Introduction 1

Is there any iron in moon dust? How much aspirin is there in a headache tablet? What trace metals are there in a tin of tuna fish? What is the purity and chemical structure of a newly prepared compound? These and a host of other questions concerning the composition and structure of matter fall within the realms of analytical chemistry. The answers may be given by simple chemical tests or by the use of costly and complex instrumentation. The techniques and methods employed and the problems encountered are so varied as to cut right across the traditional divisions of inorganic, organic and physical chemistry as well as embracing aspects of such areas as bio-chemistry, physics, engineering and economics. Analytical chemistry is therefore a subject which is broad in its scope whilst requiring a specialist and disciplined approach. An enquiring and critical mind, a keen sense of observation and the ability to pay scrupulous attention to detail are desirable characteristics in anyone seeking to become proficient in the subject. However, it is becoming increasingly recognized that the role of the analytical chemist is not to be tied to a bench using a burette and balance, but to become involved in the broader aspects of the analytical problems which are encountered. Thus, discussions with scientific and commercial colleagues, customers and other interested parties, together with on-site visits can greatly assist in the choice of method and the interpretation of analytical data thereby minimizing the expenditure of time, effort and money.

The purpose of this book is to provide a basic understanding of the principles, instrumentation and applications of chemical analysis as it is currently practised. The amount of space devoted to each technique is based upon its application in industry as determined in a national survey of analytical laboratories. Some little used techniques have been omitted altogether. The presentation is designed to aid rapid assimilation by emphasizing unifying themes common to groups of techniques and by including short summaries at the beginning of each section.

The scope of analytical chemistry

Analytical chemistry has bounds which are amongst the widest of any technological discipline. An analyst must be able to design, carry out, and interpret measurements within the context of the fundamental technological problem with which he or she is presented. The selection and utilization of suitable chemical procedures requires a wide knowledge of chemistry, whilst familiarity with and the ability to operate a varied range of instruments is essential. Finally, analysts must have a sound knowledge of the statistical treatment of experimental data to enable them to gauge the meaning and reliability of the results that they obtain.

When an examination is restricted to the identification of one or more constituents of a sample, it is known as *qualitative analysis*, while an examination to determine how much of a particular species is present constitutes a *quantitative analysis*. Sometimes information concerning the spatial arrangement of atoms in a molecule or crystalline compound is required or confirmation of the presence or position of certain organic functional groups is sought. Such examinations are described as *structural analysis* and they may be considered as more detailed forms of analysis. Any species that are the subjects of either qualitative or quantitative analysis are known as *analytes*.

There is much in common between the techniques and methods used in qualitative and quantitative analysis. In both cases, a sample is prepared for analysis by physical and chemical 'conditioning', and then a measurement of some property related to the analyte is made. It is in the degree of control over the relation between a measurement and the amount of analyte present that the major difference lies. For a qualitative analysis it is sufficient to be able to apply a test which has a known sensitivity limit so that negative and positive results may be seen in the right perspective. Where a quantitative analysis is made, however, the relation between measurement and analyte must obey a strict and measurable proportionality; only then can the amount of analyte in the sample be derived from the measurement. To maintain this proportionality it is generally essential that all reactions used in the preparation of a sample for measurement are controlled and reproducible and that the conditions of measurement remain constant for all similar measurements. A premium is also placed upon careful calibration of the methods used in a quantitative analysis. These aspects of chemical analysis are a major pre-occupation of the analyst.

The function of analytical chemistry

Chemical analysis is an indispensable servant of modern technology whilst it partly depends on that modern technology for its operation. The two have in fact developed hand in hand. From the earliest days of quantitative chemistry in the latter part of the eighteenth century, chemical analysis has provided an important basis for chemical development. For example, the combustion studies of La Voisier and the atomic theory proposed by Dalton had their bases in quantitative analytical evidence. The transistor provides a more recent example of an invention which would have been almost impossible to develop without sensitive and accurate chemical analysis. This example is particularly interesting as it illustrates the synergic development that is so frequently observed in differing fields. Having underpinned the development of the transistor, analytical instrumentation now makes extremely wide use of it. In modern technology, it is impossible to over-estimate the importance of analysis. Some of the major areas of application are listed below.

