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CALIBRATION OF CORRELATION CHROMATOGRAPHY BY EXPONENTIAL DILUTION

(Presented by O. Eisen)

Introduction

Several investigators have demonstrated the potential capability of correlation chromatography (CC) for the measurement of low concentration samples [1-6]. In CC a single sample is replaced by multiple pseudo-random injections of the sample, and so the multiplex measurement advance is realized. CC is a member of a family of multiplex measurement techniques [7]. FT NMR, FT IR and Hadamard transform (optical, mass and NMR) spectroscopy are the other examples of multiplex methods used in analytical chemistry [8,9]. The main advantages of multiplex methods over conventional ones is their ability to improve the signal to noise ratio of a measurement.

The cost one must pay for the bulkier information content of multiplex methods is that output signals cannot be directly interpreted and a computer decorrelation operation is needed to obtain final results. Although some of the multiplex measurement methods have been widely used, researchers have at the same time paid very little attention to the remaining ones. The CC belongs to the last category. Almost all the studies done in CC are the demonstrations of its capabilities rather than its application to the solving of problems of practical interest. However, a notable exception is an elegant paper by H. C. Smit et al. [4]. In gas chromatography we have an impressive example of R. Annino et al. [5], where the FID noise was suppressed about ten times, but the sample concentrations usually applied in CC measurements are not too small to be detected by conventional gas chromatography. In our opinion this is why the potential users (e.g., environmental chemists) have not been interested in this potentially advantageous technique for trace concentration measurements.

The handling of the low concentration probes of a sample causes some problems in gas chromatography. The first problem to be solved is how to calibrate a correlation chromatograph. Surprisingly, none of the investigators of CC has paid attention to this question, but at least in gas chromatography it is not a trivial problem. In CC, measurements of interest should be carried out in the signal ranges below the noise power level of the detector. The suitable methods available for generating low-concentration samples are dynamical, i.e. the sample concentration changes during the experiment. In the CC time varying input causes specific distortion of the decorrelated chromatogram — the correlation noise.

The other problem in the handling of low concentration gas samples is how to take into account adsorption—desorption of the sample on the injector and gas communication line walls.

The third problem is of a technical nature. As has been pointed out above, an interesting range of signal values in CC falls below the detector noise amplitude. So in CC we record the detector output signal whose magnitude is of the same order as that of the noise level of the detector. On the other hand, an analog to a digital converter in conventional chromatography is designed so that its resolution is in the order of the detector noise level, too. For example, in our apparatus the resolution of our analog to a digital converter is $20 \mu\text{V}$. This resolution is too low for the CC, and quantization noise effects [10] appear on the decorrelation chromatograms. This reduces the effectiveness of CC.

Finally, the fourth problem one encounters when performing measurements on the extreme sensitivity of a chromatograph is how to eliminate the base line drift which then has a significant value compared to the useful signal value.

In this paper an attempt has been made to give a solution to these problems and bring CC closer to practical needs. We have found the exponential dilution [11] to be a suitable method for calibration of the correlation chromatograph. In the theoretical part of the paper we have computed the standard deviation of the correlation noise due to exponential dilution input and shown that the nonstationarity of the input has actually no influence on the final results if proper experimental conditions are chosen. In the experimental part an exponential dilution flask is described. In this paper, a technical solution of the analog to a digital converter low resolution problem is given by increasing the detector amplifier gain. A cubic spline approximation of the base line is used to eliminate the detector voltage drift. The calibration curve for methane is given. Finally, some speculations and discussions about possibilities of CC overcome the adsorption—desorption effects are presented.

Theoretical

The standard deviation of the correlation noise. Several investigators have found that time-varying input in CC generates a specific correlation noise. Let us compute the standard deviation of the correlation noise for a linearly varying input signal.

