ELSEVIER

Analytica Chimica Acta 423 (2000) 179–185

ANALYTICA CHIMICA ACTA

www.elsevier.com/locate/aca

Systematic errors: detection and correction by means of standard calibration, Youden calibration and standard additions method in conjunction with a method response model

Reynaldo César Castells*, Marcela Alejandra Castillo

División de Química Analítica, Facultad de Ciencias Exactas, Universidad Nacional de La Plata, 47 esq. 115, 1900 La Plata, Argentina, CIDEPINT, 52 e/121 y 122, 1900 La Plata, Argentina

Received 17 April 2000; received in revised form 8 August 2000; accepted 8 August 2000

Abstract

Responses of analytical methods are interpreted by means of a simple algebraic method that considers several contributions. Types of constant and variable systematic errors are unambiguously identified on applying the model to standard calibration, Youden calibration and standard additions method performed in the presence of different matrix effects. Errors detection and composition calculation procedures emerge as mathematical consequences of this simple treatment. Matrix effects of three types are distinguished, and a definition of interference is suggested.

Keywords: Systematic errors; Youden calibration; Standard additions method; Interference; Validation

1. Introduction

Textbooks on general analytical chemistry give a poor coverage of systematic errors; even in chemometrics books [1,2] systematic errors treatment is scarce and sparse. Wilson [3], who was probably the first author to study the subject in some depth, distinguished four sources: (1) biased blanks; (2) biased calibration (contaminated standards, assumption of an incorrect response versus analyte amount functional relationship, or deficient data treatment); (3) different analytical response towards different species of a given analyte (for instance, metallic ions in the free state or complexed with matrix constituents); (4) interference.

This classification was adopted some years later by Cardone [4], who called constant errors to those of type (1) and placed errors of type (3) within the more general category of proportional errors. Constant and proportional errors are corrigible errors because they can be detected and their importance be calculated and used in the correction of analytical results. Errors of type (2) and (4) are incorrigible; the analyst must detect them on the basis of the knowledge he acquires during development of the method, which must be corrected before sample analysis. Cardone's paper emphasized the use of Youden calibration [5,6] to detect and correct for constant errors and proposed calculation methods to deal with proportional errors. We are not aware of the repercussion that his paper had by the time of its publication; however, the author returned to the subject three years later, now with an original approach [7,8]: two model numerical problems involving standard and Youden curves, single-point ratio calcu-

* Corresponding author. Fax: +54-221-427-1537
E-mail address: rcastell@dalton.quimica.unlp.edu.ar (R.C. Castells).

0003-2670/00/$ – see front matter
PII: S0003-2670(00)01125-9

Nomenclature

b_0	intercept, regression equation
b_1	slope, regression equation
P	matrix effect on the slope of the regression equation
w	sample amount
w_i	analyte amount
w_j	non-analyte amount
$w_{i,\mathrm{add}}$	added standard amount
x_i	analyte weight fraction in the sample
x_j	non-analyte weight fraction in the sample
y_i	measured response
$\hat{y}_\mathrm{i}$	predicted response

Greek symbols

β_0	intercept, linear model
β_1	slope, linear model
ε_i	random error

Subscripts

M	matrix
S	standard
SAC	standard additions calibration
YC	Youden calibration

lations and standard additions calculations were sent to a numerous group of experienced analytical chemists, warning them that data were random-error free. From a detailed analysis of the received answers the author concluded that confusion and lack of agreement about the nature of blanks and calculation procedures existed between analysts. The question to be answered is: are things different today?

Cardone's original paper [4] was very good but rather conceptual in its approach; the result of his survey is not surprising on account of the scarce treatment that the subject had received in the literature. Although some numerical examples were given, equations were reduced by the author to a minimum indispensable, and this may constitute a difficulty for readers not acquainted with the subject and used to a more symbolic language. We undertook the task of analyzing standard, Youden and standard additions plots, under different circumstances, with the help of an analytical response model that attempts accounting for its different components. This paper is focused on real samples, containing an unknown number of unidentified non-analytes. A classification of nonconstant systematic errors distinguishing two types of corrigible proportional error and including incorrigible interference as a third case resulted from this approach. A summary is presented in this paper that, hopefully, will serve to trigger the interest of the analytical community and start discussions on such an important subject.

