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CUDIF CHARTS FOR DETECTING SYSTEMATIC DIFFERENCES BETWEEN DUPLICATE DETERMINATIONS

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SUMMARY

A CUDIF chart shows a plot of the cumulative differences between duplicate determinations. From this chart, systematic differences between duplicate determinations can be detected fairly easily. The technique prevents erroneous estimates of the precision parameter. A rule of thumb is given to decide whether a systematic difference should be investigated into more detail.

1. INTRODUCTION

Cumulative sum charts (CUSUM charts) are widely used in industry. For their merits, the reader is referred to Van Dobben de Bruyn (1968) and Woodward and Goldsmith (1967). The technique can also be used to detect systematic differences between duplicate determinations. The information is presented as a plot of the sum of the cumulative differences between the duplicate determinations, which must be arranged in sequential order of measurement. This plot is called a CUDIF chart. Drawing a CUDIF chart by hand is tedious. Therefore, a computer program CUDIF was designed which carries out the computations required and plots the results in a suitable way for further processing.

2. INTERPRETATION OF A CUDIF CHART

A CUDIF chart is based on the following definitions:

Let $\{(x_{i1}, x_{i2}) \mid i = 1(1)\ N\}$ be a set of N duplicates.

Then Diff (i) : = $x_{i1} - x_{i2}$,

and Cudif (i) : = Cudif (i-1) + Diff (i),

where Cudif (0) : = 0.

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Duplicate	Difference	Cudif
1	½	½
2	-1½	-1
3	1	0
4	1	1
5	-1½	-½
6	½	0
7	-½	-½
8	-1½	-2
9	-½	-2½
10	½	-2
11	-2	-4
12	0	-4
13	1½	-2½
14	-½	-3
15	3	0
16	-½	-½
17	1½	1
18	1	2

Fig. 1 Example of a CUDIF chart.

The interpretation of a CUDIF chart is demonstrated in Fig. 1. For duplicates 1 to 6, the first determinations do not really deviate from the second, whereas for the duplicates 7 to 11 and 12 to 18 the first determinations are apparently lower and higher respectively than the second. The mean difference between the five duplicates in the second series is equal to about

$$\frac{\text{Cudif }(11) - \text{Cudif }(6)}{11-6} = \frac{(-4) - (0)}{5} = -0.80$$

In the last series of seven duplicates, the mean difference is equal to about

$$\frac{\text{Cudif }(18) - \text{Cudif }(11)}{18 - 11} = \frac{(2) - (-4)}{7} = 0.86 \ .$$

These mean differences are measures of the deviation of the slope from the vertical line. Reversely, the magnitude of the deviation of the slope from the vertical line gives the mean difference between a series of duplicates.

3. SUGGESTIONS USING THE CUDIF TECHNIQUE

CUDIF charts can be applied to observational studies, in which there may be an unknown classification of data. The CUDIF technique is used to detect possible changes in trends in the data. Analysis of duplicate measurements of e.g. an autoanalyser, given in time sequence, might reveal any change in measuring conditions.

Also CUDIF charts can be applied to experiments, in which the observer deliberately controls or varies one or more factors. In fact, the CUDIF technique can then be used as a data screening method prior to another statistical analysis method. It gives a rapid visual check on the validity of one of the assumptions of the statistical model underlying the data.

The application of CUDIF to factorial experiments can be demonstrated by an example of a 3^2 experiment with two pairs of duplicates within each cell, given in order of measurement (Table 1). Mostly such experiments

Table 1 Data of a 3^2 experiment

Factor A	Factor B			Total
	1	2	3	
1	10.0 - 10.5 9.0 - 10.5	11.0 - 10.0 10.0 - 9.0	10.0 - 10.5 10.0 - 9.5	120
2	14.0 - 15.5 13.0 - 13.5	14.5 - 14.0 14.5 - 13.0	14.0 - 15.0 14.0 - 13.0	168
3	18.0 - 19.0 17.0 - 18.0	19.5 - 18.0 17.5 - 17.0	17.5 - 19.0 18.5 - 17.0	216
Total	168	168	168	504

will be analysed by a two-way analysis of variance. However, this model needs not necessarely be correct, because e.g. the assumption that the duplicate differences should be distributed according to $N(0,\ 2\sigma^2)$, may be not satisfied. To investigate whether or not these differences deviate systematically from zero, a CUDIF chart is a skilful piece of tool. For a detailed investigation the duplicates should be sorted according to various criteria, such as

- time sequence of measurement
- per level of each factor, etc.

