characteristic of the atoms involved; this is called **secondary or fluorescence radiation**. The sample area can be large, and by examining the peak heights of the fluorescence radiation it is possible to get an indication of the sample composition. **X-ray fluorescence analysis** is a rapid process which finds application in metallurgical laboratories, in the processing of metallic ores, and in the cement industry.

Crystalline material will diffract a beam of X-rays, and X-ray powder diffractometry can be used to identify components of mixtures. These X-ray procedures are examples of **non-destructive analysis**.

Radioactivity

Methods based on radioactivity belong to the realm of radiochemistry and may involve measuring the intensity of the radiation from a naturally radioactive material; measuring radioactivity induced by exposing the sample to a **neutron source** (**activation analysis**); or **isotope dilution** and **radioimmunoassay**. Typical applications are determining trace elements for investigating pollution problems; examining geological specimens; and quality control in semiconductor manufacturing.

Kinetic methods

Kinetic methods are based on increasing the speed of a reaction by adding a small amount of a catalyst; within limits, the rate of the catalysed reaction will be governed by the amount of catalyst present. If a calibration curve is prepared showing variation of reaction rate with amount of catalyst used, then reaction rate measurements will determine how much catalyst has been added in a certain instance. This provides a sensitive method for determining submicrogram amounts of appropriate organic substances. The method can also be adapted to determine the amount of a substance in solution by adding a catalyst which will destroy it completely, and measuring the concomitant change in the absorbance of the solution for visible or ultraviolet radiation. These procedures are applied in clinical chemistry.

Optical methods

Some optical methods are particularly appropriate for organic compounds. A **refractometer** can be used to measure the refractive index of liquids. This will often provide a means of identifying a pure compound, and in conjunction with a calibration curve, it can also be used to analyse a mixture of two liquids. The **optical rotation** of optically active compounds can be measured, and polarimetric measurements can be used to identify pure substances; it can also be used for quantitative analysis.

Despite the many advantages possessed by instrumental methods, their widespread adoption has not rendered the purely chemical or classical methods obsolete; the situation is influenced by four main factors:

1. The apparatus required for classical procedures is cheap and readily available in all laboratories, but many instruments are expensive and their use will only be justified if numerous samples have to be analysed, or when dealing with the determination of substances present in minute quantities (trace, subtrace or ultratrace analysis).
2. With instrumental methods it is necessary to carry out a calibration operation using a sample of material of known composition as reference substance.

3. Although an instrumental method is ideal for a large number of routine determinations, an occasional, non-routine analysis is often simpler by a classical method. Instrument calibration can be time-consuming.
4. To obtain accurate results with instrumental methods, the reagents still need careful weighing, measuring and preparation of standard solutions. Classical analysis provides the essential training and experience.

The good chemical analyst will always appreciate the value of developing the classical skills in order to maximise the quality of instrumental procedures.

1.9 Factors affecting the choice of analytical method

Analytical techniques have different degrees of sophistication, sensitivity and selectivity, as well as different cost and time requirements. An important task for the analyst is to select the best procedure for a given determination. This will require careful consideration of the following criteria:

(a) The type of analysis required: elemental or molecular, routine or occasional.
(b) Problems arising from the nature of the material to be investigated, e.g. radioactive substances, corrosive substances, substances affected by water.
(c) Possible interference from components of the material other than those of interest.
(d) The concentration range to be investigated.
(e) The accuracy required.
(f) The facilities available, particularly the instruments.
(g) The time required to complete the analysis; this will be particularly relevant when the results are required quickly for the control of a manufacturing process. This may mean that accuracy has to be a secondary consideration; it may require expensive instruments or in-line continuous analysis.
(h) The number of analyses of similar type which have to be performed; in other words, are there a limited number of determinations or are there many repetitive analyses?
(i) Does the nature of the specimen, the kind of information sought, or the magnitude of the sample available indicate the use of non-destructive methods as opposed to the more commonly applied destructive methods? Destructive methods usually mean the sample is dissolved before analysis.

