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THE ROLE OF CHROMATOGRAPHY IN BASF

CHROMATOGRAPHIC TECHNIQUES EMPLOYED IN BASF FOR INVESTIGATORY STUDIES AND FOR PROBLEM SOLVING*

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1. INTRODUCTION

Chromatography has been employed in the analytical laboratories of BASF for many years. For instance, between 1936 and 1939 Dr. B. Weiss separated wax components on alumina and silica, and by using various solvents he was able to achieve a group separation into alkanes, monocarboxylic acids and dicarboxylic acids and a partial separation into hydroxy and keto acids. It is interesting that these early unpublished studies involved a whole series of innovations that had not been described previously in the literature. These novel features were as follows: a steel column was used, the work was carried out under pressure, the column was heated at 70°C and colourless substances were investigated (Fig. 1). It should be remembered that at that time chromatography usually involved the investigation of coloured products.

In 1952 paper chromatography was introduced, and was used for the separation and semi-quantitative determination of dinitrophenylhydrazones of carbonyl compounds and also of alcohol dinitrobenzoate derivatives. Although these methods are still of importance today, high-performance liquid chromatography (HPLC) is now usually employed.

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The first gas chromatograph was one which we built ourselves in 1955 and which incorporated a thermal conductivity cell. With the aid of this apparatus Dr. H. Kienitz carried out the first ethylene analyses. The first commercial instrument was purchased in 1956 and to our knowledge was the first gas chromatograph which was delivered to the G.F.R.

Further developments proceeded with, at times, dramatic speed, in particular as regards HPLC.

2. STATISTICS RELATING TO BASF AG

Some important statistics relating to BASF AG are presented in Table 1, which also includes some comparative data for the BASF Group. One figure which should be emphasized is the number of different products marketed by BASF, namely 6000. The number of individual chemical precursors and intermediates also produced by BASF has not been recorded. In addition it should be underlined that the 1600 buildings include an unspecified number of experimental and production plants as well as numerous research and analytical laboratories.

TABLE 1

STATISTICS FOR BASF AG AND BASF GROUP FOR 1978

	BASF AG	*BASF Group*
Employees	*ca.* 52,000	*ca.* 115,000
Total share capital	*ca.* $9000 \cdot 10^6$ DM	*ca.* $16{,}000 \cdot 10^6$ DM
Cash flow	*ca.* $10.000 \cdot 10^6$ DM	*ca.* $21{,}500 \cdot 10^6$ DM
Total area of works		6.3 km^2 (2.4 sq. miles)
No. of buildings	*ca.* 1600	
Total number of products marketed	*ca.* 6000	
Production volume	*ca.* $5.7 \cdot 10^6$ tonnes	

In this major chemical complex, which covers approximately 6.3 km^2 (2.4 square miles), fundamental analytical studies are carried out in two analytical centres. This arrangement has proved to be optimal in view of the size of the works. The Agricultural Division has its own analytical centre at Limburgerhof, outside Ludwigshafen.

Fig. 2 is an aerial view of BASF, which clearly shows the two laboratories that comprise the Analytical Centre in the northern part of the works and the Analytical Centre in the southern part.

Later data are intended to give an impression of the number of chromatographic instruments employed in BASF. In some instances, however, it was only possible to obtain statistical data tracing back developments over a relatively short period of time. The available data that cover the longest period are those referring to the increase in the number of gas chromatographs in the Central Analytical Laboratory (WHU) situated in the southern part of BASF.

These statistical data, covering a period of 20 years, are presented in Fig. 3 and

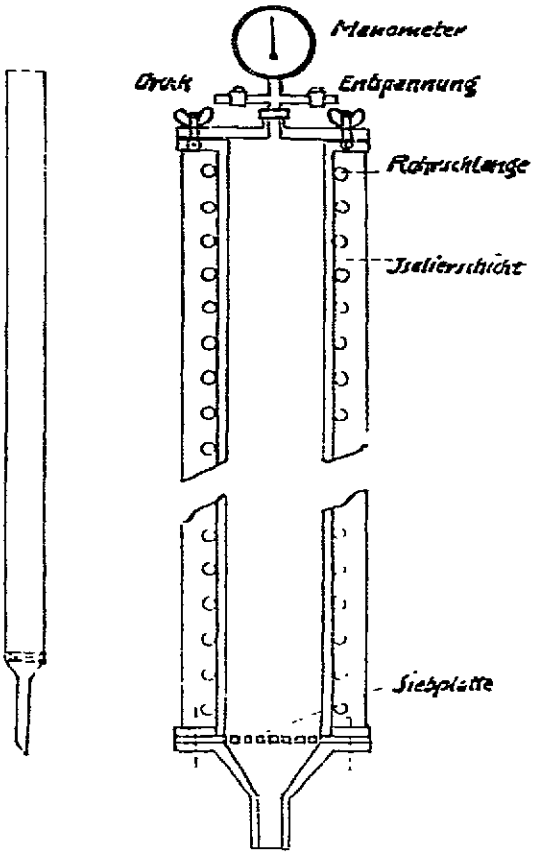


Fig. 1. Example of early chromatographic experiments at BASF AG (I.G. Farbenindustrie A.G., Ludwigshafen a. Rh.) in the period 1936–1939: low-pressure liquid chromatography at elevated temperature. Original drawing by Dr. B. Weiss ("Entspannung" = pressure release valve; "Druck" = pressure; "Rohrschlange" = coiled tube for the heating of the liquid; "Isolierschicht" = insulation layer; "Siebplatte" = sieve support).

are corrected values including active instruments only. This figure also illustrates developments in the number of samples received for analysis. In addition, the point at which the link-up with our IBM 1800 computer unit took place is indicated. The line that has been drawn gives an indication of the increase in the number of instruments and corresponds to a rate of increase of approximately 2.5 chromatographs per year.

