Trace Quantitative Analysis by Mass Spectrometry

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The authors dedicate this book to all of our mentors and colleagues,
too many to mention by name, with whom we have had the privilege of working over
many years and who have taught us so much.

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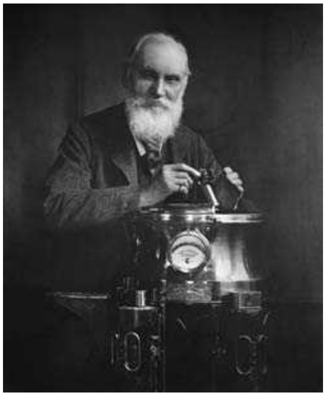
Preface



'When you can measure what you are speaking about and express it in numbers, you know something about it; but when you cannot express it in numbers, your knowledge is of a meagre and unsatisfactory kind . . . '
William Thomson (Lord Kelvin), Lecture to the Institution of Civil Engineers, 3 May 1883.

The discipline devoted to careful measurement of specific properties of the universe around us is known as *metrology*. The famous statement by William Thomson, quoted above, summarizes the importance of quantitative measurements for the testing of scientific hypotheses; indeed, without such quantitative testing, it is fair to say that hypotheses can not be regarded as scientific at all. Missing from Thomson's comment, however, is a mention of the importance of careful evaluation of the uncertainties that are present in any quantitative measurements and the resulting degree of confidence that can be placed in them and any conclusions drawn from them. These uncertainties are just as important as the 'best' quantitative measured value itself.

This book is devoted to the science and art of *chemical metrology*, taken here to mean the quantitative measurement of amounts of specific (known) chemical compounds present at trace levels (roughly defined as one part in 10^6–10^{12}) in complex matrices. Examples are drugs and their metabolites in body fluids, pesticide residues in foodstuffs, contaminants in drinking water etc. Such measurements are extremely demanding, and involve the use of a wide range of apparatus and of experimental procedures and methods of data evaluation, all of which must be used properly if reliable estimates of chemical concentrations and their associated uncertainties are to be obtained. While this is true of any chemical analysis, the modern advances in trace-level analysis are critically dependent on developments in mass spectrometry.

For several decades before its application to chemical analysis, mass spectrometry was a major tool in fundamental physics. The invention of mass spectrometry is usually attributed to Joseph John Thomson, no relative to William Thomson (Lord Kelvin) whose picture appears above. In 1897 J.J. Thomson measured the ratio of the charge of an electron to its mass, thus confirming for the first time that this then-mysterious entity possessed properties characteristic of a particle. (It is interesting that his son G.P. Thomson later emulated his father by winning a Nobel Prize, but for demonstrating that the electron *also* possesses properties characteristic of a wave!). An account of the life and work of J.J. Thomson was published (Griffiths 1997) to commemorate the centenary of the first measurement of mass-to-charge of an elementary particle.

F.W. Aston, a student of Thomson, won a Nobel Prize for using mass spectrometry to demonstrate the existence of the isotopes of the elements (Aston 1919), and for developing a higher resolution mass spectrometer that permitted measurement of atomic masses with sufficient accuracy and precision for the first reliable estimates of so-called mass defects, i.e., deviations of actual (measured) atomic masses from those predicted from the sums of the masses of the constituent elementary particles (protons, neutrons and electrons). Later, this work was extended by K.T. Bainbridge whose measurements of mass defects (Bainbridge 1932, 1936) were of sufficient accuracy and precision to confirm for the first time the famous relationship derived by Albert Einstein concerning the equivalence of mass (in this case the mass defect) and energy (in this case the binding energy of protons and neutrons within an atomic nucleus).

The first analysis of positive ions is attributed to Wien, who used a magnetic field to separate ions of different mass-to-charge ratios (Wien 1898), but the first appreciation of the potential of the new technique in chemical analysis appears to have again resulted from the work of Thomson in his famous book *Rays of Positive Electricity and Their Application to Chemical Analysis* (Thomson 1913). The present book is intended as an introduction to the use of mass spectrometry for quantitative measurements of the amounts of specific (known) chemical compounds (so-called 'target analytes') present at trace levels in complex matrices. This modern day meaning of 'quantitative mass spectrometry' is rather different from its much more specialized historical meaning in the earliest days of application of the technique to chemistry.

