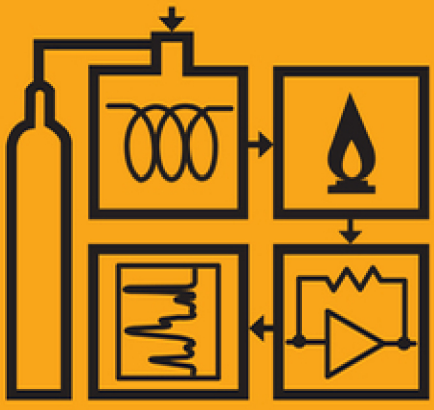
THIRD EDITION



BASIC GAS CHROMATOGRAPHY

HAROLD M. McNAIR
JAMES M. MILLER
NICHOLAS H. SNOW

WILEY

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PREFACE TO THE THIRD EDITION

Since the earliest editions of a book titled *Basic Gas Chromatography* were published by McNair and Bonelli about 50 years ago, gas chromatography has evolved and matured. Today, the gas chromatography community is large and vibrant with routine use of GC in a huge variety of scientific disciplines. GC is found in laboratories performing analyses ranging from routine and simple to cutting edge research and development. Instrument configurations include traditional benchtop instruments, smaller footprint benchtop systems, portable instruments, and fully functional instruments-on-a chip. GC is used routinely in non-laboratory settings including at-line sampling and analysis in manufacturing, and GC instruments have even flown in space.

Today, gas chromatography is undergoing a renaissance as instruments have been constructed to take full advantage of the separating power of capillary columns, along with advanced solid-state electronics for inlets and detectors. Most work is now performed using capillary columns that offer very high separating power and resolution. Routine use of GC has been greatly simplified by modern instrumentation that includes electronic control of all pneumatics, temperatures and flows and data systems that automatically perform calculations and generate reports.

Although GC has evolved, the purpose of this book remains the same as it has for 50 years: to help new users of GC get started and to remind experienced users of the fundamentals. Even as new instruments are developed, the fundamental chemistry and basic principles of chromatography remain the same.

In this edition of *Basic Gas Chromatography*, we have reorganized the content to reflect a much greater emphasis on capillary GC, with most packed column-related content placed in a new Chapter 13. The discussions of inlets and temperature programming have been expanded. The chapters on detectors have been reorganized, separating classical and spectrometric detectors. The chapters on multidimensional GC and sample preparation have been significantly updated.

We welcome Dr. Nicholas Snow of Seton Hall University to the author team and welcome back Dr. Gregory Slack of PharmAssist Laboratories as the author of Chapter 11 on sample preparation techniques. We all owe a debt of gratitude to the many colleagues and students with whom we have worked. This book is as much yours as it is ours. You have taught us more about chromatography than you will ever know.

Harold M. McNair
James M. Miller
Nicholas H. Snow

PREFACE TO THE SECOND EDITION

When the first edition of this book was published in 1998, gas chromatography (GC) was already a mature, popular separation method. Grob's encyclopedic *Modern Practice of Gas Chromatography* was already in its third (1995) edition. But the field has not remained static, and there is much new information that necessitates an update, a second edition of our book. In the meantime, Grob's book (now coedited with Barry) is in its fourth edition (2004) and comprises over 1000 pages. Miller's book on chromatography is also in its second edition (2005).

Our objectives have remained the same, as has our intention to keep the book small, basic, and fundamental. Several topics that were contained in the Special Topics chapter of the first edition have been expanded in the second. They are gas chromatography–mass spectrometry (GC-MS) and special sampling methods, now entitled simply "Sampling Methods." In addition, a new chapter on multidimensional GC has been added. Also, two new topics have been added to the Special Topics chapter, namely, fast GC and the GC analysis of nonvolatile compounds. The latter includes the original section on derivatization, supplemented with inverse GC and pyrolysis GC. The entire book has been updated with new references, resources, and websites.

The textual material for the two new chapters (11 and 12) has been written by Nicholas Snow and Gregory Slack, both former students of McNair. They are established chromatography authors in their own right, and we welcome them and thank them for their contributions. Further information about them can be found on the Acknowledgments page.

We would be remiss if we did not repeat our expression of gratitude that is included in our original Preface. Many persons have helped us and taught us, including our mentors, students, and many other colleagues. We are also indebted to our wives and families for their support and encouragement. Thank you all.