(a) Fundamental research

The first steps in unravelling the details of an unknown system frequently involve the identification of its constituents by qualitative chemical analysis. Follow-up investigations usually require structural information and quantitative measurements. This pattern appears in such diverse areas as the formulation of new drugs, the examination of meteorites, and studies on the results of heavy ion bombardment by nuclear physicists.

(b) Product development

The design and development of a new product will often depend upon establishing a link between its chemical composition and its physical properties or performance. Typical examples are the development of alloys and of polymer composites.

(c) Product quality control

Most manufacturing industries require a uniform product quality. To ensure that this requirement is met, both raw materials and finished products are subjected to extensive chemical analysis. On the one hand, the necessary constituents must be kept at the optimum levels, while on the other impurities such as poisons in foodstuffs must be kept below the maximum allowed by law.

(d) Monitoring and control of pollutants

Residual heavy metals and organo-chlorine pesticides represent two well-known pollution problems. Sensitive and accurate analysis is required to enable the distribution and level of a pollutant in the environment to be assessed and routine chemical analysis is important in the control of industrial effluents.

(e) Assay

In commercial dealings with raw materials such as ores, the value of the ore is set by its metal content. Large amounts of material are often involved, so that taken overall small differences in concentration can be of considerable commercial significance. Accurate and reliable chemical analysis is thus essential.

(f) Medical and clinical studies
The levels of various elements and compounds in body fluids are important indicators of physiological disorders. A high sugar content in urine indicating a diabetic condition and lead in blood are probably the most well-known examples.

Analytical problems and their solution

The solutions of all analytical problems, both qualitative and quantitative, follow the same basic pattern. This may be described under seven general headings.

(1) Choice of method
The selection of the method of analysis is a vital step in the solution of an analytical problem. A choice cannot be made until the overall problem is defined, and where possible a decision should be taken by the client and the analyst in consultation. Inevitably, in the method selected, a compromise has to be reached between the sensitivity, precision and accuracy desired of the results and the costs involved. For example, X-ray fluorescence spectrometry may provide rapid but rather imprecise quantitative results in a trace element problem. Atomic absorption spectrophotometry, on the other hand, will supply more precise data, but at the expense of more time-consuming chemical manipulations.

(2) Sampling
Correct sampling is the cornerstone of reliable analysis. The analyst must decide in conjunction with technological colleagues how, where, and when a sample should be taken so as to be truly representative of the parameter that is to be measured.

(3) Preliminary sample treatment
For quantitative analysis, the amount of sample taken is usually measured by mass or volume. Where a homogeneous sample already exists, it may be subdivided without further treatment. With many solids such as ores, however, crushing and mixing are prior requirements. The sample often needs additional preparation for analysis, such as drying, ignition and dissolution.

(4) Separations
A large proportion of analytical measurements is subject to interference from other constituents of the sample. Newer methods increasingly employ instrumental techniques to distinguish between analyte and interference signals. However, such distinction is not always possible and sometimes a selective chemical reaction can be used to mask the interference. If this approach fails, the separation of the analyte from the interfering component will become necessary. Where quantitative measurements are to be

made, separations must also be quantitative or give a known recovery of the analyte.

(5) Final measurement

This step is often the quickest and easiest of the seven but can only be as reliable as the preceding stages. The fundamental necessity is a known proportionality between the magnitude of the measurement and the amount of analyte present. A wide variety of parameters may be measured (Table 1.1).

Table 1.1 A general classification of important analytical techniques

Group	Property measured
gravimetric	weight of pure analyte or of a stoichiometric compound containing it
volumetric	volume of standard reagent solution reacting with the analyte
spectrometric	intensity of electromagnetic radiation emitted or absorbed by the analyte
electrochemical	electrical properties of analyte solutions
radiochemical	intensity of nuclear radiations emitted by the analyte
mass spectrometric	abundance of molecular fragments derived from the analyte
chromatographic	physico-chemical properties of individual analytes after separation
thermal	physico-chemical properties of the sample as it is heated and cooled

(6) Method validation

It is pointless carrying out the analysis unless the results obtained are known to be meaningful. This can only be ensured by proper validation of the method before use and subsequent monitoring of its performance. The analysis of validated standards is the most satisfactory approach. Validated standards have been extensively analysed by a variety of methods, and an accepted value for the appropriate analyte obtained. A standard should be selected with a matrix similar to that of the sample. In order to ensure continued accurate analysis, standards must be re-analysed at regular intervals.