In the two decades spanning about 1940–1960, the petroleum industry was the major proponent of mass spectrometry as a tool of analytical chemistry, and indeed the first few issues of *Advances in Mass Spectrometry* (essentially the proceedings of the International Conferences on Mass Spectrometry) were sponsored and published by the Petroleum Institute. Raw petroleum and its distillate fractions are incredibly complex mixtures of chemical compounds, mainly corresponding to chemical compositions $C_cH_hN_nO_oS_s$, and it is impossible to devise a complete chemical analysis of such an extremely large number of components at concentrations covering a dynamic range of many orders of magnitude. However, some knowledge of chemical composition is required by chemical engineers for optimization of the industrial processes required to produce end products with the desired properties. To this end petroleum chemists devised the concepts of compound *class*, i.e., compounds with a specified composition with respect to heteroatoms only ($N_nO_oS_s$), and compound *type*, i.e., compounds with a specified value of Z when the composition is expressed as $C_cH_{2c+Z}N_nO_oS_s$. Clearly the parameter Z is related to the degree of unsaturation. Reviews of this application of mass spectrometry have been published (Grayson 2002; Roussis 1999). The earliest methods yielded information on relative amounts of hydrocarbon compounds in a distillate, i.e. *type* analyses for the compound class with $n = o = s =$ zero. A high resolution adaptation of the original low resolution mass spectral methods was first published in 1967, and permitted determinations of 18 saturated- and aromatic-hydrocarbon types and four aromatic types containing sulfur.

Essentially, the general approach first identified specific mass-to-charge ratio (*m/z*) values in the electron ionization mass spectra that are characteristic of each compound type, and obtained a calibration based on analysis of mixtures of known composition:

$$\mathbf{S} = \mathbf{R}.\mathbf{C}$$

where **S** is a vector containing the appropriate sums of signal intensities at the *m/z* values that are characteristic for each compound type, **C** is a vector whose elements are the concentrations of these compound types, and **R** is the (square) matrix of mass spectrometric response factors determined from the calibration experiments (average response coefficients for each type are on the diagonal of the matrix and the off-diagonal elements take into account inter-type contributions to signal intensities at the characteristic *m/z* values). Quantitative analysis of an unknown thus requires inversion of the response matrix:

$$\mathbf{C} = \mathbf{R}^{-1}.\mathbf{S}$$

An example of such a type analysis for the class $C_cH_{2c+Z}S$, for both a raw petroleum feedstock and one of its products from a refinery process designed to remove the sulfur content, is shown in Figure P.1 (here the carbon number c is replaced by n). Modern developments in quantitative petroleum analysis incorporate new advances in separation science as well as in mass spectrometric technologies, especially ionization techniques and ultrahigh resolving power (Marshall 2004) and improved calibration of the response matrix (Fafet 1999).

This early and narrow interpretation of the phrase 'quantitative mass spectrometry' is now badly outdated, although petroleum analysis is still an important branch of analytical chemistry that is still being developed. However, apart from its historical importance it introduced important concepts, including calibration and response factor, that will appear throughout this book. Nowadays, quantitation by mass spectrometry generally refers to determination of target analytes (known and specified chemical species, rather than groups of compounds defined within 'classes' or 'types' as in the petroleum case), present in a complex matrix at trace levels. This book is intended as an introduction to this demanding branch of measurement science, one that is crucial for meaningful studies of a wide range of phenomena including environmental, pharmacological and biomedical studies.

