Journal of Chromatography A, 1302 (2013) 72–80

Contents lists available at SciVerse ScienceDirect

Journal of Chromatography A

journal homepage: www.elsevier.com/locate/chroma

Chromatographic background drift correction coupled with parallel factor analysis to resolve coelution problems in three-dimensional chromatographic data: Quantification of eleven antibiotics in tap water samples by high-performance liquid chromatography coupled with a diode array detector

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ARTICLE INFO

Article history:
Received 3 January 2013
Received in revised form 14 May 2013
Accepted 7 June 2013
Available online 14 June 2013

Keywords:
Chromatographic peak resolution
Second-order advantage
Antibiotics
Chromatographic background drift correction
PARAFAC

ABSTRACT

Chromatographic background drift correction has been an important field of research in chromatographic analysis. In the present work, orthogonal spectral space projection for background drift correction of three-dimensional chromatographic data was described in detail and combined with parallel factor analysis (PARAFAC) to resolve overlapped chromatographic peaks and obtain the second-order advantage. This strategy was verified by simulated chromatographic data and afforded significant improvement in quantitative results. Finally, this strategy was successfully utilized to quantify eleven antibiotics in tap water samples. Compared with the traditional methodology of introducing excessive factors for the PARAFAC model to eliminate the effect of background drift, clear improvement in the quantitative performance of PARAFAC was observed after background drift correction by orthogonal spectral space projection.

1. Introduction

Hyphenated chromatographic systems, such as high-performance liquid chromatography coupled with diode array detection (HPLC–DAD), can provide rich analytical information and are some of the most reliable and suitable methods for analyzing complex samples. However, successful applications have been limited by the coelution problems that commonly occur in the analysis of more complex samples, where chromatographic profiles of analytes of interest might be partially or completely overlapped with interferences present in matrices. Therefore, chemometric methods with the second-order advantage [1] have been introduced by analysts to separate the overlapped chromatographic peaks in a mathematical manner, which can theoretically quantify analytes of interest in the overlapped profiles. The strategy that interprets three-dimensional chromatographic data by second-order calibration has stimulated growing interest in analysts from various fields, including environmental monitoring, proteomics and metabonomics/metabolomics [2–5], by solving the problem of simultaneous quantification of multiple analytes in complicated samples containing interferences. Various chemometric methods [6–11] that are capable of providing the second-order advantage have been developed, and their successful applications in analyzing multi-way data from hyphenated chromatographic instruments have been demonstrated. However, the quality of measured data from hyphenated (chromatographic/spectroscopic) techniques is influenced by many artifacts, such as the background drift attributed to the nature of complicated matrices; these artifacts might produce invalid qualitative or quantitative results of the aforementioned chemometric methods. Aiming to provide general solutions to these artifacts, a number of methods [12–20] have been developed. A majority of these methods are devoted to efficiently eliminating background drift present in the chromatographic data. However, only a few methods [14–20] can be suitably employed for correcting background drift in two-way chromatographic data. Typical examples are multivariate curve resolution (MCR) methods [10,21]. Recently, a new chromatographic background drift correction strategy [22] was proposed

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http://dx.doi.org/10.1016/j.chroma.2013.06.009

by our research group for LC × LC × DAD data, which introduces excessive factors for alternating trilinear decomposition (ATLD) [11] to model the component of variation corresponding to the chromatographic background. Yet, it is much more complicated to efficiently remove the effect of background drift in two-way chromatographic data. Very recently, Kuligowski et al. [20] developed two straightforward background drift correction approaches to eliminate background signal contributions and facilitate the performance of multivariate curve resolution-alternating least squares (MCR-ALS).

The successful application of the background drift correction methods is built upon the assumption that background contributions can be completely eliminated by projecting the two-way chromatographic data into the subspace that is orthogonal to the space spanned by spectra of the chromatographic background. In the present work, the approach that employs orthogonal spectral signal projection (OSSP) to simultaneously treat various types of chromatographic background drift was studied in detail. Further, the analytical strategy for eliminating the influence of background drift by OSSP to improve the quantitative performance of parallel factor analysis (PARAFAC) was comprehensively investigated by a simulated chromatographic data set. Finally, this strategy was utilized to identify and quantify antibiotics in tap water samples by making use of the second-order advantage. Eleven widely-used antibiotics were used in this work: sulfacetamide (SC), sulfamerazine (SMZ), sulfamethoxazole (SMT), tetracycline (TC), pipemidic acid (PIP), pefloxacin (PEF), danofloxacin (DAN), lomefloxacin (LOM), metronidazole (MET), ornidazole (ORN), and oxytetracycline (OTC). Both qualitative and quantitative results demonstrated that a great improvement in the performance of PARAFAC could be achieved after background drift correction, as compared with the traditional chemometric methodology that introduces excessive factors for PARAFAC to model the effect of background drift.

2. Materials and methods

2.1. Reagents and instruments

The eleven analytes listed in Section 1 were purchased from Sigma–Aldrich. Methyl alcohol (HPLC-grade) was also obtained from Sigma–Aldrich. Formic acid (99 + %) was provided by Adamas Reagent Company. The Cleanert PEP 300 mg/6 mL cartridge used for solid phase extraction was obtained from Bonna-Agela Corporation (Tianjin, China). The stock solutions of analytes were diluted by 1% HCl solution, and then protected from light and stored at −20 °C. A total of 21 standard solutions were prepared, and the range of concentrations for each analyte was summarized in Table 1.

2.2. Tap water sample preparation

Five tap water samples were prepared. For each sample, no less than 1 L of water was collected in an amber glass and then percolated through a cartridge at a flow rate of less than 5 mL min^{-1}. After percolation, the cartridge was washed with 6 mL of methanol into a 10-mL graduated glass vessel and dried by a gentle flow of nitrogen at room temperature.

2.3. Validation and test sample preparation

Five validation samples containing all of the analytes were designed to investigate the reliability of the strategy. The corresponding concentrations were within the range of those in standard samples. Additionally, five test samples were prepared by mixing appropriate amounts of validation samples with tap water sample extracts.

