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Capability of detection

Part 7: Methodology based on stochastic properties of instrumental noise

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National foreword

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Capability of detection —

Part 7: Methodology based on stochastic properties of instrumental noise

Capacité de détection —

Partie 7: Méthodologie basée sur les propriétés stochastiques du bruit instrumental

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Foreword

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ISO 11843-7 was prepared by Technical Committee ISO/TC 69, *Application of statistical methods*, Subcommittee SC 6, *Measurement methods and results*.

ISO 11843 consists of the following parts, under the general title *Capability of detection*:

— *Part 1: Terms and definitions*

— *Part 2: Methodology in the linear calibration case*

— *Part 3: Methodology for determination of the critical value for the response variable when no calibration data are used*

— *Part 4: Methodology for comparing the minimum detectable value with a given value*

— *Part 5: Methodology in the linear and non-linear calibration cases*

— *Part 6: Methodology for the determination of the critical value and the minimum detectable value in Poisson distributed measurements by normal approximations*

— *Part 7: Methodology based on stochastic properties of instrumental noise*

Introduction

The series of ISO 11843 is based on the probability distributions of the net state variable (measurand) for both the linear and nonlinear calibration situations. The focus is implicitly, though sometimes explicitly, on the uncertainty associated with an estimate of the measured response predominantly coming from the baseline noise in instrumental analysis. In many, if not most, analytical instruments, the baseline noise is considered the prime cause of uncertainty when the sample amount is as low as the minimum detectable value. Within its domain of applicability, the method given in this part of ISO 11843 can dispense with the repetition of real samples, thus helping to improve global environments by saving time and energy that would be required by repetition.

The basic concept of ISO 11843-7 is the mathematical description of the probability distribution of the response variable in terms of mathematically well-defined random processes. This description straightforwardly leads to the minimum detectable value. As for the relation of the response and measurand, linear and nonlinear calibration functions can be applied. In this manner, compatibility with ISO 11843-2 and ISO 11843-5 is ensured.

The definition and applicability of the minimum detectable value are described in ISO 11843-1 and ISO 11843-2; the definition and applicability of the precision profile are described in ISO 11843-5. The precision profile expresses how the precision changes depending on the net state variable. ISO 11843-7 specifies the practical use of the fundamental concepts in ISO 11843 in case of the background noise predominance in instrumental analysis.

The minimum detectable value, x_{d}, is generally expressed in the unit of the net state variable. If the calibration function is linear, the SD or CV of the response variable estimated in this part of ISO 11843 can linearly be transformed to the SD or CV of the net state variable, which in turn can be used for the estimation of the minimum detectable value, x_{d}.

If the calibration function is nonlinear, the precision profile of the response variable in this part of ISO 11843 needs to be transformed to the precision profile of the net state variable as shown in ISO 11843-5. In this situation, the contents of ISO 11843-5 can be used for this purpose without the slightest modification.

INTERNATIONAL STANDARD ISO 11843-7:2012(E)

Capability of detection —

Part 7: Methodology based on stochastic properties of instrumental noise

1 Scope

Background noise exists ubiquitously in analytical instruments, whether or not a sample is applied to the instrument. This part of ISO 11843 is concerned with mathematical methodologies for estimating the minimum detectable value in case that the most predominant source of measurement uncertainty is background noise. The minimum detectable value can directly and mathematically be derived from the stochastic characteristics of the background noise.

It specifies basic methods to

— extract the stochastic properties of the background noise,

— use the stochastic properties to estimate the standard deviation (SD) or coefficient of variation (CV) of the response variable, and

— calculate the minimum detectable value based on the SD or CV obtained above.

The methods described in this part of ISO 11843 are useful for checking the detection of a certain substance by various types of measurement equipment in which the background noise of the instrumental output predominates over the other sources of measurement uncertainty. Feasible choices are visible and ultraviolet absorption spectrometry, atomic absorption spectrometry, atomic fluorescence spectrometry, luminescence spectrometry, liquid chromatography and gas chromatography.

2 Normative references

The following referenced documents are indispensable for the application of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 11843-1:1997, *Capability of detection — Part 1: Terms and definitions*

ISO 11843-2:2000, *Capability of detection — Part 2: Methodology in the linear calibration case*

ISO 11843-5:2008, *Capability of detection — Part 5: Methodology in the linear and non-linear calibration cases*

ISO 3534-1, *Statistics — Vocabulary and symbols — Part 1: General statistical terms and terms used in probability*

ISO 3534-2, *Statistics — Vocabulary and symbols — Part 2: Applied statistics*

ISO 3534-3, *Statistics — Vocabulary and symbols — Part 3: Design of experiments*

ISO 5725-1, *Accuracy (trueness and precision) of measurement methods and results — Part 1: General principles and definitions*

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 3534-1, ISO 3534-2, ISO 3534-3, ISO 5725-1, ISO 11843-1, ISO 11843-2, ISO 11843-5 and the following apply. A list of symbols and abbreviated terms used in this document is provided in Annex A.

3.1
precision profile
<detection capability> mathematical description of the standard deviation (SD) of the response variable [$\sigma_Y(X)$] or net state variable [$\sigma_X(X)$] as a function of the net state variable.

[ISO 11843-5:2008, 3.4]

NOTE 1 The coefficient of variation (CV) of the response variable or net state variable as a function of the net state variable is also referred to as a precision profile.

NOTE 2 Precision means the SD or CV of the observed response variable or SD or CV of the net state variable when estimated by the calibration function (ISO 11843-5).

3.2
minimum detectable value of the net state variable
x_d
value of the net state variable in the actual state that will lead, with probability 1 – β, to the conclusion that the system is not in the basic state

NOTE 1 Under the assumption that the SD, $\sigma_X(X)$, of the net state variable is constant [$(\sigma_X(X) = \sigma_X$], the minimum detectable value, x_d, is defined as

$$x_d = (k_c + k_d)\sigma_X \quad (1)$$

where

k_c denotes a coefficient to specify the probability of an error of the first kind;

k_d is a coefficient to specify the probability of an error of the second kind.

