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Selectivity in analytical chemistry: Two interpretations for univariate methods

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ABSTRACT

Selectivity is extremely important in analytical chemistry but its definition is elusive despite continued efforts by professional organizations and individual scientists. This paper shows that the existing selectivity concepts for univariate analytical methods broadly fall in two classes: selectivity concepts based on measurement error and concepts based on response surfaces (the response surface being the 3D plot of the univariate signal as a function of analyte and interferent concentration, respectively). The strengths and weaknesses of the different definitions are analyzed and contradictions between them unveiled. The error based selectivity is very general and very safe but its application to a range of samples (as opposed to a single sample) requires the knowledge of some constraint about the possible sample compositions. The selectivity concepts based on the response surface are easily applied to linear response surfaces but may lead to difficulties and counterintuitive results when applied to nonlinear response surfaces. A particular advantage of this class of selectivity is that with linear response surfaces it can provide a concentration independent measure of selectivity. In contrast, the error based selectivity concept allows only yes/no type decision about selectivity.

1. Introduction

Selectivity is one of the most important features of any analytical measurement. Without selectivity, i.e., if the measuring system responded to every substance in exactly the same way both qualitatively and quantitatively, it would not be possible to determine the concentration of any particular substance in a mixture. It is therefore logical to expect that analytical chemists have a widely accepted definition of selectivity of analytical methods. One would also expect that selectivity can be quantitated in a meaningful way, so that one could compare methods or method variants according to their selectivities.

1.1. Lack of a general definition and of a measure of selectivity

Surprisingly, there is no generally accepted definition of selectivity in analytical chemistry, as shown by a recent review [1] and opinions diverge on its measurability. Some notable sources on the subject may be mentioned here. IUPAC has issued two recommendations and a technical report about the selectivity of general analytical methods [2–4]. It has also published selectivity definitions for particular methods, like potentiometry [5]. Guidelines for good laboratory practice require selectivity tests as part of method validation [6]. Metrological organizations define selectivity of measurements, including chemical ones [7,8]. Clinical chemists appear to avoid the term selectivity and discuss interferences instead [9]. Textbooks of analytical chemistry usually devote very little space to selectivity and either redefine it in an approximate fashion or cite an IUPAC definition as it has been shown in a review [1]. No two of the mentioned sources define selectivity in exactly the same way, and none of them quantitates selectivity (except for some special techniques, like potentiometry).

The common denominator of some of the more recent recommendations by the mentioned professional organizations is that they consider an analytical method selective only if interferences do not influence the measurement result at all or at least not significantly [1]. This is a very strict and therefore quite safe definition but it has some disadvantages. Analytical chemists often develop methods which need to work reliably with a large variety of samples. The question is then how one can prove that a method will be selective (in the above very strict sense) in any future samples to be investigated. Thus the recommendations shift the burden to the analytical chemist who should define the range of future samples which can be selectively analyzed with a particular method. Recommendations for solving this task have been

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published in clinical chemistry [9], where the possible range of samples is more or less known, but similar recommendations are unlikely to be available or even possible for many other analytical problems.

The other disadvantage of the above mentioned definitions of selectivity is that while they may be satisfactory to characterize a fully developed method, they do not provide any quantitative measure of selectivity, not even an approximate one, which could guide the analytical chemist during method development in assessing and improving selectivity.

1.2. Narrowing of the problem

Interferences to an analytical method can be of many different types. One may have sample matrix effects, analytical reagents may undergo side reactions with some sample components, etc. In a frequently encountered type of interference some components of the sample may influence the measured signal in the same way as the analyte. This is a typical problem with sensors, but spectral overlaps are of the same type, and in immunoassays we also have cross sensitivities. Even if we reduce the selectivity problem to such cases (as will be done in this paper), there is no general definition and measure of selectivity available. In individual analytical techniques, though, measures of selectivity have been defined for this type of interference. In absorption spectroscopy at a single wavelength, when the Lambert Beer law is valid for mixtures, the ratio of the respective molar absorbances of the analyte and the interferent, respectively, is an obvious measure of selectivity (see below). In ion selective electrode potentiometry selectivity coefficients have been widely used. Such selectivity concepts are typically based on the response characteristics of a technique or a device in mixed solutions of the analyte and the interferent(s).

