

Limits for Qualitative Detection and Quantitative Determination

Application to Radiochemistry

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The occurrence in the literature of numerous, inconsistent and limited definitions of a detection limit has led to a re-examination of the questions of signal detection and signal extraction in analytical chemistry and nuclear chemistry. Three limiting levels have been defined: L_C —the net signal level (instrument response) above which an observed signal may be reliably recognized as “detected”; L_D —the “true” net signal level which may be *a priori* expected to lead to detection; and L_Q —the level at which the measurement precision will be satisfactory for quantitative determination. Exact defining equations as well as series of working formulae are presented both for the general analytical case and for radioactivity. The latter, assumed to be governed by the Poisson distribution, is treated in such a manner that accurate limits may be derived for both short- and long-lived radionuclides either in the presence or absence of interference. The principles are illustrated by simple examples of spectrophotometry and radioactivity, and by a more complicated example of activation analysis in which a choice must be made between alternative nuclear reactions.

IN THE COURSE of research dealing with photonuclear reactions and activation analysis, it became necessary to determine limits of detection of radiochemical procedures, to select among alternative procedures, and to optimize given procedures with respect to certain experimental parameters. Examination of the analytical and radiochemical literature for an appropriate definition of the limit of detection revealed a plethora of mathematical expressions and widely-ranging terminology. One encounters, for example, terms such as lower limit of detection (1), detection sensitivity (2), sensitivity (3), minimum detectable activity (or mass) (4, 5), and limit of guarantee for purity (6)—all used with approximately equivalent meanings. The nomenclature problem is compounded, however, because other authors make use of the same, or very similar, terms to refer not to the minimum amount that may be *detected*, but rather, to the minimum amount which may be *determined* with a given relative standard deviation (such as 10%). Still other expressions, such as the “detection limit at the 95% confidence level” are used without explicit mathematical definition, which leaves the meaning rather ambiguous. The various mathematical definitions of detection limit (or its equivalent) range from one to twenty times the standard deviation of the net signal, with the standard deviation of the blank sometimes replacing

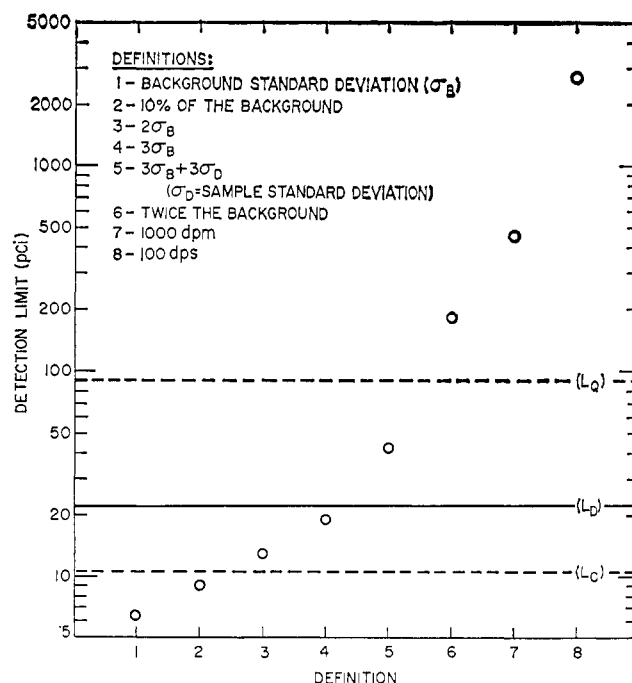


Figure 1. “Ordered” detection limits—literature definitions

The detection limit for a specific radioactivity measurement process is plotted in increasing order, according to commonly-used alternative definitions. L_C , L_D , and L_Q are the critical level, detection limit, and determination limit as derived in the text

that of the net signal. Some authors apply two-sided confidence intervals, while others use one-sided intervals. In addition, various “nonstatistical” definitions appear in which the detection limit is equated to the background, 10% of the background, 100 dps (γ -radioactivity), or 1000 dpm (α -, β -, γ -radioactivity). In order to compare some of the more commonly-used definitions, “detection limits” have been calculated for a hypothetical radioactivity experiment in which a long-lived γ -emitter was counted for 10 min with an efficiency of 10%, using a detector having a background of 20 cpm. The results, plotted in increasing order in Figure 1, are obviously unsatisfactory, for they encompass nearly three orders of magnitude!

In what follows, it will be seen that a complete discussion of the (lower) limits for a measurement process requires the introduction of three specific levels: (1) a “decision limit” at which one may decide whether or not the result of an analysis indicates detection, (2) a “detection limit” at which a given analytical procedure may be relied upon to lead to detection, and (3) a “determination limit” at which a given procedure will be sufficiently precise to yield a satisfactory quantitative estimate. Following definition of the three levels, an attempt will be made to indicate their relations to the various definitions referred to previously, and to give asymptotic expressions which may serve as convenient working definitions.

- (1) B. Altshuler and B. Pasternack, *Health Physics*, **9**, 293 (1963).
- (2) J. Wing and M. A. Wahlgren, *ANAL. CHEM.*, **39**, 85 (1967).
- (3) R. C. Koch, “Activation Analysis Handbook,” Academic Press, New York, N. Y., 1960.
- (4) D. E. Watt and D. Ramsden, “High Sensitivity Counting Techniques,” Macmillan Co., New York, N. Y., 1964.
- (5) “A Manual of Radioactivity Procedures,” Handbook 80, National Bureau of Standards, Washington, D. C., 1961.
- (6) H. Kaiser, *Z. Anal. Chem.*, **209**, 1 (1965).

The general expressions for detection and determination will be applied to radioactivity by means of the assumption of "Poisson counting statistics." In order to make the concepts generally useful, particularly in the fields of nuclear chemistry and activation analysis, the formulae will be generalized to take into account both long- and short-lived radioactivity, continuously-variable measurement parameters (such as discriminator settings), and radioactivity measurements in the presence of interfering radionuclides.