If the SD, σ_Y, of the response variable is assumed to be constant [$\sigma_Y(X) = \sigma_Y$], then the minimum detectable value can be calculated by the following equation:

$$x_d = (k_c + k_d)(\sigma_Y/|dY/dX|) \quad (2)$$

where $|dY/dX|$ denotes the absolute value of the slope of the linear calibration function and is constant.

NOTE 2 If the net state variable is normally distributed, the coefficients $k_c = k_d = 1{,}65$ specify the probabilities of an error of the first and second kinds (= 5 %) and Formula (1) can simply be written as $x_d = 3{,}30\sigma_X$.

NOTE 3 If $k_c = k_d = 1{,}65$, Formula (1) takes the form that $\sigma_X / x_d = 1/3{,}30 = 30$ %. Therefore, x_d can be found in the precision profile. x_d is located at X, the CV of which is 30 %.

NOTE 4 Different types of precision profiles are defined, but they can be transformed to each other.

For example, the SD, $\sigma_Y(X)$, of the response variable can be transformed to the SD, $\sigma_X(X)$, of the net state variable by means of the absolute value of the derivative, $|dY/dX|$, of the calibration function [$Y = f(X)$]: $\sigma_X(X) = \sigma_Y(X)/|dY/dX|$ (ISO 11843-5). This treatment is an approximation, the extent of which depends on local curvature, involving d^2Y/dX^2.

NOTE 5 Adapted from ISO 11843-5:2008.

4 Quantitative analysis and background noise

4.1 Error sources of analysis

The quantitative analysis to obtain a measurand from a sample is generally considered to consist of preparation, instrumental analysis, data handling and calibration. These steps of analysis are mechanically independent of each other and so are probabilistically independent as well.

This part of ISO 11843 applies only to instrumental analysis. However, the errors from the other steps affect the error of the final value of the measurand, as well. That is, the combined uncertainty associated with an estimate

of the measurand depends on the propagation of all uncertainties relating to the relevant steps. The following conditions are necessary for the use of ISO 11843-7.

At concentrations near the minimum detectable value in chromatography, the error from the sample injection into a chromatograph is even less important (e.g. CV = 0,3 % in a recent apparatus) than the background noise (CV = 30 % by definition). If the importance of a factor other than noise is comparable to that of the noise, the methodologies of this part of ISO 11843 are not applicable.

Data handling is usually a process to extract a signal component from noisy instrumental output such as peak height or area, which is a relative height of a summit of a peak-shaped signal or integration of intensities over a signal region, respectively. The statistical influences of this process are the major concern of this part of ISO 11843. The use of a digital or analogue filter can also be taken into account, if the noise after the filtration is analysed for this purpose.

4.2 Random processes in background

Typical examples of the response variable are area and height measured in chromatography. In this part of ISO 11843, intensity difference [Formula (6)] and area [Formulae (10) and (11)] are taken as the difference and summation of intensities Y_i of instrumental output. The response variables are usually independent of each other even if they are obtained from consecutive measurement by the same instrument. On the other hand, the consecutive intensities Y_i are formulated as a time-dependent random process, and in many cases, can be considered 1/f noise.[1]

The power spectrum, $P(f)$, of 1/f noise has a slope inversely proportional to frequency, f:

$$P(f) \propto \frac{1}{f} \tag{3}$$

when f is near zero.

In mathematical theory, the simplest model of random processes is the white noise. Let w_i denote the random variable of the white noise at point i. By definition, the mean of the white noise is zero and the SD, $\tilde{w}$, of the white noise is constant at every point i. A prominent feature of the white noise is that the noise intensities, w_i and w_j, are independent of each other, if $i \neq j$.

The Markov process is a mathematical model in which the intensities, M_i and M_j, are not independent of each other ($i \neq j$). The Markov process is treated as a major component of time-dependent changes of instrumental output [see Formula (9)]. The Markov process at point i is defined to take the form:

$$M_i = \rho M_{i-1} + m_i \tag{4}$$

where

m_i denotes the random variable of the white noise at point i ;

ρ is a constant parameter ($-1 < \rho < 1$).

5 Theories for precision

5.1 Theory based on auto-covariance function

A theory which was proposed by Winefordner[2][3][4] and his co-workers is based on an auto-covariance function

$$\psi(\tau_s) \equiv E\left[Y_{t_0+\tau_s} Y_{t_0}\right] \tag{5}$$

where $E[\cdot]$ denotes the mean of a random variable inside the square brackets over t_0.

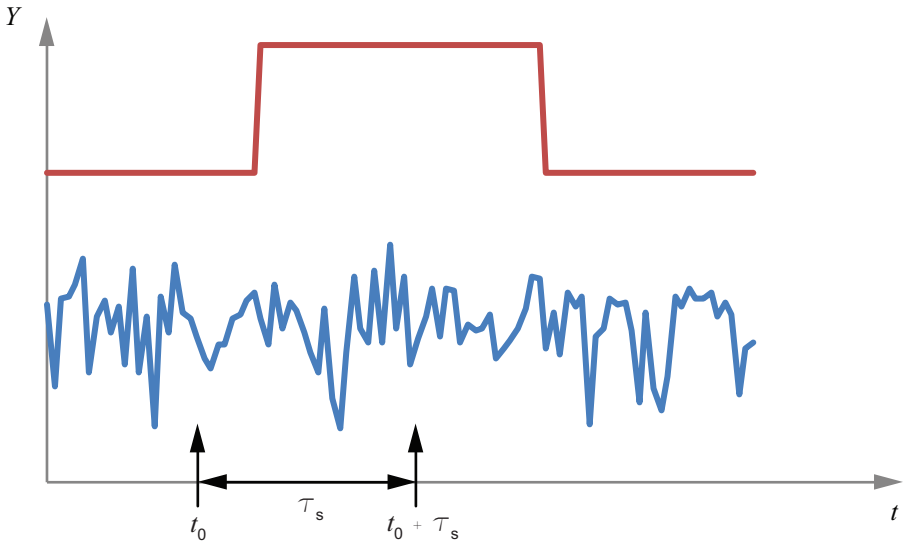


Figure 1 — Signal (upper line) and noise (lower line) with intensity difference

The upper part of Figure 1 depicts the signal as (an approximation to) a rectangular pulse. Noise (constituting background) on the signal is depicted as the oscillatory curve in the lower part of the figure. t_0 denotes a time value on the background portion of the signal and $t_0 + \tau_s$ denotes a time value on the signal itself. The measurement (signal reading) is the difference in intensities at times t_0 and $t_0 + \tau_s$. The value of the signal would be zero at t_0 in the absence of background noise. The signal has a finite value at $t_0 + \tau_s$ when a sample is measured. In the ISO 11843-7 measurement model, the signal and noise are superimposed, and this mixed random process takes the value Y_i at time t_i. The intensities at times t_0 and $t_0 + \tau_s$ are described as Y_{t_0} and $Y_{t_0+\tau_s}$, respectively, and the intensity difference is given by Formula (6).

