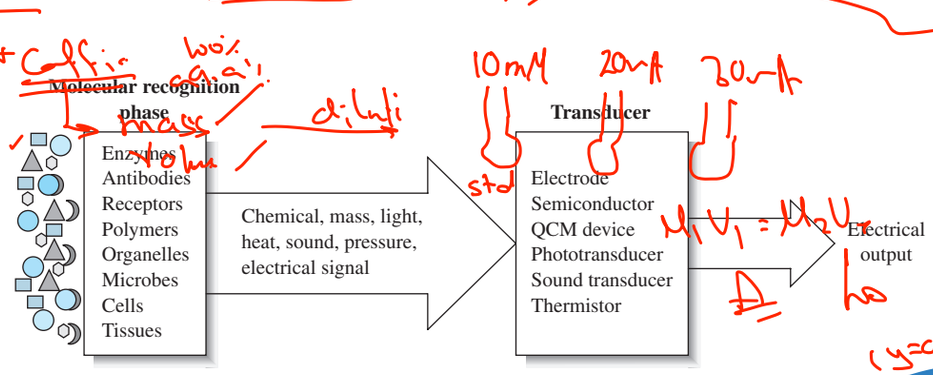

FIGURE 1-7 Chemical sensor. The sensor consists of a molecular recognition element and a transducer. A wide variety of recognition elements are possible. Shown here are some fairly selective recognition elements particularly useful with biosensors. The recognition phase converts the information of interest into a detectable characteristic, such as another chemical, mass, light, or heat. The transducer converts the characteristic into an electrical signal that can be measured.

difference 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 as long as the mass of the crystal is constant. This property of some crystalline materials is called the *piezoelectric effect* and forms the basis for the QCM. 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. This relationship 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 1 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 QCM, 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 form that is understandable by a human observer. Usually, the transduced signal takes the form of the alphanumeric or graphical 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 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. To appreciate the power and limitations of such instruments, investigators need to develop 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 CALIBRATION OF INSTRUMENTAL METHODS

A very important part of all analytical procedures is the calibration and standardization process. *Calibration* determines the relationship between the analytical response and the analyte concentration. Usually this is determined by the use of *chemical standards*.

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Almost all analytical methods require some type of calibration with chemical standards. Gravimetric methods and some coulometric methods (Chapter 24) are among the few *absolute* methods that do not rely on calibration with chemical standards. Several types of calibration procedures are described in this section.

1D-1 Comparison with Standards

Two types of comparison methods are described here, the direct comparison technique and the titration procedure.

Direct Comparison

Some analytical procedures involve comparing a property of the analyte (or the product of a reaction with the analyte) with standards such that the property being tested matches or nearly matches that of the standard. For example, in early colorimeters, the color produced as the result of a chemical reaction of the analyte was compared with the color produced by reaction of standards. If the concentration of the standard was varied by dilution, for example, it was possible to obtain a fairly exact color match. The concentration of the analyte was then equal to the concentration of the standard after dilution. Such a procedure is called a *null comparison* or *isomation method*.[3]

Titrations

Titrations are among the most accurate of all analytical procedures. In a *titration*, the analyte reacts with a standardized reagent (the titrant) in a reaction of known stoichiometry. Usually the amount of titrant is varied until chemical equivalence is reached, as indicated by the color change of a chemical indicator or by the change in an instrument response. The amount of the standardized reagent needed to achieve chemical equivalence can then be related to the amount of analyte present. The *titration* is thus a type of chemical comparison.[4]

1D-2 External-Standard Calibration

An *external standard* is prepared separately from the sample. By contrast, an *internal standard* is added to the sample itself. External standards are used to calibrate instruments and procedures when there are no interference effects from matrix components in the analyte solution. A series of such external standards containing the analyte in known concentrations is prepared. Ideally, three or more such solutions are used in the calibration process. However, in some routine analyses, two-point calibrations can be reliable.

Calibration is accomplished by obtaining the response signal (absorbance, emission intensity, electrode potential, peak area) as a function of the known analyte concentration. A calibration curve is prepared by plotting the data or by fitting them to a suitable mathematical equation, such as the slope-intercept form used in the method of linear least squares. The next step is the prediction step, where the response signal is obtained for the sample and used to *predict* the unknown analyte concentration, c_x, from the calibration curve or best-fit equation. The concentration of the analyte in the original bulk sample is then calculated from c_x by applying the appropriate dilution factors from the sample preparation steps.

