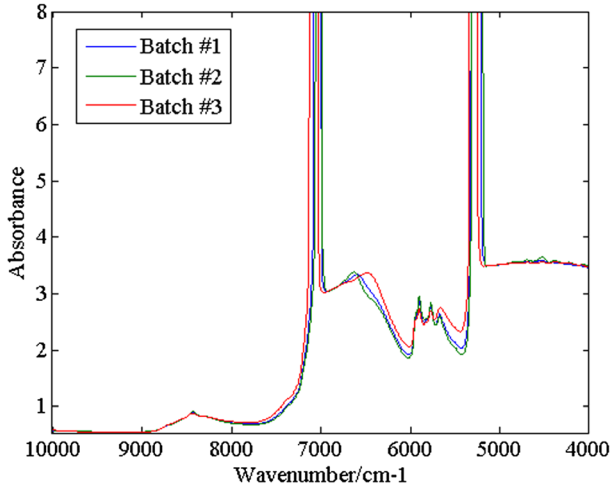


**Figure 2**. The spectra of three samples (one per batch) with chlorogenic acid content around 3 mg/mL.

cross-validation (RMSECV) was selected. The RMSE calculation is provided later [11]:

$$RMSE = \sqrt{\frac{1}{m}\Sigma_{i=1}^{m}(y_i - \hat{y}_i)^2} \quad (5)$$

where, for cross-validation, $y_i$ refers to the reference assay value for the *i*th sample and $\hat{y}_i$ denotes the predicted assay value of the *i*th sample. In Figure 3, the RMSECV curves for the raw, FIR-corrected, and OSR-corrected samples of spectrometer #1 level off around 3, 3, and 1 LVs, respectively. The corresponding regression vectors were then used to predict the assay values of samples measured on spectrometer #2.

To quantitatively compare the performance of each transfer approach, the RMSE of prediction (RMSEP) was calculated using Eq. 5, where $y_i$ denotes the reference assay value for the *i*th sample of #2 and $\hat{y}_i$ denotes the predicted value for the *i*th sample of #2. The ratio of performance to interquartile distance (RPIQ) calculated using Eq. 6 was also applied to evaluate the transferability of each transfer method [28]:

$$RPIQ = \frac{Q3 - Q1}{SEP} \quad (6)$$

where $Q1$ is the value below which we find 25% of the samples, $Q3$ is the value below which we find 75% of the samples, and SEP is exactly the RMSEP.

The number of LVs was optimized automatically using the *F*-statistic for each calibration model in the MU and FIR-corrected process. The *F*-statistic is defined as follows [29]:

$$F = \frac{RSS_{l-1}/(I - l)}{RSS_l/(I - l - 1)} \quad (7)$$

where *RSS* refers to the sum of squared residuals. *I* denotes the number of objects in the training set, and *l* is the number of LVs extracted. The extraction procedure will cease once the *F*-statistic value is less than the *F*-critical value. The *F*-critical can be identified by referring to the *F* distribution table at a significance level of 0.05. On the contrary, the extraction procedure will continue until a predefined number of LVs are reached.

The calibration model will generally produce better results with a larger number of standardization samples incorporated into the training set. However, given the analysis time and associated costs, calibration transfer methods with fewer standardization samples are practically preferred. As shown in Figure 4, once the number of standardization samples included in MU reaches 24, further increases in the number of standardization samples have little effect on the performance of the resulting model. Therefore, the number of standardization samples was set to 24 to facilitate comparison with the other transfer approaches.

Table I lists the RMSEP values for the active pharmaceutical ingredient mass in the tablet samples predicted by the model updated via MU on spectra measured with spectrometer #2. The updated model performed well at predicting the samples retained in the calibration set and test set. However, it performs worse on the validation set versus the raw PLS model. This means that the new unmodeled variation might appear in the validation set. Similar conclusions were drawn from the results presented by RPIQ.

To account for instrument-wise variations, 24 samples measured on both instruments were selected using the KS algorithm and then used to calculate the OSC weights and loadings [11]. The RMSECV curves for the OSC-corrected primary spectra data reached minimums at 3 LVs and 1 orthogonal component. Unfortunately, the results of the OSC transfer model only showed improvement on the test data and not the other two data sets.

The window size has a large effect on the performance of PDS and needs to be carefully determined. As mentioned in the literature [27], increasing the window size from 9 to 101 at increments of 4 was investigated in this study. The number of principal components (PCs) involved in the calculation of the transformation matrix was set to 2. With rigorously tuned window size (Ws), *viz.* PDS (Ws: 9), the transfer method was found to perform slightly better than the MU on this particular dataset.

