chapter**TWENTY-SEVEN**

Gas Chromatography

In **gas chromatography,** the components of a vaporized sample are separated as a result of differential distribution between a mobile gaseous phase and a liquid or a solid stationary phase held in a column. In performing a gas chromatographic separation, the sample is vaporized and injected onto the head of a chromatographic column. Elution is brought about by the flow of an inert gaseous mobile phase. In contrast to most other types of chromatography, the mobile phase does not interact with molecules of the analyte; its only function is to transport the analyte through the column.

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There are two types of gas chromatography: *gas-liquid chromatography* (GLC) and *gas-solid chromatography* (GSC). GLC is used throughout all fields of science; its name is usually shortened to *gas chromatography* (GC).[1] GSC is based on a solid stationary phase in which retention of analytes occurs because of physical adsorption. The application of GSC is limited because of semipermanent retention of active or polar molecules and severe tailing of elution peaks. Tailing is a result of the nonlinear nature of the adsorption process. Thus, this technique is not widely used except for the separation of certain low-molecular-mass gaseous species; we discuss the method briefly in Section 27F.

In GLC the analyte is partitioned between a gaseous mobile phase and a liquid phase immobilized on the surface of an inert solid packing or on the walls of a capillary tubing. The concept of GLC was first suggested in 1941 by Martin and Synge, who were also responsible for the development of liquid-liquid partition chromatography. More than a decade was to elapse, however, before the value of GLC was demonstrated experimentally[2] and this technique began to be used as a routine laboratory tool. In 1955 the first commercial apparatus for GLC appeared on the market. Since that time, the growth in applications of this technique has been phenomenal. Currently, nearly a million gas chromatographs are in use throughout the world.

27A PRINCIPLES OF GLC

The general principles of chromatography, which were developed in Chapter 26, and the mathematical relationships summarized in Section 26E are applicable to GC with only minor modifications that arise from the compressibility of gaseous mobile phases.

[1]For detailed treatment of GC, see C. Poole, ed., *Gas Chromatography*, Amsterdam: Elsevier, 2012; H. M. McNair and J. M. Miller, *Basic Gas Chromatography*, 2nd ed., Hoboken, NJ: Wiley, 2009; R. L. Grob and E. F. Barry, eds., *Modern Practice of Gas Chromatography*, 4th ed., New York: Wiley-Interscience, 2004; R. P. W. Scott, *Introduction to Analytical Gas Chromatography*, 2nd ed., New York: Marcel Dekker, 1997; W. Jennings, E. Mittlefehldt, and P. Stremple, *Analytical Gas Chromatography*, 2nd ed., Orlando, FL: Academic Press, 1997.

[2]A. T. James and A. J. P. Martin, *Analyst*, **1952**, *77*, 915–932, **DOI**: 10.1039/AN9527700915.

27A-1 Retention Volumes

To take into account the effects of pressure and temperature in GC, it is often useful to use retention volumes rather than the retention times that were discussed in Section 26B. The relationship between the two is given in Equations 27-1 and 27-2

$$V_R = t_R F \tag{27-1}$$

$$V_M = t_M F \tag{27-2}$$

where F is the average volumetric flow rate within the column; V and t are retention volumes and times, respectively; and the subscripts R and M refer to species that are retained and not retained on the column. The flow rate within the column is not directly measurable. Instead, the rate of gas flow as it exits the column is determined experimentally with a flow meter, which is discussed in Section 27B. For popular soap-bubble-type flow meters, where the gas is saturated with water, the average flow rate F is related to the measured flow rate F_m by

$$F = F_m \times \frac{T_c}{T} \times \frac{(P - P_{H_2O})}{P} \tag{27-3}$$

where T_c is the column temperature in kelvins, T is the temperature at the flow meter, and P is the gas pressure at the end of the column. Usually P and T are the ambient pressure and temperature. The term involving the vapor pressure of water, P_{H_2O}, is a correction for the pressure used when the gas is saturated with water.

Both V_R and V_M depend on the average pressure within the column—a quantity that lies intermediate between the inlet pressure P_i and the outlet pressure P (atmospheric pressure). The *pressure drop correction factor* j, also known as the *compressibility factor*, accounts for the pressure within the column being a nonlinear function of the P_i/P ratio. Corrected retention volumes V_R^0 and V_M^0, which correspond to volumes at the average column pressure, are obtained from the relationships

$$V_R^0 = jt_R F \quad \text{and} \quad V_M^0 = jt_M F \tag{27-4}$$

where j can be calculated from the relationship

$$j = \frac{3[(P_i/P)^2 - 1]}{2[(P_i/P)^3 - 1]} \tag{27-5}$$

The *specific retention volume* V_g is then defined as

$$V_g = \frac{V_R^0 - V_M^0}{m_S} \times \frac{273}{T_c} = \frac{jF(t_R - t_M)}{m_S} \times \frac{273}{T_c} \tag{27-6}$$

where m_S is the mass of the stationary phase, a quantity determined at the time of column preparation.

27A-2 Relationship between V_g and K

The specific retention volume V_g can be related to the distribution constant K_c. To do so, we substitute the expression relating t_R and t_M to k (Equation 26-12) into Equation 27-6, which gives

$$V_g = \frac{jFt_M k}{m_S} \times \frac{273}{T_c}$$

Combining this expression with Equation 27-4 yields

$$V_g = \frac{V_M^0 k}{m_S} \times \frac{273}{T_c}$$

Substituting Equation 26-9 for k gives (here, V_M^0 and V_M are identical)

$$V_g = \frac{KV_S}{m_S} \times \frac{273}{T_c}$$

The density of the liquid on the stationary phase ρ_S is given by

$$\rho_S = \frac{m_S}{V_S}$$

where V_S is the stationary-phase volume. Thus,

$$V_g = \frac{K}{\rho_S} \times \frac{273}{T_c} \tag{27-7}$$

Note that V_g at a given temperature depends only on the distribution constant of the solute and the density of the liquid making up the stationary phase.

27A-3 Effect of Mobile-Phase Flow Rate

Equation 26-23 and the relationships shown in Table 26-3 are fully applicable to GC. The longitudinal diffusion term (B/u) is more important in GLC, however, than in other chromatographic processes because of the much larger diffusion rates in gases (10^4-10^5 times greater than liquids). As a result, the minima in curves relating plate height H to flow rate (van Deemter plots) are usually considerably broadened in GC (see Figure 26-8).

27B INSTRUMENTS FOR GLC

Many changes and improvements in gas chromatographic instruments have appeared in the marketplace since their commercial introduction. In the 1970s, electronic integrators and computer-based data-processing equipment became common. The 1980s saw computers being used for automatic control of most instrument variables, such as column temperature, flow rates, and sample injection. In addition, very high-performance instruments became available at moderate costs, and perhaps most important, open tubular columns were developed capable of separating components of complex mixtures in relatively short times. Today, more than 50 instrument manufacturers offer several hundred different models of gas chromatographic equipment at costs that vary from about $1000 to more than $50,000.

The basic components of a typical instrument for performing GC are shown in Figure 27-1. A description of each component follows.

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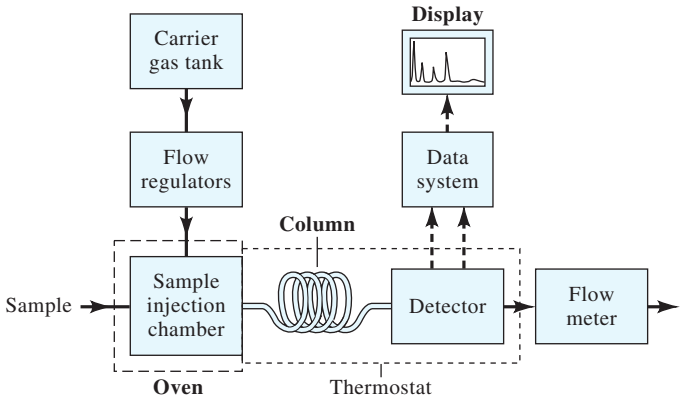


FIGURE 27-1 Block diagram of a typical gas chromatograph.

27B-1 Carrier Gas System

The mobile-phase gas in GC is called the *carrier gas* and must be chemically inert. Helium is the most common mobile-phase gas used, although argon, nitrogen, and hydrogen are also used. These gases are available in pressurized tanks. Pressure regulators, gauges, and flow meters are required to control the flow rate of the gas. In addition, the carrier gas system often contains a molecular sieve to remove impurities and water.

Flow rates are normally controlled by a two-stage pressure regulator at the gas cylinder and some sort of pressure regulator or flow regulator mounted in the chromatograph. Inlet pressures usually range from 10 to 50 psi (lb/in.^{2}) above room pressure, which lead to flow rates of 25 to 150 mL/min with packed columns and 1 to 25 mL/min for open tubular capillary columns. Generally, it is assumed that flow rates are constant if the inlet pressure remains constant. Flow rates can be established by a rotometer at the column head; this device, however, is not as accurate as the simple soap-bubble meter shown in Figure 27-2. Usually, the flow meter is located at the end of the column as shown in Figure 27-1. A soap film is formed in the path of the gas when a rubber bulb containing an aqueous solution of soap or detergent is squeezed; the time required for this film to move between two graduations on the buret is measured and converted to volumetric flow rate (see Figure 27-2). Note that volumetric flow rates and linear flow velocities are related by Equation 26-6 or 26-7. Most modern computer-controlled gas chromatographs are equipped with electronic flow meters that can be regulated to maintain the flow rate at the desired level.

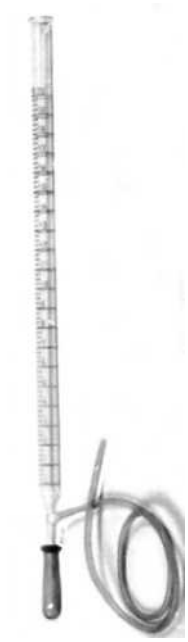


FIGURE 27-2 A soap-bubble flow meter. (Courtesy Agilent Technologies.)

27B-2 Sample Injection Systems

To achieve high column efficiency, the sample must be of a suitable size and introduced as a "plug" of vapor; slow injection or oversize samples cause band spreading and poor resolution. Calibrated microsyringes, such as those shown in Figure 27-3, are often used to inject liquid samples through a rubber or silicone diaphragm, or septum, into a heated sample port located at the head of the column. The sample port (Figure 27-4) is ordinarily about 50°C above the boiling point of the least volatile component of the sample. For ordinary packed analytical columns, sample sizes range from a few tenths of a microliter to 20 μL. Capillary columns require samples that are smaller by a factor of 100 or more. With these columns, a *sample splitter* is often needed to deliver a small known fraction (1:50 to 1:500) of the injected sample, with the remainder going to waste. Commercial gas chromatographs intended for use with capillary columns incorporate such splitters, and they also allow for *splitless injection* to improve sensitivity or for use with packed columns. With splitless inlets, the purge valve closes at injection and stays closed for 30–60 seconds. During this time the sample vapor can go

FIGURE 27-3 A set of microsyringes for sample injection. (Courtesy Hamilton Company.)

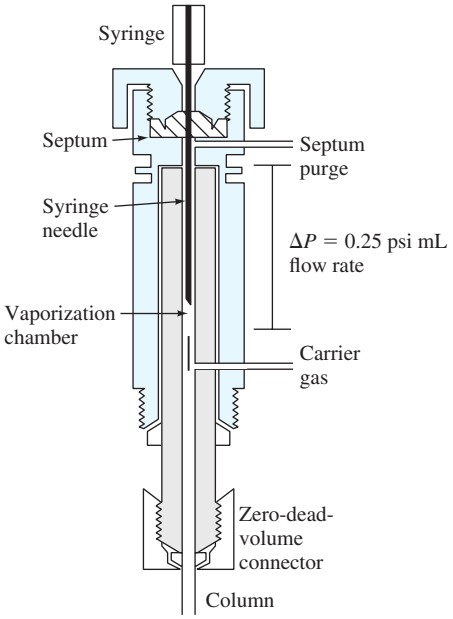


FIGURE 27-4 Cross-sectional view of a microflash vaporizer direct injector.

only onto the column. When the purge valve opens, any remaining vapor is rapidly vented. *On-column inlets* are also available for capillary GC. With this type of inlet, the entire sample is injected onto the column as a liquid, which is later vaporized by temperature programming of the column or inlet. With on-column inlets, the analyte is separated from the solvent by thermal and solvent effects.[3]

For the most reproducible sample injection, newer gas chromatographs use autoinjectors and autosamplers, such as the system shown in Figure 27-5. With such autoinjectors, syringes are filled, and the sample injected into the chromatograph auto-

[3]N. H. Snow, in *Modern Practice of Gas Chromatography*, R. L. Grob and E. F. Barry, eds., 4th ed., Chap. 9, New York: Wiley-Interscience, 2004.

