THEORETICAL ACCURACY OF THE LEAST SQUARES METHOD IN THE ISOTOPE DILUTION ANALYSIS

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The accuracy of the least squares method in the isotope dilution analysis is studied using two models, *viz.* a model of a two-parameter straight line and a model of a one-parameter straight line. The equations for the direct and the inverse isotope dilution methods are transformed into linear coordinates, and the intercept and slope of the two-parameter straight line and the slope of the one-parameter straight line are evaluated and treated.

Isotope dilution, which forms the basis of the various methods of isotope dilution analysis, can in some instances be described by a linear function[1,2], and the analysis then can be evaluated by making use of the linear least squares method. Since this approach requires that data must be measured for a number of points of the isotope dilution function, this way of performing and evaluating the analysis can be classed as a method of multiple isotope dilution. The methods of single or double isotope dilution then can be looked upon as particular cases of the multiple isotope dilution approach in which one or two points of the transformed isotope dilution function are used for the evaluation.

THEORETICAL

In the least squares method[3] applied to a two-parameter straight line equation

$$Y_k = a + bX_k \,, \tag{1}$$

where $k = p0, p1, \ldots, p(n-1)$ are members of a set of n non-negative integers, the intercept a is calculated as

$$a = \left(\sum Y_k \sum X_k^2 - \sum X_k \sum X_k Y_k\right) / \left[n \sum X_k^2 - \left(\sum X_k\right)^2\right]. \tag{2}$$

The determination of the straight line intercept by formula (*2*) will be referred to as procedure 1.

The slope of the two-parameter straight line b is calculated as

$$b = (n \sum X_k Y_k - \sum X_k \sum Y_k)/[n \sum X_k^2 - (\sum X_k)^2] . \tag{3}$$

This procedure for parameter determination will be referred to as procedure 2.

For a one-parameter straight line

$$Y_k = \beta X_k \tag{4}$$

the slope β is calculated by the least squares method[4] as

$$\beta = \sum X_k Y_k / \sum X_k^2 . \tag{5}$$

This way of determining the parameter value will be referred to as procedure 3.

The relative standard deviation of the parameter $c = a$, b, or β in dependence on $Z_k = X_k$ or Y_k, if the relative deviations $\delta Z_k/Z_k$ are mutually independent, can be expressed by equation[3]

$$s_{rc} = [\sum(\partial \ln c/\partial \ln Z_k)^2 (\delta Z_k/Z_k)^2]^{1/2} = [\sum(s_{rc}^2)_k]^{1/2} . \tag{6}$$

The mean relative standard deviation of the determination of c is

$$\bar{s}_{rc} = [\sum(s_{rc}^2)_k/\varrho]^{1/2} , \tag{7}$$

where ϱ is the number of repetitions of the analysis.

The direct isotope dilution can be expressed by the equation[5]

$$x = y_k(i_k - 1) , \tag{8}$$

where x is a constant, *viz.* the amount of the nonradioactive substance to be determined, y'_ks are variable, known amounts of the same radioactive substance, which are isotope diluted with the nonradioactive substance, and i_k is

$$i_k = s_0/s_k = A_0/A_k , \tag{9}$$

the degree of isotope dilution defined as the ratio of the specific activities of the substance before (s_0) and after (s_k) the isotope dilution, or as the ratio of activities of equal quantities of the substance before (A_0) and after (A_k) the isotope dilution. The latter alternative is of practical importance for a quantitative separation reaction using constant amounts of reagent[1,6]. This alternative also will be considered by us, which is a simplification of the problem in the sense defined by Eq. (*9*).

Coordinate pairs (y_k, s_k) or (y_k, A_k) will be regarded as a set of points, or in particular, as the k-th point of the isotope dilution function which can be expressed in an equivalent way by means of the degree of isotope dilution (*9*), (y_k, i_k), if $(Y_0 = 0, i_0 = 1)$, or by means of coordinates $(y_k, i_k - 1)$, if the point $(Y_0 = 0, i_k - i_0 = 0)$ lies in the origin of the linearized coordinate system (X_k, Y_k).

In the inverse isotope dilution method, a constant amount of the radioactive substance x is diluted with variable amounts y_k of the same nonradioactive substance; then[5]

$$x = y_k/(i_k - 1)\,. \tag{10}$$

In the linear coordinates $X_k = i_k$, $Y_k = 1/y_k$, Eq. (*8*) can be written as

$$1/y_k = -1/x + (1/x)\, i_k\,, \tag{11}$$

hence, $a = -1/x$, $b = 1/x$. Thus, x can be calculated by procedure 1 (Eq. (*2*)) as

$$x = [n \sum i_k^2 - (\sum i_k)^2]/(\sum i_k \sum i_k/y_k - \sum 1/y_k \sum i_k^2)\,. \tag{12}$$

Applying procedure 2 we have analogously from Eq. (*3*),

$$x = [n \sum i_k^2 - (\sum i_k)^2]/(n \sum i_k/y_k - \sum i_k \sum 1/y_k)\,. \tag{13}$$