Many laboratory workers totally ignore the potential costs related to any proposed analytical work. The running costs alone of many modern instruments can be extremely high and need to be used regularly and efficiently to justify the initial expenditure. It is always worth bearing in mind that single or exploratory analyses may often be carried out much more cheaply and often more quickly by a traditional titrimetric or gravimetric procedure in which only limited sample preparation may be required. Many instrumental methods amply justify their use when there are multiple analyses. The cost of analysis does not only include the actual time the equipment is used, but also a proportion of the maintenance costs and the time the instruments may be standing idle.

1.10 Interferences

Whatever the method finally chosen for the required determination, it should ideally be a **specific method**; that is to say, it should be capable of measuring the amount of desired substance accurately, no matter what other substances may be present. In practice few analytical procedures attain this ideal, but many methods are **selective**; in other words, they can be used to determine any of a limited group of ions or molecules from a much wider selection of ions or molecules. Improved selectivity is frequently achieved by carrying out the analytical procedure under carefully controlled conditions. This is particularly the case with chromatographic separations and determinations. But other substances are often present, making it harder to obtain the desired measurements directly. Interfering substances may mean that extra procedures have to be carried out to remove the interference or to prevent it from taking part in the analytical process. Ionic procedures are used for inorganic substances, whereas solvent extraction and chromatographic procedures are better for organic substances. They may be divided into six categories.

Selective precipitation Appropriate reagents may be added to convert interfering ions into precipitates which can be filtered off; careful pH control is often necessary to achieve a clean separation. Remember that precipitates tend to adsorb substances from solution, so take care to ensure that as little as possible of the substance to be determined is lost in this way.

Masking A complexing agent is added. If the resultant complexes are sufficiently stable, they will fail to react with reagents added in a later step, perhaps a titrimetric procedure or a gravimetric precipitation method.

Selective oxidation (reduction) The sample is treated with a selective oxidising or reducing agent which will react with some of the ions present; the resultant change in oxidation state will often facilitate separation. For example, to precipitate iron as hydroxide, the solution is always oxidised so that iron(III) hydroxide is precipitated; this precipitates at a lower pH than iron(II) hydroxide, which could be contaminated with the hydroxides of many bivalent metals.

Solvent extraction When metal ions are converted into chelate compounds by treatment with suitable organic reagents, the resulting complexes are soluble in organic solvents and can be extracted from the aqueous solution. Many ion association complexes containing bulky ions which are largely organic in character (e.g. the tetraphenylarsonium ion $(C_6H_5)_4As^+$) are soluble in organic solvents, so they can be used to extract appropriate metals ions from aqueous solution. Solvent extraction, along with appropriate acids and bases, may also be used to separate organic compounds from each other before quantification.

Ion exchange Insoluble ion exchange resins contain either anions or cations capable of exchanging with ions in solutions passed over them. They can be used to remove impurities from solutions or to enrich species under examination. Ion exchange is particularly valuable for concentrating low levels of ions in solution before carrying out quantitative analysis by methods of relatively low sensitivity.

Chromatography Chromatography covers a whole of range of separation techniques in which chemicals in solution travel down columns or over surfaces by means of liquids or gases and are separated from each other due to their molecular characteristics. The processes involved in chromatography are now applicable to virtually all inorganic and organic materials, except very insoluble polymers; they are of immense value in obtaining quantitative analytical data. Typical applications include drug analysis in forensic work and high-quality food analysis.

1.11 Data handling

Once the best method of dealing with interferences has been decided on and the most appropriate method of determination chosen, the analysis should be carried out in duplicate and preferably in triplicate. All analytical results should be carefully recorded in a suitable notebook to provide a permanent record of the work. Besides this, many modern instruments are either computer-operated or interfaced with computers, so the results are not only displayed on a visual display unit but also presented graphically and/or in tabular form to serve as a detailed record. Further calculations on the analytical results may be necessary to present them in the form required. Many instruments are now able to treat the raw data and to relate it to calibration charts, action limits and statistical analyses.