The curve showing the number of samples received for analysis over the last 20 years is a reflection not only of the various developments that have taken place in the field of chromatography, but also of various other factors, such as the spread of gas chromatography (GC) within BASF and the automation of GC analysis. Particularly since 1970 the use of GC techniques has spread rapidly through the many research laboratories at BASF and as a result the number of samples received by the Central Analytical Laboratory has decreased. Nevertheless, the cost units charged continued to rise, because in many instances analysis of the sample required considerably more complex chromatographic techniques, such as the use of several different columns

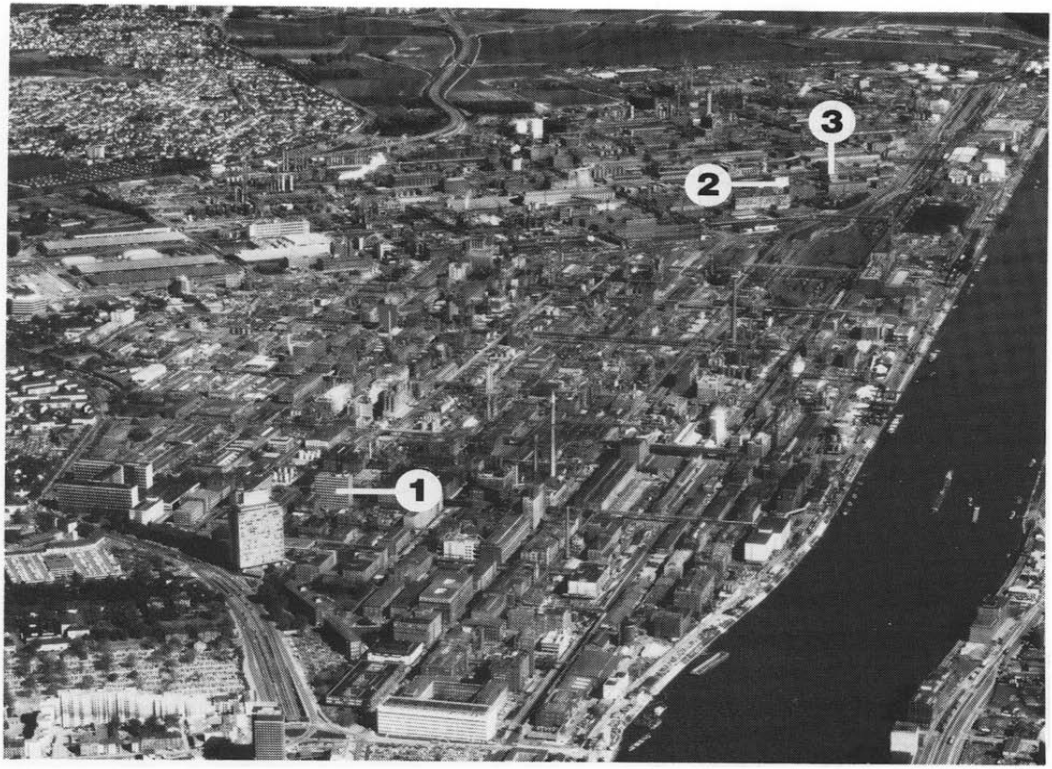


Fig. 2. Aerial view of BASF. 1 = Central Analytical Laboratory South (Untersuchungslaboratorium, WHU, E 210); 2 = Central Analytical Laboratory North, Physico-Chemical Department (Analytisches Labor, WAA, M 325); 3 = Central Analytical Laboratory North, Chemical Department (Analytisches Labor, WAA, M 320). The analytical centre of the Agricultural Division is situated at Limburgerhof Versuchsstation, outside Ludwigshafen.

and specific detectors. Following the introduction of computer evaluation and the automation of various operations there was a sharp increase in the number of samples, as it was then possible to carry out routine series of analyses. It has been our experience in the Central Analytical Laboratory, however, that the time that elapses between the introduction of a particular technical innovation and its universal application has grown steadily shorter. In this instance it was a matter of only 2–3 years before automation and the use of automatic evaluation devices became widespread throughout the works. Despite fluctuations in the number of samples received, the actual number of cost units charged for GC analysis has risen steadily, except for one or two discontinuities in the curve (Fig. 3). To complete the picture, Fig. 4 shows the increase in the number of automated injection systems for GC employed in the Analytical Centre WHU South.

Parallel to the developments that have taken place in the Analytical Centre in the southern part of the works there has been a considerable increase in the number of gas chromatographs employed in the Analytical Centre North (Oppau), as shown in Fig. 5. As precise figures are available only from about 1968 onwards, the data for earlier years have had to be estimated. The line indicating the growth rate cor-

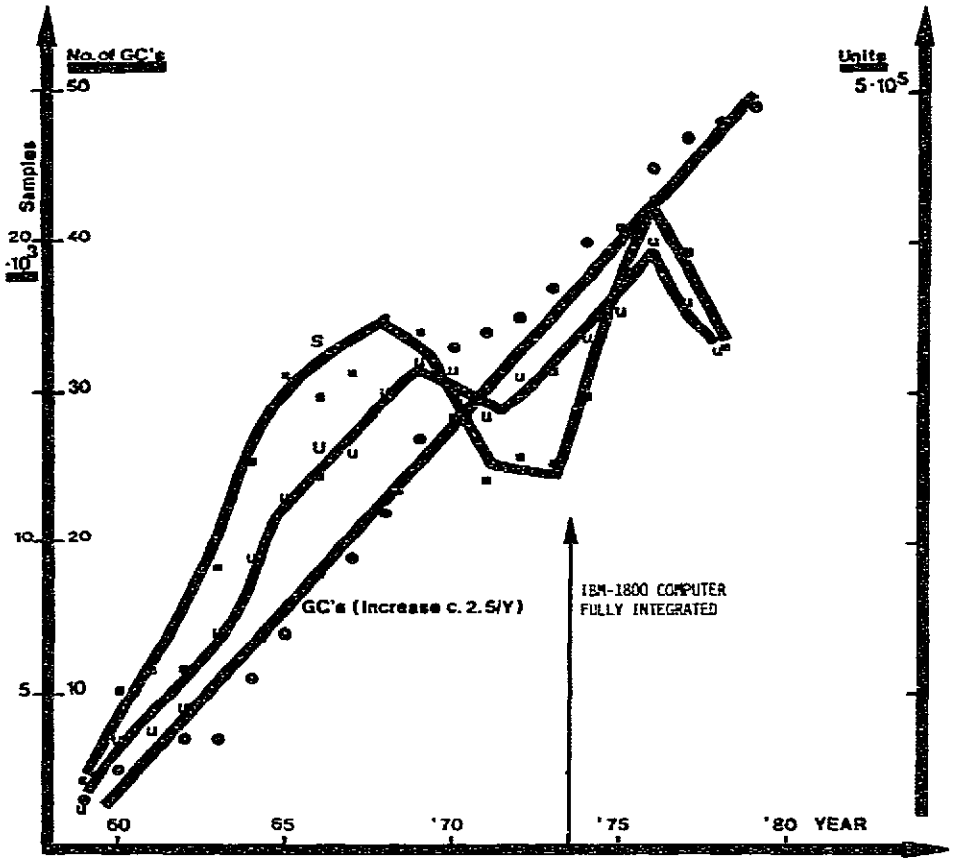


Fig. 3. Increase in the number of gas chromatographs between 1959 and 1979 in the BASF Analytical Centre, WHU South. Number of samples analysed (S) and cost units charged (U) are also compared.

responds to an increase of approximately seven gas chromatographs per year. The reason for this is that in addition to a special GC laboratory there is also a large gas-analysis laboratory.