In the linear coordinates $X_k = i_k$, $Y_k = y_k$, Eq. (*10*) can be expressed as

$$y_k = -x + x i_k \tag{14}$$

whence, by procedure 1 $(a = -x)$,

$$x = (\sum i_k \sum i_k y_k - \sum y_k \sum i_k^2)/[n \sum i_k^2 - (\sum i_k)^2] \tag{15}$$

and by procedure 2 $(b = x)$,

$$x = (n \sum i_k y_k - \sum i_k \sum y_k)/[n \sum i_k^2 - (\sum i_k)^2]\,. \tag{16}$$

Using points $(y_k, i_k - 1)$ and transformations $X_k = i_k - 1$, $Y_k = 1/y_k$, Eq. (*8*) acquires the form

$$1/y_k = (1/x)(i_k - 1)\,, \tag{17}$$

for which, by procedure 3 $(\beta = 1/x)$,

$$x = \sum (i_k - 1)^2/[\sum (i_k - 1)/y_k]\,. \tag{18}$$

Similarly, in the coordinate system $X_k = i_k - 1$, $Y_k = y_k$, Eq. (*10*) can be transformed into

$$y_k = x(i_k - 1)\,, \tag{19}$$

or which procedure 3 ($\beta = x$) affords

$$x = [\sum y_k(i_k - 1)]/\sum(i_k - 1)^2\,. \tag{20}$$

Particular Cases

In Eqs (*12*) and (*15*), where x is calculated by procedure 1, the i_k quantity stands in the numerator and in the denominator in the same power. Consequently, the set of i values for the n points of the isotope dilution function with the coordinates $i_{p1}, i_{p2}, \ldots, i_{pn}$ can be replaced by a set of their ξ-fold multiples, $\xi i_{p1}, \xi i_{p2}, \ldots, \xi i_{pn}$, without altering the value of x. We can choose $\xi = 1/s_0$ or $\xi = 1/A_0$, which are constants, and so their values need not be determined. Eq. (*12*) then can be written as

$$\begin{aligned} x &= [n \sum 1/s_k^2 - (\sum 1/s_k)^2]/[\sum 1/s_k \sum 1/(s_k y_k) - \sum 1/y_k \sum 1/s_k^2] = \\ &= [n \sum 1/A_k^2 - (\sum 1/A_k)^2]/[\sum 1/A_k \sum 1/(A_k y_k) - \sum 1/y_k \sum 1/A_k^2]\,. \end{aligned} \tag{21}$$

In the particular case of two points ($n = 2$) with the coordinates (y_p, s_p) and (y_q, s_q) or (y_p, A_p) and (y_q, A_q), Eq. (*21*) reduces to

$$x = y_p y_q (s_q - s_p)/(s_p y_q - s_q y_p) = y_p y_q (A_q - A_p)/(A_p y_q - A_q y_p) \tag{22}$$

known to be valid for the method of double direct isotope dilution[7].

Similarly, Eq. (*15*) reduces to the relation

$$x = (y_p s_p - y_q s_q)/(s_q - s_p) = (y_p A_p - y_q A_q)/(A_q - A_p) \tag{23}$$

used in the method of double inverse isotope dilution[8].

In the same manner, Eqs (*18*) and (*20*), obtained as special cases of Eq. (*5*), reduce to the initial relations (*8*) and (*10*).

Studying the precision of the direct and inverse multiple isotope dilution methods we can employ the relative standard deviation relation (*6*), which for $x = x(y_k, i_k)$ can be expressed as

$$\begin{aligned} s_{rx} = \{&\sum[(\partial \ln x)/(\partial \ln y_k)]^2 (\delta y_k/y_k)^2 + \\ &+ \sum[(\partial \ln x)/(\partial \ln i_k)]^2 (\delta i_k/i_k)^2\}^{1/2}\,, \end{aligned} \tag{24}$$

or we can make use of the mean relative standard deviation of the parameter (*7*). This deviation can be regarded as the deviation from the true x value. Suppose, for simplicity, that (*a*) $\varrho = n$, (*b*) $\delta i_k/i_k \gg \delta y_k/y_k$, the latter deviation being negligible and (*c*) $\delta i_k / i_k = s_{ri} = \text{const}$. Then we can write (*7*) and (*24*) as

$$\bar{s}_{rx} = (1/\sqrt{n}) \{\sum[(\partial \ln x)/(\partial \ln i_k)]^2\}^{1/2} s_{ri} \tag{25}$$

since according to (*9*),

$$s_{ri} = [(\delta s_0/s_0)^2 + (\delta s_k/s_k)^2]^{1/2} = [(\delta A_0/A_0)^2 + (\delta A_k/A_k)^2]^{1/2} \tag{26}$$

($\delta A/A = 1/\sqrt{N}$ where N is the number of disintegrations counted).

