Chapter 1

Introduction to Analytical Chemistry

Chapter Overview

Chemistry is the study of matter, including its composition, its structure, its physical properties, and its reactivity. Although there are many ways to study chemistry, traditionally we divide it into five areas: organic chemistry, inorganic chemistry, biochemistry, physical chemistry, and analytical chemistry. This division is historical and, perhaps, arbitrary, as suggested by current interest in interdisciplinary areas, such as bioanalytical chemistry and organometallic chemistry. Nevertheless, these five areas remain the simplest division that spans the discipline of chemistry.

Each of these traditional areas of chemistry brings a unique perspective to how a chemist makes sense of the diverse array of elements, ions, and molecules (both small and large) that make up our physical environment. An undergraduate chemistry course, therefore, is much more than a collection of facts; it is, instead, the means by which we learn to see the chemical world from a different perspective. In keeping with this spirit, this chapter introduces you to the field of analytical chemistry and highlights the unique perspectives that analytical chemists bring to the study of chemistry.

1A What is Analytical Chemistry?

"Analytical chemistry is what analytical chemists do."

This quote is attributed to C. N. Reilly (1925-1981) on receipt of the 1965 Fisher Award in Analytical Chemistry. Reilly, who was a professor of chemistry at the University of North Carolina at Chapel Hill, was one of the most influential analytical chemists of the last half of the twentieth century.

Let's begin with a deceptively simple question: What is analytical chemistry? Like all areas of chemistry, analytical chemistry is so broad in scope and so much in flux that it is difficult to find a simple definition more revealing than that quoted above. In this chapter we will try to expand upon this simple definition by saying a little about what analytical chemistry is, as well as a little about what analytical chemistry is not.

For another view of what constitutes analytical chemistry, see the article "Quo Vadis, Analytical Chemistry?", the full reference for which is Valcárcel, M. *Anal. Bioanal. Chem.* **2016**, *408*, 13-21.

Analytical chemistry often is described as the area of chemistry responsible for characterizing the composition of matter, both qualitatively (Is there lead in this paint chip?) and quantitatively (How much lead is in this paint chip?). As we shall see, this description is misleading.

Most chemists routinely make qualitative and quantitative measurements. For this reason, some scientists suggest that analytical chemistry is not a separate branch of chemistry, but simply the application of chemical knowledge.[1] In fact, you probably have performed many such quantitative and qualitative analyses in other chemistry courses.

You might, for example, have determined the concentration of acetic acid in vinegar using an acid–base titration, or used a qual scheme to identify which of several metal ions are in an aqueous sample.

Defining analytical chemistry as the application of chemical knowledge ignores the unique perspective that an analytical chemist bring to the study of chemistry. The craft of analytical chemistry is found not in performing a routine analysis on a routine sample—a task we appropriately call chemical analysis—but in improving established analytical methods, in extending these analytical methods to new types of samples, and in developing new analytical methods to measure chemical phenomena.[2]

Seven Stages of an Analytical Method

1. Conception of analytical method (birth).
2. Successful demonstration that the analytical method works.
3. Establishment of the analytical method's capabilities.
4. Widespread acceptance of the analytical method.
5. Continued development of the analytical method leads to significant improvements.
6. New cycle through steps 3–5.
7. Analytical method can no longer compete with newer analytical methods (death).

Steps 1–3 and 5 are the province of analytical chemistry; step 4 is the realm of chemical analysis.

The seven stages of an analytical method listed here are modified from Fassel, V. A. *Fresenius' Z. Anal. Chem.* **1986**, *324*, 511–518 and Hieftje, G. M. *J. Chem. Educ.* **2000**, *77*, 577–583.

Here is one example of the distinction between analytical chemistry and chemical analysis. A mining engineers evaluates an ore by comparing the cost of removing the ore from the earth with the value of its contents, which they estimate by analyzing a sample of the ore. The challenge of developing and validating a quantitative analytical method is the analytical chemist's responsibility; the routine, daily application of the analytical method is the job of the chemical analyst.

