Chapter

1

Introduction

Analytical chemistry deals with methods for determining the chemical composition of samples of matter. A qualitative method yields information about the identity of atomic or molecular species or the functional groups in the sample; a quantitative method, in contrast, provides numerical information as to the relative amount of one or more of these components.

1A CLASSIFICATION OF ANALYTICAL METHODS

Analytical methods are often classified as being either *classical* or *instrumental.* This classification is largely historical with classical methods, sometimes called *wet-chemical methods,* preceding instrumental methods by a century or more.

1A-1 Classical Methods

In the early years of chemistry, most analyses were carried out by separating the components of interest (the *analytes*) in a sample by precipitation, extraction, or distillation. For qualitative analyses, the separated components were then treated with reagents that yielded products that could be recognized by their colors, their boiling or melting points, their solubilities in a series of solvents, their odors, their optical activities, or their refractive indexes. For quantitative analyses, the amount of analyte was determined by *gravimetric* or by *titrimetric* measurements. In gravimetric measurements, the mass of the analyte or some compound produced from the analyte was determined. In titrimetric procedures, the volume or mass of a standard reagent required to react completely with the analyte was measured.

These classical methods for separating and determining analytes still find use in many laboratories. The extent of their general application is, however, decreasing with the passage of time and with the advent of instrumental methods to supplant them.

1A-2 Instrumental Methods

Early in the twentieth century, chemists began to exploit phenomena other than those used for classical methods for solving analytical problems. Thus, measurements of physical properties of analytes—such as conductivity, electrode potential, light absorption or emission, mass-to-charge ratio, and fluorescence—began to be used for quantitative analysis of a variety of inorganic, organic, and biochemical analytes. Furthermore, highly efficient chromatographic and electrophoretic techniques began to replace distillation, extraction, and precipitation for the separation of components of complex mixtures prior to their qualitative or quantitative determination. These newer methods for separating and determining chemical

species are known collectively as *instrumental methods of analysis.*

Many of the phenomena that instrumental methods are based on have been known for a century or more. Their application by most chemists, however, was delayed by lack of reliable and simple instrumentation. In fact, the growth of modern instrumental methods of analysis has paralleled the development of the electronics and computer industries.

1B TYPES OF INSTRUMENTAL METHODS

For this discussion, it is useful to consider chemical and physical characteristics that are useful for qualitative or quantitative analysis. Table 1-1 lists most of the characteristic properties that are currently used for instrumental analysis. Most of the characteristics listed in the table require a source of energy to stimulate a measurable response from the analyte. For example, in atomic emission an increase in the temperature of the analyte is required to first produce gaseous analyte atoms and then to excite the atoms to higher energy states. The excited-state atoms then emit characteristic electromagnetic radiation, which is the quantity measured by the instrument. Sources of excitation energy may take the form of a rapid thermal change as in the previous example, electromagnetic radiation from a selected region of the spectrum, application of one of the electrical quantities—voltage, current, or charge—or perhaps subtler forms intrinsic to the analyte itself.

Note that the first six entries in Table 1-1 involve interactions of the analyte with electromagnetic radiation. In the first property, radiant energy is produced by

TABLE 1-1 Chemical and Physical Properties Employed in Instrumental Methods

Characteristic Properties	Instrumental Methods
Emission of radiation	Emission spectroscopy (X-ray, UV, visible, electron, Auger); fluorescence, phosphorescence, and luminescence (X-ray, UV, and visible)
Absorption of radiation	Spectrophotometry and photometry (X-ray, UV, visible, IR); photoacoustic spectroscopy; nuclear magnetic resonance and electron spin resonance spectroscopy
Scattering of radiation	Turbidimetry; nephelometry; Raman spectroscopy
Refraction of radiation	Refractometry; interferometry
Diffraction of radiation	X-Ray and electron diffraction methods
Rotation of radiation	Polarimetry; optical rotary dispersion; circular dichroism
Electrical potential	Potentiometry; chronopotentiometry
Electrical charge	Coulometry
Electrical current	Amperometry; polarography
Electrical resistance	Conductometry
Mass	Gravimetry (quartz crystal microbalance)
Mass-to-charge ratio	Mass spectrometry
Rate of reaction	Kinetic methods
Thermal characteristics	Thermal gravimetry and titrimetry; differential scanning colorimetry; differential thermal analyses; thermal conductometric methods
Radioactivity	Activation and isotope dilution methods

the analyte; the next five properties involve changes in electromagnetic radiation brought about by its interaction with the sample. Four electrical properties then follow. Finally, four miscellaneous properties are grouped together: mass-to-charge ratio, reaction rate, thermal characteristics, and radioactivity.

The second column in Table 1-1 lists the names of instrumental methods that are based upon the various physical and chemical properties. Be aware that it is not always easy to select an optimal method from among available instrumental techniques and their classical counterparts. Some instrumental techniques are more sensitive than classical techniques, but others are not. With certain combinations of elements or compounds, an instrumental method may be more selective; with others, a gravimetric or volumetric approach may suffer less interference. Generalizations on the basis of accuracy, convenience, or expenditure of time are equally difficult to draw. Nor is it necessarily true that instrumental procedures employ more sophisticated or more costly apparatus; indeed, the modern electronic analytical balance used for gravimetric determinations is a more complex and refined instrument than some of those used in the other methods listed in Table 1-1.

As noted earlier, in addition to the numerous methods listed in the second column of Table 1-1, there is a group of instrumental procedures that are used for separation and resolution of closely related compounds. Most of these procedures are based upon chromatography or electrophoresis. One of the characteristics listed in Table 1-1 is ordinarily used to complete the analysis following chromatographic separations. Thus, for example, thermal conductivity, ultraviolet and infrared absorption, refractive index, and electrical conductance have been used for this purpose.

This text deals with the principles, the applications, and the performance characteristics of the instrumental methods listed in Table 1-1 and of chromatographic and electrophoretic separation procedures as well. No space is devoted to the classical methods, the assumption being that the reader will have encountered these techniques in earlier studies.

1C INSTRUMENTS FOR ANALYSIS

An instrument for chemical analysis converts information stored in the physical or chemical characteristics of the analyte to information that may be manipulated and interpreted by a human. Thus, an analytical instrument can be viewed as a communication device between the system under study and the investigator. To retrieve the desired information from the analyte, it is necessary to provide a stimulus, which is usually in the form of electromagnetic, electrical, mechanical, or nuclear energy as illustrated in Figure 1-1. The stimulus elicits a response from the system under study whose nature and magnitude are governed by the fundamental laws of chemistry and physics. The resulting information is contained in the phenomena that result from the interaction of the stimulus with the analyte. A familiar example is the passage of a narrow band of wavelengths of visible light through a sample to measure the extent of its absorption by the analyte. The intensity of the light is determined before and after its interaction with the sample, and the ratio of these intensities provides a measure of the analyte concentration.

Generally, instruments for chemical analysis comprise just a few basic components, some of which are listed in Table 1-2. To understand the relationships among these instrument components and the flow of information from the characteristics of the analyte through the components to the numerical or graphical output produced by the instrument, it is instructive to explore the concept of *data domains.*

1C-1 Data Domains

The measurement process is aided by a wide variety of devices that convert information from one form to another. In order to investigate how instruments function, it is important to understand the way in which information is *encoded,* or transformed from one system of information to another, as a characteristic of *electrical signals*—that is, as voltage, current, charge, or variations in these quantities. The various modes of encoding information electrically are called *data domains.* A classification scheme has been developed based on this

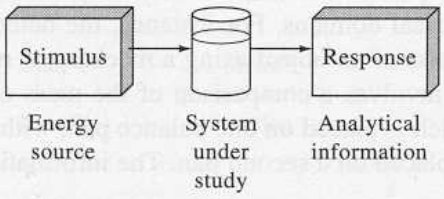

Figure 1-1 Block diagram showing the overall process of an instrumental measurement.

