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Comparison of the single channel and multichannel (multivariate) concepts of selectivity in analytical chemistry

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ABSTRACT

Different measures of selectivity are in use for single channel and multichannel linear analytical measurements, respectively. It is important to understand that these two measures express related but still distinctly different features of the respective measurements. These relationships are clarified by introducing new arguments. The most widely used selectivity measure of multichannel linear methods (which is based on the net analyte signal, NAS, concept) expresses the *sensitivity to random errors* of a determination where all bias from interferents is computationally eliminated using pure component spectra. The conventional selectivity measure of single channel linear measurements, on the other hand, helps to estimate the *bias caused by an interferent* in a biased measurement. In single channel methods expert knowledge about the samples is used to limit the possible range of interferent concentrations. The same kind of expert knowledge allows improved (lower mean squared error, MSE) analyte determinations also in "classical" multichannel measurements if those are intractable due to perfect collinearity or to high noise inflation. To achieve this goal bias variance tradeoff is employed, hence there remains some *bias* in the results and therefore the concept of single channel selectivity can be extended in a natural way to multichannel measurements. This extended definition and the resulting selectivity measure can also be applied to the so-called inverse multivariate methods like partial least squares regression (PLSR), principal component regression (PCR) and ridge regression (RR).

1. Introduction

Selectivity is a central concept in analytical chemistry [1]. Without selective methods analytical measurement of individual components' concentrations in mixtures would not be possible. A general definition of selectivity and particularly its quantification are quite difficult [2,3]. However, if a measured signal depends linearly on the concentrations of some components in the sample (e.g., in absorption spectrophotometry), acceptable measures of selectivity can be obtained. There have been, indeed, two main trends for defining the selectivity of linear methods. In measurements on a single channel (e.g., on a single wavelength or with a single sensor) selectivity is commonly defined [3–5] as the ratio of analyte sensitivity to interferent sensitivity. In multichannel (multivariate) analysis other selectivity measures have been proposed [6–8], and the one introduced by Lorber [7] (to be explained later in this paper) appears to be the most accepted.

It will be shown in this paper that this widely accepted multichannel selectivity is not a simple extension of the single channel selectivity concept. The two selectivities reflect two different approaches of analytical chemists to solve the same problem, the determination of an analyte concentration in samples where interferents may be present. It will also be shown that a direct extension of the single channel approach to multichannel measurements is possible. This may result in better analytical results and easier methods and one can also define and measure selectivity in accordance with the single channel methods.

This paper is part of an effort to clarify the concept of analytical selectivity in systems both with linear and nonlinear responses and with one or more measurement channels [2,3,9].

Scalar quantities will be denoted in this paper by lowercase letters, vectors as lowercase bold face letters, matrices as uppercase letters. Row vectors and column vectors will not be differentiated as this will be clear from the context. Vector multiplication means always the scalar product. Vector norms (Euclidean) are denoted by double vertical lines.

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2. Definitions of analytical selectivity in linear methods

2.1. Single channel linear methods

In many analytical methods the measured signal(s) depend linearly on the analyte concentration and also on the concentrations of some interferents potentially present in the investigated samples. Such techniques are, for example, absorption spectrometries, where the Lambert–Beer law has wide validity:

$$A_\lambda = s_A c_A + s_B c_B + s_C c_C + \ldots + \varepsilon \quad (1)$$

Here A_λ is the measured absorbance signal at wavelength λ, the *c–s* are concentrations, the *s–s* are sensitivities (typically all non-negative, and this non-negativity will be assumed throughout this paper) and the lower case indices denote different compounds: A is the analyte, B, C, and possibly others are interferents; ε is the random error of the absorbance measurement (not the molar absorbance coefficient). Let us assume that the sensitivities s_A, s_B, etc., are known accurately and precisely from a preceding calibration and the linear model is also accurate. If the absorbance is measured on a single wavelength (or more generally a single measurement channel is used) then the concentration of the analyte, c_A, cannot be determined from the measured absorbance alone, because the interferent concentrations c_B, c_C, etc., are also unknown and only a single equation is available. But we may have additional information which limits the possible range of c_A. A natural constraint is that all concentrations are non-negative. In many linear methods also the sensitivities are non-negative (see above). These two conditions limit the possible range of c_A between the detection limit and A_λ/s_A (neglecting the random error at this upper limit). This range is still too wide and further information is needed to estimate c_A more sharply, i.e., with less error. Before we show how, let us calculate the relative error of c_A in a single channel measurement from Eq. (1). For simplicity we consider only one interferent, B.

$$\frac{A_\lambda/s_A - c_A}{c_A} = \frac{s_B c_B}{s_A c_A} + \frac{\varepsilon}{s_A c_A} \quad (2)$$

The first term on the right hand side is the interference effect or relative bias. The bias itself is $s_B c_B/s_A$. Both depend on the ratio of the respective sensitivities, but also on the concentration(s). The ratio of sensitivities is then a characteristic quantity. Its reciprocal, s_A/s_B, may be considered the selectivity measure of the method. The higher this selectivity measure is, the less interference (relative bias) will be observed at a given ratio of the concentrations. Since in analytical chemistry the (relative) error of the analyte concentration estimate is very important, this definition of selectivity makes sense. Indeed this is the traditional definition of single channel selectivity [4,5].