Another difference between analytical chemistry and chemical analysis is that an analytical chemist works to improve and to extend established analytical methods. For example, several factors complicate the quantitative analysis of nickel in ores, including nickel's unequal distribution within the ore, the ore's complex matrix of silicates and oxides, and the presence of other metals that may interfere with the analysis. Figure 1.1 outlined one standard analytical method in use during the late nineteenth century.[3] The need for many reactions, digestions, and filtrations makes this analytical method both time-consuming and difficult to perform accurately.

1 Ravey, M. *Spectroscopy*, **1990**, *5(7)*, 11.
2 de Haseth, J. *Spectroscopy*, **1990**, *5(7)*, 11.
3 Fresenius. C. R. *A System of Instruction in Quantitative Chemical Analysis*; John Wiley and Sons: New York, 1881.

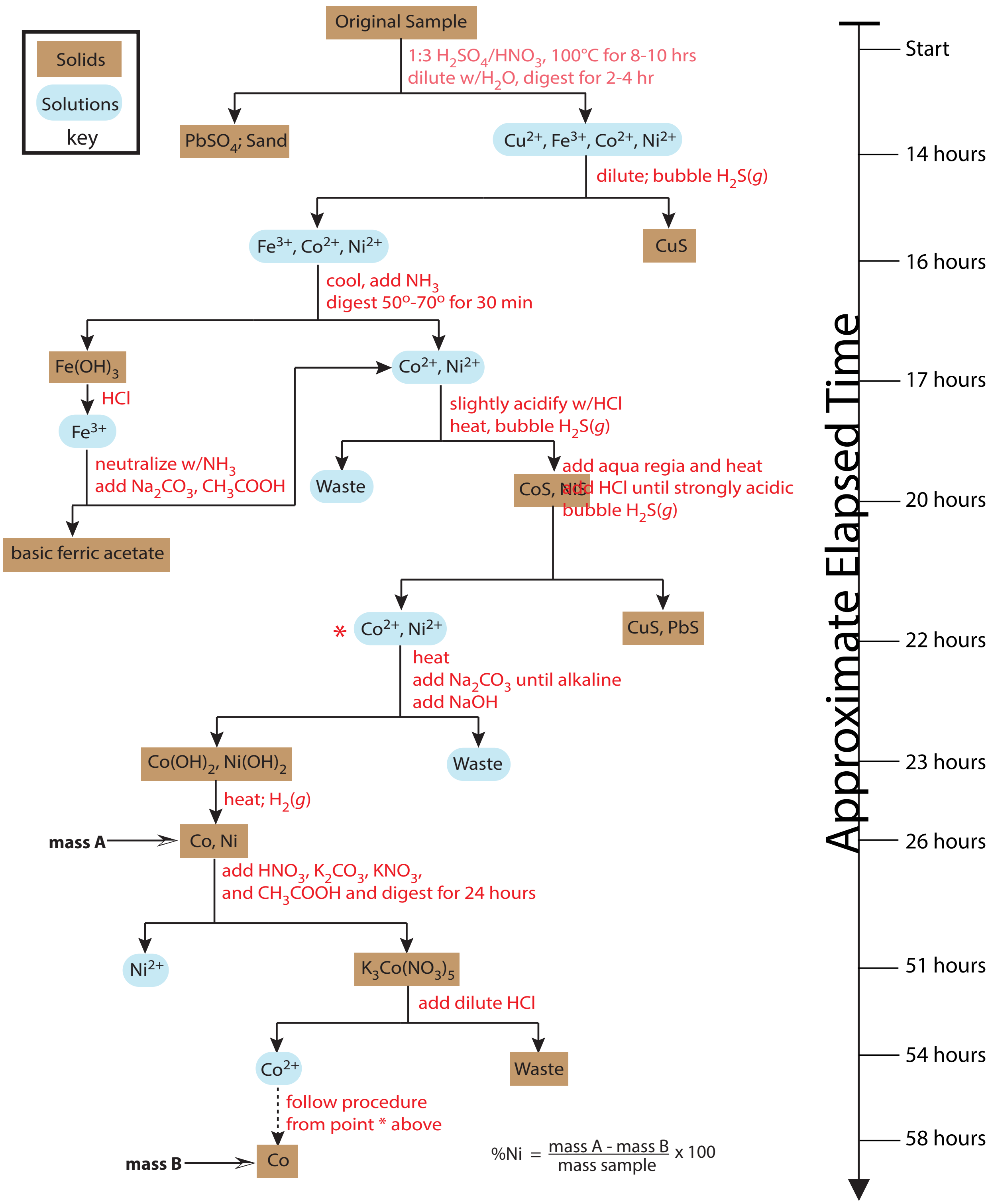
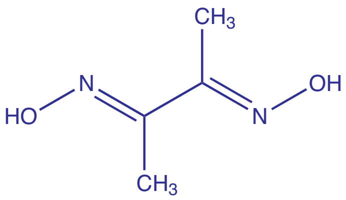


