# A model of measurement precision at low concentrations

P. M. Berthouex, D. Robert Gan

**ABSTRACT:** This paper presents a model that describes the precision of measurements at low concentrations (near the limit of detection). The total variance includes both background noise, which exists even when no analyte is present and is assumed to have a fixed variance, and analytical error, which in chemical measurements is often proportional to the concentrations of the analyte. This total variance model is used to define a limit of detection and two other measures of measurement precision. These are the Characteristic Limit, which is defined as the concentration where the variances of background noise and analytical error are equal, and the Limit of Guaranteed Purity, which defines how large the true concentration might be, in light of a given measured value. Data on lead in wastewater effluent and organic chemicals in sediment are used to illustrate the calculations and demonstrate the performance of the model. *Water Environ. Res.*, **65,** 759 (1993).

**KEYWORDS:** limit of detection, measurement error, measurement precision, variance, limit of purity, lead, organic chemicals.

The method detection limit (MDL) is based on a method's ability to determine an analyte in a sample matrix, regardless of its source of origin. Processing a test specimen by dilution, extraction, drying, etc., introduces measurement variability. It is essential that the MDL include this variability. The MDL is often thought of as being a chemical concept, but is actually a statistical concept. The MDL is estimated from data. It has no scientific meaning until it is operationally defined in terms of a measurement process and a statistical method for analyzing the measurements produced. Without a precise statistical definition, one cannot determine a numerical value for the limit of detection, or expect different laboratories to be consistent in how they determine the limit of detection.

A new approach to understanding the precision of measurements at low concentrations was proposed by Pallesen (1985) in an unpublished, and to-date uncited, note. He had no data to demonstrate his approach and this may be the reason the model was not published. The purpose of this paper is to present the Pallesen model and show how it is used. Data on lead in wastewater and organic chemicals in sediment are used to illustrate the calculations and demonstrate the performance of the model. The model accounts for the total variance of the measurements, which includes both background noise and analytical error. Background noise exists even when no analyte is present and it is assumed to have a fixed variance. The analytical errors are assumed to be proportional to the concentration of the analyte—a characteristic that is often observed in chemical data. This total variance model is used to define a limit of detection, the Characteristic Limit which is the concentration where the variances of background noise and analytical error are equal, and the Limit of Guaranteed Purity which defines how large the true concentration might be in light of a given measured value.

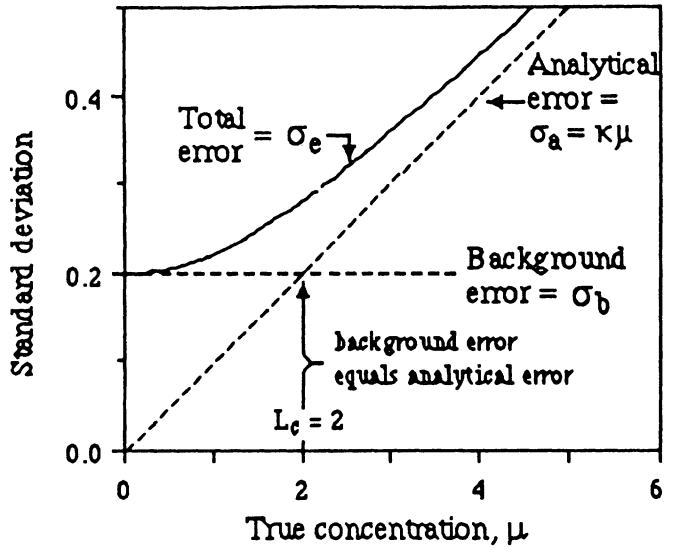
**U.S. EPA definition of the method detection limit.** Appendix B to Part 136, 40 CFR Ch. 1 (7-1-89 edition) says that "The method detection limit (MDL) is the minimum concentration of a substance that can be measured and reported with 99% confidence that the analyte concentration is greater than zero and is determined from analysis of a sample in a given matrix containing the analyte. . . . It is essential that all sample processing steps of the analytical method be included in the determination of the method of detection limit." Similar definitions are found in Glaser *et al.* (1981), Hunt and Wilson (1986), American Chemical Society (1983), Kaiser *et al.* (1968), Kaiser (1970), Holland and McElroy (1986), and Porter *et al.* (1988).