If instead of merely considering the growth rates of the two central analytical laboratories, one looks at the overall increase in the number of gas chromatographs installed throughout BASF AG, then a statistically much more balanced picture is obtained (Fig. 6). In this case the rate of increase in the total number of instruments is approximately 30 per year, and is thus considerably greater than the growth rate in the central analytical laboratories. Approximately three quarters of the instruments are employed not in the central analytical laboratories, but instead are distributed in a decentralized fashion amongst roughly a dozen analytical subcentres and a great variety of production points. There are altogether approximately 92 laboratories in which GC studies are carried out. Electronic integrators of various degrees of sophistication are available for approximately 400 gas chromatographs (channels). Seven medium-sized computers are in operation in the two analytical centres and three subcentres (Table 2).

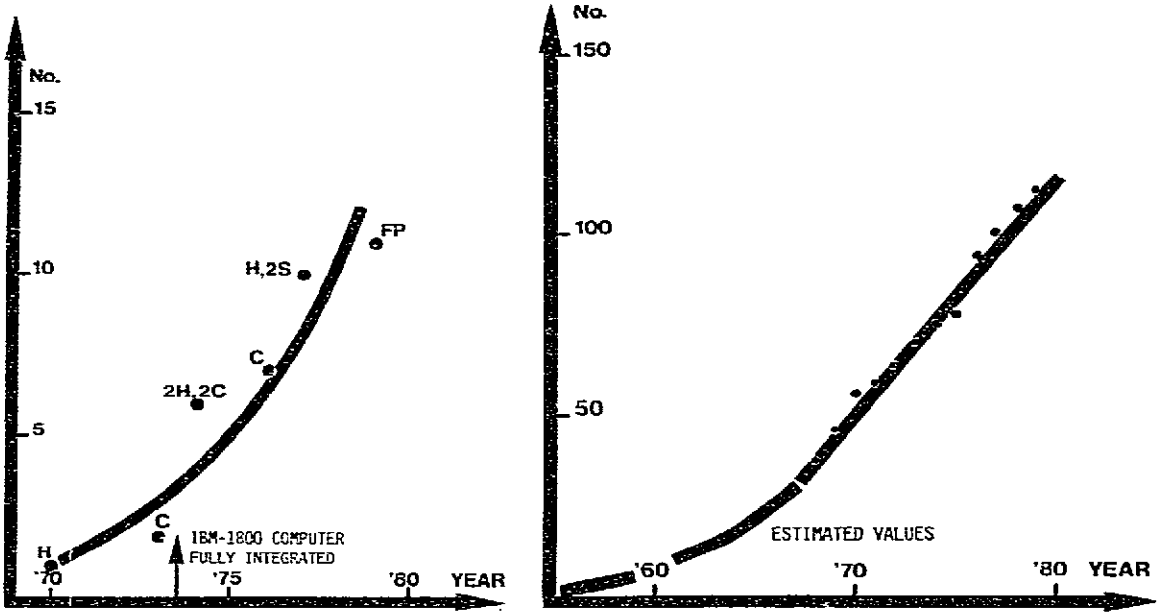


Fig. 4. Increase in the number of automated injection systems for GC between 1970 and 1979. Data from BASF Analytical Centre WHU South. Types of injection systems: H = headspace device; C = capsule device; S = syringe device; FP = flow-through plunger.

Fig. 5. Total number of gas chromatographs installed between 1955 and 1973 in BASF Analytical Centre, WAA North. Increase: *ca.* 7 gas chromatographs per year.

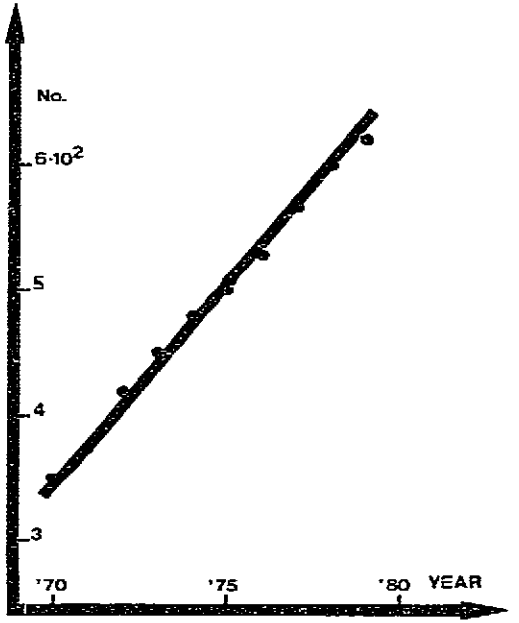


Fig. 6. Total number of gas chromatographs installed between 1970 and 1979 in BASF AG. Increase: *ca.* 30 gas chromatographs per year. No. of automated injection systems in BASF in 1979: 66 GC injectors, 10 headspace devices.

TABLE 2

TOTAL NUMBER OF INSTALLED GC AND HPLC INSTRUMENTS AND COSTS OF TLC IN BASF AG AND THE ANALYTICAL CENTRE WHU SOUTH

Type of process	*Instruments*	*No. of instruments*
GC	GC instruments	Total 620
	Automated injection + headspace systems	66 + 10
	Integrators (channels)	260 (400)
	Computers	7
HPLC, WHU/WAA Lab. only	HPLC instruments	20–30*
	Integrators, multi-channel	2*
Gel permeation chromatography	Instruments	15–20
Process GC	Instruments installed	*ca.* 80
TLC	TLC scanners	5
	TLC costs (1978), including plates + (reagents and instrumental aids)**	40,000 DM (20,000–40,000 DM)

* The total value for BASF is estimated at about 2–3 times this value.
** No other figures available for the estimation of the use of TLC at BASF AG.