GENERAL PRINCIPLES

Part of the following discussion appears elsewhere in the literature in somewhat different form, for example, in References (1 and 6). The purpose of this section is to bring together the concepts of qualitative and quantitative analysis limits, to clearly show the relationships between an *a posteriori* decision with the related confidence interval and an *a priori* "detectability," and to lay the groundwork for general application to the detection of radioactivity, to be discussed in the following section. Readers who wish fuller explication of the underlying statistical principles and methods—particularly those relating to hypothesis testing, probability distributions, and the estimation of statistical parameters—may find it helpful to consult a basic statistics text, such as Dixon and Massey (7).

Definitions and Notation. The process of measurement (experimental procedure) must be completely defined—including the measuring apparatus, method of observation, and sample nature—in order to draw valid conclusions with respect to detection capabilities. In general, the physical quantity of interest (mass, number of atoms, nuclear cross section, etc.) is not directly measurable, but is connected to that which is observed (digital counts, voltmeter deflection, etc.) through a calibration constant. The statistics of *detection* and *determination* apply directly to the observations rather than to the underlying physical quantity, and therefore, the following discussions will deal specifically with the observed (or observable) *signal* (meter reading) and its associated random fluctuations. Statistical conclusions drawn in terms of the net signal may be very simply extended to the related physical quantity by means of the calibration factor.

Symbols will be defined, in general, as they appear in the text, but it may be helpful initially to list the following:

Blank:	μ_B	limiting mean (or "true" mean)
	B	observed value
	σ_B	standard deviation
Gross Signal:	μ_{S+B}	limiting mean
	$(S + B)$	observed value
	σ_{S+B}	standard deviation
Net Signal:	$\mu_S = \mu_{S+B} - \mu_B$	limiting mean
	$S = (S + B) - B$	value derived from an observation pair
	$\sigma_S = (\sigma_{S+B}^2 + \sigma_B^2)^{1/2}$	standard deviation

The *blank* is defined as the signal resulting from a sample which is identical, in principle, to the sample of interest, except that the substance sought is absent (or small compared to σ_B). The blank thus includes the effects of interfering species.

Qualitative Analysis. It is vital at the outset to distinguish between two fundamental aspects of the problem of detection: (1) given an observed (net) signal, S , one must decide whether

a *real* signal has been detected—i.e., whether $\mu_S > 0$; (2) given a completely-specified measurement process, one must estimate the minimum *true* signal, μ_S , which may be expected to yield a sufficiently large observed signal, S , that it will be *detected*. The first aspect thus relates to the making of an *a posteriori*, *binary* (qualitative) *decision* based upon the observation, S , and a definite criterion for detection. Following such a decision one should establish either an upper limit (if "not detected") or a confidence interval (if "detected"). The second aspect relates to the making of an *a priori estimate* of the detection capabilities of a given measurement process.

Let us consider first the *a posteriori* problem. Following an experimental observation, one must decide whether or not that which was being sought was, in fact, detected. Formally known as Hypothesis Testing, such a binary, qualitative decision is subject to two kinds of error: deciding that the substance is present when it is not (α ; error of the first kind), and the converse, failing to decide that it is present when it is (β ; error of the second kind). The maximum acceptable value for α , together with the standard deviation, σ_0 , of the net signal when $\mu_S = 0$ establish the *Critical Level*, L_C , upon which decisions may be based. Operationally, an observed signal, S , must exceed L_C to yield the decision, "detected." Thus, the probability distribution of possible outcomes, when the true (net) signal is zero, intersects L_C such that the fraction, $1 - \alpha$, corresponds to the (correct) decision, "not detected."

Once L_C has been defined, an *a priori Detection Limit*, L_D , may be established by specifying L_C , the acceptable level, β , for the error of the second kind, and the standard deviation, σ_D , which characterizes the probability distribution of the (net) signal when its true value (limiting mean), μ_S , is equal to L_D . (Identification of the "true" net signal with the limiting mean assumes the absence of systematic errors. As with most discussions of detection limits, we assume that the entire measurement process may be replicated, so that errors become random in nature. Systematic errors in a calibration factor, connecting the net signal to the desired physical property, are not involved at this stage.) L_D is defined so that the probability distribution of possible outcomes (when $\mu_S = L_D$) intersects L_C such that the fraction, $1 - \beta$, will correspond to the (correct) decision, "detected." The detection limit, defined in this manner, is equivalent to the "limit of guarantee for purity" of Kaiser (6) and the "minimum detectable true activity" of Altshuler and Pasternack (1). The significance of this particular form for the definition is that it allows one to determine, for a given measurement process, the smallest (true) signal which will be "detected" with a probability $1 - \beta$, where the *a posteriori* decision mechanism has a built-in protection-level, α , against falsely concluding that a blank observation represents a "real" signal. True signals, μ_S , lying between zero and L_D will have larger values for β , and therefore, although they may be "detected," such detection cannot be considered reliable.

Mathematically, the critical level is given as

$$L_C = k_\alpha \sigma_0 \quad (1)$$

and the detection limit,

$$L_D = L_C + k_\beta \sigma_D \quad (2)$$

where k_α and k_β are abscissas of the standardized normal distribution corresponding to probability levels, $1 - \alpha$ and $1 - \beta$. The relationships between L_C , L_D , and the probability distributions for $\mu_S = 0$ and $\mu_S = L_D$ are depicted in Figure 2, where μ_B represents the limiting mean for the blank distribution, and μ_{S+B} represents the limiting mean for the (observed) signal-plus-blank distribution.

(7) W. J. Dixon and F. J. Massey, Jr., "Introduction to Statistical Analysis," 2nd ed., McGraw-Hill, New York, N. Y., 1957.

