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SELECTIVITY IN ANALYTICAL CHEMISTRY

(IUPAC Recommendations 2001)

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Abstract: The correct use of the term "selectivity" and its clear distinction from the term "specificity" are discussed. A definition of selectivity is given, and it is recommended that the use of this term be promoted and that the use of the term "specificity" be discouraged.

1. INTRODUCTION

A very important quality criterion of an analytical method is its capability to deliver signals that are free from interferences and give "true results". The ability to discriminate between the analyte and interfering components has, for many years, been expressed as the "selectivity" of a method and measurement system. One clear definition is the following: "*Selectivity* of a method refers to the extent to which it can determine particular analyte(s) in a complex mixture without interference from other components in the mixture" [1]. However, the same meaning has often been given to the term "specificity" [2]. Following earlier concern about the use of these terms [3] IUPAC clarified this overlap by expressing the view that "*Specificity* is the ultimate of *Selectivity*" [4]. The *Compendium of Analytical Nomenclature, Definitive Rules 1997*, only mentions these important terms under "related papers" in Chapters 2 and 18 [5]. As there is still a tendency to mix up these two terms, a discussion clarifying the rationale behind the need to differentiate the use of the terms is given below, followed by particular recommendations.

2. DISCUSSION

Evolution of the terminology

The use of the term "selectivity" in analytical chemistry has evolved in parallel with the development of more sensitive and discriminating methods that have a capability to identify and quantify analytes with less interference from other components, similar or dissimilar, than earlier methods were able to do. Modern methods are usually designed by combining several measurement principles introducing their own selectivity to the overall operation. In this way, very highly selective methods can be obtained.

Useful interactions

In analytical methods, several kinds of interactions can be utilized in discrimination processes. They can be based on, for example, chemical reactions, associate formation, adsorption to surfaces, inclusion phenomena, absorption of radiation, and biochemical (immunochemical or enzymatic) or electrochemical (redox) principles. In order to cope with overlap in responses to the useful interactions, modern methods usually rely on several selectivity generating steps (stages) to reduce the effects of interfering interactions.

Selectivities in methods

In current analytical chemistry, selectivities based on multistage separation and detection principles are frequently used. Other useful selectivity tools include prior reaction, extraction and distribution, mobility, or permeability differences. In all these cases, the analytical tools are chosen in relation to the analytes in such a selective way that the tools give preference for the target analyte to be appropriately ana-

lyzed, either quantitatively or qualitatively (screened). Methods for determining metals are often based on selectivity from the detection system, also called detection selectivity (e.g., atomic emission spectrometry). Techniques such as chromatography, electrophoresis, and membrane separations for all types of species tend to rely on selectivity in a separation process, often called separation selectivity. Hyphenated techniques like liquid chromatography–mass spectrometry (LC–MS), in which selectivities are combined with respect to separation and detection, can be applied when the demands for selectivity are especially high. The addition of tandem mass spectrometry as in liquid chromatography–mass spectrometry-mass spectrometry (LC–MS–MS) yields a selectivity that is rarely compromised and is often required in legal situations when positive and nonbiased identification is needed.

In recent years, combinations of sensors of different kinds and degrees of selectivity have been used in arrays. The responses are based on interactions usually evaluated in a mathematical domain (chemometrics), giving what has been called "computational selectivity" [6]. In fact, selectivity is improved by a higher number of measurements (e.g., by use of a whole spectrum over a wavelength range instead of single wavelengths and processing the spectral data by chemometric methods). The handling of near-infrared spectra in this way is a very good example of the approach [7]. Single sensors with different kinds of incorporated selectivities have also been described, where the multimode selectivity character of the sensor (e.g., a spectroelectrochemical detector using charge positioning, electrolysis potential, and spectral wavelength) was developed in order to minimize the interferences [8].

Semantic aspects

From a semantic point of view, selectivity has its origin in *seligo*, which is Latin for "to choose" or "to select" [9]. Thus, selective can mean "tending to choose carefully" [10] and selectivity "the state or quality of being selective" [11]. From these definitions, a useful concept can be found in a combination of the two terms into one expression, "Selectivity is the state or quality of choosing carefully", which fits very well the principles by which modern analytical methods are constructed.

Expressing selectivity

In the current analytical chemical literature, selectivity is very often expressed in combination with words such as adjustment [12], tuning [13], optimization [14], predetermined [15], enhancement [16,17], and coefficients [18,19], as well as selective enrichment [20,21]. The use of these expressions indicates that selectivity is regarded as something that can be graded. Analytical methods have thus been described as having good selectivity, or even high, excellent, or extreme selectivity, although Betteridge recommended that such simple qualitative terms should not be used. He put forward the idea of a "selectivity index" [22], which defined numbers of cross-reactions for descriptors α, β,γ … [22], which correspond approximately to the previous qualitative terms. Defects in the scheme were discussed later by Wilson [23], and clarification and improvements were suggested by Belcher [24] and by Inczedy [25]. Later, den Boef and Hulanicki [4] were unable to reach clear conclusions on the value of the selectivity index. Typical examples of interference, cross-reactivity, or codetermination may be found for ion-selective electrodes, ion-exchange equilibria, immunological tests, spectral overlap in spectrometry, and partly resolved peaks in the separations. In a recent textbook, it has been stated that "Selectivity gives an indication of how strongly the result is affected by other components in the sample. In various methods different factors are used to assess this selectivity in a quantitative way" [26].