At present, approximately 65 automated injection systems of various types, together with about ten headspace injection devices, are employed for GC. It is estimated that between five and ten automatic injectors for liquid chromatography are now in use.

Process GC, which should be regarded as a technical variant of GC, is employed in approximately ten installations for monitoring air quality and in about 70 units for process monitoring and regulation.

Fig. 7 shows the growth in the number of high-performance liquid chromatographic (HPLC) installations in the Analytical Centre South and the total number of samples analysed. The latter data are also broken down into the percentage of samples analysed by means of low-pressure liquid chromatography and the percentage using HPLC. The figures naturally cover only a relatively brief period, but nevertheless the curves demonstrate the rapidly increasing importance of this technique. Also in this instance the number of samples received is not a true reflection of the extent to which HPLC is employed.

These data may lead to the remarkable conclusion that, at least as far as chromatography is concerned, the bulk of the analytical work is not in fact performed in the analytical laboratories but is, instead, carried out in the various plants and subcentres. This naturally prompts the question as to what role the central analytical laboratories play in the firm. Of the roughly 700 staff employed in the two central analytical laboratories, approximately 15–20% are involved in chromatographic work. From this figure and from the volume of GC data, it is possible to estimate that

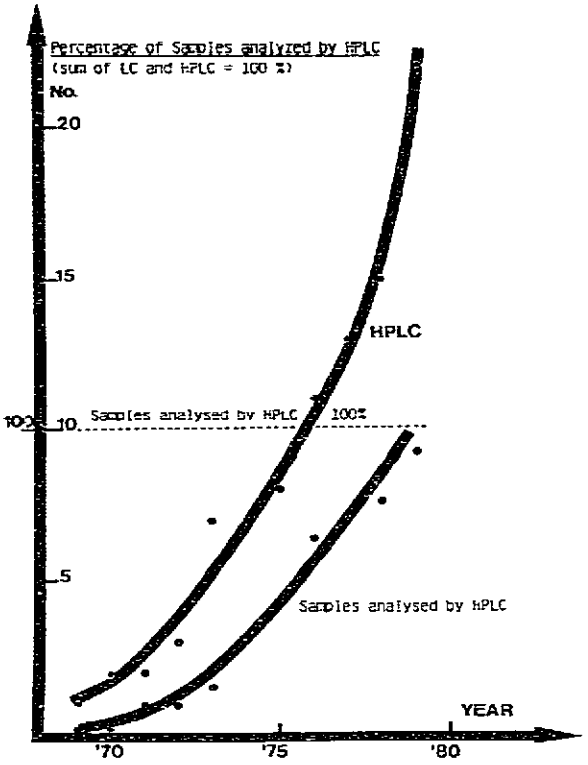


Fig. 7. Total of HPLC installations in BASF Analytical Centre WHU South.

altogether about 1000–1500 persons are partly or wholly engaged in carrying out chromatographic studies.

What the ideal number of professional analysts should be in comparison with the number of plant analysts is a particularly difficult question, to which there is no generally applicable answer. When, however, the works exceeds a certain size then a compromise develops automatically as a function of the two basic preconditions for optimal analysis, namely maximal understanding of the problem and maximal understanding of the method on the one hand, and the need to obtain rapid results on the other. One of these compromises at BASF has been the development of analytical subcentres, which function as an intermediate link between the central analytical laboratories and the analytical laboratories in the plants. At the moment there are approximately twelve such subcentres in BASF. These subcentres carry out both in-plant analyses and process control as well as analyses for production-oriented research and technical applications research.

3. FUNCTIONS AND APPLICATIONS OF CHROMATOGRAPHIC TECHNIQUES IN BASF

Naturally, for most of the problems encountered in research and development, every possible promising chromatographic technique is employed, irrespective of

whether the method will be used later for control and production purposes. A particularly important field for chromatography is in the department of technical applications, as it is here that a new product is subjected for the first time to a whole combination of investigations. These studies are carried out to resolve questions regarding production, quality control, product applicability for the customer, official approval for the product, environmental factors, etc. Examples of such tests include the analysis of monomers, studies on the migration of monomers and chemical auxiliaries from plastic utensils into foods cosmetics and drugs and consumer protection by means of predictive measurements.

Just how important these investigations are, and just how much effort these chromatographic studies involve, may be illustrated by mentioning a few examples of world-wide significance, such as the analysis of vinyl chloride in PVC and of acrylonitrile in polyacrylonitrile plastics, or the development, testing and approval of plant protection agents such as Bentazon or phenoxyalkanoic acids. Fig. 8 shows as an example acrylonitrile analysis in sunflower oil after a migration test.

In this connection, one must also mention the very active part BASF has played in the work of the Analytical Commission of the German Federal Health Authority over the last 22 years. This Commission has worked out guidelines for the analysis of everyday articles, particularly those made of plastic.

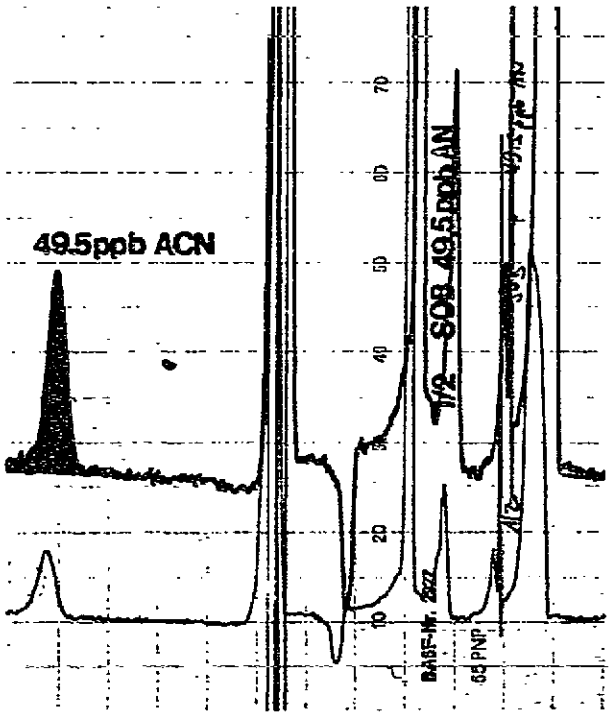
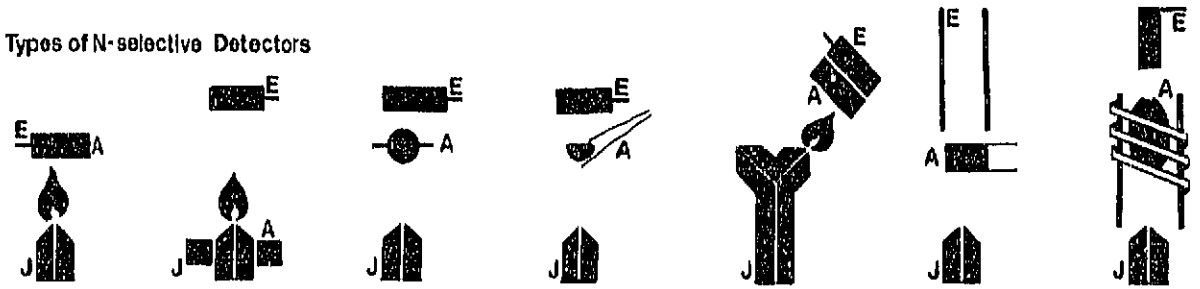


