JOURNAL OF CHROMATOGRAPHY LIBRARY - volume 42

quantitative gas chromatography

for laboratory analyses and on-line process control

Georges Guiochon

Claude L. Guillemin

FOREWORD

Gas chromatography has reached maturity. The number of scientific papers published yearly in this area is decreasing. Although there are still a few unresolved issues, many of these papers belong more to the realm of technological development than to the pursuit of science. After well above ten thousand valuable papers and many books have been published on gas chromatography, why have we written another one, and one this size?

Gas chromatography is now firmly established as one of the few major methods for the quantitative analysis of complex mixtures. It is very fast, accurate and inexpensive, with a broad scope of application. It is likely to stay forever in the analytical chemistry laboratories. Although the source of scientific literature dealing with gas chromatography is slowly drying up, the sales of gas chromatographs are still increasing. Besides replacing obsolete instruments, chromatographs are purchased to expand existing laboratories and to create new ones.

Gas chromatography has become complex and involved. Over two hundred stationary phases, more than ten detector principles and several very different column types are available for the analyst to choose from among the catalogs of over a hundred manufacturers and major retailers. Like other modern techniques of measurements, gas chromatography makes considerable use of computer technology. Digital electronics, data processors, programs for data acquisition and handling must be familiar to the analyst. Their integration to the chromatograph makes it a sophisticated piece of equipment.

These progressive changes in the nature of gas chromatography as well as its now ubiquitous use have created new needs for information which are not satisfied by the literature presently available. The analyst needs an easy way to find out about the technique as he wants to use it: how to rapidly, simply and inexpensively carry out the quantitative analyses he has to perform. He needs help in finding methods to solve his daily problems and he does not have time to seek the primary literature and to digest it. Reviews published by scientific journals are an excellent solution, but they are scattered through hundreds of volumes, are published with no logical plan and are of uneven scope and quality. Most recent books are dedicated to specialized topics and none of them discusses the specific problems of quantitative analysis. The general books and treatises available are now aging. None of them deals seriously with the practical aspects of quantitative analyses, although it is the main issue in modern gas chromatography.

We have written the present book in an attempt to fill these needs. It has always been surprising, if not shocking, to both of us that, although gas chromatography is essentially used to provide quantitative analyses, this topic is almost completely neglected in treatises, books, handbooks or textbooks. It is rarely talked about at

meetings, as if calibration were a dirty business and errors a plague and not a topic worthy of scientific discussions. We have striven to provide a complete discussion of all the problems involved in the achievement of quantitative analysis by gas chromatography, whether in the research laboratory, in the routine analysis laboratory or in process control. For this reason the presentation of theoretical concepts has been limited to the essential, while extensive explanations have been devoted to the various steps involved in the derivation of precise and accurate data. This starts with the selection of the proper instrumentation and column, continues with the choice of optimum experimental conditions and then with careful calibration and ends with the use of correct procedures for data acquisition and calculations. Finally, there is almost always something to do to reduce the errors and an entire chapter deals with this single issue. Numerous relevant examples are presented.

Although we have tried to be reasonably complete, and to present the most important and pertinent papers on each issue dealt with, we are sure that we have missed a few of them. We apologize in advance to the authors and to our readers for these lapses, which in part are due to the extreme abundance of the literature. We would like them to be brought to our attention. We shall appreciate all comments and especially those which could be useful for a further edition.

Finally we want to thank here all those who have helped us in this endeavour: those who have provided us inspiration and understanding, those who have worked with us, those who have given us ideas or clues, those who have discussed these problems with us during the years when gas chromatography was in the making and the many authors whose papers we read with delight. Their names are found in our book and they are too many to be listed here. We are especially grateful to Prof. Daniel E. Martire who read the theory section and made many constructive comments, to Mrs. Lois Ann Beaver who read the whole manuscript and made many helpful suggestions for its improvement and to Mrs. H.A. Manten who turned our set of ASCII files into a book.

