1 Introduction

Detailed knowledge of the chemical processes in plants, animals and in our environment with air, water and soil, about the safety of food and products has been made possible only through the power of modern instrumental analysis. In an increasingly short time span, more and more data are being collected. The absolute detection limits for organic substances are down in the attomole region, and counting individual molecules per unit time has already become a reality. In food safety and environmental analysis we are making measurements at the level of background contamination. Most samples subjected to chemical trace analysis carry high matrix, as are even blank samples. With the demand for decreasing detection limits by legal regulations, in the future effective sample preparation and separation procedures in association with highly selective detection techniques will be of critical importance for analysis. In addition, the number of substances requiring detection is increasing and with the broadening possibilities for analysis, so is the number of samples. The increase in analytical sensitivity is exemplified in the case of dioxins with 2,3,7,8-TCDD (tetrachlorodibenzodioxin), the most toxic food and feed contamination known today (Table 1.1).

Capillary gas chromatography (GC) is today the most important analytical method in organic chemical analysis for the determination of individual low molecular substances in complex mixtures. Mass spectrometry (MS) as the detection method gives the most meaningful data, arising from the direct determination of the substance molecule or of fragments. The results of mass spectrometry are therefore used as a reference for other indirect detection processes and finally for confirmation of the facts. The complete integration of MS and GC into a single GC-MS system has shown itself to be synergistic in every respect. While at the beginning of the 1980s MS was considered to be expensive, complicated and time-consuming or personnel-intensive, there is now hardly a GC laboratory which is not equipped with a GC-MS system. At the beginning of the 1990s MS became more widely recognized and furthermore an indispensable detection method for GC. The simple construction, clear function and an operating procedure, which has become easy because of modern computer systems, have resulted in the fact that GC-MS is widely used alongside traditional spectroscopic methods. The universal detection technique, together with high selectivity and very high sensitivity, has made GC-MS important for a broad
**Table 1.1** Sensitivity progress in mass spectrometry.

<table>
<thead>
<tr>
<th>Year</th>
<th>Instrumental technique</th>
<th>Limit of detection (pg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1967</td>
<td>GC-FID (packed column)</td>
<td>500</td>
</tr>
<tr>
<td>1973</td>
<td>GC-MS (quadrupole, packed column)</td>
<td>300</td>
</tr>
<tr>
<td>1976</td>
<td>GC-MS-SIM (magnetic instrument, capillary column)</td>
<td>200</td>
</tr>
<tr>
<td>1977</td>
<td>GC-MS (magnetic sector instrument)</td>
<td>5</td>
</tr>
<tr>
<td>1983</td>
<td>GC-HRMS (double focusing magnetic sector instrument)</td>
<td>0.15</td>
</tr>
<tr>
<td>1984</td>
<td>GC-MSD/SIM (quadrupole mass 'selective detector')</td>
<td>2</td>
</tr>
<tr>
<td>1986</td>
<td>GC-HRMS (double focusing magnetic sector instrument)</td>
<td>0.025</td>
</tr>
<tr>
<td>1989</td>
<td>GC-HRMS (double focusing magnetic sector instrument)</td>
<td>0.010</td>
</tr>
<tr>
<td>1992</td>
<td>GC-HRMS (double focusing magnetic sector instrument)</td>
<td>0.005</td>
</tr>
<tr>
<td>2006</td>
<td>GC × GC-HRMS (using comprehensive GC)</td>
<td>0.0003</td>
</tr>
<tr>
<td>2013</td>
<td>Cryogenic zone compression (t-CZC) GC-HRMS</td>
<td>0.0002</td>
</tr>
</tbody>
</table>

GC, gas chromatography; FID, flame ionization detector; MS, mass spectrometry; SIM, selected ion monitoring; and HRMS, high-resolution mass spectrometry.

The control of the chromatographic separation process still contributes significantly to the exploitation of the analytical performance of the GC-MS system (or according to Konrad Grob: "Chromatography takes place in the column!"). The analytical prediction capabilities of a GC-MS system are, however, dependent upon mastering the spectrometry. The evaluation and assessment of the data is leading to increasingly greater challenges with decreasing detection limits and the increasing number of compounds sought or found. While quantitation today is the main application for GC-MS, trace analysis methods and the appropriate data processing require additional measures for confirmation of results by mass spectrometric methods.