Calculations of degree of selectivity

Some attempts have been made in the literature to quantify selectivity (and even specificity). One of the first such treatments was that by Kaiser [27]. Later, Massart *et al*. discussed both qualitative and quantitative aspects of selectivity and specificity [28]. The latter approach involves quantification of a sen-

sitivity factor matrix, ***K***, involving n sensor responses for m components. The procedure is very demanding and requires considerable effort to arrive at conditions useful, to practicing analytical chemists, for a given complex sample. Simplifications have been considered, as well as the development of mathematical expressions for selectivity and specificity [28]. At the same time as Massart *et al*., Otto and Wegscheider compared different procedures to obtain figures of merit for the judgement of the selectivity of methods for multicomponent analysis [29]. Lorber *et al*. have used the concept of net analyte signal and selectivity defined in terms of loss of signal due to spectral overlap in multivariate calibrations with some degree of success [30,31]. A new but simpler approach to calculate and express the degree of interferences in terms of selectivity is under development [32].

3. SELECTIVITY OR SPECIFICITY

In many papers, the terms "selectivity" or "specificity" are used interchangeably. This is very unfortunate as specificity is considered as an absolute term, and thus cannot be graded. This situation clearly creates unnecessary confusion and authors can best avoid this confusion by giving preference for the use of selectivity. For chemical reactions, the remark, "A specific reaction or test is one that occurs only with the substance of interest, while a selective reaction or test is one that can occur with other substances but exhibits a degree of preference for the substance of interest. Few reactions are specific, but many exhibit selectivity" clearly expresses one author's view on the situation [33]. The phrase "exhibits a degree of preference" is consistent with the concept that selectivity is something that can be graded or, as expressed above, "referred to the extent to which a method can determine without interferences " [1]. The IUPAC statement that specificity is the ultimate of selectivity is also in line with the above concept [4]. The desire to avoid the term specificity has been expressed as "Sometimes the term specificity is used. This suggests that no component other than the analyte contributes to the result. Hardly any method is that specific (sic!) and, in general, the term should be avoided" [26]. Avoidance of the term "specificity" is, from many aspects, the simplest way to settle the problem of mixing up one definition with the other. In papers recently published in prestigious analytical chemical journals, the use of the term "selectivity" dominates, but the use of the term "specificity" has yet not been eliminated. The IUPAC recommendation herein ought to be mentioned in the "Notice for authors" in all analytical journals. At present, it is not mentioned anywhere that "selectivity" is the preferred term to use.

4. OTHER IUPAC RECOMMENDATIONS

A number of other IUPAC recommendations with regard to the use of the terms "selective", "selectivity", "specific", and "specificity" are given in the *Compendium of Chemical Terminology* [34], in addition to the clarification as to the use of selective and specific in analysis, for example, stereoselectivity, enantioselectivity, shape selectivity, chemoselectivity, and ion-selective electrodes. For some of these terms (e.g., regioselective, chemoselective, and ion-selective electrodes), use of the corresponding terms involving specificity and specific is discouraged. Selectivity (in analysis) is mentioned, but not specificity. Finally, the term "specific" (in analysis) is considered as the ultimate of selectivity. The term "specific" can of course be used without confusion to denote a physical quantity obtained after division of a measurement by mass, e.g., specific volume.

5. RECOMMENDATIONS

- *That the term "selectivity" should be promoted.* "Selectivity" is the recommended term in analytical chemistry to express the extent to which a particular method can be used to determine analytes under given conditions in the presence of other components of similar behavior. Selectivity can be graded. To avoid confusion, the use of the term "specificity" for the same concept is to be discouraged, as it is incorrect. A method is either specific or it is not. Few, if any, methods are specific.

- *Definition of selectivity.* Selectivity refers to the extent to which the method can be used to determine particular analytes in mixtures or matrices without interferences from other components of similar behavior.

6. PROBLEMS STILL TO BE SOLVED

The discussion and definition above cover most of the problems concerning selectivity facing chemists today. It might be considered that too much emphasis has been given to small molecules. In principle, however, the same terminology should be able to be applied to all analytical fields. The meaning of selectivity to procedures that determine single atoms or single molecules needs to be addressed, as does the meaning of selectivity in amplification reactions, such as the polymerase chain reaction (PCR), which are increasingly used. Selectivity for different conformers of molecules, small or (particularly) macromolecules, have to be considered. These questions will be dealt with in a future project, as well as practical ways of calculating or quantifying selectivity.

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