Chapter 1
Introduction

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Contents

Abstract This chapter gives a general introduction to chromatography. It deals with basic definitions and classifications of chromatographic methods and the reader is introduced to the chromatographic separation process. The components of a gas chromatograph are described and the application range of GC is presented. Finally, a personal view of the authors on the historical development of GC is given.

1.1 Definition and Classification of Chromatographic Methods

Gas chromatography (GC) is a powerful and widely used analytical technique to separate even complex mixtures. The term chromatography is derived from the Greek words *chromos (color)* and *graphein (write)* and was originally used in the

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theory of colors. The Russian botanist and biochemist M. S. Tswett (1872–1919) used this term in the beginning of the twentieth century to describe the separation of leaf pigments. A leaf extract was passed through a column that was filled with a powdered adsorbent [1]. A separation of the compounds was achieved in "the stream of a pure solvent," which was visible by the formation of differently colored bands. Even though the separation of pigments only covers a small fraction of chromatographic applications nowadays, the term chromatography remained not the least for historical reasons to honor its pioneer the great scientist Tswett.

According to the recommendation on nomenclature for chromatography from the "International Union of Pure and Applied Chemistry" (IUPAC) the following modern definition of chromatography applies [2, 3]:

"Chromatography is a physical method of separation in which the components to be separated are distributed between two phases, one of which is stationary (stationary phase) while the other (the mobile phase) moves in a definite direction." The mobile phase may be a gas, liquid, or supercritical fluid and is moved by gravitation, capillary forces, or pressure. It is responsible for the transport of the analytes along the stationary phase. The stationary phase may be a porous or nonporous solid or an immobilized liquid with an adequate surface area and causes retention of the analytes compared to the transport rate of the mobile phase.

A chromatographic system consists of two non-miscible phases that are in close contact to each other with one phase being stationary and the other one is moving. Analytes are distributed between the stationary and mobile phase, which is expressed by the distribution constant K. During analyte transport along the phase interface, several distribution steps take place (multiplicative distribution). As we will discuss later, differences in the distribution constant K result in different migration rates of the analytes and consequently in analyte separation.

Chromatographic methods can be classified using different criteria. A fundamental criterion is the *aggregation state of the mobile phase* (Table 1.1). The mobile phase may be gaseous, which is called gas chromatography (GC), liquid, which is called liquid chromatography (LC), or a supercritical fluid, which is called supercritical fluid chromatography (SFC).

A further criterion is the *separation mechanism*. In general, analyte distribution between stationary and mobile phase can be based on adsorption, solubility, ion exchange, size exclusion, or selective interactions. For GC only adsorption and solubility are applicable. In case of solid stationary phases adsorption chromatography takes place, called *gas solid chromatography (GSC)*. In case of liquid stationary phases solution processes take place. This partition chromatography is called *gas liquid chromatography (GLC)*. GLC is the most widely distributed GC technique. However, also mixed retention mechanisms involving both adsorption and solution can take place.

One should note that the term *distribution* is used in different meanings. In general it describes the distribution of the analytes between two phases independent of the separation mechanism. More specifically, it applies to partition chromatography describing the distribution of the analytes between two liquids (liquid liquid chromatography) or between a liquid and a gas (GLC).

Table 1.1 Classification of the most widely used chromatographic methods

Type	Mobile phase	Stationary phase	
		Solid (S)	Liquid (L)
Gas chromatography (GC)	Gas	Gas solid chromatography (GSC)	Gas liquid chromatography (GLC)
Liquid chromatography (LC)	Liquid	Liquid solid chromatography (LSC)	Liquid liquid chromatography (LLC)

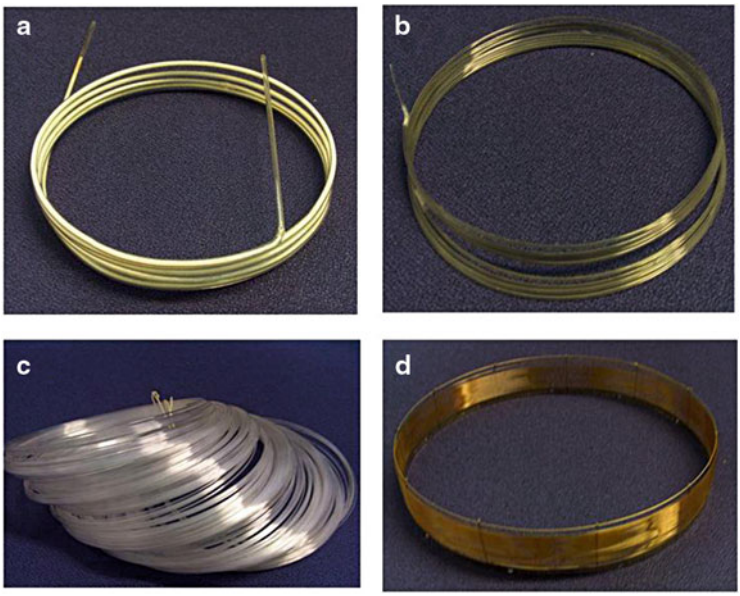


Fig. 1.1 Evolution of GC columns. The *photos* in the *upper row* show packed glass columns. (**a**) Chromosorb coated with a liquid stationary phase, (**b**) carbon adsorbent. The *lower row* shows a glass capillary column (**c**) and a fused silica capillary column (**d**)

Due to the properties of gases, GC must always be performed in closed systems. The stationary phase is located in a tube, the chromatographic column, which is purged by the mobile phase. We distinguish between packed columns and capillary columns. The different column types are shown in Fig. 1.1.