The Least-Squares Method

A typical calibration curve is shown in Figure 1-8 for the determination of Ni(II) by reaction with excess thiocyanate to form an absorbing complex $[Ni(SCN)^+]$. The absorbance of the complex is measured for a series of Ni(II) standard solutions and plotted as a function of Ni(II) concentration. The ordinate is the dependent variable, absorbance, and the abscissa is the independent variable, concentration of Ni(II). As is typical and usually desirable, the plot approximates a straight line. Note, however, that because of the indeterminate errors in the measurement process, not all the data fall exactly on the line. Thus, the investigator must try to draw the "best" straight line among the data points. *Regression analysis* provides the means for objectively obtaining such a line and also for specifying the uncertainties associated with its subsequent use. The uncertainties are related to the *residuals* shown in Figure 1-8, which are a measure of how far away from the best straight line the data points lie. The *method of least squares* (see Appendix 1, Section a1D) is often applied to obtain the equation for the line.[5]

The method of least squares is based on two assumptions. The first is that there is actually a linear relationship between the measured response y and the standard analyte concentration x. The mathematical relationship that describes this assumption is called the *regression model*, which may be represented as

$$y = mx + b$$

where b is the y intercept (the value of y when x is zero) and m is the slope of the line (see Figure 1-8). We also assume that any deviation of the individual points from the straight line arises from error in the *measurement*. That is, we assume there is no error in the x values of the points (concentrations). Both of these assumptions are appropriate for many analytical methods, but bear in mind that whenever there is significant uncertainty in the x data, basic linear least-squares analysis may not give the best straight line. In such a case, a more complex *correlation analysis* may be necessary. In addition, basic least-squares



Tutorial: Learn more about **calibration** at www.tinyurl.com/skoogpia7.

[3]See, for example, H. V. Malmstadt and J. D. Winefordner, *Anal. Chim. Acta*, **1959**, *20*, 283. **DOI**: 10.1016/0003-2670(59)80066-0; I. Ramaley and C. G. Enke, *Anal. Chem.*, 1965, 37, 1073. DOI: 10.1021/ac60227a041.

[4]See D. A. Skoog, D. M. West, F. J. Holler, and S. R. Crouch, *Fundamentals of Analytical Chemistry*, 9th ed., Belmont, CA: Brooks/Cole, 2014, Chaps. 13–17.

[5]For a discussion of using spreadsheets in linear regression analysis, see S. R. Crouch and F. J. Holler, *Applications of Microsoft® Excel in Analytical Chemistry*, 3rd ed., Belmont, CA: Cengage Learning, 2017, Chap. 4.

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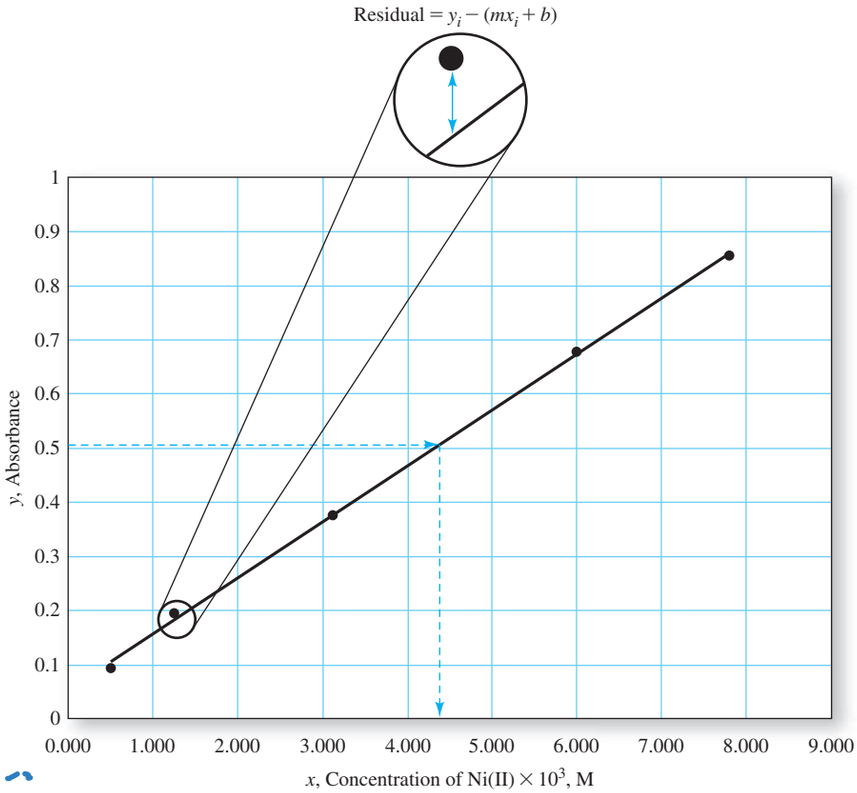