Let us assume that a detector signal is digitized after each Δt sec and injections into the chromatograph are performed after each $k \cdot \Delta t$ sec where k is an integer. The injections are performed according to the pseudo-random binary sequence (PRBS) which consists of n elements. Let us assume that PRBS is repeated r times. In general the relationship between the input and output signal is given by the following set of linear equations:

$$\begin{aligned} Y_1 &= a_1 X_1 H_1 \\ Y_2 &= a_1 X_1 H_2 + a_2 X_2 H_1 \\ Y_3 &= a_1 X_1 H_3 + a_2 X_2 H_2 + a_3 X_3 H_1 \end{aligned} \tag{1}$$

$$\begin{aligned} Y_m &= a_1 X_1 H_m + a_2 X_2 H_{m-1} + a_3 X_3 H_{m-2} + \dots + a_{m-1} X_{m-1} H_2 + a_m X_m H_1 \\ Y_{m+1} &= a_{m+1} X_1 H_1 + a_2 X_2 H_m + a_3 X_3 H_{m-1} + \dots + a_{m-1} X_{m-1} H_3 + a_m X_m H_2 \end{aligned}$$

$$\begin{aligned} Y_{(r+1)m-2} &= a_{r \cdot m - 1} X_{m-1} H_m + a_{r \cdot m} X_m H_{m-1} \\ Y_{(r+1)m-1} &= a_{r \cdot m} X_m H_m, \end{aligned}$$

where $m = n \cdot k$; Y_i is a digitized detector output signal element ($i = 1, \dots, (r+1)m - 1$); H_i , a digitized and normalized chromatogram element ($i = 1, \dots, m$); a_i , an amount of a sample injected at a time moment $t_i =$

$= (i-1)\Delta t$ ($i=1, \dots, r \cdot m$); X_i , a sequence according to which the injections are performed ($i=1, \dots, m$). If $X_i=1$, the sample is injected but if $X_i=0$, the injection is «blank». In our apparatus X_i is a sequence where between each PRBS element are $k-1$ zeroes. For example, if $\text{PRBS}=\{1, 1, 0\}$ and $k=2$, then $X=\{1, 0, 1, 0, 0, 0\}$.

It is possible to write (1) in a matrix form. Let us divide output signal vector elements in blocks with m elements in each block. Then, for arbitrary block of equations (except the first and the last one), the following matrix expression holds:

$$\begin{bmatrix} Y_i \\ Y_{i+1} \\ \vdots \\ Y_{i+m-1} \end{bmatrix} = \begin{bmatrix} a_i X_1 & a_{i-1} X_m & \dots & a_{i-m+1} X_2 \\ a_{i+1} X_2 & a_i X_1 & \dots & a_{i-m+2} X_3 \\ \dots & \dots & \dots & \dots \\ a_{i+m-1} X_n & a_{i+m-2} X_2 & \dots & a_i X_1 \end{bmatrix} \begin{bmatrix} H_1 \\ H_2 \\ \dots \\ H_m \end{bmatrix}$$

or

$$Y(i) = A(i)H, \quad (2)$$

where $i=p \cdot m+1$, p is an integer $1 \leq p < r$; H , a chromatogram vector; $Y(i)$, an output vector; $A(i)$, an $m \times m$ matrix.

If the sample concentration varies linearly during the experimental time,

$$a_{i-j} = a_i - d_i(i-j), \quad j = -(m-1) \dots (m-1), \quad (3)$$

where d_i is a constant. Using (3), it is possible to write (2) as follows:

$$Y(i) = a_i XH + d_i(NX - XN)H, \quad (4)$$

where X is a circulant matrix [12] with input sequence elements X_i in the first row; and N , a diagonal matrix with elements $N_{ij} = (i-1)\delta_{ij}$. Solving (4) for H we obtain

$$X^{-1}Y(i) = a_i H + d_i X^{-1}(NX - XN)H, \quad (5)$$

where X^{-1} is an inverse matrix of X . To find X^{-1} see [13].