The approach adopted throughout the book is to emphasize the fundamentals underlying the scientific

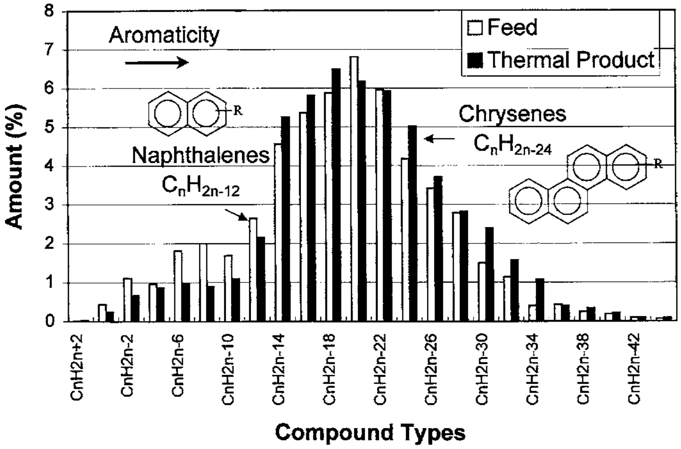


Figure P.1 Type analysis of a petroleum feedstock and its hydrocracked product for compound class $C_nH_{2n+Z}S$. Reproduced with permission from S. Roussis, *Rapid Commun. Mass Spectrom.* **13**, 1031–1051 (1999).

instruments and methodologies, illustrated by historically important developments as well as innovations that were current at the time of completing the manuscript (late summer 2007). Hopefully this will prove to be of more lasting value for the reader. However, a discussion of 'fundamentals' without any description of how 'the fundamental things apply' (see text box) to real-world problems is unlikely to be of much use to anyone, so the final chapter discusses some illustrative examples from the literature.

As mentioned above, although this book is devoted to *quantitative* analysis of specified 'target' analytes, the analyst must have a degree of confidence that the signals being measured do indeed arise from the presence of that target analyte (confirmation of analyte identity), and only from that analyte (signal purity). Therefore, even quantitative analyses inevitably involve some degree of confirmation of analyte structure and identity, and also a check for potential contributions to the recorded instrumental signals from other compounds. The degree to which such checking of analyte identity and of signal purity is necessary will vary from case to case, e.g., analysis of a synthetic pharmaceutical drug in blood plasma following a clinical dose is much less likely to require a high degree of identity confirmation than that of a chlorinated pollutant in an environmental sample. Determination of the appropriate degree of such checks is an example of application of the concept of '*Fitness for Purpose*', another major theme of this book. This principle is discussed more fully in Chapter 9.2, but will appear in several intervening chapters so a very brief introduction to the concept is presented here, based on a discussion (Bethem 2003) of its applicability to mass spectrometric analyses. The following principles are quotations from this work (Bethem 2003):

1. Ultimately it is the responsibility of the analyst to make choices, provide supporting data, and interpret results according to scientific principles and qualified judgment.
2. Analysts should use methods which are Fit for Purpose. Analysts should be able to show that their methods are Fit for Purpose.
3. Fitness for Purpose means that the uncertainty inherent in a given method is tolerable given the needs of the application area.
4. Targets for measurement uncertainty describe how accurate and precise the measurements need to be. Targets for identification confidence describe how certain one needs to be that the correct analyte has been identified.
5. Establishing method fitness consists of showing that the targets for measurement uncertainty and identification confidence have been met.

In its simplest terms, the 'Fitness for Purpose' principle corresponds to the commonsense notion that an analytical method must provide answers with sufficiently low uncertainties that the requirements of the user of the data are fully met within specified constraints of time, cost etc. On the other hand there is no point in developing, validating and using an analytical method with extremely low uncertainties in the data (high precision and accuracy) if a considerably less demanding method (generally less expensive in terms of money, time and effort) will suffice.

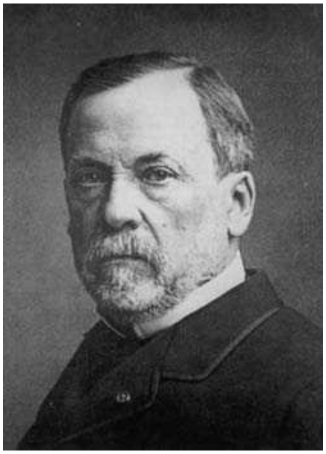
‘The Fundamental Things Apply —’

with apologies to ‘As time goes by’ by Herman Hupfeld (1931); Warner Bros. Music Corp.