2. Standard calibration (SC)

Different amounts of a high purity standard are weighed and dissolved in equal volumes of a suitable solvent; equal aliquots of each solution are subjected to the measurement procedure. Calculate the standard amounts w_i on which the measurements were performed; fit the obtained responses, $y_{i,\mathrm{S}}$, to the model

$$y_{i,\mathrm{S}} = \beta_{0,\mathrm{S}} + \beta_{1,\mathrm{S}} w_i + \varepsilon_i \tag{1}$$

where $y_{i,\mathrm{S}}$ is the measured response, ε_i is the experimental (random) error at the w_i level, $\beta_{1,S} w_i$ is the true analyte response, and $\beta_{0,\mathrm{S}}$ is a constant error, independent of analyte amount. Examples of constant error reported in literature are: (1) solubility of precipitated species in gravimetry; (2) some titration errors, as silver chromate minimum perceptible amount in Mohr halide titration or alkali consumption by acid impurities contained in ethanol used as sample solvent in fatty acids titration; (3) solvents and reagents absorbance in spectrophotometry; (4) solvents, reagents or their impurities, used in pre-chromatographic manipulation of the standards, when coelute with the analyte or its derivatives.

The result of the fitting procedure is

$$\hat{y}_{i,\mathrm{S}} = b_{0,\mathrm{S}} + b_{1,\mathrm{S}} w_i \tag{2}$$

$$b_{0,\mathrm{S}} \in \beta_{0,\mathrm{S}} \tag{3}$$

$$b_{1,\mathrm{S}} \in \beta_{1,\mathrm{S}} \tag{4}$$

where $\hat{y}_{\mathrm{i,S}}$ is the predicted response at the w_i level and symbol $\in$ is used to denote "estimate of", $b_{0,\mathrm{S}}$ the *standards blank*, that represents extrapolation to $w_i = 0$ of responses measured in the presence of finite amounts of analyte.

3. Matrix effects on sample response

Sample components different from analyte(s) are denoted by the term matrix. Matrices can affect the analyte response by two different mechanisms. Some of the matrix components, present at the time of measuring, can somehow modify the analyte response. Or some sample treatment, indispensable because of the matrix presence, can affect the response; any extraction, precipitation, adsorption or the like operations to which the sample is subjected prior to the measurement (and that are not necessary during SC) can result in a matrix effect.

Sample responses are fitted in this paper to the following model:

$$y_i = \beta_{0,S} + \beta_{0,M} + \beta_{1,S} P w_i + \varepsilon_i \quad (5)$$

where $\beta_{0,S}$, $\beta_{1,S}$ and ε_i have the same meanings as in Eq. (1); w_i is the analyte amount in the sample amount w on which the procedure was performed; $x_i = w_i/w$, represents the analyte weight fraction in the sample. $\beta_{0,M}$ is a constant matrix error, independent of sample amount, whose origin is analogous to that of $\beta_{0,S}$ (for instance, some solvent or reagent employed in sample pre-treatment and not used in SC). P is a term accounting for matrix effects on the analyte response for which at least three possibilities can be envisaged. For the sake of clarity, only the case in which P is constant through all the method linear range shall be treated at this section, leaving treatment of the other possibilities for Section 4. A constant P represents a matrix effect proportional to analyte amount but independent of matrix amount; it cannot be attributed to a non-analyte, since in this case the error would increase with matrix amount. Effects of this type, for instance, may be caused by incomplete extraction: if V_2 ml sample are extracted with V_1 ml of a non miscible solvent, the amount of analyte extracted is

$$w_{\text{extracted}} = \left\{ K \frac{(V_1/V_2)}{[1 + K(V_1/V_2)]} \right\} w_i$$

i.e. a constant fraction of the total is subjected to the measuring procedure as long as partition coefficient K remains constant.

3.1. Youden calibration (YC)

Dissolve different amounts of sample according to sample treatment procedure (not necessarily identical to that used during SC) and subject equal aliquots of each solution to the measurement procedure; w is the amount of sample on which the procedure was applied. YC plot is a representation of responses, y_i, against w.