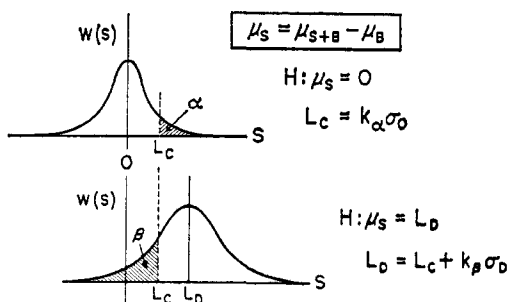


Figure 2. Hypothesis testing
Errors of the first and second kinds

Confidence Interval and Upper Limit. The preceding discussion implied that one need do no more than compare an experimental result with the decision level in order to draw a qualitative conclusion. In most cases, however, one has available an estimate of the net signal, S , and its standard deviation, σ , may be known. An interval may then be stated for μ_s , based upon $z_{1-\gamma/2}\sigma$ and corresponding to the confidence level, $1 - \gamma$. ($z_{1-\gamma/2}$ is the critical value for the standardized normal distribution such that $\text{Prob}\{z \leq z_{1-\gamma/2}\} = 1 - \gamma/2$.) If the net signal and its standard deviation are estimated by means of replication, S is replaced by \bar{S} ; σ , by s/\sqrt{n} ; and $z_{1-\gamma/2}\sigma$, by $t_{1-\gamma/2} \cdot s/\sqrt{n}$. (Here, s represents the standard deviation estimate computed from n -observations, and $t_{1-\gamma/2}$ represents the critical value for the Student's t distribution corresponding to $n - 1$ degrees of freedom.)

(1) If S (or \bar{S}) $> L_c$, the decision, "detected," should be reported, and a symmetrical confidence interval should be given: $S \pm z_{1-\gamma/2}\sigma$ (or $\bar{S} \pm t_{1-\gamma/2}s/\sqrt{n}$) where $z_{1-\gamma/2}$ (or $t_{1-\gamma/2}$) refers to a two-sided confidence interval.

(2) If S (or \bar{S}) $\leq L_c$, the decision, "not detected," should be reported, and an upper limit should be given: $S + z'_{1-\gamma}\sigma$ (or $\bar{S} + t'_{1-\gamma}s/\sqrt{n}$) where $z'_{1-\gamma}$ (or $t'_{1-\gamma}$) refers to the one-sided confidence interval. (The prime is here used to emphasize one-sided.)

Note that in the special case where $\sigma = \sigma_0$, and $z'_{1-\gamma}$ is employed, L_c is numerically equal to $z'_{1-\gamma}\sigma$. This leads to the common, mistaken practice of equating $z'_{1-\gamma}\sigma$ with the "detection limit [(95%) confidence level]." Such a statement is seriously in error because the detection limit cannot be characterized by a single "confidence level," and because it confuses the decision-making quantity ($z'_{1-\gamma}\sigma = L_c$) with L_D , which is used to assess the *a priori* detectability. To the extent that $\sigma \approx \sigma_0$, which may be satisfactory if σ is approximately constant in the region between zero and L_D , the use of $z'_{1-\gamma}\sigma$ (one-sided) to test a given result is exactly equivalent to the use of L_c for this purpose.

A second possible mistake is the confusion of an *a posteriori* upper limit with the *a priori* detection limit. Here again, the two may coincide, if the net signal happens to be L_c , and if $\sigma \approx \sigma_D$ and the one-sided confidence interval is employed. Such a coincidence is not accidental, for the detection limit is, by definition, the maximum upper limit. It must be remembered, however, that, in general, the upper limit depends upon the specific experimental result, S , whereas the detection limit *must* be independent of S , depending, rather, upon the measurement process itself.

Finally, the difference between $z\sigma$ and $t \cdot s/\sqrt{n}$ should be discussed. The use of the latter, which depends upon the variance estimate resulting from n -observations, is clearly

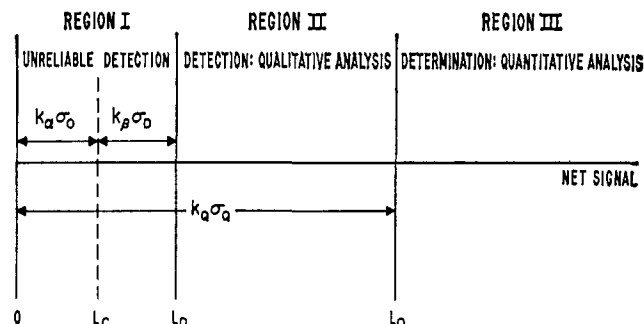


Figure 3. The three principal analytical regions

"safer" in that it takes into account possible lack of knowledge of σ . On the other hand, if σ in the region between zero and L_D is reasonably well-known (from "theory" or extensive observation), and especially if it is approximately constant, more realistic intervals and upper limits would be set through its use rather than s/\sqrt{n} . (Of course, σ/\sqrt{n} replaces σ , when \bar{S} is used in place of S .) If σ is not approximately known, and in control, in the region below L_D , it is impossible, *in principle*, to estimate a limit of detection. In any case, replicates are most desirable, if possible, and the estimate, s/\sqrt{n} , should be consistent with σ/\sqrt{n} , if the measurement process remains "in control." [An exactly equivalent, and somewhat preferable, scheme for treating replication, would include the number of observations, n , as a part of the definition of the measurement process. The standard deviation of the mean of n -observations would then be simply σ (for the over-all process) rather than σ/\sqrt{n} . The use of s/\sqrt{n} to test control rather than to set limits would be achieved by routine evaluation of s^2/σ^2 , which should be within limits set by the distribution of χ^2/ν .]

Quantitative Analysis. Neither a binary decision, based upon L_c , nor an upper limit, nor a wide confidence interval may be considered satisfactory for quantitative analysis. One wishes instead a result which is satisfactorily close to the true value (limiting mean). Therefore, for $\mu_s = L_Q$, the *Determination Limit*, the standard deviation, σ_Q , must be but a small fraction of the true value. Such a definition is similar to that used by Adams, Passmore, and Campbell who defined a "minimum working concentration" as that for which the relative standard deviation was 10% (8).