This famous song was featured in the films *Casablanca* and *Sleepless in Seattle*, as well as the well-known British TV comedy series of the same name. This is a long stretch from the subject of this book, but the above quotation from the lyrics seems appropriate.

A distinction between ‘fundamental’ and ‘applied’ science is drawn by some, including (alas) by some funding agencies! One of the themes of this book is best expressed by quoting one of the giants of 19th century science:

> *‘There does not exist a category of science to which one can give the name applied science. There are science and the applications of science, bound together as the fruit of the tree’. Louis Pasteur, ‘Revue Scientifique,’ Paris, 1871.*



Louis Pasteur

It is not essential for an experimental scientist to be familiar with and understand every detail of the theoretical underpinnings of his/her laboratory work. However, to be able to properly plan an experimental investigation so that the results can be meaningfully interpreted, it *is* essential that he/she should understand the background of the relevant theory, its basic assumptions, and the limits of its applicability and the magnitude of the consequences of the approximations involved. This general theme was a guiding principle in writing this book, and hopefully this approach will ensure that the book will have a reasonably long useful lifetime. However, fundamentals without much discussion of how they apply to real-world problems in trace analytical chemistry are not of themselves very useful, and discussions of how the ‘fundamental things apply’ will appear later in the book.

A specific example of the continuity between ‘applied’ and ‘fundamental’ research, of direct relevance to the subject of this book (see Chapter 5), is provided by the direct line of development starting from an electrostatic paint sprayer designed for industrial use, through attempts by materials scientists to prepare single molecules of synthetic polymers in the gas phase to enable fundamental studies, to the eventual award of a Nobel Prize to John B. Fenn for the invention of electrospray ionization mass spectrometry and its application to biochemistry and molecular biology.

Figure P.2 shows a generalized procedure for achieving Fitness for Purpose.

This book is not intended to cover important branches of mass spectrometry that provide accurate and precise quantitative measurements of *relative* concentrations, e.g., of variations in isotopic ratios of an element by isotope ratio mass spectrometry (IRMS) and accelerator mass spectrometry (AMS). Rather, this book is mainly concerned with determinations of absolute *amount of substance* (see Chapter 1 for a definition and explanation), particularly for compounds present at trace levels in complex matrices. (The only exception is the inclusion of a brief description of methods used to determine *differences* in levels of proteins in living cells or organisms subjected to different stimuli, e.g., disease state vs normal state).

The book covers analysis of ‘small’ ($< 2000\,\mathrm{Da}$) organic molecules, in environmental and biomedical matrices. The first book exclusively devoted to this subject (Millard 1977) is now rather out of date as a result of more recent spectacular advances in mass spectrometric technology. Very recently two excellent introductions to the subject have appeared (Duncan 2006; Lavagnini 2006). The present book differs from these with regard to their respective lengths; the present book is much longer, as a result of the attempt to provide a comprehensive introduction to all the many ancillary techniques and tools that must be coordinated to provide a reliable result for a trace-level quantitative analysis by mass spectrometry. Thus, many of the present chapters discuss matters that are common to any quantitative analytical method, not only to those in which mass spectrometry is the key component providing the final analytical signal