Harold M. McNair
James M. Miller

PREFACE TO THE FIRST EDITION

A series of books on the *Techniques in Analytical Chemistry* would be incomplete without a volume on gas chromatography (GC), undoubtedly the most widely used technique. Over 40 years in development, GC has become a mature method of analysis and one that is not likely to fade in popularity.

In the early years of development of GC, many books were written to inform analysts of latest developments. Few of them have been kept up-to-date, and few new ones have appeared, so that a satisfactory single introductory text does not exist. This book attempts to meet that need. It is based in part on the earlier work by the same title, *Basic Gas Chromatography*, co-authored by McNair and Bonelli and published by Varian Instruments. Some material is also drawn from the earlier Wiley book by Miller, *Chromatography: Concepts and Contrasts*.

We have attempted to write a brief, basic introduction to GC following the objectives for titles in this series. It should appeal to readers with varying levels of education and emphasizes a practical, applied approach to the subject. Some background in chemistry is required: mainly general organic chemistry and some physical chemistry. For use in formal class work, the book should be suitable for undergraduate analytical chemistry courses and for intensive short courses of the type offered by the American Chemical Society and others. Analysts entering the field should find it indispensable, and industrial chemists working in GC should find it a useful reference and guide.

Because the IUPAC has recently published its nomenclature recommendations for chromatography, we have tried to use them consistently to promote a unified set of definitions and symbols. Also, we have endeavored to write in such a way that the book would have the characteristics of a single author, a style especially important for beginners in the field. Otherwise, the content and coverage are appropriately conventional.

While open tubular (OT) columns are the most popular type, both open tubular and packed columns are treated throughout, and their advantages, disadvantages, and applications are contrasted. In addition, special chapters are devoted to each type of column. Chapter 2 introduces the basic instrumentation and Chapter 7 elaborates on detectors. Other chapters cover stationary phases (Chapter 4), qualitative and quantitative analysis (Chapter 8), programmed temperature (Chapter 9), and troubleshooting (Chapter 11). Chapter 10 briefly covers the important special topics of GC-MS, derivatization, chiral analysis, headspace sampling, and solid-phase micro-extraction (SPME) for GC analysis.

We would like to express our appreciation to our former professors and many colleagues who have in one way or another aided and encouraged us and to those students who, over the years, have provided critical comments that have challenged us to improve both our knowledge and communication skills.

HAROLD M. MCNAIR
JAMES M. MILLER

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The authors wish to acknowledge Chapter 11, "Sampling Methods," which was provided by Dr. Gregory C. Slack, Scientific Director at PharmAssist Laboratories, South Berlin, NY 13843.

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1

INTRODUCTION

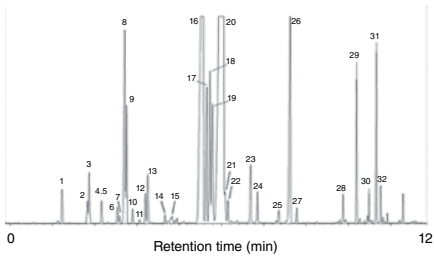
It is hard to imagine an organic analytical laboratory without a gas chromatograph. Gas chromatography (GC) is the premier technique for separation and analysis of volatile compounds. It has been used to analyze gases, liquids, and solids, with the latter usually dissolved in volatile solvents. Both organic and inorganic materials can be analyzed, and molecular weights can range from 2 to over 1000 Da.

Gas chromatographs continue to be the most widely used analytical instruments in the world. Efficient capillary columns provide high resolution, separating more than 450 components in coffee aroma, for example, or the components in a complex natural product like peppermint oil as seen in Figure 1.1. Sensitive detectors like the flame ionization detector can quantitate 50 ppb of organic compounds with a relative standard deviation of about 5%. Automated systems can handle more than 100 samples per day with minimum downtime, and all of this can be accomplished with an investment of about $20,000.

A BRIEF HISTORY

Chromatography began at the turn of the century when Ramsey [1] separated mixtures of gases and vapors on adsorbents like charcoal and Michael Tswett [2] separated plant pigments by liquid chromatography (LC). Tswett is credited

Basic Gas Chromatography, Third Edition. Harold M. McNair, James M. Miller, and Nicholas H. Snow.