Concord, Tennessee,
January 1988

GEORGES GUIOCHON
CLAUDE L. GUILLEMIN

CONTENTS

CHAPTER 1

INTRODUCTION AND DEFINITIONS

TABLE OF CONTENTS

INTRODUCTION

Gas chromatography is one of many modes of chromatography. Described for the first time in 1952 (1) it has become extremely popular because of the rapidity and ease with which complex mixtures can be analyzed, because of the very small sample required and because of the flexibility, reliability and low cost of the instrumentation required.

During the last 35 years an enormous amount of literature has been published in the field. A large number of journals publish several papers dealing with gas chromatography in every issue (2). Two journals publish only abstracts of papers published elsewhere (3,4); although striving to be complete they cannot be exhaustive. A great number of books has been published. Those most favored by the authors at some time or another in their lives are cited (5–13). This list represents a small sample of those which may be found on University library bookshelves. In the following, we shall quote, to the best extent of our knowledge, only the most important or relevant contributions.

I. DEFINITION AND NATURE OF CHROMATOGRAPHY

Chromatography is a separation process which utilizes the difference between the equilibrium coefficients of the components of the mixture to be separated between a stationary phase of large specific surface area and a moving fluid which percolates across it (5).

There are four important concepts in this definition which, together, effect the profound originality and the considerable separation power and versatility of the method.

First chromatography uses two different phases: one fixed and one mobile. Second, the mobile phase percolates across the stationary phase, and this phase has a large specific surface area. These two conditions together guarantee very fast mass transfers between the phases and rapid local equilibrium. Third, the components of the analyzed mixture must be soluble in the mobile phase and there must be a physico-chemical process of some sort which causes the components of the analyzed mixture to have some moderate affinity for the stationary phase and to equilibrate between the mobile and stationary phases. Finally, the equilibrium coefficients of

the different components of the mixture must differ sufficiently to permit their separation.

In other words, the mixture to be analyzed is dissolved in a fluid which percolates across a stationary phase. The components of the mixture equilibrate between the two phases, but a real, conventional, static equilibrium is impossible because the motion of the carrier fluid constantly displaces the equilibrium. The compounds are carried downstream by the moving fluid and separate at the same time. Since it is possible to design and build a system where components will experience a very large number of successive such equilibria, chromatography is an extremely powerful method of separation. Since physical chemistry provides a large number of equilibrium processes between two different phases, the method is very flexible.

The stationary phase can be either a solid or a liquid. In the first case adsorption is the main equilibrium process used. In the second case, to avoid the potentially disastrous effects of convective mixing, and to permit rapid exchange between the two phases, the liquid is dispersed on a solid support. This support will have a rather large specific surface area, to promote fast exchanges between the phases and rapid equilibrium, but must be inert or almost so, in order not to contribute by an adsorption process to the nature of the equilibrium between the mobile and stationary phases. This condition will be more-or-less rigidly enforced depending on the aim of the analyst: if the additional contribution of the support contributes to the separation, the so-called 'mixed mechanism' will be gratefully accepted.

The mobile phase can be either a gas or a liquid. In this book we study only gas chromatography, whose particular characteristics result from the use of a low-density, compressible fluid, of low viscosity, in which diffusion coefficients are large (1). In almost all applications it will be assumed that the behavior of the gas mobile phase is ideal. In a few cases a correction is made, using the second virial coefficient. Solubility in the mobile phase, of course, means volatility, and the components of the analyzed mixture must have a significant vapor pressure in the conditions of the analysis. There is no clear-cut threshold, and this question is discussed in more detail later, but it is quite difficult to analyze by gas chromatography (GC) compounds whose vapor pressure is not at least a few torr at the temperature at which the analysis is carried out (10). Conversely, the stationary phase must have an extremely low vapor pressure, in order to permit the achievement of a significant number of analyses under reproducible conditions.

II. PHASE SYSTEMS

This term designates the combination of mobile and stationary phases used for a given chromatographic application. In gas chromatography the mobile phase has only a very small influence on the retention data, so the choice of the proper stationary phase is of paramount importance. In some rare instances, a change of carrier gas may alter the resolution pattern to a significant degree.

References on p. 33.

