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Short Communication

Application of Kalman filter spectrophotometry in the analysis of pharmaceutical preparations — I. Sulphamethoxypyrazine and trimethroprim in sulpha compound tablets

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Introduction

The treatment of measurement data to obtain results is crucial to analytical chemistry. As all real signals contain noise, techniques are necessary to extract the useful information from the noisy signal. Various filters are available and of these the Kalman filter offers a robust, simple way of treating noisy signals in a variety of situations. The filter has its origins in control theory [1–3] but has been applied to chemical systems in recent years. Seelig and Blount [4, 5] have applied the filter to anodic stripping voltammetry. Poulisse [6–8] has described the application of a filter to multicomponent assays using UV spectrophotometry, and Brown *et al.* [9–11] have applied a similar approach to overlapping electrochemical responses.

The simultaneous assay of several components in a multicomponent mixture is increasingly important in analytical chemistry because of the simplifications it introduces in sample preparation. Although conventional multiple linear regression is used extensively in these situations, the Kalman filter approach offers an alternative with excellent performance. The assay of Sulphamethoxypyrazine compound tablets is used as an example of the application of a multicomponent Kalman filter in this paper.

Theory

The absorbance of a solution of n components, obeying the Beer–Lambert law, at a single wavelength, k, can be written in matrix notation as:

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$$Y_k = C_k \cdot X + V_k, \tag{1}$$

where Y_k is the solution absorbance at wavelength k; C_k^T is the transpose of the column *vector of specific absorbance at wavelength* k; X is the column vector of component concentrations; and V_k is the measurement noise at wavelength k.

A spectrum is a sequence of m such equations at m wavelengths ($k = 1,2, \ldots, m$; $m>n$). A multicomponent assay is the calculation of the concentration vector X, given C and the measurements Y and V.

In the application of a Kalman filter to multicomponent assay it is first necessary to define the model relating the concentration of the components at wavelength k to their concentrations at wavelength $k + 1$. As the spectrum is measured in a static solution, the concentrations are identical at all wavelengths. Thus,

$$X_{k+1} = X_k + Q, \tag{2}$$

where Q is a "noise" parameter which determines how strictly the concentration identity is enforced across the spectrum.

Next, the measurement equation (1) is used to predict the absorbance at wavelength $k + 1$ using the estimated concentrations at wavelength k. This is compared with the measured value, and the difference is used to refine the concentration values at wavelength $k + 1$. The cycle of prediction, comparison, refinement is repeated either to the end of the spectrum or until the concentration estimates do not change. Estimates of the standard deviations of the concentrations are generated simultaneously. The equations to carry out these operations are given in detail by both Poulisse and Brown.

Experimental

Equipment and reagents

The equipment used comprised: spectrophotometer, Shimadzu UV-260 double beam; computer, Apple II. Sulphamethoxypyrazine (SMPZ) and trimethroprim (TMP) were used as received. All other materials were analytical reagent quality.

Preparation of standard solutions

About 76, 80 or 84 mg SMPZ and 38, 40 or 42 mg TMP were weighed accurately and each was transferred to separate 250-ml volumetric flasks. The solids were dissolved in 10 ml methanol and diluted to volume with 0.1 N sodium hydroxide solution. Aliquots of 25.0 ml were each diluted to 100 ml with 0.1 N sodium hydroxide, and 10.0 ml aliquots of these solutions were diluted to 100 ml with 0.1 N sodium hydroxide. These final solutions formed the standard solutions.

Preparation of sample solutions

Twenty tablets were weighed and powdered. A quantity of power equivalent to about 80 mg SMPZ or about 40 mg TMP was weighed accurately and transferred to a 25-ml volumetric flask. The powder was shaken with 10 ml methanol for 5 min and the mixture was diluted to volume with 0.1 N sodium hydroxide solution. This mixture was filtered through a dry filter paper and the first 50 ml discarded. A 25.0-ml portion of the filtrate was diluted to 100 ml with 0.1 N sodium hydroxide, and a 10.0-ml aliquot of this solution was diluted to 100 ml with 0.1 N sodium hydroxide.

Spectrum measurement and calculations

The spectra of the standard and sample solutions were measured for the wavelength range 234–350 nm at 2-nm intervals using 0.1 N sodium hydroxide as a blank. Typical spectra are shown in Fig. 1.

The absorbance data at 2-nm intervals for each standard and sample were input into an Apple II multicomponent Kalman filter program based on the algorithms of Poulisse [6], using the data for the standards to form the C_k vectors. The filter was moved through the sample spectrum from low to high wavelengths and it converged rapidly to invariant concentration values. Attempts were made to use an estimate of measurement noise, in the chosen wavelength range, to calculate the covariance matrix of the filter and to use this to end the cycle of iterations when the change in concentration for an iteration was less than the corresponding variance. This approach was not entirely successful and requires further optimization.