Sample: 10% peppermint oil in dichloromethane

Column: Zebron ZB-1MS, 100% polydimethylsiloxane
10 m × 0.10 mm × 0.1 μm
Program: 45 °C, 2 min, 10 °C/min to 130 °C,
330 °C/min to 280 °C
Carrier gas: He, 0.3 mL/min, constant flow
Injection: Split 120:1, 0.2 μL, 160 °C
Detector: Mass selective

1. α-pinene
2. Sabinene
3. Beta pinene
4. Mycrene
5. 3-octanol
6. α-terpenene
7. Cymene
8. Eucalyptol
9. D-limenene
10. *cis*-ocimene
11. *Trans*-ocimene
12. γ-terpenene
13. *cis*-sabinene hydrate
14. β-terpineol
15. Linalool
16. Menthone
17. Isomentone
18. Menthone furan
19. Neomenthol
20. Menthol
21. Neoisomenthol
22. α-terpineol
23. Pulegone
24. Piperitone
25. Neomenthyl acetate
26. Menthyl acetate
27. Isomenthyl acetate
28. Burbonene
29. Caryophyllene
30. Farnescene
31. Germacrene
32. Elemene

Figure 1.1. Typical gas chromatographic separation showing the high efficiency of this method. *Source*: Courtesy of Phenomenex, Inc.

as being the "father of chromatography" principally because he coined the term *chromatography* (literally meaning "color writing") and scientifically described the process. His paper was translated into English and republished [3] because of its importance to the field. Today, of course, most chromatographic analyses are performed on materials that are not colored.

GC is that form of chromatography in which a gas is the moving phase. The important seminal work was first published in 1952 [4] when Martin and James acted on a suggestion made 11 years earlier by Martin himself in a Nobel Prize-winning paper on partition chromatography [5]. It was quickly discovered that GC was simple, fast, and applicable to the separation of many volatile materials, especially petrochemicals, for which distillation was the preferred method of separation at that time. Theories describing the process were readily tested and led to still more advanced theories. Simultaneously the demand for instruments gave rise to a new industry that responded quickly by developing new gas chromatographs with improved capabilities.

The development of chromatography in all of its forms was thoroughly explored by Ettre, who authored nearly 50 publications on chromatographic history. There are three most relevant articles: one focused on the work of Tswett, Martin, Synge, and James [6]; one emphasizing the development of instruments [7]; and a third containing over 200 references on the early development of chromatography [8].

Today GC is a mature technique and a very important one. The worldwide market for GC instruments is estimated to be between $2 and $3 billion or more than 40,000 instruments annually.

DEFINITIONS

In order to define chromatography adequately, a few terms and symbols need to be introduced, but the next chapter is the *main* source of information on definitions and symbols.

Chromatography

The "official" definitions of the International Union of Pure and Applied Chemistry (IUPAC) are:

> 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. Elution chromatography is a procedure in which the mobile phase is continuously passed through or along the chromatographic bed and the sample is fed into the system as a finite slug [9].

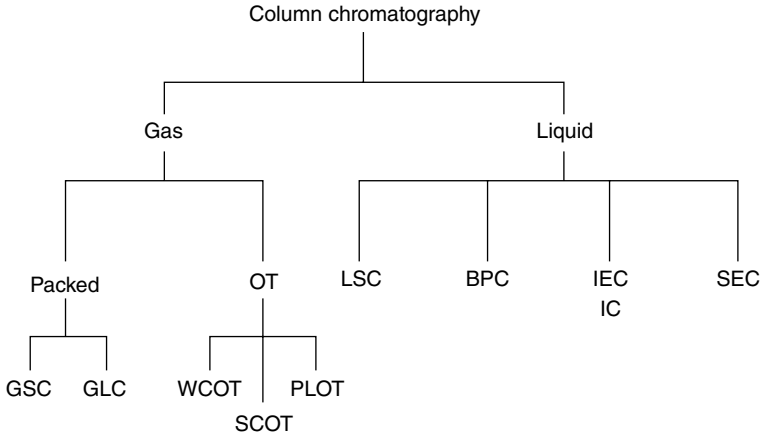


Figure 1.2. Classification of chromatographic methods. (Acronyms and abbreviations are given in Appendix A.)