Like all physical measurements, any results obtained are subject to a degree of uncertainty, and it is necessary to establish the magnitude of this uncertainty in order that meaningful results can be presented. It is therefore necessary to establish the **precision** of the results, by which we mean the extent to which they are reproducible. This is commonly expressed in terms of the numerical difference between a given experimental value and the mean value of all the experimental results. The **spread** or **range** in a set of results is the numerical difference between the highest and lowest results: this figure is also an indication of the precision of the measurements. However, the most important measures of precision are the standard deviation and the variance: these are discussed in Chapter 4.

The difference between the most probable analytical result and the true value for the sample is termed the **systematic error** in the analysis: it indicates the **accuracy** of the analysis.

1.12 Robotics

Sample preparation can often be the hardest analytical step, especially with solids, and several stages may be required, e.g. reduction of particle size (grinding), mixing for homogeneity, drying and weighing. Operations such as heating, ignition, fusion and the use of solvents are often necessary for sample dissolution. Further, there may be need for samples to be moved to various points within the laboratory. A fully automated analysis requires every operation to be automated. But laboratory robots, developed during the last decade, have enabled routine tasks to be performed sequentially without human involvement.

Owens and Eckstein have described an early robotic system that performed automatic weighing of solids and liquids, pH determination, dilution and dissolution.[1] Controlled by a microcomputer, it totally automated the pH titration of a solid sample. It calibrated the pH meter, prepared standard solutions, determined the end point, presented the data and recorded the results. An important feature is the robot arm, whose movements can often replace human hand, wrist and arm functions. Hence the robot arm can pour liquids or solids, mix liquids by shaking and transfer samples from one laboratory station to another. Some designs allow a robot hand to be interchanged automatically for a syringe that dispenses a given volume of liquid.

The first commercial laboratory robot, the Zymate Laboratory Automation System, was introduced in 1982 by the Zymark Corporation, Hopkinton MA. Strimaltis has made a survey of commercially available robot systems together with their areas of application in analytical science.[2,3] Examples include automatic Karl Fischer titrations, and determinations of dissolved oxygen and biochemical oxygen demand (BOD). The most commonly automated methods include HPLC, GC and UV/visible sample preparation and analysis. Robotic methods have several advantages over manual procedures:

1. A considerable improvement in the analytical precision.
2. A far larger sample throughput and a faster availability of analytical results.
3. An economic saving which is often achieved by an improvement in productivity, particularly if the method requires extensive and repetitive operations.

When integrated with instrumentation and computer control, laboratory robotics allows complete automation of many analytical methods. Freedom from tedious and repetitive tasks will enable the analytical scientist to develop innovatory techniques and to focus on problem solving. In the near future, developments in robot technology will undoubtedly generate new instruments, leading to major advances in laboratory practice.

1.13 Summary

Summarising, the following steps are necessary when confronted with an unfamiliar quantitative determination.

1. Sampling.
2. Literature survey and selection of possible methods of determination.
3. Consideration of interferences and procedures for their removal.

After pooling the information obtained under headings (2) and (3), a selection will be made of a suitable method for analysis along with procedures for dealing with any interferences. Once this has been done the subsequent steps can be carried out.

4. Dissolution of sample.
5. Removal or suppression of interferences.
6. Performance of the determination.
7. Statistical analysis of the results.

The final step is the presentation of the results for further data processing or in the form of a report.

1.14 References

1. G D Owens and R J Eckstein 1982 *Anal. Chem.*, **54**; 2347
2. J R Strimaltis 1989 *J. Chem. Educ.*, **66**; A8
3. J R Strimaltis 1990 *J. Chem. Educ.*, **67**; A20