Fig. 8. Determination of *ca.* 50 ppb (10^9) of acrylonitrile (ACN, AN) in sunflower oil (Sonnenblumenöl, SOB) after a migration test. Selective measurements were made using a nitrogen-selective TID in combination with the GC headspace technique.



Alkali metal source	RbBr	$RbSO_4$?	$RbSO_4$?	$RbSO_4$/RbBr	Na_2SO_4, KCl, RbCl, CsBr	Rb-Ceramic	RbBr
Form of application	Crystal	Salt-cup	Salt-cup	Pt/Ir pan	Impregnated spiral	Ceramic bed, impregnated	Quartz ampoule
Ionization, plasma	Direct flame	Direct flame	Plasma around the bed	Hydrogen plasma around the pan	Direct, flame	Direct, electric heating	Indirect electric heating
Selectivity, N/C for nitrogen	5000:1	100:1	25,000:1	20,000:1	1000:1	50,000:1	100,000:1

Fig. 9. Types of nitrogen-selective detectors. A = Alkali metal source; J = jet; E = electrode. The table shows the corresponding form of alkali metal application and, if known, the composition of the alkali metal source.

4. REVIEW OF ANALYTICAL CHROMATOGRAPHIC TECHNIQUES EMPLOYED IN BASF

Table 3 shows the GC–detector combinations which are most frequently employed. These combinations involve one- and multi-dimensional detectors. It goes without saying that GC–mass spectrometry (MS) coupling and its different variations play a very important role, both in research and also to some extent for monitoring concentrations of substances down to trace levels.

TABLE 3

GAS CHROMATOGRAPHY–DETECTOR COMBINATIONS USED AT BASF AG

GC–MS	*GC–IR and TEA*	*Selective detectors*	*GC–TLC and smell analysis*
Electron impact and chemical ionization techniques, magnetic and quadrupole instruments, high-resolution instruments	IR: Fourier transform instrument TEA: thermal-energy analyser for nitrosamine analysis	N- and P-selective detectors (TIDs) (different types), ECDs, flame photometric detectors, microwave plasma detectors, detectors for halogens and sulfur	GC–TLC combination mainly for aromatic compounds and amines; smell analysis with special smell test-tubes

Recently we have started to employ GC–infrared (IR) coupling. The Fourier transform instrument is capable of yielding complete IR spectra even when only small amounts of substance are available. Readily interpretable IR spectra can be obtained for GC peaks with a mass flow of 200 ng/sec. In addition, it is possible to exploit the high degree of separation which can now be achieved at very low sample concentrations.

BASF has traditionally produced a very wide range of nitrogen compounds, and hence nitrogen-selective detectors are of particular interest. Virtually every type of nitrogen-selective detector has been tested in our laboratories (Fig. 9).

The need for an element-specific detector, capable of responding simultaneously and specifically to different elements, has, in the meantime, been fulfilled by the microwave plasma detector. The sole disadvantage of this detector is that, depending on the element concerned, the sensitivity is 10–1000 times lower than that of a flame-ionization detector (FID).

We have continued to employ GC–thin-layer chromatography (TLC) coupling on a small scale, in particular since it has proved possible to develop this technique, which has long been known, into a GC–"smell" analysis. By means of this method it was possible to solve a series of complex smell problems, with the assistance of the human nose, but under much better defined conditions. This technique is shown in Figs. 10 and 11.

HPLC has reached a very high level of sophistication and is widely employed. Although it is perhaps almost trivial to enumerate the serious shortcomings associated with the method, nevertheless some of them should be mentioned.

The most serious problem is still the search for a detector with characteristics that can compare, even to a first approximation, with those of the FID. The chances of developing such a detector, however, appear to be slim when one considers the difference between the mobile phase in HPLC and GC.

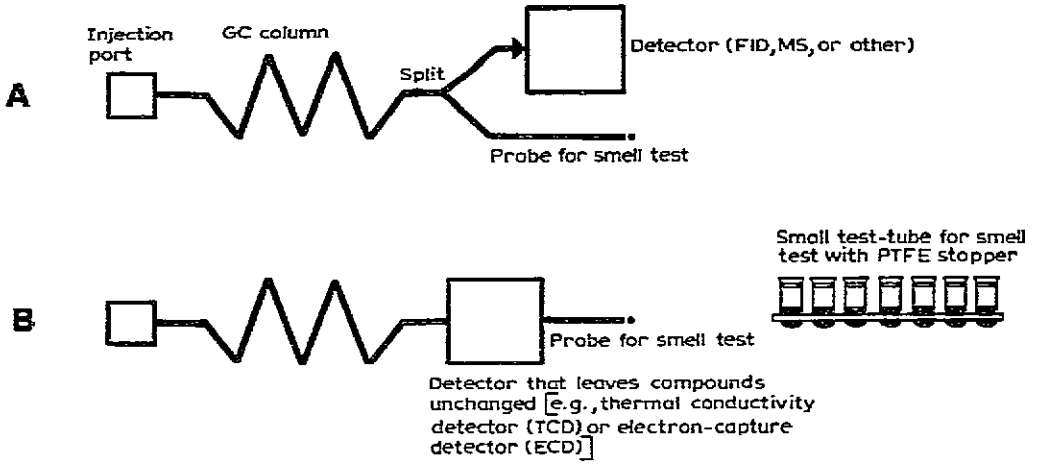


Fig. 10. Different types of experimental design for smell analysis. In order to avoid interferences due to laboratory air (smell), heat from instruments, extraneous odours, etc., the individual odour fractions (peaks) are adsorbed in small sample tubes containing an adsorbent such as silica gel. It is only in this way that the smell of the individual fractions can be assessed in a neutral atmosphere. Some of the fractions are eluted at intervals of only a few seconds (*e.g.*, with capillary columns). In this case the functional capacity of the human nose is often overstressed after a few peaks. When assessing the odour, the adsorbed substances must first be desorbed by the addition of a few drops of water. In some instances the sample must be warmed[3]. Mode A: device with split and very sensitive detector; the main stream is flowing directly to the smell probe. Mode B: the total amount of sample is passing through a non-destructive detector to the probe.