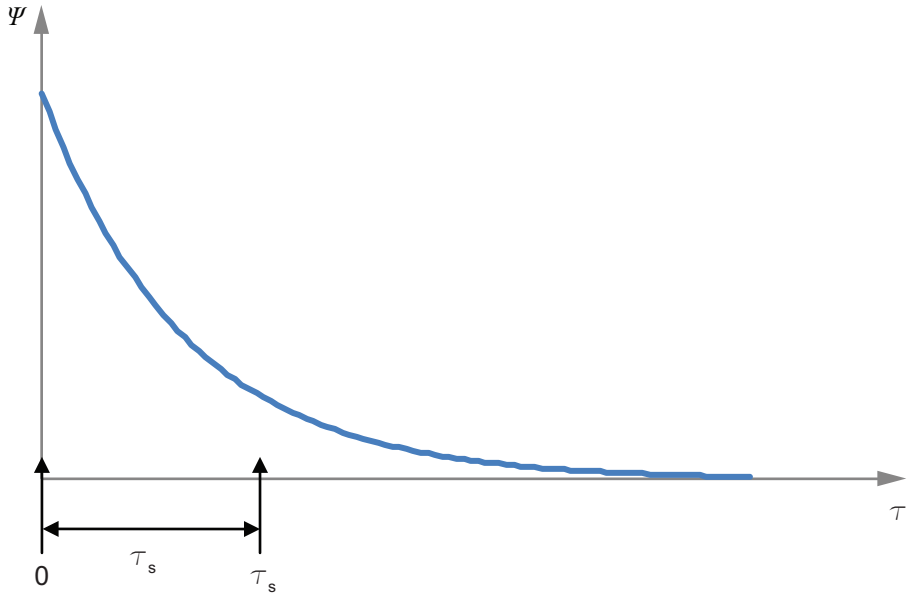


Figure 2 — Auto-covariance function of noise

The difference between the values of the auto-covariance function, $\psi(\tau)$, at 0 and τ_s gives the right side of Formula (7).

Near the minimum detectable value, which is dictated by the background fluctuation, intensity difference often applies in analytical optical spectrometry. The definition of intensity difference, e.g. signal reading corrected for background, is[2][3][4]

$$\Delta Y = Y_{t_0+\tau_s} - Y_{t_0} \tag{6}$$

Here, ΔY corresponds to the response variable Y. The variance of the intensity difference is written as shown in Formula (7)[2][3][4]. [For the derivation of Formula (7), see Annex B.]

$$\sigma_{\Delta Y}{}^2 = 2\left[\psi(0) - \psi(\tau_s)\right] \tag{7}$$

Formula (7) is of practical use when the actual auto-covariance functions, $\psi(0)$ and $\psi(\tau_s)$, are known from the observation of background noise as shown in Figure 2. The substitution of Formula (7) for Formula (2) ($\sigma_Y = \sigma_{\Delta Y}$) leads to the minimum detectable value.

Use can be made of the Wiener-Khintchine theorem,[5] which relates the auto-covariance function to the power spectral density through the Fourier transform:

$$\psi(\tau_s) = \int_0^\infty S_b(f)\left|G(f)\right|^2 \cos(2\pi f \tau_s)\,\mathrm{d}f \tag{8}$$

where

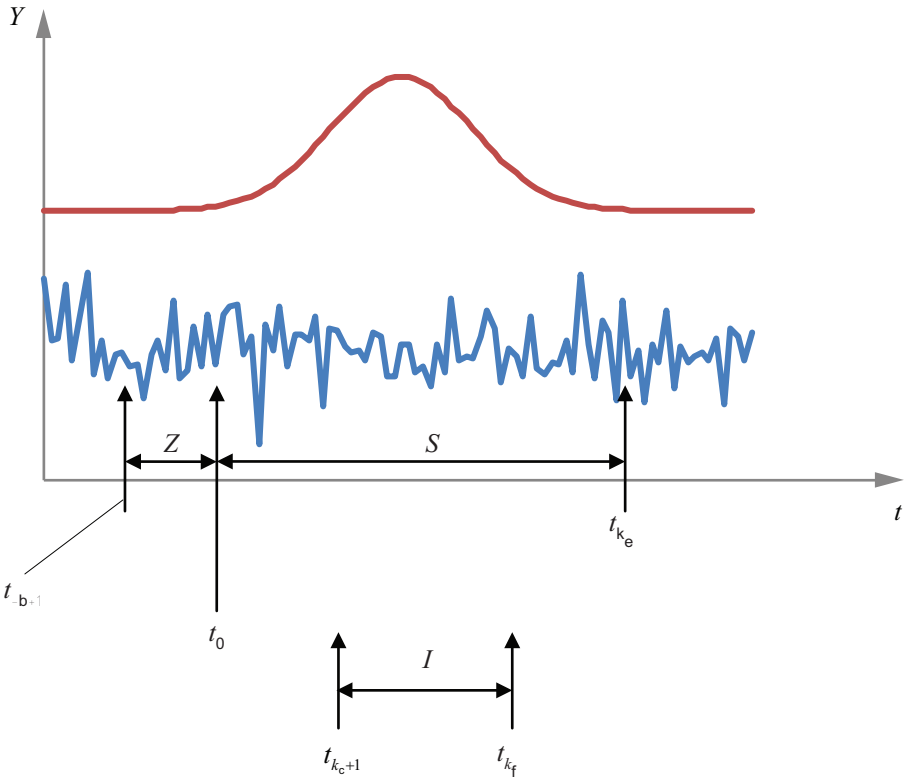
$S_b(f)$ denotes the power spectrum of the observed background noise;

$G(f)$ is the frequency response of the (linear) read-out system.