Substituting w_i for w in Eq. (5), response model for YC is obtained:

$$y_i = \beta_{0,S} + \beta_{0,M} + \beta_{1,S} P x_i w + \varepsilon_i \quad (6)$$

The result of fitting responses obtained in a YC to this model is

$$\hat{y}_i = b_{0,YC} + b_{1,YC} w \quad (7)$$

where

$$b_{0,YC} \in \beta_{0,S} + \beta_{0,M} \quad (8)$$

$$b_{1,YC} \in \beta_{1,S} P x_i \quad (9)$$

Eqs. (3) and (8) can be combined to give

$$b_{0,YC} - b_{0,S} \equiv b_{0,M} \in \beta_{0,M} \quad (10)$$

while Eqs. (4) and (9) give

$$b_{1,YC} = b_{1,S} P x_i \quad (11)$$

$b_{0,YC}$ is the *total Youden blank*; it contains the signals responsible for $b_{0,S}$ plus those arising from any sample pre-treatment, $b_{0,M}$ is *Youden blank*, its components being clear from Eq. (10).

3.2. Standard additions calibration (SAC)

Dissolve an exactly known amount of sample according to the sample procedure. Separate four equal aliquots of solution and add on three of them increasing and precisely known amounts of the standard. Equal aliquots of these four solutions are subjected to the measurement procedure. Calculate the effective mass of sample, w, and of added standard, $w_{i,\text{add}}$, taken for the measurement. A plot of the measured responses, $y_{i,\text{SAC}}$, against $w_{i,\text{add}}$ is an SAC plot.

From Eq. (5), the model to which $y_{i,\text{SAC}}$ responses have to be fitted is

$$y_{i,\text{SAC}} = \beta_{0,S} + \beta_{0,M} + \beta_{1,S} P (w_i + w_{i,\text{add}}) + \varepsilon_i \quad (12)$$

where w_i is the analyte amount present in sample amount (w) in each of the four equal aliquots.

The result of fitting SAC responses to this model is

$$\hat{y}_{i,\mathrm{SAC}} = b_{0,\mathrm{SAC}} + b_{1,\mathrm{SAC}} w_{i,\mathrm{add}} \tag{13}$$

where

$$b_{0,\mathrm{SAC}} \in \beta_{0,\mathrm{S}} + \beta_{0,\mathrm{M}} + \beta_{1,\mathrm{S}} P w_i \tag{14}$$

$$b_{1,\mathrm{SAC}} \in \beta_{1,\mathrm{S}} P \tag{15}$$

From Eqs. (4) and (15)

$$b_{1,\mathrm{SAC}} = b_{1,\mathrm{S}} P \tag{16}$$

and from Eqs. (4), (8) and (14)

$$b_{0,\mathrm{SAC}} = b_{0,\mathrm{YC}} + b_{1,\mathrm{S}} P w_i \tag{17}$$

Eq. (16) shows that a statistically significant difference between SC and SAC slopes indicates a first order analyte/matrix effect ($P \neq 1$), and that two standard additions performed on different sample amounts shall result in two parallel lines.

3.3. Sample composition calculations

Gross errors can be made when analysis is attempted by combining a single sample signal and SC ignoring constant and proportional matrix errors; the result (x_i^*), as calculated from Eq. (2), is

$$x_i^* = \frac{w_i}{w} = \frac{(y_i - b_{0,\mathrm{S}})}{b_{1,\mathrm{S}} w} \tag{18}$$

Exact result is obtained by successively using Eqs. (7), (10), (11), and (18)

$$x_i = \frac{b_{1,\mathrm{YC}}}{b_{1,\mathrm{S}}} P = \frac{(y_i - b_{0,\mathrm{YC}})}{b_{1,\mathrm{S}} w P} = \left(\frac{x_i^*}{P}\right) - \left(\frac{b_{0,\mathrm{M}}}{b_{1,\mathrm{S}} w P}\right) \tag{19}$$

The effect of constant and proportional errors on the final result of the analysis is made clear by Eq. (19); in the absence of a proportional error, Eq. (19) describes the well known asymptotic approach to the exact value as the sample size increases that is observed in the presence of constant errors [9].