A problem of almost equal gravity is the qualitative identification of the separated substance. HPLC–MS coupling, even if one day it should become a routine method, will surely never achieve the same significance as GC–MS coupling, for many reasons.

In comparison with these classical shortcomings of HPLC, experimental difficulties such as the moderate lifetime of the columns used for the widely used reversed-phase chromatography are almost insignificant. If a more exact control of the flow-rate could be achieved, this would lead to a highly desirable improvement in the precision of the method.

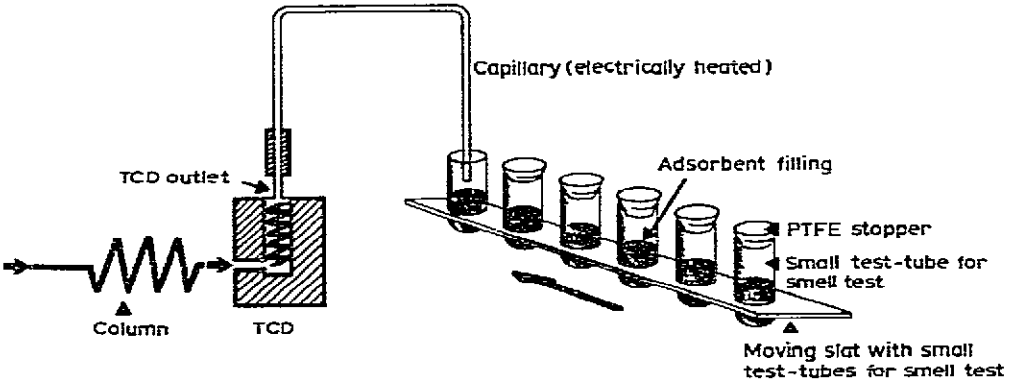


Fig. 11. Collection of fractions for subsequent sensory analysis. See also the legend to Fig. 10.

TLC is, of course, extensively employed and is unrivalled as both a qualitative and a semi-quantitative method. Nevertheless, when employed as a quantitative procedure, TLC possesses obvious disadvantages, such as only moderate accuracy, a small dynamic range, a complicated calibration procedure and a large human factor. In certain analyses these shortcomings can, in fact, be tolerated and quantitative determinations are still frequently carried out. Compared with the relative simplicity of the separation procedure it seems that the scanner operates in a very complicated fashion. The ultimate solution could be a "computerized image analyser" in which the whole adjustment and calibration process is performed by the computer. On the other hand, however, the combination of an extremely simple method of separation with an extremely complex evaluation procedure is highly undesirable.

Even though it is not immediately evident, considering the total number of GC instruments in operation, both mechanization and automation* are extensively applied not only for sample injection but also for result evaluation purposes. This has been particularly the case in the central analytical laboratories and analytical subcentres. The different types of instruments are shown schematically in Fig. 12.

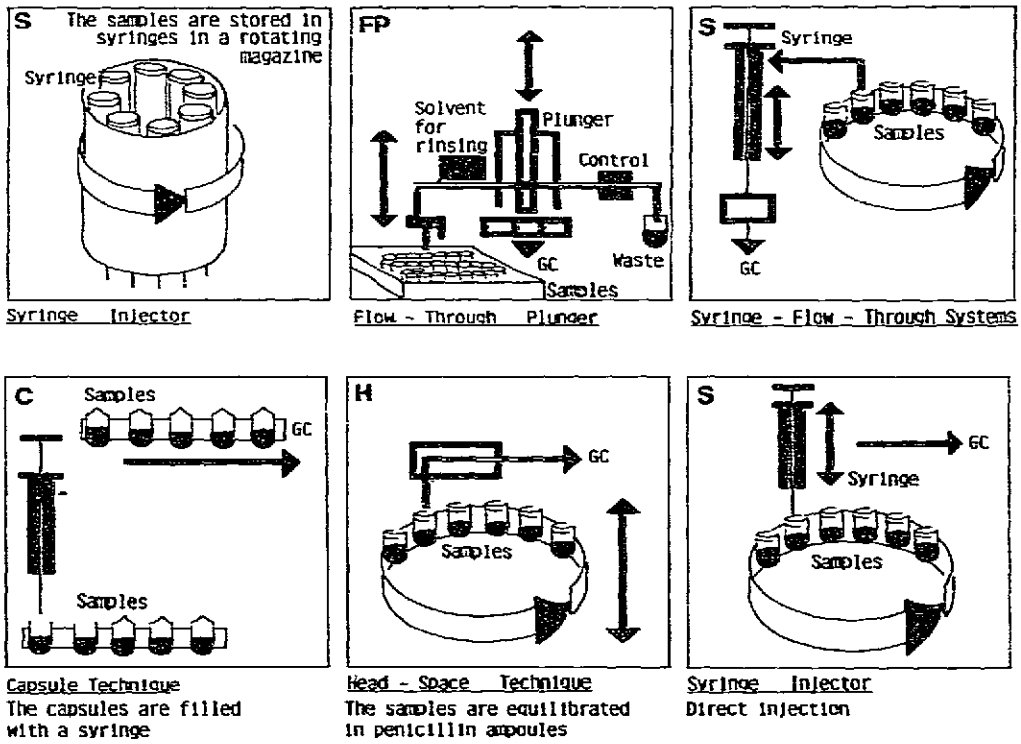


Fig. 12. Schematic representation of automated injection systems for GC. The optimal injection system must be selected with respect to the sample matrix (*e.g.*, viscosity, physical state) and the volatility of the compounds.

* Mechanization: substitution of manual work by a machine or apparatus. Automation: substitution of manual (mechanical) work, human influence and control by a device or apparatus with feed-back of results capable to make decisions (Fennel[4] and others[5–7]).