2.4. HPLC–DAD

The analysis was performed on an HPLC system (Shimadzu, Japan) composed of an LC-20AT pump, a CBM-20AT control system, a CTO-20AC column oven and an SPD-M20AT diode array detector. A reversed-phase WondaSil C18 column (150 mm × 4.6 mm, 5 μm particle size) was used for separation. Spectra were collected in a wavelength range 237–450 nm. The mobile phase was composed of 1% aqueous formic acid (A) and methyl alcohol (B) mixed with an A:B ratio (v/v) of 30:70 and delivered at a constant flow rate of 1 mL min^{-1}.

3. Theory

3.1. Background drift correction by OSSP

For a second-order chromatographic instrument, such as HPLC–DAD, a signal matrix can be generated for each sample, where each row collects a spectrum at one sampling point along the chromatographic direction, and each column gathers a chromatogram within a spectral channel. Mathematically, the response of any two-way chromatographic data, say $\mathbf{X}$, can be divided into three independent parts: the contribution of analytes $\boldsymbol{X}_{analyte}$, the chromatographic background drift $\boldsymbol{X}_{BK}$, and the instrumental noise $\boldsymbol{E}$.

$$\mathbf{X} = \mathbf{X}_{analyte} + \mathbf{X}_{BK} + \mathbf{E} \tag{1}$$

where

$$\mathbf{X}_{analyte} = \mathbf{c}_1\mathbf{s}_1^T + \mathbf{c}_2\mathbf{s}_2^T + \cdots + \mathbf{c}_N\mathbf{s}_N^T \tag{2}$$

$$\mathbf{X}_{BK} = \mathbf{c}_{BK1}\mathbf{s}_{BK1}^T + \mathbf{c}_{BK2}\mathbf{s}_{BK2}^T + \cdots + \mathbf{c}_{BKM}\mathbf{s}_{BKM}^T \tag{3}$$

In the above equations, $\mathbf{X}$ represents the measured matrix with a size of $I \times J$, where I is the number of sampling points in the chromatographic direction and J is the number of spectral channels. The response of analytes, $\mathbf{X}_{analyte}$, is a linear combination of the signals due to underlying components present in the sample. For each component, the response can be expressed as the outer product of the chromatogram ($\mathbf{c}_n$) and spectrum ($\mathbf{s}_n$). Similarly, the response of the chromatographic background drift, $\mathbf{X}_{BK}$, can also be expressed as the linear combination of the responses of underlying eluents in the mobile phase.

According to the theory proposed by Lorber [23], the spectral vector of an analyte can be divided into two subparts: the net signal part, which is orthogonal to the spectral subspace spanned by the chromatographic background ($\mathbf{s}_{BK1}$, $\mathbf{s}_{BK2}$, …, $\mathbf{s}_{BKM}$), and the background signal part that lies in the spectral subspace of chromatographic background.

$$\mathbf{s}_n = \mathbf{s}_n^{\perp} + \mathbf{s}_n^{\in} \tag{4}$$

where $\mathbf{s}_n$ is the spectrum vector of nth component, $\mathbf{s}_n^{\perp}$ and $\mathbf{s}_n^{\in}$ denote the net signal part and the background (dependent) signal part, respectively. Theoretically, the following two conditions should be met for $\mathbf{s}_n^{\perp}$ and $\mathbf{s}_n^{\in}$, respectively:

$$(\mathbf{I} - \mathbf{S}_{BK}\mathbf{S}_{BK}^{+})s_n^{\perp} = s_n^{\perp} \tag{5}$$

$$(\mathbf{I} - \mathbf{S}_{BK}\mathbf{S}_{BK}^{+})s_n^{\in} = 0 \tag{6}$$

where $\mathbf{I}$ is an identity matrix, $\mathbf{S}_{BK}$ is the spectral matrix of chromatographic background ($\mathbf{S}_{BK} = [\mathbf{s}_{BK1}, \mathbf{s}_{BK2}, \ldots, \mathbf{s}_{BKM}]$), and $\mathbf{S}_{BK}^{+}$ denotes the Moore–Penrose generalized inverse matrix of $\mathbf{S}_{BK}$. The projection matrix, $\mathbf{I} - \mathbf{S}_{BK}\mathbf{S}_{BK}^{+}$, spans the subspace that is orthogonal to the

Table 1
Quantitative results obtained using PARAFAC to analyze the simulated data. (Com.: component.).

	Before background drift correction			After background drift correction		
	Com. 1	Com. 2	Com. 3	Com. 1	Com. 2	Com. 3
R	0.9934	0.9459	0.9361	1.0000	0.9999	1.0000
RMSEC[a]	0.040	0.113	0.122	0.002	0.004	0.002
RMSEP[b]	0.087	0.209	0.126	0.003	0.006	0.003
Recovery (%)	100.8 ± 6.9	96.8 ± 23.7	96.1 ± 13.0	100.0 ± 0.3	100.2 ± 0.7	100.0 ± 0.3

[a] *RMSEC* was calculated as $\sqrt{\sum_{n=1}^{Nc}(x - x_{cal})^2/(N_c - 1)}$, where N_c is the number of calibration samples, x is actual value and x_{cal} is the estimated one. *RMSEC* was calculated for calibration samples.

[b] *RMSEP* was calculated as $\sqrt{\sum_{n=1}^{Np}(x - x_{cal})^2/(N_p - 1)}$, where N_p is the number of prediction samples. *RMSEP* was calculated for test samples.

spectral space of the chromatographic background. Theoretically, the background drift component of the two-way chromatographic data can be completely eliminated through multiplying the projection matrix by the original data, **X**:

$$\mathbf{X}(\mathbf{I} - \mathbf{S}_{BK}\mathbf{S}_{BK}{}^{+}) = \mathbf{c}_1(\mathbf{s}_1{}^{\perp})^T + \mathbf{c}_2(\mathbf{s}_2{}^{\perp})^T + \cdots + \mathbf{c}_N(\mathbf{s}_N{}^{\perp})^T + E(\mathbf{I} - \mathbf{S}_{BK}\mathbf{S}_{BK}{}^{+}) \quad (7)$$

Eq. (7) implies that the inherent bilinear structure of the two-way chromatographic data will not be influenced after projection. However, the characteristics of non-negativity of spectra might be lost, and it is unnecessary for the net signal part $\mathbf{s}_1^{\perp}$ to be identical to the original spectrum $\mathbf{s}_n$. Therefore, it is unreasonable to compare the quality of resolved spectra obtained from chemometric methods, such as MCR-ALS and PARAFAC, with the original spectra. In fact, a more reasonable methodology is to calculate the 'mathematical reference' spectra by multiplying the projection matrix by the reference spectra, and then use them as the underlying spectra of analytes. Successful applications of OSSP to eliminate the effect of background in infrared spectra or to improve the signal-to-noise ratio have been demonstrated by several groups [24–26].