The EPA gives a procedure for establishing an initial estimate of the MDL for the purpose of making samples to be used to determine the MDL. The MDL = $s \cdot t_{v,\alpha=0.001}$, where $s$ is the standard deviation computed from at least $n = 7$ aliquots of prepared solution, and $t_{v,\alpha=0.01}$ is the student's $t$ value at 99% confidence level and $v = n - 1$ degrees of freedom.

The EPA points out that the variance ($s^2$) of the analytical method may not be constant over a range of analyte concentrations, with the result that the estimated MDL would also change in proportion to the concentration of the prepared solution on which replicate measurements were made. The EPA suggests making an iterative check on the reasonability of the estimated MDL by analyzing seven additional replicate aliquots at a slightly different concentration.

**The total variance model.** The true analyte concentration, $\mu$, cannot be observed exactly. It is to be estimated from measured concentrations, $Y_i$. The measurements contain unavoidable random measurement errors, $e_i$, which are evident as variations between replicate measurements. Pallesen (1985) proposed that at low concentrations, where considerations of the limit of detection are relevant, the total error consists of background noise, $b_i$, plus analytical error, $a_i$. Both errors $a_i$ and $b_i$ are assumed to be random, independent, and normally distributed with mean values of zero. This means that the total error, $e_i$, is also random, independent, and normally distributed.

Background noise, $b_i$, exists even when the specimen being tested is blank in the analyte. It is assumed to have constant variance, $\sigma_b^2$, at all analyte concentrations. In contrast to this, the measurement error in the analytical signal, $a_i$, is assumed to be proportional to the measurement signal, $\mu$. This means that $\sigma_a = \kappa\mu$ and the variance of the analytical error is $\sigma_a^2 = \kappa^2\mu^2$. (Note that $\kappa = \sigma/\mu$ is the coefficient of variation, which is commonly used to report the precision of a measurement. This usage is most meaningful when the measurement error is



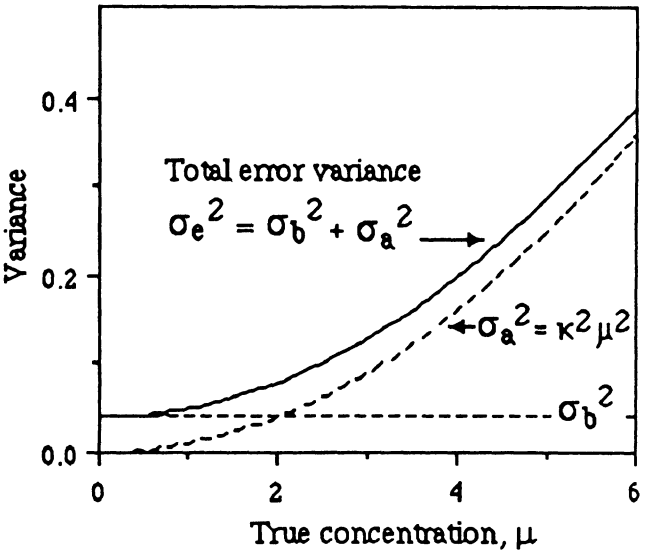




**Figure 1—The error structure of Pallesen's model.**

truly proportional to the magnitude of the concentration, a condition which does prevail for many analytical procedures.)

The relation between the true value, the measured value, and the measurement errors is

$$Y_i = \mu + e_i = \mu + a_i + b_i \quad (1)$$

and the total error variance of any measurement is

$$\sigma_e^2 = \sigma_b^2 + \sigma_a^2 = \sigma_b^2 + \kappa^2\mu^2 \quad (2)$$

The units of $Y$, $\mu$, $\sigma_e$, $\sigma_a$, $\sigma_b$ are M/L (e.g., $\mu$g/L or mg/L); variances ($\sigma_a^2$, $\sigma_e^2$, and $\sigma_b^2$) have units of $(M/L)^2$, and $\kappa$, $k_c k_p$, $k$ are dimensionless.

Both $\sigma_a^2$ and $\sigma_e^2$ decrease as the concentration decreases. When the true concentration is zero ($\mu = 0$), the only source of measurement variation is background error. In other words, $\sigma_a^2$ is also zero, and the variance of the blank is $\sigma_b^2 = \sigma_e^2$. Furthermore, when the true concentration is very low, the analytical error variance, $\sigma_a^2 = \kappa^2\mu^2$, is smaller than $\sigma_b^2$. Figure 1 shows this in terms of the variances and the standard deviations for the case where $\sigma_b^2 = 0.04$ and $\kappa = 0.1$.