Figure 1.1 Fresenius' analytical scheme for the gravimetric analysis of Ni in ores. After each step, the solid and the solution are separated by gravity filtration. Note that the mass of nickel is not determined directly. Instead, Co and Ni first are isolated and weighed together (**mass A**), and then Co is isolated and weighed separately (**mass B**). The timeline shows that it takes approximately 58 hours to analyze one sample. This scheme is an example of a gravimetric analysis, which is explored further in Chapter 8.



dimethylglyoxime

The discovery, in 1905, that dimethylglyoxime (dmg) selectively precipitates Ni^{2+} and Pd^{2+} led to an improved analytical method for the quantitative analysis of nickel.[4] The resulting analysis, which is outlined in Figure 1.2, requires fewer manipulations and less time. By the 1970s, flame atomic absorption spectrometry replaced gravimetry as the standard method for analyzing nickel in ores,[5] resulting in an even more rapid analysis. Today, the standard analytical method utilizes an inductively coupled plasma optical emission spectrometer.

Perhaps a more appropriate description of analytical chemistry is "the science of inventing and applying the concepts, principles, and…strategies for measuring the characteristics of chemical systems."[6] Analytical chemists often work at the extreme edges of analysis, extending and improving

4 Kolthoff, I. M.; Sandell, E. B. *Textbook of Quantitative Inorganic Analysis*, 3rd Ed., The Macmillan Company: New York, 1952.
5 Van Loon, J. C. *Analytical Atomic Absorption Spectroscopy*, Academic Press: New York, 1980.
6 Murray, R. W. *Anal. Chem.* **1991**, *63*, 271A.