Error of Analysis in Procedure 1

Differentiating Eq. (*12*),

$$\begin{aligned} \partial x/\partial i_k &= (2ni_k - 2\sum i_k)/(\sum i_k \sum i_k/y_k - \sum i_k^2 \sum 1/y_k) - \\ &- [n \sum i_k^2 - (\sum i_k)^2] [\sum i_k/y_k + (1/y_k) \sum i_k - \\ &-2i_k \sum 1/y_k]/(\sum i_k \sum i_k/y_k - \sum i_k^2 \sum 1/y_k)^2 \,. \end{aligned} \tag{27}$$

This relation can be modified with respect to Eqs (*8*) and (*12*) (if the deviations from the true x value are regarded, then the values of x in Eqs (*8*) and (*12*) are identical):

$$\partial x/\partial i_k = x(i_k \sum i_k - \sum i_k^2)/[n \sum i_k^2 - (\sum i_k)^2] \tag{28}$$

$$\begin{aligned} &[(\partial \ln x)/(\partial \ln i_k)]^2 = [(\partial x/\partial i_k)(i_k/x)]^2 = \\ &= [i_k^2(\sum i_k^2)^2 - 2i_k^3 \sum i_k^2 \sum i_k + i_k^4(\sum i_k)^2]/[n \sum i_k^2 - (\sum i_k)^2]^2 \,. \end{aligned} \tag{29}$$

The mean error of analysis, with regard to Eqs (*25*) and (*29*), is

$$\begin{aligned} \bar{s}_{rx} = \{[(\sum i_k^2)^3 + (\sum i_k)^2 \sum i_k^4 - 2\sum i_k \sum i_k^2 \sum i_k^3]^{1/2}/[n \sum i_k^2 - \\ - (\sum i_k)^2]\} (1/\sqrt{n}) s_{ri} \end{aligned} \tag{30}$$

and the relative standard deviation of analysis is

$$s_{rx} = \sqrt{(n)}\, \bar{s}_{rx} \,. \tag{31}$$

According to relation (*15*),

$$\begin{aligned} \partial x/\partial i_k &= [\sum i_k y_k + y_k \sum i_k - 2i_k \sum y_k]/[n \sum i_k^2 - (\sum i_k)^2] - \\ &- [\sum i_k \sum i_k y_k - \sum y_k \sum i_k^2] [2ni_k - 2\sum i_k]/[n\sum i_k^2 - (\sum i_k)^2]^2 \end{aligned} \tag{32}$$

which can be further modified with regard to Eqs (*10*) and (*15*) to give

$$\partial x/\partial i_k = x\left(\sum i_k^2 - i_k \sum i_k\right)/\left[n \sum i_k^2 - \left(\sum i_k\right)^2\right]. \tag{33}$$

Comparing the partial derivatives (*28*) and (*33*) we find them identical in their absolute value. Hence, the relative errors of analysis obtained by procedure 1 applying relations (*12*) and (*15*) for the multiple direct and multiple inverse isotope dilution can both be expressed by Eq. (*30*).

Error of Analysis in Procedure 2

From Eq. (*13*),

$$\begin{aligned}\partial x/\partial i_k &= \left(2ni_k - 2\sum i_k\right)/\left(n \sum i_k/y_k - \sum i_k \sum 1/y_k\right) - \\ &- \left[n/y_k - \sum 1/y_k\right]\left[n \sum i_k^2 - \left(\sum i_k\right)^2\right]/\left[n \sum i_k/y_k - \sum i_k \sum 1/y_k\right]^2,\end{aligned} \tag{34}$$

which with regard to Eqs (*8*) and (*13*) can be reduced to

$$\partial x/\partial i_k = x\left(ni_k - \sum i_k\right)/\left[n \sum i_k^2 - \left(\sum i_k\right)^2\right], \tag{35}$$

and consequently,

$$\left[(\partial \ln x)/(\partial \ln i_k)\right]^2 = \left[n^2 i_k^4 + i_k^2\left(\sum i_k\right)^2 - 2n i_k^3 \sum i_k\right]/\left[n \sum i_k^2 - \left(\sum i_k\right)^2\right]^2. \tag{36}$$

Inserting relation (*36*) in Eq. (*25*) we obtain

$$\begin{aligned}\bar{s}_{rx} = \Big\{&\left[\sum i_k^2\left(\sum i_k\right)^2 + n^2 \sum i_k^4 - 2n \sum i_k \sum i_k^3\right]^{1/2}/\left[n \sum i_k^2 - \right. \\ &\left. - \left(\sum i_k\right)^2\right]\Big\}\left(1/\sqrt{n}\right) s_{ri}.\end{aligned} \tag{37}$$

Eq. (*16*) gives

$$\begin{aligned}\partial x/\partial i_k &= \left(ny_k - \sum y_k\right)/\left[n \sum i_k^2 - \left(\sum i_k\right)^2\right] - \left[n \sum i_k y_k - \right. \\ &\left. - \sum i_k \sum y_k\right]\left[2ni_k - 2 \sum i_k\right]/\left[n \sum i_k^2 - \left(\sum i_k\right)^2\right]^2,\end{aligned} \tag{38}$$

which can be rearranged by means of Eqs (*16*) and (*10*) to give

$$\partial x/\partial i_k = x\left(\sum i_k - ni_k\right)/\left[n \sum i_k^2 - \left(\sum i_k\right)^2\right]. \tag{39}$$

The absolute values of the partial derivatives (*35*) and (*39*) are identical, hence, the relative error of analysis evaluated by Eqs (*13*) and (*16*) will be equal to (*37*).