Equation (5) is an approximate representation of a chromatogram that corresponds to an injected amount of a sample, a_i , at a time moment $(i-1)\Delta t$. The first member of (5) is an ideal chromatogram, and the second term in (5) is the distortion caused by a linear change of the input signal. Denote it $\Delta H(i)$. So

$$\Delta H(i) = d_i X^{-1}(NX - XN)H \quad (6)$$

is the correlation noise vector. The correlation noise has a pattern of random fluctuations of a chromatogram base line. From (6) the mean and standard deviation of the correlation noise should be calculated. The calculation is very similar to that given in our previous work [13] and is therefore omitted here. For the mean, $\Delta \bar{H}(i)$, and the standard deviation $s_{\Delta H(i)}$ we obtain

$$\begin{aligned} \Delta \bar{H}(i) &= \frac{2d_i}{n} \bar{Q}, \\ s_{\Delta H(i)} &= \frac{2|d_i|}{\sqrt{n}} \cdot s_Q, \end{aligned} \quad (7)$$

where $Q = (NX - XN)H$ and \bar{Q} is a mean and s_Q is a standard deviation of the elements of the vector Q .

The calculation of the \bar{Q} and s_Q requires some assumptions and appro-

ximations to be made. Let us assume that H consists of a single narrow peak with the retention time $l \cdot \Delta t$. So H_i is a vector with the elements $H_l=1$ and $H_i=0$ ($i \neq l$). In order to calculate the \bar{Q} and s_Q , the values of the sums $\sum_i iX_{il}$ and $\sum_i i^2X_{il}$ are needed, but as their analytical expressions are not available, we use the following estimations:

$$\sum_i iX_{il} = \frac{1}{2k} \frac{m(m+1)}{2}, \quad (8)$$

$$\sum_i i^2X_{il} = \frac{1}{2k} \frac{m(m+1)(2m+1)}{6}.$$

Now it is possible to compute \bar{Q} and s_Q . The calculation is simple but somewhat lengthy and is omitted here. For \bar{Q} and s_Q we obtain the following results:

$$\bar{Q} = -\frac{n}{2} \left(p - \frac{1}{2} \right), \quad (9)$$

$$s_Q = \frac{n}{2} \sqrt{\frac{k}{6} + k \left(p - \frac{1}{2} \right)^2},$$

where $p = l/(m+1)$.

To verify (9), vector $Q = (NX - XN)H$ was computed and \bar{Q} and s_Q were calculated by a definition. The results are presented in Fig. 1 for particular p , k and n values. An agreement between the simulation results and formulae (9) is satisfactory.

Using (7) we finally obtain the following representation for $s_{\Delta H}$:

$$s_{\Delta H} = \alpha \sqrt{n} |d_i|, \quad (10)$$

where $\alpha = \sqrt{\frac{k}{6} + k \left(p - \frac{1}{2} \right)^2}$.

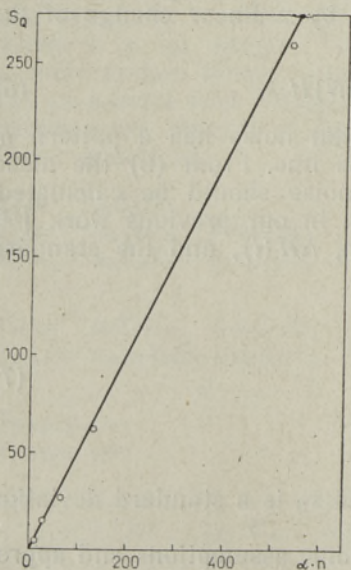
Signal to noise ratio in CC if input concentration is exponentially decreasing. Using an exponential dilution flask as an input device in CC, the sample concentration in the injector changes according to the function

$$C(t) = C_0 e^{-\frac{ut}{V}}, \quad (11)$$

where $C(t)$ is the concentration; C_0 , the constant; u , the carrier gas velocity; V , the exponential dilution flask volume.