The *Determination Limit* so defined is,

$$L_Q = k_Q \sigma_Q \quad (3)$$

where L_Q is the true value of the net signal, μ_s , having a standard deviation, σ_Q , and $1/k_Q$ is the requisite relative standard deviation.

By way of summary, the levels L_c , L_D , and L_Q are determined entirely by the error-structure of the measurement process, the risks, α and β , and the maximum acceptable relative standard deviation for quantitative analysis. L_c is used to test an experimental result, whereas L_D and L_Q refer to the capabilities of measurement process itself. The relations among the three levels and their significance in physical or chemical analysis appear in Figure 3.

Special Cases (numerical results). In order to make the significance of Equations 1-3 clearer, a number of specific choices for α , β , and the various σ 's may be helpful.

(8) P. B. Adams, W. O. Passmore, and D. E. Campbell, paper No. 14, "Symposium on Trace Characterization—Chemical and Physical," National Bureau of Standards (Oct. 1966).

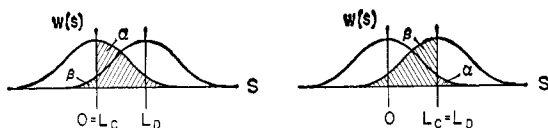


Figure 4. Extreme limits for L_c

The left-hand diagram indicates coincidence of L_c with zero; hence $\alpha = 0.50$. The right-hand diagram indicates coincidence of L_c with L_d ; hence $\beta = 0.50$

1. $\alpha = \beta$; $\sigma = \text{constant}$. If the risks of making both kinds of mistake are set equal, then $k_\alpha = k_\beta = k$, and

$$L_c = k\sigma_0 \quad (4a)$$

$$L_d = L_c + k\sigma_D = k(\sigma_0 + \sigma_D) \quad (4b)$$

If, in addition, σ is approximately constant,

$$L_c = k\sigma \quad (5a)$$

$$L_d = 2k\sigma = 2L_c \quad (5b)$$

In this case, the detection limit is just twice the critical level—a situation which obtains in the large majority of cases. Assuming that risks of 5% are acceptable, and that the random errors are normally-distributed, the constant, k , takes on the value, 1.645. The standard deviation of the net signal is derived from

$$\sigma^2 = \sigma_{S+B}^2 + \sigma_B^2 \quad (6)$$

where σ_{S+B}^2 represents the variance of the “gross” (directly-observed) signal and σ_B^2 represents the variance of the blank. If the standard deviation is approximately independent of the signal level, then

$$\sigma^2 = \sigma_{S+B}^2 + \sigma_B^2 = 2\sigma_B^2 \quad (7)$$

Making the additional requirement that $k_Q = 10$ —i.e., that $\sigma_Q \approx 10\%$ —we find that

$$L_Q = k_Q\sigma_Q = 10\sigma \quad (8)$$

The above results are summarized in Table I, which may be used to provide convenient “working” formulae for the large majority of problems. The first row is derived assuming equivalent observations of sample (plus blank) and blank, while the second row, which differs by $1/\sqrt{2}$, assumes that a long history of observations of the blank make the second term on the right in Equation 6 negligible.

2. Fixed L_d ; varying (α, β) . For a given measurement process specification of α fixes L_c . Similarly, specification of L_c or α together with the specification of β fixes L_d . For a given L_d , however, an infinite set of combinations (α, β) exist depending upon the location of L_c . For example, the value for L_d resulting from the above choice, $\alpha = \beta = 0.05$, would also obtain for all choices of L_c between zero and L_d . The extremes, $L_c = 0$ and $L_c = L_d$ (still assuming $\sigma_D = \sigma_0$), correspond to $(\alpha, \beta) = (0.5, 0.0005)$ and $(\alpha, \beta) = (0.0005, 0.5)$, respectively (see Figure 4).

3. $\mu_B = 0$. Because the above equations do not involve the magnitude of the background, *per se*, but only its standard deviation, there is no change. Such a state of affairs is reasonable, for a background of any magnitude can be set equal to zero simply by a change of scale; such a change cannot be expected to alter the detection limit.

4. $\sigma_B = 0$. In this case, the effect is profound. L_c is necessarily zero, and any net positive signal definitely indi-

Table I. “Working” Expressions for L_c, L_d, L_Q .^a

	L_c	L_d	L_Q
Paired observations	$2.33 \sigma_B$	$4.65 \sigma_B$	$14.1 \sigma_B$
“Well-known” blank	$1.64 \sigma_B$	$3.29 \sigma_B$	$10 \sigma_B$

^a Assumptions: $\alpha = \beta = 0.05$; $k_Q = 10$; $\sigma = \sigma_0 = \text{const.}$

cates detection ($\alpha = 0$). $L_d = k_\beta\sigma_D$, and $L_Q = k_Q\sigma_Q$, where σ_D and σ_Q now depend upon the net signal only.

5. $\sigma_{S+B}^2 = \mu_S + \mu_B$. Poisson statistics—to be discussed below under radioactivity. The standard deviation may not be assumed constant; it increases with signal level.

6. α or $\beta = 0.50$. If one is willing to tolerate a 50% error in wrongly identifying a false signal or in missing a true signal, either L_c becomes zero or $L_c = L_d$. That is, under these circumstances, the pair of levels, L_c and L_d , give the appearance of just a single level. This is illustrated in Figure 4. If both risks are set at 50%, then both levels coincide with zero. Therefore, any positive, net signal will be recognized as “real,” and any nonzero “true” level in a sample will be “detectable.” (That is, the detection limit is in fact zero!) However, such fantastic detection capabilities must be viewed with caution, for regardless of whether $\mu_S = 0$, or if it is just above the limit of detection, the conclusion will be wrong 50% of the time, and therefore the experiment could be performed equally well by the flipping of a coin.