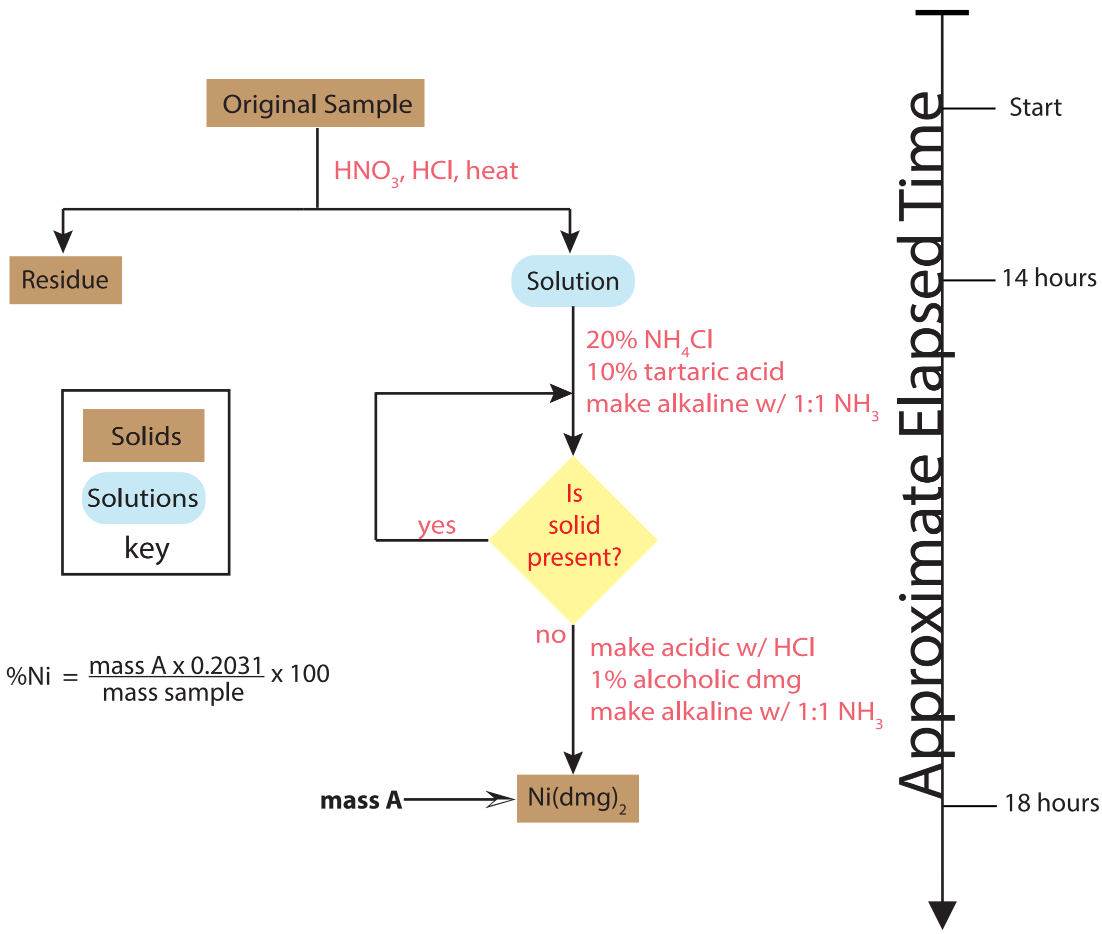


Figure 1.2 Gravimetric analysis for Ni in ores by precipitating $Ni(dmg)_2$. The timeline shows that it takes approximately 18 hours to analyze a single sample, substantially less than 58 hours for the method in Figure 1.1. The factor of 0.2301 in the equation for %Ni accounts for the difference in the formula weights of Ni and $Ni(dmg)_2$; see Chapter 8 for further details.

the ability of all chemists to make meaningful measurements on smaller samples, on more complex samples, on shorter time scales, and on species present at lower concentrations. Throughout its history, analytical chemistry has provided many of the tools and methods necessary for research in other traditional areas of chemistry, as well as fostering multidisciplinary research in, to name a few, medicinal chemistry, clinical chemistry, toxicology, forensic chemistry, materials science, geochemistry, and environmental chemistry.

You will come across numerous examples of analytical methods in this textbook, most of which are routine examples of chemical analysis. It is important to remember, however, that nonroutine problems prompted analytical chemists to develop these methods.

To an analytical chemist, the process of making a useful measurement is critical; if the measurement is not of central importance to the work, then it is not analytical chemistry.

An editorial in *Analytical Chemistry* entitled "Some Words about Categories of Manuscripts" highlights nicely what makes a research endeavour relevant to modern analytical chemistry. The full citation is Murray, R. W. *Anal. Chem.* **2008**, *80*, 4775; for a more recent editorial, see "The Scope of *Analytical Chemistry*" by Sweedler, J. V. et. al. *Anal. Chem.* **2015**, *87*, 6425.

1B The Analytical Perspective

Having noted that each area of chemistry brings a unique perspective to the study of chemistry, let's ask a second deceptively simple question: What is the analytical perspective? Many analytical chemists describe this perspective as an analytical approach to solving problems.[7] Although there likely are as many descriptions of the analytical approach as there are analytical chemists, it is convenient to define it as the five-step process shown in Figure 1.3.