TABLE 1-2 Some Examples of Instrument Components

Instrument	Energy Source (stimulus)	Analytical Information	Input Transducer	Data Domain of Transduced Information	Information Processor	Readout
Photometer	Tungsten lamp, glass filter	Attenuated light beam	Photocell	Electrical current	Meter scale	Current meter
Atomic emission spectrometer	Flame	UV or visible radiation	Photomultiplier tube	Electrical potential	Amplifier, demodulator, monochromator chopper	Chart recorder
Coulometer	DC source	Cell current	Electrodes	Electrical current	Amplifier	Chart recorder
pH meter	Sample/glass electrode	Hydrogen ion activity	Glass-calomel electrodes	Electrical potential	Amplifier, digitizer	Digital unit
X-Ray powder diffractometer	X-Ray tube, sample	Diffracted radiation	Photographic film	Latent image	Chemical developer	Black images on film
Color comparator	Sunlight	Color	Eye	Optic nerve signal	Brain	Visual color response

concept that greatly simplifies the analysis of instrumental systems and promotes understanding of the measurement process.[1] As shown in the data domains map of Figure 1-2, data domains may be broadly classified into *nonelectrical domains* and *electrical domains.*

1C-2 Nonelectrical Domains

The measurement process begins and ends in nonelectrical domains. The physical and chemical characteristics that are of interest in a particular experiment reside in these data domains. Among these characteristics are length, density, chemical composition, intensity of light, pressure, and others listed in the first column of Table 1-1.

It is possible to make a measurement entirely in nonelectrical domains. For instance, the determination of the mass of an object using a mechanical equal-arm balance involves a comparison of the mass of the object, which is placed on one balance pan, with standard masses placed on a second pan. The information repre-

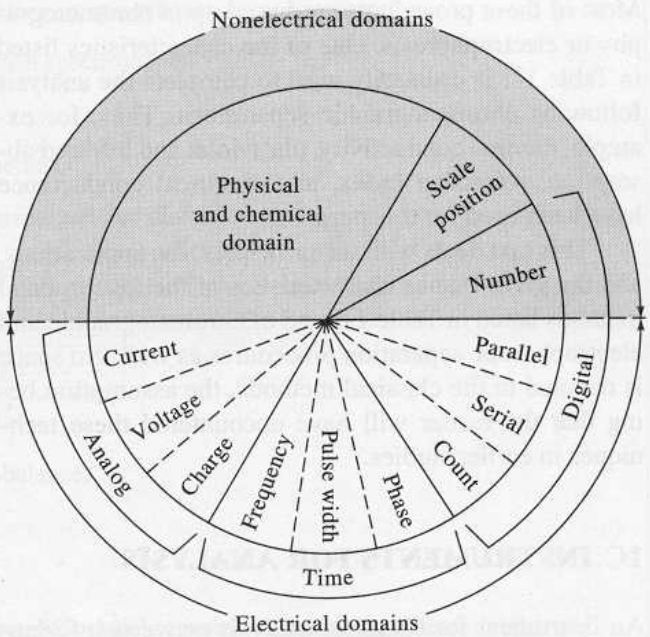

Figure 1-2 Data domains map. The upper (shaded) half of the map comprises nonelectrical domains. The bottom half is made up of electrical domains. Note that the digital domain spans both electrical and nonelectrical domains.

[1] C. G. Enke, *Anal. Chem.*, **1971,** *43,* 69A.

senting the mass of the object in standard units is encoded directly by the experimenter, who provides information processing by summing the masses to arrive at a number. In certain other mechanical balances, the gravitational force on a mass is amplified mechanically by making one of the balance arms longer than the other, thus increasing the resolution of the measurement.

The determination of the linear dimensions of an object with a ruler and the measurement of the volume of a sample of liquid with a graduated cylinder are other examples of measurements carried out exclusively in nonelectrical domains. Such measurements are often associated with classical analytical methods. The advent of inexpensive electronic signal processors, sensitive transducers, and readout devices has led to the development of a host of electronic instruments, which acquire information from nonelectrical domains, process it in electrical domains, and finally present it in nonelectrical domains once again. Electronic devices process information and transform it from one domain to another in ways analogous to the multiplication of mass in mechanical balances with unequal arms. As a consequence of the availability of these electronic devices and their rapid and sophisticated information processing, instruments that rely exclusively on nonelectrical information transfer are rapidly becoming relics of the past. Nonetheless, the information that we seek begins in the properties of the analyte and ends in a number, both of which are nonelectrical domains. The ultimate objective in all measurements is that the final numerical result must be in some manner proportional to the relevant chemical or physical characteristic of the analyte.

1C-3 Electrical Domains

The modes of encoding information as electrical quantities can be subdivided into *analog domains, time domains,* and *digital domains,* as illustrated in the bottom half of the circular map in Figure 1-2. Note that the digital domain spans three electrical domains and one nonelectrical domain because numbers presented on any type of display convey digital information and can also be encoded electrically.

Any measurement process can be represented as a series of *interdomain conversions.* For example, Figure 1-3 illustrates the measurement of the intensity of molecular fluorescence of a sample of tonic water containing a trace of quinine and, in a general way, some of the data-domain conversions that are necessary to arrive at a number expressing the intensity. The intensity of the flu-

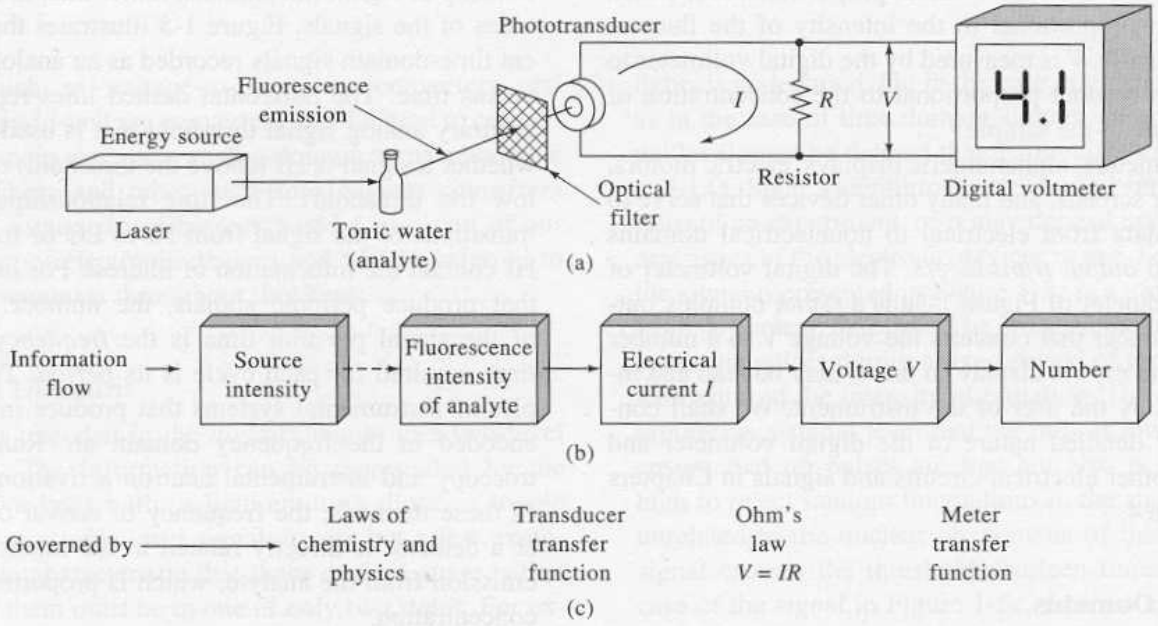

Figure 1-3 A block diagram of a fluorometer showing (a) a general diagram of the instrument, (b) a diagrammatic representation of the flow of information through various data domains in the instrument, and (c) the rules governing the data domain transformations during the measurement process.

orescence is significant in this context because it is proportional to the concentration of the quinine in the tonic water, which is ultimately the information that we desire. The information begins in the solution of tonic water as the concentration of quinine. This information is teased from the sample by applying to it a stimulus in the form of electromagnetic energy from the laser shown in Figure 1-3. The radiation interacts with the quinine molecules in the tonic water to produce fluorescence emission in a region of the spectrum characteristic of quinine and of magnitude proportional to its concentration. Radiation, and thus information, that is unrelated to the concentration of quinine is removed from the beam of light by an optical filter, as shown in Figure 1-3a. The intensity of the fluorescence emission, which is a nonelectrical domain, is encoded into an electrical domain by a special type of device called an *input transducer.* The particular type of transducer used in this experiment is a phototransducer, of which there are numerous types, some of which are discussed in Chapter 7. In this example, the input transducer converts the fluorescence from the tonic water to an electrical current, I, proportional to the intensity of the radiation. The mathematical relationship between the electrical output and the input radiant power impinging on its surface is called the *transfer function* of the transducer.

