GUIDING CONCEPTS RELATING TO TRACE ANALYSIS†

H. KAISER

Institut für Spektrochemie und angewandte Spektroskopie, 46 Dortmund, Bunsen-Kirchhoff-Str. 11, Germany

ABSTRACT

'Trace' is a term much used in colloquial language; it has many connotations and should not be 'appropriated' to denote 'scales of working' in chemistry. The concept *"scope of analysis"* is proposed instead. The quantities *"amount of substance"*, *"mass"* and *"concentration"* are critically considered and it is proposed that more use of a logarithmic presentation of concentration values should be made. The role of the *"blank portion"* of measured quantities with respect to trace determinations is pointed out; *"analytical signal"* and *"analytical noise"* are discussed. Linearization of the *"calibration function"* and elimination of the blank measures are required for extrapolation of calibration functions to low concentrations. The different calibration methods (σ, α, δ, ω) are presented; the importance of *"rating"* analysis and *"gradual"* analyses with coarsened scales is pointed out.

The 'type' of information, the *"informing power"* provided by a procedure and the *"information required"* by the analytical problem are discussed. The *"topological structure"* of a procedure is shown to be decisive for its applicability to trace determinations.

"Selectivity" and *"sensitivity"* are defined as metric quantities to be calculated from the *"calibration matrix"* of the procedure. High values of these two quantities are required for 'trace work'. *"Specificity"* is mentioned only. Finally some remarks about the *"limit of detection"* and the *"limit of guarantee of purity"* are made to clear up common mistakes, made when applying these useful concepts.

1. INTRODUCTION

Today about one third of all work in industrial chemical laboratories is said to be analytical in character, even if the chemists are not aware of this fact. Therefore we are observing an important change in the aspect of analytical chemistry as a whole. Formerly the main interest of the analyst was

---

† Not all scientific terms used in this article may be familiar to all readers, at least not in their specified narrow meaning. Several new terms also had to be defined for the subject of this paper.

To facilitate comprehension, a special notation has been used. A 'technical term' with specified meaning is set between double quotation marks (" ... "). When it is defined or appears for the first time with its full weight it is additionally printed in italics. Words which are used figuratively or with some allusion and for this reason should receive attention, are set between single quotation marks (' ... '). If a word is to be accentuated for correct comprehension of a phrase it is printed in italics. The symbol, : =, means equal (or better equivalent) by definition.

concentrated upon chemical reactions and operations used to solve isolated analytical problems. Now this whole field of applied science has become more closely integrated. Its intellectual structure has become apparent, a uniform nomenclature is being developed—slowly of course. Something like "*chemical analytics*", a comprehensive theory of chemical analysis, may emerge from all these efforts. The general problems connected with the determination of trace components had a stimulating effect in this respect. In this lecture concepts and relationships which are common to practically all work in the field of "trace determination" will be considered in a rather abstract way and without going into details of special analytical procedures.

2. THE CONCEPT OF 'TRACE'; SCALES OF WORKING

There seems to be considerable confusion about the definition of 'trace'. Some people propose that a constituent with concentration lower than 100 ppm should be named a trace. However, there are further proposals suggesting microtrace, nanotrace, picotrace and so on. Who will be able to keep this in mind without, from time to time, consulting a reference book? Standardization of nomenclature should lead to considerable simplification of the necessary vocabulary; the matter should become easier, not more complicated! The present wrestling with the standardization of the concept of trace seems to indicate that something in the approach may be wrong.

In relation to trace there are three different concepts of thinking and speaking. The first, prescientific in nature, deals with the tasks and assessments of practical life. The second is scientific and relates to the specific work of the analytical chemist. The third is more technical and deals with measuring techniques. Now the thesis is that the word 'trace' has been and still is part of the colloquial language of practical life; it has many shades of meaning. It can also be used to indicate a very small quantity, but in a vague way. However, its original meaning lies more in the sense of a track, a sign, or an effect. We may often be surprised by the fact that very small amounts of substances can have a very remarkable effect. Examples are abundant in biochemistry, semiconductor techniques, metallurgy, etc. The interest of the analyst in detecting and determining trace components is only due to such observed or expected effects. *Therefore, the word 'trace' is needed in its general qualitative meaning with all its many connotations.* It must not be stripped and degraded to a mere operator describing certain orders of magnitude in low concentrations. These can be described much better by numbers.

However there is a strange tendency, evident in glossaries and nomenclature documents, to make science easier by doing away with numbers and mathematical symbols. An IUPAC document *Recommendations on Nomenclature for Scales of Working in Analyses* in the *Information Bulletin*, February 1972, contains the following statement: 'Although numbers alone are sufficient, and indeed necessary, for the precise designation and classification of methods, it is convenient, both in written and oral communications, to designate the size ranges by suitable terms. The use of words is especially convenient when approximate ranges are to be indicated'. I fully agree with the first part of this statement, but I am afraid I must reject the second part.

The use of words *'where numbers alone are sufficient and necessary'* is by no means convenient, it is a source of endless misunderstanding. The actual problem is psychological: a clear and simple notation must be found which can be read *and spoken.* For instance, every chemist knows what the symbol pH 5 means.

In the same IUPAC recommendation a two-dimensional diagram for sample weight S and component concentration c is given. Both scales are logarithmic and by this simple trick a complete survey over the whole range of analyses is achieved. *Figure 1* shows this diagram in a slightly modified form.

Sample weight: S(in g)
Concentration: c(as decimal fraction)
Quantity of component: q(in g)

$$\log q = \log c + \log S$$
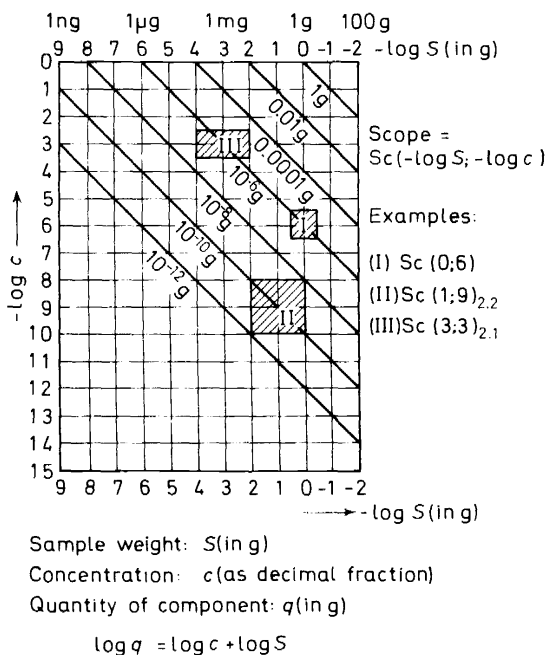
Figure 1. "Scope" of analysis: scales of working

That area of the diagram in which the analytical work in question lies may be called *"scope of analysis"*, symbolized in a mnemonic way by Sc and combined with the respective numbers in brackets. This is demonstrated for some cases in *Figure 1.* If the term "scope" is accepted, we may quite innocently continue to talk of microanalysis and trace determination, under the presupposition that the subject has once been exactly defined, for instance by Sc (5; 14).

'Scope 5; 14' is speakable, shorter and certainly clearer than the proposed verbose designation as 'ultra-micro-nano-trace-analyses'†.

It is remarkable that the sum of the two numbers in the parentheses

---

† In the IUPAC Recommendation (Information Bulletin No. 18) a *nano*trace lies between 10^{-6} ppm and 10^{-9} ppm. or simply 10^{-12} and 10^{-15}.

immediately gives the logarithm of the absolute amount of the respective component. The diagonals in this diagram are the lines of constant amounts.

It will be realized that the numbers indicating the "scope" are the negative decadic logarithms of S and c respectively. Since the values of S and c will in practically all cases be lower than unity, this convention results normally in positive numbers which is agreeable for writing and speaking. Negative numbers for S indicate sample weights greater than 1 g.

The numbers given for the "scope" should correspond to the *centre* of the area in the diagram (*Figure 1*) comprising the analytical activity in question. In order to keep this description clear and simple, only whole numbers (integers) should be given for the logarithms of S and c and—if not otherwise stated—the region about this centre should have unit square dimension, then comprising one order of magnitude both in sample weight and concentration. Other extensions can be indicated, by adding suffixes; some examples are given by the hatched areas in *Figure 1*.

This diagram may indeed bring a solution to the awkward problem of how to name and classify the analytical methods with respect to their "scope" in a precise and unambiguous manner. It is an 'open system', independent of the state of the art and the present technical requirements; it is purely descriptive, without assessment.