FIGURE 1-8 Calibration curve for the determination of Ni(II) by formation of an absorbing species. The absorbance of standards are shown as solid circles. The distance on the *y*-axis between a data point and the predicted line is called a *residual* as shown in the inset. The calibration curve is used in an inverse fashion to find the concentration of an unknown.

analysis may not be appropriate when the uncertainties in the y values vary significantly with x. In this case, it may be necessary to apply different weighting factors to the points and perform a *weighted least-squares analysis*.[6]

In cases where the data do not fit a linear model, nonlinear regression methods are available.[7] Some of these use polynomial models or multiple regression procedures. There are even computer programs that will find a model that describes a set of experimental data from an internal or user-defined set of equations.

The slope m and intercept b of the linear least-squares line are determined as in Equations a1-34 and a1-35 of Appendix 1. For determining an unknown concentration c_x from the least-squares line, the value of the instrument response y_c is obtained for the unknown, and the slope and intercept are used to calculate the unknown concentration c_x as shown in Equation 1-1.

$$c_x = \frac{y_c - b}{m} \tag{1-1}$$

The standard deviation in concentration s_c can be found from the *standard error of the estimate* s_y, also called the *standard deviation about regression*, as given in Equation 1-2,

$$s_c = \frac{s_y}{m}\sqrt{\frac{1}{M} + \frac{1}{N} + \frac{(\bar{y}_c - \bar{y})^2}{m^2 S_{xx}}} \tag{1-2}$$

where M is the number of replicate results, N is the number of points in the calibration curve (number of standards), $\bar{y}_c$ is the mean response for the unknown, and $\bar{y}$ is the mean value of y for the calibration results. The quantity S_{xx} is the sum of the squares of the deviations of x values from the mean as given in Equation a1-31 of Appendix 1.

Errors in External-Standard Calibration

When external standards are used, it is assumed that the same responses will be obtained when the same analyte concentration

[6]See P. R. Bevington and D. K. Robinson, *Data Reduction and Error Analysis for the Physical Sciences*, 3rd ed., New York: McGraw-Hill, 2003; for an Excel approach to weighted linear regression, see S. R. Crouch and F. J. Holler, *Applications of Microsoft® Excel in Analytical Chemistry*, 3rd ed., Belmont, CA: Cengage Learning, 2017, pp. 331–337.

[7]J. L. Devore, *Probability and Statistics for Engineering and the Sciences*, 9th ed., Pacific Grove, CA: Duxbury Press at Brooks/Cole, 2016.

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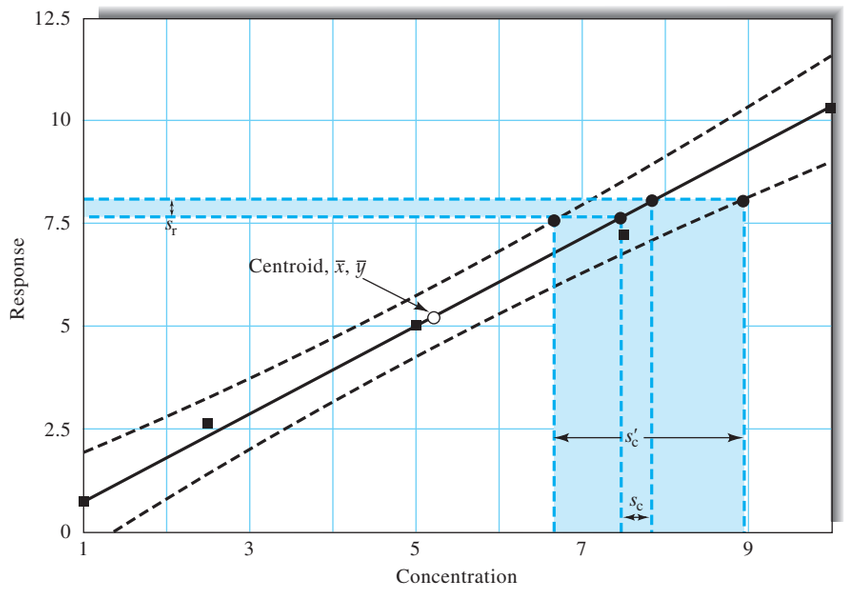