This type of chromatographic process is called *elution*. The various chromatographic processes are named according to the physical state of the mobile phase. Thus, in GC the mobile phase is a *gas*, and in LC the mobile phase is a *liquid*. Figure 1.2 shows a flow chart of the various common gas and liquid chromatographic techniques.

In GC, the sample is vaporized and carried by the mobile gas phase (the *carrier gas*) through the column. In most analyses, samples partition (equilibrate) into and out of the stationary liquid phase, based on their solubilities in the stationary phase at the given temperature. The components of the sample (called solutes or analytes) separate from one another based on their *relative* vapor pressures and affinities for the stationary phase.

Within GC, a subclassification is made according to the state of the stationary phase. If the stationary phase is a solid, the technique is called gas–solid chromatography (GSC); and if it is a liquid, the technique is called gas–liquid chromatography (GLC). Note that the names used to describe open tubular (OT or capillary) GC columns and LC columns include more detail than the simple guidelines just presented. However, all forms of GC are included in the two subdivisions, GLC and GSC. Some of the capillary columns represent GLC, while others represent GSC. Of the two major types, GLC is by far the more widely used; consequently, it receives greater attention in this work.

Obviously, the use of a gas for the mobile phase requires that the system be contained and leak-free, and this is accomplished with a glass or metal tube that is referred to as the column, which contains the stationary phase. Columns are named by specifying the stationary phase. For example, one can speak about a polydimethylsiloxane (PDMS) column, which means that the stationary liquid phase is PDMS. See Chapters 4 and 5 for details on naming columns.

The Chromatographic Process

Figure 1.3 is a schematic representation of the chromatographic process. The horizontal lines represent the column. Each line is like a snapshot of the process at a different time (increasing in time from top to bottom). In the first (top) snapshot, the sample, composed of components A and B, is introduced onto the column in a narrow zone. It is then carried through the column (from left to right) by the mobile phase.

Each component partitions between the two phases, as shown by the distributions or peaks above and below the line. Peaks above the line represent the amount of a particular component in the mobile phase, and peaks below the line represent the amount in the stationary phase. Component A has a greater distribution in the mobile phase, and as a consequence it is carried down the column faster than component B, which has a greater distribution in the stationary phase and spends more of its time there. Thus, separation of A from B occurs as they travel through the column. Eventually the components leave the column and pass through the detector as shown.

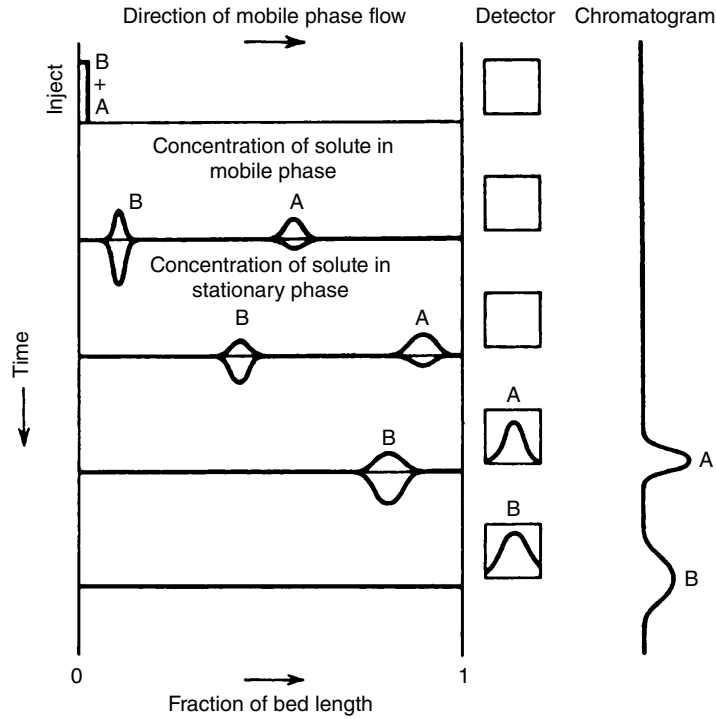


Figure 1.3. Schematic representation of the chromatographic process. *Source*: From Miller [10, p. 44]. Reproduced courtesy of John Wiley & Sons, Inc.