To complete this chapter, the third line of thought about the meaning of trace must be mentioned. The determination of 'trace' concentrations is very often a difficult problem regarding the measuring technique: at low concentrations the measurable quantity is composed of two parts, the useful "analytical signal" and the "analytical noise". This latter part may comprise any kind of accidental perturbations masking the signal. It may be very difficult to separate a relatively faint signal from the underlying analytical noise. With respect to this it has been proposed to designate small concentra-
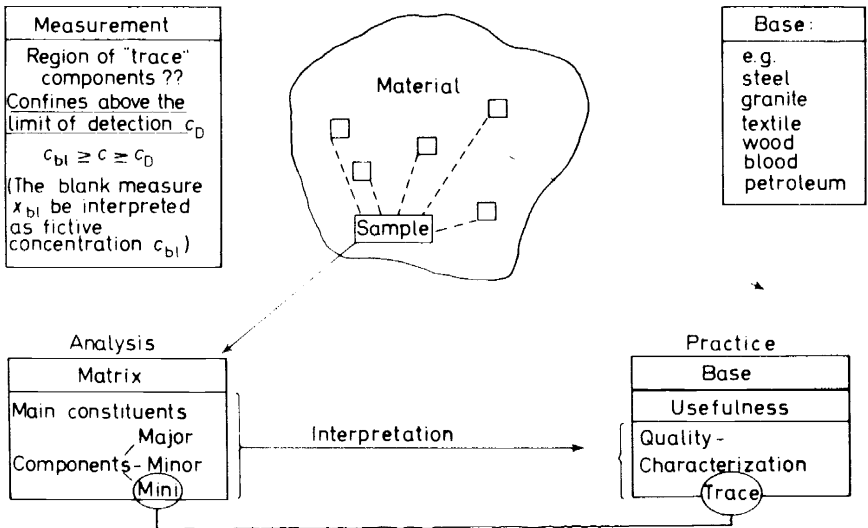

Figure 2. The logical place of the concept of "Trace"

tions as a 'trace' when the respective measure has a ratio of signal to noise smaller than unity. This, however, is confusing because the proposed characteristics may depend on the available equipment, the skill and patience of the observer and will change with technical progress. Furthermore, it has no relation at all to the importance of traces in chemistry and other sciences or in practical life. This proposal reflects only the professional worries of measurement specialists, and should therefore not be accepted.

The considerations of this section are represented in another, more condensed form in *Figure 2*, which, after the above remarks, will be self-explanatory.

3. QUANTIFICATION IN CHEMICAL ANALYSIS

In Section 2 three metric quantities, 'sample weight' S, 'concentration' c and 'quantity of component' q were used in the familiar way, without further explanation. This is not without problems. In analytical chemistry an important aim is to answer the question, how much of some substance (or several) is present in the sample? What precise meaning can the term 'how much' have in a scientific question of such unspecific generality? There are only two basic quantities which can be used to answer this question independent of all experimental parameters: *"amount of substance"* (symbol n, SI unit: mol) and *"mass"* (symbol m, SI unit: kg). However, they are not always applicable. Amount of substance† is defined only for substances conceived to consist of specified elementary units, such as atoms, molecules, electrons, etc. Mass as a purely physical quantity has no immediate connection to chemical problems, but it is closer to the practice of daily life in handling material of all kinds‡.

This embarrassing situation is overcome in practice by using relative values. The conventional term 'concentration' (symbol: c) however, which is used in chemical analysis for such relative values, has no unambiguous meaning. The resulting confusion needs clearing up—a rewarding task for IUPAC Commissions! A few remarks may be helpful:

(*a*) The original meaning of the word 'concentration' indicates the *process* of gathering around a centre. This meaning is still applicable in chemistry. (A concentrated solution has been subject to a *process* of concentration; it is then hard to say, that—as a result of such treatment—it *has* concentration.

---

† The author feels rather unhappy by this recent 'confiscation' of the old, commonly used term 'amount of...' with its broad meaning. The word is badly needed in scientific and non-scientific speech and therefore *must not* be reserved for a basic quantity "amount of substance" (SI unit: mol) which is not even applicable throughout chemistry. 'Quantity' is too overburdened to replace the confiscated word 'amount'. The author therefore had to be 'disobedient' in order to express his thoughts in this article.

If it is justified (?) to define "amount of substance" as a *'basic* quantity' (though not always applicable in chemistry) then a new term should be coined or chosen from less common words. This should indicate the main feature (indirect counting piece by piece).

‡ For liquids or gases, volumetric measurements are convenient and therefore in common use. This conceals how poor a substitute measure for the quantity of a substance its volume is. It is dependent on experimental parameters such as temperature and pressure, the state of aggregation, packing effects, adsorption, etc. Some of these influences are hardly controllable.

(b) In analytical chemistry, metallurgy and many technical fields dealing with the property of materials, 'concentration' is understood as the ratio of two measurable quantities of the same dimension (not necessarily the same unit!), indicating 'how much' of a specified substance is *contained in* another (in most cases the whole of the sample). "Concentration" in this meaning is a quantity having unit dimension (pure number); beyond that, it would be reasonable to use the same units for the physical quantities in the numerator and in the denominator, in order to make the value of the ratio independent of the special choice of units. However, concentration values (all of unit dimension)† are different when they are formed for "amount of substance", or for "mass" or "volume", or what else the case may be. The underlying quantity and also to which material or object the denominator of the ratio refers, whether to the whole of the sample or only to a part of it, or to some specified component, must be expressly stated. (When different meanings of "concentration" occur in the same context, they may be distinguished by suitable subscripts or other modifying signs.)

(c) Normally the concentration is expressed relative to the whole sample. When it is difficult to get hold of the measure for the whole sample, the concentration of a substance may be given relative to the concentration of another component present in the sample, usually the *"main constituent"*. By this division the unknown measure for the whole of the sample which occurs in both concentration values is eliminated. In other cases a reference substance (R) may be added in known amounts or weights and the concentration values for the components to be determined can be calculated with respect to this reference substance. The term *"concentration ratio"* (symbol: c_r) has been proposed in order to prevent such concentration values from being mistaken as referring to the whole sample‡.

(d) In the IUPAC *Manual of Symbols and Terminology for Physicochemical Quantities and Units* the term 'concentration' is defined as an operator in the sense of 'divided by volume' and is applied only to solutions. Here an indication of the original meaning is preserved (see (a)). This special and restricted meaning of the term concentration is against the widespread use of this word in other fields, and a concentration so defined mostly has not unit dimension.

(e) In order to bring this matter to an end, for 'concentration' in the sense of (b) and having unit dimension, the term *"content"* may be acceptable,

---

† The former incorrect expression 'dimensionless' should not be used: algebraically the dimensions of physical quantities form a multiplicative group which contains a "unity element" (not zero!).

‡ There are some 'illegal numerals' in common use which contribute to the confusion, because they are sometimes mistaken for physical quantities or units. Such numerals are:

per cent = p.c. = $\%$ ≡ 10^{-2}
(thereof: percentage = (loosely) proportion, rate)
ppm = parts per million ≡ 10^{-6}
ppb = parts per billion ≡ $\begin{cases} 10^{-9} \text{ (USA)} \\ 10^{-12} \text{ (Europe)} \end{cases}$

The term ppb is objectionable because the word billion is ambiguous. Also these numerals as such are meaningless if the 'whole' to which the term 'parts' refers, is not expressly given. Powers of ten are better and cause less errors in calculations (see also Section 4).

all the more since this term is descriptive and is already widely used. The conventional symbol c may also be used for content because from the context and the required additional statements of units, etc., it will be clear for which quantity the symbol stands. For the special cases treated in (c) the term "*content ratio*" (symbol: c_r) is proposed.

This section on quantification in general may seem to be a digression from the main topic, trace determination; however, to appreciate the following sections and to ensure their proper understanding, some floating (ambiguous?) terms in the language of the professional analyst need precise definition.

4. LOGARITHMIC PRESENTATION OF VALUES

In chemical analysis and in many technical sciences, quantities such as weight or amount of substance are not of first importance but rather ratios thereof, i.e. concentrations (contents) or, on a second level, concentration ratios. This is so because many technical qualities and physical and biological effects depend on the proportions of two or more substances.

A reasonable way of presenting proportions (ratios, fractions, etc.) over wide ranges is to use their logarithms. This in fact has been practised for a long time; in analytical chemistry diagrams (of calibration functions, for example) with one or two logarithmic scales are abundant. The power of this formal mathematical tool to provide a general survey is demonstrated by *Figure 1*†.