Formula (8) indicates the estimation of the measurement SD, Formula (7), through the noise power spectrum.

5.2 Theory based on power spectrum

A theory based on the power spectrum of the baseline, which is called FUMI (function of mutual information) [6][7][8], provides the SD values of the measured area and height in instrumental analysis. These measured values are the integration of the instrumental output over the integration region, as illustrated in Figure 3. If the signal (shape and size) is invariant, the error of measured area or height, as long as it comes from the noise alone, is equal to the area created by the noise over the integration region. That is, the measurement error is the same as the noise-created area. The SD of the noise-created areas coincides with the SD of measured heights or areas.



Key

Z zero window

S signal region

I integration region

(Additional symbols are explained in Annex A.)

Figure 3 — Signal and noise with zero window and integration area

The number of data points over the integration region is $k_f - k_c$.

In the FUMI theory, the noise intensity, Y_i, at point i is described as the mixed random processes of the white noise and Markov process:

$$Y_i = w_i + M_i \tag{9}$$

The purpose of the FUMI theory is to estimate the SD of the noise-created areas, A_F, over the integration region (see Figure 3).

In practice, especially chromatography, different modes of integration are adopted as illustrated in Figure 4. The measurement is of the integrated intensities above the baseline, which is horizontal or oblique within the domain $[k_c + 1, k_f]$. The horizontal baseline is horizontally drawn from the intensity (corrected) at the zero point, and the oblique line is drawn between the intensities at the edges of the signal region $[0, k_e]$. The latter is often useful for a slowly changing background, called “drift” in chromatography.

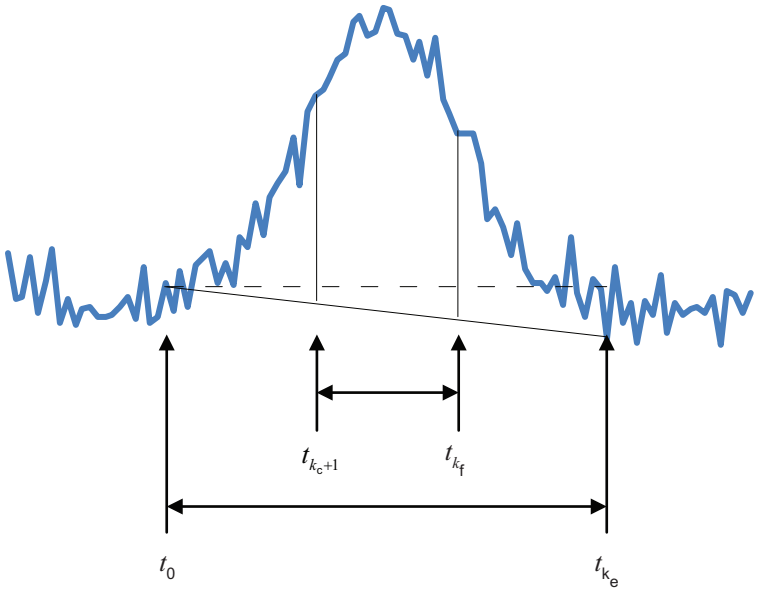


Figure 4 — Integration modes over horizontal line (broken line) and oblique line (solid line) between t_{k_c+1} and t_{k_f}

The noise-created area, which is the area between the random path and horizontal line over the integration region without signal, can be written as:

$$A_F = \sum_{i=k_c+1}^{k_f} Y_i \Delta t \tag{10}$$

where the noise intensity, Y_i, is described by Formula (9) and Δt is the time interval between consecutive data. Here, A_F means the response variable Y.

If the oblique line is used as the baseline, the noise-created area takes the form:

$$A_F = \left(\sum_{i=k_c+1}^{k_f} Y_i \Delta t \right) - A_T \tag{11}$$

where A_T denotes the area of the trapezoid created by the oblique line, horizontal line and vertical lines at the edges of the integration region from $k_c + 1$ to k_f (see Figure 4). The area of the trapezoid in Figure 4 is taken with a negative sign. The area is taken with a positive sign if the oblique line lies above the horizontal line in the integration region and with a negative sign otherwise.

The general expression of the SD, σ_F, of noise-created areas is:

$$\sigma_F = \left(E\left[{A_F}^2 \right] \right)^{1/2} \tag{12}$$

where $E[\cdot]$ denotes the ensemble mean of a random variable inside the square brackets. It should be noted that $E[A_F] = 0$, since, by definition, the ensemble mean of the noise-created area over the horizontal line [the first term in the right side of Formula (11)] is zero and the ensemble mean of the trapezoid, A_T, is zero (also see Annex C).

The above derivation is based on the assumption that there exists no uncertainty of the zero level, i.e. $Y_0 = 0$. In practice, however, this type of uncertainty exists and should be taken into account. The measurement in chromatography is usually performed relative to the zero level, which is the average of background intensities over a region referred to here as a zero window (see Figure 3).

The squared SD, σ_Y^2, of measured areas (noise-created areas) within the zero window takes the form[6][7][8]:

$$\sigma_Y{}^2 = \sigma_Z{}^2 + \sigma_F{}^2 \tag{13}$$

where σ_Z^2 denotes the variance originating from the zero window and σ_F^2 is the variance from the measured area [σ_F given by Formula (12)]. The summary of the derivation of Formulae (14) and (15) is given in Annex C. The minimum detectable value can be obtained by the substitution of Formula (13) for Formula (2).