The stationary phase is made of solid particles, preferably of narrow size distribution. Their average size is usually between 0.1 and 0.3 mm, although smaller particles have been used in some cases, to achieve very large efficiencies. From the point of view of their chemical composition, the stationary phases used can be classified into three groups:

– Adsorbents, usually with a very large specific surface area (50 to 1000 and more m^2/g). Silica, alumina, molecular sieves, activated charcoal, and graphitized carbon black have been used. Gas–solid chromatography is not a very popular method, except for the analysis of gases, or for the solution of special problems.

– Neutral, or so-called inert, supports are usually derived from diatomaceous materials, sometimes from polymers. They are impregnated with a liquid of very low vapor pressure and high thermal stability under the conditions that the column is used. There is a large variety of such liquids which have been tested, and whose characteristics are reported in the literature. The properties of these phases and the principles of stationary phase selection are discussed in Chapter 3. Changing the nature of the liquid changes the solubility of the sample components and permits the adjustment of the selectivity, i.e. of the relative position of the bands of these compounds. Dissolution of additives in the stationary phase which result in the formation of labile complexes with some of the compounds to resolve is another approach to the change of selectivity. Gas–liquid chromatography is by far the most popular method in current use.

– Adsorbents impregnated with a small amount of a low vapor pressure liquid have also been used with extremely good success to achieve difficult separations. The method is then usually referred to as gas–adsorption layer chromatography or modified gas–solid chromatography (see Chapter 7).

The mobile phase is an inert gas, such as helium, nitrogen, argon, or a gas like hydrogen, which is considered to be inert under the conditions of gas chromatography. Other gases or vapors have been used in some special cases, like steam (see Chapter 7) or anhydrous ammonia. The chemical composition of the carrier gas has only a very small effect on the retention of compounds and on their resolution. This effect is due to the variation of the second virial coefficient of interaction in the gas phase and can be neglected, except when working with very high efficiency open tubular columns.

On the other hand, the physical properties of the mobile phase, and especially the large compressibility of gases, the large value of the diffusion coefficient and the major difference between partial molar volumes in the mobile and stationary phase have a profound influence and are the reason for the considerable differences between gas chromatography and liquid chromatography.

III. SCHEMATIC DESCRIPTION OF A GAS CHROMATOGRAPH

There have been many implementations of the principles of gas chromatography, but all GC equipment is very similar in its basic principles (1-4). A schematic description is given in Figure 1.1 (see also Chapter 9, Section I). The basic components are as follows:

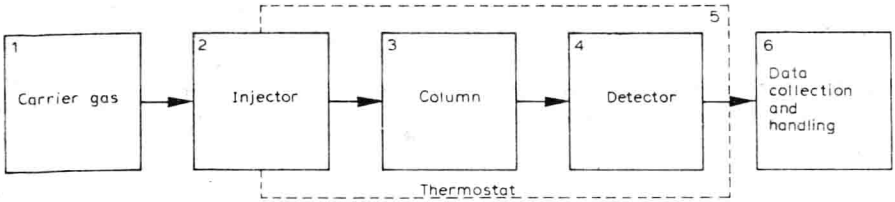

Figure 1.1. Schematic of a modular chromatograph.
1 – Source of carrier gas, at constant flow rate or constant pressure.
2 – Introduction of the sample into the carrier gas stream.
3 – Chromatographic column.
4 – Detection system.
5 – Temperature controlled oven.
6 – System for data collection and handling.

– A carrier gas supply unit, which delivers a steady stream of the carrier gas selected. The most popular systems use a flow rate controller. The mass flow rate of the carrier gas through the controller is kept constant. In other words, the number of moles of gas passing through the column per unit time is constant.

– A sampling system, which permits the injection in this stream of gas, just upstream of the column, of the proper amount of sample. This sample must be vaporized in a short enough time and introduced into the column as a cylindrical plug of vapor diluted by the carrier gas.

– The column, which is contained in a temperature-controlled oven. The temperature selected usually lies in the range ambient temperature to 350 °C, although analyses have been reported in the much larger range (−180 °C to +1000 °C).