The current from the phototransducer is then passed through a resistor R, which according to Ohm's law produces a voltage V that is proportional to I, which is in turn proportional to the intensity of the fluorescence. Finally, V is measured by the digital voltmeter to provide a readout proportional to the concentration of the quinine in the sample.

Voltmeters, alphanumeric displays, electric motors, computer screens, and many other devices that serve to convert data from electrical to nonelectrical domains are called *output transducers.* The digital voltmeter of the fluorometer of Figure 1-3a is a rather complex output transducer that converts the voltage V to a number on a liquid crystal display so that it may be read and interpreted by the user of the instrument. We shall consider the detailed nature of the digital voltmeter and various other electrical circuits and signals in Chapters 2 through 4.

Analog Domains

Information in *analog domains* is encoded as the *magnitude* of one of the electrical quantities—voltage, current, charge, or power. These quantities are continuous in both amplitude and time as shown by the typical analog signals of Figure 1-4. Magnitudes of analog quantities can be measured continuously or they can be sampled at specific points in time dictated by the needs of a particular experiment or instrumental method as discussed in Chapter 4. Although the data of Figure 1-4 are recorded as a function of time, any variable such as wavelength, magnetic field strength, or temperature may be the independent variable under appropriate circumstances. The correlation of two analog signals that result from corresponding measured physical or chemical properties is important in a wide variety of instrumental techniques, such as nuclear magnetic resonance spectroscopy, infrared spectroscopy, and differential thermal analysis.

Analog signals are especially susceptible to electrical noise that results from interactions within measurement circuits or from other electrical devices in the vicinity of the measurement system. Such undesirable noise bears no relationship to the information of interest, and methods have been developed to minimize the effects of this unwanted information. Signals, noise, and the optimization of instrumental response are discussed in Chapter 5.

Time Domains

Information is stored in time domains as the time relationship of signal fluctuations, rather than in the amplitudes of the signals. Figure 1-5 illustrates three different time-domain signals recorded as an analog quantity versus time. The horizontal dashed lines represent an arbitrary analog signal threshold that is used to decide whether a signal is HI (above the threshold) or LO (below the threshold). The time relationships between transitions of the signal from HI to LO or from LO to HI contain the information of interest. For instruments that produce periodic signals, the number of cycles of the signal per unit time is the *frequency,* and the time required for each cycle is its *period.* Two examples of instrumental systems that produce information encoded in the frequency domain are Raman spectroscopy and instrumental neutron activation analysis. In these methods, the frequency of arrival of photons at a detector is directly related to the intensity of the emission from the analyte, which is proportional to its concentration.

The time between successive LO to HI transitions is called the *period,* and the time between a LO to HI and a HI to LO transition is called the *pulse width.* De-

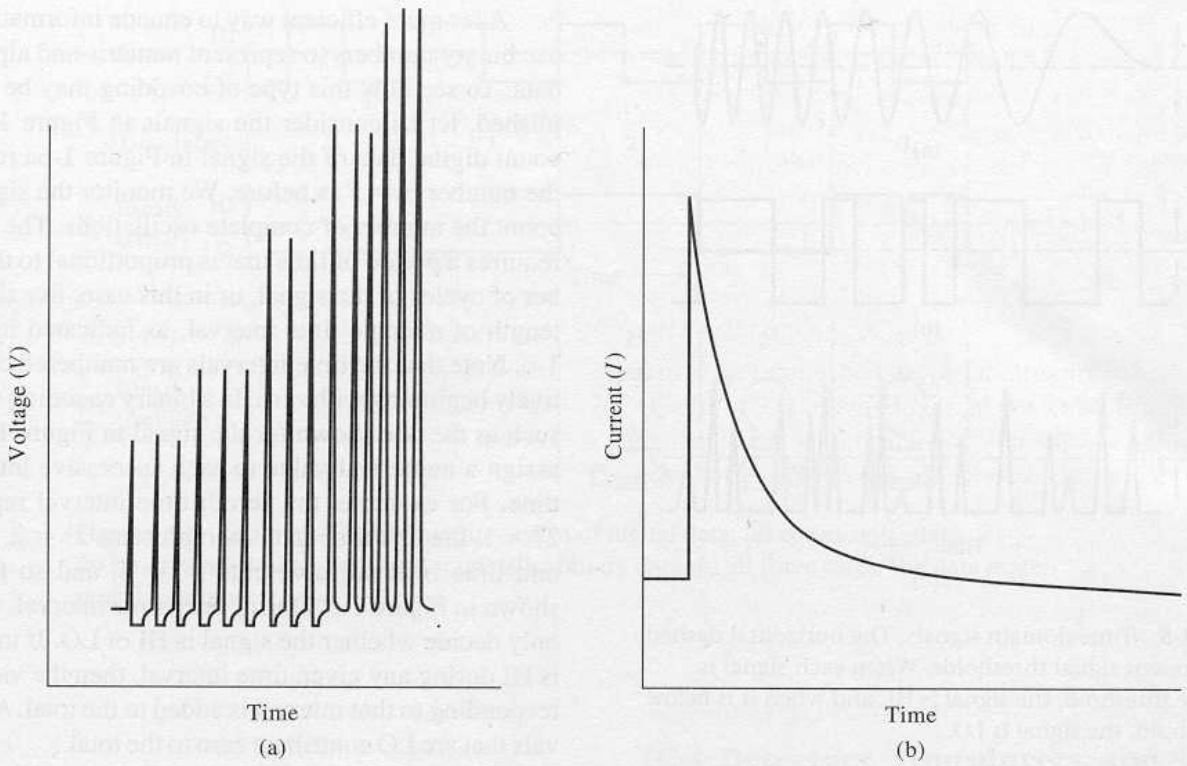

Figure 1-4 Analog signals. (a) Instrument response from the photometric detection system of a flow injection analysis experiment. A stream of reaction mixture containing plugs of red $Fe(SCN)^{2+}$ flows past a monochromatic light source and a phototransducer, which produces a changing voltage as sample concentration changes. (b) The current response of a photomultiplier tube when the light from a pulsed source falls on the photocathode of the device.

vices such as voltage-to-frequency converters and frequency-to-voltage converters may be used to convert time-domain signals to analog-domain signals and vice versa. These and other such *data domain converters* will be discussed in Chapters 3 and 4 as a part of our treatment of electronic devices and will be referred to in other contexts throughout this book.

Digital Domains

Data are encoded in the *digital domain* in a two-level scheme. The information can be represented by the state of a light bulb, a light-emitting diode, a toggle switch, or a logic level signal, to cite but a few examples. The characteristic that these devices share is that each of them must be in one of only two states. For example, lights and switches may be only ON or OFF and logic-level signals may be only HI or LO. The definition of what constitutes ON and OFF for switches and lights is understood, but in the case of electrical signals, as in the case of time domain signals, an arbitrary signal level must be defined that distinguishes between HI and LO. Such a definition may depend on the conditions of an experiment, or it may depend upon the characteristics of the electronic devices in use. For example, the signal represented in Figure 1-5c is a train of pulses from a nuclear detector. The measurement task is to count the pulses during a fixed period of time to obtain a measure of the intensity of radiation. The dashed line represents a signal level that not only is low enough to ensure that no pulses are lost but also is sufficiently high to reject random fluctuations in the signal that are unrelated to the nuclear phenomena of interest. If the signal crosses the threshold fourteen times, as in the case of the signal in Figure 1-5c, then we may be confident that fourteen nuclear events occurred. After the events have been counted, the data are then encoded in the digital domain in the form of the number 14. In

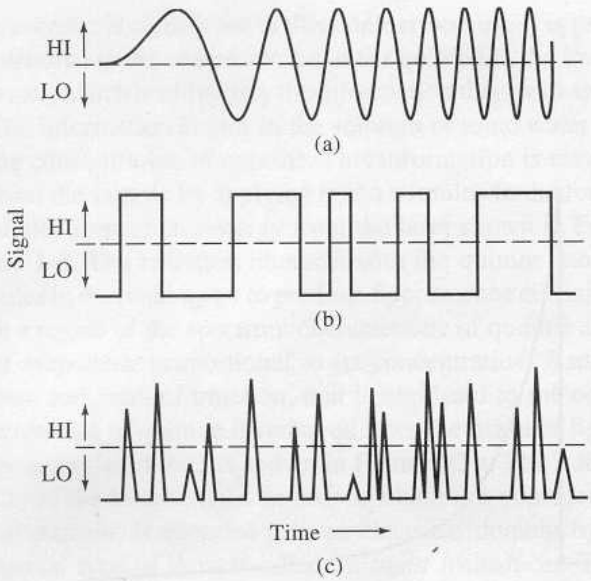

Figure 1-5 Time-domain signals. The horizontal dashed lines represent signal thresholds. When each signal is above the threshold, the signal is HI, and when it is below the threshold, the signal is LO.