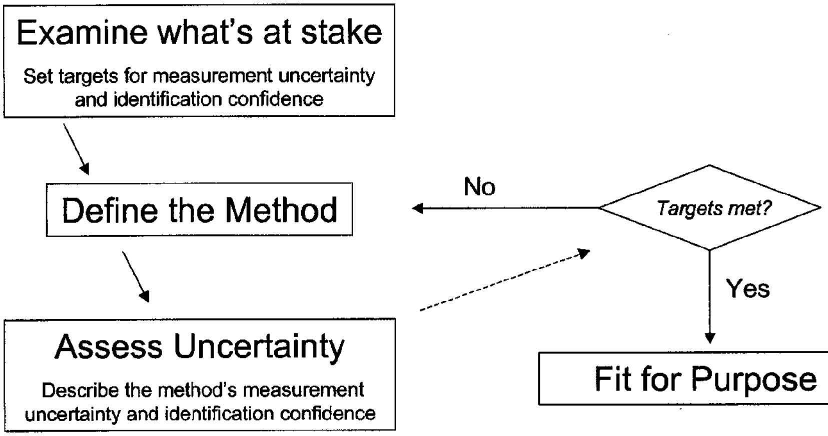


Figure P.2 Outline of a general recommended process for achieving Fitness for Purpose. Reproduced from Bethem *et al.*, *J. Amer. Soc. Mass Spectrom.* **14**, 528 (2003), with permission, copyright (2003) Elsevier.

used to estimate the concentration of the target analyte. The present book is written at a level that presupposes some basic undergraduate-level knowledge of chemistry, physics, and mathematics and statistics.

This book also treats the more recent developments of quantitative analysis of specific proteins in biological systems, even though these hardly qualify as 'small molecules'. However, it does *not* cover the important aspect of analysis of trace level metals by, e.g., ICP–MS; an excellent book covering this subject has appeared recently (Nelms 2005).

It must be emphasized that any book such as this can only be regarded as a preparation for the real learning process in this demanding practical art, namely, exposure to working on real-life problems in a real laboratory. The kinds of measurements that are addressed here really do push the various technologies involved to their current limits, and 'learning by doing' is the only truly meaningful method. This principle is well illustrated by a quotation from what might be described as 'the older literature':

> *Those who are good at archery learnt from the bow and not from Yi the Archer. Those who know how to manage boats learnt from boats and not from Wo (the legendary boatman). Those who can think learned for themselves and not from the Sages.* Kuan Yin Tze, 8th century.

The dangers involved in a sole reliance on 'learning by reading', in a practical discipline like analytical chemistry, are summarized in the following advice:

> *Il ne faut pas laisser les intellectuals jouer avec les allumettes. (Don't let the intellectuals play with the matches).* Jacques Prévert, 1900–1977.

However, it is hoped that reading this book will be useful both in providing enough background information that the first exposure to the 'learning by doing' process will not seem quite so daunting, and also will provide a useful reference thereafter. The book attempts to cover a wide range of subdisciplines, and inevitably some errors of both omission and commission will remain despite extensive checking. The authors would greatly appreciate assistance from colleagues in identifying and correcting these errors.

Robert K. Boyd, Cecilia Basic, Robert A. Bethem
October 2007

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1

Measurement, Dimensions and Units

Standards of Comparison

The US standard railroad gauge (distance between the rails) is 4 feet, 8.5 inches. That's a very strange number, why was it used? Because the first railroads were built in Britain, and the North American railroads were built by British immigrants.

Why did they build them like that? Because the first railways (lines and rolling stock) were built by the same companies that built the pre-railroad tramways, and they used the same old gauge. All right, why did 'they' use that gauge? Because the tramways used the same jigs and tools that had been used for building wagons, and the wagons used that wheel spacing.

Are we getting anywhere? Why did the wagons use that strange wheel spacing? Well, if they tried to use any other spacing the wagons would break down on some of the old long distance roads, because that's the spacing of the old wheel ruts.

So who built these old rutted roads? The first long distance roads in Europe were built by Imperial Rome for the purposes of the Roman Legions. These roads were still widely used in the 19th century. And the ruts? The initial ruts, which everyone else had to match in case they destroyed their wagons, were made by Roman war chariots. Since the chariots were made for Imperial Rome they were all alike, including the wheel spacing. So now we have an answer to the original question. The US standard railroad gauge of 4 feet, 8.5 inches is derived from the original specification for an Imperial Roman army war chariot.

The next time you are struggling with conversion factors between units and wonder how we ended up with all this nonsense, you may be closer to the truth than you knew. Because the Imperial Roman chariots were made to be just wide enough to accommodate the south ends of two war horses heading north.

