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THE DEVELOPMENT OF GAS CHROMATOGRAPHY

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SUMMARY

The development of the two major gas chromatographic techniques —based on adsorption and partition— from their beginning is summarized. In gas adsorption chromatography, the work of the pioneers is placed in the context as a precursor to the development of real gas chromatography. After the invention of gas–liquid partition chromatography, the technique underwent very rapid growth, reaching maturity within a few years. Subsequent developments in the theory, detectors and columns made it possible for the technique to reach its present advanced stage. The development of two special gas chromatographic techniques —process control and analysis, and preparative gas chromatography— is summarized separately.

INTRODUCTION

No analytical technique has gone through such rapid and intensive development as gas chromatography (GC). Practically from the beginning of modern GC, cross-fertilization of ideas by continuous contact, frequent international gatherings, and rapid publication of the newest results played a vital role in the rapid advancement of the technique. The almost immediate introduction of commercial instruments and the activities of the instrument companies, demonstrating the applicability of the new analytical method in a wide range of fields also had an important impact on the expansion of GC.

The technique of gas–liquid partition chromatography began by the pioneering work of A. T. James and A. J. P. Martin in 1951–1952. There had been, however, fairly intensive work in the nineteen thirties and forties in gas adsorption chromatography although the connection with chromatographic principles was not always recognized. By 1952, this technique also reached a mature stage and started to be utilized in analytical laboratories.

In this discussion of the development of GC we shall first deal separately with the early development of the two techniques. In each case, we will try to follow the development from its beginnings up to the point where the technique reached a mature stage. Subsequently, under the heading Second generation gas chromatography, we shall summarize the most important achievements in theory, detector and column development which permitted GC to reach the advanced stage at which it is today. Finally, the development of two special techniques —the use of GC for process analysis and control, and preparative GC— will be outlined.

The author of this paper has been intimately involved with GC since early 1957, participating in many of the developments reported here, and knows personally most of the scientists mentioned. Thus, having first-hand knowledge of the developments reported here, one could not expect him to deal with the subject as if it were a historical discussion. He will not be impersonal; still, he believes that the discussion is without bias or prejudice and represents an honest attempt to place the individual developments in their proper context.

This paper was written on the occasion of the Tenth International Symposium on Advances in Chromatography, and as a prelude to the twentieth anniversary of the First International Symposium on "Vapour Phase Chromatography", held in 1956 in London, which represented the start of the exponential development of the technique.

GAS ADSORPTION CHROMATOGRAPHY

Early period

Although the use of selective adsorption for the separation of gases and vapors has its origins in the period before the First World War, its first significant application was in the gas mask. After the War, as an extension of this research, commercial processes were developed, *e.g.*, for the recovery of raw gasoline from natural gas, and benzene and light oils from manufactured gas.

Selective adsorption was also used in various laboratory testing methods. The charcoal test widely used in the U.S.A. in the 1920s for determining the light hydrocarbon content of natural gas employed adsorption on charcoal followed by the removal of the adsorbed compounds by displacement with glycerol or mercury vapors[1].

In other methods, the adsorption was carried out at a low temperature and was followed by desorption, by raising the adsorbent's temperature. Eucken and Knick[2] modified this technique by having an oven moving slowly along the outside of the adsorbent. Turner[3] combined the two methods by using both an outside heater and mercury vapor. He also recorded the thermal conductivity of the effluent from the adsorbent; the recorder trace is similar to an integral chromatogram. An instrument based on this technique has been developed and marketed by the Burrell Corporation, Pittsburgh, Pa., U.S.A. (the "Turner–Burrell Adsorption Fractionator"). Subsequently the technique was further developed by using a "displacer gas" fed to the adsorption column by the vaporization of a liquid; this was the basis of the "Fracton", another instrument from the Burrell Corporation introduced in 1954; this unit was described by Guild at a number of meetings and, somewhat later, by Clough[4].

A displacer (carbon dioxide) was also used by Schuftan[5], who introduced the use of an interferometer as a detector.

The techniques used by these early researchers may be considered as variants of the frontal and displacement methods systematized in the nineteen forties in the institute of Tiselius, in Uppsala, Sweden. Claesson, a member of this group, reported in 1946 a number of possibilities for both techniques in gas adsorption analysis and even described a self-recording apparatus[6,7]. These techniques were further developed by Phillips and his coworkers at Oxford University[8–12].

Beginning of modern gas adsorption chromatography

Modern GC is based on elution, in a continuous flow, using an inert carrier gas. Hesse and coworkers at the University of Marburg/Lahn, in Germany, were the first to apply this technique (which they termed "adsorption distillation") to the separation of volatile organic acids; even more important, they recognized the relationship between their technique and chromatography and correctly described the chromatographic separation process using a gas as the mobile phase[13]. Hesse's work was, however, interrupted by the War and was resumed only well after the hostilities ended.

Another group connected with the early development of gas adsorption chromatography was that of Damköhler and Theile. Damköhler was Eucken's student, and thus we have a continuation of Eucken's philosophy and theories. Their results were briefly summarized in 1943[14] with the announcement that the detailed discussion would be published later, towards the end of 1944, in No, 49 of the *Beihefte der Verein deutscher Chemiker*. However, this issue was published only during the very last months of the War and did not reach many libraries; thus, it could not have any impact on future developments.

The technique of "gas adsorption chromatography" was also approached at about this time by Glueckauf, in England; the idea was briefly discussed from the theoretical point of view, in his thesis dated April 1945. In 1946, he developed a microanalytical technique for the determination of helium and neon in air which can be considered as a precursor of GC[15]. Glueckauf's first truly GC work was carried out in 1951 but due to its confidential nature (atomic energy research) was not published at that time but only briefly reported[16] in the discussion of another paper[9].

Modern gas adsorption chromatography

The first scientist to carry out true modern gas adsorption chromatography was Cremer at the University of Innsbruck who, in 1945–1950, with Prior (thesis: 1947) and Müller (thesis: 1950) developed a system consisting of a carrier-gas source, a sample introduction device, a thermostatted separation column and a thermal conductivity detector, demonstrating its application to both the analysis of light gases and physico-chemical measurements, and introducing a number of basic terms and relationships now universally used in all branches of GC[17]. Their work was published in 1951[18–20].

This period in the history of gas adsorption chromatography ended with the activities of two groups: one in the U.S.S.R. (Turkeltaub and Zhukovitskii) and the other in Czechoslovakia (Janák).

In 1950–1953, Turkeltaub, Zhukovitskii and coworkers developed the technique of "chromathermography" which in some ways resembles the technique of Eucken and Knick and Turner, *i.e.*, a moving heater applied along the chromatographic column[21–25]. This technique found fairly wide application in the U.S.S.R. but its real impact on analytical chemistry in the West was slight.