– A detector, which delivers a signal function of the composition of the carrier gas. Ideally this signal is zero when pure carrier gas exits from the column and is proportional to the concentration of any compound different from the carrier gas. Such a detector is called linear. If the proportionality coefficient is the same for all compounds the detector is called ideal. In practice, an ideal detector does not exist.

The components of a mixture, known as solutes, injected at the column inlet are carried downstream by the carrier gas. They migrate at a speed which is proportional to the carrier gas velocity, but is slower, and depends on the strength of the interaction of each of these components with the stationary phase. Accordingly, if the stationary phase has been properly selected, each component exits or, is eluted, at a different time and is resolved from the other ones. The signal of the detector permits the identification of each component from the time of elution of its band (also called its retention time), and its quantification from the size of the detector signal (its height or area).

This is the ideal situation, which is rarely encountered in practice without strenuous efforts, but is one which all chromatographers strive to achieve.

The chromatographic process is thus a sequential one. To every injection corresponds a separation followed by a detection. Whatever the implementation, the response time of the analytical system cannot be shorter than the retention time of

References on p. 33.

the compound one is interested in. If the control of a unit in a chemical plant depends on the concentration of a certain component of the exit stream, the retention time of this compound on the process control chromatograph must be shorter than the response time required for the control loop. The transfer time between the unit and the sampling system of the chromatograph must also be taken into account.

IV. CHROMATOGRAPHIC MODES

There are three different modes of chromatography: elution chromatography, frontal analysis and displacement chromatography. The first is used only for analytical applications; its implementation is discussed in detail in subsequent chapters (1–4). The principles of the other two modes are briefly described.

1. Elution Chromatography

In *elution chromatography*, the sample is injected just upstream of the column inlet, as a cylindrical plug of vapor which is diluted in the carrier gas. Each component of the mixture migrates as if it were alone, and elutes as a narrow band. If the conditions of the analysis are properly chosen, all these bands are resolved from each other, each compound is separated from the other ones, but its dilution in the carrier gas has increased.

The time width of the plug must be small compared with the distance between the two most closely eluted bands of the mixture, so that these bands do not interfere. In fact, during their elution through the column, the bands of the mixture components do broaden and their maximum concentration decreases, so the plug width needs to be rather small compared to the average width of the two closest bands. Band broadening is due to molecular diffusion and to resistance to mass transfer, which is discussed further in Chapter 4, while dilution results from band broadening, and is required by the Second Principle of Thermodynamics: the chromatographic separation of the mixture components is accompanied by their simultaneous dilution in the carrier gas, so there is no net decrease of entropy during the chromatographic process.

When the sample is not diluted enough in the carrier gas, the assumption of the independence of behavior of the different components of the mixture does not hold any longer, and the retention time of one compound depends to some extent on the amount of the other ones (see Chapter 5). Except in some cases encountered mostly in trace analysis, this situation, described as non-linear chromatography is carefully avoided in analytical applications.

2. Frontal Analysis

In *frontal analysis*, the stream of pure carrier gas is replaced suddenly, at given starting time, by a stream of gas containing diluted sample vapor. If the vapor is

diluted enough the behavior of each component can again be considered to be independent. At the column exit the composition of the eluted gas changes by successive steps, until the composition of the eluate is the same as that of the mixture entering the column. It can be shown that, within the framework of linear chromatography, the signal recorded is proportional to the integral of the signal obtained in elution chromatography. The advantage of this method over elution chromatography is the larger signal. The drawbacks are the requirement of a very much larger volume of sample, the difficulties in vaporizing it and preparing a mixture of constant composition, and difficulties in handling the data with the conventional methods using a strip chart recorder and a digital integrator. The sampling problems remain quite cumbersome, so the method finds use only in the determination of equilibrium isotherms; in this case, the requirement that the sample be dilute, which is necessary in analytical applications, in order to work in linear chromatography no longer applies.