The duplicates in Table 1 have been sorted per level of each factor. The left part of Fig. 2 shows the CUDIF chart of the duplicate differences sorted per level of factor B. For the right part the duplicates are sorted per level of factor A.

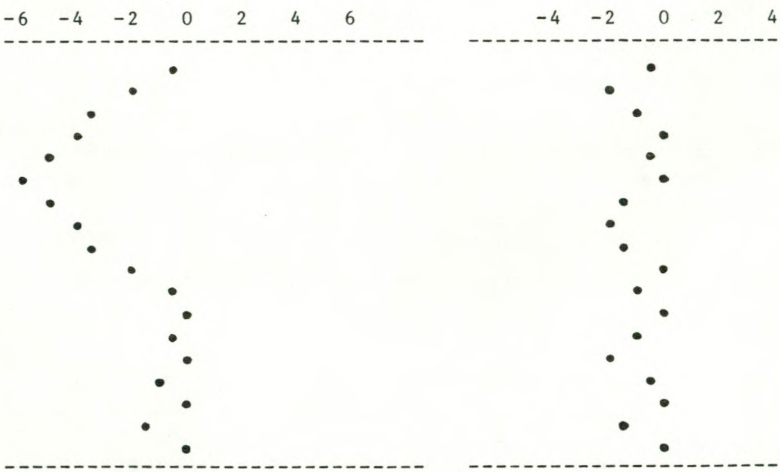


Fig. 2 CUDIF chart of the duplicate differences sorted per level of factor B (left) and per level of factor A (right).

Fig. 2 is a clear demonstration of the common necessity to try various sequences of duplicates in order to track down undesirable effects. The left chart shows systematic differences between duplicates, which are hidden in the right chart. The left chart can be divided into three parts, connected with the levels of factor B. For the first part the duplicate differences are negative, while they are positive for the second part. For the third part the differences are negative and positive alternately. The conclusion can be drawn that the statistical model used is wrong. Although the overall mean value of the duplicate differences is equal to zero, this is not true within each level of factor B. Possibly a third factor should be taken into account. After the origin of the systematic differences has been traced, a better statistical model might be formulated.

In most cases, it is difficult to provide a solution when a CUDIF chart indicates that the data are contaminated with systematic differences between duplicates. Mostly, we must confine ourselves to revealing the existence of a problem. However, it is necessary to solve the problem in physical/chemical terms in connection with future experiments, provided the magnitude of the systematic differences justifies any action.