Janák's method was developed in 1949–1950[26], as a necessity because of trade restrictions which prevented the import of a Podbielniak analyzer from the United States[17]. It represented true GC in the modern sense. Carbon dioxide was used as the mobile phase and a nitrometer as the detector; the individual fractions were measured volumetrically while carbon dioxide was absorbed by the potassium hydroxide in the nitrometer. In 1953–1955 Janák published a large number of papers on the principles and applications of this method; only a few from the early years are listed here[27–31]. The method was particularly useful in the analysis of fixed gases and light hydrocarbons.

Janák's method was widely used in the middle nineteen fifties in Europe (see *e.g.*, refs. 32 and 33) and a commercial version was also available in West Germany. The principal drawback of the system was that it needed continuous attention in order for the volume of each collected fraction to be read immediately after the emergence of a component was completed. Later, Janák also tried to automate the system[34,35]; however, the general-purpose gas chromatographs commercially available by then, with thermal conductivity detectors and automatic peak recording, proved to be more convenient. Since everything that could be analyzed in the Janák system could also be analyzed in the general-purpose gas chromatographs by simply using the appropriate adsorption column, these instruments gradually replaced the Janák system. This fact, however, does not diminish Janák's important contribution to the development of gas adsorption chromatography as a routine analytical tool.

New adsorbents

In the early work, activated carbon was initially used as the adsorbent followed by silica gel and alumina. A significant new addition was the molecular sieves introduced in 1955 by Janák[36,37]. After the introduction of gas–liquid partition chromatography, gas adsorption chromatography was used in practice almost exclusively for the analysis of inorganic gases and C_1–C_2 hydrocarbons. However, in the last 12 years, the introduction of new adsorbents resulted in a renewed interest in this technique and its use for the separation of organic compounds. In particular, four types of new phases found wide-ranging applications: the microporous polymers introduced in 1966 by Hollis[38,39], graphitized carbon blacks utilized practically simultaneously by a number of authors[40-42], the carbon molecular sieve described in 1969-1970[43,44], and Tenax introduced in 1970[45].

GAS-LIQUID PARTITION CHROMATOGRAPHY

The invention of the technique

In the advancement of chromatography as an analytical technique, the introduction of partition as the basis of separation by Martin and Synge, in 1941, is one of the most significant events, rightly recognized by the 1952 Nobel Prize in Chemistry. This work dealt with liquid–liquid partition chromatography, *i.e.*, with systems in which both the mobile and the stationary phases were liquids; however, Martin and Synge immediately recognized that the technique was not restricted to such systems. Their original paper[46] contained the following often quoted prediction:

> "The mobile phase need not be a liquid but may be a vapour ...
> Very refined separation of volatile substances should ... be
> possible in a column in which permanent gas is made to flow
> over gel impregnated with a non-volatile solvent ..."

Although this statement clearly predicted the possibility of gas–liquid chromatography, the potential of the technique was not immediately appreciated. Authors dealing with the development of GC often express their surprise at this, particularly considering the very rapid development after 1952 when proposals and suggestions were immediately tried by a number of scientists. There is, however, nothing to be surprised at: the reason for disregarding this suggestion was simply the advent of the Second World War. Communication between scientists in different countries had already been interrupted and it took some time after the War ended before it was finally re-instituted. The *Biochemical Journal* in which the paper of Martin and Synge appeared is published in England and in 1941, a large part of Europe was excluded from its circulation; it took some time after the end of the War before the back-issues could be obtained. Also, let us not forget that liquid–liquid partition chromatography (and particularly its paper chromatography version introduced by Martin and coworkers in 1944) itself revolutionized analytical chemistry, and it took a few years until this technique was fully developed.

The idea mentioned in 1941 was finally put into practice in 1951; this was done by Martin himself, now working at the National Institute for Medical Research, in London, and associated with A. T. James.

A fairly detailed account about these events was given by Martin himself[47]. At the Institute, they were engaged in research work which did not result in any success and James became so discouraged that Martin suggested that they switch to a project which must surely work: to test the prediction he made ten years earlier. A request to try to develop a more advanced method for fatty acid analysis came as a good model for the investigations. Their work succeeded fairly rapidly and soon the new technique was born; their paper was submitted for publication on June 5, 1951, and published in the first part of 1952, again in the *Biochemical Journal*[48]. This paper, followed in the same year by three others[49-51], triggered the unprecedented growth of gas chromatography.

Early development in Europe

The rapid expansion of the technique was particularly facilitated by the almost immediate contact between Martin and a few scientists in England and The Netherlands, associated with Imperial Chemical Industries, British Petroleum, National Benzole Co., Koninklijke/Shell and Unilever, to name just a few. The technique was shaped within three years into a general method applicable to a wide variety of sample types and employing over a dozen liquids as stationary phases. From this period the most important publications which, besides those of James and Martin, laid the foundation of future development should be quoted[52–57]. At the end of this period the first book on GC, by C. S. G. Phillips —himself a pioneer of the technique who, even before the publication of the paper of James and Martin, reported on additional investigations[9]—was also published[58], and commercial instruments were introduced (see below).

The theoretical treatment of Van Deemter *et al.*[59] published in 1956 provided a unified approach in relating column efficiency to the most significant characteristics of the chromatographic system. This theoretical treatment became generally known after the detailed investigations reported by Keulemans and Kwantes at the 1956 London Symposium[60] and particularly after the publication of Keulemans' book in 1957[61] which served as the basic source of information to many of us in this most important stage of the development of GC.

The role of the Gas Chromatography Discussion Group

In the summer of 1955, the scientists involved in the development of the new, exciting technique felt that the time was opportune to plan a symposium on the subject. Thus, a committee was formed under the auspices of the Hydrocarbon Research Group of the British Institute of Petroleum for this purpose and the first symposium on "vapour phase chromatography" (the initial name of the technique) was held one year later, between May 30 and June 1, 1956, in London. Nearly 400 scientists from 13 different countries attended this symposium, heard the 34 papers and participated in the very lively discussions.

Following this very successful meeting, a Gas Chromatography Discussion Group was formed which then continued the organization of these symposia on a biennial basis. The activities of this Group, and particularly the biennial symposia, served a very important role in the rapid advancement of the technique, by providing a forum for the exchange of ideas. Therefore, when dealing with the development of GC, the importance of these symposia, particularly the first three (1956, London; 1958, Amsterdam; 1960, Edinburgh), the merits of the Group and especially of D. H. Desty, the organizer of the first two symposia and the driving force of the Group in these years, must be emphasized.