And this is not yet the end! The US space shuttle has two big booster rockets attached to the sides of the main fuel tank. These are solid rocket boosters (SRBs) made in a factory in Utah. It has been alleged that the engineers who designed the SRBs would have preferred to make them a bit fatter, but the SRBs had to be shipped by train from the factory to the launch site. The railroad line from the factory happens to run through a tunnel in the mountains, and the SRBs had to fit through that tunnel. The tunnel is only slightly wider than the railroad track, and we now know the story behind the width of the track!

So, limitations on the size of crucial components of the space shuttle arose from the average width of the Roman horses' rear ends.

1.1 Introduction

All quantitative measurements are really comparisons between an unknown quantity (such as the height of a person) and a measuring instrument of some kind (e.g., a measuring tape). But to be able to communicate the results of our measurements among one another we have to agree on exactly what we are comparing our measurements to. If I say that I measured my height and the reading on the tape was 72, that does not tell you much. But if I say the value was 72 inches, that does provide some meaningful

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information provided that you know what an inch is (tradition tells us that the inch was originally defined as the length of part of the thumb of some long-forgotten potentate but that does not help us much). But even that information is incomplete as we do not know the uncertainty in the measurement. Most people understand in a general way the concepts of accuracy (deviation of the measured value from the 'true' value) and precision (a measure of how close is the agreement among repeated measurements of the same quantity) as different aspects of total uncertainty, and such a general understanding will suffice for the first few chapters of this book. However, the result of a measurement without an accompanying estimate of its uncertainty is of little value, and a more complete discussion of experimental uncertainty is provided in Chapter 8 in preparation for the practical discussions of Chapters 9 and 10.

Actually, the only correct answer to the question 'what is an inch' is that one inch is defined as exactly 2.54 centimeters (zero uncertainty in this defined conversion factor). So now we have to ask what is a centimeter, and most of us know that a centimeter is 1/100 of a meter. So what is a meter? This is starting to sound about as arbitrary as the Roman horses' hind quarters mentioned in the text box but in this case we can give a more useful if less entertaining answer: The meter is the length of the path traveled by light in vacuum during a time interval of 1/299 792 458 of a second. Note that the effect of this definition is to fix the speed of light in vacuum at exactly 299 792 458 meters per second, and that we still have not arrived at a final definition of the meter until we have defined the second (Table 1.1). This is the internationally accepted definition of the meter, established in 1983, and forms part of the International System of Units (Système Internationale d'Unites, known as SI for short). The SI establishes the standards of comparison used by all countries when the measured values of physical and chemical properties are reported. Such an international agreement is essential not only for science and technology, but also for trade. For example, consider the potential confusion arising from the following example:

1 US quart (dry) = 1.10122 litres
1 US quart (liquid) = 0.94635 litres
1 Imperial (UK/Canada) quart (liquid) = 1.136523 litres

(The litre is defined in the SI as 1/1000 of a cubic meter: $1\text{L} = 10^{-3}\,\text{m}^3$). Many other examples of such ambiguities can be given (see, for example, the unit conversions

Table 1.1 SI Base Quantities and Units

Quantity	Name of unit	Symbol	Definition
Length	meter	m	The meter is the length of the path travelled by light in vacuum during a time interval of 1/299 792 458 of a second.
Mass	kilogram	kg	The kilogram is the unit of mass; it is equal to the mass of the international prototype of the kilogram.
Time	second	s	The second is the duration of 9 192 631 770 periods of the radiation corresponding to the transition between the two hyperfine levels of the ground state of the caesium 133 atom.
Electric current	ampere	A	The ampere is that constant current which, if maintained in two straight parallel conductors of infinite length, of negligible circular cross-section, and placed one meter apart in vacuum, would produce between these conductors a force equal to 2×10^{-7} newton per meter of length.
Thermodynamic temperature	kelvin	K	The kelvin, unit of thermodynamic temperature, is the fraction 1/273.16 of the thermodynamic temperature of the triple point of water.
Amount of substance	mole	mol	The mole is the amount of substance of a system which contains as many elementary entities as there are atoms in 0.012 kilogram of carbon 12; its symbol is 'mol.' When the mole is used, the elementary entities must be specified and may be atoms, molecules, ions, electrons, other particles, or specified groups of such particles.
Luminous intensity	candela	cd	The candela is the luminous intensity, in a given direction, of a source that emits monochromatic radiation of frequency 540×10^{12} hertz and that has a radiant intensity in that direction of 1/683 watt per steradian.

