Comparison of Minimum Detectable Concentration with the IUPAC Detection Limit

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Detection capability is an important performance characteristic of a measurement process. It is characterized by ISO as minimum detectable value. Another characteristic, used in chemical measurements, was defined by IUPAC as the limit of detection. These and further closely related characteristics are compared and theoretically analysed. Directions for their use are given and exemplified using chemical trace analysis of lead.

Keywords: minimum detectable value, minimum detectable concentration, limit of detection, critical value, decision limit, limit of identification, limit of quantification.

1. INTRODUCTION

CHEMICAL MEASUREMENTS may involve material containing very small amounts of the component of interest. With regard of measurement uncertainty it is often difficult to distinguish such small amounts from zero. Therefore an important performance characteristic of a measurement process is its *detection capability*, which is usually expressed as the smallest concentration of analyte, represented by the analysed component of the sample that can be reliably distinguished from zero. The decision whether the analyte is or is not present in the laboratory sample is based on the measurement data. The detection decision is provided by a choice between two opposing statistical hypotheses about the sample. The null hypothesis H_0 states: "The sample is analyte-free". The alternative hypothesis H_1 states: "The sample is not analyte-free", which is consistent with the statement: "The sample contains a positive amount of the analyte".

Two possible types of decision errors exist in any hypothesis test: (1) the Type I error, with probability α, which occurs if the null hypothesis is rejected when it is true, called „false positive", or „false rejection", and (2) the Type II error, with probability β, called „false negative", or „false acceptance", if the null hypothesis is not rejected even when it is false. In any given situation, only one of the mentioned types of decision error is possible. If the sample does not contain the analyte, a Type I error is possible. If the sample does contain the analyte, a Type II error is possible.

A performance characteristic of any measurement process, characterizing the capability of detection, was defined by ISO 11843 [1,2] as *minimum detectable value* (MDV), sometimes called also *minimum detectable concentration* (MDC). According to ISO 11843, the concentration of analyte in the laboratory sample is the *state variable*, Z, since it represents the state of the material being analyzed. Analyte-free material is considered to be in the basic state. The difference between the state variable, Z, and its value in the basic state is called the *net state variable*, denoted by X. The state variable or the net state variable cannot be observed directly, but they are related to an observable *response variable*, Y, via a *calibration function F*, defined by the mathematical relationship $Y = F(Z)$ or $Y = F(X)$, representing the mathematical model of the measurement. In chemical measurements, the response variable Y is usually an instrument signal. The evaluation function, which is the inverse, F^{-1}, of the calibration function, gives directly the investigated analyte concentration.

Another measurement characteristic, which is frequently used in chemical measurements as a measure of detection capability, is the *limit of detection*, LOD, defined by the International Union of Pure and Applied Chemistry (IUPAC) in several recommended documents [3-5]. Even though the ISO and IUPAC working group members collaborated during the development of the respective guidelines, substantial differences between the final documents remain. The objective of this paper is therefore comparison of the ISO *minimum detectable value* with the *limit of detection* defined by IUPAC.

2. SUBJECT & METHODS

Trace analysis of lead was performed by differential pulse anodic stripping voltammetry (DPASV) using a standard three-electrode voltammetric cell with the static mercury drop electrode, a reference 3 mol/L silver-silver chloride electrode, and a platinum wire auxiliary electrode. The following parameters were set for the lead(II) determination: deposition potential ⁻1 V, equilibration time 10 s, interval time 0.1 s, initial potential ⁻0.8 V, end potential ⁻0.2 V, step potential ⁻0.002 V, modulation time 0.04 s, modulation amplitude ⁻0.05 V, experimental temperature 25 ± 0.5 °C. The data were measured by Autolab/PGSTAT 20 Electrochemical Instrument and saved into the memory of a computer, coupled to the instrument [6].

3. RESULTS

The procedures for the computation of the MDV, LOD and further related characteristics are based on the following basic assumptions: (a) the calibration function is linear, (b) measurements of the response variable are independent and

normally distributed with the standard deviation referred to as the residual standard deviation, $\hat{\sigma}$, (c) the residual standard deviation is constant, i.e. it does not depend on the state variable.

Minimum detectable value and critical value

The minimum detectable value obtained from a particular calibration is the smallest value of the net state variable which can be detected with a probability of $1-\beta$ as different from zero. The linear calibration model is given by

$$Y_{ij} = a + bx_i + \varepsilon_{ij} \quad i=1,2,\ldots,I; \quad j=1,2,\ldots,J \qquad (1)$$

where

Y_{ij}	response variable for the state i and preparation j
x_i	net state variable in the state i
ε_{ij}	random component of the sampling,

preparation and measurement errors

The *critical value*, x_C, and the *minimum detectable value*, x_D, of the net state variable are defined [7,8] by the equations

