Chapter 1

Introduction to Analytical Chemistry

Chapter Overview

Chemistry is the study of matter, including its composition and structure, its physical properties, and its reactivity. There are many ways to study chemistry, but, we traditionally divide it into five fields: organic chemistry, inorganic chemistry, biochemistry, physical chemistry, and analytical chemistry. Although this division is historical and, perhaps, arbitrary—as witnessed by current interest in interdisciplinary areas such as bioanalytical chemistry and organometallic chemistry—these five fields remain the simplest division spanning the discipline of chemistry.

Training in each of these fields provides a unique perspective to the study of chemistry. Undergraduate chemistry courses and textbooks are more than a collection of facts; they are a kind of apprenticeship. In keeping with this spirit, this chapter introduces 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 fields of chemistry, analytical chemistry is too broad and too active a discipline for us to define completely. In this chapter, therefore, we will try to say a little about what analytical chemistry is, as well as a little about what analytical chemistry is not.

Analytical chemistry is often described as the area of chemistry responsible for characterizing the composition of matter, both qualitatively (Is there any lead in this sample?) and quantitatively (How much lead is in this sample?). 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 preformed quantitative and qualitative analyses in other chemistry courses.

You might, for example, have determined the amount 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 analytical chemists bring to the study of chemistry. The craft of analytical chemistry is not in performing a routine analysis on a routine sample, which more appropriately is called chemical analysis, but in improving established analytical methods, in extending existing analytical methods to new types of samples, and in developing new analytical methods for measuring chemical phenomena.[2]

<u>Seven Stages of an Analytical Method</u>

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 given 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 this distinction between analytical chemistry and chemical analysis. Mining engineers evaluate the value of an ore by comparing the cost of removing the ore with the value of its contents. To estimate its value they analyze a sample of the ore. The challenge of developing and validating an appropriate quantitative analytical method is the analytical chemist's responsibility. After its development, the routine, daily application of the analytical method is the job of the chemical analyst.

Another distinction between analytical chemistry and chemical analysis is that analytical chemists work to improve and 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 shows a schematic outline of 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.

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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.