Assume that during the period of time $m \cdot \Delta t$ the exponential function (11) should be regarded as a linear one. Then, according to (5) and (10), we can write the signal to noise ratio, S/N , in CC as follows:

Fig. 1. Standard deviation of the elements of vector $Q = NX - XN$. Circles represent the computer simulation results. The solid line is the theoretical dependence. There $k=2$, $d=5$, $l=1$. α depends slightly on n (Eq. (9)). So on the abscissa axis the quantity $\alpha \cdot n$ is represented.



$$\left(\frac{S}{N}\right) = \frac{C(t)}{s_{\Delta H}} = \frac{C_0 e^{-\frac{ut}{V}}}{\alpha \sqrt{n} \left(\frac{u}{V}\right) C_0 e^{-\frac{ut}{V}} \Delta t}$$

or

$$\left(\frac{S}{N}\right) = \frac{V}{\alpha \sqrt{n} u \Delta t} \quad (12)$$

Let us take our experimental real values for k , n , u , Δt and V : e. g., $k=2$, $n=511$, $\Delta t=1$ sec, $u=0.2$ ml/sec and $V=600$ ml. Then $\alpha \approx 1$ and $S/N=134$. Taking into account that CC measurements are rational when the detector noise value is comparable to the signal intensity, we can conclude that the influence of the correlation noise due to the exponential dilution input should be neglected in these experimental conditions. As a linear approximation of the exponential function is not very exact in our experimental conditions, the signal—noise ratio is somewhat less. It is due to the fact that in (5) the nonlinear part of the input function is neglected.

Experimental

The experimental arrangement used is described in [14]. Instead of an injector an exponential dilution flask is used, which is filled with sample gas. The diluting gas is added through the gas sampling valve. The diluting and sample gas are thoroughly mixed in the dilution flask by means of magnetically rotated stirring vanes. The diluted gas mixture then flows out to the valve system of the chromatograph. The valve system consists of a pneumatic chromatographic valve operated by two solenoid valves monitored by a pseudo-random binary sequence (PRBS) generator. The volume of the dilution flask was $V=600$ ml, the rate of the diluting gas was constant, being the same as that of the column carrier gas. In our case we get the diluting gas flow rate $u=0.2$ ml/sec. In all experiments the pseudo-random binary sequence had $n=511$ elements, and the time interval between two pulses of the generator was $k \cdot \Delta t=2$ sec. The digitizing interval was $\Delta t=1$ sec. Thus the lengths of the chromatograms were $k \cdot n \cdot \Delta t=1022$ sec. The chromatograph used was a Perkin-Elmer Model 900 with a flame ionization detector (FID). The chromatographic column was packed with Apiezon L on Inerton AW. The oven temperature was 100°C , the carrier gas was helium and the sample gas methane. The volume of the sample gas was $10 \mu\text{l}$, and thus the concentration at the starting moment was $1.2 \cdot 10^{-5}$ g/l which yielded the signal to noise ratio approximately 10:1. Then we were able to cover a region of concentrations down to the signal to noise ratio below 1:1 at a suitable time.

The analog signals from FID were transformed to digital signals via an analog to digital converter specially designed for chromatography. To overcome the low resolution of the AKM-2 converter, the detector signal was amplified by a wide-band amplifier prior to digitization about 10 times (Fig. 2).

Computations are carried out off-line under the control of programs developed in our laboratory. The correlation (by fast Hadamard transform) program regenerates the PRBS, using the same logic as the noise generator. The results are stored on a disc for further processing. A minicomputer with 28K core memory was used. All the computer programs were written in FORTRAN.