Chapter 4, we shall explore the means for making HI-LO electronic decisions and encoding the information in the digital domain.

As suggested by the data domains map of Figure 1-2, the digital domain spans both electrical and non-electrical domains. In the example just cited, the nuclear events are accumulated by using an electronic counter and are displayed on a digital readout. When the experimenter reads and interprets the display, the number that represents the measured quantity is once again in a non-electrical domain. Each piece of HI-LO data that represents a nuclear event is a *bit* of information, which is the fundamental unit of information in the digital domain. Bits of information that are transmitted along a single electronic channel or wire may be counted by an observer or by an electronic device that is monitoring the channel; such accumulated data is termed *count digital data,* which appears in the data-domains map of Figure 1-2. For example, the signal in Figure 1-5a corresponds to the number $n = 8$ because there are eight complete cycles in the signal. The signal in the Figure 1-5b corresponds to $n = 5$, and the signal in Figure 1-5c corresponds to $n = 14$. Although effective, this means of transmitting information is not very efficient.

A far more efficient way to encode information is to use binary numbers to represent numeric and alphabetic data. To see how this type of encoding may be accomplished, let us consider the signals in Figure 1-6. The count digital data of the signal in Figure 1-6a represent the number $n = 5$ as before. We monitor the signal and count the number of complete oscillations. The process requires a period of time that is proportional to the number of cycles of the signal, or in this case, five times the length of a single time interval, as indicated in Figure 1-6. Note that the time intervals are numbered consecutively beginning with zero. In a binary encoding scheme, such as the one shown for the signal in Figure 1-6b, we assign a numerical value to each successive interval of time. For example, the zeroth time interval represents $2^0 = 1$, the first time interval represents $2^1 = 2$, the second time interval represents $2^2 = 4$, and so forth, as shown in Figure 1-6. During each time interval, we need only decide whether the signal is HI or LO. If the signal is HI during any given time interval, then the value corresponding to that interval is added to the total. All intervals that are LO contribute zero to the total.

In Figure 1-6b, the signal is HI only in interval 0 and interval 2, so the total value represented is $1 \times 2^0 + 0 \times 2^1 + 1 \times 2^2 = 5$. Thus, in the space of only three time intervals, the number $n = 5$ has been determined. In the count digital example of the signal in Figure 1-6a, five time intervals were required to determine the same number. In this limited example, the binary-coded serial data is nearly twice as efficient as the count serial data. A more dramatic example may be seen in the counting of $n = 10$ oscillations similar to those of the signal in Figure 1-6a. In the same ten time intervals, ten HI-LO bits of information in the serial binary coding scheme enable the representation of the binary numbers from 0 to $2^{10} = 1024$, or 0000000000 to 1111111111. The improvement in efficiency is 1024/10, or about 100-fold. In other words, the count serial scheme requires 1024 time intervals to represent the number 1024, while the binary coding scheme requires only ten time intervals. As a result of the efficiency of binary coding schemes, most digital information is encoded, transferred, processed, and decoded in some form of binary.

Data represented by binary coding on a single transmission line is called *serial-coded binary data,* or simply *serial data.* A common example of serial data transmission is the computer *modem,* which is a device for transmitting data between computers by telephone over a single conductor (and ground).

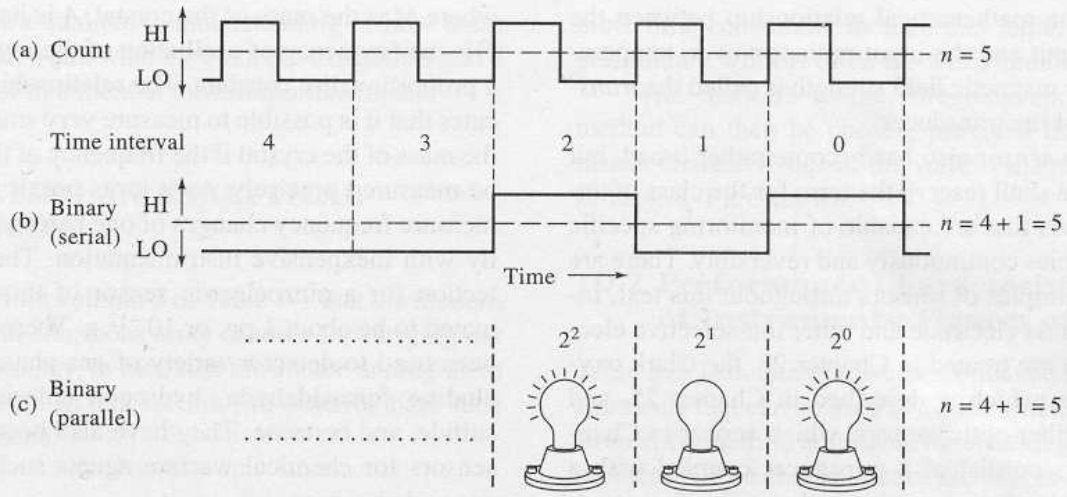

Figure 1-6 Diagram illustrating three types of digital data: (a) count serial data, (b) binary-coded serial data, and (c) parallel binary data. In all three cases, the data represent the number $n = 5$.

A still more efficient method for encoding data in the digital domain is seen in the signal of Figure 1-6c. Here, we use three light bulbs to represent the three binary digits: $2^0 = 1$; $2^1 = 2$; and $2^2 = 4$. However, we could use switches, wires, light-emitting diodes, or any of a host of electronic devices to encode the information. In this scheme, ON = 1 and OFF = 0, so that our number is encoded as shown in Figure 1-6 with the first and third lights ON and the middle light OFF, which represents $4 + 0 + 1 = 5$. This scheme is highly efficient because all of the desired information is presented to us simultaneously, just as all of the digits on the face of the digital voltmeter in Figure 1-3a appear simultaneously. Data presented in this way are referred to as *parallel* digital data. Data are transmitted within analytical instruments and computers by parallel data transmission. Since data usually travel relatively short distances within these devices, it is economical and efficient to use parallel information transfer. This economy of short distances is in contrast to the situation in which data must be transported over long distances from instrument to instrument or from computer to computer. In such instances, communication is carried out serially by using modems or other more sophisticated or faster serial data transmission schemes. We will consider these ideas in somewhat more detail in Chapter 4.

1C-4 Detectors, Transducers, and Sensors

The terms *detector, transducer,* and *sensor* are often used synonymously, but in fact the terms have somewhat different meanings. The most general of the three terms, *detector,* refers to a mechanical, electrical, or chemical device that identifies, records, or indicates a change in one of the variables in its environment, such as pressure, temperature, electrical charge, electromagnetic radiation, nuclear radiation, particulates, or molecules. This term has become a catchall to the extent that entire instruments are often referred to as *detectors.* In the context of instrumental analysis, we shall use the term *detector* in the general sense in which we have just defined it, and we shall use *detection system* to refer to entire assemblies that indicate or record physical or chemical quantities. An example is the UV (ultraviolet) detector often used to indicate and record the presence of eluted analytes in liquid chromatography.

The term *transducer* refers specifically to those devices that convert information in nonelectrical domains to information in electrical domains and the converse. Examples include photodiodes, photomultipliers, and other electronic photodetectors that produce current or voltage proportional to the radiant power of electromagnetic radiation that falls on their surfaces. Other examples include thermistors, strain gauges, and Hall effect magnetic field strength transducers. As suggested

previously, the mathematical relationship between the electrical output and the input radiant power, temperature, force, or magnetic field strength is called the *transfer function* of the transducer.