To obtain more reliable results, high-quality spectra of the chromatographic background part should be accurately provided to construct the projection matrix, $\mathbf{I} - \mathbf{S}_{BK}\mathbf{S}_{BK}^{+}$. Since it is difficult to obtain the underlying spectra of eluents, Kuligowski et al. [20] suggested two alternatives: employ the abstract spectra resolved by principal component analysis (PCA) or use the spectra estimated by simple-to-use interactive self-modeling analysis (SIMPLISMA). The retrieved spectra from the aforementioned two methods are mathematically equivalent (the results from PCA and SIMPLISMA can be treated as the results of linear combinations for each other), resulting in highly consistent solutions for the analyzed chromatographic data after background drift correction.

In the present work, the spectra of chromatographic background were estimated by using ATLD to decompose the zero-component part of the three-way data $\underline{\mathbf{X}}$, obtained by slicing a series of sample responses along the sample direction. Then Eq. (7) was adopted to eliminate the background part, followed by the application of

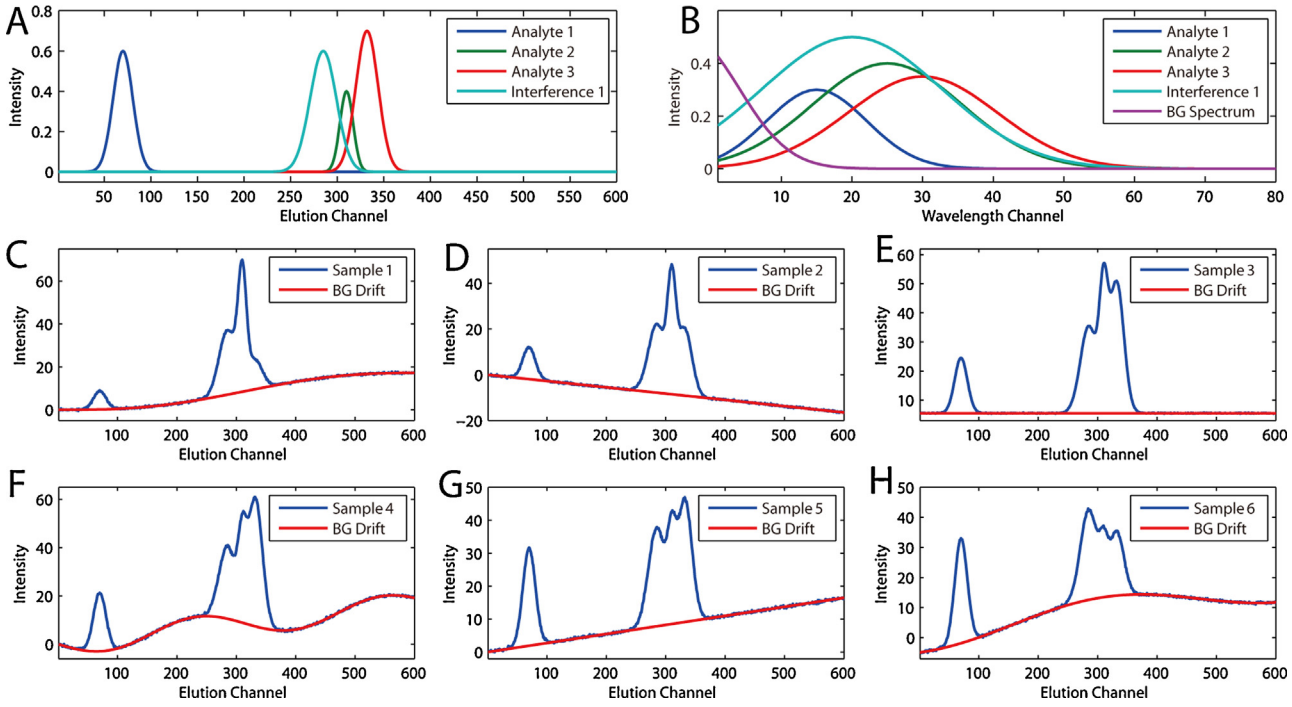

Fig. 1. Simulated chromatograms (A) and spectra (B) of components, and total chromatographic profiles of six types of simulated background drift (C)–(H). The total chromatographic profiles were calculated as the summation of the absorbance measurements under each spectral channel (BG: background drift). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