The high performance of GC lies in separation of substance mixtures and providing the transient signal for data deconvolution. With the introduction of fused silica columns, GC has become the most important and powerful separation method of analysing complex mixtures of products. GC-MS accommodates the current trend towards multi-methods or multi-component analyses (e.g. of pesticides, solvents, etc.) in an ideal way. Even isomeric compounds, which are present, for example, in essential oils, metabolic profiling, in polychlorinated biphenyls (PCBs) or dioxins, are separated by GC, while in many cases their mass spectra are almost indistinguishable. The high efficiency as a routine process is achieved through the high speed of analysis and the short turnaround time and
thus guarantees high productivity with a high sample throughput. Adaptation and optimization for different tasks only requires a quick change of column. In many cases, however, and here one is relying on the explanatory power of the mass spectrometer, one type of a medium polar column can be used for different applications by adapting the sample injection technique and modifying the method parameters.

The area of application of GC and GC-MS is limited to substances which are volatile enough to be analysed by GC. The further development of column technology in recent years has been very important for application to the analysis of high-boiling compounds. Temperature-stable phases now allow elution temperatures of up to 500 °C for stable compounds. A pyrolyser in the form of a stand-alone sample injection system extends the area of application to involatile substances by separation and detection of thermal decomposition products. A typical example of current interest for GC-MS analysis of high-boiling compounds is the determination of polyaromatic hydrocarbons, which has become a routine process using the most modern column material.

The coupling of GC with MS using fused silica capillaries has played an important role in achieving a high level of chemical analysis. In particular in the areas of environmental analysis, analysis of residues and forensic science the high information content of GC-MS analyses has brought chemical analysis into focus through sometimes sensational results. For example, it has been used for the determination of anabolic steroids in cough mixture and the accumulation of persistent organic pollutants in the food chain. With the current state of knowledge, GC-MS is an important method for monitoring the introduction, the location and fate of man-made substances in the environment, foodstuffs, chemical processes and biochemical processes in the human body. GC-MS has also made its contribution in areas such as the ozone problem, the safeguarding of quality standards in foodstuffs production, in the study of the metabolism of pharmaceuticals or plant protection agents or in the investigation of polychlorinated dioxins and furans produced in certain chemical processes, to name but a few.

The technical realization of GC-MS coupling occupies a very special position in instrumental analysis. Fused silica columns are easy to handle, can be changed rapidly and are available in many high-quality forms. New microfluidic switching technologies extend the application without compromising performance for flow switching or parallel detection solutions. The optimized carrier gas streams show good compatibility with mass spectrometers, which is true today for both carrier gases, helium and hydrogen. Coupling can therefore take place easily by directly connecting the GC column to the ion source of the mass spectrometer.

The obvious challenges of GC and GC-MS lie where actual samples contain involatile components (matrix). In this case the sample must be processed before the analysis appropriately, or suitable column-switching devices need to be considered for backflushing of high-boiling matrix components. The clean-up is generally associated with enrichment of trace components. In many methods, there is a trend towards integrating sample preparation and enrichment in a single instrument. Headspace and purge and trap techniques, thermodesorption
or SPME (solid phase microextraction) are coupled online with GC-MS and got integrated into the data systems for seamless control.

Future development will continue for a highly productive multi-compound trace analysis for the quantitation of mostly regulated target compounds. In addition, especially to comply with the aspects of food safety and product-safety requirements also non-targeted analytical techniques for the identification of potentially hazardous contaminants will evolve applying combined full scan and accurate mass capabilities.

1.1 The Historical Development of the GC-MS Technique

The foundation work in both GC and MS, which led to the current realization, was published at the end of the 1950s. At the end of the 1970s and the beginning of the 1980s, a rapid increase in the use of GC-MS in all areas of organic analysis began. The instrumental technique has now achieved a mature level for the once much specialized technique to become an indispensable routine procedure.

1910: The physicist J.J. Thompson developed the first mass spectrometer and proved for the first time the existence of isotopes ($^{20}$Ne and $^{22}$Ne). He wrote in his book ‘Rays of Positive Electricity and their Application to Chemical Analysis’: ‘I have described at some length the application of positive rays to chemical analysis: one of the main reasons for writing this book was the hope that it might induce others, and especially chemists, to try this method of analysis. I feel sure that there are many problems in chemistry which could be solved with far greater ease by this than any other method’. Cambridge 1913. In fact, Thompson developed the first isotope ratio mass spectrometer (IRMS).

1910: In the same year, M.S. Tswett published his book in Warsaw on ‘Chromophores in the Plant and Animal World’. With this he may be considered to be the discoverer of chromatography.

1918: Dempster used electron impact ionization for the first time.

1920: Aston continued the work of Thompson with his own mass spectrometer equipped with a photoplate as detector. The results verified the existence of isotopes of stable elements (e.g. $^{35}$Cl and $^{37}$Cl) and confirmed the results of Thompson.