Early development in the United States

In the United States, the first laboratories where the new technique of GC was investigated, soon after the first reports from Europe, were those of the large petroleum and chemical companies. At Gulf Research & Development Co., the technique was almost immediately applied to the study of catalysts and catalytic reactions and, in fact, the papers describing their GC system[62] and the microreactor–GC system[63] were published almost simultaneously. At Tennessee Eastman, the original work involved gas adsorption chromatography and was first presented at the 126th National American Chemical Society Meeting held in September 1954, in New York City; this was probably the first paper on GC to be given at an American national meeting. In the published text[64] gas–liquid partition chromatography is mentioned briefly, but without further discussion or data; evidently, this work was by then in progress. One year later, the same authors gave a detailed account on the possibilities of this technique[65]. Scientists from Shell Development Co. first published three papers in the March 1956 issue of *Analytical Chemistry*[66–68] with a critical discussion on apparatus requirements, applications in the hydrocarbon field, and the combination of gas adsorption and partition chromatography. The development work at Esso concentrated mostly on the use of process analysis and control and their first reports were published in 1956[69]. We shall deal with the development of process instruments later.

Other companies mentioned in the first comprehensive report on the early development of GC published in *Chemical and Engineering News* in 1956[69a] are Monsanto, DuPont, Philip Morris, American Cyanamid Co., and General Foods. It is interesting to note that at Philip Morris GC was utilized to prepare fractions of cigarette smoke for further mass spectrometric investigations.

As mentioned, probably the first presentation on GC in the U.S.A. was at the 126th National A.C.S. Meeting, in September 1954. At the 127th National A.C.S. Meeting held in Cincinnati, Ohio, in April 1955, R. H. Munch of Monsanto discussed "vapor phase chromatography" in the session honoring the first winner of the Beckman Award in Chemical Instrumentation. At this time, the potentialities of GC were already recognized; this is best shown by the fact that the *Analytical Chemistry* report on the Cincinnati Meeting, although dealing with this paper in only one paragraph, had the large bold-face title "Vapor Phase Chromatography —Tool for Analysis of Gases and Volatile Liquids"[70]. The first full-scale symposium on the technique was held during the 129th National A.C.S. Meeting, in Dallas, Texas, April 1956: nineteen papers were presented dealing with various aspects of the technique. As stated in the report published in *Analytical Chemistry*[71],

> "... no beautiful movie actress could have drawn a more appreciative and attentive audience, well equipped with cameras, than did (this) day-and-a-half Symposium ... With more than 600 at the sessions, it was a standing-room-only event."

The papers presented ranged from the use of GC to physico-chemical studies to the analysis of complex hydrocarbon fractions and tobacco smoke.

It is interesting to note that while the early European papers mostly dealt with various aspects of the technique, the first American papers rather emphasized the use of GC in quantitative analysis, and, in fact, after the introduction of commercial instruments in 1955, the quantitative aspects were considered as the most important questions. This experience led Hausdorff to remark during his presentation at the 1956 London Symposium[72] that the emphasis on quantitative analysis is, to a certain extent, much stronger in the U.S.A. than in Europe. This completely innocent remark created an uproar in the discussion by representatives of leading English and Dutch laboratories, pointing out that they were using GC overwhelmingly for quantitative analysis. The discussion itself is immaterial; however, it was important in emphasizing the ease of routine quantitative analysis by GC.

Following the success of the 1956 London Symposium, the Instrument Society of America also became involved in the organization of biennial symposia at the campus of Michigan State University, in Lansing. The first such symposium was held in August 1957. Besides these symposia, the yearly Pittsburgh Conferences on Analytical Chemistry and Applied Spectroscopy and the national and regional meetings of the American Chemical Society regularly had special sessions on gas chromatography, contributing to the exchange of ideas and the rapid advancement of the technique.

The role of the instrument companies

In the development and rapid advancement of GC the various instrument companies served a vital role in providing reliable instruments at a very early stage of the technique, picking up quickly new results and developing standard components, and also carrying out part of the basic development; and by educating the new chromatographers, helping them to solve their application problems and publishing easy-to-understand newsletters, data sheets and manuals. In fact, this latter part of their activities was considered so important for the overall advancement of the field of analytical chemistry, that the Report for Analytical Chemist in the September 1961 issue of *Analytical Chemistry* was devoted to this subject[73].

Here, we are reporting only the American companies. This does not mean to imply that instruments were not built in Europe; in fact, some British instruments (notably those built by Griffin & George, London, and Metropolitan Vickers Electrical Co., Manchester) actually predate the American models. However, in general, the impact of the American instrument companies on the overall development of the technique was greater.

The first two companies to introduce almost simultaneously a gas chromatograph to the American market in Spring 1955 were Burrell Corporation and The Perkin-Elmer Corporation. Burrell's instrument, the Kromo-Tog, resulted from their work in gas adsorption analysis. Perkin-Elmer learned the technique during visits to England by V. Z. Williams and H. H. Hausdorff. The Model 154 Vapor Fractometer was described by Ralph H. Müller in his "Instrumentation" section in the June 1955 issue of *Analytical Chemistry*[74]; by then, the instrument was in production. The Model 154 used a thermistor detector.

The 31-page brochure[75] written by Hausdorff, the chemist at Perkin-Elmer mostly responsible for this development, dealing with the theory, uses, instrumentation and general practice of GC, was distributed widely and helped many chemists to start in GC; it was also the subject of a Ralph Müller column[76] who praised the instrument manufacturers in "doing a splendid and increasingly important job in disseminating scientific and technical information".

Some weeks later these two instruments were followed by the Chromacons of Podbielniak, Chicago, Ill., the company pioneering in the development of low-temperature laboratory distillation apparatus: Podbielniak and Preston also published two basic introductory papers for novives[76a].

At the 1956 Pittsburgh Conference on Analytical Chemistry and Applied Spectroscopy, two new major instruments were introduced: the GC-1 from Beckman Instruments, Fullerton, Calif., and the Fisher-Gulf Partitioner from Fisher Scientific Co., Pittsburgh, Pa., based on the development work carried out at Gulf Research & Development Co. Later in 1956, Consolidated Electrodynamics Co., Pasadena, Calif., also introduced their gas chromatograph. In the following years, these and other companies developed newer-and-newer instruments, incorporating the most recent advances in the technique. Some of these companies were formed specifically for the development, production and marketing of new instrumentation and no report on the history of the development of gas chromatography would be complete without mentioning three of them: F & M, Wilkens Instruments & Research Co., and Hamilton Co.

F & M Scientific Company evolved from the F & M Scientific Glassware Co. founded in 1957 by Frank Martinez, a glass blower associated with DuPont's Experimental Station, in Wilmington, Del. Martinez made parts of the early gas chromatographs developed at DuPont for high-temperature work and temperature programming and was permitted to make some instruments for outside users. Seeing the potential of these instruments and particularly of temperature programming, early in 1959 two DuPont chemists, C. E. Bennett and A. J. Martin, joined Martinez and started to build and market these instruments. Their first advertising appeared in the February 1959 *Analytical Chemistry*, showing a high-temperature gas chromatograph usable up to 600°, and at about the same time, the Model 202 Linear Programmed Temperature Gas Chromatograph was also introduced. The company grew very rapidly and did much in making temperature programming an essential part of gas chromatography. In August 1965, F & M Scientific Co. was acquired by Hewlett-Packard Co.