The variance, σ_Z^2, can be described as [6][7][8]

$$\sigma_Z{}^2 = \frac{(k_\mathrm{f} - k_\mathrm{c})^2}{b}\tilde{w}^2 + \frac{(k_\mathrm{f} - k_\mathrm{c})^2}{b^2(1-\rho)^2}\left(b - 2\rho\frac{1-\rho^b}{1-\rho} + \rho^2\frac{1-\rho^{2b}}{1-\rho^2}\right)\tilde{m}^2 \tag{14}$$

and the influence of the signal integration over the signal region takes the form: [6][7][8]

$$\sigma_F{}^2 = (k_\mathrm{f} - k_\mathrm{c})\tilde{w}^2 \quad \text{(first term)}$$

$$+ \frac{1}{(1-\rho)^2}\left(k_\mathrm{f} - k_\mathrm{c} - 2\rho\frac{1-\rho^{k_\mathrm{f}-k_\mathrm{c}}}{1-\rho} + \rho^2\frac{1-\rho^{2(k_\mathrm{f}-k_\mathrm{c})}}{1-\rho^2}\right)\tilde{m}^2 \quad \text{(second term)}$$

$$+ \rho^2\frac{1-\rho^{2k_\mathrm{c}}}{1-\rho^2}\left(\frac{1-\rho^{k_\mathrm{f}-k_\mathrm{c}}}{1-\rho}\right)^2\tilde{m}^2 \quad \text{(third term)}$$

$$+ a^2\tilde{w}^2 \quad \text{(fourth term)}$$

$$+ \left\{\alpha^2\frac{1-\rho^{2k_\mathrm{e}}}{1-\rho^2} - 2\alpha\left[\left(\frac{1-\rho^{k_\mathrm{f}-k_\mathrm{c}}}{1-\rho}\right)\rho^{k_\mathrm{e}+k_\mathrm{c}-1}\left(\frac{1-\rho^{-2k_\mathrm{c}}}{1-\rho^{-2}}\right)\right] + \sum_{i=1}^{k_\mathrm{f}-k_\mathrm{c}}\left(\frac{1-\rho^{k_\mathrm{f}-k_\mathrm{c}+1-i}}{1-\rho}\rho^{k_\mathrm{e}-k_\mathrm{c}-i}\right)\right\}\tilde{m}^2 \quad \text{(fifth term)}$$

(15)

where

$$\alpha = \frac{(k_\mathrm{f} - k_\mathrm{c})(k_\mathrm{f} + k_\mathrm{c} + 1)}{2k_\mathrm{e}} \tag{16}$$

$\tilde{w}$ denotes the SD of the white noise;

$\tilde{m}$ is the SD of the white noise included in the Markov process;

ρ is the constant parameter of the Markov process;

k_c, k_f and k_e are defined in Figures 3 and 4;

b denotes the number of consecutive data points in the zero window [$-b + 1$, 0].

The five terms in Formula (15) denote the following stochastic contributions to the measurement uncertainty:

— first term: the error from the white noise in the integration domain ($k_\mathrm{f} - k_\mathrm{c}$ data points);

— second term: the error from the Markov process in the integration domain ($k_\mathrm{f} - k_\mathrm{c}$ data points);

— third term: the influence of k_c data points between the zero point and the starting point of integration;

— fourth term: the effect of the white noise in the oblique baseline;

— fifth term: the effect of the Markov process in the oblique baseline.

6 Practical use of FUMI theory

6.1 Estimation of noise parameters

All the parameters necessary for applying the FUMI theory, i.e. Formulae (13) to (16), can be uniquely determined from the experimental data. The signal parameters (b, k_c, k_f, k_e) can be set according to the shape of a target peak, as shown in Figure 3. On the other hand, the noise parameters $(\tilde{w}, \tilde{m}, \rho)$ are automatically determined from the power spectral density of the noise, as described below.

The noise power spectral density results from the Fourier transform of noise data, Y_i. The Fourier and inverse Fourier transform are

$$\hat{Y}_k = \sum_{i=0}^{N-1} Y_i W^{ki} \tag{17}$$

$$Y_i = \frac{1}{N} \sum_{k=0}^{N-1} \hat{Y}_k W^{-ki} \tag{18}$$

where

N denotes the number of data points involved in the region of the Fourier transform;

$W = \exp[-j(2\pi/N)]$;

j is the imaginary unit.

The power spectral density, $P(k)$, of the random process, Y_i, is defined as

$$P(k) = \frac{\hat{Y}_k \overline{\hat{Y}_k}}{N} \tag{19}$$

where $\overline{\hat{Y}_k}$ is the conjugate number of $\hat{Y}_k$.

If the model noise described by Formula (9) is adopted, the power spectral density of Formula (19) can be described as[6][7][8]

$$P(k) = \frac{\tilde{m}^2}{(1-\rho)\left[(1-\rho)^2 + 4\pi^2 (k/N)^2\right]} + \tilde{w}^2 \tag{20}$$

The noise parameters ($\tilde{w}, \tilde{m}$ and ρ) needed for the FUMI theory can be determined by the nonlinear least squares fitting of Formula (20) to the power spectral density of the actual background noise.

The first term of the Fourier transform, $\hat{Y}_0$, included in Formulae (19) and (20) is the dc component, and the corresponding spectral density, $P(0)$, is neglected. The frequency, k, in Formula (20), which is the integer here, ranges from 1 to $N/2$ where $N/2$ is the Nyquist frequency. A typical example of Formula (20) is illustrated in Figure 5.

In practice, frequency, k, is often expressed as Hertz. Let Δt be the time interval between consecutive data points (the intervals of an analogue-to-digital converter used for the acquisition of data, Y_i). The frequency which corresponds to k (= 1, 2,…, $N/2$) is $k/(\Delta t\, N)$.

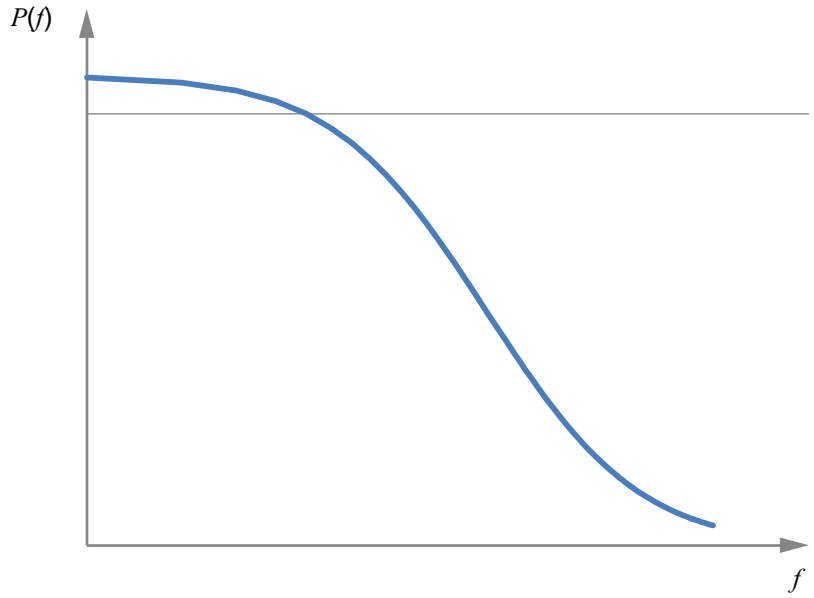


Figure 5 — Power spectral density of model noise

In practice, the power spectral density would be less smooth than the theoretical behaviour in Figure 5. If it is an observed one, it might contain small oscilations about a smooth signal.