1929: Bartky and Dempster developed the theory for a double-focussing mass spectrometer with electrostat and magnetic sector.

1934: Mattauch and Herzog published the calculations for an ion optics system with perfect focussing over the whole length of a photoplate.

1935: Dempster published the latest elements to be measured by MS, Pt and Ir. Aston thus regarded MS to have come to the end of its development.

1936: Bainbridge and Jordan determined the mass of nuclides to six significant figures, the first accurate mass application.
1937: Smith determined the ionization potential of methane (as the first organic molecule).

1938: Hustrulid published the first spectrum of benzene.

1941: Martin and Synge published a paper on the principle of gas liquid chromatography, GLC.

1946: Stephens proposed a time of flight (TOF) mass spectrometer: Velocitron.

1947: The US National Bureau of standards (NBS) began the collection of mass spectra as a result of the use of MS in the petroleum industry.

1948: Hipple described the ion cyclotron principle, known as the Omegatron which now forms the basis of the current ion cyclotron resonance (ICR) instruments.

1950: Gohlke published for the first time the coupling of a gas chromatograph (packed column) with a mass spectrometer (Bendix TOF).

1950: The Nobel Prize for chemistry was awarded to Martin and Synge for their work on GLC (1941).

1950: McLafferty, Biemann and Beynon applied MS to organic substances (natural products) and transferred the principles of organic chemical reactions to the formation of mass spectra.

1952: Cremer and co-workers presented an experimental gas chromatograph to the ACHEMA in Frankfurt; parallel work was carried out by Janák in Czechoslovakia.

1952: Martin and James published the first applications of GLC.

1953: Johnson and Nier published an ion optic with a 90° electric and 60° magnetic sector, which, because of the outstanding focussing properties, was to become the basis for many high-resolution, organic mass spectrometers (Nier/Johnson analyser).

1954: Paul published his fundamental work on the quadrupole analyser.

1955: Wiley and McLaren developed a prototype of the present TOF mass spectrometer.

1955: Desty presented the first GC of the present construction type with a syringe injector and thermal conductivity detector. The first commercial instruments were supplied by Burrell Corp., Perkin Elmer and Podbielniak Corp.

1956: A German patent was granted for the QUISTOR (quadrupole ion storage device) together with the quadrupole mass spectrometer.

1958: Paul published about his research on the quadrupole mass filter as
  – a filter for individual ions
  – a scanning device for the production of mass spectra
  – a filter for the exclusion of individual ions.

1958: Ken Shoulders manufactured the first 12 quadrupole mass spectrometers at Stanford Research Institute, California.

1958: Golay reported for the first time on the use of open tubular columns for GC.

1958: Lovelock developed the argon ionization detector as a forerunner of the electron capture detector (ECD, Lovelock and Lipsky).
1962: U. von Zahn designed the first hyperbolic quadrupole mass filter.
1964: The first commercial quadrupole mass spectrometers were developed as residual gas analyzers (Quad 200 RGAs) by Bob Finnigan and P.M. Uthe at EAI (Electronic Associates Inc., Paolo Alto, California).
1966: Munson and Field published the principle of chemical ionization (CI).
1968: The first commercial quadrupole GC-MS system for organic analysis was supplied by Finnigan Instruments Corporation to the Stanford Medical School Genetics Department.
1978: Dandenau and Zerenner introduced the technique of fused silica capillary columns.
1978: Yost and Enke introduced the triple-quadrupole technique.
1982: Finnigan obtained the first patents on ion trap technology for the mode of selective mass instability and presented the ion trap detector as the first universal MS detector with a PC data system (IBM XT).
1989: Prof. Wolfgang Paul, Bonn University, Germany, received the Nobel Prize for physics for work on ion traps, together with Prof. Hans G. Dehmelt, University of Washington in Seattle, and Prof. Norman F. Ramsay, Harvard University, USA.
2000: Alexander Makarov published a completely new mass analyser concept called Orbitrap suitable for accurate mass measurements of low ion beams.
2005: Introduction of a new type of hybrid Orbitrap mass spectrometer by Thermo Electron Corporation, Bremen, Germany, for MS/MS, very high mass resolution and accurate mass measurement on the chromatographic time scale.
2009: Amelia Peterson et al., University Wisconsin, Prof. Josh Coon group, published first results on the implementation of an EI/CI interface on a hybrid Orbitrap system for ultra-high resolution GC-MS using a GC-Quadrupole-Orbitrap configuration for full scan, SIM, MS/MS and SRM (selected reaction monitoring) at the ASMS conference.
2015: Market introduction of the first high resolution accurate mass GC-MS system using Orbitrap technology by Thermo Fisher Scientific, Austin, TX, USA.