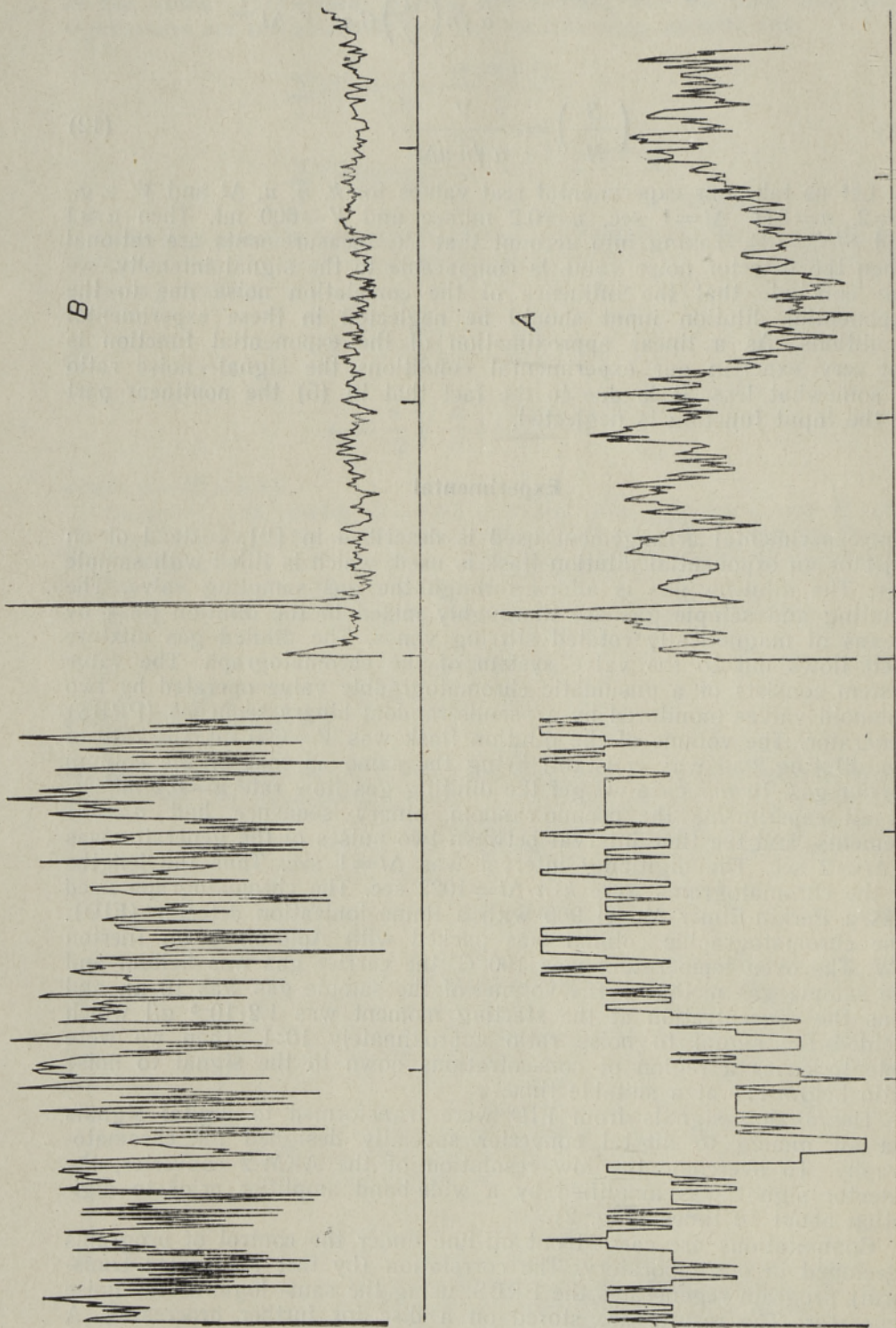


Fig. 2. Effect of detector output amplifying on correlograms. *A* detector output and computed chromatogram without amplification; *B* the same after amplifying the detector output.