Three general features of this approach deserve our attention. First, in steps 1 and 5 analytical chemists have the opportunity to collaborate with individuals outside the realm of analytical chemistry. In fact, many problems on which analytical chemists work originate in other fields. Second, the heart of the analytical approach is a feedback loop (steps 2, 3, and 4) in which the result of one step requires that we reevaluate the other steps. Finally, the solution to one problem often suggests a new problem.

Analytical chemistry begins with a problem, examples of which include evaluating the amount of dust and soil ingested by children as an indicator of environmental exposure to particulate based pollutants, resolving contradictory evidence regarding the toxicity of perfluoro polymers during combustion, and developing rapid and sensitive detectors for chemical and biological weapons. At this point the analytical approach involves a collaboration between the analytical chemist and the individual or agency working on the problem. Together they determine what information is needed and clarify how the problem relates to broader research goals or policy issues, both essential to the design of an appropriate experimental procedure.

These examples are taken from a series of articles, entitled the "Analytical Approach," which for many years was a regular feature of the journal *Analytical Chemistry*.

To design the experimental procedure the analytical chemist considers criteria, such as the required accuracy, precision, sensitivity, and detection

Chapter 3 introduces you to the language of analytical chemistry. You will find terms such accuracy, precision, and sensitivity defined there.

7 For different viewpoints on the analytical approach see (a) Beilby, A. L. *J. Chem. Educ.* **1970**, *47*, 237-238; (b) Lucchesi, C. A. *Am. Lab.* **1980**, October, 112-119; (c) Atkinson, G. F. *J. Chem. Educ.* **1982**, *59*, 201-202; (d) Pardue, H. L.; Woo, J. *J. Chem. Educ.* **1984**, *61*, 409-412; (e) Guarnieri, M. *J. Chem. Educ.* **1988**, *65*, 201-203, (f) Strobel, H. A. *Am. Lab.* **1990**, October, 17-24.