Packed columns are completely filled with fine-grained solids as stationary phase. This can either be an adsorbent (GSC) or a solid support coated with a thin film of a highly viscous liquid (GLC). Capillary columns feature an inner diameter of less than 1 mm and are open-tubular columns. The stationary phase is located on the inner wall of the column either as a thin film of a highly viscous liquid (wall-coated open-tubular column – WCOT) or as a thin layer of an adsorbent (porous layer open-tubular column – PLOT).

Liquid chromatography can either be performed as column chromatography or as planar chromatography, where the stationary phase is a thin layer on a flat support, e.g., glass, aluminum foil, or plastic (thin layer chromatography - TLC).

Regarding chromatogram development we distinguish between elution, frontal, and displacement chromatography. The selection of the process depends on the task at hand. Elution chromatography is the most widely used technique and, if not otherwise noted, the technique referred to in this book.

Elution chromatography: As in detail discussed later, the sample is injected as a discrete pulse into the moving mobile phase. This results in discrete substance bands containing the analyte and mobile phase, which are separated by bands of pure mobile phase. The elution process involves a dilution of the analytes in the mobile phase. The stationary phase is regenerated by the mobile phase.

Frontal chromatography: With this technique the sample is continuously supplied into the column. The sample itself acts as mobile phase; hence no additional mobile phase is needed. The analyte with lowest interactions with the stationary phase reaches the detector first followed by the other analytes in order of increasing interaction strength. The detector records a stepwise chromatogram. This technique is also called displacement chromatography with an intrinsic compound mixture or adsorptive filtration. The frontal technique is used for adsorptive enrichment of trace compounds from liquid samples (Solid Phase Extraction SPE) or gases as well as cleanup of solvents from polar compounds.

Displacement chromatography: With this technique the sample is injected as a discrete pulse into the mobile phase that contains a displacer. The displacer is a compound that is stronger retained than the sample analytes. The displacer moves the analytes as a plug in front of it while the analytes are sorted according to their interaction strength with the stationary phase. This technique is used in preparative chromatography to isolate pure substance from mixtures.

Gradient technique: This technique is an often used version of elution chromatography that changes a variable influencing the separation during the run. This is the column temperature in GC and solvent composition, e.g., polarity or pH, in LC.

1.2 The Chromatographic Separation Process

In simple terms chromatography can be considered as a series of discontinuous equilibrium steps that take place during a separation. In a small segment of the column (plate) an equilibrium is formed between the solute in the mobile phase and in the stationary phase, which is defined by the solute-specific distribution constant K. The portion of the solute that remains in the mobile phase is transported to the next column segment and again an equilibrium is established between mobile and stationary phase. Figure 1.2 illustrates the distribution of a solute with a distribution constant of 1 using five consecutive equilibrium steps. This model is the basis of the plate theory, which will be discussed in Chap. 2. However, we should keep in mind that this model is a simplification of the chromatographic process because it assumes that a complete equilibrium is reached in each distribution step. In reality

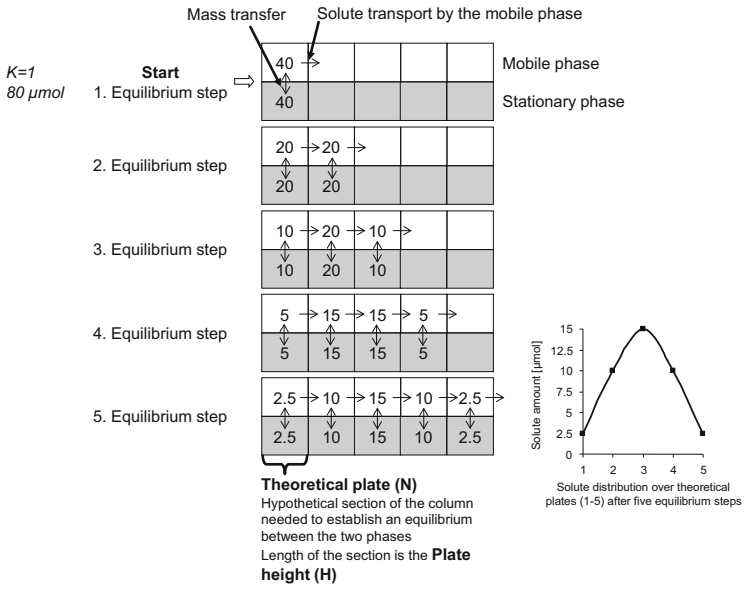


Fig. 1.2 Concept of multiplicative distribution

this is rarely the case as the mobile phase is steadily moving through the column. These aspects are considered in the kinetic theory as discussed in Chap. 2.