RADIOACTIVITY

Signal Detection. Application of the foregoing considerations to radioactivity involves the fact that the gross “signal” and “blank” observations are in digital form which in most cases may be assumed to be governed by the Poisson distribution. (Extra, non-Poisson variability of the blank is discussed below, under “Interference and Background.”) If the numbers of counts are sufficiently large, the distributions are approximately Normal, and we may therefore readily estimate the variance of the net signal and establish approximate levels of confidence and significance. Under such circumstances, the variance of the net signal (number of counts) is given by

$$\sigma^2 = \sigma_{S+B}^2 + \sigma_B^2 = (\mu_S + \mu_B) + \frac{\mu_B}{n} \quad (9)$$

(\bar{B} is assumed to have been derived from n -observations of the blank.) Note that σ is not independent of signal level as was assumed in Table I. Its variation over the range $\mu_S = 0$ to $\mu_S = L_d$ is trivial if μ_B is large, however. If $\mu_B = 10$ counts, $\sigma_D/\sigma_0 \approx 1.5$ (n -large). In the limit $\mu_B = 0$, $\sigma_D/\sigma_0 = \infty$, because $\sigma_0 = 0$. This requirement, that $\sigma_0 = 0$ and $L_c = 0$ if $\mu_B = 0$, is peculiar to the Poisson distribution, and represents one of the principal differences between the “general” case and that of radioactive decay.

Remembering that σ_0^2 is the variance when $\mu_S = 0$, and that σ_D^2 is the variance when $\mu_S = L_d$, we obtain

$$L_c = k_\alpha \sigma_0 = k_\alpha (\mu_B + \sigma_B^2)^{1/2} \quad (10)$$

$$L_d = L_c + k_\beta \sigma_D = L_c + k_\beta (L_d + \sigma_0^2)^{1/2} \quad (11)$$

Solving Equations 10 and 11 for L_d , leads to

$$L_d = L_c + \frac{k_\beta^2}{2} \left\{ 1 + \left[1 + \frac{4L_c}{k_\beta^2} + \frac{4L_c^2}{k_\alpha^2 k_\beta^2} \right]^{1/2} \right\} \quad (12)$$

Table II. "Working" Expressions for Radioactivity

	L_C (counts) ^a	L_D (counts)	L_Q (counts)
Paired observations			
$(\sigma_B^2 = \mu_B)$	$2.33 \sqrt{\mu_B}$	$2.71 + 4.65 \sqrt{\mu_B}$	$50 \left\{ 1 + \left[1 + \frac{\mu_B}{12.5} \right]^{1/2} \right\}$
"Well-known" blank			
$(\sigma_B^2 = 0)$	$1.64 \sqrt{\mu_B}$	$2.71 + 3.29 \sqrt{\mu_B}$	$50 \left\{ 1 + \left[1 + \frac{\mu_B}{25} \right]^{1/2} \right\}$
Zero blank ($\mu_B = 0$)	0	2.71	100
Asymptotic ratio ^{b,c} (S/σ_B)	1.64	3.29	10

^a Dimensions (counts) apply to the first three rows only.

^b "Well-known" blank case; for paired observations, multiply by $\sqrt{2}$.

^c Correct to within 10% if $\mu_B \geq 0, 67, 2500$ counts, respectively, for each of the three columns. For paired observations, $\mu_B \geq 0, 34, 1250$ counts, respectively.

Estimates of the mean value and the standard deviation of the blank thus allow the calculation of L_C and L_D for selected values of α and β by means of Equations 10 and 12. A considerable simplification takes place if $k_\alpha = k_\beta = k$. Equation 12 then reduces to the form,

$$L_D = k^2 + 2L_C \quad (13)$$

Equation 13 differs by the term, k^2 , from that arising in the previous discussion in which the "reasonable" assumption was made that $\sigma^2 \approx \text{const}$. Thus, even if $\sigma_B = 0 = L_C$, we see that L_D may never be equal to zero. The determination limit, L_Q , is given by

$$L_Q = k_Q \sigma_Q = k_Q (L_Q + \sigma_0^2)^{1/2} \quad (14)$$

which may be solved to yield

$$L_Q = \frac{k_Q^2}{2} \left\{ 1 + \left[1 + \frac{4\sigma_0^2}{k_Q^2} \right]^{1/2} \right\} \quad (15)$$

Again, convenient "working" expressions may be derived from Equations 9, 13, and 15 for measurements in which $\alpha = \beta = 0.05$, and $k_Q = 10$. These expressions are given in Table II.

Especially simple "working" expressions may be stated when the number of background counts, μ_B , is "large." Such simplified expressions, presented in terms of the ratio of the net signal to the standard deviation of the background ("signal/noise"), appear in the bottom row of Table II. Note the correspondence of the asymptotic ratios to the "working" expressions in Table I.

The occurrence of nonintegral values for L_D and L_Q in Table II is not at all inconsistent with integral, Poisson distributions, because L_D and L_Q represent the means of such distributions, and such means may take on any positive value, integral or nonintegral. L_C , on the other hand, represents a decision level against which an integral, experimental result must be compared. An exact, Poisson treatment would thus lead to an integer for L_C , but only discrete values for α would then be possible. The magnitude of the error in significance level, due to the assumption of normality, is worth considering with respect to the data in Table II. For example, L_D is there given as 2.71 counts for the zero blank case, and this is supposed to correspond to $\beta = 0.05$. Examination of the correct, Poisson distribution shows that the probability of

observing $S = L_C = 0$ counts when $\mu_S = L_D = 2.71$ is approximately 0.07 instead of the desired 0.05.