FIGURE 27-5 An autoinjection system with autosampler for gas chromatography. (Shimadzu Corp.)

matically. In the autosampler, samples are contained in vials on a sample turntable. The autoinjector syringe picks up the sample through a septum on the vial and injects the sample through a septum on the chromatograph. With the unit shown, up to 150 sample vials can be placed on the turntable. Injection volumes can vary from 0.1 μL with a 10-μL syringe to 200 μL with a 200-μL syringe. The reproducibility of autoinjection systems is quite good with standard deviations of replicate samples often as low as 0.3%.

For introducing gases, a sample valve, such as that shown in Figure 27-6, is often used instead of a syringe. With such devices, sample sizes can be reproduced to better than 0.5% relative. Liquid samples can also be introduced through a sampling valve. Solid samples are introduced as solutions or alternatively are sealed into thin-walled vials that can be inserted at the head of the column and punctured or crushed from the outside.

27B-3 Column Configurations and Column Ovens

Two general types of columns are used in GC, *packed columns* and *capillary columns*. In the past, the vast majority of gas chromatographic analyses used packed columns. For most current applications, packed columns have been replaced by the more efficient capillary columns.

Chromatographic columns vary in length from less than 2 to 60 m or more. They are constructed of stainless steel, glass, fused silica, or Teflon. In order to fit into an oven for thermostatting, they are usually formed as coils having diameters of 10–30 cm (see Figure 27-7). A detailed discussion of columns, column packings, and stationary phases is found in Section 27C.

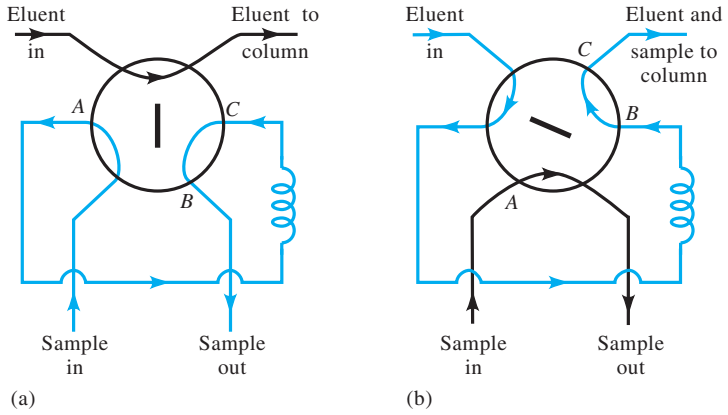


FIGURE 27-6 A rotary sample valve: valve position (a) is for filling the sample loop *ACB*; position (b) is for introduction of sample into column.

FIGURE 27-7 Fused-silica capillary columns. (Courtesy of Restek Corp., Bellefonte, PA.)

Column temperature is an important variable that must be controlled to a few tenths of a degree for precise work. Thus, the column is ordinarily housed in a thermostatted oven. The optimal column temperature depends on the boiling point of the sample and the degree of separation required. Roughly, a temperature equal to or slightly above the average boiling point of a sample results in a reasonable elution time (2 to 30 min). For samples with a broad boiling range, it is often desirable to take advantage of *temperature programming*, in which the column temperature is increased either continuously or in steps as the separation proceeds. Figure 27-8 shows the improvement in a chromatogram brought about by temperature programming.

In general, optimal resolution is associated with minimal temperature; the cost of lowered temperature, however, is an increase in elution time and therefore the time required to complete an analysis. Figures 27-8a and 27-8b illustrate this principle.

Analytes of limited volatility can sometimes be determined by forming derivatives that are more volatile. Likewise, derivatization is sometimes used to enhance detection or chromatographic performance.

27B-4 Gas Chromatographic Detectors

Dozens of detectors have been investigated and used with gas chromatographic separations.[4] We first describe the characteristics that are most desirable in a gas chromatographic detector and then discuss the most widely used devices. In some cases, gas chromatographs are coupled to spectroscopic instruments such as mass and infrared spectrometers. With such systems, the spectral device not only detects the appearance of the analytes as they elute from the column but also helps to identify them.

Characteristics of the Ideal Detector

The ideal detector for GC has the following characteristics:

1. Adequate sensitivity. Just what constitutes adequate sensitivity cannot be described in quantitative terms. For example, the sensitivities of the detectors described in this section vary by a factor of 10^7. Yet all are widely used and are adequate for certain tasks; the least sensitive are not, however, satisfactory for certain applications. In general, the sensitivities of present-day detectors lie in the range of 10^{-8} to 10^{-15} g solute/s.

[4]See L. A. Colon and L. J. Baird, in *Modern Practice of Gas Chromatography*, R. L. Grob and E. F. Barry, eds., 4th ed., Chap. 6, New York: Wiley-Interscience, 2004.

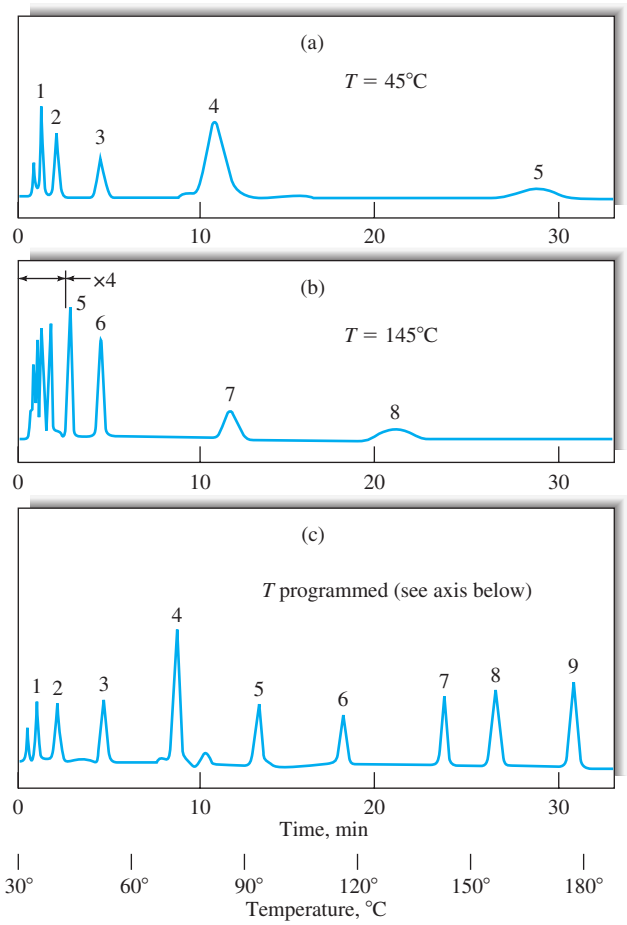


FIGURE 27-8 Effect of temperature on gas chromatograms: (a) isothermal at 45°C, (b) isothermal at 145°C, and (c) programmed at 30–180°C. (From W. E. Harris and H. W. Habgood, *Programmed Temperature Gas Chromatography*, New York: Wiley, 1966, p. 10. Reprinted with permission.)

2. Good stability and reproducibility.
3. A linear response to solutes that extends over several orders of magnitude.
4. A temperature range from room temperature to at least 400°C.
5. A short response time independent of flow rate.
6. High reliability and ease of use. The detector should be foolproof in the hands of inexperienced operators, if possible.
7. Similarity in response toward all solutes or alternatively a highly predictable and selective response toward one or more classes of solutes.
8. The detector should be nondestructive.

Needless to say, no detector exhibits all of these characteristics. Some of the most common detectors are listed in Table 27-1. Several of the most widely used detectors are described in the paragraphs that follow.

Flame Ionization Detectors

The flame ionization detector (FID) is the most widely used and generally applicable detector for GC. With an FID such as the one shown in Figure 27-9, effluent from the column is directed into a small air-hydrogen flame. Most organic compounds produce ions and electrons when pyrolyzed at the temperature of an air-hydrogen flame. Detection involves monitoring the current produced by collecting these charge carriers. A potential difference of a few hundred volts applied between the burner tip and a collector electrode located above the flame causes the ions and electrons to move toward the collector. The resulting current ($\sim 10^{-12}$ A) is then measured with a sensitive picoammeter.

The ionization of carbon compounds in the FID is not fully understood, although the number of ions produced is roughly

TABLE 27-1 Typical Gas Chromatographic Detectors

Type	Applicable Samples	Typical Detection Limit
Flame ionization	Hydrocarbons	1 pg/s
Thermal conductivity	Universal detector	500 pg/mL
Electron capture	Halogenated compounds	5 fg/s
Mass spectrometer (MS)	Tunable for any species	0.25–100 pg
Thermionic	Nitrogen and phosphorous compounds	0.1 pg/s (P), 1 pg/s (N)
Electrolytic conductivity (Hall)	Compounds containing halogens, sulfur, or nitrogen	0.5 pg Cl/s, 2 pg S/s, 4 pg N/s
Photoionization	Compounds ionized by UV radiation	2 pg C/s
Fourier transform IR (FTIR)	Organic compounds	0.2–40 ng

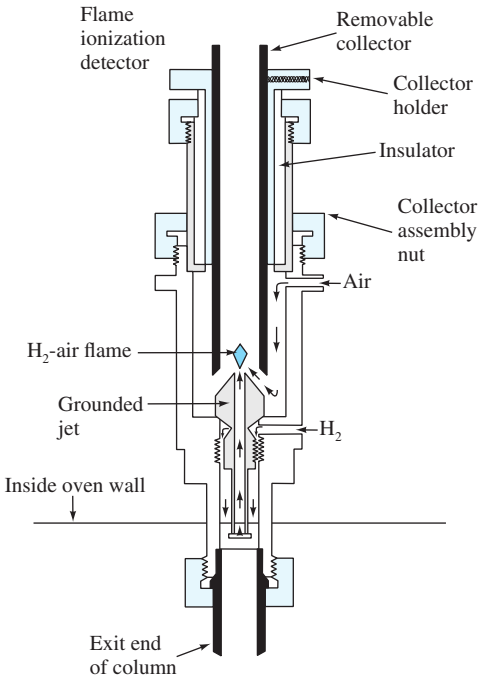


FIGURE 27-9 A typical flame ionization detector. (Courtesy of Agilent Technologies.)

proportional to the number of *reduced* carbon atoms in the flame. Because the FID responds to the number of carbon atoms entering the detector per unit of time, it is a *mass-sensitive* rather than a *concentration-sensitive* device. As such, this detector has the advantage that changes in flow rate of the mobile phase have little effect on detector response.

Functional groups, such as carbonyl, alcohol, halogen, and amine, yield fewer ions or none at all in a flame. In addition, the detector is insensitive toward noncombustible gases such as H_2O, CO_2, SO_2, CO, noble gases, and NO_x. These properties make the FID a most useful general detector for the analysis of most organic samples, including those contaminated with water and the oxides of nitrogen and sulfur.

The FID exhibits a high sensitivity ($\sim 10^{-13}$ g/s), large linear response range ($\sim 10^7$), and low noise. It is generally rugged and easy to use. Disadvantages of the FID are that it destroys the sample during the combustion step and requires additional gases and controllers.

Thermal Conductivity Detectors

The *thermal conductivity detector* (TCD), which was one of the earliest detectors for GC, is still widely used. This device contains an electrically heated source whose temperature at constant electrical power depends on the thermal conductivity of the surrounding gas. The heated element may be a fine platinum, gold, or tungsten wire or, alternatively, a small thermistor. The electrical resistance of this element depends on the thermal conductivity of the gas. Figure 27-10a shows a cross-sectional view of one of the temperature-sensitive elements in a TCD.

Twin detectors are usually used, one being located ahead of the sample-injection chamber and the other immediately beyond the column. The detector elements are labeled *sample* and *reference* in Figure 27-10b. Alternatively, the gas stream can be split. The detectors are incorporated in two arms of a bridge circuit. The bridge circuit is arranged so that the thermal conductivity of the carrier gas is canceled. In addition, the effects of variations in temperature, pressure, and electrical power are minimized.

Modulated single-filament TCDs are also available. Here, the analytical and reference gases are passed alternately over a tiny filament held in a low-volume (~5-μL) cell. The gases are switched at a frequency of 10 Hz. The output is thus a 10-Hz signal whose amplitude is proportional to the difference in thermal conductivity of the analytical and reference gases. Because the amplifier responds only to a 10-Hz signal, thermal noise in the system is largely eliminated.