The output signal of the detector gives rise to a *chromatogram* shown at the right side of Figure 1.3. The schematic in Figure 1.3 is also illustrative of the main process driving separation in GC: phase transfer equilibrium. An analyte partitions between the mobile and stationary phases as it travels along the column. The relative sizes of the peaks above and below the lines in the figure are also indicative of the relative masses of the component in each phase. The ratio of the mass in the stationary phase to the mass in the mobile phase provides the retention factor, "*k*," one of the most important chromatographic variables. Component A has more of its mass in the mobile phase, so it travels through the column faster. More details about phase equilibrium are provided in Chapter 2.

Note that Figure 1.3 also shows how an individual chromatographic peak widens or broadens as it goes through the chromatographic process. The extent of this broadening, which results from the kinetic processes at work during chromatography, is discussed in Chapter 2.

The tendency of a given component to be attracted to the stationary phase is expressed in chemical terms as an equilibrium constant called the *distribution constant*, K_c, sometimes also called the partition coefficient. The distribution constant is similar in principle to the partition coefficient that controls a liquid–liquid extraction. In chromatography, the greater the value of the constant, the greater the attraction to the stationary phase.

The distribution constant provides a numerical value for the total sorption by a solute *on* or *in* the stationary phase. As such, it expresses the extent of interaction and regulates the movement of solutes through the column. In summary, differences in distribution constants, which are controlled by thermodynamics, effect a chromatographic separation.

Additionally, the attraction can be classified relative to the *type* of *sorption* by the solute. Sorption on the surface of the stationary phase is called *ad*sorption, and sorption into the bulk of a stationary liquid phase is called *ab*sorption. These terms are depicted in comical fashion in Figure 1.4. However, most chromatographers use the term *partition* to describe the absorption process. Thus they speak about adsorption as landing on the surface of the stationary phase and partitioning as passing into the bulk of the stationary phase. Usually one of these processes is dominant for a given column, but both can be present.

Basic Chromatographic Terms and Symbols

The IUPAC has standardized chromatographic terms, symbols, and definitions for all forms of chromatography [9], and their recommendations are used in this book. However, until the IUPAC publication in 1993, uniformity did not exist, and some confusion may result from reading older publications. Table 1.1 compares some older conventions with the IUPAC recommendations.

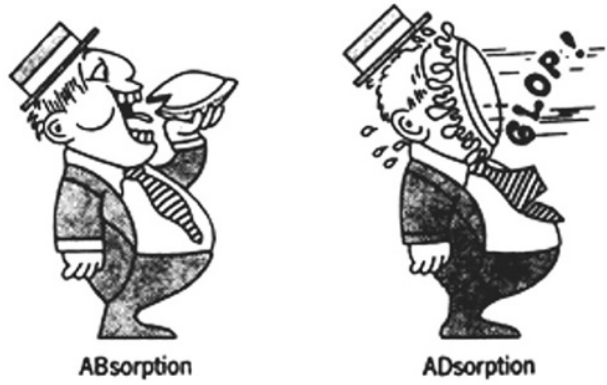


Figure 1.4. Comical illustration of the difference between absorption (partition) and adsorption. *Source*: From Miller [10, p. 45]. Reproduced courtesy of John Wiley & Sons, Inc.

TABLE 1.1 Chromatographic terms and symbols

Symbol and name recommended by the IUPAC	Other symbols and names in use
K_c distribution constant (for GLC)	K_p partition coefficient
	K_D distribution coefficient
k retention factor	k' capacity factor; capacity ratio; partition ratio
N plate number	n theoretical plate number; no. of theoretical plates
H plate height	HETP height equivalent to one theoretical plate
R retardation factor (in columns)	R_R retention ratio
R_s peak resolution	R
α separation factor	Selectivity; solvent efficiency
t_R retention time	
V_R retention volume	
V_M holdup volume	Volume of the mobile phase; V_G volume of the gas phase; V_O void volume; dead volume

Source: Data taken from Ettre [9].