4. AN EXAMPLE OF THE CUDIF TECHNIQUE FROM STATISTICAL PRACTICE

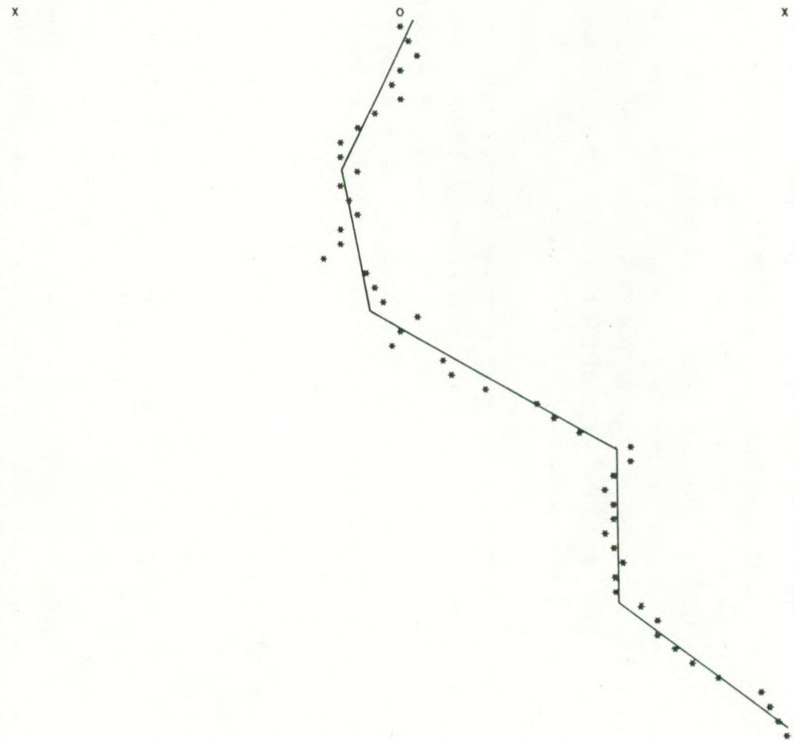
Fig. 3 shows a CUDIF chart of duplicate measurements performed in 5 different laboratories. This chart suggests that 10 single measurements were carried out in one run followed by 10 duplicate measurements in another run, giving rise to substantial differences between the duplicates. The mean difference d for each series of 10 duplicates in this figure is calculated as explained before.

Fig. 4 is a similar CUDIF chart of duplicate measurements carried out in one laboratory at 5 different temperatures (e.g. 15(5)35°C). The explanation of these systematic differences was as follows: Duplicates were determined on two different days; meanwhile thermostatted baths had been readjusted. In this case, it is possible to introduce the nested factor 'day' in an analysis of variance and to estimate the 'between-days' variability. The total variability between the duplicates is then broken down into two components of variability: 'precision' and 'between-days'. The 'precision' is estimated from the highest order interaction. The application of the CUDIF technique revealed the existence of a so far unknown source of variability. This emphasizes the desirability of the application of CUDIF.

d	$\underline{s}_e$	$\underline{s}_0$
-0.17	0.27	0.24
0.11	0.33	0.32
0.71	0.66	0.43
-0.04	0.19	0.19
0.48	0.40	0.22
Pooled	0.405	0.294

CUDIF CHART SCALE FACTOR = 4.091
5 SERIES OF 10 DUPLICATES (5 DIFFERENT LABORATORIES)

I	DIFF.	CUDIF
1	0.000	0.000
2	0.300	0.300
3	0.200	0.500
4	-0.600	-0.100
5	-0.100	-0.200
6	0.100	-0.100
7	-0.600	-0.700
8	-0.500	-1.200
9	-0.600	-1.800
10	0.100	-1.700
11	0.500	-1.200
12	-0.400	-1.600
13	0.100	-1.500
14	0.300	-1.200
15	-0.400	-1.600
16	-0.100	-1.700
17	-0.400	-2.100
18	1.100	-1.000
19	0.200	-0.800
20	0.200	-0.600
21	1.000	0.400
22	-0.400	0.000
23	-0.200	-0.200
24	1.300	1.100
25	0.300	1.400
26	1.100	2.500
27	1.400	3.900
28	0.600	4.500
29	0.600	5.100
30	1.400	6.500
31	0.100	6.600
32	-0.500	6.100
33	-0.200	5.900
34	0.300	6.200
35	-0.200	6.000
36	-0.100	5.900
37	0.100	6.000
38	0.400	6.400
39	-0.300	6.100
40	0.100	6.200
41	0.600	6.800
42	0.500	7.300
43	0.100	7.400
44	0.300	7.700
45	0.700	8.400
46	0.600	9.000
47	1.200	10.200
48	0.400	10.600
49	0.200	10.800
50	0.200	11.000



UNCORRECTED ST. DEV. = 0.405

Fig. 3 CUDIF chart of 5 series of 10 duplicate measurements by 5 laboratories.