Wilkens Instrument & Research Co. was the brainchild of K. P. Dimick, a scientist working since 1948 at the Western Utilization Research Branch of the U.S. Department of Agriculture, in the San Francisco area. He was involved in the investigation of the volatile flavor components of strawberry and applied gas chromatography at a very early stage in this work[77], also building a very simple instrument for his laboratory[77a]. (As pointed out by Dimick later in an interview[78], his nine years of research preceding the building of the first gas chromatograph could have been duplicated within one week with that instrument.) Convinced that such simple instruments had a significant market, he founded in 1956 —together with his wife and brother-in-law, K. E. Wilkens, a high-school art teacher— Wilkens Instrument & Research Co., and started to build and market a very simple instrument, the Model A-90 Aerograph gas chromatograph.

The company advanced very rapidly, particularly when introducing in 1961 the Hy-Fi, a simple flame ionization detector instrument and in 1962, the Autoprep, a low-cost laboratory instrument capable also of preparative work. One of the special merits of the company, and specifically of Dimick, was the publication of the *Aerograph Research Notes*, which explained in very simple language various aspects of the application of gas chromatography. In Spring 1966, Wilkens Instrument & Research Co. merged with Varian Associates.

The third company to be mentioned here is Hamilton Co., founded around 1958 by C. H. Hamilton, in California. Hamilton's merit is the development of high-precision microsyringes[79]. In the first years of gas chromatography, the precise high-speed introduction of very small liquid volumes represented a general problem and one can find a number of publications in the literature describing various devices for this purpose. Hamilton's microsyringes solved the problem and became universally used.

SECOND GENERATION GAS CHROMATOGRAPHY

Towards the end of the 1950s, at about the time of the Amsterdam Symposium, the basis of GC was firmly settled; at the same time certain limitations, mainly in detection capability and separation power, became clear. Fortunately, parallel developments at this time permitted the technique to overcome these limitations, providing the exponential growth experienced ever since.

These developments can be summarized in four groups: theory, detectors, columns, and temperature and flow programming. Let us see briefly the key contributions in each field.

Theory

The original paper of James and Martin[48] and the discussion of Van Deemter, Zuiderweg and Klinkenberg[59] provided us with the basic theory expressing the relationship between the various chromatographic parameters and column performance, and between retention and molecular characteristics of the sample components and liquid phases. These relationships were further refined in the following years by a number of researchers, giving us a clearer understanding of the chromatographic process. The work of Giddings should particularly be emphasized in this respect: his early work in 1955 with Eyring[80] led in 1958 to the development of the random walk theory of chromatography[81] and in 1959–1964 to a generalized non-equilibrium theory of chromatography[82,83].

A particularly important theoretical study was carried out by Golay in 1956–1958. Investigations on the GC separation process in the column by using a communication engineering picture[84] led to a mathematical theory of a chromatographic column which, in turn, led to the development of the theory, and practice, of coated open-tubular columns[85,86]. Following the development of the porous-wall open-tubular columns, he then extended his relationships to such column types[87].

Finally, we shall mention here the work of Kováts, Rohrschneider and McReynolds. In 1958, Kováts[88] proposed the so-called retention index system to express column retention. The basic difference between this system and all other expressions is that here the retention of a substance of interest is expressed on a uniform scale; with help of this system, the retention of a substance can be predicted and the selectivity of the various liquid phases characterized. Fundamental work in the first direction was carried out by Kováts and Wehrli[88,89] and Rohrschneider[90,91], while the fundamental work of Rohrschneider, further developed by McReynolds[92], serves as the basis for liquid phase characterization.

Detectors

In their original work, James and Martin[48] used an automatic titrator to detect the fractions emerging from the column. This was soon followed by the adaptation of a katharometer (thermal conductivity detector) by Ray[53], a detector which, in fact, had already been used earlier in gas adsorption chromatography by Claesson and Cremer. The first commercial instruments built in England and the United States also utilized katharometers, and most of the researchers who built their own instruments also used this type of detection with either home-constructed or commercially available detector cells. At this time, considerable work was carried out to improve the characteristics and stability of the thermal conductivity detector and in spite of its shortcomings, this detector is probably still the most widely used GC detector.

Parallel to this work, in connection with the studies in gas adsorption chromatography, the group of C. S. G. Phillips at Oxford University developed a number of other detectors for GC such as those based on the measurements of surface potential, dielectric constant, heat of adsorption and flow impedance[9].

Chronologically, the next detector was the gas density balance developed in 1954 by Martin but described only later[93,94]. This detector had the advantages that its response is independent of the structure of the substances analyzed and, if the molecular weight of the compound is known, its concentration as a weight percentage can be directly established. Later, commercial versions were also introduced but the detector has never been used widely.

A very simple, highly sensitive detector —the so-called hydrogen flame (temperature) detector— was developed in 1955 by R. P. W. Scott[95,96] and was based on the combustion of the organic compounds present in the column effluent in a hydrogen flame in an air atmosphere, and measurement of the flame temperature change during combustion. This detector had just started to be applied by a number of researchers and a commercial gas chromatograph equipped with it (the "flame chromatograph" of Shandon Scientific Co.) was also introduced in England[96] when the development of the hydrogen flame ionization detector was disclosed. This new detector was so much more sensitive that further work on Scott's detector was discontinued.

In 1958, two new detectors based on ionization principles revolutionized gas chromatography: the flame ionization detector and the argon ionization detector.

The flame ionization detector (FID) was described in 1958 almost simultaneously by two groups: by Harley, Nel and Pretorius in the Republic of South Africa[97], and by McWilliams and Dewar, at ICI of Australia and New Zealand[98,99], and almost immediately found wide application, particularly after the three papers presented two years later at the 1960 Edinburgh Symposium[100–102] established the basis of its optimization and use in quantitative analysis. Today, the FID is one of the two most widely used gas chromatographic detectors.

The argon ionization detector[103–105] is the brainchild of Lovelock, who was first to show that a normal β-ray ionization detector, such as those described by Otvos *et al.*[106,107] and Boer[108], when used with argon as the carrier gas, creates metastable argon atoms which collide with the organic vapor molecules and transfer their excitation energy. The loss in the ionization current is directly proportional to the concentration of organic vapor present. Lovelock's invention was immediately utilized commercially and the Argon Chromatograph of W. G. Pye & Co. was the sensation of the 1958 Amsterdam Symposium. Within a few months Barber-Colman Co. in the United States also introduced gas chromatographs with such ionization detectors containing an ^{90}Sr source. For some years, the relative merits of the flame *vs.* argon ionization detectors were debated at meetings and symposia, often in a very heated discussion. At the end, the FID proved to be more reliable as well as having a wider linear range. However, modifications of the original argon detector, particularly the so-called electron-capture detector[109–111], proved to be very important in the selective analysis of impurities present in trace amounts.