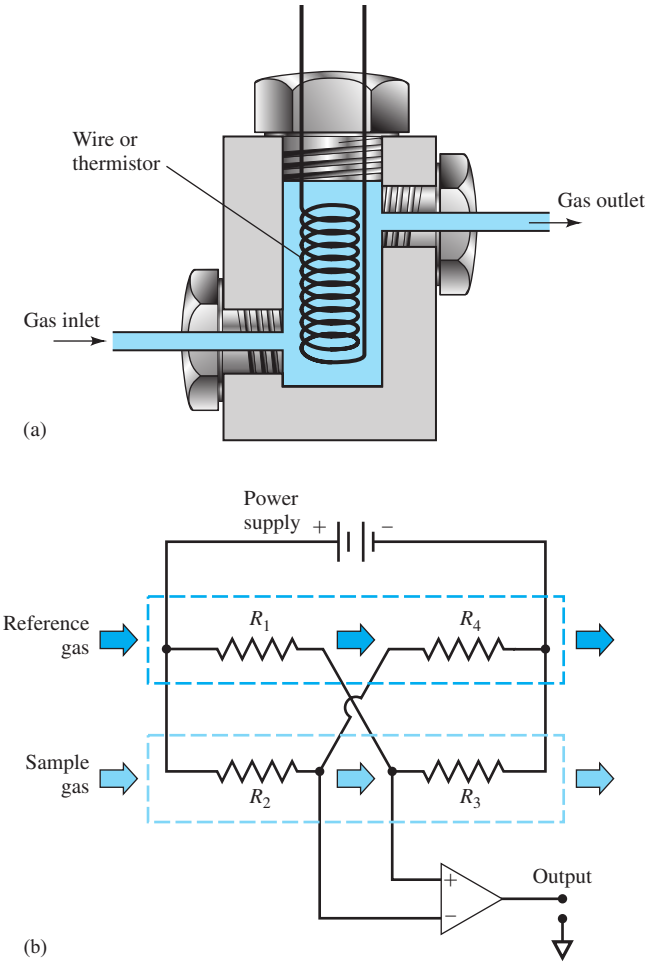


FIGURE 27-10 Schematic of (a) a thermal conductivity detector cell and (b) an arrangement of two sample detector cells (R_2 and R_3) and two reference detector cells (R_1 and R_4). (Adapted from F. Rastrelloa, P. Placidi, A. Scorzonia, E. Cozzanib, M. Messinab, I. Elmib, S. Zampollib, and G. C. Cardinali, *Sensors and Actuators A*, **2012,** *178*, 49, **DOI:** 10.1016/j.sna.2012.02.008.)

The thermal conductivities of helium and hydrogen are roughly six to ten times greater than those of most organic compounds. Thus, even small amounts of organic species cause relatively large decreases in the thermal conductivity of the column effluent, which results in a marked rise in the temperature of the detector. Detection by thermal conductivity is less satisfactory with carrier gases whose conductivities closely resemble those of most sample components.

The advantages of the TCD are its simplicity, its large linear dynamic range ($\sim 10^5$), its general response to both organic and inorganic species, and its nondestructive character, which permits collection of solutes after detection. Its chief limitation is its relatively low sensitivity ($\sim 10^{-8}$ g solute/mL carrier gas). Other detectors exceed this sensitivity by factors of 10^4 to 10^7. It should be noted that the low sensitivity of TCDs often precludes their use with capillary columns where sample amounts are very small.

Electron-Capture Detectors

The electron-capture detector (ECD) has become one of the most widely used detectors for environmental samples because it selectively responds to halogen-containing organic compounds, such as pesticides and polychlorinated biphenyls. As shown in Figure 27-11, the sample eluate from a column is passed over a radioactive β emitter, usually nickel-63. An electron from the emitter causes ionization of the carrier gas (often nitrogen) and the production of a burst of electrons. In the absence of organic species, a constant standing current between a pair of electrodes results from this ionization process. The current decreases significantly, however, in the presence of organic molecules containing electronegative functional groups that tend to capture electrons.

The ECD is selective in its response. Compounds such as halogens, peroxides, quinones, and nitro groups are detected with high sensitivity. The detector is insensitive to functional groups such as amines, alcohols, and hydrocarbons. An important application of the ECD is for the detection and quantitative determination of chlorinated insecticides.

ECDs are highly sensitive and have the advantage of not altering the sample significantly (in contrast to the FID, which consumes the sample). The linear response of the detector, however, is limited to about two orders of magnitude.

Thermionic Detectors

The thermionic detector is selective toward organic compounds containing phosphorus and nitrogen. Its response to a phosphorus atom is approximately 10 times greater than to a nitrogen atom and 10^4 to 10^6 times larger than to a carbon atom. Compared with the FID, the thermionic detector is approximately 500 times more sensitive to phosphorus-containing compounds and 50 times more sensitive to nitrogen-bearing species. These properties make thermionic detection particularly useful for sensing and determining the many phosphorus-containing pesticides.

A thermionic detector is similar in structure to the FID shown in Figure 27-9. The column effluent is mixed with hydrogen, passes through the flame tip assembly, and is ignited. The hot gas then flows around an electrically heated rubidium silicate bead, which is maintained at about 180 V with respect to the collector. The heated bead forms a plasma having a temperature of 600–800°C. Exactly what occurs in the plasma to produce unusually large numbers of ions from phosphorus- or nitrogen-containing molecules is not fully understood; but large ion currents result, which are useful for determining compounds containing these two elements.

Electrolytic Conductivity Detectors

In the Hall electrolytic conductivity detector, compounds containing halogens, sulfur, or nitrogen are mixed with a reaction gas in a small reactor tube, usually made of nickel. The reaction tube is kept at 850–1000°C. The products are then dissolved in a liquid, which produces a conductive solution. The

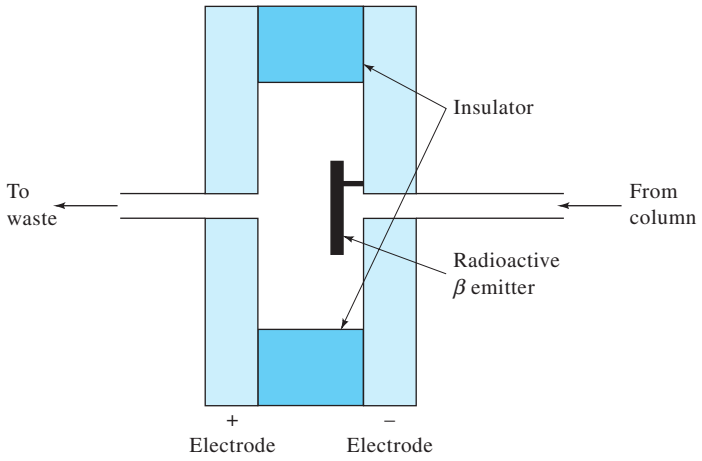


FIGURE 27-11 Schematic diagram of an ECD.

change in conductivity as a result of the ionic species in the conductance cell is then measured. A typical detector is illustrated in Figure 27-12.

In the halogen mode, hydrogen is used as the reaction gas. Halogen-containing compounds are converted to HX and dissolved in *n*-propyl alcohol as the conductivity solvent. In this mode, sulfur-containing compounds are converted to H_2S and nitrogen-containing compounds to NH_3, which do not give significant responses because both are poorly ionized in the solvent. The limit of detection is ~0.5 pg Cl/s, and the linear range is 10^6.

In the sulfur mode, the reaction gas is air, which converts the sulfur-containing compounds to SO_2. The conductivity solvent is methyl alcohol with a small amount of water. The SO_2 in the presence of water is converted to sulfite and sulfate ions. Nitrogen-containing compounds are converted to N_2 and nitrogen oxides and show little or no response. Halogen-containing compounds are converted to HX and must be removed with a postreaction scrubber prior to detection. In the sulfur mode, approximately 2 pg S/s can be detected with a linear range of three orders of magnitude.

In the nitrogen mode, hydrogen is used as the reaction gas, as in the halogen mode. However, here, water containing a small amount of an organic solvent is used as the conductivity solvent. In this solvent, the NH_3 produced is converted to NH_4^+. The HX and H_2S produced from halogen- and sulfur-containing compounds must be removed with a postreaction scrubber. The limit of detection is ~4 pg N/s with a linear range of three orders of magnitude.

Dry electrolytic conductivity detectors are also available. These differ from the conventional detectors in that they do not use a solvent but instead detect the product ions in the gas phase. The dry detector is responsive to chlorine- and bromine-containing compounds. It can be used in series with an FID.

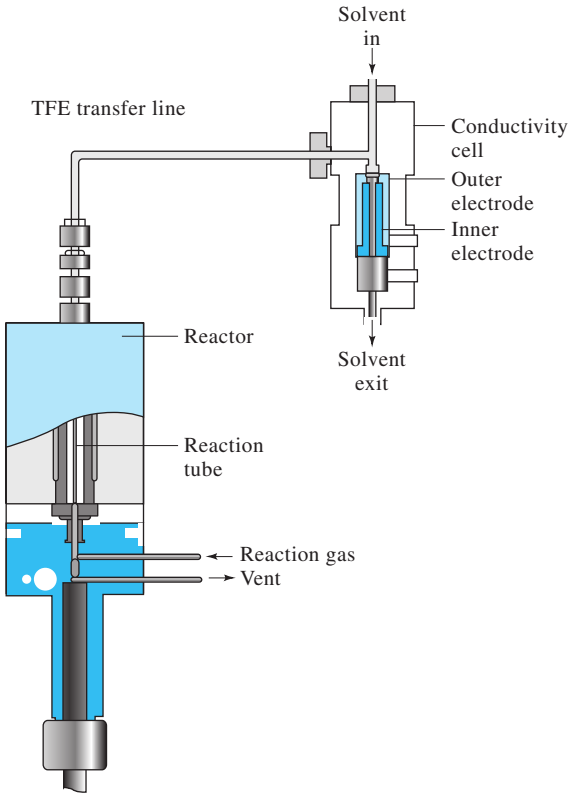


FIGURE 27-12 Diagram of a Hall electrolytic conductivity detector. (Courtesy of ThermoElectron Corp.)

Photoionization Detector

In the photoionization detector, molecules eluting from the GC column are photoionized by ultraviolet radiation from a 10.2 eV hydrogen or a 11.7 eV argon lamp. This source ionizes species with an ionization potential below the lamp energy. Compounds with a higher ionization potential do not absorb the energy and thus are not detected. The ions and electrons produced by photoionization are then collected at a pair of biased electrodes. The detector is most sensitive for aromatic hydrocarbons and organosulfur or organophosphorus compounds that are easily photoionized. The linear range is as high as seven orders of magnitude.

Atomic Emission Detectors

In the atomic emission detector (AED), the effluent from the GC column is introduced into a microwave-induced plasma (MIP), an inductively coupled plasma (ICP), or a direct current plasma (DCP). The MIP has been most widely used and is available commercially. The MIP is used in conjunction with a diode array or charge-coupled-device atomic emission spectrometer as shown in Figure 27-13. The plasma is sufficiently energetic to atomize all of the elements in a sample and to excite their characteristic atomic emission spectra. Hence, the AED is an *element-selective detector*. As shown on the right of the figure, the positionable diode array is capable of monitoring simultaneously several elements at any given setting.

Figure 27-14 illustrates the power of element-selective detection. The sample in this case consisted of a gasoline containing a small concentration of methyl tertiary butyl ether (MTBE), an antiknock agent, as well as several aliphatic alcohols in low concentrations. The upper chromatogram, obtained by monitoring the carbon emission line at 198 nm, consists of a myriad of peaks that would be very difficult to sort out and identify. In contrast, when the oxygen line at 777 nm is used to record the chromatogram (Figure 27-14b), peaks for the alcohols and for MTBE are evident and readily identifiable.

Flame Photometric Detector

The *flame photometric detector* (FPD) has been widely applied to the analysis of air and water pollutants, pesticides, and coal hydrogenation products. It is a selective detector that is primarily responsive to compounds containing sulfur and phosphorus. In this detector, the eluent is passed into a low-temperature hydrogen-air flame, which converts some of the phosphorus to

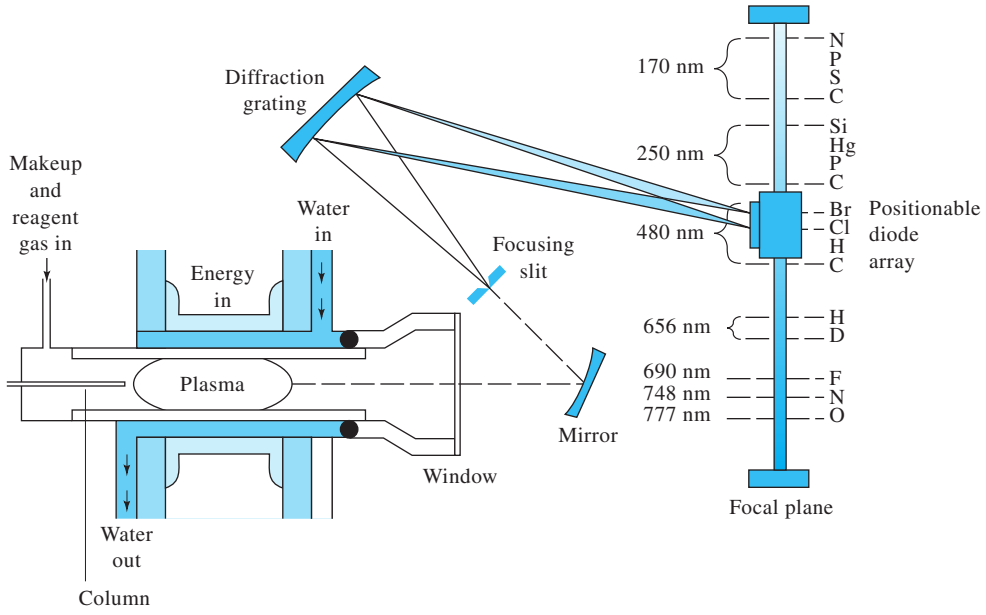


FIGURE 27-13 An AED for GC. (Courtesy of Agilent Technologies.)