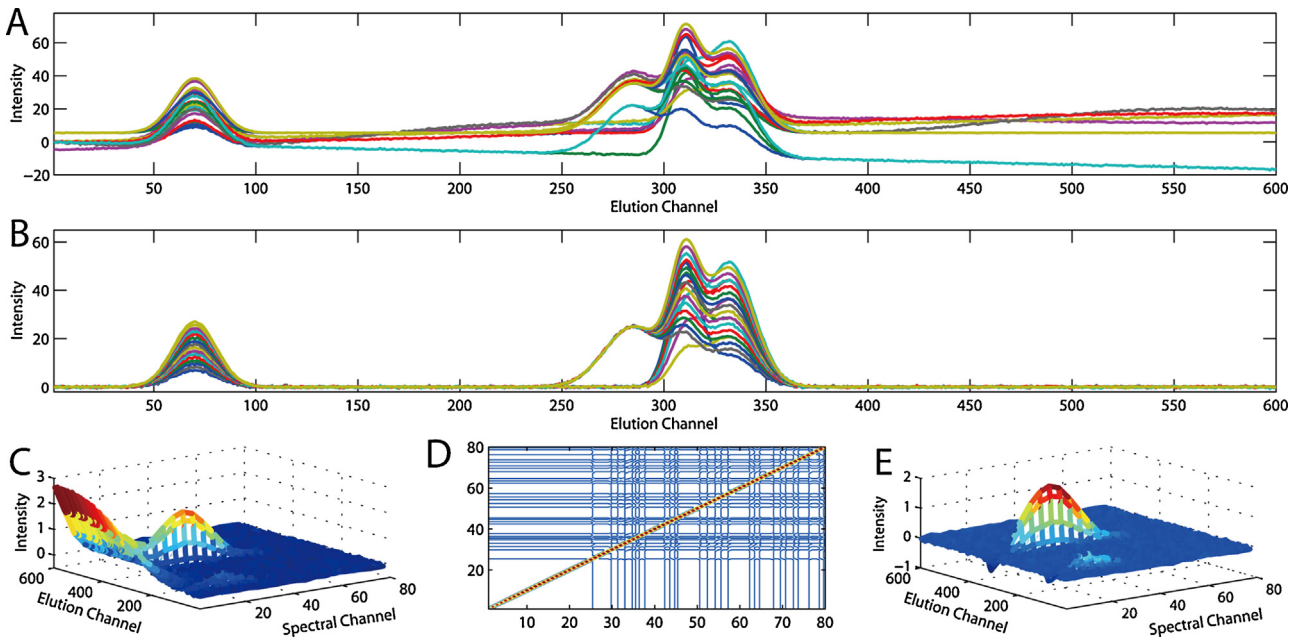

Fig. 2. Total chromatograms of twenty samples (A), and results obtained with background drift corrected by OSSP (B). For the 6th sample: (C) Original three-dimensional plots, (D) contour plot of the projection matrix, and (E) three-dimension plots after background drift correction. Note that the total chromatogram of each sample was calculated as the summation of the chromatograms under each spectral channel.

PARAFAC to resolve the coelution problem in the data and provide accurate qualitative and quantitative results.

3.2. Parallel factor analysis (PARAFAC)

The well-known PARAFAC model was originally proposed by Harshman [8] and explained by Bro [9]. This method was built upon the assumption that the analyzed three-way data, $\underline{\mathbf{X}}$, has a low-rank trilinear structure. For each element, x_{ijk}, the following trilinear model will be satisfied:

$$x_{ijk} = \sum_{n=1}^{N} a_{in} b_{jn} c_{kn} + e_{ijk} \quad (8)$$

where N is the number of components, and x_{ijk} is the measured signal at the ith elution point and jth spectral channel for the kth sample. a_{in} is the inth element of the relative chromatographic matrix $\mathbf{A}$ ($I \times N$, each column represents the normalized chromatogram of an analyte); b_{jn} is the jnth element of the relative spectral matrix $\mathbf{B}$ ($J \times N$, each column is the normalized spectrum of an analyte); c_{kn} is the knth element of the relative concentration matrix $\mathbf{C}$, ($K \times N$, each column represents the relative concentrations of an analyte in K samples). e_{ijk} is the residual part that is not accounted for by the model.

PARAFAC extracts the profiles of analytes according to a mathematical separation strategy, which retrieves the relative chromatographic matrix $\mathbf{A}$, the relative spectral matrix $\mathbf{B}$ and the relative concentration matrix $\mathbf{C}$ in an alternating least-squares manner. Basically, the overlapped chromatographic peaks will be well separated, as long as the method converges properly. More detailed descriptions of PARAFAC can be found in the literature. [3,9].

3.3. Simulated HPLC–DAD data

In order to evaluate the performance of the new strategy, which employs OSSP for chromatographic background drift correction to improve the performance of PARAFAC (for chromatographic data analysis), a simulation was designed. Fig. 1A shows the simulated chromatographic profiles of three analytes and a single interference, while the spectral profiles are shown in Fig. 1B. In addition, an eluent that has a response in the range of low spectral channels was simulated (Fig. 1B). Six various types of background drift due to changes in the composition of mobile phase have been designed. The total absorbance chromatograms of analytes, together with various types of chromatographic background drift, are shown in Fig. 1C–H. The chromatographic shapes of background drift changed dramatically among samples. A total of twenty samples were simulated in the data array: six calibration samples containing three analytes and fourteen samples with interference added. Finally, a three-way chromatographic data array with a size of $600 \times 80 \times 20$ was obtained, where 600 and 80 represent the numbers of elution channels and spectral channels, respectively.

3.4. Software

All calculations were carried out in the Matlab (MathWorks, USA) environment. Simulations and real data analysis were implemented using in-house routines. The program code can be obtained from the authors.

4. Results and discussion

4.1. Simulated chromatographic data

The total chromatograms of twenty samples are depicted in Fig. 2A, and the influence of chromatographic background drift can clearly be observed. Unfortunately, the background drift could not be eliminated by subtracting the responses of blank samples. Therefore, it was necessary to perform our background drift correction strategy in the data analysis.

First, the performance of OSSP on eliminating chromatographic background drift was investigated in the following manner. To begin, the elution range corresponding to the zero-component of the three-way data array should be estimated. Here, the zero-component elution range was simply selected as the first ten