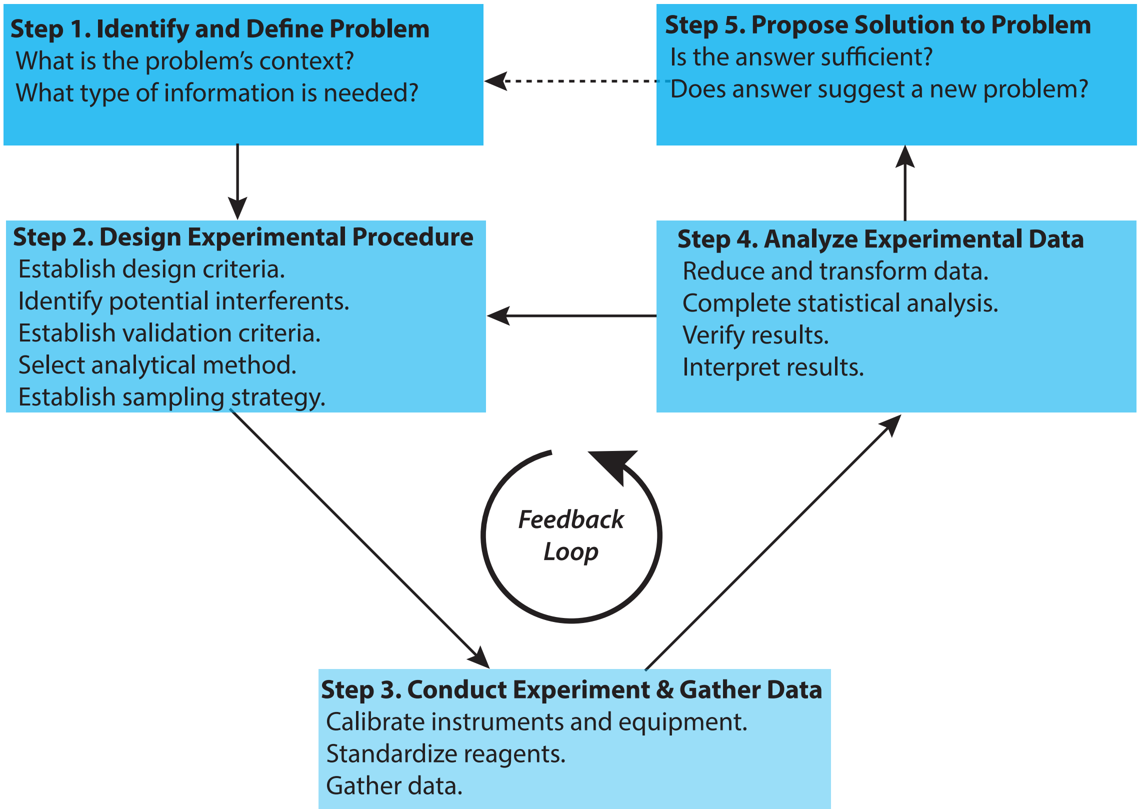


Figure 1.3 Flow diagram showing one view of the analytical approach to solving problems (modified after Atkinson.[7c]

limit, the urgency with which results are needed, the cost of a single analysis, the number of samples to analyze, and the amount of sample available for analysis. Finding an appropriate balance between these criteria frequently is complicated by their interdependence. For example, improving precision may require a larger amount of sample than is available. Consideration also is given to how to collect, store, and prepare samples, and to whether chemical or physical interferences will affect the analysis. Finally a good experimental procedure may yield useless information if there is no method for validating the results.

See Chapter 7 for a discussion of how to collect, store, and prepare samples for analysis.

The most visible part of the analytical approach occurs in the laboratory. As part of the validation process, appropriate chemical and physical standards are used to calibrate equipment and to standardize reagents.

See Chapter 14 for a discussion about how to validate an analytical method. Calibration and standardization methods, including a discussion of linear regression, are covered in Chapter 5.

The data collected during the experiment are then analyzed. Frequently the data first is reduced or transformed to a more readily analyzable form and then a statistical treatment of the data is used to evaluate accuracy and precision, and to validate the procedure. Results are compared to the original design criteria and the experimental design is reconsidered, additional trials are run, or a solution to the problem is proposed. When a solution is proposed, the results are subject to an external evaluation that may result in a new problem and the beginning of a new cycle.

Chapter 4 introduces the statistical analysis of data.

As noted earlier some scientists question whether the analytical approach is unique to analytical chemistry. Here, again, it helps to distinguish between a chemical analysis and analytical chemistry. For an analytically-oriented scientist, such as a physical organic chemist or a public health officer, the primary emphasis is how the analysis supports larger research goals that involve fundamental studies of chemical or physical processes, or that improve access to medical care. The essence of analytical chemistry, however, is in developing new tools for solving problems, and in defining the type and quality of information available to other scientists.

1C Common Analytical Problems

Many problems in analytical chemistry begin with the need to identify what is present in a sample. This is the scope of a QUALITATIVE ANALYSIS, examples of which include identifying the products of a chemical reaction,

Practice Exercise 1.1

As an exercise, let's adapt our model of the analytical approach to the development of a simple, inexpensive, portable device for completing bioassays in the field. Before continuing, locate and read the article

"Simple Telemedicine for Developing Regions: Camera Phones and Paper-Based Microfluidic Devices for Real-Time, Off-Site Diagnosis"

by Andres W. Martinez, Scott T. Phillips, Emanuel Carriho, Samuel W. Thomas III, Hayat Sindi, and George M. Whitesides. You will find it on pages 3699-3707 in Volume 80 of the journal *Analytical Chemistry*, which was published in 2008. As you read the article, pay particular attention to how it emulates the analytical approach and consider the following questions:

What is the analytical problem and why is it important?
What criteria did the authors consider in designing their experiments?
What is the basic experimental procedure?
What interferences were considered and how did they overcome them?
How did the authors calibrate the assay?
How did the authors validate their experimental method?
Is there evidence that steps 2, 3, and 4 are repeated?
Was there a successful conclusion to the analytical problem?

Don't let the technical details in the paper overwhelm you; if you skim over these you will find the paper both well-written and accessible.

Click here to review your answers to these questions.