Interference and Background. Thus far, μ_B and σ_B have been used to refer to the "blank." In observations of radioactivity one frequently approaches the situation where the blank is due only to background radiation. When such is not the case, it may be desirable to decompose the blank into its separate components: background and interfering activities. Using b to denote background and I to denote interference, the above quantities take the form,

$$\mu_B = \mu_b + \mu_I \quad (16)$$

$$\sigma_B^2 = \sigma_b^2 + \sigma_I^2 \quad (17)$$

If the variances, σ_b^2 and σ_I^2 , arise from the Poisson distribution, they will be equal to the respective mean values, μ_b and μ_I ; if the interference has instead a fixed relative standard deviation, f_I , its variance will be equal to $(f_I \mu_I)^2$. The distinction between these two situations may sometimes be quite critical in fixing the detection limit. Its significance in choosing between alternative detection systems will be discussed in a separate publication. Note that the situation may also come about where $\mu_I = 0$, but σ_I^2 corresponds to an extra (non-Poisson) component of variance. Such extra variance, which may arise from cosmic ray variations or instrument instability, must be included in the estimate of σ_0^2 and, hence, in the estimates of L_C , L_D , and L_Q .

Limits for the Related Physical Quantities. In order to make the decision, "detected" or "not detected," one needs to know only the net number of counts resulting from a specific experiment, and the critical number of counts, L_C . Limits for qualitative and quantitative analysis and upper limits or confidence intervals for actual results, however, are of value only when expressed in terms of the physical quantity of interest, such as grams or atoms. The connection is simply made by means of the relevant calibration factor. For example, the detection limit, L_D , may be related to the minimum detectable mass, $m_D(\text{g})$, by means of Equation 18,

$$L_D = K m_D \quad (18)$$

where K represents an overall calibration factor relating the detector response to the mass present. Thus, K would be equal to unity for direct (ideal) weighing; it would be equal to the absorbance per gram for spectrophotometry if the

sample cross-section is fixed; it would be equal to the number of counts per gram for activation analysis.

Although the constant, K , is not involved directly in the statistics of the detection limit, its role is fundamental, and it must be included when choosing between experimental procedures or in optimizing a given procedure. For the particular case of nuclear activation,

$$K = P(\Sigma)S(\lambda, \tau)T(\lambda, t, \Delta t)\epsilon(x) \quad (19)$$

where P = production rate (nuclei/g-sec)

S = saturation factor = $1 - e^{-\lambda\tau}$

$T = (e^{-\lambda t}/\lambda) (1 - e^{-\lambda\Delta t})$ (seconds) (a generalized counting interval relating initial counting rate to observed number of counts).

ϵ = detection efficiency (counts/disintegration) (chemical yield may be incorporated in ϵ , when appropriate).

Σ and λ are characteristic of the nuclear reaction being utilized; they represent the reaction cross section (cm^2) and product decay constant (sec^{-1}), respectively. τ , t , and Δt are the times (sec) for activation, delay (decay), and counting, respectively. x represents a variable detection parameter, such as absorber thickness, discriminator setting, etc. A similar expression may be written for the mean number of counts from an interfering radionuclide:

$$\mu_I = m_I [P(\Sigma_I)S(\lambda_I, \tau)T(\lambda_I, t, \Delta t)\epsilon_I(x)] \quad (20)$$

the mean number of background counts is given by

$$\mu_b = b(x)\Delta t \quad (21)$$

where $b(x)$ is the background rate, which also may depend upon the detection parameter, x . The preceding expressions may be incorporated into a single equation for the mass-detection limit:

$$m_D = \frac{k^2 + 2k [\mu_b + \sigma_b^2 + \mu_I + (f_I\mu_I)^2]^{1/2}}{P(\Sigma)S(\lambda, \tau)T(\lambda, t, \Delta t)\epsilon(x)} \quad (22)$$

Equation 22, although somewhat complicated, allows one to calculate the minimum detectable mass for a given activation-detection procedure, where there are no *a priori* restrictions placed upon the half-life of the product radionuclide (long- vs. short-lived) and where interference may be considered in a completely general and unrestricted manner. In order to include more than one interfering radionuclide, one simply replaces μ_I by $\sum \mu_I$ and $(f_I\mu_I)^2$ by $\sum (f_I\mu_I)^2$. If the variances of background and interference are governed by the Poisson distribution and if they are determined by "equivalent" observations, the radical in the numerator of Equation 22 takes the simpler form: $(2\mu_b + 2\mu_I)^{1/2}$. If the variances are negligible, the radical becomes $(\mu_b + \mu_I)^{1/2}$.

Systematic errors in calibration factors are not a part of the present discussion. Such errors can in no way affect the critical level, L_C , because L_C refers only to the instrumental response at which the decision is made—"detected" or "not detected." All physical quantities deduced from L_D , L_Q , or an "observed" net signal, however, contain uncertainties due to calibration factor errors. Because the calibration factor error is here considered systematic, while the observation (response) error is random, they cannot be simply compounded. As a result, the corresponding physical quantities must be characterized by error limit intervals, the upper limits of which might be used to provide "safe" estimates for m_D and m_Q .

Relative detection capability has frequently been evaluated in terms of the "figure of merit." Figure of merit, in the limit of very small (net) sample counts, is usually defined as μ_s^2/μ_b ; this expression is approximately the reciprocal of the relative variance of the net signal. Use of the above expression for comparing detector sensitivities generally involves the replacement of μ_s by the product of the sample disintegration rate and the detection efficiency, and various detectors are then compared by examining the respective ratios, ϵ^2/μ_b . Such a procedure suffers from a number of limitations, when compared to the use of Equation 22 (or the analogous equations for m_C and m_Q). The limitations include: (1) no allowance is made for short-lived radioactivity; (2) interference—especially "decaying" interference—is not considered; (3) the formula may not be applied to the comparison of critical levels or detection limits, because α - and β -type errors have not been included; (4) the approximation, $\mu_s \ll \mu_b$, is built into the formula. This last factor, which would lead one to conclude that one particular detection system is better than another, may lead to the wrong conclusion for m_D or m_Q . That is, the exact equations, of the form of Equation 22, can lead to the conclusion that the one detection system has the lower limit of detection, but that the other has the lower limit of determination.