The term *sensor* also has become rather broad, but in this text we shall reserve the term for the class of analytical devices that are capable of monitoring specific chemical species continuously and reversibly. There are numerous examples of sensors throughout this text, including the glass electrode and other ion-selective electrodes, which are treated in Chapter 23, the Clark oxygen electrode, which is described in Chapter 25, and optrodes, or fiber-optic sensors, which appear in Chapter 7. Sensors consist of a transducer coupled with a chemically selective recognition phase. So, for example, optrodes consist of a phototransducer coupled with a fiber optic that is coated on the end opposite the transducer with a substance that responds specifically to a particular physical or chemical characteristic of an analyte.

A sensor that is especially interesting and instructive is the *quartz crystal microbalance,* or QCM. This device is based on the *piezoelectric* characteristics of quartz. When quartz is mechanically deformed, an electrical potential develops across its surface. Furthermore, when a voltage is impressed across the faces of a quartz crystal, the crystal deforms. A crystal connected in an appropriate electrical circuit oscillates at a frequency that is characteristic of the mass and shape of the crystal and that is amazingly constant—provided that the mass of the crystal is constant. This property of some crystalline materials is called the *piezoelectric effect,* and forms the basis for the quartz-crystal microbalance. Moreover, the characteristic constant frequency of the quartz crystal is the basis for modern high-precision clocks, time bases, counters, timers, and frequency meters, which in turn have led to many highly accurate and precise analytical instrumental systems.

If a quartz crystal is coated with a polymer that selectively adsorbs certain molecules, the mass of the crystal increases if the molecules are present, thus decreasing the resonant frequency of the quartz crystal. When the molecules are desorbed from the surface, the crystal returns to its original frequency. The relationship between the change in frequency of the crystal ΔF and the change in mass of the crystal ΔM is given by

$$\Delta F = \frac{CF^2\Delta M}{A}$$

where M is the mass of the crystal, A is its surface area, F is the frequency of oscillation of the crystal, and C is a proportionality constant. The relationship above indicates that it is possible to measure very small changes in the mass of the crystal if the frequency of the crystal can be measured precisely. As it turns out, it is possible to measure frequency changes of one part in 10^7 quite easily with inexpensive instrumentation. The limit of detection for a piezoelectric sensor of this type is estimated to be about 1 pg, or 10^{-12} g. These sensors have been used to detect a variety of gas-phase analytes including formaldehyde, hydrogen chloride, hydrogen sulfide, and benzene. They have also been proposed as sensors for chemical warfare agents such, as mustard gas and phosgene.

The piezoelectric mass sensor presents an excellent example of a transducer converting a property of the analyte, mass in this case, to a change in an electrical quantity, the resonant frequency of the quartz crystal. This example also illustrates the distinction between a transducer and a sensor. In the quartz-crystal microbalance, the transducer is the quartz crystal, and the selective second phase is the polymeric coating. The combination of the transducer and the selective phase constitute the sensor.

1C-5 Readout Devices

A readout device is a transducer that converts information from an electrical domain to a domain that is understandable by a human observer. Usually, the transduced signal takes the form of the alphanumeric or graphic output of a cathode-ray tube, a series of numbers on a digital display, the position of a pointer on a meter scale, or, occasionally, the blackening of a photographic plate, or a tracing on a recorder paper. In some instances, the readout device may be arranged to give the analyte concentration directly.

1C-6 Microprocessors and Computers in Instruments

Most modern analytical instruments contain or are attached to one or more sophisticated electronic devices and data domain converters, such as operational amplifiers, integrated circuits, analog-to-digital and digital-to-analog converters, counters, microprocessors, and computers. In order to appreciate the power and limitations of such instruments, it is necessary that the scientist de-

velop at least a qualitative understanding of how these devices function and what they can do. Chapters 3 and 4 provide a brief treatment of these important topics.

1D SELECTING AN ANALYTICAL METHOD

It is evident from column 2 of Table 1-1 that the modern chemist has an enormous array of tools for carrying out analyses—so many, in fact, that the choice among them is often difficult. In this section, we describe how such choices are made.

1D-1 Defining the Problem

In order to select an analytical method intelligently, it is essential to define clearly the nature of the analytical problem. Such a definition requires answers to the following questions:

1. What accuracy is required?
2. How much sample is available?
3. What is the concentration range of the analyte?
4. What components of the sample will cause interference?
5. What are the physical and chemical properties of the sample matrix?
6. How many samples are to be analyzed?

The answer to question 1 is of vital importance because it determines how much time and care will be needed for the analysis. The answers to questions 2 and 3 determine how sensitive the method must be and how wide a range of concentrations must be accommodated. The answer to question 4 determines the selectivity required of the method. The answers to question 5 are important because some analytical methods in Table 1-1 are applicable to solutions (usually aqueous) of the analyte. Other methods are more easily applied to gaseous samples, while still other methods are suited to the direct analysis of solids.

The number of samples to be analyzed (question 6) is also an important consideration from the economic standpoint. If this number is large, considerable time and money can be spent on instrumentation, method development, and calibration. Furthermore, if the number is large, a method should be chosen that requires the least operator time per sample. On the other hand, if only a few samples are to be analyzed, a simpler but more time-consuming method that requires little or no preliminary work is often the wiser choice.

With answers to the foregoing six questions, a method can then be chosen, provided that the performance characteristics of the various instruments shown in Table 1-1 are known.

1D-2 Performance Characteristics of Instruments; Figures of Merit

Table 1-3 lists quantitative performance criteria of instruments that can be used to decide whether a given instrumental method is suitable for attacking an analytical problem. These characteristics are expressed in numerical terms that are called *figures of merit.* Figures of merit permit us to narrow the choice of instruments for a given analytical problem to a relatively few. Selection among these few can then be based upon the qualitative performance criteria listed in Table 1-4.

In this section, we define each of the six figures of merit listed in Table 1-3. These figures are then used throughout the remainder of the text in discussing various instruments and instrumental methods.

TABLE 1-3 Numerical Criteria for Selecting Analytical Methods

Criterion	Figure of Merit
1. Precision	Absolute standard deviation, relative standard deviation, coefficient of variation, variance
2. Bias	Absolute systematic error, relative systematic error
3. Sensitivity	Calibration sensitivity, analytical sensitivity
4. Detection limit	Blank plus three times standard deviation of a blank
5. Concentration range	Concentration limit of quantitation (LOQ) to concentration limit of linearity (LOL)
6. Selectivity	Coefficient of selectivity

TABLE 1-4 Other Characteristics to Be Considered in Method Choice

1. Speed
2. Ease and convenience
3. Skill required of operator
4. Cost and availability of equipment
5. Per-sample cost

Precision

As we show in Section a1A, Appendix 1, the precision of analytical data is the degree of mutual agreement among data that have been obtained in the same way. Precision provides a measure of the random, or indeterminate, error of an analysis. Figures of merit for precision include *absolute standard deviation, relative standard deviation, coefficient of variation,* and *variance.* These terms are defined in Table 1-5.

Bias

As shown in Section a1A-2, Appendix 1, bias provides a measure of the systematic, or determinate, error of an analytical method. Bias is defined by the equation

$$\text{bias} = \mu - x_t \qquad (1\text{-}1)$$

where μ is the population mean for the concentration of an analyte in a sample that has a true concentration of x_t. Determining bias involves analyzing one or more standard reference materials whose analyte concentration is known. Sources of such materials are given in references 3 and 4 in Section a1A-2 of Appendix 1. The results from such an analysis will, however, contain both random and systematic errors; but if a sufficient number of analyses are performed, the mean value may be determined with a given level of confidence. As shown in Section a1B-2, Appendix 1, the mean of 20 or 30 replicate analyses can ordinarily be taken as a good estimate of the population mean μ in Equation 1-1. Any difference between this mean and the known value analyte concentration of the standard reference material can be attributed to bias.

If performing 20 replicate analyses on a standard is impractical, the probable presence or absence of bias can be evaluated as shown in Example a1-7 in Appendix 1.

TABLE 1-5 Figures of Merit for Precision of Analytical Methods

Terms	Definition*
Absolute standard deviation, s	$s = \sqrt{\dfrac{\sum_{i=1}^{N}(x_i - \bar{x})^2}{N-1}}$
Relative standard deviation (RSD)	$\text{RSD} = \dfrac{s}{\bar{x}}$
Standard deviation of the mean, s_m	$s_m = s/\sqrt{N}$
Coefficient of variation, CV	$\text{CV} = \dfrac{s}{x} \times 100\%$
Variance	s^2

*x_i = numerical value of the ith measurement.