Error of Analysis in Procedure 3

According to Eqs (*18*) and (*8*),

$$\partial x/\partial i_k = 2(i_k - 1)/[\sum(i_k - 1)/y_k] - [\sum(i_k - 1)^2/(y_k)]/[\sum(i_k - 1)/y_k]^2 = .$$
$$= x(i_k - 1)/[\sum(i_k - 1)^2]\,, \qquad (40)$$

whence

$$[(\partial \ln x)/(\partial \ln i_k)]^2 = i_k^2(i_k - 1)^2/[\sum(i_k - 1)^2]^2\,. \qquad (41)$$

According to Eqs (*25*) and (*41*),

$$\bar{s}_{rx} = \{[\sum i_k^2(i_k - 1)^2]^{1/2}/[\sum(i_k - 1)^2]\}\,(1/\sqrt{n})\,s_{ri}\,. \qquad (42)$$

Applying relation (*20*) and with regard to Eq. (*10*),

$$\partial x/\partial i_k = y_k/[\sum(i_k - 1)^2] - [2(i_k - 1)\sum y_k(i_k -$$
$$- 1)]/[\sum(i_k - 1)^2]^2 = -x(i_k - 1)/[\sum(i_k - 1)^2]\,. \qquad (43)$$

The absolute values of the partial derivatives (*40*) and (*43*) being equal, the error of analysis in procedure 3 for the multiple direct and multiple inverse isotope dilution according to Eqs (*18*) and (*20*) can be expressed by the same relation, *viz.* Eq. (*42*).

Particular Cases

If x is to be determined by Eqs (*22*) and (*23*), then a minimum of two different nonzero points are necessary. At $n = 2$, $\sum i_k = i_p + i_q$, $\sum i_k^2 = i_p^2 + i_q^2$, *etc.*, and the mean relative square error of determination, which in this case is identical with the relative standard deviation, can be written according to Eq. (*30*) as

$$s_{rx} = [i_p i_q/(|i_q - i_p|)]\,s_{ri}\,. \qquad (44)$$

This equation expresses the error of the double isotope dilution methods due to inaccuracies in the radioactivity measurements[9].

For the single determination by means of Eqs (*8*) and (*10*), at least one point is necessary (the second point is implicit in the equation and lies in the coordinate origin); then $\sum i_k = i_k$, $\sum(i_k - 1) = i_k - 1$, and the relative error of analysis, identical with the relative standard deviation, is according to (*42*)

$$s_{rx} = [i_k/(i_k - 1)]\,s_{ri}\,. \qquad (45)$$

This equation gives the error of analysis due to the inaccuracy in the radioactivity measurements in the simple direct or inverse isotope dilution[5].

The mean relative standard deviation of analysis in procedures 1, 2, and 3 are given in Table I (data for Table I are summarized in Table II).

TABLE I

Mean relative standard deviations of analysis $\bar{s}_{rx}$, in % (s_{ri} = 1%), in procedures 1, 2 and 3 according to Eqs (*30*), (*37*) and (*42*)

Points selected from the Table II	Deviations for procedure		
	1	2	3
1,2,3	205[a]	205	98·0
4,5,6	21·7	21·0	10·2
7,8,9	3·41	2·69	1·41
0,10,11	1·47	0·736	0·603[b]
0,10,11,12	1·47	0·550	0·419[b]
0,10,11,12,13	1·47	0·439	0·320[b]
0,10,11,12,13,14	1·46	0·366	0·259[b]
10,11,12	4·41	1·099	0·484
10,11,12,13	3·68	0·743	0·358
10,11,12,13,14	3·31	0·559	0·284
11,12,13	9·60	1·486	0·427
11,12,13,14	6·79	0·950	0·323
12,13,14	16·1	1·88	0·398
15,16,17	$2{\cdot}17 \cdot 10^3$	21·0	0·337
18,19,20	$2{\cdot}05 \cdot 10^5$	205	0·334

[a] At high errors the analyses have no real meaning; [b] point 0 is included in the isotope dilution function, the values are calculated for $i_0 \rightarrow 1 + 0$.

TABLE II

Values of the degree of isotope dilution i_k in the various points k of the isotope dilution function (y_k, i_k)

k	i_k	k	i_k
0	1	11	5
1	1·001	12	7
2	1·003	13	9
3	1·005	14	11
4	1·01	15	101
5	1·03	16	103
6	1·05	17	105
7	1·1	18	1 001
8	1·3	19	1 003
9	1·5	20	1 005
10	3		

Have a function

$$n\varphi = n\bar{s}_{\mathrm{rx}}/s_{\mathrm{ri}} = \sqrt{(n)}\, s_{\mathrm{rx}}/s_{\mathrm{ri}}\,. \tag{46}$$

It can be proved that

$$\lim_{n\to\infty} n\varphi = f(i_{\mathrm{p}}, i_{\mathrm{q}}) \tag{47}$$

where $f(i_{\mathrm{p}}, i_{\mathrm{q}}) = \text{const}$ for the fixed limit values of the isotope dilution degree, $i_{\mathrm{p}} = i_{\mathrm{p1}} < i_{\mathrm{p2}} < \ldots < i_{\mathrm{pn}} = i_{\mathrm{q}}$. The proof will be given for procedure 3. For $n \to \infty$, the sum can be replaced by an integral by the Monte Carlo method[10],

$$\lim_{n\to\infty} \sum_{k=\mathrm{p1}}^{\mathrm{pn}} f(i_k)/n = \int_{i_{\mathrm{p}}}^{i_{\mathrm{q}}} f(i)\,\mathrm{d}i \Big/ \int_{i_{\mathrm{p}}}^{i_{\mathrm{q}}} \mathrm{d}i\,. \tag{48}$$