(7) The assessment of results

Results obtained from an analysis must be assessed by the appropriate statistical methods and their meaning considered in the light of the original problem.

The nature of analytical methods

It is common to find analytical methods classified as *classical* or *instrumental*, the former comprising 'wet chemical' methods such as gravimetry and titrimetry. Such a classification is historically derived and largely artificial as there is no fundamental difference between the methods in the two groups. All involve the correlation of a physical measurement with the analyte concentration. Indeed, very few analytical methods are entirely instrumental, and most involve chemical manipulations prior to the instrumental measurement.

A more satisfactory general classification is achieved in terms of the physical parameter that is measured (Table 1.1).

Trends in analytical methods and procedures

There is constant development and change in the techniques and methods of analytical chemistry. Better instrument design and a fuller understanding of the mechanics of analytical processes enable steady improvements to be made in sensitivity, precision, and accuracy. These same changes contribute to more economic analysis as they frequently lead to the elimination of time-consuming separation steps. The ultimate development in this direction is a non-destructive method, which not only saves time but leaves the sample unchanged for further examination or processing.

The automation of analysis, sometimes with the aid of laboratory robots, has become increasingly important. For example, it enables a series of bench analyses to be carried out more rapidly and efficiently, and with better precision, whilst in other cases continuous monitoring of an analyte in a production process is possible. Two of the most important developments in recent years have been the incorporation of microprocessor control into analytical instruments and their interfacing with micro- and minicomputers. The microprocessor has brought improved instrument control, performance and, through the ability to monitor the condition of component parts, easier routine maintenance. Operation by relatively inexperienced personnel can be facilitated by simple interactive keypad dialogues including the storage and re-call of standard methods, report generation and diagnostic testing of the system. Microcomputers with sophisticated data handling and graphics software packages have likewise made a considerable impact on the collection, storage, processing, enhancement and interpretation of analytical data. *Laboratory Information and Management Systems* (LIMS), for the automatic logging of large numbers of samples, *Chemometrics*, which involve computerized and often sophisticated statistical analysis of data, and *Expert Systems*, which provide interactive computerized guidance and assessments in the solving of analytical problems, have all become important in optimizing chemical analysis and maximizing the information it provides.

Analytical problems continue to arise in new forms. Demands for analysis at 'long range' by instrument packages steadily increase. Space probes, 'borehole logging' and deep sea studies exemplify these requirements. In other fields, such as environmental and clinical studies, there is increasing recognition of the importance of the exact chemical form of an element in a sample rather than the mere level of its presence. Two well-known examples are the much greater toxicity of organo-lead and organo-mercury compounds compared with their inorganic counterparts. An identification and determination of the element in a specific chemical form presents the analyst with some of the more difficult problems.

Glossary of terms

The following list of definitions, though by no means exhaustive, will help both in the study and practice of analytical chemistry.

Accuracy
The closeness of an experimental measurement or result to the true or accepted value (p. 13).

Analyte
Constituent of the sample which is to be studied by quantitative measurements or identified qualitatively.

Assay
A highly accurate determination, usually of a valuable constituent in a material of large bulk, e.g. minerals and ores. Also used in the assessment of the purity of a material, e.g. the physiologically active constituent of a pharmaceutical product.

Background
That proportion of a measurement which arises from sources other than the analyte itself. Individual contributions from instrumental sources, added reagents and the matrix can, if desired, be evaluated separately.

Blank
A measurement or observation in which the sample is replaced by a simulated matrix, the conditions otherwise being identical to those under which a sample would be analysed. Thus, the blank can be used to correct for background effects and to take account of analyte other than that present in the sample which may be introduced during the analysis, e.g. from reagents.