This exercise provides you with an opportunity to think about the analytical approach in the context of a real analytical problem. Practice exercises such as this provide you with a variety of challenges ranging from simple review problems to more open-ended exercises. You will find answers to practice exercises at the end of each chapter.

Use this link to access the article's abstract from the journal's web site. If your institution has an on-line subscription you also will be able to download a PDF version of the article.

screening an athlete's urine for a performance-enhancing drug, or determining the spatial distribution of Pb on the surface of an airborne particulate. An early challenge for analytical chemists was developing simple chemical tests to identify inorganic ions and organic functional groups. The classical laboratory courses in inorganic and organic qualitative analysis, still taught at some schools, are based on this work.[8] Modern methods for qualitative analysis rely on instrumental techniques, such as infrared (IR) spectroscopy, nuclear magnetic resonance (NMR) spectroscopy, and mass spectrometry (MS). Because these qualitative applications are covered adequately elsewhere in the undergraduate curriculum, they receive no further consideration in this text.

Perhaps the most common analytical problem is a QUANTITATIVE ANALYSIS, examples of which include the elemental analysis of a newly synthesized compound, measuring the concentration of glucose in blood, or determining the difference between the bulk and the surface concentrations of Cr in steel. Much of the analytical work in clinical, pharmaceutical, environmental, and industrial labs involves developing new quantitative methods to detect trace amounts of chemical species in complex samples. Most of the examples in this text are of quantitative analyses.

A good resource for current examples of qualitative, quantitative, characterization, and fundamental analyses is *Analytical Chemistry's* annual review issue that highlights fundamental and applied research in analytical chemistry. Examples of review articles in the 2015 issue include "Analytical Chemistry in Archaeological Research," "Recent Developments in Paper-Based Microfluidic Devices," and "Vibrational Spectroscopy: Recent Developments to Revolutionize Forensic Science."

Another important area of analytical chemistry, which receives some attention in this text, are methods for characterizing physical and chemical properties. The determination of chemical structure, of equilibrium constants, of particle size, and of surface structure are examples of a CHARACTERIZATION ANALYSIS.

The purpose of a qualitative, a quantitative, or a characterization analysis is to solve a problem associated with a particular sample. The purpose of a FUNDAMENTAL ANALYSIS, on the other hand, is to improve our understanding of the theory that supports an analytical method and to understand better an analytical method's limitations.

1D Key Terms

characterization analysis	fundamental analysis	qualitative analysis
quantitative analysis		

1E Chapter Summary

Analytical chemists work to improve the ability of chemists and other scientists to make meaningful measurements. The need to work with smaller samples, with more complex materials, with processes occurring on shorter time scales, and with species present at lower concentrations challenges

8 See, for example, the following laboratory texts: (a) Sorum, C. H.; Lagowski, J. J. *Introduction to Semimicro Qualitative Analysis*, 5th Ed.; Prentice-Hall: Englewood, NJ, 1977; (b) Shriner, R. L.; Fuson, R. C.; Curtin, D. Y. *The Systematic Identification of Organic Compounds*, 5th Ed.; John Wiley and Sons: New York, 1964.

analytical chemists to improve existing analytical methods and to develop new ones.

Typical problems on which analytical chemists work include qualitative analyses (What is present?), quantitative analyses (How much is present?), characterization analyses (What are the sample's chemical and physical properties?), and fundamental analyses (How does this method work and how can it be improved?).

1F Problems

1. For each of the following problems indicate whether its solution requires a qualitative analysis, a quantitative analysis, a characterization analysis, and/or a fundamental analysis. More than one type of analysis may be appropriate for some problems.

   (a) The residents in a neighborhood near a hazardous-waste disposal site are concerned that it is leaking contaminants into their groundwater.

   (b) An art museum is concerned that a recently acquired oil painting is a forgery.

   (c) Airport security needs a more reliable method for detecting the presence of explosive materials in luggage.

   (d) The structure of a newly discovered virus needs to be determined.

   (e) A new visual indicator is needed for an acid–base titration.

   (f) A new law requires a method for evaluating whether automobiles are emitting too much carbon monoxide.