$\bar{x}$ = mean of N measurements = $\dfrac{\sum_{i=1}^{N} x_i}{N}$

Ordinarily in developing an analytical method, every effort is made to identify the source of bias and eliminate it or correct for it by the use of blanks and by instrument calibration.

Sensitivity

There is general agreement that the sensitivity of an instrument or a method is a measure of its ability to discriminate between small differences in analyte concentration. Two factors limit sensitivity: the slope of the calibration curve and the reproducibility or precision of the measuring device. Of two methods that have equal precision, the one that has the steeper calibration curve will be the more sensitive. A corollary to this statement is that if two methods have calibration curves with equal slopes, the one that exhibits the better precision will be the more sensitive.

The quantitative definition of sensitivity that is accepted by the International Union of Pure and Applied Chemists (IUPAC) is *calibration sensitivity,* which is the slope of the calibration curve at the concentration of interest. Most calibration curves that are used in analytical chemistry are linear and may be represented by the equation

$$S = mc + S_{\text{bl}} \qquad (1\text{-}2)$$

where S is the measured signal, c is the concentration of the analyte, S_{bl} is the instrumental signal for a blank, and m is the slope of the straight line. The quantity S_{bl} should be the y-intercept of the straight line. With such curves, the calibration sensitivity is independent of the concentration c and is equal to m. The calibration sensitivity as a figure of merit suffers from its failure to take into account the precision of individual measurements.

Mandel and Stiehler[2] recognized the need to include precision in a meaningful mathematical statement of sensitivity and proposed the following definition for *analytical sensitivity*, γ:

$$\gamma = m/s_S \tag{1-3}$$

Here, m is again the slope of the calibration curve, and s_S is the standard deviation of the measurement.

The analytical sensitivity offers the advantage of being relatively insensitive to amplification factors. For example, increasing the gain of an instrument by a factor of five will produce a fivefold increase in m. Ordinarily, however, this increase will be accompanied by a corresponding increase in s_S, thus leaving the analytical sensitivity more or less constant. A second advantage of analytical sensitivity is that it is independent of the measurement units for S.

A disadvantage of analytical sensitivity is that it is often concentration dependent since s_S may vary with concentration.

Detection Limit

The most generally accepted qualitative definition of detection limit is that it is the minimum concentration or mass of analyte that can be detected at a known confidence level. This limit depends upon the ratio of the magnitude of the analytical signal to the size of the statistical fluctuations in the blank signal. That is, unless the analytical signal is larger than the blank by some multiple k of the variation in the blank owing to random errors, it is impossible to detect the analytical signal with certainty. Thus, as the limit of detection is approached, the analytical signal and its standard deviation approach the blank signal S_{bl} and its standard deviation s_{bl}. The minimum distinguishable analytical signal S_m is then taken as the sum of the mean blank signal $\bar{S}_{bl}$ plus a multiple k of the standard deviation of the blank. That is,

$$S_m = \bar{S}_{bl} + ks_{bl} \tag{1-4}$$

Experimentally, S_m can be determined by performing 20 to 30 blank measurements, preferably over an extended period of time. The resulting data are then treated statistically to obtain $\bar{S}_{bl}$ and s_{bl}. Finally, the slope from Equation 1-4 is used to convert S_m to c_m, which is defined as the detection limit. That is, the detection limit is given by

$$c_m = \frac{S_m - \bar{S}_{bl}}{m} \tag{1-5}$$

As pointed out by Ingle,[3] numerous alternatives, based correctly or incorrectly on t and z statistics (Section a1B-2, Appendix 1), have been used to determine a value for k in Equation 1-4. Kaiser[4] argues that a reasonable value for the constant is $k = 3$. He points out that it is wrong to assume a strictly normal distribution of results from blank measurements and that when $k = 3$, the confidence level of detection will be 95% in most cases. He further argues that little is to be gained by using a larger value of k—and thus a greater confidence level. Long and Winefordner,[5] in a discussion of detection limits, also recommend the use of $k = 3$.

EXAMPLE 1-1

A least-squares analysis of calibration data for the determination of lead based upon its flame emission spectrum yielded the equation

$$S = 1.12\, c_{Pb} + 0.312$$

where c_{Pb} is the lead concentration in parts per million and S is a measure of the relative intensity of the lead emission line. The following replicate data were then obtained:

Concn, ppm Pb	No. of Replications	Mean Value of S	s
10.0	10	11.62	0.15
1.00	10	1.12	0.025
0.000	24	0.0296	0.0082

[2] J. Mandel and R. D. Stiehler, *J. Res. Natl. Bur. Std.*, **1964,** *A53,* 155.

[3] J. D. Ingle Jr., *J. Chem. Educ.*, **1970,** *42,* 100.

[4] H. Kaiser, *Anal. Chem.*, **1987,** *42,* 53A.

[5] G. L. Long and J. D. Winefordner, *Anal. Chem.*, **1983,** *55,* 712A.

Calculate **(a)** the calibration sensitivity, **(b)** the analytical sensitivity at 1 and 10 ppm of Pb, and **(c)** the detection limit.

(a) By definition, the calibration sensitivity m is the slope of the straight line. Thus, $m = 1.12$.

(b) At 10 ppm Pb, $\gamma = m/s_S = 1.12/0.15 = 7.5$. At 1 ppm Pb, $\gamma = 1.12/0.025 = 45$.

(c) Applying Equation 1-4,

$$S_m = 0.0296 + 3 \times 0.0082 = 0.054$$

Substituting into Equation 1-5 gives

$$c_m = \frac{0.054 - 0.0296}{1.12} = 0.022 \text{ ppm Pb.}$$

Dynamic Range

Figure 1-7 illustrates the definition of the *dynamic range* of an analytical method, which extends from the lowest concentration at which quantitative measurements can be made (limit of quantitation, or LOQ) to the concentration at which the calibration curve departs from linearity (limit of linearity, or LOL). The lower limit of quantitative measurements is generally taken to be equal to ten times the standard deviation of repetitive measurements on a blank, or $10s_{bl}$. At this point, the relative standard deviation is about 30% and decreases rapidly as concentrations become larger. At the limit of detection, the relative standard deviation is 100%.

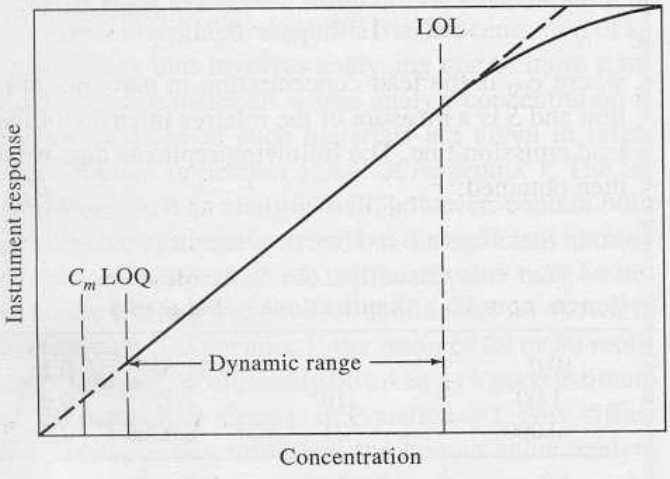

Figure 1-7 Useful range of an analytical method. LOQ = limit of quantitative measurement; LOL = limit of linear response.

To be very useful, an analytical method should have a dynamic range of at least two orders of magnitude. Some methods have applicable concentration ranges of five to six orders of magnitude.

Selectivity

Selectivity of an analytical method refers to the degree to which the method is free from interference by other species contained in the sample matrix. Unfortunately, no analytical method is totally free from interference from other species, and frequently steps must be taken to minimize the effects of these interferences.

Consider, for example, a sample containing an analyte A as well as potential interfering species B and C. If c_A, c_B, and c_C are the concentrations of the three species and m_A, m_B, and m_C are their calibration sensitivities, then the total instrument signal will be given by a modified version of Equation 1-3. That is,

$$S = m_A c_A + m_B c_B + m_C c_C + S_{bl} \qquad (1\text{-}6)$$

Let us now define the selectivity coefficient for A with respect to B as

$$k_{B,A} = m_B/m_A \qquad (1\text{-}7)$$

The selectivity coefficient then gives the relative response of the method to species B as compared with A. A similar coefficient for A with respect to C is

$$k_{C,A} = m_C/m_A \qquad (1\text{-}8)$$

Substituting these relationships into Equation 1-4 leads to

$$S = m_A(c_A + k_{B,A}c_B + k_{C,A}c_C) + S_{bl} \qquad (1\text{-}9)$$

Selectivity coefficients can range from zero (no interference) to values a good deal greater than unity. Note that a coefficient is negative when the interference causes a reduction in the intensity of the output signal of the analyte. For example, if the presence of interferant B causes a reduction in S in Equation 1-7, m_B will carry a negative sign, as will $k_{B,A}$.