In trace determination the logarithmic presentation of concentrations has four decisive advantages:

(a) With a logarithmic scale of equal spacing through all orders of magnitude there would be no compression at low concentration values nor undue extension at the upper end.

(b) It is evident and constantly demonstrated that the value 'zero' for concentrations cannot be accepted as a result of an analysis, because it can never be verified. Now, the corresponding point on a logarithmic scale ($-\infty$) is inaccessible.

(c) On a logarithmic scale a concentration ratio is represented by a constant difference; the same is true for *relative* errors.

(d) A very strong point in this respect is the fact that many analytical curves will approach a straight line when they are represented in a diagram with either one or two logarithmic scales. (This is exact for all simple power functions.) Particularly in trace analysis a straight-line calibration plot is needed for extrapolation to low concentration values. (This point will be treated later in connection with the question of calibration.)

In spite of these facts—so often used in practice, but not duly appreciated —logarithmic variables have not found much favour in chemical analysis. The reason may be twofold: firstly, the word 'logarithm' is awkward and secondly it evokes the idea of a special, inconvenient operation which must

---

† In this diagram S (sample weight) stands for the product of the numerical value and the unit; S (in g) is therefore a pure number for which the logarithm can be formed.

be performed. This is a psychological barrier. Instead of thinking in terms of concentration c which every time must be transformed, log c should be considered as the appropriate metric quantity describing numerically the composition of some material; it is not always necessary to remember the origin of this quantity. What is needed is a good speakable name and symbol.

There is such a symbol already used in chemistry: it is the letter p in the symbol pH which was formed from the latin term 'potentia hydrogenii'. The letter p indicates the power of ten, and therefore is nothing more than the negative decadic logarithm of the quantity which follows. In some branches of analytical chemistry, for instance in electrochemical analysis (in connection with ion-sensitive electrodes) the letter p is already used to symbolize the logarithm of concentrations other than the hydrogen concentration for which it was originally coined.

Therefore, it is herewith proposed to use the letter p *as a special operator in the field of chemical analysis, indicating that the negative logarithm of the quantity which follows has to be taken.* This would provide a simple and speakable symbol. For example pc would be the negative decadic logarithm of the concentration c, $p[S(in g)]$ that for the sample weight, pc_{Cu} or more simply pCu symbolizes the concentration of copper in a matrix which must be specified. If units and the type of material are always adequately specified, any confusion will be unlikely.

5. ANATOMY OF THE MEASURED VALUE

In analytical chemistry the procedure does not give the answer to the analytical question directly: it provides measured values of "*indicating quantities*" (weight, volume, potential, absorbance, spectrum line intensity, etc.). These measures must be evaluated and interpreted to obtain the final analytical result.

Each measured value is composed of two essentially different portions. One portion is intended because it is correlated with the quantity of the substance to be determined. This useful, informative portion of the measure may be called the "*(analytical) signal*". The other portion, in most cases a small one, is produced or influenced by other non-specific sources. This useless, but inevitable portion may be called the "*blank measure*" because it does not contribute to the desired information. In chemical analysis the blank measure can often be directly determined by making "*blank analyses*". This is a familiar procedure. In the region of high concentrations the blank portion of the measure may often be negligible. However, for trace determinations the two portions contained in the total measure must be properly separated or at least taken into account, otherwise the analytical results derived from the measured values will be systematically wrong. In particular near the limit of detection the blank portion of the total measure may be much greater than the analytical signal. The difference—total measure minus blank measure—may be called "*net measure*". Strictly speaking it is not identical with the "analytical signal" since the net measure may still contain accidental errors from the blank measure. However, a constant blank measure of whatever size can always be compensated either by calculation or by experimental means, presupposing that the blank portion can be measured precisely enough.

42

However, there are limitations: in principle all measured values are subject to 'errors'. Conventionally these are distinguished as being either systematic or accidental, yet there is no sharp distinction between systematic and accidental errors. Unnoticed changes of experimental parameters are often the cause of errors which may appear to be accidental, but which are systematic in nature and could be eliminated if the appropriate parameter were measured. The classification depends partly on the controls which are applied, using knowledge, skill, work, equipment and time.

Accidental errors are uncontrollable either for reasons of principle or practice. They may be caused by the inherent limitations of all measurements (uncertainty principle, quantized nature of energy and particle structure of matter, thermal agitation) or by external perturbations and imperfections in the measuring procedure.

A series of measured values x_i taken on the same sample will lie more or less widely scattered around their average $\bar{x}$ because of the unpredictable accidental errors. "*Scatter*" is a good general term for this conjuncture. The degree of scatter in such a series is formally described by the "*standard deviation*" $s = \left[\sum_{i=1}^{n} (n-1)^{-1} (x_i - \bar{x})^2\right]^{\frac{1}{2}}$.

The different items and steps in an analytical procedure contribute to the scatter of the result in a complex way depending on the degree of correlation between their respective accidental fluctuations. This can be investigated by statistical methods and used to optimize a procedure. When the different sources of scatter are independent in the sense of probability theory, the 'law of propagation of errors', which is quadratic in the standard deviations, is applicable.

For trace determinations the scatter of the blank measures sets a limit on the detectability of the substance to be determined (see Section 11). For low concentrations one is uncertain whether, and to what degree, an observed measure is really due to the amount of the wanted substance in the sample or whether it is caused by uncontrolled chance perturbations of the blank measures. The sources for such perturbations are manifold. They range from accidental contaminations of reagents, losses through sputtering or adsorption, temperature or pressure fluctuations, instabilities in light sources, shot effect in detectors, electronic 'noise' in amplifiers, granularity of photographic plates and random errors of weighing or titration to failings of the observer.

In general, the combined effect of all these sources in the production of "*blank scatter*" cannot be calculated theoretically. *The decisive step is therefore an experimental approach*[1]. In practice the blank scatter for each analytical procedure can be found numerically by making a sufficiently large number (at least 20) of blank analyses and then treating the measures x_{bl} statistically. The average $\bar{x}_{bl}$ and the standard deviation s_{bl} are calculated. *This value s_{bl} of the standard deviation for blank analyses is the only reasonable measure for the "blank scatter"*, (which recently has often been called "(analytical) noise")†. (See end of this section).

---

† There is no reason to replace the generally accepted word "standard deviation" (symbol: s) for a well-defined statistical concept by the vague expression 'root mean square value' (symbol: RMS) which is nothing more than an abbreviation for an 'empty' mathematical operation.

A series of analyses, on a blank sample, which is made in order to determine the blank scatter must be planned with critical consideration so that *all* causes for perturbations involved in the analytical procedure can play their full part. In this respect a particular difficulty must be mentioned. The series of 20 (or more) blank analyses is only a small section (a statistical 'sample') of the whole (theoretically perhaps infinite) *"population"* or *"universe"* for which it is hoped to be representative. It must be 'random', not biased, and to ensure this one must have some idea of the parent population before the program of a statistical investigation is set up. *Statistical figures are meaningless if the population to which they refer has not been expressly stated*[2].

A series of analyses of a certain kind, performed in one place during an hour or a day, may not be representative for the universe of the same analyses made over a period of a year or in different laboratories. Accidental perturbations may not be perceptible during an hour because they produce a constant deviation of all measured values; during a day they may appear as a drift, observed over a year they can be totally random. Therefore, *no formal rules for calculation can dispense with a critical investigation of each individual case.*

This remark applies specially to the determination of the blank scatter of an analytical procedure. For economic or practical reasons this is often made with a shortened model of the procedure. But then the question arises, are these the 'correct' blank measures, representative for the full procedure?

The term for the random fluctuations of the blank measures, the "blank scatter" (being a *disturbance* to the desired analytical measurement), which has come into fashion in recent years is "*(analytical) noise*". This impressive term was originally coined for the field of telecommunication where the "blank scatter", the atmospherics in a radio receiver or the thermal fluctuations in the entrance resistor of an amplifier, can be made audible as 'noise' in a loudspeaker.

The use of the term "(analytical) noise" in chemical analysis should not mislead one into supposing, by analogy, that the main source of fluctuations is to be found in the electronic part of the apparatus. Other sources of fluctuations often affect the blank measure (and the signal) more seriously; the electronic 'noise', even if perceptible, may be of no importance.

The chemical, physical and environmental random perturbations listed above, and many others, vary so widely in appearance, temporal distribution and frequency that it is certainly hard to subsume all this under "(analytical) noise", a term which always evokes its original sensuous meaning. It connotes depreciation: noise is a nuisance. Therefore to keep the picture clear:

(*i*) Fluctuations of the (analytical) signal, which may carry information, must not be called "noise".