Many other detectors have been developed in the last 20 years but only three have found wide application: the coulometric detector, the thermionic detectors and the flame photometric detector. All three types are important in the selective detection of certain substance groups.

The coulometric detector was developed in 1960 by Coulson and Cavanagh[112]. It is selective for chlorine-containing organic compounds and is based on the combustion of the column effluent and automatic titration of the absorbed chloride with silver ions generated by a coulometric system.

The thermionic detectors represent modifications of the flame ionization detectors and are based on an enhanced response of a flame containing alkali metal ions to certain heteroatoms present in an organic compound entering the flame. The first such detector was described in 1961 by Cremer *et al.*[113] but the widely used versions of the detector selective for halogen and phosphorus compounds are based on the work of Karmen and Giuffrida, in 1964[114,115]. By modifying the detector construction, the alkali metal compound, the electronic field and experimental conditions, the detector can also be rendered selective to nitrogen-containing organic compounds. Such a detector was first described in 1967 by scientists at the University of Missouri[116] and in the last 8 years its construction has undergone a number of changes making it more-and-more reliable.

The flame photometric detector is a modified flame ionization detector where the glow area is viewed by means of a narrow path filter and a photomultiplier tube for the characteristic wavelength emission of sulfur or phosphorus. The introduction of this principle into GC in 1966 is due to Brody and Chaney[117]; since that time a growing number of publications have dealt with the application of this detector, particularly since the increased use of phosphorus- and sulfur-containing pesticides.

Columns

The original work of James and Martin[48] was carried out by using columns prepared from tubes of 4 mm I.D., in lengths of 4–11 feet, filled with a packing consisting of a liquid phase distributed on the surface of relatively inert porous particles. These packed columns still represent the majority of separation systems used today, although their efficiency has a definite limit. At the 1956 London Symposium a 20-m long column with 10,000 theoretical plates was considered as a feasibility but not a reality[60]; two years later, at the 1958 Amsterdam Symposium, R. P. W. Scott described a packed column having a length of 50 feet and an efficiency of 30,000 theoretical plates[118] and this is about the ultimate performance one can expect from a packed column.

The real breakthrough in higher column performance is due to Golay who, in 1956, started to investigate the operation of a GC column from a theoretical point of view[84]. In subsequent work a packed column was considered as equivalent to a bundle of capillary tubes coated with the liquid phase, with an inside diameter of the order of the support particles' size. Out of curiosity, a long Tygon tubing was once substituted for a regular packed column to see how such a capillary would behave; this resulted in the surprising finding that while in regular packed columns an enormous discrepancy existed between the theoretical and practical performance, the two were close for this capillary tube. This is how the open-tubular (capillary) columns, which contain no "packing" and the liquid phase is coated on the inside smooth wall of the column tubing, were born.

Golay's first detailed report was presented at the 1957 Lansing Symposium[85] followed one year later by a thorough theoretical discussion at the Amsterdam Symposium[86] where he also gave some practical results. At the same meeting Dijkstra and De Goey of Unilever also presented results obtained on similar columns[119]. These discussions revolutionized high-resolution GC, providing columns with efficiencies of many hundred thousand theoretical plates. Within one year five groups —Desty and coworkers at British Petroleum[120,121], Scott at Benzole Producers[122], Condon at Perkin-Elmer[123], as well as Zlatkis at the University of Houston[124] and Lipsky at Yale University[125,126], both in cooperation with Lovelock— showed practical applications in a number of fields. Further use of open-tubular columns was greatly facilitated by the simultaneous introduction of the two ionization detectors which provided satisfactory sensitivity for the small sample sizes encountered with these columns, by the development of the proper GC systems including the special sample introduction systems, and by detailed investigations on the optimum performance of these columns. In this respect, besides those quoted above who continued their involvement in this field, the activities of Halász' group at Frankfurt University, Teranishi and coworkers at the Western Regional Laboratory of the U.S. Department of Agriculture, Schomburg at the Max-Planck-Institut für Kohlenforschung, in Mülheim/Ruhr, three Texas groups, Durrett, Simmons and Dvoretzky at Shell Oil Co., Schwartz at Shell Development Co. and Hollis at Dow Chemical Co., as well as the members of Perkin-Elmer's Applications Groups, should be mentioned.

The next step in the further development of open-tubular columns was based on a proposal of Golay[127] to increase the sample capacity of these columns while decreasing the liquid film thickness by preparing a porous layer on the inside surface of the column tubing. Apart from a few isolated trials this proposal was put into practice by Horváth (thesis: 1963) in Halász' laboratory at the University of Frankfurt, West Germany, by developing the so-called support-coated open-tubular columns[40,128]. These columns were then studied extensively from both the scientific and practical points of view, and made commercially available by Perkin-Elmer's Applications Group in 1965–1968[129,130]. Today, these columns are used in a large number of laboratories for day-to-day, routine applications.

The third important step in the utilization of open-tubular columns was the development of highly efficient and reliable columns made of glass. The methods of preparation of the capillary tubing had been already described in 1960 by Desty and coworkers[131] and Kreyenbuhl[132], but it took some time until the techniques of surface preparation and coating were fully understood. Intensive pioneering work in this field has been carried out at a number of places in both Europe and the United States such as by Grob, in Zürich, by Bruner, Cartoni and Liberti, in Rome, by Tesařík and Novotný, in Czechoslovakia, continued by Novotný, in the United States, by Guiochon and his group, in Paris, by students and coworkers of Keulemans, at the Technische Hogeschool, in Eindhoven, by Horning and his Institute, in Houston, Texas, and by Schomburg, at the Max-Planck-Institut in Mülheim; this work is still continuing.

Returning to packed columns, one of the major difficulties at the beginning was to obtain reliable support materials. The diatomaceous earth type supports used in the first years were produced for other purposes (mainly as filter aids), and much work had to be done by the individual user to ensure uniform particle size and the required inertness. With the advancement of GC, however, a number of companies specializing in GC supplies carried out considerable work in producing reliable support materials of narrow mesh cuts, and the merits of May & Baker, in Great Britain, and of Johns-Manville Corp., Applied Science Laboratories, Analabs, Inc., and Supelco, in the United States should particularly be emphasized. These companies also pioneered in providing reliable and pure stationary phases and in the introduction of a number of new phases.

A significant advancement in preparing inert supports took place in 1959–1960 with the development of silanization of the diatomaceous earth type material using dichlorodimethylsilane[133] or hexamethyldisilazane[134].