Selectivity coefficients are useful figures of merit for describing the selectivity of analytical methods. Unfortunately, they are not widely used except to characterize the performance of ion-selective electrodes (Chapter 23). Example 1-2 illustrates the use of selectivity coefficients when they are available.

EXAMPLE 1-2

The selectivity coefficient for an ion-selective electrode for K^+ with respect to Na^+ is reported to be 0.052. Calculate the relative error in the determination of K^+ in a solution that has a K^+ concentration of 3.00×10^{-3} M if the Na^+ concentration is **(a)** 2.00×10^{-2} M; **(b)** 2.00×10^{-3} M; **(c)** 2.00×10^{-4} M. Assume that S_{bl} for a series of blanks was approximately zero.

(a) Substituting into Equation 1-9 yields

$$S = m_{K^+}(c_{K^+} + k_{Na^+,K^+}c_{Na^+}) + 0$$

$$S/m_{K^+} = 3.00 \times 10^{-3} + 0.052 \times 2.00 \times 10^{-2} = 4.04 \times 10^{-3}$$

If Na^+ were not present

$$S/m_{K^+} = 3.00 \times 10^{-3}$$

The relative error in c_{K^+} will be identical to the relative error in S/m_{K^+} (see Section a1B-5, Appendix 1). Therefore,

$$E_{rel} = \frac{4.04 \times 10^{-3} - 3.00 \times 10^{-3}}{3.00 \times 10^{-3}} \times 100\% = 35\%$$

Proceeding in the same way we find

(b) $E_{rel} = 3.5\%$

(c) $E_{rel} = 0.35\%$

1E CALIBRATION OF INSTRUMENTAL METHODS

With two exceptions, all types of analytical methods require *calibration,* a process that relates the measured analytical signal to the concentration of analyte.[6] The three most common calibration methods include the preparation and use of a calibration curve, the standard addition method, and the internal standard method.

[6] The two exceptions are gravimetric and coulometric methods. In both of these cases, the relationship between the quantity measured and the concentration of analyte can be computed from accurately known physical constants.

1E-1 Calibration Curves

To use the calibration curve technique, several standards containing exactly known concentrations of the analyte are introduced into the instrument, and the instrumental response is recorded. Ordinarily, this response is corrected for the instrument output obtained with a blank. Ideally, the blank contains all of the components of the original sample except for the analyte. The resulting data are then plotted to give a graph of corrected instrument response versus analyte concentration.

Figure 1-8 shows a typical *calibration curve* (also called a *working curve* or an *analytical curve*). Plots, such as this, that are linear over a significant concentration range (the *dynamic range*) are often obtained and are desirable because they are less subject to error than are nonlinear curves. Not uncommonly, however, nonlinear plots are observed, which require a larger number of calibration data to establish accurately the relationship between the instrument response and concentration. Usually, an equation is developed for the calibration curve by a least-squares technique (Appendix a1C) so that sample concentrations can be computed directly.

The success of the calibration curve method is critically dependent upon how accurately the analyte concentrations of the standards are known and how closely the matrix[7] of the standards resemble that of the samples to be analyzed. Unfortunately, matching the matrix of complex samples is often difficult or impossible, and matrix effects lead to interference errors. To minimize matrix effects, it is often necessary to separate the analyte from the *interferent* before measuring the instrument response.

1E-2 Standard Addition Methods

Standard addition methods are particularly useful for analyzing complex samples in which the likelihood of matrix effects is substantial. A standard addition method can take several forms.[8] One of the most common forms involves adding one or more increments of a standard solution to sample aliquots of the same size.

[7] The term *matrix* refers to the collection of all of the various constituents making up an analytical sample. In addition to the analyte, the sample matrix includes all of the other constituents of the sample, which are sometimes referred to as the *concomitants.*

[8] See M. Bader, *J. Chem. Educ.*, **1980,** *57,* 703.

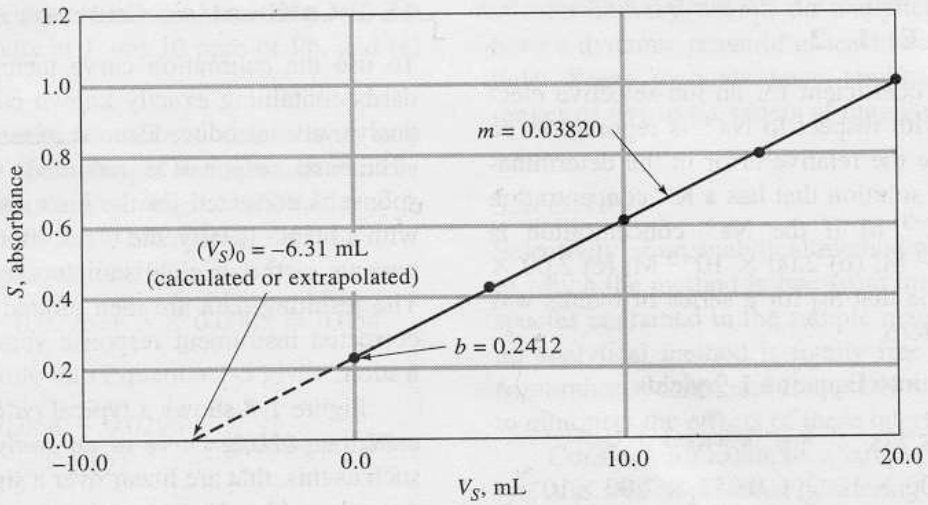

Figure 1-8 Linear calibration plot for the method of standard additions. The concentration of the unknown solution may be calculated from the slope m and the intercept b, or it may be determined by extrapolation as explained in the text.

This process is often called *spiking* the sample. Each solution is then diluted to a fixed volume before measurement. It should be noted that when the amount of sample is limited, standard additions can be carried out by successive introductions of increments of the standard to a single measured volume of the unknown. Measurements are made on the original sample and on the sample plus the standard after each addition. In most versions of the standard addition method, the sample matrix is nearly identical after each addition, the only difference being the concentration of the analyte or, in cases involving the addition of an excess of an analytical reagent, the concentration of the reagent. All other constituents of the reaction mixture should be identical because the standards are prepared in aliquots of the sample.

Assume that several identical aliquots V_x of the unknown solution with a concentration c_x are transferred to volumetric flasks having a volume V_t. To each of these flasks is added a variable volume V_s mL of a standard solution of the analyte having a known concentration c_s. Suitable reagents are then added, and each solution is diluted to volume. Instrumental measurements are then made on each of these solutions to yield an instrument response S. If the instrument response is proportional to concentration, as it must be if the standard addition method is to be applicable, we may write

$$S = \frac{kV_s c_s}{V_t} + \frac{kV_x c_x}{V_t} \tag{1-10}$$

where k is a proportionality constant. A plot of S as a function of V_s is a straight line of the form

$$S = mV_s + b$$

where the slope m and the intercept b are given by

$$m = \frac{kc_s}{V_t}$$

and

$$b = \frac{kV_x c_x}{V_t}$$

Just such a plot is depicted in Figure 1-8.