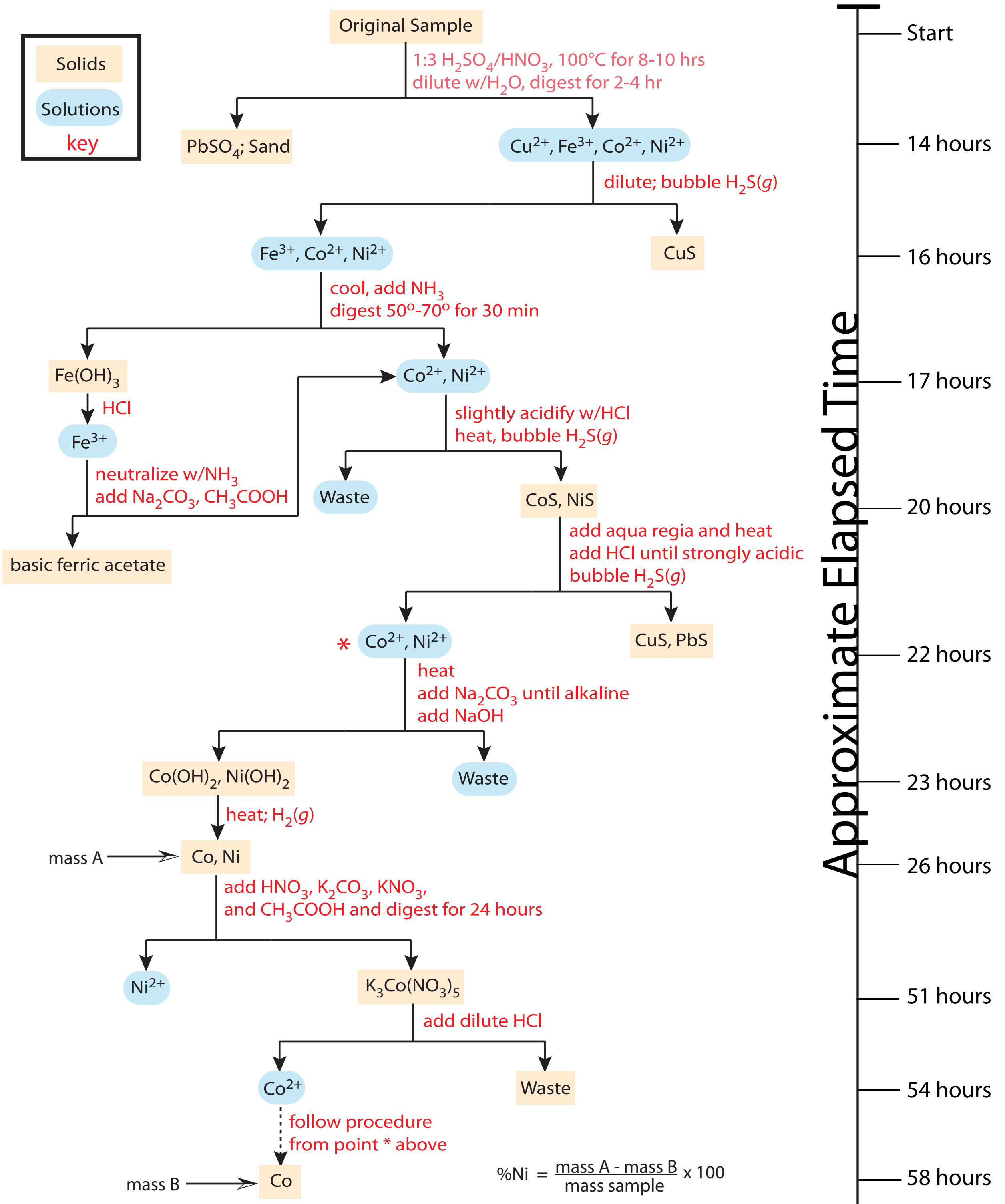
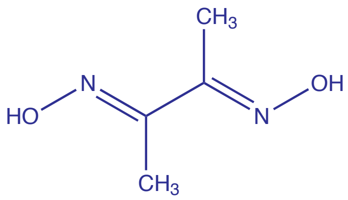


Figure 1.1 Fresenius' analytical scheme for the gravimetric analysis of Ni in ores. Note that the mass of nickel is not determined directly. Instead, Co and Ni are isolated and weighed (mass A), and then Co is isolated and weighed (mass B). The timeline shows that after digesting a sample, it takes approximately 44 hours to complete an analysis. This scheme is an example of a gravimetric analysis in which mass is the important measurement. See Chapter 8 for more information about gravimetric procedures.



dimethylglyoxime

The development, in 1905, of dimethylglyoxime (dmg), a reagent that selectively precipitates Ni^{2+} and Pd^{2+}, led to an improved analytical method for the quantitative analysis of nickel.[4] The resulting analysis, as shown in Figure 1.2, requires fewer manipulations and less time after completing the sample's dissolution. 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.

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

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.