Similar to PDS, the window size significantly influences the performance of FIR. Thus, a window size scanning between 5 and 250 at intervals of 10 was examined. A transfer window of 175 points performed well in this application, which reflected

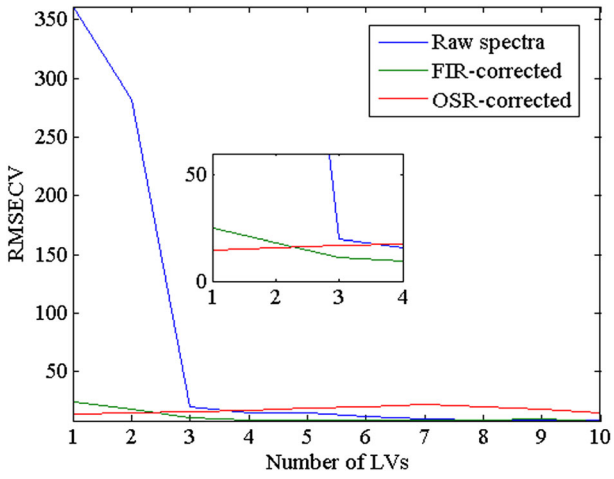


**Figure 3**. Calibration curves used for determining the PLS model complexity on the raw (3 LVs), FIR-corrected (3 LVs), and OSR-corrected (1 LV) spectra of the pharmaceutical tablet data.

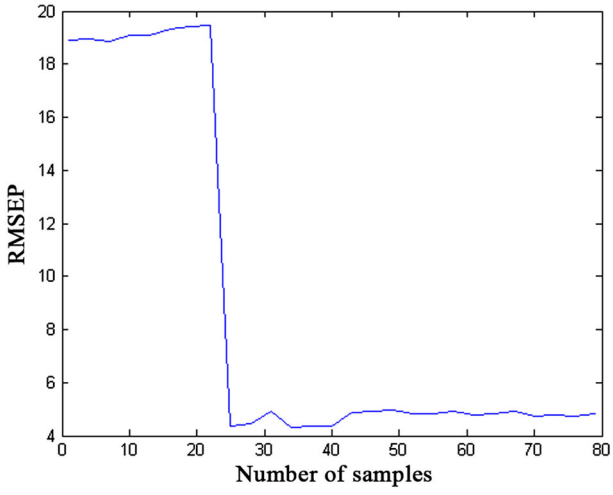


**Figure 4**. The effect of the number of standardization samples on the performance of the updated model. The RMSEP values were calculated for the assay value of the active ingredient in the pharmaceutical tablet samples (excluding the 24 standardization samples) predicted from spectra recorded with the secondary instrument.

**Table I.** Summary of root-mean-squared error of prediction and ratio of performance to interquartile distance values of the pharmaceutical tablets after transfer of instrument #2 spectra

| Method | Calibration | | Test | | Validation | |
|---|---|---|---|---|---|---|
| | RMSEP | RPIQ | RMSEP | RPIQ | RMSEP | RPIQ |
| PLS[a] | 4.30 | 7.64 | 6.57 | 3.04 | 4.61 | 0.57 |
| PDS[a] | 3.85 | 8.54 | 5.67 | 3.52 | 4.01 | 0.66 |
| FIR[b] | 3.62 | 9.08 | 3.55 | 5.63 | 4.97 | 0.53 |
| OSC[b] | 5.07 | 6.48 | 5.67 | 3.52 | 4.85 | 0.54 |
| MU[b] | 4.17 | 7.88 | 4.65 | 4.30 | 4.84 | 0.55 |
| OSR[b] | 3.93 | 8.36 | 3.64 | 5.49 | 3.50 | 0.76 |
| PLS[c] | 3.82 | 8.61 | 4.96 | 4.03 | 4.33 | 0.6 |

RMSEP, root-mean-squared error of prediction; RPIQ, ratio of performance to interquartile distance; PLS, partial least squares; PDS, piecewise direct standardization; FIR, finite impulse response; OSC, orthogonal signal correction; MU, model updating; OSR, orthogonal space regression.
[a]denotes the PLS calibration model built using the raw spectra of the calibration samples measured on instrument #1.
[b]signifies the PLS model built on the corrected spectra of the calibration set measured on instrument #1.
[c]refers to the calibration model constructed using the spectra of the calibration set measured on instrument #2.

the broad nature of the NIR spectra. This window was nearly half of the total number of points in the dataset reduced for this study. The results reported in Table I indicate that the RPIQ for both PDS and FIR methods are consistently larger than that of the raw PLS except the validation RPIQ for the FIR algorithm. This means that FIR is more sensitive to the unmodeled variations in the validation set versus PDS.