at: http://www.megaconverter.com/Mega2/index.html). Such discrepancies may not seem to be very important when only a single quart is considered, but in international trade where literally millions of quarts of some commodity might be traded, the 19 % difference between the two definitions of the liquid quart could lead to extreme difficulties if the ambiguity were not recognized and taken into account. In a lecture on 'Money as the measure of value and medium of exchange', delivered in 1763 at the University of Glasgow, Adam Smith commented (Smith 1763, quoted in Ashworth 2004):

> 'Natural measures of quantity, such as fathoms, cubits, inches, taken from the proportion of the human body, were once in use with every nation. But by a little observation they found that one man's arm was longer or shorter than another's, and that one was not to be compared with the other; and therefore wise men who attended to these things would endeavour to fix upon some more accurate measure, that equal quantities might be of equal values. Their method became absolutely necessary when people came to deal in many commodities, and in great quantities of them.'

It is precisely this kind of uncertainty that the SI is designed to avoid in both science and in trade and commerce. In this regard it is unfortunate to note that even definitions of words used to denote numbers are still subject to ambiguity. For example, in most countries 'one billion' (or the equivalent word in a country's official language) is defined as 10^{12} (a million million), but in the USA (and increasingly in other English-speaking countries) a billion is used to represent 10^9 (a thousand million) and 10^{12} is referred to as a 'trillion'. In view of this ambiguity it is always preferable to use scientific numerical notation.

1.2 The International System of Units (SI)

An excellent source of information about the SI can be found at the website of the US National Institute for Standards and Technology (NIST): http://physics.nist.gov/cuu/Units/index.html

Here we shall be mainly concerned with those quantities that directly affect quantitative measurements of amounts of chemical substances by mass spectrometry. However, it is appropriate to briefly describe some general features of the SI.

Early History of the SI

There is a strong French connection with the SI, including its name and the location in Paris of the central organization that coordinates this international agreement (Bureau International des Poids et Mesures, or BIPM), and the international guiding body CIPM (Comité International de Poids et Mesures, i.e., International Committee for Weights and Measures). This connection was established at the time of the French Revolution when the revolutionary government decided that the chaotic state of weights and measures in France had to be fixed. The intellectual leader in this initiative, that resulted in the so-called Metric System, was the chemist Antoine Lavoisier, famous for his demonstration that combustion involves reaction with oxygen and that water is formed by combustion of two parts of hydrogen with one of oxygen. His efforts resulted in the creation of two artifacts made of platinum (chosen because of its resistance to oxidation), one representing the meter as the new unit of length between two scratch marks on the platinum bar, and the other the kilogram. These artifacts were housed in the Archives de la République in Paris in 1799, and this represents the first step taken towards establishment of the modern SI.

Sadly, Lavoisier did not live to see this realization of his ideas. Despite his fame, and his services to science and his country (he was a liberal by the standards of pre-revolutionary France and played an active role in the events leading to the Revolution and, in its early years, formulated plans for many reforms), he fell into disfavour because of his history as a former farmer-general of taxes, and was guillotined in 1794. After his arrest and a trial that lasted less than a day, Lavoisier requested postponement of his execution so that he could complete some experiments, but the presiding judge infamously refused: 'L'état n'a pas besoin de savants' (the state has no need of intellectuals).

Antoine Lavoisier

Any system of measurement must decide what to do about the fact that there are literally thousands of physical properties that we measure, each of which is expressed as a measured number of some well-defined unit of measurement. It would be impossible to set up primary standards for the units of each and every one of these thousands of physical quantities, but fortunately there is no need to do so since there are many relationships connecting the measurable quantities to one another. A simple example that is of direct importance to the subject of this book is that of volume; as mentioned above, the SI unit of volume (cubic meter) is simply related to the SI unit for length via the physical relationship between the two quantities. So the first question to be settled concerns how many, and which, physical quantities should be defined as SI base quantities (sometimes referred to as dimensions), for which the defined units of measurement can be combined appropriately to give the SI units for all other measurable quantities.