ILLUSTRATIONS

In order to make clear the application of the preceding formulae, three examples will be given, one selected arbitrarily from among "standard" methods of chemical analysis, another dealing with the simple detection of radioactivity, and a third dealing with a more complex problem in activation analysis.

(1) SPECTROPHOTOMETRY

The fundamental relation governing the absorption of light by matter may be written,

$$A = \mu cl + A_0 \quad (23)$$

where A and A_0 are the absorbances for samples having concentrations, c and 0, respectively; l is the cell path length; μ is the absorptivity. In order to relate the problem to the preceding discussion, we make the following identifications.

(a) A_0 = blank, μ_B , which is here set equal to zero, by adjustment of the transmittance reading to 100% using a "blank" sample.

(b) σ_B = standard deviation of the blank absorbance $\neq 0$.

(c) A = net signal, μ_s , which here equals the gross signal, because A_0 has been set equal to zero.

(d) $K = \mu l$, the calibration factor.

(e) σ_s = standard deviation of the net signal, A .

Experimental observations on the spectrophotometric determination of thorium using thorian, yielded: $\sigma_B = 0.0020$, and $K = 58.2 \text{ l/g}$ (9). The sample standard deviation, σ_s , was observed to be relatively constant and equal to σ_B , over the concentration range studied. A particular sample analyzed was observed to give a response (absorbance) of 0.0060. Using these data and expressions for paired observations from Table I, we find the following:

Decision: $L_C = 2.33 \sigma_B = 0.0047$. Thus, the observed response, 0.0060, leads to the decision, "detected."

(9) L. A. Currie, G. M. France III, and P. A. Mullen, National Bureau of Standards, unpublished data (1964).

Table III. Detection of Potassium in Sodium

Reaction	Target nuclide ^a	Product ^b	Detection limit (g)	
			Interference-free	$m(\text{Na}) = 1 \text{ g}$
(n, γ)	⁴¹ K (6.9%)	⁴² K (12.4 hr)	1.3×10^{-10}	0.26
	²³ Na (100%)	²⁴ Na (15 hr)		
(γ, n)	³⁹ K (93.1%)	³⁸ K (7.7 min)	7.7×10^{-10}	6.0×10^{-7}
	²³ Na (100%)	²² Na (2.6 yr)		

^a Isotopic abundance listed in parentheses.^b Half-life listed in parentheses

Confidence Interval: Because the signal is considered detected, we may set a confidence interval, rather than an upper limit. The absorbance interval for the signal at the 95% level of confidence is $0.0060 \pm 1.96 (0.0020)$. The corresponding thorium concentration interval, assuming negligible error in the calibration constant, is 36 to 170 $\mu\text{g/l}$, and the estimate of the mean is 103 $\mu\text{g/l}$.

Detection Limit: $L_D = 4.65 \sigma_B = 0.0093$. Thus, the minimum detectable concentration (that which will give a signal exceeding L_D , 95% of the time) is equal to 160 $\mu\text{g/l}$.

Determination Limit: $L_Q = 14.1 \sigma_B = 0.0282$. Therefore, in order to obtain a precision (relative standard deviation) as small as 10%, one must have a thorium concentration of 480 $\mu\text{g/l}$.

(2) RADIOACTIVITY

Let us next consider the detection of the 7.7-min positron-emitter, ³⁸K. We shall assume that the radionuclide is detected by means of the 0.51-MeV positron annihilation quanta using a sodium iodide crystal having a background of 20 cpm and a detection efficiency (for ³⁸K) of 32%. Our aim will be to calculate the various limits in terms of activity (disintegration rate) instead of mass. As will be shown in a separate publication, the counting interval, Δt , which leads to the minimum detection limit is approximately twice the half-life; we shall therefore take $\Delta t = 15.4 \text{ min}$. Equation 18 here takes the form, $L_D = Ka_D$, where a_D represents the minimum detectable activity, and $K = \epsilon T$. Because the delay time, t , is not involved in the present example, $T = (1 - e^{-\lambda \Delta t})/\lambda$. (For long-lived species, T , the "effective counting interval," reduces to Δt , the physical counting interval.) Using the fact that $\mu_B = 20 \text{ cpm} \times 15.4 \text{ min}$, one may calculate L_C , L_D , and L_Q directly from the formulae for paired observations given in the first row of Table II. The above value for ϵ may then be combined with $T = 8.33 \text{ min}$, in order to determine a_C , a_D , and a_Q . The results are given below:

$$a_C = 15.3 \text{ dpm}$$

$$a_D = 31.6 \text{ dpm}$$

$$a_Q = 114 \text{ dpm}$$

Let us suppose that an observation of sample plus background gives a total of 340 counts. The net signal would then be 32 counts (assuming that the background observation yielded 308 counts), and its estimated standard deviation would be 25.4 counts. L_C , as calculated from Table II, is equal to 40.8 counts, and therefore such an observation would lead to the conclusion, "not detected." (The comparison might be made on the basis of the corresponding disintegration rates, 12 dpm-observed, and $15.3 \text{ dpm} = a_C$, but the conversion from counts to dpm is unnecessary for making the decision.) The upper limit (95% confidence level) for the net signal is

equal to $32 + 1.645 (25.4) = 73.8$ counts; this is equivalent to a disintegration rate of 27.6 dpm.

The effect of half-life on the above limits is notable. For example, if ³⁸K had a very long half-life, $T \rightarrow 15.4 \text{ min}$ and a_D would be reduced to 17.1 dpm. A long half-life, of course, would make useful a longer counting interval. If the interval were 10^3 min , for example, the minimum detectable activity would be further reduced to 2.06 dpm. Thus, when half-life is the only variable, one can detect considerably smaller activities for long-lived species than for those which are short-lived.