This paper investigates if the common selectivity concepts used in analytical chemistry are meaningful, i.e. free of internal contradictions and mutually compatible. This work appears to be the first one to carry out such analysis. It is based among others on our experience with selectivity problems of ion selective electrodes [10–13], numerous method validations following guidelines for Good Laboratory Practice (GLP) [14,15] and investigations about the selectivity of molecularly imprinted polymers [16,17]. An impulse to this work has been given by important recent recognitions about the selectivity of ion selective electrodes [18–21] supported by a large body of experimental data. This study was also motivated by the work of M. Valcarcel and coworkers, who have also recognized the lack of general approaches to analytical selectivity and contributed to the clarification of the term selectivity [22].

2. Selectivity concepts and their properties in the univariate case

The problem discussed here is defined as follows. An analytical output quantity (a signal or an estimate of the analyte concentration, in either case a scalar quantity) is influenced by two components' concentration (Fig. 1). One of these components is considered the analyte, the other the interferent. It is assumed that the response to the analyte alone is a strictly monotonous function of the analyte concentration. The interferent is supposed to affect the measurement in a similar manner to the analyte. This means here that the interferent alone would also give a monotonous calibration line with the same direction as the analyte. For simplicity we shall assume that the calibration lines are both monotonously increasing. It is also assumed that the addition of any of the two components to any mixture of them will increase the output value. All these assumptions are satisfied by many analytical methods.

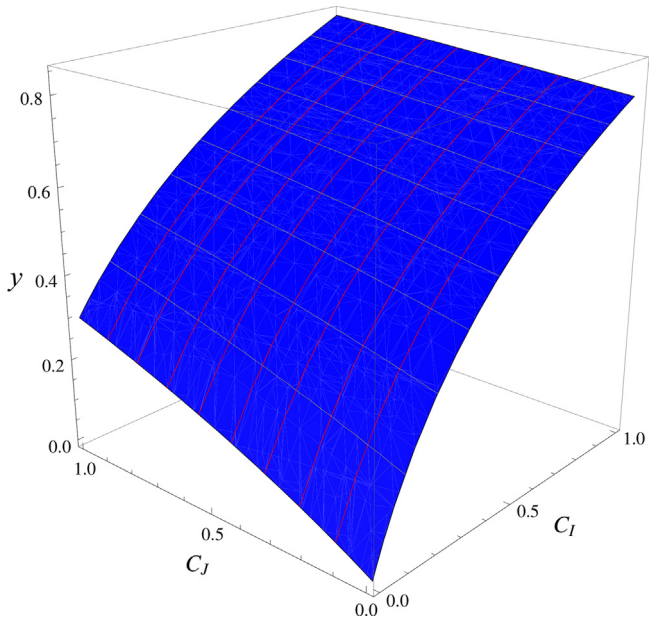

Fig. 1. A general response surface (y: measured signal, c_I: analyte concentration, c_J: interferent concentration).

The main ideas of the paper will be introduced by discussing first the simplest possible case, i.e., that of linear response in both concentration variables.

2.1. Linear response function

Let the measured signal, y, be a homogeneous linear function of the two concentrations, i.e.,

$$y = f(c_I, c_J) = k_I c_I + k_J c_J \tag{1}$$

here I denotes the analyte, J the interferent, c with a subscript stands for the respective concentration. The k-s are constants. (The equation might also include an additive constant. This would, however, not influence the final result.) The analyst wants to estimate the concentration of the analyte from the measured signal, y. Without having any further information, this is not possible, because there are two unknown concentrations but only one equation. As additional information the analyst may know, for example, that the ratio of interferent to analyte concentration is less than a certain value in all future samples. In another scenario the analyst may ascertain by a quick test or by sample preparation that the interferent concentration is less than a certain value. In either case a rational approach is to consider at first the total signal to be due to the analyte alone. By this procedure one obtains the highest possible value of the analyte concentration (because of the monotonicity criteria made above) which is in accordance with the measured signal value and the additional condition at the same time. This estimate of the analyte concentration may be in error, but as will be shown immediately, the maximum of this error may be estimated and compared with the required tolerance level.

The biased estimate, $\hat{c}_I$, of the analyte concentration is calculated, as proposed above, by dividing the signal, y, by k_I, which is the slope of the calibration line in pure I solutions:

$$\hat{c}_I = \frac{y}{k_I} = \frac{k_I c_I + k_J c_J}{k_I} = c_I + \frac{k_J}{k_I} c_J \tag{2}$$