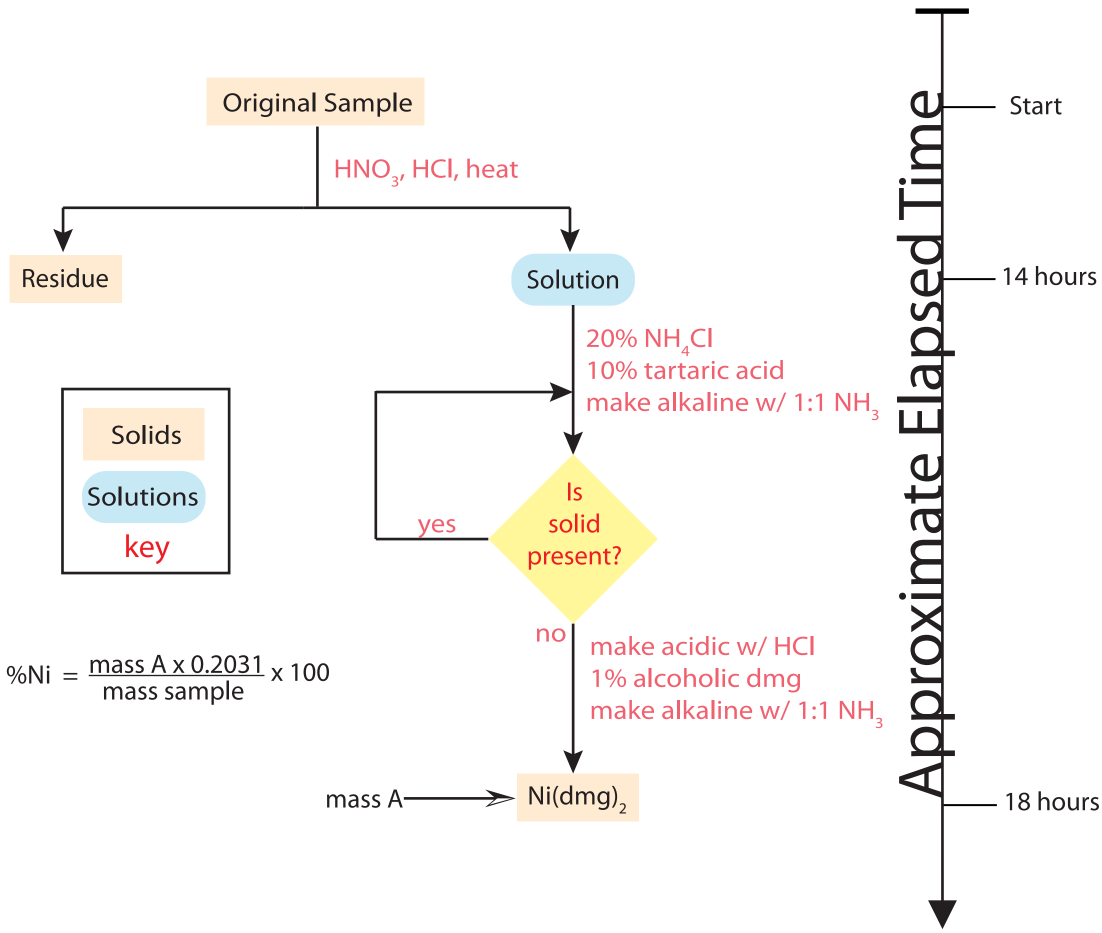


Figure 1.2 Gravimetric analysis for Ni in ores by precipitating $Ni(dmg)_2$. The timeline shows that it takes approximately four hours to complete an analysis after digesting the sample, which is 10x shorter than for the method in Figure 1.1. The factor of 0.2301 in the equation for %Ni accounts for the difference in the formula weights for Ni and $Ni(dmg)_2$; see Chapter 8 for further details.

typically operate at the extreme edges of analysis, extending and improving 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 the 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.

The next time you are in the library, look through a recent issue of an analytically oriented journal, such as *Analytical Chemistry*. Focus on the titles and abstracts of the research articles. Although you may not recognize all the terms and analytical methods, you will begin to answer for yourself the question "What is analytical chemistry?"

A recent editorial in *Analytical Chemistry* entitled "Some Words about Categories of Manuscripts" nicely highlights what makes a research endeavour relevant to modern analytical chemistry. The full citation is Murray, R. W. *Anal. Chem.* **2008**, *80*, 4775.

1B The Analytical Perspective

Having noted that each field of chemistry brings a unique perspective to the study of chemistry, we now 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 are probably as many descriptions of the analytical approach as there are analytical chemists, it is convenient for our purpose 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 may collaborate with individuals outside the realm of analytical chemistry. In fact, many problems on which analytical chemists work originate in other fields. Second, the analytical approach includes a feedback loop (steps 2, 3, and 4) in which the result of one step may require reevaluating 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 may involve a collaboration between the analytical chemist and the individual or agency

These examples are taken from a series of articles, entitled the "Analytical Approach," which was a regular feature of the journal *Analytical Chemistry*, a bimonthly publication of the American Chemical Society. The first issue of each month continues to publish a variety of engaging articles highlighting current trends in analytical chemistry.