Although for both FIR and OSR, no identical samples need to be measured on all instruments, the performance of OSR is relatively better than that of FIR in terms of the RMSE and the RPIQ for the validation set. Additionally, the prediction powers of the OSR-corrected model on the three datasets are consistently better than those of the raw PLS. The performance of OSR on the test and validation data is even better than that of the recalibrated PLS model. These results indicate that the spectral variation between spectrometers might be eliminated efficiently by OSR.

The results illustrate that the application of transfer methods (i.e. PDS, OSC, FIR, MU, and OSR) on the calibration and test spectra measured on spectrometer #2 reduces the prediction errors to some extent. From the validation set, it can be concluded that both the FIR and the MU methods are more sensitive to unmodeled variances compared with the other methods. After the spectra was corrected with OSR, the prediction performance of the model built on the spectra of instrument #1 is comparable to or even better than that of the model constructed using the spectra measured on instrument #2. Therefore, the OSR algorithm can correct for the difference between instruments.

### 4.2. The chlorogenic acid data

The saturated spectra regions 5149–5353 $cm^{-1}$ and 6958–7162 $cm^{-1}$ (Figure 2) have no contribution to the calibration model built on the spectra from batch #1 and were eliminated from the full spectra. Significant differences among spectra can be observed because of the inevitable batch-wise variation, If the calibration model built for batch #1 is directly applied to the spectra collected on new batches, the resulting prediction errors will be substantially large. To make the calibration model applicable, more sophisticated calibration transfer is required. The widely used PDS is unsuitable for this specific data because there are no identical samples.

In Figure 5, the RMSECV curves for the raw, OSR-corrected, and FIR-corrected samples display minimums at 4, 1, and 3 LVs, respectively. The corresponding regression vectors were then applied to the batches #2 and #3 samples. The predicted values are separately plotted against their reference values in Figures 6 and 7. The RMSEP and RPIQ results for the OSR-transformation and FIR-transformation samples are reported in Table II. Amazingly, the FIR with an optimal window size of 205 failed to improve the prediction performance on batches #2 and #3 samples. No significant improvement was achieved even upon optimization of window. This suggests that removing the wavelength-dependent scatter effect is insufficient to maintain the calibration model for the particular data. Nevertheless,it was found that OSR employing the first five samples was able to incorporate sufficient new property information into the resulting calibration model. That makes the transfer approach more executable. The batch-wise variations in the DOSC-pretreated spectra were corrected using a linear function, which was obtained by regressing the VSS of the secondary batch on that of the primary batch. Thus, there is no need to rebuild the calibration model.

To illustrate the necessity of VSS, five samples from the primary batch (#1) and five samples from each of the secondary batch (i.e. batches #2 and #3) were selected and pooled to construct the OSC model. With the batch-wise orthogonal variance removed, the RMSECV curves for the primary samples showed minimums at 2 LVs. From Table II, it can be concluded that the transferability of the OSC method is limited for the chlorogenic acid dataset.

The results of the OSR approach are shown in Figures 6 and 7 for each batch. To facilitate the comparison with OSR, an updated PLS model was constructed using all the samples from the primary batch (batch #1) and five KS-selected samples from

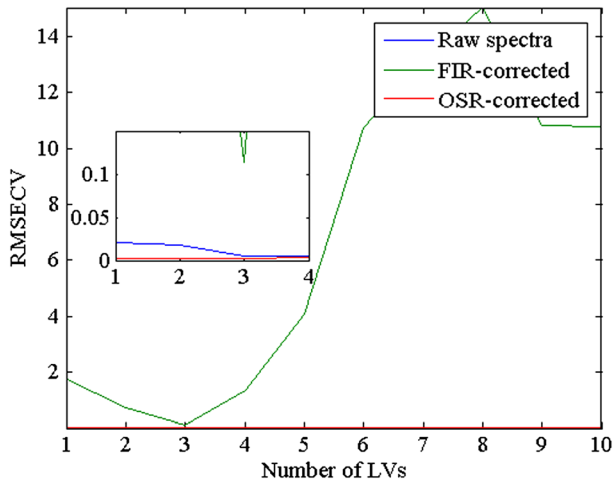


**Figure 5.** Calibration curves for raw (4 LVs), FIR-corrected (3 LVs), and OSR-corrected (1 LV) spectra on the chlorogenic acid data.