The concept of multiplicative distribution demonstrates that solute distribution over the column segments follows a normal distribution and an ideal chromatographic peak in elution chromatography has a Gaussian peak shape.

1.3 Components of a Gas Chromatograph

An instrument used for gas chromatography is called a gas chromatograph and consists of the following main parts:

– **Carrier gas supply**
  It provides a continuous flow of the mobile phase through the column. Since the mobile phase transports the solutes through the column, it is often called *carrier gas*. Ultrapure helium, hydrogen, or nitrogen are used as carrier gases. Most laboratories use high-pressure gas cylinders with a two-stage pressure gauge to supply gases or they are equipped with central gas supply. Hydrogen can also be

conveniently and safely produced on-site by a hydrogen generator. The operation principle is based on the electrolysis of water.

- **Injector**
  It is a device to introduce gaseous or liquid samples onto the column head. Liquid samples are commonly injected using a microliter syringe while gases are applied by a gastight syringe or gas valves. Modern instruments are equipped with an autosampler to automatically inject the samples allowing user-independent processing of sample batches.
- **Column**
  The column is often considered as the heart of the GC system. Packed columns or capillary columns with liquid or solid stationary phases are used.
- **Column oven**
  The column oven houses the column. The oven is an air thermostat to provide a constant (isothermal) or defined (programmed) increased of the column temperature. The column oven is always equipped with a ventilator to guarantee a strong air circulation, because air has a poor heat conductivity.
- **Detector**
  The detector is a device to record the solutes upon leaving the column. An electric signal is produced, in most cases amplified, and sent to the data system.
- **Data processor**
  It is used to register, store, and analyze the data produced.

Figure 1.3 shows a general scheme of a gas chromatograph, which is independent of the vendor or instrument type, e.g., benchtop laboratory GC, process control GC, or miniaturized mobile GC for on-site analysis.

As mentioned above, the heart of a GC is the chromatographic column. It contains the stationary phase and is continuously purged by the mobile phase. The chromatographic separation takes place in the column. The sample is introduced into the injector, if needed transferred into the gas phase, and transported onto the column by the mobile phase. At the column head partitioning of the solute into the stationary phase takes place and this portion is not available for transport by the mobile phase (see Fig. 1.2). The distribution of solutes between stationary and mobile phase is determined by their vapor pressure (and polarity depending on the polarity of the stationary phase) in GLC. The higher the vapor pressure of a solute the higher is its portion in the mobile phase and the faster is it transported through the column. On its way through the column multiple phase transfer reactions take place (multiple solution/vaporization or adsorption/desorption, respectively) resulting in different dwell times (retention time) of the individual analytes in the stationary phase. Ideally, the differently retained analytes leave the column one by one and reach the detector. The latter produces a signal, which is amplified, digitalized, and stored for further analysis.

The detector signal is plotted over the time that has passed since the sample has been injected. This representation is called *chromatogram* or in GC more precisely *gas chromatogram*. Figure 1.4 shows a hypothetical gas chromatogram.

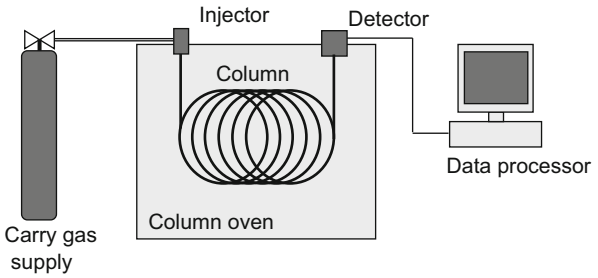
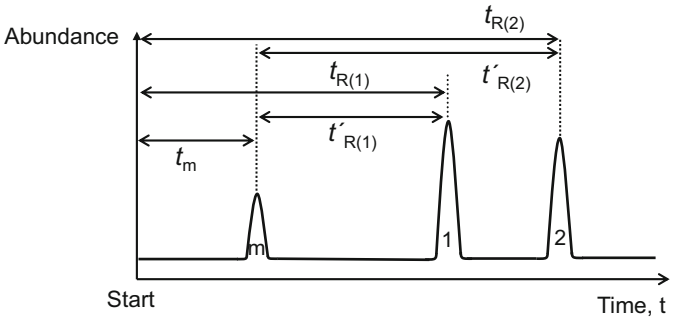


Fig. 1.3 Scheme of a typical GC system (gas chromatograph)



t_m Hold-up time equals retention time of an unretained compound
t_R Total retention time
t'_R Adjusted retention time

Fig. 1.4 Hypothetical gas chromatogram for two components 1 and 2

The *x* axis represents the time (retention time) and the *y* axis the signal intensity (abundance). If only carrier gas reaches the detector a flat line is recorded, the so-called baseline. It commonly shows slight fluctuations, which are called baseline noise or background noise. An increasing signal intensity indicates that a solute leaves the column and reaches the detector. Ideally, the signal follows normal distribution and has a typical Gaussian shape. These signals are called *peaks*. A peak is characterized by its position in the chromatogram, expressed as *retention time* (t_r) and its *height* and *width*. Early peaks represent solutes that are only slightly retained in the stationary phase. The longer the solutes are retained in the stationary phase the later they appear in the chromatogram.