FIGURE 1-9 Effect of calibration curve uncertainty. The dashed lines show confidence limits for concentrations determined from the regression line. Note that uncertainties increase at the extremities of the plot. Usually, we estimate the uncertainty in analyte concentration only from the standard deviation of the response. Calibration curve uncertainty can significantly increase the uncertainty in analyte concentration from s_c to s_c'.

is present in the sample and in the standard. Thus, the calibration functional relationship between the response and the analyte concentration must apply to the sample as well. Usually, in a determination, the raw response from the instrument is not used. Instead, the raw analytical response is corrected by measuring a *blank*. An *ideal blank* is identical to the sample but without the analyte. In practice, with complex samples, it is too time-consuming or impossible to prepare an ideal blank and a compromise must be made. Most often a real blank is either a *solvent blank*, containing the same solvent in which the sample is dissolved, or a *reagent blank*, containing the solvent plus all the reagents used in sample preparation.

Even with blank corrections, several factors can cause the basic assumption of the external-standard method to break down. Matrix effects, due to extraneous species in the sample that are not present in the standards or blank, can cause the same analyte concentrations in the sample and standards to give different responses.[8] Differences in experimental variables at the times at which blank, sample, and standard are measured can also invalidate the established calibration function. Even when the basic assumption is valid, errors can still occur because of contamination during the sampling or sample preparation steps.

[8]The *matrix* includes the analyte and other constituents, which are termed *concomitants*.

Also, systematic errors can occur during the calibration process. For example, if the standards are prepared incorrectly, an error will occur. The accuracy with which the standards are prepared depends on the accuracy of the gravimetric and volumetric techniques and equipment used. The chemical form of the standards must be identical to that of the analyte in the sample; the state of oxidation, isomerization, or complexation of the analyte can alter the response. Once prepared, the concentration of the standards can change because of decomposition, volatilization, or adsorption onto container walls. Contamination of the standards can also result in higher analyte concentrations than expected. A systematic error can occur if there is some bias in the calibration model. For example, errors can occur if the calibration function is obtained without using enough standards to obtain good statistical estimates of the parameters.

Random errors can also influence the accuracy of results obtained from calibration curves, as illustrated in Figure 1-9. The uncertainty in the concentration of analyte s_c' obtained from a calibration curve is lowest when the response is close to the mean value $\bar{y}$. The point $\bar{x}, \bar{y}$ represents the centroid of the regression line. Note that measurements made near the center of the curve will give less uncertainty in analyte concentration than those made at the extremes.

Multivariate Calibration

The least-squares procedure just described is an example of a univariate calibration procedure because only one response is

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used per sample. The process of relating multiple instrument responses to an analyte or a mixture of analytes is known as *multivariate calibration*. Multivariate calibration methods[9] have become quite popular in recent years as new instruments become available that produce multidimensional responses (absorbance of several samples at multiple wavelengths, mass spectrum of chromatographically separated components, etc.). Multivariate calibration methods are very powerful. They can be used to simultaneously determine multiple components in mixtures and can provide redundancy in measurements to improve precision because repeating a measurement N times provides a $\sqrt{N}$ improvement in the precision of the mean value (see Appendix 1, Section a1B-1). They can also be used to detect the presence of interferences that would not be identified in a univariate calibration.

1D-3 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.[10] One of the most common forms involves adding one or more increments of a standard solution to sample aliquots containing identical volumes. This process is often called *spiking* the sample. Each solution is then diluted to a fixed volume before measurement. Note 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 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 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 and corrected for any blank response to yield a net instrument response S. If the blank-corrected instrument response is proportional to concentration, as is assumed in the standard-addition method, we may write

$$S = \frac{kV_s c_s}{V_t} + \frac{kV_x c_x}{V_t} \tag{1-3}$$

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

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

Such a standard-addition plot is shown in Figure 1-10.