CUDIF CHART SCALE FACTOR = 5.114

5 SERIES OF 10 DUPLICATES (5 DIFFERENT TEMPERATURES)

d	s_e	s_0	I	DIFF.	CUDIF
			1	1.000	1.000
			2	-0.400	0.600
			3	-0.200	0.400
			4	1.300	1.700
0.71	0.66	0.43	5	0.300	2.000
			6	1.100	3.100
			7	1.400	4.500
			8	0.600	5.100
			9	0.600	5.700
			10	1.400	7.100
			11	-0.300	6.800
			12	0.000	6.800
			13	0.100	6.900
			14	0.700	7.600
0.09	0.25	0.24	15	0.000	7.600
			16	0.100	7.700
			17	0.400	8.100
			18	-0.600	7.500
			19	0.300	7.800
			20	0.200	8.000
			21	-0.100	7.900
			22	-0.100	7.800
			23	0.500	8.300
			24	-0.500	7.800
0.08	0.21	0.21	25	-0.100	7.700
			26	-0.100	7.600
			27	0.300	7.900
			28	0.300	8.200
			29	0.200	8.400
			30	0.400	8.800
			31	-0.200	8.600
			32	-0.600	8.000
			33	0.200	8.200
			34	-0.600	7.600
-0.24	0.40	0.36	35	0.200	7.800
			36	-0.300	7.500
			37	-1.400	6.100
			38	-0.300	5.800
			39	0.200	6.000
			40	0.400	6.400
			41	-0.500	5.900
			42	0.800	6.700
			43	-0.100	6.600
			44	0.200	6.800
0.10	0.28	0.27	45	0.200	7.000
			46	-0.100	6.900
			47	-0.400	6.500
			48	0.400	6.900
			49	0.500	7.400
			50	0.000	7.400
Pooled	0.397	0.314			

UNCORRECTED ST. DEV. = 0.397

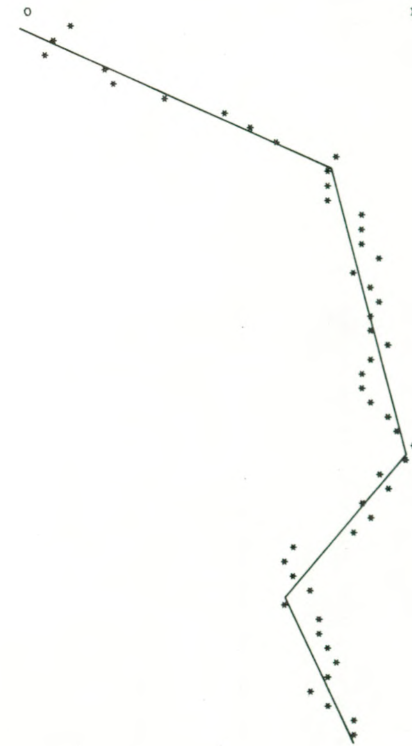


Fig. 4 CUDIF chart of 5 series of 10 duplicate measurements by one laboratory.

5. ESTIMATION OF THE PRECISION IN THE PRESENCE OF SYSTEMATIC DIFFERENCES

The program CUDIF allows estimation of the precision if systematic duplicate differences are present.

Let the mathematical model be

$$\begin{cases} \underline{x}_1 = \mu + \underline{e}_1, \\ \underline{x}_2 = \mu - \delta + \underline{e}_2, \\ \underline{e}_j \sim N(0,\sigma_0^{\,2}) \quad j = 1,2 \end{cases}$$

Then

$$\underline{\bar{x}} = \mu - \tfrac{1}{2}\delta + \tfrac{1}{2}\underline{e}_1 + \tfrac{1}{2}\underline{e}_2,$$
$$\underline{x}_1 - \underline{\bar{x}} = \tfrac{1}{2}(\delta + \underline{e}_1 - \underline{e}_2) = -(\underline{x}_2 - \underline{\bar{x}}).$$

The empirical (uncorrected) variance estimate on the basis of a pair of duplicates

$$\underline{s}_e^{\,2} = \sum_{j=1}^{2} (\underline{x}_j - \underline{\bar{x}})^2 = \tfrac{1}{2}(\delta + \underline{e}_1 - \underline{e}_2)^2$$

has an expected value $\sigma_e^{\,2} = \sigma_0^{\,2} + \tfrac{1}{2}\delta^2$.

