ACS SENSORS

pubs.acs.org/acssensors

Editorial

I'm Sensitive about Sensitivity

Cite This: *ACS Sens.* 2022, 7, 1235−1236

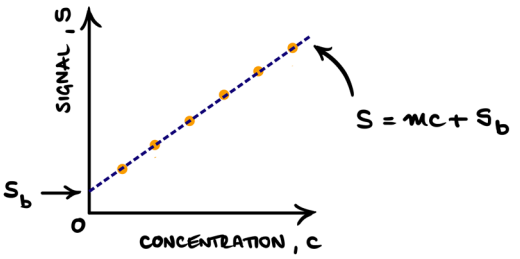
Read Online

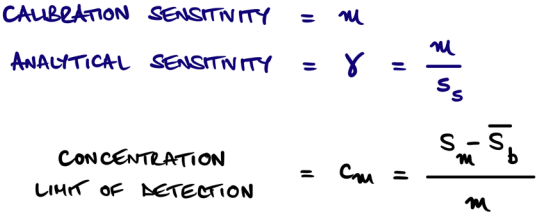
ACCESS | Metrics & More | Article Recommendations

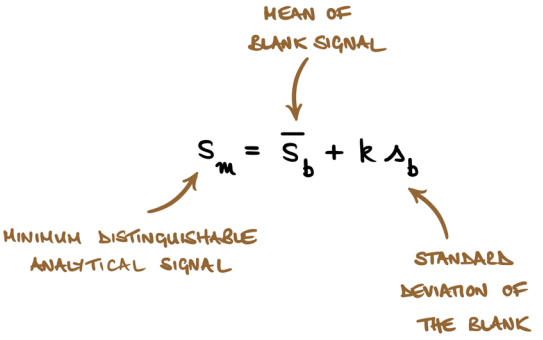
One of the perks of being an Associate Editor for *ACS Sensors* is the chance to talk to the community through editorials. Often these highlight current trends or future opportunities for the field, but sometimes they provide an editor with a chance to grumble (many apologies, Justin). This month, I'd like to spend a couple of minutes talking about the use of the terms "sensitivity" and "limit of detection" in sensor science.

I do not think it would be a great surprise to find out that almost all articles published in our journal contain both figures of merit, often on numerous occasions. We include and attempt to quantify them because they are important and often provide us with valuable information about our sensor or analytical method. What may be more surprising is that, despite having very different definitions, they are regularly used in an interchangeable fashion, with little regard for their true meanings. As an Associate Editor, I can confirm that this happens far more often than you might think! "*So what*?" you might say, "*does it make that much difference*?" I would argue that it often does. Not least because they are different quantities, but also because there are multiple definitions for each figure of merit and differences of opinion with regard to which definitions are correct.

Since my aim is not to provide an in-depth analysis, let me make some simple definitions that are widely accepted from a chemical standpoint. But before I begin, please note that our discussion of sensitivity should not be confused with the use of the term when characterizing diagnostic tests, in which sensitivity refers to the probability that a test will yield a positive result if the tested individual does have the disease. Most analytical chemists would agree that the sensitivity of an analytical method or instrument in some way quantifies its ability to discriminate between small differences in the concentration (or mass) of a target analyte (Note: This quantity will have units of "signal units per unit concentration" or "signal units per unit mass". For the purposes of my discussion, I will consider only concentrations going forward). The simplest definition of "calibration sensitivity", and the one recognized by IUPAC, is the slope of the calibration curve at the concentration of interest (m in my sketch).[1,2] Since the calibration curve will only be linear over some range of concentrations, calibration sensitivity must always be accompanied by a statement of this range; it is meaningless if the range is omitted. Such a figure of merit is simple to calculate, but does ignore measurement precision. Accordingly, Mendel and Stiehler introduced the concept of "analytical sensitivity", which accounts for both the gradient of the calibration curve and analytical precision, and is defined as the calibration sensitivity divided by the standard deviation of the analytical signal measurement (s_s).[3]







The limit of detection is in some ways easier to define, but in others a more complex beast. As a starting point, the limit of detection can be broadly defined as the smallest concentration that can be detected with a defined level of confidence.[4] This is of course rather vague, but tells us that random experimental errors are unavoidable and that the limit of detection will