Besides the introduction of the open-tubular columns, the most significant breakthrough in column technology was the introduction of packed columns with very low (2–3%) liquid phase loading by Horning and coworkers[135]. The application of such columns with silanized supports opened an entirely new field for GC: the analysis of steroids and other biologically important substances, and of pesticides.

Temperature and flow programming

In the initial development of GC the analysis was carried out by maintaining the column temperature constant until all peaks of interest emerged. Such an isothermal operation, however, has definite shortcomings if a wide boiling-range mixture is analyzed because the conditions are optimized only for a relatively small region of the chromatogram: for the earlier part, the temperature is too high while for the later part, it is too low.

In their early work, James and Martin[51] altered the column temperature at a point in the chromatogram in order to elute high-boiling components in a reasonable time. Another approach used in the 1950s was to connect a number of GC units in series so that the detector outlet of a preceding unit was linked to the column inlet of the following unit, and to have each column at a different temperature. For example, a three-stage instrument was developed in 1956–1957 at the U.S. Bureau of Mines laboratory, at Bartlesville, Okla., for the analysis of automobile exhaust gases, permitting the separation of more than 50 components[136], and, in 1957, a commercially available instrument (the Model 188 of Perkin-Elmer) was also introduced.

A better method for the analysis of wide-boiling samples is temperature programming. In this technique the column temperature is raised with a predetermined heating rate (linear or non-linear) during analysis. In this way, each sample component can emerge at its optimum temperature.

Programmed-temperature GC was first used as early as 1952 by the group of C. S. G. Phillips, in connection with the separation of organic halides[9] and a few reports can also be found in the literature from subsequent years; however, the technique achieved general acceptance only after the fundamental work of Dal Nogare and coworkers[137–139] and the activities of the founders of F & M Scientific Co.[140]. The theoretical background of temperature-programmed GC was elaborated almost simultaneously by Habgood and Harris[141], Giddings[142], Said[143] and Rowan[144], while the technique was extended to open-tubular columns by Teranishi and coworkers[145]. Today, most gas chromatographs permit the use of temperature programming.

A major problem in temperature programming might arise from the exponentially increasing baseline due to the change in the bleeding rate of the liquid phase. The solution to this problem was presented in 1961 by Emery and Koerner of Monsanto[146] who developed the dual column, baseline-compensation technique. The original system was related to thermal conductivity detectors but one year later, a commercial instrument utilizing the same technique with flame ionization detectors (Perkin-Elmer Model 800) was also introduced and the performance of such systems had been studied in detail[147].

Besides temperature, the carrier-gas flow is also a variable which can be changed during analysis. In their first work[48] James and Martin utilized a stepwise increase of the flow rate (inlet pressure) in order to reduce the analysis time. Following the general acceptance of temperature programming, Purnell, in his book published in 1962[148], specifically suggested the use of flow programming as an approach which "would certainly lead to results equivalent in many respects to those of temperature programming". However, flow programming as a technique was established only in 1964–1965 when a number of groups described results obtained by using this variation of GC[149–153]. Soon flow programmer accessories also became commercially available but the technique never gained wide acceptance.

SPECIAL TECHNIQUES

Process analysis and control

The application of GC in automated on-stream process analysis and control started very early, in the middle 1950s. At that time, on-line process analyzers based on ultraviolet and infrared spectroscopy were already in use; these were then fairly quickly replaced by the gas chromatographs.

Initial development work on this application of GC was carried out by the large petroleum and chemical companies. Detailed information is mostly available only about the American companies, although, naturally, similar activities have also been carried out in Europe. For example, at the 1956 London Symposium, in the discussion of Hausdorff's paper[72], Amesz mentioned the GC analysis of plant streams at Shell's refinery in Holland, and the report on the Congress on Modern Analytical Chemistry in Industry organized by the (British) Society for Analytical Chemistry and held in June 1957 at St. Andrews, in Scotland[154], quotes Keulemans who said that automated analysis of gas streams was being carried out at Shell, without giving further details. The first paper on the development of a process analyzer at Koninklijke/Shell was presented at the 1958 Amsterdam Symposium[155]; as stated there, the unit described had been in use in pilot plant work for about two years. We also know about activities at the Billingham Division of ICI[154] and Harvey and coworkers described at a symposium held in September 1957 in Swansea[156] a unit used by ICI for the automatic analysis of a 98% pure isobutane stream. In 1957, the automatic GC analysis of a butane distillation stream at Böhlen, G.D.R., was also reported[157].

Automatic gas chromatographs for on-stream process analysis must fulfil very stringent requirements concerning the stability of the carrier-gas flow, the column and its temperature, and the detector. Also, special automated sampling valves are needed which take the proper samples at the start of each analytical cycle. Thus, besides the basic development in GC, the introduction of process analyzers also required considerable development work in instrumentation.

The first process analyzer reported in the literature was developed by Esso Research & Engineering Co. and installed in 1956 at Esso's Bayway Refinery polymerization plant[69]. The analyzer was used for the analysis of propane in propylene and employed a fairly unique system. An adsorption column was used because of fear that air used as the carrier gas would oxidize the liquid phase and thus the column might deteriorate quickly. The detector was based on the measurement of the heat of adsorption. One year later, in September 1957, at the 132nd National American Chemical Society Meeting held in New York City, Dudenbostel and Skarstrom reported on well over one year of successful experience with this unit[158]. The analyzer was described in detail at a meeting held by the New York Academy of Sciences, in April 1958[159].

In 1956, other process gas chromatographs had also been developed and installed. Spracklen described a unit developed and built by the Specialized Instruments Department of Carbide & Carbon Co. for the measurement of the purity of chlorine streams[160,161]. The work at Monsanto Chemical Company's Plastics Division, in Texas, was summarized by Zinn and coworkers during the 1957 Lansing Symposium[162]. Phillips Petroleum Co., in Bartlesville, Okla., had a number of units built and Ayers, the principal scientist involved in this work, presented a detailed report on them at the same Lansing Symposium[163]. Phillips Petroleum Co. also cooperated with Perkin-Elmer in the development of their automatic process gas chromatograph: the first ten units were built in 1956 and the final design was introduced to the market in the first half of 1957[164].

Apart of the very early work at Esso, the first generation process gas chromatographs utilized thermal conductivity detection. After the development of the ionization detectors, they were soon adapted to process analyzers. For a short time, units with argon ionization detectors were also built in Europe but in the long term, the flame ionization detector was found more reliable for such use.