Calibration

(1) A procedure which enables the response of an instrument to be related to the mass, volume or concentration of an analyte in a sample by first measuring the response from a sample of known composition or from a known amount of the analyte, i.e. a *standard*. Often, a series of standards is used to prepare a *calibration curve* in which instrument response is plotted as a function of mass, volume or concentration of the analyte over a given range. If the plot is linear, a *calibration factor*

(related to the slope of the curve) may be calculated. This facilitates the rapid computation of results without reference to the original curve.

(2) Determination of the accuracy of graduation marks on volumetric apparatus by weighing measured volumes of water, or determinations of the accuracy of weights by comparison with weights whose value is known with a high degree of accuracy.

Concentration

The amount of a substance present in a given mass or volume of another substance. The abbreviations w/w, w/v and v/v are sometimes used to indicate whether the concentration quoted is based on the weights or volumes of the two substances. Concentration may be expressed in several ways. These are shown in Table 1.2.

Table 1.2 Alternative methods of expressing concentration*

Units	Name and symbol	
moles of solute per dm^3	mol dm^{-3}, M	
equivalents of solute per dm^3	normal, N	
milli-equivalents of solute per dm^3	meq dm^{-3}	
grams of solute per dm^3	g dm^{-3}	
parts per million	ppm (γ)	
milligrams of component per kg	mg kg^{-1}	
milligrams of solute per dm^3	mg dm^{-3}	
parts per billion	ppb	
nanograms of component per kg	ng kg^{-1}	
nanograms of solute per dm^3	ng dm^{-3}	
parts per trillion	ppt	
picograms of component per kg	pg kg^{-1}	
picograms of solute per dm^3	pg dm^{-3}	
parts per hundred	% (w/w, w/v, v/v)	
millimoles of solute per 100 cm^3	mM%	
grams of solute per 100 cm^3	g%	
milligrams of solute per 100 cm^3	mg%	
micrograms of solute per 100 cm^3	μg%	
nanograms of solute per 100 cm^3	ng%	
micrograms of solute per cm^3	μg cm^{-3}	≡ ppm
micrograms per gram	μg g^{-1}	
nanograms of solute per cm^3	ng cm^{-3}	≡ ppb
nanograms per gram	ng g^{-1}	
picograms of solute per cm^3	pg cm^{-3}	≡ ppt
picograms per gram	pg g^{-1}	

* The table includes most of the methods of expressing concentration that are in current use, although some are not consistent with SI.

Constituent
A component of a sample; it may be further classified as:

major	$>10\%$
minor	0.01–10%
trace	1–100 ppm (0.0001–0.01%)
ultratrace	<1 ppm

Detection limit
The smallest amount or concentration of an analyte that can be detected by a given procedure and with a given degree of confidence (p. 25).

Determination
A quantitative measure of an analyte with an accuracy of considerably better than 10% of the amount present.

Equivalent
That amount of a substance which, in a specified chemical reaction, produces, reacts with or can be indirectly equated with one mole (6.023×10^{23}) of hydrogen ions. This confusing term is *obsolete* but its use is still to be found in some analytical laboratories.

Estimation
A semi-quantitative measure of the amount of an analyte present in a sample, i.e. an approximate measurement having an accuracy no better than about 10% of the amount present.

Interference
An effect which alters or obscures the behaviour of an analyte in an analytical procedure. It may arise from the sample itself, from contaminants or reagents introduced during the procedure or from the instrumentation used for the measurements.

Internal standard
A compound or element added to *all* calibration standards and samples in a constant known amount. Sometimes a major constituent of the samples to be analysed can be used for this purpose. Instead of preparing a conventional calibration curve of instrument response as a function of analyte mass, volume or concentration, a *response ratio* is computed for each calibration standard and sample, i.e. the instrument response for the analyte is divided by the corresponding response for the fixed amount of added internal standard. Ideally, the latter will be the same for each pair of measurements but variations in experimental conditions may alter the responses of both analyte and internal standard. However, their *ratio* should be unaffected and should therefore be a more reliable function of

the mass, volume or concentration of the analyte than its response alone. The analyte in a sample is determined from its response ratio using the calibration graph and should be independent of sample size.