Information gained from a chromatogram will be discussed in detail in the following chapters. It only should be mentioned that the peak position (retention time) in the chromatogram delivers information on the identity of the separated analyte while the peak size (height or area) is a measure for relative concentration or amount of the analyte. Peak width and shape indicate column performance and working conditions.

1.4 Application of Gas Chromatography

The use of a gaseous mobile phase to transport analytes through the column inevitably implies that GC is only suitable for volatile analytes. But, the criteria volatility does not mean that the column temperature has to be above the boiling point of the solutes to keep them completely in the gaseous phase. At a given column temperature it is sufficient that a part of the analytes is in the gas phase for their distribution between the stationary and mobile phase and to enable their transport through the column. The key criterion is a sufficient vapor pressure at the column temperature (estimated at about 60 Torr). The column temperature for liquid stationary phases can be significantly lower than the boiling point of the analytes as demonstrated in the chromatogram in Fig. 1.5 for the separation of polycyclic aromatic hydrocarbons (PAHs). These high boiling hydrocarbons consist of two to five fused aromatic rings and are partly carcinogenic and teratogenic. They are broadly distributed and are formed during the incomplete combustion of organic material. Their boiling points range between 218 and 500 °C. The US Environmental Protection Agency EPA classified 16 PAHs as priority environmental toxins that are often analyzed in environmental samples as representatives of the more than 100 possible isomeric and congeneric compounds.

As the example shows, GC is definitely suited for the separation of high boiling compounds as long as they do not decompose at higher temperatures. In general, GC column temperatures range from room temperature up to 350 °C, though the application area of GC extends to volatile and thermally stable compounds (boiling point up to 380–400 °C) that can be transferred into the gas phase without decomposition or reaction with other sample components. GC is the method of choice for the analysis of compounds meeting these requirements.

As it is well known, volatility depends on the size and polarity of the molecule. The higher the molecular weight and/or polarity the lower is the volatility. Consequently, one has to consider both parameters, since larger nonpolar molecules might be more volatile than small polar molecules. A polar group in a large molecule has a lower influence compared to a polar group in a small molecule. Compounds containing more than one polar group, e.g., sugars, amino acids, often exhibit a very low volatility and are only amenable to GC after chemical transformation into more volatile derivatives.

Therefore, the domain of GC are nonpolar or weakly polar compounds, such as gaseous, liquid, or solid compounds with less than 60 carbon atoms and a molecular mass and boiling point below 600 Da and 500 °C, respectively. In simple terms all compounds that can be smelled reach the human nose over the gas phase and are therefore analyzable by GC. Nevertheless, some high boiling compounds, such as long-chain saturated hydrocarbons up to a carbon number of 100, or triglycerides, can be measured by GC due to their thermal stability.

There are several options to make higher boiling compounds amenable to GC analysis. Polar, less volatile, or thermally fragile substances can be transformed into stable, volatile, and less polar derivatives by chemical reaction, such as silylation,

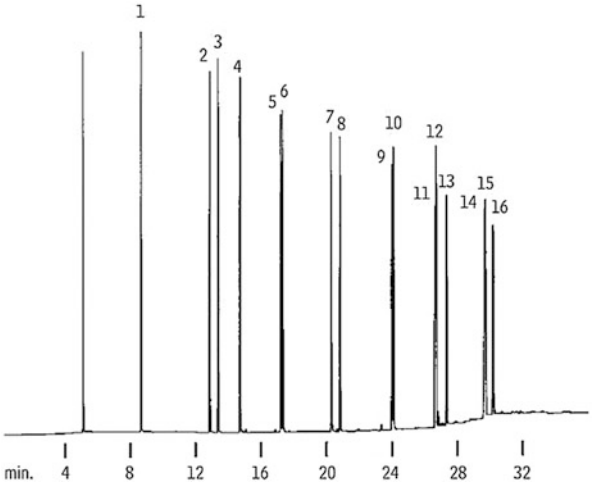


Fig. 1.5 GC analysis of PAHs (US EPA Method 610) on an Rtx-5 column (30 m × 0.32 mm ID, 0.25 µm film thickness). Injection: 0.5 µL cold on-column, temperature program: 35 °C (4 min), 10 °C/min to 325 °C, carrier gas: H_2 (40 cm/s), detection: FID. Peaks: (1) naphthalene, (2) acenaphthylene, (3) acenaphthene, (4) fluorene, (5) phenanthrene, (6) anthracene, (7) fluoranthene, (8) pyrene, (9) benzo[a]anthracene, (10) chrysene, (11) benzo[b]fluoranthene, (12) benzo[k] fluoranthene, (13) benzo[a]pyrene, (14) indeno[1,2,3-cd]pyrene, (15) dibenzo[a,h]anthracene, (16) benzo[ghi]perylene. Figure reprinted with permission from Restek searchable chromatogram library (GC_EV00376, http://www.restek.com/chromatogram/view/GC_EV00376; accessed 12/2013)

alkylation, or acylation (see Chap. 17). The introduction of "detector specific groups" by derivatization can also lead to a more selective and sensitive detection. In addition, nonvolatile compounds can be degraded by controlled thermal breakdown (pyrolysis GC) into smaller molecules analyzable by GC (see Chap. 25).