(*ii*) *The scatter of blank measures* (which is undesirable) *may be called* "*(analytical) noise*". (This does not include any possible transformation into real, audible noise.)

(*iii*) The scatter of the total measure '*contains*' some 'noise' but it *is not* 'noise'.

This 'dissection' of the measured value will facilitate the treatment of such concepts as "precision", "accuracy", "limit of detection" and "limit of guarantee of purity".

6. TREATMENT OF CALIBRATION FUNCTIONS

Calibration is a necessary operation when building up a quantitative analytical procedure. (Testing the validity of a stoichiometric conversion factor with standard samples† of known composition is nothing more than a relatively simple calibration process.) It may be executed once or repeatedly, depending on the stability of the procedure.

By analysing standard samples with known concentrations (c_I, c_{II}, c_{III} in *Figure 3*) the *"calibration function"* $x = g(c)$, correlating the measurable quantity x with concentration c, is experimentally established.
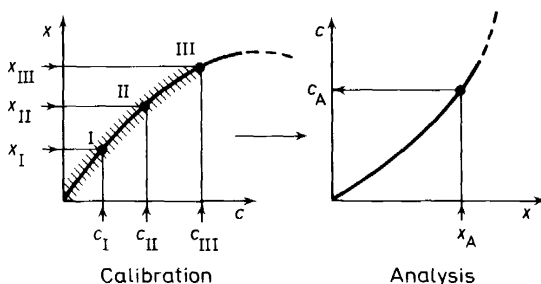

Figure 3. Calibration curve and analytical curve as inverse functions. Points I, II, and III refer to standard samples used for calibration. The hatched region around the calibration curve is the uncertainty region due to accidental errors

The *"analytical function"* $c = f(x)$—which is used to derive the required concentration c_A from the measure x_A gained during an analysis—is the inverse of the calibration function (*Figure 3*). This distinction is essential for multicomponent analyses, where *systems of interdependent functions* normally occur[3].

For trace determinations, reliable standard samples may not be available for the desired low concentrations, but only for relatively high ones. In these cases, one is forced to extrapolate the calibration function into the desired low range, sometimes through several orders of magnitude. This task requires a high degree of critical judgment because small deviations at the start may cause grave systematic errors in the low range.

In order to make extended extrapolation practicable, two basic requirements should be fulfilled:

(a) *The calibration function must be linear*! If not, it must be 'linearized' by a suitable transformation of the variables x and/or c.

(b) The calibration function must be established for the net measure only, *the blank portion of the measure must be eliminated*.

---

† It has been proposed to reserve the term "standard sample" for samples which have been *officially* analysed and issued by some authoritative organization and consequently to name samples from other sources as 'reference sample' or 'calibration sample'.

The first condition means that the *shape* of the curve or function must be known in advance, so that its course in the (x, c) plane is predictable, once its *location* has been determined. This requires two parameters (or points). When more than two points are available for calibration they should be used to locate the (straight) line more precisely and not to work out details of a special shape, which will be very uncertain due to the inevitable errors of measurement.

Examples for linearization of calibration curves are abundant. Among them are such familiar procedures as the use of "absorbance" in spectrophotometric analysis, the representation of the Scheibe–Lomakin equation in emission spectrochemical analysis in a double logarithmic grid and the Kinoshita formula for "photographic transmittance" in mass spectrometry.

The second condition, elimination of the blank portion of the measure, is imperative when the blank portion is irregularly changing in size. Then the net measure (standing for the "analytical signal") must be excised from the total measure. When the blank portion is constant but not additive in its contribution, a linear calibration curve may not be attainable without having first eliminated the blank.

Even when blank and signal measure are strictly additive and a linear calibration curve exists, it may be advisable to subtract the blank measure in order to emphasize the uncertainty of the remaining small signal for low
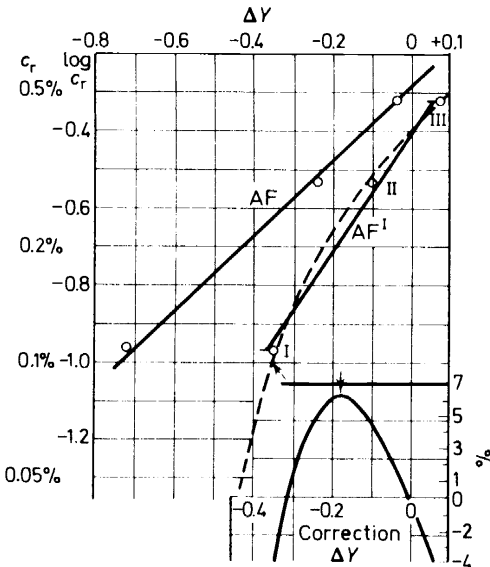

Figure 4. Analytical functions for the spectrochemical determination of Mn in Al-alloys. AF—true function (straight line) for the net measure (background eliminated): AF[1]—"Ersatzfunction" (straight line assumed) for the total measure: dotted curve –true calibration function (curve for the total measure (background not eliminated))
The curve in the lower right corner is the correction curve for the concentration values gained from AF[1]. Points I, II and III correspond to standard samples

concentrations. In such cases the masking of the signal by the blank is easily demonstrated when the concentration is plotted in a logarithmic scale. Then the constant blank measure gives the asymptote along which the uncorrected curve runs down and eventually vanishes in the blank scatter.

The practical (not theoretical) necessity of eliminating the blank portion of the measure is demonstrated in *Figure 4* by an actual example[4]. It is so much more illustrative as it deals with the analysis for a minor component and not just for a 'trace'. The diagram shows, in three different forms, the analytical function for the spectrochemical determination of Mn (from 0.1 to 0.5 per cent) in an Al–Mg alloy, containing about 94 per cent of Al. These data were measured with a medium quartz spectrograph and a Feussner spark ($C \approx 8000$ pF, $L \approx 6$ μH). On the abscissa, ΔY is the usual symbol for the logarithm of the intensity ratio of two spectrum lines. The analysis line was Mn 2949 Å and the reference line Al 3050 Å.

The analytical procedure was well constructed, yielding a relative standard deviation below 0.02 in routine work; it was calibrated for the desired short range with three standard samples. Background was present in the spectrum due to the continuous radiation of the hard spark and the slit width set at 0.035 mm to allow precise photographic intensity measurements. This background—the blank measure under the analysis line—appeared relatively weak with the chosen exposure and did not immediately suggest the need for elimination. The points I, II and III for the standard samples are directly measured without subtracting the background intensity.

What will happen in practice? The analyst, not knowing the shape of the curve and being uncertain about the accuracy of the concentrations given for the standards, and considering the possible errors of his measured values, will assume a straight line as the probably correct analytical function. He will perhaps make a least squares fit to ease his conscience and arrive at the *"Ersatz-function"*† AF^I. Elimination of the background, however,—which is a bit complicated in photographic photometry—leads to the *"true analytical function"* (AF) for which a straight line is the best assumption, in keeping with the general experience in spectrochemical analysis. This line may be extrapolated to low concentrations.

A backwards calculation from this straight line, AF, is the only reliable way to the "true analytical *curve*" (dotted in *Figure 4*) which is valid for the directly measured values of ΔY, not corrected for background (total measure). This curve has an asymptote, $\Delta Y = -0.61$, corresponding to the constant background intensity. Either one of these 'true functions', straight line or curve, may be used together with the net measure or the total measure, respectively; they contain the same information. There may be, however, minor differences in the attainable precision of results‡.

Now the "Ersatz-function" AF^I, also a straight line, must be discussed. The systematic errors of the results which are caused by the use of this

---

† This German word for substitute has a depreciating connotation such as 'in default of something better'.

‡ Results from the straight line may be affected by random errors in the individual background measurements; results from the curve by fluctuations of the background radiation against the assumed constant value.

incorrect analytical function are immediately seen by comparing this line, AF^t, with the true curve. The differences can be read from the correction curve plotted in the corner of *Figure 4*. In the middle of the range the derived Mn values will be more than 6 per cent too low and near the ends 4 per cent too high. The high precision ($s < 0.02$) of this good procedure is thus wasted by the poor accuracy of the calibration. It will be realized that this "Ersatz-function" must not be extrapolated. The systematic errors of the results become greater, the more the original range is extended. This special example was discussed at some length, because the possibly fatal role of the blank portion of a measure in setting up a correct analytical function may not be generally known.