Masking
Treatment of a sample with a reagent to prevent interference with the response of the analyte by other constituents of the sample (p. 40).

Matrix
The remainder of the sample of which the analyte forms a part.

Method
The overall description of the instructions for a particular analysis.

Precision
The random or indeterminate error associated with a measurement or result. Sometimes called the variability, it can be represented statistically by the standard deviation or relative standard deviation (coefficient of variation) (p. 14).

Primary standard
A substance whose purity and stability are particularly well established and with which other standards may be compared.

Procedure
A description of the practical steps involved in an analysis.

Reagent
A chemical used to produce a specified reaction in relation to an analytical procedure.

Sample
A substance or portion of a substance about which analytical information is required.

Sensitivity

(1) The change in the response from an analyte relative to a small variation in the amount being determined. The sensitivity is equal to the slope of the calibration curve, being constant if the curve is linear.
(2) The ability of a method to facilitate the detection or determination of an analyte.

Standard

(1) A pure substance which reacts in a quantitative and known stoichiometric manner with the analyte or a reagent.

(2) The pure analyte or a substance containing an accurately known amount of it which is used to calibrate an instrument or to standardize a reagent solution.

Standard addition
A method of quantitative analysis whereby the response from an analyte is measured before and after adding a known amount of that analyte to the sample. The amount of analyte originally in the sample is determined from a calibration curve or by simple proportion if the curve is linear. The main advantage of the method is that all measurements of the analyte are made

Table 1.3 Physical quantities and units including SI and CGS

	SI		CGS	
Physical quantity	Unit	Symbol	Unit	Symbol
length, l	metre	m	centimetre	cm
mass, m	kilogram	kg	gram	g
time, t	second	s	second	s
energy, E	joule	J	erg	—
			electron volt	eV
			calorie	cal
thermodynamic temperature, T	kelvin	K	kelvin	K
amount of substance, n	mole	mol	mole	mol
force, F	newton	N	dyne	—
volume, V	cubic metre	m^3	cubic centimetre	cm^3 (ml)
	cubic decimetre	dm^3	litre	l
electric current, I or i	ampere	A	ampere	A
electric potential difference, E	volt	V	volt	V
electric resistance, R	ohm	Ω	ohm	Ω
electric conductance, G	siemens	S	mho	Ω^{-1}
quantity of electricity, Q	coulomb	C	coulomb	C
electric capacitance, C	farad	F	farad	F
frequency, ν	hertz	Hz	cycles per second	cps
wavenumber, σ ($\bar{\nu}$)			reciprocal centimetre	cm^{-1}
wavelength, λ	metre	m	centimetre	cm
	millimetre	mm	millimetre	mm
	micrometre	μm	micron	μ
	nanometre	nm	millimicron	mμ
			Ångström	Å
magnetic flux density, B	tesla	T	gauss	G
disintegration rate	curie	Ci	curie	Ci
	becquerel	Bq		
nuclear cross-sectional area	barn	b	barn	b

in the same matrix which eliminates interference effects arising from differences in the overall composition of sample and standards (pp. 30, 114).

Standardization
Determination of the concentration of an analyte or reagent solution from its reaction with a standard or primary standard.

Technique
The principle upon which a group of methods is based.

Validation of methods
In order to ensure that results yielded by a method are as accurate as possible, it is essential to validate the method by analysing standards which have an accepted analyte content, and a matrix similar to that of the sample. The accepted values for these validated standards are obtained by extensive analysis, using a range of different methods. Internationally accepted standards are available.

Physical quantities relevant to analytical measurements and the units and symbols used to express them are given in Table 1.3. Both SI and CGS units have been included because of current widespread use of the latter and for ease of comparison with older literature. However, only the SI nomenclature is now officially recognized and the use of the CGS system should be progressively discouraged.

Further reading

Skoog, D. A. & West, D. M., *Fundamentals of Analytical Chemistry* (4th edn), CBS College Publishing, New York, 1982.