$$x_C = \frac{y_C - \hat{a}}{\hat{b}} = t_{1-\alpha}(v)\frac{\hat{\sigma}}{\hat{b}}\sqrt{1 + \frac{1}{IJ} + \frac{\overline{x}^2}{s_{xx}}} \qquad (2)$$

$$x_D = \delta(v, \alpha, \beta)\frac{\hat{\sigma}}{\hat{b}}\sqrt{1 + \frac{1}{IJ} + \frac{\overline{x}^2}{s_{xx}}} \qquad (3)$$

where

$t_{1-\alpha}(v)$	$(1-\alpha)$ % quantile of the t- distribution with $v = (IJ - 2)$ degrees of freedom
δ	non-centrality parameter of the non-central t-distribution
$\hat{\sigma}$	estimated residual standard deviation of the regression analysis of model (1)

$$S_{xx} = J \sum_{i=1}^{I}(x_i - \overline{x})^2$$

Limit of detection and limit of identification

In chemical measurements, the *limit of detection*, LOD, is the smallest concentration (or the mass) of the analyte, x_D, that can be detected with a specified degree of certainty. Its old traditional definition, given by IUPAC in the seventies of the 20th century, is based on the mean, μ_b, and the population standard deviation of the blank, σ_b, which represents an analyte-free sample. In practice, its value y_D in the signal domain has been commonly approximated by the arithmetic mean of the blank $\overline{y}_b$ plus the k_D - multiple of the blank standard deviation $\hat{\sigma}_b$ (denoted as s_b in chemical literature). In the common case when $k_D = 3$, the LOD in the signal domain is $y_D = \overline{y}_b + 3s_b$. Factor $k_I = 6$ is recommended for the *limit of identification*, LOI. Then the LOD and LOI in the concentration domain are defined by $LOD = (y_D - \hat{a})/\hat{b}$ and $LOI = (y_I - \hat{a})/\hat{b}$, respectively. However, according to some authors the first limit is called the *critical level* and only the second limit is called the limit of detection.

Statistically much more correct is the approach using the *one-sided upper confidence limit* of the calibration line [5], according to which the LOD in the concentration domain is defined by

$$LOD = [t_{1-\alpha}(v)\,\hat{\sigma}/\hat{b}\,][1 + 1/N + \overline{\overline{x}}^2/\sum_{n=1}^{N}(x_n - \overline{x})^2]^{1/2}$$

where $N = IJ$ (I – the number of standard solutions, J – the number of parallel measurements).

The LOI is defined in the same way except the additional factor of two; $LOI = 2\,LOD$ [5].

Comparison of the minimum detectable value with the limit of detection

Comparison of the ISO measurement characteristics, the critical level, x_C, and the minimum detectable value, x_D, with the IUPAC recommended characteristics LOD and LOI for the electrochemical trace analysis of lead is summarized in Tab.1.

Tab.1...Determination of lead by DPSAV – comparison of the critical value and the minimum detectable value with the limit of detection and the limit of identification.

I	8	v	30	I	8	v	6
J	4	$t(v, 0.01)$	2.4573	J	1	$t(v, 0.01)$	3.1427
N	32	$\delta(v, 0.01, 0.01)$	4.8793	N	8	$\delta(v, 0.01, 0.01)$	6.2127
$\hat{a}$	20.86	x_C	0.2495	$\hat{a}$	20.86	x_C	0.2445
$\hat{b}$	7.449	x_D	0.4955	$\hat{b}$	7.449	x_D	0.4833
$\hat{\sigma}$	0.7199	LOD	0.2495	$\hat{\sigma}$	0.4868	LOD	0.2445
		LOI	0.4991			LOI	0.4889

Note: The estimate of the blank standard deviation $s_b = 0.01639$, therefore the LOD and LOI defined by the traditional $3s_b$ and $6s_b$ approach are: $LOD(3s_b) = 0.2439$, $LOI(6s_b) = 0.4878$.

4. DISCUSSION / CONCLUSIONS

According to the results summarized in Table 1, the LOD, utilized mostly in chemical literature, is identical to the ISO critical level, x_C, and the LOI is considerably similar to the minimum detectable value, x_D. The latter similarity is due to the close values of the non-centrality parameter

$\delta(v, \alpha, \beta)$ and the doubled t- critical value $2\,t_{1-\alpha}(v)$. It is valid not only for the larger number of degrees of freedom in the left part of Table 1 (first four columns) but also for smaller v in its right part (last four columns) where four individual measurements for each state i are substituted by their means and $J = 1$ is used instead of $J = 4$. The values of x_C, x_D, LOD and LOI were found comparable in both cases despite higher values of $\delta(v, 0.01, 0.01)$ and higher critical t-values for the case with $v = 6$, due to smaller standard deviation $\hat{\sigma}$. The selection of $\alpha = 0.01$ and $\beta = 0.01$ was influenced by the IUPAC recommendation [5] where this is considered as the best choice. However, the mentioned conclusions were proved valid also for the selection $\alpha = \beta = 0.05$.

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