7 For several different viewpoints 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.

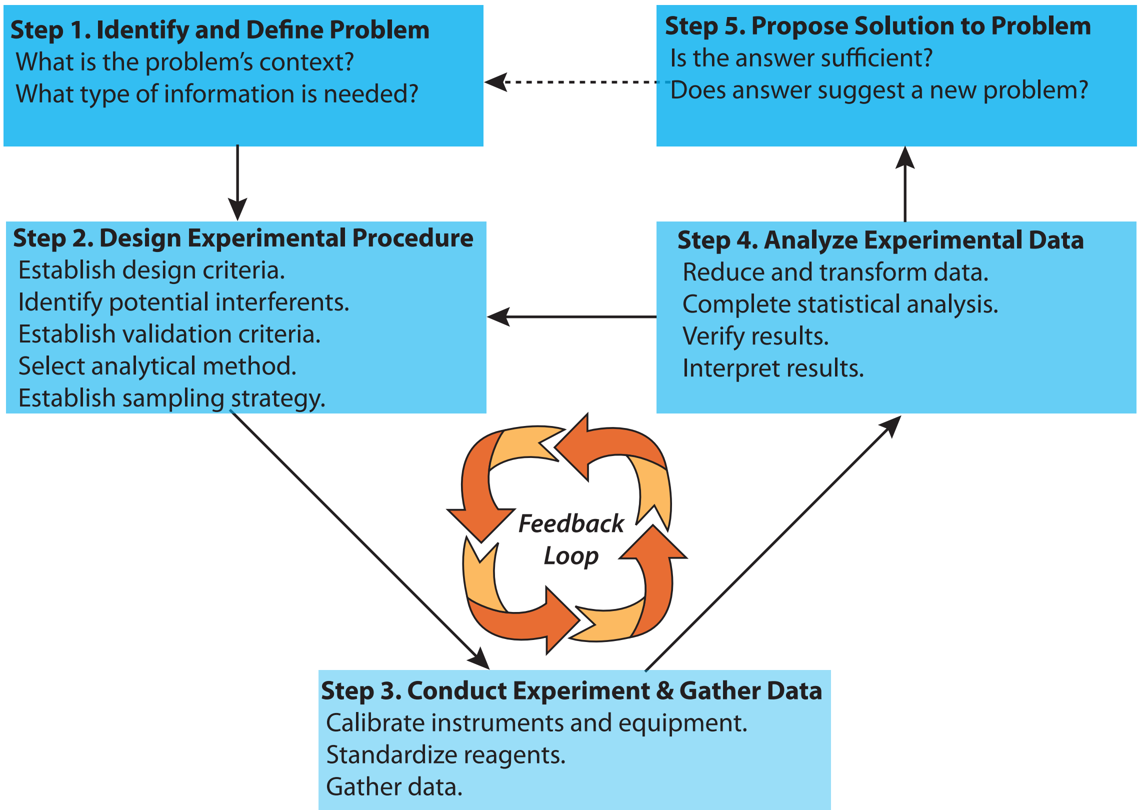


Figure 1.3 Flow diagram showing one view of the analytical approach to solving problems (modified after Atkinson.[7c]

working on the problem. Together they determine what information is needed. It also is important for the analytical chemist to understand how the problem relates to broader research goals or policy issues. The type of information needed and the problem's context are essential to designing an appropriate experimental procedure.

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

To design the experimental procedure the analytical chemist considers criteria such as the desired accuracy, precision, sensitivity, and detection limits; the urgency with which results are needed; the cost of a single analysis; the number of samples to be analyzed; and the amount of sample available for analysis. Finding an appropriate balance between these parameters is frequently complicated by their interdependence. For example, improving precision may require a larger amount of sample. Consideration is also given to collecting, storing, and preparing samples, and to whether chemical or physical interferences will affect the analysis. Finally a good experimental procedure may still yield useless information if there is no method for validating the results.

See Chapter 7 for information about collecting, storing, and preparing samples.

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 any equipment and to standardize any reagents.