In many cases, it is not needed to map the complete sample composition but only to analyze the volatile sample components. The required analyte transfer into the gas phase, often considered as a disadvantage of GC, offers an elegant option to combine sample introduction with an analyte/matrix separation. In this context a number of solvent-free sample preparation and enrichment techniques have been developed (see Chap. 11).

If we examine the application criteria of GC (volatility) and HPLC (solubility) it is evident that both methods are perfectly complementary. However, there is some overlap as several compounds can be analyzed by both methods. When selecting a method we should keep in mind that HPLC offers milder conditions, e.g., separation at room temperature, while capillary GC offers higher separation efficiency.

The analytical use of GC to analyze mixtures or sample purity is the main application area of GC. GC is also employed for physicochemical measurements to determine thermodynamic and kinetic parameters (see Chap. 24). Furthermore, GC can be used for micro-preparative isolation of pure substances from mixtures. Preparative GC using packed columns played a major role in the 1960s, but nowadays has been replaced mostly by preparative liquid chromatography.

1.5 History and Development of Gas Chromatography

The historical development of GC has been presented in several excellent books and articles [4–7] and the interested reader is referred to these publications for a detailed insight in GC history. Here, we do not intend to present a complete historical synopsis of GC development, but only show selected, certainly incomplete, milestones that reflect our personal view of the developments in the past (see Tables 1.2 and 1.3).

In 1952 Archer J.P. Martin and Richard L.M. Synge were awarded the Nobel Prize for their invention of liquid–liquid partition chromatography, which they first described in a publication entitled "A new form of chromatogram employing two liquid phases" in 1941 [8]. In this publication they already pointed out that the mobile phase can also be a gas:

> The mobile phase need not be a liquid but may be a vapour... very refined separations of volatile substances should therefore be possible in a column in which permanent gas is made to flow over gel impregnated with a non-volatile solvent in which the substance to be separated approximately obey Raoult's law. When differences of volatility are too small to permit a ready separation by these means, advantage may be taken in some cases of deviation from Raoult's law, as in azeotropic distillation. Possible the method may also be found to be of use in the separation of isotopes... [8].

This concept was first implemented by Archer Martin and Anthony James in 1951. The corresponding publication on the separation of free fatty acids in 3.3 m glass columns appeared the same year the Nobel Prize was awarded [9]. The stationary phase consisted of silicone DC 550 modified with 10 % stearic acid and was impregnated on Kieselguhr (Celite 545) as support material. Detection was carried out using a titration cell with an automatic burette. The gaseous fatty acids were absorbed in the water of the titration cell and continuously titrated using NaOH and phenol red as indicator. The result was a stepwise titration curve that was graphical transformed in a differential curve. The experimental setup and theoretical background of partition chromatography were extensively discussed.

This fundamental publication is often considered as the beginning of gas chromatography, but this is only true for partition gas chromatography using a liquid stationary phase. The origin of gas adsorption chromatography using a solid stationary phase dates back much longer with fundamental contributions by P. Schuftan, G. Hesse, G. Damköhler, E. Cremer, N.M. Turkeltaub, A.A Žuchovičkij, and J. Janak. In 1941, the same year Martin suggested to use a gaseous mobile phase [8], Hesse succeeded to separate small molecules with a molecular mass below 200 Da using adsorption chromatography, which was previously not achieved [10]. He could show that the insufficient adsorption of small molecules on the adsorbent surface due to the presence of solvents impeded their analysis and used gases instead. Basically, he wrote: "Solvents with an even lower affinity to the adsorbent compared to the analytes can be found among gases. Using them transfers the chromatographic adsorption analysis from the liquid into the gaseous state" [10]. With the designed apparatus that resembled a distillation setup,

Table 1.2 The early period of gas chromatography

Year	Milestones
1944–1947	Gas-solid chromatography (Cremer) • Theoretical fundamentals of separation • Instrument with hydrogen as carrier gas and thermal conductivity detector for gas separation (Cremer and Prior)
1952	Gas–liquid chromatography (James and Martin) • Automated titration was used for detection of fatty acids
1953	GC instrument with CO_2 as carrier gas and volumetric detection by CO_2 absorption (Janak), patented in 1955
1955	First commercial GC instrument with thermal conductivity cell as detector Column coupling (parallel or serial)
1956	Theory of band broadening (Van Deemter)
1958	Flame ionization detector – FID (McWilliam and Dewar/Pretorius et al.) Temperature-programmed GC (Dal, Nogare) Retention index concept (Kováts) Application of GC in process control Static headspace GC First radiation ionization detector: argon ionization detector (Lovelock)
1958	Theory of capillary gas chromatography (Golay) First commercial microsyringe (10 µL, Hamilton)
1959	Direct coupling to mass spectrometry (Gohlke) Pyrolysis GC
1960	Electron capture detector – ECD (Lovelock and Lipsky) SIM mode in GC-MS (Henneberg)

the authors successfully applied the principle of GC to the separation of benzene and cyclohexane and other pairs of analytes with similar boiling point. However, the principle was not called chromatography but adsorption distillation in the publication. Due to the Second World War and the difficult and turbulent time afterwards, Hesse was not able to continue this work directly.