In the region of higher concentrations, where the calibration curve is first established, the blank measures may appear negligible but when the extrapolation is made they have a disproportionate effect. There are examples where the blank portion in the measured quantity may not be observed when it alone is present, e.g. when it is below the threshold of an instrument. Nevertheless, it may have a strong effect, when raised above such a threshold, as a part of the total measure. In such cases, an unusual shape, slope or position of the calibration curve may cause an experienced observer to suspect that some correction for hidden interferences must be carried out.

All this may seem rather complicated, when explained in abstract, scientific terms as in the last two sections. It can be grasped more easily and is unlikely to be forgotten by means of a striking analogy, taken from daily life, which fits in every detail†.

The weight of a captain is to be measured. He is not cooperative and does not like to be put on a balance. A clandestine way to gain the required information would be by ordering a diver to read the diving depth of the ship on a measuring rod twice, with and without the captain on board. Everything is there: the distance from the bottom of the basin to the normal depth of the keel is the "blank measure" and the small difference of the two readings is the "net measure". Calibration is necessary in order to find the relation of the difference in position of the keel (the "signal") and the difference in weight. The ripples in the basin may cause "blank scatter" (noise?) by rocking the ship. This up and down movement of the keel may be big enough to completely mask the small displacement which is to be measured. In this case the weight of the captain is below the "limit of detection" of this ingeneous method. Elimination of the blank portion is necessary because the bottom of the basin may be uneven. This can be controlled by measuring the depth of the water.

This odd story illustrates exactly the situation of the analyst involved in trace determinations. It may be helpful to convince salesmen, technicians, judges and other laymen in chemistry who demand reliable analytical results for traces, how difficult the work is and how carefully the results must be interpreted.

7. CALIBRATION METHODS FOR TRACE DETERMINATION

During any analysis the sample under investigation is compared with the

---

† R. Hoppe, Giessen provided me with this analogy—it may be an old joke.

standard samples which were used to calibrate the analytical procedure. For many common, routine procedures this may have been done long ago. Analyses for traces, however, are very often special problems with individual difficulties and therefore require as a rule immediate comparison of analysis and standard samples in the course of each particular analysis. The standard samples 'lead' the analysis samples through the whole procedure thereby controlling the experimental conditions ("leader samples").

There are three main calibration methods used for trace determinations:

σ-Calibration (with *synthetic* standard samples)

α-Calibration (with *analysed* standard samples)

δ-Calibration (by *differential* additions)

Of these methods, σ-calibration is the most fundamental. However, it may not be possible to prepare such samples from pure substances and to transfer them into a state in which they are of the 'same kind' as the analysis sample, with respect to all operations to which they are submitted during the course of an analysis. The conventional way of equalizing different samples by solution may not be feasible for two reasons: dilution of the original material may reduce the detectability of the trace components, and reconcentration of the solutions may bring up the impurities dragged in by the large quantities of reagents.

Pure substances are not generally available. Often their impurities must first be investigated. Special purification procedures must occasionally be developed and the correct dosage and homogeneous distribution of very small quantities evokes serious problems. In particular, this is so for sensitive organic compounds and biochemicals which are easily destroyed.

α-Calibration with pre-analysed samples is an exception in trace determination. Such samples are available only for a few basic materials, e.g. metals. If they cover the desired concentration range this presupposes that the problem of how to analyse such samples and to calibrate this procedure must have been solved already. This means a regression to σ-calibration. Furthermore, the interest in the determination of ever lower concentrations devaluates standard samples which have been prepared some time ago.

α-Calibration has a side branch, much used in biochemical and pharmacological analysis. The analytical procedure is calibrated with some standard sample whose content has been determined in some arbitrarily agreed unit, mostly based on the observation of some biological effect of interest. Examples are the international units for antibiotics or those for vitamins. This ω-calibration (with agreed units) may also be useful in future for non-biological trace determinations.

The most important calibration method for trace determinations is the δ-calibration (by differential additions). Small, but known quantities of the component to be determined are added to the sample undergoing analysis. This is like scanning the calibration function in small differential steps[5-7].

This δ-calibration method is the only one that permits a quantitative determination of very small traces when the basic material of the sample cannot be obtained completely free from impurities. When the calibration curve scanned by successive additions shows a reasonable course, then it may be possible to extrapolate this function downwards and thereby determine the unknown content which was originally present in the analytical

49

sample. The main problem is to ensure that the added quantity of the component is in the same physical and chemical condition as that part of the component which was originally present or which was previously added. The whole of the component must behave in the same way when undergoing analysis.

Reliable calibration may well be considered as the very crux of trace determinations. It may be unattainable, not in principle, but in practice. Sometimes one may be partly successful on a lower level, when the analytical task includes comparison of different samples. Since the analytical functions in general are monotonous the different samples can be arranged in an order (greater, smaller, equal in content) by comparing the measured values. Often the measurable quantities are simply rated by inspection and the samples are accordingly classified (into 'pigeon-holes'). This type of procedure, with truncated calibration, may be called *"rating analysis"*[2].

Another way should be mentioned. Sometimes it may be possible not to locate the analytical curve in the x/c-plane, but to somehow assess its slope. This may be based on previous experience, or on theoretical insight, and in general it presupposes elimination of the blank portion of the measures, and a nearly linear curve. Then, by dividing the measured values for the different samples which are to be compared, the *proportional values* of their contents can be established. Some reservation should be observed; nevertheless such information may be most valuable for trace characterization and may provide guidance, e.g. for the selection and purification of substances.

There is a paradox peculiar to trace determination near the limit of detection. Such work may require sophisticated operations and high precision measurements, sometimes also expensive equipment, but with all that, the precision of the analytical result may be very poor because it is derived from the small difference of two large quantities (remember the captain's weight to be measured on a ship!). Yet even more, this poor precision may not be needed and may be thrown away in favour of a rough assignment of concentration values to measures. In geochemical prospecting for example, it may be sufficient to give the concentrations of the different elements according to powers of ten. Finer subdivisions are also often used, mostly in geometrical progression (constant differences in pc!). For this purpose the *"preferred numbers"* of ISO are useful; such series as

$$\dots 1 \quad 1.6 \quad 2.5 \quad 4.0 \quad 6.3 \quad 10 \dots$$

or,

$$\dots 1 \quad\quad 3.2 \quad\quad 10 \dots$$

A good name for this type of analysis may be *"gradual analysis"*[2] (The term 'semiquantitative', so often found in the literature, makes no sense!). The *recorded* values of concentration are the labels of pigeon-holes in which samples whose contents spread over a certain range are gathered. For the underlying-calibration, *"broad band-calibration"*, the problem of ensuring that the analytical samples and the standard samples are of the same kind is considerably simplified. The broad band, representing the calibration function in the x/c-plane, at least partially swallows up the deviations caused by different general composition of the samples (*"matrix effects"*). This opens the way to more or less 'universal' analytical procedures, which are so important for questions of pollution.

It should be remarked that the distribution of errors in "gradual analysis" (putting a sample in the wrong box) follows a Poisson distribution rather than a normal Gauss distribution (see Nalimov[8]). The standard deviation of the results is therefore that of the respective Poisson distribution.

Consequently, a sharp distinction must be made between the precision of the measurements and that of the coarsened concentration values derived from them. The arsenal of instruments (sometimes expensive) and high-precision measuring techniques is not used in order to arrive at precise results, but to push the limit of detection downwards as far as possible and to achieve at least some result in the desired low concentration range (see Laqua et al.[9]).

8. TYPE OF INFORMATION AND INFORMING POWER

There is a large variety of analytical principles, methods and complete procedures to choose from for work on trace determinations. The selection of an optimum procedure for some specified task can be difficult. In general, the analytical task is not only chemical in nature, but there are secondary conditions to be considered as well such as the availability of time, money, equipment, personnel and training, and furthermore experience, routine and habit versus daring, innovation and scientific fashions. In any case a *detailed* and complete specification of the analytical task and related problems should, in a first approach, lead to a reduced number of competing possible solutions. It is possible, even at this early stage, that some wishes and conditions are recognized as being incompatible. The main object of this first screening, however, is to select procedures which will give the right *'type of information'* (desired knowledge) and which will probably be suitable for the desired "scope of analysis" (see Section 2). At a second stage, structural, functional and statistical features of the procedures must be considered.

As well as producing the right *type* of information the analytical procedure must have an *"informing power"*, P_{inf}, (a formal metric quantity, measurable in the unit "bit") which is greater than the amount of information, M_{inf} (also in bit) required by the analytical problem for communicating (e.g. on punched or magnetic tape) the desired knowledge[2].

This *"information requirement"*, can be found by a logical analysis of the task. How many alternatives (yes-no decisions) are necessary to build up the desired message right from the bottom? Each alternative needs 1 bit for its representation in a binary code with no redundancy. The number of alternatives by which the wanted information can be composed gives M_{inf}, the value of the "information requirement" in bit.