Received: May 5, 2022
Published: May 27, 2022

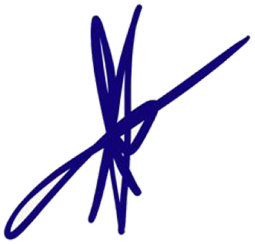
https://doi.org/10.1021/acssensors.2c00982
ACS Sens. 2022, 7, 1235−1236

depend on the ratio of the signal to the magnitude of statistical fluctuations in the blank signal. As shown in the sketch, the limit of detection (c_m) should be quantified by determining the minimum distinguishable analytical signal through multiple (typically 20−30) blank measurements and substitution of this value into the equation describing the calibration curve. Although there has been much discussion regarding the choice of the multiple, k, a value of 3 is widely accepted by most (including IUPAC and the ACS) as being ideal.[4−6] It should also be remembered that other related figures of merit, such as limit of blank (LoB) and limit of quantitation (LoQ), can be used to assess the minimum concentrations that can be reliably measured using an analytical procedure under given conditions.[7]

What should be clear from this fleeting analysis is that, as defined, both figures of merit are quite different in their meaning and often reported in an inconsistent manner. This can lead to uncertainty when sensitivity or limit of detection values are used to compare different analytical procedures, sensors, and instruments. Put simply, any declaration of analytical sensitivity must be accompanied by a statement of the concentration (or concentration range) at which the sensitivity has been calculated, and quoted limits of detection must explicitly state the multiple, k. In addition to this being the correct thing to do, such an approach is the only way to ensure that different assays and methods can be compared in a consistent, fair, and meaningful manner. On the flipside, perhaps I should not be overly surprised about this lack of consistency. Despite the fact that our journal is part of a chemistry publishing house, our authors and contributors come from varied backgrounds, ranging from molecular biology to civil engineering to geology. Accordingly, the language and reporting of scientific ideas will naturally vary between individuals. That said, a clear definition of what is meant by terms such a sensitivity is always sensible and prevents confusion.

Finally, while the limit of detection and analytical sensitivity are useful figures of merit, they are not the be-all and end-all when assessing sensor performance. In this regard, it should not be forgotten that clinical decision levels for a range of biomarkers and species, such as glucose, albumin, creatinine, and cholesterol, are of 10 orders of magnitude higher than the limit of detection of most diagnostic tests. In such a situation, the limit of detection is a rather unimportant figure of merit. Indeed, while advances and progress in sensor and assay technologies are most commonly measured by shifts to lower and lower limits of detection, other factors, such as cost, time-to-result, simplicity, and shelf lifetime will be far more important factors in determining whether a test is fit for purpose.

So, my request is simple. When using sensitivity and limit of detection to characterize a sensor or analytical method, think about what these values are telling you and report them in a consistent and complete manner. This allows for meaningful comparisons between existing sensors and tests and makes an editor's job much, much easier.



Andrew J. deMello, Associate Editor, *ACS Sensors*

AUTHOR INFORMATION

Complete contact information is available at:
https://pubs.acs.org/10.1021/acssensors.2c00982

Notes

Views expressed in this editorial are those of the author and not necessarily the views of the ACS.

REFERENCES

(1) Ingle, J. D. Sensitivity and Limit of Detection in Quantitative Spectrometric Methods. *J. Chem. Educ.* **1974**, *51*, 100.
(2) Currie, L. A. Nomenclature in evaluation of analytical methods including detection and quantification capabilities (IUPAC Recommendations 1995). *Pure Appl. Chem.* **1995**, *67*, 1699.
(3) Mandel, J.; Stiehler, R. D. Sensitivity-A Criterion for the Comparison of Methods of Test. *Journal of Research of the National Bureau of Standards* **1954**, *53*, 155.
(4) Long, G. L.; Winefordner, J. D. Limit of detection. A closer look at the IUPAC definition. *Anal. Chem.* **1983**, *55*, 712A.
(5) Kaiser, H. Quantitation in Elemental Analysis. *Anal. Chem.* **1970**, *42*, 26A.
(6) Kaiser, H. Report for analytical chemists. II. Quantitation in elemental analy. *Anal. Chem.* **1970**, *42*, 26A.
(7) Armbruster, D. A.; Pry, T. Limit of Blank, Limit of Detection and Limit of Quantitation. *Clinical Biochemist Reviews* **2008**, *29*, S49.

https://doi.org/10.1021/acssensors.2c00982
ACS Sens. 2022, 7, 1235−1236