INTERNATIONAL UNION OF PURE
AND APPLIED CHEMISTRY

ANALYTICAL CHEMISTRY DIVISION
COMMISSION ON GENERAL ASPECTS OF ANALYTICAL CHEMISTRY[ζ]

SELECTIVITY IN ANALYTICAL CHEMISTRY

RECOMMENDATIONS FOR ITS USE.

(IUPAC Recommendations 2000)

Prepared for publication by

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Abstract

The correct use of the term selectivity and its clear distinction from the term specificity is discussed. Recommendations are made with regard to (a) the definition of selectivity and (b) that the use of the term selectivity be promoted.

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 capacity to identify and quantify analytes with less interference from other components, similar or dissimilar,than the earlier methods were able to do. The modern methods are usually designed in such a way that different kinds of selectivities are combined in order to end up with a signal or response that does not exhibit significant ambiguities due to overlap in response(s) from other analytes.

Useful interactions. Analytical methods can utilise several kinds of interactions in discrimination processes. They can be based on e.g. chemical reactions, associate formation, adsorption to surfaces, inclusion phenomena, absorption of radiation, 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 analysed, 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 techniques for all types of species tend to rely on selectivity in a separation process, also called separation selectivity. Hyphenated techniques, like LC-MS, which combine selectivities with respect to detection and separation can be applied when the demands for selectivity are especially high. The addition of tandem mass spectrometry as in LC-MS-MS yields a selectivity that is rarely compromised and is often required in legal situations when positive and non-biased 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 that way is a very good example of this 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 minimise 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 a useful concept can be found in a combination of the two terms into one expression,” *Selectivity is the state 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), optimisation (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 … , which correspond approximately to the previous qualitative terms. Defects in the scheme were discussed later by Wilson (23) and clarification and improvements 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 in the separations, expressed as separation factors or resolutions . A recent textbook has stated ”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. There are some attempts in the literature, where the degree of selectivity or even specificity has been given a quantitative treatment. 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 sensitivity factor matrix, K, involving *n* sensor responses for *m* components. The procedure is very demanding and it requires considerable effort to arrive at conditions useful to practising 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).A new but simpler approach to calculate and express the degree of interferences in terms of selectivity is under development (30).

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 can not be graded. This situation clearly creates unnecessary confusions and can best be avoided by authors 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 authors´ view on the situation (31). 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 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 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** (32) 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 are 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 by mass e.g. specific volume.

5. Recommendation

1) *That the term Selectivity be promoted.* Selectivity is the recommended term in analytical chemistry to express the extent to which a particular method can determine analytes under given conditions in the presence of interferences from other components in the matrix. Selectivity can be graded. To avoid confusion the use of the term specificity for the same concept is to be discouraged.

2) *Definition of Selectivity.* Selectivity of a method refers to the extent to which it can determine particular analytes under given conditions in mixtures or matrices, simple or complex, without interferences from other components .

6. Problems yet to be settled

The discussion and definition above cover most of the problems concerning *selectivity* facing chemists today. There might be considered to be too much emphasis on small molecules, however, in principle, the same terminology has to be applied all over the analytical field. Procedures are now being put forward for atom or single molecule determination. What does this mean with respect to selectivity? A discussion is needed on how to evaluate and express selectivity in connection with amplification reactions, such as 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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