6.2 Procedures for estimation of SD

The FUMI theory requires the instrumental output to estimate the SD of measured areas, which in turn leads to the minimum detectable value. The complete set of steps is illustrated in Figure 6.

Digital instrumental output such as chromatograms and spectra is required for extracting both the signal and noise parameters. The signal parameters involve the signal region ranging from point 0 to point k_e, the integration region from point $k_c + 1$ to point k_f, and the zero window from point 0 to $-b + 1$ (see Figure 3). The signal region is made up of $k_e + 1$ data points, the integration region of $k_e - k_c$ data points, and the zero window b data points.

The signal parameters are arbitrary, but the following instruction will be useful in practice. For a Gaussian signal like that in Figure 3, the signal region may be $\pm 3\sigma$ or $\pm 4\sigma$ around the signal centre, where σ denotes the standard deviation (width) and the signal centre is the mean of the Gaussian signal ($k_e = 6\sigma$ or 8σ). In many cases, the peak height or entire area is the typical measurement. For the peak height measurement, $k_f = k_c + 1$. For the entire area measurement, $k_f = k_e - 1$ and $k_c = 0$. In either measurement, the number of data points in the integration region is $k_f - k_c$. The integration over a part of the signal region, as shown in Figure 3, is also effective from the viewpoint of precision. The zero window may be set empirically as a region even narrower than the signal region, as shown in Figure 3.

Unlike the signal parameters, the noise parameters ($\tilde{w}$, $\tilde{m}$ and ρ) are uniquely determined according to the stochastic properties of background noise. Some examples in liquid chromatography are given in Table 1. The first step is to identify a region from the background noise that has no significant signal contribution.

The second step is the Fourier transform of the background noise in this region to give the power spectral density according to Formula (20). If the number, N, of data points in Formula (20) is limited to the nth power of 2 in the fast Fourier transform (FFT) used, 512 or 1 024 data points will be appropriate for the FFT region for the signal region of 50 or 100 data points.

The third step is the least-squares fitting of the theoretical curve [Formula (20)] to the power spectral density obtained as mentioned above. A small number of data points in the FFT region (e.g. 32) have a tendency, in some situations, to bias the exact estimation of the noise parameters.

The signal and noise parameters determined as mentioned above are substituted for Formulae (13) to (16) to provide the final value of the FUMI theory (precision).

The applicability of the FUMI theory is rather wide, but there are two typical situations where it is not.

— One is that the predominant error source is not background noise. In mass spectroscopy, if the ionization process produces much more error than the noise, the FUMI theory underestimates the SD of measured areas.

— The other situation is where actual instrumental noise includes the noise that cannot successfully be approximated by the mixed processes of the white noise and Markov process. An example is spike noise of high intensity.

The minimum detectable value can be found graphically from the precision profile as the net state variable at which the CV of the net state variable is 30 %. This method is also applicable for the CV of the response variable, since the precision profile of the net state variable is identical to that of the response variable if the calibration function is linear.[9][10] In the case of nonlinear calibration, however, the precision profiles of the response variable and the net state variable are different. In this case, the method given in ISO 11843-5 applies to the transformation of the different precision profiles and the minimum detectable value can be estimated as well.

Table 1 — Example of noise parameters estimation in liquid chromatography[6]

	$\tilde{w}$	$\tilde{m}$	ρ
Experiment A	14	3,7	0,99
Experiment B	12	9,0	0,94
Experiment C	14	5,6	0,99