There are two options to calculate sample composition:

1. From one SAC and YC, by Eqs. (16) and (17):

$$x_i = \frac{(b_{0,\mathrm{SAC}} - b_{0,\mathrm{YC}})}{b_{1,\mathrm{SAC}} w} \tag{20}$$

   Again, the error induced by many authors that preconize the relationship $x_i = b_{0,\mathrm{SAC}}/\mathrm{b}_{1,\mathrm{SAC}}\, w$ is made evident.

2. An option introduced by Cardone [10] is to perform two SAC, adding the standard to different sample weights, w and w'. SAC responses can be written as

$$y_{i,\mathrm{SAC}} = b_{0,\mathrm{SAC}} + b_{1,\mathrm{SAC}} w \left(\frac{w_{i,\mathrm{add}}}{w}\right) \tag{21}$$

$$y_{1,\mathrm{SAC}'} = b_{0,\mathrm{SAC}'} + b_{1,\mathrm{SAC}} w' \left(\frac{w_{i,\mathrm{add}}}{w'}\right) \tag{22}$$

   with $b_{0,\mathrm{SAC}} = b_{0,\mathrm{YC}} + b_{1,\mathrm{SAC}} x_i w$ and $b_{0,\mathrm{SAC}'} = b_{0,\mathrm{YC}} + b_{1,\mathrm{SAC}} x_i w'$. It is easily demonstrated that two straight lines should be obtained when plotting both SAC responses against $(w_{i,\mathrm{add}}/w)$, with intersection point at $(w_{i,\mathrm{add}}/w)^*$, calculated as

$$\left(\frac{w_{i,\mathrm{add}}}{w}\right)^* = \frac{(b_{0,\mathrm{SAC}'} - b_{0,\mathrm{SAC}})}{[b_{1,\mathrm{SAC}}(w - w')]} = -x_i \tag{23}$$

   It can, furthermore, be demonstrated that the ordinate at the intersection of both straight lines, y_{i,SAC^*}, is given by

$$y_{i,\mathrm{SAC}^*} = b_{0,\mathrm{YC}} \tag{24}$$

4. Other types of matrix effects

Section 3 summarized the simplest case of matrix effects on analyte signal and the ways to detect and correct for it. Two cases in which P is not constant are treated at this section.

$$P = f(w_j) = f(x_j w) \tag{25}$$

A matrix effect is produced by an unidentified non-analyte j, present in the sample at a weight fraction $x_j = w_j/w$, which does not produce a signal or produces a signal that can be perfectly differentiated from the one corresponding to the analyte; the analyte signal is, however, modified by compound j, and the magnitude of this change depends exclusively on w_j.

Sample response model, obtained by substituting Eq. (25) in Eq. (5), shows that y_i can be nonlinear in w. This introduces uncertainties in the measurement of the Youden total blank and makes calculation methods that can dispense with the knowledge of $b_{0,\mathrm{YC}}$ highly desirable.

SAC responses are linear in $w_{i,\mathrm{add}}$; the result of fitting responses to the model is identical to Eq. (13), but the intercept and slope now depend on the sample weight w to which the standard was added:

$$b_{0,\mathrm{SAC}} = b_{0,\mathrm{YC}} + b_{1,\mathrm{S}} f(x_j w) w_i \tag{26}$$

$$b_{1,\mathrm{SAC}} = b_{1,\mathrm{S}} f(x_j w) \tag{27}$$

As in the former case, a statistically significant difference between SC and SAC slopes indicates an analyte/matrix interactional effect. However, plots of two SAC performed by adding standards on two different sample amounts will not be parallel, and this constitutes a criterion to detect this type of matrix effect.

Two standard additions on two samples with different weights, w and w', constitute also the best way towards the calculation of the sample composition, since knowledge of $b_{0,\mathrm{YC}}$ becomes unnecessary. It is easily demonstrated that when plotting responses obtained in both standard additions, $y_{i,\mathrm{SAC}}$ and $y_{i,\mathrm{SAC}'}$, against $(w_{i,\mathrm{add}}/w)$ and $(w_{i,\mathrm{add}}/w')$, respectively, two straight lines are obtained with a point of intersection at

$$\left(\frac{w_{i,\mathrm{add}}}{w}\right)^* = \left(\frac{b_{0,\mathrm{SAC}'} - b_{0,\mathrm{SAC}}}{w b_{1,\mathrm{SAC}} - w' b_{1,\mathrm{SAC}'}}\right) = -x_i \tag{28}$$

Furthermore, the ordinate at the intersection point is given by Eq. (24).