**The characteristic limit.** The Characteristic Limit, $L_c$, is defined as the true concentration where the background error variance equals the analytical error variance. That is, when the concentration $\mu = L_c$

$$\sigma_b^2 = \sigma_a^2 = \kappa^2\mu^2 \quad (3)$$

and $\sigma_b = \kappa\mu = \kappa L_c$. This condition determines

$$L_c = \frac{\sigma_b}{\kappa} = \frac{\sigma_a}{\kappa} = k_c\sigma_b \quad (4)$$

where $k_c = 1/\kappa$. If the true mean is less than $L_c$, then the uncertainty of the measurement is mostly background error, whereas for $\mu < L_c$ the uncertainty is mostly analytical error. For the example shown in Figure 1, $L_c = 2$.

**The limit of detection.** The limit of detection (MDL) is the smallest measured value $Y$ for which the analyst will conclude that the result $\mu = 0$ is highly improbable. It is a common, though sometimes questioned practice (Gilbert, 1987; Rhodes, 1981), for a chemist measuring $Y$ less than the MDL, to state that the analyte of interest was "not detected" and to refuse to record the numerical value produced by the instrument. A measurement $Y >$ MDL is "detected" and the measured value is reported.

The MDL is defined as

$$\text{MDL} = k_d\sigma_b \quad (5)$$

Figure 2 is the graphical definition of MDL that is constructed assuming that $Y$ is normally distributed with variance $\sigma_b^2$ and that the true mean of the blanks is zero. Assuming mean zero is convenient, but it is recognized that in practice the mean of

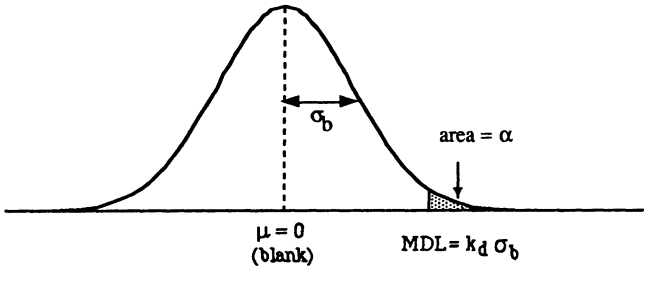



**Figure 2—Graphical definition of the method limit of detection.**

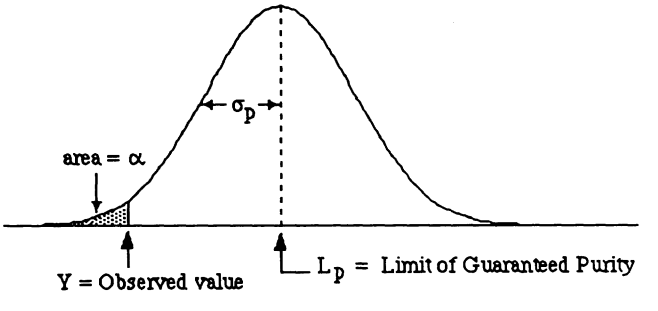



**Figure 3—Graphical definition of the limit of guaranteed purity.**

**Table 1—Typical lead data (Laboratory B).**

| Pb Spike Added | Replicate Observations (μg/L) | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 0 μg/L | 2.5 | 3.8 | 2.2 | 2.2 | 3.1 | 2.6 | | | | | | | | |
| 1.25 μg/L | 2.8 | 2.7 | 3.4 | 2.4 | 3.0 | 3.7 | 4.6 | 4.3 | 4.0 | 1.7 | 2.2 | 2.4 | 3.5 | 2.2 |
| | 3.6 | 3.1 | 3.2 | 2.8 | 2.7 | 3.1 | | | | | | | | |
| 2.50 μg/L | 4.5 | 3.7 | 3.8 | 4.4 | 5.4 | 3.9 | 4.1 | 3.7 | 4.8 | 3.3 | 4.7 | 4.4 | 3.0 | 4.5 |
| 5.00 μg/L | 3.9 | 5.0 | 5.4 | 4.9 | 6.2 | | | | | | | | | |
| 10.00 μg/L | 12.2 | 13.8 | 9.9 | 10.5 | 10.9 | | | | | | | | | |

instrument readings on blanks may be a positive value. Or, if the concentration is estimated by subtracting a blank correction, the measured value may be negative even though the actual concentration cannot be.