(3) ACTIVATION ANALYSIS

The foregoing principles will next be applied to a somewhat more complex example in which one must consider both the effects of various product half-lives and the effects of interference arising from alternative nuclear projectiles. The problem to be examined is whether reactor neutrons or linac bremsstrahlung are better for the detection of potassium. The minimum detectable mass will be estimated for the interference-free situation, and also for that in which the potassium is accompanied by 1 gram of sodium. Details of the calculation will not be presented here, but only the input data and the results. The results were calculated directly from Equation 22. The input assumptions follow:

- thermal neutron flux— $10^{13} \text{ (n/cm}^2\text{-sec)}$.
- bremsstrahlung flux distribution— $10^{14}/E \text{ (quanta/MeV-min-cm}^2\text{)}$ (electron beam energy well above the giant resonance).
- irradiation time and counting time— 10^3 min or two half-lives (potassium product) whichever is less.
- delay time—negligible.
- nuclear cross sections—taken from the literature.
- interference correction accuracy, $f_I = 1\%$.
- detection—paired observations, sodium-iodide counting of the positron annihilation peak (bremsstrahlung-produced activity) or the 1.51 MeV ⁴²K γ -peak (neutron-produced activity). Interferences due to sodium activities were estimated from the respective gamma ray spectra. The backgrounds and detection efficiencies are as follows:

Reaction	Background	Efficiency (γ -efficiency \times branching)	
		K	Na
(n, γ)	12 cpm	0.014	0.0097
(γ, n)	20 cpm	0.32	0.29

Minimum detectable masses of potassium are given in Table III. Note that the minimum detectable activity calculated for ³⁸K in the preceding example applies also to the present example; the minimum detectable mass differs only by the production factor, $P(\Sigma)$, which here equals $4.11 \times 10^{10} \text{ dpm/g}$ for ³⁸K.

The results given in Table III indicate that both a reactor and an electron linear accelerator provide excellent detection capabilities for potassium in the absence of interference, the reactor being somewhat better. The importance of Equation 22 for detection limit estimation in the presence of interference, however, becomes quite clear upon examination of the last column of Table III. Here, the detection limit by bremsstrahlung irradiation has become about one thousand times poorer, and thermal neutron activation has become practically useless.

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Graphical Technique for Estimating Activity Levels Produced in Thermal- and Fission-Neutron Irradiation

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We describe a rapid and flexible graphical method for estimating the activity induced in neutron irradiations. This method, applicable to several activation problems, is applied here to thermal- and fission-neutron irradiations, which are widely used in activation analysis with reactors. The calculated saturation activities of the products of most activation reactions are represented on two activation charts. We develop a graphical technique, using a transparent overlay, to obtain corrections for the saturation, decay, and counting factors. The principal advantage of this method is that the corrections due to these factors can be applied to any saturation activity of the chart, which already contains all the nuclear information required for estimation of induced radioactivity. Most simple activity calculations can be performed quickly and accurately; the technique is also useful in estimating the best irradiation and decay times to enhance selected activities in composite samples. We give the numerical values for the construction of charts of saturation activities for thermal- and fission-neutron irradiation and for the overlay. Calculation techniques are explained and clarified with typical examples.

THE CALCULATION of induced radioactivity is required in many activation problems. Generally, the same mathematical formalism is applied, with different values of nuclear constants and time parameters. The search for nuclear constants and the solution of equations for composite samples is often time-consuming. We here develop a graphical method for representing nuclear data and solving activation equations; this method can be successfully applied to several activation problems, flux monitoring, and radioisotope production with reactors and accelerators. (The two activation charts and the transparent overlay are available as a courtesy from General Radioisotope Processing Corp., 3120 Crow Canyon Road, San Ramon, Calif. 94583.) The specific applications to thermal- and fission-neutron activation have been chosen because of their wide and frequent use in activation analysis with reactors.

Several nomographs for calculating induced radioactivity have been published (1-3). To use most of these, it is first

necessary to find the nuclear parameters in the literature. Concise summaries of sensitivities for thermal-neutron activation have also been published (4, 5). These generally apply to selected counting and irradiation conditions.

The techniques described here combine, in compact form, the essential nuclear data with a quick and flexible graphical calculation method. The various factors appearing in the activity equation, including the saturation, decay, and counting-time corrections, can easily be determined. Also, qualitative information of optimal irradiation and decay times, which are often desired in activation analysis, can be obtained graphically rather than by using numerical computer techniques (6).

GRAPHICAL METHOD FOR COMPUTATION

The Activation Equation. In calculating induced radioactivity, we assume that the irradiated sample is so small that it produces no significant attenuation of the flux of incident particles. The total disintegration rate of a radioisotope produced by irradiation of an element of natural isotopic composition in a constant flux is then given by

$$A = \frac{mfN_0\phi\sigma}{100 M} [(1 - \exp(-\ln 2 \times t_i/T_{1/2})) \exp(-\ln 2 \times t_d/T_{1/2})] = A_{sat}SD = N^* \ln 2/T_{1/2} \quad (1)$$

where m is the mass of the irradiated element, f is the isotopic abundance (%) of the isotope that undergoes the reaction, N_0 is Avogadro's number, ϕ is neutron flux, σ is the cross section, M is the atomic weight of the irradiated element, $T_{1/2}$ is the half-life of the induced activity, t_i is the irradiation time, t_d is the decay time (between the end of irradiation and the beginning of counting), A_{sat} is $\frac{mfN_0\phi\sigma}{100 M}$, the saturation activity, S is $[(1 - \exp(-\ln 2 \times t_i/T_{1/2}))]$, the saturation factor, D is $\exp(-\ln 2 \times t_d/T_{1/2})$, the decay factor, and N^* is the number of decaying nuclei.

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- (2) E. Ricci, *Nucleonics*, **22**, No. 8, 105 (1964).
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