3. Displacement Chromatography

In *displacement chromatography* an amount of sample, more-or-less dilute, is introduced into the column and the carrier gas stream is immediately replaced by a stream of a mixture of this gas and of a vapor which interacts with the stationary phase more strongly than any component of the mixture. This vapor pushes the sample in front of it and each component of this sample displaces the components which interact less strongly than itself with the stationary phase. At the column exit, the successive elution of the bands of the mixture components takes place. These bands closely follow each other, with some interference between each neighbor. For proper displacement behavior, a relatively large concentration of sample is required. For these reasons, the method is more suited to preparative applications than to analytical ones. Furthermore, regeneration of the column, with elimination of the displacement agent, is required before a second run can be made. This may need time.

As the present book deals only with analyses carried out by gas chromatography, we do not discuss further the problems of frontal analysis or displacement chromatography, nor those of preparative chromatography.

V. THE CHROMATOGRAPHIC PROCESS

There are three different approaches to account for the chromatographic process: (i) the stochastic method which uses probabilities to describe the behavior of the molecules of a compound during their elution and is best illustrated by the random walk model (see Chapter 4), (ii) the use of mass-balance equations, the classical method of chemical engineering (see Chapter 5), (iii) the analogy with the Craig machine, which is a cascade of liquid–liquid extractors.

Each of these approaches is best suited to a different purpose. The analogy to the Craig machine, although it is somewhat arbitrary, illustrates very well some of the basic concepts of chromatography. The random walk approach permits an excellent,

References on p. 33.

although somewhat elementary, discussion of the influence of the resistance to mass-transfer on band broadening. The analytical solution of the set of mass-balance equations is not possible in cases which are of real practical interest, so the method can give only the necessary numerical solutions, but does not supply the concepts or images which are required to understand the chromatographic processes.

In this section, we give an outline of the Craig machine, in order to illustrate the basic concepts of chromatography (5–11). We do not give a detailed presentation of its theory, however, as it does not really apply to chromatography and does not readily extend to it.

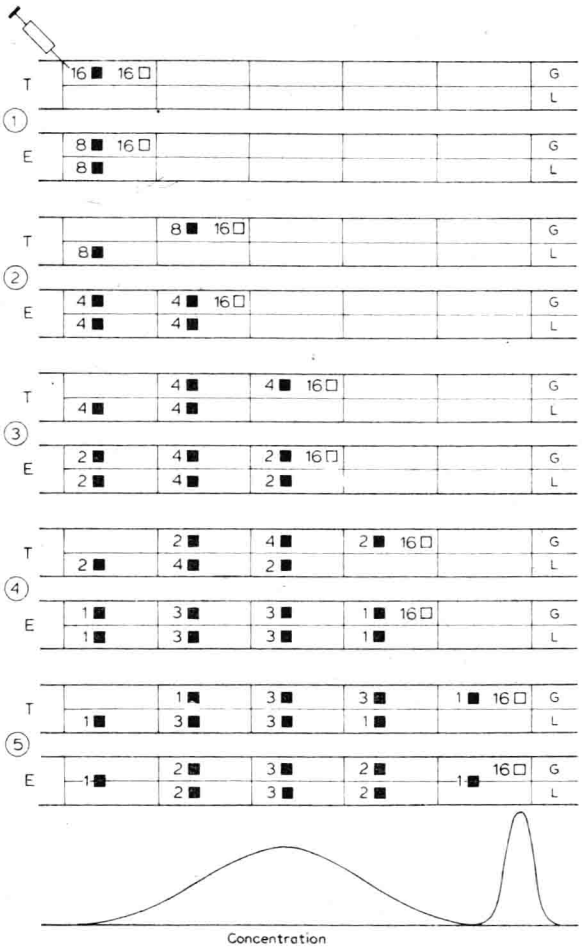

Figure 1.2. Schematic of the chromatographic process, considered as an automatic Craig machine. Succession of transfer steps (T) and equilibrium steps (E).
G denotes the gas phase, L the stationary phase in a chromatographic column.
The lower curve gives the concentration profiles of the two compounds in the Craig machine.