A possible origin for this type of matrix effect is some kind of association between compounds i and j to give a complex species (ij) with formation constant $K = [ij]/[i][j]$. If c_i and c_j are used to denote analyte and non-analyte analytical concentrations at the moment of performing the measurement, free species i concentration shall be given by $[i] = c_i - [ij] = c_i - K[i][j]$, from which

$$[i] = \frac{c_i}{(1 + K[j])} \tag{29}$$

If only free species i is detected by the method, sample response model (Eq. (5)) can be written as

$$\begin{aligned} y_i &= \beta_{0,\mathrm{S}} + \beta_{0,\mathrm{M}} + \beta_{1,\mathrm{S}}[i]V + \varepsilon_i \\ &= \beta_{0,\mathrm{S}} + \beta_{0,\mathrm{M}} + \beta_{1,\mathrm{S}}\{1 + K[j]\}^{-1} w_i + \varepsilon_i \end{aligned} \tag{30}$$

where V is solution volume and $c_i V = w_i$. The term between brackets is P, and two possible situations may be considered:

1. When $c_j \gg c_i$, $[j] = c_j - K[i][j] \cong c_j$; under these conditions P is constant at constant w and V even though $c_i = (w_i + w_{i,\mathrm{add}})/V$ changes. SAC plots shall be straight lines with slopes and intercepts given by Eqs. (26) and (27).
2. When $c_j \cong c_i$, $[j]$ depends on c_i, P is not constant and SAC plot may show curvature. P becomes a function both of analyte and non-analyte concentrations, and this takes us to the next type of matrix effect.

$$P = f(w_i, w_j) \tag{31}$$

Cases in which P obeys this functional relationship constitute *interference* from the sample matrix. Interference, within the context of this paper, means an incorrigible error (in the sense that it cannot be corrected by means of an adequate data treatment), caused by non-analytes present in the sample (interferents), whose magnitude depends on both analyte and non-analyte concentrations. A case of an interference was mentioned in point (2) above; origins of interferences, however, are much more complex: imagine, for instance, that non-analyte j, besides complexing with analyte i, generates its own response and that this cannot be differentiated from that of the analyte. Very complex interference effects were shown by Tyson [11] for Ca (II) atomic absorption signals in the presence of Al (III), where $P \cong \exp[-\text{constant}\ (w_j/w_i)]$. A detailed knowledge of the interference mechanism is necessary in order to formulate function $f(w_i, w_j)$ on rational grounds, and this knowledge is often not available. Anyway, from the general forms adopted by sample and SAC response models:

$$y_i = \beta_{0,\mathrm{S}} + \beta_{0,\mathrm{M}} + \beta_{1,\mathrm{S}} f(x_i w, x_j w) x_i w + \varepsilon_i \tag{32}$$

$$\begin{aligned} y_{i,\mathrm{SAC}} = {} & \beta_{0,\mathrm{S}} + \beta_{0,\mathrm{M}} + \beta_{1,\mathrm{S}} f(w_i + w_{i,\mathrm{add}}, w_j) w_i \\ & + \beta_{1,\mathrm{S}} f(w_i + w_{i,\mathrm{add}}, w_j) w_{i,\mathrm{add}} + \varepsilon_i \end{aligned} \tag{33}$$

it can be expected that linear YC and SAC plots only result in some specific situations.

One of those situations occurs when the interference is additive, in which case analyte and interferent contribute in additive and independent form to the apparent signal. Examples of this type are well known: simultaneous precipitation of interferent in gravimetric analysis, peak overlapping in chromatography, positive interference of absorbing non-analytes in spectrophotometry, etc. Sample response model can in these cases be written as

$$y_i = \beta_{0,S} + \beta_{0,M} + \beta_{1,S(i)} w_i + \beta_{1,S(j)} w_j + \varepsilon_i \quad (34)$$

where $\beta_{1,S(i)}$ and $\beta_{1,S(j)}$ are used to denote analyte and interferent theoretical slopes in their respective SC models. Eq. (34) can easily arranged to the form

$$y_i = \beta_{0,S} + \beta_{0,M} + \beta_{1,S(i)} \left[1 + \left(\frac{\beta_{1,S(j)} w_j}{\beta_{1,S(i)} w_i} \right) \right] w_i + \varepsilon_i \quad (35)$$

in order to demonstrate its coincidence with the general expression valid for interference (Eq. (31)), with P given by the square bracket.