The computer link-up (*e.g.*, in WHU) enabled automatic injectors to be employed for the first time on a large scale. Following this development, the use of these devices in production and control laboratories spread very rapidly. The introduction of automated chromatographs in the central analytical laboratories brought with it the following benefits:

In special routine analyses it was possible to carry out many more determinations at a lower cost, owing to continuous day and night operation. For instance, the introduction of the first automated capsule system meant that the cost of some routine series could be cut by 60%. During the period from Friday evening to Monday morning it was possible for one unsupervised instrument to perform between 100 and 200 analyses automatically and to provide fully evaluated sets of results. Of course, it goes without saying that for work of this kind it is essential to have a flexibly programmable computer, which prints out a complete analytical report as well as a list of control functions for the evaluation algorithms.

A further advantage is the fact that when such automatic analysers are employed, better reproducibility and hence in some instances also higher accuracy can be achieved, if it is possible to reduce the measuring error by means of appropriate calibration and test runs.

Two examples are given in Tables 4, 5 and 6, for the analysis of Bentazon and vitamin E acetate, and a gas chromatogram is shown in Fig. 13.

TABLE 4

CALIBRATION FACTORS FOR BENTAZON AS METHYL DERIVATIVE

Fluctuations during a continuous cycle of measurements of the same sample (automated injection, computer evaluation). The cycle was: cal. 1, sample 1A, sample 1B, cal. 2, sample 2A, etc. A constant calibration factor ($f = 1.73$) was used to show the oscillations of the analytical results during repeated analysis of one sample during an uninterrupted cycle of measurement.

Time (min)	*Calibration No.*	*Nominal value for Bentazon (%)*	*Effective value found for Bentazon (%)*
0	1	99.4	100.2
99	2	99.4	100.0
205	3	99.4	99.7
417	4	99.4	100.7
524	5	99.4	99.5
630	6	99.4	98.0
737	7	99.4	97.3
843	8	99.4	99.8
950	9	99.4	98.3

The search for the best combination of separation parameters could be considerably accelerated and also reduced in cost by employing an "automatic method optimizer". Such a device would pre-programme temperatures, temperature programmes, gas pressures and flow-rates as well as eluent flow-rates and gradients for a large number of analytical runs. First steps have already been taken in this direction,

TABLE 5

CALIBRATION FACTORS FOR BENTAZON (AS METHYL DERIVATIVE) WITH OCTADECANE AS INTERNAL STANDARD[1]

Measurements on different days, during which the column was held at a working temperature of 205°C. Day-to-day oscillations of the calibration factor; these oscillations can be eliminated by differential calibration and analytical cycles with the following order of measurement: standard mixture 1 (f_1), sample A1, sample A2, standard mixture 2 (f_2), sample B1, sample B2, etc. The mean of results A1 and A2 is corrected by the mean of factors 1 and 2 (measured with standard mixtures 1 and 2).

Date	*Time (h)*	*Calibration factors*			*Samples measured*
		f_1	f_2	$\bar{f}$	
7.3.78	f_1: 18.40	1.742	1.731	1.74	2
	f_2: 20.16				
	f_3: 21.56	f_3 1.726		1.73	2
9.3.78	f_1: 11.48	1.750	1.706	1.73	
	f_2: 13.30				2
10.3.78	f_1: 11.28	1.740	1.674	1.71	
	f_2: 13.10				2
11.3.78	f_1: 10.58	1.734	1.726	1.73	
	f_2: 12.37				2

TABLE 6

CALIBRATION FACTORS (f) FOR THE DETERMINATION OF VITAMIN E ACETATE WITH SQUALANE AS INTERNAL STANDARD

The table shows the extreme discrepancies that can occur if the analytical result is obtained with automated injection plus computer evaluation on the one hand, and manual injection and planimetry on the other. These differences in reproducibility occur especially during analysis with an internal standard (see corresponding chromatogram in Fig. 13).

$f = \frac{F_{St}\, M_V}{F_V\, M_{St}}$, where F_{St} = peak area of standard peak (squalane), F_V = peak area of vitamin E acetate, M_{St} = mass of standard, M_V = mass of vitamin E acetate.

f	
Manual injection, evaluation of peaks by planimetry	*Automated injection, evaluation of peaks by computer*
1.143	1.114
1.163	1.121
1.171	1.106
1.259	1.095
1.062	1.125
1.271	1.119
1.186	1.117
	1.119
Mean: 1.179	1.115
S*: 0.071	0.010
$S_{rel.}$**: 6.0%	0.87%

* Standard deviation.

** Coefficient of variation (%).

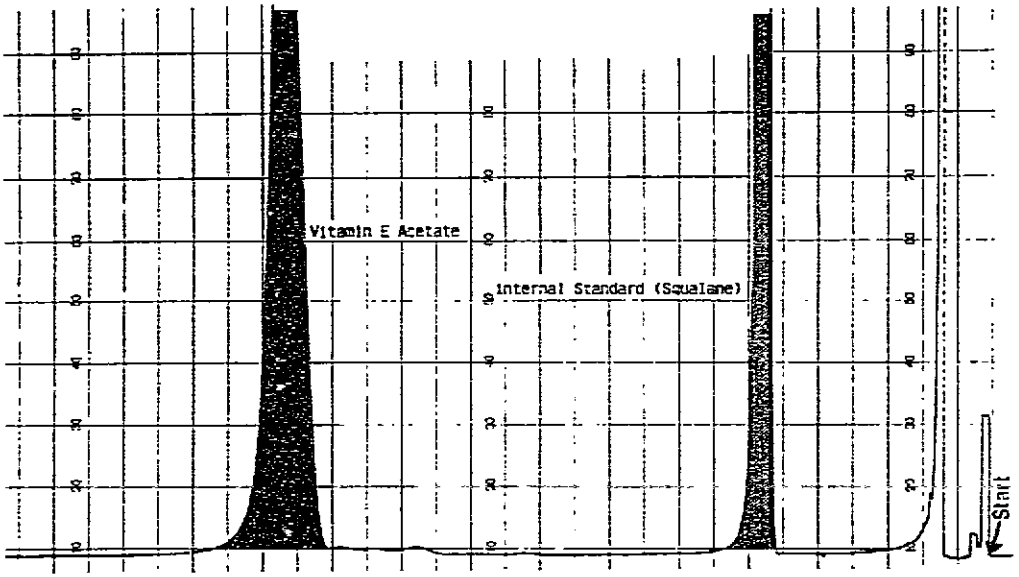


Fig. 13. Gas chromatogram of a vitamin E acetate test sample. Conditions: glass column (2 m × 4 mm I.D.) coated with 5% SE-30; temperature, 252°C (isothermal).

even though the instruments are not completely satisfactory and to date only limited experience has been gained in their use.