The coefficient $k_d$ is chosen such that the probability of $Y$ being greater than MDL is kept suitably low; that is $P(Y > \text{MDL}) = (1 - \alpha)100\%$. The coefficient $k_d$ corresponding to any given $\alpha$ value can be found in a table of the normal distribution. For example, $k_d = 1.645$ for $\alpha = 0.05$ (5%), $k_d = 1.960$ for $\alpha = 0.025$, and $k_d = 3.00$ for $\alpha = 0.0013$. Note that the U.S. EPA definition of the MDL chooses $k_d =$ so $\alpha = 0.01$ (1%).

**The limit of guaranteed purity.** In constructing the limit of detection, the uncertainty embodied in the measurement $Y$ was counted to the benefit of the hypothesis that $\mu = 0$. To state the amount of impurity that might be in a specimen, the uncertainty embodied in $Y$ should be counted to benefit the hypothesis that $\mu$ is larger than $Y$. Pallesen (1985), based on an idea from Kaiser (1968, 1970), defined the Limit of Guaranteed Purity, $L_p$, as "the largest value of $\mu$ that reasonably can be hypothesized consistent with a particular measured value $Y$." This sets an effective upper limit on the value of $\mu$, given a measured value $Y$.

The definition of $L_p$, shown in Figure 3, is

$$L_p = Y + k_p\sigma_p \tag{6}$$

where $\sigma_p$ is the standard deviation when $\mu = Y + k_p\sigma_p$. This definition is applicable even when $Y <$ MDL, so long as a numerical value for $Y$ is reported.

From equations 2 and 6, the total error variance $\mu = Y + k_p\sigma_p$ is

$$\sigma_p^2 = \sigma_b^2 + \sigma_a^2 = \sigma_b^2 + \kappa^2\mu^2 = \sigma_b^2 + \kappa^2(Y + k_p\sigma_p)^2 \tag{7}$$

Substituting the relations $k_c = 1/\kappa = k_d = Y/\sigma_b$, and solving for $\sigma_p$ gives

$$\sigma_p = \sigma_b\left(\frac{k_c^2}{k_c^2 - k_p^2}\right)\left(\frac{k_pk_d}{k_c^2} + \frac{1}{k_c}\sqrt{k_c^2 - k_p^2 + k_d^2}\right) \tag{8}$$

which holds for the condition that $k_p\kappa < 1$. (If $k_p\kappa > 1$ there is a solution and no Limit of Guaranteed Purity exists). For the special case where $k_d = k_p = k$,

$$\sigma_p = \sigma_b\left(\frac{k_c^2 + k^2}{k_c^2 - k^2}\right) \tag{9}$$

This condition is easily satisfied since $\kappa$ is always less than 1, unless the measurement process is so poor as to be virtually useless. For most acceptable measurement methods, $\kappa$ is probably 0.05 – 0.4. This requires $k_p$ to be in the range of 2.5 to 20. Following the same argument used to select $k_d$, it is recommended to use $k_p = 3.0$, corresponding to $\alpha = 0.13\%$. That is, using $k_p = 3$, we can state with approximately 99% confidence that $Y < Lp$.

To be safely on the high side when a numerical value is not reported for $Y$, $L_p$ is computed using $Y = \text{MDL} = k_d\sigma_b$, which gives $L_p = k_d\sigma_b + k_p\sigma_p$. Of course, $L_p$ calculated in this manner is larger than would be obtained from equation 6 if an actual value of $Y <$ MDL had been retained. This is one price that is paid for censoring the data at the limit of detection. Using the same value for $k_d$ and $k_p$ ($k_d = k_p = k$) gives

$$L_p\,(Y = \text{MDL}) = \frac{2k\sigma_b}{1 - k^2\kappa^2} \tag{10}$$

**Example—lead data.** Several laboratories measured lead in 50 samples prepared from filtered activated sludge effluent. Six of the samples were just the unspiked effluent matrix, which was expected to have a low concentration of lead (but not zero). Twenty specimens were spiked with 1.25 μg/L Pb, 14 were spiked with 2.5 μg/L, 5 were spiked with 5 mg/L, and 5 were spiked