So far, we have discussed only process analysis. However, as already pointed out in 1957 by Ayers[163], the next logical step was the introduction of the analyzer output signal into an automatic control system: he also described a unit where the GC analyzer automatically re-set a temperature and a flow controller in a de-butanizer distillation column. Two years later, at the 1959 Lansing Symposium, Turner of Beckman dealt in detail with the problems of process control systems incorporating GC analyzers and gave a number of examples for their application[165]. Since that time, this application has advanced further and today, one can rarely find a chemical or petroleum plant without some kind of GC analyzer automatically monitoring and controlling the process.

Preparative gas chromatography

Since gas chromatography is a separation technique it is natural that the possibility of using the process for the separation and collection of sizeable amounts of highly pure substances was considered since the technique's beginnings. As stated by James[166], he and Martin had already tried in the early 1950s to scale up the columns to a diameter of 25 mm as compared to the conventional 4–6 mm, in order to be able to collect pure fractions. Soon afterward Evans and Tatlow at Birmingham University used the technique to separate fluorinated hydrocarbons[167] using a horizontal column of about 3 cm diameter and 5 m length; a few grams of pure substances could be separated in a single run. They presented a second report one year later, at the 1956 London Symposium[168]. At the same meeting, Whitham of Shell Research in Great Britain[169] described the unit built by them. It utilized columns of 12.7 mm diameter; since the efficiency of the column was less than that obtainable with a standard analytical column, the resolution was improved by increasing the length to 8.3 m. Sample volumes were of the order of 0.1–0.2 ml.

One year later, at the 1957 Lansing Symposium, Kirkland[170] described a laboratory unit built at DuPont which was capable of separating highly pure gases, liquids, and low-melting solids, in amounts up to 10 g or even higher. The columns had a diameter of 31 mm and were made in lengths of 6 feet. Sample sizes up to 10 ml (liquid) were introduced.

In 1957, another preparative unit was also described by Heilbronner *et al.* at the Eidgenössische Technische Hochschule, in Zürich[171]. Their unit had a repetitive automated sample introduction system and also automated fraction collection having the collectors in a turntable. By repetitive injection and collection there was no need for larger diameter columns.

The same principle was also advocated by Atkinson and Tuey of May & Baker in their paper presented at the 1958 Amsterdam Symposium[172]: to use a column with moderate diameter, only somewhat larger than is common for analytical purposes, and repeat the separation and collection. The columns used by them had a diameter of 20 mm.

At this time, the difficulty of preparing larger diameter columns without much loss in efficiency became evident and thus future development followed three directions. The first two utilized columns with a diameter only somewhat larger than that of the analytical columns while in the third case the preparation and efficiency of large diameter columns were improved. Besides these, special units have also been developed.

In the first direction a number of columns were used in one unit and were installed parallel to each other. Relatively large sample volumes were introduced into the equipment and, after evaporation, mixed with the carrier gas; this mixture was then split to the columns. The column effluents were combined and carried to the collectors. The first commercial laboratory preparative gas chromatograph*, the Megachrom, introduced by Beckman in 1958 was based on these principles. This instrument was first described by Carle and Johns in May 1958[173]; a detailed report on selected applications was presented one year later[174]. This instrument utilized a number of 5/8 inch (16 mm) diameter columns parallel to each other: eight 6-ft. columns, four 12-ft. columns, two 24-ft. columns or one 48-ft. column. The carrier gas was recirculated after suitable cleaning by adsorption on charcoal; the carrier gas throughput was 0.5–15 l/min. A 100-fold scale-up in sample size could be achieved in optimum cases with the instrument.

The use of parallel columns was found to have many problems, mainly in matching them so that the same compound had exactly the same retention time through each column. Therefore, they were slowly replaced by systems representing the second direction of the development: using columns with moderate diameter but with automatic operation utilizing repetitive sample injection and fraction collection. The pro-

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* The preparative instruments of Podbielniak predate this instrument; however, we shall deal with them later, when discussing the large-scale units.

posal of Ambrose and Collerson in 1956[175] was the first description of this idea and at the 1956 London Symposium some preliminary results were also given[176]. However, they used only gaseous samples. The two instruments developed by the group at the E.T.H.[171] and at May & Baker[172] showed for the first time such fully developed systems with liquid sample introduction. Similar systems were also developed at other laboratories, such as by Felton at DuPont[177,178] and by Catalette and coworkers in France[179].

This principle was utilized in the Autoprep, the instrument introduced by Wilkens Instruments & Research Co. in 1962[180,181]. This instrument utilized spiral columns of 3/8 inch (9 mm) diameter in lengths up to 20 ft.

Many other systems based on automatic cycling have been described in the literature and also introduced commercially. Naturally, their development required very detailed investigations and scores of publications deal with the various problems related to automatic injection, fraction collection and the programming mechanism as well as with other aspects of preparative gas chromatography (*e.g.* Felton's bibliography[178] lists 68 references up to the end of 1963); however, it is beyond the limits of this article to give even a brief review of them.

The third direction in preparative GC was towards the use of large diameter columns. As already mentioned, such columns were used from the very beginning; Podbielniak Inc. also introduced towards the end of 1956 the "Vapor Phase Chromaneer Plants" using columns of 25–100 mm diameter, in lengths of 6 m or more. These instruments (or, probably more correctly, pilot plants) could be used up to 200° and were capable of separating 280–700 l of gaseous materials per day; however, other than advertising material, I could not find any data on actual performance.

By about the 1956 London Symposium, it became clear that if one goes above a certain diameter, the column efficiency seriously deteriorates and therefore has to be compensated for by increasing the column length. The first quantitative data on columns having various diameters were given by Carle and Johns[173] and this observation was the reason that in the Megachrom, the column diameter was not increased above 16 mm. Similarly, in Germany, Bayer and Witsch[182] reported problems at diameters above 10–20 mm. The reason for this deterioration of the efficiency is the presence of velocity differences in the cross-section of the column and this was derived by Golay in 1959 based on theoretical considerations[183]. To overcome this effect, Golay suggested the insertion of mixing washers into the column at periodic intervals. The presence of these profiles was actually demonstrated by Huyten and coworkers[184] and Frisone[185] first used such washers consisting of filter-paper rings saturated with the liquid phase. A number of different suggestions have also been made such as inserting radial metal baffles[186], porous metal or PTFE disks[187,188], or constructing columns with special geometry[189].

A further problem in preparing large-diameter columns was the manner in which they were packed. A variety of methods have been described of which the fluidization method of Guillemin[190] and the percolation method of Bayer *et al.*[191] are particularly noteworthy.

Truly large-diameter (30–120 cm) columns for production-scale GC have been developed in the United States by Abcor. These columns also used baffles consisting of disks with diameters less than that of the column, placed at regular intervals along the length of the column[192]. For some time these systems evoked considerable interest[193]; however, evidently their use presented economic problems and today, very little is heard about them. More moderate systems utilizing 1-foot diameter columns up to a length of 5 m were described in 1969 by Carel and coworkers of the Continental Oil Co., in Ponca City, Okla.[194]; in these units, total sample volumes up to 500 ml have been successfully separated.