Eqs (*42*), (*46*), (*47*) and (*48*) give

$$\begin{aligned}\lim_{n\to\infty} (n\varphi) &= \lim_{n\to\infty} \{n^{1/2}[\textstyle\sum i_k^2(i_k - 1)^2]^{1/2}/\sum(i_k - 1)^2\} = \\ &= \left[\int_{i_{\mathrm{p}}}^{i_{\mathrm{q}}} i^2(i-1)^2\,\mathrm{d}i \Big/ \int_{i_{\mathrm{p}}}^{i_{\mathrm{q}}} \mathrm{d}i\right]^{1/2} \Big/ \left[\int_{i_{\mathrm{p}}}^{i_{\mathrm{q}}} (i-1)^2\,\mathrm{d}i \Big/ \int_{i_{\mathrm{p}}}^{i_{\mathrm{q}}} \mathrm{d}i\right] = \\ &= \{[18(i_{\mathrm{q}}^5 - i_{\mathrm{p}}^5) - 45(i_{\mathrm{q}}^4 - i_{\mathrm{p}}^4) + 30(i_{\mathrm{q}}^3 - i_{\mathrm{p}}^3)]\,(i_{\mathrm{q}} - \\ &- i_{\mathrm{p}})/10\}^{1/2}/[(i_{\mathrm{q}} - i_{\mathrm{p}})^3 - 3(i_{\mathrm{q}} - i_{\mathrm{p}})^2 + 3(i_{\mathrm{q}} - i_{\mathrm{p}})] = f_3(i_{\mathrm{p}}, i_{\mathrm{q}})\,. \end{aligned} \tag{49}$$

As i_{p} approaches i_{q}, $\sum i_k^2(i_k - 1)^2 \to n i_{\mathrm{q}}^2(i_{\mathrm{q}} - 1)^2$, $\sum(i_k - 1)^2 \to n(i_{\mathrm{q}} - 1)^2$, and

$$\lim_{i_{\mathrm{p}}\to i_{\mathrm{q}}} f_3(i_{\mathrm{p}}, i_{\mathrm{q}}) = i_{\mathrm{q}}/(i_{\mathrm{q}} - 1)\,. \tag{50}$$

The nearing of the φ and $n\varphi$ functions to their limiting values with increasing n, for procedures 1, 2, and 3, is shown in Table III. The limit values for the three procedures are given in Tables IV–VI, respectively. By means of these limits, for a sufficient number of points of the isotope dilution function, the errors of analysis can be expressed, with a sufficient accuracy, by the simple equations

$$\bar{s}_{\mathrm{rx}} = [f(i_{\mathrm{p}}, i_{\mathrm{q}})/n]\, s_{\mathrm{ri}} \tag{51}$$

$$s_{\mathrm{rx}} = [f(i_{\mathrm{p}}, i_{\mathrm{q}})/\sqrt{n}]\, s_{\mathrm{ri}}\,. \tag{52}$$

It is seen from Table III that for $i_{\mathrm{p}} = 3$, $i_{\mathrm{q}} = 4$, and $n = 3$, $f_3(i_{\mathrm{p}}, i_{\mathrm{q}}) = 1{\cdot}44$, and for $n \geqq 21$, $f_3(i_{\mathrm{p}}, i_{\mathrm{q}}) = 1{\cdot}42$; hence, a number of $n \geqq 3$ can be regarded as sufficient for the conditions in question.

DISCUSSION

The accuracy of the least squares method in the isotope dilution analysis was studied within the scope of two models: a model of a two-parameter straight line (*1*) and a model of a one-parameter straight line (*4*). The isotope dilution process was transformed to linear coordinates, and the intercept of the two-parameter straight line was determined by procedure 1, the slope of the two-parameter straight line was determined by procedure 2, and the slope of the one-parameter straight line was determined by procedure 3.

Two major simplifications were adopted: first, the radioactivity measurements on all the samples were assumed to have the same relative standard deviation, hence, $\delta i/i = s_{ri} =$ const, and second, the inaccuracy in the radioactivity measurements was assumed to exceed greatly that in the amounts of the substance added, hence, $\delta i/i \gg \delta y/y$, the radiometric error constituting the principal source of statistical error in the isotope dilution analysis. In identical conditions (identical set of degrees of isotope dilution, identical relative error of radioactivity measurements, and identical procedure for data evaluation), the accuracy of the multiple direct isotope dilution analysis methods is equal to that of the multiple inverse isotope dilution analysis

TABLE III

Values of the function $\varphi = \bar{s}_{rx}/s_{ri}$ and $n\varphi$ in procedures 1, 2 and 3 on the interval $i \in \langle 3, 4 \rangle$ according to Eqs (*30*), (*37*) and (*42*), respectively[a]

Number of points *n*	φ 1	φ 2	φ 3	$n\varphi$ 1	$n\varphi$ 2	$n\varphi$ 3
3	9·90	2·89	0·480	29·7	8·66	1·44
6	5·94	1·72	0·238	35·6	10·3	1·43
11	3·50	1·01	0·130	38·5	11·1	1·43
21	1·92	0·554	0·068	40·3	11·6	1·42
51	0·812	0·235	0·028	41·4	12·0	1·42
101	0·414	0·120	0·014	41·8	12·1	1·42
201	0·209	0·060	0·007	42·1	12·1	1·42
501	0·084	0·024	0·003	42·2	12·2	1·42
1 001	0·042	0·012	0·001	42·2	12·2	1·42
2 001	0·021	0·006	0·001	42·2	12·2	1·42
5 001	0·008	0·002	0·000	42·3	12·2	1·42
10 001	0·004	0·001	0·000	42·3	12·2	1·42
∞	0	0	0	42·3	12·2	1·42

[a] Uniform division of the interval ($i_p = 3$, $i_q = 4$) by the number of points $n - 2$ (two points are the end ones).