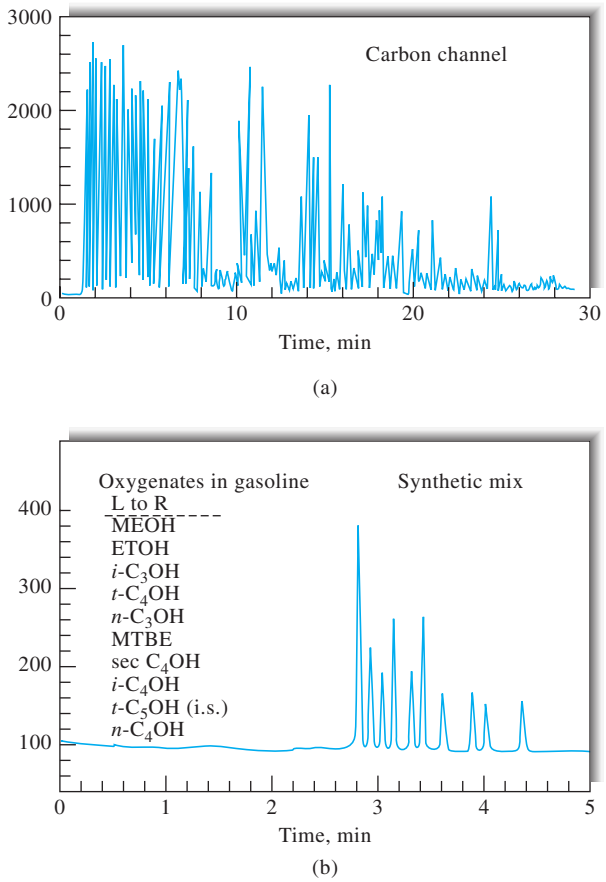


FIGURE 27-14 Chromatogram for a gasoline sample containing a small amount of MTBE and several aliphatic alcohols. (a) Monitoring a carbon emission line and (b) monitoring an oxygen emission line. (Courtesy of Agilent Technologies.)

an HPO species that emits bands of radiation centered at about 510 and 526 nm. Sulfur in the sample is simultaneously converted to S_2, which emits a band centered at 394 nm. However, the sulfur chemiluminescence detector discussed later in this section provides lower detection limits and wider linear working range than does the FPD. Suitable filters are used to isolate the appropriate bands, and their intensity is recorded photometrically. Other elements that have been detected by flame photometry include the halogens, nitrogen, and several metals, such as tin, chromium, selenium, and germanium.

Mass Spectrometry Detectors

One of the most powerful detectors for GC is the mass spectrometer. Mass spectrometers and applications of mass spectrometry are discussed in Chapters 11 and 20. The combination of GC with mass spectrometry is known as *GC/MS*.[5] As discussed in Chapter 11, a mass spectrometer measures the mass-to-charge ratio (m/z) of ions that have been produced from the sample. Most of the ions produced are singly charged ($z = 1$) so that mass spectrometrists often speak of measuring the mass of ions when mass-to-charge ratio is actually measured. Currently, nearly fifty instrument companies offer GC/MS equipment. The flow rate from capillary columns is generally low enough that the column output can be fed directly into the ionization chamber of the mass spectrometer. A schematic of a typical system is shown in Figure 27-15. Prior to the advent of capillary columns in GC,

[5]For additional information, see O. D. Sparkman, Z. E. Penton, and F. G. Kitson, *Gas Chromatography and Mass Spectrometry*, 2nd ed., Amsterdam: Elsevier, 2011; M. C. McMaster, *GC/MS: A Practical User's Guide*, 2nd ed., New York: Wiley, 2008.

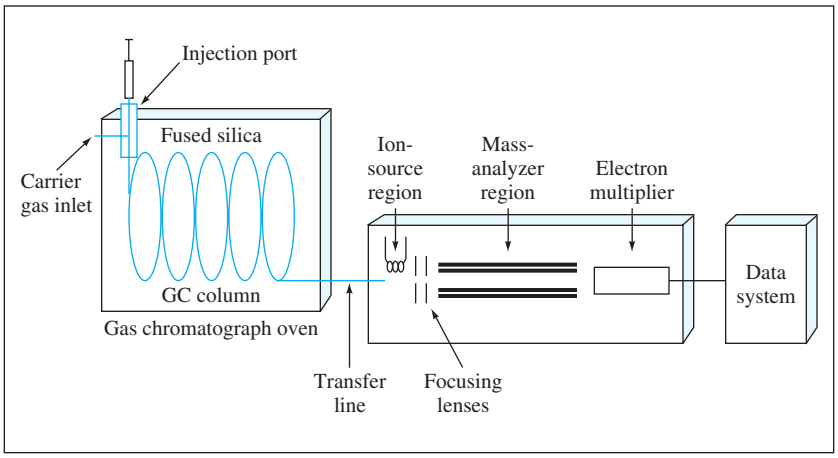


FIGURE 27-15 Schematic of a typical capillary GC/MS system. The effluent from the GC is passed into the inlet of the mass spectrometer, where the molecules in the gas are fragmented, ionized, analyzed, and detected.

when packed columns were used, it was necessary to minimize the large volumes of carrier gas eluting from the GC. Various jet, membrane, and effusion separators were used for this purpose. However, in many cases such devices also removed a significant amount of the analyte and were thus quite inefficient. Currently, capillary columns are invariably used in GC/MS instruments, and such separators are no longer needed.

Thermal degradation of components can be a difficulty in GC/MS. Not only can the GC injection port and GC column cause degradation but also the heated metal surfaces in the mass spectrometer ion source may cause problems. Lowering the temperature can minimize degradation. Often, however, the mass spectrometer can be used to identify decomposition products, which can lead to chromatographic modifications that solve the degradation problem.

The most common ion sources used in GC/MS are electron ionization and chemical ionization. Ion sources for mass spectrometry are discussed in detail in Section 20B. The most common mass analyzers are quadrupole and ion-trap analyzers. These analyzers are described in Sections 11B-2 and 20C-3. Time-of-flight mass analyzers are also used, but not as frequently as quadrupoles and ion traps.

In GC/MS, the mass spectrometer scans the masses repetitively during a chromatographic experiment. If the chromatographic run is 10 minutes, for example, and a scan is taken each second, 600 mass spectra are recorded. The data can be analyzed by the data system in several different ways. First, the ion abundances in each spectrum can be summed and plotted as a function of time to give a *total-ion chromatogram*. This plot is similar to a conventional chromatogram. One can also display the mass spectrum at a particular time during the chromatogram to identify the species eluting at that time. Finally, a single mass-to-charge (m/z) value can be selected and monitored throughout the chromatographic experiment, a technique known as *selected-ion monitoring*. Mass spectra of selected ions obtained during a chromatography experiment are known as *mass chromatograms*.

GC/MS instruments have been used for the identification of thousands of components that are present in natural and biological systems. For example, these procedures have permitted characterization of the odor and flavor components of foods, identification of water pollutants, medical diagnosis based on breath components, and studies of drug metabolites.

An example of one application of GC/MS is shown in Figure 27-16. The upper figure is the total-ion chromatogram of a five-component mixture. Also shown are mass chromatograms at $m/z = 74$ and $m/z = 93$. From these, the identities of components 1, 2, and 5 can be determined.

Mass spectrometry can also be used to obtain information about incompletely separated components. For example, the mass spectrum of the front edge of a GC peak may be different from that of the middle part of the peak or the trailing edge if the peak is due to more than one component. With mass spectrometry, we can not only determine that a peak is due to more than one species but also identify the various unresolved components. GC has also been coupled to tandem mass spectrometers or to Fourier transform mass spectrometers to give GC/MS/MS or GC/MS^n systems. These are extremely powerful tools for identifying components in mixtures.

GC Coupled with Spectroscopic Detection

GC is often coupled with the selective techniques of spectroscopy and electrochemistry to provide powerful tools for separating and identifying the components of complex mixtures. Combinations of GC with mass spectrometry (GC/MS), Fourier

Animation: Learn more about **GC/MS** at www.tinyurl.com/skoogpia7

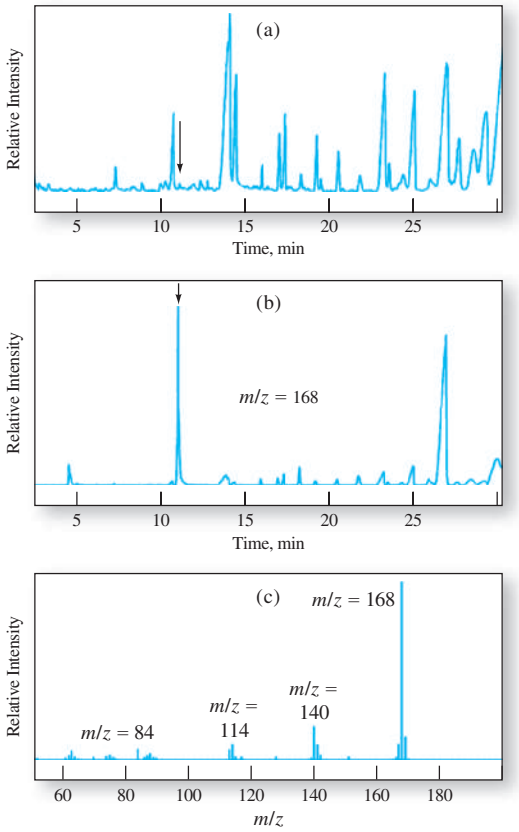


FIGURE 27-16 Typical outputs for a GC/MS system. In (a) the total ion chromatogram of an extract from a termite sample is shown. In (b) the ion at $m/z = 168$ was monitored during the chromatogram. In (c), the complete mass spectrum of the compound eluting at $t = 10.46$ minutes is presented, allowing it to be identified as β-carboline norharmane, an important alkaloid. (Adapted from S. Itakura, S. Kawabata, H. Tanaka, and A. Enoki, *J. Insect Sci.*, **2008**, *8*, 13.)

transform infrared spectroscopy (GC/FTIR), nuclear magnetic resonance spectroscopy, and electroanalytical methods are sometimes termed *hyphenated methods*.[6]

In early systems, the eluates from the GC column were collected as separate fractions in a cold trap, and a nondestructive, nonselective detector was used to indicate their appearance. The composition of each fraction was then investigated by nuclear magnetic resonance spectrometry, infrared spectroscopy, or by electroanalytical measurements. A serious limitation to this approach was the very small (usually micromolar) quantities of solute contained in a fraction.

Most modern hyphenated methods monitor the effluent from the chromatographic column continuously by spectroscopic methods. The combination of two techniques based on different principles can achieve tremendous selectivity. Today's computer-based GC instruments incorporate large databases for comparing spectra and identifying compounds.

Other Types of Detectors

Several other types of GC detectors are useful for specific applications. The *sulfur chemiluminescence detector* is based on the reaction between certain sulfur compounds and ozone. The resulting luminescence intensity is proportional to the concentration of sulfur. This detector has proven particularly useful for the determination of pollutants such as mercaptans. In the sulfur chemiluminescence detector, the eluent is mixed with hydrogen and air, and combustion takes place as in the FID. The resulting gases are then mixed with ozone, and the intensity of the emission produced is measured. The linear range is about five orders of magnitude, and the limit of detection for sulfur is approximately 0.5 pg/s. The sulfur chemiluminescence detector has also been adapted to supercritical fluid chromatography.

The nitrogen-specific chemiluminescence detector is quite similar to the sulfur detector. The nitrous oxide combustion product reacts with ozone to produce chemiluminescence. The detector responds linearly to nitrogen over about four orders of magnitude. The limit of detection for nitrogen is about 5 pg/s. The detector can be used for organic nitrogen compounds and for inorganic compounds such as ammonia, hydrazine, HCN, and nitrogen oxides.

27C GAS CHROMATOGRAPHIC COLUMNS AND STATIONARY PHASES

The pioneering gas-liquid chromatographic studies in the early 1950s were carried out on packed columns in which the stationary phase was a thin film of liquid retained by adsorption on the surface of a finely divided, inert solid support. From theoretical studies made during this early period, it became apparent that unpacked columns having inside diameters of a few tenths of a millimeter could provide separations superior to those on packed columns in both speed and column efficiency.[7] In such *capillary columns*, the stationary phase was a film of liquid a few tenths of a micrometer thick that uniformly coated the interior of a capillary tubing. In the late 1950s such *open tubular columns* were constructed and the predicted performance characteristics were confirmed experimentally in several laboratories, with open tubular columns having 300,000 plates or more being described.[8] Today, open tubular columns predominate in GC

[6]For reviews on hyphenated methods, see C. L. Wilkins, *Science*, **1983**, *222*, 291, **DOI**: 10.1126/science.6353577; C. L. Wilkins, *Anal. Chem*., **1989**, *59*, 571A, **DOI**: 10.1021/ac00135a001.

[7]For a thorough discussion of packed and capillary column technology, see E. F. Barry and R. L. Grob, *Columns for Gas Chromatography*, Hoboken, NJ: Wiley-Interscience, 2007.