The first gas chromatograph was constructed in the group of Erika Cremer at the University of Innsbruck in the end of the Second World War. They separated gas mixtures using a silica-filled column. Detection of the separated compounds was carried out using a thermal conductivity cell. A correlation between elution order and the adsorption heat was shown. The respective publication entitled "On the migration speed of zones in chromatographic analysis" was submitted to the journal Naturwissenschaften in 1944 and accepted for publication. But in the turmoil of the war publication was postponed and it took more than 30 years for it to be finally published in Chromatographia [11].

The work by James and Martin discussed above was the first of three publications in a row that were published in the "Biochemical Journal" in 1952 [9, 12, 13]. They were dealing with the GC separation of polar compounds that were long considered as problematic for GC. Before long the advantages of GC were recognized as fast, relatively simple, accurate and reliable, cost-effective, and low sample amounts needed combined with high detection sensitivity and high resolution.

Table 1.3 Development of capillary gas chromatography

Year	Milestones
1957–1958	Fundamental theory on open-tubular columns (Golay) First glass capillary columns
1958–1959	Flame ionization detector (FID) First commercial microsyringes Capillary columns made from plastic, copper, and stainless steel tubing (Desty) Split injection (Desty)
1958–1973	Patent on open-tubular columns (Perkin-Elmer)
1959–1960	Glass open-tubular columns (Desty) • Glass capillary drawing machine
1960s	Era of glass open-tubular columns • Self-made glass open-tubular columns GC-MS with quadrupole mass analyzer GC-TOFMS
1968	Capillary column switching system (Dean)
1970s	Surface treatment and coating procedures (many research groups) Silicon phases (polysiloxanes) PLOT columns Wide-bore open-tubular columns Splitless injection technique Microprocessor based instruments Improvements in detector technology Computing integrators
1979	Thin-walled, flexible fused silica columns – FS columns (Dandeneau and Zerenner)
1980s	Immobilized stationary phases (cross-linking, chemical bonding) Thick film columns High-temperature GC Fundamental basis of injection processes (K. Grob) • On-column injection, PTV injection, large volume injection (LVI) Autosamplers GC-MS/MS (triple quadrupole) GC-ICPMS
1990s	Improved column technology: greater inertness, lower column bleeding PC control of GC operation and data handling Electronic pneumatic control of carrier gas Hyphenated techniques (commercialized): GC-MS, GC-AED, GC-FTIR, LC-GC coupling Solid phase microextraction – SPME (Pawliszyn) and derived techniques Fast GC Micro-GC and field portable instruments
1991	Comprehensive two-dimensional GC (Liu and Phillips)
Since 2000	Gas generators for on-site production of hydrogen as carrier gas Better automation and integration of sample preparation Robotic systems for automated sample preparation

Soon a meteoric rise of GC started and it became widely distributed and well accepted. Already 3 years after publication of the first papers commercial instruments were launched by American and British companies assembling components for the separation and detection of the analytes. Further instruments as compact or

modular systems followed within a short period of time. As Table 1.3 shows many important instrumental GC developments occurred in the 1950s and were further refined as technology advanced. This included the implementation of temperature-programmed GC to analyze compounds over a broad boiling point range. Headspace GC enabled the analysis of volatile analytes in the presence of high boiling or nonvolatile matrix components without laborious and complicated sample preparation steps.

Before long GLC became much more distributed than GSC due to its many advantages, such as greater variety of stationary phases, lower column temperature used for separation, or higher sample capacity. Nevertheless, GSC is still the method of choice for the analysis of gases and low boiling analytes (see Chap. 18).

After the Second World War the rapidly growing field of petroleum industry and petrol chemistry was the first big application area of GC. The analysis of hydrocarbon isomers that possess very similar properties required powerful separation techniques and furthered the breakthrough of GC. It replaced the standard distillation techniques for the analysis of gaseous and liquid mixtures within a short period of time.