A least-squares analysis (Appendix 1, Section a1D) 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_s, 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

$$c_x = \frac{bc_s}{mV_x} \tag{1-4}$$

The standard deviation in concentration can then be obtained by first calculating the standard deviation in volume s_V and then using the relationship between volume and concentration. The standard deviation in volume is found from Equation 1-2 with a few alterations. Because we extrapolate the calibration curve to the x-axis in the standard-addition method, the value of y for the unknown is 0 and the $1/M$ term is absent. Hence, the equation for s_V becomes

$$s_V = \frac{s_y}{m}\sqrt{\frac{1}{N} + \frac{(0 - \bar{y})^2}{m^2 S_{xx}}} \tag{1-5}$$

As shown by the dashed line of Figure 1-10, 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 $(V_s)_0$, 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

$$S = \frac{kV_s c_s}{V_t} + \frac{kV_x c_x}{V_t} = 0 \tag{1-6}$$

By solving Equation 1-6 for c_x, we obtain

$$c_x = -\frac{(V_s)_0 c_s}{V_x} \tag{1-7}$$

The standard deviation in concentration s_c is then

$$s_c = s_V\left(\frac{c_s}{V_x}\right) \tag{1-8}$$

[9] For a more extensive discussion, see K. Varmuza and P. Filzmoser, *Introduction to Multivariate Statistical Analysis in Chemometrics*, Boca Raton, FL: CRC Press, 2009; K. R. Beebe, R. J. Pell, and M. B. Seasholtz, *Chemometrics: A Practical Guide*, New York: Wiley, 1998, Chap. 5; H. Martens and T. Naes, *Multivariate Calibration*, New York: Wiley, 1989.

[10] See M. Bader, *J. Chem. Educ.*, **1980**, *57*, 703, **DOI**: 10.1021/ed057p703.

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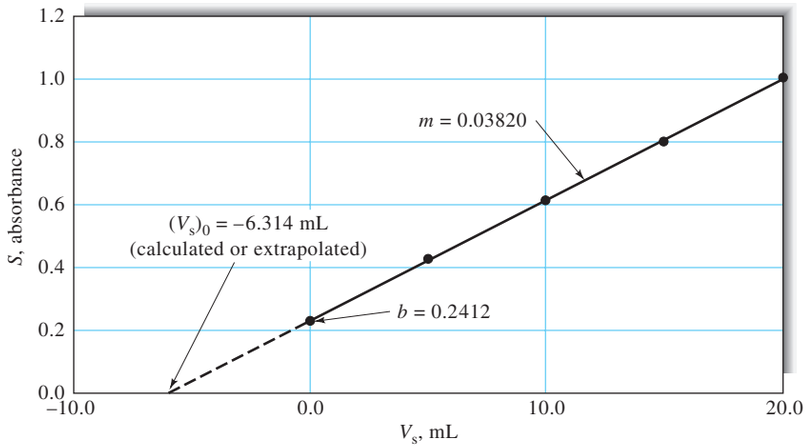

FIGURE 1-10 Linear calibration plot for the method of standard additions. The concentration of the unknown solution may be calculated from the slope m and the intercept b, or it may be determined by extrapolation, as explained in the text.

Example 1-1 shows the uses of these quantities.

EXAMPLE 1-1

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 the standard deviation in the concentration of Fe^{3+}.

Solution

(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 1-10, demonstrates that there is a linear relationship between the solution absorbance and the added amount of iron.

To obtain the equation for the line in Figure 1-10 ($S = mV_s + b$), we follow the procedure illustrated in Example a1-11 in Appendix 1. The result, shown in the spreadsheet in Figure 1-11, is $m = 0.0382$ and $b = 0.2412$ and thus

$$S = 0.0382V_s + 0.2412$$

From Equation 1-4, or from the spreadsheet, we obtain

$$c_x = \frac{0.2412 \times 11.1}{0.0382 \times 10.00} = 7.01 \text{ ppm } Fe^{3+}$$