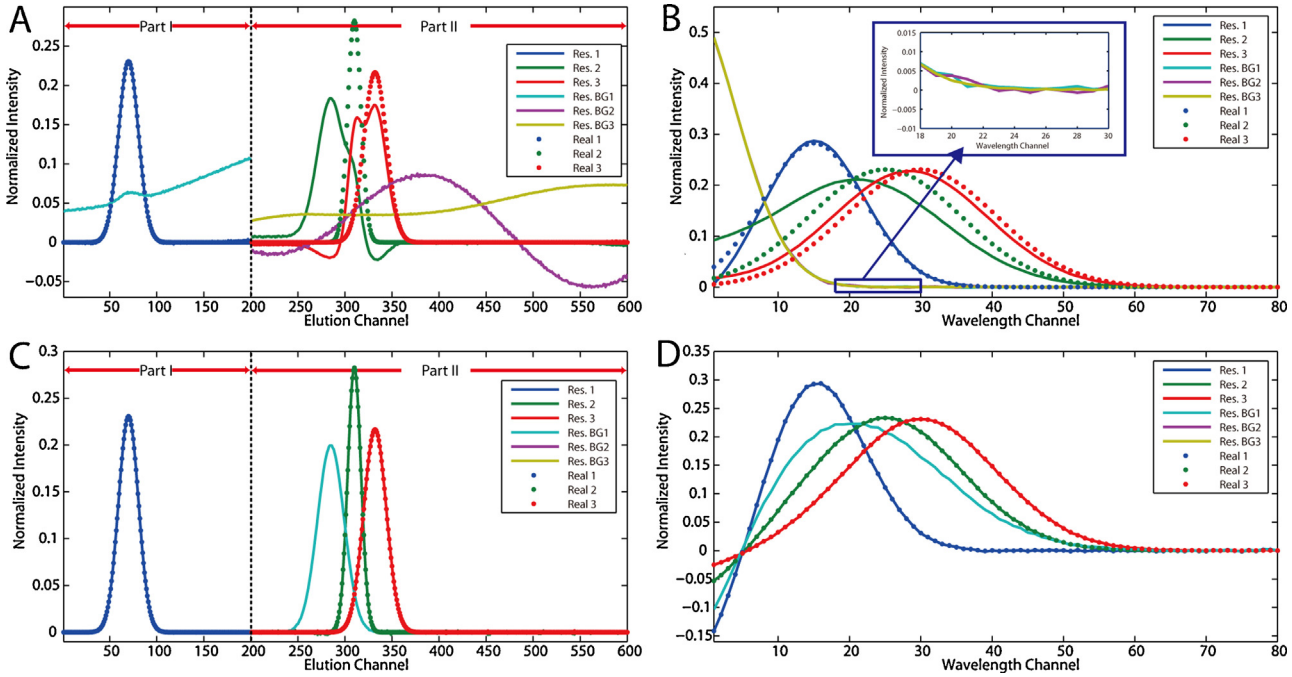

Fig. 3. Resolved chromatograms (A) and spectra (B) by using PARAFAC to analyze the original chromatographic data. Resolved chromatograms (C) and spectra (D) by using PARAFAC to decompose the data with background drift corrected by OSSP. (Res.: resolved profiles; Int.: interference.) Note that the chromatographic data were divided into two segments for convenience of analysis according to the parts shown in (A) and (C). For part I of (A), $N = 2$ was employed, and $N = 4$ was employed for part II of (A). For part I of (C), $N = 1$ was used, and $N = 3$ for part II. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

elution channels, as the chromatographic background shape in this elution range had no significant changes among samples. Next the number of components should be estimated. In this work, the underlying number of components ($N = 1$) was temporarily used for ATLD, and the spectrum of an eluent was immediately retrieved. Then the projection matrix, $\mathbf{I} - \mathbf{S}_{BK}\mathbf{S}_{BK}^{+}$, was calculated accordingly. Finally, the chromatographic background drift was efficiently removed by multiplying the projection matrix by the data $\mathbf{X}$, see Eq. (7). The total chromatograms of the data after background drift correction are shown in Fig. 2B. A comparison with the profiles shown in Fig. 2A clearly indicates that various types of background drift were successfully corrected.

A graphical implementation of OSSP to correct background drift is illustrated in Fig. 2C–E. In the original two-way chromatograms (Fig. 2C), one can observe clearly that significant background drift was present in the first 20 spectral channels. However, the drift was efficiently removed through multiplying by the projection matrix (shown as contour plot in Fig. 2D), and satisfactory results were

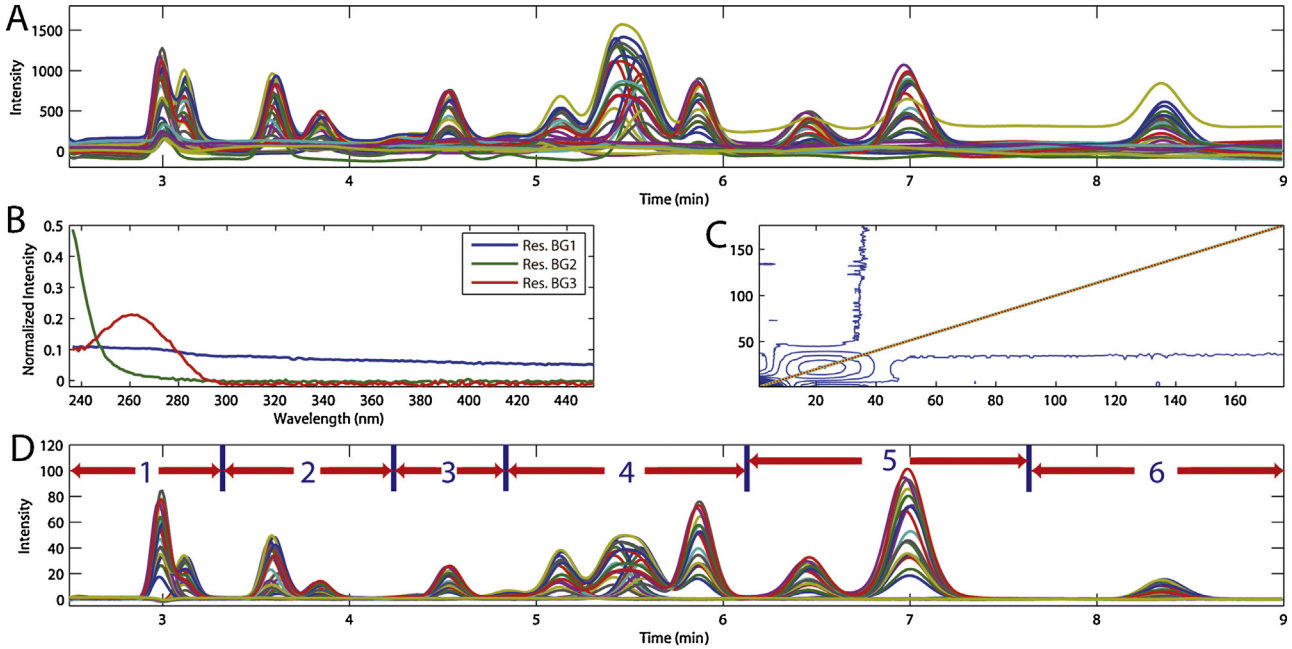

Fig. 4. Total chromatograms of 31 samples (A), resolved spectra for three components in background by ATLD (B), projection matrix (C) and results obtained after background drift correction (D). (BG: background drift.). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

Table 2
Elution ranges and concentration levels of 11 antibiotics and the number of components used in PARAFAC.