The "informing power" P_{inf} of an analytical procedure can be estimated in a simple way. For a procedure based on the measurement of one quantity x only, which may display S distinguishable values (steps, mainly depending on precision) the informing power is simply:

$$P_{inf} = \log_2 S$$

Most classical procedures are of this type, yielding an informing power of a few bit. (S = 1000 corresponds to 10 bit only). If n different, independent quantities are measured, it is

$$P_{inf} = \sum_{i=1}^{n} \log_2 S_i \approx n \log_2 \overline{S} \tag{1}$$

When however, a second variable appears in the role of a parameter v, which changes the conditions for the measurement of the first 'indicating' quantity x, then the number of discernible steps of this parameter enters instead of the factor n in equation (1). Such a parameter is mainly found in spectroscopic measurements (v in the following formula may stand for frequency, wavelength or energy, but also for a sliding potential or temperature, or for the run-off time, etc.) The following formula[2] gives the informing power of an analytical procedure with a variable parameter v, which yields a (spectral) "*resolution*", R, in the range from v_a to v_b, and with a number, S, of discernible steps for the 'indicating' measurable quantity (e.g. intensity, absorbance, peak height):

$$P_{inf} = \int_{v_a}^{v_b} R(v) \times \log_2 S(v) \times \frac{dv}{v}$$

$$\approx \overline{R} \log_2 \overline{S} \times \ln \frac{v_b}{v_a} \tag{2}$$

With instruments of high resolving power (optical and mass spectrometers) an informing power of the order of 10^6 bit is (theoretically) attainable†.

The high "*resolving power*" R_0 of the instrument may not be usable in practice because the practical "resolution" R is limited by the observed phenomenon: broad bands in the infrared or ultraviolet spectra, or wide empty regions in a spectrum where nothing can be measured are good examples. Therefore, in equation (2), R must be regarded as the practical resolution which is determined *jointly* by the dispersing instrument (spectrometer), the observed phenomenon (width of lines, bands or energy levels) and experimental conditions (slit width, admitted region, etc.). Yet the remaining fraction is still remarkable.

This inherent superiority in informing power is one logical reason why the classical procedures of chemical analysis had to be replaced by physical procedures—mainly spectroscopic ones in a general sense—in order to solve complex multicomponent universal analytical problems, which are also frequent in trace determination.

9. TOPOLOGICAL STRUCTURES OF ANALYTICAL PROCEDURES

A second reason why physical procedures have replaced classical procedures of chemical analysis can be found in the different *topological structure* of procedures derived from various principles[10]. It is imperative, for trace work, that the analysis proceeds with a minimum of operations, reactions and reagents in order to avoid contamination and loss.

---

† H. Wolter (Marburg) derived this formula for the 'channel-capacity' of a spectrometer (unpubl.). He imparted it during a discussion in 1964. Here the same formula is applied to a total analytical procedure.

Figure 5 gives schematically the basic structures occurring in analytical procedures. The topological *'tree'* (A) gives the interrelation of steps in a 'classical' procedure, characterized by a sequence of many operations branching out more and more in the course of the analysis. Such procedures are designed according to a building-brick principle. They are therefore very versatile, but easily exposed to contamination and loss, because the probability of such undesirable events increases with the number of steps, and there is hardly an internal control. Such procedures are generally not the first choice for serial analysis or automation. However, they are relatively inexpensive with respect to equipment, but tedious and time consuming.

By way of contrast, the topological structure of a *'bundle'* (B) is characteristic for procedures in which the principal analytical step—separation of the different components—is achieved in one operation by spatial dispersion, using only one physical principle. All procedures based on optical spectroscopy, from infrared down to γ-ray and also mass and electron spectroscopy, have this structure, at least in the very core of the method. The spectroscopic separation as such is 'clean'. In optical spectroscopy in particular, the various substances are not 'touched'—their signals, the frequencies, which are not subject to external contamination, are separated.

Preliminary stages of sample preparation—mostly of simple topological structure—are more exposed. These stages include such operations as solution, enrichment of traces, elimination of the matrix and application of additives.

Another simple structure which corresponds dually (in the mathematical sense) to that of a bundle is the *'chain'* structure (C). It represents those procedures where the separation is reached by the actual passage of time† or by the variation of a time-dependent parameter. Again there is only one operative principle. Examples are electrochemical separations, fractional distillation or extraction and chromatography.

The *'point'* structure (P) in *Figure 5* is a degenerate form of either (B) or (C); it is based on one simple measurement without any separation‡.

Analytical procedures of type (B) and (C) based on a single analytical principle are straightforward, inspite of sometimes using complicated equipment. They operate technically and not humanly and therefore can be automated, generally without difficulty. When they are thoroughly developed, they are reliable and 'robust'. Thus they may be adapted to routine serial analysis; those of structure (B) can also be adapted to rapid analysis.

The "resolution" provided by the variable dispersive parameter may be used to achieve a relatively high "informing power", which is important for multicomponent analyses. At the same time high resolution allows the separation of the analytical signal from the underlying blank measure and thereby a reduction of the analytical noise ("blank scatter"), which results in low detection limits.

---

† A chain structure is not given when a *steady* phenomenon in its *spatial* dispersion is *scanned* during some period by a single detecting device, instead of a simultaneous multi-channel measurement which may require very expensive equipment. If time is available, a slow pace may save money which otherwise would have been spent on instruments.

‡ Other more complicated topological structures ('networks', N)[10] occurring in the elucidation of molecular structures are not considered in this paper.
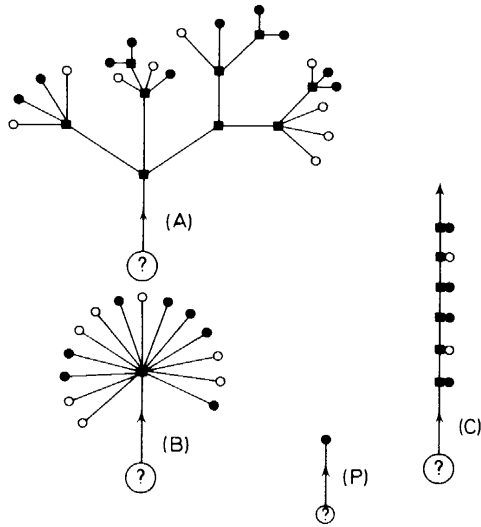
Figure 5. Topological structures of analytical procedures: A = tree (arbor); B = bundle (local); C = chain (temporal); P = point: ■, operations; ◯, no result; ●, result

The combination of all these features explains the progress in trace determination brought about in the last few decades by instrumental methods of analysis.

10. SELECTIVITY AND SENSITIVITY OF PROCEDURES FOR MULTICOMPONENT ANALYSIS

An analytical procedure is said to be fully "*selective*", when it enables the different components in the sample to be determined independently of each other. Therefore, the analyst using such a procedure, can *select* which of the components are to be determined and which are not, without any risk of errors due to disregarding some components of minor interest.

"Selectivity" is a valuable characteristic of procedures which may be used for trace determinations for two reasons. Firstly, selective procedures are by nature less affected by contaminations than non-selective ones, because in their logical structure they have fewer cross-connections through which contaminants may influence the results for the desired components. Secondly, the difficulties in calibrating the procedure for several components are greatly reduced, because the various calibration functions are not interdependent.

The colloquial phrase 'more or less selective' indicates that "selectivity" is understood to be a metric quantity—so far lacking precise definition. A sensible numerical value for the "selectivity" Ξ of a given analytical procedure can be derived from the system of calibration functions, which represents the relationship between concentrations c_i and measurable quantities x_i in

54

a multicomponent analysis. A general derivation has been given elsewhere[3]; for the special case of trace determination a simpler method leads to the same result.

As was stated above, trace determinations require linear calibration and analytical functions in order to permit reliable extrapolation. If necessary, the functions must be 'linearized' by suitable transformation of the variables (see Section 6). Therefore, a system of linear equations, valid for the whole range of analysis, can be assumed for the calibration functions. The number of components and also that of the measurable quantities may be n. (The contents, c_k and the measures x_i, are supposed to be 'independent' in the mathematical sense.) The system of calibration functions is then:

$$x_1 = \gamma_{11}c_1 + \gamma_{12}c_2 + \ldots \gamma_{1n}c_n$$

$$x_2 = \gamma_{21}c_1 + \gamma_{22}c_2 + \ldots \gamma_{2n}c_n$$

$$\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots$$

$$x_n = \gamma_{n1}c_1 + \gamma_{n2}c_2 + \ldots \gamma_{nn}c_n$$

(3)

The matrix of this system

$$\gamma_{11}\gamma_{12}\cdots\gamma_{1n}$$

$$\gamma_{21}\gamma_{22}\cdots\gamma_{2n}$$

$$\ldots\ldots\ldots\ldots\ldots$$

$$\gamma_{n1}\gamma_{n2}\cdots\gamma_{nn}$$

(4)

which may be called the "*calibration matrix*" of the procedure, contains the total information on the relationships of the variables.