[8]In 1987 a world record for length of an open tubular column and number of theoretical plates was set, as attested in the *Guinness Book of Records*, by Chrompack International Corporation of the Netherlands. The column was a fused-silica column drawn in one piece and having an internal diameter of 0.32 mm and a length of 2.1 km, or 1.3 miles. The column was coated with a 0.1 m film of polydimethyl siloxane. A 1300 m section of this column contained more than 2 million plates.

because, with no packing, columns can be narrower and longer, leading to higher efficiencies than with packed columns.

Despite such spectacular performance characteristics, capillary columns did not gain widespread use until more than two decades after their invention. The reasons for the delay were several, including small sample capacities; fragility of columns; mechanical problems associated with sample introduction and connection of the column to the detector; difficulties in coating the column reproducibly; short lifetimes of poorly prepared columns; tendencies of columns to clog; and patents, which limited commercial development to a single manufacturer (the original patent expired in 1977). The most significant development in capillary GC occurred in 1979 when fused-silica capillaries were introduced. Since then an impressive list of commercially available capillary columns for various applications has appeared. As a result, the majority of applications that have appeared in the past few years use capillary columns.[9]

27C-1 Capillary Columns

Capillary columns are also called open tubular columns because of the open flow path through them. They are of two basic types: *wall-coated open tubular* (WCOT) and *support-coated open tubular* (SCOT) columns.[10] Wall-coated columns are simply capillary tubes coated with a thin layer of the stationary phase. In SCOT columns, the inner surface of the capillary is lined with a thin film (~30 μm) of a support material, such as diatomaceous earth. This type of column holds several times as much stationary phase as does a wall-coated column and thus has a greater sample capacity. Generally, the efficiency of a SCOT column is less than that of a WCOT column but significantly greater than that of a packed column.

Early WCOT columns were constructed of stainless steel, aluminum, copper, or plastic. Later, glass columns began to be used. Often, the glass was etched with gaseous hydrochloric acid, strong aqueous hydrochloric acid, or potassium hydrogen fluoride to give a rough surface, which bonded the stationary phase more tightly. The most widely used capillary columns are *fused-silica wall-coated* (FSWC) *open tubular columns*. Fused-silica capillaries are drawn from specially purified silica that contains minimal amounts of metal oxides. These capillaries have much thinner walls than glass columns. The tubes are given added strength by an outside protective polyimide coating, which is applied as the capillary tubing is drawn. The resulting columns are quite flexible and can be bent into coils with diameters of a few inches. Figure 27-7 shows fused-silica open tubular columns. Fused-silica capillary columns are available commercially and offer several important advantages such as physical strength, much lower reactivity toward sample components, and flexibility. For most applications, they have replaced the older-type WCOT glass columns.

The most widely used silica open tubular columns have inside diameters of 0.32 and 0.25 mm. Higher-resolution columns are also available with diameters of 0.20 and 0.15 mm. Such columns are more troublesome to use and are more demanding on the injection and detection systems. Thus, a sample splitter must be used to reduce the size of the sample injected onto the column and a more sensitive detector system with a rapid response time is required.

Larger 530-μm capillaries, sometimes called *megabore columns*, are also available commercially. These columns will tolerate sample sizes that are similar to those for packed columns. The performance characteristics of megabore open tubular columns are not as good as those of smaller-diameter columns but are significantly better than those of packed columns.

Table 27-2 compares the performance characteristics of fused-silica capillary columns with other types of wall-coated columns as well as with support-coated and packed columns.

27C-2 Packed Columns

Modern packed columns are fabricated from glass or metal tubing; they are typically 2–3 m long and have inside diameters of 2–4 mm. These tubes are densely packed with a uniform, finely divided packing material, or solid support, coated with a thin layer (0.05–1 μm) of the stationary liquid phase. Columns are usually formed as coils with diameters of roughly 15 cm to permit convenient thermostatting in an oven.

Solid Support Materials

The packing, or solid support in a packed column, holds the liquid stationary phase in place so that as large a surface area as possible is exposed to the mobile phase. The ideal support consists of small, uniform, spherical particles with good mechanical strength and a specific surface area of at least 1 m^2/g. In addition, the material should be inert at elevated temperatures and be uniformly wetted by the liquid phase. No material is yet available that meets all of these criteria perfectly.

The earliest, and still the most widely used, packings for GC were prepared from naturally occurring diatomaceous earth, which consists of the skeletons of thousands of species of single-celled plants that once inhabited ancient lakes and seas. Figure 27-17 is an enlarged photo of a diatom obtained with a scanning electron microscope. Such plants received their nutrients and disposed of their wastes via molecular diffusion through their pores. As a result, their remains are well-suited as support materials because GC is also based on the same kind of molecular diffusion.

Particle Size of Supports

As shown in Figure 26-11, the efficiency of a gas chromatographic column increases rapidly with decreasing particle

[9]For more information on columns in GC, see E. F. Barry, in *Modern Practice of Gas Chromatography*, R. L. Grob and E. F. Barry, eds., 4th ed., Chap. 3, New York: Wiley-Interscience, 2004.

[10]For a detailed description of open tubular columns, see M. L. Lee, F. J. Yang, and K. D. Bartle, *Open Tubular Column Gas Chromatography: Theory and Practice*, New York: Wiley, 1984.

TABLE 27-2 Properties and Characteristics of Typical GC Columns

	Type of Column			
	FSWC*	WCOT†	SCOT‡	Packed
Length, m	10–100	10–100	10–100	1–6
Inside diameter, mm	0.1–0.3	0.25–0.75	0.5	2–4
Efficiency, plates/m	2000–4000	1000–4000	600–1200	500–1000
Sample size, ng	10–75	10–1000	10–1000	$10–10^6$
Relative pressure	Low	Low	Low	High
Relative speed	Fast	Fast	Fast	Slow
Flexibility?	Yes	No	No	No
Chemical inertness	Best →			Poorest

*Fused silica, wall-coated open tubular column.

†Wall-coated open tubular metal, plastic, or glass columns.

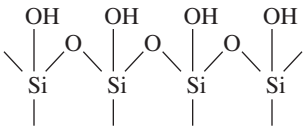
‡Support-coated open tubular column (also called porous-layer open tubular, or PLOT).

FIGURE 27-17 A photomicrograph of a diatom. Magnification 5000×. (BIOPHOTO ASSOCIATES/Getty Images)

diameter of the packing. The pressure difference required to maintain an acceptable flow rate of carrier gas, however, varies inversely as the square of the particle diameter; the latter relationship has placed lower limits on the size of particles used in GC because it is not convenient to use pressure differences that are greater than about 50 psi. As a result, the usual support particles are 60–80 mesh (250–170 μm) or 80–100 mesh (170–149 μm).

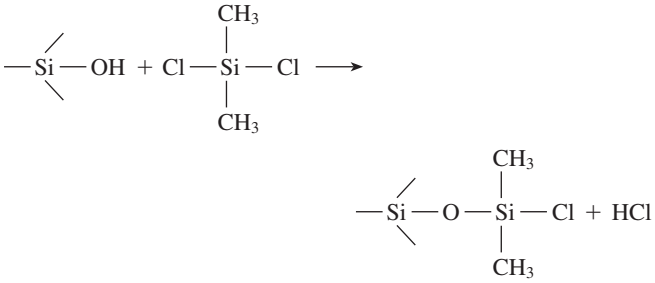
27C-3 Adsorption on Column Packings or Capillary Walls

A problem that has plagued GC from its beginning has been the physical adsorption of polar or polarizable analyte species, such as alcohols or aromatic hydrocarbons, on the silicate surfaces of column packings or capillary walls. Adsorption causes distorted peaks, which are broadened and often exhibit a tail (recall Figure 26-5). Adsorption occurs with silanol groups that form on the surface of silicates by reaction with moisture. Thus, a fully hydrolyzed silicate surface has the structure

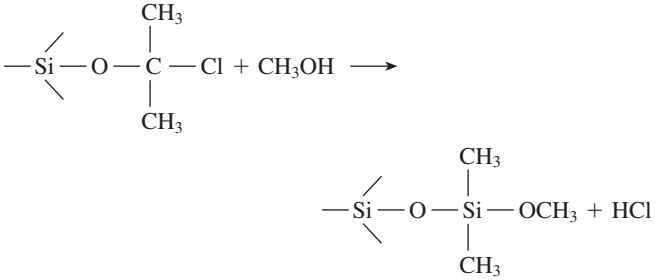


The SiOH groups on the support surface have a strong affinity for polar organic molecules and tend to retain them by adsorption.

Support materials can be deactivated by silanization with dimethylchlorosilane (DMCS). The reaction is



When the support is washed with methanol, the second chloride is replaced by a methoxy group. That is,



Silanized surfaces of column packings may still show a residual adsorption, which apparently occurs with metal oxide impurities in the diatomaceous earth. Acid washing prior to silanization removes these impurities. Fused silica used for manufacturing open tubular columns is largely free of this type of impurity. Because of this, fewer problems with adsorption arise with fused-silica columns.

27C-4 The Stationary Phase

Desirable properties for the immobilized liquid phase in a gas-liquid chromatographic column include (1) *low volatility* (ideally, the boiling point of the liquid should be at least 100°C higher than the maximum operating temperature for the column); (2) *thermal stability*; (3) *chemical inertness*; and (4) *solvent characteristics* such that k and α (Sections 26B-5 and 26B-6, respectively) values for the solutes to be resolved fall within a suitable range.

Many liquids have been proposed as stationary phases in the development of GLC. Currently, fewer than a dozen are commonly used. The proper choice of stationary phase is often crucial to the success of a separation. Qualitative guidelines for stationary-phase selection can be based on a literature review, an Internet search, prior experience, or advice from a vendor of chromatographic equipment and supplies.

The retention time for an analyte on a column depends on its distribution constant, which in turn is related to the chemical nature of the liquid stationary phase. To separate various sample components, their distribution constants must be sufficiently different to accomplish a clean separation. At the same time, these constants must not be extremely large or extremely small because large distribution constants lead to prohibitively long retention times and small constants produce such short retention times that separations are incomplete.

To have a reasonable residence time in the column, an analyte must show some degree of compatibility (solubility) with the stationary phase. Here, the principle of "like dissolves like" applies, where "like" refers to the polarities of the analyte and the immobilized liquid. The polarity of a molecule, as indicated by its dipole moment, is a measure of the electric field produced by separation of charge within the molecule. Polar stationary phases contain functional groups such as —CN, —CO, and —OH. Hydrocarbon-type stationary phases and dialkyl siloxanes are nonpolar, but polyester phases are highly polar. Polar analytes include alcohols, acids, and amines; solutes of medium polarity include ethers, ketones, and aldehydes. Saturated hydrocarbons are nonpolar. Generally, the polarity of the stationary phase should match that of the sample components. When the match is good, the order of elution is determined by the boiling point of the eluents.

Classification of Stationary Phases

Many different schemes have been reported to classify stationary phases and thereby simplify stationary-phase selection. Most of these are based on solute probes that test specific interactions between the solute and the liquid phase by measuring solute retention characteristics. Two of the most important classifications are based on the work of Rohrschneider and McReynolds.[11] The result was the production of lists of stationary phases and the compound classes that can be separated by each phase (see Table 27-3). Likewise, numerical values, known as McReynolds constants, are available that can guide the user in selecting a stationary phase to separate analytes having different functional groups, such as alcohols from aldehydes or ketones.[12]

[11]L. Rohrschneider, *J. Chromatogr.*, **1966**, *22*, 6, **DOI**: 10.1016/S0021-9673(01)97064-5; W. O. McReynolds, *J. Chromatogr. Sci.*, **1970**, *8*, 685, **DOI**: 10.1093/chromsci/8.12.685.

[12]J. A. Dean, *Analytical Chemistry Handbook*, pp. 4.34–4.37, New York: McGraw-Hill, 1995.

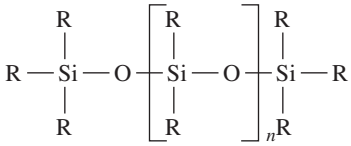
TABLE 27-3 Some Common Liquid Stationary Phases for Gas-Liquid Chromatography

Stationary Phase	Common Trade Name	Maximum Temperature, °C	Common Applications
Polydimethyl siloxane	OV-1, SE-30	350	General-purpose nonpolar phase, hydrocarbons, polynuclear aromatics, steroids, PCBs
5% Phenyl-polydimethyl siloxane	OV-3, SE-52	350	Fatty acid methyl esters, alkaloids, drugs, halogenated compounds
50% Phenyl-polydimethyl siloxane	OV-17	250	Drugs, steroids, pesticides, glycols
50% Trifluoropropyl-polydimethyl siloxane	OV-210	200	Chlorinated aromatics, nitroaromatics, alkyl-substituted benzenes
Polyethylene glycol	Carbowax 20M	250	Free acids, alcohols, ethers, essential oils, glycols
50% Cyanopropyl-polydimethyl siloxane	OV-275	240	Polyunsaturated fatty acids, rosin acids, free acids, alcohols

Some Widely Used Stationary Phases

Table 27-3 lists the most widely used stationary phases for both packed and open tubular column GC in order of increasing polarity. These six liquids can probably provide satisfactory separations for 90% or more of samples encountered.