**Table 2—Averages ($\bar{x}$) and variances ($s_e^2$) at each lead concentration level for five laboratories.**

| | Laboratory A | | Laboratory B | | Laboratory C | | Laboratory D | | Laboratory E | |
|---|---|---|---|---|---|---|---|---|---|---|
| Spike Added (μg/L) | Ave. (μg/L) | Var. (μg/L)² | Ave. (μg/L) | Var. (μg/L)² | Ave. (μg/L) | Var. (μg/L)² | Ave. (μg/L) | Var. (μg/L)² | Ave. (μg/L) | Var. (μg/L)² |
| 0 | 2.30 | 0.45 | 2.73 | 0.38 | 1.90 | 0.12 | 1.09 | 0.22 | 1.50 | 0.06 |
| 1.25 | 2.55 | 0.67 | 3.07 | 0.55 | 2.76 | 0.22 | 1.82 | 0.37 | 1.65 | 0.68 |
| 2.5 | 4.55 | 1.24 | 4.16 | 0.41 | 4.53 | 0.36 | 3.08 | 0.43 | 3.21 | 0.66 |
| 5.0 | 8.14 | 2.31 | 5.08 | 0.70 | 6.90 | 0.44 | 4.59 | 0.44 | 5.16 | 0.75 |
| 10.0 | 11.90 | 2.64 | 11.46 | 2.42 | 11.23 | 1.26 | 9.12 | 1.15 | 10.66 | 1.15 |

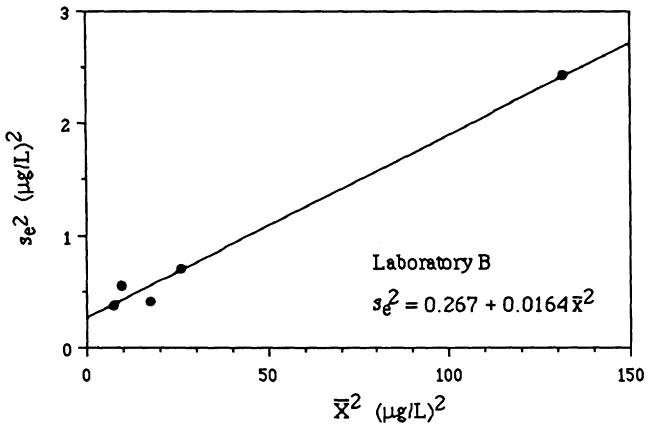



**Figure 4—Plots of $s_e^2$ vs. $\bar{x}^2$ for lead data from Table 1.**

with 10 mg/L lead. The laboratories did not know the concentration range of the specimens, how many concentration levels were represented, or that some specimens were unspiked background effluent matrix (Berthouex, 1991). A typical data set is given in Table 1.

Estimates of $\mu$ and $\sigma_e^2$ are available from the data by computing the averages $\bar{x}$ and variances $s_e^2$ from the replicate measurements at the various concentration levels. These values for five laboratories are given in Table 2. The parameters $\sigma_b$ and $\kappa$ are estimated by regression using equation 2, $s_e^2 = \sigma_b^2 + \kappa^2\bar{x}^2$. As shown in Figure 4, the intercept estimates $\sigma_b^2$ and the slope estimates of $\kappa^2$. Table 3 gives the MDL ($=3\sigma_b$) and $L_c$ ($=k_c\sigma_b$) and the values of $\sigma_b^2$ and $\kappa^2$ that were used to compute them.

Table 4 lists a few values for the Limit of Guaranteed Purity. These were computed using the Laboratory A values of $\sigma_b$ = 0.85 μg/L, $\kappa$ = 0.12, and $k_p$ = 3. Equation 10 was used for observations that are below the MDL (MDL = $3\sigma_b$ = 2.55 μg/L). Equation 9 was used to compute $\sigma_p$ and $L_p$ is computed from equation 6.

Suppose that the measured value is $Y$ = 1 μg/L. If, however, the chemist retained and reported the value $Y$ = 1 μg/L, equations 9 and 6 can be used to compute $\sigma_p$ = 0.85(77.89/59.89) = 1.106, and $L_p$ = 1 + 3(1.106) = 4.4 μg/L. On the other hand, if the chemist claims total ignorance about measurements in the range of zero to 2.55 μg/L and reports $Y \leq$ MDL, $L_p$ is computed from equation 10, giving $L_p$ = 2(3)(0.85)/[1 − (9)(68.89)] = 5.86 μg/L. This makes the situation seem considerably worse than the value of $L_p$ = 4.4 μg/L obtained when the chemist reports the numerical value $Y$ = 1 μg/L.