See Chapter 14 for a discussion about validating analytical methods. 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 is reduced or transformed to a more readily analyzable form. 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.[1] Here, again, it helps to distinguish between a chemical analysis and analytical chemistry. For other analytically oriented scientists, such as a physical organic chemist or a public health officer, the primary emphasis is how the analysis supports larger research goals involving fundamental studies of chemical or physical processes, or improving 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.

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. It might be helpful to 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 of repeating steps 2, 3, and 4?
Was there a successful conclusion to the problem?

Don't let the technical details in the paper overwhelm you. If you skim over these you will find that the paper is 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. Boxed 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 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.

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, screening an athlete's urine for the presence of a performance-enhancing drug, or determining the spatial distribution of Pb on the surface of an airborne particulate. Much of the early work in analytical chemistry involved the development of 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] Currently, most qualitative analyses use methods such as infrared (IR) spectroscopy and nuclear magnetic resonance (NMR) spectroscopy. These qualitative applications are covered adequately elsewhere in the undergraduate curriculum and, so, will receive no further consideration in this text.

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

Current research in the areas of quantitative analysis, qualitative analysis, and characterization analysis are reviewed biennially (odd-numbered years) in *Analytical Chemistry's* series of "Application Reviews." The 2007 issue, for example, reviews forensic science, water, pharmaceuticals, geochemistry, and protemics, to name a few.

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

The purpose of a qualitative, quantitative, or 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 behind an analytical method. Extending and improving the theory on which an analytical method is based, studying an analytical method's limitations, and designing and modifying existing analytical method are examples of fundamental studies in analytical chemistry.

Current research in the area of fundamental analysis is reviewed biennially (even-numbered years) in Analytical Chemistry's series of "Fundamental Reviews." The 2008 issue, for example, reviews fiber-optic chemical sensors and biosensors, thermal analysis, chiral separations, chemometrics, and solid state NMR, to name a few.

1D Key Terms

characterization analysis | fundamental analysis | qualitative analysis | quantitative analysis

As you review this chapter, try to define a key term in your own words. Check your answer by clicking on the key term, which will take you to the page where it was first introduced. Clicking on the KEY TERM there, will bring you back to this page so that you can continue with another key term.

8 See, for example, the following laboratory texts: (a) Sorum, C. H.; Lagowski, J. J. *Introduction to Semimicro Qualitative Analysis*, 5th Ed.; Prenctice-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.

1E Chapter Summary

Analytical chemists work to improve the ability of all chemists to make meaningful measurements. Chemists working in the other traditional areas of chemistry, as well as in interdisciplinary fields such as medicinal chemistry, clinical chemistry, and environmental chemistry, need better tools for analyzing materials. 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 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 (Who 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, or a fundamental analysis. More than one type of analysis may be appropriate for some problems.

   (a) A hazardous-waste disposal site is believed to be leaking contaminants into the local groundwater.

   (b) An art museum is concerned that a recent acquisition 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," by several scientists working 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. Write an essay summarizing the nature of the problem and how it was solved. As a guide, refer to Figure 1.3 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

Literature 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 visiting a doctor, he or she may ask the nurse to 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 fewer resources because lab equipment is expensive, and because there may be a shortage of trained personnel 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 and quantitatively performing clinical assays in less than ideal circumstances.

What criteria did the authors consider in designing their experiments?

In considering solutions to this problem, the authors identify seven important criteria for the device: it must be inexpensive; it must operate without the need for much electricity, so that it can be taken to remote sites; it must be adaptable to many types of assays; its operation 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 the development of a paper-based microfluidic device that allows anyone to run an analysis 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. Digital pictures of the microfluidic device are taken with a cell phone camera and sent to an off-site physician who analyzes the picture using image editing software and interprets 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 could 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 possible presence in samples of particulate materials that might interfere with the analyses. Paper is a natural filter for particulate materials and the authors found that samples containing dust, sawdust, and pollen did 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 containing 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, allowing for duplicate analyses and providing 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 repetitive paths 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.

In summary, the authors report the successful development of an inexpensive, portable, and easy-to-use device for running clinical samples in developing countries.

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