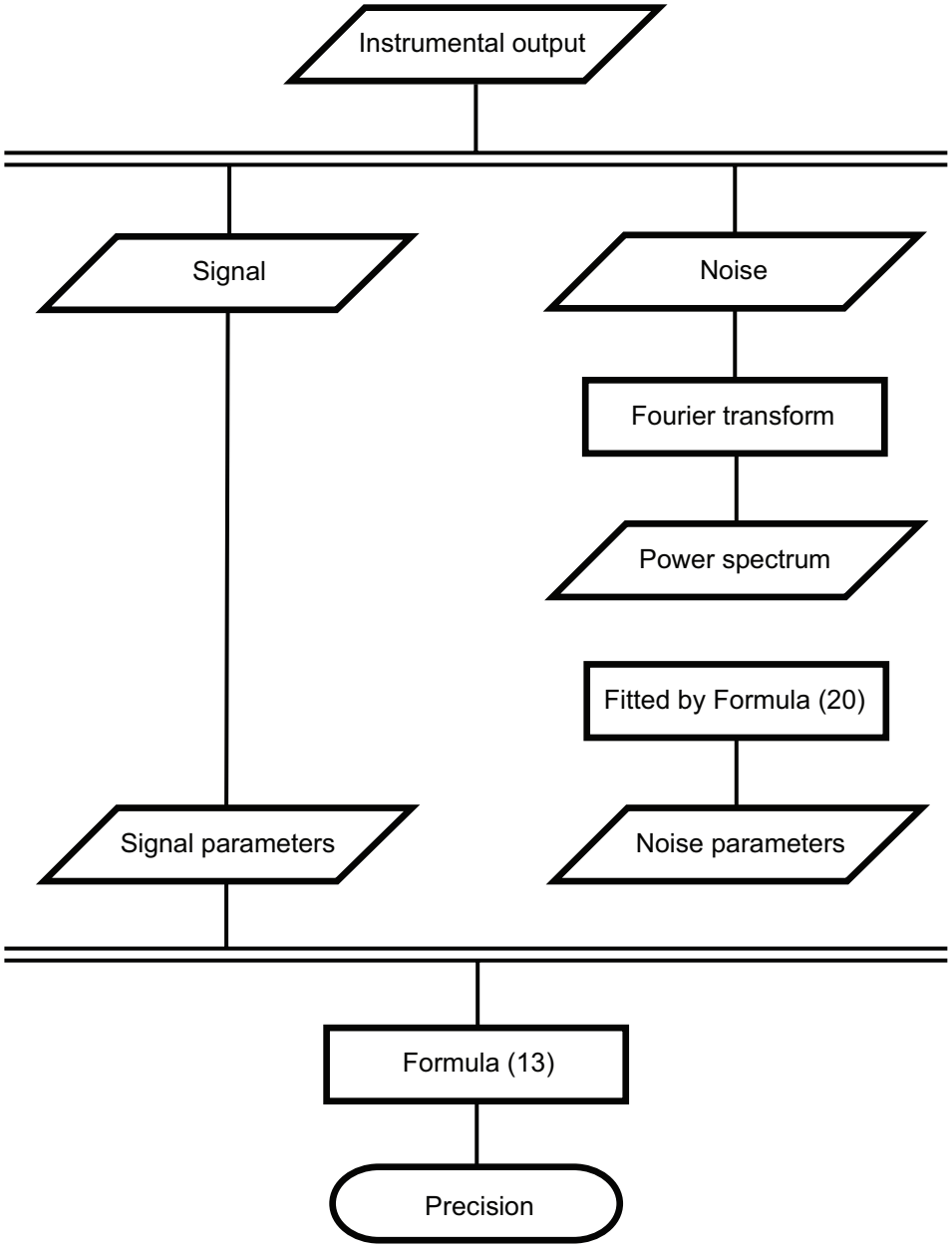


Figure 6 — Procedures of FUMI theory

Annex A
(informative)

Symbols and abbreviated terms used in this part of ISO 11843

SD	standard deviation
CV	coefficient of variation (SD divided by the mean)
X	net state variable
Y	response variable (measured area or height)
t_i	one of a set of uniformly spaced time values t_1, t_2, …
Δt	$t_{i+1} - t_i$, length of time interval for analogue-to-digital conversion in data acquisition
Y_i	intensity of instrumental output at time t_i, (sum of Y_i means Y)
Y_t	intensity of instrumental output at time t (sum of Y_t means Y)
x_d	minimum detectable value of net state variable
k_c	coefficient to specify the probability of an error of the first kind
k_d	coefficient to specify the probability of an error of the second kind
$\sigma_Y(X)$	SD of response variable as a function of X
$\sigma_X(X)$	SD of net state variable as a function of X
$\lvert dY/dX \rvert$	derivative of calibration function
$E[\cdot]$	mean of a random variable inside the square brackets
$\psi(\tau)$	auto-covariance function with lag τ, defined by Formula (5)
w_i	random variable at point i of the white noise with mean zero and SD $\tilde{w}$
$\tilde{w}$	SD of the white noise w_i
M_i	random variable of the Markov process at point i
m_i	white noise included in Markov process at point i, defined by Formula (4)
$\tilde{m}$	SD of the white noise m_i included in Markov process
ρ	ratio for retaining the previous state, defined by Formula (4)
A_F	noise-created area, which is the area created by the noise alone
FUMI	abbreviation of function of mutual information

Annex B
(informative)

Derivation of Formula (7)

The variance of the intensity difference between points t_0 and $t_0 + \tau_s$ can be written as: [2-4]

$$\sigma_{\Delta Y}{}^2 = E\left[\left(Y_{t_0+\tau_s} - Y_{t_0}\right)^2\right] = E\left[Y_{t_0+\tau_s}{}^2\right] + E\left[Y_{t_0}{}^2\right] - 2E\left[Y_{t_0+\tau_s} Y_{t_0}\right] \tag{B.1}$$

From the definition of the auto-covariance function [Formula (5)], the second term of the right side of Formula (B.1) can be described as

$$\psi(0) \equiv E\left[Y_{t_0}{}^2\right] \tag{B.2}$$

The stationarity assumption of the background fluctuation equalizes the first and second terms of the right side of Formula (B.1):

$$E\left[Y_{t_0+\tau_s}{}^2\right] = E\left[Y_{t_0}{}^2\right] \tag{B.3}$$

Under the stationarity assumption, this equation means that the variance of the background fluctuation is constant over time. Then, Formula (B.1) can be written as:

$$\sigma_{\Delta Y}{}^2 = 2\psi(0) - 2E\left[Y_{t_0+\tau_s} Y_{t_0}\right] \tag{B.4}$$

Noticing the definition of the auto-covariance [Formula (5)], we can obtain Formula (7).

Annex C
(informative)

Derivation of Formulae (14) to (16)

The fundamental assumption on the derivation of Formulae (14) to (16) is that the random variables of the white noise are independent of each other:

$$E\left[w_i w_j\right] = 0 \qquad \text{if } i \neq j \tag{C.1}$$

$$E\left[w_i w_j\right] = \tilde{w}^2 \qquad \text{if } i = j \tag{C.2}$$

$$E\left[m_i m_j\right] = 0 \qquad \text{if } i \neq j \tag{C.3}$$

$$E\left[m_i m_j\right] = \tilde{m}^2 \qquad \text{if } i = j \tag{C.4}$$

$$E\left[w_i m_j\right] = 0 \tag{C.5}$$

where Formula (C.5) holds true under any condition. The derivation in this annex takes the case of the oblique baseline, since the resulting equations can include the case of the horizontal baseline as well.