TABLE IV

Values of $\lim_{n\to\infty} n\varphi = f(i_p, i_q)$ for procedure 1 (see Table III and Eqs (*46*), (*47*), (*51*), and (*52*))

i_q \ i_p	1	2	3	4	5	6	7	8	9	10	100	1 000	∞
1	∞												
2	7·62	∞											
3	6·60	21·5	∞										
4	6·73	15·2	42·3	∞									
5	7·16	13·6	27·4	70·0	∞								
6	7·71	13·2	22·9	43·0	105	∞							
7	8·31	13·2	21·0	34·4	62·0	146	∞						
8	8·96	13·5	20·1	30·5	48·3	84·5	195	∞					
9	9·62	13·9	19·8	28·4	41·8	64·4	111	250	∞				
10	10·3	14·3	19·8	27·3	38·1	54·7	82·9	140	313	∞			
100	75·6	78·3	81·1	83·9	86·9	89·9	93·0	96·2	99·6	103	∞		
1 000	733	735	738	741	743	746	748	751	754	756	1 029	∞	
∞	∞	∞	∞	∞	∞	∞	∞	∞	∞	∞	∞	∞	∞

The least value is $f(i_p, i_q) = f(1, 3) = 6{\cdot}60$; ($f(2, 6) \approx 2f(1, 3)$, $f(3, 9) \approx 3f(1, 3)$, *etc.*).

methods, and the mean relative standard deviation of analysis can be expressed by Eqs (*30*), (*37*), and (*42*). The same conclusions were found to apply to the single and double isotope dilution methods even if the inaccuracy in the substance additions was taken into account[5,9].

In procedure 1, in contrast to procedures 2 and 3, the data of the isotope-undiluted sample need not be known, which allows the experimenter to use higher quantities of the substance. The double isotope dilution methods are a particular case of procedure 1 using two points of the isotope dilution function with different, nonzero isotope dilutions. The single isotope dilution methods are a particular case of procedure 3, a single point of the isotope dilution function $(y_k, i_k - 1)$ being used for the determination.

If a sufficiently high number of points of the isotope dilution function are available, with a constant value of the relative error of the activity measurements ($s_{ri} = \sqrt{2} \,.\, \delta A/A = \text{const}$), the accuracy of the analysis depends on the function $f(i_p, i_q)$, i_p and i_q being the lower and upper limits of the sequence of the degrees of isotope dilution. It follows from Tables IV–VI that for finite values, the order for procedures 1, 2, and 3 is

$$f_1(i_p, i_q) > f_2(i_p, i_q) > f_3(i_p, i_q) > 1\,.$$

The accuracy of the procedures decreases in the reverse order (Table I).

TABLE V

Values of $f(i_p, i_q)$ for procedure 2 (see Eqs (*51*) and (*52*))

i_p i_q	1	2	3	4	5	6	7	8	9	10	100	1 000	∞
1	∞												
2	5·37	∞											
3	3·71	8·76	∞										
4	3·18	5·37	12·2	∞									
5	2·92	4·26	7·06	15·7	∞								
6	2·77	3·71	5·37	8·76	19·1	∞							
7	2·67	3·39	4·53	6·49	10·5	22·6	∞						
8	2·60	3·18	4·04	5·37	7·62	12·2	26·0	∞					
9	2·55	3·03	3·71	4·70	6·21	8·76	13·9	29·5	∞				
10	2·51	2·92	3·49	4·26	5·37	7·06	9·91	15·7	32·9	∞			
100	2·22	2·25	2·28	2·31	2·34	2·37	2·40	2·44	2·47	2·51	∞		
1 000	2·19	2·20	2·20	2·20	2·20	2·21	2·21	2·21	2·22	2·22	2·51	∞	
∞	2·19	2·19	2·19	2·19	2·19	2·19	2·19	2·19	2·19	2·19	2·19	2·19	∞

The lowest value is $f(i_p, i_q) = f(i_p, \infty) = 2{\cdot}19$.