Discussion and results

Accurate trace analysis is practically possible only with a continuous sample flow. In CC this situation is realized, and one must choose the same kind of calibration method. Either high concentrations of appropriate gas mixtures or pure gases should be used for calibration purposes. By running calibration standards and samples under the same operating conditions, systematic errors due to adsorption, reactions and other factors should be eliminated. Careful calibration in the case of ppm concentrations is best performed with the dynamic system of an exponential gas diluter. The system is simple and gives a straight calibration curve when the concentration is plotted versus time on a semilog scale. The advantage of this is that neither the diluting gas flow rate nor the initial sample size affects the linearity of the dilution rate.

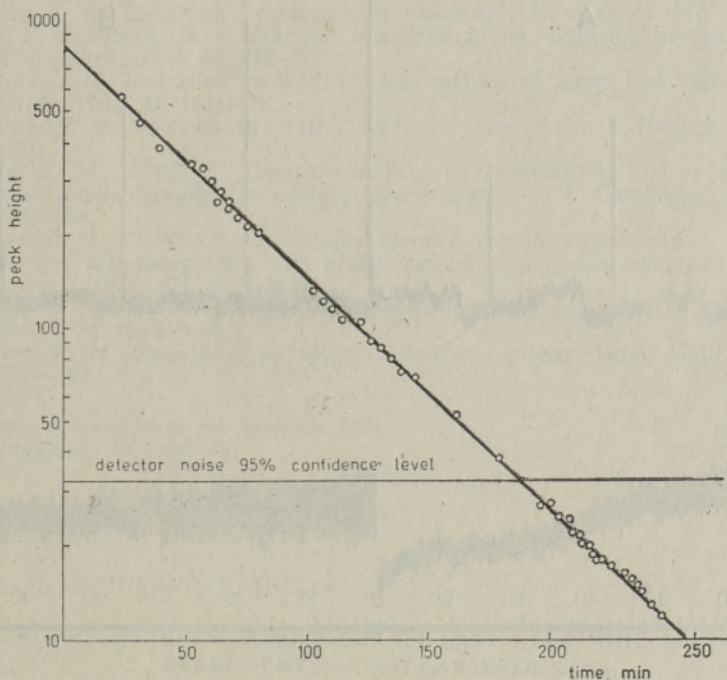


Fig. 3. Detector calibration curve for methane. The solid line is the computed curve for $b=0.02 \text{ min}^{-1}$.

Figure 3 presents the calibration curve for methane at a dilution gas flow rate of 12.1 ml/min. This curve covers the concentration range from $1.2 \times 10^{-5} \text{ g/l}$ to 10^{-7} g/l . The lowest level is below the detector noise for a single injection by the valve system. (The volume of a single injection was 200 μl .)

Good agreement between the calculated ratio $b=u/V$ and the experimental one was obtained, which evidenced the small effect of adsorption—desorption in our case. The advantage of the continuous dosage can be seen here where a surface of full adsorption capacity is saturated. Further investigations are carried out to get calibration curves for other samples and to obtain a rule of adsorption—desorption which may be the main source of the systematic error in trace analysis [15], and the exponential dilution method seems to be useful for that purpose.

In order to obtain a peak height or area with accuracy, one needs a chromatogram with a flat baseline. In correlation chromatography the drift of the detector output signal has a significant influence on the chromatogram computed.

Previous experience suggests that in the absence of a good analytical model the use of the spline function is one of the best approaches to the treatment of experimental data. For the base line approximation we used the spline fitting method of C. H. Reinsch [16] where knots were placed in minimum points of an output curve. It provides the smoothest possible curve that fits the base line with specified accuracy. The suitability of the fit can be judged by the computed chromatograms, and it can be improved, if necessary, by varying the number of knots.