**Table 3—Estimates of $\sigma_b$, $\kappa$, $L_c$ ($=k_c\sigma_b$), and MDL ($=3\sigma_b$) for lead.**

| Laboratory | $\sigma_b$ (μg/L) | $\kappa$ | $k_c$ | $L_c$ (μg/L) | MDL (μg/L) |
|---|---|---|---|---|---|
| A | 0.85 | 0.12 | 8.3 | 7.16 | 2.55 |
| B | 0.52 | 0.13 | 7.8 | 4.06 | 1.56 |
| C | 0.34 | 0.09 | 11.1 | 3.77 | 1.02 |
| D | 0.52 | 0.10 | 10.0 | 5.20 | 1.56 |
| E | 0.66 | 0.10 | 10.0 | 6.60 | 1.98 |

Note: $L_c = k_c\sigma_b = \sigma_b/\kappa$ and MDL = 3 $\sigma_b$.

**Table 4—Example values of $\sigma_p$ and $L_p$ for some reported values of Y.**

| Reported Y (μg/L) | $\sigma_p$ (μg/L) | $L_p$ (μg/L) |
|---|---|---|
| 1 | 1.106 | 4.4 |
| Y < MDL | | 5.9 |
| 3 | 1.149 | 6.4 |
| 4 | 1.264 | 7.8 |
| 5 | 1.391 | 9.2 |
| 6 | 1.528 | 10.6 |
| 8 | 1.828 | 13.5 |
| 10 | 2.149 | 16.4 |

**Example—organic chemicals.** This second example uses data on six organic chemicals (Clayton *et al.*, 1986). A single quantity of uncontaminated sediment was used as the source matrix for all test specimens. Standard solutions containing known amounts of the analytes (in acetone) were used to spike the sediment matrix to target concentration levels of approximately 0.2 μg/L, 0.8 μg/L and 1.0 μg/L. The sediments were then extracted and the extracts were analyzed by gas chromatography. Control samples (spike = 0) were handled in a similar manner.

Figure 5 is an example plot for chloronaphthalene. The estimated values for the six chemicals are given in Table 5. The estimated values of $\sigma_b^2$ for anthracene and fluoranthene were about $10^{-6}$, but could statistically be considered as zero. The true variance cannot be negative and, for practical reasons, we are reluctant to report the variance as zero. Therefore, for these two chemicals, the variances of the controls (spike = 0) were used to compute the results in Table 5.

## Summary

This paper has presented Pallesen's total variance model (Pallesen, 1985) that stipulates both random analytical error can be used to the precision of measurements at low concentration. The method detection limit (MDL) was defined in the usual way, in terms of a multiple of the standard deviation of the background noise, ($\sigma_b$). The quantity $\sigma_b$ can be estimated by regression using the proposed model, $\sigma_e^2 = \sigma_b^2 + (k\mu)^2$. This was illustrated using measurements on lead in wastewater and organic chemicals in soil. A Characteristic Limit, $L_c$, was defined as the concentration where the variance of background error equals the variance of random analytical errors. At low concen-