Consequently, any systematic difference causes overestimation of the precision of the method (expressed in the standard deviation).
This result enables us to estimate $\sigma_0^{\,2}$ as

$$\underline{s}_0^{\,2} = \underline{s}_e^{\,2} - \tfrac{1}{2}d^2$$

where d: = ΔCudif/n over the range (n points) where the CUDIF chart is fairly straight.
For this range,

$$\underline{s}_e^{\,2} = \frac{1}{2n} \sum_{n} (\mathrm{Diff})^2.$$

The value of the uncorrected standard deviation estimate, $\underline{s}_e$, for the whole series is printed at the bottom of the chart.

For the estimation of the corrected variance, $\underline{s}_0^{\,2}$, from a CUDIF chart consisting of a series of intersecting straight lines (as is the case in Figs. 3 and 4), the slopes of these lines and the number of points on it should be taken into account:

- the corrected variance of the measurements of Fig. 3, consisting of 5 groups of equal size, is
  $\underline{s}_0^{\,2} = 0.405^2 - \tfrac{1}{2}[1/5(0.17^2 + 0.11^2 + 0.71^2 + 0.04^2 + 0.48^2)] =$
  $= 0.0863$ and $\underline{s}_0 = 0.294$;

- the corrected variance for Fig. 4 is calculated in a similar way
  $\underline{s}_0^{\,2} = 0.397^2 - \tfrac{1}{2}[1/5(0.71^2 + 0.09^2 + 0.08^2 + 0.24^2 + 0.10^2)] =$
  $= 0.0988$ and $\underline{s}_0 = 0.314$.

In both cases, it is assumed that the estimates of $\underline{s}_0$ for the five parts of each chart do not differ systematically. This can be verified by calculating $\underline{s}_0$ for each part of the chart: see the tables on the left-hand side of Figs. 3 and 4.
Table 2 gives the ratios of the maximum and minimum variances tested against the critical values. It is clear that the assumptions concerning $\underline{s}_0$ were confirmed.

Table 2 Ratios of maximum and minimum variances

Figure	Variance ratio	Critical point*	Remark
3	$\underline{s}_{e_{max}}^{\,2} / \underline{s}_{e_{min}}^{\,2} = 12.4$	9.6 (1% point)	significant
	$\underline{s}_{0_{max}}^{\,2} / \underline{s}_{0_{min}}^{\,2} = 5.5$	7.11 (5% point)	not significant
4	$\underline{s}_{e_{max}}^{\,2} / \underline{s}_{e_{min}}^{\,2} = 9.6$	9.6 (1% point)	significant
	$\underline{s}_{0_{max}}^{\,2} / \underline{s}_{0_{min}}^{\,2} = 4.4$	7.11 (5% point)	not significant

* Biometrika Tables for Statisticians, Vol. 1, 3rd ed., Table 31. ($\underline{s}_e$ estimates have 10 df and $\underline{s}_0$ estimates, 9 df).

6. JUDGEMENT OF SYSTEMATIC DIFFERENCES IN A CUDIF CHART

6.1 A rule of thumb

To judge whether systematic differences in a CUDIF chart can be ignored from a practical point of view, the following rule of thumb may be used:

Systematic differences in a CUDIF chart can be ignored if the absolute value of the largest systematic difference is less than half the uncorrected standard deviation $\underline{s}_e$

$$|d|_{max} < \tfrac{1}{2}\underline{s}_e \ .$$

The degree of overestimation of $\underline{s}_0$ has a maximum value of less than 7%.

6.2 Mathematical justification

Suppose the CUDIF chart consists of m parts, each with n_i ($i = 1, m$) points. The total number of points N is

$$N = \sum_{i=1}^{m} n_i \ .$$

Suppose also that the systematic difference d_i of a certain part of the chart is equal to

$$d_i = \frac{\underline{s}_e}{\alpha_i} \qquad i = 1, \ldots\ldots, m$$

where $|\alpha_i| \geqq 2$.