Another large-scale preparative GC system was described by a French group[195]. Their pilot plant had a throughput of about 10 tons/year and utilized columns with a diameter of 12.5 cm. Two examples given in their report are the upgrading of 99.9% *n*-pentane to a purity of 99.996% and the enrichment to 50% of a heavy fraction present in the original cut in a concentration of only 100 ppm. We also know from private discussions that preparative GC is used to a limited extent for production purposes in the U.S.S.R., with columns having a diameter of 1 ft. or more.

Finally, we should briefly mention the special systems developed for relatively large-scale production of pure substances using more-or-less GC principles.

At the 1956 London Symposium, Freund and coworkers of the Hungarian Petroleum and Gas Research Institute described a continuous pilot plant developed for the recovery of acetylene from the end gas of the partial oxidation of methane[196]; the theoretical calculations related to the continuous chromatographic "column" were presented one year later at the 1957 Lansing Symposium[197]. A different continuous GC system was described in 1958 by Scott[198]. This unit was used at the Watford plant of Benzole Producers to recover 99% pure benzene from a coal gas stream. Of course, in neither case should one really speak about a column, in the usual chromatographic sense.

Other types of continuous systems utilized circular columns which were rotated past fixed inlet and outlet ports. Such systems were developed in the late 1950s[199–202]. In 1966 Glasser also described similar equipment[203]. A more advanced system was developed by Barker and his group at the University of Birmingham, in the early 1960s[204,205]. In this system, the sample mixture is introduced into the column in the carrier-gas stream and held within the column by rotation at a predetermined speed, until the individual components are separated sufficiently so that they can be eluted and collected separately. Since the inception of this "chromatographic machine", Barker and his group have further developed it and demonstrated its applicability to a number of sample types. The system, in different versions, is also manufactured commercially in Great Britain.

There have been questions as to whether the systems mentioned above can truly be considered as based on chromatographic principles and opinions are not uniform. However, the last system to be mentioned is clearly based on truly chromatographic principles. This system was developed in the early 1960s at the S.N.A.M. Laboratory in Italy[206–208]. It consisted of 100 small-diameter (6–8 mm) straight-packed columns placed on the circumference of a revolving metal cylinder. The evaporated sample is injected successively into the columns and the exits of the columns slide over a stationary ring with the traps. Since a particular component will reach the exit of each column at the same time, it will be collected in the same trap. This unit (called the Roto-Prep) has also been produced in a limited quantity.

Undoubtly there have been many other preparative GC systems developed since the inception of GC at various places and used more-or-less successfully there.

A number of other commercial systems have also been developed and marketed but most of them have been withdrawn. The basic problem in preparative GC is that the technique used, the system, and the analytical conditions depend much more on the specific application than in the case of analytical work, and general-purpose instruments always have serious limitations when one tries to adapt them to a specific problem. The same is true for specially constructed large-scale systems: they are designed for a given application and it is not certain that they can be adapted for other uses while still maintaining their performance. We must add that in the case of production-type applications, economic questions also play a vital role. These are the reasons that preparative GC is not as widespead as it was originally envisaged.

THE FUTURE

It is not always easy to predict the future and in GC, we have had both good and bad experiences in this respect. Starting with the good, Martin was correct in 1956, when he predicted the use of capillary columns and in 1957, when he stated that the principal detector of the future would be based on ionization of the molecules and that pyrolysis–GC would have a great future. On the other hand, this author remembers well the predictions in the second part of the 1950s that preparative GC would replace whole distillation plants, or the enthusiasm around 1960, at the start of automobile exhaust control, when it was taken for granted that in a few years every gasoline station would have a gas chromatograph to check the exhaust of our automobiles...

Today, the technique of GC is at such an advanced stage that it is hard to predict further new major developments. There will be breakthroughs in the application of GC, mainly in biochemistry and clinical chemistry, but even here, we are at a stage where the field now has to catch up with us. Today, we can show definite patterns for certain illnesses but biochemistry is not yet sure about their interpretation and particularly about the role of certain compounds present or absent in these patterns. We certainly can expect better and more reliable columns; the present upsurge in glass open-tubular columns indicates this trend. We can also expect some improvement in our detectors although their sensitivity, particularly that of the selective detectors, is already very high and we can detect sub-ppb concentrations ($<10^{-7}\%$)*. Still, even more information can be obtained by the simultaneous use of selective detectors and this is certainly a field where future developments can be expected.

It is likely that the "new" in the future will mostly come in instrumentation. Here, we have an interesting situation. At the moment, the electronics industry is undergoing such rapid development that its full impact on scientific and process instruments, and thus also on our gas chromatographs, cannot be fully comprehended. We are at a stage where the electronic engineer is coming to us with new devices and asks us to try to fully utilize them.

Today, almost every instrument company is redesigning its instruments to

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* I do not know how far the extent of this sensitivity is generally fully appreciated: a detectability of 0.25 ppb with a selective detector is analogous to a space-ship picking out a single person from the whole population of the world and telling us that he (or she) has red hair...

incorporate these new microprocessors and, within a few years, completely new instrumentation can be expected*. These new instruments will be radically different in many respects: they will "think", always adjust to the optimum conditions and the operator will have only a start button to push.

A further significant development can be expected in data evaluation, a field deliberately omitted from this discussion. As the moment, we already have a number of automated data systems from minicomputers through the dedicated small computers to the large computer systems. The newest developments in electronics will result in increased performance (speed, memory, storage capacity) permitting even the small data systems to do more while in the case of the medium or large systems we shall be able to combine various instruments, compare their results with a data bank, and identify the unknowns based on the combined data and the stored information. The work of Jellum and his group at the University of Oslo in detecting metabolic disorders with the help of complex gas chromatograph–mass spectrometer–computer systems[210] already shows the potentialities of this approach.

At the 1957 Lansing Symposium, A. J. P. Martin spoke about the "Past, Present and Future of Gas Chromatography"[211]. He finished his address with the following prediction:

> "If we tie the gas chromatograph to other pieces of laboratory equipment, we have the possibility of almost the automatic chemist. We can separate a substance on the gas chromatograph, we can take every column which is reasonable in turn, and substances as they run from the column can go directly to various instruments such as nuclear magnetic resonance, ultraviolet, visible, infrared spectroscopy, and we can have a mass spectrograph working as well. Here you have the uniting instrument of the gas chromatograph in the center with its slaves clustered around. The calculating machine in the background will have the records of all previous substances separated . . . and it will come out with a sheet typed at the end with the name of the compound and the weight per cent in the mixture. We may even get it to the stage where it will work out the structure too."

Could it be that Dr. Martin was also correct in this prediction?

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* See the report of Petruzzi about Atwood's recent speech[209].

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