In 1956 the British Institute of Petroleum launched a symposium series that still takes place on a biannually in Europe as "International Symposium on Chromatography" (ISC). A key event for the further development was the meeting in Amsterdam in 1958 presenting three groundbreaking innovations: the flame ionization detector (FID), the argon ionization detector as a precursor of the electron capture detector (ECD), and the separation in capillary columns. The flame ionization detector turned out to be an extremely powerful detector for almost all organic compounds. It provided lower limits of detection, higher robustness, and faster response rates compared to the previously used thermal conductivity detector and soon became standard equipment in commercial gas chromatographs. The development of the FID was also essential for the successful introduction of capillary gas chromatography. The ECD allowed the selective and sensitive detection of analytes with a high electron affinity, such as compounds containing halogen atoms, or aromatics, which is important for the application of GC in environmental analysis.

Finally, Marcel Golay demonstrated in Amsterdam that capillary columns offer a higher separation power than packed columns. Although this was confirmed by several research groups within a short period of time, packed columns remained the dominating column type for over 20 years. However, their length is limited and their separation power is low. At that time GC users mainly modified the selectivity of the stationary phase to obtain different solubilities for the analytes in the stationary phase. Back then, over 300 different stationary phases were used. Today, capillary columns are the dominating column type, but packed columns are still used for simple separations in the industrial area due to their high robustness and sample capacity.

In addition to hydrocarbon analysis soon further application areas of GC opened up, such as the analysis of flavor and fragrances, fatty acid analysis (as fatty acid methyl esters – FAMEs) in medicine and food, environmental analysis, and the use

in chemical industry, pharmacology, toxicology, and biochemistry. The use of GC in these areas not only replaced laborious and insufficient analytical methods, it also significantly broadened our knowledge on the composition of complex mixtures and the presence of trace components in food, medicinal plants, and other biological samples, and in the environment. The progress in GC also stimulated the development of HPLC and CE and furthered the transition from classical analytical chemistry to instrumental analysis.

The application of GC for process control and process engineering in chemical industry started already in 1958 and developed on its own. For the on-site use of GC in production facilities fully automated, robust, low-maintenance, reliable, and explosion-proof instruments featuring stable retention times had to be constructed. Consequently, a process GC contains 2 units that can be placed separately: The *analyzer* is on-site and contains the gas supply, sample preparation and injection, column, and detector in an explosion-proof chassis. The *data analysis unit* is often placed outside the production line in a control station. The sampling of gases or liquids is carried out using valves and the chromatographic column is operated under isothermal conditions. Multiple column techniques and column switching are employed to obtain analysis times that are process compatible. All events are time controlled. Recently, more and more miniaturized instruments are employed.

The preferred material for capillary columns was initially stainless steel, copper, alumina, and nylon. In 1960 Desty et al. introduced a glass drawing machine to produce coiled glass capillaries heralding the era of glass capillaries [14]. Still, in the beginning, the efficient glass capillary columns were only used in a few laboratories for several reasons:

- The easy breakability of glass required new sealing ferrules and operators skilled in the production, installation, and general handling of these columns.
- The reproducible injection of low sample volumes compatible with capillary columns was initially difficult. The first solution for this problem was the introduction of the split technique.
- Lower gas flow rates had to be managed reproducibly and instruments had to be modified to minimize dead volume in injector, connections, and detector.
- Poor coating performance of thin-film stationary phases on the inner wall of capillary columns resulting in asymmetric peaks, lower column temperature limits, and low column lifetime.

The breakthrough was presented by Dandeneau and Zerrener in 1979 [15] at the "3. International Symposium on Glass Capillary Chromatography" in Hindelang, a symposium series that emerged from the conference series "Symposium on Capillary Chromatography" initiated by R. E. Kaiser in 1975. Dandeneau and Zerrener presented fused silica capillary columns (FS columns) made from pure silica that, due to their low wall thickness, were coated on the outside with a protective layer using mainly polyimide. The low wall thickness resulted in a higher flexibility enabling easy column handling, and installation in the GC oven was much easier compared to glass capillary columns. They were also more inert due to a very low content of metal oxides.

A key problem of capillary column production was the generation of a homogenous and even at higher temperatures firmly adhering film of the stationary phase on the ideally inert inner wall of the capillary. In the 1970s and 1980s several research groups were dealing with this aspect. Several pretreatments of the inner glass surface and coating options were tested. An essential progress was the in situ cross-linking of the polymer chains and bonding with the pretreated inner wall. This allowed the immobilization of up to 5-μm thick films. Since the end of the 1980s cross-linking and cross-bonding are state of the art in commercial column production. Solvent stability of the columns was an important precondition for the development of injection techniques for highly diluted samples in the 1980s, such as splitless, on-column, and programmed temperature vaporizer (PTV) injection (see Chap. 5). The successful establishment of these injection techniques was facilitated by the in-depth investigation of the processes in the injector and column head during the injection of liquid samples especially by K. Grob [16, 17], which substantially increased our knowledge in this field.

A broad range of commercially available FS capillary columns ended the era of self-drawn and coated glass capillaries in the 1980s. Simultaneously, the diversity in polar stationary phases was reduced down to a few polysiloxane-based phases and polyethylene glycol. At that time, many manufacturers and users believed that the high separation efficiency of nonpolar columns enables most separations and phase selectivity was neglected. But after a while the importance of polar stationary phases was rediscovered.