From a CUDIF chart consisting of m parts, the corrected variance $\underline{s}_0^{\,2}$ is estimated as

$$\underline{s}_0^{\,2} = \underline{s}_e^{\,2} - \tfrac{1}{2}\overline{d^2}$$

$$= \underline{s}_e^{\,2} - \frac{1}{2N} \sum_{i=1}^{m} n_i \frac{\underline{s}_e^{\,2}}{\alpha_i^{\,2}}$$

$$= \underline{s}_e^{\,2}\left(1 - \frac{1}{2N}\sum_{i=1}^{m}\frac{n_i}{\alpha_i^{\,2}}\right)$$

or

$$\underline{s}_0 = \underline{s}_e\left(1 - \frac{1}{2N}\sum_{i=1}^{m}\frac{n_i}{\alpha_i^{\,2}}\right)^{\frac{1}{2}}.$$

As $\frac{1}{2N}\sum_{i=1}^{m}\frac{n_i}{\alpha_i^{\,2}} \leqq 1/8$, the expression for s_0 may be approximated by

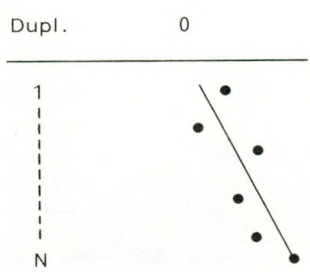
$$\underline{s}_0 \cong \underline{s}_e\left(1 - \frac{1}{4N}\sum_{i=1}^{m}\frac{n_i}{\alpha_i^{\,2}}\right).$$

(The error is smaller than $(1 - 1/8)^{\frac{1}{2}} - (1 - 1/16) = 0.0021 \cong 0.2\%$)

Now we investigate 3 cases with $n_i = N/m$. This simplifies the above relation to

$$\underline{s}_0 \cong \underline{s}_e\left(1 - \frac{1}{4m}\sum_{i=1}^{m}\frac{1}{\alpha_i^{\,2}}\right).$$

<u>Case 1</u> $m = 1,\ \alpha = 2$

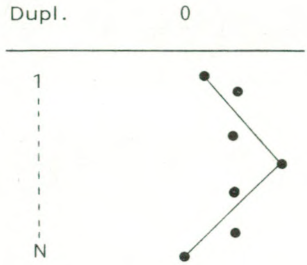


$$\underline{s}_0 = \underline{s}_e\ (1 - \tfrac{1}{4}.\tfrac{1}{4}) = 0.9375\ \underline{s}_e$$

$$\underline{s}_e = 1.067\ \underline{s}_0$$

Ignoring the systematic difference d, $\underline{s}_e$ overestimates $\underline{s}_0$ by less than 7%.

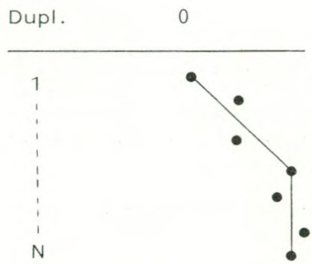
<u>Case 2</u> $m = 2,\ \alpha_1 = 2,\ \alpha_2 = -2$



$\underline{s}_0 = \underline{s}_e\ [1 - 1/8(\frac{1}{4} + \frac{1}{4})] = 0.9375\ \underline{s}_e$

As expected this result is equal to that in Case 1.

<u>Case 3</u> $m = 2,\ \alpha_1 = 2,\ \alpha_2 = \infty$



$\underline{s}_0 = \underline{s}_e\ [1 - 1/8(\frac{1}{4} + 0)] = 0.969\ \underline{s}_e$

$\underline{s}_e = 1.032\ \underline{s}_0$

$\underline{s}_0$ is now overestimated by $\underline{s}_e$ by 3.2%.