YC results should be fitted to the model

$$y_i = \beta_{0,S} + \beta_{0,M} + [\beta_{1,S(i)} x_i + \beta_{1,S(j)} x_j] w + \varepsilon_i \quad (36)$$

that obviously corresponds to a straight line. Also SAC plots are straight lines, whose intercepts and slopes are estimates of the following model parameters:

$$b_{0,SAC} \in \beta_{0,S} + \beta_{0,M} \beta_{1,S(i)} w_i + \beta_{1,S(j)} w_j \quad (37)$$

$$b_{1,SAC} \in \beta_{1,S(i)} \quad (38)$$

Then, using Eqs. (4) and (8)

$$b_{0,SAC} = b_{0,YC} + b_{1,S(i)} w_i + b_{1,S(j)} w_j \quad (39)$$

$$b_{1,SAC} = b_{1,S(i)} \quad (40)$$

By Eq. (40), SAC is unable to detect this type of interference. This makes additive interference highly insidious, and a good practice when interference is suspected is to slightly modify method conditions (as a change in wavelength or in mobile phase composition) in order to detect if new signals are generated. Eq. (39) reflects the impossibility of differentiating between analyte and interferent signals by means of normal standard additions method. Additive signals as those in Eq. (39) can be differentiated by means of some multiple-sensor instrument, as UV absorbance measurement at several wavelengths and data treatment by the generalized standard additions method (GSAM) [12,13]. This method, however, demands knowledge of number and identity of interferents and, furthermore, standards of each of them must be available in order to be added in perfectly known amounts to the sample. These requirements are of illusory fulfilment in most real samples analysis, as those performed on biological samples, and the analyst should better somehow modify his technique to obtain analyte and interferent separate signals.

5. Conclusions

This paper demonstrates that it is possible to establish clear, mathematical relationships between different types of systematic errors associated with chemical analysis. Blanks are unambiguously defined and three classes of variable error are clearly specified according with type of matrix/analyte interaction. Data gathered in standard calibration, Youden calibration and standard additions method, when treated by the procedures described in the paper, enable errors detection and correction.

Acknowledgements

This work was sponsored by CONICET (Consejo Nacional de Investigaciones Científicas y Técnicas de la República Argentina), by Agencia Nacional de Promoción Científica y Tecnológica (contract BID 802/OC-AR) and by CICPBA (Comisión de Investigaciones Científicas de la Provincia de Buenos Aires). M.A.C. acknowledges contract UNLP-FOMEC for a fellowship.

References

[1] D.L. Massart, B.G.M. Vandeginste, L.M.C. Buydens, S. De Jong, P.J. Lewi, J. Smeyers-Verbeke, Handbook of Chemometrics and Qualimetrics: Part A, Elsevier, Amsterdam, 1997.
[2] M.A. Sharaf, D.L. Illman, B.R. Kowalski, Chemometrics, Wiley, New York, 1986.
[3] A.L. Wilson, Talanta 21 (1974) 1109.
[4] M.J. Cardone, J. Assoc. Off. Anal. Chem. 66 (1983) 1283.
[5] W.J. Youden, Anal. Chem. 19 (1947) 946.

[6] F.J. Linning, J. Mandel, J.M. Peterson, Anal. Chem. 26 (1954) 1102.
[7] M.J. Cardone, Anal. Chem. 58 (1986) 433.
[8] M.J. Cardone, Anal. Chem. 58 (1986) 438.
[9] D.A. Skoog, D.M. West, Fundamentals of Analytical Chemistry, 3rd Edition, Holt, Rinchart & Winston, New York, 1976, p. 81.
[10] M.J. Cardone, Anal. Chem. 59 (1987) 2818.
[11] J.F. Tyson, Analyst 109 (1984) 313.
[12] B.E.H. Saxberg, B.R. Kowalski, Anal. Chem. 51 (1979) 1031.
[13] C. Jochum, P. Jochum, B.R. Kowalski, Anal. Chem. 53 (1981) 85.