Let us divide the column into a series of short reactors, each of unit volume. In each of these reactors, equilibrium of the sample composition between the two phases takes place. The continuous chromatographic process is thus replaced by a succession of a number of two-step processes. In the first step, a volume of gas is transferred from each reactor to the next one; the first reactor is filled with pure carrier gas. In the second step, the reactors are left still, so that equilibrium can be reached in each of the reactors. The sequence is repeated a sufficient number of times to permit elution of all sample components.

Although we somewhat arbitrarily introduced a discontinuity in the process, this model correctly identifies the two basic phenomena which underlie chromatography: downstream transfer by the mobile phase and equilibrium between the two phases.

If we assume, for example, that we have (cf Figure 1.2) 32 molecules in a sample of a mixture, 16 black ones and 16 white ones, with partition coefficients 0.5 and 0.0 respectively, a very crude assumption indeed, the process takes place as follows (cf Figure 1.2).

First step

During the *first transfer*, the 32 molecules are introduced into the first reactor.

During the *first equilibrium,* the white molecules are not soluble in the liquid stationary phase. They all stay in the gas phase, while the black molecules partition between the two phases, and at equilibrium there are 8 black molecules in the gas phase, 8 in the stationary phase.

Second step

Second transfer: The gas phase of the first reactor is transferred to the second one, with the 16 white molecules and the 8 black ones it contains. The other 8 black molecules stay in the stationary phase of the first reactor. The proper volume of pure carrier gas is introduced into this reactor.

Second equilibrium: In the first reactor there remain no white molecules. The black ones equilibrate between the two phases, 4 molecules on average are in the gas and 4 in the stationary phase. In the second reactor the 16 white molecules remain in the gas phase, while the 8 black ones partition between the two phases. At equilibrium there are 4 black molecules in the gas phase and 4 in the stationary phase.

Third step

Third transfer: The gas phase of the second reactor is transferred to a third one with the 16 white and 4 black molecules it contains, the gas of the first reactor is transferred to the second one with the 4 black molecules it contains, and the first reactor is filled with pure carrier gas.

References on p. 33.

Third equilibrium: In the first and second reactors there are no white molecules. They are all in the third one, where they stay in the gas phase since they are not soluble in the liquid phase. The first reactor contains 4 black molecules and at equilibrium there are 2 in each phase. The second reactor is already at equilibrium, with 4 black molecules in each phase. The third reactor also contains 4 molecules, 2 in each phase.

Fourth step

Fourth transfer: The gas phase of the third reactor is transferred to a fourth one, with the 16 white molecules and the 2 black ones it contains. The gas phase of the second reactor is transferred to the third one, with its 4 black molecules and the gas phase of the first reactor is transferred to the second reactor with the 2 black molecules it contains. The first reactor is filled with pure carrier gas.

Fourth equilibrium: Only the fourth reactor contains the non-soluble white molecules. The black molecules are now distributed between the four reactors as follows: 2 in the first one (1 in each phase), 6 in both the second and third reactors (3 in each phase, in each reactor), and 2 in the fourth reactor (1 in each phase).

A distribution curve of the two compounds is given in Figure 1.2. The progressive dilution of the retained compounds, their separation when their distribution coefficients are different and the shape of their distribution among the different reactors now appear clearly. Their profile is given by the binomial distribution (5). When the number of reactors is large this distribution tends towards the Gaussian law.

Assuming a large number of reactors and a Gaussian distribution, it is possible to relate the number of reactors to the properties of the profile. This number is given by the classical relationship:

$$N = 16\left(\frac{t_R}{w}\right)^2 \tag{1}$$

where t_R is the time of the maximum of the distribution and w its base width. By analogy to distillation columns and other systems where continuous separation processes take place, this number has been called the number of equilibrium stages or, more classically, the number of theoretical plates.

VI. DIRECT CHROMATOGRAPHIC DATA

From the data recorded during a chromatographic analysis, five parameters can be measured for each peak, assuming it is well enough resolved from its neighbors (cf Figure 1.3). From these parameters, which vary a great deal when experimental conditions are changed, a number of more fundamental data can be calculated (cf next section).