Results and Discussion

A typical plot of estimated concentrations against wavelength as the filter moves across the spectrum is given in Fig. 2. Table 1 shows the results of six recovery

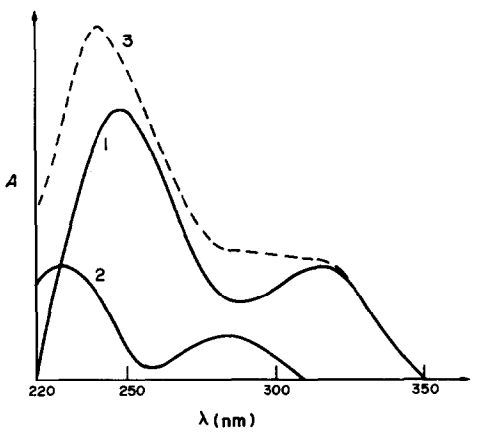

Figure 1
Absorption curves: 1, sulphamethoxypyrazine (8 g ml^{-1}); 2, trimethroprim (4 g ml^{-1}); 3, mixture.

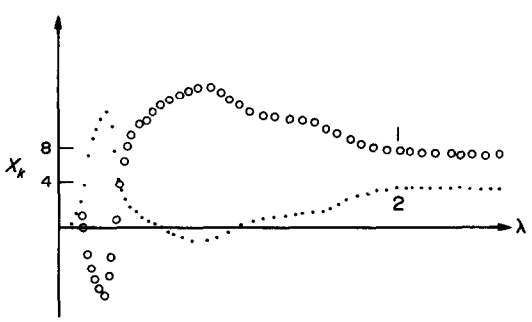

Figure 2
Estimated concentrations X_k by using Kalman filtering.

Table 1
Recovery of sulphamethoxypyrazine and trimethroprim

Batch No.	TMP Added (mg)	TMP Recovery (mg)	TMP Recovery (%)	SMPZ Added (mg)	SMPZ Recovery (mg)	SMPZ Recovery (%)
1	44.18	44.80	101.4	78.55	78.72	100.2
2	41.92	42.40	101.1	81.59	81.60	100.0
3	38.78	39.20	101.1	79.30	79.28	99.97
4	38.87	39.20	100.8	82.93	83.02	100.1
5	36.64	36.80	100.4	79.26	79.34	100.1
6	40.41	40.60	100.5	80.52	80.56	100.0
Mean Recovery			100.9			100.1
SD			0.39			0.09
RSD (%)			0.38			0.09

Table 2
Comparison of five assay methods

Batch	Method 1 TMP	Method 1 SMPZ	Method 2 TMP	Method 2 SMPZ	Method 3 TMP	Method 3 SMPZ	Method 4 TMP	Method 4 SMPZ	Method 5 TMP	Method 5 SMPZ
1. Content (%)	100.2	100.7	100.0	100.6	99.4	99.2	98.8	99.2	98.4	99.2
SD	0.53	0.26	0.28	0.11	0.98	0.45	0.44	0.45	0.56	0.45
2. Content (%)	99.9	99.7	99.2	99.4	99.4	99.6	98.8	99.6	99.6	99.6
SD	0.44	0.35	0.45	0.08	1.74	0.38	0.49	0.38	0.74	0.38
3. Content (%)	99.3	101.2	99.2	100.6	100.3	99.9	98.8	99.9	99.4	99.9
SD	0.67	0.06	0.44	0.06	1.00	0.53	0.36	0.53	0.63	0.53

Method 1: Kalman filter.
Method 2: *Shanghai Drug Standard* [12].
Method 3: Dual-wavelength method using 271 and 318 nm.
Method 4: Three-wavelength method using 229, 304 and 447 nm.
Method 5: Orthogonal function method for determination of TMP using third-degree polynomial with six points at 12 nm intervals in the range 238–298 nm.

experiments for the two components. Recoveries of 100.9% (% relative standard deviation, RSD, 0.39%) and 100.1% (% RSD 0.09%) for TMP and SMPZ, respectively are excellent.

Table 2 gives the results of the assay of three batches of tablets by the Kalman filter method and by four other existing methods. Good agreement between the methods is seen in both the assay value and the standard deviation.

The good agreement with the existing methods and the good recoveries and standard deviations demonstrate the viability of using the multicomponent Kalman filter in the assay of pharmaceutical products. The filter is simple to programme and use, and does not require the matrix inversion operations needed for the multiple linear regression calculations. Because of its simplicity, it is possible to consider the use of such a filter in the on-line computation of assay results as a spectrum is being recorded.

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