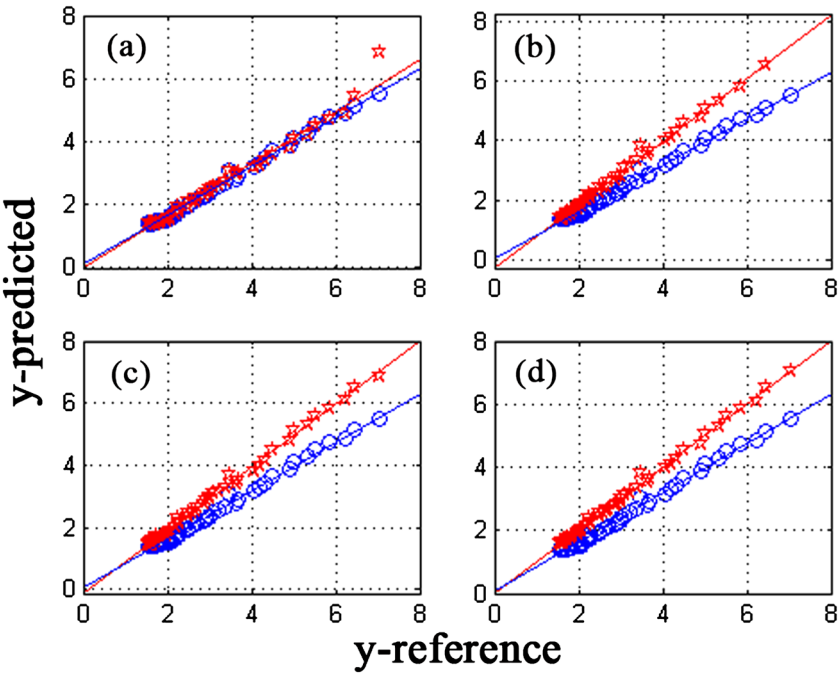


**Figure 6**. The prediction results for batch #2. The predicted values of the raw PLS model are represented by blue circle. The predicted values of the FIR model, OSR model, MU model, and the recalculated PLS model are shown in subplots (a)–(d) using red pentagon, respectively.

the secondary batch (batch #2 or #3). The updated model was then used to predict the remaining samples of the secondary batch. For all the two batch-wise transfers (Figures 6 and 7), the MU predictions approach the ideal calibration line. However, the MU procedures complicate the mode transfer process because the corresponding regression vectors needs to be re-estimated.

An examination of the results for OSR and MU in Table II reveals that the prediction errors for these methods are similar. This is not surprising because both methods incorporate samples from the primary and secondary batches. In addition, it is interesting to note that the number of LVs identified for both data sets using OSR was one. This suggests that only the variation pertinent to the property of interest was preserved [30]. Although significant improvement was acquired for the prediction of #2 and #3 samples, the RMSEP values of MU and OSR were still consistently larger than those of the recalculated PLS model. This phenomenon can be attributed to the unaccounted variation in the remaining samples. In brief, the success of the OSR on the

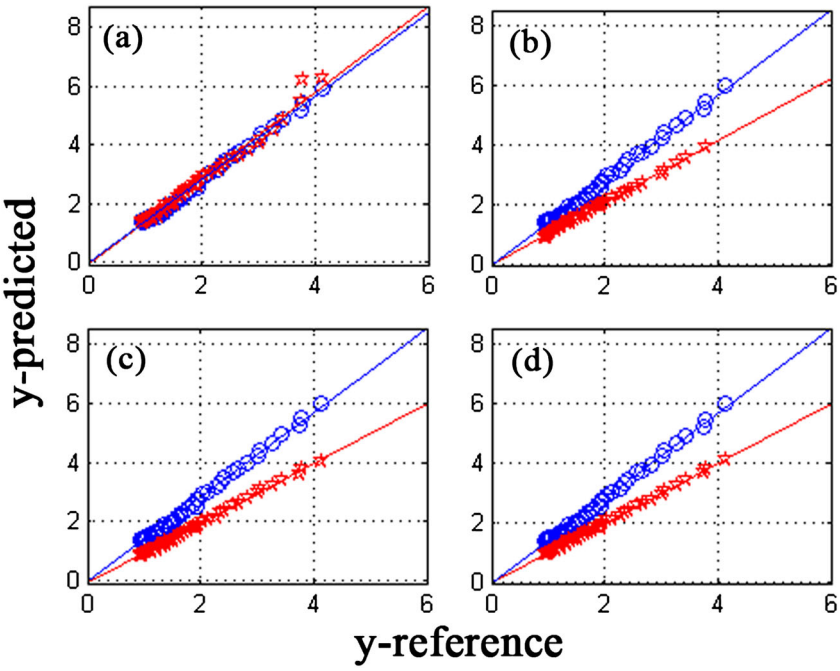


**Figure 7**. The prediction results for batch #3. Details are shown in Figure 6.

**Table II.** Summary of the root-mean-squared error of prediction and ratio of performance to interquartile distance values predicted by different transfer techniques