The corresponding system of analytical functions, leading from the measured values x_i to the desired contents c_k is also linear; its matrix is the inverted calibration matrix. The inversion is possible only when the determinant of the calibration matrix is sufficiently different from zero.

$$\det(\gamma_{ik}) \neq 0 \tag{5}$$

The elements $\gamma_{ik} = \partial x_i / \partial c_k$ are none other than the "*partial sensitivities*" of the individual measures towards variations of the contents of the different components.

Obviously, an analytical procedure would be called "*fully selective*" when only the elements of the principal diagonal of its calibration matrix, the γ_{ii}, $i = 1, \ldots, n$ are non-zero. The procedure would then break down into n independent sub-procedures—at least as regards calibration and evaluation. Each of the components (i) to be determined would then be measured by its own measurable quantity, which depends only on the content of this one component. (This may occur, for example, in atomic absorption spectroscopy or in mass spectroscopy.)

A procedure of 'some' selectivity should at least allow an approximate solution of the equations, by neglecting in a first step all coefficients outside the principal diagonal[3, 10]. In this first step, one proceeds *as if* the analytical procedure were fully selective. This iteration process for solution only converges, when in each row of the calibration matrix the element in the diagonal is larger than all other elements of the same row taken together.

The mathematical condition for convergence can be used to derive a numerical definition of "*selectivity*" Ξ in the following expression:

$$\Xi := \underset{i=1\ldots n}{\text{Min}} \frac{|\gamma_{ii}|}{\sum\limits_{k=1}^{n} |\gamma_{ik}| - |\gamma_{ii}|} - 1 \tag{6}$$

For a "fully selective" procedure, Ξ becomes very great (formally infinite); when the value of Ξ is zero or negative, there is no selectivity at all, the variables being too greatly entangled. Analyses for traces require procedures with Ξ values as high as possible.

Procedures which are not selective may nevertheless be very useful for the determination of several components in high concentrations. The system of calibration functions can always be solved for the contents when the determinant of the calibration matrix is sufficiently different from zero. This remark leads to a definition of the "*sensitivity*" H of a complex analytical procedure as a whole[3, 10]:

$$H_{(n)} := \det (\gamma_{ik}) \quad \text{for } i,k = 1\ldots n \tag{7}$$

For a simple analytical procedure ($n = 1$; one component, one measured quantity), its "sensitivity" $H_{(1)}$ is defined as the slope dx/dc of its calibration curve. In algebraic terms this is the ratio of the difference Δx of the measure x which is due to a (small) change Δc of the concentration c. In exact mathematical language, this leads to the differential quotient dx/dc as the transfer factor from c on x ($\Delta x = \Delta c \times dx/dc$)†.

The generalization of the differential quotient as a transfer factor on a *system* of functions is the determinant of the matrix (γ_{ik}) whose elements are all partial differential quotients $\partial x_i / \partial c_k$. In 'differential calculus' the symbol

$$\frac{\partial(x_1, x_2, \ldots x_n)}{\partial(c_1, c_2, \ldots c_n)}$$

is used for $\det (\gamma_{ik})$. With this symbol the 'transfer equation'

is generalized to

$$\Delta x = \frac{dx}{dc} \times \Delta c \tag{8}$$

$$\Delta x_1 \, \Delta x_2 \ldots \Delta x_n = \frac{\partial(x_1, x_2, \ldots x_n)}{\partial(c_1, c_2, \ldots c_n)} \times \Delta c_1 \, \Delta c_2 \ldots \Delta c_n \tag{9}$$

Now the formal condition for solvability of the system of equations, namely $\det (\gamma_{ik}) \neq 0$, reveals its practical significance. When the "sensivity" H of the procedure is zero (or very low), then at least one of the measurable quantities x_i is 'dead' and does not respond to changes of the concentrations; the system is not suitable to derive analytical results. The same consideration applies to the inverse system of the analytical functions, leading in the other direction from the x_i to the c_i. It must not be 'dead' either. Therefore the sensitivity of an analytical procedure must not be too high, because the

---

† This definition is in agreement with the common use of this term in most scientific and technical fields. In chemical analyses "sensitivity" *must not* be used ambiguously as just another word for "power of detection", "limit of detection" or "threshold of measure" or something else; there is also no logical relation to 'trace' or 'micro-sample'.

product of the determinants of the two inverse matrices is 1. For this 'transfer factor' a value near 'one' may normally be appropriate.

In trace determination where wide ranges of concentration must be covered and the functional relationship of measures and concentrations is critical, the question of an appropriate sensitivity should find special attention. (It should be noted that the numerical values will depend on the chosen units for the c and for the x. The choice made should be such that convenient figures result.)

Another concept of this group is "*specificity*" Ψ. An analytical procedure is called "*fully specific*" when it gives an "analytical signal" solely for one particular component ('species') but is 'dead' for all other components which may also be present in the sample. A fully specific procedure has a calibration matrix in which only one of the elements in the principal diagonal is not zero[3].

Full specificity is required in trace determination when some specified substance only, is to be determined, in case this substance cannot be separated from the other components or from the matrix for practical or economic reasons, or because the investigated object might otherwise be destroyed.

"Specificity" ends near the limit of detection, because there, an observed measure may not only be caused by the presence of the specific substance in question, but also be unspecific random perturbations from uncontrolled sources.

11. LIMIT OF DETECTION AND LIMIT OF GUARANTEE OF PURITY

Extensive discussion of the "*limit of detection*" is not necessary here because in recent years a broad agreement on principles has been achieved. Some difficulties of comprehension however, still remain. These are often due to the fact that the didactic side of the problem is not realized. Concepts applicable to *all* analytical procedures *must* have great generality. They are definite but contain only essentials; when such general ideas are applied to concrete special cases, then a thorough interpretation is needed.

It is now generally agreed that the problem of the limit of detection is statistical by nature. It is related to the idea of the ratio "(analytical) signal" to "(analytical) noise". There are some misunderstandings about analytical noise as was pointed out in Section 5. There is a tendency to use this notion with too narrow a meaning. "(Analytical) noise" is identical with "blank scatter" and the only reasonable measure for this is the value s_{bl} of the standard deviation for blank analyses.

The statistical definition of the limit of detection cannot remove the uncertainty of a may-be-signal which is nearly submerged in the random fluctuations of the blank measures. A criterion is therefore *agreed by convention*. The difference between the analytical measure x and the mean blank value $\bar{x}_{bl}$ must be greater than a definite multiple k of the standard deviation s_{bl} of the blanks. Smaller measures are discarded as not sound. It should be realized that this is a freely made decision, justified by reason[11-14].

There has been some discussion in recent years about the appropriate value of the factor k. The proposals range from $k = 1$ to $k = 10$. What is not duly considered in these discussions is that the formally calculated

'confidence limit' for a normal distribution cannot be applied in most cases, for two reasons. Firstly, most distributions near the limit of detection are not normal, many are asymmetric. Secondly, the values for the standard deviation and the average of the blank measures are 'estimates' only, calculated mostly from relatively short statistical series. Discussion has shown that this question cannot be left open because reliable communication of results needs definite rules. The dissenting opinions are now converging. Experience has proven that it is appropriate to choose $k = 3$. If at least 20 blank analyses are carried out, and k is taken as 3, then the risk of erroneously eliminating a measure as not sound, is at most a few per cent[12, 14].

The measure x_D at the limit of detection is therefore to be defined by the equation†

$$x_D := \overline{x}_{bl} + 3s_{bl}^*$$ (10)

In this formula the standard deviation for the blank measures is marked by an asterisk. This was done in order to accentuate the symbolic character of this equation, which needs specific interpretation for each particular case. The appropriate blank scatter which makes small signals not detectable in *actual* analyses must be investigated. For example, the particular blank measure found during an analysis may be used not only for comparison with the suspected signal but also to eliminate the blank portion (e.g. background under a spectrum line). In such cases the accidental uncertainty of the blank interferes twice, mostly in different functional ways. This must be accounted for, when the appropriate s_{bl}^* is chosen. The question is decisive for the correct use of formula (10). The problem has been extensively discussed previously[12, 14].