Elution range	Analyte	Concentration level[a] ($\mu g\,mL^{-1}$)	Elution range (min)	Number of components for PARAFAC-ALS	
				Before background correction	After background correction
I	Metronidazole	0.41–2.07	2.9–3.2	3	3
	Sulfacetamide	0.52–2.08	3.0–3.3	3	3
II	Pipemidic acid	0.15–0.77	3.7–4.1	4	3
III	Sulfamerazine	0.49–2.43	4.4–4.8	4	3
IV	Pefloxacin	0.40–1.98	4.9–5.4	5	4
	Tetracycline	1.39–5.56	5.2–5.7	5	4
	Oxytetracycline	1.28–4.28	5.3–5.9	5	4
	Ornidazole	0.80–4.00	5.7–6.2	5	4
V	Danofloxacin	0.35–1.74	6.1–6.8	3	2
	Lomefloxacin	0.81–4.04	6.6–7.4	3	2
VI	Sulfamethoxazole	0.81–1.04	8.1–8.8	2	1

[a] Values in calibration (standard) samples.

achieved (Fig. 2E). Notably, as demonstrated in Section 3, the characteristics of non-negativity of spectra were not guaranteed in the processed two-way chromatographic data (Fig. 2E).

Provided that the background drift was successfully corrected, a three-way chromatographic data array could be obtained by slicing the two-way data array along the sample direction; PARAFAC was used to resolve the coelution problem to accurately quantify analytes of interest, even in the presence of unknown compounds. To provide a distinct comparison with the traditional chemometric analysis strategy, the results provided by using excessive factors for PARAFAC to model the effect of background drift were obtained. The entire data set was divided into two segments according to the elution ranges of analytes for the analysis: the elution range corresponding to the first analyte (channels 1–200) and the elution range containing the second and third analytes as well as an interference (channels 201–800).

Three excessive components were introduced for PARAFAC to model the background drift. In Fig. 3A and B, the resolved chromatographic and spectral profiles obtained by implementing PARAFAC on the original three-way data array were respectively depicted. A brief examination of Fig. 3A and B reveals that only the simulated results for the first analyte are acceptable. (Note that the reference spectra of analytes are the 'mathematical reference' spectra calculated according to the descriptions in Section 3). On the contrary, resolved chromatographic profiles for the other three components (the other two analytes as well as the interference) seemed to be the result of the linear combination of the underlying components. Particularly, the qualitative results for the second analyte were obviously unacceptable and were composed of what appears to be a mixture of chromatograms of the second analyte and the interference; it seems that the influences of background drift in the second segment could not be efficiently modeled by excessive components.

Fortunately, significant improvement in qualitative results could be achieved by using PARAFAC to analyze the chromatographic data, with background drift correction by OSSP. The profiles shown in Fig. 3C and D demonstrated that the retrieved qualitative results are highly consistent with the underlying components. Moreover, the results in Fig. 3C and D imply that the problem of overlapped chromatographic peaks was satisfactorily resolved by the 'mathematical separation' strategy of PARAFAC. Comparison of the profiles shown in Fig. 3 also indicated that the effect of background drift was efficiently eliminated. To further demonstrate the improvement in quantitative capability of PARAFAC with background drift correction, statistical parameters including the correlation coefficient (R), the root mean square error of calibration (*RMSEC*) and the root mean square error of prediction (*RMSEP*), were summarized in Table 1; these parameters show remarkable improvement in the performance of PARAFAC when coupled with OSSP.

4.2. Real chromatographic data

Fig. 4A highlights the total chromatograms of the 21 standard samples, along with those of 5 validation samples and 5 test samples. Coelution of analytes was readily observed under the optimized chromatographic separation conditions. In addition, the presence of differential sample-to-sample background drift would certainly have an adverse effect on PARAFAC results. Therefore, PARAFAC was performed only after background drift correction by OSSP.

The spectra of eluents were estimated by implementing ATLD on the zero-component elution range (channels 1–100) of three-way data. (It is important to note that isocratic elution was used in this work, and the selected range covered the background spectra.) As depicted in Fig. 4B, three absorbing components were successfully resolved: the blue line might correspond to the spectrum of instrumental background; the green line possibly denotes the spectrum of eluent; and the red line represents a contaminant in the column. Then the projection matrix was constructed according to $\mathbf{I} - \mathbf{S}_{BK}\mathbf{S}_{BK}^{+}$ (contour plot shown in Fig. 4C). Finally, background drift was accurately removed by multiplying the projection matrix on the original two-way chromatographic data (Fig. 4D). OSSP provided high-quality background drift correction results; however, a part of the useful signals was distorted, and thus the signal-to-noise ratio may have decreased. This artifact is a risk of the projection method that one should always be aware of in real applications, particularly when the spectrum of the analyzed compound is highly correlated with those of eluents.

Before the employment of PARAFAC, the entire data array was divided into six smaller segments, according to the elution ranges of analytes of interest (Fig. 4D). In addition, the elution ranges of eleven analytes are listed in Table 2. It is obvious from Fig. 4D and Table 2 that the amount of overlap for each of the eleven compounds varied widely: in elution range I, compounds metronidazole and sulfacetamide were eluted; in elution range II, pipemidic acid was present; in elution range III, the single analyte sulfamerazine was present; in elution range IV, compounds pefloxacin, tetracycline, oxytetracycline and ornidazole were eluted; in elution range V, compounds danofloxacin and lomefloxacin were present; in elution range VI, sulfamethoxazole was well separated from the ten previously eluted analytes.

Since another challenge for the employment of trilinear decomposition was the time shift problem, the run-to-run time shift was also investigated (Fig. 4D). However, it seems that the time shift problem is not apparent in Fig. 4D. In practical applications, however, time shift alignment should be implemented initially if time shift among samples is significant [27,28]. The number of components for PARAFAC for each segment was estimated by the core-consistence value [29], and the results are summarized in