From these examples it is clear that in any two line segments with $\alpha_1 = 2$, the degree of overestimation of $\underline{s}_0$ lies between 7% and 3.2%, when $2 \leqq |\alpha_2| < \infty$. Moreover, we feel that in this case the degree of overestimation of $\underline{s}_0$ increases if $n_1 > n_2$, the limiting case being Case 1, and decreases if $n_2 > n_1$.

In the 3 examples given, we confined ourselves to cases where all n_i were equal. This limitation does not result in any loss of generality in the argumentation, for the minimum value of the function

$\left(1 - \frac{1}{4N} \sum_{i=1}^{m} \frac{n_i}{\alpha_i^{\,2}}\right)$, subject to the constraints $n_i \geqq 1$ and $|\alpha_i| \geqq 2$,

is independent of the n_i values.

The above expression reaches its minimum value if

$$\frac{1}{4N} \sum_{i=1}^{m} \frac{n_i}{\alpha_i^2} \quad \text{has a maximum value.}$$

The maximum value is obtained when each of the terms n_i/α_i^2 has a maximum, or, given n_i, when the denominators α_i^2 have a minimum value.

As $|\alpha_i| \geqq 2$, $(i = 1, \ldots, m)$, the minimum value of α_i^2 is 4.

Hence, the maximum value is $\frac{1}{4N} \sum_{i=1}^{m} \frac{n_i}{\alpha_i^2} = \frac{1}{16N} \sum_{i=1}^{m} n_i = 0.067$.

The above equation shows that the maximum value does not depend on the individual values of the n_i's, because

$\sum_{i=1}^{m} n_i = N$, so that the maximum degree of overestimation of $\underline{s}_0$ by

$\underline{s}_e$ is not influenced by the individual n_i's.

6.3 Decision procedure

When the rule of thumb is applied to a CUDIF chart, the decision procedure to be followed is:

- Find that part of the chart with the 'steepest slope' (having the largest deviation from the vertical line);
- Calculate for this part of the chart the systematic difference d between the duplicates;
- Divide the uncorrected standard deviation $\underline{s}_e$ by 2 and compare the result with the systematic difference (d);
- If $|d| < \frac{1}{2}\underline{s}_e$: Ignore the irregularities in the CUDIF chart.

  If $|d| \geqq \frac{1}{2}\underline{s}_e$: A problem is detected. Try to solve it in physical/chemical terms in connection with future experiments.
  The precision is overestimated.

We now apply this procedure to the example in Fig. 3 in which the third part of the chart has the steepest slope. The corresponding systematic difference $|d| = 0.71$. This value is greater than $\frac{1}{2}\underline{s}_e = 0.20$. We conclude that serious problems exist and that $\underline{s}_e$ overestimates the precision. The corrected standard deviation can be derived according to the procedure given in Section 5 (the result is 0.294). An explanation for the existence of the systematic differences should be found in order to be able to avoid them in a subsequent experiment. In this example, it is possible to introduce the nested factor 'run' or 'day' in an analysis of variance (cf. end of Section 4). The same holds for Fig. 4.

7. SCALE FACTOR FOR THE COMPUTER PROGRAM

To plot the CUDIF chart entirely between positions 30 and 121 on the output sheet, a scale factor, s, is used which can be calculated by the program according to

$$s = \frac{45}{\max\ |\mathrm{Cudif}|}$$

where (max|Cudif|) is the - empirical - maximum absolute cumulative sum value of all the differences between duplicate determinations.

It is also possible to assign an a priori value to s. This may be useful when different charts have to be compared. The value of s should then be chosen in such a way that all charts are plotted entirely between positions 30 and 121 on the output sheets. If too high a value of s is chosen, the points with too highly negative or positive Cudif values are plotted continuously on the other side of the chart, thus starting at positions 121 and 30 respectively.

8. REFERENCES

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R.H. Woodward and P.L. Goldsmith, Cumulative Sum Techniques. Oliver & Boyd, Edinburgh/London (1967).

Note. For details about the computer program, please contact R. van Splunter.

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