In procedure 1, $f_1(i_p, i_q)$ increases without bounds with i_p increasing within the interval $1 \leqq i_p \leqq i_q$. As i_q is varied over the region of $i_p \leqq i_q < \infty$, the function passes from ∞ over a minimum to ∞. The minima lie approximately at $(i_p, i_q) \approx$ $\approx (1, 3), (2, 6), (3, 9), (4, 10)$, *etc.*; the value of the function in the minima increases without bounds with increasing arguments, starting from the lowest value of 6·60 which is the optimum value for the analysis. (Other values on the line of minimum are approximately equal to i_p . 6·60.) This increase can be explained in terms of the fact that as in procedure 1 the (i_p, i_q) values increase, the result of analysis is determined from an increased distance from the origin of the coordinate system. The accuracy of analysis may not be improved if the number of points is increased (Table I, arrows 4, 5, 6). The relative standard deviation of analysis (Eq. (*52*)) decreases proportionally to $1/\sqrt{n}$, but $f_1(i_p, i_q)$ can increase more rapidly than $\sqrt{n}$, and so the overall effect can be an enhanced error; for instance (Table IV), $f_1(2, 8) = 13{\cdot}5$, whereas $f_1(2, 100) = 78{\cdot}3$. To compensate for the increase in the error of analysis, the number of points of the isotope dilution function would have to be increase approximately 34 times. Since for $i_p \to i_q$ we have $\lim f(i_p, i_q) = \infty$, the analysis

TABLE VI

Values of $f(i_p,i_q)$ for procedure 3 (see Eqs (*51*) and (*52*))

$i_q \backslash i_p$	1	1·1	2	3	4	5	6	7	8	9	10	100	1 000	∞
1	∞[a]													
1·1	18·6[b]	11·0[c]												
2	3·05	2·90	2·00											
3	2·19	2·14	1·72	1·50										
4	1·91	1·87	1·61	1·42	1·33									
5	1·76	1·74	1·55	1·39	1·30	1·25								
6	1·68	1·66	1·51	1·38	1·29	1·23	1·20							
7	1·62	1·61	1·49	1·37	1·28	1·22	1·19	1·17						
8	1·58	1·57	1·47	1·37	1·28	1·22	1·18	1·16	1·14					
9	1·55	1·54	1·45	1·36	1·29	1·23	1·19	1·16	1·14	1·12				
10	1·53	1·52	1·44	1·36	1·29	1·23	1·19	1·16	1·13	1·12	1·11			
100	1·36	1·36	1·35	1·34	1·34	1·33	1·32	1·32	1·32	1·31	1·30	1·01		
1 000	1·34	1·34	1·34	1·34	1·34	1·34	1·34	1·34	1·34	1·34	1·34	1·28	1·00	
∞	1·34[d]	1·34	1·34	1·34	1·34	1·34	1·34	1·34	1·34	1·34	1·34	1·34	1·34	1·00[e]

[a] $\lim\limits_{i_p \to i_q \to 1} f(i_p, i_q) = \infty$; [b] the values in the column are $\lim\limits_{i_p \to 1+0} f(i_p, i_q)$; [c] the diagonal values are $\lim\limits_{i_p \to i_q} f(i_p, i_q) = i_q/(i_q - 1)$; [d] $\lim\limits_{i_q \to \infty} f(i_p, i_q) = \sqrt{(18/10)} = 1{\cdot}34$; [e] $\lim\limits_{i_p \to i_p \to \infty} f(i_p, i_q) = 1$.

cannot be evaluated by procedure 1 base on a single point of the isotope dilution function. The advantage of procedure 1 against procedurse 2 and 3, is that H, however procedure 1 does not require the knowledge of the s_0 or A_0 values is offset to an extent by the lowered accuracy of analysis.

In procedure 2, the function $f_2(i_p, i_q)$ increases withiut bounds with increasing $i_p \in \langle 1, i_q \rangle$ and decreases monotonically down to 2·19 with increasing $i_q \in \langle i_p, \infty)$ (Table V). The accuracy remains unaffected by replacement of the $i_{p1}, i_{p2}, \ldots, i_{pn}$ sequence by its ξ-fold multiple, $\xi i_{p1}, \xi i_{p2}, \ldots, \xi i_{pn}$. Since $f_2(i_p \to i_q) \to \infty$, the analysis cannot be evaluated based on a single point of the isotope dilution function. For an optimum evaluation, the minimum i_p and maximum i_q values should be chosen, but only a small improvement (about 1·3 times) in the accuracy is achieved at $i_q > 5$.

In procedure 3, $f_3(i_p, i_q)$ approaches a limit of $i_q/(i_q - 1)$ with $i_p \to i_q; i_p \in (1, i_q\rangle$ (Table VI). As the $i_q \in \langle i_p, \infty)$ is increased, f_3 decreases form the above value down to a value of 1·34; at $i_p > 3$, the function passes through minima whose coordinates are approximately $(i_p, i_q) \approx (4, 7), (5, 7), (6, 8), (7, 9), (8, 10)$, *etc.* The $f_3(i_p, i_q)$ values in the minima decrease in the range of 1·28 to 1·13, and decrease further to the absolutely lowest value of $f(i_p, i_q) = 1$. The local minima, then, are not very deep and the decrease in the $f_3(i_p, i_q)$ value is statistically insignificant from the analytical point of view. The analysis can also be evaluated based on a single point of the isotope dilution function because for $i_p \to i_q$, $\lim f_3(i_p, i_q) = i_q/(i_q - 1)$. The least squares method then reduces to the single isotope dilution method. If the analysis corresponding to this point is repeated n times (*i.e.*, both the A_0 and the A_q activities are measured n times), the accuracy of determination of x by the least squares method and by the method of single isotope dilution using the average $\bar{i}_q = \overline{A_0/A_q}$ will be identical (see below).