In parallel with the developments in column technology, GC instrument technology matured. The first-generation instruments were made for packed columns; later instruments could be upgraded for the use with capillary columns. At the end of the 1970s instruments specifically configured for the requirements of capillary GC reached the market. Next to the technological progress instrumental development is still driven by the increasing analytical demand to meet higher quality control criteria or tightened laws, regulations, or guidelines that request analyte identification and quantification at constantly lowered detection limits and the need to analyze complex and difficult sample matrices. Accuracy, precision, reliability, robustness, easy to use, automation, low costs, and analytical speed play an increasing role. In this context the use of computer technology to store and analyze the data and the electronic control of temperature and carrier gas flow/pressure became essential.

In the second half of the 1980s the evolution of GC slowed down to less spectacular improvements and refinements. A new boost started in the 1990s with the introduction of solid phase microextraction (SPME), comprehensive two-dimensional GC (GC×GC), and a new instrument generation with electronic temperature and gas flow control as well as a higher degree of automation. That provided the user in research and routine laboratories with extended capabilities, such as high reproducibility of retention times, fast GC, or improved trace analysis, that could not or only limited be realized with the older instrument generation.

In 1989, R. B. Belardi and J. Pawliszyn [18] introduced the concept of solid phase microextraction, which became commercially available in 1993. It combines

a solvent free analyte extraction by a coated silica fiber with the subsequent thermal desorption/evaporation of the analytes from the fiber in the hot GC injector. Initially, this easy to use and automatable technique was not accepted without reservations, but soon intensive research on solvent-free or solvent-reduced micro-techniques for extraction and sample preparation was sparked, such as stir bar sorptive extraction (SBSE, Twister), in-tube extraction, or membrane techniques (see Chap. 11).

Comprehensive two-dimensional GC (GC×GC) constituted a tremendous methodical progress at the end of the last century (see Chap. 13). It is sometimes even considered as the most important innovation in GC since the introduction of FS columns. Even though GC column switching by coupling two or more chromatographic columns of different selectivity by means of a device for the time-controlled switching of the carrier gas flow has been used for over 50 years (multidimensional GC, GC-GC) it only allowed the multidimensional separation of a few selected segments of the chromatogram. A complete two-dimensional separation of the whole sample in *one* run was first carried out by Z. Liu and J. Phillips [19] using a thermal modulator between two chromatographic columns. The modulator cuts the eluate from the first column into small segments and transfers them subsequently onto the second column. An indispensable basis for GC×GC was the previously evolved theory and practical application of fast GC in short narrow columns (see Chap. 12). Within a short period of time GC×GC sparked a lot of interest due its high separation power for the complete separation of complex samples. It was shown that the compound diversity in complex samples, such as mineral oil, environmental samples, plant extracts, etc., was much greater than previously expected. In the meantime the instrumentation for GC×GC became commercially available.

An important technological progress was the hyphenation of GC to mass spectrometry (MS); see Chap. 9. The advantages of MS over other GC detectors are the high detection sensitivity, the potential to use it as universal or mass-selective detector, and the option to gain structural information from the mass spectra. The online coupling of GC-MS was first performed in 1956 with packed columns and later with capillary columns. Both techniques operate in the gas phase making them highly compatible. But there is a gas flow delivered at the end of the GC column and atmospheric pressure is present while the MS operates under high vacuum. The low gas flow rates of capillary columns in combination with the high pumping performance of modern vacuum pumps enabled the unproblematic hyphenation of both techniques. GC-MS has been a routine technique for more than 25 years. It provided a new quality in particular for the trace analysis. Efficiency, ease of use, and robustness of the instruments were constantly improved and mass spectral libraries extended. In addition to quadrupole and ion trap mass analyzers, triple-quadrupole instruments (Triple Quads) and time-of-flight (TOF) systems are used for GC-MS in recent years.

At this stage, gas chromatography presents itself as a widely used and matured technique. Currently, it is estimated that about 400,000–500,000 GC systems are in use worldwide. Still, the development of GC has not reached its end, but advances

are to be expected in the details. Currently, hot topics are high sample throughput, reduction of analysis time, improved trace analysis, integration of sample preparation and enrichment within the GC instrument, further automation in particular in data analysis, and the replacement of helium as carrier gas. The further improvement of column technology and the development of stable polar stationary phases and stationary phases with tailored selectivity are constantly demanded. For example, the introduction of ionic liquids as highly polar stationary phases that first became commercially available in 2008 meets the demand for new polar stationary phases.

Modern instrument technology and software simplify the use of GC and analyses can be performed by less trained personnel. Nevertheless, the high methodical and instrumental potential of GC can only be fully used if the operator is familiar with the theoretical and practical aspects of GC.

Unfortunately, the chromatographic literature was and still today is not consistent in the use of terminology and symbols, which may cause confusion. Therefore, the "International Union of Pure and Applied Chemistry" (IUPAC) published a "Nomenclature for Chromatography" in 1974 [2] that was updated 20 years later [20]. This nomenclature is mainly used in this book. A compendium of the most important terms is given in the appendix.

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