Five of the liquids listed in Table 27-3 are polydimethyl siloxanes that have the general structure



In the first of these, polydimethyl siloxane, the —R groups are all $—CH_3$, giving a liquid that is relatively nonpolar. In the other polysiloxanes shown in the table, a fraction of the methyl groups are replaced by functional groups such as phenyl ($—C_6H_5$), cyanopropyl ($—C_3H_6CN$), and trifluoropropyl ($—C_3H_6CF_3$). The percentage description in each case gives the amount of substitution of the named group for methyl groups on the polysiloxane backbone. Thus, for example, 5% phenyl-polydimethyl siloxane has a phenyl ring bonded to 5% (by number) of the silicon atoms in the polymer. These substitutions increase the polarity of the liquids to various degrees.

The fifth entry in Table 27-3 is a polyethylene glycol with the structure

$$HO—CH_2—CH_2—(O—CH_2—CH_2)_n—OH$$

This compound is used widely for separating polar species. Figure 27-18 illustrates applications of the phases listed in Table 27-3 for open tubular columns.

Bonded and Cross-Linked Stationary Phases

Commercial columns are advertised as having bonded or cross-linked stationary phases. The purpose of bonding and cross-linking is to provide a longer-lasting stationary phase that is not disrupted at elevated temperatures or during temperature programming. With use, untreated columns slowly lose their stationary phase because of "bleeding," in which a small amount of immobilized liquid is carried out of the column during the elution process. Such columns are also recommended for on-column injection where a large solvent volume is used. Indeed, cross-linked or bonded columns may be backflushed to remove contaminants without significant loss of stationary phase.

Bonding involves attaching a monomolecular layer of the stationary phase to the silica surface of the column by a chemical reaction. For commercial columns, the nature of the reaction is usually proprietary.

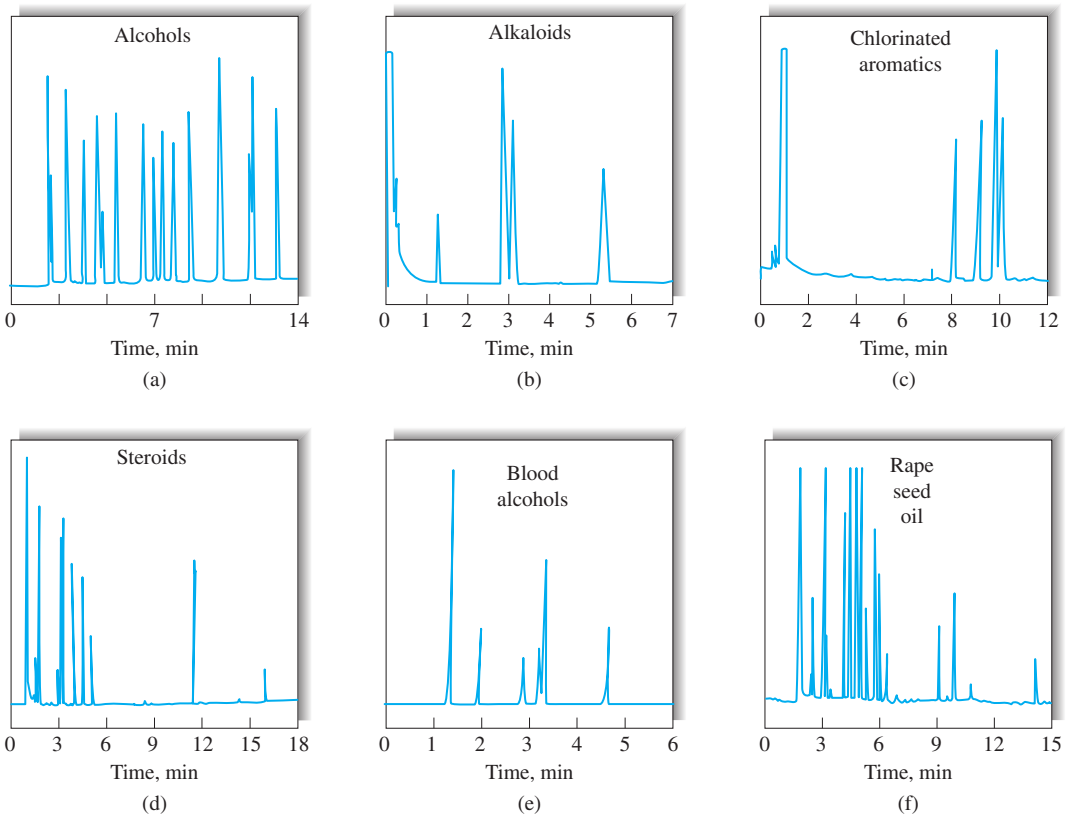


FIGURE 27-18 Typical chromatograms from open tubular columns coated with (a) polydimethyl siloxane, (b) 5% (phenyl methyldimethyl) siloxane, (c) 50% (phenyl methyldimethyl) siloxane, (d) 50% poly(trifluoropropyl-dimethyl) siloxane, (e) polyethylene glycol, and (f) 50% poly(cyanopropyl-dimethyl) siloxane. (Source: Agilent Technologies.)

Cross-linking is carried out *in situ* after a column is coated with one of the polymers listed in Table 27-3. One way of cross-linking is to incorporate a peroxide into the original liquid. When the film is heated, reaction between the methyl groups in the polymer chains is initiated by a free radical mechanism. The polymer molecules are then cross-linked through carbon-to-carbon bonds. The resulting films are less extractable and have considerably greater thermal stability than do untreated films. Cross-linking has also been initiated by exposing the coated columns to gamma radiation.

Film Thickness

Commercial columns are available having stationary phases that vary in thickness from 0.1 to 5 μm. Film thickness primarily affects the retentive character and the capacity of a column as discussed in Section 26C-3. Thick films are used with highly volatile analytes because such films retain solutes for a longer time, thus providing a greater time for separation to take place. Thin films are useful for separating species of low volatility in a reasonable length of time. For most applications with 0.25- or 0.32-mm columns, a film thickness of 0.25 μm is recommended. With megabore columns, 1- to 1.5-μm films are often used. Today, columns with 8-μm films are marketed.

Chiral Stationary Phases

In recent years, much effort has been devoted to developing methods for the separation of enantiomers by gas or liquid chromatography.[13] Two approaches have been used. One is based on forming derivatives of the analyte with an optically active reagent that forms a pair of diastereomers that can be separated on an achiral column. The alternative method is to use a chiral liquid as the stationary phase. A number of amino acid–derived chiral phases have been developed for this purpose, and others are becoming available commercially.

27D APPLICATIONS OF GC

To evaluate the importance of GC, we must distinguish between the two roles the method plays. First, GC is a tool for performing separations. In this role, GC methods are unsurpassed when applied to complex organic, metal-organic, and biochemical systems made up of volatile species or species that can be derivatized to yield volatile substances. The second role that GC plays is in the completion of an analysis. In this role, retention times or volumes are used for qualitative identification, and peak heights or peak areas provide quantitative information. For qualitative purposes, GC is much more limited than most of the spectroscopic methods considered in earlier chapters. Thus, an important trend in the field has been in the direction of combining the remarkable separation capabilities of GC with the superior identification properties of such instruments as mass, infrared, and nuclear magnetic resonance spectrometers (see Section 27B-4).

[13]For a review of chiral stationary-phase separations by GC, see J. V. Hinshaw, *LC-GC*, **1993**, *11*, 644; E. F. Barry, in *Modern Practice of Gas Chromatography*, R. L. Grob and E. F. Barry, eds., 4th ed., Chap. 3, New York: Wiley-Interscience, 2004.

27D-1 Qualitative Analysis

Gas chromatograms are widely used to establish the purity of organic compounds. The appearance of additional peaks reveals any contaminants present, and the areas under these peaks provide estimates of the extent of contamination. Such areas are only estimates because different components may have widely differing detector response factors. Gas chromatographic techniques are also useful for evaluating the effectiveness of purification procedures.

In theory, GC retention times should be useful for identifying components in mixtures. In fact, however, the applicability of such data is limited by the number of variables that must be controlled to obtain reproducible results. Nevertheless, GC provides an excellent means of confirming the presence or absence of a suspected compound in a mixture, provided that an authentic sample of the substance is available. No new peaks in the chromatogram of the mixture should appear on addition of the known compound, and enhancement of an existing peak should be observed. The evidence is particularly convincing if the effect can be duplicated on different columns and at different temperatures.

On the other hand, because a chromatogram provides only a single piece of information about each species in a mixture (the retention time), the application of the technique to the qualitative analysis of complex samples of unknown composition is limited. This limitation has been largely overcome by linking chromatographic columns directly with ultraviolet, infrared, and mass spectrometers to produce hyphenated instruments as discussed elsewhere.

Selectivity Factors

We have seen (Section 26B-6) that the selectivity factor α for compounds A and B is given by the relationship

$$\alpha = \frac{K_B}{K_A} = \frac{(t_R)_B - t_M}{(t_R)_A - t_M} = \frac{(t'_R)_B}{(t'_R)_A}$$

where $(t'_R)_A = [(t_R)_A - t_M]$ is the adjusted retention time for species A. If a standard substance is chosen as compound B, then α can provide an index for identification of compound A, which is largely independent of column variables other than temperature. Numerical tabulations of selectivity factors for pure compounds relative to a common standard can be prepared and then used for the characterization of solutes. Unfortunately, finding a universal standard that yields selectivity factors of reasonable magnitude for all types of analytes is impossible. Thus, the amount of selectivity factor data available in the literature is presently limited.

The Retention Index

The retention index I was first proposed by E. Kovats in 1958 for identifying solutes from chromatograms.[14] The retention index for any given solute can be calculated from a chromatogram of a mixture of that solute with at least two normal alkanes having retention times that bracket that of the solute. The retention index scale is based on normal alkanes. By definition, the retention index for a normal alkane is equal to 100 times the number of carbons in the compound *regardless of the column packing, the*

[14]E. Kovats, *Helv. Chim. Acta*, **1958**, *41*, 1915, **DOI**: 10.1002/hlca.19580410703.

temperature, or other chromatographic conditions. The retention indexes for all compounds other than normal alkanes vary, often by several hundred retention index units, with column variables.

It has long been known that within a homologous series, a plot of the logarithm of adjusted retention time ($t'_R = t_R - t_M$) versus the number of carbon atoms is linear, provided the lowest member of the series is excluded. Such a plot for C_4 to C_9 normal alkane standards is shown in Figure 27-19. Also indicated on the ordinate are log-adjusted retention times for three compounds on the same column and at the same temperature. Their retention indexes are then obtained by multiplying the corresponding abscissa values by 100. Thus, the retention index for toluene is 749, and for benzene it is 644.

Normally, a graphical procedure is not required to determine retention indexes. Instead, adjusted retention data are calculated by interpolation from a chromatogram of a mixture of the solute of interest and two or more alkane standards.

It is important to reiterate that the retention index *for a normal alkane* is independent of temperature and column packing. Thus, *I* for heptane, by definition, is always 700. In contrast, retention indexes of all other solutes may, and often do, vary widely from one column to another. For example, the retention index for acenaphthene on a cross-linked polydimethyl siloxane stationary phase at 140°C is 1460. With 5% phenyl-polydimethyl siloxane as the stationary phase, it is 1500 at the same temperature, and with polyethylene glycol as the stationary phase, the retention index is 2084.

The retention index system has the advantage of being based on readily available reference materials that cover a wide boiling range. In addition, the temperature dependence of retention indexes is relatively small.

The use of retention data on two or more GC columns can improve the chances of correctly identifying an unknown compound. The columns can be used in separate experiments or sometimes they can be used in tandem. The use of two or more columns in series is termed *multidimensional chromatography*.[15] Likewise, the responses of two or more GC detectors can greatly aid in qualitative identification.

The combination of GC with various spectroscopic detectors, particularly with mass spectrometry, can greatly aid in identifying components. In fact, GC/MS is now the premier technique for separating and identifying species in mixtures.

The National Institute for Standards and Technology maintains NIST Standard Reference Database 1A, which contains mass spectral data on nearly 250,000 compounds and retention indices on 70,000 of those. Along with the database, the agency has developed a sophisticated software application to search and match experimental spectra and retention indices to those of known compounds.[16]

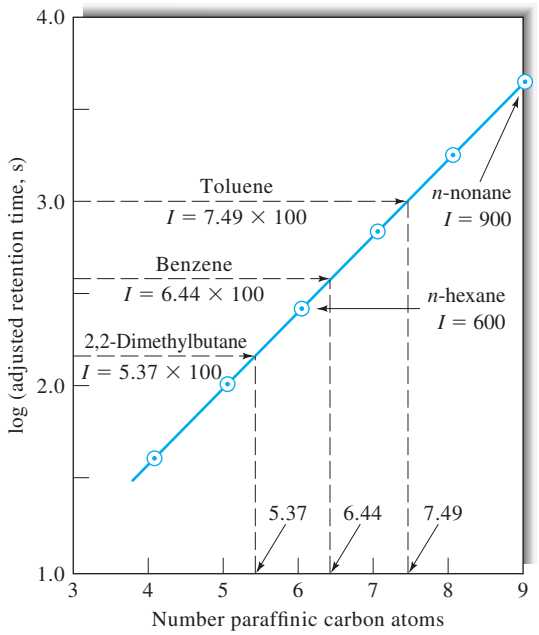


FIGURE 27-19 Graphical illustration of the method for determining retention indexes for three compounds. Stationary phase: squalane. Temperature: 60°C. Retention indexes for normal alkane standards nonane and hexane are indicated.