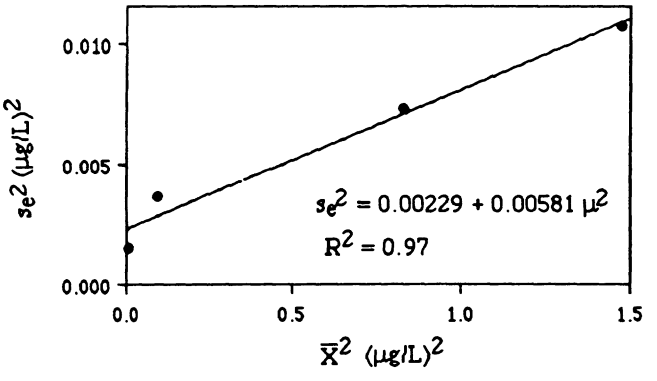



**Figure 5—Plot of $s_e^2$ vs. $\bar{x}^2$ for 2-chloronaphthalene.**

**Table 5—Estimates of the parameters $\sigma_b^2$, $\kappa$, the Characterstic Limit, and the MDL.**

| Chemical | $\sigma_b^2$ $(\mu g/L)^2$ | $\sigma_b$ ($\mu$g/L) | $\kappa^2$ | $\kappa$ | $k_c$ | $L_c$ ($\mu$g/L) | MDL ($\mu$g/L) |
|---|---|---|---|---|---|---|---|
| 2-Chloronaphthalene | 0.00229 | 0.048 | 0.0058 | 0.076 | 13.11 | 0.63 | 0.14 |
| Dimethylphthalate* | 0.00165 | 0.041 | 0.0103 | 0.101 | 9.86 | 0.40 | 0.12 |
| Hexachlorobenzene | 0.00006 | 0.008 | 0.0054 | 0.073 | 13.65 | 0.11 | 0.02 |
| Anthracene | 0.00011 | 0.010 | 0.0055 | 0.074 | 13.54 | 0.14 | 0.03 |
| Phenanthrene | 0.00022 | 0.015 | 0.0034 | 0.058 | 17.21 | 0.26 | 0.04 |
| Fluoranthene | 0.00012 | 0.010 | 0.0090 | 0.095 | 10.53 | 0.11 | 0.03 |

* One outlier removed.

trations, below $L_c$, background error dominates the analytical error; at high concentrations random analytical error dominates. A Limit of Guaranteed Purity was defined as the largest true concentration that is plausible, at a high level of confidence, given a particular measured concentration. This limit can be calculated even when the observed value is below the limit of detection.

## Acknowledgments

**Authors.** P. M. Berthouex is on staff at The University of Wisconsin—Madison in the Department of Civil and Environmental Engineering. D. Robert Gan is with Eder Associates Consulting Engineers in Madison, Wisconsin. Correspondence should be addressed to Prof. P. M. Berthouex, Dept. of Civil and Environmental Engineering, University of Wisconsin—Madison, 1415 Johnson Drive, Madison, WI 53706.

*Submitted for publication March 4, 1992; revised manuscript submitted October 29, 1992; accepted for publication January 21, 1993. The deadline for discussions of this paper is January 15, 1994. Discussions should be submitted to the Executive Editor. The authors will be invited to prepare a single Closure for all discussions received before that date.*

## References

American Chemical Society, Committee on Environmental Improvement (1983) Principles of Environmental Analysis. *Anal. Chem.*, **55,** 2210.

Berthouex, P. M. (1991) A Study of the Precision of Lead Measurements at Concentrations Near the Method Limit of Detection. Technical Report No. 9, Wisconsin Consortium for Applied Water Pollution Control Research, University of Wisconsin—Madison, Wis.

Clayton, C. A., Hines, J. W., Hartwell, T. D., and Burrows, P. M. (1986) Demonstration of a Technique for Estimating Detection Limits with Specified Assurance Probabilities, Report RTI/2575/05-01F. Office of Standards and Regulations, U.S. EPA, Washington, D.C.

Gilbert, Richard O. (1987) Statistical Methods for Environmental Pollution Monitoring, Van Nostrand Reinhold Co., New York, N.Y.

Glaser, J. A., Foerst, D. L., McKee, G. D., Quave, S. A., and Budde, W. L. (1981) Trace analyses for wastewaters, *Environ. Sci. Technol.*, **15,** 1426.

Holland, D. M., and McElroy, F. F. (1986) Analytical Method Comparison by Estimates of Precision and Lower Detection Limit. *Environ. Sci. Technol.*, **20,** 1157.

Hunt, D. T. E., and Wilson, A. L. (1986) The Chemical Analysis of Water, 2nd ed., The Royal Society of Chemistry, London, Eng.

Kaiser, H. H., and Menzes, A. C. (1968) Two Papers on the Limit of Detection of a Complete Analytical Procedure. Adam Hilger Ltd, London, Eng.

Kaiser, H. H. (1970) Quantitation in Elemental Analysis, Part II. *Anal. Chem.*, **42,** 26A.

Pallesen, Lars (1985) The Interpretation of Analytical Measurements Made Near the Limit of Detection, unpublished report, IMSOR, Technical University of Denmark.

Porter, Paul S., Ward, R. C., and Bell, H. F. (1988) The Detection Limit. *Environ. Sci. Technol.*, **22,** 856.

Rhodes, R. C. (1981) Much Ado About Next to Nothing, Or What to Do with Measurements Below the Detection Limit, *Environmetrics 81: Selected Papers,* SIAM-SIMS Conference Series No. 8, Philadelphia, 157.