The distribution constant, K_c, has just been discussed as the controlling factor in the partitioning equilibrium between a solute and the stationary phase. It is defined as the concentration of the solute A in the stationary phase divided by its concentration in the mobile phase:

$$K_c = \frac{[A_s]}{[A_m]} \tag{1.1}$$

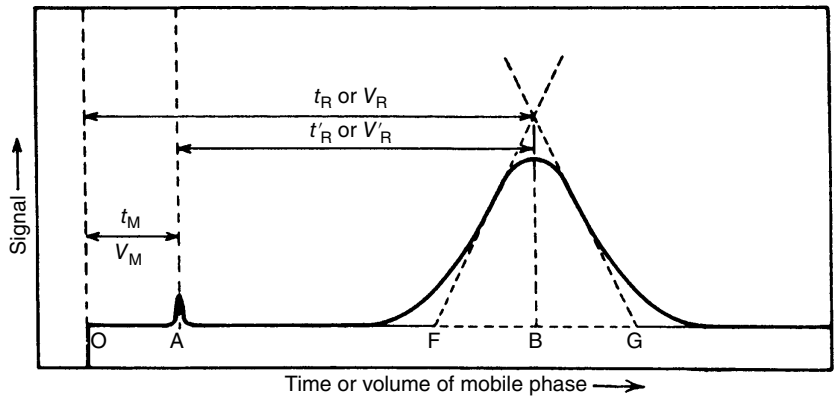


Figure 1.5. Typical chromatogram. *Source*: From Miller [10, p. 46]. Reproduced courtesy of John Wiley & Sons, Inc.

This constant is a true thermodynamic value that is temperature dependent; it expresses the relative tendency of a solute to distribute itself between the two phases. Differences in distribution constants result in differential migration rates of solutes through a column.

Figure 1.5 shows a typical chromatogram for a single solute, A, with an additional small peak early in the chromatogram. Solutes like A are retained by the column and are characterized by their *retention times or retention volumes*, (t_R, or V_R). The retention time and volume for solute A are depicted in the figure as the distance from the point of injection to the peak maximum. The retention time is the time required for the solute to elute from the column, which is related to the volume of carrier gas necessary to elute solute A by the flow rate, F_c, assuming constant flow:

$$V_R = t_R \times F_c \quad \text{or} \quad t_R = \frac{V_R}{F_c} \tag{1.2}$$

Unless specified otherwise, a constant flow rate is assumed and retention time is proportional to retention volume, and both can be used to represent the same concept. Retention time is far more commonly used than retention volume, so it is used primarily in this book. A discussion of retention volume is provided in Chapter 14.

The small early peak represents a solute that does not sorb in the stationary phase—it passes straight through the column without stopping. The IUPAC [9] has selected the name *holdup volume* for V_M and defined it as "the volume of the mobile phase (MP) required to elute the un-retained compound from the chromatographic column and reported at column temperature and ambient pressure." The analogous time parameter is *holdup time*, t_M, "the time

required for the MP to pass through the chromatographic column." Further, because the original terms were found to be misleading or superfluous, the IUPAC [11] recommends that the common term *dead volume* not be used. In GC, air or methane is often used as the unretained component, and the peak labeled A in Figure 1.5 is sometimes referred to as the *air or methane peak*.

The relationships between retention volume, time, and flow are derived in the text by Karger et al. [12] and an article by Snow [13]. Equation (1.3), one of the fundamental chromatographic equations, relates the retention time, t_R, as the sum of time spent moving in the mobile phase, t_m, and time spent sorbed not moving in the stationary phase, t'_R:

$$t_R = t_m + t'_R \tag{1.3}$$

An understanding of the chromatographic process can be deduced by reexamining Eqs. (1.2) and (1.3). The total time required for the elution of a solute can be seen to be composed of two parts: the time required for the solute to pass through the gas that fills the column, t_m, and the time spent while the solute is not moving but is stationary on or in the stationary phase, t'_R. The latter is determined by the distribution constant (the solute's tendency to sorb) and the amount of stationary phase in the column V_S. There are only two things a solute can do: move with the flow of mobile phase when it is in the mobile phase or sorb into the stationary phase and remain immobile. The sum of these two effects provides the total retention time or volume, t_R, or V_R.

OVERVIEW: ADVANTAGES AND DISADVANTAGES

GC has several important advantages as summarized in the list below.

Advantages of Gas Chromatography

- Fast analysis, typically minutes.
- Efficient, providing high resolution.
- Sensitive, easily detecting ppm and often ppb.
- Nondestructive, making possible online coupling, e.g. to a mass spectrometer.
- Highly accurate quantitative analysis, typical RSDs of 1–5%.
- Requires small samples, typically μL.
- Reliable and relatively simple.
- Inexpensive.