This value may be determined by graphical extrapolation as the figure also illustrates. The extrapolated value represents the volume of reagent corresponding to zero instrument response (absorbance), which in this case is −6.314 mL. The unknown concentration of the analyte in the original solution is then calculated from Equation 1-7 as follows:

$$c_x = -\frac{(V_s)_0 c_s}{V_x} = \frac{6.314 \text{ mL} \times 11.1 \text{ ppm}}{10.00 \text{ mL}}$$

$$= 7.01 \text{ ppm } Fe^{3+}$$

(b) The standard deviation in concentration can be obtained from the standard deviation in the volume intercept (Equation 1-5) and Equation 1-8 as shown in the spreadsheet of Figure 1-11. The result is $s_c = 0.16$ ppm. Hence, the concentration of Fe in the unknown is 7.01 ± 0.16 ppm.

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 signals resulting from the diluted sample and the diluted sample plus standard, respectively. Dividing the second equation by the first gives, after rearranging,

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

The single-addition method is somewhat dangerous because it presumes a linear relationship and provides no check of this assumption. The multiple-addition method at least gives a check on the linearity supposition.

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	A	B	C	D	E	F	G	H	I	J
1	**Determination of Fe in Natural Water by Colorimetry with Multiple Additions**									
2	Concentration of standard, c_s	11.10	ppm							
3	Volume of unknown used, V_x	10.00	mL							
4	**Volume of standard added**	**Absorbance, *A***								
5	0.00	0.240								
6	5.00	0.437								
7	10.00	0.621								
8	15.00	0.809								
9	20.00	1.009								
10										
11	**Regression Equation**									
12	Slope	0.0382								
13	Intercept	0.2412								
14	Volume intercept	-6.31414								
15	Concentration of unknown	7.01	ppm							
16	**Error Analysis**									
17	Standard error in *y*	0.004858								
18	*N*	5								
19	S_{xx}	250								
20	*y* bar	0.6232								
21	Standard deviation in volume	0.143011								
22	Standard deviation in *c*	0.16								
23	**Spreadsheet Documentation**									
24	Cell B12=SLOPE(B5:B9,A5:A9)									
25	Cell B13=INTERCEPT(B5:B9,A5:A9)									
26	Cell B14=-B13/B12									
27	Cell B15=-B14*B2/B3									
28	Cell B17=STEYX(B5:B9,A5:A9)									
29	Cell B18=COUNT(B5:B9)									
30	Cell B19=DEVSQ(A5:A9)									
31	Cell B20=AVERAGE(B5:B9)									
32	Cell B21=(B17/B12)*SQRT(1/B18+((0-B20)^2)/((B12^2)*B19))									
33	Cell B22=B21*B2/B3									

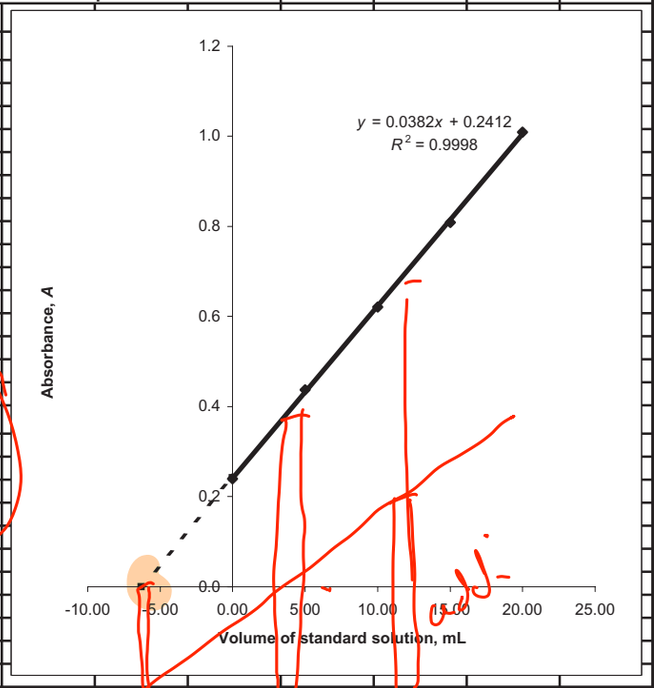

FIGURE 1-11 Spreadsheet for standard-addition Example 1-1.

1D-4 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 such 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 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.