At one time it was thought to be more 'elegant' to work with a minimum possible number of dimensions and their defined units of measurement, and this pseudo-esthetic criterion gave rise to the three-dimensional centimeter-gram-second (cgs) and meter-kilogram-second (MKS) systems. However, it soon became apparent that utility and convenience were more important than perceived elegance! As a simple example, consider Coulomb's Law for the electrostatic force F between two electric charges q_1 and q_2 separated by a distance r in a vacuum:

$$F = k_o . q_1 . q_2 / r^2$$

In the simple form of Coulomb's Law as used with the cgs system, the Coulomb's Law Constant k_o is treated as a dimensionless constant with value 1. (This is not the case in the SI, where $k = 1/(4\pi\varepsilon_o)$ where ε_o is the permittivity of free space $= 8.854187817 \times 10^{-12}\,s^4A^2kg^{-1}m^{-3}$). By Newton's Second Law of Motion, force is given as (mass × acceleration), i.e., $(\text{mass} \times \text{length} \times \text{time}^{-2})$, so in the cgs system $q_1 \cdot q_2$ corresponds to $(\text{mass} \times \text{length}^3 \times \text{time}^{-2})$; thus, in such a three-dimensional measurement system, electrical charge q corresponds to $(\text{mass}^{\frac{1}{2}} \times \text{length}^{\frac{3}{2}} \times \text{time}^{-1})$. This very awkward (and inelegant!) result involving fractional exponents becomes even more cumbersome when magnetism is considered. Once it was accepted that usefulness was the only criterion for deciding on the base physical quantities (dimensions) and their units of measurement, it was finally agreed that the most useful number of dimensions for the SI was seven. Some of these seven are of little or no direct consequence for this book, but for the sake of completeness they are all listed in Table 1.1. Some important SI units, that are derived from the base units but have special names and symbols, are listed in Table 1.2.

The two base quantities (and their associated SI units) that are most important for quantitative chemical analysis are amount of substance (mole) and mass (kilogram), although length (meter) is also important via its derived quantity volume in view of the convenience introduced by our common use of volume concentrations for liquid solutions. (Note, however, that the latter will in principle vary with temperature as a result of expansion or contraction of the liquid).

The kilogram is unique among the SI base units for two reasons. Firstly, the unit of mass is the only one whose name contains a prefix (this is a historical accident arising from the old centimeter-gram-second system of measurement mentioned above). Names and symbols for decimal multiples and submultiples of the unit of mass are formed

Table 1.2 Some SI Derived units with special names and symbols[a]

Derived quantity	Name of unit	Symbol	Relationship to SI base units	Relationship to other SI units
Plane angle	radian	rad	$m.m^{-1}$ (= 1)	—
Solid angle	steradian	sr	$m^2.m^{-2}$ (= 1)	—
Frequency	hertz	Hz	s^{-1}	—
Force	newton	N	$m.kg.s^{-2}$	—
Pressure	pascal	Pa	$m^{-1}.kg.s^{-2}$	$N.m^{-2}$
Energy	joule	J	$m^2.kg.s^{-2}$	N.m; $Pa.m^3$
Power	watt	W	$m^2.kg.s^{-3}$	$J.s^{-1}$
Electric charge	coulomb	C	A.s	—
Electric potential difference	volt	V	$m^2 \cdot kg \cdot s^{-3} \cdot A^{-1}$	$W.A^{-1}$
Electric resistance	ohm	Ω	$m^2 \cdot kg \cdot s^{-3} \cdot A^{-2}$	$V.A^{-1}$
Magnetic flux density	tesla	B	$kg \cdot s^{-2} \cdot A^{-1}$	
Celsius temperature	degree Celsius	°C	K[b]	—

a for a complete list and discussion, see Taylor (1995) and Taylor (2001).
b the *size* of the two units is the same, but Celsius temperature (°C) = thermodynamic temperature (K) − 273.15 (the ice point).