The slope of the oblique baseline passing the zero point ($Y_0 = 0$) and the intensity at k_e is Y_{k_e}/k_e. Therefore, the heights of the edges of the integration region are written as

$$\frac{Y_{k_e}}{k_e}\left(k_c + 1\right) \quad \text{at } k_c + 1 \tag{C.6}$$

$$\frac{Y_{k_e}}{k_e} k_f \qquad \text{at } k_f \tag{C.7}$$

where Y_i is given by Formula (9). The trapezoid created by the oblique line, horizontal lines and vertical lines (see Figure 4) has the area:

$$A_T = \alpha Y_{k_e} \tag{C.8}$$

where α is given by Formula (16). Formula (11) for the noise-created area takes the form:

$$A_F = \left(\sum_{i=k_c+1}^{k_f} Y_i \right) - \alpha Y_{k_e} \tag{C.9}$$

where Δt of Formula (11) is assumed to be unity. The variance of Formula (C.9) is the objective equation [Formula (15)].

Before the derivation, the sum of the Markov process is taken as a simple example of measured area. If $M_0 = 0$, then the Markov process defined by Formula (4) also takes the form:

$$M_1 = m_1 \tag{C.10}$$

$$M_2 = \rho m_1 + m_2 \tag{C.11}$$

...

$$M_k = \rho^{k-1} m_1 + \rho^{k-2} m_2 + \ldots + \rho m_{k-1} + m_k \tag{C.12}$$

The sum of the Markov process can be written as:

$$\left(\sum_{i=1}^{k} M_i \right) = (1 + \rho + \rho^2 + \ldots + \rho^{k-1}) m_1 + (1 + \rho + \rho^2 + \ldots + \rho^{k-2}) m_2 + \ldots + (1 + \rho) m_{k-1} + m_k \tag{C.13}$$

By definition, $E[m_i] = 0$, the mean of Formula (C.13) is zero, but its variance has a finite value:

$$E\left[\left(\sum_{i=1}^{k} M_i \right)^2 \right] = (1 + \rho + \rho^2 + \ldots + \rho^{k-1})^2 \tilde{m}^2 + (1 + \rho + \rho^2 + \ldots + \rho^{k-2}) \tilde{m}^2 + \ldots + (1 + \rho) \tilde{m}^2 + \tilde{m}^2 \tag{C.14}$$

This equation takes a simple form:

$$E\left[\left(\sum_{i=1}^{k} M_i \right)^2 \right] = \frac{\tilde{m}^2}{(1-\rho)^2} \left(k - 2\rho \frac{1-\rho^k}{1-\rho} + \rho^2 \frac{1-\rho^{2k}}{1-\rho^2} \right) \tag{C.15}$$

The substitution of $k_f - k_c$ for k in Formula (C.15) leads to the second term of Formula (15). The first term of Formula (15) is the sum of the white noise over $k_f - k_c$ points. The other terms of Formula (15) can be obtained by the consideration of Formulae (C.1) to (C.5) and (C.9) to (C.15)[7]. In addition, $E[A_F] = 0$ under the assumption that $E[w_i] = 0$ and $E[m_i] = 0$.

The uncertainty associated with the zero level setting can be derived in a similar way.[8] The zero level, L_0, is defined here as the average of b consecutive data:

$$L_0 = \frac{1}{b} \left(\sum_{i=1}^{b} Y_i \right) \tag{C16}$$

where Y_i is given by Formula (9). The zero level setting means that the background correction is made throughout the integration region, creating the following area within the integration region:

$$(k_f - k_c) L_0 \tag{C.17}$$

Therefore, the uncertainty associated with the zero level takes the form:

$$\sigma_Z{}^2 = (k_f - k_c)^2 E\left[L_0{}^2 \right] \tag{C.18}$$

where $E[L_0] = 0$ by definition. If Formula (C.13) is used instead of $\sum_{i=1}^{b} Y_i$ in Formula (C.16), the resulting equation corresponds to the second term of Formula (14).[8] The first term of Formula (14) is the influence of the white noise only.

Bibliography

[1] INGLE, J.D. Jr. and S.R. CROUCH. *Spectrochemical Analysis*. Prentice-Hall, Inc., New Jersey, 1988

[2] ALKEMADE, C.Th.J., W. SNELLEMAN, G.D. BOUTILIER, B.D. POLLARD, J.D. WINEFORDNER, T.L. CHESTER and N. OMENETTO. A review and tutorial discussion of noise and signal-to-noise ratios in analytical spectrometry-I. Fundamental principles of signal-to-noise ratios. *Spectrochim. Acta*, **33B**, pp. 383-399, 1978

[3] BOUTILIER, G.D., B.D. POLLARD, J.D. WINEFORDNER, T.L. CHESTER and N. OMENETTO. A review and tutorial discussion of noise and signal-to-noise ratios in analytical spectrometry-II. Fundamental principles of signal-to-noise ratios. *Spectrochim. Acta*, **33B**, pp. 401-415, 1978

[4] ALKEMADE, C.Th. J., W. SNELLEMAN, G.D. BOUTILIER and J.D. WINEFORDNER. A review and tutorial discussion of noise and signal-to-noise ratios in analytical spectrometry-III. Multiplicative noises. *Spectrochim. Acta*, **35B**, pp. 261-270, 1980

[5] HINO, M. *Spectral Analysis (Supekutoru Kaiseki)*. Asakura Shoten, Tokyo, 1982

[6] HAYASHI, Y. and R. MATSUDA. Deductive prediction of measurement precision from signal and noise in liquid chromatography. *Anal. Chem.*, **66**(18), pp. 2874-2881, 1994

[7] HAYASHI, Y. and R. MATSUDA. Prediction of precision from signal and noise measurement in liquid chromatography: Mathematical relationship between integration domain and precision, *Chromatographia*, **41**, pp. 75-83, 1995

[8] POE, R.B., Y. HAYASHI and R. MATSUDA. Precision-optimization of wavelengths in diode-array detection in separation science. *Anal. Sci.*, **13**, pp. 951-962, 1997

[9] KOTANI, A., Y. YUAN, B. YANG, Y. HAYASHI, R. MATSUDA and F. KUSU. Selection of the optimal solvent grade for the mobile phase in HPLC with electrochemical detection based on FUMI theory. *Anal. Sci.*, **25**, pp. 925-929, 2009

[10] KOTANI, A., S. KOJIMA, Y. HAYASHI, R. MATSUDA and F. KUSU, Optimization of capillary liquid chromatography with electrochemical detection for determining femtogram levels of baicalin and baicalein on the basis of the FUMI theory. *J. Pharm. Biomed. Anal.*, **48**, pp. 780-787, 2008

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