| Method | Batch 2 | | Batch 3 | |
|---|---|---|---|---|
| | RMSEP | RPIQ | RMSEP | RPIQ |
| PLS[a] | 0.61 | 3.01 | 0.78 | 1.36 |
| FIR[b] | 0.63 | 2.92 | 0.81 | 1.31 |
| OSC[b] | 0.65 | 2.83 | 0.63 | 1.69 |
| MU[b] | 0.15 | 12.24 | 0.07 | 15.19 |
| OSR[b] | 0.13 | 14.13 | 0.08 | 13.29 |
| PLS[c] | 0.08 | 22.96 | 0.05 | 21.26 |

RMSEP, root-mean-squared error of prediction; RPIQ, ratio of performance to interquartile distance; PLS, partial least squares; PDS, piecewise direct standardization; FIR, finite impulse response; OSC, orthogonal signal correction; MU, model updating; OSR, orthogonal space regression.
[a]denotes the model built using the raw spectra of batch #1.
[b]denotes the model built using the corrected spectra of batch #1.
[c]indicates the model built on spectra from each batch.

chlorogenic acid data fully demonstrates the ability to correct for batch-wise variation.

## 5. CONCLUSIONS

In this work, OSR is proposed to perform calibration transfer in cases where the standardization samples are difficult to measure on a secondary setting. The chlorogenic acid results collected from different batches demonstrate that the difference between batches can be corrected through OSR, without requiring the use of standardization samples. The performance of OSR was also compared with other calibration transfer methods using pharmaceutical tablet data. The results illustrate that the variations between spectra of different instruments can be successfully corrected by using OSR. In brief, OSR can be used to transfer calibration models between primary situations and secondary situations, whether the standardization samples are provided or not.

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## APPENDIX

An outline of the proposed OSR method is shown below.

Optionally transform, center, and scale the raw data to give the matrices **X** ($I \times J$), **Y** ($I \times K$) for the primary set and **Xt** ($m \times J$), **Yt** ($m \times K$) for the secondary set.

(1) $\hat{\mathbf{Y}} = \mathbf{X}\left(\mathbf{X}'\mathbf{X}\right)^{-1}\mathbf{X}'\mathbf{Y}$. Project **Y** onto **X**.
(2) $\mathbf{X}o = \mathbf{X} - \hat{\mathbf{Y}}\left(\hat{\mathbf{Y}}'\hat{\mathbf{Y}}\right)^{-1}\hat{\mathbf{Y}}'\mathbf{X}$. Deflate the pertinent part of **X** with respect to $\hat{\mathbf{Y}}$.
(3) $\mathbf{T}a = \mathbf{PCA}$ (**Xo**, *no*). Find *no* major PCs of the orthogonal part of X, that is, **Xo**.
(4) $\mathbf{W} = \mathbf{X}^{-}\mathbf{T}a$. Estimate the projection matrix with respect to generalized inverse $\mathbf{X}^{-}$. where $\mathbf{X}^{-}$ is calculated using a PCR solution between **X** and **T***a* with the number of PCs for the PCR solution equals the number of singular values of **X** larger than a tolerance (*tol*).
(5) $\mathbf{T} = \mathbf{XW}$. Calculate the estimated scores.
(6) $\mathbf{P} = \mathbf{X}'\mathbf{T}(\mathbf{T}'\mathbf{T})^{-1}$. Calculate the loadings.
(7) $\mathbf{X}corr = \mathbf{X} - \mathbf{TP}'$. Calculate the corrected matrix **X***corr*.
(8) $\mathbf{Xt}' = \mathbf{Xt} - \mathbf{XtWP}'$. Calculate the corrected matrix for the secondary data set.
(9) $\mathbf{v}_{\text{primary}} = bias + slope \cdot \mathbf{v}_{\text{transferred}}$. Fit *bias* and *slope* between the two virtual standardization spectra, using ordinary least squares, where $\mathbf{v}_{\text{primary}}$ is calculated as the mean of DOSC-corrected primary spectra divided by its corresponding property values and $\mathbf{v}_{\text{transferred}}$ refers to the median (or mean) of *n* DOSC-corrected secondary spectra divided by its corresponding property values.
(10) $\mathbf{x}_{\mathbf{t}}^{\mathbf{tran}} = bias + slope \cdot \mathbf{x}_{\mathbf{t}}^{\mathbf{corr}}$. Correct the differences between instruments or batches.