2. Read the article "When Machine Tastes Coffee: Instrumental Approach to Predict the Sensory Profile of Espresso Coffee," which discusses work completed at the Nestlé Research Center in Lausanne, Switzerland. You will find the article on pages 1574-1581 in Volume 80 of *Analytical Chemistry*, published in 2008. Prepare an essay that summarizes the nature of the problem and how it was solved. Do not worry about the nitty-gritty details of the mathematical model developed by the authors, which relies on a combination of an analysis of variance (ANOVA), a topic we will consider in Chapter 14, and a principle component regression (PCR), at topic that we will not consider in this text. Instead, focus on the results of the model by examining the visualizations in Figures 3 and 4. As a guide, refer to Figure 1.3 in this chapter for a model of the analytical approach to solving problems.

Use this link to access the article's abstract from the journal's web site. If your institution has an on-line subscription you also will be able to download a PDF version of the article.

1G Solutions to Practice Exercises

Practice Exercise 1.1

What is the analytical problem and why is it important?

A medical diagnoses often relies on the results of a clinical analysis. When a patient visits a doctor, he or she may draw a sample of your blood and send it to the lab for analysis. In some cases the result of the analysis is available in 10-15 minutes. What is possible in a developed country, such as the United States, may not be feasible in a country with less access to expensive lab equipment and with fewer trained personnel available to run the tests and to interpret the results. The problem addressed in this paper, therefore, is the development of a reliable device for rapidly performing a clinical assay under less than ideal circumstances.

What criteria did the authors consider in designing their experiments?

In considering a solution to this problem, the authors identify seven important criteria for the analytical method: it must be inexpensive; it must operate without the need for much electricity, so that it can be used in remote locations; it must be adaptable to many types of assays; its must not require a highly skilled technician; it must be quantitative; it must be accurate; and it must produce results rapidly.

What is the basic experimental procedure?

The authors describe how they developed a paper-based microfluidic device that allows anyone to run an analysis simply by dipping the device into a sample (synthetic urine, in this case). The sample moves by capillary action into test zones containing reagents that react with specific species (glucose and protein, for this prototype device). The reagents react to produce a color whose intensity is proportional to the species' concentration. A digital photograph of the microfluidic device is taken using a cell phone camera and sent to an off-site physician who uses image editing software to analyze the photograph and to interpret the assay's result.

This is an example of a colorimetric method of analysis. Colorimetric methods are covered in Chapter 10.

What interferences were considered and how did they overcome them?

In developing this analytical method the authors considered several chemical or physical interferences. One concern was the possibility of non-specific interactions between the paper and the glucose or protein, which might lead to non-uniform image in the test zones. A careful analysis of the distribution of glucose and protein in the text zones showed that this was not a problem. A second concern was the possibility that particulate materials in the sample might interfere with the analyses. Paper is a natural filter for particulate materials and the authors found that samples containing dust, sawdust, and pollen do not interfere with the analysis for glucose. Pollen, however, is an interferent for the protein analysis, presumably because it, too, contains protein.

How did the author's calibrate the assay?

To calibrate the device the authors analyzed a series of standard solutions that contained known concentrations of glucose and protein. Because an image's intensity depends upon the available light, a standard sample is run with the test samples, which allows a single calibration curve to be used for samples collected under different lighting conditions.

How did the author's validate their experimental method?

The test device contains two test zones for each analyte, which allows for duplicate analyses and provides one level of experimental validation. To further validate the device, the authors completed 12 analyses at each of three known concentrations of glucose and protein, obtaining acceptable accuracy and precision in all cases.

Is there any evidence of repeating steps 2, 3, and 4?

Developing this analytical method required several cycles through steps 2, 3, and 4 of the analytical approach. Examples of this feedback loop include optimizing the shape of the test zones and evaluating the importance of sample size.

Was there a successful conclusion to the analytical problem?

Yes. The authors were successful in meeting their goals by developing and testing an inexpensive, portable, and easy-to-use device for running clinical samples in developing countries.

Click here to return to the chapter.