27D-2 Quantitative Analysis

The peak height or peak area of an eluate from a GC column has been widely used for quantitative and semiquantitative analyses. An accuracy of 1% relative is attainable under carefully controlled conditions using either the external or the internal standard method. As with most analytical tools, reliability is directly related to the control of variables; the nature of the sample also plays a part in determining the potential accuracy. The general discussion of quantitative chromatographic analysis given in Section 26F-2 applies to GC as well as to other types; therefore, no further consideration of this topic is given here.

27E ADVANCES IN GC

Although GC is quite a mature technique, there have been many developments in recent years in theory, instrumentation, columns, and practical applications. We discuss here some developments in high-speed GC and in miniaturized GC systems.

27E-1 High-Speed GC[17]

Researchers in GC have often focused on achieving ever higher resolution to separate more and more complex mixtures. In most separations, conditions are varied to separate the most difficult-to-separate pair of components, the so-called *critical pair*. Many of the components of interest, under these conditions, are highly overseparated. The basic idea of high-speed

[15]For reviews of two-dimensional GC, see M. Adahchour, J. Beens, R. J. J. Vreuls, U. A. Th. Brinkman, *Trends Anal. Chem.* (*TRAC*), **2006**, *25*, 438, **DOI**: 10.1016/j.trac.2006.03.002; **2006**, *25*, 540, **DOI**: 10.1016/j.trac.2006.04.004; **2006**, *25*, 726, **DOI**: 10.1016/j.trac.2006.03.005.

[16]*NIST Standard Reference Database 1A*, Gaithersburg, MD: National Institute of Standards and Technology, 2014, http://tinyurl.com/ncozs4c.

[17]For more information, see R. D. Sacks, in *Modern Practice of Gas Chromatography*, R. L. Grob and E. F. Barry, eds., 4th ed., Ch. 5, New York: Wiley-Interscience, 2004.

GC is that, for many separations of interest, higher speed can be achieved albeit at the expense of some selectivity and resolution.

The principles of high-speed separations can be demonstrated by substituting Equation 26-5 into Equation 26-11

$$\frac{L}{t_R} = u \times \frac{1}{1 + k_n} \tag{27-8}$$

where k_n is the retention factor for the last component of interest in the chromatogram. If we rearrange Equation 27-8 and solve for the retention time of the last component of interest, we obtain

$$t_R = \frac{L}{u} \times (1 + k_n) \tag{27-9}$$

Equation 27-9 tells us that we can achieve faster separations by using short columns, higher-than-usual carrier gas velocities and small retention factors. For example, if we reduce the column length L by a factor of 4 and increase the carrier-gas velocity u by a factor of 5, the analysis time t_R is reduced by a factor of 20. The price paid is reduced resolving power caused by increased band broadening and reduced peak capacity (the number of peaks that will fit in the chromatogram).

Research workers in the field have been designing instrumentation and chromatographic conditions to optimize separation speed at the lowest cost in terms of resolution and peak capacity.[18] They have designed systems to achieve tunable columns and high-speed temperature programming. A tunable column is a series combination of a polar and a nonpolar column. Figure 27-20 shows the separation of twelve compounds prior to initiating a programmed temperature ramp and nineteen compounds after the temperature program was begun. The total time required was 140 s. These workers have also been using high-speed GC with mass spectrometry detection including time-of-flight detection.[19]

27E-2 Miniaturized GC Systems

For many years there has been a desire to miniaturize GC systems to the microchip level. Miniature GC systems are useful in space exploration, in portable instruments for field use, and in environmental monitoring. Early work reported on GC columns etched onto a microchip.[20] However, the relatively poor chromatographic performance of such devices led to removal of the column from the chip in the commercial systems that were produced.

Microfabricated columns have been designed using substrates of silicon, several metals, and polymers.[21] Relatively deep, narrow channels are etched into the substrate. These channels have low dead volume to reduce band broadening and high surface area to increase stationary-phase volume. A complete microfabricated GC system has been described.[22] Figure 27-21 shows the microfabricated GC column and

[18]H. Smith and R. D. Sacks, *Anal. Chem.*, **1998**, *70*, 4960, **DOI**: 10.1021/ac980463b.

[19]C. Leonard and R. Sacks, *Anal. Chem.*, **1999**, *71*, 5177, **DOI**: 10.1021/ac990631f.

[20]See S. C. Terry et al., *IEEE Trans. Electron Devices*, **1979**, *26*, 1880, **DOI**: 10.1109/T-ED.1979.19791; J. B. Angell et al., *Sci. Am.*, **1983**, *248* (4), 44, **DOI**: 10.1038/scientificamerican0483-44.

[21]G. Lambertus et al., *Anal. Chem.*, **2004**, *76*, 2629, **DOI**: 10.1021/ac030367x.

[22]D. Gaddes et al., *J. Chromatograph. A*, **2014**, *1349*, 96, **DOI**: 10.1016/j.chroma.2014.04.087.

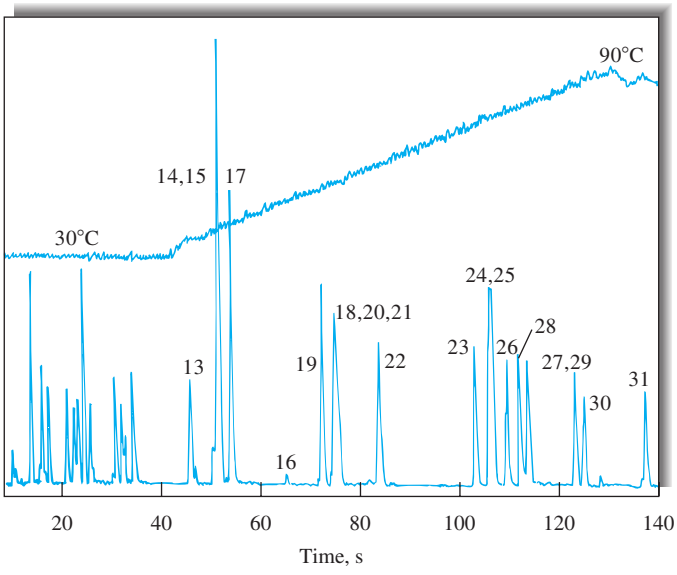


FIGURE 27-20 High-speed chromatogram obtained with isothermal operation (30°C) for 37 s followed by a 35°C/min temperature ramp to 90°C. (From H. Smith and R. D. Sacks, *Anal. Chem.*, **1998**, *70*, 4960. Copyright 1998 American Chemical Society.)

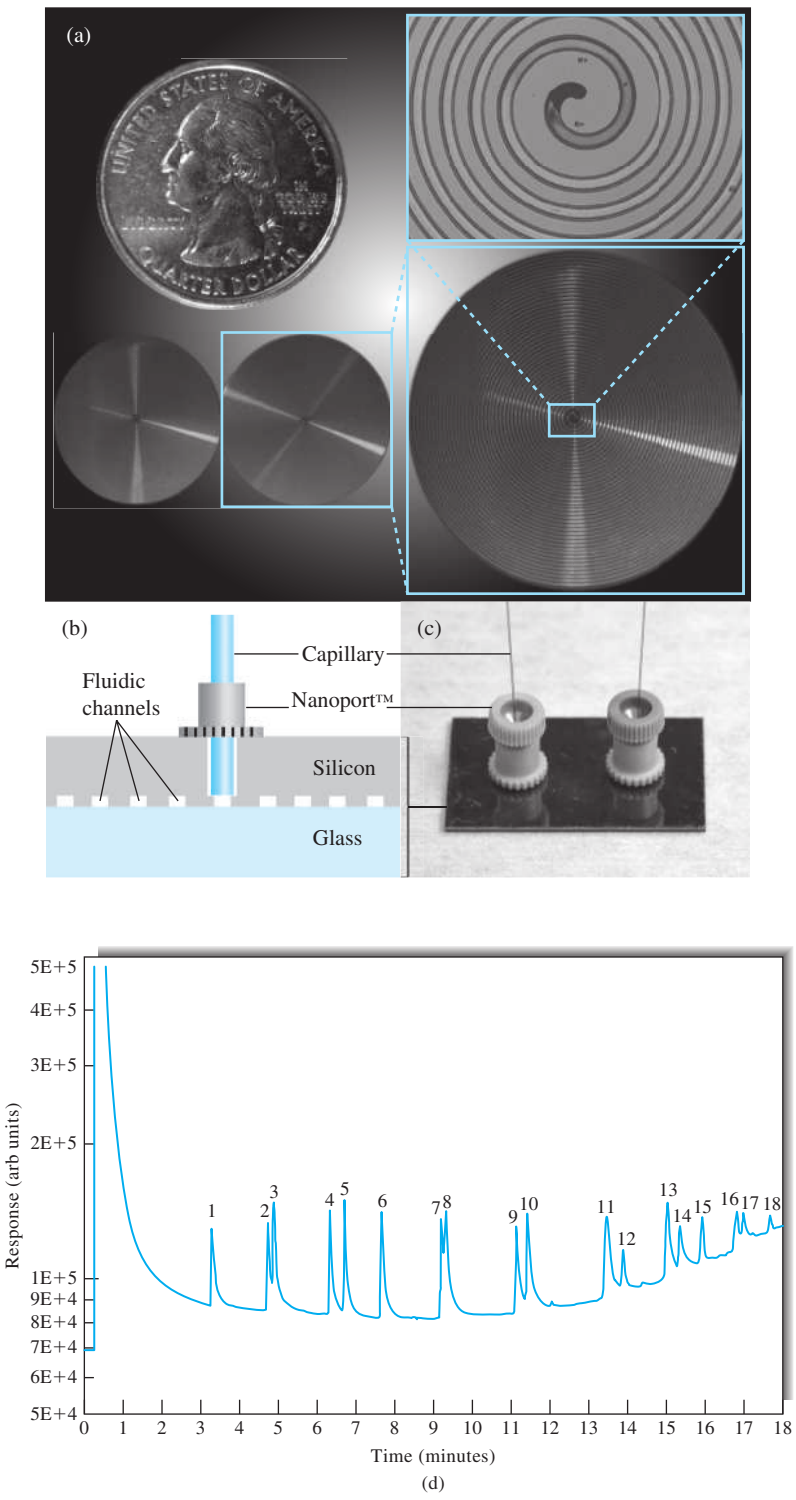


FIGURE 27-21 (a) Photo of a 2-m microfabricated GC column in relation to a U.S. quarter dollar. The two insets on the right show the column at two different zoom levels. The lighter regions in the images are the channel tracks and the darker regions are bonded silicon wall regions. (b) Schematic illustration in cross-sectional view of the capillary tubing to GC column fluidic channel connection. (c) Photo of the assembled GC column. The column with the fluid connections are carefully aligned and attached at the inlet and outlet. The silica tubing connects the injection port to the column. (d) Separation of a mixture of polycyclic aromatic hydrocarbons on the column shown in (a)–(c). The separation was started at 45°C and was ramped to 325°C at a rate of 15°C/min. All 18 components of the mixture were successfully separated. (D. Gaddes et al., *J. Chromatograph. A,* **2014**, *1349,* 96. With permission.)

various connections to tubing and an injection port (a, b, and c). A chromatogram of a mixture of polycyclic aromatic hydrocarbons is also shown (d).

27F GAS-SOLID CHROMATOGRAPHY

GSC is based on adsorption of gaseous substances on solid surfaces. Distribution constants are generally much larger than those for GLC. As a result, GSC is useful for the separation of species that are not retained by gas-liquid columns, such as the components of air, hydrogen sulfide, carbon disulfide, nitrogen oxides, carbon monoxide, carbon dioxide, and the rare gases.

GSC is performed with both packed and open tubular columns. For the latter, a thin layer of the adsorbent is affixed to the inner walls of the capillary. Such columns are sometimes called *porous-layer open tubular*, or PLOT, columns.

27F-1 Molecular Sieves

Molecular sieves are aluminum silicate ion exchangers, whose pore size depends on the kind of cation present. Commercial preparations of these materials are available in particle sizes of 40–60 mesh to 100–120 mesh. The sieves are classified according to the maximum diameter of molecules that can enter the pores. Commercial molecular sieves come in pore sizes of 4, 5, 10, and 13 Å. Molecules smaller than these dimensions penetrate into the interior of the particles where adsorption takes place. For such molecules, the surface area is enormous when compared with the area available to larger molecules. Thus, molecular sieves can be used to separate small molecules from large. For example, a 6-ft, 5-Å packing at room temperature will easily separate a mixture of helium, oxygen, nitrogen, methane, and carbon monoxide in the order given.