A least-squares analysis (Section a1C, Appendix 1) can be used to determine m and b; c_x can then be obtained from the ratio of these two quantities and the known values of c_x, V_x, and V_s. Thus,

$$\frac{b}{m} = \frac{kV_x c_x / V_t}{kc_s / V_t} = \frac{V_x c_x}{c_s}$$

or

$$c_x = \frac{bc_s}{mV_x} \tag{1-11}$$

A value for the standard deviation in c_x can then be obtained by assuming that the uncertainties in c_s, V_s, and V_t are negligible with respect to those in m and b. Then, the relative variance of the result $(s_c/c_x)^2$ is assumed to be the sum of the relative variances of m and b. That is,

$$\left(\frac{s_c}{c_x}\right)^2 = \left(\frac{s_m}{m}\right)^2 + \left(\frac{s_b}{b}\right)^2$$

where s_m is the standard deviation of the slope and where s_b is the standard deviation of the intercept. Taking the square root of this equation gives

$$s_c = c_x \sqrt{\left(\frac{s_m}{m}\right)^2 + \left(\frac{s_b}{b}\right)^2} \qquad (1\text{-}12)$$

Alternatively, a manual plot of the data may be constructed, and the linear portion of the plot may be extrapolated to the left of the origin, as shown by the dashed line of Figure 1-8. The difference between the volume of the standard added at the origin (zero) and the value of the volume at the intersection of the straight line with the x-axis, or the x-intercept $(V_x)_0$, is the volume of standard reagent equivalent to the amount of analyte in the sample. In addition, the x-intercept corresponds to zero instrument response, so that we may write

$$S = \frac{kV_s c_s}{V_t} + \frac{kV_x c_x}{V_t} = 0 \qquad (1\text{-}13)$$

By solving Equation 1-13 for c_x, we obtain

$$c_x = -\frac{(V_s)_0 c_s}{V_x}$$

EXAMPLE 1-3

Ten-millimeter aliquots of a natural water sample were pipetted into 50.00-mL volumetric flasks. Exactly 0.00, 5.00, 10.00, 15.00, and 20.00 mL of a standard solution containing 11.1 ppm of Fe^{3+} were added to each, followed by an excess of thiocyanate ion to give the red complex $Fe(SCN)^{2+}$. After dilution to volume, the instrument response S for each of the five solutions, measured with a colorimeter, was found to be 0.240, 0.437, 0.621, 0.809, and 1.009, respectively. **(a)** What was the concentration of Fe^{3+} in the water sample? **(b)** Calculate a standard deviation of the slope and of the intercept and the standard deviation for the concentration of Fe^{3+}.

(a) In this problem, $c_s = 11.1$ ppm, $V_x = 10.00$ mL, and $V_t = 50.00$ mL. A plot of the data, shown in Figure 1-8, demonstrates that there is a linear relationship between the instrument response and the iron concentration.

To obtain the equation for the line in Figure 1-8 ($S = mV_s + b$), we follow the procedure illustrated in Example a1-12 in Appendix 1. The result is $m = 0.03820$ and $b = 0.2412$ and thus

$$S = 0.03820\ V_s + 0.2412$$

Substituting into Equation 1-11 gives

$$c_x = \frac{0.2412 \times 11.1}{0.03820 \times 10.00} = 7.01 \text{ ppm } Fe^{3+}$$

This value may be determined by graphical extrapolation as illustrated in the figure as well. The extrapolated value represents the volume of reagent corresponding to zero instrument response, which in this case is -6.31 mL. The unknown concentration of the analyte in the original solution is then calculated as follows:

$$c_x = -\frac{(V_s)_0 c_s}{V_x} = \frac{6.31 \text{ mL} \times 11.1 \text{ ppm}}{10.00 \text{ mL}} = 7.01 \text{ ppm } Fe^{3+}$$

(b) Equations a1-35 and a1-36 give the standard deviation of the intercept and the slope. That is, $s_b = 3.8 \times 10^{-3}$ and $s_m = 3.1 \times 10^{-4}$.

Substituting into Equation 1-12 gives

$$s_c = 7.01\sqrt{\left(\frac{3.82 \times 10^{-3}}{0.2412}\right)^2 + \left(\frac{3.07 \times 10^{-4}}{0.0382}\right)^2} = 0.12 \text{ ppm } Fe^{3+}$$

In the interest of saving time or sample, it is possible to perform a standard addition analysis by using only two increments of sample. Here, a single addition of V_s mL of standard would be added to one of the two samples, and we can write

$$S_1 = \frac{kV_x c_x}{V_t}$$

$$S_2 = \frac{kV_x c_x}{V_t} + \frac{kV_s c_s}{V_t}$$

where S_1 and S_2 are the analytical signals resulting from the diluted sample and the diluted sample plus standard,

respectively. Dividing the second equation by the first gives upon rearrangement

$$c_x = \frac{S_1 c_s V_s}{(S_2 - S_1)V_x}$$

1E-3 The Internal Standard Method

An *internal standard* is a substance that is added in a constant amount to all samples, blanks, and calibration standards in an analysis. Alternatively, it may be a major constituent of samples and standards that is present in a large enough amount that its concentration can be assumed to be the same in all cases. Calibration then involves plotting the ratio of the analyte signal to the internal standard signal as a function of the analyte concentration of the standards. This ratio for the samples is then used to obtain their analyte concentrations from a calibration curve.

An internal standard, if properly chosen and used, can compensate for several types of both random and systematic errors. Thus, if the analyte and internal standard signals respond proportionally to random instrumental and method fluctuations, the ratio of these signals is independent of these fluctuations. If the two signals are influenced in the same way by matrix effects, compensation of these effects also occurs. In those instances where the internal standard is a major constituent of samples and standards, compensation for errors that arise in sample preparation, solution, and cleanup may also occur.

A major difficulty in applying the internal standard method is that of finding a suitable substance to serve as the internal standard and of introducing that substance into both samples and standards in a reproducible way. The internal standard should provide a signal that is similar to the analyte signal in most ways but sufficiently different so that the two signals are readily distinguishable by the instrument. The internal standard must be known to be absent from the sample matrix so that the only source of the standard is the added amount. For example, lithium is a good internal standard for the determination of sodium or potassium in blood serum because the chemical behavior of lithium is similar to both analytes, but it does not occur naturally in blood.

As an example, the internal standard method is often used in the determination of trace elements in metals by emission spectroscopy. Thus, in determining parts per million of antimony and tin in lead to be used for the manufacture of storage batteries, the relative intensity of a strong line for each of the minor constituents might be compared with the intensity of a weak line for lead. Ordinarily, these ratios would be less affected by variables that arise in causing the samples to emit radiation. In the development of any new internal standard method, we must verify that changes in concentration of analyte do not affect the signal intensity that results from the internal standard. In order for such a procedure to be successful, a good deal of time and effort would need to be expended in preparing a set of pure lead samples that contains exactly known concentrations of antimony and tin.

1F QUESTIONS AND PROBLEMS

1-1 What is a transducer in an analytical instrument?

1-2 What is the information processor in an instrument for measuring the color of a solution visually?

1-3 What is the detector in a spectrograph in which spectral lines are recorded photographically?

1-4 What is the transducer in a smoke detector?

1-5 What is a data domain?

1-6 What are analog domains? How is information encoded in analog domains?

1-7 List four output transducers and describe how they are used.

1-8 What is a figure of merit?

1-9 The following calibration data were obtained by an instrumental method for the determination of the species X in aqueous solution.

Concn X, C_X ppm	No. Replications, N	Mean Analytical Signal, S	Standard Deviation, ppm
0.00	25	0.031	0.0079
2.00	5	0.173	0.0094
6.00	5	0.422	0.0084
10.00	5	0.702	0.0084
14.00	5	0.956	0.0085
18.00	5	1.248	0.0110

(a) Calculate the calibration sensitivity.
(b) Calculate the analytical sensitivity at each concentration.
(c) Calculate the coefficient of variation for the mean for each of the replicate sets.
(d) What is the detection limit for the method?

1-10 A 25.0-mL sample containing Cu^{2+} gave an instrument signal of 23.6 units (corrected for a blank). When exactly 0.500 mL of 0.0287 M $Cu(NO_3)_2$ was added to the solution, the signal increased to 37.9 units. Calculate the molar concentration of Cu^{2+} assuming that the signal was directly proportional to the analyte concentration.

1-11 Exactly 5.00-mL aliquots of a solution containing phenobarbital were measured into 50.00-mL volumetric flasks and made basic with KOH. The following volumes of a standard solution of phenobarbital containing 2.000 μg/mL of phenobarbital were then introduced into each flask and the mixture was diluted to volume: 0.000, 0.500, 1.00, 1.50, and 2.00 mL. A fluorometer reading for each of these solutions was 3.26, 4.80, 6.41, 8.02, and 9.56, respectively.
(a) Plot the data.
(b) Using the plot from (a), calculate the concentration of phenobarbital in the unknown.
(c) Derive a least-squares equation for the data.
(d) Compute the concentration of phenobarbital from the equation in (c).
(e) Calculate a standard deviation for the concentration obtained in (d).