The selectivity, s_A/s_B, is the ratio of two sensitivities. As the sensitivities express signal changes per unit concentration change, their ratio shows the necessary change in c_B to bias c_A by one concentration unit. For the same reason *the reciprocal of the selectivity shows the (change of) bias in* c_A *caused by unit change in* c_B. This formulation will be extended later in this paper to multichannel methods.

Two things need to be noted here. First, the selectivity, s_A/s_B is used in the estimation of the bias, not the random error. This will be very important later in the discussion of multichannel selectivity. Second, s_A/s_B is not sufficient alone to estimate the relative bias. The concentration ratio, c_B/c_A is also needed. Although the individual concentrations c_A and c_B, respectively, are unknown, the analyst may have some information about their ratio. For example the analyst may know from experience with the samples at hand that the ratio c_B/c_A is less than 0.01 in all samples, i.e., $c_B/c_A < 0.01$. This inequality is a very useful constraint. For example if $s_A/s_B = 2$, then the bias in the determination of the analyte concentration is found from Eq. (2) to be less than $0.5 \times 0.01 = 0.005$, i.e. 0.5%.

Generalizing what has been said above, Eq. (1) is an underdetermined linear "equation system" consisting of a single equation with two unknown concentrations. To obtain a sufficiently close estimate of the analyte concentration, further information is needed about the concentration variables. Such information may be further equations, which are derived from additional measurements, like absorbance readings at multiple wavelengths. This is the case in multichannel measurements, where the goal may be to completely eliminate the bias due to interferents. This will be discussed later. But the analyst may not want to eliminate the effect of interferents completely, since she *needs only to keep the total uncertainty of* c_A *below certain, predetermined limit* [10]. Therefore she may be satisfied to know that the first term on the right hand side of Eq. (2) is below a certain limit. For a method with given selectivity this means she needs to make sure that the concentration ratio c_B/c_A is less than a certain limit. Mathematically this is a constraint on the two variables in the form of an inequality:

$$\frac{c_B}{c_A} \le u_{\lim} \quad (3)$$

where $u_{\lim}$ is an upper limit. The analyst may know from experience with earlier samples that this limit is never exceeded; she may even ascertain this in new samples by some semiquantitative tests. Alternatively it may be enough to know or to prove that c_B is less than a certain limit, if one knows simultaneously that c_A is higher than a certain minimum in every sample. Occasionally the analyst may not know these relationships a priori, but she may perform a sample pretreatment operation which leads to the required relation. It is also possible that a method developer includes in the description of the method that some concentrations, or concentration ratios, must not exceed a certain value for the method to be sufficiently accurate. Such considerations are very common in some areas of analytical chemistry, e.g., in ion selective electrode potentiometry. But less explicitly than in potentiometry, they are used in essentially all single channel analytical measurements, because analytical chemists do not bother with interferents which are extremely unlikely to be present in samples in appreciable concentrations compared to the analyte. Interferents with very low sensitivity values can also be mostly disregarded because the bias caused by them is well within the tolerance limits. This sort of neglecting minor interferences does not work in some *multichannel* measurement methods, where the mere assumption that an interferent may be present, can be the cause of very large analytical errors. One goal of this paper is to show how to avoid this situation.

2.2. Selectivity concepts for multichannel linear methods

Some decades ago it became feasible to make quickly and at low cost multichannel analytical measurements, e.g., in the form of full spectra or of sensor array readings. In many instances this had made possible to obtain fully determined or even overdetermined equation systems of the kind of Eq. (1). This means that, if the determinant of the equation system is not zero, and if the pure component spectra are all available, then all concentrations in the equation system can be determined *without bias* caused by other components in the equations. (Other sources of bias, like unmodeled interferents, imprecise calibration, unmodeled nonlinearities, etc. are not being considered here). Such measurements are therefore totally selective ("specific") for the analyte (and also for the interferents). It was therefore thought that the necessity for using selectivity, as a measure of bias caused by interferents, became superfluous with multichannel measurements. There were, however, other, new problems discovered, which were attributable to the interferences. Therefore