(Sometimes the letter σ is used as a symbol for standard deviation. But then it refers to the whole "population", mostly an imagined infinite set of measurements. The symbol s which is used here, denotes the 'estimate' of σ, derived from a finite series (a 'statistical sample') and therefore stands for those values which are attainable in practice.)

The content c_D at the limit of detection follows then from the analytical function, as

$$c_D = f(x_D)$$ (11)

This is the smallest value for the content which the analytical procedure in question can ever yield *and therefore, is a characteristic feature of the procedure itself.*
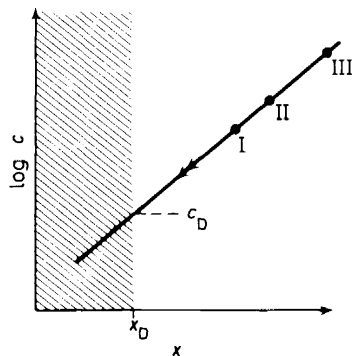
Near the limit of detection c_D all quantitative determinations of the content are rather imprecise; it follows from the definition that, depending on the slope of the analysis function, the relative standard deviation for c_D must be about 0.3. Therefore, the demand, frequently brought forward, to raise the precision *at* the limit of detection is a *contradictio in adjecto.*

For the optimization of analytical procedures with respect to trace deter-

---

† In previous papers the author has used a bar underneath the letter symbols when they are correlated to the limit of detection. e.g. x and c. A bar underneath is the mathematical symbol for a lower bound. However, it is easily overlooked and liable to printing errors. Therefore, the editor has proposed to use 'D' as a subscript, hence x_D and c_D in this paper.

minations, it should be realized that the limit of detection depends in different ways on the experimental parameters. This is schematically shown in *Figure 6*. The measure x_D at the limit of detection is found by statistical considerations. The hatched zone below x_D is the 'forbidden' region where the random perturbations are too high. The concentration c_D at the limit of detection however, is found as the point where the extrapolated calibration line enters the forbidden region. The limit of detection can be decreased in two ways: either by pushing the border of the forbidden region to the left, which means reducing the blank scatter, or by shifting the calibration curve downwards. For atomic spectrochemical analysis this has been extensively discussed by Laqua *et al*[9].

Figure 6. Definition of the limit of detection c_D: x_D is the value of the measured physical quantity at the limit of detection. Hatched zone below x_D—random perturbations too high for detection of analytical signal. Straight line through calibration points I, II and III is extrapolated into the perturbation zone

The limit of detection c_D is a figure of merit for the analytical procedure as such, not for the individual analysis. All analytical results which can be obtained by this procedure must be $> c_D$. If the desired substance has not been found, it must *never* be asserted that the content is below the limit of detection c_D. The "*limit of guarantee for purity*", c_G, which one would wish to indicate if the required substance could not be detected, is always higher than the limit of detection of the procedure. It is *not* a characteristic property of the analytical procedure as such, but it provides an *interpretation for an 'empty' result* obtained by analysing a particular, concrete sample[12–14].

For an entirely homogeneous sample and with the same statistical significance on which the limit of detection was based, we have for the measure x_G at the "limit of guarantee of purity"

$$x_G := \bar{x}_{bl} + 6s^*_{bl} \tag{12}$$

and for the concentration c_G, which will most probably not be exceeded (see *Figure 7*)

$$c_G = f(x_G) \tag{13}$$

If however, the sample is inhomogeneous we must consider the unhappy chance that a piece or a spot with an accidentally low concentration was

59

analysed. To accept responsibility for a guaranteed degree of purity, we must set a higher limit. Let the heterogeneity of the sample *under the given experimental conditions* be described by a standard deviation s_S and let s be the standard deviation of the procedure at the concentrations in question. Then the measure x_G can be calculated from the more general formula

$$x_G = \bar{x}_{bl} + 3s_{bl}^* + 3(s_S^2 + s^2)^{\frac{1}{2}} \qquad (14)$$

This formula can lead to ridiculously high concentrations—for instance, if a procedure for local microanalysis has been misused to determine an average content. However, for such failure, the analyst and not the theory should be blamed[13, 14].
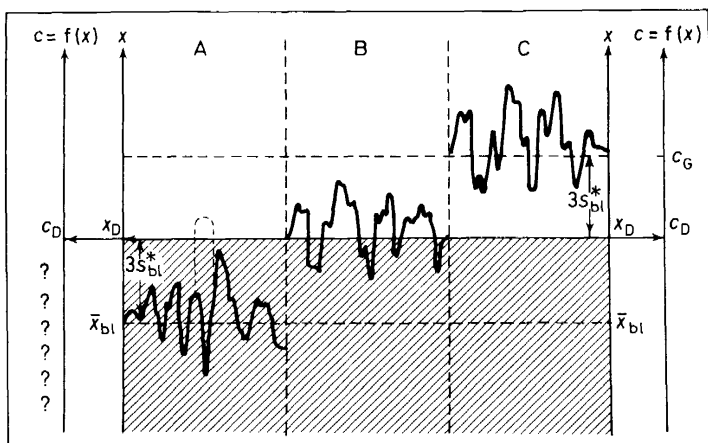

Figure 7. Schematic diagram of fluctuating measures demonstrating limit of detection c_D and limit of guarantee of purity c_G: A—all observed values below the limit of detection in the zone of blank scatter; B—concentration of sample at the limit of detection will not be detected in 50 per cent of all cases due to downward fluctuations and C—limit of guarantee of purity must be higher than limit of detection in order to also detect all accidently low measures

With the idea of guarantee we are back to the demands of life in a complex society. We started there an hour ago with the concept of 'trace' which has its legitimate place in practical life. In the meantime we took a meditative promenade on a bridge high above the jungle of daily work, yet always with the intention of finding ways or roads through. The charms of 'chemical analytics' as applied science may have been felt: intellectual effort and pleasure, technical skill, experience gathered in centuries and all this devoted to human life.

ACKNOWLEDGEMENT

corrections, pointing to obscurities, contradiction and approval. These discussions in spoken, written or printed form went on for more than three decades.

The author is particularly indebted to his colleagues, past and present, in the Institut für Spektrochemie, the members of the IUPAC Commission V.4, on Spectrochemical and Other Optical Methods of Analysis, and to the organizers of the Kyoto Conference who gently forced him by their kind invitation to compose all this.

REFERENCES

[1] H. Kaiser and H. Specker, *Z. Anal. Chem.*, **149**, 46 (1956).
[2] H. Kaiser, *Anal. Chem.*, **42**, No. 2, 24A, No. 4, 26A (1970).
[3] H. Kaiser, *Z. Anal. Chem.*, **260**, 252 (1972).
[4] H. Kaiser, *Spectrochim. Acta*, **3**, 297 (1947).
[5] A. Gatterer, *Spectrochim. Acta*, **1**, 513 (1941).
[6] F. Rosendahl, *Spectrochim. Acta*, **10**, 201 (1957/58).
[7] G. Ehrlich and R. Gerbatsch, *Z. Anal. Chem.*, **209**, 35 (1965).
[8] V. V. Nalimov, *The Application of Mathematical Statistics to Chemical Analysis*, p. 92, Pergamon Press, Oxford (1963).
[9] K. Laqua, W. D. Hagenah and H. Waechter, *Z. Anal. Chem.*, **225**, 142 (1967).
[10] H. Kaiser, *Methodicum Chimicum*, Vol. 1, Ch. 1 (ed. F. Korte) Georg Thieme Verlag, Stuttgart, in the press. (English version to appear with Academic Press.)
[11] H. Kaiser, *Spectrochim. Acta*, **3**, 40 (1947).
[12] H. Kaiser, *Z. Anal. Chem.*, **209**, 1 (1965).
[13] H. Kaiser, *Z. Anal. Chem.*, **216**, 80 (1966).
[14] H. Kaiser and A. C. Menzies, *The Limit of Detection of a Complete Analytical Procedure*, Adam Hilger, London (1968) (contains translations of Ref. 12 and 13).

Generally accepted scientific terms and symbols, which were used in this article may be found in the following IUPAC documents:

(a) Recommendations for the Presentation of the Results of Chemical Analysis, *Pure and Appl. Chem.*, **18**, 439 (1969).

(b) Manual of Symbols and Terminology for Physicochemical Quantities and Units, *Pure and Appl. Chem.*, **21**, 3 (1970).

(c) Nomenclature, Symbols, Units and their Usage in Spectrochemical Analysis—I, *Pure and Appl. Chem.*, **30**, 651 (1972).