In procedure 3, the isotope dilution function linearizes also in the reversed coordinates ($X_k \to Y_k$, $Y_k \to X_k$); then in Eqs (*4*) and (*5*), β is substituted by $1/\beta$, and for the direct isotope dilution, Eq. (*18*) is replaced by $x = (\sum(i_k - 1)/y_k)/\sum(1/y_k^2)$, and for the inverse isotope dilution, Eq. (*20*) is replaced by $x = \sum y_k^2/\sum y_k(i_k - 1)$. The absolute values of the partial derivatives $\partial x/\partial i_k$ in the two cases are expressed by relation (*40*) and the error of analysis is expressed by Eq. (*42*), similarly as when Eqs (*18*) and (*20*) hold true.

In procedure 3 with $i_p \geqq 2$, the relative standard deviation of analysis can be approximated by

$$s_{rx} = [(1{\cdot}5 \pm 0{\cdot}5)/\sqrt{n}]\, s_{ri}\,, \qquad (53)$$

the statistical significance of results being the same on a confidence level of $\alpha = 0{\cdot}05$.

An advantage of the least squares method using n different points of the isotope dilution function over the method using n times one and the same point of the function lies in the possibility of verifying the linearity of the isotope dilution function (in the coordinates in question). This linearity is an *a priori* condition for obtaining accurate x values in all the above procedures and variants of isotope dilution analysis.

Apart from the least squares approach, the more accurate but also more sophisticated approach of the maximum likelihood method[10] can be applied; lower values of the $f(i_p, i_q)$ function should then emerge. However, procedure 3 affords values which are sufficiently near to the absolute minimum value, which is unity (Table VI).

The s_{ri} value, which is a significant parameter describing the accuracy of the result of analysis, was regarded constant. Other assumptions as to the accuracy of the activity measurements in relation to the accuracy of analysis can be found in papers[11,12]. A value of $s_{ri} = 1\%$ is obtained, for a negligible background, if 20 000 disintegrations are counted for either of the (A_0, A_k) pair, because then $s_{ri} = [(1/20\,000) + (1/20\,000)]^{1/2}$. If the measurements are carried out n times for a pair (A_0, A_q), the degree of isotope dilution being determined as $\bar{i}_q = \overline{A_0/A_q}$, then the relative standard deviation of the determination of the degree of isotope dilution is

$$s_{r\bar{i}} = s_{ri}/\sqrt{n} = \bar{s}_{ri}\,. \qquad (54)$$

If, then, x is determined for the $\bar{i}_q$ value by the single isotope dilution method, the error of analysis, Eq. (*45*), is

$$s_{rx} = [\bar{i}_q/(\bar{i}_q - 1)]\, s_{r\bar{i}} \approx [i_q/(i_q - 1)]\,(1/\sqrt{n})\, s_{ri}\,. \qquad (55)$$

The error is statistically equal to that obtained in procedure 3 by using the least squares method (see above).

If, on the other hand, a single measurement is made of A_0, whereas A_q is measured $(2n - 1)$ times (the total number of measurements of the (A_0, A_q) pair is n), then

$$\delta i/i = [(\delta A_0/A_0)^2 + (\delta A_q/A_q)^2/(2n - 1)]^{1/2}\,; \qquad (56)$$

for $n \to \infty$, $\delta i/i = (\sqrt{(2)}/2)\, s_{ri}$ and $s_{rx} = [i_q/(i_q - 1)]\,(\sqrt{(2)}/2)\, s_{ri}$. Hence, this overall n-fold measurement of the A_0, A_q activities has an insignificant effect; the error of analysis is not lower than 0·7 times that obtained from a single measurement of A_0 and A_q.

The above procedures do not cover all the conceivable variants for isotope dilution analysis[13]. The aim of this study was also to introduce a mathematical approach, which can be of importance for the clasification of the isotope dilution methods.

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LIST OF SYMBOLS

X_k, Y_k	coordinates of straight lines $Y_k = a + bX_k$ or $Y_k = \beta X_k$
$a, b, \beta = c$	straight line parameters (regression coefficients)
$k = p0, p1, \ldots, p(n-1)$	a set of n non-negative integers
$\delta Z_k/Z_k$	relative deviation of $Z_k(Z_k = X_k, Y_k, y_k, i_k, A_k, s_k)$
s_{rc}	relative standard deviation of c $(c = x, i)$
$\bar{s}_{rc}$	mean relative standard deviation of c
ϱ	number of repetitions of analysis
x	amount of substance to be determined $(x = -a, -1/a, b, 1/b, \beta, 1/\beta)$
y_k	variable amounts of substance analyzed $(i_k = f(y_k))$
i_k	degree of isotope dilution $(i_k = A_0/A_k = s_0/s_k)$
$\bar{i}_k$	mean i_k values
A_0, A_k	activities of equal quantities of substance before and after the isotope dilution, respectively
s_0, s_k	specific activities of substance before and after the isotope dilution, respectively
ξ	constant
N	number of disintegrations counted
$\varphi = \bar{s}_{rx}/s_{ri}$	
$\lim\limits_{n \to \infty} n\varphi = f(i_p, i_q)$	
p, q	beginning and end of $\langle i_p, i_q \rangle$ interval

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