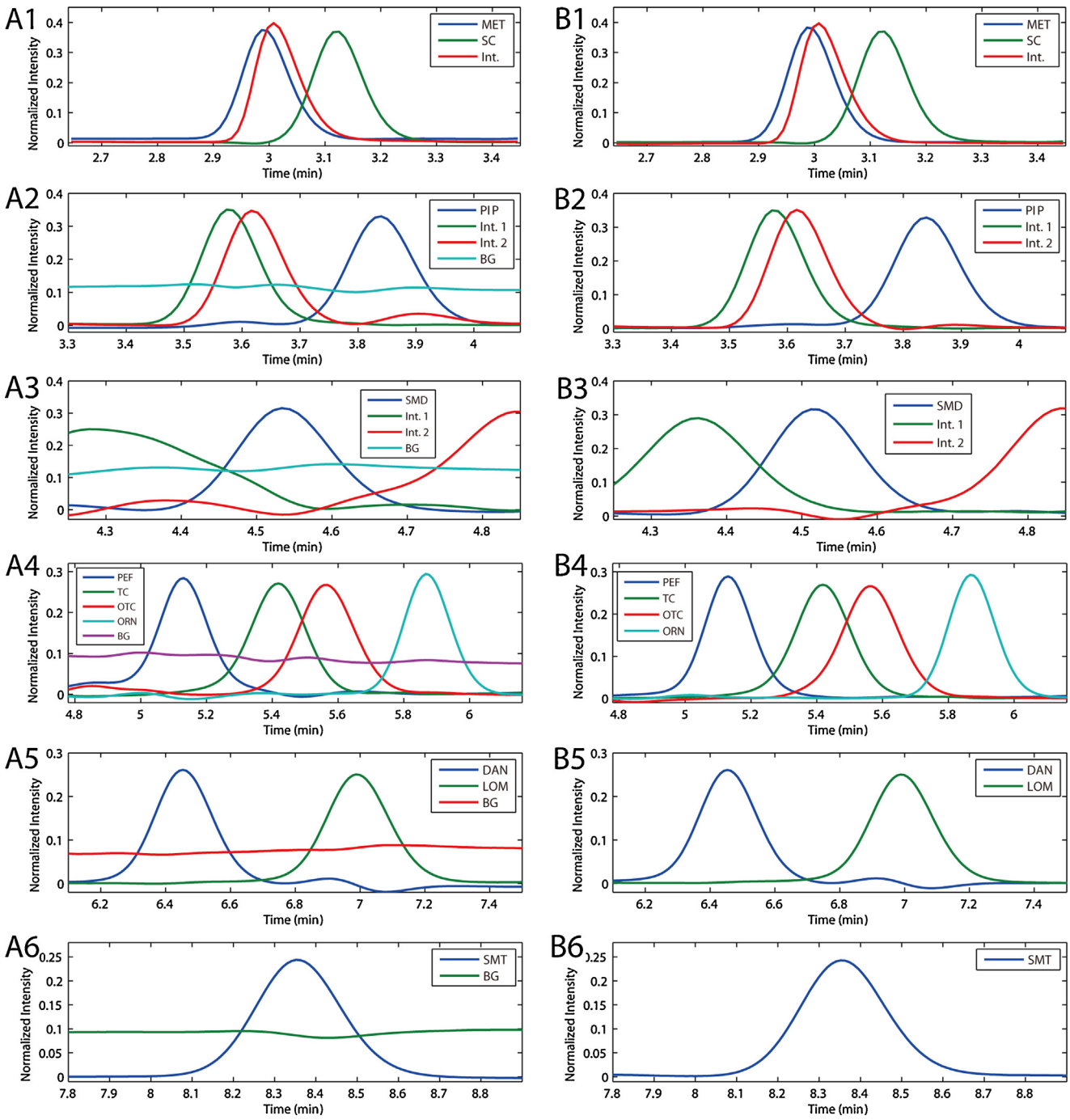

Fig. 5. Resolved chromatograms by using PARAFAC to decompose the original data (left column) and the data with background drift correction (right column). The first to sixth rows correspond to the first to sixth elution ranges shown in Fig. 4D, respectively. Abbreviations: BG: the resolved chromatogram of background drift; while Int.: interference.

Table 2. The number of components for most elution ranges was larger in the original data array than after background drift correction by OSSP, indicating that background drift made a significant contribution to the measured signal.

Resolved chromatographic profiles for each of the six segments were independently shown in the six rows of Fig. 5. In the left column of Fig. 5, results obtained by analyzing the data using PARAFAC without background drift correction are shown, whereas results with background drift correction are shown in the right column of Fig. 5. Although excessive factors were employed to model the influence of background, the recovered chromatograms of several constituents were still affected by these artifacts (Fig. 5A2, A3 and A4). In fact, higher numbers of components were also used for PARAFAC without OSSP correction; however, the results seemed to show little improvement. Therefore, the traditional chemometric strategy that employs excessive factors for PARAFAC to model the effect of background drift is insufficient, and one should perform a separate analysis to account for the influences of background drift. The resolved profiles in the right column of Fig. 5 clearly indicate that reasonable profiles were obtained by using PARAFAC to interpret chromatographic data processed with OSSP. Moreover, the chromatograms in Fig. 5 indicate that the overlapped chromatographic peaks of antibiotics can be successfully separated by the mathematical separation strategy using PARAFAC, which would

