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POINT OF VIEW

The Case of the Limit of Detection

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Students learn early on in science courses that reliable results can only be achieved from accurate measurements. In some of the first general chemistry classes, but even more intensively in analytical chemistry classes, students are introduced to the concept of significant figures.[1] They learn that a measurement is only as true and precise as the instrument used to carry it out, and that the level of skill of the measurer (and how they interpret and report the measurement) is also important. A classic example to introduce significant figures involves the measurement of an object's length using a ruler. Let us say that the object is a string, and one has two rulers available to measure it. The first ruler has 1-cm markings, while the second one presents 0.1-cm markings. When performing any measurement, students learn that more accurate results will be achieved if one estimates and includes an additional digit to the measurement. Thus, as an example, let us say that the string's length is determined to be between 3 and 4 cm using the first ruler. The measurer will then estimate the tenths decimal place and report the string's length as 3.4 cm, for example. Although considered significant, the tenths place (*i.e.*, 4) is an estimate and, therefore, it is uncertain. The other digit (*i.e.*, 3) is both significant and certain. Using the second ruler, the string's length falls between 3.4 and 3.5 cm. The measurer will again estimate an additional decimal place and report the length as 3.48 cm. In this example, the digits 3 and 4 are both significant and certain, while the hundredths place (*i.e.*, 8) is significant but uncertain.

Now, how does the concept of significant figures relate to limit of detection (LOD)?

There are different interpretations for LOD,[2-5] but it simply is the lowest concentration of analyte generating an instrument response that is statistically different from (and higher than) that recorded for the blank. According to the International Union of Pure and Applied Chemistry (IUPAC), the LOD is calculated as three times the standard deviation of the instrument response for the blank (S_b), divided by the calibration curve slope (m), *i.e.*, LOD = $3S_b/m$. The value S_b is calculated from repeated measurements of the blank solution, usually 10 - 20 replicates (n = 10 - 20). Considering a normal distribution, 99.86% of the data is < $(\bar{x} + 3S)$ (*i.e.*, < than the value corresponding to three standard deviations above the mean). Therefore, the LOD calculated at $3S_b$ is statistically different from, and has a 99.86% chance of being larger than the blank.[4]

At the LOD, the instrument response recorded for the analyte is certainly not due to the random variation of the blank signal (almost 100% certain). However, there is no certainty associated with the analyte concentration. In other words, one knows the analyte is present, but cannot quantify it with an adequate level of confidence. Considering S_b as noise, the analyte's signal-to-noise ratio (S/N) at the LOD is 3 (*i.e.*, the instrument response recorded for the analyte is three times higher than the noise). Because S/N is the reciprocal of the relative standard deviation (RSD), analyte signal variations higher than 33% (RSD = 1/3) are expected at the LOD. Therefore, the concentration corresponding to the LOD is, by definition, uncertain. Going back to the concept of significant figures, the LOD must be reported with a single digit, which is significant but uncertain.

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Many researchers fail to follow these fundamental concepts of statistics and analytical chemistry, as LODs are often reported with several significant figures (!). Perhaps, it is due to a natural difficulty to connect concepts learned at different points in one's education. Nevertheless, "the case of the LOD" may foster an awareness that could facilitate the identification of instances in which the connection between different concepts is essential: from adequate reporting of analytical results to new ideas and discoveries.

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