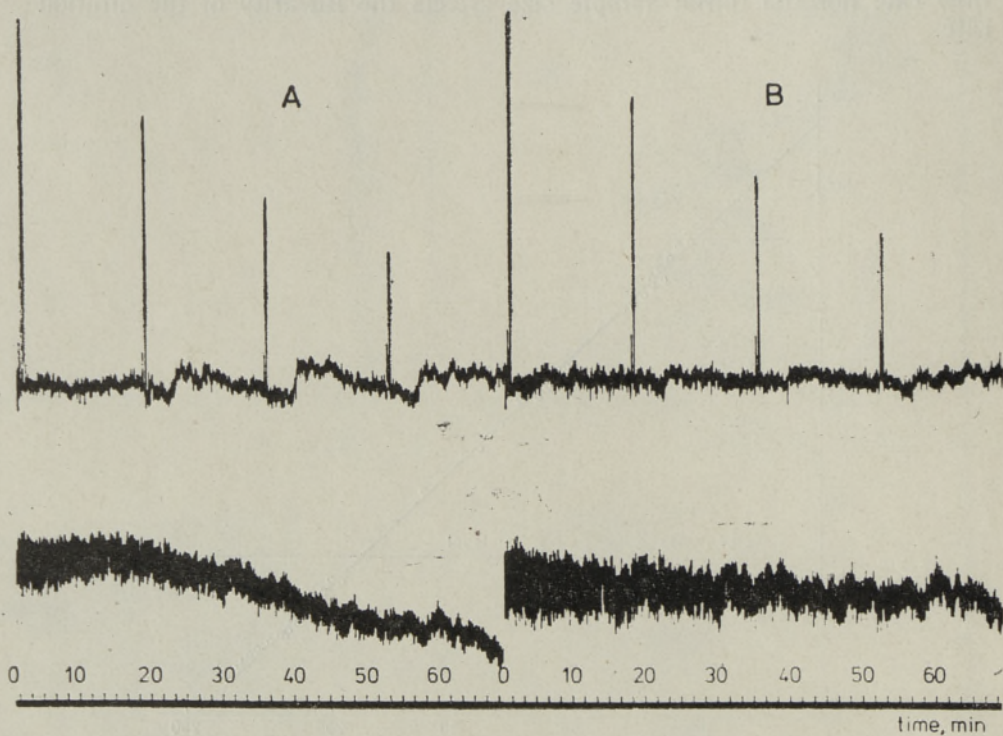


Fig. 4. Effect of base line drift on correlograms. A) detector output and computed chromatograms without base line compensation; B) the same, after base line approximation by spline function and subtraction.

The effect of that base line approximation can be seen in Fig. 4, which shows how important the base line drift compensation is. We preferred to do this in that form before the fast Hadamard transform was used to compute chromatograms.

The concentration level 10^{-7} g/l for CH_4 is of course higher than the possible one for measuring in contemporary gas chromatography with sample concentration. However, the aim of this work was first to demonstrate how various distortions in correlation chromatography should be overcome rather than to develop a new method of CH_4 determination. Thus no attempts were undertaken to minimize inherent noise of the particular chromatograph in use.

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KORRELATSIOONKROMATOGRAAFI KALIBREERIMINE SISENDI EKSPONENTSIAALSE LAHJENDUSEGA

Artiklis on näidatud, et sobivate katsetingimuste korral võib kromatogrammide arvutamisel sisendi eksponentsiaalsest lahjendusest tingitud korrelatsioonimüra mitte arvestada.

M. КОЭЛЬ, М. КАЛЮРАНД, Э. КЮЛЛИК

КАЛИБРОВКА КОРРЕЛЯЦИОННОГО ХРОМАТОГРАФА МЕТОДОМ ЭКСПОНЕНЦИАЛЬНОГО РАЗБАВЛЕНИЯ ПРОБЫ

Показано, что метод экспоненциального разбавления пробы можно применять для калибровки корреляционного хроматографа. В подходящих условиях эксперимента влиянием корреляционного шума, обусловленного экспоненциальным разбавлением пробы, можно пренебречь.