Figure 27-22a shows a typical molecular sieve chromatogram. In this application two packed columns were used, one an ordinary gas-liquid column and the other a molecular sieve column. The former retains only the carbon dioxide and passes the remaining gases at rates corresponding to the carrier rate. When the carbon dioxide elutes from the first column, a switch briefly directs the flow around the second column to avoid permanent adsorption of the carbon dioxide on the molecular sieve. After the carbon dioxide signal has returned to zero, the flow is switched back through the second column, thereby permitting separation and elution of the remainder of the sample components.

27F-2 Porous Polymers

Porous polymer beads of uniform size are manufactured from styrene cross-linked with divinylbenzene (Section 28F-2). The pore size of these beads is uniform and is controlled by the amount of cross-linking. Porous polymers have found considerable use in the separation of gaseous polar species such as hydrogen sulfide, oxides of nitrogen, water, carbon dioxide, methanol, and vinyl chloride. A typical application of an open tubular column lined with a porous polymer (PLOT column) is shown in Figure 27-22b.

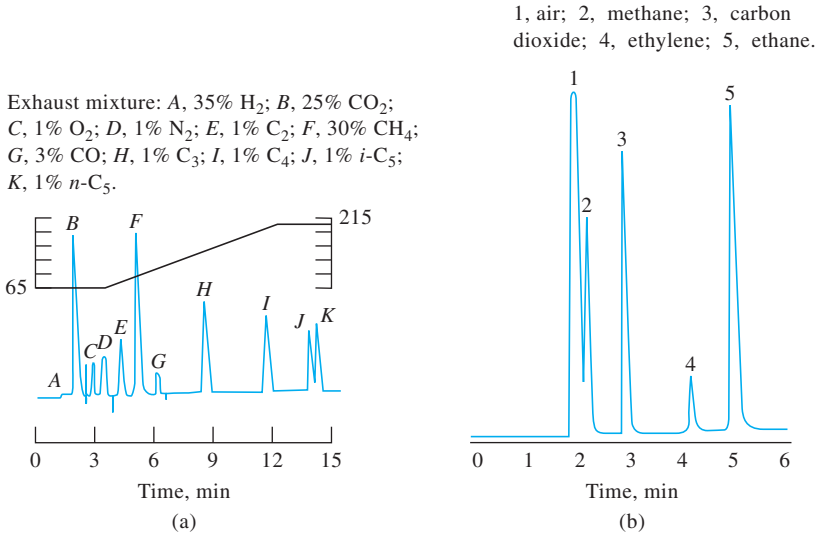


FIGURE 27-22 Typical gas-solid chromatographic separations: (a) a 5 ft. × 1/8 in. molecular sieve column; (b) a 30 m × 0.53 mm PLOT column. C_n = hydrocarbon with *n* carbons.

» QUESTIONS AND PROBLEMS

*Answers are provided at the end of the book for problems marked with an asterisk.

Problems with this icon are best solved using spreadsheets.

27-1 How do gas-liquid and gas-solid chromatography differ?

27-2 How does a soap-bubble flow meter work?

27-3 What is meant by temperature programming in GC? Why is it frequently used?

27-4 Define (a) retention volume, (b) corrected retention volume, (c) specific retention volume.

27-5 What is the difference between a concentration-sensitive and a mass-sensitive detector? Are the following detectors mass or concentration sensitive? (a) thermal conductivity, (b) atomic emission, (c) thermionic, (d) electron captive, (e) flame photometric, (f) flame ionization.

27-6 Describe the principles of operation for the detectors listed in Question 27-5.

27-7 What are the major advantages and the principal limitations of each of the detectors listed in Question 27-5?

***27-8** What is the difference between a total-ion chromatogram and a mass chromatogram?

27-9 Discuss why the combination of GC and mass spectrometry is so powerful.

27-10 What are *hyphenated* GC methods? Briefly describe two hyphenated methods.

***27-11** What is the packing material used in most packed GC columns?

27-12 How do the following open tubular columns differ?

(a) PLOT columns **(b)** WCOT columns **(c)** SCOT columns

27-13 What are megabore open tubular columns? Why are they used?

***27-14** What are the advantages of fused-silica capillary columns compared with glass or metal columns?

27-15 What properties should the stationary-phase liquid for GC possess?

***27-16** What is the effect of stationary-phase film thickness on gas chromatograms?

27-17 Why are gas chromatographic stationary phases often bonded and cross-linked? What do these terms mean?

27-18 List the variables that lead to (a) band broadening and (b) band separation in GLC.

27-19 What are retention indexes? Describe how they are determined.

27-20 The same polar compound is gas chromatographed on an SE-30 (very nonpolar) column and then on a Carbowax 20M (very polar column). How will $K = c_S/c_M$ vary between the two columns?

***27-21** Use the retention data given in the following table to calculate the retention index of 1-hexene.

Sample	Retention Time, min
Air	0.571
n-pentane	2.16
n-hexane	4.23
1-hexene	3.15

QUESTIONS AND PROBLEMS (continued)

***27-22** A GC column was operated under the following conditions:

column: 1.10 m × 2.0 mm, packed with Chromosorb P; mass of stationary liquid added, 1.40 g; density of liquid, 1.02 g/mL

pressures: inlet, 26.1 psi above room; room, 748 torr

measured outlet flow rate: 25.3 mL/min

temperature: room, 21.2°C; column, 102.0°C

retention times: air, 18.0 s; methyl acetate, 1.98 min; methyl propionate, 4.16 min; methyl *n*-butyrate, 7.93 min

peak widths of esters at base: 0.19, 0.39, and 0.79, respectively

Calculate

(a) the average flow rate in the column.

(b) the corrected retention volumes for air and the three esters.

(c) the specific retention volumes for the three components.

(d) the distribution constants for each of the esters.

(e) a corrected retention volume and retention time for methyl *n*-hexanoate.

***27-23** From the data in Problem 27-22, calculate

(a) the retention factor k for each component.

(b) selectivity factor α for each adjacent pair of compounds.

(c) the average number of theoretical plates and plate height for the column.

(d) the resolution for each adjacent pair of compounds.

27-24 The stationary-phase liquid in the column described in Problem 27-23 was didecylphthalate, a solvent of intermediate polarity. If a nonpolar solvent such as a silicone oil had been used instead, would the retention times for the three compounds be larger or smaller? Why?

27-25 One method for quantitative determination of the concentration of constituents in a sample analyzed by GC is the area-normalization method. Here, complete elution of all of the sample constituents is necessary. The area of each peak is then measured and corrected for differences in detector response to the different eluates. This correction involves dividing the area by an empirically determined correction factor. The concentration of the analyte is found from the ratio of its corrected area to the total corrected area of all peaks. For a chromatogram containing three peaks, the relative areas were found to be 16.4, 45.2, and 30.2 in the order of increasing retention time. Calculate the percentage of each compound if the relative detector responses were 0.60, 0.78, and 0.88, respectively.

27-26 Determine the concentration of species in a sample using the peak areas and relative detector responses for the five gas chromatographic peaks given in the following table. Use the area-normalization method described in Problem 27-25.

Also shown are the relative responses of the detector. Calculate the percentage of each component in the mixture.

Compound	Relative Peak Area	Relative Detector Response
A	32.5	0.70
B	20.7	0.72
C	60.1	0.75
D	30.2	0.73
E	18.3	0.78

27-27 What would be the effect of the following on the plate height of a column? Explain.

(a) Increasing the mass of the stationary phase relative to the packing mass.

(b) Decreasing the rate of sample injection.

(c) Increasing the injection port temperature.

(d) Increasing the flow rate.

(e) Reducing the particle size of the packing.

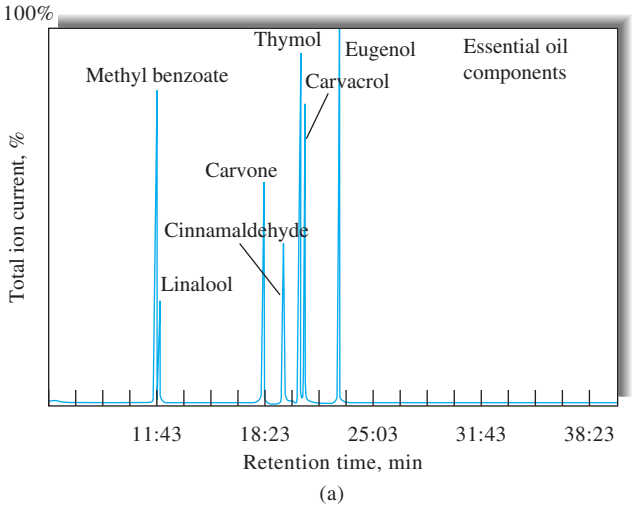
(f) Decreasing the column temperature.

* **27-28** What kinds of mixtures are separated by GSC?

27-29 Why is GSC not used nearly as extensively as GLC?

Challenge Problem

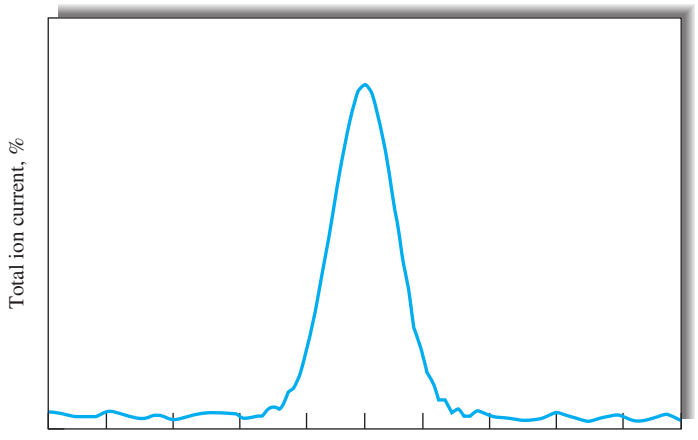
27-30 Cinnamaldehyde is the component responsible for cinnamon flavor. It is also a potent antimicrobial compound present in essential oils (see M. Friedman, N. Kozukue, and L. A. Harden, *J. Agric. Food Chem.*, **2000**, *48*, 5702, **DOI**: 10.1021/jf000585g). The GC response of an artificial mixture containing six essential oil components and methyl benzoate as an internal standard is shown in part (a) of the figure.



(a)

QUESTIONS AND PROBLEMS (continued)

(a) An idealized enlargement of the region near the cinnamaldehyde peak is given in part (b) of the figure. Determine the retention time for cinnamaldehyde.



Enlarged chromatogram

(b)

(b) From part (b) of the figure, determine the number of theoretical plates for the column.

(c) The fused-silica column was 0.25 mm × 30 cm with a 0.25-μm film. Determine the height equivalent to a theoretical plate from the data in parts (a) and (b).

(d) Quantitative data were obtained by using methyl benzoate as the internal standard. The following results were found for calibration curves of cinnamaldehyde, eugenol, and thymol. The values under each component represent the peak area of the component divided by the peak area of the internal standard.

Concentration, mg sample/ 200 μL	Cinnamaldehyde	Eugenol	Thymol
0.50	—	0.4	—
0.65	—	—	1.8
0.75	1.0	0.8	—
1.10	—	1.2	—
1.25	2.0	—	—
1.30	—	—	3.0
1.50	—	1.5	—
1.90	3.1	2.0	4.6
2.50	4.0	—	5.8

Determine the calibration curve equations for each component. Include the R^2 values.

(e) From the data in part (d), determine which of the components has the highest calibration curve sensitivity? Which has the lowest?

(f) A sample containing the three essential oils in part (d) gave the peak areas relative to the internal standard area: cinnamaldeyde, 2.6; eugenol, 0.9; thymol, 3.8. Determine the concentrations of each of the oils in the sample and the standard deviations in concentration.

(g) A study was made of the decomposition of cinnamaldehyde in cinnamon oil. The oil was heated for various times at different temperatures. The following data were obtained:

Temp, °C	Time, min	Cinnamaldehyde, %
25, initial		90.9
40	20	87.7
—	40	88.2
—	60	87.9
60	20	72.2
—	40	63.1
—	60	69.1
100	20	66.1
—	40	57.6
—	60	63.1
140	20	64.4
—	40	53.7
—	60	57.1
180	20	62.3
—	40	63.1
—	60	52.2
200	20	63.1
—	40	64.5
—	60	63.3
210	20	74.9
—	40	73.4
—	60	77.4

Determine whether temperature has a statistical effect on the decomposition of cinnamaldehyde using analysis of variance (ANOVA). (For how to perform ANOVA, see S. R. Crouch and F. J. Holler, *Applications of Microsoft® Excel in Analytical Chemistry*, 3rd ed., Chap. 3, Belmont, CA: Cengage Learning, 2017.) In the same way, determine if time of heating has an effect.

(h) Using the data in part (g), assume that decomposition begins at 60°C and test the hypothesis that there is no effect of temperature or time.