A particular publication[2] illustrates very clearly the fact that all the problems and questions associated with GC, such as automation, calibration, choice of test substances, switching technique, column preparation and separation theory, are also arising in HPLC, albeit much more rapidly.

Of the many special chromatographic techniques which are known some are employed extensively in BASF, whilst others are themselves the objects of further research (Table 7).

Pyrolysis gas chromatography is employed in all its forms, using packed and capillary columns as well as in combination with every conceivable microchemical reaction.

In recent years, the headspace technique has gained considerably importance,

TABLE 7

SPECIAL CHROMATOGRAPHIC TECHNIQUES USED AT BASF AG

1.	Pyrolysis gas chromatography*
2.	Reversion gas chromatography[8]
3.	Headspace technique*
4.	Hyperfluid chromatography
5.	Column-switching according to Deans*
6.	Preparative HPLC
7.	Gel-permeation chromatography*

* Widely used.

particularly with automated instruments. Whilst the first automated headspace instrument was employed at BASF as early as 1970, this technique has only achieved worldwide popularity in the last few years. This has been the result of migration experiments carried out in connection with trace- and ultra-trace determinations of monomers such as vinyl chloride and acrylonitrile in plastic goods and in other products into which monomers may migrate.

Although GC techniques have reached a highly advanced level, there are nevertheless areas where interesting technical developments are still taking place, for instance the column-switching technique of Deans. Despite several years of research and development in this field, only recently have relatively simple routine instruments that do not require complicated procedures for the adjustment and optimization of the switching time become commercially available. The Deans column-switching technique is now beginning to be employed for laboratory purposes at BASF. On the other hand, in our central analytical laboratories this method is at present the principal competitor to the capillary technique.

Preparative HPLC has recently attracted growing interest. The application of Fourier transform technique in infrared and nuclear magnetic resonance spectroscopy often enables very impressive spectra to be obtained using only microgram amounts of sample, and therefore minor components of complex mixtures can also be identified. One of the liquid-phase chromatographic techniques employed extensively is gel-permeation chromatography. This method is not restricted to the characterization of molecular weight distributions, but in addition the aim is always to achieve a qualitative identification of separated components using a specific detector such as a laser detector.

As modern analysis is expensive, it seems justifiable to ask how the maximum of information can be obtained at minimal cost. The main problem here is surely one of achieving the closest possible cooperation between the analyst and the chemist who synthesizes the sample. In this way it would also be possible to reduce the risk of producing exactly reproducible, but incorrect, analytical results.

5. PROBLEMS, REQUIREMENTS, INSTRUMENTATION (EXAMPLES)

First, some questions can be posed. Is the high cost of chromatography the result of the high cost of the instruments? Is the large amount of work which chromatography entails due to the tendency of the instruments to develop faults and require repairs, or is it a consequence of the instruments being inadequately adapted to the analytical problems encountered? Why do workers in the field of chromatography have to waste so much of their time on problems involving purely technical details, upon which the success or failure of a method often depends?

For a start, one often has the feeling that the actual chromatographic parts of the instrument, namely the separation columns with their inlets and outlets, are not considered the key section of the whole apparatus. All sorts of publications and discussions had dealt for a long time with topics such as dead space and peak broadening, techniques for their measurement and calculation, and the effects of contaminated connection capillaries. It never ceases to amaze one that successful principles of instrument construction are discarded after only one or two production series, and are only readopted after prolonged discussions or as a consequence of

economic failures in certain laboratories or companies. Completely different schools of thought exist even with regard to fundamental questions of standardization, such as modular construction, modular dimensions and amount of space required for modules. It is practically impossible to install an FID amplifier from company X in an instrument from company Y without the assistance of an electronics expert. With standardization of electronic–electrical connections it would merely be necessary to insert a normed module. It seems to be a law of nature that FIDs in instruments from different manufacturers are not interchangeable! Even detectors from relatively similar models made by the same firm are usually not interchangeable. There is a similar lack of standardization of the connections for glass columns. Only a small number of companies have at least standardized the distance between the two connections so that glass columns may be interchanged. With hundreds or even thousands of glass columns in a large analytical laboratory and with up to ten different types of gas chromatographs, it requires considerable effort to maintain flexibility. The large analytical laboratories are therefore particularly anxious to see standardization of constructional elements and connection sizes in the above-mentioned areas.

In HPLC the relative ease of combination of the various instrumental units has led to competition between the manufacturers, and this has certainly been the decisive factor contributing to the exceptionally rapid development of HPLC instruments.

In view of the extremely positive developments that have occurred in liquid and thin-layer chromatography, we should also like to see clear and precise specification (standardization) of the stationary phases used in GC. Unfortunately, research in this area has been largely neglected. In connection with these remarks, a further problem, which still remains completely unsolved, should be mentioned, namely the standardization of glass capillary columns.

As increasing costs render mechanization and automation[4–7] of chromatographic processes essential, further development work in this direction must be carried out, particularly in GC and HPLC.

We still experience considerable difficulties with automatic injectors, especially with matrix and viscosity problems, and cross-contamination continues to cause many problems. Unfortunately some autosamplers cannot tolerate even limited variations in the viscosity of the samples. In certain instances instruments cannot be employed as a consequence of cross-contamination at the trace level. There is still no problem-free, routine injection device available for quantitative capillary GC.

It is well known, of course, that the computer is only as good as the program supplied by the analyst, and that computers often produce rubbish, albeit very reproducibly. The instruments should not degenerate to "black boxes" and the analyst must retain a complete understanding of their mode of operation. We shall not discuss here the subject of the "apparent achievements" of the microprocessor, which sometimes seem to lead to easier operation, but often are only a hindrance when one is working.

6. SUMMARY

The statistical data presented and the widespread use of all the major available chromatographic techniques underline that chromatography is a very powerful analytical tool at BASF. In order to develop effective analytical methods economically

and to avoid developments in the wrong direction, it is necessary in the future to have more direct cooperation between analysts, instrument manufacturers and chemists working on synthesis.

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