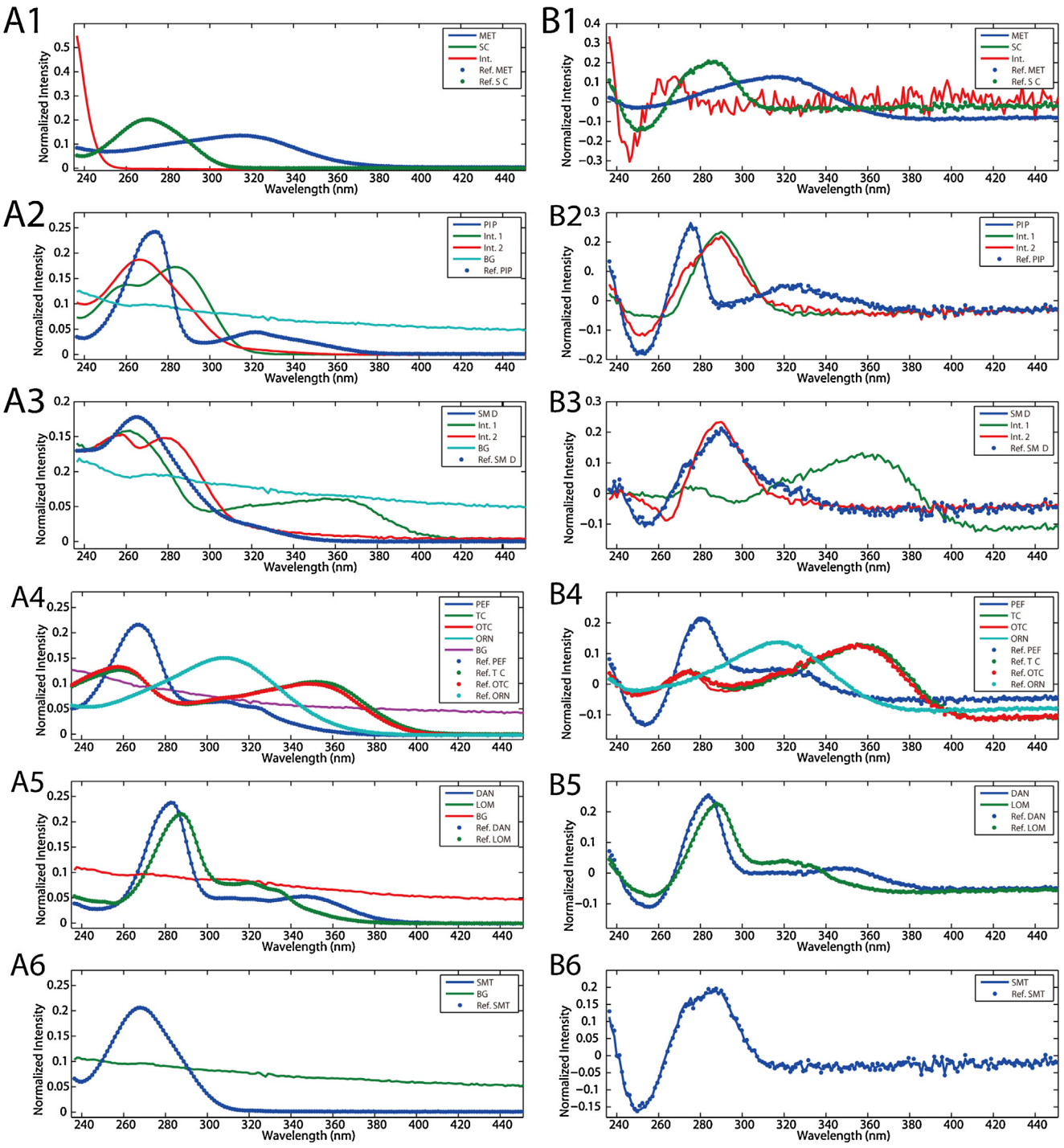

Fig. 6. Resolved spectra by using PARAFAC to decompose the original data (left column) and on the data with background drift correction (right column). The first to sixth rows correspond to the first to sixth elution ranges shown in Fig. 4D, respectively (BG: the resolved chromatogram of background drift; Int.: interference; Ref.: the reference spectrum of a compound obtained through multiplying the projection matrix by the original reference spectrum). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

definitely benefit the practical applications of chromatographic techniques to quantify antibiotics in water samples.

In the resolved and reference spectra for the analytes (Fig. 6), one can see that the spectra of eluents present in background were found in all elution segments without background correction (left column of Fig. 6). Additionally, the non-negativity for the resolved spectra of analytes was lost with background drift corrected by OSSP (the right column of Fig. 6), which is consistent with the results shown in Fig. 3D. Moreover, the resolved spectra in the second column of Fig. 6 seem slightly noisy when compared with those shown in the first column of Fig. 6; this might be due to the fact that a part of useful information embedded in the background spectra (background spectra in Fig. 4B) was removed through background drift correction, and thus the signal-to-noise ratio was reduced. Nevertheless, these retrieved spectra were consistent with the underlying 'mathematical reference' spectra.

The quantitative results for eleven antibiotics were summarized in Table 3. The simulated results (with and without background

Table 3
Quantitative results obtained by using PARAFAC to interpret real chromatographic data with and without background drift.

	Analyte										
	MET	SC	PIP	SMD	PEF	TC	OTC	ORN	DAN	LOM	SMT
Before correction											
R	0.9931	0.9968	0.9953	0.9988	0.9964	0.9979	0.9980	0.9959	0.9925	0.9971	0.9972
RMSEC	0.116	0.045	0.024	0.037	0.053	0.102	0.071	0.112	0.066	0.096	0.095
RMSEP	0.153	0.085	0.038	0.062	0.235	0.382	0.210	0.136	0.070	0.252	0.129
Recovery (%)	**100.0 ± 13.5**	102.4 ± 6.9	105.4 ± 8.3	101.0 ± 3.9	**120.0 ± 14.2**	109.3 ± 6.2	102.5 ± 7.6	104.7 ± 6.7	100.7 ± 8.4	107.6 ± 4.5	105.1 ± 4.1
After correction											
R	0.9988	0.9988	0.9981	0.9956	0.9960	0.9989	0.9986	0.9972	0.9959	0.9980	0.9976
RMSEC	0.031	0.028	0.015	0.071	0.055	0.073	0.061	0.093	0.049	0.080	0.088
RMSEP	0.053	0.070	0.018	0.100	0.096	0.358	0.226	0.107	0.058	0.249	0.105
Recovery (%)	102.8 ± 3.3	104.3 ± 3.6	102.3 ± 3.0	105.3 ± 5.9	106.3 ± 3.9	107.7 ± 7.7	99.3 ± 8.5	103.6 ± 2.6	104.6 ± 2.9	107.5 ± 3.9	103.4 ± 3.4

correction) did not show a statistical difference when compared with the actual ones (using the *t*-test under 95% confidence level); close investigation of these values revealed improvement in PARAFAC after background drift correction. Additionally, these results demonstrated that quantification of analytes in tap water samples can be performed by OSSP coupled with PARAFAC to interpret three-dimensional chromatographic data, regardless of background drift and coelution.

5. Conclusion

In the present work, the chromatographic background drift correction strategy based on OSSP was described in detail, and a relatively simple implementation of this strategy was presented. The results demonstrated that the combination of OSSP with PARAFAC can be used to resolve coelution problems in chromatographic analysis; therefore, more accurate quantitative results for analytes of interest can be achieved, regardless of the presence of background drift and unknown interferences. The analytical strategy described in this work would find potential application in the analysis of antibiotics in real samples using hyphenated chromatographic techniques.

Acknowledgements

The authors would like to acknowledge the National Natural Science Foundation of China (Grant No. 21175041) and the National Basic Research Program (Grant No. 2012CB910602) for financial support. In addition, the author Hai-Yan Fu would like to thank the open funds of the State Key Laboratory of Chemo/Biosensing and Chemometrics (Hunan University) (No. 201111) and the National Natural Science Foundation of China (No. 21205145) for financial support. Finally, the authors would like to thank Enago (www.enago.cn) for the English language review.

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