An example of the determination of sodium in blood by flame spectrometry using lithium as an internal standard is shown in Figure 1-12. The upper figure shows the normal calibration curve of sodium intensity versus sodium concentration in ppm. Although a fairly linear plot is obtained, quite a bit of scatter is observed. The lower plot shows the intensity ratio of sodium to lithium plotted against the sodium concentration in ppm. Note the improvement in the calibration curve when the internal standard is used.

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 and that the internal standard does not suppress or enhance the analyte signal.

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	A	B	C	D	E	F	G	H	I	J	K
1	**Method of internal standards for flame spectrometry**										
2	1000 ppm Li added as internal standard										
3	Na conc., ppm	I_{Na}	I_{Li}	I_{Na}/I_{Li}							
4	0.10	0.11	86	0.001279							
5	0.50	0.52	80	0.0065							
6	1.00	1.8	128	0.014063							
7	5.00	5.9	91	0.064835							
8	10.00	9.5	73	0.130137							
9	Unknown	4.4	95	0.046316							
10	**Regression equation**										
11	Slope	0.012975									
12	Intercept	0.000285									
13	Concentration of unknown	3.54759									
14	**Error analysis**										
15	Standard error in *y*	0.000556									
16	*N*	5									
17	S_{xx}	71.148									
18	*y* bar (average ratio)	0.043363									
19	*M*	1									
20	Standard deviation in *c*	0.046925									
21	**Documentation**										
22	Cell D4=B4/C4										
23	Cell B11=SLOPE(D4:D8,A4:A8)										
24	Cell B12=INTERCEPT(D4:D8,A4:A8)										
25	Cell B13=(D9-B12)/B11										
26	Cell B15=STEYX(D4:D8,A4:A8)										
27	Cell B16=COUNT(A4:A8)										
28	Cell B17=DEVSQ(A4:A8)										
29	Cell B18=AVERAGE(D4:D8)										
30	Cell B19=enter no. of replicates										
31	Cell B20=B15/B11*SQRT(1/B19+1/B16+((D9-B18)^2)/((B11^2)*B17))										
32											
33											

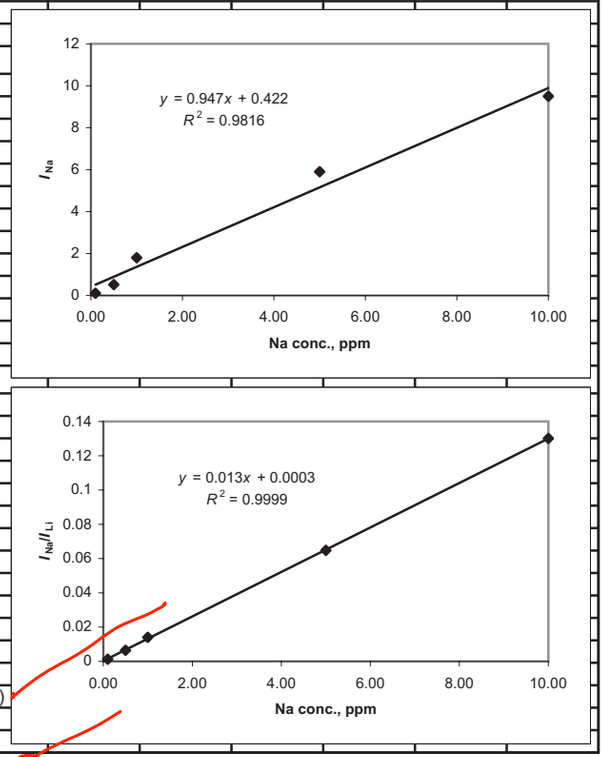

FIGURE 1-12 Spreadsheet to illustrate the internal-standard method for the flame spectrometric determination of sodium.

1E SELECTING AN ANALYTICAL METHOD

Column 2 of Table 1-1 shows that today we have an enormous array of tools for performing chemical analyses. There are so many, in fact, that the choice among them is often difficult. In this section, we briefly describe how such choices are made.

1E-1 Defining the Problem

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 might 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, and 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 an 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 these six questions, a method can then be chosen, provided that the performance characteristics of the various instruments shown in Table 1-1 are known.

1E-2 Performance Characteristics of Instruments

Table 1-3 lists quantitative instrument performance criteria that can be used to decide whether a given instrumental method is suitable for attacking an analytical problem.

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